

**UNITED STATES
 SECURITIES AND EXCHANGE COMMISSION**
 Washington, D.C. 20549

AMENDMENT NO. 3
 TO

FORM S-1
 REGISTRATION STATEMENT
 UNDER
 THE SECURITIES ACT OF 1933

Aprea Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

<p>Delaware (State or other jurisdiction of incorporation or organization)</p>	<p>2834 (Primary Standard Industrial Classification Code Number)</p>	<p>84-2246769 (I.R.S. Employer Identification No.)</p>
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535 Boylston Street
 Boston MA 02116
 (617) 463-9385
 (Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Christian S. Schade
 President and Chief Executive Officer

Aprea Therapeutics, Inc.
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Approximate date of commencement of proposed sale to the public:
 As soon as practicable after this Registration Statement is declared effective.

- If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box.
- If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.
- If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.
- If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company
 Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	AMOUNT TO BE REGISTERED(1)	PROPOSED MAXIMUM OFFERING PRICE PER SHARE	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE(1)(2)	AMOUNT OF REGISTRATION FEE(3)
Common Stock, par value \$0.001 per share	5,750,000	\$16.00	\$92,000,000	\$11,150.40

- (1) Includes the additional shares that the underwriters have an option to purchase. See "Underwriting."
 (2) Estimated solely for purposes of calculating the registration fee in accordance with Rule 457(a) under the Securities Act of 1933, as amended.
 (3) Previously paid.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion
Preliminary Prospectus dated September 27, 2019

PROSPECTUS

5,000,000 Shares



Common Stock

This is Aprea Therapeutics, Inc.'s initial public offering. We are offering 5,000,000 shares of our common stock.

We expect the public offering price to be between \$14.00 and \$16.00 per share. Prior to this offering, there has been no market for our common stock. We have applied to list our common stock on the Nasdaq Global Select Market under the symbol "APRE."

We are an "emerging growth company" and a "smaller reporting company" under federal securities laws and are subject to reduced public company disclosure standards for this prospectus and future filings. See "Summary—Implications of Being an Emerging Growth Company and Smaller Reporting Company."

Investing in the common stock involves risks that are described in the "Risk Factors" section beginning on page 12 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per share	Total
Public offering price	\$	\$
Underwriting discount(1)	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) We have agreed to reimburse the underwriters for certain FINRA-related expenses. We refer you to "Underwriting" beginning on page 188 of this prospectus for additional information regarding underwriting compensation.

The underwriters may also exercise their option to purchase up to an additional 750,000 shares from us, at the public offering price, less underwriting discounts and commissions, within 30 days after the date of this prospectus.

The shares will be ready for delivery on or about _____, 2019.

Joint Book-Running Managers

J.P. Morgan

Morgan Stanley

RBC Capital Markets

The date of this prospectus is _____, 2019.

Explanatory Note

On September 20, 2019, we consummated the corporate reorganization as described in this prospectus under the section titled "Corporate Reorganization," pursuant to which all of the issued and outstanding stock and options of Aprea Therapeutics AB, a corporation domiciled in Sweden, were exchanged for common stock, preferred stock or options, as applicable, of Aprea Therapeutics, Inc., the issuer of the common stock being offered in this offering. As a result of this corporate reorganization, Aprea Therapeutics AB became a wholly-owned subsidiary of Aprea Therapeutics, Inc., a recently formed holding company with nominal assets and no liabilities, contingencies, or commitments, which has not conducted any operations prior to this offering other than acquiring the entire issued and outstanding stock of Aprea Therapeutics AB.

We refer to these transactions throughout the prospectus included in this registration statement collectively as the "Holdco Reorganization." See "Corporate Reorganization" for further detail regarding these transactions.

The audited consolidated financial statements for 2017 and 2018 and the notes thereto, the unaudited interim condensed consolidated financial statements for the six months ended June 30, 2019 and 2018 and the notes thereto, and selected historical consolidated financial data and other financial information included in this registration statement are those of Aprea Therapeutics AB and do not give effect to the Holdco Reorganization. The balance sheet of Aprea Therapeutics, Inc. at July 11, 2019, included in this registration statement, does not give effect to the Holdco Reorganization.

Immediately prior to the completion of this offering, and with the consent of shareholders representing a majority of our outstanding preferred shares, all outstanding shares of our convertible preferred stock, including the shares issued as part of the Holdco Reorganization, will convert into an aggregate of 13,028,292 shares of our common stock. Shares of the common stock of Aprea Therapeutics, Inc. are being offered by the prospectus included in this registration statement.

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Through and including _____, 2019 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

We are responsible for the information contained in this prospectus. We have not, and the underwriters have not, authorized anyone to provide you with any information other than what is provided in this prospectus. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you or any representation that others may make to you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of any sale of the common stock. Our business, liquidity position, financial condition, prospects or results of operations may have changed since the date of this prospectus.

This prospectus contains forward-looking statements that are subject to a number of risks and uncertainties, many of which are beyond our control. See "Risk Factors" and "Special Note Regarding Forward-Looking Statements."

For investors outside the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside

the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

In this prospectus, unless otherwise stated or the context otherwise requires, references to "Aprea," "the company," "we," "us," "our" and similar references refer to Aprea Therapeutics, Inc. and its consolidated subsidiaries, after giving effect to the Holdco Reorganization, and to Aprea Therapeutics AB and its consolidated subsidiaries prior to giving effect to the Holdco Reorganization.

Presentation of financial and operating data

Unless otherwise indicated, the historical financial and operating information presented in this prospectus as of and for the years ended December 31, 2017 and 2018 and for the six months ended June 30, 2018 and 2019 is that of Aprea Therapeutics AB.

Certain amounts and percentages included in this prospectus have been rounded. Accordingly, in certain instances, the sum of the numbers in a column of a table may not exactly equal the total figure for that column.

The audited consolidated financial statements for the years ended December 31, 2017 and 2018 and the notes thereto, the unaudited interim condensed consolidated financial statements for the six months ended June 30, 2018 and 2019 and the notes thereto, represent the operations of Aprea Therapeutics AB and its consolidated subsidiaries and do not give effect to the Holdco Reorganization. The balance sheet of Aprea Therapeutics, Inc. at July 11, 2019, included in this registration statement, does not give effect to the Holdco Reorganization. On September 20, 2019, we consummated the corporate reorganization as described under the section titled "Corporate Reorganization." In this prospectus, we refer to this transaction as the "Holdco Reorganization." We expect that the Holdco Reorganization will not have a material effect on our consolidated financial statements.

Industry and market data

We obtained the industry, market and competitive position data used throughout this prospectus from our own internal estimates and research, as well as from independent market research, industry and general publications and surveys, governmental agencies and publicly available information in addition to research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires. In addition, while we believe the industry, market and competitive position data included in this prospectus is reliable and based on reasonable assumptions, such data involve risks and uncertainties and are subject to change based on various factors, including those discussed in "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by third parties or by us.

Trademarks and tradenames

Aprea and other trademarks or service marks of Aprea appearing in this prospectus are the property of Aprea. The other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Summary

This summary highlights, and is qualified in its entirety by, the more detailed information and financial statements included elsewhere in this prospectus. This summary does not contain all of the information that may be important to you. You should read and carefully consider the entire prospectus, especially our financial statements and the notes thereto appearing at the end of this prospectus and the "Risk Factors" section of this prospectus, before deciding to invest in our common stock. Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to "Aprea," "the company," "we," "us" and "our" refer to Aprea Therapeutics, Inc. and its consolidated subsidiaries, after giving effect to the Holdco Reorganization described herein, and to Aprea Therapeutics AB, referred to herein as Aprea AB, and its consolidated subsidiaries prior to giving effect to the Holdco Reorganization.

Aprea Therapeutics overview

We are a clinical-stage biopharmaceutical company focused on developing and commercializing novel cancer therapeutics that reactivate mutant p53 tumor suppressor protein. p53 is the protein expressed from the *TP53* gene, the most commonly mutated gene in cancer. We believe that mutant p53 is an attractive therapeutic target due to the high incidence of p53 mutations across a range of cancer types and its involvement in key cellular activities such as apoptosis. Cancer patients with mutant p53 face a significantly inferior prognosis even when treated with the current standard of care, and a large unmet need for these patients remains. Our lead product candidate, APR-246, is a small molecule p53 reactivator that is in late-stage clinical development for hematologic malignancies, including myelodysplastic syndromes, or MDS, and acute myeloid leukemia, or AML. APR-246 has received Orphan Drug and Fast Track designations from the FDA for MDS, and Orphan Drug designation from the EMA for MDS, AML and ovarian cancer, and we believe APR-246 will be a first-in-class therapy if approved by applicable regulators. We have commenced a pivotal Phase 3 trial of APR-246 with azacitidine for frontline treatment of *TP53* mutant MDS and expect initial data from this trial in the second half of 2020. Our pivotal Phase 3 trial is supported by data from two ongoing Phase 1b/2 investigator initiated trials, one in the U.S. and one in France, testing APR-246 with azacitidine as frontline treatment in *TP53* mutant MDS and AML patients.

In the ongoing U.S. Phase 1b/2 trial, sponsored by Dr. David Sallman of the H. Lee Moffitt Cancer Center and Research Institute, or Moffitt, we have observed an objective response rate, or ORR, of 88% and a complete remission, or CR, rate of 59% in 41 response-evaluable MDS/AML patients treated with APR-246 and azacitidine, as of July 2019 and we expect a final CR endpoint in the second half of 2019. In MDS patients, the CR rate was 61%, with an additional 27% achieving non-CR responses. In AML patients, the CR rate was 50%, with an additional 38% achieving non-CR responses. In addition, 46% of evaluable patients were able to discontinue treatment in order to proceed to allogeneic hematopoietic stem cell transplantation, or allo-HCT. Allo-HCT is currently the only recognized therapy believed to increase the likelihood of long term survival for *TP53* mutant MDS and AML patients in remission. In the ongoing French Phase 1b/2 trial, sponsored by Groupe Francophone des Myelodysplasies, or GFM, under lead investigator Prof. Pierre Fenaux, we have observed an ORR of 75% and a CR rate of 56% in 16 response-evaluable patients treated with APR-246 and azacitidine, as of July 2019 and we expect a final CR endpoint in the first half of 2020. In MDS patients, the CR rate was 55%, with an additional 18% achieving non-CR responses. In AML patients, the CR rate was 60%, with an additional 20% achieving non-CR responses. We expect the results of our pivotal Phase 3 trial and the U.S. and French Phase 1b/2 trials will be submitted in support of marketing applications to the FDA and EMA. We are also developing a next-generation small molecule p53 reactivator, APR-548, for potential use in multiple hematologic malignancies and other oncologic indications, and expect to file an IND with the FDA in the first half of 2020. We

currently retain global development and commercialization rights to all of our preclinical and clinical product candidates, which are summarized in the following figure:

Molecule	Target Indication	Treatment Line	Preclinical	Phase 1	Phase 2	Phase 3	Milestones
APR-246	TP53 Mutant MDS	Frontline (U.S.)	Combination with azacitidine				Top-line data second half 2020
		Frontline (U.S. trial) ⁽¹⁾	Combination with azacitidine				Final CR primary endpoint and duration of response second half 2019
	TP53 Mutant MDS / AML	Frontline (French trial) ⁽¹⁾	Combination with azacitidine				Final CR primary endpoint first half 2020
		Post-Transplant Maintenance	Combination with azacitidine				Full enrollment second half 2020
	TP53 Mutant AML	Frontline and Relapsed / Refractory	Combination with Bcl-2 inhibitor ⁽²⁾				First patient enrollment Q4 2019
APR-548	TP53 Mutant MDS / AML					IND submission first half 2020	

- (1) Investigator-initiated trial
(2) With or without azacitidine

We believe that targeting p53 and thereby reactivating key intrinsic cellular functions has the potential to significantly impact patients' lives and treatment strategies for a wide variety of cancers. p53 is a tumor suppressor protein that in its normal state functions to sense DNA damage and induce cell cycle arrest, DNA damage repair, senescence and cellular apoptosis. Mutant p53 is an attractive target because it is widely mutated across hematologic and solid tumors and is associated with an aggressive clinical and molecular phenotype. In preclinical studies and clinical trials, mutations in p53 and the apoptotic pathway have been shown to play a key role in cancer genesis, proliferation and resistance to currently marketed therapeutic agents. Many approved and clinical stage oncology drugs are more effective with a functional p53 pathway. Our approach is to restore normal function to p53, thereby re-enabling a cell's ability to undergo apoptosis. Accordingly, we believe that by targeting p53, our drug candidates may enhance the ability of other anti-cancer therapies to induce cancer cell death. In addition, we believe that our approach may counteract resistance mechanisms that characterize many of the most aggressive cancers.

We believe there is a significant market opportunity for therapies targeting mutant p53 because these mutations occur in more than half of all tumors and confer an inferior prognosis relative to patients with wild type p53. Based on the importance of p53 mutations as disease-driver mutations, the sensitivity of hematopoietic cells to oxidative stress and continued unmet medical need, we have initially focused our clinical development on hematological malignancies, MDS and AML, with mutations in the TP53 gene.

MDS is a collection of bone marrow disorders in which malignant hematopoietic cells prevent the production of healthy, mature blood cells. As of 2019, there are an estimated 200,000 MDS patients

worldwide, with 68,000 of these in the United States and 69,000 MDS patients across the five major markets of the European Union and Japan.

AML is the most common form of adult leukemia, with the highest incidence in patients age 60 years and older. Like MDS, AML is characterized by proliferation of abnormal immature white blood cells which impair production of normal blood cells. There are an estimated 213,000 AML patients worldwide, with 37,000 of these in the United States, and 41,000 across the five major markets of the European Union and Japan.

MDS and AML can develop *de novo* or may arise secondary to progression of other hematologic disorders or from chemotherapy or radiation treatment for a different, prior malignancy. Secondary MDS and AML carry a worse prognosis than *de novo* disease. Mutations in *TP53* occur in approximately 20% of patients with newly diagnosed MDS/AML and in more than 30% of patients with therapy-related MDS/AML.

Treatment with azacitidine is the standard of care for frontline therapy in *TP53* mutant MDS and AML, with an ORR of approximately 40-50%, a CR rate of approximately 10-20% and median overall survival, or OS, of approximately 7-8 months. There are no established curative pharmacologic therapies for MDS and AML. Allo-HCT is currently the only recognized therapy believed to increase the likelihood of long term survival for *TP53* mutant MDS and AML patients in remission; however, many patients are not candidates for allo-HCT due to lack of sufficient clinical response to therapy, advanced age, comorbidities or lack of a suitable donor. Unfortunately, even for those *TP53* mutant MDS and AML patients who receive allo-HCT, the post-transplantation prognosis is poor: *TP53* mutations are associated with a 4-fold increased risk of death and 1-year relapse-free survival of only 30% following transplantation.

Given the poor prognosis for patients with *TP53* mutant MDS and AML, there is a significant need for more effective therapies in this population, particularly if such treatments have a favorable safety profile, and a mechanism of action that targets mutant p53 directly, and may be used in combination with existing or future treatment options.

We have assembled an outstanding team, which includes world-class scientific and clinical oncology leaders, to execute on our mission to create novel p53-reactivating therapies to help patients suffering with cancer. Together with our board of directors, our scientific founders and members of our management team have significant experience in drug discovery and development and finance. Collectively, we believe our team's strong capabilities position us to build a leading biotech company focused on developing novel cancer therapies to address the significant unmet medical need of patients with p53 mutant malignancies, for whom there are limited effective therapeutic options.

Our drug candidates

Our lead product candidate, APR-246, is a small molecule that has demonstrated reactivation of mutant p53 in clinical trials. Promising clinical data support the application of APR-246 across a variety of hematologic malignancies and other oncologic indications. APR-246 is a pro-drug that is administered intravenously and forms the active moiety, 2-methylene-quinuclidin-3-one, or MQ, under physiological conditions. APR-246 has been shown to induce apoptosis in cancer cells with mutant p53 in Phase 1/2 trials. We believe the mechanism of action and current adverse event profile of APR-246 may provide the basis for its combination with both conventional and novel therapies, such as targeted therapies, chemotherapy, radiotherapy and immuno-therapy. APR-246 has received Orphan Drug and Fast Track designations from the FDA for MDS, and Orphan Drug designation from the EMA for MDS, AML and ovarian cancer.

We are conducting and supporting multiple clinical trials of APR-246:

- **Pivotal Phase 3 MDS Trial-** We are currently enrolling a pivotal Phase 3 randomized, controlled trial evaluating APR-246 with azacitidine as frontline therapy in HMA-naïve *TP53* mutant MDS patients. The first patient was enrolled in January 2019 and we anticipate full enrollment in our Phase 3 trial in the first quarter of 2020 and top-line data from this trial in the second half of 2020.
- **U.S. Phase 1b/2 MDS/AML Trial-** We are supporting an investigator-initiated Phase 1b/2 single-arm, open-label trial in the United States, sponsored by Dr. David Sallman of the H. Lee Moffitt Cancer Center and Research Institute, or Moffitt, evaluating APR-246 with azacitidine as frontline therapy in HMA-naïve patients with *TP53* mutant MDS or AML. We are collaborating with Moffitt on this trial by supplying APR-246, in addition to providing financial support. The primary endpoint of the trial is CR rate and enrollment has completed with 55 patients. Top-line results on the CR rate primary endpoint and median duration of response are expected in the second half of 2019. The regimen achieved an ORR of 88% and a CR rate of 59% in 41 response-evaluable patients as of July 2019. In MDS patients, the CR rate was 61%, with an additional 27% achieving non-CR responses. In AML patients, the CR rate was 50%, with an additional 38% achieving non-CR responses. In addition, 46% of evaluable MDS/AML patients were able to discontinue treatment in order to proceed to allo-HCT. By intention-to-treat analysis, and with a median follow up of 10.5 months, median OS was 11.6 months (95% confidence interval: 9.2 - 14.0 months) with significantly prolonged OS of 12.8 months in responding patients versus 3.9 months in non-responding patients ($p < 0.0001$).
- **French Phase 1b/2 MDS/AML Trial-** We are supporting a parallel investigator-initiated Phase 1b/2 single-arm, open-label trial in France, sponsored by Groupe Francophone des Myelodysplasies, or GFM, under lead investigator Prof. Pierre Fenaux, evaluating APR-246 with azacitidine as frontline therapy in HMA-naïve patients with *TP53* mutant MDS or AML. We are collaborating with GFM on this trial by supplying APR-246, in addition to providing financial support. The primary endpoint of the trial is CR rate and enrollment has completed with 53 patients. Top-line results on the CR rate primary endpoint are expected in the first half of 2020. All patients are to receive the recommended Phase 2 dose from the U.S. Phase 1b/2 MDS/AML Trial. As of July 2019, the regimen has achieved an ORR of 75% and CR rate of 56% in 16 response-evaluable patients. In MDS patients, the CR rate was 55%, with an additional 18% achieving non-CR responses. In AML patients, the CR rate was 60%, with an additional 20% achieving non-CR responses. Responding patients who proceed to allo-HCT are eligible to continue receiving APR-246 with azacitidine as post-transplant maintenance therapy.
- **Phase 2 MDS/AML Post-Transplant Trial-** We are currently enrolling our single-arm, open-label Phase 2 trial evaluating APR-246 with azacitidine as post-transplant maintenance therapy in *TP53* mutant MDS and AML patients who have received allo-HCT. The primary endpoint is relapse-free survival at 12 months. We anticipate full enrollment in the first half of 2020.
- **Phase 1/2 AML Trials-** Based on *in vitro* data evidencing synergistic activity between APR-246 and a Bcl-2 inhibitor, we have designed and plan to conduct Phase 1/2 clinical trials in frontline and relapsed/refractory AML assessing APR-246 with a Bcl-2 inhibitor with or without azacitidine. We anticipate the first patient to be enrolled in the fourth quarter of 2019.

Our second product candidate, APR-548, is a next-generation p53 reactivator with the potential for oral administration. APR-548 is a unique analog of APR-246 and therefore a pro-drug of MQ. We have filed a patent application in support of composition of matter and methods of use intellectual property protection for APR-548. APR-548 exhibits high oral bioavailability in preclinical testing and is being developed in an oral dosage form. We are currently conducting Investigational New Drug, or IND, enabling preclinical trials of APR-548 and anticipate submitting an IND in the first half of 2020.

Our strategy

Our mission is to be the leading player in the development and commercialization of p53-targeted cancer therapies. The key elements of our strategy are to:

- Rapidly develop and commercialize our lead mutant p53 reactivator product candidate, APR-246, in frontline combination therapy for *TP53* mutant MDS
- Expand the clinical opportunity for APR-246 by pursuing development of combination therapy for post-transplant maintenance in *TP53* mutant MDS and AML
- Rapidly develop APR-246 for frontline and relapsed/refractory *TP53* mutant AML
- Advance our next-generation p53 reactivator, APR-548
- Explore additional oncology indications for APR-246 and APR-548
- Maximize the commercial opportunity of our product candidates across global markets

Risks associated with our business

Our ability to execute on our business strategy is subject to a number of risks, which are discussed more fully in the section of this prospectus entitled "Risk Factors." You should carefully consider these risks before making an investment in our common stock. These risks include, among others, the following:

- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability. As of June 30, 2019, we had an accumulated deficit of \$71.2 million.
- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability. We have never generated revenues and may never be profitable. Our lead product candidate, APR-246, is currently in multiple clinical trials and all of our other product candidates are in preclinical research.
- We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements into 2023. We expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to enable us to complete each of our ongoing clinical trials. We do not expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient, however, to enable us to conduct through completion any additional clinical trials of APR-246 or to otherwise complete the development of APR-246. Accordingly, we will need substantial additional funding, which may not be available to us on acceptable terms or at all, to complete development of APR-246 and to fund development of our next-generation p53 reactivator, APR-548. If we are unable to raise capital when needed, we may be forced to delay, reduce and/or eliminate our research and drug development programs or commercialization efforts.
- We are substantially dependent on the success of APR-246 and cannot be certain that we will receive marketing approval for APR-246 or will successfully commercialize APR-246 even if we receive such marketing approval.
- If we experience delays or difficulties in the enrollment of patients in clinical trials, we may not be able to initiate or complete clinical trials for our product candidates on a timely basis.
- The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

- If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs, experience delays in completing, or ultimately be unable to complete, the development of our product candidates or be unable to obtain marketing approval.
- We rely on third parties to conduct our clinical trials, some aspects of our research and preclinical studies and the manufacturing of our product candidates. If these third parties do not perform satisfactorily, including by failing to meet deadlines for the completion of such trials, research and studies, we could be delayed in our clinical development activities or in our efforts to obtain marketing approval of our product candidates.
- The chemical structure of APR-246 is in the public domain. Accordingly, we do not own or license any composition of matter patents claiming the compound of APR-246 and will not in the future own or license any composition of matter patents claiming the chemical structure of APR-246 as described in the public domain. Our patent portfolio for APR-246 currently consists of method-of-use and formulation patent claims, and dosing, manufacturing processes, and crystalline solid form provisional patent application claims. If we are unable to obtain or maintain patent and other intellectual property-related protection of our proprietary technologies and our product candidates, including APR-246, their respective components, formulations, methods used to manufacture them and methods of treatment, if the scope of the patent protection obtained is not sufficiently broad, or if we are unable to successfully defend our patents against third-party challenges or enforce our patents against third-parties, our competitors and other third parties could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize any product candidate we may develop and our technology may be adversely affected.
- Our commercial success depends in part on the ability to avoid and successfully defend claims that we have infringed, misappropriated or otherwise violated the intellectual property of a third party.

Our corporate information

We were incorporated under the laws of the State of Delaware in May 2019 under the name Aprea Therapeutics, Inc. On September 20, 2019, we consummated the Holdco Reorganization, pursuant to which all of the issued and outstanding stock and options of Aprea Therapeutics AB, or Aprea AB, were exchanged for common stock, preferred stock or options, as applicable, of Aprea Therapeutics, Inc. As a result of the HoldCo Reorganization, Aprea AB, became a wholly-owned subsidiary of Aprea Therapeutics, Inc. See "Corporate Reorganization" for additional information.

We are a holding company. We conduct substantially all of our operations through our subsidiaries. Our subsidiary, Aprea AB, a corporation domiciled in Sweden, was originally incorporated in 2002 and commenced principal operations in 2006, and holds substantially all of our intellectual property assets. Our executive offices are located at 535 Boylston Street, Boston, MA 02116, and our telephone number is 617-463-9385. Our website address is www.aprea.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Implications of being an emerging growth company and smaller reporting company

As a company with less than \$1.07 billion of revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an emerging growth company for up to five years, or until such earlier time as we have more than \$1.07 billion in annual revenue, the market value of our stock held by non-affiliates is more than \$700 million (and we have been a public company for at least 12 months).

and have filed one annual report on Form 10-K with the Securities and Exchange Commission, or the SEC) or we issue more than \$1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to other public companies that are not emerging growth companies. These provisions include:

- reduced disclosure about our executive compensation arrangements;
- exemption from the non-binding stockholder advisory votes on executive compensation or golden parachute arrangements;
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting; and
- reduced disclosure of financial information in this prospectus, such as being permitted to include only two years of audited financial information and two years of selected financial information in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure.

We have taken advantage of some reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock. In addition, the JOBS Act permits an emerging growth company to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, as a result, upon completion of this offering we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies that are not emerging growth companies.

We are also a "smaller reporting company," as such term is defined in Rule 12b-2 under the Securities Exchange Act of 1934, or the Exchange Act, meaning that the market value of our common stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than \$700 million and our annual revenue is less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our common stock held by non-affiliates is less than \$250 million or (ii) our annual revenue is less than \$100 million during the most recently completed fiscal year and the market value of our common stock held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

The Offering

Common stock offered by us	5,000,000 shares
Underwriters' option to purchase additional shares	We have granted the underwriters a 30-day option to purchase up to 750,000 additional shares at the public offering price, less underwriting discounts and commissions.
Common stock to be outstanding after the offering	19,209,865 shares (or 19,959,865 shares if the underwriters exercise in full their option to purchase additional shares)
Use of proceeds	We estimate that our net proceeds from this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$66.6 million, or \$77.0 million if the underwriters exercise their option to purchase additional shares in full, assuming an initial public offering price of \$15.00 per share, which is the mid-point of the price range set forth on the cover page of this prospectus. We intend to use the net proceeds from the offering to fund: (i) future Phase 1b/2 clinical studies of APR-246 for solid tumor and hematological malignancies as well as additional future clinical studies to be determined if the data derived from such Phase 1b/2 clinical studies is favorable; (ii) continued research and development activities for APR-548, including ongoing IND-enabling studies and a first-in-human clinical trial; (iii) the ongoing preclinical and clinical development of APR-246, including preparation and submission of a New Drug Application (NDA) in MDS; and (iv) general research and development activities, working capital and other general corporate activities including the buildout of infrastructure to support the advancement of our product candidates. See "Use of Proceeds" on page 77 for a more complete description of the intended use of proceeds from this offering.
Directed share program	The underwriters have reserved up to 3% of the shares of common stock being offered by this prospectus (excluding the shares of common stock that may be issued upon the underwriters' exercise of their option to purchase additional common stock) for sale to our directors, officers, employees, business associates and related persons of the Company. The number of shares of common stock available for sale to the general public will be reduced to the extent these individuals purchase such reserved shares. Any reserved shares that are not so purchased will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus. See "Underwriting—Directed Share Program."

Risk factors

See the "Risk Factors" section beginning on page 12 of this prospectus, as well as other information included in this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.

Proposed Nasdaq Global Select Market symbol

"APRE"

The number of shares of our common stock to be outstanding after the completion of this offering is based on 14,209,865 shares outstanding as of June 30, 2019, after giving effect to the Holdco Reorganization which took place on September 20, 2019 and the 1 for 1.6045 split of our common stock which took place on September 26, 2019 and assumes the conversion of our outstanding convertible preferred stock into 13,028,292 shares of common stock immediately prior to the completion of this offering, and excludes:

- 2,761,794 shares of common stock, with a weighted-average exercise price of \$1.66 per share, issuable upon exercise of stock options outstanding as of June 30, 2019 under our 2016 Stock Incentive Plan; and
- 2,488,206 shares of common stock reserved for issuance pursuant to future awards under our 2019 Stock Incentive Plan or our Employee Stock Purchase Plan, plus any future increases in the number of shares of common stock reserved for issuance under our 2019 Stock Incentive Plan or our Employee Stock Purchase Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year.

Unless otherwise indicated or the context otherwise requires, information in this prospectus reflects and assumes the following:

- the 1 for 1.6045 split of our common stock which took place on September 26, 2019;
- the issuance of 2,807 shares of common stock from the exercise of stock options on March 25, 2019, which were registered pursuant to Swedish law with the Swedish Companies Registration office on August 27, 2019;
- no exercise of outstanding options or warrants;
- the completion of the Holdco Reorganization;
- no exercise by the underwriters of their option to purchase up to an additional 750,000 shares of our common stock;
- the conversion of all of our outstanding shares of convertible preferred stock into an aggregate of 13,028,292 shares of common stock immediately prior to the completion of this offering; and
- the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the completion of this offering.

Summary Financial Data

You should read the following summary financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus. We have derived the statement of operations data for the years ended December 31, 2017 and 2018 and the balance sheet data as of December 31, 2018 from our audited financial statements appearing at the end of this prospectus. The consolidated statements of operations data for the six months ended June 30, 2018 and 2019 and the consolidated balance sheet data at June 30, 2019 are derived from our unaudited condensed consolidated financial statements included in this prospectus. The unaudited condensed consolidated financial statements include, in the opinion of management, all adjustments that management considers necessary for the fair presentation of the consolidated financial information set forth in those statements. Our historical results are not necessarily indicative of results that should be expected in any future period.

	Years ended December 31,		Six months ended June 30,	
	2017	2018	2018	2019
	(unaudited)			
Consolidated Statement of Operations Data:				
Operating expenses:				
Research and development	\$ 13,392,631	\$ 14,194,732	\$ 7,492,788	\$ 7,998,270
General and administrative	2,459,744	2,294,671	1,166,520	2,347,915
Total operating expenses	15,852,375	16,489,403	8,659,308	10,346,185
Other income (expense):				
Interest expense	(15)	(182)	(188)	(7,439)
Foreign currency gain	662,140	961,316	949,158	1,615,974
Total other income (expense)	662,125	961,134	948,970	1,608,535
Net loss	\$ (15,190,250)	\$ (15,528,269)	\$ (7,710,338)	\$ (8,737,650)
Net loss per share attributable to common stockholders, basic and diluted(1)	\$ (13.17)	\$ (13.45)	\$ (6.68)	\$ (7.43)
Weighted average common shares outstanding, basic and diluted(1)	1,153,069	1,154,368	1,154,107	1,176,417
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)(1)		\$ (1.65)		\$ (0.62)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)(1)		9,428,873		14,075,669

(1) See Note 2 to our audited and unaudited interim financial statements included elsewhere in this prospectus for an explanation of the method used to calculate basic and diluted net loss per share and unaudited pro forma net basic and diluted loss per share as well as the weighted-average number of shares used in the computation of the per share amounts.

The following table sets forth summary balance sheet data as of June 30, 2019:

- on an actual basis (including 2,807 shares of common stock from the exercise of stock options on March 25, 2019, which were registered pursuant to Swedish law with the Swedish Companies Registration Office on August 27, 2019);
- on a pro forma basis to give effect to (i) the Holdco Reorganization described under the section titled "Corporate Reorganization", (ii) the 1 for 1.6045 split of our common stock which took place on September 26, 2019, (iii) the conversion of all of our outstanding shares of convertible preferred stock into an aggregate of 13,028,292 shares of common stock immediately prior to the completion of this offering and (iv) the filing and effectiveness of our amended and restated certificate of incorporation; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 5,000,000 shares of our common stock in this offering at an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	June 30, 2019		
	Actual	Pro forma	Pro forma as adjusted(1)
Consolidated Balance Sheet Data:			
Cash and cash equivalents	\$ 60,994,738	\$ 60,994,738	\$ 127,544,738
Working capital(2)	56,215,210	56,215,210	122,765,210
Total assets	62,214,654	62,214,654	128,764,654
Total liabilities	5,878,053	5,878,053	5,878,053
Convertible preferred stock	118,188,993	—	—
Total stockholders' equity (deficit)	(61,852,392)	56,336,601	122,886,601

- (1) A \$1.00 increase or decrease in the assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by \$4.7 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. An increase or decrease of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease the pro forma as adjusted amount of each of cash, cash and cash equivalents, working capital, total assets and total stockholders' equity by \$14.0 million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions. This pro forma as adjusted information is illustrative only and will depend on the actual initial public offering price and other terms of this offering determined at pricing.
- (2) We define working capital as current assets less current liabilities. See our financial statements for further details regarding our current assets and current liabilities.

Risk Factors

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should consider carefully the risks described below, together with the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus. We believe the risks described below are the risks that are material to us as of the date of this prospectus. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks related to our financial position and need for additional capital

We have incurred significant losses in each year since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since our inception, we have incurred significant losses on an aggregate basis. Our net loss was \$8.7 million for the six months ended June 30, 2019, and \$15.5 million for the year ended December 31, 2018. Our accumulated deficit was \$71.2 million as of June 30, 2019 and \$62.5 million as of December 31, 2018. We have not generated any revenue to date from sales of any drugs and have financed our operations principally through private placements of our preferred stock. We have devoted substantially all of our efforts to research and development. Our lead product candidate, APR-246, is in clinical development, and our other product candidates are in preclinical research. As a result, we expect that it will be several years, if ever, before we have any product candidates ready for commercialization. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter.

To become and remain profitable, we must develop, obtain approval for and eventually commercialize a drug or drugs with significant market potential, either on our own or with a collaborator. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those drugs for which we may obtain marketing approval and establishing and managing any collaborations for the development, marketing and/or commercialization of our product candidates. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business and/or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if at all. If we are unable to obtain product approvals or generate significant commercial revenues, our business will be materially harmed.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability. We have never generated revenues and may never be profitable.

We are an early-stage company. Aprea Therapeutics AB, or Aprea AB, was originally incorporated in 2002 and commenced operations in 2006. We were incorporated in May 2019. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our lead product candidate, APR-246, identifying potential product candidates, conducting preclinical studies of our product candidates and conducting clinical trials of our product candidates. All of our product candidates other than APR-246 are in preclinical research. We have not yet demonstrated our ability to successfully complete large-scale, pivotal clinical trials, obtain marketing approvals, manufacture commercial-scale drug products or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful drug commercialization. Typically, it takes about six to ten years to develop a new drug from the time it is in Phase 1 clinical trials to when it is approved for treating patients, but in many cases it may take longer. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We may need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any particular quarterly or annual periods as indications of future operating performance.

We will need substantial additional funding, which may not be available to us on acceptable terms or at all. If we are unable to raise capital when needed, we may be forced to delay, reduce and/or eliminate our research and drug development programs or future commercialization efforts.

Developing drug products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct clinical trials of, and seek marketing approval for, APR-246 and our other product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time for any such product candidate. Furthermore, commencing upon the completion of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce and/or eliminate our research and drug development programs or future commercialization efforts.

We plan to use the net proceeds from this offering to fund our ongoing clinical trials of APR-246 and additional research and clinical development activity related to APR-246 and other programs and for working capital and other general corporate purposes, which may include additional research, hiring additional personnel, capital expenditures and the costs of operating as a public company. We will be required to expend significant funds in order to advance the development of APR-246, as well as any other product candidates. In any event, the net proceeds from this offering and our existing cash and cash equivalents will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our product candidates. Accordingly, we will be required to

obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements into 2023. Our estimate as to how long we expect the net proceeds from this offering, together with our existing cash and cash equivalents, to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of our current and future clinical trials of APR-246 for our current targeted indications;
- the scope, progress, results and costs of drug discovery, preclinical research and clinical trials for APR-246 and our other product candidates;
- the number of future product candidates that we pursue and their development requirements;
- the costs, timing and outcome of regulatory review of our product candidates;
- the extent to which we acquire or invest in businesses, products and technologies, including entering into or maintaining licensing or collaboration arrangements for product candidates on favorable terms, although we currently have no commitments or agreements to complete any such transactions;
- the costs and timing of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining, defending and enforcing our intellectual property rights and defending intellectual property-related claims;
- our headcount growth and associated costs as we expand our business operations and our research and development activities; and
- the costs of operating as a public company.

Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, restrict our operations or require us to relinquish rights to our product candidates.

We expect our expenses to increase in connection with our planned operations. Until such time, if ever, as we can generate substantial revenues from the sale of drugs, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and/or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. In addition, debt financing, if available, would result in fixed

payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technology, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, reduce and/or eliminate our product candidate development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks related to the discovery, development and commercialization of our product candidates

We are substantially dependent on the success of our lead product candidate, APR-246, which is currently in multiple clinical trials. Our clinical trials of APR-246 may not be successful. If we are unable to obtain approval for and commercialize APR-246 or experience significant delays in doing so, our business will be materially harmed.

Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, APR-246, our lead product candidate. We are investing a majority of our efforts and financial resources in the research and development of APR-246. Our other product candidates are in earlier stages of development. Our business depends entirely on the successful development and commercialization of our product candidates. We currently have no drugs approved for sale and generate no revenues from sales of any products, and we may never be able to develop a marketable product.

APR-246 will require additional clinical development, evaluation of clinical, preclinical and manufacturing activities, marketing approval in multiple jurisdictions, substantial investment and significant marketing efforts before we generate any revenues from product sales. We are not permitted to market or promote APR-246, or any other product candidates, before we receive marketing approval from the FDA and comparable foreign regulatory authorities, and we may never receive such marketing approvals.

The success of APR-246 will depend on several factors, including the following:

- successful and timely completion of our ongoing clinical trials of APR-246;
- initiation and successful patient enrollment and completion of additional clinical trials on a timely basis;
- our ability to demonstrate APR-246's safety, tolerability and efficacy to the FDA or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals for APR-246;
- obtaining and maintaining patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- successfully defending and enforcing our rights in our intellectual property portfolio;
- avoiding and successfully defending against any claims that we have infringed, misappropriated or otherwise violated any intellectual property of any third party;

- the performance of our future collaborators, if any;
- the extent of, and our ability to timely complete, any required post-marketing approval commitments imposed by FDA or other applicable regulatory authorities;
- establishment of supply arrangements with third-party raw materials and drug product suppliers and manufacturers who are able to manufacture clinical trial and commercial quantities of APR-246 drug substance and drug product and to develop, validate and maintain a commercially viable manufacturing process that is compliant with current good manufacturing practices, or cGMP, at a scale sufficient to meet anticipated demand and over time enable us to reduce our cost of manufacturing;
- establishment of scaled production arrangements with third-party manufacturers to obtain finished products that are compliant with cGMP and appropriately packaged for sale;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors;
- the availability of coverage and adequate reimbursement and pricing by third-party payors and government authorities;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments; and
- our ability to compete with other therapies.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator. Accordingly, we cannot assure you that we will ever be able to generate revenue through the sale of APR-246. If we are not successful in commercializing APR-246, or are significantly delayed in doing so, our business will be materially harmed.

We may find it difficult to enroll patients in our clinical trials given the relatively smaller patient population who have the diseases for which our product candidates are being developed. If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. In particular, because our clinical trials of APR-246 are focused on indications with relatively small patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.

Patient enrollment may be affected if our competitors have ongoing clinical trials for product candidates that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' product candidates. Patient enrollment may also be affected by other factors, including:

- size and nature of the patient population;
- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;

- patient eligibility criteria for the trial in question;
- patients' and clinicians' perceived risks and benefits of the product candidate under study;
- competing clinical trials;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- continued enrollment of prospective patients by clinical trial sites.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

The reactivation of p53 is a novel and unproven therapeutic approach and our development of APR-246 may never lead to a marketable product.

We are developing APR-246 for its ability to reactivate the tumor suppressor protein p53, the protein product of the *TP53* gene and the most commonly mutated gene in cancer. We are also developing a next-generation p53 reactivator, APR-548, for potential use in multiple hematologic malignancy indications. We believe that mutant p53 is an attractive target for novel cancer therapy due to the high incidence of p53 mutations across a range of cancer types and the universally inferior prognosis for cancer patients with mutated p53. However, to our knowledge, no one has advanced a product candidate with this mechanism of action into clinical development. The scientific evidence to support the feasibility of developing these product candidates is both preliminary and limited. For instance, even though APR-246 has shown promising results in preclinical studies and early-stage clinical trials, we may not succeed in demonstrating safety and efficacy of APR-246 in larger-scale clinical trials, including our pivotal Phase 3 clinical trial. Advancing APR-246 as a novel product to reactivate p53 creates significant challenges for us, including:

- obtaining marketing approval, as obtaining regulatory approval of a p53 reactivator from the FDA or comparable foreign regulatory authorities has never been done before;
- educating medical personnel regarding the potential efficacy and safety benefits, as well as the challenges, of incorporating our product candidates, if approved, into treatment regimens; and
- establishing the sales and marketing capabilities to gain market acceptance, if approved.

If serious adverse or unacceptable side effects are identified during the development of our product candidates or we observe limited efficacy of our product candidates, we may need to abandon or limit the development of one or more of our product candidates.

Adverse events or unacceptable side effects caused by, or other unexpected properties of, our product candidates could cause us, any future collaborators, an institutional review board, or IRB, or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in the (i) delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities, (ii) approval with significant restrictions on distribution or (iii) required labeling information regarding safety concerns, if approved.

In general, our clinical trials of APR-246 include cancer patients who are very sick and whose health is deteriorating, and we expect that additional clinical trials of APR-246 and our other product candidates will include similar patients with deteriorating health. Multiple patients in our trials have experienced adverse events, including serious adverse events. The most commonly reported adverse events include nausea, vomiting, constipation, dizziness and neutropenia. Some patients in our trials have experienced serious adverse events. See "Business—Our Approach." In the U.S. Phase 1b/2 MDS/AML Trial, serious adverse events, regardless of causality, reported for more than one patient were: febrile neutropenia (27%), lung infection (9%), infections and infestations (5%), respiratory failure (5%), sepsis (5%), vomiting (5%), chest pain (4%), dehydration (4%), intracranial hemorrhage (4%) and multi-organ failure (4%). In the Phase 1b/2 Clinical Trial of APR 246 in Platinum Sensitive Ovarian Cancer (PiSARRO), serious adverse events, regardless of causality, reported in more than one patient were: device related infection (17%), vomiting (17%), febrile neutropenia (8%), infection (6%), small intestinal obstruction (6%) and thrombocytopenia (6%).

Some patients have died during their participation in the clinical trials for APR-246, and there has been one death reported by an investigator as possibly related to both APR-246 and azacitidine. We believe this death may have been caused by the underlying disease, other comorbidities from which such patient was suffering or the other co-administered treatments. Any deaths occurring in our clinical trials, whether related to our product candidate or not, could affect perceptions relating to our product candidate.

If any of our product candidates are associated with adverse events or undesirable side effects or have properties that are unexpected, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. We, or any future collaborators, may abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, results of operations, financial condition and prospects significantly.

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, interim results of a clinical trial do not necessarily predict final results, and the results of our clinical trials may not satisfy the requirements of the FDA or comparable foreign regulatory authorities.

We currently have no drugs approved for sale and we cannot guarantee that we will ever have marketable drugs. Clinical failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we or any future collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. We will be required to demonstrate with substantial evidence through adequate and well-controlled clinical trials that our product candidates are safe and effective for use in treating specific conditions in order to obtain marketing approvals for their commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that future larger registration clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate safety and efficacy to the satisfaction of the FDA and non-U.S. regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. Product candidates that have shown promising results in preclinical studies and early-stage clinical trials may still suffer significant setbacks in subsequent registration clinical trials. Additionally, the outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later-stage clinical trials.

From time to time, we may publish or report interim or preliminary data from our clinical trials. Interim or preliminary data from clinical trials that we may conduct may not be indicative of the final

results of the trial and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Interim or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the interim or preliminary data. As a result, interim or preliminary data should be viewed with caution until the final data are available.

In addition, the design of a clinical trial can determine whether its results will support approval of a drug and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and conduct a clinical trial to support marketing approval. Further, if our product candidates are found to be unsafe or lack efficacy, we will not be able to obtain marketing approval for them and our business would be harmed. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in preclinical studies and earlier clinical trials.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain marketing approval to market our product candidates.

We have multiple clinical trials of APR-246 currently ongoing. In the event that an adverse safety issue, clinical hold or other adverse finding occurs in one or more of our clinical trials of APR-246, such event could adversely affect our other clinical trials of APR-246. Moreover, there is a relatively limited safety data set for product candidates that are designed to reactivate p53. An adverse safety issue or other adverse finding in a clinical trial conducted by a third party with a product candidate reactivate p53, could adversely affect our clinical trials of APR-246.

Further, our product candidates may not be approved even if they achieve their primary endpoints in Phase 3 clinical trials or registration trials. The FDA or non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal clinical trial that has the potential to result in approval by the FDA or another regulatory authority. In addition, any of these regulatory authorities may also approve a product candidate for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. In addition, the FDA or other comparable foreign regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our product candidates.

Before obtaining marketing approvals for the commercial sale of any product candidate for a target indication, we must demonstrate with substantial evidence gathered in preclinical studies and adequate and well-controlled clinical trials, and, with respect to approval in the United States, to the satisfaction of the FDA and other comparable foreign regulatory authorities, that the product candidate is safe and effective for use for that target indication. There is no assurance that the FDA or other comparable foreign regulatory authorities will consider our future clinical trials to be sufficient to serve as the basis for approval of one of our product candidates for any indication. The FDA and other comparable foreign regulatory authorities retain broad discretion in evaluating the results of our clinical trials and in determining whether the results demonstrate that a product candidate is safe and effective. If we are required to conduct additional clinical trials of a product candidate than we expect prior to its approval, we will need substantial additional funds and there is no assurance that the results of any such additional clinical trials will be sufficient for approval.

Clinical drug development is a lengthy and expensive process, with an uncertain outcome. If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs, experience delays in completing, or ultimately be unable to complete, the development of our product candidates or be unable to obtain marketing approval.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial, such as the results of our ongoing clinical trials of APR-246, do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs.

We do not know whether ongoing clinical trials will be completed on schedule or at all, or whether future clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- obtaining regulatory authorization to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining institutional review board or ethics committee approval at each clinical trial site;
- recruiting suitable patients to participate in a trial;
- developing and validating any companion diagnostic to be used in the trial, to the extent we are required to do so;
- patients failing to comply with the clinical trial protocol or dropping out of a trial;
- clinical trial sites failing to comply with the clinical trial protocol or dropping out of a trial;
- addressing any conflicts with new or existing laws or regulations;
- the need to add new clinical trial sites;
- manufacturing sufficient quantities of product candidate for use in clinical trials and ensuring clinical trial material is provided to clinical sites in a timely manner; or
- obtaining advice from regulatory authorities regarding the statistical analysis plan to be used to evaluate the clinical trial data or other trial design issues.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon drug development programs;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors, including our CROs, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we, our investigators, or any of the overseeing IRBs or ethics committees might decide to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- any future collaborators that conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are insufficiently positive to support marketing approval, or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are narrower or more limited in scope than intended or desired;
- obtain marketing approval subject to significant use or distribution restrictions or with labeling that includes significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the drug removed from the market after obtaining marketing approval.

Our drug development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Furthermore, we rely on third-party CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and while we have agreements governing their committed activities, we have limited influence over their actual performance. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring drugs to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other strategic arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

The failure to obtain required regulatory clearances or approvals for any companion diagnostic tests that we may pursue may prevent or delay approval of any of our product candidates. Moreover, the commercial success of any of our product candidates that require a companion diagnostic will be tied to the receipt of any required regulatory clearances or approvals and the continued availability of such tests.

In connection with the clinical development of our product candidates for certain indications, we may work with collaborators to develop or obtain access to companion diagnostic tests to identify appropriate patients for our product candidates. We may rely on third parties for the development, testing and manufacturing of these companion diagnostics, the application for and receipt of any required regulatory clearances or approvals, and the commercial supply of these companion diagnostics. The FDA and foreign regulatory authorities regulate companion diagnostics as medical devices that will likely be subject to clinical trials in conjunction with the clinical trials for product candidates, and which will require separate regulatory clearance or approval prior to commercialization. This process could include additional meetings with health authorities, such as a pre-submission meeting and the requirement to submit an investigational device exemption. In the case of a companion diagnostic that is designated as "significant risk device," approval of an investigational device exemption by the FDA and IRB is required before such diagnostic is used in conjunction with the clinical trials for a corresponding product candidate. We or our third-party collaborators may fail to obtain the required regulatory clearances or approvals, which could prevent or delay approval of our product candidates. In addition, the commercial success of any of our product candidates that require a companion diagnostic will be tied to and dependent upon the receipt of required regulatory clearances or approvals and the continued ability of such third parties to make the companion diagnostic commercially available to us on reasonable terms in the relevant geographies.

We may not be successful in our efforts to identify or discover additional potential product candidates.

Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential product candidates;
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and/or achieve market acceptance; and
- potential product candidates may not be safe or effective in treating their targeted diseases.

Research programs to identify new product candidates require substantial technical, financial and human resources. If we are unable to identify suitable compounds for preclinical and clinical development, our business would be harmed.

If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability, or that of any future collaborators, to market the drug could be compromised.

Clinical trials of our product candidates must be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our product candidates receives marketing approval and we, or others, discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we, or any future collaborators, may be required to recall the drug, change the way the drug is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- the drug may become less competitive in the marketplace; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well-established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenues from sales of drugs and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to alternative therapies;
- the prevalence and severity of any side effects;

- whether the product is designated under physician and other provider treatment guidelines as a first-, second- or third-line therapy;
- our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;
- the product's convenience and ease of administration for patients and healthcare practitioners compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- limitations or warnings, including distribution or use restrictions and safety information contained in the product's approved labeling;
- the strength of sales, marketing and distribution support;
- changes in the standard of care for the targeted indications for the product; and
- the availability of coverage by, and the amount of reimbursement from, government payors, managed care plans and other third-party payors.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The pharmaceutical and biotechnology industries generally, and the cancer drug sector specifically, are highly competitive and characterized by rapidly advancing technologies, evolving understanding of disease etiology and a strong emphasis on proprietary drugs. We face competition with respect to APR-246, our lead product candidate, and will face competition with respect to any product candidates that we may seek to discover and develop or commercialize in the future, from major pharmaceutical, specialty pharmaceutical and biotechnology companies. There are a number of major pharmaceutical, specialty pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of drugs for the treatment of cancer. Potential competitors also include academic institutions and governmental agencies and public and private research institutions.

There are a large number of companies developing or marketing treatments for cancer, including the indications for which we may develop product candidates. Many of the companies that we compete or may compete against in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Small or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of the currently-approved drug therapies are branded and subject to patent protection and may be established as the standard of care for treatment of indications for which we may choose to seek regulatory approvals. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors, and, even if our product candidates were to be approved, there can be no assurance that our product candidates would displace existing treatments. In addition to currently marketed therapies, there are also a number of drugs in late-stage clinical development to treat cancer, including the indications for which we are developing product candidates. These clinical-stage product candidates may provide efficacy, safety, convenience and other benefits that are not provided by currently-marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain regulatory approval.

We are developing our lead product candidate, APR-246, to reactivate p53 for the treatment of various cancers. We are aware of other product candidates that are in clinical development for the treatment of various cancers through the reactivation of p53. Although there is a subset of drugs that directly target the p53 pathway, there are many cancer drugs that claim to affect the p53 pathway by upstream or complementary pathways. We are aware of selective small molecule inhibitors that are designed to target the p53-MDM2 interaction in various stages of clinical development being tested by F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., or collectively Roche, Amgen Inc., Novartis AG, Daiichi Sankyo Co., Ltd, and Aileron Therapeutics, Inc. If APR-246 were to be approved for the indications for which we currently have ongoing clinical trials, it will compete with currently-marketed drugs or drugs that may be approved for marketing by the FDA or comparable foreign regulatory authorities in the future and such competition will not be limited to drugs that act through the reactivation of p53.

Our business and operations would suffer in the event of IT system failures, cybersecurity attacks, data breaches, or vulnerabilities in our or our third-party vendors' information security program or defenses.

Our business relies upon information technology systems operated by us and by our third party service providers. These systems may fail or experience operational disruption, experience cybersecurity attacks, or be damaged by computer viruses and unauthorized access. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to intellectual property, proprietary business information and personal information). It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. While we are currently in the process of developing and implementing policies and procedures to ensure the security and integrity of our information technology systems and confidential and proprietary information, we do not currently have any such policies and procedures formally in place. If we fail to develop and maintain adequate policies and procedures for the protection of our information technology systems and confidential and proprietary information, we may be vulnerable to security breaches or disruptions and system breakdowns or other damage or interruptions. We also have outsourced elements of our operations to third parties, and as a result we manage a number of third-party vendors and other contractors and consultants who have access to or store our confidential information. We do not conduct audits or formal evaluations of our third-party vendors' information technology systems and cannot be sure that our third-party vendors have sufficient measures in place to ensure the security and integrity of their information technology systems and our confidential and proprietary information. If our third-party vendors fail to protect their information technology systems and our confidential and proprietary information, we may be vulnerable to disruptions in service and unauthorized access to our confidential or proprietary information and we could incur liability and reputational damage and the further development and commercialization of our product candidates could be delayed. While we have not, to our knowledge, experienced any material IT system failures or

cybersecurity attacks to date, we cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, breaches in our systems or those of our third-party vendors and other contractors and consultants, or other cyber incidents that could have a material adverse effect upon our reputation, business, operations or financial condition. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs, business operations, a breach of sensitive personal information or a loss or corruption of critical data assets including trade secrets or other proprietary information. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Such IT system failures, cybersecurity attacks or vulnerabilities to our or our third-party vendors' information security programs or defenses could result in legal liability, reputational damage, business interruption, and our competitive position could be harmed and the further development and commercialization of our products or any future products could be delayed or disrupted. Moreover, containing and remediating any IT system failure, cybersecurity attack or vulnerability may require significant investment of resources. Furthermore, significant security breaches or disruptions of our internal information technology systems or those of our third-party vendors and other contractors and consultants could result in the loss, misappropriation and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and personal information), which could result in financial, legal, business and reputational harm to us.

If we are required to in the future and if we are unable to successfully develop companion diagnostic tests for our product candidates that require such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these product candidates.

We may be required by the FDA to develop, either by ourselves or with collaborators, companion diagnostic tests for our product candidates for certain indications. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. We have no prior experience with medical device or diagnostic test development. If we choose to develop and seek FDA approval for companion diagnostic tests on our own, we will require additional personnel. We may rely on third parties for the design, development and manufacture of companion diagnostic tests for our therapeutic product candidates that require such tests. If these parties are unable to successfully develop companion diagnostics for these therapeutic product candidates, or experience delays in doing so, we may be unable to enroll enough patients for our current and planned clinical trials, the development of these therapeutic product candidates may be adversely affected, these therapeutic product candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these therapeutics that obtain marketing approval. Any failure to successfully develop this companion diagnostic may cause or contribute to delayed enrollment of this trial, and may prevent us from initiating or completing further clinical trials to support marketing approval for our product candidates. As a result, our business, results of operations and financial condition could be materially harmed.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale or marketing of pharmaceutical drugs. We are not currently a party to a strategic collaboration that provides us with access to a collaborator's resources in selling or marketing drugs. To achieve commercial success for any approved drug for which sales and marketing is not the responsibility of any strategic collaborator that we may have in the future, we must either develop a sales and marketing organization or outsource these functions to other third parties. In the future, we may choose to build

a sales and marketing infrastructure to market or co-promote some of our product candidates if and when they are approved, or enter into collaborations with respect to the sale and marketing of our product candidates.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any commercial launch of a product candidate. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- limitations or restrictions on the ability of sales personnel to appropriately market the product to physicians or other healthcare professionals;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- inability to obtain sufficient coverage and reimbursement from third-party payors and governmental agencies.

If we enter into arrangements with third parties to perform sales and marketing services, our revenues from the sale of drugs or the profitability of these revenues to us are likely to be lower than if we were to market and sell any drugs that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of our product candidates that receive marketing approval, or such authorities do not grant our product candidates appropriate periods of data or market exclusivity before approving generic versions of our product candidates, the sales of our product candidates could be adversely affected.

Once an NDA is approved, the drug covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations." Manufacturers may seek marketing approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials demonstrating safety and efficacy. Rather, the applicant generally must show that its drug is pharmaceutically equivalent to the reference listed drug, in that it has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug, and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic drugs may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic drugs are generally able to offer them at lower prices.

Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug is typically lost to the generic drug.

The FDA may not approve an ANDA for a generic drug until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another version of such product candidate where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing product candidate. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for product candidates containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Manufacturers may seek to launch these generic drugs following the expiration of the marketing exclusivity period, even if we still have patent protection for our drug.

Competition that our product candidates may face from generic versions of our product candidates could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates. Our future revenues, profitability and cash flows could also be materially and adversely affected and our ability to obtain a return on the investments we have made in those product candidates may be substantially limited if our product candidates, if and when approved, are not afforded the appropriate periods of non-patent exclusivity.

Even if we obtain regulatory approval of any product candidate, the approved product may be subject to post-approval studies and will remain subject to ongoing regulatory requirements. If we fail to comply, or if concerns are identified in subsequent studies, our approval could be withdrawn, and our product sales could be suspended.

If we are successful at obtaining regulatory approval for APR-246 or any of our other product candidates, regulatory agencies in the United States and other countries where a product will be sold may require extensive additional clinical trials or post-approval clinical trials that are expensive and time-consuming to conduct. These trials may reveal side effects or other harmful effects in patients that use our products after they are on the market, which may result in the limitation or withdrawal of our drugs from the market. Alternatively, we may not be able to conduct such additional trials, which might force us to abandon our efforts to develop or commercialize certain product candidates. Even if post-approval studies are not requested or required, after our products are approved and on the market, there might be safety issues that emerge over time that require a change in product labeling, additional postmarket studies or clinical trials, imposition of distribution and use restrictions under a Risk Evaluation and Mitigation Strategy, or REMS, or withdrawal of the product from the market, which would cause our revenue to decline.

Additionally, any products that we may successfully develop will be subject to ongoing regulatory requirements after they are approved. These requirements will govern the manufacturing, packaging, marketing, distribution, and use of our products. If we fail to comply with such regulatory requirements, approval for our products may be withdrawn, and product sales may be suspended. We

may not be able to regain compliance, or we may only be able to regain compliance after a lengthy delay, significant expense, lost revenues and damage to our reputation.

Even if we are able to commercialize any product candidate, such product candidate may become subject to unfavorable pricing regulations, third-party coverage and reimbursement policies or healthcare reform initiatives, which could harm our business.

The regulations that govern marketing approval, pricing, coverage and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement and coverage for these products and related treatments will be available from government authorities, private health insurers and other organizations, and if reimbursement and coverage is available, the level of reimbursement and coverage. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the healthcare industry in the United States and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for medical products. We cannot be sure that coverage and reimbursement will be available for any drug that we commercialize and, if coverage and reimbursement are available, we cannot be sure as to the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, may be incorporated into existing payments for other items or services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for new products that we develop and for which we obtain marketing approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any drugs that we may develop. Our insurance policies may be inadequate and may potentially expose us to unrecoverable risk.

We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and will face an even greater risk if we commercially sell any drugs that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or drugs caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or drugs that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any drugs that we may develop.

We currently hold clinical trial liability insurance coverage for up to \$3.0 million, but that coverage may not be adequate to cover any and all liabilities that we may incur. We would need to increase our insurance coverage when we begin the commercialization of our product candidates, if ever. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of our products, if any.

In some countries, particularly member states of the European Union, or, the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we, or our future collaborators, may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Risks related to our dependence on third parties

We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.

We currently rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials of APR-246 and expect to continue to rely upon third parties to conduct additional clinical trials of APR-246 and our other product candidates. We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical studies. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our drug development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan, study protocols for the trial, statistical analysis plan and other study-specific documents (for example, monitoring and blinding plans). Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practice, or GCP, International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use, or ICH, guidelines, and regulations regarding the informed consent process, safety reporting requirements, data collection guidelines, and other regulations for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The European Medicines Agency, or EMA, also requires us to comply with similar standards. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP and other applicable regulations. In addition, our clinical trials must be conducted with product produced under current Good Manufacturing Practices, or cGMP, regulations. Our failure to comply with these regulations may require us to conduct new clinical trials, which would delay the marketing approval process. We also are required to register certain ongoing clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of such third parties could delay clinical development or marketing approval of our product candidates or commercialization of our product candidates, producing additional losses and depriving us of potential revenue from sales of drugs.

We are currently dependent on a single third party manufacturer for the manufacture of the active pharmaceutical ingredient for APR-246. This reliance on a single third party increases the risk that we will not have sufficient quantities of our product candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities or personnel, and we currently have no plans to build our own clinical or commercial scale manufacturing capabilities. We currently contract with third parties for the manufacture of our product candidates for certain preclinical trials and clinical trial materials, including raw materials and consumables necessary for their manufacture, consistent with applicable cGMP requirements. We intend to continue to contract for these materials in the future, including commercial manufacture if our product candidates receive marketing approval.

The active pharmaceutical ingredient, or API, for APR-246 is currently manufactured by a single contract manufacturer. Although we may do so in the future, we do not currently have arrangements in place for redundant supply of the API for APR-246. We contract with a different manufacturer for formulation of drug product, sterile fill of vials, labeling and packaging, and the storage and distribution of APR-246 to clinical sites.

We expect to rely on third-party manufacturers or third-party collaborators for the manufacture of our product candidates for commercial supply of any of our product candidates for which we or any of our future collaborators obtain marketing approval. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible failure of the third party to manufacture our product candidate according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the possible termination or nonrenewal of agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the possible breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the possible failure of the third party to manufacture our product candidates according to our specifications;
- the possible mislabeling of clinical supplies, potentially resulting in issues including the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or the EMA pursuant to inspections that will be conducted after we submit our NDA to the FDA or our MAA to the EMA. We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP regulations for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the

FDA or other regulatory bodies, they will not be able to secure and/or maintain marketing approval for their manufacturing facilities. In addition, we do not have complete control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, the EMA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved.

Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and harm our business and results of operations.

Any drugs that we may develop may compete with other product candidates and drugs for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

We do not currently have arrangements in place for redundant supply of the API of APR-246. If our current contract manufacturer cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or drugs may adversely affect our future profit margins and our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis.

Although we currently plan to retain all commercial rights to APR-246 and our product candidates, we may enter into strategic collaborations for the development, marketing and commercialization of APR-246 and our other product candidates. If those collaborations are not successful, the development, marketing and/or commercialization of our product candidates that are the subject of such collaborations would be harmed.

As we further develop APR-246, we may build a commercial infrastructure with the capability to directly market it to a variety of markets and geographies. Although we currently plan to retain all commercial rights to APR-246 and our product candidates, we may enter into strategic collaborations for the development, marketing and commercialization of APR-246 and our other product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we do enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development, marketing and/or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;

- collaborators may not perform their obligations as expected;
- collaborators may not pursue development, marketing and/or commercialization of our product candidates or may elect not to continue or renew development, marketing or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, drugs that compete directly or indirectly with our product candidates or product candidates;
- a collaborator with marketing and distribution rights to one or more drugs may not commit sufficient resources to the marketing and distribution of such drug or drugs;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly obtain, maintain, defend and enforce our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- we may lose certain valuable rights under circumstances identified in any collaboration arrangement that we enter into, such as if we undergo a change of control;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development, marketing and/or commercialization of the applicable product candidates;
- collaborators may learn about our discoveries, data, proprietary information, trade secrets, or compounds and use this knowledge to compete with us in the future; and
- the number and type of our collaborations could adversely affect our attractiveness to future collaborators or acquirers.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all.

Risks related to our intellectual property

If we are unable to obtain and maintain intellectual property protection for APR-246 or any other product candidates we develop or for our technology, our competitors could develop and commercialize products or technology similar or identical to ours, and our ability to successfully commercialize APR-246 or any product candidates we may develop, and our technology may be adversely affected.

Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, which include APR-246 and others, their respective components, formulations, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges.

We seek to protect our proprietary position by filing patent applications in the United States and abroad relating to our product candidates as well as other technologies that are important to our business. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The chemical structure of APR-246 is in the public domain. Accordingly, we do not own or license any composition of matter patents claiming the compound of APR-246 and will not in the future own or license any composition of matter patents claiming the chemical structure of APR-246 as described in the public domain. Our patent portfolio for APR-246 currently consists of method-of-use and formulation patent claims, and dosing, manufacturing processes, and crystalline solid form provisional patent application claims. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technologies. Any failure to obtain or maintain patent protection with respect to APR-246 and our other product candidates could have a material adverse effect on our business, financial condition, results of operations and growth prospects. If it is later determined that our activities or product candidates infringe, misappropriate or otherwise violate the intellectual property of third parties we may be liable for damages, enhanced damages or subjected to an injunction, any of which could have a material adverse effect on our business.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. During the course of business we have decided not to pursue certain products or processes and have not pursued certain corresponding intellectual property. However, we may decide to pursue such products or processes again in the future. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain and involves complex legal and factual questions for which many legal principles remain unresolved. In recent years patent rights have been the subject of significant litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued in the United States or in other jurisdictions which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products.

Our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art, including our own previously filed patent applications and scientific publications, allow our inventions to be patentable over the prior art. We are aware of certain scientific publications by our inventors and other third parties that disclose subject matter, including the composition of APR-246, relating to certain of our patents, that may be used by third parties to challenge the validity and enforceability of our patents and patent applications. If such third parties are successful, we could lose valuable patent rights. In the United States, an inventor's own publication cannot be used as prior art to the inventor's patent application on the same subject matter when published less than one year before the effective filing date of the patent application. Such a publication may be considered prior art in certain jurisdictions that do not provide such a grace period. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. In addition, the U.S. Patent and Trademark Office, or USPTO, might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common

inventor. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties, certain of these parties have and others may in the future breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in the patent claims of our patents being narrowed, invalidated or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, some of our owned patents and patent applications may in the future be co-owned with third parties. If we do not have exclusive control of the grant of licenses under any such third-party co-owners' interest in such patents or patent applications or we are otherwise unable to secure such exclusive rights, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our co-owned patents in order to enforce such patents against third parties, and such cooperation may not be provided to us.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or otherwise provide us with a competitive advantage. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions, including APR-246 based on patent exclusivity. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects.

Our proprietary position for APR-246 depends upon patents that consist of method-of-use and formulation patent claims, which may not prevent a competitor or other third party from using the same product candidate for another use or in another formulation.

Composition-of-matter patent claims on the active pharmaceutical ingredient, or API, in pharmaceutical drug products are generally considered to be the favored form of intellectual property protection for drug products because such patents may provide protection without regard to any particular method of use or manufacture or formulation of the API used. The chemical structure of APR-246 is in the public domain. Accordingly, we do not own or license any composition of matter patents claiming the compound of APR-246 and will not in the future own or license any composition of matter patents claiming the chemical structure of APR-246 as described in the public domain.

Method-of-use patent claims protect the use of a product for the specified method and dosing or formulation patent claims cover dosing regimens or formulations of the API. These types of patent claims do not prevent a competitor or other third party from marketing an identical API for an indication that is outside the scope of the method claims or from developing a different dosing regimen

or formulation that is outside the scope of the dosing or formulation claims. Moreover, with respect to method-of-use patents, even if competitors or other third parties do not actively promote their product for our targeted indications or uses for which we may obtain patents, physicians may recommend that patients use these products off-label, or patients may do so themselves. Although off-label use may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute. In addition, there are numerous publications and other prior art that may be relevant to our patents and may be used to challenge the validity of such patents in litigation or other intellectual property-related proceedings. If such challenges are successful, our patents may be narrowed or found to be invalid and we may lose valuable intellectual property rights. Any of the foregoing could have a material adverse effect on our business, financial conditions and results of operations and prospects.

Issued patents covering our product candidates and other technologies could be narrowed or found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.

If we seek to enforce a patent covering our product candidates or other technologies against a third party, that third party could assert that such patent is invalid or unenforceable. In patent litigation in the United States, challenges to validity or enforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of patentable subject matter, lack of novelty, obviousness, inadequate written description, indefiniteness, or lack of enablement. Grounds for an unenforceability assertion could be an allegation that relevant information was withheld from or a misleading statement was made to the USPTO during prosecution.

In addition, third parties may raise claims challenging the validity or enforceability of our patents before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include preissuance submission of prior art to the USPTO and re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our priority of invention or other features of patentability with respect to our patents and patent applications. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our product candidates or other technologies and compete directly with us, without payment to us.

In the United States, an inventor's own publication may not be effective prior art to the inventor's patent application on the same subject matter when published less than one year before the effective filing date of the patent application. Such a publication might be considered prior art in certain jurisdictions that do not provide such a grace period. For those non-US jurisdictions, reliance on non-patent exclusivity may provide sufficient competitive protection to exclude others from commercializing generic versions of our products.

Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. If we are unsuccessful in any such proceeding or other priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products. Any of the foregoing could have a material adverse effect on our business, results of operations, financial condition and prospects.

We may be subject to other claims challenging the inventorship of our patents and other intellectual property.

We may also be subject to claims that former employees, collaborators or other third parties have an interest in our patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates or other technologies. Litigation may be necessary to defend against these and other claims challenging inventorship of our patents, trade secrets or other intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates and other technologies. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

If we do not obtain patent term extension or data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate. However, we may not be granted an extension in the United States and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and growth prospects could be materially harmed.

We may not be successful in obtaining, through acquisitions, in-licenses or otherwise, rights that may be necessary to our product candidates or other technologies.

The growth of our business may depend in part on our future ability to acquire or in-license any relevant third-party proprietary rights that we may identify as necessary or important to our business operations. For example, our programs may involve additional product candidates that may require the use of additional proprietary rights held by third parties. Our product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may develop products containing our compounds and pre-existing pharmaceutical compounds. These pharmaceutical compounds may be covered by intellectual property rights held by others. We may be required by the FDA or comparable foreign regulatory authorities to provide a companion diagnostic test or tests with our product candidates. These diagnostic test or tests may be covered by intellectual property rights held by others. We may be unable to acquire or in-license such third-party intellectual property rights. We may fail to obtain any of

these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe, misappropriate or otherwise violate intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license to such intellectual property rights, any such license may be non-exclusive, which may allow our competitors access to the same technologies licensed to us.

Additionally, we sometimes collaborate with academic institutions and clinical research organizations to accelerate our research or development, including our research or development of APR-246, under written agreements with these institutions and organizations. In certain cases, these institutions and organizations may own or jointly own with us inventions that are created under such collaborations and provide us with an option to negotiate a license to any of the institution's rights in such inventions. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution or organization may offer the intellectual property rights to others, potentially blocking our ability to pursue our program and allowing third parties to compete with us.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. If we are unable to successfully obtain rights to third-party intellectual property that may be necessary, we may have to abandon development of such program and our business, results of operations, financial condition and prospects could suffer.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates and technology.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent regardless of whether another inventor had made the invention earlier. In March 2013, under the Leahy-Smith America Invents Act, or America Invents Act, the United States moved from a "first-to-invent" to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after March 2013, but before us, could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either (i) file any patent application related to our product candidates or other technologies or (ii) invent any of the inventions claimed in our patents or patent applications.

The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party in a district court action. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights, all of which could have a material adverse effect on our business and financial condition. Accordingly, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents, or we may be required to defend against claims of infringement. In addition, our patents also may become involved in inventorship, priority, validity or unenforceability disputes. To counter or defend against such claims can be expensive and time consuming. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. For example, in an infringement proceeding, a court may decide that a patent owned by us is invalid or unenforceable. There is also the risk that, even if the validity of these patents is upheld, the court will refuse to stop the third party on the ground that such third party's activities do not infringe our owned patents, including finding that the other party's use of our patented technology falls under the safe harbor to patent infringement under 35 U.S.C. § 271(e)(1). Even if resolved in our favor, these lawsuits are expensive and would consume time and other resources, including distracting our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

We may not be able to detect infringement against our patents which may be more difficult for formulation patents. Even if we detect infringement by a third party of our patents, we may choose not to pursue litigation against or settlement with the third party. If we later sue such third party for patent infringement, the third party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us to enforce our patents against such third party.

If another party questions the patentability of any of our claims in our U.S. patents, the third party can request that the USPTO review the patent claims such as in an *inter partes* review, *ex parte* re-exam or post-grant review proceedings. These proceedings are expensive and may result in a loss of scope of some claims or a loss of the entire patent. In addition to potential USPTO review proceedings, we may become a party to patent opposition proceedings in the European Patent Office, or EPO, or similar proceedings in other foreign patent offices, where either our foreign patents are challenged. The costs of these opposition or similar proceedings could be substantial, and may result in a loss of scope of some claims or a loss of the entire patent. An unfavorable result at the USPTO, EPO or other patent office may result in the loss of our right to exclude others from practicing one or more of our inventions in the relevant country or jurisdiction, which could have a material adverse effect on our business.

If we are sued for infringing, misappropriating or otherwise violating patents or other intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. We cannot guarantee that our product candidates and other technologies that we have developed, are developing or may develop in the future will not infringe existing or future patents owned by third parties. U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields relating to our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert our product candidates infringe the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates or other technologies, could be found to be infringed by our product candidates or other technologies. In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications covering our product candidates or technology. If any such patent applications issue as patents, and if such patents

have priority over our patent applications or patents, we may be required to obtain rights to such patents owned by third parties which may not be available on commercially reasonable terms or at all, or may only be available on a non-exclusive basis.

If a third party claims that we infringe its intellectual property rights, we may face a number of issues even if we believe such claims are without merit, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate, may divert our management's attention from our core business and may impact our reputation;
- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, including APR-246, or from using our proprietary technologies, unless the third party licenses its patent rights to us, which it is not required to do;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our product candidates or such license is only available on a non-exclusive basis; and
- redesigning our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or growth prospects.

We may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in an *ex-parte* re-exam, *inter partes* review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party's patent in patent opposition proceedings in the EPO, or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies.

We may not be able to protect our intellectual property rights with patents throughout the world.

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive, and the laws of some foreign countries may not protect our rights to the same extent as the laws of the United States. Competitors may use our technology in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as in the United States. These products may compete with our product candidates in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in

foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings to enforce our intellectual property rights or proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business and could put our patents at risk of being invalidated or interpreted narrowly.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and growth prospects may be adversely affected.

Obtaining and maintaining our patent protection depends upon compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent prosecution process and following the issuance of a patent. In some cases, an inadvertent failure to comply with such requirements can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance could result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case if our patent were in force, which would have a material adverse effect on our business.

We may be subject to claims that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees, consultants or advisors or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their current or former employers. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources.

Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our platform technology and discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and we have limited control over the protection of trade secrets used by our collaborators and suppliers. Although we seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with parties who have access them, such as our employees, consultants, and outside scientific advisors, contractors and collaborators, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite our efforts, any of these parties might breach the agreements and intentionally or inadvertently disclose our trade secret information and we may not be able to obtain adequate remedies for such breaches. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Moreover, our competitors or other third parties may independently develop equivalent knowledge, methods and know-how.

Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts inside and outside the United States sometimes are less willing or unwilling to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. If any of our trade secrets were determined to be lawfully obtained or independently developed by a competitor or other third party, we may not be able to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position, business, results of operations and prospects would be materially and adversely harmed.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to the pharmaceutical compounds used in our product candidates but that are not covered by the claims of our patents;

- the APIs in our current product candidates will eventually become commercially available in generic drug products, and no patent protection may be available with regard to formulation or method of use;
- we, or our future licensors or collaborators, might not have been the first to file patent applications for these inventions;
- we, or our future licensors or collaborators, might not have been the first to make the inventions covered by our issued patents or pending patent applications;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our current or future pending or licensed patent applications will not result in issued patents;
- it is possible that public disclosures or publications, including disclosures or publications made by us, could be used in an attempt to invalidate our patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- it is possible that others may circumvent our patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our proprietary rights to the same extent as the laws of the United States;
- the claims of our issued patents or patent applications, if and when issued, may not cover our product candidates;
- our issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- we have engaged in scientific collaborations in the past and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- we may choose not to pursue patent protection in order to maintain certain trade secrets or know-how, and a third party may subsequently obtain a patent covering such intellectual property;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Risks related to regulatory and marketing approval and other legal compliance matters

We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our product candidates.

We have never obtained marketing approval for a product candidate. The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. It is possible that the FDA and comparable foreign regulatory authorities may refuse to accept for filing and substantive review any new drug applications, or NDAs, marketing authorization applications, or MAA, that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates. If the FDA, or comparable foreign regulatory authorities do not accept or approve our NDAs or MAAs for our product candidates, it may require that we conduct additional clinical, nonclinical or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other regulatory authority-required studies, approval of any NDA, MAA or other application that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA or comparable foreign regulatory authorities to approve our NDAs or our MAAs.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us, or any future collaborators, from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of drugs are subject to extensive regulation by the FDA and comparable foreign regulatory authorities, whose laws and regulations may differ from country to country. We, and any future collaborators, are not permitted to market our product candidates in the United States or in other countries until we or they receive approval of an NDA from the FDA or marketing approval from comparable foreign regulatory authorities. Our product candidates are in early stages of development and are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the United States and abroad, is a lengthy, expensive and uncertain process. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of

manufacturing facilities by, the regulatory authorities. The FDA or other comparable foreign regulatory authorities have substantial discretion and may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Our product candidates could fail to receive marketing approval, or marketing approval for our product candidates could be limited or delayed, for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission and applications or to obtain marketing approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the FDA or comparable foreign regulatory authorities may fail to approve any companion diagnostics that may be required in connection with approval of our therapeutic product candidates
- the FDA or the applicable foreign regulatory agency may fail to approve the formulation, labeling and/or the specifications for our product candidate
- changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted drug application; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of clinical trial results may result in our failing to obtain marketing approval to market APR-246, which would significantly harm our business, results of operations and prospects. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical studies, clinical trials or other studies and testing. In addition, varying interpretations of the data obtained from preclinical studies and clinical trials could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we, or any collaborators we may have in the future, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved drug not commercially viable.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability or that of any collaborators we may have to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad. Any approval we are granted for our product candidates in the United States would not assure approval of our product candidates in foreign jurisdictions.

In order to market and sell our product candidates in the EU and many other jurisdictions, we, and any collaborators we may have in the future, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside of the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside of the United States, it is required that the drug be approved for reimbursement before the drug can be approved for sale in that country. We, and any collaborators we may have in the future, may not obtain approvals from regulatory authorities outside of the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA.

On June 23, 2016, the electorate in the United Kingdom, or the U.K., voted in favor of leaving the EU, commonly referred to as Brexit. The U.K. government communicated the notice of withdrawal to the EU on March 29, 2017. As part of the withdrawal process, the U.K. government and the EU negotiated a withdrawal agreement that was approved by the U.K. Prime Minister and the leaders of EU member states. However, under U.K. law, such agreement also requires the approval of the U.K. parliament, and the U.K. parliament has to date refused to approve the agreement. While negotiations are continuing, there remains considerable uncertainty around the withdrawal. As a result, the EU and the U.K. have agreed to delay the date on which the U.K. will leave the EU to October 31, 2019, although if the U.K. parliament approves the withdrawal agreement prior to that date, it is possible that the U.K. may leave the EU on an earlier date; however, failure to obtain parliamentary approval of an agreed withdrawal agreement may, absent a revocation of the U.K.'s notification to withdraw or some other further delay, mean that the U.K. would leave the EU on October 31, 2019 with no agreement (a so-called "hard Brexit"). Absent delay or mitigating legislative measures by individual EU Member States, in the event of a hard Brexit the trade relationship between the U.K. and the EU would be solely based on World Trade Organization terms, thereby hindering current levels of mutual market access.

If the U.K. and the EU do reach a deal on or before October 31, 2019 (or any later withdrawal date which may subsequently be agreed between the U.K. and the EU) or if the U.K.'s withdrawal takes effect on the terms of the existing withdrawal agreement, a transition period may start that lasts until December 31, 2020. Based upon the currently proposed transition plan, during this period, the U.K. would, with some exceptions, remain subject to EU law. It would also maintain access to the EU's single market. During this transition phase, the U.K. and EU would also start negotiations on their future trade relationship.

The consequences for the economies of the U.K. and the EU member states as a result of the U.K.'s withdrawal from the EU are unknown and unpredictable, especially in the case of a hard Brexit. Given the lack of comparable precedent, it is unclear what the broader macro-economic and financial implications the U.K. leaving the EU with no agreements in place would have.

Since a significant proportion of the regulatory framework in the U.K. is derived from EU directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of our product candidates in the U.K. or the EU. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the U.K. and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the U.K. and/or EU for our product candidates, which could significantly and materially harm our business.

We, or any future collaborators, may not be able to obtain or maintain orphan drug exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA or the European Commission from approving competing products.

Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. APR-246 has received orphan drug designation from the FDA for use in the treatment of high-risk myelodysplastic syndromes, or MDS, and orphan drug designation from the EMA for MDS, acute myeloid leukemia, or AML, and ovarian cancer. We may seek orphan drug designations for APR-246 for other indications or for other of our product candidates. There can be no assurances that we will be able to obtain such designations.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, the company that obtains the first FDA approval for a designated orphan drug for a rare disease receives marketing exclusivity for use of that drug for the designated condition for a period of seven years. Once a product receives orphan drug exclusivity, a second product that is considered to be the same drug for the same indication generally may be approved during the exclusivity period only if the second product is shown to be "clinically superior" to the original orphan drug in that it is more effective, safer or otherwise makes a "major contribution to patient care" or the holder of exclusive approval cannot assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated.

The European Commission can grant orphan drug product designation to products for which the sponsor can establish that it is intended for the diagnosis, prevention, or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the European Union, or (2) a life threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that sales of the drug in the European Union would generate a sufficient return to justify the necessary investment. In addition, it must be established that there is no other satisfactory method approved in the European Union of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan drug designation is not a marketing authorization. It is a designation that provides a number of benefits, including fee reductions, regulatory assistance, and the possibility to apply for a centralized EU marketing authorization, as well as 10 years of market exclusivity following a marketing authorization. During this market exclusivity period, neither the EMA, nor the European Commission nor the EU member states can accept an application or grant a marketing authorization for a 'similar medicinal product.' A 'similar medicinal product' is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market

exclusivity period for the authorized therapeutic indication may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, a competing similar medicinal product may in limited circumstances be authorized prior to the expiration of the market exclusivity period, including if it is shown to be safer, more effective or otherwise clinically superior to our product. Our product can lose orphan designation, and the related benefits, prior to us obtaining a marketing authorization if it is demonstrated that the orphan designation criteria are no longer met.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing drug products. If this happens, marketing approval for our product candidate may be delayed due to the first-approved product's orphan drug exclusivity, unless we demonstrate clinical superiority. We may not be able to demonstrate that our product is clinically superior to a first-approved product with orphan drug exclusivity, i.e., that it provides greater safety or efficacy or a major contribution to patient care. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Even if we, or any collaborators we may have in the future, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our product candidates could require substantial expenditure of resources and may limit how we, or they, manufacture and market our product candidates, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved drug and its manufacturer and marketer are subject to ongoing review and extensive regulation. These requirements include submissions of safety and other post-marketing information and reports, user fee requirements, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. We, and any collaborators we may have in the future, must also comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the drug's approved labeling. Thus, we, and any collaborators we may have in the future, may not be able to promote any drugs we develop for indications or uses for which they are not approved.

The FDA or comparable foreign regulatory authorities may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a drug. For example, the approval may be subject to limitations on the indicated uses for which the drug may be

marketed or to the conditions of approval, including the requirement to implement a REMS or comparable foreign equivalents, like the EU Risk Management Plan, or RMP, which could include requirements for a restricted distribution system. Manufacturers of approved drugs and those manufacturers' facilities are also required to comply with extensive FDA or comparable foreign regulatory authorities requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA or comparable foreign regulatory authorities to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or our future collaborators, receive marketing approval for one or more of our product candidates, we, and our future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and our future collaborators, are not able to comply with post-approval regulatory requirements, regulatory agencies or enforcement authorities may:

- issue warning letters;
- impose civil or criminal penalties;
- suspend regulatory approval;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us or our collaborators;
- impose restrictions on our operations, including closing our or our collaborators' manufacturing facilities; or
- seize or detain products or require a recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our product candidates, if approved. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

The regulatory requirements and policies may change, and additional government regulations may be enacted for which we may also be required to comply. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. If we or any future collaboration partner are not able to maintain regulatory compliance, we or such collaboration partner, as applicable, may face government enforcement action and our business will suffer. Moreover, our or our future collaborators' ability to market any future drugs could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

The FDA's and other comparable regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.

In December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. Notably, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs, within the Office of Management and Budget, on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an Executive Order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued Executive Orders relating to the review of federal regulations; however, it is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Any of our product candidates for which we, or our future collaborators, obtain marketing approval in the future will be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our product candidates following approval.

Any of our product candidates for which we, or our future collaborators, obtain marketing approval in the future, will be subject to continual review by the FDA or comparable foreign regulatory authorities.

For example in the United States, the FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or our future collaborators, do not market any of our product candidates for which we, or they, receive marketing approval for only their

approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our product candidates or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- litigation involving patients taking our drug;
- restrictions on such drugs, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a drug;
- restrictions on drug distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the drugs from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of drugs;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- restrictions on coverage by third-party payors;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of drugs;
- drug seizure; or
- injunctions or the imposition of civil or criminal penalties.

Recently enacted and future legislation, and a change in existing government regulations and policies, may increase the difficulty and cost for us and our future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of our future collaborators, to profitably sell any drugs for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we, or our future collaborators, may receive for any approved drugs.

In the United States, the Congress and recent presidential administrations have enacted or are considering a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products, if approved, and to do so profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting

changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access.

In the United States, the pharmaceutical industry has been a particular focus of efforts to reform the healthcare system and has been significantly affected by major legislative initiatives, including the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, "PPACA"), which contains provisions that may potentially affect the profitability of our products, including, for example, increased rebates for products sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs, and expansion of the entities eligible for discounts under the Public Health Services pharmaceutical pricing program. There have been judicial and Congressional challenges to the PPACA, as well as efforts by the Trump administration to repeal or replace certain aspects of the PPACA that contribute to regulatory uncertainty that could affect the profitability of our products. Since January 2017, President Trump has signed several Executive Orders and other directives designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements mandated by the PPACA. In December 2018, a federal district court in Texas ruled the individual mandate was unconstitutional and could not be severed from the PPACA. As a result, the court ruled the remaining provisions of the PPACA were also invalid, though the court declined to issue a preliminary injunction with respect to the PPACA. In April 2019, in a brief filed in the Fifth Circuit Court of Appeals, the Trump Administration took the position that the individual mandate was unconstitutional, that it could not be severed from the PPACA, and, as a result, the PPACA must be invalidated in its entirety. The case is pending before the Fifth Circuit, and it remains unclear whether, and to what extent, the PPACA may be affected by the Fifth Circuit's and possibly other courts' rulings.

While Congress has not enacted legislation to comprehensively repeal the PPACA, at least two bills affecting the implementation of the PPACA have been signed into law, including the repeal, effective January 1, 2019, of the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain fees mandated by the PPACA, including the so-called "Cadillac" tax on certain high-cost employer-sponsored health insurance plans and the annual fee imposed on certain health insurance providers. Moreover, effective January 1, 2019, the Bipartisan Budget Act of 2018, among other things, further amends portions of the Social Security Act implemented as part of the PPACA to increase from 50% to 70% the point-of-sale discount that pharmaceutical manufacturers participating in the Coverage Gap Discount Program provide to eligible Medicare Part D beneficiaries during the coverage gap phase of the Part D benefit, commonly referred to as the "donut hole," and to reduce standard beneficiary cost sharing in the coverage gap from 30% to 25% in most Medicare Part D plans. In the future, there may be additional challenges and/or amendments to the PPACA. It remains to be seen precisely what any new legislation will provide, when or if it will be enacted, and what impact it will have on the availability and cost of healthcare items and services, including drug products.

Other legislative changes have been proposed and adopted since PPACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions in Medicare payments to providers of up to 2% per fiscal year that started in April 2013 and, due to subsequent statutory amendments, will continue through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, which, among other changes, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These legislative changes may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

More recently, the cost of prescription pharmaceuticals has been the subject of considerable discussion in the United States. Congress has begun developing legislation and the Trump Administration has proposed and begun implementing regulatory reforms to further increase transparency around prices and price increases, lower out-of-pocket costs for consumers, and decrease spending on prescription drugs by government programs. Congress has conducted or is in the process of conducting inquiries into the prescription drug industry's pricing practices. The Trump Administration's budget proposal for fiscal year 2019 contained additional drug price control measures that could be enacted in future legislation, including, for example, measures to end Medicare Part B coverage of medications and to shift those medication costs to Medicare Part D, to allow some states to negotiate prescription drug prices under Medicaid and to eliminate cost sharing for generic drugs for low-income patients. While several proposed reform measures will require Congress to pass legislation to become effective, Congress and the Trump Administration have each indicated that it will continue to seek new legislative and/or regulatory measures to address prescription drug costs. At the state level, legislatures are increasingly passing legislation and states are implementing regulations designed to control spending on, and patient out-of-pocket costs for, drug products. Implementation of cost containment measures or other healthcare reforms that affect the pricing and/or availability of drug products may impact our ability to generate revenue, attain or maintain profitability, or commercialize products for which we may receive regulatory approval in the future.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and/or new payment methodologies, and place additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels and imposition of more rigorous coverage criteria or new payment methodologies may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any coverage or reimbursement policies instituted by Medicare or other federal health care programs may result in a similar policies from private payors. The implementation of cost containment measures or other healthcare reforms may affect our ability to generate revenue, attain or maintain profitability, or commercialize our product candidates. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to that of other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for drug products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent drug labeling and post-marketing testing and other requirements.

We may seek a breakthrough therapy designation for APR-246 or one or more of our other product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster development or regulatory review or approval process.

We may seek a breakthrough therapy designation for APR-246 or one or more of our other product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA may also be eligible for priority review if supported by clinical data at the time the NDA is submitted to the FDA, and parts of the NDA may be submitted and reviewed on a rolling basis.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. Even if we receive breakthrough therapy designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

A fast track designation by the FDA for APR-246 may not actually lead to a faster development or regulatory review or approval process.

If a drug is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a drug sponsor may apply for FDA fast track designation. Although we have received a fast track designation for APR-246 for the treatment of patients with myelodysplastic syndrome having a *TP53* mutation, this does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with fast track designation compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

We may seek priority review designation for APR-246 or one or more of our other product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster development or regulatory review or approval process.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months from the 60-day filing date, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily mean

a faster development or regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties, including criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Although we do not currently have any products on the market, we are subject to a variety of regulatory requirements, including healthcare statutory and regulatory requirements and enforcement by the U.S. federal and state governments and the foreign governments of the countries in which we conduct our business. Even though we are not in a position to make patient referrals and do not bill Medicare, Medicaid, or other government or commercial third-party payers, our relationships with healthcare providers, physicians and third-party payors will subject us to healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Our future arrangements with healthcare providers, physicians and third-party payors and patients may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include, without limitation, the following:

- *The Federal Anti-Kickback Statute*—An intent-based federal criminal statute that prohibits, among other things, any person from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made, in whole or in part, by a federal health care program, such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. The PPACA, among other things, amended the intent requirement of the federal Anti-Kickback Statute, so that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. The Anti-Kickback Statute has also been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and individuals, such as prescribers, patients, purchasers, and formulary managers on the other the other hand. A conviction for violation of the Anti-Kickback Statute results in criminal fines and requires mandatory exclusion from participation in federal health care programs. Although there are a number of statutory exceptions and regulatory safe harbors to the federal Anti-Kickback Statute that protect certain common industry practices from prosecution, the exceptions and safe harbors are narrowly drawn, and arrangements may be subject to scrutiny or penalty if they do not fully satisfy all elements of an available exception or safe harbor. The Anti-Kickback Statute safe harbors, including the discount safe harbor, are the subject of possible regulatory reforms. Any changes to the safe harbors may impact our future contractual and other arrangements with pharmacy benefit managers, third-party payors, wholesalers and distributors, healthcare providers and prescribers, and other entities, as well as our future pricing strategies.
- *The Federal Civil False Claims Act*—Imposes civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or knowingly making using or causing to be made or used a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages

and significant per-claim penalties, currently set at \$11,181 to \$22,363 per false claim or statement for penalties assessed after January 29, 2018, with respect to violations occurring after November 2, 2015. Among other reasons, pharmaceutical companies have been investigated and/or subject to government enforcement actions asserting liability under the federal civil False Claims Act in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes (e.g., under the Medicaid Drug Rebate Program), and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. In addition, manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Criminal prosecution is also possible for making or presenting a false, fictitious or fraudulent claim to the federal government.

- *The Federal Criminal Statute on False Statements Relating to Health Care Matters*—Makes it a crime to knowingly and willfully falsify, conceal, or cover up a material fact, make any materially false, fictitious, or fraudulent statements or representations, or make or use any materially false writing or document knowing the same to contain any materially false, fictitious, or fraudulent statement or entry in connection with the delivery of or payment for federally funded healthcare benefits, items, or services.
- *HIPAA Criminal Federal Health Care Fraud Statute*—Enacted as part of the Health Insurance Portability and Accountability Act of 1996, makes it a crime to knowingly and willfully falsify, conceal, or cover up a material fact, make any materially false, fictitious, or fraudulent statements or representations, or make or use any materially false writing or document knowing the same to contain any materially false, fictitious, or fraudulent statement or entry in connection with the delivery of or payment for federally funded healthcare benefits, items, or services.
- *The Federal Civil Monetary Penalties Law*—Authorizes the imposition of substantial civil monetary penalties against an entity, such as a pharmaceutical manufacturer, that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal healthcare programs to provide items or services reimbursable by a federal healthcare program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment.
- *HIPAA Health Information Privacy and Security*—The Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, or collectively, HIPAA, imposes privacy, security, and breach reporting obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouse as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including, among other requirements, mandatory contractual terms and technical safeguards to protect the privacy, security and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties

directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.

- *The Federal Physician Payments Sunshine Act*—Requires "applicable manufacturers" of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the State Children's Health Insurance Program, among others, to track and report annually to the federal government (for disclosure to the public) certain payments and other transfers of value they make to "covered recipients." The term covered recipients includes physicians, teaching hospitals, and, for reports submitted on or after January 1, 2022, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse midwives. Failure to submit required information may result in civil monetary penalties.
- *The Federal Food, Drug, and Cosmetic Act*—Prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices.
- *Analogous State and Foreign Laws*—There are state and foreign law equivalents of the above federal laws, such as the Anti-Kickback Statute and the False Claims Act, which may apply to items or services reimbursed by any third-party payor, including commercial insurers (i.e., so-called "all-payor anti-kickback laws"). Similarly, there are state and foreign laws that govern the privacy and security of health information, biometric information or more general personally identifiable information, including state health information privacy laws, data breach notification laws, marketing privacy laws, and certain comprehensive privacy legislation such as the new California Consumer Privacy Act which govern the collection, use, disclosure, and protection of health-related and other personal information, many of which differ from each other in significant ways and, with respect to state laws, are often not pre-empted by HIPAA, or govern data that we may have that is outside the scope of HIPAA, thus requiring additional compliance efforts. These privacy and data protection laws are also evolving, requiring continual evaluation and investment in compliance programs.
- *State and Foreign Laws Regulating Pharmaceutical Manufacturer Compliance Programs and Other Practices*—Some state and foreign laws require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or to track and report gifts, compensation, or other remuneration to physicians and other healthcare providers. Several U.S. states and localities have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports, and/or make periodic public disclosures on sales, marketing, pricing, clinical trials, and other activities. Other state laws prohibit certain marketing-related activities including the provision of gifts, meals or other items to certain healthcare providers, and restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs. In addition, several recently passed state laws require disclosures related to state agencies and/or commercial purchasers with respect to certain price increases that exceed a certain level as identified in the relevant statutes. Some of these laws and regulations contain ambiguous requirements that government officials have not yet clarified. Given the lack of clarity in the laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent federal and state laws and regulations.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, guidance, case law or other applicable law. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, exclusion from

participation in federal health care programs, such as Medicare and Medicaid, disbursement, reputational harm, additional oversight and reporting obligations pursuant to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with applicable laws and regulations, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to market our products, if approved, and adversely impact our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws and regulations, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, it may be costly to us in terms of money, time and resources, and they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we may establish, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance

may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of hazardous and flammable materials, including chemicals and biological materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must comply with numerous laws and regulations in each jurisdiction in which we plan to operate, such as the applicable anti-bribery, anti-corruption, anti-money laundering regulations. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the DOJ. The Securities and Exchange Commission, or SEC, is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

We are also subject to other laws and regulations governing our international operations, including applicable import and export control regulations, economic sanctions on countries and persons administered or enforced by the U.S. government (including, without limitation, the Office of Foreign Assets Control of the U.S. Department of the Treasury), anti-money laundering laws, customs requirements and currency exchange regulations, collectively referred to as the trade control laws. We can provide no assurance that we will be completely effective in ensuring our compliance with all applicable legal requirements, including trade control laws. If we are not in compliance with applicable trade control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions

and remedial measures, and legal expenses, which could have an adverse impact on our business, results of operations, financial condition and prospects. Likewise, any investigation of any potential violations of these trade control laws by U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations, financial condition and prospects.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and product candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting.

Security breaches, loss of data and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability, which could adversely affect our business and our reputation.

In the ordinary course of our business, we collect and store sensitive data, including personally identifiable information, intellectual property and proprietary business information owned or controlled by ourselves and other parties. We manage and maintain our applications and data utilizing a combination of on-site systems, managed data centers and cloud-based data centers. We utilize external security and infrastructure vendors to manage our information technology systems and data centers. These applications and data encompass a wide variety of business-critical information, including research and development information, commercial information, and business and financial information. We face a number of risks relative to protecting this critical information, including loss of access risk, inappropriate use or disclosure, inappropriate modification, and the risk of our being unable to adequately monitor, audit and modify our controls over our critical information. This risk extends to the third-party vendors and subcontractors we use to manage this sensitive data.

The secure processing, storage, maintenance and transmission of this critical information are vital to our operations and business strategy. Although we take measures to protect sensitive data from unauthorized access, use or disclosure, and are in the process of developing policies and procedures to protect our information technology systems and confidential and proprietary information, we do not currently have any such policies and procedures formally in place and our information technology and infrastructure may be vulnerable to attacks by hackers or viruses or breached due to employee error, malfeasance or other malicious or inadvertent disruptions. Any such breach or interruption could compromise our networks and the information stored there could be accessed by unauthorized parties, manipulated, publicly disclosed, lost or stolen. Any such access, breach or other loss of information could result in legal claims or proceedings, and liability under federal or state laws that protect the privacy of personal information, such as the Health Insurance Portability and Accountability Act of 1996, or HIPAA, the Health Information Technology for Economic and Clinical Health Act, or HITECH, and regulatory penalties. Notice of breaches must be made to affected individuals, the Secretary of the Department of Health and Human Services, and for extensive breaches, notice may need to be made to the media or State Attorneys General. Such a notice could harm our reputation and our ability to compete. Although we have implemented security measures and are in the process of implementing formal, dedicated enterprise policies and procedures to prevent unauthorized access to patient data, we do not currently have any such policies and procedures formally in place and there is no guarantee we can protect our data from breach. Unauthorized access, loss or dissemination could also damage our reputation or disrupt our operations, including our ability to conduct our analyses, process claims and appeals, conduct research and development activities, collect, process and prepare

company financial information, provide information about our tests and other patient and physician education and outreach efforts through our website, and manage the administrative aspects of our business.

Penalties for violations of these laws vary. For instance, penalties for failure to comply with a requirement of HIPAA and HITECH vary significantly, and include civil monetary penalties of up to \$55,910 per violation, not to exceed approximately \$1.68 million per calendar year for each provision of HIPAA that is violated and, in certain circumstances, criminal penalties with fines up to \$250,000 per violation and/or imprisonment. However, a single breach incident can result in multiple violations, which can lead to significant financial penalties. In addition, numerous breach incidents could lead to possible penalties in excess of \$1.68 million. A person who knowingly obtains or discloses individually identifiable health information in violation of HIPAA may face a criminal penalty of up to \$50,000 and up to one-year imprisonment. The criminal penalties increase if the wrongful conduct involves false pretenses or the intent to sell, transfer or use identifiable health information for commercial advantage, personal gain or malicious harm.

Further, various states, such as California and Massachusetts, have implemented similar privacy laws and regulations, such as the California Confidentiality of Medical Information Act, that impose restrictive requirements regulating the use and disclosure of health information and other personally identifiable information. These laws and regulations are not necessarily preempted by HIPAA, particularly if a state affords greater protection to individuals than HIPAA. Where state laws are more protective, we have to comply with the stricter provisions. In addition to fines and penalties imposed upon violators, some of these state laws also afford private rights of action to individuals who believe their personal information has been misused. California's patient privacy laws, for example, provide for penalties of up to \$250,000 and permit injured parties to sue for damages. The interplay of federal and state laws may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and data we receive, use and share, potentially exposing us to additional expense, adverse publicity and liability. Further, as regulatory focus on privacy issues continues to increase and laws and regulations concerning the protection of personal information expand and become more complex, these potential risks to our business could intensify.

Compliance with U.S. and international data protection laws and regulations could cause us to incur substantial costs or require us to change our business practices and compliance procedures in a manner adverse to our business. Moreover, complying with these various laws could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. We do not currently have formal policies and procedures in place, and have not conducted any internal or external audits, to ensure our compliance with all applicable data protection laws and regulations. Additionally, we do not currently have policies and procedures in place for assessing our third-party vendors' compliance with applicable data protection laws and regulations. Failure by us or by our third-party vendors to comply with U.S. and international data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity and could negatively affect our operating results and business. Claims that we or our third-party vendors have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we or our third-party vendor, as applicable, are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

We are subject to the GDPR, which applies extra-territorially and implements stringent operational requirements on controllers (e.g., sponsors) and processors (e.g., CROs, laboratories) of personal data, including, for example, high standards for obtaining valid consent from individuals to process their personal data (where consent is the legal ground relied upon), the requirements to provide detailed disclosures to individuals, restrictions on transfers of personal data from the EEA, short timelines for personal data breach notifications to data protection authorities, limitations on retention of personal data, additional considerations where processing health data and other "special categories of personal data" and specific obligations where third-party processors are engaged. Further, the GDPR provides that EU Member States may establish their own laws and regulations further restricting the processing of genetic data, biometric data, health data and other personal data, which could limit our ability to use and share such personal data or could cause our costs to increase. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. We do not currently have any formal data privacy policies and procedures in place and have not completed an assessment of whether we are in compliance with the GDPR. The GDPR also grants certain privacy rights to individuals (e.g., the right to access or erase their personal data). If our or our vendors' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims for financial or non-financial loss by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. If so, this could result in government-imposed fines or orders requiring that we change our practices, which could adversely affect our business.

Risks related to employee matters and managing growth

Our future success depends on our ability to retain our President and Chief Executive Officer, our Senior Vice President and Chief Scientific Officer, Chief Medical Officer, Vice President of Business Development and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Christian S. Schade, our President and Chief Executive Officer, Scott M. Coiante, our Senior Vice President and Chief Financial Officer, Lars Abrahmsen, Ph.D., our Senior Vice President and Chief Scientific Officer, Eyal C. Attar, M.D., our Senior Vice President and Chief Medical Officer, and Gregory A. Korbel, Ph.D., our Vice President of Business Development, as well as the other principal members of scientific team. Our agreements with Mr. Schade, Mr. Coiante, Dr. Abrahmsen, Dr. Attar and Dr. Korbel do not prevent them from terminating their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. However, the loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us

and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we may establish, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

We expect to expand our development and regulatory capabilities and potentially our sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical operations, regulatory affairs and, potentially, sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks related to tax matters

We have significant deferred tax assets, which may become devalued if we do not generate sufficient future taxable income, applicable corporate tax rates are reduced or if we experience an ownership change.

Our total gross deferred tax assets as of December 31, 2018 were \$12.8 million. Of that amount, \$12.5 million relates to gross deferred tax assets in Aprea AB. Our anticipated activities are also expected to result in future significant net operating losses in the United States and Sweden resulting in additional deferred tax assets. Utilization of most deferred tax assets is dependent on generating sufficient future taxable income in the appropriate jurisdiction and/or entity. The company has provided a valuation allowance of \$12.7 million on our net deferred tax assets as of December 31, 2018, based on all available evidence, it is considered more likely than not that all the recorded deferred tax assets

will not be realized in a future period. Additionally, most of our deferred tax assets are determined by reference to applicable corporate income tax rates in Sweden or the United States. Accordingly, in the event of a reduction of any such corporate income tax rates, the carrying value of certain of our deferred tax assets would decrease.

Moreover, our ability to use our net operating losses and other deferred tax assets to offset future taxable income in Sweden and the United States may be significantly limited if we experience an ownership change. For Swedish income tax purposes, an ownership change will generally occur when one, or several shareholders together, acquire shares representing more than 50 percent of the voting power over a five year period (under special provisions in Chapter 40 of the Swedish Income Tax Act; 1999:1229). Such an ownership change results in the forfeiture of tax losses carried forward exceeding 200 percent of the cost of the change of control. In this calculation, capital contributions to the company prior to the ownership change and in the preceding two years should reduce the cost of the change of control. Due to potential ownership changes under the Swedish Income Tax Act, we may be limited in our ability to realize a tax benefit on our deferred tax assets, whether or not we attain profitability in future years.

For U.S. federal income tax purposes, an ownership change will generally occur when the percentage of our stock (by value) owned by one or more "5 percent shareholders" (as defined in the U.S. Internal Revenue Code of 1986, as amended) has increased by more than 50% over the lowest percentage owned by such shareholders at any time during the prior three years (calculated on a rolling basis). We anticipate that we will incur losses in the United States in the foreseeable future related to our research and development activities. Due to potential ownership changes under Section 382 of the Code, we may be limited in our ability to realize a tax benefit from the use of our deferred tax assets, whether or not we attain profitability in future years.

In addition, our ability to utilize any future net operating losses may be limited by the recently enacted Pub. L. 115-97, commonly known as the Tax Cuts and Jobs Act of 2017 ("TCJA"). Under the TCJA, the amount of our net operating losses that we are permitted to deduct in any taxable year is limited to 80% of our taxable income in such year, where taxable income is determined without regard to the net operating loss deduction itself, while allowing unused net operating losses to be carried forward indefinitely.

For these reasons, a material devaluation in our deferred tax assets due to insufficient taxable income, lower corporate income tax rates or ownership change would have an adverse effect on our results of operations and financial condition.

We may have taxable income as a result of the purging election we will make following the Holdco Reorganization

While not entirely clear, we intend to treat Aprea AB as having been a passive foreign investment company, or PFIC, for U.S. federal income tax purposes prior to the Holdco Reorganization and treat Aprea Therapeutics, Inc. as having succeeded to the tax basis and holding periods of those shareholders in Aprea AB that exchanged their shares for our common stock. Based on such treatment, and absent a purging election as described below, the stock of Aprea AB held by Aprea Therapeutics, Inc. would have retained its status as stock of a PFIC with respect to all periods prior to the Holdco Reorganization (the "PFIC Taint") and therefore, absent a prior election by those shareholders to treat Aprea AB as a qualified electing fund, Aprea Therapeutics, Inc., would have been subject to certain adverse U.S. federal income tax consequences with respect to distributions received on such stock and gain recognized on the disposition of such stock. In order to purge the PFIC Taint on the stock of Aprea AB, and avoid such adverse tax consequences, following the Holdco Reorganization we intend to make a purging election in the form of a deemed dividend election under which, for U.S. federal income tax purposes, Aprea AB will be deemed to have made a distribution to

Aprea Therapeutics, Inc. of all of its current and accumulated earnings and profits as determined for U.S. federal income tax purposes. Because we do not expect Aprea AB to have had any accumulated or current year earnings and profits, we do not expect the purging election to result in any incremental U.S. federal income taxes. We note, however, that earnings and profits are determined only at the end of the taxable year and no assurance can be given that Aprea AB will not have any earnings and profits.

We may be subject to current taxation on some of the income of our foreign subsidiaries even absent any cash distributions

Because we hold directly or indirectly all of the shares of our foreign subsidiaries, including Aprea AB, such subsidiaries are treated as controlled foreign corporations ("CFC") for U.S. federal income tax purposes. For U.S. federal income tax purposes, Aprea Therapeutics, Inc. will therefore need to include in its taxable income each year Aprea AB's "subpart F income," and "global intangible low-taxed income", if any, even if no distributions are made.

Our foreign subsidiaries may directly become subject to U.S. federal income tax and be subject to a branch profits tax in the United States, which could reduce our after-tax returns and the value of our shares.

We currently intend to conduct substantially all of our businesses and operations in a manner such that our foreign subsidiaries will not be treated as engaged in a trade or business in the United States and will not be subject to additional U.S. income tax or branch profits tax. However, it is not entirely clear when a foreign subsidiary is treated as being engaged in a trade or business in the United States for U.S. federal income tax purposes. Accordingly, we cannot assure you that the Internal Revenue Service ("IRS") will not contend, perhaps successfully, that our foreign subsidiaries were engaged in a trade or business in the United States or are subject to more U.S. income tax than they currently incur. A foreign corporation deemed to be so engaged would be subject to U.S. federal income tax, as well as branch profits tax, on its income that is treated as effectively connected with the conduct of that trade or business unless the corporation is entitled to relief under an applicable tax treaty, which is determined on an annual basis.

The ongoing effects of the 2017 Tax Cuts and Jobs Act and GILTI could make our results difficult to predict.

Our effective tax rate may fluctuate in the future as a result of the TCJA, which included significant enacted changes in U.S. income tax law many aspects of which are not entirely clear and with respect to which guidance is mostly available only in proposed form. The enacted tax legislation included, among other new provisions, a reduction in the corporate tax rate, new limitations on the deductibility of net interest, the base erosion and anti-abuse minimum tax and new rules related to the global intangible low-taxed income of our foreign subsidiaries ("GILTI"). GILTI may require us to include in taxable income certain income of our foreign subsidiaries that are CFCs, though we may be eligible to claim foreign tax credits with respect to some of the taxes paid by such subsidiaries. While the U.S. tax authorities issued formal guidance as well as final and proposed regulations for GILTI, there are still certain aspects of the TCJA that remain unclear. We will continue to review the impact of GILTI and the other changes resulting from the TCJA as further guidance is issued. Any further guidance may result in changes to the interpretations and assumptions we made and actions we may take, which as a result may impact the amounts recorded with respect to international provisions of the TCJA, possibly materially.

Changes in U.S. federal income tax law and other jurisdictions could materially adversely affect an investment in our common shares.

It is possible that tax laws in the United States and other jurisdictions will be changed. It remains difficult to predict whether or when there will be any tax law changes or further guidance by the

authorities in the U.S. or elsewhere in the world that will have a material adverse effect on our business.

Risks related to our common stock and this offering

After this offering, our executive officers, directors and principal stockholders will exert significant control over matters submitted to stockholders for approval. This may prevent new investors from influencing significant corporate decisions.

Upon the completion of this offering, our executive officers and directors and our stockholders which own more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own shares representing approximately 70.0% of our common stock, not including any shares purchased by these stockholders in this offering. As a result, if these stockholders were to choose to act together, they would be able to exert significant control over matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company, or other significant corporate decisions, on terms that other stockholders may desire.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws that will become effective upon the completion of this offering may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

An active trading market for our common stock may not develop.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters. Although we have applied to list our common stock on The Nasdaq Global Select Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop or is not sustained, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares, or at all.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

The initial public offering price of our common stock is substantially higher than the pro forma as adjusted net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our pro forma as adjusted net tangible book value per share after this offering. To the extent shares are issued under outstanding options, you will incur further dilution. Based on the initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover of this prospectus, you will experience immediate dilution of \$6.35 per share, representing the difference between our pro forma as adjusted net tangible book value per share after giving effect to this offering and the assumed initial public offering price per share. In addition, purchasers of common stock in this offering will have contributed approximately 35% of the aggregate price paid by all purchasers of our stock but will own only approximately 26% of our common stock outstanding after this offering.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.

Our stock price is likely to be volatile. The stock market in general and the market for pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of APR-246 and any of our other product candidates;

- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- the success of existing or new competitive products or technologies;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- establishment or termination of collaborations for our product candidates or development programs;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and our resources, which could harm our business.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates.

Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies or smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an emerging growth company for up to five years, or until such earlier time as we have more than \$1.07 billion in annual revenue, the market value of our stock held by non-affiliates is more than \$700 million or we issue more than \$1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, being permitted to present only two years of audited financial statements and a correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this prospectus, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In this prospectus, we have taken advantage of reduced reporting obligations. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. An emerging growth company can therefore delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. However, we are choosing to "opt out" of such extended transition period, and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for public companies that are not emerging growth companies. The JOBS Act provides that our decision to opt out of the extended transition period for complying with new or revised accounting standards is irrevocable.

We are also a "smaller reporting company," as such term is defined in Rule 12b-2 of the Exchange Act, meaning that the market value of our common stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than \$700 million and our annual revenue is less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our common stock held by non-affiliates is less than \$250 million or (ii) our annual revenue is less than \$100 million during the most recently completed fiscal year and the market value of our common stock held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

We will incur increased costs as a result of operating as a public company as we become subject to additional laws, regulations and listing exchange standards, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, and particularly after we are no longer an "emerging growth company" or a "smaller reporting company," we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and NASDAQ have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. There is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Accounting principles and related pronouncements, implementation guidelines and interpretations we apply to a wide range of matters that are relevant to our business, including, but not limited to, revenue recognition, leases and stock-based compensation, are complex and involve subjective assumptions, estimates and judgments by our management. Changes in accounting pronouncements or their interpretation or changes in underlying assumptions, estimates or judgments by our management could significantly change our reported or expected financial performance.

In connection with the preparation of our financial statements as of and for the years ended December 31, 2017 and 2018, the Company and our independent registered public accounting firm identified a material weakness in the Company's internal control over financial reporting. If we are not able to remediate the material weakness and otherwise to maintain an effective system of internal control over financial reporting in the future, investors may lose confidence in the accuracy and completeness of our financial reports, and the market price of our common stock could be materially and adversely affected.

To date, we have not conducted an evaluation and testing of our internal control required by Section 404 of the Sarbanes-Oxley Act. We may experience situations in the future where our evaluation and testing processes required by Section 404 of the Sarbanes-Oxley Act, or work performed by independent registered accountants, may identify one or more material weaknesses in our internal controls over financial reporting that will result in our inability to assert that our internal control over financial reporting is effective. During our evaluation and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports.

In connection with the audits of our financial statements, we and our independent registered public accounting firm identified a material weakness related to our financial statement closing process, primarily related to the lack of sufficient skilled employees with U.S. GAAP and SEC reporting knowledge and experience for the purposes of timely and reliable financial reporting. Specifically, the material weakness identified relates to a lack of internal resources sufficient to prepare and review our consolidated financial statements and related disclosures in accordance with U.S. GAAP and financial reporting requirements set forth by the SEC.

Under standards established by the Public Company Accounting Oversight Board, a material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected and corrected on a timely basis.

We are working to remediate the material weakness and are taking steps to strengthen our internal control over financial reporting such as, for example, the recent hiring of Scott M. Coiante as Chief Financial Officer. Additionally, we plan to further develop and implement formal policies, processes and documentation procedures relating to the financial reporting of the Company. The actions that we are taking are subject to ongoing executive management review, and will also be subject to audit committee oversight. If we are unable to successfully remediate the material weakness, or if in the future, we identify further material weaknesses in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we will be required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The Nasdaq Global Select Market or other adverse consequences that would materially harm our business. In addition, we could become subject to investigations by NASDAQ, the SEC, and other regulatory authorities, and become subject to litigation from investors and stockholders, which could harm our reputation and our financial condition, or divert financial and management resources from our core business.

Because we do not anticipate paying any cash dividends on our common stock for the foreseeable future, capital appreciation, if any, of our common stock will be your sole source of gain.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have outstanding 19,209,865 shares of common stock based on the number of shares outstanding as of June 30, 2019 (including 2,807 shares of common stock from the exercise of stock options on March 25, 2019, which were registered pursuant to Swedish law with the Swedish Companies Registration Office on August 27, 2019).

Of these shares of our common stock, the 5,000,000 shares to be sold in this offering, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering, unless purchased by our affiliates. All of the remaining shares are currently restricted as a result of securities laws or lock-up agreements but will be able to be sold after the offering as described in the "Shares Eligible for Future Sale" section of this prospectus. Moreover, after this offering, holders of approximately 14,200,000 shares of our common stock will have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriting" section of this prospectus.

Our certificate of incorporation that will become effective upon the completion of this offering designates the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors, officers and employees.

Our certificate of incorporation that will become effective upon the completion of this offering provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf under Delaware law, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or bylaws, any action asserting a claim against us governed by the internal affairs doctrine, or any other action asserting an "internal corporate claim," as defined in Section 115 of the Delaware General Corporation Law. These exclusive-forum provisions do not apply to claims under the Securities Act of 1933, as amended, or the Securities Act, or the Exchange Act. This exclusive forum provision may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find the exclusive-forum provision in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could harm our results of operations.

Special Note Regarding Forward-Looking Statements

This prospectus contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "potential," "seek," "should," "target," "will," "would," and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- estimates of our expenses, capital requirements and our needs for additional financing;
- the prospects of APR-246 and other product candidates, which are still in development;
- outcome and results of ongoing or future preclinical studies and clinical trials of APR-246;
- the design of our multiple clinical trials, including the sample size, trial duration, endpoint definition, event rate assumptions and eligibility criteria;
- our expectations regarding the timing of data from our Phase 3 and additional clinical trials;
- market acceptance or commercial success of APR-246 and the degree of acceptance among physicians, patients, patient advocacy groups, health care payors and the medical community;
- our expectations regarding competition, potential market size, the size of the patient populations for APR-246, if approved for commercial use, and market acceptance;
- our ability to maintain regulatory approval of APR-246, and any related restrictions, limitations and/or warnings in the label of APR-246;
- the scope of protection we are able to establish and maintain for intellectual property rights covering APR-246;
- potential claims relating to our intellectual property and third-party intellectual property;
- the duration of our intellectual property estate that will provide protection for APR-246;
- developments relating to our competitors and our industry;
- our sales, marketing or distribution capabilities and our ability to commercialize APR-246, if we obtain regulatory approval;
- current and future agreements with third parties in connection with the manufacturing, commercialization, packaging and distribution of APR-246;
- our expectations regarding the ability of our current contract manufacturing partners to produce APR-246 in the quantities and timeframe that we will require;
- our expectations regarding our future costs of goods;
- our ability to attract, retain and motivate key personnel and increase the size of our organization;
- our ability to establish collaborations in lieu of obtaining additional financing;
- the impact of government laws and regulations;
- our anticipated use of proceeds from this offering;

- our financial performance; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act or a smaller reporting company under the Exchange Act.

These forward-looking statements are based on management's current expectations, estimates, forecasts, and projections about our business and the industry in which we operate and management's beliefs and assumptions and are not guarantees of future performance or development and involve known and unknown risks, uncertainties, and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this prospectus may turn out to be inaccurate. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under "Risk Factors" and elsewhere in this prospectus. Potential investors are urged to consider these factors carefully in evaluating the forward-looking statements. These forward-looking statements speak only as of the date of this prospectus. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. You should read this prospectus with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

Use of Proceeds

We estimate that the net proceeds from our issuance and sale of 5,000,000 shares of our common stock in this offering will be approximately \$66.6 million, assuming an initial public offering price of \$15.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds will be approximately \$77.0 million.

A \$1.00 increase (decrease) in the assumed initial public offering price of \$15.00 per share would increase (decrease) the aggregate net proceeds to us from this offering by approximately \$4.7 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1,000,000 shares in the number of shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately \$14.0 million, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the initial public offering price or the number of shares by these amounts would have a material effect on our uses of the proceeds from this offering, although it may accelerate the time at which we will need to seek additional capital.

We intend to use the net proceeds from the offering as follows:

- Approximately \$20.0 million to \$30.0 million to fund future Phase 1b/2 clinical studies of APR-246 for solid tumor and hematological malignancies as well as additional future clinical studies to be determined if the data derived from such Phase 1b/2 clinical studies is favorable;
- Approximately \$10.0 million to \$15.0 million to fund continued research and development activities for APR-548, including ongoing IND-enabling studies and a first-in-human clinical trial;
- Approximately \$5.0 million to \$10.0 million to fund the ongoing preclinical and clinical development of APR-246, including preparation and submission of a New Drug Application (NDA) in MDS; and
- The remainder to fund general research and development activities, working capital and other general corporate activities including the buildout of infrastructure to support the advancement of our product candidates.

Our expected use of proceeds from this offering represents our current intentions based on our present plans and business condition. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the proceeds to be received upon the completion of this offering or the actual amounts that we will spend on the uses set forth above. We may also use a portion of the proceeds to in-license, acquire or invest in additional businesses, technologies, products or assets. Although we have no specific agreements, commitments or understandings with respect to any in-licensing activity or acquisition, we evaluate these opportunities and engage in related discussions with other companies from time to time.

The net proceeds from this offering, together with our cash and cash equivalents, may not be sufficient for us to conduct through completion any additional existing clinical trials of APR-246 or to otherwise complete the development of APR-246.

The amount and timing of our actual expenditures will depend on numerous factors, including the results of our research and development efforts, the timing and outcome of any ongoing or future clinical trials, and the timing and outcome of regulatory submissions. As a result, our management will have broad discretion over the use of the proceeds from this offering.

Pending the use of the proceeds from this offering, we may invest the proceeds in interest-bearing, investment-grade securities, certificates of deposit and/or U.S. government securities.

Dividend Policy

We have never declared or paid any dividends on our common stock. We do not anticipate declaring or paying any cash dividends on our common stock in the foreseeable future. Any future determination to declare and pay cash dividends, if any, will be made at the discretion of our board of directors and will depend on a variety of factors, including applicable laws, our financial condition, results of operations, contractual restrictions, capital requirements, business prospects, general business or financial market conditions and other factors our board of directors may deem relevant.

Aprea AB

Prior to the Holdco Reorganization, the capital structure of Aprea AB consisted of four classes of equity interests: ordinary shares; Series A preferred shares; Series B preferred shares; and Series C preferred shares.

Corporate reorganization

On September 20, 2019, we engaged in a series of transactions, which we refer to collectively as the Holdco Reorganization. As a result of the Holdco Reorganization, Aprea AB became a wholly-owned subsidiary of Aprea Therapeutics, Inc. and our consolidated financial statements will be reported from Aprea Therapeutics, Inc. We, Aprea AB, and the holders of all of the issued and outstanding equity interests of Aprea AB entered into a Share Contribution and Exchange Agreement, dated as of June 13, 2019, pursuant to which the Holdco Reorganization was effected.

In May 2019, we formed Aprea Therapeutics, Inc. as a stand-alone entity. The remaining steps to the Holdco Reorganization that were effected on September 20, 2019 included:

- Each holder of Aprea AB equity interests contributed, transferred, granted, assigned and delivered to us all of its right, title and interest in and to all Aprea AB equity interests owned by such holder;
- In exchange for each Aprea AB ordinary share contributed by a holder, we issued to such holder one share of our common stock;
- In exchange for each Aprea AB Series A preferred share contributed by a holder, we issued to such holder one share of our Series A preferred stock;
- In exchange for each Aprea AB Series B preferred share contributed by a holder, we issued to such holder one share of our Series B preferred stock;
- In exchange for each Aprea AB Series C preferred share contributed by a holder, we issued to such holder one share of our Series C preferred stock; and
- Each outstanding option to purchase Aprea AB ordinary shares issued by Aprea AB pursuant to the 2016 Stock Incentive Plan was cancelled, and we issued to the holder of such Aprea AB option, a substitute option to purchase, on the same terms and conditions as were applicable to such Aprea AB option, shares of our common stock pursuant to our 2019 Stock Incentive Plan; except that with respect to vested options held by U.S. employees, we assumed such options and exercised them for newly issued shares of Aprea.

Immediately prior to the completion of this offering, with the consent of shareholders representing a majority of our outstanding preferred shares, all outstanding shares of our convertible preferred stock, including the shares of our Series A preferred stock, Series B preferred stock and Series C preferred stock issued as part of the Holdco Reorganization will be converted into shares of our common stock on a 1-for-1.6045 basis. As a result of the Holdco Reorganization and such subsequent conversion, the former holders of all of the issued and outstanding equity interests of Aprea AB will have received 100% of our outstanding common stock as of immediately prior to the completion of the offering.

Capitalization

The following table sets forth our cash and cash equivalents and our capitalization as of June 30, 2019:

- on an actual basis with respect to Aprea AB (including 2,807 shares of common stock from the exercise of stock options on March 25, 2019, which were registered pursuant to Swedish law with the Swedish Companies Registration Office on August 27, 2019);
- on a pro forma basis to give effect to (i) the Holdco Reorganization described under the section titled "Corporate Reorganization"; (ii) the 1 for 1.6045 split of our common stock which took place on September 26, 2019; (iii) the conversion of all of our outstanding shares of convertible preferred stock into an aggregate of 13,028,292 shares of common stock immediately prior to the completion of this offering and (iv) the filing and effectiveness of our amended and restated certificate of incorporation; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 5,000,000 shares of our common stock in this offering at an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the completion of this offering will depend on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table together with our financial statements and the related notes appearing at the end of this prospectus

	June 30, 2019		
	Actual	Pro forma	Pro forma as adjusted
Cash and cash equivalents	\$ 60,994,738	\$ 60,994,738	\$ 127,544,738
Convertible preferred stock:			
Series A convertible preferred stock, \$0.11 par value; 612,446 shares issued and outstanding actual; no shares outstanding, pro forma and pro forma as adjusted	6,483,044	—	—
Series B convertible preferred stock, \$0.11 par value; 7,235,969 shares issued and outstanding actual; no shares outstanding, pro forma and pro forma as adjusted	49,742,942	—	—
Series C convertible preferred stock, \$0.11 par value; 5,179,877 shares issued and outstanding actual; no shares outstanding, pro forma and pro forma as adjusted	61,963,007	—	—
Total convertible preferred stock	<u>118,188,993</u>	<u>—</u>	<u>—</u>
Stockholders' Deficit			
Common stock, \$0.11 par value actual, \$0.001 par value pro forma and pro forma as adjusted; 1,181,573 shares issued and outstanding actual; 14,209,865 shares issued and outstanding, pro forma 19,209,865 shares issued and outstanding, and pro forma as adjusted	129,974	14,210	19,210
Additional paid-in capital	19,971,732	138,276,489	204,821,489
Accumulated other comprehensive loss	(10,747,992)	(10,747,992)	(10,747,992)
Accumulated deficit	(71,206,106)	(71,206,106)	(71,206,106)
Total stockholders' equity (deficit)	<u>(61,852,392)</u>	<u>56,336,601</u>	<u>122,886,601</u>
Total Capitalization	<u>\$ 56,336,601</u>	<u>\$ 56,336,601</u>	<u>\$ 122,886,601</u>

A \$1.00 increase or decrease in the assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by \$4.7 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. An increase or decrease of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease the pro forma as adjusted amount of each of cash, cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by \$14.0 million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions.

The table above does not include:

- 2,761,794 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2019, at a weighted average exercise price of \$1.66 per share; and
- 2,488,206 shares of common stock reserved for issuance pursuant to future awards under our 2019 Stock Incentive Plan or our Employee Stock Purchase Plan, plus any future increases in the number of shares of common stock reserved for issuance under our 2019 Stock Incentive Plan or our Employee Stock Purchase Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year.

Dilution

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value (deficit) as of June 30, 2019 was \$(61.9) million, or \$(83.99) per share of our common stock. Our historical net tangible book value (deficit) is the amount of our total assets less our total liabilities and convertible preferred stock, which is not included in our stockholders' deficit. Historical net tangible book value (deficit) per share represents historical net tangible book value (deficit) divided by the number of shares of our common stock outstanding as of June 30, 2019 (including 2,807 shares of common stock from the exercise of stock options on March 25, 2019, which were registered pursuant to Swedish law with the Swedish Companies Registration Office on August 27, 2019).

Our pro forma net tangible book value as of June 30, 2019 was \$56.3 million, or \$6.36 per share of our common stock. Pro forma net tangible book value represents the amount of our total assets less our total liabilities, after giving effect to (i) the Holdco Reorganization described under the section titled "Corporate Reorganization," pursuant to which all of the issued and outstanding stock of Aprea Therapeutics AB was exchanged for common stock, preferred stock or options, as applicable, of Aprea Therapeutics, Inc., (ii) the 1 for 1.6045 split of our common stock which took place on September 26, 2019 and (iii) the conversion of all of our outstanding shares of convertible preferred stock into an aggregate of 13,028,292 shares of our common stock immediately prior to the completion of this offering. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares of common stock outstanding as of June 30, 2019 (including 2,807 shares of common stock from the exercise of stock options on March 25, 2019, which were registered pursuant to Swedish law with the Swedish Companies Registration Office on August 27, 2019), after giving effect to the Holdco Reorganization, the 1 for 1.6045 split of our common stock which took place on September 26, 2019 and the automatic conversion of all outstanding shares of our preferred stock into common stock immediately prior to the completion of this offering.

After giving further effect to our sale of 5,000,000 shares of common stock in this offering at the initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of June 30, 2019 would have been \$122.9 million, or \$8.65 per share. This represents an immediate increase in pro forma as adjusted net tangible book value of \$4.68 per share to our existing stockholders and an immediate dilution in pro forma as adjusted net tangible book value of \$6.35 per share to new investors purchasing common stock in this offering. Dilution per share to new investors purchasing common stock in this offering is determined by subtracting pro forma as adjusted net

tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		\$ 15.00
Historical net tangible book value (deficit) per share as of June 30, 2019	\$ (52.35)	
Pro forma increase in net tangible book value per share attributable to the conversion of our Convertible Preferred Stock immediately prior to the completion of this offering	\$ 56.31	
Pro forma net tangible book value per share as of June 30, 2019	\$ 3.96	
Increase in pro forma net tangible book value per share attributable to new investors participating in this offering	\$ 4.68	8.65
Pro forma as adjusted net tangible book value per share after this offering		
Dilution in pro forma net tangible book value per share to new investors participating in this offering		\$ 6.35

A \$1.00 increase or decrease in the assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease our pro forma as adjusted net tangible book value by \$4.7 million, our pro forma as adjusted net tangible book value per share after this offering by \$0.33 and dilution per share to new investors purchasing shares in this offering by \$0.67, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. An increase of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase the pro forma as adjusted net tangible book value per share after this offering by \$0.98 and decrease the dilution per share to new investors participating in this offering by \$0.98, assuming no change in the assumed initial public offering price and after deducting estimated underwriting discounts and commissions. A decrease of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease the pro forma as adjusted net tangible book value per share after this offering by \$14.0 million and increase the dilution per share to new investors participating in this offering by \$0.98, assuming no change in the assumed initial public offering price and after deducting estimated underwriting discounts and commissions.

If the underwriters exercise their option to purchase additional shares in full, our pro forma as adjusted net tangible book value per share after this offering would be \$9.38 per share, representing an immediate increase in pro forma as adjusted net tangible book value per share of \$5.42 to existing stockholders and an immediate dilution in pro forma as adjusted net tangible book value per share of \$5.62 to new investors purchasing common stock in this offering, assuming an initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If any shares are issued upon exercise of outstanding options, you will experience further dilution.

The following table summarizes, on a pro forma as adjusted basis, as of June 30, 2019, the differences between the number of shares of common stock purchased from us, the total consideration paid to us and the average price per share paid by existing stockholders and by new investors purchasing shares of common stock in this offering. The calculation below is based on an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on

the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares purchased		Total consideration		Average price per share
	Number	Percent	Amount	Percent	
Existing stockholders before this offering	14,209,865	74%	\$ 136,926,976	65%	\$ 9.64
Investors participating in this offering	5,000,000	26%	75,000,000	35%	15.00
Total	19,209,865	100.0%	\$ 211,926,976	100.0%	

A \$1.00 increase or decrease in the assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease the total consideration paid by new investors by \$5.0 million and, in the case of an increase, would increase the percentage of total consideration paid by new investors by two percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by new investors by two percentage points, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. An increase or decrease of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease the total consideration paid by new investors by \$15.0 million and, in the case of an increase, would increase the percentage of total consideration paid by new investors by four percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by new investors by four percentage points, assuming no change in the assumed initial public offering price.

The table above assumes no exercise of the underwriters' option to purchase additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to 71% of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors participating in the offering would be increased to 29% of the total number of shares of our common stock outstanding after this offering.

The number of shares purchased from us by existing stockholders is based on 14,209,865 shares of our common stock outstanding as of June 30, 2019 (including 2,807 shares of common stock from the exercise of stock options on March 25, 2019, which were registered pursuant to Swedish law with the Swedish Companies Registration Office on August 27, 2019), after giving effect to (i) the Holdco Reorganization described under the section titled "Corporate Reorganization," pursuant to which all of the issued and outstanding stock of Aprea Therapeutics AB was exchanged for common stock, preferred stock or options, as applicable, of Aprea Therapeutics, Inc., (ii) the 1 for 1.6045 split of our common stock which took place on September 26, 2019 and (iii) the conversion of all outstanding shares of our convertible preferred stock, including the shares issued as part of the Holdco Reorganization, into an aggregate of 13,028,292 shares of our common stock, immediately prior to the completion of this offering, and excludes:

- 2,761,794 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2019, at a weighted average exercise price of \$1.66 per share; and
- 2,488,206 shares of common stock reserved for issuance pursuant to future awards under our 2019 Stock Incentive Plan or our Employee Stock Purchase Plan, plus any future increases in the number of shares of common stock reserved for issuance under our 2019 Stock Incentive Plan or our Employee Stock Purchase Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year.

Selected Financial Data

You should read the following selected financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the statement of operations data for the years ended December 31, 2017 and 2018 and the balance sheet data as of December 31, 2017 and 2018 from our audited financial statements appearing at the end of this prospectus. The consolidated statements of operations data for the six months ended June 30, 2018 and 2019 and the consolidated balance sheet data at June 30, 2019 are derived from our unaudited condensed consolidated financial statements included in this prospectus. The unaudited condensed consolidated financial statements include, in the opinion of management, all adjustments that management considers necessary for the fair presentation of the consolidated financial information set forth in those statements. Our historical results are not necessarily indicative of results that should be expected in any future period.

	Years ended December 31,		Six months ended June 30,	
	2017	2018	2018	2019
Consolidated Statement of Operations Data:				
Operating expenses:				
Research and development	\$ 13,392,631	\$ 14,194,732	\$ 7,492,788	\$ 7,998,270
General and administrative	2,459,744	2,294,671	1,166,520	2,347,915
Total operating expenses	15,852,375	16,489,403	8,659,308	10,346,185
Other income (expense):				
Interest expense	(15)	(182)	(188)	(7,439)
Foreign currency gain	662,140	961,316	949,158	1,615,974
Total other income (expense)	662,125	961,134	948,970	1,608,535
Net loss	\$ (15,190,250)	\$ (15,528,269)	\$ (7,710,338)	\$ (8,737,650)
Net loss per share attributable to common stockholders, basic and diluted(1)	\$ (13.17)	\$ (13.45)	\$ (6.68)	\$ (7.43)
Weighted average common shares outstanding, basic and diluted(1)	1,153,069	1,154,368	1,154,107	1,176,417
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)(1)	\$ (1.65)	\$ (1.65)	\$ (0.62)	\$ (0.62)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)(1)	9,428,873	9,428,873	14,075,669	14,075,669

(1) See Note 2 to our audited and unaudited interim financial statements included elsewhere in this prospectus for an explanation of the method used to calculate basic and diluted net loss per share and unaudited pro forma basic and diluted net loss per share as well as the weighted-average number of common shares used in the computation of the per share amounts.

	December 31,		June 30,
	2017	2018	2019
Consolidated Balance Sheet Data:			
Cash and cash equivalents	\$ 24,401,488	\$ 65,675,931	\$ 60,994,738
Working capital(1)	20,430,334	61,129,968	56,215,210
Total assets	24,761,804	66,022,638	62,214,654
Total liabilities	4,301,013	4,868,109	5,878,053
Convertible preferred stock	56,225,986	112,590,631	118,188,993
Total stockholders' deficit	(35,765,195)	(51,436,102)	(61,852,392)

(1) We define working capital as current assets less current liabilities.

You should read the following discussion and analysis of our financial condition and results of operations together with the "Selected Financial Data" section of this prospectus and our financial statements and the related notes included at the end of this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risks and uncertainties, such as statements of our plans, objectives, expectations and intentions. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company focused on developing and commercializing novel cancer therapeutics that reactivate mutant p53 tumor suppressor protein. p53 is the protein expressed from the *TP53* gene, the most commonly mutated gene in cancer. We believe that mutant p53 is an attractive therapeutic target due to the high incidence of p53 mutations across a range of cancer types and its involvement in key cellular activities such as apoptosis. Cancer patients with mutant p53 face a significantly inferior prognosis even when treated with the current standard of care, and a large unmet need for these patients remains. Our lead product candidate, APR-246, is a small molecule p53 reactivator that is in late-stage clinical development for hematologic malignancies, including myelodysplastic syndromes, or MDS, and acute myeloid leukemia, or AML. APR-246 has received Orphan Drug and Fast Track designations from the FDA for MDS, and Orphan Drug designation from the EMA for MDS, AML and ovarian cancer, and we believe APR-246 will be a first-in-class therapy if approved by applicable regulators. We have commenced a pivotal Phase 3 trial of APR-246 with azacitidine for frontline treatment of *TP53* mutant MDS and expect initial data from this trial in the second half of 2020. Our pivotal Phase 3 trial is supported by data from two ongoing Phase 1b/2 investigator initiated trials, one in the U.S. and one in France, testing APR-246 with azacitidine as frontline treatment in *TP53* mutant MDS and AML patients.

In the ongoing U.S. Phase 1b/2 trial, sponsored by Dr. David Sallman of the H. Lee Moffitt Cancer Center and Research Institute, or Moffitt, we have observed an objective response rate, or ORR, of 88% and a complete remission, or CR, rate of 59% in 41 response-evaluable MDS/AML patients treated with APR-246 and azacitidine, as of July 2019 and we expect a final CR endpoint in the second half of 2019. In MDS patients, the CR rate was 61%, with an additional 27% achieving non-CR responses. In AML patients, the CR rate was 50%, with an additional 38% achieving non-CR responses. In addition, 46% of evaluable patients were able to discontinue treatment in order to proceed to allogeneic hematopoietic stem cell transplantation, or allo-HCT. Allo-HCT is currently the only recognized therapy believed to increase the likelihood of long term survival for *TP53* mutant MDS and AML patients in remission. In the ongoing French Phase 1b/2 trial, sponsored by Groupe Francophone des Myelodysplasies, or GFM, under lead investigator Prof. Pierre Fenaux, we have observed an ORR of 75% and a CR rate of 56% in 16 response-evaluable patients treated with APR-246 and azacitidine, as of July 2019 and we expect a final CR endpoint in the first half of 2020. In MDS patients, the CR rate was 55%, with an additional 18% achieving non-CR responses. In AML patients, the CR rate was 60%, with an additional 20% achieving non-CR responses. We expect the results of our pivotal Phase 3 trial and the U.S. and French Phase 1b/2 trials will be submitted in support of marketing applications to the FDA and EMA. We are also developing a next-generation small molecule p53 reactivator, APR-548, for potential use in multiple hematologic malignancies and other oncologic indications, and expect to file an IND with the FDA in the first half of 2020. We have assembled a management team with extensive experience in the discovery and development of novel oncology drugs. Our management team is supported by our world-class scientific advisors and leading

life science investors in their mission to successfully develop p53-reactivating therapies for cancer patients.

Aprea Therapeutics AB, or Aprea AB, was originally incorporated in 2002 and commenced principal operations in 2006. In connection with this initial public offering, we incorporated Aprea Therapeutics, Inc. in May 2019. We completed the Holdco Reorganization on September 20, 2019, as a result of which all of the issued and outstanding stock of Aprea AB was exchanged for common stock, preferred stock or options, as applicable, of Aprea Therapeutics, Inc. As a result of such transactions, Aprea AB became a wholly-owned subsidiary of Aprea Therapeutics, Inc. For more information, please see the section titled "Corporate Reorganization".

We have devoted substantially all of our resources to developing our product candidates, including APR-246, building our intellectual property portfolio, business planning, raising capital and providing general and administrative support for these operations. To date, we have financed our operations through private placements of preferred stock. Through June 30, 2019, we had received net proceeds of \$136.9 million from our sales of preferred and common stock.

Since our inception, we have incurred significant losses on an aggregate basis. Our ability to generate product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our product candidates. Our net losses were \$8.7 million for the six months ended June 30, 2019 and \$15.2 million and \$15.5 million for the years ended December 31, 2017 and 2018, respectively. As of June 30, 2019, we had an accumulated deficit of \$71.2 million. These losses have resulted primarily from costs incurred in connection with research and development activities, patent investment, and general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years.

We anticipate that our expenses will increase substantially if and as we:

- conduct our current and future clinical trials and additional preclinical research of APR-246;
- initiate and continue research and preclinical and clinical development of our other product candidates;
- seek to identify and develop additional product candidates;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials, if any;
- establish a sales, marketing, manufacturing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- require the manufacture of larger quantities of our product candidates for clinical development and potentially commercialization;
- maintain, expand, protect and enforce our intellectual property portfolio;
- acquire or in-license other drugs and technologies;
- defend against any claims of infringement, misappropriation or other violation of third-party intellectual property;
- hire and retain additional clinical, quality control and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our drug development, any future commercialization efforts and our transition to a public company; and
- operate as a public company.

Upon the completion of this offering, we expect to incur additional costs associated with operating as a public company. Furthermore, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution.

As a result, we will need additional financing to support our continuing operations. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity or debt financings or other sources, which may include collaborations with third parties. We may be unable to raise additional funds or enter into other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of June 30, 2019, we had cash and cash equivalents of \$61.0 million. We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements into 2023. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "—Liquidity and Capital Resources."

Components of our results of operations

Revenue

We have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. If our development efforts for APR-246 or other product candidates that we may develop in the future are successful and result in marketing approval or collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from collaboration or license agreements that we may enter into with third parties.

Operating expenses

Our expenses since inception have consisted solely of research and development costs and general and administrative costs.

Research and development expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates, and include:

- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct research, preclinical activities and clinical trials on our behalf as well as contract manufacturing organizations, or CMOs, that manufacture our product candidates for use in our preclinical and clinical trials;
- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;

- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials;
- expenses related to compliance with regulatory requirements; and
- facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expense research and development costs as incurred. We recognize costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as prepaid or accrued research and development expenses.

We typically use our employee and infrastructure resources across our development programs. We track outsourced development costs and milestone payments made to our research partners by product candidate or development program, but we do not allocate personnel costs or other internal costs to specific development programs or product candidates.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase for the foreseeable future as we initiate additional clinical trials of APR-246, pursue later stages of clinical development of APR-246, initiate clinical trials for product candidates other than APR-246 and continue to discover and develop additional product candidates.

We cannot determine with certainty the duration and costs of the current or future clinical trials of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any our product candidates for which we obtain marketing approval. We may never succeed in obtaining marketing approval for any of our product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of our ongoing clinical trials of APR-246, as well as of any future clinical trials of APR-246 or other product candidates and other research and development activities that we may conduct;
- uncertainties in clinical trial design and patient enrollment rates;
- significant and changing government regulation and regulatory guidance;
- the timing and receipt of any marketing approvals; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the U.S. Food and Drug Administration, or FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience

significant trial delays due to patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development.

We are currently conducting multiple clinical trials of APR-246: our Phase 3 trial in the United States for the treatment of *TP53* mutant MDS with azacitidine, our Phase 1b/2 trials in the United States and France for the treatment of MDS and AML with azacitidine, and our Phase 2 trial of post-transplant maintenance therapy with azacitidine in MDS and AML. At this time, we cannot reasonably estimate the cost for initiating and completing other clinical trials of APR-246 and preclinical studies of APR-246, as it will be highly dependent on the clinical data from ongoing clinical trials as well as any target disease subpopulations chosen for further evaluation.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, corporate and business development and administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our general and administrative personnel headcount to support personnel in research and development and to support our operations generally as we increase our research and development activities and activities related to the potential commercialization of our product candidates. We also expect to incur increased expenses associated with being a public company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements; director and officer insurance costs; and investor and public relations costs.

Other income and expense

Interest income and expense

Interest expense consists of bank charges and fees incurred on our cash and cash equivalents. We anticipate that our interest income will increase in the future as we expect our investment balances to be higher due to anticipated cash proceeds from this offering.

Foreign currency gain

Our consolidated financial statements are presented in U.S. dollars, which is our reporting currency. The financial position and results of operations of our subsidiaries Aprea AB and Aprea Personal AB are measured using the foreign subsidiaries' local currency as the functional currency. Aprea AB cash accounts holding U.S. dollars are remeasured based upon the exchange rate at the date of remeasurement with the resulting gain or loss included in the consolidated statement of operations and comprehensive loss. Expenses of such subsidiaries have been translated into U.S. dollars at average exchange rates prevailing during the period. Assets and liabilities have been translated at the rates of exchange on the consolidated balance sheet date. The resulting translation gain and loss adjustments are recorded directly as a separate component of shareholders' equity and as other comprehensive loss on the consolidated statement of operations and comprehensive loss.

Income taxes

Since Aprea AB's inception in 2002, we have not recorded any U.S. federal, state or foreign income tax expense or benefits for the net losses we have incurred in any year, due to our uncertainty of realizing a benefit from those items. We have provided a valuation allowance for the full amount of

the net deferred tax assets as, based on all available evidence, it is considered more likely than not that all the recorded deferred tax assets will not be realized in a future period. At December 31, 2018, we had \$61.6 million, \$0.5 million and \$0.4 million of foreign, federal and state net operating loss carryforwards, respectively, that expire at various dates through 2036. Certain of these foreign, federal and state net operating loss carryforwards may be subject to Internal Revenue Code Section 382 or similar provisions, which impose limitations on their utilization amounts.

Critical accounting policies and use of estimates

Our management's discussion and analysis of financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of our financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, costs and expenses and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing at the end of this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Accrued research and development expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses at each balance sheet. This process involves reviewing open contract and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research activities on our behalf and conducting preclinical studies and clinical trials on our behalf;
- investigative sites or other service providers in connection with clinical trials;
- vendors in connection with preclinical and clinical development activities; and
- vendors related to product manufacturing and development and distribution of preclinical and clinical supplies.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CROs that conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing fees, we estimate the time period over which services will be performed, enrollment of

patients, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Stock-based compensation

We measure stock options and other stock-based awards granted to employees and directors based on their fair value on the date of the grant and recognize compensation expense of those awards, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. We apply the straight-line method of expense recognition to all awards with only service-based vesting conditions and apply the graded-vesting method to all awards with performance-based vesting conditions or to awards with both service-based and performance-based vesting conditions.

For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed in accordance with the FASB issued ASU No. 2018-07, Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. The new standard largely aligns the accounting for share-based payment awards issued to employees and nonemployees by expanding the scope of ASC 718 to apply to nonemployee share-based transactions, as long as the transaction is not effectively a form of financing.

We estimate the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield.

Determination of fair value of common stock

As a privately held company, there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors as of the date of each option grant, with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Our common stock valuations were prepared using a hybrid method, which used market approaches to estimate our enterprise value. The hybrid method is a probability-weighted expected return method, or PWERM, where the equity value in one or more scenarios is calculated using an option-pricing method, or OPM. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The

common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. These third-party valuations were performed at various dates, which resulted in valuations of our common stock of \$0.92 per share as of May 31, 2016, \$1.01 per share as of October 2, 2017 and \$3.18 per share as of December 31, 2018.

In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status and results of preclinical studies and clinical trials for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used significantly different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could have been materially different.

Once a public trading market for our common stock has been established in connection with the completion of this offering, it will no longer be necessary for our board of directors to estimate the fair value of our common stock in connection with our accounting for granted stock options and other such awards we may grant, as the fair value of our common stock will be determined based on the quoted market price of our common stock.

Options granted

The following table summarizes by grant date the number of shares subject to options granted between January 1, 2017 and June 30, 2019, the per share exercise price of the options, the fair value

of common stock underlying the options on each grant date, and the per share estimated fair value of the options:

<u>Grant date</u>	<u>Number of shares subject to options granted</u>	<u>Per share exercise price of options</u>	<u>Fair value of common stock per share on date of option grant</u>	<u>Per share estimated fair value of options</u>
January 3, 2017	91,456	\$ 0.92	\$ 0.92	\$ 0.66
February 16, 2017	32,892	\$ 0.92	\$ 0.92	\$ 0.67
March 30, 2017	185,088	\$ 0.07	\$ 0.92	\$ 0.82
November 24, 2017	353,788	\$ 1.01	\$ 1.01	\$ 0.74
July 31, 2018	24,067	\$ 1.01	\$ 1.01	\$ 0.69
February 28, 2019	984,596	\$ 3.19	\$ 3.19	\$ 2.23

Income taxes

We account for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in our tax returns. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amounts and the tax bases of the assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. Potential for recovery of deferred tax assets is evaluated by considering several factors, including estimating the future taxable profits expected, estimating future reversals of existing taxable temporary differences, considering taxable profits in carryback periods, and considering prudent and feasible tax planning strategies.

We account for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity, and changes in facts or circumstances related to a tax position. As of each balance sheet date, we did not have any uncertain tax positions.

Emerging growth company and smaller reporting company status

We are an emerging growth company, as defined in the JOBS Act. Under this act, emerging growth companies are permitted to delay adopting new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We may remain classified as an EGC until the end of the fiscal year in which the fifth anniversary of this offering occurs, although if the market value of our common stock that is held by non-affiliates exceeds \$700 million as of any June 30 before that time or if we have annual gross revenues of \$1.07 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than \$1 billion of non-convertible debt over a three-year period.

We are also a "smaller reporting company," as such term is defined in Rule 12b-2 of the Exchange Act, meaning that the market value of our common stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than \$700 million and our

annual revenue is less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our common stock held by non-affiliates is less than \$250 million or (ii) our annual revenue is less than \$100 million during the most recently completed fiscal year and the market value of our common stock held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Results of operations

Comparison of the six months ended June 30, 2018 and 2019

The following table summarizes our results of operations for the six months ended June 30, 2018 and 2019:

	Six months ended June 30,		Change
	2018	2019	
Operating expenses:			
Research and development	\$ 7,492,788	\$ 7,998,270	\$ 505,482
General and administrative	1,166,520	2,347,915	1,181,395
Total operating expenses	8,659,308	10,346,185	1,686,877
Other income (expense):			
Interest expense	(188)	(7,439)	(7,251)
Foreign currency gain	949,158	1,615,974	666,816
Total other income (expense)	948,970	1,608,535	659,565
Net loss	\$ (7,710,338)	\$ (8,737,650)	\$ (1,027,312)

Research and development expenses

	Six months ended June 30,		Change
	2018	2019	
APR-246	\$ 5,866,561	\$ 6,314,584	\$ 448,023
Other early-stage development programs	336,144	673,435	337,291
Unallocated research and development expenses	1,290,083	1,010,251	(279,832)
Total research and development expenses	\$ 7,492,788	\$ 7,998,270	\$ 505,482

Research and development expenses for the six months ended June 30, 2018 were \$7.5 million, compared to \$8.0 million for the six months ended June 30, 2019. The increase of \$0.5 million was primarily related to the advancement of our clinical product candidate APR-246.

General and administrative expenses

General and administrative expenses for the six months ended June 30, 2018 were \$1.2 million, compared to \$2.3 million for the six months ended June 30, 2019. The increase of \$1.2 million was primarily related to a \$0.9 million increase in legal and accounting fees.

Other income and expense

Foreign currency gain for the six months ended June 30, 2018 was \$0.9 million compared to \$1.6 million for the six months ended June 30, 2019. The increase of \$0.7 million was primarily due to a strengthening of the U.S. dollar against the Swedish Krona during the six months ended June 30, 2019. Interest expense for the six months ended June 30, 2018 and 2019 consisted of an insignificant amount of banking charges or fees and in 2019 interest expense derived from the new lease accounting.

Comparison of the years ended December 31, 2017 and 2018

The following table summarizes our results of operations for the years ended December 31, 2017 and 2018:

	Years ended December 31,		Change
	2017	2018	
Operating expenses:			
Research and development	\$ 13,392,631	\$ 14,194,732	\$ 802,101
General and administrative	2,459,744	2,294,671	(165,073)
Total operating expenses	15,852,375	16,489,403	637,028
Other income (expense):			
Interest expense	(15)	(182)	(167)
Foreign currency gain	662,140	961,316	299,176
Total other income (expense)	662,125	961,134	299,009
Net loss	\$ (15,190,250)	\$ (15,528,269)	\$ (338,019)

Research and development expenses

	Years ended December 31,		Change
	2017	2018	
APR-246	\$ 9,388,373	\$ 10,957,970	\$ 1,569,597
Other early-stage development programs	1,243,991	656,692	(587,299)
Unallocated research and development expenses	2,760,267	2,580,070	(180,197)
Total research and development expenses	\$ 13,392,631	\$ 14,194,732	\$ 802,101

Research and development expenses for the year ended December 31, 2017 were \$13.4 million, compared to \$14.2 million for the year ended December 31, 2018. The increase of \$0.8 million was primarily related to the advancement of our clinical product candidate APR-246.

General and administrative expenses

General and administrative expenses for the year ended December 31, 2017 were \$2.5 million, compared to \$2.3 million for the year ended December 31, 2018.

Other income and expense

Other income and expense for the year ended December 31, 2017 consisted of an insignificant amount of banking charges or fees and a foreign currency gain of \$0.7 million. Other income and expense for the year ended December 31, 2018 consisted of an insignificant amount of banking fees on our cash balances and a foreign currency gain of \$1.0 million.

Liquidity and capital resources

Since our inception, we have incurred significant losses on an aggregate basis. We have not yet commercialized any of our product candidates, which are in various phases of preclinical and clinical development, and we do not expect to generate revenue from sales of any products for several years, if at all. To date, we have financed our operations through private placements of our preferred and common stock. Through June 30, 2019, we had received net proceeds of \$136.9 million from our sales of preferred and common stock. As of June 30, 2019, we had cash, cash and cash equivalents of \$61.0 million.

Cash flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Years ended December 31,		Six months ended June 30,	
	2017	2018	2018	2019
Net cash provided by (used in):				
Operating activities	\$ (14,002,118)	\$ (15,250,234)	\$ (8,246,834)	\$ (9,797,443)
Investing activities	—	(3,702)	(4,734)	(6,189)
Financing activities	23,343,863	56,366,742	1,415	5,621,480
Net increase (decrease) in cash and cash equivalents	<u>\$ 9,341,745</u>	<u>\$ 41,112,806</u>	<u>\$ (8,250,153)</u>	<u>\$ (4,182,152)</u>

Operating activities

The cash used in operating activities resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital. Net cash used in operating activities was \$8.2 million for the six months ended June 30, 2018 compared to \$9.8 million for the six months ended June 30, 2019. The increase in cash used in operating activities of \$1.6 million was primarily attributable to an increase in our net loss of \$1.0 million and an increase in foreign currency gains of \$0.7 million.

Net cash used in operating activities was \$15.3 million for the year ended December 31, 2018 compared to \$14.0 million for the year ended December 31, 2017. The increase in cash used in operating activities of \$1.3 million was primarily attributable to an increase in our net loss of \$0.3 million, an increase in non-cash expenses of \$0.4 million, resulting primarily from an increase in foreign currency gains of \$0.3 million and a decrease in stock-based compensation of \$0.1 million, and a decrease in the components of working capital of \$0.5 million.

Investing activities

During the six months ended June 30, 2019 and 2018, we used an insignificant amount of cash in investing activities, consisting of the purchase of property and equipment of \$6,189 and \$4,734, respectively.

During the year ended December 31, 2018, we used an insignificant amount of cash in investing activities, consisting of the purchase of property and equipment of \$3,702. There was no cash used in investing activities during the year ended December 31, 2017.

We expect that investing activities will increase over the next several years.

Financing activities

Net cash provided by financing activities was \$5.6 million for the six months ended June 30, 2019 compared to \$1,415 for the six months ended June 30, 2018. The increase in cash provided by financing activities of \$5.6 million was primarily attributable to the issuance of Series C convertible preferred stock in February 2019 for net proceeds of \$5.6 million.

Net cash provided by financing activities was \$56.4 million for the year ended December 31, 2018 compared to \$23.3 million for the year ended December 31, 2017. The increase in cash provided by financing activities of \$33.1 million was attributable to the issuance of Series C convertible preferred stock in November 2018 for net proceeds of \$56.4 million. In October 2017, we issued Series B convertible preferred stock for net proceeds of \$23.3 million.

Funding requirements

We expect our expenses to increase substantially in connection with our ongoing development activities related to APR-246 and other product candidates and programs which are still in the early stages of clinical development. In addition, commencing upon the completion of this offering, we expect to incur additional costs associated with operating as a public company. We expect that our expenses will increase substantially if and as we:

- conduct our current and future clinical trials and additional preclinical research of APR-246;
- initiate and continue research and preclinical and clinical development of our other product candidates;
- seek to identify and develop additional product candidates;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials, if any;
- establish a sales, marketing, manufacturing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- require the manufacture of larger quantities of our product candidates for clinical development and potentially commercialization;
- maintain, expand, protect and enforce our intellectual property portfolio;
- acquire or in-license other drugs and technologies;
- defend against any claims of infringement, misappropriation or other violation of third-party intellectual property;
- hire and retain additional clinical, quality control and scientific personnel;
- build out new facilities or expand existing facilities to support our ongoing development activity;
- add operational, financial and management information systems and personnel, including personnel to support our drug development, any future commercialization efforts and our transition to a public company; and
- operate as a public company.

As of June 30, 2019, we had cash and cash equivalents of \$61.0 million. We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements into 2023. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with the development of APR-246 and other product candidates and programs and because the extent to which we may enter into collaborations with third parties for development of our product candidates is unknown, we are unable to estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of our current and future clinical trials of APR-246 for our current targeted indications;
- the scope, progress, results and costs of drug discovery, preclinical research and clinical trials for APR-246 and our other product candidates;
- the number of future product candidates that we pursue and their development requirements;
- the costs, timing and outcome of regulatory review of our product candidates;
- the extent to which we acquire or invest in businesses, products and technologies, including entering into or maintaining licensing or collaboration arrangements for product candidates on favorable terms, although we currently have no commitments or agreements to complete any such transactions;
- the costs and timing of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining, protecting and enforcing our intellectual property rights and defending intellectual property-related claims;
- our headcount growth and associated costs as we expand our business operations and our research and development activities; and
- the costs of operating as a public company.

Developing drug products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval for any product candidates or generate revenue from the sale of any products for which we may obtain marketing approval. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Adequate additional funds may not be available to us on acceptable terms, or at all. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be diluted, and the terms of these securities may include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. Additional debt or preferred equity financing, if available, may involve agreements that include restrictive covenants that may limit our ability to take specific actions, such as incurring debt, making capital expenditures or declaring dividends, which could adversely impact our ability to conduct our business, and may require the issuance of warrants, which could potentially dilute your ownership interest.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technology, future revenue streams, research programs, or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or collaborations, strategic alliances or licensing arrangements with third parties when needed, we may be required to delay, limit, reduce and/or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual obligations and commitments

The following table summarizes our contractual obligations at June 30, 2019:

	Payments due by period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
Operating leases(1)	\$ 310,973	\$ 122,783	\$ 188,190	\$ —	\$ —
Total	\$ 310,973	\$ 122,783	\$ 188,190	\$ —	\$ —

(1) Represents minimum payments due for our lease of office and laboratory space in Boston, Massachusetts under an operating lease agreement that, as amended, expires in 2021.

We enter into contracts in the normal course of business with CROs and CMOs for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts do not contain any minimum purchase commitments and are cancelable by us upon prior notice of 30 days and, as a result, are not included in the table of contractual obligations above. Payments due upon cancellation consist only of payments for services provided and expenses incurred up to the date of cancellation.

Internal control over financial reporting

In connection with the audit of our financial statements, we and our independent registered public accounting firm identified a material weakness in our internal control over financial reporting primarily related to the lack of sufficient skilled employees with U.S. GAAP and SEC reporting knowledge and experience for the purposes of timely and reliable financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected and corrected on a timely basis. We are currently establishing more robust processes to strengthen our internal control over financial reporting. See "Risk Factors—In connection with the preparation of our financial statements as of and for the years ended December 31, 2017 and 2018, the Company and our independent registered public accounting firm identified a material weakness in the Company's internal control over financial reporting. If we are not able to remediate the material weakness and otherwise to maintain an effective system of internal control over financial reporting in the future, investors may lose confidence in the accuracy and completeness of our financial reports, and the market price of our common stock could be materially and adversely affected."

We are working to remediate the material weakness and are taking steps to strengthen our internal control over financial reporting, such as, for example, the recent hiring of Scott M. Coiante as Chief Financial Officer. Additionally, we plan to further develop and implement formal policies, processes and documentation procedures relating to the financial reporting of the Company. The actions that we are taking are subject to ongoing executive management review, and will also be subject to audit committee oversight.

Off-balance sheet arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Recently issued accounting pronouncements

We have reviewed all recently issued standards and have determined that, other than as disclosed in Note 2 to our financial statements appearing at the end of this prospectus, such standards will not have a material impact on our financial statements or do not otherwise apply to our operations.

Quantitative and qualitative disclosures about market risk*Interest Rate Risk*

We are exposed to market risk related changes in interest rates. As of June 30, 2019, our cash equivalents consisted of bank deposits and money market accounts. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, historical fluctuations in interest income have not been significant for us.

Foreign Currency Exchange Rate Risk

We face market risk to the extent that changes in foreign currency exchange rates affect our non-U.S. dollar functional currency foreign subsidiaries' revenues, expenses, assets and liabilities. The financial position and results of operations of our subsidiaries Aprea AB and Aprea Personal AB are measured using the foreign subsidiaries' local currency as the functional currency. Aprea AB cash accounts holding U.S. dollars are remeasured based upon the exchange rate at the date of remeasurement with the resulting gain or loss included in the consolidated statement of operations and comprehensive loss.

Our investments in foreign subsidiaries with a functional currency other than the U.S. dollar are generally considered long-term. In addition, we do not believe that we currently have any significant direct foreign exchange risk. Accordingly, we have not used any derivative financial instruments to hedge exposure to such risk.

Overview

We are a clinical-stage biopharmaceutical company focused on developing and commercializing novel cancer therapeutics that reactivate mutant p53 tumor suppressor protein. p53 is the protein expressed from the *TP53* gene, the most commonly mutated gene in cancer. We believe that mutant p53 is an attractive therapeutic target due to the high incidence of p53 mutations across a range of cancer types and its involvement in key cellular activities such as apoptosis. Cancer patients with mutant p53 face a significantly inferior prognosis even when treated with the current standard of care, and a large unmet need for these patients remains. Our lead product candidate, APR-246, is a small molecule p53 reactivator that is in late-stage clinical development for hematologic malignancies, including myelodysplastic syndromes, or MDS, and acute myeloid leukemia, or AML. APR-246 has received Orphan Drug and Fast Track designations from the FDA for MDS, and Orphan Drug designation from the EMA for MDS, AML and ovarian cancer, and we believe APR-246 will be a first-in-class therapy if approved by applicable regulators. We have commenced a pivotal Phase 3 trial of APR-246 with azacitidine for frontline treatment of *TP53* mutant MDS and expect initial data from this trial in the second half of 2020. Our pivotal Phase 3 trial is supported by data from two ongoing Phase 1b/2 investigator initiated trials, one in the U.S. and one in France, testing APR-246 with azacitidine as frontline treatment in *TP53* mutant MDS and AML patients.

In the ongoing U.S. Phase 1b/2 trial, sponsored by Dr. David Sallman of the H. Lee Moffitt Cancer Center and Research Institute, or Moffitt, we have observed an objective response rate, or ORR, of 88% and a complete remission, or CR, rate of 59% in 41 response-evaluable MDS/AML patients treated with APR-246 and azacitidine, as of July 2019 and we expect a final CR endpoint in the second half of 2019. In MDS patients, the CR rate was 61%, with an additional 27% achieving non-CR responses. In AML patients, the CR rate was 50%, with an additional 38% achieving non-CR responses. In addition, 46% of evaluable patients were able to discontinue treatment in order to proceed to allogeneic hematopoietic stem cell transplantation, or allo-HCT. Allo-HCT is currently the only recognized therapy believed to increase the likelihood of long term survival for *TP53* mutant MDS and AML patients in remission. In the ongoing French Phase 1b/2 trial, sponsored by Groupe Francophone des Myelodysplasies, or GFM, under lead investigator Prof. Pierre Fenaux, we have observed an ORR of 75% and a CR rate of 56% in 16 response-evaluable patients treated with APR-246 and azacitidine, as of July 2019 and we expect a final CR endpoint in the first half of 2020. In MDS patients, the CR rate was 55%, with an additional 18% achieving non-CR responses. In AML patients, the CR rate was 60%, with an additional 20% achieving non-CR responses. We expect the results of our pivotal Phase 3 trial and the U.S. and French Phase 1b/2 trials will be submitted in support of marketing applications to the FDA and EMA. We are also developing a next-generation small molecule p53 reactivator, APR-548, for potential use in multiple hematologic malignancies and other oncologic indications, and expect to file an IND with the FDA in the first half of 2020. We have assembled a management team with extensive experience in the discovery and development of novel oncology drugs. Our management team is supported by our world-class scientific advisors and leading life science investors in their mission to successfully develop p53-reactivating therapies for cancer patients.

Our lead programs are summarized below. We currently retain global development and commercialization rights to all of our product candidates:

Molecule	Target Indication	Treatment Line	Preclinical	Phase 1	Phase 2	Phase 3	Milestones
APR-246	TP53 Mutant MDS	Frontline (U.S.)	Combination with azacitidine				Top-line data second half 2020
		Frontline (U.S. trial) ⁽¹⁾	Combination with azacitidine				Final CR primary endpoint and duration of response second half 2019
	TP53 Mutant MDS / AML	Frontline (French trial) ⁽¹⁾	Combination with azacitidine				Final CR primary endpoint first half 2020
		Post-Transplant Maintenance	Combination with azacitidine				Full enrollment second half 2020
	TP53 Mutant AML	Frontline and Relapsed / Refractory	Combination with Bcl-2 inhibitor ⁽²⁾				First patient enrollment Q4 2019
APR-548	TP53 Mutant MDS / AML					IND submission first half 2020	

(1) Investigator-initiated trial

(2) With or without azacitidine

We believe that targeting p53 and thereby reactivating key intrinsic cellular functions has the potential to significantly impact patients' lives and treatment strategies for a wide variety of cancers. p53 is a tumor suppressor protein that in its normal state functions to sense DNA damage and induce cell cycle arrest, DNA damage repair, senescence and cellular apoptosis. Mutant p53 is an attractive target because it is widely mutated across hematologic and solid tumors and is associated with an aggressive clinical and molecular phenotype. In preclinical studies and clinical trials, mutations in p53 and the apoptotic pathway have been shown to play a key role in cancer genesis, proliferation and resistance to currently marketed therapeutic agents. Many approved and clinical stage oncology drugs are more effective with a functional p53 pathway. Our approach is to restore normal function to p53, thereby re-enabling a cell's ability to undergo apoptosis. Accordingly, we believe that by targeting p53, our drug candidates may enhance the ability of other anti-cancer therapies to induce cancer cell death. In addition, we believe that our approach may counteract resistance mechanisms that characterize many of the most aggressive cancers. Although we have observed single agent activity in preclinical testing of APR-246, our current clinical program is focused on combination therapy based on the strong additive or synergistic effects we have observed in combination with multiple conventional chemotherapeutic drugs, DNA hypomethylating agents, or HMAs, inhibitors of anti-apoptotic proteins and immuno-oncology checkpoint blockade agents.

Our lead product candidate, APR-246, is a small molecule that has demonstrated reactivation of mutant p53 in clinical trials. Promising clinical data support the application of APR-246 across a variety of hematologic malignancies and other oncologic indications. APR-246 is a pro-drug that is administered intravenously and forms the active moiety, 2-methylene-quinuclidin-3-one, or MQ, under

physiological conditions. APR-246 has been shown to induce apoptosis in cancer cells with mutant p53 in Phase 1/2 trials. We believe the mechanism of action and current adverse event profile of APR-246 may provide the basis for its combination with both conventional and novel therapies, such as targeted therapies, chemotherapy, radiotherapy and immuno-therapy. APR-246 has received Orphan Drug and Fast Track designations from the FDA for MDS, and Orphan Drug designation from the EMA for MDS, AML and ovarian cancer.

We are conducting and supporting multiple clinical trials of APR-246:

- **Pivotal Phase 3 MDS Trial**—We are currently enrolling a pivotal Phase 3 randomized, controlled trial evaluating APR-246 with azacitidine as frontline therapy in HMA-naïve *TP53* mutant MDS patients. The trial has a target enrollment of 154 patients randomized in a 1:1 ratio to either the azacitidine control arm or to the APR-246 + azacitidine experimental arm, with a primary endpoint of CR rate. The first patient was enrolled in January 2019 and we anticipate full enrollment in our Phase 3 trial in the first quarter of 2020 and top-line data from this trial in the second half of 2020.
- **U.S. Phase 1b/2 MDS/AML Trial**—We are supporting an investigator-initiated Phase 1b/2 single-arm, open-label trial in the United States, sponsored by Dr. David Sallman of the H. Lee Moffitt Cancer Center and Research Institute, or Moffitt, evaluating APR-246 with azacitidine as frontline therapy in HMA-naïve patients with *TP53* mutant MDS or AML. We are collaborating with Moffitt on this trial by supplying APR-246, in addition to providing financial support. The primary endpoint of the trial is CR rate and enrollment has completed with 55 patients. Top-line results on the CR rate primary endpoint and median duration of response are expected in the second half of 2019. The regimen achieved an ORR of 88% and a CR rate of 59% in 41 response-evaluable patients as of July 2019. In MDS patients, the CR rate was 61%, with an additional 27% achieving non-CR responses. In AML patients, the CR rate was 50%, with an additional 38% achieving non-CR responses. In addition, 46% of evaluable MDS/AML patients were able to discontinue treatment in order to proceed to allo-HCT. By intention-to-treat analysis, and with a median follow up of 10.5 months, median OS was 11.6 months (95% confidence interval: 9.2 – 14.0 months) with significantly prolonged OS of 12.8 months in responding patients versus 3.9 months in non-responding patients ($p < 0.0001$). Analysis of peer-reviewed published data in *TP53* mutant MDS and AML suggests frontline azacitidine monotherapy provides an ORR of 40-50% for AML, CR rates of approximately 20% and median OS of 7-8 months.
- **French Phase 1b/2 MDS/AML Trial**—We are supporting a parallel investigator-initiated Phase 1b/2 single-arm, open-label trial in France, sponsored by Groupe Francophone des Myelodysplasies, or GFM, under lead investigator Prof. Pierre Fenaux, evaluating APR-246 with azacitidine as frontline therapy in HMA-naïve patients with *TP53* mutant MDS or AML. We are collaborating with GFM on this trial by supplying APR-246, in addition to providing financial support. The primary endpoint of the trial is CR rate and enrollment has completed with 53 patients. Top-line results on the CR rate primary endpoint are expected in the first half of 2020. All patients are to receive the recommended Phase 2 dose from the U.S. Phase 1b/2 MDS/AML Trial. As of July 2019, the regimen has achieved an ORR of 75% and CR rate of 56% in 16 response-evaluable patients. In MDS patients, the CR rate was 55%, with an additional 18% achieving non-CR responses. In AML patients, the CR rate was 60%, with an additional 20% achieving non-CR responses. Responding patients who proceed to allo-HCT are eligible to continue receiving APR-246 with azacitidine as post-transplant maintenance therapy.
- **Phase 2 MDS/AML Post-Transplant Trial**—We are currently enrolling our single-arm, open-label Phase 2 trial evaluating APR-246 with azacitidine as post-transplant maintenance therapy in *TP53* mutant MDS and AML patients who have received allo-HCT. The primary endpoint is

relapse-free survival at 12 months. Target enrollment is 31 patients and we anticipate full enrollment in the second half of 2020. Analysis of the historical, peer-reviewed published data in *TP53* mutant MDS and AML patients who undergo bone marrow transplant suggests that *TP53* mutation is associated with a 4-fold increased risk of death following transplantation and a 1-year relapse-free survival of only 30%.

- **Phase 1/2 AML Trials**—Based on *in vitro* data evidencing synergistic activity between APR-246 and a Bcl-2 inhibitor, we have designed and plan to conduct Phase 1/2 clinical trials in frontline and relapsed/refractory AML assessing APR-246 with a Bcl-2 inhibitor with or without azacitidine. We anticipate the first patient to be enrolled in the fourth quarter of 2019.

Our second product candidate, APR-548, is a next-generation p53 reactivator with the potential for oral administration. APR-548 is a unique analog of APR-246 and therefore a pro-drug of MQ. APR-548 exhibits high oral bioavailability in preclinical testing and is being developed in an oral dosage form. We are currently conducting Investigational New Drug, or IND, enabling preclinical studies of APR-548 and anticipate submitting an IND in the first half of 2020.

We have assembled an outstanding team, which includes world-class scientific and clinical oncology leaders, to execute on our mission to create novel p53-reactivating therapies to help patients suffering with cancer. Together with our board of directors, our scientific founders and members of our management team have significant experience in drug discovery and development and finance. Collectively, we believe our team's strong capabilities position us to build a leading biotech company focused on developing novel cancer therapies to address the significant unmet medical need of patients with p53 mutant malignancies, for whom there are limited effective therapeutic options.

Our strategy

Our mission is to be the leading player in the development and commercialization of p53-targeted cancer therapies. The key elements of our strategy are to:

- **Rapidly develop and commercialize our lead mutant p53 reactivator, APR-246, in frontline combination therapy for *TP53* mutant MDS.** We are currently advancing APR-246 with azacitidine through Phase 3 clinical development in *TP53* mutant MDS. We are initially targeting frontline *TP53* mutant MDS, where there are few approved therapies, no approved p53-targeted therapies and a continued high unmet medical need. We believe the data generated to date support compelling clinical activity in this underserved patient population.
- **Expand the clinical opportunity for APR-246 by pursuing development of combination therapy for post-transplant maintenance in *TP53* mutant MDS and AML.** Allo-HCT is currently considered the only curative option for patients with *TP53* mutant MDS/AML, and even with transplantation the outcomes for these patients remain poor. We are currently advancing APR-246 as post-transplant maintenance therapy in *TP53* mutant MDS and AML in the French Phase 1b/2 MDS/AML Trial and our Phase 2 MDS/AML Post-Transplant Trial. We believe that this approach may offer an opportunity to quickly expand the commercial potential of APR-246.
- **Rapidly develop APR-246 for frontline and relapsed/refractory *TP53* mutant AML.** We are currently advancing the clinical development of APR-246 in frontline *TP53* mutant AML through the U.S. Phase 1b/2 MDS/AML Trial and the French Phase 1b/2 MDS/AML Trial. While these frontline trials are evaluating APR-246 with azacitidine, we also intend to evaluate additional combination regimens with a Bcl-2 inhibitor with or without azacitidine in both frontline and relapsed/refractory AML patients. We believe that the treatment of these patients may offer an opportunity to significantly expand the commercial potential of APR-246.
- **Advance our next-generation p53 reactivator, APR-548.** We are developing a next-generation small molecule p53 reactivator with the potential to be delivered in an oral dosage form. We intend to

initially develop APR-548 in *TP53* mutant MDS/AML. We believe that an oral p53-reactivating drug will improve patient convenience and compliance, if approved, including for patients receiving prolonged therapy in the maintenance setting.

- **Explore additional oncology indications for APR-246 and APR-548.** We are evaluating combination treatment with our product candidates in additional hematologic and solid tumor indications where mutant and dysfunctional p53 is a driver of disease. We have preclinical models that show synergistic effects of APR-246 with a variety of anti-cancer agents including multiple conventional chemotherapeutic drugs, HMAs, inhibitors of anti-apoptotic proteins and immuno-oncology checkpoint blockade agents. Based on our preclinical data, we believe there is potential to expand APR-246 and APR-548 into additional oncological indications.
- **Maximize the commercial opportunity of our product candidates across global markets.** We currently retain worldwide development and commercialization rights to all of our product candidates. We intend to retain commercial rights to our product candidates in the United States and may elect to build a focused commercial oncology organization to market any of our product candidates that are approved. Outside of the United States, we may elect to selectively evaluate strategic partnership opportunities for our product candidates with partners whose development and commercial capabilities complement our own.

Our approach

Background on p53, a key tumor suppressor protein

TP53 is the most widely mutated gene in human cancers. Since its discovery in 1979, p53 has been extensively studied by researchers and the pharmaceutical industry due to its central role in preventing the initiation and progression of liquid and solid tumors. p53 has long been referred to as "the guardian of the genome" because it is the body's first line of cellular defense against cancers. Among its multiple biologic functions, p53 regulates a variety of tumor suppressive responses including cell cycle arrest, DNA repair, apoptosis, and senescence.

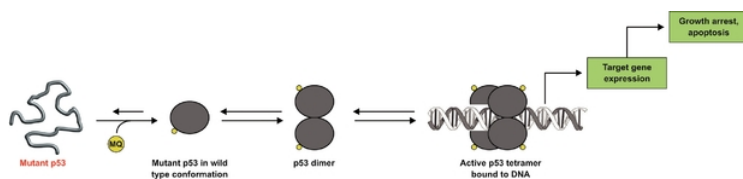
p53 is activated when DNA damage is detected and when oxidative or other cellular stresses exceed thresholds for normal cellular function. The result of p53 activation is to facilitate the repair of the cell or trigger killing of the damaged cell, through a process known as apoptosis, before it can become cancerous and replicate. Given that the mutational status of p53 in a tumor has a strong impact on sensitivity to commonly used anti-cancer drugs and radiotherapy, p53 is important both as clinical marker and as a novel therapeutic target. Importantly, mutations in p53 not only diminish tumor suppression function but also often lead to the acquisition of new pro-tumor functions.

To date, more than 25,000 unique *TP53* mutations have been reported and thus a key challenge in the development of p53-targeted therapies is the vast number of mutations that compromise tumor suppression activity. Incidence of *TP53* mutations increases after treatment with chemotherapy or radiation. The most common of these are missense mutations, involving the site-specific exchange of one amino acid for another, and account for 75% of all p53 mutations; however, even the six most frequently mutated "hotspot" missense mutations in p53 collectively represent only ~30% of all missense mutations. Therefore, we believe that a therapeutic agent that targets a small subset of *TP53* mutations would be of limited benefit. To circumvent these challenges, previous drug development efforts have primarily focused on gene therapy delivery of wild type p53 or drugs that disrupt interaction with proteins that control p53 activation and abundance. We believe the more effective approach is our direct conformational reactivation of mutant p53 and restoration of wild-type structure and activity, independent of the type of mutation.

Our approach to re-activating p53

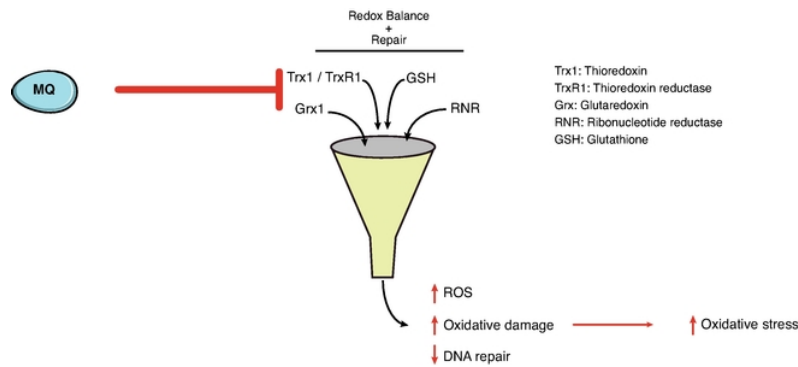
One of the most attractive features of apoptosis activation as a cancer therapy is its potential to induce tumor regression rather than to simply stop tumor growth. However, pro-apoptotic agents that cannot discriminate between malignant and normal cells carry a significant risk of side effects. This is an important issue with traditional cancer treatments: radiotherapy and chemotherapy induce apoptosis only as a secondary effect of the cellular damage they induce. These treatments affect most proliferating cells without distinction between malignant or normal cells. Our product candidates, in contrast, are designed to reactivate mutant, non-functional p53 to restore normal apoptotic functions in cancer cells without triggering apoptosis in normal cells, thereby selectively enhancing the effects of other chemotherapy drugs in malignant cancer cells with mutant p53.

APR-246 and the MQ, have been extensively studied. MQ-modified mutant p53 protein has been shown to induce significant levels of apoptosis, indicating that covalent binding of MQ activates mutant p53 and induces a p53-dependent apoptotic response. Experiments by our founders looking directly at the conformational state of p53 protein in cells have confirmed that binding of MQ stabilizes mutant p53 in the functional, wild type conformation. Structural biology studies performed by our collaborators have produced the first-ever crystal structures of several single-site missense mutant p53 forms bound to DNA. These structures confirm both the sites of MQ binding to mutant p53 and the stabilization of mutant p53 by MQ in the wild type conformation. Reactivation of mutant p53 via stabilization of the properly folded wild type conformation is the key step in our product candidates' mechanism of action. The following diagram illustrates this mechanism.



In *in vitro* and *in vivo* experiments, our lead p53 re-activating product candidate, APR-246, via MQ, impaired tumor cells' capacity to respond to oxidative stress. In parallel to binding mutant p53, and as published by Liu et al, Nat Commun, 2017, 14844, MQ depletes intracellular glutathione, or GSH, and induces reactive oxygen species, or ROS. Furthermore, as published in Peng et al, Cell Death Dis, 2013, e881, MQ has been shown to inhibit the reductase activities of the redox enzyme thioredoxin reductase, or TrxR1, and convert the enzyme to a dedicated oxidase, thereby increasing levels of ROS. Additional results reported in Haffo et al, Sci. Reports, 2018, 12671, have demonstrated MQ inhibition of thioredoxin, or Trx1, and glutaredoxin, or Grx1, which further augment oxidative stress, and ribonucleotide reductase, or RNR, which decreases the cell's ability to repair damaged DNA. These effects on the cellular redox system, illustrated in the following diagram, may contribute to the anticancer activity of APR-246 as well as the selectivity for effects on cancer cells versus healthy normal cells. Malignant cells have higher levels of ROS than healthy cells and are thus more

susceptible to increased stress that can trigger pro-apoptotic responses. MQ-induced oxidative stress is therefore an important secondary feature of the mechanism of action.



Cell fate is a function of the extent and severity of cellular stresses, such as oxidative stress and DNA damage. A network of proteins translates information about cellular stress into biochemical signals and relays this information back to p53, the center of the network. p53 integrates these biochemical signals and becomes activated to initiate cell cycle arrest. When cellular stress and damage are sufficiently high, such as with chemotherapy, p53 initiates apoptosis. MQ restores the ability of a cell to respond to oxidative stress and DNA damage via reactivation of mutant p53 and induces heightened oxidative stress signals to which reactivated p53 can respond. The overlap of these features of the mechanism of action may in turn provide more efficient induction of apoptosis.

Market opportunity for p53 re-activating product candidates

We believe there is a significant market opportunity for therapies targeting mutant p53 because these mutations occur in more than half of all tumors and confer an inferior prognosis relative to patients with wild type p53. Preclinical anti-tumor activity has been observed with APR-246 in a wide variety of hematological and solid tumor models and cell lines as reviewed and referenced in Perdrix et al, Cancer 2017, 9, 172. Given the importance of p53 mutations as disease-driver mutations, the sensitivity of hematopoietic cells to oxidative stress and continued unmet medical need, we are initially focused in our clinical development on hematological malignancies, MDS and AML, with TP53 mutations.

Myelodysplastic syndromes—disease background and opportunity

MDS is a collection of bone marrow disorders in which malignant hematopoietic cells prevent production of healthy, mature blood cells. Low blood cell counts, called cytopenias, are a hallmark feature of MDS and are a principal cause of morbidity and mortality from infection and bleeding. MDS can develop *de novo* or may arise secondary to chemotherapy or radiation treatment for a different, prior malignancy or following an antecedent hematological disorder. Treatment-related MDS is associated with increased complex chromosomal abnormalities and carries a worse prognosis than *de novo* MDS. As of 2019, there are an estimated 200,000 MDS patients worldwide, with 68,000 of these in the United States and 69,000 MDS patients across the five major markets of the European Union and Japan. Globally, MDS prevalence is expected to increase 2-3% annually in mature markets and 3-4% annually in emerging markets as populations age. MDS predominantly affects older adults, with

approximately 75% of patients aged 60 years or older at diagnosis. Around 30% of patients diagnosed with MDS will progress to AML, with the rate being higher for patients with more advanced disease.

MDS patients are segmented into different risk groups according to the number of cytopenias, bone marrow blast percentage, and cytogenetic abnormalities. The presence of three or more coincident structural genetic abnormalities is classified as a complex karyotype, which correlates with poor prognosis, low response to intensive chemotherapy, high rate of relapse and inferior survival. Mutations in *TP53* occur in approximately 20% of patients with *de novo* MDS and in more than 30% of patients with therapy-related MDS who develop disease secondary to chemotherapy or radiation treatment for other cancers. Sequencing of a panel of commonly mutated genes, including *TP53*, is standard practice in the diagnosis of MDS.

Historically, treatment response rates in *TP53* mutant MDS patients have been poor regardless of therapy. Treatment with azacitidine is the standard of care for frontline therapy in *TP53* mutant MDS, with ORR of 40-45%, a CR rate of 20% and median OS of approximately 7-8 months. There are no established curative pharmacologic therapies for MDS. Allo-HCT is currently the only recognized therapy believed to increase the likelihood of long term survival for *TP53* mutant MDS patients; however, many patients are not candidates for allo-HCT due to lack of sufficient clinical response to initial therapy, advanced age, comorbidities or lack of a suitable donor. Unfortunately, even for those *TP53* mutant MDS patients who receive allo-HCT, the post-transplantation prognosis is poor: *TP53* mutations are associated with a 4-fold increased risk of death and 1-year relapse-free survival of only 30% following transplantation.

Given the poor prognosis for patients with *TP53* mutant MDS there is a significant need for more effective therapies in this population, particularly if such treatments have a favorable safety profile, and a mechanism of action that targets mutant p53 directly, and may be used in combination with existing or future treatment options.

Acute myeloid leukemia—disease background and opportunity

AML is the most common form of adult leukemia, with the highest incidence in patients aged 60 years and older. AML is characterized by proliferation of abnormal immature white blood cells which, like MDS, impairs production of normal blood cells. AML can develop *de novo* or may arise secondary to progression of other hematologic disorders or from chemotherapy or radiation treatment for a different, prior malignancy; secondary AML carries a worse prognosis than *de novo* AML. As of 2019, there are an estimated 213,000 AML patients worldwide, with 37,000 of these in the United States and 41,000 across the five major European Union markets and Japan. Globally, AML prevalence is expected to increase approximately 1-2% annually in mature markets and 2-3% in emerging markets.

AML patients are segmented into different risk groups according to cytogenetic abnormalities. The presence of three or more coincident structural genetic abnormalities is classified as a complex karyotype, which correlates with adverse prognosis, low response to intensive chemotherapy, high rate of relapse and inferior survival. Mutations in *TP53* occur in approximately 20% of patients with newly diagnosed AML, more than 30% of patients with therapy-related AML and approximately 70-80% of patients with complex karyotype. Sequencing of a panel of commonly mutated genes, including *TP53*, is standard practice in the diagnosis of AML.

Historically, treatment response rates in *TP53* mutant AML patients have been poor regardless of therapy. Treatment with azacitidine is the standard of care therapy for frontline therapy in *TP53* mutant AML, with 40-50% ORR, 10-20% CR rate and OS of 7-8 months. Similar to MDS, allo-HCT is currently the only recognized therapy believed to increase the likelihood of long term survival for *TP53* mutant AML patients; however, many patients are not candidates for allo-HCT due to lack of sufficient clinical response to therapy, advanced age, comorbidities or lack of a suitable donor. Unfortunately, even for those *TP53* mutant AML patients who receive allo-HCT, the post-transplantation prognosis is

poor: *TP53* mutations are associated with a 4-fold increased risk of death and 1-year relapse-free survival of only 30% following transplantation.

Given the poor prognosis for patients with *TP53* mutant AML there is a significant need for more effective therapies in this population, particularly if such treatments have a favorable safety profile, and a mechanism of action that targets mutant p53 directly, and may be used in combination with existing or future treatment options.

Our lead product candidate, APR-246

Our lead product candidate, APR-246, is a small molecule that has demonstrated reactivation of mutant p53 in both clinical trials and preclinical studies. Promising clinical and preclinical data support the application of APR-246 across a variety of hematologic malignancies and other oncologic indications. Based on its mechanism of action of p53 reactivation and the complementary increase in oxidative stress, as well as its potential synergy with anti-cancer agents as evidenced in preclinical studies, APR-246 treatment may be effective in a broad range of clinical settings. We are currently focusing our clinical development of APR-246 on hematologic malignancies.

Clinical trials of APR-246 in MDS and AML

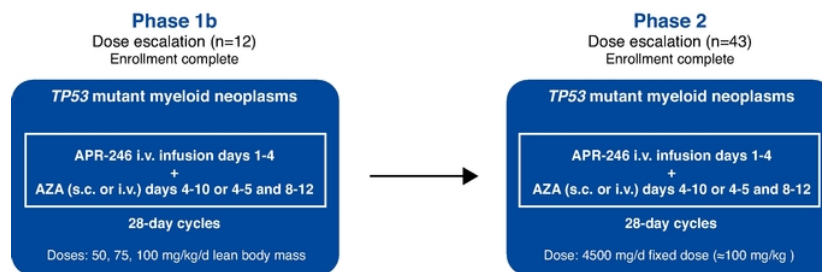
We are currently evaluating APR-246 with azacitidine for the treatment of *TP53* mutant MDS and/or AML patients in 4 clinical trials, including frontline therapy and post-allo-HCT maintenance therapy. We plan to initiate an additional trial in the fourth quarter of 2019 to evaluate APR-246 with a Bcl-2 inhibitor with or without azacitidine for the treatment of frontline and relapsed/refractory, or R/R, AML.

The Pivotal Phase 3 MDS Trial

Our pivotal Phase 3 trial commenced enrollment in January 2019. Patients are randomized in a 1:1 ratio to either the azacitidine control arm or to the APR-246 + azacitidine test arm. The primary endpoint is CR rate with secondary endpoints including ORR, duration of response, progression-free survival, or PFS, leukemia-free survival, or LFS, OS, and proportion transitioning to allo-HCT. Serious adverse events, regardless of causality, reported in more than one patient as of September 18, 2019 were: febrile neutropenia 19%, lung infection (9%), pyrexia 6%, muscle weakness 4%, pericarditis 4%, pneumonitis 4%, hypotension (4%), sepsis (4%). There has been one death, resulting from respiratory failure, in a patient receiving both APR-246 and azacitidine and reported by an investigator as possibly related to both study drugs. There has been one death, resulting from pneumonitis, in a patient receiving azacitidine monotherapy and reported by an investigator as possibly related. The target enrollment is 154 patients and we anticipate completing enrollment in the first quarter of 2020 and expect top-line CR data in the second half of 2020.

The U.S. Phase 1b/2 MDS/AML Trial

We are supporting an investigator-initiated Phase 1b/2 single-arm, open-label, multi-center trial in the United States of APR-246 with azacitidine in HMA-naïve patients with *TP53* mutant myeloid neoplasms including MDS and AML. Enrollment commenced in May 2017 and was completed in March 2019. The Phase 1b part enrolled 12 patients and was conducted as a dose escalation in a modified 3+3 design at dose levels of 50 mg/kg/d, 75 mg/kg/d and 100 mg/kg/d, calculated by lean body mass. The Phase 2 part enrolled 43 patients with all patients receiving a fixed dose of 4500 mg/d APR-246, a dose that our population pharmacokinetic analysis has identified as approximately equivalent to the highest Phase 1b dose, 100 mg/kg/d by lean body mass. A lead-in phase, beginning two weeks prior to starting cycle 1 of combination therapy with azacitidine, was conducted only in the Phase 1b part. The purpose of the lead-in phase was to establish the adverse event profile of APR-246 in this patient population and to APR-246-induced p53 reactivation. The protocol specifies administration of APR-246 as a 6-hour intravenous infusion daily for four consecutive days, with administration of 75 mg/m²/d azacitidine by sub-cutaneous injection or intravenously beginning on Day 4 after completion of APR-246 infusion and continuing for 6 additional days. The image below shows the design of the U.S. Phase 1b/2 MDS/AML Trial.



Baseline characteristics of patients enrolled in the trial are shown in the following table. Patients with MDS, AML, chronic myelomonocytic leukemia, or CMML, and MDS-myeloproliferative neoplasm overlap, or MDS-MPN, were allowed to enroll in the trial. Most patients were higher risk MDS (35/55, 64%) or AML (11/55, 20%), with complex karyotypes, cytopenias and transfusion dependence.

Baseline characteristics

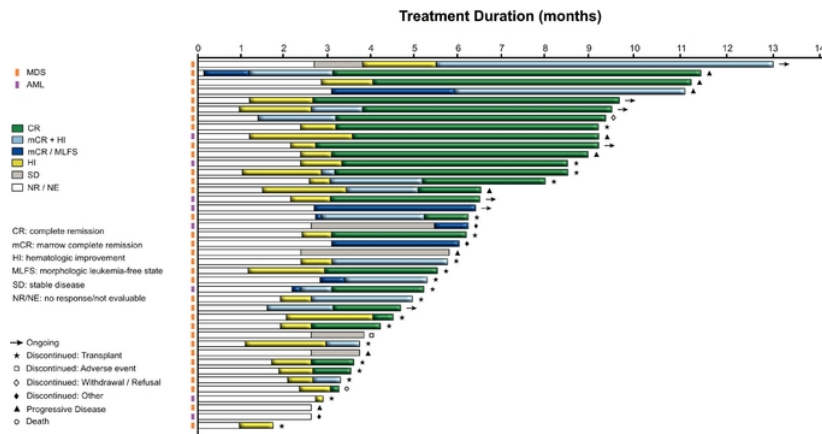
	All patients (n=55)
Female / Male, n	29 / 26
Age in years, median (range)	66 (34 - 85)
Age Category, n (%)	
< 65	23 (42)
≥ 65	32 (58)
ECOG PS(1) at treatment start, n (%)	
0	17 (31)
1	34 (62)
2	4 (7)
Disease type, n (%)	
MDS	40 (73)
IPSS-R(2): Intermediate	4 (7)
IPSS-R: High	8 (15)
IPSS-R: Very High	28 (51)
AML	11 (20)
CMML(3)	2 (4)
MDS-MPN(4)	2 (4)
Therapy-related(5), n (%)	18 (33)
Chemotherapy	16 (29)
Radiation	3 (5)
Complex karyotype, n (%)	47 (85)
TP53 VAF(6)%, median (range)	27 (1 - 79)
Bone marrow blast %, median (range)	8 (0 - 30)
Hematology, median (range)	
ANC(7), 10 ³ /mL	1.19 (0.02 - 15.98)
Hgb(8), g/dL	8.6 (6.7 - 13.8)
Platelets, 10 ³ /mL	46 (0 - 845)
WBC(9), 10 ³ /mL	2.4 (0.6 - 30.8)
Transfusion dependence, n (%)	
RBC(10)	36 (65)
Platelets	12 (22)

(1) Eastern Cooperative Oncology Group performance status

- (2) Revised International Prognostic Scoring System
- (3) Chronic myelomonocytic leukemia
- (4) Myelodysplastic syndromes-myeloproliferative neoplasms overlap
- (5) Patients treated for prior cancer(s)
- (6) Variant allele frequency
- (7) Absolute neutrophil count
- (8) Hemoglobin
- (9) White blood cell
- (10) Red blood cell

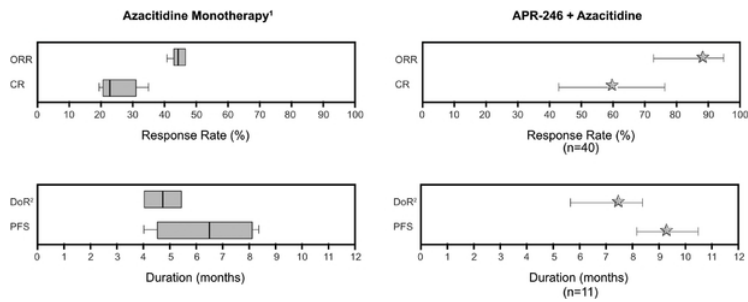
The median age of all enrolled patients was 66 years, consistent with MDS and AML affecting mostly older patients. Of the MDS patients in the trial, 36/40 were high or very high risk by IPSS-R. Across all patients, 33% had documented therapy-related disease and 85% had complex karyotypes. High risk patients with complex karyotypes and *TP53* mutation have been reported to have the poorest prognosis of all MDS and AML patients. The median bone marrow blast percentage was 8%. Hematologic parameters were reflective of the frequently severe cytopenias attendant with MDS and AML, and were underscored by transfusion dependence at baseline in 65% of patients.

Of the 51 MDS and AML patients treated with the combination of APR-246 and azacitidine, 41 had at least one serial bone marrow biopsy performed and were evaluable for response in accordance with trial protocol as of July 2019. In this subset of 41 evaluable patients, responses were reported in 29/33 (88%) MDS patients and 7/8 (88%) AML patients. In MDS patients, the CR rate was 61%, with an additional 27% achieving non-CR responses. In AML patients, the CR rate was 50%, with an additional 38% achieving non-CR responses. Nineteen of 41 (46%) MDS/AML patients discontinued treatment for allo-HCT, as transplant is viewed as a potentially curative option for patients with *TP53* mutant MDS and AML. Treatment duration and responses are shown in the figure below. The median time to first response is 1.9 months in MDS patients and 2.2 months in AML patients. By intention-to-treat analysis in all 55 patients, and with a median follow up of 10.5 months, median OS was 11.6 months (95% confidence interval: 9.2 – 14.0 months) with significantly prolonged OS of 12.8 months in responding patients versus 3.9 months in non-responding patients ($p < 0.0001$). In the subset of 41 MDS/AML patients, median OS was 12.2 months (95% confidence interval: 9.8 – 14.6 months).



Treatment with azacitidine is the standard of care for frontline therapy in *TP53* mutant MDS and AML, with ORR of 40-45% and a CR rate of 20%. A limited number of peer-reviewed publications have reported the duration of response, or DoR, and PFS in this patient population; from the available public data, DoR is approximately 4-5 months and PFS is approximately 4-8 months. In the 41 evaluable patients in the U.S. trial, ORR was 88% (95% confidence interval: 73 - 95%) and CR rate was 59% (95% confidence interval: 43 - 75%). For the evaluable Phase 1b patients, where the data is mature, DoR was 7.5 months (95% confidence interval: 5.8 - 8.4 months) and PFS was 9.3 months (95% confidence interval: 8.2 - 10.6 months) as of the data cutoff. These data are summarized in the following figure.

Rates and Duration of Response



(1) Data from Sallman et al, 2018 Annual Meeting of the American Society of Hematology, poster 1817; Bally et al, *Leukemia Res.*, 2014; Takahashi et al, *Oncotarget*, 2016; Kulasekararaj, *Br. J. Haematol.*, 2013; Bejar et al, *Blood*, 2014; Falconi et al, *Leukemia*, 2018.
 (2) Duration of response

Reported adverse events, or AEs, are mostly low-grade (Grade 1 or 2). Grade 3 or higher AEs are mostly associated with the underlying disease. In the APR-246 monotherapy lead-in phase there were no dose-limiting toxicities, no serious adverse events attributed to APR-246 and all treatment-related AEs were low-grade. The following chart summarizes the AEs reported in more than one patient during the APR-246 monotherapy lead-in phase.

AEs reported in > 1 patient during APR-246 monotherapy lead-in phase (n=12)

<u>Adverse event, n (%)</u>	<u>Any grade</u>	<u>Grade ≥ 3</u>
Nausea	5 (42)	0 (0)
Peripheral sensory neuropathy	5 (42)	0 (0)
Back pain	3 (25)	0 (0)
Febrile neutropenia	2 (17)	2 (17)
Anemia	2 (17)	2 (17)
Headache	2 (17)	0 (0)
Dizziness	2 (17)	0 (0)

The most common AEs observed across all cycles of treatment in the trial, as of the cutoff date and regardless of causality, are summarized in the following chart. Only three patients (5%) discontinued treatment due to AE. Serious adverse events, regardless of causality, reported for more than one patient were: febrile neutropenia (27%), lung infection (9%), infections and infestations (5%), respiratory failure (5%), sepsis (5%), vomiting (5%), chest pain (4%), dehydration (4%), intracranial hemorrhage (4%) and multi-organ failure (4%).

Most common reported AEs with APR-246 + azacitidine treatment, regardless of causality (≥20%)

Data cutoff: July 15, 2019 (n=55)

<u>Adverse event, n (%)</u>	<u>Any grade</u>	<u>Grade ≥ 3</u>
Nausea	35 (65)	0 (0)
Vomiting	24 (44)	1 (2)
Fatigue	23 (42)	0 (0)
Constipation	22 (40)	0 (0)
Dizziness	19 (35)	1 (2)
Diarrhea	19 (35)	1 (2)
Febrile neutropenia	18 (31)	18 (33)
Neutropenia	16 (29)	16 (29)
Edema—limbs	16 (29)	1 (2)
Infections and infestations	16 (29)	6 (11)
Dyspnea	16 (29)	2 (4)
Peripheral sensory neuropathy	15 (27)	0 (0)
Leukopenia	15 (27)	14 (25)
Thrombocytopenia	15 (27)	13 (24)
Cough	15 (27)	1 (2)
Headache	14 (25)	0 (0)
Pruritus	13 (24)	0 (0)
Mucositis oral	12 (22)	0 (0)
Fever	12 (22)	1 (2)
Skin and subcutaneous tissue disorders	12 (22)	0 (0)
Tremor	11 (20)	1 (2)
Anorexia	11 (20)	0 (0)
Alanine aminotransferase increased	11 (20)	1 (2)
Lung infection	11 (20)	9 (16)

The most common AEs, determined by an investigator to be possibly, probably or definitely related to APR-246 or azacitidine, are summarized in the following chart.

Most common reported AEs with possible, probable or definite relation to APR-246 or azacitidine (≥10%)

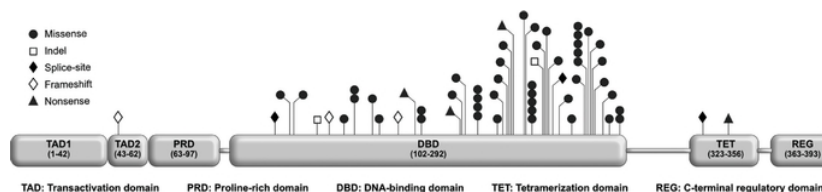
Data cutoff: July 15, 2019 (n=55)

Adverse event, n (%)	Any grade	Grade ≥ 3
Nausea	32 (58)	0 (0)
Vomiting	24 (44)	1 (2)
Dizziness	17 (31)	1 (2)
Constipation	13 (24)	0 (0)
Peripheral sensory neuropathy	12 (22)	0 (0)
Leukopenia	12 (22)	11 (20)
Thrombocytopenia	11 (20)	9 (16)
Neutropenia	10 (18)	10 (18)
Fatigue	8 (15)	0 (0)
Tremor	8 (15)	0 (0)
Pruritus	7 (13)	0 (0)
Diarrhea	6 (11)	0 (0)
Anorexia	6 (11)	0 (0)

Fifty-eight *TP53* mutations, representing 49 unique mutations, were identified in the subset of 41 evaluable MDS and AML patients. Consistent with prior published findings, the majority of these were missense mutations (79%) and located in the DNA-binding domain (93%). Other *TP53* mutations sequenced in the 41 evaluable MDS and AML patients included insertion-deletion mutations (3%), splice-site mutations (5%), frameshift mutations (5%) and nonsense mutations (7%). The distribution of *TP53* mutations by type and breadth of mutations by response are shown in the figure below.

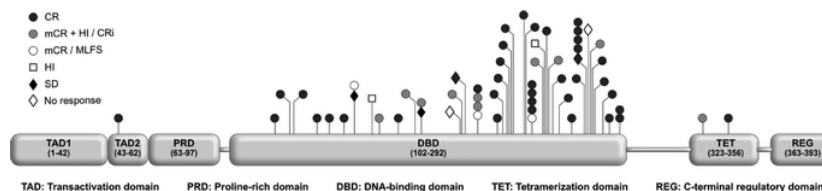
***TP53* mutations by type in evaluable MDS/AML patients**

Data cutoff: July 15, 2019 (n=41)



***TP53* mutations by best response in evaluable MDS/AML patients**

Data cutoff: July 15, 2019 (n=41)



We are supporting an ongoing investigator-initiated single-arm, open-label Phase 1b/2 trial in France by the Groupe Francophone des Myélodysplasies, or GFM, under lead investigator Prof. Pierre Fenaux, to expand the adverse event and efficacy data set in MDS and AML patients treated with the combination of APR-246 and azacitidine. The trial was initiated in September 2018 and reached final enrollment of 53 patients in July 2019. The median age of enrolled patients is 73 years. Thirty-four of 53 patients (64%) had a diagnosis of MDS and 19/53 (36%) with AML. At baseline, 74% of MDS patients were very high risk by IPSS-R. Complex karyotype was found in 89% of enrolled patients.

The protocol specifies administration of 4500 mg/d APR-246 as a 6-hour intravenous infusion daily for four consecutive days, with administration of 75 mg/m²/d azacitidine by sub-cutaneous injection or intravenously beginning on Day 4 after completion of APR-246 infusion and continuing for 6 additional days. Patients who receive benefit from frontline therapy and undergo allo-HCT are eligible to continue with post-transplant maintenance therapy with APR-246 and azacitidine. As of July 2019, of the 53 patients enrolled, there were 11 MDS patients and 5 AML patients that had at least one serial bone marrow biopsy performed and were evaluable for response in accordance with trial protocol. Responses were achieved in 8/11 (73%) of MDS patients with 55% CR rate, and 4/5 (80%) of AML patients with a 60% CR rate, for a combined 75% ORR and 56% CR rate. As demonstrated in the following table, these data from the French Phase 1b/2 MDS/AML Trial are qualitatively consistent with data from the U.S. Phase 1b/2 MDS/AML Trial.

Comparison of best response in French Phase 1b/2 MDS/AML Trial and U.S. Phase 1b/2 MDS/AML Trial

	French phase 1b/2 MDS/AML trial (n=11)	U.S. phase 1b/2 MDS/AML trial (n=33)
MDS		
ORR, %	73	88
CR, %	55	61
mCR + HI, %	9	21
mCR, %	0	3
HI, %	9	3
AML		
ORR, %	80	88
CR, %	60	50
MLFS, %	20	25
HI, %	0	13
Combined MDS + AML		
ORR, %	75	88
CR, %	56	59
mCR + HI / CRi / CRp, %	6	17
mCR / MLFS, %	6	7
HI, %	6	5

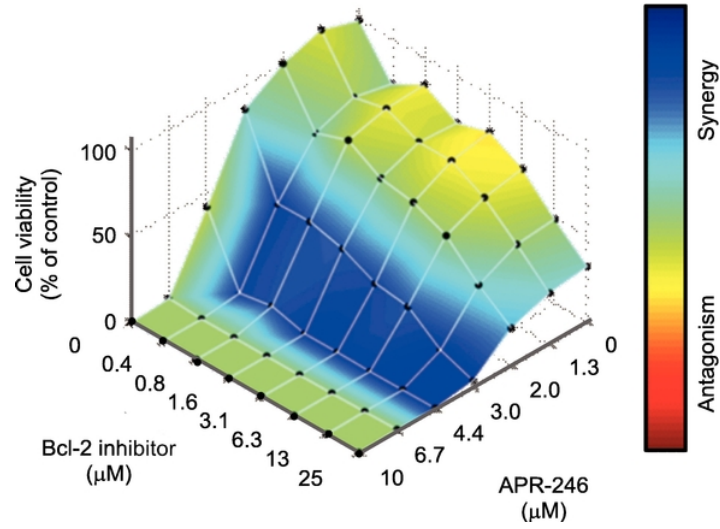
Serious adverse events, regardless of causality, reported in more than one patient in the French Phase 1b/2 MDS/AML Trial were: Febrile neutropenia (23%), device related infection (9%), sepsis (8%), pneumonia (6%), cerebellar syndrome (4%), lung disorder (4%), lung infection (4%), subdural hematoma (4%), urinary tract infection (4%).

There is a significant unmet medical need for more effective therapies for patients with *TP53* mutant AML and MDS following allo-HCT given that the one year post-transplant relapse-free survival, or RFS, rate is only 30%. In the second quarter of 2019, we opened enrollment to our Phase 2 MDS/AML Post-Transplant Trial to evaluate the benefit of APR-246 with azacitidine on RFS in *TP53* mutant MDS and AML patients who have received allo-HCT. The protocol specifies administration of 3700 mg/d APR-246 as a 6-hour intravenous infusion daily on days 1 through 4, with administration of 35 mg/m²/d azacitidine by sub-cutaneous injection or intravenously on days 1 through 5. Patients may receive a maximum of 12 cycles of maintenance therapy in the Phase 2 MDS/AML Post-Transplant Trial. Target enrollment in the trial is 31 patients and the primary endpoint is 1-year RFS. In addition, we will evaluate the adverse event profile of APR-246 with azacitidine as maintenance treatment post-HCT.

The Phase 1/2 AML Trials

We have designed and plan to conduct a Phase 1/2 clinical trial evaluating the adverse event profile and efficacy of treatment with APR-246 and ABT-199/venetoclax, the Bcl-2 inhibitor, with or without azacitidine, in frontline and R/R *TP53* mutant AML. Bcl-2 is a pro-survival protein that is frequently expressed at high levels in tumor cells and acts to restrict apoptosis. Inhibition of Bcl-2 protein relieves its anti-apoptotic function, thereby augmenting apoptosis. In preclinical trials, we have observed strong synergy when APR-246 and the Bcl-2 inhibitor are combined in the *TP53* mutant AML cell line, KBM3, as shown in the figure below, and believe that this combination may provide meaningful improvements in durable responses for *TP53* mutant AML patients with previously untreated and relapsed/refractory AML.

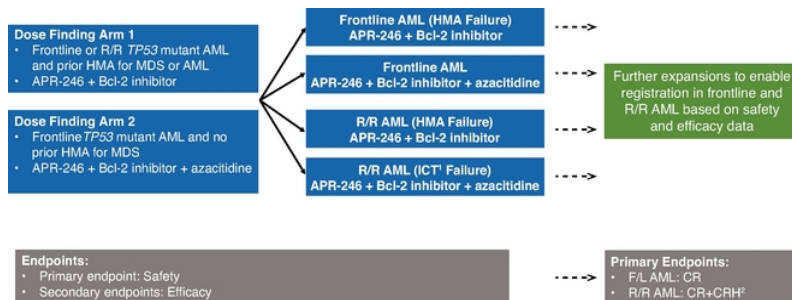
Strong synergy⁽¹⁾ is observed in *TP53* mutant cells treated with APR-246 and the Bcl-2 inhibitor



(1) Synergy analyzed using the Highest Single Agent (HSA) method.

Under the anticipated trial design, frontline and R/R *TP53* mutant AML patients who have received prior HMA therapy will receive treatment with APR-246 and the Bcl-2 inhibitor, and frontline patients who are HMA-naïve will receive treatment with APR-246, Bcl-2 inhibitor and azacitidine. We intend to expand the number of patients in individual arms of the trial, as warranted by adverse event and efficacy data, to enable a path to registration in frontline and R/R AML. We anticipate enrollment of the first patient in the fourth quarter of 2019. The following figure shows the design of the Phase 1/2 AML Trials.

Design of the Phase 1/2 AML Trials



- (1) Intensive chemotherapy
(2) CR with partial hematologic recovery

Clinical development in solid tumors

Phase 1b/2 Clinical Trial of APR-246 in Platinum-Sensitive Ovarian Cancer, or PiSARRO

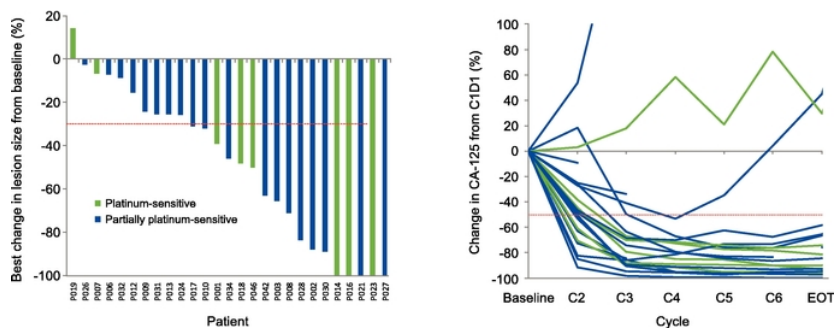
As part of the early development strategy, APR-246 was evaluated in clinical trials in ovarian cancer and this decision was based on the anticipated market size and high prevalence of *TP53* mutation of greater than 95% in high-grade serous ovarian cancer, or HGSOC. In March 2014, a Phase 1b trial was initiated as a part of a combined Phase 1b/2 protocol in platinum-sensitive HGSOC to evaluate APR-246 with carboplatin and pegylated liposomal doxorubicin, or PLD. All patients had previously been treated with platinum-based antineoplastic agents and all had accumulation of p53, as assessed by immunohistochemistry, or IHC, as a surrogate marker of mutant p53. Archival samples were available for 29 patients, of which 27 had DNA of sufficient quality for sequencing and all 27 were confirmed to be *TP53* mutant.

The completed Phase 1b part of the trial was conducted as a dose-escalation in 35 platinum-sensitive and partially platinum-sensitive patients. The primary trial objectives of the Phase 1b portion were to assess the adverse event profile of APR-246 with carboplatin and PLD, to determine a recommended Phase 2 dose level, or RP2D, and to evaluate the pharmacokinetics of APR-246 with carboplatin and PLD. Tumor response was a secondary objective.

The most frequently reported APR-246-related AEs were nausea, dizziness and fatigue, of which most were low-grade. A limited number of APR-246-related grade 3+ AEs were reported, including neutropenia (37%), vomiting (14%), thrombocytopenia (9%), dizziness (6%), anemia (6%), fatigue (3%), headache (3%) and decreased appetite (3%). Serious adverse events, regardless of causality, reported in more than one patient were: device related infection (17%), vomiting (17%), febrile neutropenia (8%), infection (6%), small intestinal obstruction (6%) and thrombocytopenia (6%).

Although efficacy was not a Phase 1b trial objective, tumor response was evaluated. A 67% ORR was observed in 27 patients who were evaluable for radiological response according to RECIST 1.1.

including 11% with complete response and 56% with partial response. In addition, an 84% ORR was observed in 25 patients who were evaluable for CA-125 response according to Gynecologic Cancer InterGroup, or GCIIG, criteria. Reductions in lesion size and declines in CA-125 are shown in the following figure below. All patients who were evaluable by RECIST 1.1 achieved a best response of stable disease or better, where stable disease indicates lack of objective response but without disease progression. The median time between prior platinum therapy and disease progression prior to enrollment in the trial, known as platinum free interval, or PFI, was 9.4 months, and 40% of patients had received more than one prior line of platinum-based chemotherapy. Two-thirds of patients enrolled in the trial were partially platinum-sensitive, with PFI 6-12 months. The remaining one-third of patients were platinum-sensitive, with PFI greater than 12 months. The median progression-free survival, or PFS, was 10.2 months across all patients and was 10 months and 11.4 months in partially platinum-sensitive and platinum sensitive patients, respectively. The median OS was 24.3 months. This was the first clinical trial of APR-246 with cytotoxic chemotherapy and we believe that the data demonstrated that the agent can be combined with carboplatin and PLD at standard doses.



Data supporting the carboplatin and PLD doublet as a treatment option in platinum-sensitive HGSOc were generated in the CALYPSO trial, a phase 3 clinical trial sponsored by an international consortium of 10 cancer research organizations. The CALYPSO trial enrolled 976 patients, randomized to receive either carboplatin and PLD (48%) or carboplatin and paclitaxel (52%). All patients had received a maximum of two prior lines of chemotherapy; in the carboplatin and PLD arm, 88% had received one prior line and 12% had received two prior lines. The median interval since last chemotherapy, or therapy-free interval, was 15.2 months in the carboplatin and PLD arm, of whom 35% had a therapy-free interval of 6-12 months and 65% had a therapy-free interval in excess of 12 months. The most frequently reported AEs in the carboplatin and PLD arm included neutropenia (80%), nausea (78%), fatigue (78%), anemia (66%), constipation (55%) and vomiting (49%). The most common grade 3+ AEs included neutropenia (35%), thrombocytopenia (16%) and anemia (8%). In the carboplatin and PLD arm PFS was reported as 11.3 months and OS as 30.7 months. Median PFS in the carboplatin and PLD arm was greater than the 9.4 months PFS in the carboplatin and paclitaxel arm (hazard ratio: 0.821, 95% CI, 0.72 – 0.94, $P = 0.005$). Response rates were not reported for the CALYPSO trial. Whereas the CALYPSO trial enrolled a majority of patients with treatment-free interval exceeding 12 months, our PiSARRO Phase 1b trial enrolled a majority of patients with partially platinum-sensitive disease which is generally recognized as a patient population with inferior treatment outcomes.

In the third quarter of 2016, enrollment commenced in the Phase 2 portion of the PiSARRO trial and concluded at 211 patients. The Phase 2 part was an open-label, randomized, controlled multi-center trial to assess whether patients with platinum-sensitive recurrent HGSOc would benefit from treatment with APR-246 in combination with carboplatin/PLD chemotherapy regimen. All patients were

required to have accumulation of p53 as assessed by immunohistochemistry, a surrogate marker of mutant p53.

Patients were randomized in a 1:1 ratio to receive either APR-246 with carboplatin and PLD or carboplatin and PLD only, with treatment to be repeated every 28 days for up to six cycles. Enrollment was concluded in April 2018. The primary endpoint for the Phase 2 part is PFS, defined as the time from registration to the time of disease progression or relapse or death, or the date of last tumor assessment without any such event. Serious adverse events, regardless of causality, reported in more than one patient were: small intestine obstruction (4%), thrombocytopenia (2%), dyspnea (2%), nausea (2%), renal impairment (2%), vomiting (2%), abdominal pain, (1%) anemia (1%), constipation (1%), dehydration (1%), dizziness (1%), infectious pleural effusion (1%), large intestine perforation (1%), urinary tract infection (1%). Upon receipt of final data, we intend to conduct a subset analysis of clinical and molecular characteristics that may influence response and PFS in these patients, and anticipate completing this analysis in the first half of 2020.

Phase 2 clinical trial of APR-246 in platinum-resistant ovarian cancer, or PiSARRO-R

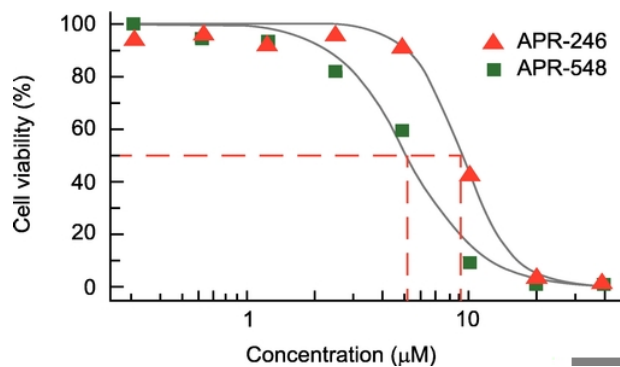
In July 2017 we initiated an open-label, multicenter Phase 2 trial, PiSARRO-R, to evaluate the adverse event profile and preliminary efficacy of varying infusion regimens of APR-246 with systemic PLD chemotherapy in platinum-resistant HGSOc. The trial enrolled 36 patients and all patients were required to have recurrent disease with PFI between 4 weeks and 6 months, and accumulation of p53 as assessed by immunohistochemistry, a surrogate marker of mutant p53. The majority (69%) of patients had received 2 or more prior lines of chemotherapy. Patients received either a 4500 mg/d fixed dose of APR-246 as a 6 hour intravenous infusion (n=28, 78%), or the same or lower fixed dose over 3 or 4 hours (n=8, 22%) for four consecutive days, followed by 40 mg/m² PLD on Day 4. The most frequently reported APR-246-related AEs were nausea, vomiting and dizziness. Limited APR-246-related grade 3+ AEs were reported, of which only anemia (n=3, 8%) was observed in more than one patient. Serious adverse events, regardless of causality, reported in more than one patient were: Intestinal obstruction (n=3, 8%) and infection (n=2, 6%). We believe the available adverse event data from the trial demonstrates that reduced duration infusion regimens with APR-246 are feasible.

As part of the PiSARRO trials, we are collaborating with the European Network for Translational Research in Ovarian Cancer, or EUTROC, with the aim to identify predictive markers of efficacy, tolerability and clinical pharmacology.

Our second product candidate, APR-548

We are developing a next-generation small molecule mutant p53 reactivator, APR-548, a novel pro-drug of MQ that has the potential to be administered in an oral dosage form. We intend to initially develop APR-548 in TP53 mutant hematological malignancies. We believe that an oral p53-reactivating drug will improve patient convenience and compliance, if approved, including for patients receiving prolonged therapy in the maintenance setting.

In preclinical testing we have observed potency with APR-548 that is superior to that of APR-246 in a Saos-2 osteosarcoma cell line expressing an Arg273His mutant p53 and the MIA-PaCa-2 pancreatic cancer cell line harboring an Arg248Trp mutant p53. The half maximal inhibitory concentration, or IC₅₀, in the Saos-2 cell line was calculated to be 5.6 mM ± 1.0 mM (n=3) for APR-548 and 9.5 mM ± 1.2 mM (n=37) for APR-246, representing an approximately 40% reduction in IC₅₀ with APR-548. In the MIA-PaCa-2 cell line, the IC₅₀ for APR-548 was calculated to be 6.0 mM (n=1) versus 19 mM (n=1) for APR-246, representing a nearly 70% reduction in IC₅₀ with APR-548.

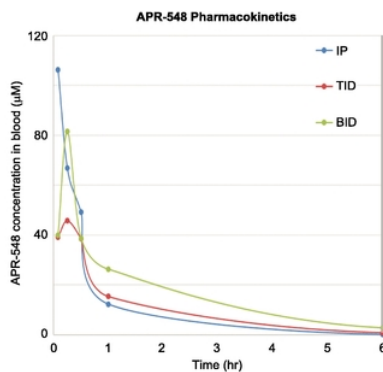
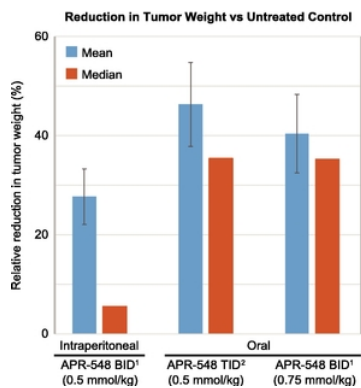


(1) Half-maximal inhibitory concentration

In xenograft studies in which mice were implanted with a breast adenocarcinoma cell line, MDA-MB-231-*luc*, we tested the *in vivo* efficacy of APR-548 when administered by twice-daily intraperitoneal (i.p.) injection, or by twice-daily or three times daily oral (PO) gavage. In these studies, mice received APR-548 for three cycles where each cycle consisted of 5 consecutive days of dosing followed by 2 days without dosing. Tumor growth inhibition was measured on day 33 post-inoculation, 3 days after the final dosing in the final cycle. In mice receiving APR-548 via oral administration, we observed reductions in tumor weight relative to untreated control mice. Results from these studies are summarized in the following table.

Xenograft Study	No. of mice	APR-548/dose (mmol/kg)	Doses/day	Dosing interval (hours)	Route	Tumor growth inhibition (%)
#1	8	0.18	2	8	i.p.	20 ± 2
	8	0.50	2	8	i.p.	26 ± 2
#2	8	0.25	2	8	i.p.	15 ± 2
	8	0.50	3	4	PO	24 ± 2
	8	0.75	2	8	PO	36 ± 5
#3	8	0.50	2	8	i.p.	28 ± 6
	8	0.50	3	4	PO	46 ± 8
	8	0.75	2	8	PO	40 ± 8
	8	0.75	2	1.50	PO	28 ± 5
#4	8	0.19	2	8	PO	3 ± 0.4
	8	0.38	2	8	PO	19 ± 3
	8	0.75	2	8	PO	40 ± 6
	8	1.50	1	—	PO	32 ± 4

In xenograft study #3 we assessed APR-548 pharmacokinetics and confirmed that circulating blood concentrations of APR-548 exceeded levels expected to be efficacious, as determined from *in vitro* results. Results from this xenograft study are summarized graphically in the following figure.



- (1) Twice daily
(2) Three times daily

In *in vivo* studies in mouse and dog, we observed high oral bioavailability of APR-548 when dosed as either an aqueous solution or as a solid in capsules. Observed oral bioavailability ranged from 75% to greater than 99%, and with no significant effect of feeding on absorption. Results from these studies are summarized in the following table.

Species	No. of animals	APR-548 dose (mg/kg)	Route	Bioavailability (%)
Mouse (C57Bl/6N)	18	20	PO (solution)	80
Mouse (CD-1)	9	50	PO (solid in capsule)	97
Mouse (CD-1)	9	50	PO (solution)	99
Dog, fed	3	10	PO (solid in capsule)	84
Dog, fasted	3	10	PO (solid in capsule)	83
Dog, fed	3	10	PO (solution)	80
Dog, fasted	3	10	PO (solution)	75

Based on results obtained through our preclinical *in vitro* and *in vivo* studies, we have initiated a series of studies required for IND submission. In our *in vitro* studies, APR-548 has not demonstrated inhibition or induction of metabolic enzymes at concentrations up to 300 nM. Studies testing APR-548 as an inhibitor or substrate of protein transporters have shown weak inhibition, with $IC_{50} > 150$ nM, is limited to the OCT2 transporter. Additional studies have shown no significant effects when tested at 10 nM in a screen of 87 different receptors, transporters and enzymes, and no effect on the human *ether-a-go-go* channel, or hERG, in a manual patch clamp assay at concentrations up to 100 nM. Metabolic studies have shown that APR-548 is metabolized slowly and all metabolites produced in human cells are also produced in our mouse and dog toxicology species. Pivotal repeat-dose GLP toxicology studies in both mouse and dog toxicology species have been initiated.

We have developed a scalable, high-purity process for the manufacture of APR-548 and have completed physical characterization studies to survey the landscape of APR-548 polymorphs with properties favorable for the development of an oral formulation to be used in clinical trials.

Manufacturing

We currently contract with third parties for the manufacture of our product candidates for certain preclinical trials and clinical trial materials, including raw materials and consumables necessary for their manufacture, consistent with applicable cGMP requirements. We intend to continue to contract for these materials in the future, including commercial manufacture if our product candidates receive marketing approval. We do not own or operate cGMP manufacturing facilities, nor do we currently plan to build our own cGMP manufacturing capabilities for the production of our product candidates for clinical or commercial use. Although we rely upon contract manufacturers for the manufacture of our product candidates for IND-enabling trials and clinical trials, we have personnel with extensive manufacturing experience who oversee our contract manufacturers. In the future, we may also rely upon collaboration partners, in addition to contract manufacturers, for the manufacture of our product candidates or any products for which we obtain marketing approval.

The active pharmaceutical ingredient, or API, for APR-246 is currently manufactured by a single contract manufacturer. Although we may do so in the future, we do not currently have arrangements in place for redundant supply of the API for APR-246. We contract with a different manufacturer for formulation of drug product, sterile fill of vials, labeling and packaging, and the storage and distribution of APR-246 to clinical sites. We believe that these third parties have sufficient capacity to meet our current demand and, in the event they fail to meet our demand, we believe that adequate alternative sources for the supply of materials for APR-246 exist. We intend to identify and qualify additional manufacturers to provide the API and other services for APR-246 prior to seeking marketing approval for APR-246.

We believe that, because APR-246 is a small molecule, it can be manufactured through reliable and reproducible synthetic processes from readily available raw materials and then purified and packaged for clinical use. We believe that the chemistry process is amenable to scale-up and requires only customary equipment in the manufacturing process.

We have a service agreement and quality agreement with Syngene International Private Limited for the manufacture of API. We have a service agreement with Cobra Biopharma for the clinical manufacture, labeling and packaging of formulated drug product. We have a manufacturing and supply agreement with Siegfried Hameln GmbH for the commercial manufacture, supply, labeling and packaging of formulated drug product.

Manufacturing clinical products is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance. Our contract manufacturers are required to comply with current good manufacturing practice regulations, which are regulatory requirements for the production of pharmaceuticals that will be used in humans.

Competition

The pharmaceutical and biotechnology industries generally, and the cancer drug sector specifically, are highly competitive and characterized by rapidly advancing technologies, evolving understanding of disease etiology and a strong emphasis on proprietary drugs. While we believe that our product candidates, development capabilities, experience and scientific knowledge provide us with competitive advantages, we face significant potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

There are a large number of companies developing or marketing treatments for cancer, including the indications for which we may develop product candidates. Many of the companies that we compete against or may compete against in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Small or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience and price, in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

The most common methods of treating patients with cancer are surgery, radiation and therapy with drugs or biologics. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of the currently-approved drug therapies are branded and subject to patent protection and may be established as standard of care for the treatment of indications for which we may choose to seek regulatory approvals. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors, and even if our drug candidates were to be approved, there can be no assurance that our drugs would displace existing treatments.

In addition to currently marketed therapies, there are also a number of drugs in late-stage clinical development to treat cancer, including for the treatment of the indications for which we are developing product candidates. These clinical-stage drug candidates may provide efficacy, safety, convenience and other benefits that are not provided by currently-marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain regulatory approval.

We are developing our lead product candidate, APR-246, to reactivate p53 for the treatment of various cancers. We are aware of other product candidates that are in clinical development as potential treatments of various cancers through the reactivation of p53. Although there is a subset of drugs that directly target the p53 pathway, there are many cancer drugs that claim to affect the p53 pathway by upstream or complementary pathways. We are aware of molecules in development that also are being explored for p53 upregulation / activation in various stages of clinical development being tested by CDG Therapeutics, Inc., Innovation Pharmaceuticals, Inc., MedVax Technologies, Inc., PMV Pharmaceuticals, Inc., and Senhwa Biosciences, Inc., among others. We are also aware of selective small molecule inhibitors that are designed to target the p53-MDM2 interaction in various stages of clinical development being tested by F-Hoffman La Roche Ltd and Hoffman La Roche Inc., or collectively Roche, Amgen Inc., Novartis AG, Aileron Therapeutics and Daiichi Sankyo Co., Ltd., including testing MDM2 inhibitors in combination with a variety of other anti-cancer agents. Finally, we are aware of several small molecules that are designed to inhibit the activity of Bcl-2 and the related protein Mcl-1 and relieve inhibition of the apoptotic cascade. Abbvie Inc.'s venetoclax has been approved in AML and chronic lymphocytic leukemia; companies with Bcl-2 or Mcl-1 inhibitors in various stages of preclinical or clinical development include Amgen Inc., Servier SAS, AstraZeneca Plc and Pfizer Inc., among others.

If APR-246 was approved for the indications for which we currently have ongoing clinical trials, it will compete with currently-marketed drugs and will likely compete with other drugs that are currently in clinical development, each as discussed below.

MDS / AML

The front-line treatments for patients with higher-risk MDS in the United States are combination chemotherapy or HMAs such as Dacogen (decitabine) or Vidaza (azacitidine). We are aware of several ongoing clinical trials aimed at expanding the use of approved chemotherapy and immunomodulatory agents in higher-risk MDS, as well as several new clinical programs testing novel technologies in this area, including product candidates from Abbvie Inc., argenx, Astex Pharmaceuticals, Inc., Celgene Corporation, CTI BioPharma Corp., Cyclacel Pharmaceuticals, Inc., Eisai Co., Ltd., Karyopharm Therapeutics Inc., Onconova Therapeutics, Inc., and Takeda Pharmaceutical Company Limited.

Intellectual property

We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the methods-of-use, formulations, dosing, manufacturing processes, and crystalline solid form of one or more of our product candidates, including APR-246, and composition of matter of our other product candidates, related technology, and other inventions that are important to our business.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions, and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets, and operate without infringing the valid and enforceable patents and other proprietary rights of third parties.

A third party may hold intellectual property, including patent rights, which are important or necessary to the development or commercialization of our product candidates. If it becomes necessary for us to use patented or proprietary technology of third parties to develop or commercialize our product candidates, we may need to seek a license from such third parties. Our business could be harmed, possibly materially, if we are unable to obtain such a license on terms that are commercially reasonable, or at all.

We may seek to expand our intellectual property estate by filing patent applications directed to dosage forms, methods of treatment, diagnostics, and additional compounds and their derivatives. Specifically, we have sought and will continue to seek patent protection in the United States and internationally for novel compositions of matter covering the compounds of our product candidates other than APR-246 and a crystal form of APR-246, the chemistries and processes for manufacturing these compounds, and the use of these compounds in a variety of therapies. The chemical structure of APR-246 is in the public domain. Accordingly, we do not own or license any composition of matter patents claiming the compound of APR-246 and will not in the future own or license any composition of matter patents claiming the chemical structure of APR-246 as described in the public domain.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags actual discoveries, we cannot be certain of the priority of inventions covered by pending patent

applications. Moreover, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office, or USPTO, to determine priority of invention or in post-grant challenge proceedings at the USPTO or at a foreign patent office, such as inter partes review and post grant review proceedings at the USPTO and opposition proceedings at the European Patent Office, that challenge priority of invention or other features of patentability. Such proceedings could result in substantial cost, even if the eventual outcome is favorable to us. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

Patent portfolio

As of September 18, 2019, our exclusively owned patent portfolio includes five U.S. issued patents, three pending U.S. provisional patent applications, approximately 113 foreign issued patents and approximately 10 pending foreign patent applications. The claims of these owned patents and patent applications are directed toward various aspects of our product candidates and research programs. Specifically, the claims of these patents and patent applications include compositions of matter for product candidates other than APR-246 and a crystal form of APR-246, methods-of-use, drug product formulations, dosing, diagnostics and methods of manufacture.

APR-246 Method of Use Family

As of September 18, 2019, we exclusively own a patent family directed to methods-of-uses of APR-246. This patent family includes one U.S. issued patent and approximately 33 patents granted in Europe (validated in Austria, Belgium, Bulgaria, Switzerland-Lichtenstein, Cyprus, Czech Republic, Germany, Denmark, Estonia, Spain, Finland, France, United Kingdom, Greece, Hungary, Ireland, Iceland, Italy, Lithuania, Luxembourg, Monaco, Netherlands, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia and Turkey), Australia, Canada, India, and Japan. The issued patents in this family are expected to expire in 2025, not giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity, or other governmental fees.

APR-246 Formulation Family

As of September 18, 2019, we exclusively own a patent family directed to formulations of APR-246. This patent family includes one U.S. issued patent and approximately 40 issued patents in Europe (validated in Austria, Belgium, Switzerland-Lichtenstein, Cyprus, Czech Republic, Germany, Denmark, Estonia, Spain, Finland, France, United Kingdom, Greece, Hungary, Ireland, Italy, Lithuania, Luxembourg, Latvia, Monaco, Malta, Netherlands, Norway, Poland, Portugal, Sweden, Slovakia, San Marino and Turkey), Australia, Canada, China, Israel, Japan, South Korea, Philippines, Russia, Singapore, and South Africa. This patent family also includes approximately 5 pending patent applications in Brazil, China, Hong Kong, India, and Thailand. The granted patents and pending applications, if issued, in this family are expected to expire in 2031, not giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity, or other governmental fees.

APR-246 Dosing Family

As of September 18, 2019, we exclusively own a pending U.S. provisional patent application directed to dosing regimens involving APR-246, which was filed in 2019. This provisional patent application is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing of our provisional patent application. If we do not timely file any non-provisional patent applications, we may lose our priority date with respect to our provisional patent application and any patent protection on the inventions disclosed in our provisional patent application. Any future U.S. patents that may issue from this provisional patent application (assuming the necessary non-provisional patent applications are timely filed and all other

applicable requirements are satisfied) are expected to expire in 2040, not giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity, or other governmental fees.

APR-246 Process and Solid Form Family

As of September 18, 2019, we exclusively own a pending U.S. provisional patent application directed to improved processes for large scale preparation of APR-246 and to a crystalline solid form comprising APR-246, which was filed in 2019. This provisional patent application is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing of our provisional patent application. If we do not timely file any non-provisional patent applications, we may lose our priority date with respect to our provisional patent application and any patent protection on the inventions disclosed in our provisional patent application. Any future U.S. patents that may issue from this provisional patent application (assuming the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) are expected to expire in 2040, not giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity, or other governmental fees.

Combination Therapy Of APR-246 With A Bcl-2 Inhibitor

As of September 18, 2019, we exclusively own a pending U.S. provisional patent application directed to a method of treatment using a combination therapy of APR-246 with a Bcl-2 inhibitor. This provisional patent application is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing of our provisional patent application. If we do not timely file any non-provisional patent applications, we may lose our priority date with respect to our provisional patent application and any patent protection on the inventions disclosed in our provisional patent application. Any future U.S. patents that may issue from this provisional patent application (assuming the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) are expected to expire in 2040, not giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity, or other governmental fees.

Next-Generation Patent Family/APR-548

As of September 18, 2019, we exclusively own a patent family directed to next-generation p53 reactivators, including APR-548. Four European pending patent applications have been filed in 2018 and one European pending patent application has been filed in 2019. In this patent family, one European patent application is pending with claims directed to compositions of matter and methods-of-use of APR-548. Any future patents that may issue from these patent applications (assuming all applicable requirements are satisfied) are expected to expire in 2039 and 2040, not giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity, or other governmental fees.

Intellectual property protection

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the Hatch-Waxman Act permits a patent holder to apply for patent term extension of a patent that covers an FDA-approved drug, which, if granted, can extend the patent term of such patent to compensate for part of the patent term lost during the FDA regulatory review process. This extension can be for up to five years beyond the original expiration date of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory

review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to an approved drug may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended.

Similar provisions are available in Europe and other non-United States jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates. While we intend to seek patent term extensions to any of our patents in any jurisdiction where such extensions are available, there is no guarantee that the applicable authorities, including the FDA and the USPTO in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to our reliance on patent protection for our inventions, product candidates and research programs, we also rely on trade secrets and confidentiality agreements to protect our technology, know-how and other aspects our business that are not amenable to, or that we do not consider appropriate for, patent protection. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. However, such confidentiality agreements and invention assignment agreements can be breached and we may not have adequate remedies for any such breach. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

Government Regulation

Government regulation and product approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the EU, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of drug products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and approval of drugs in the United States

In the United States, the FDA approves drug products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with applicable requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution,

injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each proposed indication;
- preparation and submission to the FDA of an NDA requesting marketing for one or more proposed indications;
- review by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product candidate or disease. A clinical hold may occur at any time during the life of an IND and may affect one or more specific trials or all trials conducted under the IND.

Preclinical studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as *in vitro* and animal studies to assess the potential safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

The IND and IRB processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support

of a request for an IND, a sponsor must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. The sponsor may be a company seeking to develop the drug or, as in the case of an investigator-initiated trial, the sponsor may be an investigator who is conducting the trial. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA regulatory requirements in order to use the study as support for an IND or application for marketing approval. Specifically, FDA has promulgated regulations governing the acceptance of foreign clinical trials not conducted under an IND, establishing that such studies will be accepted as support for an IND or application for marketing approval if the study was conducted in accordance with GCP, including review and approval by an independent ethics committee, or IEC, and use of proper procedures for obtaining informed consent from subjects, and the FDA is able to validate the data from the study through an on-site inspection if FDA deems such inspection necessary. The GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies. If a marketing application is based solely on foreign clinical data, the FDA requires that the foreign data be applicable to the U.S. population and U.S. medical practice; the studies must have been performed by clinical investigators of recognized competence; and the FDA must be able to validate the data through an on-site inspection or other appropriate means, if the FDA deems such an inspection to be necessary.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Human clinical trials in support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

- Phase 1:* The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- Phase 2:* The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3:* The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.
- Phase 4:* Post-approval studies, which are conducted following initial approval, are typically conducted to gain additional experience and data from treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious AEs occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, and purity of the final drug. Additionally, appropriate packaging must be selected and tested

and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from several alternative sources, including investigator-initiated trials that are not sponsored by company. Under federal law, the submission of most NDAs is additionally subject to an application user fee, which for federal fiscal year 2019 is \$2,588,478. The sponsor of an approved NDA is also subject to annual program fees, which for fiscal year 2019 are \$309,915 per eligible product.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the filing date, and most applications for "priority review" products are meant to be reviewed within six months of the filing date. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing (such as APIs), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation and priority review designation. In May 2014, the FDA published a final Guidance for Industry titled "Expedited Programs for Serious Conditions-Drugs and Biologics," which provides guidance on the FDA programs that are intended to facilitate and expedite development and review of new product candidates as well as threshold criteria generally applicable to concluding that a product candidate is a candidate for these expedited development and review programs.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated approval pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, including total or partial suspension of production, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription drug products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription drug product samples and impose requirements to ensure accountability in distribution.

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme allowing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the API, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. An applicant may submit an ANDA suitability petition to request the FDA's prior permission to submit an abbreviated application for a drug that differs from the RLD in route of administration, dosage form, or strength, or for a drug that has one different active ingredient in a fixed-combination drug product (i.e., a drug product with multiple active ingredients). At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists may consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years from the date the NDA is approved, unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; it does, however, block the FDA from approving ANDAs during the period of exclusivity. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant, and for which the applicant has not obtained a right of reference. If the 505(b)(2) applicant can establish that reliance on FDA's previous findings of safety and effectiveness is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional bridging studies or measurements, including clinical trials, to support the change from the previously approved reference drug. The FDA may then approve the new product candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Hatch-Waxman patent certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods-of-use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or 505(b)(2) application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from granting final approval of the application until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired.

Pediatric studies and exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act of 2012, sponsors must also submit pediatric study plans prior to the assessment data.

Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If the sponsor of a product with orphan designation receives the first FDA approval for that drug for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same

indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

Patent term restoration and extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA less any time the applicant did not act with due diligence during the period, plus the time between the submission date of an NDA and the ultimate approval date less any time the applicant did not act with due diligence during the period. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We plan to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

FDA approval and regulation of companion diagnostics

A therapeutic product may rely upon an *in vitro* companion diagnostic for use in selecting the patients that will be more likely to respond to that therapy. If safe and effective use of a therapeutic depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the drug therapeutic and *in vitro* companion diagnostic device on issues related to co-development of the products.

If FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. The review of *in vitro* companion diagnostics in conjunction with the review of our therapeutic treatments for cancer will, therefore, likely involve coordination of review by the FDA's

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval, or PMA. The FDA has generally required *in vitro* companion diagnostics intended to select the patients who will respond to cancer treatment to obtain a PMA for that diagnostic simultaneously with approval of the drug. We expect that any companion diagnostic developed for use with APR-246 will utilize the PMA pathway.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee of \$322,147 for most PMAs for FY 2019. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards are not maintained or problems are identified following initial marketing.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to

comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the U.S.

The 21st Century Cures Act

On December 13, 2016, then-President Obama signed 21st Century Cures Act, or the Cures Act, into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the PHS Act to reauthorize and expand funding for the NIH. The Cures Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the PHS Act, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of "real world evidence" to help support approval of new indications for approved drugs; provides a new "limited population" approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a "regenerative advanced therapy," thereby making it eligible for certain expedited review and approval designations.

Regulations outside the United States

Regulations and procedures governing approval of drug products in the EU

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of drug products in the EU generally follows the same lines as in the United States and involves satisfactorily completing preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication, as well as the submission to the relevant competent authorities of a marketing authorisation application, or MAA, and actual granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval. Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on Good Clinical Practice, a system for the approval of clinical trials in the EU has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a EU member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states.

Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by an investigational drug product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the EU adopted a new Clinical Trials Regulation, (EU) No 536/2014, which will replace the current Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the EU, the new EU clinical trials legislation was passed as a regulation that is directly applicable in all EU member states without the need for implementation into the member states' national laws. All clinical trials performed in the EU are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (EU) No 536/2014 becomes applicable. According to the current plans of the European Medicines Agency, or EMA, the new Clinical Trials Regulation will become applicable in 2020. The Clinical Trials Directive 2001/20/EC will, however, still apply three years from the date of entry into application of the Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for old system.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trial in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the EU portal; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states; a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed jointly by all member states concerned. Part II is assessed separately by each member state concerned; strictly defined deadlines for the assessment of clinical trial applications; and the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Clinical Trials Regulation.

Marketing Authorization. To obtain a marketing authorization for a product under EU regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in EU member states (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EU. In the case of pediatric patients, Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan drug products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the

assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a drug product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Regulatory data protection in the EU. In the EU, new chemical entities approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic drug product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of authorization and renewals. A marketing authorization shall be valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization shall be valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the EU market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Orphan drug designation and exclusivity. Regulation (EC) No 141/2000 on orphan drug products provides that a drug shall be designated as an orphan drug if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or that the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Regulation (EC) No 847/2000 sets out criteria and procedures governing designation of orphan drugs in the EU. Specifically, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, the EMA or the member state competent authorities, cannot accept another application for a marketing authorization, or grant a marketing authorization, for a similar drug product for the same indication. The period of market exclusivity is extended by two years for medicines that have also complied with an agreed PIP.

This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for ODD, for example because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of "clinical superiority" by a similar drug product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply).

Regulatory requirements after a marketing authorization has been obtained. In case an authorization for a drug in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of drug products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed, has to be ensured.
- The manufacturing of authorized drugs, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the EU, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and identity.
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and EU member state laws.

Authorization to market companion diagnostics in the EU.

In the European Economic Area, or EEA, *in vitro* medical devices are currently required to conform with the essential requirements of the European Union Directive on *in vitro* diagnostic medical devices (Directive No 98/79/EC, as amended). To demonstrate compliance with the essential requirements, the manufacturer must undergo a conformity assessment procedure. The conformity assessment varies according to the type of medical device and its classification. The conformity assessment of *in vitro* diagnostic medical devices can require the intervention of an accredited EEA Notified Body. If successful, the conformity assessment concludes with the drawing up by the manufacturer of an EC Declaration of Conformity entitling the manufacturer to affix the CE mark to its products and to sell them throughout the EEA. On April 5, 2017, the EU adopted the new In Vitro Device Regulation (EU) 2017/746, or IVDR, which repeals and replaces Directive No 98/79/EC. Unlike directives, which must be implemented into the national laws of the EU member states, a regulation is directly applicable, i.e., without the need for adoption of EU member state laws implementing them, in all EEA member states. The IVDR, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU for *in vitro* diagnostic medical devices and ensure a high level of safety and health while supporting innovation. The IVDR

will not become fully applicable until five years following its entry into force. Once applicable, the IVDR will among other things:

- strengthen the rules on placing devices on the market and reinforce surveillance once they are available;
- establish explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance and safety of devices placed on the market;
- improve the traceability of medical devices throughout the supply chain to the end-user or patient through a unique identification number; and
- set up a central database to provide patients, healthcare professionals and the public with comprehensive information on products available in the EU.

Brexit and the regulatory framework in the United Kingdom

On June 23, 2016, the electorate in the U.K., voted in favor of leaving the EU, commonly referred to as Brexit. The U.K. government communicated the notice of withdrawal to the EU on March 29, 2017. Since the regulatory framework for drug products in the U.K. covering quality, safety and efficacy of drug products, clinical trials, marketing authorization, commercial sales and distribution of drug products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the U.K. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the U.K.

Pharmaceutical coverage, pricing and reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients and healthcare providers are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other comparable government authorities. Even if our product candidates are approved, sales of our products will depend, in part, on the extent to which third-party payors, including federal health care programs in the United States, such as Medicare and Medicaid, and commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that a payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged for, examining the medical necessity of, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication. Coverage and reimbursement by a third-party payer may depend upon a number of factors, including, without limitation, the third-party payer's determination that use of a therapeutic product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payer supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover our product candidates could reduce health care provider prescribing and/or patient utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. In addition, prices for drugs may be reduced by mandatory discounts or rebates required by federal health care programs or private payers and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. It is difficult to predict how Medicare coverage and reimbursement policies will be applied to products for which the company receives marketing approval in the future and coverage and reimbursement under different federal health care programs is not always consistent. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products for which we receive marketing approval.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for our product candidates will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our product candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the EU, pricing and reimbursement schemes vary widely from member state to member state. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies (so called health technology assessment, or HTA) in order to obtain reimbursement or pricing approval. EU member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased

the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on healthcare costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare law and regulation

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare and Medicaid Services, or CMS, other divisions of the U.S. Department of Health and Human Services (such as the Office of Inspector General and the Health Resources and Service Administration), the U.S. Department of Justice, and individual U.S. Attorney offices, and state and local governments. For example, sales, marketing and scientific/educational grant programs may have to comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the privacy and security provisions of HIPAA, and similar state laws, each as amended, as applicable. Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to these broadly applicable healthcare laws and regulations that may constrain our business and/or financial arrangements.

Restrictions under applicable federal and state healthcare laws and regulations, include, without limitation, the following:

- *The Federal Anti-Kickback Statute*—An intent-based federal criminal statute that prohibits, among other things, any person from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made, in whole or in part, by a federal health care program, such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. The PPACA, among other things, amended the intent requirement of the federal Anti-Kickback Statute, so that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. The Anti-Kickback Statute has also been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and individuals, such as prescribers, patients, purchasers, and formulary managers on the other the other hand. A conviction for violation of the Anti-Kickback Statute results in criminal fines and requires mandatory exclusion from participation in federal health care programs. Although there are a number of statutory exceptions and regulatory safe harbors to the federal Anti-Kickback Statute that protect certain common industry practices from prosecution, the exceptions and safe harbors are narrowly drawn, and arrangements may be subject to scrutiny or penalty if they do not fully satisfy all elements of an available exception or safe harbor. The Anti-Kickback Statute safe harbors, including the discount safe harbor, are the subject of possible regulatory reforms. Any changes to the safe harbors may impact our future contractual and other arrangements with pharmacy benefit managers, third-party payors, wholesalers and distributors, healthcare providers and prescribers, and other entities, as well as our future pricing strategies.

- *The Federal Civil False Claims Act*—Imposes civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or knowingly making using or causing to be made or used a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at \$11,181 to \$22,363 per false claim or statement for penalties assessed after January 29, 2018, with respect to violations occurring after November 2, 2015. Among other reasons, pharmaceutical companies have been investigated and/or subject to government enforcement actions asserting liability under the federal civil False Claims Act in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes (e.g., under the Medicaid Drug Rebate Program), and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. In addition, manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Criminal prosecution is also possible for making or presenting a false, fictitious or fraudulent claim to the federal government.
- *The Federal Criminal Statute on False Statements Relating to Health Care Matters*—Makes it a crime to knowingly and willfully falsify, conceal, or cover up a material fact, make any materially false, fictitious, or fraudulent statements or representations, or make or use any materially false writing or document knowing the same to contain any materially false, fictitious, or fraudulent statement or entry in connection with the delivery of or payment for federally funded healthcare benefits, items, or services.
- *HIPAA Criminal Federal Health Care Fraud Statute*—Enacted as part of the Health Insurance Portability and Accountability Act of 1996, makes it a crime to knowingly and willfully falsify, conceal, or cover up a material fact, make any materially false, fictitious, or fraudulent statements or representations, or make or use any materially false writing or document knowing the same to contain any materially false, fictitious, or fraudulent statement or entry in connection with the delivery of or payment for federally funded healthcare benefits, items, or services.
- *The Federal Civil Monetary Penalties Law*—Authorizes the imposition of substantial civil monetary penalties against an entity, such as a pharmaceutical manufacturer, that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal healthcare programs to provide items or services reimbursable by a federal healthcare program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment.
- *HIPAA Health Information Privacy and Security*—HIPAA imposes privacy, security, and breach reporting obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouse as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including, among other requirements, mandatory contractual terms and technical safeguards to protect the privacy, security and transmission of individually identifiable health information, and require notification

to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.

- *The Federal Physician Payments Sunshine Act*—Requires "applicable manufacturers" of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the State Children's Health Insurance Program, among others, to track and report annually to the federal government (for disclosure to the public) certain payments and other transfers of value they make to "covered recipients." The term covered recipients includes physicians, teaching hospitals, and, for reports submitted on or after January 1, 2022, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse midwives. Failure to submit required information may result in civil monetary penalties.
- *The Federal Food, Drug and Cosmetic Act*—A set of laws, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices.
- *Analogous State and Foreign Laws*—There are state and foreign law equivalents of the above federal laws, such as the Anti-Kickback Statute and the False Claims Act, which may apply to items or services reimbursed by any third-party payor, including commercial insurers (i.e., so-called "all-payor anti-kickback laws"), as well as state and foreign laws that govern the privacy and security of health information or personally identifiable information in certain circumstances, including state health information privacy and data breach notification laws which govern the collection, use, disclosure, and protection of health-related and other personal information, many of which differ from each other in significant ways and, with respect to state laws, are often not pre-empted by HIPAA, thus requiring additional compliance efforts.
- *State and Foreign Laws Regulating Pharmaceutical Manufacturer Compliance Programs and Other Practices*—Some state and foreign laws require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or to track and report gifts, compensation, or other remuneration to physicians and other healthcare providers. Several U.S. states and localities have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports, and/or make periodic public disclosures on sales, marketing, pricing, clinical trials, and other activities. Other state laws prohibit certain marketing-related activities including the provision of gifts, meals or other items to certain healthcare providers, and restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs. In addition, several recently passed state laws require disclosures related to state agencies and/or commercial purchasers with respect to certain price increases that exceed a certain level as identified in the relevant statutes. Some of these laws and regulations contain ambiguous requirements that government officials have not yet clarified. Given the lack of clarity in the laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent federal and state laws and regulations.

We expect that one or more of our products, if approved, may be eligible for coverage under Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain drug products, that are medically necessary to treat a beneficiary's health condition. In addition, one or more of our products, if approved, may be covered and reimbursed under other federal health care programs, such as Medicaid and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing

Program, the manufacturer must extend discounts to entities that participate in the program. As part of the requirements to participate in these government programs, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average manufacturer price and best price.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, guidance, case law or other applicable law. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, exclusion from participation in federal health care programs, such as Medicare and Medicaid, disgorgement, reputational harm, additional oversight and reporting obligations pursuant to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with applicable laws and regulations, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to market our products, if approved, and adversely impact our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws and regulations, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, it may be costly to us in terms of money, time and resources, and they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

U.S. healthcare reform

In the United States and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of our future collaborators, to profitably sell any drugs for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we, or our future collaborators, may receive for any approved drugs. For example, the PPACA has substantially changed healthcare financing and delivery by both governmental and private insurers. Among the PPACA provisions of importance to the pharmaceutical industry, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain federal programs identified in the PPACA;
- expansion of beneficiary eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price" for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of the types of entities eligible for the 340B drug discount program;
- establishment of the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount, which increased to 70% starting in 2019, off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- establishment of the Center for Medicare and Medicaid Innovation within the Centers for Medicare and Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- reporting of certain financial arrangements between manufacturers of drugs, biologics, devices, and medical supplies and physicians and teaching hospitals under the Physician Payments Sunshine Act; and
- annual reporting of certain information regarding drug samples that manufacturers and distributors provide to licensed practitioners.

There have been judicial and Congressional challenges to the PPACA, as well as efforts by the Trump administration to repeal or replace certain aspects of the PPACA that contribute to regulatory uncertainty that could affect the profitability of our products. Since January 2017, President Trump has signed several Executive Orders and other directives designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements mandated by the PPACA. In December 2018, a federal district court in Texas ruled the individual mandate was unconstitutional and could not be severed from the PPACA. As a result, the court ruled the remaining provisions of the PPACA were also invalid, though the court declined to issue a preliminary injunction with respect to the PPACA. In April 2019, in a brief filed in the Fifth Circuit Court of Appeals, the Trump Administration took the position that the individual mandate was unconstitutional, that it could not be severed from the PPACA, and, as a result, the PPACA must be invalidated in its entirety. The case is pending before the Fifth Circuit, and it remains unclear whether, and to what extent, the PPACA may be affected by the Fifth Circuit's and possibly other courts' rulings.

While Congress has not enacted legislation to comprehensively repeal the PPACA, at least two bills affecting the implementation of the PPACA have been signed into law, including the repeal, effective January 1, 2019, of the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain fees mandated by the PPACA, including the so-called "Cadillac" tax on certain high-cost employer-sponsored health insurance plans, the annual fee imposed on certain health insurance providers, and the medical device excise tax on non-exempt medical devices. Moreover, effective January 1, 2019, the Bipartisan Budget Act of 2018, among other things, further amends portions of the Social Security Act implemented as part of the PPACA to increase from 50% to 70% the point-of-sale discount that pharmaceutical manufacturers participating in the Coverage Gap Discount Program provide to eligible Medicare Part D beneficiaries during the coverage gap phase of the Part D benefit, commonly referred to as the "donut hole," and to reduce standard beneficiary cost sharing in the coverage gap from 30% to 25% in most Medicare Part D plans. In the future, there may be additional challenges and/or amendments to the PPACA. It remains to be seen precisely what any new legislation will provide, when or if it will be enacted, and what impact it will have on the availability and cost of healthcare items and services, including drug products.

More recently, the cost of prescription pharmaceuticals has been the subject of considerable discussion in the United States. Congress has begun developing legislation and the Trump Administration has proposed and begun implementing regulatory reforms to further increase transparency around prices and price increases, lower out-of-pocket costs for consumers, and decrease spending on prescription drugs by government programs. Congress has conducted or is in the process of conducting inquiries into the prescription drug industry's pricing practices. The Trump Administration's budget proposal for fiscal year 2019 contained additional drug price control measures that could be enacted in future legislation, including, for example, measures to end Medicare Part B coverage of medications and to shift those medication costs to Medicare Part D, to allow some states to negotiate prescription drug prices under Medicaid and to eliminate cost sharing for generic drugs for low-income patients. While several proposed reform measures will require Congress to pass legislation to become effective, Congress and the Trump Administration have each indicated that it will continue to seek new legislative and/or regulatory measures to address prescription drug costs. At the state level, legislatures are increasingly passing legislation and states are implementing regulations designed to control spending on and patient out-of-pocket costs for drug products. Implementation of cost containment measures or other healthcare reforms that affect the pricing and/or availability of drug products may impact our ability to generate revenue, attain or maintain profitability, or commercialize products for which we may receive regulatory approval in the future.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and/or new payment methodologies, and place additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels and imposition of more rigorous coverage criteria or new payment methodologies may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any coverage or reimbursement policies instituted by Medicare or other federal health care programs may result in a similar policies from private payors. The implementation of cost containment measures or other healthcare reforms may affect our ability to generate revenue, attain or maintain profitability, or commercialize our drug candidates. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

Legal proceedings

We are not currently subject to any legal proceedings.

Facilities

We have facilities in Boston, Massachusetts and Stockholm, Sweden. Our Boston facilities consist of office space of approximately 2,295 square feet under an operating lease agreement that expires in 2021. Our Stockholm facilities consist of office and laboratory space of approximately 3,980 square feet under an operating lease agreement that expires in 2022.

Employees

As of September 26, 2019, we had 14 full-time employees. Of the workforce, 9 employees are directly engaged in research and development with the rest providing administrative, business and operations support. We are not bound by any collective bargaining agreements. We consider the relationship with our employees to be good. We also use outside consultants and contractors with unique expertise and skills for limited engagements. As of September 26, 2019, we utilized multiple outside consultants or contractors that represented approximately 4 full-time equivalents to supplement our full-time workforce.

Management

The following table sets forth the name, age as of September 26, 2019 and position of each of our executive officers and directors.

Name	Age	Position
Executive Officers		
Christian S. Schade	58	President and Chief Executive Officer and Director
Scott M. Coiante	52	Senior Vice President, Chief Financial Officer
Eyal C. Attar, M.D.	49	Senior Vice President, Chief Medical Officer
Lars Abrahmsen, Ph.D.	61	Senior Vice President, Chief Scientific Officer
Gregory A. Korbelt, Ph.D.	43	Vice President of Business Development
Non-Employee Directors		
Scott M. Rocklage, Ph.D.	65	Chairman of the Board of Directors
Guido Magni, M.D., Ph.D.	66	Director
Johan Christenson, M.D., Ph.D.	61	Director
Jonathan Hepple, Ph.D.	48	Director
Bernd R. Seizinger, M.D., Ph.D.	62	Director
John B. Henneman, III	57	Director

Executive officers

Christian S. Schade has served as our President and Chief Executive Officer and as a member of our board of directors since June 2016. Mr. Schade has more than 30 years of private and public pharmaceutical and biotechnology industry experience, as well as broad corporate finance expertise from his tenure in the investment banking industry. Prior to joining Aprea Therapeutics, he was Chief Executive Officer of Novira Therapeutics, which was acquired in December 2015 by Johnson & Johnson in an all-cash transaction. Prior to joining Novira, Mr. Schade was Executive Vice President and Chief Financial Officer at Omthera, a NASDAQ-listed specialty pharmaceuticals company focused on the development and commercialization of new therapies for dyslipidemia. At Omthera, Mr. Schade was responsible for all corporate finance, accounting and business development activities, and led the sale of Omthera in July 2013 to AstraZeneca. He also was Executive Vice President and Chief Financial Officer at NYSE-listed NRG Energy, and from 2000 to 2009, he was Senior Vice President of Administration and Chief Financial Officer at Medarex, a biopharmaceutical company focused on antibody-based therapeutic products for oncology, inflammation, autoimmune disorders and infectious diseases. Mr. Schade played a pivotal role in the acquisition of Medarex by Bristol-Myers Squibb, leading the negotiations for the sale and the eventual merger-integration process of the research, development and administrative functions. Before joining Medarex, Mr. Schade served as Managing Director at Merrill Lynch in London and held various corporate finance and capital markets positions in New York and London for both Merrill Lynch and JP Morgan Chase & Co. Mr. Schade currently serves on the board of directors of Integra Life Sciences Inc. and has previously served on the board of directors of Indivior PLC. Mr. Schade received an M.B.A. from the Wharton School at the University of Pennsylvania and an A.B. from Princeton University.

We believe Mr. Schade is qualified to serve as our President and Chief Executive Officer and on our board of directors because of his extensive experience in leadership and management roles at various life sciences companies.

Scott M. Coiante has served as our Senior Vice President, Chief Financial Officer since August 2019. Mr. Coiante joined Aprea from Agile Therapeutics, or Agile, where he was Senior Vice President and Chief Financial Officer. Having served at Agile since 2010, he played a leadership role in the company and in the development of the internal finance and accounting infrastructure. Prior to joining

Agile, he was from 2002 Vice President of Finance and Treasurer at Medarex, Inc., formerly a NASDAQ listed biotech company that was acquired in 2009 by Bristol Myers Squibb. From 1989 to 2002, Mr. Coiante held management positions of increasing responsibilities at Ernst & Young LLP. Mr. Coiante received a B.S. in Accounting from Villanova University.

Eyal C. Attar, M.D. has served as our Senior Vice President, Chief Medical Officer since April 2019. Dr. Attar joined Aprea from Agios Pharmaceuticals, where he was Senior Medical Director and IDH Hematology Medical Lead. Having served at Agios since 2014, Dr. Attar played a leadership role in the clinical development and approval of IDHIFA and TIBSOVO for patients with relapsed/refractory AML. Prior to Agios, he served on the clinical staff at the Massachusetts General Hospital Cancer Center, where Dr. Attar was a member of the Center for Leukemia and Assistant Professor of Medicine at Harvard Medical School. He completed his residency in Internal Medicine at Brigham and Women's Hospital and held fellowships in hematology and oncology in the Dana-Farber Partners Cancer Care Hematology/Oncology Fellowship Program. Dr. Attar received his medical degree from the University of North Carolina School of Medicine.

Lars Abrahmsen, Ph.D. has served as our Senior Vice President, Chief Scientific Officer since October 2014. Dr. Abrahmsen has more than 30 years of experience in research and drug development in the pharmaceutical industry, both with small molecules and biopharmaceuticals. Beginning with postdoctoral work at Genentech, he has also worked at Biovitrum, Pharmacia&Upjohn, Pharmacia and KabiGen. More recently he served as Chief Scientific Officer at Affibody from 2004-2010 and as SVP of Protein Therapeutics at Algeta from 2010-2013. Dr. Abrahmsen has experience from discovery research to preclinical development and has primarily focused on projects within oncology and metabolic diseases. Dr. Abrahmsen received a Ph.D. in Biochemistry and an M.S. in Chemistry, both from the Royal Institute of Technology in Stockholm, Sweden.

Gregory A. Korbel, Ph.D. has served as our Vice President of Business Development since July 2016. Dr. Korbel has 12 years of experience in the biotechnology and pharmaceutical industries. Prior to joining Aprea Therapeutics, he was Director of Business Development and Operations at Novira Therapeutics, which was acquired in December 2015 by Johnson & Johnson, and served as Director of Research Operations subsequent to the acquisition. In addition to consulting for venture capital and biotechnology firms, he formerly served as Senior Scientist at Invitrogen/Life Technologies. Dr. Korbel received an M.B.A. from the Wharton School at the University of Pennsylvania, a Ph.D. in Chemistry from Harvard University and a B.A. from Vanderbilt University.

Non-employee directors

Scott M. Rocklage, Ph.D. has served as a member of our board of directors since 2016 and as Chairman of our board of directors since June 2017. Dr. Rocklage joined 5AM Ventures in 2003 as a Venture Partner, became a Managing Partner in 2004 and transitioned to Founding Partner in 2017. Dr. Rocklage has over three decades of healthcare management experience with strategic leadership responsibilities that led to FDA approval of three U.S. New Drug Applications (Omniscan™, Teslascan® and Cubicin®). He has served as Chairman and CEO of Cubist Pharmaceuticals, President and CEO of Nycomed Salutar and has also held R&D positions at Salutar and Catalytica. Dr. Rocklage formerly served as Board Chairman of Relypsa (acquired by Vifor Pharma) and Novira (acquired by J&J). He currently serves as Board Chairman of Expansion, Kinestral and Cidara (NASDAQ: CDTX) and is a Board member at NodThera and Nouscom. He was formerly Executive Chairman of Ilypsa (acquired by Amgen), Miikana (acquired by Entremed) and Semprus (acquired by Teleflex). Dr. Rocklage received his B.S. in Chemistry from the University of California, Berkeley and his Ph.D. in Chemistry from MIT where he conducted research in the laboratory of Richard R. Schrock (Nobel Prize in Chemistry in 2005). He is an inventor or co-inventor of over 30 U.S. patents and has produced more than 100 peer-reviewed publications.

We believe Dr. Rocklage is qualified to serve on our board of directors because of his extensive leadership and investment experience in the life sciences sector and strong scientific background.

Guido Magni, M.D., Ph.D. has served as a member of our board of directors since March 2016. Dr. Magni has served a Partner with Versant Ventures since February 2012. Dr. Magni previously served as a Managing Director of EuroVentures, a Versant incubator, where he was intimately involved in several biotech investments including Synosia (sold to Biotie Therapies), Flexion and Okairos. Dr. Magni was previously the Global Head of the Medical Science Department of Roche Pharmaceuticals in Basel, Switzerland. During his twelve-year term at Roche, Dr. Magni oversaw the development and the registration of a large number of new chemical and biological entities including Cellcept, Pegasys, Mabthera, Xeloda, Herceptin, Tamiflu and Tarceva. Currently, Dr. Magni serves on the Board of Biotie and AM Pharma, with previous board positions at Adolor Corporation and Anabasis Pharma before their recent acquisitions. Dr. Magni was trained at the University of Padua with a specialization in neuro-psychiatry. He is the co-author of over 100 peer-reviewed papers.

We believe Dr. Magni is qualified to serve on our board of directors because of his management and investment experience in the life sciences sector and medical and scientific background.

Johan Christenson, M.D., Ph.D. has served as a member of our board of directors since 2016. Dr. Christenson is a Partner of HealthCap. Prior to joining HealthCap in 2001, Dr. Christenson was with SEB Företagsinvest (the venture capital arm of SEB) to supervise its health care portfolio. He has senior management experience from Astra Pain Control as Project Director and AstraZeneca as Global Product Director and member of the global therapy area management team of pain and inflammation. Dr. Christenson received his medical training at the Karolinska Institute and received his Ph.D. in basic neuroscience in 1991. He served as a lecturer in neuroscience and also held a position as Assistant Dean at the Karolinska Institute Graduate School for two years. Dr. Christenson has four years of clinical specialist training in paediatrics and paediatric neurology.

We believe Dr. Christenson is qualified to serve on our board of directors because of his management and investment experience in the life sciences sector and medical and scientific background.

Jonathan Hepple, Ph.D. has served as a member of our board of directors since April 2015. Dr. Hepple is a co-founder of Rosetta Capital Limited, where he has served as a Partner since January 2009. He has more than twenty years investment experience in the life sciences industry. He started his investment career at Rothschilds Asset Management and he was also a partner at Seroba Life Sciences where he was on the boards of Covagen and Opsona. Dr. Hepple has held Board Director and Observer roles in portfolio companies such as Catalyst Biosciences, Glycomimetics, Novimmune, Procertus and Tranzyme. He has served on the board of Clanotech AB since June 2013. He received his Ph.D. from Cambridge University for cancer research.

We believe Dr. Hepple is qualified to serve on our board of directors because of his experience as an investor and board member in the life sciences industry, as well as his scientific background.

Bernd R. Seizinger, M.D., Ph.D. has served as a member of our board of directors since 2015. Dr. Seizinger is a board member in a number of companies, including Opsona (Dublin, Ireland), Agennix AG (Princeton, NJ; Houston, TX; Munich, Germany) and TriMod Ltd. (Dublin, Ireland). He is Chairman of Opsona Ltd. And acting Chairman of Trimod Ltd. From 1998 to 2009, Dr. Seizinger was President and Chief Executive Officer of GPC Biotech before it merged with Agennix AG. Prior to his corporate appointments, he was at Massachusetts General Hospital and Harvard Medical School.

We believe Dr. Seizinger is qualified to serve on our board of directors because of his perspective and experience as a leader and board member in the life sciences industry, as well as his strong medical and scientific background.

John B. Henneman III has been a member of our board of directors since August 2019. Mr. Henneman has more than 25 years of combined financial and operational management experience in the life sciences industry. From July 2018 until November 2018, Mr. Henneman served as the Chief Administrative Officer of NewLink Genetics Corporation, a biotechnology company, and prior to that, served as NewLink's Executive Vice President and Chief Financial Officer from October 2014 to July 2018. From 1998 to 2014, Mr. Henneman served at Integra LifeSciences Holdings Corp., a publicly-held medical device company, in various capacities. Before becoming Integra's Chief Financial Officer in 2007, Mr. Henneman was Chief Administrative Officer, responsible for Integra's regulatory affairs, quality systems, clinical affairs, human resources, information systems and legal affairs functions, the management of Integra's surgical instruments business, and Integra's business development function. Mr. Henneman serves on the boards of directors of R1 RCM, Inc., a publicly-held revenue cycle technology and management services company, SeaSpine Holdings Corporation, a publicly-held medical technology company, and Alafair Biosciences, Inc., a privately-held medical device company. Mr. Henneman is also senior advisor to Prettybrook Partners, a private equity firm, and a consultant to SparkMed Advisors LLC, which provides consulting and other services to start-up medical device and biotechnology companies.

We believe Mr. Henneman is qualified to serve on our board of directors because of his senior management experience at NewLink and Integra and his service on the boards of R1 RCM, Inc. and SeaSpine, as well as his extensive experience in the areas of finance, financial accounting, business transactions, and mergers and acquisitions, qualify him to serve on our board of directors.

Board composition and election of directors

Board composition

Our board of directors currently consists of seven members. After the completion of this offering, the number of directors will be fixed by our board of directors, subject to the terms of our amended and restated certificate of incorporation and amended and restated bylaws. Each of our current directors will continue to serve as a director until the election and qualification of his or her successor, or until his or her earlier death, resignation or removal.

Our certificate of incorporation and bylaws that will become effective as of the closing date of this offering provide that the authorized number of directors may be changed only by resolution of our board of directors. Our certificate of incorporation and bylaws will also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of our shares of common stock present in person or by proxy and entitled to vote, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

We have no formal policy regarding board diversity. Our priority in selection of board members is identification of members who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business and understanding of the competitive landscape.

Director independence

Under the rules of NASDAQ, independent directors must comprise a majority of a listed company's board of directors within one year of the completion of its initial public offering. In addition, the rules of NASDAQ require that, subject to specified exceptions, each member of a listed company's audit, compensation and corporate governance and nominating committees be independent. Our board of directors has determined that Scott M. Rocklage, Johan Christenson, John B. Henneman III, Jonathan Hepple, Guido Magni and Bernd R. Seizinger qualify as "independent"

directors in accordance with the NASDAQ listing requirements. The NASDAQ independence definition includes a series of objective tests, such as that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his family members has engaged in various types of business dealings with us. In addition, as required by NASDAQ rules, our board of directors has made a subjective determination as to each independent director that no relationships exist, which, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Classified board of directors

In accordance with our amended and restated certificate of incorporation to be in effect immediately prior to the completion of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Effective upon the completion of this offering, we expect that our directors will be divided among the three classes as follows:

- the Class I directors will be Bernd R. Seizinger, M.D., Ph.D. and Jonathan Hepple, Ph.D. and their term will expire at the annual meeting of stockholders to be held in 2020;
- the Class II directors will be Guido Magni, M.D., Ph.D. and Johan Christenson, M.D., Ph.D. and their term will expire at the annual meeting of stockholders to be held in 2021; and
- the Class III directors will be Christian S. Schade, Scott M. Rocklage, Ph.D. and John B. Henneman, III and their term will expire at the annual meeting of stockholders to be held in 2022.

Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control of our company.

Board committees

Audit committee

Upon the completion of this offering, our board of directors will have an audit committee and our board of directors will adopt an audit committee charter, which will define the audit committee's principal functions, including oversight related to:

- our accounting and financial reporting process;
- appointing our independent registered public accounting firm;
- evaluating the independent registered public accounting firm's qualifications, independence and performance;
- the compensation, retention, oversight of the work of, and termination of the independent registered public accounting firm;
- discussing with management and the independent registered public accounting firm the results of the annual audit and the review of our quarterly financial statements;
- pre-approving all audit and permitted non-audit and tax services to be provided;

- monitoring the rotation of partners of the independent registered public accounting firm on our engagement team in accordance with requirements established by the SEC;
- reviewing our financial statements and our management's discussion and analysis of financial condition and results of operations to be included in our annual and quarterly reports to be filed with the SEC;
- reviewing our critical accounting policies and estimates; and
- reviewing the audit committee charter and the committee's performance at least annually.

Upon the completion of this offering, our audit committee will be composed of John B. Henneman III, Bernd R. Seizinger and Jonathan Hepple. John B. Henneman III serves as the chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and NASDAQ. Our board of directors has determined that John B. Henneman III is an audit committee financial expert as defined under the applicable rules of the SEC and has the requisite financial sophistication as defined under the applicable rules and regulations of NASDAQ. Under the rules of the SEC, members of the audit committee must also meet heightened independence standards. However, a minority of the members of the audit committee may be exempt from the heightened audit committee independence standards for one year from the date of effectiveness of the registration statement of which this prospectus forms a part. Each of the members of our audit committee is independent under the applicable rules and regulations of NASDAQ. The audit committee will operate under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

Compensation committee

Upon the completion of this offering, our board of directors will have a compensation committee and our board of directors will adopt a compensation committee charter, which will define the compensation committee's principal functions, including recommending policies relating to compensation and benefits of our directors, officers and employees. Among other matters, the compensation committee will review and recommend corporate goals and objectives relevant to compensation of our Chief Executive Officer, evaluate the performance of our Chief Executive Officer in light of those goals and objectives and recommend to our board of directors the compensation of the Chief Executive Officer based on such evaluations. The compensation committee will also recommend to our board of directors the issuance of stock options and other awards under our stock plans. The compensation committee will review and evaluate, at least annually, the performance of the compensation committee and its members, including adherence by the compensation committee to its charter. Upon the completion of this offering, our compensation committee will be composed of Scott M. Rocklage, John B. Henneman III and Johan Christenson. Scott M. Rocklage serves as the chairperson of the committee. Each of the members of our compensation committee is independent under the applicable rules and regulations of NASDAQ and is a "non-employee director" as defined in Rule 16b-3 promulgated under the Securities Exchange Act. The compensation committee will operate under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

Nominating and corporate governance committee

Upon the completion of this offering, our board of directors will have a nominating and corporate governance committee and our board of directors will adopt a nominating and corporate governance committee charter. The nominating and corporate governance committee will be responsible for making recommendations to our board of directors regarding candidates for directorships and the size and composition of our board of directors. Among other matters, the nominating and corporate governance committee will be responsible for developing and monitoring compliance with our corporate governance guidelines and reporting and making recommendations to our board of directors concerning governance

matters. Upon the completion of this offering, our nominating and corporate governance committee will be composed of Guido Magni, Bernd R. Seizinger and Jonathan Hepple. Guido Magni serves as the chairman of the committee. Each of the members of our nominating and corporate governance committee is an independent director under the applicable rules and regulations of NASDAQ relating to nominating and corporate governance committee independence. The nominating and corporate governance committee will operate under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

Compensation committee interlocks and insider participation

None of our executive officers serves, or in the past year has served, as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee. None of the members of our compensation committee is, or has ever been, an officer or employee of our company.

Code of business conduct and ethics

We plan to adopt a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, which will be effective upon the completion of this offering. Following this offering, we will post a copy of the code on the Corporate Governance section of our website. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Limitations on liability and indemnification

Our amended and restated certificate of incorporation, which will become effective immediately prior to the completion of this offering, contains provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation, which will become effective immediately prior to the completion of this offering, provides that we are required to indemnify our directors and officers to the fullest extent permitted by Delaware law. Our amended and restated certificate of incorporation also provides that, subject to limited exceptions, we are obligated to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permits us to secure insurance on behalf of any current or former director or officer against any liability asserted against such person, whether or not we would have the power to indemnify such person against such liability under our amended and restated certificate of incorporation or otherwise. We have entered and expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by our board of directors. With specified exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys'

fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these provisions of our amended and restated certificate of incorporation and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and our stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage.

Fiscal 2018 director compensation

We currently do not have a formal non-employee director compensation policy. We did not make any equity awards or non-equity awards to, or pay any other compensation to any of the non-employee members of our board of directors for their service as a director in 2018 with the exception of Dr. Seizinger. Pursuant to a letter agreement with us, Dr. Seizinger is entitled to receive an annual cash retainer of \$28,727, paid annually in arrears, for his service on the board of directors. We reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of directors and committee meetings. Mr. Schade, our chief executive officer and a member of our board of directors, did not receive any compensation for his service as a member of our board of directors during 2018. Mr. Schade's compensation for service as an employee for fiscal year 2018 is presented below in the "2018 Summary compensation table."

The following table sets forth information regarding compensation earned by our non-employee directors during 2018. As noted above, Dr. Seizinger is the only non-employee director who received compensation during 2018.

<u>Name</u>	<u>Fees Earned or Paid in Cash (\$)</u>	<u>Total (\$)(1)</u>
Bernd R. Seizinger, M.D., Ph.D.	28,727	28,727

(1) As of December 31, 2018, Dr. Seizinger held stock options to acquire 263,970 shares of our common stock following the consummation of the offering and the payment of a subscription price established in 2015. None of our other non-employee directors held any other outstanding equity awards with respect to us as of December 31, 2018.

After the completion of this offering, our board of directors intends to approve a compensation policy for our non-employee directors. This policy will be intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

Following this offering, we expect to offer our non-employee directors the following compensation for their service on our board of directors and its committees:

<u>Director Compensation Element</u>	<u>Amount</u>
Board Cash Retainer	\$ 35,000
Committee Cash Retainer	
—Audit	\$ 7,500
—Compensation	\$ 5,000
—Governance	\$ 4,000
Committee Chair Cash Retainer	
—Audit	\$ 7,500
—Compensation	\$ 5,000
—Governance	\$ 4,000
Annual Stock Compensation	\$ 150,000
Value of Initial Stock-Based Awards for Newly Elected Directors	\$ 185,000

Executive Compensation

This section describes the material elements of compensation awarded to, earned by or paid to each of our named executive officers in 2018. We are an "emerging growth company," within the meaning of the JOBS Act and a smaller reporting company under the Exchange Act, and have elected to comply with the reduced compensation disclosure requirements available to emerging growth companies under the JOBS Act. Our named executive officers for 2018 were Christian S. Schade, Lars Abrahmsen and Gregory A. Korbel. This section also provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place in perspective the data presented in the tables and narrative that follow.

Overview

Our current executive compensation program is intended to align executive compensation with our business objectives and to enable us to attract, retain and reward executive officers who contribute to our long-term success. The compensation paid or awarded to our executive officers is generally based on a qualitative assessment of each individual's performance compared against the business objectives established for the fiscal year as well as our historical compensation practices. In the case of new hire executive officers, their compensation is primarily determined based on the negotiations of the parties as well as our historical compensation practices. For 2018, the material elements of our executive compensation program were base salary and annual cash bonuses.

In preparing to become a public company, we have begun a thorough review of all elements of our executive compensation program, including the function and design of our equity incentive program. We expect that our executive compensation program will evolve to reflect our status as a newly publicly-traded company, while still supporting our overall business and compensation objectives. In connection with this offering, our board of directors has retained the services of Willis Towers Watson, an independent executive compensation consultant, to help advise on our post-offering executive compensation program, as described further below.

Compensation of named executive officers

Base salaries

In 2018, we paid annual base salaries of \$412,000 to Mr. Schade, \$192,505 to Dr. Abrahmsen and \$226,600 to Dr. Korbel. We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary. Following a market review by Willis Towers Watson, the compensation committee adjusted the base salaries of Mr. Schade and Dr. Abrahmsen to \$500,000 and \$220,000, respectively, to be effective upon consummation of this offering.

Annual cash bonuses

Although we do not have a formal performance-based bonus plan, each executive is eligible to receive a discretionary bonus pursuant to the terms of his employment agreement or offer letter, as applicable. Under such terms of employment, the target bonus opportunities, as a percentage of base salary, for Mr. Schade, Dr. Abrahmsen and Dr. Korbel are 40%, 25%, and 20%, respectively. From time to time, our board of directors has approved discretionary annual cash bonuses to employees, including our named executive officers, based on a qualitative assessment of prior year performance. Mr. Schade, Dr. Abrahmsen and Dr. Korbel earned cash bonuses of \$181,280, \$52,139, and \$49,852, respectively, for services performed during 2018. Following a market review by Willis Towers Watson, the compensation committee adjusted the annual bonus targets of Mr. Schade and Dr. Abrahmsen to 50% and 30% of base salary, respectively, to be effective upon consummation of this offering.

Equity awards

Although we do not have a formal policy with respect to the grant of equity incentive awards to our named executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide recipients, including our named executive officers, with a strong link to our long-term performance, create an ownership culture and help to align the interests of our award recipients and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incents the award recipient to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options. None of our named executive officers received equity awards in 2018, although each held outstanding equity awards as of December 31, 2018 a result of prior year equity grants. In connection with this offering, our board of directors granted stock option awards to certain employees of the Company, including each of the named executive officers. Accordingly, Mr. Schade, Dr. Abrahmsen and Mr. Korbel received stock option awards with respect to 306,085, 77,630 and 64,322 shares, respectively, and with an exercise price equal to the initial public offering price and which vest 25% on the one-year anniversary of the date of grant and monthly thereafter, subject to early vesting in the event of a change in control or certain terminations of employment.

2018 Summary compensation table

The following table sets forth information regarding compensation awarded to, earned by or paid to our named executive officers during 2018.

<u>Name and principal position</u>	<u>Year</u>	<u>Salary (\$)</u>	<u>Bonus \$(1)</u>	<u>Option awards (\$)</u>	<u>All other compensation \$(2)</u>	<u>Total (\$)</u>
Christian S. Schade(3) President and Chief Executive Officer	2018	412,000	181,280	—	—	593,280
Lars Abrahmsen, Ph.D. Senior Vice President, Chief Scientific Officer	2018	192,505	52,139	—	62,190	306,834
Gregory A. Korbel, Ph.D. Vice President of Business Development	2018	226,600	49,852	—	—	276,452

(1) The amounts reported in the "Bonus" column represent discretionary annual cash bonuses awarded to our named executive officers.

(2) Consists of pension plan contributions for Dr. Abrahmsen.

(3) Mr. Schade serves as a member of our board of directors but does not receive any additional compensation for his service as a director.

Outstanding equity awards at 2018 fiscal year-end

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2018:

	Option awards				
	Vesting commencement date	Number of securities underlying unexercised option exercisable (#)(1)	Number of securities underlying unexercised option unexercisable (#)(1)	Option exercise price (\$/share)	Option expiration date
Christian S. Schade	4/20/17	351,956	175,979(2)	0.92	9/14/2026
	11/24/18	43,454	116,995	1.01	11/24/2027
Lars Abrahmsen, Ph.D.	4/20/17	70,391	35,196	0.92	9/14/2026
	11/21/18	15,209	40,948	1.01	11/24/2027
Gregory A. Korbel, Ph.D.	7/5/17	48,481	31,764	0.92	9/14/2026
	2/16/18	14,706	17,383	0.92	2/16/2027
	11/24/18	6,517	17,550	1.01	11/24/2027

(1) Twenty-five percent of these options vested on the Vesting Commencement Date, with the remaining options vesting in equal monthly installments on the first day of every calendar month during the following three year period.

(2) These options are subject to accelerated vesting in the event Mr. Schade's employment is terminated by us without "cause" or by him due to "good reason" within 12 months following a change in control.

Employment agreements, severance and change in control agreements

We entered into employment agreements with each of Mr. Schade, Dr. Abrahmsen and Dr. Korbel. These agreements set forth the initial terms and conditions of each executive's employment with us, including base salary, target annual bonus opportunity and standard employee benefit plan participation. Except as noted below, these employment agreements provide for "at will" employment. The terms "cause," "good reason" and "change in control" referred to below are defined in each named executive officer's employment agreement.

In connection with this offering, we expect to enter into new employment agreements with the Company's named executive officers that will set forth the initial terms of their employment, including base salary and annual bonus target levels. In addition, the employment agreements are expected to provide for severance benefits following a termination by the Company without "cause," the expiration of the employment agreement term upon non-renewal by the Company or resignation by the named executive officer due to "good reason" as follows: (i) severance payments equal to nine-months of base salary (12-months in the case of Mr. Schade); (ii) a prorated target bonus for the year of termination; and (iii) the payment of an amount equal to the employer's portion of healthcare continuation coverage for a period of up to nine-months (12-months in the case of Mr. Schade), with the severance amount and healthcare continuation increasing to 12-months (18-months in the case of Mr. Schade) for a qualifying termination of employment following a change in control of the Company. The severance benefits under the employment agreements will be subject to the named executive officer's execution of a release of claims in favor of the Company and compliance with restrictive covenants relating to non-competition, non-solicitation and confidentiality.

Christian S. Schade

We entered into an employment letter agreement with Mr. Schade in April 2016. Under the terms of the letter agreement, in the event that he is terminated by us without "cause" or he terminates his employment for "good reason," death or disability he will be entitled to receive, upon execution and effectiveness of a release of claims, (i) continued payment of his then-current base salary for a period

of 12 months following termination and (ii) a direct payment by us of the medical, vision and dental coverage premiums due to maintain any COBRA coverage for which he is eligible and has appropriately elected through the earlier of (x) 12 months following termination and (y) the date he becomes employed by another entity or individual. Upon a termination without "cause" or due to "good reason," death or disability during this 12 month period following "change of control" Mr. Schade is entitled to a prorated target bonus for the year of such termination. Further, in the event Mr. Schade's employment is terminated by us without "cause" or by him due to "good reason" within 12-months following a change in control, the outstanding options granted under the letter agreement will vest in full.

In the event that we terminate Mr. Schade with cause or he resigns without good reason, then he will not be entitled to receive severance benefits.

Under the letter agreement, Mr. Schade is prohibited from disclosing our confidential information and is subject to non-competition and non-solicitation restrictive covenants for 12-months post-termination.

Lars Abrahmsen, Ph.D.

We entered into an employment agreement with Dr. Abrahmsen in March 2016. Dr. Abrahmsen's employment agreement may be terminated by us upon six-month prior written notice. Under the terms of Dr. Abrahmsen's employment agreement, we are required to compensate Dr. Abrahmsen up to 60% of his average monthly remuneration during the 12-month non-compete period under his employment agreement. Dr. Abrahmsen is also subject to a non-solicit restrictive covenant for six-months following termination and prohibitions on the disclosure of our confidential information.

Gregory A. Korbel, Ph.D.

We entered into an employment letter agreement with Dr. Korbel in July 2016.

In the event that he is terminated by us without "cause" or his employment termination due to death or disability, he will be entitled to receive, upon execution and effectiveness of a release of claims, (i) continued payment of his then-current base salary for a period of three months following termination (six months if such termination occurs within the 12 month period immediately following a "change of control") and (ii) a direct payment by us of the medical, vision and dental coverage premiums due to maintain any COBRA coverage for which he is eligible and has appropriately elected through the earlier of (i) the date his base salary continuation ceases following termination and (ii) the date he becomes employed by another entity or individual.

In the event that we terminate Dr. Korbel with cause or he resigns, then he will not be entitled to receive severance benefits.

Under the letter agreement, Dr. Korbel is prohibited from disclosing our confidential information and is subject to non-competition and non-solicitation restrictive covenants for 12-months post-termination.

Pension Plan

Our company policy is to provide a pension plan, the Pension Plan, to all of our employees in Sweden. Contributions for each employee are calculated as an age-adjusted percentage of base salary. All contributions to the Pension Plan begin at the time of employment and cease upon termination of employment, with contributions distributed to the participant at retirement. Other than the Pension Plan, the Company does not maintain any retirement programs for its employees.

Stock option and other compensation plans

2016 Stock option program

The 2016 Stock Incentive Plan of Aprea AB, or 2016 Plan, was approved by the board of directors and stockholders of Aprea AB in October 2016. Under the 2016 Plan, we have reserved for issuance an aggregate of 3,402,418 shares of common stock of Aprea AB. The number of shares of common stock reserved for issuance is subject to adjustment in the event of a stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in our capitalization.

The board of directors of Aprea AB has acted as administrator of the 2016 Plan. The administrator has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, and to determine the specific terms and conditions of each award, subject to the provisions of the 2016 Plan. Persons eligible to participate in the 2016 Plan are those employees, officers and directors of, and consultants to, the company as selected from time to time by the administrator in its discretion.

The term and per share option exercise price of each option under the 2016 Plan is determined by the administrator. The option may not be exercised until the occurrence of a "Trade Sale" or "IPO," as defined in the 2016 Plan; provided, however, that option holders may also exercise their options when they leave their employment with the Company.

The 2016 Plan provides that upon the occurrence of a "Trade Sale," as defined in the 2016 Plan, our board of directors may take one or more of the following actions as to some or all awards outstanding under the 2016 Plan: (1) decide on a period for exercise of the stock options; (2) resolve to have these terms and conditions continue following the closing date of the Trade Sale; (3) allow a grant of equivalent rights to acquire securities in a new company as the option holder had in us immediately before the Trade Sale in which case any rights under the stock options shall lapse as a consequence thereof; (4) allow an amendment of the awards' terms and conditions to the effect that, following the Trade Sale, a new company assumes our rights and obligations under the 2016 Plan and that the holder's right to subscribe for shares in accordance with the 2016 Plan shall relate to shares in such new company; (5) resolve to pay the option holder in cash the difference between the share price in the Trade Sale and the exercise price, meaning that the stock option cannot be exercised into shares and that the stock option will lapse or (6) any combination of the foregoing. The 2016 Plan provides that upon the occurrence of an "IPO," as defined in the 2016 Plan, our board of directors shall decide on an exercise period.

The administrator may amend, the 2016 Plan at any time, subject to stockholder approval where such approval is required by applicable law. The administrator of the 2016 Plan may also amend, any outstanding award, provided that no amendment to an award may materially and adversely affect a participant's rights without his or her consent.

The 2016 Plan will terminate automatically upon September 30, 2026. As of June 30, 2019, options to purchase 2,761,794 shares of common stock were outstanding under the 2016 Plan. In connection with the Holdco Reorganization and prior to the completion of this Offering, each outstanding option to purchase common stock of Aprea AB issued pursuant to the 2016 Plan will be canceled, and we will issue to the holder of each such Aprea AB option, a substitute option to purchase shares of our common stock pursuant to our 2019 Plan. See "Corporate Reorganization" for further detail regarding these transactions. Our board of directors has determined not to make any further awards under the 2016 Plan following the completion of this offering.

2019 Stock incentive plan

In connection with this offering, our board of directors expects to adopt, and our current stockholders expect to approve, the 2019 Stock Incentive Plan, or the 2019 Plan, prior to the effective date of this offering. The 2019 Plan will replace the 2016 Plan, as described above.

The purposes of the 2019 Plan are to align the interests of our stockholders and those eligible for awards, to retain officers, directors, employees, and other service providers, and to encourage them to act in our long-term best interests. Our 2019 Plan provides for the grant of incentive stock options (within the meaning of Internal Revenue Code Section 422), nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units, other stock awards, and performance awards. Officers, directors, employees, consultants, agents and independent contractors who provide services to us or to any subsidiary of ours are eligible to receive awards under the 2019 Plan. The material terms of the 2019 Plan are expected to be as follows:

Stock subject to the plan. The number of shares reserved for issuance under the 2019 Plan, including shares issuable upon exercise of options substituted for those originally issued under the 2016 Plan as well as stock options previously issued to our director, Bernd Seizinger, under a separate plan in 2015, is 5,000,000, plus an annual increase added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2020 and continuing until, and including, the fiscal year ending December 31, 2029. The annual increase will be equal to the lesser of (i) 4% of the number of shares of common stock outstanding on the first day of such fiscal year, (ii) 5,000,000 shares of our common stock or (iii) such other amount determined by our board of directors. To the extent an equity award granted under the 2019 Plan, including awards granted in exchange for awards under the 2016 Plan or any other prior equity plan of the Company (other than any substitute award), expires or otherwise terminates without having been exercised or paid in full, or is settled in cash, the shares subject to such award will become available for future grant under the 2019 Plan. In addition, to the extent shares subject to an award granted under the 2019 Plan or a prior equity plan of the Company are withheld to satisfy a participant's tax withholding obligation upon the exercise or settlement of such award (other than any substitute award) or to pay the exercise price of a stock option, such shares will become available for future grant under the 2019 Plan.

Plan administration. Our compensation committee will administer the 2019 Plan. Our board of directors has the authority to amend and modify the plan, subject to any stockholder approval required by applicable law or stock exchange rules. Subject to the terms of the 2019 Plan, our compensation committee will have the authority to determine the eligibility for awards and the terms, conditions, and restrictions, including vesting terms, the number of shares subject to an award, and any performance goals applicable to grants made under the 2019 Plan. The compensation committee also will have the authority, subject to the terms of the 2019 Plan, to construe and interpret the 2019 Plan and awards, and amend outstanding awards at any time.

Stock options and stock appreciation rights. Our compensation committee may grant incentive stock options, nonstatutory stock options, and stock appreciation rights under the 2019 Plan, provided that incentive stock options are granted only to employees. Other than with respect to options issued in substitution of awards granted under the 2016 Plan and other prior plans, the exercise price of stock options and stock appreciation rights under the 2019 Plan will be fixed by the compensation committee, but must equal at least 100% of the fair market value of our common stock on the date of grant. The term of an option or stock appreciation right may not exceed ten years; provided, however, that an incentive stock option held by an employee who owns more than 10% of all of our classes of stock, or of certain of our affiliates, may not have a term in excess of five years, and must have an exercise price of at least 110% of the fair market value of our common stock on the grant date. Subject to the provisions of the 2019 Plan, the compensation committee will determine the remaining terms of the options and stock appreciation rights (e.g., vesting). Upon a participant's termination of service, the

participant may exercise his or her option or stock appreciation right, to the extent vested (unless the compensation committee permits otherwise), as specified in the award agreement.

Stock awards. Our compensation committee will decide at the time of grant whether an award will be in the form of restricted stock, restricted stock units, or other stock award. The compensation committee will determine the number of shares subject to the award, vesting, and the nature of any performance measures. Unless otherwise specified in the award agreement, the recipient of restricted stock will have voting rights and be entitled to receive dividends with respect to his or her shares of restricted stock. The recipient of restricted stock units will not have voting rights, but his or her award agreement may provide for the receipt of dividend equivalents. Our compensation committee may grant other stock awards that are based on or related to shares of our common stock, such as awards of shares of common stock granted as bonus and not subject to any vesting conditions, deferred stock units, stock purchase rights, and shares of our common stock issued in lieu of our obligations to pay cash under any compensatory plan or arrangement.

Performance awards. Our compensation committee will determine the value of any performance award, the vesting and nature of the performance measures, and whether the award is denominated or settled in cash or in shares of our common stock. The performance goals applicable to a particular award will be determined by our compensation committee at the time of grant.

Transferability of awards. The 2019 Plan does not allow awards to be transferred other than by will or the laws of inheritance following the participant's death, and options may be exercised, during the lifetime of the participant, only by the participant. However, an award agreement may permit a participant to assign an award to a family member by gift or pursuant to a domestic relations order, or to a trust, family limited partnership or similar entity established for one of the participant's family members. A participant may also designate a beneficiary who will receive outstanding awards upon the participant's death.

Certain adjustments. If any change is made in our common stock subject to the 2019 Plan, or subject to any award agreement under the 2019 Plan, without the receipt of consideration by us, such as through a stock split, stock dividend, extraordinary distribution, recapitalization, combination of shares, exchange of shares or other similar transaction, appropriate adjustments will be made in the number, class, and price of shares subject to each outstanding award and the numerical share limits contained in the plan.

Change in control. Subject to the terms of the applicable award agreement, upon a "change in control" (as defined in the 2019 Plan), our board of directors may, in its discretion, determine whether some or all outstanding options and stock appreciation rights will become exercisable in full or in part, whether the restriction period and performance period applicable to some or all outstanding restricted stock awards and restricted stock unit awards will lapse in full or in part and whether the performance measures applicable to some or all outstanding awards will be deemed to be satisfied. Our board of directors may further require that shares of stock of the corporation resulting from such a change in control, or a parent corporation thereof, be substituted for some or all of our shares of common stock subject to an outstanding award and that any outstanding awards, in whole or in part, be surrendered to us by the holder and be immediately cancelled by us in exchange for a cash payment, shares of common stock of the corporation resulting from or succeeding us or a combination of both cash and such shares of stock.

Clawback. Awards granted under the 2019 Plan and any cash payment or shares of our common stock delivered pursuant to an award are subject to forfeiture, recovery, or other action pursuant to the applicable award agreement or any clawback or recoupment policy that we may adopt.

Plan termination and amendment. Our board of directors has the authority to amend, suspend, or terminate the 2019 Plan, subject to any requirement of stockholder approval required by law or stock

exchange rules. Our 2019 Plan will terminate on the ten-year anniversary of its approval by our board of directors, unless we terminate it earlier.

New plan benefits. The compensation committee has the discretion to grant awards under the 2019 Plan, and therefore it is not possible at the time of filing of this prospectus to determine future awards that will be received by our named executive officers or others under the 2019 Plan. All officers, directors, employees, consultants, agents and independent contractors of the Company and its subsidiaries are eligible for consideration to participate in the 2019 Plan.

In connection with this offering, our board of directors granted stock option awards to certain employees of the Company with respect to an aggregate amount of 807,353 shares, and with an exercise price equal to the initial public offering price and which vest 25% on the one-year anniversary of the date of grant and monthly thereafter, subject to early vesting in the event of a change in control or certain terminations of employment.

2019 Employee stock purchase plan

In connection with this offering, our board of directors will adopt and our current stockholders expect to approve the Aprea Therapeutics, Inc. Employee Stock Purchase Plan, or the ESPP, to be effective upon the completion of this offering.

Generally, all of our employees (including those of our consolidated subsidiaries, other than those subsidiaries excluded from participation by our board of directors or compensation committee) who have been employed for at least 90 days are eligible to participate in the ESPP. The ESPP permits employees to purchase our common stock through payroll deductions during six-month offering periods. Participants may authorize payroll deductions of a specific percentage of compensation of up to 15%, with such deductions being accumulated for six-month purchase periods beginning on the first business day of each offering period and ending on the last business day of each offering period. Under the terms of the ESPP, the purchase price per share with respect to an offering period will equal the lesser of (i) 85% of the fair market value of a share of our common stock on the first business day of such offering period and (ii) 85% of the fair market value of a share of our common stock on the last business day of such offering period, although the compensation committee has discretion to change the purchase price with respect to future offering periods, subject to the terms of the ESPP. No employee may participate in an offering period if the employee owns 5% or more of the total combined voting power or value of our stock or the stock of any of our subsidiaries. No participant may purchase more than 5,000 shares of our common stock during any offering period.

250,000 shares of our common stock, subject to adjustment for stock splits, stock dividends or other changes in our common stock, have been reserved for issuance under the ESPP. Subject to the adjustment provisions contained in the ESPP, the maximum number of shares of our common stock available under the ESPP will automatically increase on the first trading day in January of each calendar year, commencing January 1, 2020, by an amount equal to the lesser of 1% of the shares of our common stock issued and outstanding on December 31 of the immediately preceding calendar year, 250,000 shares of our common stock or such lesser amount as is determined by our board of directors.

The ESPP will be administered by the compensation committee or a designee of the compensation committee. The ESPP may be amended by our board of directors or the compensation committee but may not be amended without prior stockholder approval to the extent required by Section 423 of the Code. The ESPP shall continue in effect until the earlier of (i) the termination of the ESPP by our board of directors or the compensation committee pursuant to the terms of the ESPP and (ii) the ten-year anniversary of the effective date of the ESPP, with no new offering periods commencing on or after such ten-year anniversary.

Certain relationships and related persons transactions

Since January 1, 2016, we have engaged in the following transactions in which the amount involved exceeded \$120,000 and any of our directors, executive officers or beneficial holders of more than 5% of any class of our voting securities, or any of their affiliates, had a material interest. We believe that all of these transactions were on terms comparable to terms that could have been obtained from unrelated third parties.

Series A preferred stock financing

In October 2011, the board of Aprea AB resolved to issue 145,469 Series A preferred shares in Aprea AB at a price per share of \$22.22, for an aggregate purchase price of \$3.2 million. In March 2016, Aprea AB issued 466,977 Series A preferred shares in Aprea AB at a price per share of \$6.96 in connection with the repayment of loans made to the Company by KDev Group (includes KDev Investments, KCIF Co-Investment Fund KB and Karolinska Development). These Series A preferred shares in Aprea AB were contributed and exchanged for shares of Series A preferred stock in the Company in connection with the Holdco Reorganization. The following table sets forth the number of shares of our Series A preferred stock owned by our directors, executive officers and 5% stockholders, and their affiliates, and the aggregate purchase price paid for those shares, in each case, after giving effect to the Holdco Reorganization.

Name	Shares of Series A preferred stock purchased	Aggregate purchase price(1)
KDev Group	579,647	\$ 5,753,978

(1) Includes \$3,249,627 in connection with the repayment of loans made to the Company.

Series B preferred stock financing

In March 2016, Aprea AB, the shareholders of the Company and a number of investors entered into a Series B investment agreement for the issue of up to 7,235,969 Series B preferred shares in Aprea AB in one or more closings. In March 2016, Aprea AB issued 3,322,762 Series B preferred shares at a price per share of \$6.81, for an aggregate purchase price of \$22.6 million. In March 2016, Aprea AB also issued 590,445 Series B preferred shares in Aprea AB at a price per share of \$6.81 in connection with the repayment of loans made to the Company by existing investors totaling \$4.1 million. In October 2017, Aprea AB issued 3,322,762 Series B preferred shares at a price per share of \$7.02, for an aggregate purchase price of \$23.3 million. These Series B preferred shares in Aprea AB were contributed and exchanged for shares of Series B preferred stock in the Company in connection with the Holdco Reorganization. The following table sets forth the number of shares of our Series B preferred stock owned by our directors, executive officers and 5% stockholders, and their affiliates, and the aggregate purchase price paid for those shares, in each case, after giving effect to the Holdco Reorganization.

Name	Shares of Series B preferred stock purchased	Aggregate purchase price
5AM Ventures	1,993,658	\$ 13,783,254
HealthCap	1,661,382	\$ 11,490,331
KDev Group(1)	590,445	\$ 4,108,818
Sectoral Asset Management	996,826	\$ 6,898,961
Versant	1,993,658	\$ 13,786,556

(1) Includes \$4,108,818 in connection with the repayment of loans made to the Company.

Series C preferred stock financing

In November 2018, Aprea AB, certain shareholders of the Company and a number of investors entered into a Series C investment agreement for the issue of 4,712,698 Series C preferred shares in Aprea AB at a price per share of \$12.08, for an aggregate purchase price of \$56.7 million. In February 2019, Aprea AB, certain shareholders of the Company and a number of investors entered into an additional Series C investment agreement for the issue of 467,179 Series C preferred shares in Aprea AB at a price per share of \$12.10, for an aggregate purchase price of \$5.6 million. These Series C preferred shares in Aprea AB were contributed and exchanged for shares of Series C preferred stock in the Company in connection with the Holdco Reorganization. The following table sets forth the number of shares of our Series C preferred stock owned by our directors, executive officers and 5% stockholders, and their affiliates, and the aggregate purchase price paid for those shares, in each case, after giving effect to the Holdco Reorganization.

Name	Shares of Series C preferred stock purchased	Aggregate purchase price
5AM Ventures	512,994	\$ 6,164,954
HealthCap	427,496	\$ 5,147,150
KDev Group	430,467	\$ 5,180,090
Redmile(1)	1,868,718	\$ 22,472,429
Sectoral Asset Management	467,179	\$ 5,614,984
Versant	512,995	\$ 6,197,369

(1) Includes 1,454,926 shares held by Redmile Biopharma Investments I, L.P. and 413,792 shares held by RAF L.P.

Registration rights agreement

We are a party to an amended and restated registration rights agreement, dated as of September 20, 2019 (the "Registration Rights Agreement"), with our existing stockholders, including certain holders of five percent or more of our common stock and their affiliates and entities affiliated with certain of our directors. The Registration Rights Agreement provides these holders the right, following the completion of this offering, to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. See "Description of Capital Stock—Registration Rights" for additional information regarding these registration rights.

Employment agreements

See the "Executive Compensation—Employment agreements, severance and change in control agreements" section of this prospectus for a further discussion of these arrangements.

Indemnification agreements

Our amended and restated certificate of incorporation, which will become effective immediately prior to the completion of this offering, provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we plan to enter into indemnification agreements with each of our officers and directors that may be broader in scope than the specific indemnification provisions contained in the Delaware General Corporation Law. See "Management—Limitation on Liability and Indemnification" for additional information regarding these agreements.

Policies and procedures for related person transactions

Following this offering, pursuant to the written charter of our audit committee adopted in September of 2019, our audit committee of the board of directors will be responsible for reviewing and

approving, prior to our entry into any such transaction, all related person transactions involving a principal stockholder, a member of the board of directors, senior management or an immediate family member of any of the aforementioned individuals. In addition, our code of business conduct and ethics requires that our officers and employees avoid taking for themselves personally opportunities that are discovered through the use of our property, information or position or use of our property, information or position for personal gain.

Principal Stockholders

The following table sets forth information with respect to the beneficial ownership of our common stock as of September 26, 2019 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of September 26, 2019, through the exercise of any stock option or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 14,209,865 shares of our common stock outstanding as of September 26, 2019, which reflects the 1 for 1.6045 split of our common stock which took place on September 26, 2019 and the conversion of all outstanding shares of convertible preferred stock, including the shares issued as part of the Holdco Reorganization, into 13,028,292 shares of common stock immediately prior to the completion of this offering. The percentage of shares beneficially owned after this offering is computed on the basis of shares of common stock outstanding immediately after the completion of this offering (assuming no exercise of the underwriters' option to purchase additional shares of our common stock). Shares of our common stock that a person has the right to acquire within 60 days of September 26, 2019, are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group.

The table below does not reflect any shares of common stock that directors, executive officers and entities may purchase in this offering through the directed share program described under

Name of beneficial owner	Number of shares beneficially owned	Percentage of shares beneficially owned	
		Before offering	After offering
5.0% Stockholders			
KDev Group(1)	2,444,837	17.21%	12.73%
Versant(2)	2,519,322	17.73%	13.11%
5AM Ventures(3)	2,519,320	17.73%	13.11%
HealthCap(4)	2,099,438	14.77%	10.93%
Redmile Group(5)	1,868,718	13.15%	9.73%
Sectoral Asset Management(6)	1,470,339	10.35%	7.65%
Executive Officers and Directors			
Christian S. Schade(7)	553,327	3.75%	2.80%
Lars Abrahmsen, Ph.D.(8)	122,666	*	*
Eyal C. Attar, MD	—	*	*
Scott M. Coiante	—	*	*
Gregory A. Korb, Ph.D.(9)	100,964	*	*
Guido Magni, M.D., Ph.D.(2)	2,519,322	17.73%	13.11%
Scott M. Rocklage, Ph.D.(3)	2,519,320	17.73%	13.11%
Johan Christenson, M.D., Ph.D.(4)	2,099,438	14.77%	10.93%
Jonathan Hepple, Ph.D.(1)	1,992,591	14.02%	10.37%
Bernd R. Seizinger, M.D., Ph.D.(10)	263,970	1.82%	1.36%
John B. Henneman III(11)	—	*	*
All directors and executive officers as a group (11 persons)(12)	10,171,598	66.70%	50.23%

* Represents beneficial ownership of less than 1% of our outstanding stock.

- (1) Consists of (i) 481,909 shares of common stock issuable upon conversion of shares of Series A convertible preferred stock held of record by KDev Investments, (ii) 37,169 shares of common stock issuable upon conversion of shares of Series A convertible preferred stock held of record by KCIF Co-Investment Fund KB, (iii) 60,569 shares of common stock issuable upon conversion of shares of Series A convertible preferred stock held of record by Karolinska Development, (iv) 510,035 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock held of record by KDev Investments, (v) 19,841 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock held of record by KCIF Co-Investment Fund KB, (vi) 60,569 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock held of record by Karolinska Development, (vii) 233,591 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock held of record by KDev Investments, (viii) 34,321 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock held of record by KCIF Co-Investment Fund KB, (ix) 162,555 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock held of record by Karolinska Development, (x) 767,056 shares of common stock held of record by KDev Investments and (xi) 77,222 shares of common stock held of record by KCIF Co-Investment Fund KB, or collectively, the KDev Group Entities. Jonathan Hepple is co-founder and director of Rosetta Capital Limited, the investment manager of certain private investment vehicles that own shares of KDev Investments. Dr. Hepple does not share voting and investment power over the shares held by any of the KDev Group Entities and disclaims beneficial ownership of all shares held by the KDev Group Entities except to the extent of his pecuniary interest therein. Dr. Hepple is a member of our board of directors. The address for each of these entities is c/o KDev Group, Tomtebodavägen 23A, 171 65 Solna, Sweden.
- (2) Consists of (i) 1,993,658 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock, (ii) 512,995 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock and (iii) 12,670 shares of common stock. Guido Magni, a partner of Versant Venture

Management, LLC, does not share voting and investment power over the shares held of record by Versant. Dr. Magni disclaims beneficial ownership of all shares held by Versant except to the extent of his pecuniary interest therein. Dr. Magni is a member of our board of directors. The address for Versant is 15 Boulevard F.W. Raiffeisen, 2411 Luxembourg.

- (3) Consists of (i) 1,913,910 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock held of record by 5AM Ventures IV, L.P. (ii) 79,746 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock held of record by 5AM Co-Investors IV, L.P., (iii) 492,475 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock held of record by 5AM Ventures IV, L.P. (iv) 20,519 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock held of record by 5AM Co-Investors IV, L.P., (v) 12,163 shares of common stock held of record by 5AM Ventures IV, L.P. and (vi) 507 shares of common stock held of record by 5AM Co-Investors IV, L.P. Scott Rocklage, a Managing Member of 5AM Partners IV, LLC, the General Partner of 5AM Ventures IV, L.P. and 5AM Co-Investors IV, L.P., may be deemed to share voting and investment power over the shares held of record by 5AM Ventures IV, L.P. and 5AM Co-Investors IV, L.P. Dr. Rocklage is a member of our board of directors. The address for each of these entities is c/o 5AM Ventures, 501 2nd Street, Suite 350, San Francisco, CA 94107.
- (4) Consists of (i) 1,661,382 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock, (ii) 427,496 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock and (iii) 10,559 shares of common stock. Johan Christenson, a partner of HealthCap VII Advisor AB, is acting as advisor to HealthCap VII L.P. Dr. Christenson disclaims beneficial ownership of all shares held by HealthCap except to the extent of his pecuniary interest therein. Dr. Christenson is a member of our board of directors. The address for HealthCap is 18 Avenue d'Orchys CH-1006 Lausanne, Switzerland.
- (5) Consists of (i) 1,454,926 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock held of record by Redmile Biopharma Investments I, L.P. and (ii) 413,792 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock held of record by RAF, L.P. (together with Redmile Biopharma Investments I, L.P., the "Redmile Funds"). Redmile Group, LLC is the investment manager to the Redmile Funds and, in such capacity, exercises shared voting and dispositive power over the securities held by the Redmile Funds and may be deemed to beneficially own such securities. Jeremy Green serves as the managing member of Redmile Group, LLC and as such shares voting and dispositive power over the securities held by the Redmile Funds, Redmile Group, LLC and Mr. Green each disclaim beneficial ownership of these securities, except to the extent of its or his pecuniary interest in such securities, if any. The address for each of the above person and entities is One Letterman Drive, Building D, Suite D3-300, San Francisco, CA 94129.
- (6) Consists of (i) 996,826 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock, (ii) 467,179 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock and (iii) 6,334 shares of common stock. The address for Sectoral Asset Management is 1010 Sherbrooke St. West, #1610, Montreal, QC Canada H3A 2R7.
- (7) Consists of (i) 160 shares of common stock issued in connection with the initial capital contribution to the Company, and (ii) 553,167 shares of common stock issuable upon the exercise of stock options exercisable within 60 days of September 26, 2019.
- (8) Consists of 122,666 shares of common stock issuable upon the exercise of stock options exercisable within 60 days of September 26, 2019.
- (9) Consists of 100,964 shares of common stock issuable upon the exercise of stock options exercisable within 60 days of September 26, 2019.
- (10) Consists of 263,970 shares of common stock issuable upon the exercise of stock options exercisable within 60 days of September 26, 2019.
- (11) Does not include options to purchase shares of common stock, to be valued at \$185,000 based on the initial public offering price of the Company's common stock, approved for grant to Mr. Henneman, which grant is contingent and effective upon the effectiveness of the registration statement of which this prospectus forms a part. The final number of shares will not be calculated until the price of the initial public offering of the Company's common stock has been finalized and will be computed using the Black-Scholes option-pricing model.
- (12) Consists of shares described in notes.

Description of Capital Stock

General

Following the completion of this offering and the completion of the Holdco Reorganization as described in the "Corporate Reorganization" section of this prospectus, and the conversion of all outstanding shares of our convertible preferred stock into common stock immediately prior to the completion of this offering, our authorized capital stock will consist of 400,000,000 shares of common stock, par value \$0.001 per share, and 40,000,000 shares of preferred stock, par value \$0.001 per share, all of which preferred stock will be undesignated. The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the certificate of incorporation and the bylaws that will become effective as of the closing date of this offering. We have filed copies of these documents as exhibits to our registration statement of which this prospectus forms a part. The descriptions of the common stock and preferred stock reflect changes to our capital structure that will occur as of immediately prior to the completion of this offering.

Common stock

As of June 30, 2019, we had outstanding 14,209,865 shares of common stock (including 2,807 shares of common stock from the exercise of stock options on March 25, 2019, which were registered pursuant to Swedish law with the Swedish Companies Registration Office on August 27, 2019), reflecting the completion of the Holdco Reorganization and the 1 for 1.6045 split of our common stock and assuming the automatic conversion of all outstanding shares of our preferred stock into 13,028,292 shares of common stock immediately prior to the completion of this offering, which were held of record by 25 stockholders.

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter, except as otherwise disclosed below. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred stock

Under the terms of our certificate of incorporation that will become effective as of the closing date of this offering, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third

party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. As of immediately prior to the completion of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Stock options

As of June 30, 2019, options to purchase 2,761,794 shares of our common stock at a weighted average exercise price of \$1.66 per share were outstanding, of which no options to purchase shares of our common stock were exercisable.

Registration rights

We are party to an amended and restated registration rights agreement, dated as of September 20, 2019, pursuant to which certain of our stockholders, including certain holders of five percent or more of our capital stock and their affiliates and entities affiliated with certain of our directors, have the right to demand that we file a registration statement for their shares of our common stock or request that their shares of our common stock be covered by a registration statement that we are otherwise filing, including, in each case, shares of our common stock that were issued upon conversion of convertible preferred stock. These shares are referred to as registrable securities. Such stockholders have agreed not to exercise their registration rights during the lock-up period for this offering. See "Shares Eligible for Future Sale—Lock-Up Agreements."

Demand registration rights

At any time after 180 days following the completion of this offering, the shareholders, as defined in the Registration Rights Agreement, holding not less than fifty percent of the registrable securities have the right to demand that we file, a registration statement to register all or a portion of their registrable securities, provided that the expected aggregate proceeds to be received from the sale of the registrable securities to be sold under the registration statement is equal to or exceeds \$10.0 million. We are not obligated to file a registration statement pursuant to this demand provision (i) on more than one occasion within any six-month period or (ii) if at the time of such request, four or more such demand registrations and underwritten takedowns, as defined in the Registration Rights Agreement, have previously been effected or deemed effected.

Form S-3 registration rights

In addition, if, at any time after the first anniversary of this offering, we become eligible to file a registration statement on Form S-3 under the Securities Act, subject to specified limitations, a shareholder or a group of shareholders, as defined in the Registration Rights Agreement, may demand in writing that we register on Form S-3 all or part of the registrable securities held by them. We are not obliged to effect more than one such underwritten takedown, as defined in the Registration Rights Agreement, within any six-month period.

Piggyback registration rights

If, at any time after the completion of this offering, we propose to file a registration statement to register any of our common stock under the Securities Act (other than (i) a registration statement on Form S-3 or (ii) a registration statement relating to any employee benefit plan), either for our own account or for the account of any of our stockholders that are not holders of registrable securities, the holders of our registrable securities are entitled to notice of registration and, subject to specified exceptions, we will be required to use our commercially reasonable efforts to register the registrable securities then held by them that they request that we register.

Expenses of registration

Pursuant to the Registration Rights Agreement, we are required to pay all registration expenses, including registration fees, printing expenses, fees and disbursements of our counsel and accountants and reasonable fees and disbursements of one counsel representing all shareholders, as defined in the Registration Rights Agreement, participating in the offering, other than any underwriting discounts and commissions attributable to the sale of registrable securities, as defined in the Registration Rights Agreement.

The Registration Rights Agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify shareholders, as defined in the Registration Rights Agreement, beneficially owning registrable securities covered by a registration statement in the event of material misstatements or omissions in the registration statement attributable to us, and each shareholder, as defined in the Registration Rights Agreement, is obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Anti-Takeover effects of Delaware law and our charter and bylaws

Delaware law contains, and upon the completion of this offering our certificate of incorporation and our bylaws will contain, provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

Staggered board; removal of directors

Upon the completion of this offering, our certificate of incorporation and bylaws will divide our board of directors into three classes with staggered three-year terms. In addition, a director will only be able to be removed for cause and only by the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in an annual election of directors. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, will only be able to be filled by vote of a majority of our directors then in office. The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder action by written consent; special meetings

Upon the completion of this offering, our certificate of incorporation will provide that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of such holders and may not be effected by any consent in writing by such holders. Upon the completion of this offering, our certificate of incorporation and bylaws will also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our chairman of the board, our Chief Executive Officer or our board of directors.

Advance notice requirements for stockholder proposals

Upon the completion of this offering, our bylaws will establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of persons for election to our board of directors. Stockholders at an annual meeting will only be able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the

meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities.

Delaware business combination statute

Upon the completion of this offering, we will be subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Amendment of certificate of incorporation and bylaws

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Effective as of the closing date of this offering, our bylaws may be amended or repealed by a majority vote of our board of directors or by the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above under "—Staggered board; removal of directors" and "—Stockholder action by written consent; special meetings."

Exclusive forum selection

Effective as of the closing date of this offering, our certificate of incorporation will provide that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the Court of Chancery of the State of Delaware (or if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on behalf of our company under Delaware law, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, (3) any action asserting a claim against our company arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or bylaws, (4) any action asserting a claim against our company governed by the internal affairs doctrine or (5) any other action asserting an "internal corporate claim," as defined in Section 115 of the Delaware General Corporation Law. These exclusive-forum provisions do not apply to claims under the Securities Act or the Exchange Act. Any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and consented to this provision. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against us or our directors and officers.

Listing on The Nasdaq Global Select Market

We have applied to have our common stock listed on The Nasdaq Global Select Market under the symbol "APRE."

Authorized but unissued shares

The authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing requirements of The Nasdaq Global Select Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make it more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Transfer agent and registrar

The transfer agent and registrar for our common stock will be Computershare Trust Company, N.A. The transfer agent and registrar's address is 150 Royall St., Canton, MA 02021.

Shares Eligible for Future Sale

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital in the future. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after the completion of this offering due to contractual and legal restrictions on resale described below. Future sales of our common stock in the public market either before (to the extent permitted) or after restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price of our common stock at such time and our ability to raise equity capital at a time and price we deem appropriate.

Sale of restricted shares

Based on the number of shares of our common stock outstanding as of September 26, 2019, and after giving effect to the Holdco Reorganization and the conversion of all outstanding shares of our convertible preferred stock for common stock, upon the completion of this offering, we will have outstanding an aggregate of approximately 19,209,865 shares of common stock. Of these shares, all of the shares of common stock to be sold in this offering will be freely tradable in the public market without restriction or further registration under the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering will be "restricted securities" as such term is defined in Rule 144. These restricted securities were issued and sold by us, or will be issued and sold by us, in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, based on the number of shares of our common stock outstanding as of September 26, 2019, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

<u>Approximate number of shares</u>	<u>First date available for sale into public market</u>
14,179,428 shares	180 days after the date of this prospectus upon expiration of the lock-up agreements referred to below, subject in some cases to applicable volume limitations under Rule 144

Lock-Up agreements

In connection with this offering, we, our directors, executive officers and holders of substantially all outstanding shares have agreed with the underwriters, subject to certain exceptions, to not to dispose of or hedge any shares of our common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of the lock-up agreement continuing through the date 180 days after the date of this prospectus, except with the prior written consent of J.P. Morgan Securities LLC and Morgan Stanley & Co. LLC. These agreements are subject to certain customary exceptions. See the section titled "Underwriting" for additional information.

Prior to the completion of the offering, certain of our employees, including our executive officers, and/or directors may enter into written trading plans that are intended to comply with Rule 10b5-1 under the Exchange Act. Sales under these trading plans would not be permitted until the expiration of the lock-up agreements relating to the offering described above.

Following the lock-up periods set forth in the agreements described above, and assuming that the representatives of the underwriters do not release any parties from these agreements, all of the shares of our common stock that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

Directed share program

At our request, the underwriters have reserved up to 3% of the shares for sale at the initial public offering price to those who are directors, officers, employees, business associates and related persons to us through a directed share program. The number of shares available for sale to the general public will be reduced by the number of directed shares purchased by participants in the program. Except for certain of our officers, directors and employees who have entered into lock-up agreements, each person buying shares through the directed share program has agreed that, for a period of 180-days from the date of this prospectus, he or she will not, without the prior written consent of Morgan Stanley & Co. LLC, dispose of or hedge any shares purchased in the program or any securities convertible into or exchangeable or redeemable for our common stock with respect to shares purchased in the program. For certain officers, directors and employees purchasing shares through the directed share program, the lock-up agreements described above with respect to the underwriting agreement shall govern with respect to their purchases. Any directed shares not purchased will be offered by the underwriters to the general public on the same basis as all other shares offered. We have agreed to indemnify the underwriters against certain liabilities and expenses, including liabilities under the Securities Act, in connection with the sales of the directed shares.

Rule 144

In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, a person (or persons whose shares are required to be aggregated) who is not deemed to have been one of our "affiliates" for purposes of Rule 144 at any time during the three months preceding a sale, and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months, including the holding period of any prior owner other than one of our "affiliates," is entitled to sell those shares in the public market (subject to the lock-up agreement referred to above, if applicable) without complying with the manner of sale, volume limitations or notice provisions of Rule 144, but subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than "affiliates," then such person is entitled to sell such shares in the public market without complying with any of the requirements of Rule 144 (subject to the lock-up agreement referred to above, if applicable). In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, our "affiliates," as defined in Rule 144, who have beneficially owned the shares proposed to be sold for at least six months are entitled to sell in the public market, upon expiration of any applicable lock-up agreements and within any three-month period, a number of those shares of our common stock that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 192,098 shares of common stock immediately after this offering (calculated as of September 26, 2019); or
- the average weekly trading volume of our common stock on The Nasdaq Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Such sales under Rule 144 by our "affiliates" or persons selling shares on behalf of our "affiliates" are also subject to certain manner of sale provisions, notice requirements and to the availability of current public information about us. Notwithstanding the availability of Rule 144, the holders of substantially all of our capital stock and options have entered into lock-up agreements as referenced above and their restricted securities will become eligible for sale (subject to the above limitations under Rule 144) upon the expiration of the restrictions set forth in those agreements.

Rule 701

In general, under Rule 701 as currently in effect, any of our employees, directors, officers, consultants or advisors who acquired common stock from us in connection with a written compensatory stock or option plan or other written agreement in compliance with Rule 701 under the Securities Act before the effective date of the registration statement of which this prospectus is a part (to the extent such common stock is not subject to a lock-up agreement) is entitled to rely on Rule 701 to resell such shares beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act in reliance on Rule 144, but without compliance with the holding period requirements contained in Rule 144. Accordingly, subject to any applicable lock-up agreements, beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act, under Rule 701 persons who are not our "affiliates," as defined in Rule 144, may resell those shares without complying with the minimum holding period or public information requirements of Rule 144, and persons who are our "affiliates" may resell those shares without compliance with Rule 144's minimum holding period requirements (subject to the terms of the lock-up agreement referred to above, if applicable).

Registration rights

Based on the number of shares of common stock outstanding as of September 26, 2019, after the completion of this offering, the holders of approximately 14,200,000 shares of our common stock, or their transferees, will, subject to any lock-up agreements they have entered into, be entitled to certain rights with respect to the registration of the offer and sale of those shares under the Securities Act. For a description of these registration rights, please see the section titled "Description of Capital Stock—Registration Rights." If the offer and sale of these shares are registered, they will be freely tradable without restriction under the Securities Act.

Stock plans

We intend to file with the SEC a registration statement under the Securities Act covering the shares of common stock reserved for issuance under our 2019 Stock Incentive Plan and 2019 Employee Stock Purchase Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the completion of this offering. Accordingly, shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

Material U.S. Federal Income Tax Considerations to Non-U.S. Holders

The following is a summary of material U.S. federal income tax consequences of the purchase, ownership and disposition of shares of our common stock as of the date hereof. Except where noted, this summary deals only with common stock that was acquired in this offering and that is held as a capital asset by a non-U.S. holder (as defined below).

A "non-U.S. holder" means a beneficial owner of shares of our common stock (other than an entity treated as a partnership for U.S. federal income tax purposes) that is not, for U.S. federal income tax purposes, any of the following:

- an individual citizen or resident of the United States;
- a corporation (or any other entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if it (1) is subject to the primary supervision of a court within the United States and one or more U.S. persons as defined under the Code have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

This summary is based upon provisions of the Internal Revenue Code of 1986, as amended (the "Code"), and regulations, rulings and judicial decisions as of the date hereof. Those authorities may be changed, perhaps retroactively, so as to result in U.S. federal income consequences different from those summarized below. This summary does not address all aspects of U.S. federal income taxes and does not deal with foreign, state, local or other tax considerations that may be relevant to non-U.S. holders in light of their particular circumstances. In addition, it does not represent a detailed description of the U.S. federal income tax consequences applicable to you if you are subject to special treatment under the U.S. federal income tax laws (including if you are a U.S. expatriate, foreign pension fund, "controlled foreign corporation," "passive foreign investment company" or a partnership or other pass-through entity for U.S. federal income tax purposes). We cannot assure you that a change in law will not alter significantly the tax considerations that we describe in this summary.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds shares of our common stock, the tax treatment of a partner and the partnership will generally depend upon the status of the partner and the activities of the partnership. If you are a partnership or a partner of a partnership holding our common stock, you should consult your tax advisors.

If you are considering the purchase of our common stock, you should consult your own tax advisors concerning the particular U.S. federal income tax consequences to you of the purchase, ownership and disposition of our common stock, as well as the consequences to you arising under other U.S. federal tax laws and the tax laws of any state, local or other taxing jurisdiction.

Dividends

We have never paid cash dividends on our common stock and we do not anticipate paying any cash dividends in the foreseeable future. See "Dividend Policy." If we make a distribution of cash or other property (other than certain *pro rata* distributions of our stock) in respect of shares of our common stock, the distribution generally will be treated as a dividend for U.S. federal income tax purposes to the extent it is paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Any portion of a distribution that exceeds our current and accumulated earnings and profits generally will be treated first as a tax-free return of capital, causing a

reduction in the adjusted tax basis of a non-U.S. holder's common stock, and to the extent the amount of the distribution exceeds a non-U.S. holder's adjusted tax basis in shares of our common stock, the excess will be treated as gain from the disposition of shares of our common stock (the tax treatment of which is discussed below under "—Gain on Disposition of Common Stock").

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. However, dividends that are effectively connected with the conduct of a trade or business by the non-U.S. holder within the United States (and, if required by an applicable income tax treaty, are attributable to a U.S. permanent establishment) are not subject to the withholding tax, provided certain certification and disclosure requirements are satisfied. Instead, such dividends are subject to U.S. federal income tax on a net income basis in the same manner as if the non-U.S. holder were a U.S. person as defined under the Code. Any such effectively connected dividends received by a foreign corporation may be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty.

A non-U.S. holder who wishes to claim the benefit of an applicable treaty rate and avoid backup withholding, as discussed below, for dividends will be required (a) to provide the applicable withholding agent with a properly executed IRS Form W-BEN or Form W-8BEN-E (or other applicable form) certifying under penalty of perjury that such holder is not a U.S. person as defined under the Code and is eligible for treaty benefits or (b) if our common stock is held through certain foreign intermediaries, to satisfy the relevant certification requirements of applicable U.S. Treasury regulations. Special certification and other requirements apply to certain non-U.S. holders that are pass-through entities rather than corporations or individuals.

A non-U.S. holder eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

Gain on disposition of common stock

Subject to the discussion of backup withholding and FATCA below, any gain realized by a non-U.S. holder on the sale or other disposition of our common stock generally will not be subject to U.S. federal income tax unless:

- the gain is effectively connected with a trade or business of the non-U.S. holder in the United States (and, if required by an applicable income tax treaty, is attributable to a U.S. permanent establishment of the non-U.S. holder);
- the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of that disposition, and certain other conditions are met; or
- we are or have been a "United States real property holding corporation" for U.S. federal income tax purposes and certain other conditions are met.

A non-U.S. holder described in the first bullet point immediately above will be subject to tax on the gain derived from the sale or other disposition in the same manner as if the non-U.S. holder were a U.S. person as defined under the Code. In addition, if any non-U.S. holder described in the first bullet point immediately above is a foreign corporation, the gain realized by such non-U.S. holder may be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. An individual non-U.S. holder described in the second bullet point immediately above will be subject to a 30% (or such lower rate as may be specified by an applicable income tax treaty) tax on the gain derived from the sale or other disposition, which gain may be offset by U.S. source capital losses even though the individual is not considered a resident of the United States.

Generally, a corporation is a "United States real property holding corporation" if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests and its other assets used or held for use in a trade or business (all as determined for U.S. federal income tax purposes). We have not been, are not and do not anticipate becoming a U.S. real property holding corporation for U.S. federal income tax purposes. If we are or become a "United States real property holding corporation," however, so long as our common stock is regularly traded on an established securities market during the calendar year in which the sale or other disposition occurs, only a non-U.S. holder who holds or held (at any time during the shorter of the five-year period preceding the date of disposition or the holder's holding period) more than 5% of our common stock will be subject to U.S. federal income tax on the sale or other disposition of our common stock.

Information reporting and backup withholding

Distributions paid to a non-U.S. holder and the amount of any tax withheld with respect to such distributions generally will be reported to the IRS. Copies of the information returns reporting such distributions and any withholding may also be made available to the tax authorities in the country in which the non-U.S. holder resides under the provisions of an applicable income tax treaty.

A non-U.S. holder will not be subject to backup withholding on dividends received if such holder certifies under penalty of perjury that it is a non-U.S. holder (and the payor does not have actual knowledge or reason to know that such holder is a U.S. person as defined under the Code), or such holder otherwise establishes an exemption.

Information reporting and, depending on the circumstances, backup withholding will apply to the proceeds of a sale or other disposition of our common stock made within the United States or conducted through certain U.S.-related financial intermediaries, unless the beneficial owner certifies under penalty of perjury that it is a non-U.S. holder (and the payor does not have actual knowledge or reason to know that the beneficial owner is a U.S. person as defined under the Code), or such owner otherwise establishes an exemption.

Backup withholding is not an additional tax and any amounts withheld under the backup withholding rules will be allowed as a refund or a credit against a non-U.S. holder's U.S. federal income tax liability provided the required information is timely furnished to the IRS.

Additional withholding requirements under FATCA

Pursuant to sections 1471 through 1474 of the Code, commonly known as the Foreign Account Tax Compliance Act ("FATCA"), a 30% withholding tax may be imposed on certain payments to you or to certain foreign financial institutions, investment funds and other non-U.S. persons receiving payments on your behalf if you or such persons are subject to, and fail to comply with, certain information reporting requirements. Such payments will include U.S.-source dividends and the gross proceeds from the sale or other disposition of stock that can produce U.S.-source dividends. Payments of dividends that you receive in respect of shares of our common stock could be affected by this withholding if you are subject to FATCA information reporting requirements and fail to comply with them or if you hold shares of our common stock through a non-U.S. person (e.g., a foreign bank or broker) that fails to comply with these requirements (even if payments to you would not otherwise have been subject to FATCA withholding). Pursuant to recently proposed regulations, the U.S. Treasury Department has indicated its intent to eliminate the requirements under FATCA of withholding on gross proceeds. The U.S. Treasury Department has indicated that taxpayers may rely on these proposed regulations pending their finalization. An intergovernmental agreement between the United States and your country of residence (or the country of residence of the non-U.S. person receiving payments on your behalf) may

modify the requirements described above. You should consult your own tax advisors regarding the relevant U.S. law and other official guidance on FATCA withholding.

If a dividend payment is both subject to withholding under FATCA and subject to the withholding tax discussed above under "—Dividends," the withholding under FATCA may be credited against, and therefore reduce, such other withholding tax. You should consult your own tax advisors regarding these requirements and whether they may be relevant to your ownership and disposition of our common stock.

Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC, Morgan Stanley & Co. LLC and RBC Capital Markets, LLC are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the representatives. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the initial public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	
Morgan Stanley & Co. LLC	
RBC Capital Markets, LLC	
Total	5,000,000

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of \$ _____ per share. Any such dealers may resell shares to certain other brokers or dealers at a discount of up to \$ _____ per share from the initial public offering price. After the initial offering of the shares to the public, if all of the common shares are not sold at the initial public offering price, the underwriters may change the offering price and the other selling terms. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to 750,000 additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ _____ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option to purchase additional shares exercise	With full option to purchase additional shares exercise
Per Share	\$ _____	\$ _____
Total	\$ _____	\$ _____

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and

commissions, will be approximately \$3.2 million. We have agreed to reimburse the underwriters for expenses of up to \$35,000 related to clearance of this offering with the Financial Industry Regulatory Authority, or FINRA.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or file with the Securities and Exchange Commission a registration statement under the Securities Act, relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC and Morgan Stanley & Co. LLC for a period of 180 days after the date of this prospectus, other than the shares of our common stock to be sold hereunder and any shares of our common stock issued upon the exercise of options granted under our existing stock incentive plans.

Our directors, executive officers and holders of substantially all outstanding shares have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 180 days after the date of this prospectus, may not, without the prior written consent of J.P. Morgan Securities LLC and Morgan Stanley & Co. LLC, (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

The restrictions described in the immediately preceding paragraph do not apply to, among other items, transfers or dispositions of shares of common stock:

- as a bona fide gift or gifts or for bona fide estate planning purposes;
- to immediate family members or any trust or other legal entity for the direct or indirect benefit of the party subject to the lock-up restrictions or the immediate family of such person;
- by will, other testamentary document or intestate succession subject to the lockup restrictions;

- to any corporation, partnership, limited liability company, trust or other business entity under the ownership of the party or managers, managing members, partners, stockholders, all subject to the lock-up restrictions;
 - as transfers to affiliates, investment funds or other entities controlled or managed by the party subject to the lock-up restrictions;
 - pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all holders of our common stock involving a change of control; provided that in the event such tender offer, merger, consolidation or other such transaction is not completed, the shares of our common stock shall remain subject to the lock-up restrictions;
 - the exercise of outstanding warrants or options to purchase shares of common stock granted under any stock incentive plan or stock purchase plan of ours, provided that the underlying shares shall continue to be subject to the lock-up restrictions;
 - transfers or surrenders to the Company of shares of common stock pursuant to any contractual arrangement that provides the Company with an option to repurchase such shares in connection with the termination of the party subject to the lock-up's employment or service relationship with us, or on a cashless or "net exercise" basis or to cover tax withholding obligations of the party subject to the lock-up, in connection with the vesting or exercise of such shares of common stock or other securities; and
 - transactions relating to common stock or other securities convertible into or exercisable or exchangeable for common stock acquired in this offering or in open market transactions after the completion of this offering
- provided that in the case of any transfer or distribution pursuant to the subclauses above, (i) each donee or distributee shall sign and deliver a lock-up letter in the form executed by the party subject to the lock up restrictions and (ii) no filing or other public announcement under Section 16(a) of the Exchange Act of 1934, as amended, or the Exchange Act, shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5 after the restricted period has ended);
- and the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of shares of common stock during the restricted period and (ii) no filing under the Exchange Act or other public announcement shall be required or voluntarily made by or on behalf of the party subject to the lock-up restrictions regarding the establishment of such plan.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

We have applied to list our common stock on The Nasdaq Global Select Market under the symbol "APRE."

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be "covered" shorts, which are short positions in an amount not greater than the underwriters' option to purchase additional shares referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase

additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on NASDAQ, in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters expect to consider a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our common shares, or that the shares will trade in the public market at or above the initial public offering price.

Other relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates may in the future provide various commercial banking, financial advisory or investment banking advice or other services in the ordinary course of their business, for which they will receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their respective affiliates, officers, directors and employees may effect transactions for their own

account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of our securities and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in our securities.

Directed share program

At our request, the underwriters have reserved up to 3% of the shares of common stock to be issued by the Company and offered by this prospectus for sale, at the initial public offering price, to directors, officers, employees, business associates and related persons of the Company. If purchased by these persons, these shares will be subject to a 180-day lock-up restriction. The number of shares of common stock available for sale to the general public will be reduced to the extent these individuals purchase such reserved shares. Any reserved shares that are not so purchased will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus.

Selling restrictions

General

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Australia

This prospectus is not a disclosure document under Chapter 6D of the Australian Corporations Act, has not been lodged with the Australian Securities and Investments Commission and does not purport to include the information required of a disclosure document under Chapter 6D of the Australian Corporations Act. Accordingly, (i) the offer of the securities under this prospectus is only made to persons to whom it is lawful to offer the securities without disclosure under Chapter 6D of the Australian Corporations Act under one or more exemptions set out in section 708 of the Australian Corporations Act, (ii) this prospectus is made available in Australia only to those persons as set forth in clause (i) above, and (iii) the offeree must be sent a notice stating in substance that by accepting this offer, the offeree represents that the offeree is such a person as set forth in clause (i) above, and, unless permitted under the Australian Corporations Act, agrees not to sell or offer for sale within Australia any of the securities sold to the offeree within 12 months after its transfer to the offeree under this prospectus.

Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale

of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the representatives are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant Member State"), no offer of shares may be made to the public in that Relevant Member State other than:

- A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or
- C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The Company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly, any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression "an offer to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances that do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances that do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares that are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan, or the Financial Instruments and Exchange Law, and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term, as used in this prospectus means any person resident in Japan, including any corporation or other entity organized under the laws of Japan) or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person that is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold

investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document, nor any other offering or marketing material relating to the shares or this offering, may be publicly distributed or otherwise made publicly available in Switzerland. Neither this document nor any other offering or marketing material relating to this offering, the Company, or the shares has been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

United Arab Emirates

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for this prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus, you should consult an authorized financial advisor.

United Kingdom

This document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49 (2) (a) to (d) of the Order (all such persons together being referred to as "relevant persons").

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Legal Matters

The validity of the shares of our common stock offered hereby is being passed upon for us by Sidley Austin LLP, New York, New York. Certain legal matters relating to this offering will be passed upon for the underwriters by Davis Polk & Wardwell LLP, New York, New York.

Experts

The consolidated financial statements of Aprea Therapeutics AB at December 31, 2017 and 2018, and for each of the two years in the period ended December 31, 2018, appearing in this Prospectus and Registration Statement have been audited by Ernst & Young AB, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The balance sheet of Aprea Therapeutics, Inc. at July 11, 2019, appearing in this Prospectus and Registration Statement has been audited by Ernst & Young AB, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and is included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The registered business address of Ernst & Young AB is Box 7850, 103 99, Stockholm, Sweden.

Where You Can Find More Information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock we are offering to sell. This prospectus, which constitutes part of the registration statement, does not include all of the information contained in the registration statement and the exhibits, schedules and amendments to the registration statement. Some items are omitted in accordance with the rules and regulations of the SEC. For further information with respect to us and our common stock, we refer you to the registration statement and to the exhibits, schedules and amendments to the registration statement. Statements contained in this prospectus about the contents of any contract, agreement or other document filed as an exhibit are not necessarily complete, and, in each instance, we refer you to the copy of the contract, agreement or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

Upon completion of this offering, we will be subject to the information reporting requirements of the Securities Exchange Act, and we will file reports, proxy statements and other information with the SEC. We intend to furnish our stockholders with annual reports containing financial statements certified by an independent registered public accounting firm. We also maintain a website at www.aprea.com. The information contained on, or that can be accessed through, our website is not a part of, and is not incorporated into, this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

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To the Stockholder and the Board of Directors of Aprea Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheet of Aprea Therapeutics, Inc. (the Company) at July 11, 2019 and the related notes. In our opinion, the balance sheet presents fairly, in all material respects, the financial position of the Company at July 11, 2019, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

The balance sheet is the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's balance sheet based on our audit. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the balance sheet is free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audit included performing procedures to assess the risks of material misstatement of the balance sheet, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the balance sheet. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the balance sheet. We believe that our audit provides a reasonable basis for our opinion.

/s/ Ernst & Young AB

We have served as the Company's auditor since 2019.

Stockholm, Sweden

August 20, 2019,

Except for the stock split described in Note 1, as to which the date is September 27, 2019.

Aprea Therapeutics, Inc.

Balance Sheet

As of July 11, 2019 (date of initial capital contribution)

	July 11, 2019
Assets	
Current assets:	
Cash and cash equivalents	\$ 100
Total current assets	<u>100</u>
Total assets	<u>\$ 100</u>
Liabilities and Stockholders' Equity	
Total liabilities	\$ —
Stockholders' deficit:	
Common stock, \$0.001 par value; 160 shares authorized, issued and outstanding.	—
Additional paid-in capital	<u>100</u>
Total stockholders' equity	<u>100</u>
Total liabilities and stockholders' equity	<u>\$ 100</u>

See accompanying notes to financial statements.

1. Nature of business and basis of presentation

Nature of business—Aprea Therapeutics, Inc. ("ATI" or the "Company") was incorporated in Delaware on May 3, 2019 and the date of its initial capital contribution was July 11, 2019.

The authorized share capital of ATI consists of 160 shares of capital stock, par value \$0.001 per share, which has been issued. ATI was incorporated with nominal assets and liabilities for the purpose of becoming a holding company for Aprea Therapeutics AB and Aprea (U.S.) Inc. and for the purposes of consummating a corporate reorganization.

On September 20, 2019, the Company consummated a corporate reorganization, pursuant to which all of the issued and outstanding stock and options of Aprea Therapeutics AB, or Aprea AB, were exchanged for common stock, preferred stock or options, as applicable, of Aprea Therapeutics, Inc. As a result, Aprea Therapeutics AB, became a wholly-owned subsidiary of Aprea Therapeutics, Inc.

Basis of presentation—The accompanying financial statements are prepared in conformity with accounting principles generally accepted in the United States ("U.S. GAAP"). Separate statements of income, changes in equity and cash flows have not been presented in the financial statements because there have been no operations in the Company at the balance sheet date.

Prior to the completion of its initial public offering, the Company will approve a 1-for-1.6045 stock split of the Company's common stock. All share and per share amounts in the balance sheet and notes thereto have been retroactively adjusted for all periods presented to give effect to this split.

To the Stockholders and the Board of Directors of Aprea Therapeutics AB

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Aprea Therapeutics AB (the Company) as of December 31, 2017 and 2018, the related consolidated statements of operations and comprehensive income (loss), convertible preferred stock and stockholders' deficit and cash flows for each of the two years in the period ended December 31, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young AB

We have served as the Company's auditor since 2015.

Stockholm, Sweden

August 20, 2019,

Except for the stock split described in Note 1, as to which the date is September 27, 2019.

Aprea Therapeutics AB
Consolidated Balance Sheets

	December 31,	
	2017	2018
Assets		
Current assets:		
Cash and cash equivalents	\$ 24,401,488	\$ 65,675,931
Prepaid expenses and other current assets	329,859	322,146
Total current assets	24,731,347	65,998,077
Property and equipment, net	30,336	24,450
Other noncurrent assets	121	111
Total assets	<u>\$ 24,761,804</u>	<u>\$ 66,022,638</u>
Liabilities, Convertible Preferred Stock and Stockholders' Deficit		
Current liabilities:		
Accounts payable	\$ 1,661,813	\$ 1,739,337
Accrued expenses	2,639,200	3,128,772
Total current liabilities	4,301,013	4,868,109
Total liabilities	4,301,013	4,868,109
Commitments and contingencies (Note 6)		
Convertible preferred stock:		
Series A convertible preferred stock, \$0.11 par value; 612,446 shares issued and outstanding at December 31, 2018 and 2017 (liquidation preference of \$6,483,044 at December 31, 2018)	6,483,044	6,483,044
Series B convertible preferred stock, \$0.11 par value; 7,235,969 shares issued and outstanding at December 31, 2018 and 2017 (liquidation preference of \$58,874,347 at December 31, 2018)	49,742,942	49,742,942
Series C convertible preferred stock, \$0.11 par value; 4,712,698 and 0 shares issued and outstanding at December 31, 2018 and 2017, respectively (liquidation preference of \$57,115,312 at December 31, 2018)	—	56,364,645
Total convertible preferred stock	56,225,986	112,590,631
Stockholders' deficit:		
Common stock, \$0.11 par value; 1,155,366 and 1,153,061 shares issued and outstanding at December 31, 2018 and 2017, respectively.	126,838	127,091
Additional paid-in capital	19,335,560	19,666,588
Accumulated other comprehensive loss	(8,287,406)	(8,761,325)
Accumulated deficit	(46,940,187)	(62,468,456)
Total stockholders' deficit	(35,765,195)	(51,436,102)
Total liabilities, convertible preferred stock and stockholders' deficit	<u>\$ 24,761,804</u>	<u>\$ 66,022,638</u>

See accompanying notes to consolidated financial statements.

Aprea Therapeutics AB

Consolidated Statements of Operations and Comprehensive Loss

	Years ended December 31,	
	2017	2018
Operating expenses:		
Research and development	\$ 13,392,631	\$ 14,194,732
General and administrative	2,459,744	2,294,671
Total operating expenses	15,852,375	16,489,403
Other income (expense):		
Interest expense	(15)	(182)
Foreign currency gain	662,140	961,316
Total other income (expense)	662,125	961,134
Net loss	\$ (15,190,250)	\$ (15,528,269)
Other comprehensive income (loss):		
Foreign currency translation	\$ 495,160	\$ (473,919)
Total comprehensive loss	\$ (14,695,090)	\$ (16,002,188)
Net loss per share attributable to common stockholders, basic and diluted	\$ (13.17)	\$ (13.45)
Weighted-average common shares outstanding, basic and diluted	1,153,069	1,154,368
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		\$ (1.65)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)		9,428,873

See accompanying notes to consolidated financial statements

Consolidated Statements of Convertible Preferred Stock and Stockholders' Deficit

	Convertible preferred stock								Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' deficit
	Series A		Series B		Series C		Common stock					
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at January 1, 2017	612,446	\$ 6,483,044	3,913,207	\$ 26,399,079	—	\$ —	1,153,061	\$ 126,838	\$ 18,940,120	\$ (8,782,566)	\$ (31,749,937)	\$ (21,465,545)
Issuance of Series B convertible preferred stock, net of issuance costs of \$47,047	—	—	3,322,762	23,343,863	—	—	—	—	—	—	—	—
Stock-based compensation	—	—	—	—	—	—	—	—	395,440	—	—	395,440
Foreign currency translation	—	—	—	—	—	—	—	—	—	495,160	—	495,160
Net loss	—	—	—	—	—	—	—	—	—	—	(15,190,250)	(15,190,250)
Balance at December 31, 2017	612,446	\$ 6,483,044	7,235,969	\$ 49,742,942	—	\$ —	1,153,061	\$ 126,838	\$ 19,335,560	\$ (8,287,406)	\$ (46,940,187)	\$ (35,765,195)
Issuance of Series C convertible preferred stock, net of issuance costs of \$3,278,302	—	—	—	—	4,712,698	56,364,645	—	—	—	—	—	—
Exercise of stock options	—	—	—	—	—	—	2,305	253	1,844	—	—	2,097
Stock-based compensation	—	—	—	—	—	—	—	—	329,184	—	—	329,184
Foreign currency translation	—	—	—	—	—	—	—	—	—	(473,919)	—	(473,919)
Net loss	—	—	—	—	—	—	—	—	—	—	(15,528,269)	(15,528,269)
Balance at December 31, 2018	612,446	\$ 6,483,044	7,235,969	\$ 49,742,942	4,712,698	\$ 56,364,645	1,155,366	\$ 127,091	\$ 19,666,588	\$ (8,761,325)	\$ (62,468,456)	\$ (51,436,102)

See accompanying notes to consolidated financial statements.

Aprea Therapeutics AB
Consolidated Statements of Cash Flows

	Years ended December 31,	
	2017	2018
Cash flows from operating activities:		
Net loss	\$ (15,190,250)	\$ (15,528,269)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	7,932	8,316
Stock-based compensation	395,440	329,184
Foreign currency gain	(662,140)	(961,316)
Changes in operating assets and liabilities:		
Prepaid expense and other current assets	4,041	(19,452)
Accounts payable	327,054	214,380
Accrued expenses and other liabilities	1,115,805	706,923
Net cash used in operating activities	<u>(14,002,118)</u>	<u>(15,250,234)</u>
Cash flows from investing activities:		
Purchases of property and equipment	—	(3,702)
Net cash used in investing activities	<u>—</u>	<u>(3,702)</u>
Cash flows from financing activities:		
Proceeds from the exercise of stock options	—	2,097
Proceeds from issuance of Series B convertible preferred, net	23,343,863	—
Proceeds from issuance of Series C convertible preferred, net	—	56,364,645
Net cash provided by financing activities	<u>23,343,863</u>	<u>56,366,742</u>
Increase in cash	9,341,745	41,112,806
Effect of exchange rate changes on cash	1,394,568	161,637
Cash and cash equivalents—beginning of year	13,665,175	24,401,488
Cash and cash equivalents—end of year	<u>\$ 24,401,488</u>	<u>\$ 65,675,931</u>

See accompanying notes to consolidated financial statements.

1. Nature of business and basis of presentation

Nature of business—Aprea Therapeutics AB (the “Company”) is a clinical-stage biopharmaceutical company focused on developing and commercializing novel cancer therapeutics that reactivate mutant tumor suppressor protein p53. p53 is the protein expressed from the *TP53* gene, the most commonly mutated gene in cancer. The Company began operations in 2006. Its principal offices are in Stockholm, Sweden and Boston, Massachusetts.

Basis of presentation and management plans—The accompanying financial statements are prepared in conformity with accounting principles general accepted in the United States (“U.S. GAAP”). The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business.

Since its inception, the Company has devoted substantially all of its efforts to business planning, research and development, recruiting management and technical staff, and raising capital, and has financed its operations through the issuance of convertible preferred stock (“Preferred Stock”) and common stock.

The Company is subject to risks common to companies in the biopharmaceutical industry. There can be no assurance that the Company’s research and development will be successfully completed, that adequate protection for the Company’s intellectual property will be maintained, that any therapeutic products developed will obtain required regulatory approval or that any approved or consumer products will be commercially viable. Even if the Company’s development efforts are successful, it is uncertain when, if ever, the Company will generate significant product sales.

The Company’s management believes that the December 31, 2018 cash balance of \$65,675,931, along with the gross proceeds of \$5,645,248 from the issuance of Series C convertible preferred stock (“Series C Preferred”) from a new investor in February 2019, will be sufficient to fund the Company’s operations into the third quarter of 2021. In the event that additional funds are not available thereafter, management would expect to significantly reduce expenditures to conserve cash, which would involve scaling back or curtailing new development activity.

Prior to the completion of its initial public offering, the Company will approve a 1-for-1.6045 stock split of the Company’s preferred and common stock. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this split.

2. Summary of significant accounting policies

Principles of consolidation—The consolidated financial statements include the accounts of Aprea Therapeutics AB and its wholly owned subsidiaries Aprea Personal AB, which was incorporated in May 2009, and Aprea US, Inc., which was incorporated in June 2016. All intercompany transactions and balances have been eliminated.

Use of estimates—The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, and expenses as of and during the reporting period. The Company bases estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. The Company assesses estimates on an ongoing basis; however,

2. Summary of significant accounting policies (continued)

actual results could materially differ from those estimates. Significant items subject to such estimates and assumptions include fair value of stock-based compensation expense.

Unaudited pro forma financial information—The Company is planning a proposed offer and sale by Aprea Therapeutics, Inc., a Delaware corporation and successor entity, of common stock in an initial public offering (the "IPO"). Prior to the completion of the IPO, pursuant to a corporate reorganization, the Company became a wholly-owned subsidiary of Aprea Therapeutics, Inc. In connection with the corporate reorganization, each issued and outstanding share of Series A, Series B and Series C convertible preferred stock of the Company was exchanged on a one for one basis into shares of Series A, Series B and Series C convertible preferred stock of Aprea Therapeutics, Inc. Each share of common stock of the Company was exchanged on a one for one basis in to shares of common stock of Aprea Therapeutics, Inc. Prior to consummation of the IPO, all outstanding shares of Series A, Series B and Series C convertible preferred stock of Aprea Therapeutics, Inc. will be converted into common stock.

The unaudited pro forma basic and diluted weighted average common shares outstanding used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the years ended December 31, 2017 and 2018 give effect to the automatic conversion of all outstanding shares of convertible preferred stock into shares of common stock as if the conversion had occurred on the later of January 1, 2017 or the issuance date of the convertible preferred stock for the year ended December 31, 2017, and on the later of January 1, 2018 or the issuance date of the convertible preferred stock for the year ended December 31, 2018.

Foreign currency and currency translation—The functional currency for Aprea Therapeutics AB and its wholly owned foreign subsidiary, Aprea Personal AB, is the Swedish Krona. Assets and liabilities of Aprea Therapeutics AB and Aprea Personal AB are translated into United States dollars at the exchange rate in effect on the balance sheet date. Revenues and expenses are translated at the average exchange rate in effect during the period. Unrealized translation gains and losses are recorded as a cumulative translation adjustment, which is included in the consolidated statements of convertible preferred stock and stockholders' deficit as a component of accumulated other comprehensive loss. Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the local currency are included in other income (expense), net in the consolidated statements of operations as incurred.

Concentrations of credit risk—Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash. Periodically, the Company may maintain deposits in financial institutions in excess of government insured limits. Management believes that the Company is not exposed to significant credit risk as the Company's deposits are held at financial institutions that management believes to be of high credit quality, and the Company has not experienced any losses on these deposits.

Cash and cash equivalents—The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents.

Deferred initial public offering costs—The Company capitalizes deferred initial public offering ("IPO") costs, which primarily consist of direct, incremental legal, professional, accounting and other third-party fees relating to the Company's initial public offering, within other non-current assets. The

Notes to Financial Statements (Continued)

2. Summary of significant accounting policies (continued)

deferred IPO costs will be offset against IPO proceeds upon the consummation of an offering. Should the planned IPO be abandoned, the deferred issuance costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. There were no deferred IPO costs as of December 31, 2018.

Property and equipment—Property and equipment are recorded at cost. Expenditures for repairs and maintenance are expensed as incurred. When assets are retired or disposed of, the assets and related accumulated depreciation are eliminated from the accounts, and any resulting gain or loss is included in the determination of net income or loss. Fixed assets acquired for research and development purposes are assessed for alternative future use. Depreciation is provided using the straight-line method over the estimated useful lives of the related assets. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset.

<u>Asset category</u>	<u>Estimated useful life</u>
Computer equipment and software	5 years
Furniture and fixtures	5 years
Laboratory equipment and office furniture	5 years
Leasehold improvements	Remainder of lease term

Impairment of long-lived assets—Periodically, the Company evaluates its long-lived assets, which consist primarily of property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset exceeds the fair value of the asset. To date, no impairments have occurred.

Fair value of financial instruments—Fair value is defined as the price that would be received upon sale of an asset or paid to transfer a liability between market participants at measurement dates. ASC Topic 820, Fair Value Measurement ("ASC 820"), establishes a three-level valuation hierarchy for instruments measured at fair value. The hierarchy is based on the transparency of inputs to the valuation of an asset or liability as of the measurement date. The hierarchy defines three levels of valuation inputs, of which the first two are considered observable and the last is considered unobservable:

- Level 1 inputs: Quoted prices in active markets for identical assets or liabilities.
- Level 2 inputs: Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.
- Level 3 inputs: Unobservable inputs developed using estimates or assumptions developed by the Company, which reflect those that a market participant would use in pricing the asset or liability.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Notes to Financial Statements (Continued)

2. Summary of significant accounting policies (continued)

Convertible preferred stock—The Company has classified convertible preferred stock ("Preferred Stock") as temporary equity in the accompanying balance sheets due to certain change in control events that are outside of the Company's control, including sale or transfer of control of the Company, as holders of the Preferred Stock could cause redemption of the shares in these situations. The Company does not accrete the carrying values of the Preferred Stock to the redemption values since a liquidation event was not considered probable as of December 31, 2018. Subsequent adjustments of the carrying values to the ultimate redemption values will be made only if it becomes probable that such a liquidation event will occur.

Research and development costs—Research and development costs are charged to expense as incurred. Research and development expense consists of expenses incurred in performing research and development activities, including salaries and benefits, materials and supplies, preclinical expenses, stock-based compensation expense, depreciation of equipment, contract services, and other outside expenses. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using or information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development.

Patent costs—All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Stock-based compensation—The Company measures stock options and other stock-based awards granted to employees and directors based on their fair value on the date of the grant and recognize compensation expense of those awards, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. The Company applies the straight-line method of expense recognition to all awards with only service-based vesting conditions and apply the graded-vesting method to all awards with performance-based vesting conditions or to awards with both service-based and performance-based vesting conditions.

For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed in accordance with the FASB issued ASU No. 2018-07, Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. The new standard largely aligns the accounting for share-based payment awards issued to employees and nonemployees by expanding the scope of ASC 718 to apply to nonemployee share-based transactions, as long as the transaction is not effectively a form of financing.

The Company estimates the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of the Company's common stock and assumptions the Company makes for the volatility of its common stock, the expected term of its stock options, the risk-free interest rate for a period that approximates the expected term of its stock options and its expected dividend yield.

Notes to Financial Statements (Continued)

2. Summary of significant accounting policies (continued)

Determination of fair value of common stock

As there has been no public market for the Company's common stock to date, the estimated fair value of its common stock has been determined by its board of directors as of the date of each option grant, with input from management, considering the Company's most recently available third-party valuations of common stock and its board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. The Company's common stock valuations were prepared using a hybrid method, which used market approaches to estimate its enterprise value. The hybrid method is a probability-weighted expected return method, or PWERM, where the equity value in one or more scenarios is calculated using an option-pricing method, or OPM. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. These third-party valuations were performed at various dates, which resulted in valuations of the Company's common stock of \$0.92 per share as of May 31, 2016, \$1.01 per share as of October 2, 2017 and \$3.18 per share as of December 31, 2018.

In addition to considering the results of these third-party valuations, the Company's board of directors considered various objective and subjective factors to determine the fair value of its common stock as of each grant date, including:

- the prices at which the Company sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to its common stock at the time of each grant;
- the progress of the Company's research and development programs, including the status and results of preclinical studies and clinical trials for its product candidates;
- the Company's stage of development and commercialization and its business strategy;
- external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry;
- the Company's financial position, including cash on hand, and its historical and forecasted performance and operating results;
- the lack of an active public market for the Company's common stock and its preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of the Company in light of prevailing market conditions; and

Notes to Financial Statements (Continued)

2. Summary of significant accounting policies (continued)

- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if the Company had used significantly different assumptions or estimates, the fair value of its common stock and its stock-based compensation expense could have been materially different.

Income taxes—The Company accounts for income tax in accordance with ASC 740-10, Income Taxes ("ASC 740-10"), which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the Company's financial statements and tax returns. Deferred tax assets and liabilities are determined based upon the differences between the financial statement carrying amounts and the tax bases of existing assets and liabilities and for loss and credit carryforwards, using enacted tax rates expected to be in effect in the year in which the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if it is more likely than not that these assets may not be realized. The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes.

Net loss per share—The Company has reported losses since inception and has computed basic net loss per share attributable to common stockholders by dividing net loss attributable to common stockholders by the weighted-average number of common shares outstanding for the period, without consideration for potentially dilutive securities. The Company computes diluted net loss per common share after giving consideration to all potentially dilutive common shares, including options to purchase common stock and convertible preferred stock, outstanding during the period determined using the treasury-stock and if-converted methods, except where the effect of including such securities would be antidilutive. Because the Company has reported net losses since inception, these potential common shares have been anti-dilutive and basic and diluted loss per share were the same for all periods presented.

Basic and diluted net loss per share attributable to common stockholders was calculated as follows:

	<u>Year ended December 31,</u>	
	<u>2017</u>	<u>2018</u>
Numerator:		
Net loss	\$ (15,190,250)	\$ (15,528,269)
Denominator—basic and diluted:		
Weighted average common shares outstanding, basic and diluted	1,153,069	1,154,368
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (13.17)</u>	<u>\$ (13.45)</u>

Notes to Financial Statements (Continued)

2. Summary of significant accounting policies (continued)

The following table sets forth the potentially dilutive securities that have been excluded from the calculation of diluted net loss per share because to include them would be anti-dilutive (in common stock equivalent shares):

	<u>Year ended December 31,</u>	
	<u>2017</u>	<u>2018</u>
Series A convertible preferred stock	612,446	612,446
Series B convertible preferred stock	7,235,969	7,235,969
Series C convertible preferred stock	—	4,712,698
Options to purchase common stock	1,897,206	1,844,188
Total shares of common stock equivalents	<u>9,745,621</u>	<u>14,405,301</u>

Pro forma net loss per share—Unaudited pro forma net loss per share attributable to common stockholders is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all the convertible preferred stock into shares of common stock as if such conversion had occurred at the beginning of the period presented or the date of original issuance, if later.

The following table summarizes the Company's unaudited pro forma net loss per share attributable to common stockholders:

	<u>Year ended</u>
	<u>December 31, 2018</u>
Numerator:	
Net loss attributable to common stockholders, basic and diluted	\$ (15,528,269)
Denominator:	
Weighted average common shares outstanding—basic and diluted	1,154,368
Assumed conversion of Series A, Series B and Series C convertible preferred stock	<u>8,274,505</u>
Pro forma weighted average common shares outstanding, basic and diluted	9,428,873
Pro forma net loss per share attributable to common stockholders, basic and diluted	<u>\$ (1.65)</u>

Notes to Financial Statements (Continued)

2. Summary of significant accounting policies (continued)

Recently issued accounting pronouncements

In March 2016, the FASB issued ASU No. 2016-09, Compensation—Stock Compensation ("ASU No. 2016-09"), which amends ASC Topic 718, Compensation—Stock Compensation. ASU No. 2016-09 identifies areas for simplification involving several aspects of accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, an option to recognize gross stock compensation expense with actual forfeitures recognized as they occur, as well as certain classifications on the statement of cash flows. The amendments are effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods. The Company adopted ASU No. 2016-09 effective January 1, 2017. The adoption of ASU No. 2016-09 did not have a material impact on the Company's financial statements. Upon adoption, the Company elected to account for forfeitures as they occur. The Company did not have any excess tax benefits associated with stock option exercises and therefore there was no deferred tax asset recorded upon adoption.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments* ("ASU No. 2016-15"). This guidance addresses the presentation and classification of certain cash receipts and cash payments in the statement of cash flows. The standard is effective for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. Early adoption is permitted. The Company adopted ASU No. 2016-15 effective January 1, 2017. The adoption of ASU No. 2016-15 did not have a material impact on the Company's financial statements.

In February 2016, the FASB issued ASU 2016-02, "*Leases (Topic 842)*." Under ASU 2016-02, lessees will be required to recognize, for all leases of 12 months or more, a liability to make lease payments and a right-of-use asset representing the right to use the underlying asset for the lease term. Additionally, the guidance requires improved disclosures to help users of financial statements better understand the nature of an entity's leasing activities. This ASU is effective for nonpublic reporting companies for interim and annual periods beginning after December 15, 2019, with early adoption permitted, and must be adopted using a modified retrospective approach. The Company is currently assessing the impact of the adoption of this authoritative guidance on its financial statements.

In June 2018, the FASB issued ASU No. 2018-07, "*Compensation—Stock Compensation*", which expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees, except for specific exceptions. This ASU is effective for annual or any interim periods beginning after December 15, 2019. The Company is currently assessing the impact of adopting this authoritative guidance on its financial statements.

In May 2017, the FASB issued ASU No. 2017-09, "*Compensation—Stock Compensation*", which clarifies the guidance about which changes to the terms and conditions of a share-based payments award require an entity to apply modification accounting in Topic 718. This ASU is effective for annual or any interim periods beginning after December 15, 2017. The Company adopted this standard on January 1, 2018, which did not impact the consolidated financial statements as the Company has not modified the terms and conditions of any share-based payments during the year ended December 31, 2018.

Notes to Financial Statements (Continued)

3. Property and equipment

Property and equipment as of December 31, 2017 and 2018 consist of the following:

	December 31,	
	2017	2018
Lab equipment	\$ 72,123	\$ 69,770
Furniture & Fixtures	16,313	16,313
Computer equipment	13,828	12,689
Property and equipment, at cost	102,264	98,772
Less accumulated depreciation and amortization	(71,928)	(74,322)
Property and equipment—net	\$ 30,336	\$ 24,450

Depreciation expense for years ended December 31, 2017 and 2018 was \$7,932 and \$8,316, respectively.

4. Fair value measurements

The Company's financial instruments consist of accounts payable. The carrying amount of accounts payable is considered a reasonable estimate of fair value due to the short-term maturity.

The accounting standard for fair value measurements provides a framework for measuring fair value and requires expanded disclosures regarding fair value measurements. Fair value is defined as the proceeds that would be received for an asset or the exit price that would be paid to transfer a liability in the principal or most advantageous market in an orderly transaction between market participants on the measurement date.

All fair value measurements are classified in the three-tier fair value hierarchy, which categorizes the inputs used in measuring fair value. These categories include (in descending order of priority) Level 1, defined as observable inputs, such as quoted prices in active markets for identical securities; Level 2, defined as inputs other than quoted prices included in Level 1 that are either directly or indirectly observable; and Level 3, defined as significant unobservable inputs in which little or no market data exists, therefore, requiring an entity to develop its own assumptions.

5. Accrued expenses

Accrued expenses at December 31, 2017 and 2018 consist of the following:

	December 31,	
	2017	2018
Professional fees	\$ 33,886	\$ 80,771
Compensation and benefits	717,218	624,298
Research and development	1,817,292	2,178,086
Other	70,804	245,617
Total accrued expenses	\$ 2,639,200	\$ 3,128,772

Notes to Financial Statements (Continued)

6. Commitments

Operating leases—In August 2016, the Company entered into an operating lease for office in Boston, Massachusetts that expires in December 2021. The Company leased office space in Solna, Sweden under an annual operating lease that expired on June 30, 2019. Additionally, the Company entered into a new operating lease for office and laboratory space in Solna, Sweden that is effective July 1, 2019 and expires in June 2022. Base rent for this lease is approximately \$125,000 annually.

Rent expense for the years ended December 31, 2017 and 2018 was \$242,263 and \$263,518, respectively.

Future minimum lease payments as of December 31, 2018 are as follows:

<u>Years ending December 31,</u>	<u>Amount</u>
2019	\$ 121,635
2020	123,930
2021	126,225
Thereafter	—
Total future minimum lease payments	\$ 371,790

7. Income taxes

Components of the net loss consist of the following:

	<u>Year ended December 31,</u>	
	<u>2017</u>	<u>2018</u>
Foreign	\$ (15,185,931)	\$ (15,713,032)
Domestic	(4,319)	184,763
Net loss	\$ (15,190,250)	\$ (15,528,269)

A reconciliation of the effect of applying the federal statutory rate to the net loss and the effective income tax rate:

	<u>Year ended December 31,</u>	
	<u>2017</u>	<u>2018</u>
Statutory federal income tax rate	34.0%	21.0%
Earnings in jurisdictions taxed at rates different from the statutory U.S. federal tax rate	(12.0)%	1.0%
Permanent differences	(0.1)%	0.4%
Changes in valuation allowance	(21.5)%	(16.7)%
Rate change due to TCJA	(0.4)%	0.0%
Rate change due to Swedish tax reform	0.0%	(5.7)%
Effective income tax rate	0.0%	0.0%

Notes to Financial Statements (Continued)

7. Income taxes (continued)

Significant components of the Company's deferred taxes as of December 31, 2017 and 2018 are as follows:

	December 31,	
	2017	2018
Deferred tax assets:		
Net operating loss carryforward	\$ 11,108,800	\$ 12,816,395
Capitalized research and development	5,694	1,951
Gross deferred tax assets	11,114,494	12,818,346
Valuation allowance	(11,053,983)	(12,661,874)
Total deferred tax assets	60,511	156,472
Deferred tax liabilities:		
Fixed assets	(2,297)	(2,050)
Stock Compensation	(58,214)	(154,422)
Total deferred tax liabilities	(60,511)	(156,472)
Net deferred tax assets (liabilities)	\$ —	\$ —

The Company has no income tax expense due to operating losses incurred for the years ended December 31, 2017 and 2018. The Company has provided a valuation allowance for the full amount of the net deferred tax assets as, based on all available evidence, it is considered more likely than not that all the recorded deferred tax assets will not be realized in a future period. At December 31, 2018, the Company has \$61.6 million, \$0.5 million and \$0.4 million of foreign, federal and state net operating loss carryforwards, respectively, that expire at various dates through 2036. Certain of these foreign, federal and state net operating loss carryforwards may be subject to Internal Revenue Code Section 382 or similar provisions, which impose limitations on their utilization.

The valuation allowance increased in 2018 by \$2.5 million, due to the increase in the deferred tax assets by the same amounts; primarily due to net operating loss carryforwards. Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. Under the provisions of the U.S. Internal Revenue Code and Sweden tax law, certain changes in the Company's ownership, including a sale of the Company or significant changes in ownership due to sales of equity, may have limited, or may limit in the future, the amount of net operating loss carryforwards that could be used annually to offset future taxable income. For U.S. and Swedish income tax purposes, the Company has not completed a study to assess whether a change of control has occurred or whether there have been changes of control since the Company's formation due to the complexity and cost associated with such study and because there could be additional changes in control in the future. As a result, the Company is not able to estimate the effect of the change in control, if any, on the Company's ability to utilize U.S. or Swedish net operating losses or other tax attribute carryforwards the future. For Swedish income tax purposes, the Company has estimated that approximately \$12.5 million of its net operating losses may be subject to limitations in accordance with the country's group contribution restriction laws.

The Company files tax returns in Sweden, the United States, Pennsylvania and Massachusetts, and all tax years since inception remain open to examination by the major taxing jurisdictions to which the Company is subject, as carryforward attributes generated in years past may still be adjusted upon

Notes to Financial Statements (Continued)

7. Income taxes (continued)

examination by the Internal Revenue Service (IRS) or other authorities if they have or will be used in a future period. The Company is not currently under examination by the IRS or any other jurisdictions for any tax years.

As of December 31, 2018, the Company had no uncertain tax positions. The Company has elected to recognize interest and penalties related to income tax matters as a component of income tax expense, of which no interest or penalties were recorded for the years ended December 31, 2017 and 2018.

In June 2018, Sweden promulgated changes to the Swedish regulations on corporate income taxation. The law will apply from January 1, 2019. Among other things, the changes decrease the corporate income tax rate in two steps from 22% to 21.4% as of January 1, 2019 and 20.6% as of January 1, 2020. U.S. GAAP requires companies to revalue their deferred tax assets and deferred tax liabilities as of the date of enactment, with the resulting tax effects accounted for in the reporting period of enactment. This revaluation resulted in an overall reduction of deferred taxes of \$0.7 million and a corresponding reduction in the valuation allowance. As such, there was no net impact to the Company's statement of operations as a result of the reduction in tax rates.

In December 2017, what is commonly known as the Tax Cuts and Jobs Act (the Tax Act), was signed into law. Among other things, the Tax Act permanently lowers the corporate federal income tax rate to 21% from the statutory rate of 35%, effective for tax years including or commencing January 1, 2018. As a result of the reduction of the corporate federal income tax rate to 21%, U.S. GAAP requires companies to revalue their deferred tax assets and deferred tax liabilities as of the date of enactment, with the resulting tax effects accounted for in the reporting period of enactment. This revaluation resulted in an overall reduction of deferred taxes of \$0.1 million and a corresponding reduction in the valuation allowance. As such, there was no net impact to the Company's statement of operations as a result of the reduction in tax rates.

8. Convertible preferred stock

The Company has 20,000,000 shares authorized for all classes of equity combined.

Series A Preferred

In June 2011, the Company issued 145,469 shares of Series A Preferred for gross proceeds of \$3,233,417. In March 2016, the Company issued 466,977 shares of Series A Preferred as settlement of its outstanding bridge loans totaling \$3,249,627. All 612,446 shares of Series A Preferred were issued to related parties.

As of December 31, 2018, the rights and preferences of the Series A Preferred are as follows:

Conversion—Each share of Series A Preferred may be converted at any time, at the option of the holder, into a share of common stock. The Series A Preferred automatically converts into shares of common stock when 1) shareholders representing a majority of the outstanding preferred shares calls for such conversion or 2) at the closing of an initial public offering of the Company's common stock at a per share price of at least one and a half (1.5) times the average amount (EUR 16.05 based on all Series C preferred shares issued as of December 31, 2018) paid per Series C preferred share (as adjusted for share splits and similar) and aggregate proceeds in excess of EUR 50,000,000.

Notes to Financial Statements (Continued)

8. Convertible preferred stock (continued)

Dividends—Holders of Series A Preferred do not accrue dividends.

Voting rights—Preferred Stock and common stock vote together as one class on an as converted basis. Common stock voting rights on certain matters are subject to the powers, preferences, and rights of the Preferred Stock. Holders are entitled to vote on all matters and shall have the number of votes equal to the number of shares of common stock into which the shares of Preferred Stock held by such holder are then convertible.

Series B Preferred

In March 2016, the Company issued 3,322,762 shares of Series B Preferred for gross proceeds of \$22,609,485, or \$22,290,261 net of issuance costs. The Company also issued 590,445 shares of Series B Preferred in settlement of its outstanding bridge loans totaling \$4,108,818. In October 2017, the Company issued 3,322,762 Series B preferred shares at a price per share of \$7.02, for an aggregate purchase price of \$23,349,617. All 7,235,969 shares of Series B Preferred were issued to related parties.

As of December 31, 2018, the rights and preferences of the Series B Preferred are as follows:

Conversion—Each share of Series B Preferred may be converted at any time, at the option of the holder, into a share of common stock. The Series B Preferred automatically converts into shares of common stock when 1) shareholders representing a majority of the outstanding preferred shares calls for such conversion or 2) at the closing of an initial public offering of the Company's common stock at a per share price of at least one and a half (1.5) times the average amount (EUR 16.05 based on all Series C preferred shares issued as of December 31, 2018) paid per Series C preferred share (as adjusted for share splits and similar) and aggregate proceeds in excess of EUR 50,000,000.

Dividends—Holders are entitled to dividends of 8%, compounded annually if not paid. No dividends have been declared or paid as of December 31, 2018. The company has not accrued dividends on the Series B Preferred since dividends are only payable upon the occurrence of a liquidation event, including the transfer of more than fifty percent of the Company's outstanding shares or the transfer of substantially all of the Company's intellectual property. Approximately \$8,806,426 of accrued dividends that were payable through December 31, 2018 was added to the stated liquidation preference amount of the Series B Preferred, which totaled \$58,874,347 at December 31, 2018.

Voting rights—Preferred Stock and common stock vote together as one class on an as converted basis. Common stock voting rights on certain matters are subject to the powers, preferences, and rights of the Preferred Stock. Holders are entitled to vote on all matters and shall have the number of votes equal to the number of shares of common stock into which the shares of Preferred Stock held by such holder are then convertible.

Series C Preferred

In November 2018, the Company issued 4,712,698 shares of Series C Preferred for gross proceeds of \$56,725,342 or \$56,364,645 net of issuance costs. A total of 4,219,849 shares of Series C Preferred were issued to related parties.

Notes to Financial Statements (Continued)

8. Convertible preferred stock (continued)

As of December 31, 2018, the rights and preferences of the Series C Preferred are as follows:

Conversion—Each share of Series C Preferred may be converted at any time, at the option of the holder, into a share of common stock. The Series C Preferred automatically converts into shares of common stock when 1) shareholders representing a majority of the outstanding preferred shares calls for such conversion or 2) at the closing of an initial public offering of the Company's common stock at a per share price of at least one and a half (1.5) times the average amount (EUR 16.05 based on all Series C preferred shares issued as of December 31, 2018) paid per Series C preferred share (as adjusted for share splits and similar) and aggregate proceeds in excess of EUR 50,000,000.

Dividends—Holders are entitled to dividends of 8%, compounded annually if not paid. No dividends have been declared or paid as of December 31, 2018. The company has not accrued dividends on the Series C Preferred since dividends are only payable upon the occurrence of a liquidation event, including the transfer of more than fifty percent of the Company's outstanding shares or the transfer of substantially all of the Company's intellectual property. Approximately \$389,970 of accrued dividends that were payable through December 31, 2018 was added to the stated liquidation preference amount of the Series C Preferred, which totaled \$57,115,312 at December 31, 2018.

Voting rights—Preferred Stock and common stock vote together as one class on an as converted basis. Common stock voting rights on certain matters are subject to the powers, preferences, and rights of the Preferred Stock. Holders are entitled to vote on all matters and shall have the number of votes equal to the number of shares of common stock into which the shares of Preferred Stock held by such holder are then convertible.

Liquidation preference

Upon liquidation, dissolution, or winding up of business, the Preferred Stock holders are entitled to receive a liquidation preference in priority to holders of common stock at the original issue price plus, in the case of Series B and Series C Preferred, any unpaid accumulated dividends as follows:

- 1) If a liquidation event occurs prior to the Company achieving a certain clinical milestone, Series C Preferred shareholders shall receive an amount per Series C Preferred share equal to the original subscription price per Series C Preferred share (as adjusted for share splits and similar) plus unpaid accumulated dividends. Secondly, after the Series C Preferred shareholders have received full payment, the Series B Preferred shareholders shall receive an amount per Series B preferred share equal to the original subscription price per Series B Preferred share (as adjusted for share splits and similar) plus unpaid accumulated dividends. Thirdly, after the Series B and C Preferred shareholders have received full payment, the Series A Preferred shareholders shall receive an amount per Series A preferred share equal to the original subscription price per Series A Preferred share (as adjusted for share splits and similar). When the Preferred A, B and C shareholders are satisfied in full, any excess assets available for distribution will be allocated ratably among holders of common stock and preferred stock based on their pro rata shareholdings on an as-if-converted basis.
- 2) If a liquidation event occurs after the Company achieves a certain clinical milestone, Series B and C Preferred shareholders, based on their pro rata shareholdings, shall receive an amount per Series B and C Preferred share equal to the original subscription price per Series B and C Preferred share (as adjusted for share splits and similar) plus unpaid accumulated dividends.

Notes to Financial Statements (Continued)

8. Convertible preferred stock (continued)

Secondly, after the Series B and C Preferred shareholders have received full payment, the Series A Preferred shareholders shall receive an amount per Series A preferred share equal to the original subscription price per Series A Preferred share (as adjusted for share splits and similar). When the Preferred A, B and C shareholders are satisfied in full, any excess assets available for distribution will be allocated ratably among holders of common stock and preferred stock based on their pro rata shareholdings on an as-if-converted basis.

The liquidation preferences apply to each series of preferred stock only to the extent the holders would receive less than three times their respective original purchase prices.

9. Common stock

The Company has 1,155,366 shares of common stock outstanding as of December 31, 2018. During 2018, the Company issued 2,305 shares of common stock to employees for aggregate consideration of \$2,097 as a result of stock option exercises. No common stock was issued during 2017.

The holders of common stock are entitled to one vote for each share of common stock. Subject to the payment in full of all preferential dividends to which the holders of the Preferred Stock are entitled, the holders of common stock shall be entitled to receive dividends out of funds legally available. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, after the payment or provision for payment of all debts and liabilities of the Company and all preferential amounts to which the holders of Preferred Stock are entitled with respect to the distribution of assets in liquidation, the holders of common stock shall be entitled to share ratably in the remaining assets of the Company available for distribution.

10. Stock option plan

In October 2016, the Board of Directors adopted the 2016 Amended and Restated Stock Option Program (the "Plan"), which provided for the grant of stock options to the Company's employees, officers, directors, and outside consultants for the purchase of up to 1,224,824 shares of the Company's common stock. During 2017, the Plan was amended to provide up to 1,946,849 shares of the Company's common stock. During 2018, the Plan was further amended to provide up to 3,069,999 shares of the Company's common stock. Holders of stock options shall be entitled to exercise the vested portion of the stock option provided that a trade sale, as defined in the plan, or initial public offering has occurred. The holders of stock options may also exercise the vested portion of the stock option within six months of termination of employment.

Stock options generally vest over a four-year period and expire in October 2026. The Board of Directors has the discretion to provide for accelerated vesting. At December 31, 2018, there were 1,487,466 shares available for future grant under the Plan.

The Company recorded stock-based compensation expense of \$395,440 and \$329,814 during the years ended December 31, 2017 and 2018, respectively. As of December 31, 2018, there was \$386,388 of unrecognized compensation cost related to nonvested share-based compensation arrangements granted under the Plan, which is expected to be recognized over a weighted-average period of approximately 2.1 years.

The fair value of each option award is estimated on the date of grant using Black-Scholes, with the assumptions noted in the table below. Expected volatility for the Company's common stock was

Notes to Financial Statements (Continued)

10. Stock option plan (continued)

determined based on an average of the historical volatility of a peer group of similar public companies. The expected term of options granted to employees was calculated using the simplified method, which represents the average of the contractual term of the option and the weighted-average vesting period of the option. The Company uses the simplified method because it does not have sufficient historical option exercise data to provide a reasonable basis upon which to estimate expected term. The contractual life of the option was used for the expected life of options granted to non-employee. The assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free rate for periods within the expected life of the option is based upon the Swedish Government Bond Rate in effect at the time of grant.

In determining the exercise prices for options granted, the Company's Board of Directors has considered the fair value of the common stock as of the measurement date. The fair value of the common stock at each award grant date was based upon a variety of factors, including the results obtained from an independent third-party valuation, the Company's financial position and historical financial performance, the status of technological developments within the Company's proposed products, an evaluation or benchmark of the Company's competition, the current business climate in the marketplace, the illiquid nature of the common stock, arm's length sales of the Company's capital stock, including Preferred Stock, the effect of the rights and preferences of the preferred shareholders, and the prospects of a liquidity event, among others.

The assumptions used in Black-Scholes for the years ended December 31, 2017 and 2018 are as follows:

	Year ended December 31,	
	2017	2018
Expected volatility	71.9% - 75.4%	71.5%
Risk-free rate	2.3% - 2.5%	2.9%
Expected dividend yield	0%	0%
Expected term in years	8.6 - 9.7	8.2

Notes to Financial Statements (Continued)

10. Stock option plan (continued)

A summary of option activity under the Plan during the years ended December 31, 2017 and 2018 are as follows:

	Number of options	Weighted-average exercise price per share	Weighted average remaining contractual term (in years)	Aggregate intrinsic value
Outstanding at January 1, 2017	1,237,292	\$ 1.85	9.2	\$ 66,498
Granted	663,224	0.73		
Exercised	—	—		
Cancelled/Forfeited	(3,310)	0.92		
Outstanding at December 31, 2017	1,897,206	\$ 1.46	8.3	\$ 360,691
Granted	24,067	1.01		
Exercised	(2,306)	0.92		
Cancelled/Forfeited	(74,779)	17.31		
Outstanding at December 31, 2018	1,844,188	\$ 0.82	7.6	\$ 4,382,781
Exercisable at December 31, 2018	2,807	\$ 0.92	0.3	\$ 6,388
Vested or expected to vest at December 31, 2018	1,844,188	\$ 0.82	7.6	\$ 4,382,781

The weighted-average grant date fair value of options granted during the years ended December 31, 2017 and 2018, was \$0.75 and \$0.69 per share, respectively.

11. Subsequent events

In February 2019, the Company raised \$5,645,248 in gross proceeds through the issuance of 467,179 Series C convertible preferred shares.

On September 20, 2019, the Company consummated a corporate reorganization, pursuant to which all of the issued and outstanding stock and options of Aprea Therapeutics AB, or Aprea AB, was exchanged for common stock, preferred stock or options, as applicable, of Aprea Therapeutics, Inc. As a result, Aprea Therapeutics AB, became a wholly-owned subsidiary of Aprea Therapeutics, Inc.

In September 2019, the Company's Board of Directors and stockholders approved a 1-for-1.6045 stock split of the Company's preferred and common stock. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this split.

Aprea Therapeutics AB

Condensed Consolidated Balance Sheets

(Unaudited)

	December 31, 2018	June 30, 2019	Pro forma June 30, 2019
Assets			
Current assets:			
Cash and cash equivalents	\$ 65,675,931	\$ 60,994,738	\$ 60,994,738
Deferred offering costs	—	624,624	624,624
Prepaid expenses and other current assets	322,146	291,991	291,991
Total current assets	65,998,077	61,911,353	61,911,353
Property and equipment, net	24,450	25,662	25,662
Right of use lease asset	—	277,531	277,531
Other noncurrent assets	111	108	108
Total assets	<u>\$ 66,022,638</u>	<u>\$ 62,214,654</u>	<u>\$ 62,214,654</u>
Liabilities, Convertible Preferred Stock and Stockholders' Equity (Deficit)			
Current liabilities:			
Accounts payable	\$ 1,739,337	\$ 2,323,719	\$ 2,323,719
Accrued expenses	3,128,772	3,260,109	3,260,109
Lease liability—current	—	112,315	112,315
Total current liabilities	4,868,109	5,696,143	5,696,143
Lease liability—noncurrent	—	181,910	181,910
Total liabilities	4,868,109	5,878,053	5,878,053
Commitments and contingencies (Note 6)			
Convertible preferred stock:			
Series A convertible preferred stock, \$0.11 par value; 612,446 shares issued and outstanding at December 31, 2018 and June 30, 2019 (liquidation preference of \$6,483,044 at June 30, 2019)	6,483,044	6,483,044	—
Series B convertible preferred stock, \$0.11 par value; 7,235,969 shares issued and outstanding at December 31, 2018 and June 30, 2019 (liquidation preference of \$61,127,463 at June 30, 2019)	49,742,942	49,742,942	—
Series C convertible preferred stock, \$0.11 par value; 4,712,698 and 5,179,877 shares issued and outstanding at December 31, 2018 and June 30, 2019, respectively (liquidation preference of \$65,188,827 at June 30, 2019)	56,364,645	61,963,007	—
Total convertible preferred stock	112,590,631	118,188,993	—
Stockholders' equity (deficit):			
Common stock, \$0.11 par value at December 31, 2018 and June 30, 2019, \$0.001 par value at pro forma June 30, 2019; 1,155,366, 1,181,573 and 14,209,865 shares issued and outstanding at December 31, 2018, June 30, 2019 and pro forma June 30, 2019, respectively.	127,091	129,974	14,210
Additional paid-in capital	19,666,588	19,971,732	138,276,489
Accumulated other comprehensive loss	(8,761,325)	(10,747,992)	(10,747,992)
Accumulated deficit	(62,468,456)	(71,206,106)	(71,206,106)
Total stockholders' equity (deficit)	(51,436,102)	(61,852,392)	56,336,601
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	<u>\$ 66,022,638</u>	<u>\$ 62,214,654</u>	<u>\$ 62,214,654</u>

See accompanying notes to condensed consolidated financial statements.

Aprea Therapeutics AB

Condensed Consolidated Statements of Operations and Comprehensive Loss

(Unaudited)

	Six Months Ended June 30,	
	2018	2019
Operating expenses:		
Research and development	\$ 7,492,788	\$ 7,998,270
General and administrative	1,166,520	2,347,915
Total operating expenses	<u>8,659,308</u>	<u>10,346,185</u>
Other income (expense):		
Interest expense	(188)	(7,439)
Foreign currency gain	949,158	1,615,974
Total other income (expense)	<u>948,970</u>	<u>1,608,535</u>
Net loss	<u>\$ (7,710,338)</u>	<u>\$ (8,737,650)</u>
Other comprehensive loss:		
Foreign currency translation	(1,176,208)	(1,986,667)
Total comprehensive loss	<u>(8,886,546)</u>	<u>(10,724,317)</u>
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (6.68)</u>	<u>\$ (7.43)</u>
Weighted average basic and diluted shares of common stock outstanding	<u>1,154,107</u>	<u>1,176,417</u>
Pro forma net loss per share attributable to common stockholders, basic and diluted	<u>\$ (0.62)</u>	
Pro forma weighted average common shares outstanding, basic and diluted		<u>14,075,669</u>

See accompanying notes to condensed consolidated financial statements.

Condensed Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

(Unaudited)

	Convertible Preferred Stock								Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Series A		Series B		Series C		Common Stock					
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance, December 31, 2017	612,446	\$ 6,483,044	7,235,969	\$ 49,742,942	—	\$ —	1,153,061	\$ 126,838	\$ 19,335,560	\$ (8,287,406)	\$ (46,940,187)	\$ (35,765,195)
Exercise of stock options	—	—	—	—	—	—	1,503	165	1,250	—	—	1,415
Stock-based compensation	—	—	—	—	—	—	—	—	169,854	—	—	169,854
Foreign currency translation	—	—	—	—	—	—	—	—	—	(1,176,208)	—	(1,176,208)
Net loss	—	—	—	—	—	—	—	—	—	—	(7,710,338)	(7,710,338)
Balance, June 30, 2018	612,446	\$ 6,483,044	7,235,969	\$ 49,742,942	—	\$ —	1,154,564	\$ 127,003	\$ 19,506,664	\$ (9,463,614)	\$ (54,650,525)	\$ (44,480,472)
Balance, December 31, 2018	612,446	\$ 6,483,044	7,235,969	\$ 49,742,942	4,712,698	\$ 56,364,645	1,155,366	\$ 127,091	\$ 19,666,588	\$ (8,761,325)	\$ (62,468,456)	\$ (51,436,102)
Issuance of Series C convertible preferred stock, net of issuance costs of \$53,509	—	—	—	—	467,179	5,598,362	—	—	—	—	—	—
Exercise of stock options	—	—	—	—	—	—	26,207	2,883	20,235	—	—	23,118
Stock-based compensation	—	—	—	—	—	—	—	—	284,909	—	—	284,909
Foreign currency translation	—	—	—	—	—	—	—	—	—	(1,986,667)	—	(1,986,667)
Net loss	—	—	—	—	—	—	—	—	—	—	(8,737,650)	(8,737,650)
Balance, June 30, 2019	612,446	\$ 6,483,044	7,235,969	\$ 49,742,942	5,179,877	\$ 61,693,007	1,181,573	\$ 129,974	\$ 19,971,732	\$ (10,747,992)	\$ (71,206,106)	\$ (61,852,392)
Exchange and conversion of preferred stock and common stock of Aprea Therapeutics AB into common stock of Aprea Therapeutics Inc.	(612,446)	(6,483,044)	(7,235,969)	(49,742,942)	(5,179,877)	(61,693,007)	13,028,292	(115,764)	118,304,757	—	—	118,188,993
Balance, June 30, 2019 pro forma	—	\$ —	—	\$ —	—	\$ —	14,209,865	\$ 14,210	\$ 138,276,489	\$ (10,747,992)	\$ (71,206,106)	\$ 56,336,601

See accompanying notes to condensed consolidated financial statements.

Aprea Therapeutics AB

Condensed Consolidated Statements of Cash Flows

(Unaudited)

	Six Months Ended June 30,	
	2018	2019
Cash flows from operating activities:		
Net loss	\$ (7,710,338)	\$ (8,737,650)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	4,263	4,739
Stock-based compensation	169,854	284,909
Amortization of right of use lease asset	—	51,853
Foreign currency gain	(949,158)	(1,615,974)
Changes in operating assets and liabilities:		
Deferred offering costs	—	(624,624)
Prepaid expense and other current assets	91,530	19,721
Accounts payable	(51,369)	640,719
Accrued expenses and other liabilities	198,384	232,679
Lease liability	—	(53,815)
Net cash used in operating activities	<u>(8,246,834)</u>	<u>(9,797,443)</u>
Cash flows from investing activities:		
Purchases of property and equipment	(4,734)	(6,189)
Net cash used in investing activities	<u>(4,734)</u>	<u>(6,189)</u>
Cash flows from financing activities:		
Proceeds from the exercise of stock options	1,415	23,118
Proceeds from issuance of Series C preferred, net	—	5,598,362
Net cash provided by financing activities	<u>1,415</u>	<u>5,621,480</u>
Decrease in cash	(8,250,153)	(4,182,152)
Effect of exchange rate changes on cash and cash equivalents	(547,286)	(499,041)
Cash and cash equivalents—beginning of period	24,401,488	65,675,931
Cash and cash equivalents—end of period	<u>\$ 15,604,049</u>	<u>\$ 60,994,738</u>
Non-cash activities:		
Cumulative effect of change in accounting principle—ASC 842 adoption	\$ —	\$ 329,384

See accompanying notes to condensed consolidated financial statements.

Notes to Condensed Consolidated Financial Statements

(Unaudited)

1. Nature of business and basis of presentation

Nature of business—Aprea Therapeutics AB (the "Company") is a clinical-stage biopharmaceutical company focused on developing and commercializing novel cancer therapeutics that reactivate mutant tumor suppressor protein p53. p53 is the protein expressed from the *TP53* gene, the most commonly mutated gene in cancer. The Company began operations in 2006. Its principal offices are in Solna, Sweden and Boston, Massachusetts.

Basis of presentation and management plans—The accompanying financial statements are prepared in conformity with accounting principles generally accepted in the United States ("U.S. GAAP"). The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business.

Since its inception, the Company has devoted substantially all of its efforts to business planning, research and development, recruiting management and technical staff, and raising capital, and has financed its operations through the issuance of convertible preferred stock ("Preferred Stock") and common stock.

The Company is subject to risks common to companies in the biopharmaceutical industry. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be maintained, that any therapeutic products developed will obtain required regulatory approval or that any approved or consumer products will be commercially viable. Even if the Company's development efforts are successful, it is uncertain when, if ever, the Company will generate significant product sales.

The Company's management believes that the June 30, 2019 cash balance of \$60,994,738 will be sufficient to fund the Company's operations into the third quarter of 2021. In the event that additional funds are not available thereafter, management would expect to significantly reduce expenditures to conserve cash, which would involve scaling back or curtailing new development activity.

Prior to its initial public offering, the Company approved a 1-for-1.6045 stock split of the Company's preferred and common stock. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this split.

2. Summary of significant accounting policies

Principles of consolidation—The consolidated financial statements include the accounts of Aprea Therapeutics AB and its wholly owned subsidiaries Aprea Personal AB, which was incorporated in May 2009, and Aprea US, Inc., which was incorporated in June 2016. Management has concluded it has a single reporting segment for purposes of reporting financial condition and results of operations. All intercompany transactions and balances have been eliminated.

Unaudited interim condensed consolidated financial statements—The accompanying condensed consolidated balance sheet as of June 30, 2019, the condensed consolidated statements of operations and comprehensive loss and cash flows for the six months ended June 30, 2018 and 2019, and the condensed consolidated statement of convertible preferred stock and stockholders (deficit) equity for the six months ended June 30, 2019 are unaudited. The unaudited condensed consolidated financial

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

2. Summary of significant accounting policies (continued)

statements have been prepared on the same basis as the audited consolidated financial statements, and in management's opinion, include all adjustments, consisting of only normal recurring adjustments, necessary for the fair statement of the Company's financial position as of June 30, 2019 and its results of operations and comprehensive loss and cash flows for six months ended June 30, 2018 and 2019. The financial data and the other financial information disclosed in the notes to these condensed consolidated financial statements related to the six month periods are also unaudited. The results of operations for the six months ended June 30, 2019 are not necessarily indicative of the results to be expected for the full fiscal year or any other period.

Use of estimates—The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, and expenses as of and during the reporting period. The Company bases estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. The Company assesses estimates on an ongoing basis; however, actual results could materially differ from those estimates. Significant items subject to such estimates and assumptions include fair value of common stock and stock based compensation expense.

Unaudited pro forma financial information—The Company is planning an offer and sale by Aprea Therapeutics, Inc., a Delaware corporation and successor entity, of common stock in an initial public offering (the "IPO"). Prior to the completion of the IPO, pursuant to a corporate reorganization, the Company became a wholly owned subsidiary of Aprea Therapeutics, Inc. In connection with the corporate reorganization, each issued and outstanding share of Series A, Series B and Series C convertible preferred stock of the Company was exchanged on a one for one basis into shares of Series A, Series B and Series C convertible preferred stock of Aprea Therapeutics, Inc.

Each share of common stock of the Company (\$0.11 par value) was also exchanged on a one for one basis into shares of common stock of Aprea Therapeutics, Inc. (\$0.001 par value). Immediately prior to consummation of the IPO, all outstanding shares of Series A, Series B and Series C convertible preferred stock of Aprea Therapeutics, Inc. will be converted into common stock, on a 1 for 1.6045 basis.

The accompanying unaudited pro forma balance sheet as of June 30, 2019 has been prepared to give effect to the corporate reorganization and automatic conversion of all outstanding shares of convertible preferred stock into 13,028,292 shares of common stock of Aprea Therapeutics, Inc. as if

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

2. Summary of significant accounting policies (continued)

the corporate reorganization and automatic conversion had occurred on June 30, 2019 as illustrated below:

	Series A Preferred Stock	Series B Preferred Stock	Series C Preferred Stock	Common Stock	Additional Paid-in Capital
Aprea Therapeutics AB as of June 30, 2019	\$ 6,483,044	\$ 49,742,942	\$ 61,963,007	\$ 129,974	\$ 19,971,732
Adjustments to reflect:					
Exchange of common stock	—	—	—	(128,792)	128,792
Exchange and conversion of preferred stock:					
Series A Preferred	(6,483,044)	—	—	612	6,482,432
Series B Preferred	—	(49,742,942)	—	7,236	49,735,706
Series C Preferred	—	—	(61,963,007)	5,180	61,957,827
Pro forma of Aprea Therapeutics, Inc. as of June 30, 2019	\$ —	\$ —	\$ —	\$ 14,210	\$ 138,276,489

The unaudited pro forma basic and diluted weighted average common shares outstanding used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the six months ended June 30, 2019 give effect to the automatic conversion of all outstanding shares of convertible preferred stock into shares of common stock as if the conversion had occurred on the later of January 1, 2019 or the issuance date of the convertible preferred stock for the six months ended June 30, 2019.

Foreign currency and currency translation—The functional currency for Aprea Therapeutics AB and its wholly owned foreign subsidiary, Aprea Personal AB, is the Swedish Krona. Assets and liabilities of Aprea Therapeutics AB and Aprea Personal AB are translated into United States dollars at the exchange rate in effect on the balance sheet date. Revenues and expenses are translated at the average exchange rate in effect during the period. Unrealized translation gains and losses are recorded as a cumulative translation adjustment, which is included in the consolidated statements of convertible preferred stock and stockholders' deficit as a component of accumulated other comprehensive loss. Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the local currency are included in other income and expense in the condensed consolidated statements of operations and comprehensive loss as incurred.

Concentrations of credit risk—Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash. Periodically, the Company may maintain deposits in financial institutions in excess of government insured limits. Management believes that the Company is not exposed to significant credit risk as the Company's deposits are held at financial institutions that management believes to be of high credit quality, and the Company has not experienced any losses on these deposits.

Cash and cash equivalents—The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents.

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

2. Summary of significant accounting policies (continued)

Deferred offering costs—The Company capitalizes deferred IPO costs, which primarily consist of direct, incremental legal, professional, accounting and other third-party fees relating to the Company's initial public offering. The deferred IPO costs will be offset against IPO proceeds upon the consummation of an offering. There were \$0 and \$624,624 of deferred IPO costs as of December 31, 2018 and June 30, 2019, respectively.

Property and equipment—Property and equipment are recorded at cost. Expenditures for repairs and maintenance are expensed as incurred. When assets are retired or disposed of, the assets and related accumulated depreciation are eliminated from the accounts, and any resulting gain or loss is included in the determination of net income or loss. Fixed assets acquired for research and development purposes are assessed for alternative future use. Depreciation is provided using the straight-line method over the estimated useful lives of the related assets. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset.

<u>Asset category</u>	<u>Estimated useful life</u>
Computer equipment and software	5 years
Furniture and fixtures	5 years
Laboratory equipment and office furniture	5 years
Leasehold improvements	Remainder of lease term

Impairment of long-lived assets—Periodically, the Company evaluates its long-lived assets, which consist primarily of property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset exceeds the fair value of the asset. To date, no impairments have occurred.

Fair value of financial instruments—The accounting standard for fair value measurements provides a framework for measuring fair value and requires expanded disclosures regarding fair value measurements. Fair value is defined as the price that would be received upon sale of an asset or paid to transfer a liability between market participants at measurement dates. ASC Topic 820, Fair Value Measurement ("ASC 820"), establishes a three-level valuation hierarchy for instruments measured at fair value. The hierarchy is based on the transparency of inputs to the valuation of an asset or liability as of the measurement date. The hierarchy defines three levels of valuation inputs, of which the first two are considered observable and the last is considered unobservable:

- Level 1 inputs: Quoted prices in active markets for identical assets or liabilities.
- Level 2 inputs: Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.
- Level 3 inputs: Unobservable inputs developed using estimates or assumptions developed by the Company, which reflect those that a market participant would use in pricing the asset or liability.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

2. Summary of significant accounting policies (continued)

degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The Company's financial instruments consist of accounts payable. The carrying amount of accounts payable is considered a reasonable estimate of fair value due to the short-term maturity.

Convertible preferred stock—The Company has classified convertible preferred stock ("Preferred Stock") as temporary equity in the accompanying balance sheets due to certain change in control events that are outside of the Company's control, including sale or transfer of control of the Company, as holders of the Preferred Stock could cause redemption of the shares in these situations. The Company does not accrete the carrying values of the Preferred Stock to the redemption values since a liquidation event was not considered probable as of June 30, 2019. Subsequent adjustments of the carrying values to the ultimate redemption values will be made only if it becomes probable that such a liquidation event will occur.

Accounting for leases—In February 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016 02, "Leases" ("ASC 842") to enhance the transparency and comparability of financial reporting related to leasing arrangements. Under this new lease standard, most leases are required to be recognized on the balance sheet as right-of-use assets and lease liabilities. Disclosure requirements have been enhanced with the objective of enabling financial statement users to assess the amount, timing, and uncertainty of cash flows arising from leases. Prior to January 1, 2019, GAAP did not require lessees to recognize assets and liabilities related to operating leases on the balance sheet. The new standard establishes a right-of-use ("ROU") model that requires a lessee to recognize a ROU asset and corresponding lease liability on the balance sheet for all leases with a term longer than 12 months. Leases will be classified as finance or operating, with classification affecting the pattern and classification of expense recognition in the income statement as well as the reduction of the right of use asset.

The Company has adopted the standard effective January 1, 2019, using the modified retrospective method. The new standard provides a number of optional practical expedients in transition. The Company has elected to apply the 'package of practical expedients' which allow us to not reassess (i) whether existing or expired arrangements contain a lease, (ii) the lease classification of existing or expired leases, or (iii) whether previous initial direct costs would qualify for capitalization under the new lease standard. The Company has also elected to apply (i) the practical expedient which allows us to not separate lease and non-lease components, for new leases entered into after adoption and (ii) the short-term lease exemption for all leases with an original term of less than 12 months, for purposes of applying the recognition and measurements requirements in the new standard. For the impact to the Company's consolidated financial statement upon adoption of the new leasing standard, see Note 3 to our unaudited condensed consolidated financial statements.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on specific facts and circumstances, the existence of an identified asset(s), if any, and the Company's control over the use of the identified asset(s), if applicable. Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of future lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

2. Summary of significant accounting policies (continued)

readily determinable. As such, the Company will utilize the incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. As of the ASC 842 effective date, the Company's incremental borrowing rate is approximately 4.3% based on the remaining lease term of the applicable leases.

The Company has elected not to separate lease and non-lease components as a single component. Operating leases are recognized on the balance sheet as ROU lease assets, lease liabilities current and lease liabilities non-current. Fixed rents are included in the calculation of the lease balances while variable costs paid for certain operating and pass-through costs are excluded. Lease expense is recognized over the expected term on a straight-line basis.

Research and development costs—Research and development costs are charged to expense as incurred. Research and development expense consists of expenses incurred in performing research and development activities, including salaries and benefits, materials and supplies, preclinical expenses, stock-based compensation expense, depreciation of equipment, contract services, and other outside expenses. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using or information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued expense.

Patent costs—All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Stock-based compensation—The Company measures stock options and other stock based awards granted to employees and directors based on their fair value on the date of the grant and recognize compensation expense of those awards, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. The Company applies the straight-line method of expense recognition to all awards with only service based vesting conditions.

For stock based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed in accordance with the FASB issued ASU No. 2018-07, Compensation Stock Compensation (Topic 718): Improvements to Nonemployee Share Based Payment Accounting. The new standard largely aligns the accounting for share based payment awards issued to employees and nonemployees by expanding the scope of ASC 718 to apply to nonemployee share based transactions, as long as the transaction is not effectively a form of financing.

The Company estimates the fair value of each stock option grant on the date of grant using the Black Scholes option pricing model, which uses as inputs the fair value of the Company's common stock and assumptions the Company makes for the volatility of its common stock, the expected term of its stock options, the risk free interest rate for a period that approximates the expected term of its stock options and its expected dividend yield.

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

2. Summary of significant accounting policies (continued)*Determination of Fair Value of Common Stock*

As there has been no public market for the Company's common stock to date, the estimated fair value of its common stock has been determined by its board of directors as of the date of each option grant, with input from management, considering the Company's most recently available third party valuations of common stock and its board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately Held Company Equity Securities Issued as Compensation.

The Company's common stock valuations were prepared using a hybrid method, which used market approaches to estimate its enterprise value. The hybrid method is a probability weighed expected return method, or PWERM, where the equity value in one or more scenarios is calculated using an option pricing method, or OPM. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. The PWERM is a scenario based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The common stock value is based on the probability weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. These third party valuations were performed at various dates, which resulted in valuations of the Company's common stock of \$0.92 per share as of May 31, 2016, \$1.01 per share as of October 2, 2017 and \$3.18 per share as of December 31, 2018.

In addition to considering the results of these third-party valuations, the Company's board of directors considered various objective and subjective factors to determine the fair value of its common stock as of each grant date, including:

- the prices at which the Company sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to its common stock at the time of each grant;
- the progress of the Company's research and development programs, including the status and results of preclinical studies and clinical trials for its product candidates;
- the Company's stage of development and commercialization and its business strategy;
- external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry;
- the Company's financial position, including cash on hand, and its historical and forecasted performance and operating results;
- the lack of an active public market for the Company's common stock and its preferred stock;

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

2. Summary of significant accounting policies (continued)

- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of the Company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if the Company had used significantly different assumptions or estimates, the fair value of its common stock and its stock-based compensation expense could have been materially different.

Income taxes—The Company accounts for income tax in accordance with ASC 740-10, Income Taxes ("ASC 740-10"), which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the Company's financial statements and tax returns. Deferred tax assets and liabilities are determined based upon the differences between the financial statement carrying amounts and the tax bases of existing assets and liabilities and for loss and credit carryforwards, using enacted tax rates expected to be in effect in the year in which the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if it is more likely than not that these assets may not be realized. The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company recognizes interest and penalties, if any, related to uncertain tax positions in income tax expense.

Net loss per share—The Company has reported losses since inception and has computed basic net loss per share attributable to common stockholders by dividing net loss attributable to common stockholders by the weighted-average number of common shares outstanding for the period, without consideration for potentially dilutive securities. The Company computes diluted net loss per common share after giving consideration to all potentially dilutive common shares, including options to purchase common stock and convertible preferred stock, outstanding during the period determined using the treasury-stock and if-converted methods, except where the effect of including such securities would be antidilutive. Because the Company has reported net losses since inception, these potential common shares have been anti-dilutive and basic and diluted loss per share have been the same.

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

2. Summary of significant accounting policies (continued)

Basic and diluted net loss per share attributable to common stockholders was calculated as follows:

	Six Months Ended June 30,	
	2018	2019
Numerator:		
Net loss	\$ (7,710,338)	\$ (8,737,650)
Denominator—basic and diluted:		
Weighted-average common shares outstanding, basic and diluted	1,154,107	1,176,417
Net loss per share—basic and diluted	\$ (6.68)	\$ (7.43)

The following table sets forth the potentially dilutive securities that have been excluded from the calculation of diluted net loss per share because to include them would be anti-dilutive (in common stock equivalent shares):

	Six Months Ended June 30,	
	2018	2019
Series A convertible preferred stock	612,446	612,446
Series B convertible preferred stock	7,235,969	7,235,969
Series C convertible preferred stock	—	5,179,877
Options to purchase common stock	1,860,631	2,761,794
Total shares of common stock equivalents	9,709,046	15,790,086

Pro forma net loss per share—Unaudited pro forma net loss per share attributable to common stockholders is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all the convertible preferred stock into shares of common stock as if such conversion had occurred at the beginning of the period presented or the date of original issuance, if later.

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

2. Summary of significant accounting policies (continued)

The following table summarizes the Company's unaudited pro forma net loss per share attributable to common stockholders:

	Six Months ended June 30, 2019
Numerator:	
Net loss attributable to common stockholders, basic and diluted	\$ (8,737,650)
Denominator:	
Weighted average common shares outstanding—basic and diluted	1,176,417
Assumed conversion of Series A, Series B and Series C convertible preferred stock	12,899,252
Denominator for pro forma basic and diluted loss per common share	14,075,669
Pro forma basic and diluted net loss per common share	\$ (0.62)

Recently issued accounting pronouncements—not yet adopted

In June 2018, the FASB issued ASU No. 2018-07, "Compensation—Stock Compensation", which expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees, except for specific exceptions. This ASU is effective for annual or any interim periods beginning after December 15, 2019. The Company is currently assessing the impact of adopting this authoritative guidance on its financial statements.

3. Leases

On January 1, 2019, the Company adopted ASC 842 using the modified retrospective transition approach allowed under ASU 2018-11 which releases companies from presenting comparative periods and related disclosures under ASC 842 and requires a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption (Note 2). The Company is party to two operating leases for office or laboratory space. The Company's finance leases are immaterial both individually and in the aggregate. The Company has elected to apply the short-term lease exception to all leases of one year or less. As of June 30, 2019, this exception applies to one operating lease for office and laboratory space, which is for a term of one year, and expired June 30, 2019. Rent expense for six months ended June 30, 2018 and 2019 was \$64,474 and \$69,524, respectively, which are included in operating expenses.

Further, the Company has applied the guidance in ASC 842 to our corporate office and laboratory leases and have determined that these should be classified as operating leases. Consequently, as a result of the adoption of ASC 842, we recognized a ROU lease asset of approximately \$329,384 with a corresponding lease liability of approximately \$348,040 based on the present value of the minimum rental payments of such leases. In accordance with ASC 842, the beginning balance of the ROU lease asset was reduced by the existing deferred rent liability at inception of approximately \$18,656. In the consolidated balance sheets at June 30, 2019, the Company has a ROU asset balance of \$277,531 and a current and non-current lease liability of \$112,315 and \$181,910, respectively, relating to the ROU lease

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

3. Leases (continued)

asset. The balance of both the ROU lease asset and the lease liabilities primarily consists of future payments under the Company's office lease in Boston, Massachusetts.

The Company is party to an operating lease in Boston, Massachusetts for office and laboratory space. The lease commenced in November 2016 with the initial term set to expire in December 2021. This office lease does not have any renewal options. The Company was party to an operating lease in Solna, Sweden that had month-to-month payments and expired on June 30, 2019. Additionally, the Company entered into a new operating lease for office and laboratory space in Solna, Sweden that is effective July 1, 2019 and expires in June 2022. Base rent for this lease is approximately \$128,000 annually.

Quantitative information regarding the Company's leases for the six months ended June 30, 2019 is as follows:

Lease Cost	Classification	Six Months Ended June 30, 2019
Operating lease cost	General and administrative expenses	\$ 51,853
Other Information		
Operating cash flows paid for amounts included in the measurement of lease liabilities		\$ 60,818
Operating lease liabilities arising from obtaining right-of-use assets		—
Weighted average remaining lease term (years)		2.5
Weighted average discount rate		4.3%

Future lease payments under noncancellable leases are as follows at June 30, 2019:

Future Lease Payments	Operating Leases
2019	\$ 60,818
2020	123,930
2021	126,225
Thereafter	—
Total Lease Payments	\$ 310,973
Less: Imputed Interest	(16,748)
Total Lease Liabilities	\$ 294,225

As most of the Company's leases do not provide an implicit rate, we use the Company's incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments. The Company uses the incremental borrowing rate on January 1, 2019 for operating leases that commenced prior to that date.

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

4. Property and equipment

Property and equipment as of December 31, 2018 and June 30, 2019 consist of the following:

	December 31, 2018	June 30, 2019
Lab equipment	\$ 69,770	\$ 73,722
Furniture & Fixtures	16,313	16,313
Computer equipment	12,689	12,279
Property and equipment, at cost	98,772	102,314
Less accumulated depreciation and amortization	(74,322)	(76,652)
Property and equipment—net	<u>\$ 24,450</u>	<u>\$ 25,662</u>

Depreciation expense for six months ended June 30, 2018 and 2019 was \$4,263 and \$4,739, respectively.

5. Accrued expenses

Accrued expenses at December 31, 2018 and June 30, 2019 consist of the following:

	December 31, 2018	June 30, 2019
Professional fees	\$ 80,771	\$ 318,668
Compensation and benefits	624,298	434,133
Research and development	2,178,086	2,102,926
Other	245,617	404,382
Total accrued expenses	<u>\$ 3,128,772</u>	<u>\$ 3,260,109</u>

6. Commitments

The Company's commitments are disclosed in the audited financial statements included in this Registration Statement as of and for the year ended December 31, 2018. Since the date of such financial statements, there have been no material changes to the Company's commitments. Further, the Company's commitments related to lease agreements are disclosed in Note 3 to our unaudited condensed consolidated financial statements included elsewhere in this Registration Statement.

7. Income taxes

The Company has no income tax expense due to operating losses incurred for the six months ended June 30, 2018 and 2019. The Company has provided a valuation allowance for the full amount of the net deferred tax assets as, based on all available evidence, it is considered more likely than not that all the recorded deferred tax assets will not be realized in a future period. At December 31, 2018, the Company had \$61.6 million, \$0.5 million and \$0.4 million of foreign, federal and state net operating loss carryforwards, respectively, that expire at various dates through 2036. Certain of these foreign, federal and state net operating loss carryforwards may be subject to Internal Revenue Code Section 382 or similar provisions, which impose limitations on their utilization amounts.

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

7. Income taxes (continued)

Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. Under the provisions of the U.S. Internal Revenue Code and Sweden tax law, certain substantial changes in the Company's ownership, including a sale of the Company or significant changes in ownership due to sales of equity, may have limited, or may limit in the future, the amount of net operating loss carryforwards that could be used annually to offset future taxable income. For U.S. and Swedish income tax purposes, the Company has not completed a study to assess whether a change of control has occurred or whether there have been changes of control since the Company's formation due to the complexity and cost associated with such study and because there could be additional changes in control in the future. As a result, the Company is not able to estimate the effect of the change in control, if any, on the Company's ability to utilize U.S. or Swedish net operating losses or other tax attribute carryforwards in the future. For Swedish income tax purposes, the Company has estimated that approximately \$12.5 million of its net operating losses may be subject to limitations in accordance with the country's group contribution restriction laws at December 31, 2018.

The Company files tax returns in Sweden, the United States, Pennsylvania and Massachusetts, and all tax years since inception remain open to examination by the major taxing jurisdictions to which the Company is subject, as carryforward attributes generated in years past may still be adjusted upon examination by the Internal Revenue Service (IRS) or other authorities if they have or will be used in a future period. The Company is not currently under examination by the IRS or any other jurisdictions for any tax years.

As of December 31, 2018 and June 30, 2019, the Company had no uncertain tax positions or related interest and penalties accrued.

In June 2018, Sweden passed law on changes to the Swedish regulations on corporate income taxation. The law applies from January 1, 2019. Among other things, the changes decrease the corporate income tax rate in two steps from 22% to 21.4% as of January 1, 2019 and 20.6% as of January 1, 2020. U.S. GAAP requires companies to revalue their deferred tax assets and deferred tax liabilities as of the date of enactment, with the resulting tax effects accounted for in the reporting period of enactment. This revaluation resulted in an overall reduction of deferred taxes of \$0.7 million and a corresponding reduction in the valuation allowance. As such, there was no net impact to the Company's statement of operations as a result of the reduction in tax rates.

8. Convertible preferred stock

The Company has 20,000,000 shares authorized for all classes of equity combined.

Series A Preferred

In June 2011, the Company issued 145,469 shares of Series A Preferred for gross proceeds of \$3,233,417. In March 2016, the Company issued 466,977 shares of Series A Preferred as settlement of its outstanding bridge loans totaling \$3,249,627. All 612,446 shares of Series A Preferred were issued to related parties.

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

8. Convertible preferred stock (continued)

As of June 30, 2019, the rights and preferences of the Series A Preferred are as follows:

Conversion—Each share of Series A Preferred may be converted at any time, at the option of the holder, into a share of common stock. The Series A Preferred automatically converts into shares of common stock when 1) shareholders representing a majority of the outstanding preferred shares calls for such conversion or 2) at the closing of an initial public offering of the Company's common stock at a per share price of at least one and a half (1.5) times the average amount (EUR 16.05 based on all Series C preferred shares issued as of June 30, 2019) paid per Series C preferred share (as adjusted for share splits and similar) and aggregate proceeds in excess of EUR 50,000,000.

Dividends—Holders of Series A Preferred do not accrue dividends.

Voting rights—Preferred Stock and common stock vote together as one class on an as converted basis. Common stock voting rights on certain matters are subject to the powers, preferences, and rights of the Preferred Stock. Holders are entitled to vote on all matters and shall have the number of votes equal to the number of shares of common stock into which the shares of Preferred Stock held by such holder are then convertible.

Series B Preferred

In March 2016, the Company issued 3,322,762 shares of Series B Preferred for gross proceeds of \$22,609,485. The Company also issued 590,445 shares of Series B Preferred in settlement of its outstanding bridge loans totaling \$4,108,818. In October 2017, the Company issued 3,322,762 Series B preferred shares at a price per share of \$7.02, for an aggregate purchase price of \$23,349,617. All 7,235,769 shares of Series B Preferred were issued to related parties.

As of June 30, 2019, the rights and preferences of the Series B Preferred are as follows:

Conversion—Each share of Series B Preferred may be converted at any time, at the option of the holder, into a share of common stock. The Series B Preferred automatically converts into shares of common stock when 1) shareholders representing a majority of the outstanding preferred shares calls for such conversion or 2) at the closing of an initial public offering of the Company's common stock at a per share price of at least one and a half (1.5) times the average amount (EUR 16.05 based on all Series C preferred shares issued as of June 30, 2019) paid per Series C preferred share (as adjusted for share splits and similar) and aggregate proceeds in excess of EUR 50,000,000.

Dividends—Holders are entitled to dividends of 8%, compounded annually if not paid. No dividends have been declared or paid as of June 30, 2019. The company has not accrued dividends on the Series B Preferred since dividends are only payable upon the occurrence of a liquidation event, including the transfer of more than fifty percent of the Company's outstanding shares or the transfer of substantially all of the Company's intellectual property. Approximately \$11,059,542 of accrued dividends that were payable through June 30, 2019 was added to the stated liquidation preference amount of the Series B Preferred, which totaled \$61,127,463 at June 30, 2019.

Voting rights—Preferred Stock and common stock vote together as one class on an as converted basis. Common stock voting rights on certain matters are subject to the powers, preferences, and rights of the Preferred Stock. Holders are entitled to vote on all matters and shall have the number of votes

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

8. Convertible preferred stock (continued)

equal to the number of shares of common stock into which the shares of Preferred Stock held by such holder are then convertible.

Series C Preferred

In November 2018, the Company issued 4,712,698 shares of Series C Preferred for gross proceeds of \$56,725,342. In February 2019, the Company issued 467,179 shares of Series C Preferred for gross proceeds of \$5,651,872. A total of 4,219,849 shares of Series C Preferred were issued to related parties.

As of June 30, 2019, the rights and preferences of the Series C Preferred are as follows:

Conversion—Each share of Series C Preferred may be converted at any time, at the option of the holder, into a share of common stock. The Series C Preferred automatically converts into shares of common stock when 1) shareholders representing a majority of the outstanding preferred shares calls for such conversion or 2) at the closing of an initial public offering of the Company's common stock at a per share price of at least one and a half (1.5) times the average amount (EUR 16.05 based on all Series C preferred shares issued as of June 30, 2019) paid per Series C preferred share (as adjusted for share splits and similar) and aggregate proceeds in excess of EUR 50,000,000.

Dividends—Holders are entitled to dividends of 8%, compounded annually if not paid. No dividends have been declared or paid as of June 30, 2019. The company has not accrued dividends on the Series C Preferred since dividends are only payable upon the occurrence of a liquidation event, including the transfer of more than fifty percent of the Company's outstanding shares or the transfer of substantially all of the Company's intellectual property. Approximately \$2,811,614 of accrued dividends that were payable through June 30, 2019 was added to the stated liquidation preference amount of the Series C Preferred, which totaled \$65,188,827 at June 30, 2019.

Voting rights—Preferred Stock and common stock vote together as one class on an as converted basis. Common stock voting rights on certain matters are subject to the powers, preferences, and rights of the Preferred Stock. Holders are entitled to vote on all matters and shall have the number of votes equal to the number of shares of common stock into which the shares of Preferred Stock held by such holder are then convertible.

Liquidation preference

Upon liquidation, dissolution, or winding up of business, the Preferred Stock holders are entitled to receive a liquidation preference in priority to holders of common stock at the original issue price plus, in the case of Series B and Series C Preferred, any unpaid accumulated dividends as follows:

- 1) If a liquidation event occurs prior to the Company achieving a certain clinical milestone, Series C Preferred shareholders shall receive an amount per Series C Preferred share equal to the original subscription price per Series C Preferred share (as adjusted for share splits and similar) plus unpaid accumulated dividends. Secondly, after the Series C Preferred shareholders have received full payment, the Series B Preferred shareholders shall receive an amount per Series B preferred share equal to the original subscription price per Series B Preferred share (as adjusted for share splits and similar) plus unpaid accumulated dividends. Thirdly, after the Series B and C Preferred shareholders have received full payment, the

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

8. Convertible preferred stock (continued)

Series A Preferred shareholders shall receive an amount per Series A preferred share equal to the original subscription price per Series A Preferred share (as adjusted for share splits and similar). When the Preferred A, B and C shareholders are satisfied in full, any excess assets available for distribution will be allocated ratably among holders of common stock and preferred stock based on their pro rata shareholdings on an as-if-converted basis.

- 2) If a liquidation event occurs after the Company achieves a certain clinical milestone, Series B and C Preferred shareholders, based on their pro rata shareholdings, shall receive an amount per Series B and C Preferred share equal to the original subscription price per Series B and C Preferred share (as adjusted for share splits and similar) plus unpaid accumulated dividends. Secondly, after the Series B and C Preferred shareholders have received full payment, the Series A Preferred shareholders shall receive an amount per Series A preferred share equal to the original subscription price per Series A Preferred share (as adjusted for share splits and similar). When the Preferred A, B and C shareholders are satisfied in full, any excess assets available for distribution will be allocated ratably among holders of common stock and preferred stock based on their pro rata shareholdings on an as-if-converted basis.

The liquidation preferences apply to each series of preferred stock only to the extent the holders would receive less than three times their respective original purchase prices.

9. Common stock

The Company has 1,181,573 shares of common stock outstanding as of June 30, 2019. During the first six months of 2018 and 2019, the Company issued 1,503 and 26,207 shares of common stock to employees for aggregate consideration of \$1,415 and \$23,118, respectively, as a result of stock option exercises.

The holders of common stock are entitled to one vote for each share of common stock. Subject to the payment in full of all preferential dividends to which the holders of the Preferred Stock are entitled, the holders of common stock shall be entitled to receive dividends out of funds legally available. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, after the payment or provision for payment of all debts and liabilities of the Company and all preferential amounts to which the holders of Preferred Stock are entitled with respect to the distribution of assets in liquidation, the holders of common stock shall be entitled to share ratably in the remaining assets of the Company available for distribution.

10. Stock option plan

In October 2016, the Board of Directors adopted the 2016 Amended and Restated Stock Option Program (the "Plan"), which provided for the grant of stock options to the Company's employees, officers, directors, and outside consultants for the purchase of up to 1,224,824 shares of the Company's common stock. During 2017, the Plan was amended to provide up to 1,946,849 shares of the Company's common stock. During 2018, the Plan was further amended to provide up to 3,069,999 shares of the Company's common stock. Holders of stock options shall be entitled to exercise the vested portion of the stock option provided that a trade sale, as defined in the plan, or initial public

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

10. Stock option plan (continued)

offering has occurred. The holders of stock options may also exercise the vested portion of the stock option within six months of termination of employment.

Stock options generally vest over a four-year period and expire in October 2026. The Board of Directors has the discretion to provide for accelerated vesting. At June 30, 2019, there were 543,647 shares available for future grant under the Plan.

The Company recorded stock-based compensation expense of \$169,854 and \$284,909 during the six months ended June 30, 2018 and 2019, respectively. As of June 30, 2019, there was \$2,271,127 of unrecognized compensation cost related to nonvested share-based compensation arrangements granted under the Plan, which is expected to be recognized over a weighted-average period of approximately 2.9 years.

The fair value of each option award is estimated on the date of grant using Black-Scholes, with the assumptions noted in the table below. Expected volatility for the Company's common stock was determined based on an average of the historical volatility of a peer group of similar public companies. The expected term of options granted to employees was calculated using the simplified method, which represents the average of the contractual term of the option and the weighted-average vesting period of the option. The Company uses the simplified method because it does not have sufficient historical option exercise data to provide a reasonable basis upon which to estimate expected term. The contractual life of the option was used for the expected life of options granted to non-employee. The assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free rate for periods within the expected life of the option is based upon the Swedish Government Bond Rate in effect at the time of grant.

In determining the exercise prices for options granted, the Company's Board of Directors has considered the fair value of the common stock as of the measurement date. The fair value of the common stock at each award grant date was based upon a variety of factors, including the results obtained from an independent third-party valuation, the Company's financial position and historical financial performance, the status of technological developments within the Company's proposed products, an evaluation or benchmark of the Company's competition, the current business climate in the marketplace, the illiquid nature of the common stock, arm's length sales of the Company's capital stock, including Preferred Stock, the effect of the rights and preferences of the preferred shareholders, and the prospects of a liquidity event, among others.

The assumptions used in Black-Scholes for the six months ended June 30, 2018 and 2019 are as follows:

	Six Months ended June 30,	
	2018	2019
Expected volatility	n/a	73.5%
Risk-free rate	n/a	2.6%
Expected dividend yield	n/a	0%
Expected term in years	n/a	7.6

Notes to Condensed Consolidated Financial Statements (Continued)

(Unaudited)

10. Stock option plan (continued)

A summary of option activity under the Plan at December 31, 2018 and June 30, 2019 are as follows:

	Number of options	Weighted-average exercise price per share	Weighted average remaining contractual term (in years)	Aggregate intrinsic value
Outstanding at December 31, 2018	1,844,188	\$ 0.82	7.6	\$ 4,382,781
Granted	984,596	3.19		
Exercised	(26,207)	0.97		
Cancelled/Forfeited	(40,783)	0.99		
Outstanding at June 30, 2019	2,761,794	\$ 1.66	7.2	\$ 4,234,886
Exercisable at June 30, 2019	—	—	—	—
Vested or expected to vest at June 30, 2019	2,761,794	\$ 1.66	7.2	\$ 4,234,886

The weighted-average grant date fair value of options granted during the six months ended June 30, 2019, was \$2.23 per share. No options were granted during the six months ended June 30, 2018.

11. Subsequent events

On September 20, 2019, the Company consummated a corporate reorganization, pursuant to which all of the issued and outstanding stock and options of Aprea Therapeutics AB, or Aprea AB, was exchanged for common stock, preferred stock or options, as applicable, of Aprea Therapeutics, Inc. As a result, Aprea Therapeutics AB, became a wholly-owned subsidiary of Aprea Therapeutics, Inc.

In September 2019, the Company's Board of Directors and stockholders approved a 1-for-1.6045 stock split of the Company's preferred and common stock. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this split.

5,000,000 shares



Common stock

Prospectus

J.P. Morgan

Morgan Stanley

RBC Capital Markets

, 2019

Information not required in prospectus

Item 13. Other expenses of issuance and distribution.

The following table sets forth the expenses to be incurred in connection with the offering described in this Registration Statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimates except the Securities and Exchange Commission's registration fee, the Financial Industry Regulatory Authority, Inc. filing fee and the NASDAQ listing fee.

	<u>Amount</u>
Securities and Exchange Commission registration fee	\$ 11,151
Financial Industry Regulatory Authority, Inc. filing fee	14,300
NASDAQ listing fee	150,000
Accountants' fees and expenses	900,000
Legal fees and expenses	1,500,000
Transfer Agent's fees and expenses	25,000
Printing fees and expenses	300,000
Miscellaneous fees and expenses	299,549
Total expenses	<u>\$ 3,200,000</u>

Item 14. Indemnification of directors and officers.

Section 102 of the Delaware General Corporation Law permits a corporation to eliminate the personal liability of its directors for monetary damages for a breach of fiduciary duty as a director, except where the director breached his or her duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Upon completion of this offering, our certificate of incorporation will provide that none of our directors shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the Delaware General Corporation Law prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the Delaware General Corporation Law provides that a corporation has the power to indemnify a director, officer, employee, or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he or she is or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Upon the completion of this offering, our certificate of incorporation will provide that we will indemnify each person who was or is a party or is threatened to be made a party or is involved in any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or

investigative (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our certificate of incorporation that will be effective as of the closing date of this offering also provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred by him or her or on his or her behalf in connection therewith. If we do not assume the defense, expenses must be advanced to an Indemnitee under certain circumstances.

We plan to enter into indemnification agreements with each of our executive officers and directors. In general, these agreements provide that we will indemnify the director or executive officer to the fullest extent permitted by law for claims arising in his or her capacity as a director or executive officer of our company or in connection with their service at our request for another corporation or entity. The indemnification agreements also provide for procedures that will apply in the event that a director or executive officer makes a claim for indemnification and establish certain presumptions that are favorable to the director or executive officer.

We maintain a general liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

The underwriting agreement we will enter into in connection with the offering of common stock being registered hereby provides that the underwriters will indemnify, under certain conditions, our directors and officers (as well as certain other persons) against certain liabilities arising in connection with such offering.

Insofar as the forgoing provisions permit indemnification of directors, executive officers, or persons controlling us for liability arising under the Securities Act of 1933, as amended, or the Securities Act, we have been informed that, in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Item 15. Recent sales of unregistered securities.

The following list sets forth information regarding all securities sold or granted by us since January 1, 2016, which were not registered under the Securities Act, and the consideration, if any, received by us for such securities:

- (1) In March 2016 and October 2017, Aprea AB issued and sold an aggregate of 7,235,969 shares of its Series B preferred stock to five accredited investors at a purchase price of \$6.81 and \$7.02, respectively, per share for aggregate proceeds of approximately \$50.0 million in cash.
- (2) In November 2018 and February 2019, Aprea AB issued and sold an aggregate of 5,179,877 shares of its Series C preferred stock to six accredited investors at a purchase price of \$12.08 and \$12.10, respectively, per share for aggregate proceeds of approximately \$62.3 million in cash.
- (3) In connection with the formation and initial capitalization of Aprea Therapeutics, Inc., on July 11, 2019, Aprea Therapeutics, Inc. issued 160 shares of its common stock to Chris Schade, our Chief Executive Officer, for an aggregate purchase price of \$100.
- (4) Since January 1, 2016, we have granted stock options to purchase an aggregate of 2,973,085 shares of our common stock with exercise prices of \$0.92, \$1.01, \$3.18 and \$10.95 per share, to our employees, directors and consultants pursuant to our 2016 Stock Incentive Plan. Since January 1, 2016, we have issued an aggregate of 28,512 shares of our common stock upon exercise of stock options granted pursuant to our 2016 Stock Incentive Plan, for an aggregate consideration of \$25,215 in cash.

The offers, sales and issuances of the securities described in Items 15(1), 15(2) and 15(3) were exempt from registration under the Securities Act under Section 4(a)(2) of the Securities Act as transactions by an issuer not involving a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions was an accredited person and had adequate access, through employment, business or other relationships, to information about the registrant.

The offers, sales and issuances of the securities described in Item 15(4) were exempt from registration under the Securities Act under either (1) Rule 701 in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701 or (2) Section 4(a)(2) of the Securities Act as transactions by an issuer not involving any public offering. The recipients of such securities were the registrant's employees, consultants or directors and received the securities under the registrant's 2016 Stock Incentive Plan. The recipients of securities in each of these transactions represented their intention to acquire the securities for investment only and not with view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions.

(a) Exhibits.

The following exhibits are filed as part of this Registration Statement:

- ##1.1 [Form of Underwriting Agreement](#)
- ##3.1 [Certificate of Incorporation of the Registrant](#)
- ##3.2 [Bylaws of the Registrant, as currently in effect](#)
- ##3.3 [Amended and Restated Certificate of Incorporation of Registrant, as currently in effect.](#)
- 3.4 [Certificate of Amendment to the Amended and Restated Certificate of Incorporation of the Registrant.](#)
- 3.5 [Form of Amended and Restated Certificate of Incorporation of the Registrant \(to be effective upon the completion of this offering\)](#)
- ##3.6 [Form of Amended and Restated Bylaws of the Registrant \(to be effective upon the completion of this offering\).](#)
- 4.1 [Specimen common stock certificate of the Registrant](#)
- 5.1 [Opinion of Sidley Austin LLP](#)
- +10.1 [Form of 2019 Stock Incentive Plan and form of agreements thereunder](#)
- ##+10.2 [Form of 2019 Employee Stock Purchase Plan](#)
- ##+10.3 [Service Agreement, between Aprea AB and Syngene International Private Limited](#)
- ##10.4 [Amended and Restated Registration Rights Agreement by and among the Registrant and the shareholders party thereto](#)
- ##+10.5 [Form of Indemnification Agreement between the Registrant and each of its directors and executive officers](#)
- +10.6 [Employment Agreement between the Registrant and Christian S. Schade](#)
- +10.7 [Form of Executive Employment Agreement](#)
- +10.8 [Employment Agreement between the Registrant and Lars Abrahmsen, Ph.D.](#)
- +10.9 [Employment Agreement between the Registrant and Gregory A. Korbel, Ph.D.](#)
- +10.10 [Employment Agreement between the Registrant and Scott M. Coiante.](#)
- ##+10.11 [Master Manufacturing and Supply Agreement, between Aprea Therapeutics AB and Siegfried Hameln GmbH](#)
- 23.1 [Consent of Ernst & Young AB, independent registered public accounting firm](#)
- 23.2 [Consent of Sidley Austin LLP \(included in Exhibit 5.1\)](#)
- ##24.1 [Power of Attorney](#)

Previously filed.

+ Indicates a management contract or compensatory plan.

† Portions of this exhibit (indicated by bracketed asterisks) have been omitted as the Company has determined that (i) the omitted information is not material and (ii) the omitted information would likely cause competitive harm to the Company if publicly disclosed.

(b) Financial statement schedules.

No financial statement schedules are provided because the information called for is not required or is shown either in the financial statements or the related notes.

Item 17. Undertakings.

- (a) The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.
- (b) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.
- (c) The undersigned registrant hereby undertakes that:
 - (1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
 - (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Signature

Title

Date

*

John B. Henneman, III

Director

September 27, 2019

*By:

/s/ SCOTT M. COIANTE

Scott M. Coiante
Attorney-in-fact

CERTIFICATE OF AMENDMENT TO THE
AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
APREA THERAPEUTICS, INC.

Aprea Therapeutics, Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "**DGCL**"), does hereby certify that:

ONE: The original name of this corporation is Aprea Therapeutics, Inc., and the date of filing of the original Certificate of Incorporation of this corporation with the Secretary of State of the State of Delaware was May 3, 2019.

TWO: That the Certificate of Incorporation of this corporation was amended and restated on September 20, 2019 (as so amended, the "**Amended and Restated Certificate of Incorporation**").

THREE: This Certificate of Amendment to the Amended and Restated Certificate of Incorporation (the "**Certificate of Amendment**") has been duly adopted in accordance with Section 242 of the DGCL and amends the provisions of the Corporation's Amended and Restated Certificate of Incorporation (the "**Restated Certificate**").

FOUR: This Certificate of Amendment has been approved and duly adopted by the Board of Directors of the Corporation.

FIVE: The terms and provisions of this Certificate of Amendment have been duly approved by written consent of the required number of shares of outstanding stock of the Corporation pursuant to Subsection 228(a) of the DGCL and written notice pursuant to Subsection 228(e) of the DGCL has been or will be given to those stockholders whose written consent has not been obtained.

SIX: The following is hereby inserted into paragraph A of Article IV immediately before the first sentence therein:

"Effective upon the filing of this Certificate of Amendment to the Amended and Restated Certificate of Incorporation with the Secretary of State of the State of Delaware (the "**Effective Time**"), every 1 share of Common Stock then issued and outstanding or held in the treasury of the Corporation immediately prior to the Effective Time shall automatically be split into 1.6045 shares of Common Stock, without any further action by the holders of such shares (the "**Stock Split**"). The Stock Split shall occur automatically without any further action by the holders of the shares of Common Stock and Preferred Stock affected thereby. All rights, preferences and privileges of the Common Stock and the Preferred Stock shall be appropriately adjusted to reflect the Stock Split in accordance with this Amended and Restated Certificate of Incorporation."

[Remainder of page intentionally left blank]

IN WITNESS WHEREOF, this Certificate of Amendment, having been duly adopted in accordance with Section 242 of the DGCL, has been duly executed by a duly authorized officer of the corporation on this 26th day of September 2019.

APREA THERAPEUTICS, INC.

Signature: /s/ CHRISTIAN S. SCHADE

Name: Christian S. Schade

Title: President and Chief Executive Officer

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

OF

APREA THERAPEUTICS, INC.

a Delaware corporation

Aprea Therapeutics, Inc., a corporation organized and existing under the laws of the State of Delaware (the "**Corporation**"), hereby certifies as follows:

A. The name of the Corporation is Aprea Therapeutics, Inc. The Corporation's original certificate of incorporation was filed with the office of the Secretary of State of the State of Delaware on May 3, 2019

B. This amended and restated certificate of incorporation was duly adopted in accordance with Sections 242 and 245 of the General Corporation Law of the State of Delaware, as amended (the "**DGCL**"), restates and amends the provisions of the Corporation's certificate of incorporation and has been duly approved by the written consent of the stockholders of the Corporation in accordance with Section 228 of the DGCL.

C. The text of the certificate of incorporation of this Corporation is hereby amended and restated to read in its entirety as follows:

ARTICLE I
NAME

The name of the Corporation is Aprea Therapeutics, Inc.

ARTICLE II
REGISTERED OFFICE

The address of the Corporation's registered office in the State of Delaware is 1209 Orange Street, City of Wilmington, County of New Castle, Delaware 19801. The name of its registered agent at such address is The Corporation Trust Company.

ARTICLE III
PURPOSE

The purpose of the Corporation is to engage in any lawful act or activity for which corporations may be organized under the DGCL.

ARTICLE IV
CAPITAL STOCK

4.1 Authorized Capital Stock. The total number of shares of all classes of capital stock that the Corporation is authorized to issue is 440,000,000 shares, consisting of 400,000,000 shares of common stock, par value \$0.001 per share ("Common Stock"), and 40,000,000 shares of preferred stock, par value \$0.001 per share ("Preferred Stock").

4.2 Increase or Decrease in Authorized Capital Stock. The number of authorized shares of Common Stock or Preferred Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority in voting power of the stock of the Corporation entitled to vote generally in the election of directors, irrespective of the provisions of Section 242(b)(2) of the DGCL (or any successor provision thereto), voting together as a single class, without a separate vote of the holders of the class or classes the number of authorized shares of which are being increased or decreased, unless a vote by any holders of one or more series of Preferred Stock is required by the express terms of any series of Preferred Stock as provided for or fixed pursuant to the provisions of Section 4.4 of this Certificate of Incorporation (as defined below).

4.3 Common Stock.

(a) The holders of shares of Common Stock shall be entitled to one vote for each such share on each matter properly submitted to the stockholders of the Corporation on which the holders of shares of Common Stock are entitled to vote. The holders of shares of Common Stock shall not have cumulative voting rights. Except as otherwise required by law or this amended and restated certificate of incorporation of the Corporation (as further amended from time to time in accordance with the provisions hereof and including, without limitation, the terms of any certificate of designation with respect to any series of Preferred Stock, this "Certificate of Incorporation"), and subject to the rights of the holders of shares of Preferred Stock, if any, at any annual or special meeting of the stockholders of the Corporation, the holders of shares of Common Stock shall have the right to vote for the election of directors of the Corporation and on all other matters properly submitted to the stockholders of the Corporation for their vote; provided, however, that, except as otherwise required by law, holders of shares of Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation that relates solely to the terms, number of shares, powers, designations, preferences or relative, participating, optional or other special rights (including, without limitation, voting rights), or to qualifications, limitations or restrictions thereof, of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to this Certificate of Incorporation or pursuant to the DGCL.

(b) Subject to the rights of the holders of shares of Preferred Stock, the holders of shares of Common Stock shall be entitled to receive such dividends and other distributions (payable in cash, property or capital stock of the Corporation) when, as and if declared thereon by the board of directors of the Corporation (the "Board") from time to time out of any assets or funds of the Corporation legally available therefor and shall share equally on a per share basis in such dividends and distributions.

(c) In the event of any voluntary or involuntary liquidation, dissolution or winding-up of the Corporation, after payment or provision for payment of the debts and other liabilities of the Corporation, and subject to the rights of the holders of shares of Preferred Stock in respect thereof, the holders of shares of Common Stock shall be entitled to receive all of the remaining assets of the Corporation available for distribution to its stockholders, ratably in proportion to the number of shares of Common Stock held by them.

4.4 Preferred Stock.

(a) The Board is expressly authorized to issue from time to time shares of Preferred Stock in one or more series pursuant to a resolution or resolutions providing for such issue duly adopted by the Board. The Board is further authorized, subject to limitations prescribed by law, to fix by resolution or resolutions and to set forth in a certification of designation filed pursuant to the DGCL the powers, designations, preferences and relative, participating, optional or other special rights, if any, and the qualifications, limitations or restrictions thereof, if any, of any wholly unissued series of Preferred Stock, including, without limitation, dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including, without limitation, sinking fund provisions), redemption price or prices and liquidation preferences of any such series, and the number of shares constituting any such series and the designation thereof, or any of the foregoing.

(b) The Board is further authorized to increase (but not above the total number of authorized shares of the class) or decrease (but not below the number of shares of any such series then outstanding) the number of shares of any series of Preferred Stock, the number of which was fixed by it, subsequent to the issuance of shares of such series then outstanding, subject to the powers, preferences and rights, and the qualifications, limitations and restrictions thereof, stated in this Certificate of Incorporation or the resolution of the Board originally fixing the number of shares of such series. If the number of shares of any series of Preferred Stock is so decreased, then the shares constituting such decrease shall resume the status that they had prior to the adoption of the resolution originally fixing the number of shares of such series.

ARTICLE V
BOARD OF DIRECTORS

5.1 General Powers. The business and affairs of the Corporation shall be managed by or under the direction of the Board.

5.2 Number of Directors; Election; Term.

(a) The number of directors that shall constitute the entire Board shall be fixed from time to time exclusively by the Board in accordance with the bylaws of the Corporation (as amended from time to time in accordance with the provisions hereof and thereof, the "**Bylaws**"), subject to the rights of holders of any series of Preferred Stock with respect to the election of directors, if any.

(b) Subject to the rights of holders of any series of Preferred Stock with respect to the election of directors, the directors of the Corporation shall be divided into three classes as nearly equal in number as is practicable, hereby designated Class I, Class II and Class III. The Board is

authorized to assign members of the Board already in office to such classes. The term of office of the initial Class I directors shall expire upon the election of directors at the first annual meeting of stockholders following the effectiveness of this Article V; the term of office of the initial Class II directors shall expire upon the election of directors at the second annual meeting of stockholders following the effectiveness of this Article V; and the term of office of the initial Class III directors shall expire upon the election of directors at the third annual meeting of stockholders following the effectiveness of this Article V. At each annual meeting of stockholders, commencing with the first annual meeting of stockholders following the effectiveness of this Article V, each of the successors elected to replace the directors of a class whose term shall have expired at such annual meeting shall be elected to hold office until the third annual meeting next succeeding his or her election and until his or her respective successor shall have been duly elected and qualified. Subject to the rights of holders of any series of Preferred Stock with respect to the election of directors, if the number of directors that constitutes the Board is changed, any newly created directorships or decrease in directorships shall be so apportioned by the Board among the classes as to make all classes as nearly equal in number as is practicable, provided that no decrease in the number of directors constituting the Board shall shorten the term of any incumbent director.

(c) Notwithstanding the foregoing provisions of this Section 5.2, and subject to the rights of holders of any series of Preferred Stock with respect to the election of directors, each director shall serve until such director's successor is duly elected and qualified or until such director's earlier death, resignation or removal.

(d) Elections of directors need not be by written ballot unless the Bylaws shall so provide.

(e) Notwithstanding any of the other provisions of this Article V, whenever the holders of any one or more series of Preferred Stock issued by the Corporation shall have the right, voting separately by series, to elect directors at an annual or special meeting of stockholders, the election, term of office, filling of vacancies and other features of such directorships shall be governed by the terms of the certificate of designation for such series of Preferred Stock, and such directors so elected shall not be divided into classes pursuant to this Article V unless expressly provided by such terms. During any period when the holders of any series of Preferred Stock have the right to elect additional directors as provided for or fixed pursuant to the provisions of this Article V, then upon commencement and for the duration of the period during which such right continues; (i) the then otherwise total authorized number of directors of the Corporation shall automatically be increased by such specified number of directors, and the holders of such Preferred Stock shall be entitled to elect the additional directors so provided for or fixed pursuant to such provisions, and (ii) each such additional director shall serve until such director's successor shall have been duly elected and qualified, or until such director's right to hold such office terminates pursuant to such provisions, whichever occurs earlier, subject to such director's earlier death, resignation or removal. Except as otherwise provided by the Board in the resolution or resolutions establishing such series, whenever the holders of any series of Preferred Stock having such right to elect additional directors are divested of such right pursuant to the provisions of such series of stock, the terms of office of all such additional directors elected by the holders of such stock, or elected to fill any vacancies resulting from the death, resignation or removal of such additional directors, shall forthwith

terminate, and the total authorized number of directors of the Corporation shall be reduced accordingly.

5.3 Removal. Subject to the rights of holders of any series of Preferred Stock with respect to the election of directors, a director may be removed from office by the stockholders of the Corporation only for cause.

5.4 Vacancies and Newly Created Directorships. Subject to the rights of holders of any series of Preferred Stock with respect to the election of directors, vacancies occurring on the Board for any reason and newly created directorships resulting from an increase in the number of directors shall, unless the Board determines by resolution that any such vacancies or newly created directorships shall be filled by the affirmative vote of the stockholders, except as otherwise required by law, be filled only by vote of a majority of the remaining members of the Board, although less than a quorum, or by a sole remaining director, and not by the stockholders. A person so elected by the Board to fill a vacancy or newly created directorship shall hold office until the next election of the class for which such person shall have been assigned by the Board and until such person's successor shall be duly elected and qualified or until such director's earlier death, resignation or removal.

ARTICLE VI
AMENDMENT OF BYLAWS

In furtherance and not in limitation of the powers conferred by statute, the Board is expressly authorized to adopt, amend, alter or repeal the Bylaws. The Bylaws may also be adopted, amended, altered or repealed by the stockholders of the Corporation by the affirmative vote of the holders of at least a majority of the voting power of all then outstanding shares of capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class; provided, however, that, in the case of any adoption, amendment, alteration or repeal of the Bylaws by the stockholders of the Corporation, notwithstanding any other provision of the Bylaws, and in addition to any other vote that may be required by law or the terms of any series of preferred stock, the affirmative vote of the holders of at least seventy-five percent (75%) of the voting power of all of the then outstanding shares of capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required to amend, alter, repeal or adopt any provision inconsistent with Sections 1.3, 1.7(b), 1.11, 1.13, 1.16, 1.17, 2.1, 2.8, 2.9, 2.10, 2.13 or 2.14 or Article VI of the Bylaws.

ARTICLE VII
STOCKHOLDERS

7.1 No Action by Written Consent of Stockholders. Except as otherwise expressly provided by the terms of any series of Preferred Stock permitting the holders of such series of Preferred Stock to act by written consent, any action required or permitted to be taken by the stockholders of the Corporation must be effected at a duly called annual or special meeting of the stockholders of the Corporation, and the ability of stockholders to act by written consent in lieu of a meeting of the stockholders is specifically denied.

7.2 Special Meetings. Except as otherwise expressly provided by the terms of any series of Preferred Stock permitting the holders of such series of Preferred Stock to call a special meeting of the holders of such series, special meetings of the stockholders of the Corporation may be called only by the Board, the chairperson of the Board, the chief executive officer or president (in the absence of a chief executive officer), and the ability of the stockholders to call a special meeting of the stockholders is hereby specifically denied.

7.3 Advance Notice. Advance notice of stockholder nominations for the election of directors and of business to be brought by stockholders before any meeting of the stockholders of the Corporation shall be given in the manner provided in the Bylaws.

ARTICLE VIII
LIMITATION OF LIABILITY AND INDEMNIFICATION

8.1 Limitation of Personal Liability. No director of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except to the extent such exemption from liability or limitation thereof is not permitted under the DGCL, as it presently exists or may hereafter be amended from time to time. If the DGCL is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the DGCL, as so amended.

8.2 Indemnification and Advancement of Expenses. The Corporation shall indemnify its directors and officers to the fullest extent authorized or permitted by the DGCL, as now or hereafter in effect, and such right to indemnification shall continue as to a person who has ceased to be a director or officer of the Corporation and shall inure to the benefit of such person's heirs, executors and personal and legal representatives. A director's or officer's right to indemnification conferred by this Section 8.2 shall include the right to be paid by the Corporation the expenses incurred in defending or otherwise participating in any proceeding in advance of its final disposition, provided that such director or officer presents to the Corporation a written undertaking to repay such amount if it shall ultimately be determined that such director or officer is not entitled to be indemnified by the Corporation under this Article VIII or otherwise. Notwithstanding the foregoing, except for proceedings to enforce any director's or officer's rights to indemnification or to advancement of expenses, the Corporation shall not be obligated to indemnify any director or officer, or advance expenses of any director, (or such director's or officer's heirs, executors or personal or legal representatives) in connection with any proceeding (or part thereof) initiated by such person unless such proceeding (or part thereof) was authorized by the Board.

8.3 Non-Exclusivity of Rights. The rights to indemnification and advancement of expenses conferred in Section 8.2 of this Certificate of Incorporation shall neither be exclusive of, nor be deemed in limitation of, any rights to which any person may otherwise be or become entitled or permitted under this Certificate of Incorporation, the Bylaws, any statute, agreement, vote of stockholders or disinterested directors or otherwise.

8.4 Insurance. To the fullest extent authorized or permitted by the DGCL, the Corporation may purchase and maintain insurance on behalf of any current or former director or officer of the Corporation against any liability asserted against such person, whether or not the

Corporation would have the power to indemnify such person against such liability under the provisions of this Article VIII or otherwise.

8.5 Persons Other Than Directors and Officers. This Article VIII shall not limit the right of the Corporation, to the extent and in the manner permitted by law, to indemnify and to advance expenses to, or to purchase and maintain insurance on behalf of, persons other than those persons described in the first sentence of Section 8.2 of this Certificate of Incorporation or to advance expenses to persons other than directors of the Corporation.

8.6 Effect of Modifications. Any amendment, repeal or modification of any provision contained in this Article VIII shall, unless otherwise required by law, be prospective only (except to the extent such amendment or change in law permits the Corporation to further limit or eliminate the liability of directors or officers) and shall not adversely affect any right or protection of any current or former director or officer of the Corporation existing at the time of such amendment, repeal or modification with respect to any acts or omissions occurring prior to such amendment, repeal or modification.

ARTICLE IX
MISCELLANEOUS

9.1 Forum for Certain Actions.

(a) Forum. Unless a majority of the Board, acting on behalf of the Corporation, consents in writing to the selection of an alternative forum (which consent may be given at any time, including during the pendency of litigation), the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another state court located within the State of Delaware or, if no court located within the State of Delaware has jurisdiction, the federal district court for the District of Delaware) shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of the Corporation under Delaware law, (ii) any action asserting a claim of breach of a fiduciary duty owed by any current or former director, officer or other employee of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim against the Corporation or any of its directors, officers or other employees arising pursuant to any provision of the DGCL, this Certificate of Incorporation or the Bylaws (in each case, as may be amended from time to time), (iv) any action asserting a claim against the Corporation or any of its directors, officers or other employees governed by the internal affairs doctrine of the State of Delaware, or (v) any other action asserting an "internal corporate claim," as defined in Section 115 of the DGCL, in all cases subject to the court's having personal jurisdiction over all indispensable parties named as defendants. Nothing herein contained shall be construed to preclude stockholders that assert claims under the Securities Act of 1933, as amended, the Securities Exchange Act of 1934, as amended, or any successor thereto, from bringing such claims in state or federal court, subject to applicable law.

(b) Personal Jurisdiction. If any action the subject matter of which is within the scope of subparagraph (a) of this Section 9.1 is filed in a court other than a court located within the State of Delaware (a "*Foreign Action*") in the name of any stockholder, such stockholder shall be deemed to have consented to (i) the personal jurisdiction of the state and federal courts located within the State of Delaware in connection with any action brought in any such court to

enforce subparagraph (a) of this Section 9.1 (an “**Enforcement Action**”) and (ii) having service of process made upon such stockholder in any such Enforcement Action by service upon such stockholder’s counsel in the Foreign Action as agent for such stockholder.

(c) Enforceability. If any provision of this Section 9.1 shall be held to be invalid, illegal or unenforceable as applied to any person, entity or circumstance for any reason whatsoever, then, to the fullest extent permitted by law, the validity, legality and enforceability of such provision in any other circumstance and of the remaining provisions of this Section 9.1, and the application of such provision to other persons or entities and circumstances shall not in any way be affected or impaired thereby.

9.2 Amendment. The Corporation reserves the right to amend, alter or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by this Certificate of Incorporation and the DGCL; and all rights, preferences and privileges herein conferred upon stockholders of the Corporation by and pursuant to this Certificate of Incorporation in its present form or as hereafter amended are granted subject to the right reserved in this Section 9.2. In addition to any other vote that may be required by law, applicable stock exchange rule or the terms of any series of Preferred Stock, the affirmative vote of the holders of at least a majority of the voting power of all then outstanding shares of capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required to amend, alter, repeal or adopt any provision of this Certificate of Incorporation. Notwithstanding any other provision of this Certificate of Incorporation, and in addition to any other vote that may be required by law, applicable stock exchange rule or the terms of any series of Preferred Stock, the affirmative vote of the holders of at least seventy-five percent (75%) of the voting power of all then outstanding shares of capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required to amend, alter, repeal or adopt any provision of this Certificate of Incorporation inconsistent with the purpose and intent of Article V, Article VI, Article VII or this Article IX (including, without limitation, any such Article as renumbered as a result of any amendment, alternation, repeal or adoption of any other Article).

9.3 Severability. If any provision or provisions of this Certificate of Incorporation shall be held to be invalid, illegal or unenforceable as applied to any circumstance for any reason whatsoever the validity, legality and enforceability of such provision in any other circumstance and of the remaining provisions of this Certificate of Incorporation (including, without limitation, each portion of any paragraph of this Certificate of Incorporation containing any such provision held to be invalid, illegal or unenforceable) shall not in any way be affected or impaired thereby.

IN WITNESS WHEREOF, the Corporation has caused this amended and restated Certificate of Incorporation to be signed by a duly authorized officer of the Corporation on this day of , 2019.

By: Christian Schade
Title: President and Chief Executive Officer

ZQ|CERT#|COY|CLS|RGSTRY|ACCT#|TRANSTYPE|RUN#|TRANS#

COMMON STOCK
PAR VALUE \$0.001

COMMON STOCK



APREA THERAPEUTICS, INC.

INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE

SEE REVERSE FOR CERTAIN DEFINITIONS

CUSIP 03836J 1

Certificate Number
ZQ00000000

THIS CERTIFIES THAT

MR. SAMPLE & MRS. SAMPLE & MR. SAMPLE & MRS. SAMPLE

is the owner of

ZERO HUNDRED THOUSAND ZERO HUNDRED AND ZERO

THIS CERTIFICATE IS TRANSFERABLE IN WHOLE OR IN PART BY THE SIGNATURES DESIGNATED BY THE TRANSFER AGENT, AVAILABLE ONLINE AT www.computershare.com

FULLY-PAID AND NON-ASSESSABLE SHARES OF COMMON STOCK OF

Aprea Therapeutics, Inc. (hereinafter called the "Company"), transferable on the books of the Company in person or by duly authorized attorney, upon surrender of this Certificate properly endorsed. This Certificate and the shares represented hereby, are issued and shall be held subject to all of the provisions of the Certificate of Incorporation, as amended, and the By-Laws, as amended, of the Company (copies of which are on file with the Company and with the Transfer Agent), to all of which each holder, by acceptance hereof, assents. This Certificate is not valid unless countersigned and registered by the Transfer Agent and Registrar.

Witness the facsimile seal of the Company and the facsimile signatures of its duly authorized officers.

FACSIMILE SIGNATURE TO COME

President

FACSIMILE SIGNATURE TO COME

Secretary



DATED DD-MMM-YYYY

COUNTERSIGNED AND REGISTERED:
COMPUTERSHARE TRUST COMPANY, N.A.
TRANSFER AGENT AND REGISTRAR,

By _____ AUTHORIZED SIGNATURE

SECURITY INSTRUCTIONS ON REVERSE



PO BOX 45004, Providence, RI 02940-3004

MR. A. SAMPLE
DESIGNATION (IF ANY)

ADD 1
ADD 2
ADD 3
ADD 4



CUSIP/IDENTIFIER	Holder ID	Insurance Value	Number of Shares	DTC	Certificate Numbers	Num/No. Denom.	Total
XXXXXXXXXX	XXXXXXXXXX	1,000,000.00	123456	12345678	12345678	12345678	1
							2
							3
							4
							5
							6
							7
							Total Transaction

APREA THERAPEUTICS, INC.

THE COMPANY WILL FURNISH WITHOUT CHARGE TO EACH SHAREHOLDER WHO SO REQUESTS, A SUMMARY OF THE POWERS, DESIGNATIONS, PREFERENCES AND RELATIVE, PARTICIPATING, OPTIONAL OR OTHER SPECIAL RIGHTS OF EACH CLASS OF STOCK OF THE COMPANY AND THE QUALIFICATIONS, LIMITATIONS OR RESTRICTIONS OF SUCH PREFERENCES AND RIGHTS, AND THE VARIATIONS IN RIGHTS, PREFERENCES AND LIMITATIONS DETERMINED FOR EACH SERIES, WHICH ARE FIXED BY THE CERTIFICATE OF INCORPORATION OF THE COMPANY, AS AMENDED, AND THE RESOLUTIONS OF THE BOARD OF DIRECTORS OF THE COMPANY, AND THE AUTHORITY OF THE BOARD OF DIRECTORS TO DETERMINE VARIATIONS FOR FUTURE SERIES. SUCH REQUEST MAY BE MADE TO THE OFFICE OF THE SECRETARY OF THE COMPANY OR TO THE TRANSFER AGENT. THE BOARD OF DIRECTORS MAY REQUIRE THE OWNER OF A LOST OR DESTROYED STOCK CERTIFICATE, OR HIS LEGAL REPRESENTATIVES, TO GIVE THE COMPANY A BOND TO INDEMNIFY IT AND ITS TRANSFER AGENTS AND REGISTRARS AGAINST ANY CLAIM THAT MAY BE MADE AGAINST THEM ON ACCOUNT OF THE ALLEGED LOSS OR DESTRUCTION OF ANY SUCH CERTIFICATE.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM - as tenants in common	UNIF GIFT MIN ACT Custodian.....
		(Cust) (Minor)
TEN ENT - as tenants by the entireties		under Uniform Gifts to Minors Act.....
		(State)
JT TEN - as joint tenants with right of survivorship and not as tenants in common	UNIF TRF MIN ACT Custodian (until age.....)
		(Cust) (Minor) (State)
		under Uniform Transfers to Minors Act.....

Additional abbreviations may also be used though not in the above list.

For value received, _____ hereby sell, assign and transfer unto _____ PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING POSTAL ZIP CODE, OF ASSIGNEE)

_____ Shares
of the Common Stock represented by the within Certificate, and do hereby irrevocably constitute and appoint _____ Attorney
to transfer the said stock on the books of the within-named Company with full power of substitution in the premises.

Dated: _____ 20____
Signature: _____
Signature: _____

Signature(s) Guaranteed: Medallion Guarantee Stamp
THE SIGNATURE(S) SHOULD BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (Banks, Stockbrokers, Savings and Loan Associations and Credit Unions) WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM, PURSUANT TO S.E.C. RULE 17A-15.

Notice: The signature to this assignment must correspond with the name as written upon the face of the certificate, in every particular, without alteration or enlargement, or any change whatever.

SECURITY INSTRUCTIONS

THIS IS WATERMARKED PAPER. DO NOT ACCEPT WITHOUT NOTING WATERMARK. HOLD TO LIGHT TO VERIFY WATERMARK.



The IRS requires that the named transfer agent ("we") report the cost basis of certain shares or units acquired after January 1, 2011. If your shares or units are covered by the legislation, and you requested to sell or transfer the shares or units using a specific cost basis calculation method, then we have processed as you requested. If you did not specify a cost basis calculation method, then we have defaulted to the first in, first out (FIFO) method. Please consult your tax advisor if you need additional information about cost basis.
If you do not keep in contact with the issuer or do not have any activity in your account for the time period specified by state law, your property may become subject to state unclaimed property laws and transferred to the appropriate state.

1534201

SIDLEYSIDLEY AUSTIN LLP
787 SEVENTH AVENUE
NEW YORK, NY 10019
+1 212 839 5300
+1 212 839 5599 FAX

AMERICA · ASIA PACIFIC · EUROPE

September 27, 2019

Aprea Therapeutics, Inc.
535 Boylston Street
Boston, MA 02116Re: 5,750,000 shares of common stock, \$0.001 par value per share

Ladies and Gentlemen:

We refer to the Registration Statement on Form S-1, File No. 333-233662, filed by Aprea Therapeutics, Inc., a Delaware corporation (the "Company"), with the Securities and Exchange Commission (the "SEC") under the Securities Act of 1933, as amended (the "Securities Act"), as amended by Amendment No. 1 filed with the SEC on September 23, 2019, Amendment No. 2 filed with the SEC on September 25, 2019, and Amendment No. 3 being filed with the SEC on the date hereof (as so amended, the "Registration Statement"). The Registration Statement relates to the registration under the Securities Act of 5,750,000 shares (including an aggregate of 750,000 shares that may be sold by the Company pursuant to the exercise of the underwriters' option to purchase additional shares under the Underwriting Agreement (as defined below)) of common stock, \$0.001 par value per share (the "New Shares"), of the Company. The New Shares are to be sold by the Company pursuant to an underwriting agreement among the Company and the Underwriters named therein, the form of which has been filed as Exhibit 1.1 to the Registration Statement (the "Underwriting Agreement").

This opinion letter is being delivered in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act.

We have examined (i) the Registration Statement; (ii) the form of the Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation") of the Company to be filed with the Secretary of State of the State of Delaware prior to the closing of the sale of the New Shares contemplated by the Registration Statement, filed as Exhibit 3.5 to the Registration Statement; (iii) the form of the Amended and Restated Bylaws of the Company to be effective prior to the closing of the sale of the New Shares contemplated by the Registration Statement, filed as Exhibit 3.6 to the Registration Statement; (iv) the form of the Underwriting Agreement; and (v) the resolutions adopted by the board of directors of the Company relating to the Registration Statement and the issuance of the New Shares by the Company. We have also examined originals, or copies of originals certified to our satisfaction, of such agreements, documents, certificates and statements of the Company and other corporate documents and instruments, and have examined such questions of law, as we have considered relevant and necessary as a basis for this opinion letter. We have assumed the authenticity of all documents

Sidley Austin (NY) LLP is a Delaware limited liability partnership doing business as Sidley Austin LLP and practicing in affiliation with other Sidley Austin partnerships.

submitted to us as originals, the genuineness of all signatures, the legal capacity of all persons and the conformity with the original documents of any copies thereof submitted to us for examination. As to facts relevant to the opinions expressed herein, we have relied without independent investigation or verification upon, and assumed the accuracy and completeness of certificates, letters and oral and written statements and representations of public officials and officers and other representatives of the Company. We have also assumed that the Certificate of Incorporation will be approved by all requisite action of the stockholders of the Company and will be duly filed with the Secretary of State of the State of Delaware prior to the sale of the New Shares.

Based on the foregoing, we are of the opinion that the New Shares will be validly issued, fully paid and non-assessable when: (i) the Registration Statement, as finally amended, shall have been declared effective under the Securities Act; (ii) the Company's board of directors or a duly authorized committee thereof shall have duly adopted final resolutions setting the price of the New Shares; and (iii) certificates representing the New Shares shall have been duly executed, countersigned and registered and duly delivered to the purchasers thereof against payment of the agreed consideration therefor in an amount not less than the par value thereof or, if any New Shares are to be issued in uncertificated form, the Company's books shall reflect the issuance of such New Shares to the purchasers thereof against payment of the agreed consideration therefor in an amount not less than the par value thereof, all in accordance with the Underwriting Agreement as executed and delivered by the parties thereto.

This opinion letter is limited to the General Corporation Law of the State of Delaware. We express no opinion as to the laws, rules or regulations of any other jurisdiction, including, without limitation, the federal laws of the United States of America or any state securities or blue sky laws.

We hereby consent to the filing of this opinion letter as an Exhibit to the Registration Statement and to all references to our Firm included in or made a part of the Registration Statement. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act.

Very truly yours,

/s/ Sidley Austin LLP

APREA THERAPEUTICS, INC.

2019 EQUITY INCENTIVE PLAN

ADOPTED BY THE BOARD OF DIRECTORS: September 19, 2019

APPROVED BY THE STOCKHOLDERS: September 26, 2019

TERMINATION DATE: September 19, 2029

I. INTRODUCTION

1.1 PURPOSES. The purposes of the Aprea Therapeutics, Inc. 2019 Equity Incentive Plan (this “**Plan**”) are (i) to align the interests of the Company’s stockholders and the recipients of awards under this Plan by increasing the proprietary interest of such recipients in the Company’s growth and success, (ii) to advance the interests of the Company by attracting and retaining Non-Employee Directors, officers, other employees, consultants, independent contractors and agents and (iii) to motivate such persons to act in the long-term best interests of the Company and its stockholders.

1.2 CERTAIN DEFINITIONS.

“**Agreement**” means the written or electronic agreement evidencing an award hereunder between the Company and the recipient of such award.

“**Board**” means the Board of Directors of the Company.

“**Change in Control**” has the meaning set forth in [Section 5.3\(a\)](#).

“**Code**” means the Internal Revenue Code of 1986, as amended.

“**Committee**” means the Compensation Committee of the Board, or a subcommittee thereof, or such other committee designated by the Board, in each case, consisting of two or more members of the Board, each of whom is intended to be (i) a “Non-Employee Director” within the meaning of Rule 16b-3 under the Exchange Act and (ii) “independent” within the meaning of the rules of NASDAQ or, if the Common Stock is not listed on NASDAQ, within the meaning of the rules of the principal stock exchange on which the Common Stock is then traded.

“**Common Stock**” means the common stock, par value \$0.001 per share, of the Company, and all rights appurtenant thereto.

“**Company**” means Aprea Therapeutics, Inc., a Delaware corporation, or any successor thereto.

“**Exchange Act**” means the Securities Exchange Act of 1934, as amended.

“**Exchange Act Person**” means any natural person, entity, or “group” (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that “Exchange Act Person”

does not include: (i) the Company or any Subsidiary; (ii) any employee benefit plan of the Company or any Subsidiary or any trustee or other fiduciary holding securities under an employee benefit plan of the Company or any Subsidiary; (iii) an underwriter temporarily holding securities pursuant to an offering of such securities; (iv) an entity owned, directly or indirectly, by the stockholders of the Company in substantially the same proportions as their ownership of stock of the Company; or (v) any natural person, entity, or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act) that, as of the effective date of this Plan, is the owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities.

"Fair Market Value" means the closing transaction price of a share of Common Stock as reported on NASDAQ on the date as of which such value is being determined or, if the Common Stock is not listed on NASDAQ, the closing transaction price of a share of Common Stock on the principal national stock exchange on which the Common Stock is traded on the date as of which such value is being determined or, if there shall be no reported transactions for such date, on the next preceding date for which transactions were reported; *provided, however*, that if the Common Stock is not listed on a national stock exchange or if Fair Market Value for any date cannot be so determined, Fair Market Value shall be determined by the Committee by whatever means or method as the Committee, in the good faith exercise of its discretion, shall at such time deem appropriate and in compliance with Section 409A of the Code; *provided, further*, in the case of grants made in connection with the Initial Public Offering, Fair Market Value shall mean the price per share at which shares of Common Stock are initially offered for sale to the public by the Company's underwriters in the Initial Public Offering.

"Free-Standing SAR" means a SAR which is not granted in tandem with, or by reference to, an option, which entitles the holder thereof to receive, upon exercise, shares of Common Stock (which may be Restricted Stock) or, to the extent set forth in the applicable Agreement, cash or a combination thereof, with an aggregate value equal to the excess of the Fair Market Value of one share of Common Stock on the date of exercise over the base price of such SAR, multiplied by the number of such SARs that are exercised.

"Incentive Stock Option" means an option to purchase shares of Common Stock that meets the requirements of Section 422 of the Code, or any successor provision, which is intended by the Committee to constitute an Incentive Stock Option.

"Initial Public Offering" means an initial public offering of the Common Stock of the Company registered on Form S-1 (or any successor form under the Securities Act of 1933, as amended).

"Non-Employee Director" means any member of the Board who is not an officer or employee of the Company or any Subsidiary.

"Nonstatutory Stock Option" means an option to purchase shares of Common Stock which is not an Incentive Stock Option.

"Other Stock Award" means an award granted pursuant to Section 3.4 of the Plan.

“Performance Award” means a right to receive an amount of cash, Common Stock, or a combination of both, contingent upon the attainment of specified Performance Measures within a specified Performance Period.

“Performance Measures” means the criteria and objectives, established by the Committee, which shall be satisfied or met (i) as a condition to the grant or exercisability of all or a portion of an option or SAR or (ii) during the applicable Restriction Period or Performance Period as a condition to the vesting of the holder’s interest, in the case of a Restricted Stock Award, of the shares of Common Stock subject to such award, or, in the case of a Restricted Stock Unit Award, Other Stock Award or Performance Award, to the holder’s receipt of the shares of Common Stock subject to such award or of payment with respect to such award. Such criteria and objectives may include one or more of the following corporate-wide or subsidiary, division, operating unit, line of business, project, geographic or individual measures: the attainment by a share of Common Stock of a specified Fair Market Value for a specified period of time; increase in stockholder value; earnings per share; return on or net assets; return on equity; return on investments; return on capital or invested capital; total stockholder return; earnings or income of the Company before or after taxes and/or interest; earnings before interest, taxes, depreciation and amortization (“**EBITDA**”); EBITDA margin; operating income; revenues; operating expenses, attainment of expense levels or cost reduction goals; market share; cash flow, cash flow per share, cash flow margin or free cash flow; interest expense; economic value created; gross profit or margin; operating profit or margin; net cash provided by operations; price-to-earnings growth; and strategic business criteria, consisting of one or more objectives based on meeting specified goals relating to publication, clinical or regulatory milestones, research and development achievements, market penetration, customer acquisition, business expansion, cost targets, customer satisfaction, reductions in errors and omissions, reductions in lost business, management of employment practices and employee benefits, supervision of litigation, supervision of information technology, quality and quality audit scores, efficiency, acquisitions or divestitures, coverage decisions, licenses, collaborations, joint ventures or promotional arrangements and such other goals as the Committee may determine whether or not listed herein, or any combination of the foregoing. Each such goal may be expressed on an absolute or relative basis and may include comparisons based on current internal targets, the past performance of the Company (including the performance of one or more subsidiaries, divisions, or operating units) or the past or current performance of other companies or market indices (or a combination of such past and current performance). In addition to the ratios specifically enumerated above, performance goals may include comparisons relating to capital (including, but not limited to, the cost of capital), shareholders’ equity, shares outstanding, assets or net assets, sales, or any combination thereof. The applicable performance measures may be applied on a pre- or post-tax basis and may be adjusted to include or exclude components of any performance measure, including, without limitation, foreign exchange gains and losses, asset writedowns, acquisitions and divestitures, change in fiscal year, unbudgeted capital expenditures, special charges such as restructuring or impairment charges, debt refinancing costs, extraordinary or noncash items, unusual, infrequently occurring, nonrecurring or one-time events affecting the Company or its financial statements or changes in law or accounting principles (“**Adjustment Events**”). In the sole discretion of the Committee, the Committee may amend or adjust the Performance Measures or other terms and conditions of an outstanding award in recognition of any Adjustment Events. Performance Measures shall be subject to such other special rules and conditions as the Committee may establish at any time.

“Performance Period” means any period designated by the Committee during which (i) the Performance Measures applicable to an award shall be measured and (ii) the conditions to vesting applicable to an award shall remain in effect.

“Restricted Stock” means shares of Common Stock which are subject to a Restriction Period and which may, in addition thereto, be subject to the attainment of specified Performance Measures within a specified Performance Period.

“Restricted Stock Award” means an award of Restricted Stock under this Plan.

“Restricted Stock Unit” means a right to receive one share of Common Stock or, in lieu thereof and to the extent set forth in the applicable Agreement, the Fair Market Value of such share of Common Stock in cash, which shall be contingent upon the expiration of a specified Restriction Period and which may, in addition thereto, be contingent upon the attainment of specified Performance Measures within a specified Performance Period.

“Restricted Stock Unit Award” means an award of Restricted Stock Units under this Plan.

“Restriction Period” means any period designated by the Committee during which either (i) the Common Stock subject to a Restricted Stock Award may not be sold, transferred, assigned, pledged, hypothecated or otherwise encumbered or disposed of, except as provided in this Plan or the Agreement relating to such award, or (ii) the conditions to vesting applicable to a Restricted Stock Unit Award or Other Stock Award shall remain in effect.

“SAR” means a stock appreciation right, which may be a Free-Standing SAR or a Tandem SAR.

“Stock Award” means a Restricted Stock Award, Restricted Stock Unit Award or Other Stock Award.

“Subject Person” has the meaning set forth in [Section 5.8\(a\)\(1\)](#).

“Subsidiary” means any corporation, limited liability company, partnership, joint venture, or similar entity in which the Company owns, directly or indirectly, an equity interest possessing more than 50% of the combined voting power of the total outstanding equity interests of such entity.

“Substitute Award” means an award granted under this Plan upon the assumption of, or in substitution for, outstanding equity awards previously granted by a company or other entity in connection with a corporate transaction, including a merger, combination, consolidation, or acquisition of property or stock or upon the substitution of Nonstatutory Stock Options for options of Aprea Therapeutics AB in connection with the reorganization of Aprea Therapeutics AB; *provided, however*, that in no event shall the term “Substitute Award” be construed to refer to an award made in connection with the cancellation and repricing of an option or SAR.

“Tandem SAR” means an SAR which is granted in tandem with, or by reference to, an option (including a Nonstatutory Stock Option granted prior to the date of grant of the SAR),

which entitles the holder thereof to receive, upon exercise of such SAR and surrender for cancellation of all or a portion of such option, shares of Common Stock (which may be Restricted Stock) or, to the extent set forth in the applicable Agreement, cash or a combination thereof, with an aggregate value equal to the excess of the Fair Market Value of one share of Common Stock on the date of exercise over the base price of such SAR, multiplied by the number of shares of Common Stock subject to such option, or portion thereof, which is surrendered.

“**Tax Date**” has the meaning set forth in [Section 5.5](#).

“**Ten Percent Holder**” has the meaning set forth in [Section 2.1\(a\)](#).

1.3 ADMINISTRATION. This Plan shall be administered by the Committee. Any one or a combination of the following awards may be made under this Plan to eligible persons: (i) options to purchase shares of Common Stock in the form of Incentive Stock Options or Nonstatutory Stock Options; (ii) SARs in the form of Tandem SARs or Free-Standing SARs; (iii) Stock Awards in the form of Restricted Stock, Restricted Stock Units or Other Stock Awards; and (iv) Performance Awards. The Committee shall, subject to the terms of this Plan, select eligible persons for participation in this Plan and determine the form, amount and timing of each award to such persons and, if applicable, the number of shares of Common Stock subject to an award, the number of SARs, the number of Restricted Stock Units, the dollar value subject to a Performance Award, the purchase price or base price associated with the award, the time and conditions of exercise or settlement of the award, and all other terms and conditions of the award, including, without limitation, the form of the Agreement evidencing the award. The Committee may, in its sole discretion and for any reason at any time, take action such that (i) any or all outstanding options and SARs shall become exercisable in part or in full, (ii) all or a portion of the Restriction Period applicable to any outstanding awards shall lapse, (iii) all or a portion of the Performance Period applicable to any outstanding awards shall lapse and (iv) the Performance Measures (if any) applicable to any outstanding awards shall be deemed to be satisfied at the target, maximum or any other level. The Committee shall, subject to the terms of this Plan, interpret this Plan and the application thereof, establish rules and regulations it deems necessary or desirable for the administration of this Plan, and may impose, incidental to the grant of an award, conditions with respect to the award, such as limiting competitive employment or other activities. All such interpretations, rules, regulations and conditions shall be conclusive and binding on all parties.

The Committee may delegate some or all of its power and authority hereunder to the Board (or any members thereof) or, subject to applicable law, to a subcommittee of the Board, a member of the Board, the Chief Executive Officer or other executive officer of the Company as the Committee deems appropriate; *provided, however*, that the Committee may not delegate its power and authority to a member of the Board, the Chief Executive Officer or other executive officer of the Company with regard to the selection for participation in this Plan of an officer, director or other person subject to Section 16 of the Exchange Act or decisions concerning the timing, pricing or amount of an award to such an officer, director or other person.

No member of the Board or Committee, and neither the Chief Executive Officer nor any other executive officer to whom the Committee delegates any of its power and authority

hereunder, shall be liable for any act, omission, interpretation, construction or determination made in connection with this Plan in good faith, and the members of the Board and the Committee and the Chief Executive Officer or other executive officer shall be entitled to indemnification and reimbursement by the Company in respect of any claim, loss, damage or expense (including attorneys' fees) arising therefrom to the full extent permitted by law (except as otherwise may be provided in the Company's Certificate of Incorporation and/or Bylaws) and under any directors' and officers' liability insurance that may be in effect from time to time.

1.4 ELIGIBILITY. Participants in this Plan shall consist of such officers, other employees, Non-Employee Directors, consultants, independent contractors, agents, and persons expected to become officers, other employees, Non-Employee Directors, consultants, independent contractors and agents of the Company and its Subsidiaries as the Committee in its sole discretion may select from time to time. Participants shall also consist of persons to whom Nonstatutory Stock Options are granted in substitution for options of Aprea Therapeutics AB in connection with the reorganization of Aprea Therapeutics AB. The Committee's selection of a person to participate in this Plan at any time shall not require the Committee to select such person to participate in this Plan at any other time. Except as otherwise provided for in an Agreement, for purposes of this Plan, references to employment by the Company shall also mean employment by a Subsidiary, and references to employment shall include service as a Non-Employee Director, consultant, independent contractor or agent. The Committee shall determine, in its sole discretion, the extent to which a participant shall be considered employed during an approved leave of absence. Notwithstanding anything herein to the contrary, the aggregate value of cash compensation to be paid and the grant date fair value of equity awards that may be granted during any fiscal year of the Company to any Non-Employee Director shall not exceed \$500,000; ~~provided, however,~~ such limit shall be multiplied by 1.5 for the first fiscal year in which a Non-Employee Directors commences service on the Board.

1.5 SHARES AVAILABLE. Subject to adjustment as provided in Section 5.7 and to all other limits set forth in this Plan, 5,000,000 shares of Common Stock shall initially be available for all awards under this Plan, including in respect of Nonstatutory Stock Options issued in substitution for options of Aprea Therapeutics AB in connection with the reorganization of Aprea Therapeutics AB, but excluding future Substitute Awards. Subject to adjustment as provided in Section 5.7, no more than 5,000,000 shares of Common Stock in the aggregate may be issued under the Plan in connection with Incentive Stock Options. The number of shares of Common Stock available under the Plan shall increase annually on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2020, and continuing until (and including) the fiscal year ending December 31, 2029, with such annual increase equal to the lesser of (i) 5,000,000 shares of Common Stock, (ii) 4% of the number of shares of Common Stock issued and outstanding on December 31 of the immediately preceding calendar year, and (iii) an amount determined by the Board. The number of shares of Common Stock that remain available for future grants under this Plan shall be reduced by the sum of the aggregate number of shares of Common Stock that become subject to outstanding options, outstanding Free-Standing SARs, outstanding Stock Awards and outstanding Performance Awards denominated in shares of Common Stock.

To the extent that shares of Common Stock subject to an outstanding option, SAR, Stock Award or Performance Award granted under the Plan, other than Substitute Awards other than

the Nonstatutory Stock Options granted in substitution for options of Aprea Therapeutics AB in connection with the reorganization of Aprea Therapeutics AB, are not issued or delivered by reason of (i) the expiration, termination, cancellation or forfeiture of such award (excluding shares subject to an option cancelled upon settlement in shares of a related Tandem SAR or shares subject to a Tandem SAR cancelled upon exercise of a related option) or (ii) the settlement of such award in cash, then such shares of Common Stock shall again be available under this Plan. In addition, shares of Common Stock subject to an award under this Plan shall again be available for issuance under this Plan if such shares are (x) shares that were subject to an option or stock-settled SAR and were not issued or delivered upon the net settlement or net exercise of such option or SAR or (y) shares delivered to or withheld by the Company to pay the purchase price or the withholding taxes related to an outstanding award. Notwithstanding anything herein to the contrary, shares repurchased by the Company on the open market with the proceeds of an option exercise shall not again be available under this Plan.

The number of shares of Common Stock available for awards under this Plan shall not be reduced by (i) the number of shares of Common Stock subject to Substitute Awards or (ii) available shares under a stockholder approved plan of a company or other entity which was a party to a corporate transaction with the Company (as appropriately adjusted to reflect such corporate transaction) which become subject to awards granted under this Plan (subject to applicable stock exchange requirements).

Shares of Common Stock to be delivered under this Plan shall be made available from authorized and unissued shares of Common Stock, or authorized and issued shares of Common Stock reacquired and held as treasury shares or otherwise or a combination thereof.

II. STOCK OPTIONS AND STOCK APPRECIATION RIGHTS

2.1 STOCK OPTIONS. The Committee may, in its discretion, grant options to purchase shares of Common Stock to such eligible persons as may be selected by the Committee. Each option, or portion thereof, that is not an Incentive Stock Option, shall be a Nonstatutory Stock Option. To the extent that the aggregate Fair Market Value (determined as of the date of grant) of shares of Common Stock with respect to which options designated as Incentive Stock Options are exercisable for the first time by a holder during any calendar year (under this Plan or any other plan of the Company, or any parent or Subsidiary) exceeds the amount (currently \$100,000) established by the Code, such options shall constitute Nonstatutory Stock Options.

Options shall be subject to the following terms and conditions and shall contain such additional terms and conditions, not inconsistent with the terms of this Plan, as the Committee shall deem advisable:

(a) **Number of Shares and Purchase Price.** The number of shares of Common Stock subject to an option and the purchase price per share of Common Stock purchasable upon exercise of the option shall be determined by the Committee; *provided, however*, that the purchase price per share of Common Stock purchasable upon exercise of an option shall not be less than 100% of the Fair Market Value of a share of Common Stock on the date of grant of such option; *provided further*, that if an Incentive Stock Option shall be granted to any person who, at the time such option is granted, owns capital stock possessing more than 10% of the total

combined voting power of all classes of capital stock of the Company (or of any parent or Subsidiary) (a "**Ten Percent Holder**"), the purchase price per share of Common Stock shall not be less than the price (currently 110% of Fair Market Value) required by the Code in order to constitute an Incentive Stock Option.

Notwithstanding the foregoing, in the case of an option that is a Substitute Award, the purchase price per share of the shares subject to such option may be less than 100% of the Fair Market Value per share on the date of grant, provided, that the excess of: (a) the aggregate Fair Market Value (as of the date such Substitute Award is granted) of the shares subject to the Substitute Award, over (b) the aggregate purchase price thereof does not exceed the excess of: (x) the aggregate fair market value (as of the time immediately preceding the transaction giving rise to the Substitute Award, such fair market value to be determined by the Committee) of the shares of the predecessor company or other entity that were subject to the grant assumed or substituted for by the Company, over (y) the aggregate purchase price of such shares.

(b) **Option Period and Exercisability.** The period during which an option may be exercised shall be determined by the Committee; *provided, however*, that no option may be exercised later than ten years after its date of grant; *provided further*, that if an Incentive Stock Option shall be granted to a Ten Percent Holder, such option may not be exercised later than five years after its date of grant. The Committee may, in its discretion, establish Performance Measures which shall be satisfied or met as a condition to the grant of an option or to the exercisability of all or a portion of an option. The Committee shall determine whether an option shall become exercisable in cumulative or non-cumulative installments and in part or in full at any time. An exercisable option, or portion thereof, may be exercised only with respect to whole shares of Common Stock.

(c) **Method of Exercise.** An option may be exercised (i) by giving written notice to the Company specifying the number of whole shares of Common Stock to be purchased and accompanying such notice with payment therefor in full (or arrangement made for such payment to the Company's satisfaction) either: (A) in cash; (B) by delivery (either actual delivery or by attestation procedures established by the Company) of shares of Common Stock having a Fair Market Value, determined as of the date of exercise, equal to the aggregate purchase price payable by reason of such exercise; (C) authorizing the Company to withhold whole shares of Common Stock which would otherwise be delivered having an aggregate Fair Market Value, determined as of the date of exercise, equal to the amount necessary to satisfy such obligation; (D) in cash by a broker-dealer acceptable to the Company to whom the holder has submitted an irrevocable notice of exercise; (E) in any other form of legal consideration that may be acceptable to the Committee and specified in the Agreement; or (F) a combination of (A), (B), (C) and (E), in each case to the extent set forth in the Agreement relating to the option; (ii) if applicable, by surrendering to the Company any Tandem SARs which are cancelled by reason of the exercise of the option; and (iii) by executing such documents as the Company may reasonably request. Any fraction of a share of Common Stock which would be required to pay such purchase price shall be disregarded and the remaining amount due shall be paid in cash by the holder. No shares of Common Stock shall be issued and no certificate representing Common Stock shall be delivered until the full purchase price therefor and any withholding taxes thereon, as described in Section 5.5, have been paid (or arrangement made for such payment to the

Company's satisfaction).

2.2 STOCK APPRECIATION RIGHTS. The Committee may, in its discretion, grant SARs to such eligible persons as may be selected by the Committee. The Agreement relating to an SAR shall specify whether the SAR is a Tandem SAR or a Free-Standing SAR.

SARs shall be subject to the following terms and conditions and shall contain such additional terms and conditions, not inconsistent with the terms of this Plan, as the Committee shall deem advisable:

(a) **Number of SARs and Base Price.** The number of SARs subject to an award shall be determined by the Committee. Any Tandem SAR related to an Incentive Stock Option shall be granted at the same time that such Incentive Stock Option is granted. The base price of a Tandem SAR shall be the purchase price per share of Common Stock of the related option. The base price of a Free-Standing SAR shall be determined by the Committee; *provided, however*, that such base price shall not be less than 100% of the Fair Market Value of a share of Common Stock on the date of grant of such SAR (or, if earlier, the date of grant of the option for which the SAR is exchanged or substituted).

Notwithstanding the foregoing, in the case of an SAR that is a Substitute Award, the base price per share of the shares subject to such SAR may be less than 100% of the Fair Market Value per share on the date of grant, provided, that the excess of: (a) the aggregate Fair Market Value (as of the date such Substitute Award is granted) of the shares subject to the Substitute Award, over (b) the aggregate base price thereof does not exceed the excess of: (x) the aggregate fair market value (as of the time immediately preceding the transaction giving rise to the Substitute Award, such fair market value to be determined by the Committee) of the shares of the predecessor company or other entity that were subject to the grant assumed or substituted for by the Company, over (y) the aggregate base price of such shares.

(b) **Exercise Period and Exercisability.** The period for the exercise of an SAR shall be determined by the Committee; *provided, however*, that (i) no Tandem SAR may be exercised later than the expiration, cancellation, forfeiture or other termination of the related option and (ii) no Free-Standing SAR may be exercised later than ten years after its date of grant. The Committee may, in its discretion, establish Performance Measures which shall be satisfied or met as a condition to the grant of an SAR or to the exercisability of all or a portion of an SAR. The Committee shall determine whether an SAR may be exercised in cumulative or non-cumulative installments and in part or in full at any time. An exercisable SAR, or portion thereof, may be exercised, in the case of a Tandem SAR, only with respect to whole shares of Common Stock and, in the case of a Free-Standing SAR, only with respect to a whole number of SARs. If an SAR is exercised for shares of Restricted Stock, a certificate or certificates representing such Restricted Stock shall be issued in accordance with [Section 3.2\(c\)](#), or such shares shall be transferred to the holder in book entry form with restrictions on the shares duly noted, and the holder of such Restricted Stock shall have such rights of a stockholder of the Company as determined pursuant to [Section 3.2\(d\)](#). Prior to the exercise of a stock-settled SAR, the holder of such SAR shall have no rights as a stockholder of the Company with respect to the shares of Common Stock subject to such SAR.

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(c) **Method of Exercise.** A Tandem SAR may be exercised by (i) giving written notice to the Company specifying the number of whole SARs which are being exercised, (ii) surrendering to the Company any options which are cancelled by reason of the exercise of the Tandem SAR and (iii) executing such documents as the Company may reasonably request. A Free-Standing SAR may be exercised by (A) giving written notice to the Company specifying the whole number of SARs which are being exercised and (B) executing such documents as the Company may reasonably request. No shares of Common Stock shall be issued and no certificate representing Common Stock shall be delivered until any withholding taxes thereon, as described in [Section 5.5](#), have been paid (or arrangement made for such payment to the Company's satisfaction).

2.3 TERMINATION OF EMPLOYMENT OR SERVICE. All of the terms relating to the exercise, cancellation or other disposition of an option or SAR (i) upon a termination of employment with or service to the Company of the holder of such option or SAR, as the case may be, whether by reason of disability, retirement, death, or any other reason; or (ii) during a paid or unpaid leave of absence, shall be determined by the Committee and set forth in the applicable Agreement.

2.4 NO REPRICING. The Committee shall not, without the approval of the stockholders of the Company, (i) reduce the purchase price or base price of any previously granted option or SAR, (ii) cancel any previously granted option or SAR in exchange for another option or SAR with a lower purchase price or base price or (iii) cancel any previously granted option or SAR in exchange for cash or another award if the purchase price of such option or the base price of such SAR exceeds the Fair Market Value of a share of Common Stock on the date of such cancellation, in each case, other than in connection with a Change in Control or the adjustment provisions set forth in [Section 5.7](#).

2.5 NO DIVIDEND EQUIVALENTS. Notwithstanding anything in an Agreement to the contrary, the holder of an option or SAR shall not be entitled to receive dividend equivalents with respect to the number of shares of Common Stock subject to such option or SAR.

III. STOCK AWARDS

3.1 STOCK AWARDS. The Committee may, in its discretion, grant Stock Awards to such eligible persons as may be selected by the Committee. The Agreement relating to a Stock Award shall specify whether the Stock Award is a Restricted Stock Award, a Restricted Stock Unit Award or, in the case of an Other Stock Award, the type of award being granted.

3.2 TERMS OF RESTRICTED STOCK AWARDS. Restricted Stock Awards shall be subject to the following terms and conditions and shall contain such additional terms and conditions, not inconsistent with the terms of this Plan, as the Committee shall deem advisable.

(a) **Number of Shares and Other Terms.** The number of shares of Common Stock subject to a Restricted Stock Award and the Restriction Period, Performance Period (if any) and Performance Measures (if any) applicable to a Restricted Stock Award shall be determined by the Committee.

(b) **Vesting and Forfeiture.** The Agreement relating to a Restricted Stock Award shall provide, in the manner determined by the Committee, in its discretion, and subject to the

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provisions of this Plan, for the vesting of the shares of Common Stock subject to such award (i) if the holder of such award remains continuously in the employment of the Company during the specified Restriction Period and (ii) if specified Performance Measures (if any) are satisfied or met during a specified Performance Period, and for the forfeiture of the shares of Common Stock subject to such award (x) if the holder of such award does not remain continuously in the employment of the Company during the specified Restriction Period or (y) if specified Performance Measures (if any) are not satisfied or met during a specified Performance Period.

(c) **Stock Issuance.** During the Restriction Period, the shares of Restricted Stock shall be held by a custodian in book entry form with restrictions on such shares duly noted or, alternatively, a certificate or certificates representing a Restricted Stock Award shall be registered in the holder's name and may bear a legend, in addition to any legend which may be required pursuant to [Section 5.6](#), indicating that the ownership of the shares of Common Stock represented by such certificate is subject to the restrictions, terms and conditions of this Plan and the Agreement relating to the Restricted Stock Award. All such certificates shall be deposited with the Company, together with stock powers or other instruments of assignment (including a power of attorney), each endorsed in blank with a guarantee of signature if deemed necessary or appropriate, which would permit transfer to the Company of all or a portion of the shares of Common Stock subject to the Restricted Stock Award in the event such award is forfeited in whole or in part. Upon termination of any applicable Restriction Period (and the satisfaction or attainment of applicable Performance Measures), subject to the Company's right to require payment of any taxes in accordance with [Section 5.5](#), the restrictions shall be removed from the requisite number of any shares of Common Stock that are held in book entry form, and all certificates evidencing ownership of the requisite number of shares of Common Stock shall be delivered to the holder of such award.

(d) **Rights with Respect to Restricted Stock Awards.** Subject to the terms and conditions of a Restricted Stock Award, the holder of such award shall have all rights as a stockholder of the Company, including, but not limited to, voting rights, the right to receive dividends and the right to participate in any capital adjustment applicable to all holders of Common Stock; *provided, however*, that a distribution or dividend with respect to shares of Common Stock, including a regular cash dividend, shall be deposited with the Company and shall be subject to the same restrictions as the shares of Common Stock with respect to which such distribution was made.

3.3 TERMS OF RESTRICTED STOCK UNIT AWARDS. Restricted Stock Unit Awards shall be subject to the following terms and conditions and shall contain such additional terms and conditions, not inconsistent with the terms of this Plan, as the Committee shall deem advisable.

(a) **Number of Shares and Other Terms.** The number of shares of Common Stock subject to a Restricted Stock Unit Award, including the number of shares that are earned upon the attainment of any specified Performance Measures, and the Restriction Period, Performance Period (if any) and Performance Measures (if any) applicable to a Restricted Stock Unit Award shall be determined by the Committee.

(b) **Vesting and Forfeiture.** The Agreement relating to a Restricted Stock Unit Award shall provide, in the manner determined by the Committee, in its discretion, and subject

to the provisions of this Plan, for the vesting of such Restricted Stock Unit Award (i) if the holder of such award remains continuously in the employment of the Company during the specified Restriction Period and (ii) if specified Performance Measures (if any) are satisfied or met during a specified Performance Period, and for the forfeiture of the shares of Common Stock subject to such award (x) if the holder of such award does not remain continuously in the employment of the Company during the specified Restriction Period or (y) if specified Performance Measures (if any) are not satisfied or met during a specified Performance Period.

(c) **Settlement of Vested Restricted Stock Unit Awards.** The Agreement relating to a Restricted Stock Unit Award shall specify (i) whether such award may be settled in shares of Common Stock or cash or a combination thereof and (ii) whether the holder thereof shall be entitled to receive dividend equivalents, and, if determined by the Committee, interest on, or the deemed reinvestment of, any deferred dividend equivalents, with respect to the number of shares of Common Stock subject to such award. Any dividend equivalents with respect to Restricted Stock Units shall be subject to the same restrictions as such Restricted Stock Units. Prior to the settlement of a Restricted Stock Unit Award, the holder of such award shall have no rights as a stockholder of the Company with respect to the shares of Common Stock subject to such award.

3.4 OTHER STOCK AWARDS. Subject to the limitations set forth in the Plan, the Committee is authorized to grant other awards that may be denominated or payable in, valued in whole or in part by reference to, or otherwise based on, or related to, shares of Common Stock, including without limitation shares of Common Stock granted as a bonus and not subject to any vesting conditions, dividend equivalents, deferred stock units, stock purchase rights and shares of Common Stock issued in lieu of obligations of the Company to pay cash under any compensatory plan or arrangement, subject to such terms as shall be determined by the Committee. The Committee shall determine the terms and conditions of such awards, which may include the right to elective deferral thereof, subject to such terms and conditions as the Committee may specify in its discretion. Any dividend equivalent rights granted with respect to an award shall be subject to the same vesting conditions as the underlying award.

3.5 TERMINATION OF EMPLOYMENT OR SERVICE. All of the terms relating to the satisfaction of Performance Measures and the termination of the Restriction Period or Performance Period relating to a Stock Award, or any forfeiture and cancellation of such award (i) upon a termination of employment with or service to the Company of the holder of such award, whether by reason of disability, retirement, death, or any other reason; or (ii) during a paid or unpaid leave of absence, shall be determined by the Committee and set forth in the applicable Agreement.

IV. PERFORMANCE AWARDS

4.1 PERFORMANCE AWARDS. The Committee may, in its discretion, grant Performance Awards to such eligible persons as may be selected by the Committee.

4.2 TERMS OF PERFORMANCE AWARDS. Performance Awards shall be subject to the following terms and conditions and shall contain such additional terms and conditions, not inconsistent with the terms of this Plan, as the Committee shall deem advisable.

(a) **Value of Performance Awards and Performance Measures.** The method of determining the value of the Performance Award and the Performance Measures and Performance Period applicable to a Performance Award shall be determined by the Committee.

(b) **Vesting and Forfeiture.** The Agreement relating to a Performance Award shall provide, in the manner determined by the Committee, in its discretion, and subject to the provisions of this Plan, for the vesting of such Performance Award if the specified Performance Measures are satisfied or met during the specified Performance Period and for the forfeiture of such award if the specified Performance Measures are not satisfied or met during the specified Performance Period.

(c) **Settlement of Vested Performance Awards.** The Agreement relating to a Performance Award shall specify whether such award may be settled in shares of Common Stock (including shares of Restricted Stock) or cash or a combination thereof. If a Performance Award is settled in shares of Restricted Stock, such shares of Restricted Stock shall be issued to the holder in book entry form or a certificate or certificates representing such Restricted Stock shall be issued in accordance with [Section 3.2\(c\)](#) and the holder of such Restricted Stock shall have such rights as a stockholder of the Company as determined pursuant to [Section 3.2\(d\)](#). Any dividends or dividend equivalents with respect to a Performance Award shall be subject to the same restrictions as such Performance Award. Prior to the settlement of a Performance Award in shares of Common Stock, including Restricted Stock, the holder of such award shall have no rights as a stockholder of the Company.

4.3 TERMINATION OF EMPLOYMENT OR SERVICE. All of the terms relating to the satisfaction of Performance Measures and the termination of the Performance Period relating to a Performance Award, or any forfeiture and cancellation of such award (i) upon a termination of employment with or service to the Company of the holder of such award, whether by reason of disability, retirement, death, or any other reason; or (ii) during a paid or unpaid leave of absence, shall be determined by the Committee and set forth in the applicable Agreement.

V. GENERAL

5.1 EFFECTIVE DATE AND TERM OF PLAN. This Plan shall be submitted to the stockholders of the Company for approval within 12 months of Board approval and, if approved, shall be effective as of the date of such Board approval. This Plan shall terminate on the tenth anniversary of Board approval of the Plan, unless terminated earlier by the Board. Termination of this Plan shall not affect the terms or conditions of any award granted prior to termination. Awards hereunder may be made at any time prior to the termination of this Plan, provided that no Incentive Stock Option may be granted later than ten years after the date on which the Plan was approved by the Board.

5.2 AMENDMENTS. The Board may amend this Plan as it shall deem advisable; *provided, however*, that no amendment to the Plan shall be effective without the approval of the Company's stockholders if (i) stockholder approval is required by applicable law, rule or regulation, including any rule of NASDAQ or any other stock exchange on which the Common Stock is then traded, or (ii) such amendment seeks to modify the Non-Employee Director compensation limit set forth in [Section 1.4](#) or the terms of [Section 2.4](#) hereof; *provided further*,

that no amendment may materially impair the rights of a holder of an outstanding award without the consent of such holder.

5.3 AGREEMENT. Each award under this Plan shall be evidenced by an Agreement setting forth the terms and conditions applicable to such award. No award shall be valid until an Agreement is executed by the Company and, to the extent required by the Company, executed or electronically accepted by the recipient of such award. Upon such execution or acceptance and delivery of the Agreement to the Company within the time period specified by the Company, such award shall be effective as of the effective date set forth in the Agreement.

5.4 NON-TRANSFERABILITY. No award shall be transferable other than by will, the laws of descent and distribution or pursuant to beneficiary designation procedures approved by the Company or, to the extent expressly permitted in the Agreement relating to such award, to the holder's family members, a trust or entity established by the holder for estate planning purposes, a charitable organization designated by the holder or pursuant to a domestic relations order, in each case, without consideration. Except to the extent permitted by the foregoing sentence or the Agreement relating to an award, each award may be exercised or settled during the holder's lifetime only by the holder or the holder's legal representative or similar person. Except as permitted by the second preceding sentence, no award may be sold, transferred, assigned, pledged, hypothecated, encumbered or otherwise disposed of (whether by operation of law or otherwise) or be subject to execution, attachment or similar process. Upon any attempt to so sell, transfer, assign, pledge, hypothecate, encumber or otherwise dispose of any award, such award and all rights thereunder shall immediately become null and void.

5.5 TAX WITHHOLDING. The Company shall have the right to require, prior to the issuance or delivery of any shares of Common Stock or the payment of any cash pursuant to an award made hereunder, payment by the holder of such award of any federal, state, local or other taxes which may be required to be withheld or paid in connection with such award. An Agreement may provide that (i) the Company shall withhold whole shares of Common Stock which would otherwise be delivered to a holder, having an aggregate Fair Market Value determined as of the date the obligation to withhold or pay taxes arises in connection with an award (the "**Tax Date**"), or withhold an amount of cash which would otherwise be payable to a holder, in the amount necessary to satisfy any such obligation or (ii) the holder may satisfy any such obligation by any of the following means: (A) a cash payment to the Company; (B) delivery (either actual delivery or by attestation procedures established by the Company) to the Company of previously owned whole shares of Common Stock having an aggregate Fair Market Value, determined as of the Tax Date, equal to the amount necessary to satisfy any such obligation; (C) authorizing the Company to withhold whole shares of Common Stock which would otherwise be delivered having an aggregate Fair Market Value, determined as of the Tax Date, or withhold an amount of cash which would otherwise be payable to a holder, in either case equal to the amount necessary to satisfy any such obligation; (D) in the case of the exercise of an option, a cash payment by a broker-dealer acceptable to the Company to whom the holder has submitted an irrevocable notice of exercise; (E) any other form of payment that may be acceptable to the Committee and specified in the Agreement or (F) any combination of (A), (B), (C) and (E), in each case to the extent set forth in the Agreement relating to the award. Shares of Common Stock to be delivered or withheld may not have an aggregate Fair Market Value in excess of the amount determined by applying the minimum statutory withholding rate (or, if permitted by the Company, such other

rate as shall not cause adverse accounting consequences under the accounting rules then in effect, and is permitted under applicable IRS withholding rules). Any fraction of a share of Common Stock which would be required to satisfy such an obligation shall be disregarded and the remaining amount due shall be paid in cash by the holder.

5.6 RESTRICTIONS ON SHARES. Each award made hereunder shall be subject to the requirement that if at any time the Company determines that the listing, registration or qualification of the shares of Common Stock subject to such award upon any securities exchange or under any law, or the consent or approval of any governmental body, or the taking of any other action is necessary or desirable as a condition of, or in connection with, the delivery of shares thereunder, such shares shall not be delivered unless such listing, registration, qualification, consent, approval or other action shall have been effected or obtained, free of any conditions not acceptable to the Company. The Company may require that certificates evidencing shares of Common Stock delivered pursuant to any award made hereunder bear a legend indicating that the sale, transfer or other disposition thereof by the holder is prohibited except in compliance with the Securities Act of 1933, as amended, and the rules and regulations thereunder.

5.7 ADJUSTMENT. In the event of any equity restructuring (within the meaning of Financial Accounting Standards Board Accounting Standards Codification Topic 718, Compensation—Stock Compensation or any successor or replacement accounting standard) that causes the per share value of shares of Common Stock to change, such as a stock dividend, stock split, spinoff, rights offering, or recapitalization through an extraordinary cash dividend, the number and class of securities available under this Plan, the terms of each outstanding option and SAR (including the number and class of securities subject to each outstanding option or SAR and the purchase price or base price per share), the terms of each outstanding Stock Award (including the number and class of securities subject thereto), and the terms of each outstanding Performance Award (including the number and class of securities subject thereto, if applicable) shall be appropriately adjusted by the Committee, such adjustments to be made in the case of outstanding options and SARs in accordance with Section 409A of the Code. In the event of any other change in corporate capitalization, including a merger, consolidation, reorganization, or partial or complete liquidation of the Company, such equitable adjustments described in the foregoing sentence may be made as determined to be appropriate and equitable by the Committee to prevent dilution or enlargement of rights of participants. In either case, the decision of the Committee regarding any such adjustment shall be final, binding and conclusive.

5.8 CHANGE IN CONTROL.

(a) For purposes of this Plan, "**Change in Control**" means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(1) any Exchange Act Person becomes the owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities other than by virtue of a merger, consolidation or similar transaction. Notwithstanding the foregoing, a Change in Control shall not be deemed to occur (A) on account of the acquisition of securities by the Company or any Subsidiary, (B) on

account of the acquisition by any employee benefit plan (or related trust) sponsored or maintained by the Company or any Subsidiary, (C) on account of the acquisition of securities of the Company by an investor, any affiliate thereof or any other Exchange Act Person that acquires the Company's securities in a transaction or series of related transactions the primary purpose of which is to obtain financing for the Company through the issuance of equity securities or (D) solely because the level of ownership held by any Exchange Act Person (the "**Subject Person**") exceeds the designated percentage threshold of the outstanding voting securities as a result of a repurchase or other acquisition of voting securities by the Company reducing the number of shares outstanding, provided that if a Change in Control would occur (but for the operation of this sentence) as a result of the acquisition of voting securities by the Company or any Subsidiary, and after such share acquisition, the Subject Person becomes the owner of any additional voting securities that, assuming the repurchase or other acquisition had not occurred, increases the percentage of the then outstanding voting securities owned by the Subject Person over the designated percentage threshold, then a Change in Control shall be deemed to occur;

- (2) there is consummated a merger, consolidation, or similar transaction involving (directly or indirectly) the Company and, immediately after the consummation of such merger, consolidation, or similar transaction, the stockholders of the Company immediately prior thereto do not own, directly or indirectly, either (A) outstanding voting securities representing more than 50% of the combined outstanding voting power of the surviving entity in such merger, consolidation or similar transaction or (B) more than 50% of the combined outstanding voting power of the parent of the surviving entity in such merger, consolidation, or similar transaction, in each case in substantially the same proportions as their ownership of the outstanding voting securities of the Company immediately prior to such transaction;
- (3) the stockholders of the Company approve or the Board approves a plan of complete dissolution or liquidation of the Company, or a complete dissolution or liquidation of the Company shall otherwise occur, except for a liquidation into a parent corporation; or
- (4) there is consummated a sale, lease, exclusive license, or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries, other than a sale, lease, license, or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries to an entity, more than 50% of the combined voting power of the voting securities of which are owned by stockholders of the Company in substantially the same proportions as their ownership of the outstanding voting securities of the Company immediately prior to such sale, lease, license, or other disposition.

Notwithstanding the foregoing definition or any other provision of this Plan, (A) the term Change in Control shall not include a sale of assets, merger, or other transaction effected exclusively for the purpose of changing the domicile of the Company and (B) with respect to any nonqualified deferred compensation that becomes payable on account of the Change in Control, the transaction or event described in clause (1), (2), (3) or (4) shall also constitute a "change in control event," as defined in Treasury Regulation § 1.409A-3(i)(5) if required in order for the payment not to violate Section 409A of the Code.

- (b) Subject to the terms of the applicable Agreements, in the event of a Change in Control, the Board, as constituted prior to the Change in Control, may, in its discretion:
- (1) require that (i) some or all outstanding options and SARs shall become exercisable in full or in part, either immediately or upon a subsequent termination of employment, (ii) the Restriction Period applicable to some or all outstanding Stock Awards shall lapse in full or in part, either immediately or upon a subsequent termination of employment, (iii) the Performance Period applicable to some or all outstanding awards shall lapse in full or in part, and (iv) the Performance Measures applicable to some or all outstanding awards shall be deemed to be satisfied at the target, maximum or any other level;
 - (2) require that shares of capital stock of the corporation resulting from or succeeding to the business of the Company pursuant to such Change in Control, or a parent corporation thereof, or other property be substituted for some or all of the shares of Common Stock subject to an outstanding award, with an appropriate and equitable adjustment to such award as determined by the Board in accordance with Section 5.7; and/or
 - (3) require outstanding awards, in whole or in part, to be surrendered to the Company by the holder, and to be immediately cancelled by the Company, and to provide for the holder to receive (i) a cash payment in an amount equal to (A) in the case of an option or an SAR, the aggregate number of shares of Common Stock then subject to the portion of such option or SAR surrendered, whether or not vested or exercisable, multiplied by the excess, if any, of the Fair Market Value of a share of Common Stock as of the date of the Change in Control, over the purchase price or base price per share of Common Stock subject to such option or SAR, (B) in the case of a Stock Award or a Performance Award denominated in shares of Common Stock, the number of shares of Common Stock then subject to the portion of such award surrendered to the extent the Performance Measures applicable to such award have been satisfied or are deemed satisfied pursuant to Section 5.8(b)(1), whether or not vested, multiplied by the Fair Market Value of a share of Common Stock as of the date of the Change in Control, and (C) in the case of a Performance Award denominated in cash, the value of the Performance Award then subject to the portion of such award surrendered to the extent the Performance Measures applicable to such award have been satisfied or are deemed satisfied pursuant to Section 5.8(b)(1); (ii) shares of capital stock of the corporation resulting from or succeeding to the business of the Company

pursuant to such Change in Control, or a parent corporation thereof, having a fair market value not less than the amount determined under clause (i) above; or (iii) a combination of the payment of cash pursuant to clause (i) above and the issuance of shares pursuant to clause (ii) above.

5.9 DEFERRALS. The Committee may determine that the delivery of shares of Common Stock or the payment of cash, or a combination thereof, upon the settlement of all or a portion of any award made hereunder shall be deferred, or the Committee may, in its sole discretion, approve deferral elections made by holders of awards. Deferrals shall be for such periods and upon such terms as the Committee may determine in its sole discretion, subject to the requirements of Section 409A of the Code.

5.10 NO RIGHT OF PARTICIPATION, EMPLOYMENT OR SERVICE. Unless otherwise set forth in an employment agreement, no person shall have any right to participate in this Plan. Neither this Plan nor any award made hereunder shall confer upon any person any right to continued employment by or service with the Company, any Subsidiary or any affiliate of the Company or affect in any manner the right of the Company, any Subsidiary or any affiliate of the Company to terminate the employment or service of any person at any time without liability hereunder.

5.11 RIGHTS AS STOCKHOLDER. No person shall have any right as a stockholder of the Company with respect to any shares of Common Stock or other equity security of the Company which is subject to an award hereunder unless and until such person becomes a stockholder of record with respect to such shares of Common Stock or equity security.

5.12 DESIGNATION OF BENEFICIARY. To the extent permitted by the Company, a holder of an award may file with the Company a written designation of one or more persons as such holder's beneficiary or beneficiaries (both primary and contingent) in the event of the holder's death or incapacity. To the extent an outstanding option or SAR granted hereunder is exercisable, such beneficiary or beneficiaries shall be entitled to exercise such option or SAR pursuant to procedures prescribed by the Company. Each beneficiary designation shall become effective only when filed in writing with the Company during the holder's lifetime on a form prescribed by the Company. The spouse of a married holder domiciled in a community property jurisdiction shall join in any designation of a beneficiary other than such spouse. The filing with the Company of a new beneficiary designation shall cancel all previously filed beneficiary designations. If a holder fails to designate a beneficiary, or if all designated beneficiaries of a holder predecease the holder, then each outstanding award held by such holder, to the extent vested or exercisable, shall be payable to or may be exercised by such holder's executor, administrator, legal representative or similar person.

5.13 AWARDS SUBJECT TO CLAWBACK. The awards granted under this Plan and any cash payment or shares of Common Stock delivered pursuant to such an award are subject to forfeiture, recovery by the Company or other action pursuant to the applicable Agreement or any clawback or recoupment policy which the Company may adopt from time to time, including without limitation any such policy which the Company may be required to adopt under the Dodd-Frank Wall Street Reform and Consumer Protection Act and implementing rules and regulations thereunder, or as otherwise required by law.

5.14 **GOVERNING LAW.** This Plan, each award hereunder and the related Agreement, and all determinations made and actions taken pursuant thereto, to the extent not otherwise governed by the Code or the laws of the United States, shall be governed by the laws of the State of Delaware and construed in accordance therewith without giving effect to principles of conflicts of laws.

5.15 **FOREIGN EMPLOYEES.** Without amending this Plan, the Committee may grant awards to eligible persons who are foreign nationals and/or reside outside of the United States on such terms and conditions different from those specified in this Plan as may in the judgment of the Committee be necessary or desirable to foster and promote achievement of the purposes of this Plan and, in furtherance of such purposes the Committee may make such modifications, amendments, procedures, subplans and the like as may be necessary or advisable to comply with provisions of laws in other countries or jurisdictions in which the Company or its Subsidiaries operates or has employees.

APREA THERAPEUTICS, INC.
2019 STOCK INCENTIVE PLAN
STOCK OPTION AWARD NOTICE

[Name]

September 20, 2019

In substitution of your options with respect Aprea Therapeutics AB in connection with the corporate reorganization of Aprea Therapeutics AB, you have been awarded an option to purchase shares of Common Stock of Aprea Therapeutics, Inc., a Delaware corporation (the "Company"), The option is granted pursuant to the terms and conditions of the Aprea Therapeutics, Inc. 2019 Stock Incentive Plan (the "Plan") and the Stock Option Agreement (together with this Award Notice, the "Agreement"). Copies of the Plan and the Stock Option Agreement are attached hereto. Capitalized terms not defined herein shall have the meanings specified in the Plan or the Agreement.

Option: You have been awarded a Nonstatutory Stock Option to purchase from the Company [] shares of its Common Stock, par value \$0.001 per share (the "Common Stock"), subject to adjustment as provided in Section 4.2 of the Agreement.

Original Option Date: []

Exercise Price: \$[] per share, subject to adjustment as provided in Section 4.2 of the Agreement.

Vesting Schedule: Except as otherwise provided in the Plan, the Agreement or any other agreement between the Company or any of its Subsidiaries and Holder, (i) one quarter of the shares subject to the Option on the Original Option Date vested on the first day of the first calendar quarter beginning at least twelve (12) months after the Original Option Date and (ii) 1/36th of the shares subject to the Option on the Original Option Date vested or shall vest thereafter on a monthly basis on each monthly anniversary of the Original Option Date, if, and only if, you are, and have been, continuously (except for any absence for vacation, leave, etc. in accordance with the Company's or its Subsidiaries' policies): (a) employed by the Company or any of its Subsidiaries; (b) serving as a Non-Employee Director or (c) providing services to the Company or any of its Subsidiaries as an advisor or consultant, in each case, from the date of this Agreement through and including such date.

Exercise Limitations: Except as otherwise provided in the Plan, the Agreement or any other agreement between the Company or any of its Subsidiaries and Holder, you shall be entitled to exercise the Option, to the extent vested, from and after the earlier to occur of an Initial Public Offering, Acquisition or Asset Transfer (each as defined in the Company's Amended and Restated Certificate of Incorporation).

Expiration Date:

Except to the extent earlier terminated pursuant to Section 2.2 of the Agreement or earlier exercised pursuant to Section 2.3 of the Agreement, the Option shall terminate at 5:00 p.m., U.S. Eastern time, on September 30, 2026.

APREA THERAPEUTICS, INC.

By: _____
Name: Christian S. Schade
Title: President and Chief Executive Officer

Acknowledgment, Acceptance and Agreement:

By signing below and returning this Award Notice to Aprea Therapeutics, Inc., I hereby acknowledge receipt of the Agreement and the Plan, accept the Option granted to me and agree to be bound by the terms and conditions of this Award Notice, the Agreement and the Plan.

Holder

Date

**APREA THERAPEUTICS, INC.
2019 STOCK INCENTIVE PLAN**

Stock Option Agreement

In substitution of options with respect to Aprea Therapeutics AB in connection with the corporate reorganization of Aprea Therapeutics AB, Aprea Therapeutics, Inc., a Delaware corporation (the "Company"), hereby grants to the individual ("Holder") named in the award notice attached hereto (the "Award Notice") as of September 20, 2019, pursuant to the provisions of the Aprea Therapeutics, Inc. 2019 Stock Incentive Plan (the "Plan"), an option to purchase from the Company the number of shares of the Company's Common Stock, par value \$0.001 per share ("Common Stock"), set forth in the Award Notice at the price per share set forth in the Award Notice (the "Exercise Price"). (the "Option"), upon and subject to the terms and conditions set forth below, in the Award Notice and in the Plan. Capitalized terms not defined herein shall have the meanings specified in the Plan.

1. Option Subject to Acceptance of Agreement. The Option shall be null and void unless Holder shall accept this Agreement by executing the Award Notice in the space provided therefor and returning an original execution copy of the Award Notice to the Company (or electronically accepting this Agreement within the Holder's stock plan account with the Company's stock plan administrator according to the procedures then in effect).

2. Time and Manner of Exercise of Option.

2.1. Maximum Term of Option. In no event may the Option be exercised, in whole or in part, after the expiration date set forth in the Award Notice (the "Expiration Date").

2.2. Vesting and Exercise of Option. The Option shall become vested and exercisable in accordance with the vesting schedule set forth in the Award Notice (the "Vesting Schedule") if, and only if, Holder is, and has been, continuously (except for any absence for vacation, leave, etc. in accordance with the Company's or its Subsidiaries' policies): (i) employed by the Company or any of its Subsidiaries; (ii) serving as a Non-Employee Director or (iii) providing services to the Company or any of its Subsidiaries as an advisor or consultant, in each case, from the Original Option Date through and including the applicable vesting date. The Option shall also be subject to the following terms and conditions:

(a) Voluntary Resignation by Holder, Termination by Company Other Than for Cause or Termination Due to Retirement, Death or Disability. If Holder's employment with the Company terminates due to

(i) Holder's voluntary resignation, (ii) termination by the Company other than for Cause, (iii) Holder's retirement pursuant to the terms of Holder's employment agreement with the Company or applicable regulatory requirements, (iv) death or (v) termination by the Company due to physical disability, the Option, to the extent vested on the effective date of such termination of employment, may thereafter be exercised by Holder (or, in the event of Holder's death, Holder's estate) until and including the earlier to occur of (i) the date which is six (6) months after the date of such termination of employment and (ii) the Expiration Date. Except to the extent the Option is vested and exercisable as of Holder's termination of

employment under this Section 2.2(a), the unvested portion of the Option shall terminate immediately upon such termination of employment.

(b) Termination by Company for Cause. If Holder's employment with the Company is terminated by the Company for Cause, then the Option, whether or not vested, shall terminate immediately upon such termination of employment.

(c) Change in Control. In the event Holder's employment is terminated by the Company without Cause or by Holder due to Good Reason, in each case, within one-year following a Change in Control, the Option, to the extent it is then outstanding, shall become fully vested and may thereafter be exercised by Holder until and including the earlier to occur of (i) the date which is one-year after the date of such termination of employment and (ii) the Expiration Date.

(d) Definitions.

(i) Cause. For purposes of this Agreement, "Cause" shall mean, in the sole discretion of the Board: (1) conduct by Holder in connection with Holder's service to the Company or any affiliate that is fraudulent, unlawful or grossly negligent; (2) Holder's material breach of Holder's material responsibilities to the Company or any affiliate or Holder's willful failure to comply with reasonable and lawful directives of the Board; (3) Holder's material breach of Holder's material representations, warranties, covenants and/or obligations under Holder's employment agreement; (4) material misconduct by Holder that seriously discredits or damages the Company or any affiliate; or (5) nonperformance or unsatisfactory performance of Holder's material duties or responsibilities to the Company or any affiliate. In the case of each of (2), (3), (4) and (5) as determined in good faith by the Board after written notice to Holder providing reasonable details of the alleged breach and not less than a 30 day period to cure the alleged breach.

(ii) Good Reason. For purposes of this Agreement, "Good Reason" shall mean that Holder has complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following actions undertaken by the Company without Holder's express prior written consent: (1) a material diminution in Holder's position, responsibilities, authority or function; (2) a material reduction in Holder's base salary and/or annual target bonus opportunity; provided, however, that Good Reason shall not be deemed to have occurred in the event of a reduction in Holder's base salary and/or annual target bonus opportunity that is pursuant to a reduction program affecting substantially all of the senior level employees of the Company and that does not adversely affect Holder to a greater extent than other similarly situated senior level employees; or (3) a change of more than 50 miles in the geographic location at which Holder must regularly report to work and perform services, except for required travel on business of the Company; provided, however, that "Good Reason" shall not include, following a Change of Control, a reduction in title, position, responsibilities or duties solely by virtue of the Company being acquired and made part of, or operating as a subsidiary or division of a larger company or organization, as long as Holder's new duties and responsibilities are reasonably commensurate with Holder's experience. For purposes of the "Good Reason" definition, "Good Reason Process" shall mean that: (v) Holder has reasonably determined in good faith that a "Good Reason" has occurred; (w) Holder has notified the Board in writing of the first occurrence

of the Good Reason condition within 60 days of the first occurrence of such condition; (x) Holder has cooperated in good faith with the efforts of the Company, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the condition; (y) notwithstanding such efforts, the Good Reason condition continues to exist; and (z) Holder terminates employment within 60 days after the end of the Cure Period. If the Good Reason condition is cured by the Company during the Cure Period, Good Reason shall be deemed not to have occurred.

2.3. Method of Exercise. Subject to the limitations set forth in this Agreement, the Option, to the extent vested, may be exercised by Holder (a) by delivering to the Company an exercise notice in the form prescribed by the Company specifying the number of whole shares of Common Stock to be purchased and by accompanying such notice with payment therefor in full (or by arranging for such payment to the Company's satisfaction) either (i) in cash, (ii) by delivery to the Company (either actual delivery or by attestation procedures established by the Company) of shares of Common Stock having an aggregate Fair Market Value, determined as of the date of exercise, equal to the aggregate purchase price payable pursuant to the Option by reason of such exercise, (iii) by authorizing the Company to withhold whole shares of Common Stock which would otherwise be delivered having an aggregate Fair Market Value, determined as of the date of exercise, equal to the amount necessary to satisfy such obligation, (iv) except as may be prohibited by applicable law, in cash by a broker-dealer acceptable to the Company to whom Holder has submitted an irrevocable notice of exercise or (v) by a combination of (i), (ii) and (iii), and (b) by executing such documents as the Company may reasonably request. Any fraction of a share of Common Stock which would be required to pay such purchase price shall be disregarded and the remaining amount due shall be paid in cash by Holder. No share of Common Stock or certificate representing a share of Common Stock shall be issued or delivered until the full purchase price therefor and any withholding taxes thereon, as described in Section 4.1, have been paid.

2.4. Termination of Option. In no event may the Option be exercised after it terminates as set forth in this Section 2.4. The Option shall terminate, to the extent not earlier terminated pursuant to Section 2.2 or exercised pursuant to Section 2.3, on the Expiration Date. Upon the termination of the Option, the Option and all rights hereunder shall immediately become null and void.

3. Transfer Restrictions and Investment Representations.

3.1. Nontransferability of Option. The Option may not be transferred by Holder other than by will or the laws of descent and distribution or pursuant to the designation of one or more beneficiaries on the form prescribed by the Company. Except to the extent permitted by the foregoing sentence, (i) during Holder's lifetime the Option is exercisable only by Holder or Holder's legal representative, guardian or similar person and (ii) the Option may not be sold, transferred, assigned, pledged, hypothecated, encumbered or otherwise disposed of (whether by operation of law or otherwise) or be subject to execution, attachment or similar process. Upon any attempt to so sell, transfer, assign, pledge, hypothecate, encumber or otherwise dispose of the Option, the Option and all rights hereunder shall immediately become null and void.

3.2. Investment Representation. Holder hereby represents and covenants that (a) any shares of Common Stock purchased upon exercise of the Option will be purchased for investment and not with a view to the distribution thereof within the meaning of the Securities Act of 1933, as amended (the "Securities Act"), unless such purchase has been registered under the Securities Act and any applicable state securities laws; (b) any subsequent sale of any such shares shall be made either pursuant to an effective registration statement under the Securities Act and any applicable state securities laws, or pursuant to an exemption from registration under the Securities Act and such state securities laws; and (c) if requested by the Company, Holder shall submit a written statement, in a form satisfactory to the Company, to the effect that such representation (x) is true and correct as of the date of any purchase of any shares hereunder or (y) is true and correct as of the date of any sale of any such shares, as applicable. As a further condition precedent to any exercise of the Option, Holder shall comply with all regulations and requirements of any regulatory authority having control of or supervision over the issuance or delivery of the shares and, in connection therewith, shall execute any documents which the Board or the Committee shall in its sole discretion deem necessary or advisable.

4. Additional Terms and Conditions.

4.1. Withholding Taxes. (a) As a condition precedent to the issuance of Common Stock following the exercise of the Option, Holder shall, upon request by the Company, pay to the Company in addition to the purchase price of the shares, such amount as the Company may be required, under all applicable federal, state, local or other laws or regulations, to withhold and pay over as income or other withholding taxes (the "Required Tax Payments") with respect to such exercise of the Option. If Holder shall fail to advance the Required Tax Payments after request by the Company, the Company may, in its discretion, deduct any Required Tax Payments from any amount then or thereafter payable by the Company to Holder.

(b) Holder may elect to satisfy his or her obligation to advance the Required Tax Payments by any of the following means: (i) a cash payment to the Company; (ii) delivery to the Company (either actual delivery or by attestation procedures established by the Company) of previously owned whole shares of Common Stock having an aggregate Fair Market Value, determined as of the date on which such withholding obligation arises (the "Tax Date"), equal to the Required Tax Payments; (iii) authorizing the Company to withhold whole shares of Common Stock which would otherwise be delivered to Holder upon exercise of the Option having an aggregate Fair Market Value, determined as of the Tax Date, equal to the Required Tax Payments; (iv) except as may be prohibited by applicable law, a cash payment by a broker-dealer acceptable to the Company to whom Holder has submitted an irrevocable notice of exercise or (v) any combination of (i), (ii) and (iii). Shares of Common Stock to be delivered or withheld may not have a Fair Market Value in excess of the minimum amount of the Required Tax Payments (or such higher withholding rate as permitted by the Committee and which does not result in adverse accounting consequences for the Company). Any fraction of a share of Common Stock which would be required to satisfy any such obligation shall be disregarded and the remaining amount due shall be paid in cash by Holder. No share of Common Stock or certificate representing a share of Common Stock shall be issued or delivered until the Required Tax Payments have been satisfied in full.

4.2. Adjustment. In the event of any equity restructuring (within the meaning of Financial Accounting Standards Board Accounting Standards Codification Topic 718, Compensation—Stock Compensation) that causes the per share value of shares of Common Stock to change, such as a stock dividend, stock split, spinoff, rights offering or recapitalization through an extraordinary dividend, the number and class of securities subject to the Option and the Exercise Price shall be equitably adjusted by the Committee, such adjustment to be made in accordance with Section 409A of the Code. In the event of any other change in corporate capitalization, including a merger, consolidation, reorganization, or partial or complete liquidation of the Company, such equitable adjustments described in the foregoing sentence may be made as determined to be appropriate and equitable by the Committee (or, if the Company is not the surviving corporation in any such transaction, the board of directors of the surviving corporation) to prevent dilution or enlargement of rights of participants. The decision of the Committee regarding any such adjustment shall be final, binding and conclusive.

4.3. Compliance with Applicable Law. The Option is subject to the condition that if the listing, registration or qualification of the shares subject to the Option upon any securities exchange or under any law, or the consent or approval of any governmental body, or the taking of any other action is necessary or desirable as a condition of, or in connection with, the purchase or issuance of shares hereunder, the Option may not be exercised, in whole or in part, and such shares may not be issued, unless such listing, registration, qualification, consent, approval or other action shall have been effected or obtained, free of any conditions not acceptable to the Company. The Company agrees to use reasonable efforts to effect or obtain any such listing, registration, qualification, consent, approval or other action.

4.4. Issuance or Delivery of Shares. Upon the exercise of the Option, in whole or in part, the Company shall issue or deliver, subject to the conditions of this Agreement, the number of shares of Common Stock purchased against full payment therefor. Such issuance shall be evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company. The Company shall pay all original issue or transfer taxes and all fees and expenses incident to such issuance, except as otherwise provided in Section 4.1.

4.5. Option Confers No Rights as Stockholder. Holder shall not be entitled to any privileges of ownership with respect to shares of Common Stock subject to the Option unless and until such shares are purchased and issued upon the exercise of the Option, in whole or in part, and Holder becomes a stockholder of record with respect to such issued shares. Holder shall not be considered a stockholder of the Company with respect to any such shares not so purchased and issued.

4.6. Option Confers No Rights to Continued Employment. In no event shall the granting of the Option or its acceptance by Holder, or any provision of this Agreement or the Plan, give or be deemed to give Holder any right to continued employment by the Company, any Subsidiary or any affiliate of the Company or affect in any manner the right of the Company, any Subsidiary or any affiliate of the Company to terminate the employment of any person at any time.

4.7. Decisions of Board or Committee. The Board or the Committee shall have the right to resolve all questions which may arise in connection with the Option or its

exercise. Any interpretation, determination or other action made or taken by the Board or the Committee regarding the Plan or this Agreement shall be final, binding and conclusive.

4.8. Successors. This Agreement shall be binding upon and inure to the benefit of any successor or successors of the Company and any person or persons who shall, upon the death of Holder, acquire any rights hereunder in accordance with this Agreement or the Plan.

4.9. Notices. All notices, requests or other communications provided for in this Agreement shall be made, if to the Company, to Aprea Therapeutics, Inc., Attn: Treasury Department, 535 Boylston Street, Boston MA 02116, and if to Holder, to the last known mailing address of Holder contained in the records of the Company. All notices, requests or other communications provided for in this Agreement shall be made in writing either (a) by personal delivery, (b) by facsimile or electronic mail with confirmation of receipt, (c) by mailing in the United States mails or (d) by express courier service. The notice, request or other communication shall be deemed to be received upon personal delivery, upon confirmation of receipt of facsimile or electronic mail transmission or upon receipt by the party entitled thereto if by United States mail or express courier service; provided, however, that if a notice, request or other communication sent to the Company is not received during regular business hours, it shall be deemed to be received on the next succeeding business day of the Company.

4.10. Governing Law. This Agreement, the Option and all determinations made and actions taken pursuant hereto and thereto, to the extent not governed by the Code or the laws of the United States, shall be governed by the laws of the State of Delaware and construed in accordance therewith without giving effect to principles of conflicts of laws.

4.11. Agreement Subject to the Plan. This Agreement is subject to the provisions of the Plan and shall be interpreted in accordance therewith. In the event that the provisions of this Agreement and the Plan conflict, the Plan shall control. The Holder hereby acknowledges receipt of a copy of the Plan.

4.12. Entire Agreement. This Agreement and the Plan constitute the entire agreement of the parties with respect to the subject matter hereof and supersede in their entirety all prior undertakings and agreements of the Company and the Holder with respect to the subject matter hereof and may not be modified adversely to the Holder's interest except by means of a writing signed by the Company and the Holder.

4.13. Partial Invalidation. The invalidity or unenforceability of any particular provision of this Agreement shall not affect the other provisions hereof and this Agreement shall be construed in all respects as if such invalid or unenforceable provisions were omitted.

4.14. Amendment and Waiver. The provisions of this Agreement may be amended or waived only by the written agreement of the Company and the Holder, and no course of conduct or failure or delay in enforcing the provisions of this Agreement shall affect the validity, binding effect or enforceability of this Agreement.

**APREA THERAPEUTICS, INC.
2019 STOCK INCENTIVE PLAN
STOCK OPTION AWARD NOTICE**

Bernd Seizinger
September 20, 2019

In connection with the corporate reorganization of Aprea Therapeutics AB, you have been awarded stock options representing the right to acquire shares of Common Stock of Aprea Therapeutics, Inc., a Delaware corporation (the "Company") in substitution of your stock options granted under that certain agreement entered into between you, Aprea Therapeutics AB and Aprea Personal AB on September 4, 2015. The stock options are granted pursuant to the terms and conditions of the Aprea Therapeutics, Inc. 2019 Stock Incentive Plan (the "Plan") and the Stock Option Agreement (together with this Award Notice, the "Agreement") and, subject to the payment of the subscription price by you, are immediately exercisable upon the consummation of the initial public offering of the Company's common stock. Copies of the Plan and the Stock Option Agreement are attached hereto. Capitalized terms not defined herein shall have the meanings specified in the Plan or the Agreement.

Stock Options: You hold stock options with respect to [] shares of the Company's Common Stock, par value \$0.001 per share (the "Common Stock"), subject to adjustment as provided in Section 4.2 of the Agreement.

Original Grant Date: []

Vesting Commencement Date: []

Subscription Price: \$0.12 per share, subject to adjustment as provided in Section 4.2 of the Agreement.

Vesting Schedule: The stock options shall vest upon the earlier to occur of (i) a sale or other transfer of any part of the shares in the Company, in a single transaction or series of transactions with one or more bona fide third parties resulting in that such person(s) or entity(-ies) together with any person or entity acting in concert with such person(s) or entity(-ies) holding (whether directly or indirectly) more than 50% of the total number of shares (in aggregate calculated on a fully diluted basis) in the Company or other holding company of the Company's business, or the sale of all or substantially all assets of the Company (whether through a share transaction or an asset transaction or the granting of a license constituting substantially the entire value of the Company or (ii) a listing (including, but not limited to, a spin-off) of the shares in the Company or other holding company of the Company's business on a stock exchange or other marketplace for public trading in shares, whether through a primary or a secondary offering (the events in clauses (i) and (ii) are referred to as an "Exercise Event").

Exercise Limitations:

Except as otherwise provided in the Plan, the Agreement or any other agreement between the Company or any of its Subsidiaries and Holder, the Option shall only be exercisable after the occurrence of an Exercise Event.

Expiration Date:

Except to the extent earlier settled or terminated pursuant to Section 2.2 of the Agreement, the stock options shall terminate on September 4, 2025.

APREA THERAPEUTICS, INC.

By: _____

Name:

Title:

Acknowledgment, Acceptance and Agreement:

By signing below and returning this Award Notice to Aprea Therapeutics, Inc., I hereby acknowledge receipt of the Agreement and the Plan and agree to be bound by the terms and conditions of this Award Notice, the Agreement and the Plan.

The Holder acknowledges and understands that (i) the substitution of the Stock Options issued to Holder by Aprea Personal AB with the Option under the Agreement, or the acquisition of Common Stock upon the exercise of the Option may be treated as taxable events for United States Federal, state, local and foreign income tax purposes, including the application of the passive foreign investment company rules, and may be subject to tax withholding, (ii) it is Holder's responsibility to consult with Holder's tax advisors with respect to the tax treatment of the substitution and acquisition, and (iii) the Company, Aprea Personal AB, Aprea Therapeutics AB and their respective advisors do not provide any tax advice with respect to such substitution or acquisition.

Holder

Date

Signature Page to Stock Option Agreement

**APREA THERAPEUTICS, INC.
2019 STOCK INCENTIVE PLAN**

Stock Option Agreement

In substitution of stock options with respect to Aprea Therapeutics AB in connection with the corporate reorganization of Aprea Therapeutics AB, Aprea Therapeutics, Inc., a Delaware corporation (the "Company"), hereby grants to the individual ("Holder") named in the award notice attached hereto (the "Award Notice") as of September 20, 2019, pursuant to the provisions of the Aprea Therapeutics, Inc. 2019 Stock Incentive Plan (the "Plan"), stock options to acquire from the Company the number of shares of the Company's Common Stock, par value \$0.001 per share ("Common Stock"), set forth in the Award Notice at the subscription price per share set forth in the Award Notice (the "Subscription Price") (the "Option"), upon and subject to the terms and conditions set forth below, in the Award Notice and in the Plan. Capitalized terms not defined herein shall have the meanings specified in the Plan.

1. Acceptance of Agreement. This Agreement shall be null and void unless Holder shall accept this Agreement by executing the Award Notice in the space provided therefor and returning an original execution copy of the Award Notice to the Company (or electronically accepting this Agreement within the Holder's stock plan account with the Company's stock plan administrator according to the procedures then in effect).

2. Time and Manner of Acquisition of Shares.

2.1. Maximum Term. In no event may the Option be exercised, in whole or in part, after the expiration date set forth in the Award Notice (the "Expiration Date").

2.2. Vesting and Settlement of Option. The Option shall become vested and automatically exercised upon the occurrence of an Exercise Event, as described in the Award Notice if, and only if, (i) Holder is, and has been, continuously (except for any absence for vacation, leave, etc. in accordance with the Company's or its Subsidiaries' policies): (a) serving as a Non-Employee Director or (b) providing services to the Company or any of its Subsidiaries as an advisor or consultant, in each case, from the Grant Date through and including the occurrence of an Exercise Event and (ii) the Exercise Event occurs within four years after the termination other than for Cause of Holder's service to the Company as a Non-Employee Director or advisor or consultant. Termination shall be deemed to be for "Cause" if the Holder (A) has acted in material breach of applicable laws and regulations, (B) has acted in material breach of fiduciary duties in relation to the Company, (C) has acted in material breach of contractual undertakings in relation to the Company or its affiliates or the Company's direct or indirect shareholders, (D) has accepted a position in or in any other way advising, promoting or investing in a company competing with the Company, (E) has solicited, or attempted to solicit, employees, consultants, directors, suppliers, customers or partners of the Company away from the Company, or (F) has suspended payments, entered into liquidation, either voluntary or compulsory, been declared bankrupt or otherwise may be deemed to be insolvent.

2.3. Settlement of Option. Subject to the limitations set forth in this Agreement, upon the occurrence of an Exercise Event and subject to the Holder's payment of the Subscription Price set forth in the Award Notice, the Company shall issue or deliver, subject to the conditions of this Agreement, the number of shares of Common Stock acquired hereunder. Such issuance shall occur as soon as practicable following the Exercise Event (but in any event no later than the March 15th immediately following the year in which the Exercise Event occurs). The Subscription Price shall be paid by the Holder to the Company in cash or, if permitted by applicable law, by reducing the Holder's other compensation from the Company. No shares of Common Stock or certificate representing a share of Common Stock shall be issued or delivered until the full Subscription Price has been paid and such issuance shall be evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company. The Company shall pay all original issue or transfer taxes and all fees and expenses incident to such issuance.

3. Transfer Restrictions and Investment Representations.

3.1. Nontransferability of Option. The Option may not be transferred by Holder other than by will or the laws of descent and distribution or pursuant to the designation of one or more beneficiaries on the form prescribed by the Company. Upon any attempt to so sell, transfer, assign, pledge, hypothecate, encumber or otherwise dispose of the Option, the Option and all rights hereunder shall immediately become null and void.

3.2. Investment Representation. Holder hereby represents and covenants that (a) any shares of Common Stock acquired upon the exercise of the Option will be acquired for investment and not with a view to the distribution thereof within the meaning of the Securities Act of 1933, as amended (the "Securities Act"), unless such acquisition has been registered under the Securities Act and any applicable state securities laws; (b) any subsequent sale of any such shares shall be made either pursuant to an effective registration statement under the Securities Act and any applicable state securities laws, or pursuant to an exemption from registration under the Securities Act and such state securities laws; and (c) if requested by the Company, Holder shall submit a written statement, in a form satisfactory to the Company, to the effect that such representation (x) is true and correct as of the date of any acquisition of any shares hereunder or (y) is true and correct as of the date of any sale of any such shares, as applicable. As a further condition precedent to any acquisition of shares hereunder, Holder shall comply with all regulations and requirements of any regulatory authority having control of or supervision over the issuance or delivery of the shares and, in connection therewith, shall execute any documents which the Board or the Committee shall in its sole discretion deem necessary or advisable.

4. Additional Terms and Conditions.

4.1. Tax Consequences. The Holder acknowledges and understands that (i) the substitution of the Stock Options issued to Holder by Aprea Personal AB with the Option hereunder, or the acquisition of Common Stock upon the exercise of the Option hereunder may be treated as taxable events for United States Federal, state, local and foreign income tax purposes, including the application of the passive foreign investment company rules, and may be subject to tax withholding, and (ii) it is Holder's responsibility to consult with Holder's tax

advisors with respect to the tax treatment of the substitution and acquisition, and (iii) the Company, Aprea Personal AB, Aprea Therapeutics AB and their respective advisors do not provide any tax advice with respect to such substitution or acquisition.

4.2. Adjustment. In the event of any equity restructuring (within the meaning of Financial Accounting Standards Board Accounting Standards Codification Topic 718, Compensation—Stock Compensation) that causes the per share value of shares of Common Stock to change, such as a stock dividend, stock split, spinoff, rights offering or recapitalization through an extraordinary dividend, the number and class of securities subject to the Agreement and the Subscription Price shall be equitably adjusted by the Committee. In the event of any other change in corporate capitalization, including a merger, consolidation, reorganization, or partial or complete liquidation of the Company, such equitable adjustments described in the foregoing sentence may be made as determined to be appropriate and equitable by the Committee (or, if the Company is not the surviving corporation in any such transaction, the board of directors of the surviving corporation) to prevent dilution or enlargement of rights of participants. The decision of the Committee regarding any such adjustment shall be final, binding and conclusive.

4.3. Compliance with Applicable Law. The Option is subject to the condition that if the listing, registration or qualification of the shares subject to the Option upon any securities exchange or under any law, or the consent or approval of any governmental body, or the taking of any other action is necessary or desirable as a condition of, or in connection with, the purchase or issuance of shares hereunder, and shares subject to this Agreement may not be issued, unless such listing, registration, qualification, consent, approval or other action shall have been effected or obtained, free of any conditions not acceptable to the Company. The Company agrees to use reasonable efforts to effect or obtain any such listing, registration, qualification, consent, approval or other action.

4.4. Option Confers No Rights as Stockholder. Holder shall not be entitled to any privileges of ownership with respect to shares of Common Stock subject to the Option unless and until such shares are acquired and issued in accordance with this Agreement, and Holder becomes a stockholder of record with respect to such issued shares. Holder shall not be considered a stockholder of the Company with respect to any such shares not so issued.

4.5. Option Confers No Rights to Continued Service. In no event shall the granting of the Option or its acceptance by Holder, or any provision of this Agreement or the Plan, give or be deemed to give Holder any right to continued service with the Company, any Subsidiary or any affiliate of the Company or affect in any manner the right of the Company, any Subsidiary or any affiliate of the Company to terminate the service of any person at any time.

4.6. Decisions of Board or Committee. The Board or the Committee shall have the right to resolve all questions which may arise in connection with the Option. Any interpretation, determination or other action made or taken by the Board or the Committee regarding the Plan or this Agreement shall be final, binding and conclusive.

4.7. Successors. This Agreement shall be binding upon and inure to the benefit of any successor or successors of the Company and any person or persons who shall,

upon the death of Holder, acquire any rights hereunder in accordance with this Agreement or the Plan.

4.8. Notices. All notices, requests or other communications provided for in this Agreement shall be made, if to the Company, to Aprea Therapeutics, Inc., Attn: Treasury Department, 535 Boylston Street, Boston MA 02116, and if to Holder, to the last known mailing address of Holder contained in the records of the Company. All notices, requests or other communications provided for in this Agreement shall be made in writing either (a) by personal delivery, (b) by facsimile or electronic mail with confirmation of receipt, (c) by mailing in the United States mails or (d) by express courier service. The notice, request or other communication shall be deemed to be received upon personal delivery, upon confirmation of receipt of facsimile or electronic mail transmission or upon receipt by the party entitled thereto if by United States mail or express courier service; provided, however, that if a notice, request or other communication sent to the Company is not received during regular business hours, it shall be deemed to be received on the next succeeding business day of the Company.

4.9. Governing Law. This Agreement, the Option and all determinations made and actions taken pursuant hereto and thereto, to the extent not governed by the Code or the laws of the United States, shall be governed by the laws of the State of Delaware and construed in accordance therewith without giving effect to principles of conflicts of laws.

4.10. Agreement Subject to the Plan. This Agreement is subject to the provisions of the Plan and shall be interpreted in accordance therewith. In the event that the provisions of this Agreement and the Plan conflict, the Plan shall control. The Holder hereby acknowledges receipt of a copy of the Plan.

4.11. Entire Agreement. This Agreement and the Plan constitute the entire agreement of the parties with respect to the subject matter hereof and supersede in their entirety all prior undertakings and agreements of the Company and the Holder with respect to the subject matter hereof, including, without limitation, the Agreement on Terms for Aprea AB Incentive Plan for Bernd Seizinger, and may not be modified adversely to the Holder's interest except by means of a writing signed by the Company and the Holder.

4.12. Partial Invalidity. The invalidity or unenforceability of any particular provision of this Agreement shall not affect the other provisions hereof and this Agreement shall be construed in all respects as if such invalid or unenforceable provisions were omitted.

4.13. Amendment and Waiver. The provisions of this Agreement may be amended or waived only by the written agreement of the Company and the Holder, and no course of conduct or failure or delay in enforcing the provisions of this Agreement shall affect the validity, binding effect or enforceability of this Agreement.

4.14. Counterparts. The Award Notice may be executed in two counterparts, each of which shall be deemed an original and both of which together shall constitute one and the same instrument.

EMPLOYMENT AGREEMENT

THIS EMPLOYMENT AGREEMENT (the "Agreement") between APREA THERAPEUTICS, INC., a Delaware corporation (the "Company"), and Christian S. Schade (the "Executive"), is made and entered into as of September 26, 2019, and will become effective, if at all, upon the date of closing of the Company's initial public offering of stock pursuant to an effective registration statement filed under the Securities Act of 1933, as amended (the "Effective Date").

WHEREAS, the Company desires to continue to employ Executive on the terms and conditions contained herein;

WHEREAS, the Company and Executive previously entered into an employment letter agreement, dated as of April 2016 (the "Prior Agreement");

WHEREAS, Executive desires to continue to be employed by and render services to the Company upon and subject to the terms, conditions and other provisions set forth herein.

NOW THEREFORE, in consideration of the promises and mutual covenants and agreements contained herein, the adequacy of all of which consideration is hereby acknowledged, the parties hereby agree as follows:

- 1. Agreement and Term.** The Company hereby agrees to continue to employ Executive, and Executive hereby accepts such employment and agrees to render such services to the Company, on the terms and conditions set forth in this Agreement. Unless terminated earlier as set forth in Section 4 herein, Executive's employment and the term under this Agreement shall commence under the terms set forth herein on the Effective Date and shall continue until the third-anniversary of the Effective Date (the "Initial Term") and, thereafter, shall be extended automatically for successive one-year terms, unless either Executive or the Company gives contrary written notice not less than 60 days in advance of the expiration of the Initial Term or any succeeding term of this Agreement. The Initial Term, together with any extension thereof in accordance with this Section 1, shall be referred to herein as the "Term."
- 2. Positions and Authority.** Executive shall serve in the positions of President and Chief Executive Officer of the Company, or in such other positions as the parties may agree. On the Effective Date, Executive shall continue to serve as a member of the Board of Directors of the Company (the "Board") and, during the Term, the Company shall cause Executive to be nominated for election as a member of the Board. Executive agrees to serve in the officer positions referred to in this Section 2 and continue to serve as a director of the Company, and to perform diligently and to the best of his abilities the duties and services appertaining to such offices as set forth in the Bylaws of the Company, as well as such additional duties and services appropriate to such offices that the parties may agree upon from time to time. Upon the Effective Date, Executive's principal place of work shall be located in Boston, Massachusetts.

During the Term, Executive shall devote Executive's full business time and efforts to the business and affairs of the Company and its subsidiaries, provided that the Executive shall be entitled to serve as a member of the board of directors of a reasonable number of other companies, to serve on civic, charitable, educational, religious, public interest or public service boards, and to

manage the Executive's personal and family investments, in each case, to the extent such activities do not materially interfere with the performance of the Executive's duties and responsibilities hereunder. Executive shall not become a director of any for profit entity without first receiving the approval of the Nominating and Corporate Governance Committee of the Board.

3. Compensation and Benefits

(a) Base Salary. As compensation for Executive's performance of Executive's duties hereunder, Company shall pay to Executive an initial Base Salary of \$500,000 per year, payable in accordance with the normal payroll practices of the Company. The Base Salary shall be reviewed for increases but not decreases by the Compensation Committee of the Board (the "Compensation Committee") in good faith, based upon the Company's and Executive's performance and the Company's pay philosophy, not less often than annually. The term "Base Salary," shall refer to the Base Salary as may be in effect from time to time.

(b) Annual Incentive Compensation. During the Term, Executive shall be eligible to participate in the annual cash bonus program maintained for senior executive officers of the Company (the "Annual Incentive Program"), with an initial target annual bonus opportunity equal to 50% of Base Salary. The actual amount of the annual bonus earned by and payable to Executive for any year or portion of a year, as applicable, shall be determined upon the satisfaction of goals and objectives established by the Compensation Committee, and shall be subject to such other terms and conditions of the Annual Incentive Program as in effect from time to time. Each bonus paid under the Annual Incentive Program shall be paid to Executive no later than March 15th of the calendar year following the calendar year in which the bonus is earned.

(c) Long-Term Incentive Grants. During the Term, Executive shall be eligible to participate in the long-term incentive program maintained for senior executive officers of the Company (the "LTI Program"), with a LTI Program target opportunity and LTI Program Vehicles determined by the Compensation Committee for each year of participation.

(d) Employee Benefits and Perquisites. During the Term, the Executive shall be entitled to receive all benefits and perquisites of employment generally available to other members of the Company's senior executive management, upon Executive's satisfaction of the eligibility or participation criteria therefor. The Company reserves the right to modify or terminate employee benefits and perquisites at its discretion.

(e) Business Expenses. Subject to Section 17, Executive shall be reimbursed for reasonable travel and other expenses incurred in the performance of Executive's duties on behalf of the Company in a manner consistent with the Company's policies regarding such reimbursements, as may be in effect from time to time.

4. Termination of Employment. (a) The Term shall end upon the first to occur of: (i) the expiration of the term of this Agreement pursuant to Section 1 hereof; (ii) Termination due to Disability (as defined below); (iii) termination of Executive's employment by the Company for any reason other than Termination due to Disability; (iv) Executive's death; or (v) termination of Executive's employment by Executive for any reason. Upon the termination of Executive's employment with the Company for any reason, Executive shall be deemed to have resigned from

the Board and all other positions with the Company or any of its Affiliates held by Executive as of the date immediately preceding Executive's termination of employment.

(b) If Executive's employment ends for any reason, except as otherwise contemplated in this Section 4, Executive shall cease to have any rights to salary, bonus (if any) or other benefits, other than (i) the earned but unpaid portion of Executive's Base Salary through the date of termination or resignation, (ii) a lump-sum payment in respect of accrued but unused vacation days at the Executive's per-business-day Base Salary rate, (iii) any unpaid expense or other reimbursements due to Executive, and (iv) any other amounts or benefits required to be paid or provided by law or under any plan, program, policy or practice of the Company.

(c) Termination without Cause or for Good Reason. If Executive's employment hereunder shall be terminated by the Company without Cause, termination upon the expiration of the Term following notice of non-renewal by the Company, or by Executive for Good Reason, then in addition to the payments and benefits described in Section 4(b) and subject to Section 17 and Executive's continuing compliance with Section 5 of this Agreement:

(i) the Company shall pay Executive an amount equal to 12 months of the Executive's Base Salary (the "Severance Payment"), payable during the 12-month period following such termination of employment, with the Severance Payment commencing as soon as administratively feasible within 60 days following Executive's termination of employment and the first installment payment including the portion of the Severance Payment that was payable prior to such first payment date; provided, however, if the Executive's employment is terminated under circumstances entitling the Executive to severance under this Section 4(c) within 12 months following a Change in Control (a "CIC Qualifying Termination"), then the Severance Payment and period to pay the Severance Payment shall be increased to 18 months;

(ii) the Company shall pay Executive an annual bonus for the year of termination equal to the Executive's target annual bonus opportunity, payable within 60 days following the Executive's termination of employment, subject to proration based on the number of days in the calendar year that have elapsed prior to the date of termination;

(iii) following the Executive's termination of employment, the Company shall pay to the Executive (or to the Executive's family in the event of Executive's death) on a monthly basis an amount equal to the monthly amount of the Consolidated Omnibus Budget Reconciliation Act of 1985 continuation coverage premium for such month, at the same level and cost to the Executive (or the Executive's family in the event of Executive's death) as immediately preceding the Executive's termination of employment, under the Company group medical plan in which the Executive participated immediately preceding the Executive's termination of employment, less the amount of the Executive's portion of such monthly premium as in effect immediately preceding the Executive's termination of employment, until the earlier of (A) 12 months after the Executive's termination of employment and (B) the Executive and Executive's family have obtained other substantially similar healthcare coverage; provided, however, if the Executive experiences a CIC Qualifying Termination, then the number of months set forth in clause (A) of this sentence shall be increased to 18 months;

For the avoidance of doubt, Executive shall not be entitled to the benefits described in this Section 4(c) for a Termination due to Disability, termination of Executive's employment for Cause, Executive's death, or termination of Executive's employment by Executive for any reason other than for Good Reason.

(d) Section 280G. Notwithstanding anything to the contrary in this Agreement, Executive expressly agrees that if the payments and benefits provided for in this Agreement or any other payments and benefits which Executive has the right to receive from the Company and its Affiliates (collectively, the "Payments"), would constitute a "parachute payment" (as defined in Section 280G(b)(2) of the Internal Revenue Code of 1986, as amended (the "Code")), then the Payments shall be either (i) reduced (but not below zero) so that the present value of the Payments will be one dollar (\$1.00) less than three times Executive's "base amount" (as defined in Section 280G(b)(3) of the Code) and so that no portion of the Payments received by Executive shall be subject to the excise tax imposed by Section 4999 of the Code or (ii) paid in full, whichever produces the better net after-tax position to Executive. The reduction of Payments, if any, shall be made by reducing first any Payments that are exempt from Section 409A of the Code and then reducing any Payments subject to Section 409A of the Code in the reverse order in which such Payments would be paid or provided (beginning with such payment or benefit that would be made last in time and continuing, to the extent necessary, through to such payment or benefit that would be made first in time). The determination as to whether any such reduction in the Payments is necessary shall be made by the Compensation Committee in good faith. If a reduced Payment is made or provided and, through error or otherwise, that Payment, when aggregated with other payments and benefits from Company (or its Affiliates) used in determining if a "parachute payment" exists, exceeds one dollar (\$1.00) less than three times Executive's base amount, then Executive shall immediately repay such excess to the Company.

(e) Certain Definitions.

"Affiliate" shall mean all persons and entities directly or indirectly controlling, controlled by or under common control with the Company, where control may be by management authority, or an equity interest of 50% or more (direct or indirect).

"Cause" shall mean, in the sole discretion of the Board:

- (i) conduct by Executive in connection with Executive's service to the Company or any Affiliate that is fraudulent, unlawful or grossly negligent;
- (ii) Executive's material breach of Executive's material responsibilities to the Company or any Affiliate or Executive's willful failure to comply with reasonable and lawful directives of the Board;
- (iii) Executive's material breach of Executive's material representations, warranties, covenants and/or obligations under this Agreement;
- (iv) material misconduct by Executive that seriously discredits or damages the Company or any Affiliate;

- (v) nonperformance or unsatisfactory performance of Executive's material duties or responsibilities to the Company or any Affiliate;
- (vi) violation of the Company's or any of its Affiliates' policies including, without limitation, the Company's Code of Conduct and policies on equal employment opportunity and prohibition of unlawful harassment; and/or
- (vii) the conviction of, or plea of nolo contendere to, any felony or a misdemeanor involving dishonesty or fraud

In the case of each of (ii), (iii), (iv), (v) and (vi) as determined in good faith by the Board after written notice to Executive providing reasonable details of the alleged breach and not less than a 30 day period to cure the alleged breach; provided that the Company may suspend Executive's employment, access, authority and duties during such cure period.

"Change in Control" shall have the meaning assigned to such term in the Company's 2019 Equity Incentive Plan.

"Good Reason" shall mean that Executive has complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following actions undertaken by the Company without Executive's express prior written consent:

- (i) the changing of Executive's position from President and Chief Executive Officer of the Company;
- (ii) a material diminution in Executive's responsibilities, authority or function as President and Chief Executive Officer of the Company;
- (iii) a material reduction in Executive's Base Salary and/or annual target bonus opportunity; provided, however, that Good Reason shall not be deemed to have occurred in the event of a reduction in Executive's Base Salary and/or annual target bonus opportunity that is pursuant to a reduction program affecting substantially all of the senior level employees of the Company and that does not adversely affect Executive to a greater extent than other similarly situated senior level employees; or
- (iv) a change of more than 50 miles in the geographic location at which Executive must regularly report to work and perform services, except for required travel on business of the Company; provided, however, that "Good Reason" shall not include, following a Change of Control, a reduction in title, position, responsibilities or duties solely by virtue of the Company being acquired and made part of, or operating as a subsidiary or division of a larger company or organization, as long as Executive's new duties and responsibilities are reasonably commensurate with Executive's experience.

"Good Reason Process" shall mean that: (i) Executive has reasonably determined in good faith that a "Good Reason" has occurred; (ii) Executive has notified the Board in writing of the first occurrence of the Good Reason condition within 60 days of the first occurrence of such condition; (iii) Executive has cooperated in good faith with the efforts of the Company, for a

period not less than 30 days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) Executive terminates employment within 60 days after the end of the Cure Period. If the Good Reason condition is cured by the Company during the Cure Period, Good Reason shall be deemed not to have occurred.

"Termination due to Disability," shall mean Executive's termination of employment as a result of Executive becoming incapacitated for a period of at least 180 days by accident, sickness or other circumstance that renders Executive mentally or physically incapable of performing the material duties as President and Chief Executive Officer of the Company.

5. Restrictive Covenants.

(a) Confidential Information and Restricted Activities. By signing this Agreement, Executive represents that Executive has carefully read and considered all the terms and conditions of this Agreement, including the restraints imposed on Executive pursuant to this Section 5 (collectively, the "Restrictive Covenant Agreements"). For purposes of the Restrictive Covenant Agreements, "Company," shall mean the Company and its Affiliates. Executive agrees that during Executive's employment and for the twelve month period after Executive's employment with the Company ends for any reason (the "Restricted Period") Executive will not (without the Company's prior written consent), whether as owner, partner, shareholder, director, consultant, agent, employee, co-venturer or otherwise, (i) engage, participate or invest in any business activity anywhere in the world that develops, markets or sells any products, or performs or sells any services that directly or indirectly target the pharmacological restoration of normal function to wild type or missense-mutant P53 in oncologic applications; provided that this shall not prohibit any investment by Executive in publicly traded stock of a company representing less than two percent of the stock of such company, (ii) (A) solicit or attempt to solicit, or (B) take away or divert from the Company, or attempt to take away or divert from the Company, the business or patronage of any customer(s) known to Executive with respect to which Executive was involved in soliciting, in each case at any time during the twelve-month period that immediately preceded the termination of Executive's employment with the Company and with which, as a result of Executive's employment with the Company, Executive had business dealings or about which Executive acquired confidential information, or (iii) (A) recruit or attempt to recruit, solicit or attempt to solicit, hire or attempt to hire, interfere with or endeavor to entice away or (B) assist in recruiting or attempting to recruit, soliciting or attempting to solicit, hiring or attempting to hire, interfering with or enticing away any person who is or was employed by the Company or is or was an agent, representative or consultant of the Company within the six-month period preceding the termination of Executive's employment with the Company. Executive agrees without reservation that these restraints are necessary for the reasonable and proper protection of the Company, and that each and every one of the restraints is reasonable in respect to subject matter, length of time and geographic area. Executive further understands that Executive's obligations under the Restrictive Covenant Agreements will continue in accordance with their express terms regardless of any changes in Executive's title, position, duties, salary, compensation or benefits or other terms and conditions of employment. Executive expressly consents to be bound by the provisions of the Restrictive Covenant Agreements for the benefit of the Company or any Affiliate or successor to whose employ Executive may be transferred.

(b) Return of Property. All files, letters, notes, memoranda, reports, records, data, sketches, drawings, notebooks, layouts, charts, quotations and proposals, specification sheets, program listings, blueprints, models, prototypes, or other written, photographic or other tangible material containing Company information, whether created by Executive or others, which come into Executive's custody or possession, are the exclusive property of the Company to be used by Executive only in the performance of Executive's duties for the Company. Any property situated on the Company's premises and owned by the Company, including without limitation computers, disks and other storage media, filing cabinets or other work areas, is subject to inspection by the Company at any time with or without notice. In the event of the termination of Executive's employment for any reason, Executive will deliver to the Company all files, letters, notes, memoranda, reports, records, data, sketches, drawings, notebooks, layouts, charts, quotations and proposals, specification sheets, program listings, blueprints, models, prototypes, or other written, photographic or other tangible material containing proprietary information, and other materials of any nature pertaining to the proprietary information of the Company and to Executive's work performed for the Company, and will not take or keep in Executive's possession any of the foregoing or any copies.

(c) Developments. Executive will make full and prompt disclosure to the Company of all inventions, discoveries, designs, developments, methods, modifications, improvements, processes, algorithms, databases, computer programs, formulae, techniques, trade secrets, graphics or images, audio or visual works, and other works of authorship (collectively, "Developments"), whether or not patentable or copyrightable, that are created, made, conceived or reduced to practice by Executive (alone or jointly with others) or under Executive's direction during the period of Executive's employment. Executive acknowledges that all work performed by Executive is on a "work for hire" basis, and Executive hereby does assign and transfer and, to the extent any such assignment cannot be fully made at present, will assign and transfer, to the Company and its successors and assigns all Executive's right, title and interest in all Developments that (i) relate to the business of the Company or any customer of or supplier to the Company or any of the products or services being researched, developed, manufactured, commercialized, marketed or sold by the Company or that may be used with such products or services; or (ii) result from tasks assigned to Executive by the Company; or (iii) result from the use of premises or personal property (whether tangible or intangible) owned, leased or contracted for by the Company ("Company-Related Developments"), and all related patents, patent applications, trademarks and trademark applications, copyrights and copyright applications, and other intellectual property rights in all countries and territories worldwide and under any international conventions ("Intellectual Property Rights"). To preclude any possible uncertainty, Executive has provided on Exhibit A to this Agreement a complete list of Developments that Executive has, alone or jointly with others, conceived, developed or reduced to practice prior to the commencement of Executive's employment with the Company that Executive considers to be Executive's property or the property of third parties and that Executive wishes to have excluded from the scope of this Agreement ("Prior Inventions"). Executive has also listed on Exhibit A all patents and patent applications in which Executive is named as an inventor, other than those that have been assigned to the Company, ("Other Patent Rights"). If no such disclosure is set forth on Exhibit A, Executive represents that there are no Prior Inventions or Other Patent Rights. If, in the course of Executive's employment with the Company, Executive incorporates a Prior Invention into a Company product, process or machine or other work done for the Company, Executive hereby grants to the Company a nonexclusive, royalty-free, irrevocable, worldwide license (with the full right to sublicense) to

make, have made, modify, use and sell such Prior Invention. Notwithstanding the foregoing, Executive will not incorporate, or permit to be incorporated, Prior Inventions in any Company-Related Development without the Company's prior written consent. This Agreement does not obligate Executive to assign to the Company any Development that, in the sole judgment of the Company, reasonably exercised, is developed entirely on Executive's own time and does not relate to the business efforts or research and development efforts in which, during the period of Executive's employment, the Company actually is engaged or reasonably would be engaged, and does not result from the use of premises or equipment owned or leased by the Company. However, Executive will also promptly disclose to the Company any such Developments for the purpose of determining whether they qualify for such exclusion. Executive understands that to the extent this Agreement is required to be construed in accordance with the laws of any state that precludes a requirement in an employee agreement to assign certain classes of inventions made by an employee, this [Section 5\(c\)](#) will be interpreted not to apply to any invention which a court rules and /or the Company agrees falls within such classes. Executive also hereby waives all claims to any moral rights or other special rights which Executive may have or accrue in any Company-Related Developments.

(d) **Enforcement of Agreement; Relief.** Executive acknowledges and agrees that the Restrictive Covenant Agreements and all other provisions of this Agreement that are intended to endure beyond the terms of Executive's employment shall survive the termination of Executive's employment and that any violation of any of the Restrictive Covenant Agreements will cause immediate and irreparable damage to the Company, entitling it to specific performance, injunctive relief and other equitable remedies. Executive specifically consents to the issuance of temporary, preliminary, and permanent injunctive relief to enforce the terms of this Agreement. In addition to injunctive relief, the Company is entitled to all money damages available under the law. If Executive breaches any of the covenants contained in the Restrictive Covenant Agreements, in addition to the Company's other legal and equitable remedies, the Company may cease any termination benefits to which Executive might otherwise be entitled. Any such termination of the termination benefits by the Company in the event of a breach by Executive shall not affect Executive's ongoing obligations to the Company including pursuant to the Release.

(e) **Notice of Intent to Resign.** In the event Executive wishes to voluntarily terminate Executive's employment, Executive agrees to provide the Company with four (4) weeks advance written notice (the "**Notice Period**") of Executive's intent to do so, and, if Executive intends or contemplates alternative employment, Executive also agrees to provide the Company with accurate information concerning such alternative employment in sufficient detail to allow the Company to meaningfully exercise its rights under this [Section 5](#). After receipt of such notice, the Company, in its sole, absolute and unreviewable discretion, may (i) require Executive to continue working during the Notice Period, (ii) relieve Executive of some or all of his work responsibilities during the Notice Period, or (iii) shorten the Notice Period and make Executive's voluntary termination of employment effective immediately. Notwithstanding the foregoing, if Executive provides notice of resignation, in no event shall Executive's separation of employment be considered an involuntary termination by the Company, even if the effective date of termination is accelerated by the Company.

(f) **Non-Disparagement.** Executive agrees during and following the Term not to make, or cause to be made, any statement, observation, or opinion, or communicate any information

(whether oral or written, directly or indirectly) that (i) accuses or implies that the Company or its Affiliates engaged in any wrongful, unlawful or improper conduct, whether relating to Executive's employment (or the termination thereof), the business or operations of the Company or its Affiliates, or otherwise or (ii) disparages, impugns, or in any way reflects adversely upon the business or reputation of the Company or its Affiliates. Nothing herein will be deemed to preclude Executive from providing truthful testimony or information pursuant to subpoena, court order, or similar legal process, instituting and pursuing legal action, or engaging in other legally protected speech or activities.

(g) Protected Rights. Notwithstanding anything in this Agreement to the contrary, Executive understands that nothing contained in this Agreement limits the Executive's ability to report possible violations of law or regulation to or file a charge or complaint with the Securities and Exchange Commission, the Equal Employment Opportunity Commission, the National Labor Relations Board, the Occupational Safety and Health Administration, the Department of Justice, the Congress, any Inspector General, or any other federal, state or local governmental agency or commission or regulatory authority (collectively, "Government Agencies"). Executive further understands that this Agreement does not limit his ability to communicate with any Government Agencies or otherwise participate in any investigation or proceeding that may be conducted by any Government Agency, including providing documents or other information, without notice to the Company. Furthermore (i) Executive shall not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that: (A) is made (x) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney; and (y) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal, and (ii) if Executive files a lawsuit for retaliation by the Company for reporting a suspected violation of law, Executive may disclose a trade secret to his or her attorney and use the trade secret information in the court proceeding, if Executive files any document containing the trade secret under seal and does not disclose the trade secret except pursuant to court order.

(h) Breach. Executive acknowledges that the restrictions contained in this Agreement are fair, reasonable, and necessary for the protection of the legitimate business interests of the Company, that the Company will suffer irreparable harm in the event of any actual or threatened breach by Executive, and that it is difficult to measure in money the damages which will accrue to the Company by reason of a failure by Executive to perform any of Executive's obligations under this Section 5. Accordingly, if the Company or any of its Affiliates institutes any action or proceeding to enforce their rights under this Section 5, to the extent permitted by applicable law, Executive hereby waives the claim or defense that the Company or its Affiliates has an adequate remedy at law, Executive shall not claim that any such remedy at law exists, and Executive consents to the entry of a restraining order, preliminary injunction, or other preliminary, provisional, or permanent court order to enforce this Agreement, and expressly waives any security that might otherwise be required in connection with such relief. Executive also agrees that any request for such relief by the Company shall be in addition and without prejudice to any claim for monetary damages and/or other relief which the Company might elect to assert. In the event Executive violates any provision of this Section 5, the Company shall be entitled to recover all costs and expenses of enforcement, including reasonable attorneys' fees, and the time periods set forth above shall be extended for the period of time Executive remains in violation of the provisions.

(i) Release. Executive's execution of a complete and general release of any and all of Executive's potential claims (other than for benefits and payments described in this Agreement or any other vested benefits with the Company and/or its Affiliates) against the Company, any of its Affiliates, and their respective successors and any officers, employees, agents, directors, attorneys, insurers, underwriters, and assigns of the Company or its Affiliates and/or successors, is an express condition of Executive's right to receive termination payments and benefits under this Agreement. Executive shall be required to execute within 45 days after Executive's termination of employment (or such shorter period of time as specified by the Company) the Company's standard form of general waiver and release agreement which documents the release required under this Section 5.

6. Survival. Sections 5, 6, 8, 10, and 12 - 17, and such other provisions hereof as may so indicate shall survive and continue in full force and effect in accordance with their respective terms, notwithstanding any termination of the Term.

7. Notices. Any notice provided for in this Agreement shall be in writing and shall be delivered (i) personally, (ii) by certified mail, postage prepaid, (iii) by Federal Express or other reputable courier service regularly providing evidence of delivery (with charges paid by the party sending the notice), or (iv) by facsimile or a PDF or similar attachment to an email, provided that such telecopy or email attachment shall be followed within one (1) business day by delivery of such notice pursuant to clause (i), (ii) or (iii) above. Any such notice to a party shall be addressed at the address set forth below (subject to the right of a party to designate a different address for itself by notice similarly given):

If to the Company:

APREA THERAPEUTICS, INC.
535 Boylston Street
Boston, MA 02116
Attention: Chair of the Compensation Committee

If to Executive:

Christian S. Schade
At the most recent address on file with the Company

With a copy to:

Sidley Austin LLP
Attn: Geoffrey W. Levin, Esq.
787 Seventh Avenue
New York, NY 10019

8. Indemnification. During the Term, the Company agrees that it shall indemnify Executive and provide Executive with Directors & Officers liability insurance coverage to the same extent that it indemnifies and/or provides such insurance coverage to Board members and other most senior executive officers of the Company

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9. Entire Agreement. This Agreement constitutes the entire agreement and understanding between the parties with respect to the subject matter hereof and supersedes and preempts any prior understandings, agreements or representations by or between the parties, written or oral, which may have related in any manner to the subject matter hereof, including, without limitation, the Prior Agreement.

10. No Conflict. Executive represents and warrants that Executive is not bound by any employment contract, restrictive covenant, or other restriction preventing Executive from carrying out Executive's responsibilities for the Company, or which is in any way inconsistent with the terms of this Agreement. Executive further represents and warrants that Executive shall not disclose to the Company or induce the Company to use any confidential or proprietary information or material belonging to any previous employer or others.

11. Successors and Assigns. This Agreement shall inure to the benefit of and be enforceable by Executive and his heirs, executors and personal representatives, and the Company and its successors and assigns. Any successor or assignee of the Company shall assume the liabilities of the Company hereunder.

12. Governing Law. This Agreement shall be governed by the internal laws (as opposed to the conflicts of law provisions) of the State of Delaware.

13. Amendment and Waiver. The provisions of this Agreement may be amended or waived only with the prior written consent of the Company and Executive, and no course of conduct or failure or delay in enforcing the provisions of this Agreement shall affect the validity, binding effect or enforceability of this Agreement.

14. Withholding. All payments and benefits under this Agreement are subject to withholding of all applicable taxes and other required deductions.

15. Clawbacks. The payments to Executive pursuant to this Agreement are subject to forfeiture or recovery by the Company or other action pursuant to any clawback or recoupment policy which the Company may adopt from time to time, including without limitation any such policy or provision that the Company has included in any of its existing compensation programs or plans or that it may be required to adopt under the Dodd-Frank Wall Street Reform and Consumer Protection Act and implementing rules and regulations thereunder, or as otherwise required by law.

16. Company Policies. Executive shall be subject to additional Company policies as they may exist from time-to-time, including policies with regard to stock ownership by senior executives and policies regarding trading of securities.

17. Code Section 409A. This Agreement is intended to comply with the requirements of Section 409A of the Code, and shall be interpreted and construed consistently with such intent. The payments to Executive pursuant to this Agreement are also intended to be exempt from Section 409A of the Code to the maximum extent possible, under either the separation pay exemption pursuant to Treasury regulation §1.409A-1(b)(9)(iii) or as short-term deferrals pursuant to Treasury regulation §1.409A-1(b)(4), and for such purposes, each payment to Executive under this Agreement shall be considered a separate payment. In the event the terms of this Agreement

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would subject Executive to taxes or penalties under Section 409A of the Code ("409A Penalties"), the Company and Executive shall cooperate diligently to amend the terms of the Agreement to avoid such 409A Penalties, to the extent possible. To the extent any amounts under this Agreement are payable by reference to Executive's "termination of employment" such term and similar terms shall be deemed to refer to Executive's "separation from service," within the meaning of Section 409A of the Code. Executive hereby agrees to be bound by the Company's determination of its "specified employees" (as such term is defined in Section 409A of the Code) provided such determination is in accordance with any of the methods permitted under the regulations issued under Section 409A of the Code. Notwithstanding any other provision in this Agreement, to the extent any payments made or contemplated hereunder constitute nonqualified deferred compensation, within the meaning of Section 409A, then (i) each such payment which is conditioned upon Executive's execution of a release and which is to be paid or provided during a designated period that begins in one taxable year and ends in a second taxable year, shall be paid or provided in the later of the two taxable years and (ii) if Executive is a specified employee (within the meaning of Section 409A of the Code) as of the date of Executive's separation from service, each such payment that is payable upon Executive's separation from service and would have been paid prior to the six-month anniversary of Executive's separation from service, shall be delayed until the earlier to occur of (A) the first day of the seventh month following Executive's separation from service or (B) the date of Executive's death. Any reimbursement payable to Executive pursuant to this Agreement shall be conditioned on the submission by Executive of all expense reports reasonably required by Employer under any applicable expense reimbursement policy, and shall be paid to Executive within 30 days following receipt of such expense reports, but in no event later than the last day of the calendar year following the calendar year in which Executive incurred the reimbursable expense. Any amount of expenses eligible for reimbursement, or in-kind benefit provided, during a calendar year shall not affect the amount of expenses eligible for reimbursement, or in-kind benefit to be provided, during any other calendar year. The right to any reimbursement or in-kind benefit pursuant to this Agreement shall not be subject to liquidation or exchange for any other benefit. To the extent that the Severance Payment payable hereunder is deemed to be a substitute for a payment provided under another agreement with the Executive, then the Severance Payment payable hereunder shall be paid at the same time and in the same form as such substituted payment to the extent required to comply with Section 409A of the Code.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first written above.

APREA THERAPEUTICS, INC.

By: /s/ Scott M. Coiante

Name: Scott M. Coiante
Title: Senior Vice President, Chief Financial Officer

EXECUTIVE

By: /s/ Christian S. Schade

Name: Christian S. Schade
Title: President and Chief Executive Officer

FORM OF EMPLOYMENT AGREEMENT

THIS EMPLOYMENT AGREEMENT (the "Agreement") between APREA THERAPEUTICS, INC., a Delaware corporation (the "Company"), and [] (the "Executive"), is made and entered into as of [], 20 [] (the "Effective Date").

WHEREAS, the Company desires to continue to employ Executive on the terms and conditions contained herein;

WHEREAS, the Company and Executive previously entered into an employment letter agreement, dated as of [] (the "Prior Agreement");

WHEREAS, Executive desires to continue to be employed by and render services to the Company upon and subject to the terms, conditions and other provisions set forth herein.

NOW THEREFORE, in consideration of the promises and mutual covenants and agreements contained herein, the adequacy of all of which consideration is hereby acknowledged, the parties hereby agree as follows:

1. Agreement and Term. The Company hereby agrees to continue to employ Executive, and Executive hereby accepts such employment and agrees to render such services to the Company, on the terms and conditions set forth in this Agreement. Unless terminated earlier as set forth in Section 4 herein, Executive's employment and the term under this Agreement shall commence under the terms set forth herein on the Effective Date and shall continue until the third-anniversary of the Effective Date (the "Initial Term") and, thereafter, shall be extended automatically for successive one-year terms, unless either Executive or the Company gives contrary written notice not less than 60 days in advance of the expiration of the Initial Term or any succeeding term of this Agreement. The Initial Term, together with any extension thereof in accordance with this Section 1, shall be referred to herein as the "Term."
2. Positions and Authority. Executive shall serve in the position of [] of the Company, or in such other position as the parties may agree. Executive agrees to serve in the officer position referred to in this Section 2, and to perform diligently and to the best of his abilities the duties and services appertaining to such offices as set forth in the Bylaws of the Company, as well as such additional duties and services appropriate to such offices that the parties may agree upon from time to time. Upon the Effective Date, Executive's principal place of work shall be located in Boston, Massachusetts.

During the Term, Executive shall devote Executive's full business time and efforts to the business and affairs of the Company and its subsidiaries, provided that the Executive shall be entitled to serve as a member of the board of directors of a reasonable number of other companies, to serve on civic, charitable, educational, religious, public interest or public service boards, and to manage the Executive's personal and family investments, in each case, to the extent such activities do not materially interfere with the performance of the Executive's duties and responsibilities

hereunder. Executive shall not become a director of any for profit entity without first receiving the approval of the Chief Executive Officer of the Company.

3. Compensation and Benefits

(a) Base Salary. As compensation for Executive's performance of Executive's duties hereunder, Company shall pay to Executive an initial Base Salary of \$[] per year, payable in accordance with the normal payroll practices of the Company. The Base Salary shall be reviewed for increases but not decreases by the Compensation Committee of the Board (the "Compensation Committee") in good faith, based upon the Company's and Executive's performance and the Company's pay philosophy, not less often than annually. The term "Base Salary," shall refer to the Base Salary as may be in effect from time to time.

(b) Annual Incentive Compensation. During the Term, Executive shall be eligible to participate in the annual cash bonus program maintained for senior executive officers of the Company (the "Annual Incentive Program"), with an initial target annual bonus opportunity equal to []% of Base Salary. The actual amount of the annual bonus earned by and payable to Executive for any year or portion of a year, as applicable, shall be determined upon the satisfaction of goals and objectives established by the Compensation Committee, and shall be subject to such other terms and conditions of the Annual Incentive Program as in effect from time to time. Each bonus paid under the Annual Incentive Program shall be paid to Executive no later than March 15th of the calendar year following the calendar year in which the bonus is earned.

(c) Long-Term Incentive Grants. During the Term, Executive shall be eligible to participate in the long-term incentive program maintained for senior executive officers of the Company (the "LTI Program"), with a LTI Program target opportunity and LTI Program Vehicles determined by the Compensation Committee for each year of participation.

(d) Employee Benefits and Perquisites. During the Term, the Executive shall be entitled to receive all benefits and perquisites of employment generally available to other members of the Company's senior executive management, upon Executive's satisfaction of the eligibility or participation criteria therefor. The Company reserves the right to modify or terminate employee benefits and perquisites at its discretion.

(e) Business Expenses. Subject to Section 17, Executive shall be reimbursed for reasonable travel and other expenses incurred in the performance of Executive's duties on behalf of the Company in a manner consistent with the Company's policies regarding such reimbursements, as may be in effect from time to time.

4. Termination of Employment. (a) The Term shall end upon the first to occur of: (i) the expiration of the term of this Agreement pursuant to Section 1 hereof; (ii) Termination due to Disability (as defined below); (iii) termination of Executive's employment by the Company for any reason other than Termination due to Disability; (iv) Executive's death; or (v) termination of Executive's employment by Executive for any reason. Upon the termination of Executive's employment with the Company for any reason, Executive shall be deemed to have resigned from all positions with the Company or any of its Affiliates held by Executive as of the date immediately preceding Executive's termination of employment.

(b) If Executive's employment ends for any reason, except as otherwise contemplated in this Section 4, Executive shall cease to have any rights to salary, bonus (if any) or other benefits, other than (i) the earned but unpaid portion of Executive's Base Salary through the date of termination or resignation, (ii) a lump-sum payment in respect of accrued but unused vacation days at the Executive's per-business-day Base Salary rate, (iii) any unpaid expense or other reimbursements due to Executive, and (iv) any other amounts or benefits required to be paid or provided by law or under any plan, program, policy or practice of the Company.

(c) Termination without Cause or for Good Reason. If Executive's employment hereunder shall be terminated by the Company without Cause, termination upon the expiration of the Term following notice of non-renewal by the Company, or by Executive for Good Reason, then in addition to the payments and benefits described in Section 4(b) and subject to Section 17 and Executive's continuing compliance with Section 5 of this Agreement:

(i) the Company shall pay Executive an amount equal to nine months of the Executive's Base Salary (the "Severance Payment"), payable during the nine-month period following such termination of employment, with the Severance Payment commencing as soon as administratively feasible within 60 days following Executive's termination of employment and the first installment payment including the portion of the Severance Payment that was payable prior to such first payment date; provided, however, if the Executive's employment is terminated under circumstances entitling the Executive to severance under this Section 4(c) within 12 months following a Change in Control (a "CIC Qualifying Termination"), then the Severance Payment and period to pay the Severance Payment shall be increased to 12 months;

(ii) the Company shall pay Executive an annual bonus for the year of termination equal to the Executive's target annual bonus opportunity, payable within 60 days following the Executive's termination of employment, subject to proration based on the number of days in the calendar year that have elapsed prior to the date of termination;

(iii) following the Executive's termination of employment, the Company shall pay to the Executive (or to the Executive's family in the event of Executive's death) on a monthly basis an amount equal to the monthly amount of the Consolidated Omnibus Budget Reconciliation Act of 1985 continuation coverage premium for such month, at the same level and cost to the Executive (or the Executive's family in the event of Executive's death) as immediately preceding the Executive's termination of employment, under the Company group medical plan in which the Executive participated immediately preceding the Executive's termination of employment, less the amount of the Executive's portion of such monthly premium as in effect immediately preceding the Executive's termination of employment, until the earlier of (A) nine months after the Executive's termination of employment and (B) the Executive and Executive's family have obtained other substantially similar healthcare coverage; provided, however, if the Executive experiences a CIC Qualifying Termination, then the number of months set forth in clause (A) of this sentence shall be increased to 12 months;

For the avoidance of doubt, Executive shall not be entitled to the benefits described in this Section 4(c) for a Termination due to Disability, termination of Executive's employment for

Cause, Executive's death, or termination of Executive's employment by Executive for any reason other than for Good Reason.

(d) Section 280G. Notwithstanding anything to the contrary in this Agreement, Executive expressly agrees that if the payments and benefits provided for in this Agreement or any other payments and benefits which Executive has the right to receive from the Company and its Affiliates (collectively, the "Payments"), would constitute a "parachute payment" (as defined in Section 280G(b)(2) of the Internal Revenue Code of 1986, as amended (the "Code")), then the Payments shall be either (i) reduced (but not below zero) so that the present value of the Payments will be one dollar (\$1.00) less than three times Executive's "base amount" (as defined in Section 280G(b)(3) of the Code) and so that no portion of the Payments received by Executive shall be subject to the excise tax imposed by Section 4999 of the Code or (ii) paid in full, whichever produces the better net after-tax position to Executive. The reduction of Payments, if any, shall be made by reducing first any Payments that are exempt from Section 409A of the Code and then reducing any Payments subject to Section 409A of the Code in the reverse order in which such Payments would be paid or provided (beginning with such payment or benefit that would be made last in time and continuing, to the extent necessary, through to such payment or benefit that would be made first in time). The determination as to whether any such reduction in the Payments is necessary shall be made by the Compensation Committee in good faith. If a reduced Payment is made or provided and, through error or otherwise, that Payment, when aggregated with other payments and benefits from Company (or its Affiliates) used in determining if a "parachute payment" exists, exceeds one dollar (\$1.00) less than three times Executive's base amount, then Executive shall immediately repay such excess to the Company.

(e) Certain Definitions.

"Affiliate" shall mean all persons and entities directly or indirectly controlling, controlled by or under common control with the Company, where control may be by management authority, or an equity interest of 50% or more (direct or indirect).

"Cause" shall mean, in the sole discretion of the Board:

- (i) conduct by Executive in connection with Executive's service to the Company or any Affiliate that is fraudulent, unlawful or grossly negligent;
- (ii) Executive's material breach of Executive's material responsibilities to the Company or any Affiliate or Executive's willful failure to comply with reasonable and lawful directives of the Board;
- (iii) Executive's material breach of Executive's material representations, warranties, covenants and/or obligations under this Agreement;
- (iv) material misconduct by Executive that seriously discredits or damages the Company or any Affiliate;
- (v) nonperformance or unsatisfactory performance of Executive's material duties or responsibilities to the Company or any Affiliate;

(vi) violation of the Company's or any of its Affiliates' policies including, without limitation, the Company's Code of Conduct and policies on equal employment opportunity and prohibition of unlawful harassment; and/or

(vii) the conviction of, or plea of nolo contendere to, any felony or a misdemeanor involving dishonesty or fraud

In the case of each of (ii), (iii), (iv), (v) and (vi) as determined in good faith by the Board after written notice to Executive providing reasonable details of the alleged breach and not less than a 30 day period to cure the alleged breach; provided that the Company may suspend Executive's employment, access, authority and duties during such cure period.

"Change in Control" shall have the meaning assigned to such term in the Company's 2019 Equity Incentive Plan.

"Good Reason" shall mean that Executive has complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following actions undertaken by the Company without Executive's express prior written consent:

(i) the changing of Executive's position from [];

(ii) a material diminution in Executive's responsibilities, authority or function as [] of the Company;

(iii) a material reduction in Executive's Base Salary and/or annual target bonus opportunity; provided, however, that Good Reason shall not be deemed to have occurred in the event of a reduction in Executive's Base Salary and/or annual target bonus opportunity that is pursuant to a reduction program affecting substantially all of the senior level employees of the Company and that does not adversely affect Executive to a greater extent than other similarly situated senior level employees; or

(iv) a change of more than 50 miles in the geographic location at which Executive must regularly report to work and perform services, except for required travel on business of the Company; provided, however, that "Good Reason" shall not include, following a Change of Control, a reduction in title, position, responsibilities or duties solely by virtue of the Company being acquired and made part of, or operating as a subsidiary or division of a larger company or organization, as long as Executive's new duties and responsibilities are reasonably commensurate with Executive's experience.

"Good Reason Process" shall mean that: (i) Executive has reasonably determined in good faith that a "Good Reason" has occurred; (ii) Executive has notified the Board in writing of the first occurrence of the Good Reason condition within 60 days of the first occurrence of such condition; (iii) Executive has cooperated in good faith with the efforts of the Company, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) Executive terminates employment within 60 days after the end of the Cure Period. If the Good Reason

condition is cured by the Company during the Cure Period, Good Reason shall be deemed not to have occurred.

“Termination due to Disability,” shall mean Executive’s termination of employment as a result of Executive becoming incapacitated for a period of at least 180 days by accident, sickness or other circumstance that renders Executive mentally or physically incapable of performing the material duties as [].

5. Restrictive Covenants.

(a) Confidential Information and Restricted Activities. By signing this Agreement, Executive represents that Executive has carefully read and considered all the terms and conditions of this Agreement, including the restraints imposed on Executive pursuant to this Section 5 (collectively, the “Restrictive Covenant Agreements”). For purposes of the Restrictive Covenant Agreements, “Company,” shall mean the Company and its Affiliates. Executive agrees that during Executive’s employment and for the twelve month period after Executive’s employment with the Company ends for any reason (the “Restricted Period”) Executive will not (without the Company’s prior written consent), whether as owner, partner, shareholder, director, consultant, agent, employee, co-venturer or otherwise, (i) engage, participate or invest in any business activity anywhere in the world that develops, markets or sells any products, or performs or sells any services that directly or indirectly target the pharmacological restoration of normal function to wild type or missense-mutant P53 in oncologic applications; provided that this shall not prohibit any investment by Executive in publicly traded stock of a company representing less than two percent of the stock of such company, (ii) (A) solicit or attempt to solicit, or (B) take away or divert from the Company, or attempt to take away or divert from the Company, the business or patronage of any customer(s) known to Executive with respect to which Executive was involved in soliciting, in each case at any time during the twelve-month period that immediately preceded the termination of Executive’s employment with the Company and with which, as a result of Executive’s employment with the Company, Executive had business dealings or about which Executive acquired confidential information, or (iii) (A) recruit or attempt to recruit, solicit or attempt to solicit, hire or attempt to hire, interfere with or endeavor to entice away or (B) assist in recruiting or attempting to recruit, soliciting or attempting to solicit, hiring or attempting to hire, interfering with or enticing away any person who is or was employed by the Company or is or was an agent, representative or consultant of the Company within the six-month period preceding the termination of Executive’s employment with the Company. Executive agrees without reservation that these restraints are necessary for the reasonable and proper protection of the Company, and that each and every one of the restraints is reasonable in respect to subject matter, length of time and geographic area. Executive further understands that Executive’s obligations under the Restrictive Covenant Agreements will continue in accordance with their express terms regardless of any changes in Executive’s title, position, duties, salary, compensation or benefits or other terms and conditions of employment. Executive expressly consents to be bound by the provisions of the Restrictive Covenant Agreements for the benefit of the Company or any Affiliate or successor to whose employ Executive may be transferred.

(b) Return of Property. All files, letters, notes, memoranda, reports, records, data, sketches, drawings, notebooks, layouts, charts, quotations and proposals, specification sheets, program listings, blueprints, models, prototypes, or other written, photographic or other tangible

material containing Company information, whether created by Executive or others, which come into Executive's custody or possession, are the exclusive property of the Company to be used by Executive only in the performance of Executive's duties for the Company. Any property situated on the Company's premises and owned by the Company, including without limitation computers, disks and other storage media, filing cabinets or other work areas, is subject to inspection by the Company at any time with or without notice. In the event of the termination of Executive's employment for any reason, Executive will deliver to the Company all files, letters, notes, memoranda, reports, records, data, sketches, drawings, notebooks, layouts, charts, quotations and proposals, specification sheets, program listings, blueprints, models, prototypes, or other written, photographic or other tangible material containing proprietary information, and other materials of any nature pertaining to the proprietary information of the Company and to Executive's work performed for the Company, and will not take or keep in Executive's possession any of the foregoing or any copies.

(c) **Developments.** Executive will make full and prompt disclosure to the Company of all inventions, discoveries, designs, developments, methods, modifications, improvements, processes, algorithms, databases, computer programs, formulae, techniques, trade secrets, graphics or images, audio or visual works, and other works of authorship (collectively, "**Developments**"), whether or not patentable or copyrightable, that are created, made, conceived or reduced to practice by Executive (alone or jointly with others) or under Executive's direction during the period of Executive's employment. Executive acknowledges that all work performed by Executive is on a "work for hire" basis, and Executive hereby does assign and transfer and, to the extent any such assignment cannot be fully made at present, will assign and transfer, to the Company and its successors and assigns all Executive's right, title and interest in all Developments that (i) relate to the business of the Company or any customer of or supplier to the Company or any of the products or services being researched, developed, manufactured, commercialized, marketed or sold by the Company or that may be used with such products or services; or (ii) result from tasks assigned to Executive by the Company; or (iii) result from the use of premises or personal property (whether tangible or intangible) owned, leased or contracted for by the Company ("**Company-Related Developments**"), and all related patents, patent applications, trademarks and trademark applications, copyrights and copyright applications, and other intellectual property rights in all countries and territories worldwide and under any international conventions ("**Intellectual Property Rights**"). To preclude any possible uncertainty, Executive has provided on **Exhibit A** to this Agreement a complete list of Developments that Executive has, alone or jointly with others, conceived, developed or reduced to practice prior to the commencement of Executive's employment with the Company that Executive considers to be Executive's property or the property of third parties and that Executive wishes to have excluded from the scope of this Agreement ("**Prior Inventions**"). Executive has also listed on **Exhibit A** all patents and patent applications in which Executive is named as an inventor, other than those that have been assigned to the Company, ("**Other Patent Rights**"). If no such disclosure is set forth on **Exhibit A**, Executive represents that there are no Prior Inventions or Other Patent Rights. If, in the course of Executive's employment with the Company, Executive incorporates a Prior Invention into a Company product, process or machine or other work done for the Company, Executive hereby grants to the Company a nonexclusive, royalty-free, irrevocable, worldwide license (with the full right to sublicense) to make, have made, modify, use and sell such Prior Invention. Notwithstanding the foregoing, Executive will not incorporate, or permit to be incorporated, Prior Inventions in any Company-Related Development without the Company's prior written consent. This Agreement does not

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obligate Executive to assign to the Company any Development that, in the sole judgment of the Company, reasonably exercised, is developed entirely on Executive's own time and does not relate to the business efforts or research and development efforts in which, during the period of Executive's employment, the Company actually is engaged or reasonably would be engaged, and does not result from the use of premises or equipment owned or leased by the Company. However, Executive will also promptly disclose to the Company any such Developments for the purpose of determining whether they qualify for such exclusion. Executive understands that to the extent this Agreement is required to be construed in accordance with the laws of any state that precludes a requirement in an employee agreement to assign certain classes of inventions made by an employee, this **Section 5(c)** will be interpreted not to apply to any invention which a court rules and /or the Company agrees falls within such classes. Executive also hereby waives all claims to any moral rights or other special rights which Executive may have or accrue in any Company-Related Developments.

(d) **Enforcement of Agreement; Relief.** Executive acknowledges and agrees that the Restrictive Covenant Agreements and all other provisions of this Agreement that are intended to endure beyond the terms of Executive's employment shall survive the termination of Executive's employment and that any violation of any of the Restrictive Covenant Agreements will cause immediate and irreparable damage to the Company, entitling it to specific performance, injunctive relief and other equitable remedies. Executive specifically consents to the issuance of temporary, preliminary, and permanent injunctive relief to enforce the terms of this Agreement. In addition to injunctive relief, the Company is entitled to all money damages available under the law. If Executive breaches any of the covenants contained in the Restrictive Covenant Agreements, in addition to the Company's other legal and equitable remedies, the Company may cease any termination benefits to which Executive might otherwise be entitled. Any such termination of the termination benefits by the Company in the event of a breach by Executive shall not affect Executive's ongoing obligations to the Company including pursuant to the Release.

(e) **Notice of Intent to Resign.** In the event Executive wishes to voluntarily terminate Executive's employment, Executive agrees to provide the Company with four (4) weeks advance written notice (the "**Notice Period**") of Executive's intent to do so, and, if Executive intends or contemplates alternative employment, Executive also agrees to provide the Company with accurate information concerning such alternative employment in sufficient detail to allow the Company to meaningfully exercise its rights under this **Section 5**. After receipt of such notice, the Company, in its sole, absolute and unreviewable discretion, may (i) require Executive to continue working during the Notice Period, (ii) relieve Executive of some or all of his work responsibilities during the Notice Period, or (iii) shorten the Notice Period and make Executive's voluntary termination of employment effective immediately. Notwithstanding the foregoing, if Executive provides notice of resignation, in no event shall Executive's separation of employment be considered an involuntary termination by the Company, even if the effective date of termination is accelerated by the Company.

(f) **Non-Disparagement.** Executive agrees during and following the Term not to make, or cause to be made, any statement, observation, or opinion, or communicate any information (whether oral or written, directly or indirectly) that (i) accuses or implies that the Company or its Affiliates engaged in any wrongful, unlawful or improper conduct, whether relating to Executive's employment (or the termination thereof), the business or operations of the Company or its

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Affiliates, or otherwise or (ii) disparages, impugns, or in any way reflects adversely upon the business or reputation of the Company or its Affiliates. Nothing herein will be deemed to preclude Executive from providing truthful testimony or information pursuant to subpoena, court order, or similar legal process, instituting and pursuing legal action, or engaging in other legally protected speech or activities.

(g) **Protected Rights.** Notwithstanding anything in this Agreement to the contrary, Executive understands that nothing contained in this Agreement limits the Executive's ability to report possible violations of law or regulation to or file a charge or complaint with the Securities and Exchange Commission, the Equal Employment Opportunity Commission, the National Labor Relations Board, the Occupational Safety and Health Administration, the Department of Justice, the Congress, any Inspector General, or any other federal, state or local governmental agency or commission or regulatory authority (collectively, "**Government Agencies**"). Executive further understands that this Agreement does not limit his ability to communicate with any Government Agencies or otherwise participate in any investigation or proceeding that may be conducted by any Government Agency, including providing documents or other information, without notice to the Company. Furthermore (i) Executive shall not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that: (A) is made (x) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney; and (y) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal, and (ii) if Executive files a lawsuit for retaliation by the Company for reporting a suspected violation of law, Executive may disclose a trade secret to his or her attorney and use the trade secret information in the court proceeding, if Executive files any document containing the trade secret under seal and does not disclose the trade secret except pursuant to court order.

(h) **Breach.** Executive acknowledges that the restrictions contained in this Agreement are fair, reasonable, and necessary for the protection of the legitimate business interests of the Company, that the Company will suffer irreparable harm in the event of any actual or threatened breach by Executive, and that it is difficult to measure in money the damages which will accrue to the Company by reason of a failure by Executive to perform any of Executive's obligations under this **Section 5**. Accordingly, if the Company or any of its Affiliates institutes any action or proceeding to enforce their rights under this **Section 5**, to the extent permitted by applicable law, Executive hereby waives the claim or defense that the Company or its Affiliates has an adequate remedy at law, Executive shall not claim that any such remedy at law exists, and Executive consents to the entry of a restraining order, preliminary injunction, or other preliminary, provisional, or permanent court order to enforce this Agreement, and expressly waives any security that might otherwise be required in connection with such relief. Executive also agrees that any request for such relief by the Company shall be in addition and without prejudice to any claim for monetary damages and/or other relief which the Company might elect to assert. In the event Executive violates any provision of this **Section 5**, the Company shall be entitled to recover all costs and expenses of enforcement, including reasonable attorneys' fees, and the time periods set forth above shall be extended for the period of time Executive remains in violation of the provisions.

(i) **Release.** Executive's execution of a complete and general release of any and all of Executive's potential claims (other than for benefits and payments described in this Agreement or

any other vested benefits with the Company and/or its Affiliates) against the Company, any of its Affiliates, and their respective successors and any officers, employees, agents, directors, attorneys, insurers, underwriters, and assigns of the Company or its Affiliates and/or successors, is an express condition of Executive's right to receive termination payments and benefits under this Agreement. Executive shall be required to execute within 45 days after Executive's termination of employment (or such shorter period of time as specified by the Company) the Company's standard form of general waiver and release agreement which documents the release required under this Section 5.

6. Survival. Sections 5, 6, 8, 10, and 12 - 17, and such other provisions hereof as may so indicate shall survive and continue in full force and effect in accordance with their respective terms, notwithstanding any termination of the Term.

7. Notices. Any notice provided for in this Agreement shall be in writing and shall be delivered (i) personally, (ii) by certified mail, postage prepaid, (iii) by Federal Express or other reputable courier service regularly providing evidence of delivery (with charges paid by the party sending the notice), or (iv) by facsimile or a PDF or similar attachment to an email, provided that such telecopy or email attachment shall be followed within one (1) business day by delivery of such notice pursuant to clause (i), (ii) or (iii) above. Any such notice to a party shall be addressed at the address set forth below (subject to the right of a party to designate a different address for itself by notice similarly given):

If to the Company:

APREA THERAPEUTICS, INC.
535 Boylston Street
Boston, MA 02116
Attention: Chief Executive Officer

If to Executive:

[]
At the most recent address on file with the Company

With a copy to:

Sidley Austin LLP
Attn: Geoffrey W. Levin, Esq.
787 Seventh Avenue
New York, NY 10019

8. Indemnification. During the Term, the Company agrees that it shall indemnify Executive and provide Executive with Directors & Officers liability insurance coverage to the same extent that it indemnifies and/or provides such insurance coverage to Board members and other most senior executive officers of the Company

9. Entire Agreement. This Agreement constitutes the entire agreement and understanding between the parties with respect to the subject matter hereof and supersedes and preempts any prior understandings, agreements or representations by or between the parties, written or oral,

which may have related in any manner to the subject matter hereof, including, without limitation, the Prior Agreement.

10. No Conflict. Executive represents and warrants that Executive is not bound by any employment contract, restrictive covenant, or other restriction preventing Executive from carrying out Executive's responsibilities for the Company, or which is in any way inconsistent with the terms of this Agreement. Executive further represents and warrants that Executive shall not disclose to the Company or induce the Company to use any confidential or proprietary information or material belonging to any previous employer or others.
11. Successors and Assigns. This Agreement shall inure to the benefit of and be enforceable by Executive and his heirs, executors and personal representatives, and the Company and its successors and assigns. Any successor or assignee of the Company shall assume the liabilities of the Company hereunder.
12. Governing Law. This Agreement shall be governed by the internal laws (as opposed to the conflicts of law provisions) of the State of Delaware.
13. Amendment and Waiver. The provisions of this Agreement may be amended or waived only with the prior written consent of the Company and Executive, and no course of conduct or failure or delay in enforcing the provisions of this Agreement shall affect the validity, binding effect or enforceability of this Agreement.
14. Withholding. All payments and benefits under this Agreement are subject to withholding of all applicable taxes and other required deductions.
15. Clawbacks. The payments to Executive pursuant to this Agreement are subject to forfeiture or recovery by the Company or other action pursuant to any clawback or recoupment policy which the Company may adopt from time to time, including without limitation any such policy or provision that the Company has included in any of its existing compensation programs or plans or that it may be required to adopt under the Dodd-Frank Wall Street Reform and Consumer Protection Act and implementing rules and regulations thereunder, or as otherwise required by law.
16. Company Policies. Executive shall be subject to additional Company policies as they may exist from time-to-time, including policies with regard to stock ownership by senior executives and policies regarding trading of securities.
17. Code Section 409A. This Agreement is intended to comply with the requirements of Section 409A of the Code, and shall be interpreted and construed consistently with such intent. The payments to Executive pursuant to this Agreement are also intended to be exempt from Section 409A of the Code to the maximum extent possible, under either the separation pay exemption pursuant to Treasury regulation §1.409A-1(b)(9)(iii) or as short-term deferrals pursuant to Treasury regulation §1.409A-1(b)(4), and for such purposes, each payment to Executive under this Agreement shall be considered a separate payment. In the event the terms of this Agreement would subject Executive to taxes or penalties under Section 409A of the Code ("409A Penalties"), the Company and Executive shall cooperate diligently to amend the terms of the Agreement to avoid such 409A Penalties, to the extent possible. To the extent any amounts under this Agreement

are payable by reference to Executive's "termination of employment" such term and similar terms shall be deemed to refer to Executive's "separation from service," within the meaning of Section 409A of the Code. Executive hereby agrees to be bound by the Company's determination of its "specified employees" (as such term is defined in Section 409A of the Code) provided such determination is in accordance with any of the methods permitted under the regulations issued under Section 409A of the Code. Notwithstanding any other provision in this Agreement, to the extent any payments made or contemplated hereunder constitute nonqualified deferred compensation, within the meaning of Section 409A, then (i) each such payment which is conditioned upon Executive's execution of a release and which is to be paid or provided during a designated period that begins in one taxable year and ends in a second taxable year, shall be paid or provided in the later of the two taxable years and (ii) if Executive is a specified employee (within the meaning of Section 409A of the Code) as of the date of Executive's separation from service, each such payment that is payable upon Executive's separation from service and would have been paid prior to the six-month anniversary of Executive's separation from service, shall be delayed until the earlier to occur of (A) the first day of the seventh month following Executive's separation from service or (B) the date of Executive's death. Any reimbursement payable to Executive pursuant to this Agreement shall be conditioned on the submission by Executive of all expense reports reasonably required by Employer under any applicable expense reimbursement policy, and shall be paid to Executive within 30 days following receipt of such expense reports, but in no event later than the last day of the calendar year following the calendar year in which Executive incurred the reimbursable expense. Any amount of expenses eligible for reimbursement, or in-kind benefit provided, during a calendar year shall not affect the amount of expenses eligible for reimbursement, or in-kind benefit to be provided, during any other calendar year. The right to any reimbursement or in-kind benefit pursuant to this Agreement shall not be subject to liquidation or exchange for any other benefit. To the extent that the Severance Payment payable hereunder is deemed to be a substitute for a payment provided under another agreement with the Executive, then the Severance Payment payable hereunder shall be paid at the same time and in the same form as such substituted payment to the extent required to comply with Section 409A of the Code.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first written above.

APREA THERAPEUTICS, INC.

By: _____

Name:

Title:

EXECUTIVE

By:

Name:

Title:

APREA AB
AND
LARS ABRAHMSÉN

EMPLOYMENT AGREEMENT



EMPLOYMENT AGREEMENT

This Employment Agreement (the "Agreement") is entered into on this day between

- (1) **Aprea AB**, Reg. No. 556631-2285, Nobels väg 3, 171 65 Solna, a company duly incorporated and organised under the laws of Sweden, (the "Company"); and
- (2) **Lars Abrahmsén**, , 114 22 Stockholm (the "Employee").

1 Commencement date and term of employment

1.1 The employment, effective with this agreement, commenced on March 1, 2016.

1.2 This Agreement supersedes all other written or oral agreements between the Company, or any associated company, and the Employee due to the employment. For the purposes of this Agreement, "associated company" means a legal entity directly or indirectly controlling or controlled by or under common control with the Company, irrespective of the country of registration of such legal entity. For the avoidance of doubt, this agreement is an extension of a previous agreement effective December 1, 2015, Appendix II.

2 Position

2.1 The Employee shall hold the position of Senior Vice President and Chief Scientific Officer and be stationed at the Company's premises in Solna or at any other premises in Sweden occupied by the Company in the future.

2.2 The Company and the Employee (jointly the "Parties") agree that the nature of the Company's business demands flexibility and that reallocation of duties, etc. from time to time is a constituent part of, and a precondition for, the employment relationship between the Company and the Employee. The position of the Employee implies that the Employee may be required from time to time to travel within and outside Sweden in order to promote the Company's interests in the best possible way.

2.3 The Parties agree that it is essential for the Company's business and a condition for employment with the Company that its employees are service-minded and that they conduct themselves appropriately and act in all respects as good ambassadors of the Company.

3 Working hours and other engagements

3.1 The working hours comprise forty (40) hours per week exclusive of lunch breaks.

3.2 The position demands that additional hours are worked from time to time. No compensation shall be paid for any overtime worked since this, among other things, has been taken into account when determining the salary level.

3.3 During the employment the Employee shall not, either personally or through any legal entity, be engaged in any other employment or carry out other work without the prior written consent of the Company.

4 Salary and other remuneration

4.1 The Employee is entitled to a monthly salary of SEK 133,333. The salary is paid in arrears before the expiry of each calendar month

4.2 In addition to the salary, the Employee is eligible for a bonus targeted at 25% of the adjusted base salary. For 2016 the bonus will be calculated on a 12 month calendar period, notwithstanding the effective date of this agreement. Bonus payments are discretionary and will be based on achievement of Company and individual performance objectives. The Company reserves the right to unilaterally decide on any changes to, or cessation of, the bonus.

4.3 The salary and bonus target are normally subject to annual review.

5 Pension and insurance

5.1 The Employee's employment will expire by the end of the month of the Employee's 67th birthday.

5.2 The Employee shall be entitled to insurance and pension benefits in accordance with the Company's policy as applicable from time to time.

6 Work equipment

For the performance of the Employee's duties, the Company will provide such equipment that the Company deems necessary from time to time.

7 Expenses

7.1 Entertainment expenses incurred in compliance with Company regulations will be reimbursed and such expenses must be itemised and verified.

7.2 Expenses drawn on the Company's credit card (which will be available for the Employee's use), which the Employee has not accounted for in accordance with the Company's expense reporting policy within one (1) month of the due date of the credit card company's invoice, may be set off by the Company against the Employee's net salary.

8 Vacation

The Employee is entitled to 30 days paid vacation per each yearly period of service to be taken at such times as agreed with the Company. Vacation pay is calculated in accordance with the Company's policy as applicable from time to time. In conjunction with the cessation of employment, any vacation pay paid in advance may be deducted from any salary and accrued vacation pay.

9 Sick pay

In case of absence due to sickness the provisions of the Swedish Sick Pay Act (*Sw. lagen om sjuklön (1991:1047)*) shall apply.

10 Personal data and data security

10.1 The Employee confirms that the Company has informed the Employee of the Company's use of employees' personal data in accordance with the provisions of the Swedish Personal Data Protection Act (Sw. *personuppgiftslagen (1998:204)*).

10.2 The Employee agrees to comply with the Company's policies regarding the use of the Company's computers, e-mail system, Internet services and other software programs. The Employee is aware and acknowledges that the Company has unrestricted access to all material and e-mail correspondence and an overview of Internet usage that is saved in or performed via the Company's data system.

11 Intellectual property rights

11.1 All rights to any material and results within the Company's field of activity, and all intellectual property rights related thereto (including but not limited to all patents, inventions, trademark rights, copyrights and neighbouring rights, rights in computer software and database rights, design rights, trade secrets and know-how including the rights to registrations or applications for these rights), which are made, written, designed or produced by the Employee during the term of the Employee's employment shall exclusively vest in the Company, irrespective of whether such material, results and intellectual property rights are produced during or outside of working hours and irrespective of whether produced with the use of the Company's facilities. This applies irrespective of whether the Employee has been instructed or has taken own initiative to produce such material, results and intellectual property rights. The Company shall have a right to freely develop and alter such material, results and intellectual property rights and to licence and assign them to third parties, with or without a reference to the Employee's name. The above-mentioned right of the Company includes any patent applications for inventions that have been created through the participation of the Employee and which have been filed within six (6) months after the termination of the employment, provided that the invention falls within the Company's field of activity and that the Employee is unable to reasonably prove that the invention was made after the employment was terminated.

11.2 The Employee shall not be entitled, directly or indirectly, to use or exploit the material, results and intellectual property rights referred to in Section 11 in any manner whatsoever during the term of the Employee's employment or thereafter unless obtaining a written confirmation regarding such use from the Company. However, this Section 11.2 shall not prevent the Employee from using such material, results and/or intellectual property rights to the extent such use is necessary for the Employee's performance of his/her normal contractual duties under this Agreement. In cases of uncertainty, the Employee shall always obtain written approval from the Company.

11.3 The Employee confirms that the compensation agreed in this Agreement for the performed work is reasonable and constitutes satisfactory compensation for the assignment in Section 11 and hereby waives any claims for royalty or other compensation for the assignment, exploitation or use of the assigned rights, to the extent permitted by law. The Employee furthermore undertakes not to make any claims against the Company's, its subsidiaries' or successors' ownership or other rights to the assigned rights in Section 11.

11.4 The Employee agrees to inform the Company in writing of all inventions, ideas, discoveries, developments or improvements wholly or partially made by the Employee during the term of the Employee's employment. Such information shall be given continuously, and without delay after creation.

11.5 The Employee agrees and undertakes without any additional compensation, during or after the Employee's employment, to execute all such deeds and documents that, in the Company's sole discretion, are necessary or desirable in order for the Company to be able to protect, register, maintain and in any other way fully enjoy the Company's rights referred to under this Section 11.

12 Confidentiality

12.1 The Employee shall not at any time during the employment or thereafter utilise, reproduce or disclose to any person or firm or company (unless required by the performance of the Employee's duties under this Agreement or by law) any information in respect of the Company or any of its associated companies that the Employee will gain access to through the employment and that the Company reasonably wishes to keep confidential.

12.2 Confidential information shall include, without limitation and in whatever form, information concerning the Company and its associated companies:

- business, current and potential business relations, business plans, strategic plans investigations, finances and financial statements;
- employees, terms of employment and other human resources matters;
- customers, suppliers and distributors;
- prices and pricing policies, marketing, sales methods, contracts;
- trade secrets, know-how, methods, software programs, new products and services, safety devices, etc.

12.3 Confidential information shall not include information that enters the public domain, other than through a breach by the Employee of an obligation of confidentiality owed to the Company or its associated companies.

12.4 The Employee agrees that the Employee will not, during the employment with the Company, improperly use or disclose any proprietary information or trade secrets of any former or concurrent employer or other person or entity. Further, the Employee will not bring into the Company any proprietary information or trade secret of any such employer, person or entity unless consented to in writing by such employer, person or entity.

13 Non-competition

13.1 The Parties hereby agree that the Employee in the course of the employment will gain access to company-specific trade secrets that cannot be protected through patents or other similar registrations and which may cause the Company considerable harm if used for the benefit of a competing business. The Parties furthermore agree that it is a precondition for the Employee's employment that the Company can disclose such

information to the Employee in the knowledge that it will not be used to engage in or promote a business that competes with the Company's (or any associated company's) business. The Employee thus agrees to refrain, during the term of this Agreement and for a period of six (6) months after its termination, directly or indirectly, whether alone or as a partner, officer, employee, director or executive or consultant, from engaging, participating or investing in any business activity anywhere in the world that develops, markets or sells any products, or performs or sells any services that directly or indirectly target the pharmacological restoration of normal function to wild type or missense-mutant p53 in oncologic applications .

- 13.2 Subject to the exceptions stated below in this section, the Company shall, as compensation for the inconvenience that the existing non-competition covenant causes the Employee after the expiry of the employment, pay the Employee per month the difference between the Employee's average monthly remuneration (both fixed and variable) paid by the Company during the twelve (12) months preceding the time of termination of the employment and the (lower) salary which the Employee earns, or reasonably could have earned from any new employment or proceeds of any business activity. However, the monthly compensation payable by the Company shall never exceed sixty (60) per cent of the Employee's average monthly remuneration as set out above during the restrictive period of the non-competition covenant. For the avoidance of doubt, if the Employee, despite reasonable efforts to minimise the Employee's loss of income, does not obtain new employment or is not engaged in any business activity after the employment with the Company has terminated, the Company shall pay the Employee per month sixty (60) per cent of the Employee's average monthly remuneration as set out above during the restrictive period of this non-competition covenant. The right to compensation according to this section presupposes that there is a causal relationship between the Employee's undertaking in accordance with the non-competition covenant and the loss of income that is caused by its application. Compensation shall not be paid in case of the Employee's breach of this non-competition covenant.
- 13.3 After the expiry of employment, the Employee is obliged to inform the Company of the level of the Employee's current salary from any new employment or proceeds of any business activity. Such written information shall be provided to the Company no later than on the 15th day of each month. In the absence of such written information, it shall be understood that the Employee has not suffered any loss of income with regards to the concerned month, but Section 13.1 shall still apply.
- 13.4 Compensation according to Section 13.2 above shall not be paid during any period for which the Employee receives severance pay from the Company or if the employment expires: (i) due to the Employee's retirement; or (ii) due to cancellation of this Agreement with immediate effect or the Company's immediate dismissal of the Employee.
- 13.5 During the term of employment, as well as in the event of either party's termination of the employment and as long as the non-competition covenant is in force, the Company may unilaterally subject to one (1) month's prior written notice either limit the application of the non-competition covenant or completely release the Employee from the non-competition covenant. In the event of a full release from the non-competition

covenant, the Company shall be released from the obligation to pay compensation in accordance with Section 13.2 above.

14 Non-solicitation

14.1 During the term of this Agreement and for six (6) months following the termination thereof, the Employee shall not, directly or indirectly, engage or participate in professional contacts with anyone who, during the twelve (12) months preceding the termination of the Employee's employment, has been a customer or client of the Company or any of its associated companies or is a potential customer or client who has been actively approached by the Company or any of its associated companies, with the intention of persuading such customer or client/potential customer or client to change the business relationship, to cease to do business with or to refrain from initiating a business relationship with the Company or any of its associated companies. The Company may through written notification release the Employee from this obligation in specific cases.

14.2 During the term of this Agreement and for six (6) months following the termination thereof, the Employee shall not directly or indirectly solicit or attempt to solicit employees of the Company, or any of its associated companies, or use their services for any means other than for the benefit of the Company. The Company may through written notification release the Employee from this obligation in specific cases.

15 Termination of employment

15.1 This Agreement may be terminated by the Company subject to six (6) months' notice and by the Employee subject to six (6) months' notice. In the event the employment agreement extends beyond the end of the month of the Employee's 67th birthday, such extension shall be governed by provisions of the Swedish Employment Protection Act.

15.2 The Company is entitled to terminate the employment summarily without notice in the event of the Employee's gross misconduct or material breach of any of the terms of this Agreement. However, notwithstanding such termination, the Employee's obligations pursuant to Section 11 (Intellectual Property Rights), Section 12 (Confidentiality), Section 13 (Non-competition) and Section 14 (Non-solicitation) shall remain in full force and effect.

15.3 In conjunction with the expiry of the employment, the Employee shall deliver up to the Company all reports, papers, correspondence, documents and any other materials (including copies thereof) supplied, or entrusted to the Employee or in the Employee's possession in connection with this employment and/or relating to the Company, its associated companies and/or their businesses and the same shall at all times remain the sole property of the Company or the associated company as the case may be.

16 Amendments

This Agreement may only be amended by an instrument in writing duly executed by the Parties.

17 **Governing law**

17.1 This Agreement shall be governed by and construed in accordance with the laws of Sweden.

17.2 Any dispute, controversy or claim arising out of or in connection with this Agreement, or the breach, termination or invalidity thereof, shall be settled by arbitration in accordance with the Swedish Arbitration Act (*Sw. lagen (1999:116) om skiljeförfarande*).

17.3 The arbitral tribunal shall be composed by one (1) arbitrator. In case the Parties are unable to agree on the appointment of the arbitrator, the arbitrator shall be appointed by the Arbitration Institute of the Stockholm Chamber of Commerce.

17.4 The Parties undertake and agree that all arbitral proceedings conducted by reference to this arbitration section will be kept strictly confidential. This confidentiality undertaking shall cover all information disclosed in the course of such arbitral proceedings, as well as any decision or award that is made or declared during the proceedings. Information covered by this confidentiality undertaking may not, in any form, be disclosed to a third party without the written consent of both Parties hereto. Notwithstanding the foregoing, a party shall not be prevented from disclosing such information in order to secure its interests against the other Party in connection with a dispute or if required to do so by law, any applicable stock exchange regulations or the regulations of any other recognised market place.

17.5 The Company shall, unless the arbitrator holds that the Employee has caused the initiation of arbitral proceedings without reasonable cause, pay the arbitrator's fees and, if applicable, the fees of the Arbitration Institute of the Stockholm Chamber of Commerce. Other costs, such as legal fees, shall be apportioned between the Parties in accordance with the provisions of the Swedish Code of Judicial Procedure (*Sw. rättegångsbalken (1942:740)*).

This Agreement has been duly executed in two (2) original copies of which each of the Parties has received one.

Place: Stockholm

Date: September 7, 2016

Aprea AB

/s/ Christian S. Schade
Christian S, Schade
CEO

/s/ Lars Abrahmsén

Lars Abrahmsén

July 15, 2016

Greg Korbel
3929 Netherfield Road
Philadelphia, PA 19129

Dear Greg:

On behalf of Aprea (US), Inc. (the "Company"), a wholly-owned U.S. subsidiary of Aprea AB ("Aprea"), I am pleased to confirm the terms and conditions of your employment as set forth below in this letter agreement (this "Agreement"). Certain capitalized terms used in this Agreement without definition are defined in Section 14.

1. **Position.** Effective as of July 15, 2016, you will serve as the Vice President, Business Development, of the Company. As Vice President, Business Development, you will have overall responsibility for the business development strategy and operations of the Company. You will report to the Company's Chief Executive Officer. It is understood and agreed that, while you render services to the Company, you will not engage in any other employment, consulting or other business activities, except for business and professional activities that do not interfere with your obligations under this Agreement and that are first disclosed to and approved by the Company's Chief Executive Officer or Board of Directors (the "Board").
 2. **Place of Performance.** Your primary place of performance will be offices of the Company located in or around Boston, Massachusetts, and from time-to-time you may be required to travel to Company or Aprea offices located in Sweden and other geographic locations in connection with the performance of your duties.
 3. **Salary.** The Company will pay you a salary at the rate of U.S. \$220,000 per year, payable in accordance with its standard payroll practices and subject to applicable deductions and withholdings. Your salary will be subject to periodic review and increase at the Board's discretion in conjunction with the Company's annual performance reviews.
 4. **Bonus Compensation.** You will be eligible for a bonus targeted at 20% of your base salary. For 2016, you will receive a prorated bonus based upon the fraction of the calendar year remaining from the commencement date of your employment. Bonus payments are discretionary and will be based on achievement of Company and individual performance objectives, as determined by the Board in consultation with the Chief Executive Officer. Payment of any bonus compensation shall be made in a single lump sum payment no later than March 15 of the year following the year to which the bonus relates. Payment of your bonus compensation is not contingent on continued employment; if you are awarded a bonus, so long as you have not voluntarily terminated your employment or been terminated by the Company for Cause, the bonus will be paid to you regardless of whether you are still employed by the Company on the date on which the lump sum bonus payment is otherwise payable.
 5. **Benefits/Vacation.** You will be eligible to participate in the employee benefits and insurance programs generally made available to full-time executive officers of the Company, including 20 days of paid time off and the Company's standard medical and dental programs.
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6. **At-Will Employment, Accrued Obligations.** Your employment will be “at will,” meaning you or the Company may terminate it at any time for any or no reason. In the event of the termination of your employment for any reason, the Company shall pay you the Accrued Obligations, defined as (a) your base salary through the date of termination, (b) an amount equal to the value of your accrued unused vacation days, and (c) the amount of any expenses properly incurred by you on behalf of the Company prior to any such termination and not yet reimbursed.

7. **Termination Without Cause or by Reason of Death or Disability.** In the event that (a) the Company terminates your at-will employment without Cause, or your employment terminates by reason of your death or Disability, and (b) you (and/or your representative, if applicable) (i) enter into, do not revoke, and comply with the terms of a separation agreement in a form acceptable to the Company, which shall include a release against the Company, Aprea and related persons and entities (the “Release”); (ii) resign from any and all positions, including, without implication of limitation, as a director, trustee, and officer, that you then hold with the Company, Aprea or any Affiliate of the Company; and (iii) return all property belonging to the Company, Aprea or its Affiliates (“Company Property”) and comply with any instructions related to deleting and purging duplicates of such Company property (collectively, the “Termination Benefits Conditions”), the Company will continue your base salary for three months (six months if such termination occurs during the twelve-month period that immediately follows a Change of Control) (the “Termination Benefits”). Any severance payments due hereunder shall commence (and, if applicable, any prorated bonus payment shall be made) as soon as administratively feasible within 60 days after your termination of employment provided you have timely executed and returned the Release and, if a revocation period is applicable, you have not revoked the Release. Solely for purposes of Section 409A of the Internal Revenue Code of 1986, as amended (the “Code”), each installment payment is considered a separate payment. To the full extent permitted by Code Section 409A, it is intended that any severance benefit hereunder shall be exempt from the requirements of Code Section 409A by reason of either (1) the exemption set forth in Treas. Regs. Section 1.409A-1(b)(9)(iii) or (2) the short-term deferral rule under Treas. Regs. Section 1.409A-1(b)(4).

8. **Termination of Employment Due to Your Resignation or Termination by the Company for Cause.** In the event your employment is terminated as a result of your (a) resignation for any reason, or (b) termination for Cause by the Company, you will not be eligible for any Termination Benefits.

9. **Confidential Information and Restricted Activities.** By signing this Agreement, you represent that you have carefully read and considered all the terms and conditions of this Agreement, including the restraints imposed on you pursuant to Sections 9, 10 and 11 of this Agreement (collectively, the “Restrictive Covenant Agreements”). For purposes of the Restrictive Covenant Agreements, “Company” shall mean the Company and its Affiliates. You agree that during your employment and for the twelve month period after your employment with the Company ends for any reason (the “Restricted Period”) you will not (without the Company’s prior written consent), whether as owner, partner, shareholder, director, consultant, agent, employee, co-venturer or otherwise, (a) engage, participate or invest in any business activity anywhere in the world that develops, markets or sells any products, or performs or sells any services that directly or indirectly target the pharmacological restoration of normal function to

wild type or missense-mutant P53 in oncologic applications; provided that this shall not prohibit any investment by you in publicly traded stock of a company representing less than two percent of the stock of such company, (b) (i) solicit or attempt to solicit, or (ii) take away or divert from the Company, or attempt to take away or divert from the Company, the business or patronage of any customer(s) known to you or with respect to which you were involved in soliciting, in each case at any time during the twelve-month period that immediately preceded the termination of your employment with the Company and with which, as a result of your employment with the Company, you had business dealings or about which your acquired confidential information, or (c) (i) recruit or attempt to recruit, solicit or attempt to solicit, hire or attempt to hire, interfere with or endeavor to entice away or (ii) assist in recruiting or attempting to recruit, soliciting or attempting to solicit, hiring or attempting to hire, interfering with or enticing away any person who is or was employed by the Company or is or was an agent, representative or consultant of the Company within the six-month period preceding the termination of your employment with the Company. You agree without reservation that these restraints are necessary for the reasonable and proper protection of the Company, and that each and every one of the restraints is reasonable in respect to subject matter, length of time and geographic area. Any breach of any of the Restrictive Covenant Agreements is likely to cause the Company substantial and irrevocable damage and therefore, in the event of such breach, the Company, in addition to such other remedies which may be available, will be entitled to specific performance and other injunctive relief. If you breach any of the covenants contained in the Restrictive Covenant Agreements, in addition to the Company's other legal and equitable remedies, the Company may cease any Termination Benefits to which you might otherwise be entitled. Any such termination of the Termination Benefits by the Company in the event of a breach by you shall not affect your ongoing obligations to the Company including pursuant to the Release. You further understand that your obligations under the Restrictive Covenant Agreements will continue in accordance with their express terms regardless of any changes in your title, position, duties, salary, compensation or benefits or other terms and conditions of employment. You expressly consent to be bound by the provisions of the Restrictive Covenant Agreements for the benefit of the Company or any Affiliate or successor to whose employ you may be transferred.

10. Return of Property. All files, letters, notes, memoranda, reports, records, data, sketches, drawings, notebooks, layouts, charts, quotations and proposals, specification sheets, program listings, blueprints, models, prototypes, or other written, photographic or other tangible material containing Company information, whether created by you or others, which come into your custody or possession, are the exclusive property of the Company to be used by you only in the performance of your duties for the Company. Any property situated on the Company's premises and owned by the Company, including without limitation computers, disks and other storage media, filing cabinets or other work areas, is subject to inspection by the Company at any time with or without notice. In the event of the termination of your employment for any reason, you will deliver to the Company all files, letters, notes, memoranda, reports, records, data, sketches, drawings, notebooks, layouts, charts, quotations and proposals, specification sheets, program listings, blueprints, models, prototypes, or other written, photographic or other tangible material containing proprietary information, and other materials of any nature pertaining to the proprietary information of the Company and to your work performed for the Company, and will not take or keep in your possession any of the foregoing or any copies.

11. Developments. You will make full and prompt disclosure to the Company of all inventions, discoveries, designs, developments, methods, modifications, improvements, processes, algorithms, databases, computer programs, formulae, techniques, trade secrets, graphics or images, audio or visual works, and other works of authorship (collectively "Developments"), whether or not patentable or copyrightable, that are created, made, conceived or reduced to practice by you (alone or jointly with others) or under your direction during the period of your employment. You acknowledge that all work performed by you is on a "work for hire" basis, and you hereby do assign and transfer and, to the extent any such assignment cannot be fully made at present, will assign and transfer, to the Company and its successors and assigns all your right, title and interest in all Developments that (a) relate to the business of the Company or any customer of or supplier to the Company or any of the products or services being researched, developed, manufactured, commercialized, marketed or sold by the Company or that may be used with such products or services; or (b) result from tasks assigned to you by the Company; or (c) result from the use of premises or personal property (whether tangible or intangible) owned, leased or contracted for by the Company ("Company-Related Developments"), and all related patents, patent applications, trademarks and trademark applications, copyrights and copyright applications, and other intellectual property rights in all countries and territories worldwide and under any international conventions ("Intellectual Property Rights"). To preclude any possible uncertainty, you have provided on Exhibit A to this Agreement a complete list of Developments that you have, alone or jointly with others, conceived, developed or reduced to practice prior to the commencement of your employment with the Company that you consider to be your property or the property of third parties and that you wish to have excluded from the scope of this Agreement ("Prior Inventions"). You have also listed on Exhibit A all patents and patent applications in which you are named as an inventor, other than those that have been assigned to the Company, ("Other Patent Rights"). If no such disclosure is set forth on Exhibit A, you represent that there are no Prior Inventions or Other Patent Rights. If, in the course of your employment with the Company, you incorporate a Prior Invention into a Company product, process or machine or other work done for the Company, you hereby grant to the Company a nonexclusive, royalty-free, irrevocable, worldwide license (with the full right to sublicense) to make, have made, modify, use and sell such Prior Invention. Notwithstanding the foregoing, you will not incorporate, or permit to be incorporated, Prior Inventions in any Company-Related Development without the Company's prior written consent. This Agreement does not obligate you to assign to the Company any Development that, in the sole judgment of the Company, reasonably exercised, is developed entirely on your own time and does not relate to the business efforts or research and development efforts in which, during the period of your employment, the Company actually is engaged or reasonably would be engaged, and does not result from the use of premises or equipment owned or leased by the Company. However, you will also promptly disclose to the Company any such Developments for the purpose of determining whether they qualify for such exclusion. You understand that to the extent this Agreement is required to be construed in accordance with the laws of any state that precludes a requirement in an employee agreement to assign certain classes of inventions made by an employee, this Section 12 will be interpreted not to apply to any invention which a court rules and /or the Company agrees falls within such classes. You also hereby waive all claims to any moral rights or other special rights which you may have or accrue in any Company-Related Developments.

12. Enforcement of Agreement; Relief. You acknowledge and agree that the Restrictive Covenant Agreements and all other provisions of this Agreement that are intended to endure beyond the terms of your employment shall survive the termination of your employment and that any violation of any of the Restrictive Covenant Agreements will cause immediate and irreparable damage to the Company, entitling it to injunctive relief and other equitable remedies. You specifically consent to the issuance of temporary, preliminary, and permanent injunctive relief to enforce the terms of this Agreement. In addition to injunctive relief, the Company is entitled to all money damages available under the law.

13. Definitions. For purposes of this Agreement:

“Affiliates” means all persons and entities directly or indirectly controlling, controlled by or under common control with the Company, where control may be by management authority, or an equity interest of 50% more (direct or indirect).

“Cause” means, in the sole discretion of the Chief Executive Officer: (i) conduct by you in connection with your service to the Company or any Affiliate that is fraudulent, unlawful or grossly negligent; (ii) your material breach of your material responsibilities to the Company or any Affiliate or your willful failure to comply with reasonable and lawful directives of the Board or written policies of the Company that results in harm to the Company or any Affiliate; (iii) material breach by you of your material representations, warranties, covenants and/or obligations under the this Agreement; (iv) material misconduct by you that seriously discredits or damages the Company or any Affiliate; and/or (v) nonperformance or unsatisfactory performance of your material duties or responsibilities to the Company or any Affiliate; in the case of each of (ii), (iii), (iv) and (v) as determined in good faith by the Chief Executive Officer after written notice to you providing reasonable details of the alleged breach and not less than a 30 day period to cure the alleged breach; provided that the Company may suspend your employment, access, authority and duties during such cure period.

“Change of Control” will mean the occurrence of any of the following events after the date hereof:

(i) the acquisition of the Company by another person or entity (other than an Affiliate) by means of any transaction or series of related transactions (including, without limitation, any reorganization, merger or consolidation or stock transfer, but excluding any such transaction effected primarily for the purpose of changing the domicile of the Company or any of its Affiliates), unless the Company stockholders of record immediately prior to such transaction or series of related transactions hold, immediately after such transaction or series of related transactions, at least 50% of the voting power of the surviving or acquiring entity; provided that neither the sale by the Company or any of its Affiliates of its securities for the purposes of raising additional funds nor any trading in the Company’s capital stock after such time, if any, as the Company shall have a class of securities registered under the Securities Exchange Act of 1934 shall constitute a Change of Control hereunder; or

(ii) a sale, exclusive worldwide license or other disposition of all or substantially all of the assets of the Company other than to an Affiliate.

14. Tax Matters.

All payments and forms of compensation referred to in this Agreement are subject to reduction to reflect applicable withholding and payroll taxes and other deductions required by law. You hereby acknowledge that neither the Company has no duty to design its compensation policies in a manner that minimizes your tax liabilities, and you will not make any claim against the Company or any of its Affiliates, or the Board related to tax liabilities arising from your compensation.

Anything in this Agreement to the contrary notwithstanding, if at the time of your separation from service within the meaning of Section 409A of the Code, the Company determines that you are a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that you becomes entitled to under this Agreement on account of your separation from service would be considered deferred compensation subject to the 20% additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (a) six months and one day after your separation from service, or (b) your death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six-month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule. All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by you during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit. To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon your termination of employment, then such payments or benefits shall be payable only upon your "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h). the Company and you intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with (or are exempt from) Section 409A of the Code. The Company makes no representation or warranty and shall have no liability to you or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

In the event that the Company determines in good faith that any payments or benefits (whether made or provided pursuant to this Agreement or otherwise) provided to you constitute

“parachute payments” within the meaning of Section 280G of the Code (“Parachute Payments”) and may be subject to an excise tax imposed pursuant to Section 4999 of the Code, the Parachute Payments will be reduced to an amount determined by the Company in good faith to be the maximum amount that may be provided to you (after taking into account the value of the Restrictive Covenant Agreements, reasonable compensation for services, and any other available exemption) without resulting in any portion of such Parachute Payments being subject to such excise tax (the amount of such reduction, the “Cutback Benefits”); provided, however, that no such reduction shall apply if either (a) the Company’s stockholders approve the Cutback Benefits (in accordance with the procedure described below) or (b) upon your request, the Company does not seek such stockholder approval and your net after-tax benefit, after applying the excise tax required by Section 4999 of the Code with respect to the full amount of the Parachute Payments (without reduction), would be more than your net after-tax benefit after subtracting the Cutback Benefits. You shall be entitled to select which Parachute Payments (of those that are not considered to be deferred compensation under Section 409A of the Code) shall be reduced hereunder; provided that if you fail to so select promptly, the Company shall select which Parachute Payments (of those that are not considered to be deferred compensation under Section 409A of the Code) will be reduced. Parachute Payments that are considered to be deferred compensation under Section 409A of the Code shall be reduced only to the extent that the complete reduction of the Parachute Payments in the preceding sentence is insufficient to eliminate the imposition of the excise tax imposed under Section 4999 of the Code. Notwithstanding the foregoing, if applicable to the Company at that time, upon your request, the Company shall use reasonable efforts to obtain the approval of the Cutback Benefits by the Company’s stockholders in the manner contemplated by Q&A 7 of Treas. Reg. Section 1.280G-1, it being understood and agreed that the Company does not guarantee that such approval will be obtained. If the Company seeks but fails to attain the required stockholder approval described in the immediately preceding sentence, you will forfeit the Cutback Benefits.

15. Interpretation, Amendment and Enforcement. This Agreement, the Restrictive Covenant Agreements, and any other agreements evidencing equity grants to you by the Company and its Affiliates constitute the complete agreement between you and the Company, contain all of the terms of your employment with the Company and supersede any prior agreements, representations or understandings (whether written, oral or implied) between you and the Company or its Affiliates relating to the subject matter herein. The terms of such agreements and the resolution of any disputes as to the meaning, effect, performance or validity of this Agreement or arising out of, related to, or in any way connected with, this Agreement, your employment with the Company or any other relationship between you and the Company and its Affiliates (the “Disputes”) will be governed by the laws of the State of Delaware, excluding laws relating to conflicts or choice of law. You and the Company submit to the exclusive personal jurisdiction of the federal and state courts located in the State of Delaware in connection with any Dispute or any claim related to any Dispute.

16. Assignment. Neither you nor the Company may make any assignment of this Agreement or any interest in it, by operation of law or otherwise, without the prior written consent of the other; provided, however, that the Company may assign its rights and obligations under this Agreement (including, without limitation, the Restrictive Covenant Agreements) without your

consent to one of its Affiliates or to any person with whom the Company or Aprea shall hereafter effect a reorganization, consolidate with, or merge into or to whom it transfers all or substantially all of its properties or assets. This Agreement shall inure to the benefit of and be binding upon you and the Company, and each of our respective successors, executors, administrators, heirs and permitted assigns.

17. Severability. In case any provisions (or portions thereof) contained in this Agreement (including the Restrictive Covenant Agreements) shall, for any reason, be held invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect the other provisions of this Agreement, and this Agreement shall be construed as if such invalid, illegal or unenforceable provision had never been contained herein. If, moreover, any one or more of the provisions contained in this Agreement shall for any reason be held to be excessively broad as to duration, geographical scope, activity or subject, it shall be construed by limiting and reducing it, so as to be enforceable to the extent compatible with the applicable law as it shall then appear.

18. Miscellaneous. This Agreement may not be modified or amended, and no breach shall be deemed to be waived, unless agreed to in writing by you and a duly authorized officer or board member of the Company. The headings and captions in this Agreement are for convenience only and in no way define or describe the scope or content of any provision of this Agreement. The words "include," "includes" and "including" when used herein shall be deemed in each case to be followed by the words "without limitation." This Agreement may be executed in two or more counterparts, each of which shall be an original and all of which together shall constitute one and the same instrument. A facsimile or electronic transmission of a scanned copy of a signed counterpart signature page to this Agreement shall be deemed to be an originally executed copy for purposes of this Agreement.

19. Other Terms. By signing this Agreement, you confirm to the Company that you have no contractual commitments or other legal obligations that would or may prohibit you from entering into this Agreement or performing your duties for the Company.

To indicate your acceptance of this Agreement, please sign and date this Agreement in the space provided below and return it to me by July 15, 2016. We look forward to working with you.

Very truly yours,

APREA (US), Inc.

By: /s/ Christian S. Schade
Christian S. Schade
Chief Executive Officer

Accepted and Agreed:

/s/ Greg Korb
Greg Korb

Dated: July 15, 2016

EXHIBIT A

Prior Inventions and Other Patent Rights

None.

EMPLOYMENT AGREEMENT

THIS EMPLOYMENT AGREEMENT (the "Agreement") between APREA THERAPEUTICS, INC., a Delaware corporation (the "Company"), and Scott M. Coiante (the "Executive"), is made and entered into as of September 26, 2019, and will become effective, if at all, upon the date of closing of the Company's initial public offering of stock pursuant to an effective registration statement filed under the Securities Act of 1933, as amended (the "Effective Date").

WHEREAS, the Company desires to continue to employ Executive on the terms and conditions contained herein;

WHEREAS, the Company and Executive previously entered into an employment letter agreement, dated as of August 5, 2019 (the "Prior Agreement");

WHEREAS, Executive desires to continue to be employed by and render services to the Company upon and subject to the terms, conditions and other provisions set forth herein.

NOW THEREFORE, in consideration of the promises and mutual covenants and agreements contained herein, the adequacy of all of which consideration is hereby acknowledged, the parties hereby agree as follows:

1. Agreement and Term. The Company hereby agrees to continue to employ Executive, and Executive hereby accepts such employment and agrees to render such services to the Company, on the terms and conditions set forth in this Agreement. Unless terminated earlier as set forth in Section 4 herein, Executive's employment and the term under this Agreement shall commence under the terms set forth herein on the Effective Date and shall continue until the third-anniversary of the Effective Date (the "Initial Term") and, thereafter, shall be extended automatically for successive one-year terms, unless either Executive or the Company gives contrary written notice not less than 60 days in advance of the expiration of the Initial Term or any succeeding term of this Agreement. The Initial Term, together with any extension thereof in accordance with this Section 1, shall be referred to herein as the "Term."

2. Positions and Authority. Executive shall serve in the position of Senior Vice President, Chief Financial Officer of the Company, or in such other position as the parties may agree. Executive agrees to serve in the officer position referred to in this Section 2, and to perform diligently and to the best of his abilities the duties and services appertaining to such offices as set forth in the Bylaws of the Company, as well as such additional duties and services appropriate to such offices that the parties may agree upon from time to time. Upon the Effective Date, Executive's principal place of work shall be located in Boston, Massachusetts.

During the Term, Executive shall devote Executive's full business time and efforts to the business and affairs of the Company and its subsidiaries, provided that the Executive shall be entitled to serve as a member of the board of directors of a reasonable number of other companies, to serve on civic, charitable, educational, religious, public interest or public service boards, and to manage the Executive's personal and family investments, in each case, to the extent such activities do not materially interfere with the performance of the Executive's duties and responsibilities

hereunder. Executive shall not become a director of any for profit entity without first receiving the approval of the Chief Executive Officer of the Company.

3. Compensation and Benefits

(a) Base Salary. As compensation for Executive's performance of Executive's duties hereunder, Company shall pay to Executive an initial Base Salary of \$350,000 per year, payable in accordance with the normal payroll practices of the Company. The Base Salary shall be reviewed for increases but not decreases by the Compensation Committee of the Board (the "Compensation Committee") in good faith, based upon the Company's and Executive's performance and the Company's pay philosophy, not less often than annually. The term "Base Salary," shall refer to the Base Salary as may be in effect from time to time.

(b) Annual Incentive Compensation. During the Term, Executive shall be eligible to participate in the annual cash bonus program maintained for senior executive officers of the Company (the "Annual Incentive Program"), with an initial target annual bonus opportunity equal to 35% of Base Salary. The actual amount of the annual bonus earned by and payable to Executive for any year or portion of a year, as applicable, shall be determined upon the satisfaction of goals and objectives established by the Compensation Committee, and shall be subject to such other terms and conditions of the Annual Incentive Program as in effect from time to time. Each bonus paid under the Annual Incentive Program shall be paid to Executive no later than March 15th of the calendar year following the calendar year in which the bonus is earned.

(c) Long-Term Incentive Grants. During the Term, Executive shall be eligible to participate in the long-term incentive program maintained for senior executive officers of the Company (the "LTI Program"), with a LTI Program target opportunity and LTI Program Vehicles determined by the Compensation Committee for each year of participation.

(d) Employee Benefits and Perquisites. During the Term, the Executive shall be entitled to receive all benefits and perquisites of employment generally available to other members of the Company's senior executive management, upon Executive's satisfaction of the eligibility or participation criteria therefor. The Company reserves the right to modify or terminate employee benefits and perquisites at its discretion.

(e) Business Expenses. Subject to Section 17, Executive shall be reimbursed for reasonable travel and other expenses incurred in the performance of Executive's duties on behalf of the Company in a manner consistent with the Company's policies regarding such reimbursements, as may be in effect from time to time.

4. Termination of Employment. (a) The Term shall end upon the first to occur of: (i) the expiration of the term of this Agreement pursuant to Section 1 hereof; (ii) Termination due to Disability (as defined below); (iii) termination of Executive's employment by the Company for any reason other than Termination due to Disability; (iv) Executive's death; or (v) termination of Executive's employment by Executive for any reason. Upon the termination of Executive's employment with the Company for any reason, Executive shall be deemed to have resigned from all positions with the Company or any of its Affiliates held by Executive as of the date immediately preceding Executive's termination of employment.

(b) If Executive's employment ends for any reason, except as otherwise contemplated in this Section 4, Executive shall cease to have any rights to salary, bonus (if any) or other benefits, other than (i) the earned but unpaid portion of Executive's Base Salary through the date of termination or resignation, (ii) a lump-sum payment in respect of accrued but unused vacation days at the Executive's per-business-day Base Salary rate, (iii) any unpaid expense or other reimbursements due to Executive, and (iv) any other amounts or benefits required to be paid or provided by law or under any plan, program, policy or practice of the Company.

(c) Termination without Cause or for Good Reason. If Executive's employment hereunder shall be terminated by the Company without Cause, termination upon the expiration of the Term following notice of non-renewal by the Company, or by Executive for Good Reason, then in addition to the payments and benefits described in Section 4(b) and subject to Section 17 and Executive's continuing compliance with Section 5 of this Agreement:

(i) the Company shall pay Executive an amount equal to nine months of the Executive's Base Salary (the "Severance Payment"), payable during the nine-month period following such termination of employment, with the Severance Payment commencing as soon as administratively feasible within 60 days following Executive's termination of employment and the first installment payment including the portion of the Severance Payment that was payable prior to such first payment date; provided, however, if the Executive's employment is terminated under circumstances entitling the Executive to severance under this Section 4(c) within 12 months following a Change in Control (a "CIC Qualifying Termination"), then the Severance Payment and period to pay the Severance Payment shall be increased to 12 months;

(ii) the Company shall pay Executive an annual bonus for the year of termination equal to the Executive's target annual bonus opportunity, payable within 60 days following the Executive's termination of employment, subject to proration based on the number of days in the calendar year that have elapsed prior to the date of termination;

(iii) following the Executive's termination of employment, the Company shall pay to the Executive (or to the Executive's family in the event of Executive's death) on a monthly basis an amount equal to the monthly amount of the Consolidated Omnibus Budget Reconciliation Act of 1985 continuation coverage premium for such month, at the same level and cost to the Executive (or the Executive's family in the event of Executive's death) as immediately preceding the Executive's termination of employment, under the Company group medical plan in which the Executive participated immediately preceding the Executive's termination of employment, less the amount of the Executive's portion of such monthly premium as in effect immediately preceding the Executive's termination of employment, until the earlier of (A) nine months after the Executive's termination of employment and (B) the Executive and Executive's family have obtained other substantially similar healthcare coverage; provided, however, if the Executive experiences a CIC Qualifying Termination, then the number of months set forth in clause (A) of this sentence shall be increased to 12 months;

For the avoidance of doubt, Executive shall not be entitled to the benefits described in this Section 4(c) for a Termination due to Disability, termination of Executive's employment for

Cause, Executive's death, or termination of Executive's employment by Executive for any reason other than for Good Reason.

(d) Section 280G. Notwithstanding anything to the contrary in this Agreement, Executive expressly agrees that if the payments and benefits provided for in this Agreement or any other payments and benefits which Executive has the right to receive from the Company and its Affiliates (collectively, the "Payments"), would constitute a "parachute payment" (as defined in Section 280G(b)(2) of the Internal Revenue Code of 1986, as amended (the "Code")), then the Payments shall be either (i) reduced (but not below zero) so that the present value of the Payments will be one dollar (\$1.00) less than three times Executive's "base amount" (as defined in Section 280G(b)(3) of the Code) and so that no portion of the Payments received by Executive shall be subject to the excise tax imposed by Section 4999 of the Code or (ii) paid in full, whichever produces the better net after-tax position to Executive. The reduction of Payments, if any, shall be made by reducing first any Payments that are exempt from Section 409A of the Code and then reducing any Payments subject to Section 409A of the Code in the reverse order in which such Payments would be paid or provided (beginning with such payment or benefit that would be made last in time and continuing, to the extent necessary, through to such payment or benefit that would be made first in time). The determination as to whether any such reduction in the Payments is necessary shall be made by the Compensation Committee in good faith. If a reduced Payment is made or provided and, through error or otherwise, that Payment, when aggregated with other payments and benefits from Company (or its Affiliates) used in determining if a "parachute payment" exists, exceeds one dollar (\$1.00) less than three times Executive's base amount, then Executive shall immediately repay such excess to the Company.

(e) Certain Definitions.

"Affiliate" shall mean all persons and entities directly or indirectly controlling, controlled by or under common control with the Company, where control may be by management authority, or an equity interest of 50% or more (direct or indirect).

"Cause" shall mean, in the sole discretion of the Board:

- (i) conduct by Executive in connection with Executive's service to the Company or any Affiliate that is fraudulent, unlawful or grossly negligent;
- (ii) Executive's material breach of Executive's material responsibilities to the Company or any Affiliate or Executive's willful failure to comply with reasonable and lawful directives of the Board;
- (iii) Executive's material breach of Executive's material representations, warranties, covenants and/or obligations under this Agreement;
- (iv) material misconduct by Executive that seriously discredits or damages the Company or any Affiliate;
- (v) nonperformance or unsatisfactory performance of Executive's material duties or responsibilities to the Company or any Affiliate;

(vi) violation of the Company's or any of its Affiliates' policies including, without limitation, the Company's Code of Conduct and policies on equal employment opportunity and prohibition of unlawful harassment; and/or

(vii) the conviction of, or plea of nolo contendere to, any felony or a misdemeanor involving dishonesty or fraud

In the case of each of (ii), (iii), (iv), (v) and (vi) as determined in good faith by the Board after written notice to Executive providing reasonable details of the alleged breach and not less than a 30 day period to cure the alleged breach; provided that the Company may suspend Executive's employment, access, authority and duties during such cure period.

"Change in Control" shall have the meaning assigned to such term in the Company's 2019 Equity Incentive Plan.

"Good Reason" shall mean that Executive has complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following actions undertaken by the Company without Executive's express prior written consent:

(i) the changing of Executive's position from Senior Vice President, Chief Financial Officer;

(ii) a material diminution in Executive's responsibilities, authority or function as Senior Vice President, Chief Financial Officer;

(iii) a material reduction in Executive's Base Salary and/or annual target bonus opportunity; provided, however, that Good Reason shall not be deemed to have occurred in the event of a reduction in Executive's Base Salary and/or annual target bonus opportunity that is pursuant to a reduction program affecting substantially all of the senior level employees of the Company and that does not adversely affect Executive to a greater extent than other similarly situated senior level employees; or

(iv) a change of more than 50 miles in the geographic location at which Executive must regularly report to work and perform services, except for required travel on business of the Company; provided, however, that "Good Reason" shall not include, following a Change of Control, a reduction in title, position, responsibilities or duties solely by virtue of the Company being acquired and made part of, or operating as a subsidiary or division of a larger company or organization, as long as Executive's new duties and responsibilities are reasonably commensurate with Executive's experience.

"Good Reason Process" shall mean that: (i) Executive has reasonably determined in good faith that a "Good Reason" has occurred; (ii) Executive has notified the Board in writing of the first occurrence of the Good Reason condition within 60 days of the first occurrence of such condition; (iii) Executive has cooperated in good faith with the efforts of the Company, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) Executive terminates employment within 60 days after the end of the Cure Period. If the Good Reason

condition is cured by the Company during the Cure Period, Good Reason shall be deemed not to have occurred.

“Termination due to Disability,” shall mean Executive’s termination of employment as a result of Executive becoming incapacitated for a period of at least 180 days by accident, sickness or other circumstance that renders Executive mentally or physically incapable of performing the material duties as Senior Vice President, Chief Financial Officer.

5. Restrictive Covenants.

(a) Confidential Information and Restricted Activities. By signing this Agreement, Executive represents that Executive has carefully read and considered all the terms and conditions of this Agreement, including the restraints imposed on Executive pursuant to this Section 5 (collectively, the “Restrictive Covenant Agreements”). For purposes of the Restrictive Covenant Agreements, “Company,” shall mean the Company and its Affiliates. Executive agrees that during Executive’s employment and for the twelve month period after Executive’s employment with the Company ends for any reason (the “Restricted Period”) Executive will not (without the Company’s prior written consent), whether as owner, partner, shareholder, director, consultant, agent, employee, co-venturer or otherwise, (i) engage, participate or invest in any business activity anywhere in the world that develops, markets or sells any products, or performs or sells any services that directly or indirectly target the pharmacological restoration of normal function to wild type or missense-mutant P53 in oncologic applications; provided that this shall not prohibit any investment by Executive in publicly traded stock of a company representing less than two percent of the stock of such company, (ii) (A) solicit or attempt to solicit, or (B) take away or divert from the Company, or attempt to take away or divert from the Company, the business or patronage of any customer(s) known to Executive with respect to which Executive was involved in soliciting, in each case at any time during the twelve-month period that immediately preceded the termination of Executive’s employment with the Company and with which, as a result of Executive’s employment with the Company, Executive had business dealings or about which Executive acquired confidential information, or (iii) (A) recruit or attempt to recruit, solicit or attempt to solicit, hire or attempt to hire, interfere with or endeavor to entice away or (B) assist in recruiting or attempting to recruit, soliciting or attempting to solicit, hiring or attempting to hire, interfering with or enticing away any person who is or was employed by the Company or is or was an agent, representative or consultant of the Company within the six-month period preceding the termination of Executive’s employment with the Company. Executive agrees without reservation that these restraints are necessary for the reasonable and proper protection of the Company, and that each and every one of the restraints is reasonable in respect to subject matter, length of time and geographic area. Executive further understands that Executive’s obligations under the Restrictive Covenant Agreements will continue in accordance with their express terms regardless of any changes in Executive’s title, position, duties, salary, compensation or benefits or other terms and conditions of employment. Executive expressly consents to be bound by the provisions of the Restrictive Covenant Agreements for the benefit of the Company or any Affiliate or successor to whose employ Executive may be transferred.

(b) Return of Property. All files, letters, notes, memoranda, reports, records, data, sketches, drawings, notebooks, layouts, charts, quotations and proposals, specification sheets, program listings, blueprints, models, prototypes, or other written, photographic or other tangible

material containing Company information, whether created by Executive or others, which come into Executive's custody or possession, are the exclusive property of the Company to be used by Executive only in the performance of Executive's duties for the Company. Any property situated on the Company's premises and owned by the Company, including without limitation computers, disks and other storage media, filing cabinets or other work areas, is subject to inspection by the Company at any time with or without notice. In the event of the termination of Executive's employment for any reason, Executive will deliver to the Company all files, letters, notes, memoranda, reports, records, data, sketches, drawings, notebooks, layouts, charts, quotations and proposals, specification sheets, program listings, blueprints, models, prototypes, or other written, photographic or other tangible material containing proprietary information, and other materials of any nature pertaining to the proprietary information of the Company and to Executive's work performed for the Company, and will not take or keep in Executive's possession any of the foregoing or any copies.

(c) **Developments.** Executive will make full and prompt disclosure to the Company of all inventions, discoveries, designs, developments, methods, modifications, improvements, processes, algorithms, databases, computer programs, formulae, techniques, trade secrets, graphics or images, audio or visual works, and other works of authorship (collectively, "**Developments**"), whether or not patentable or copyrightable, that are created, made, conceived or reduced to practice by Executive (alone or jointly with others) or under Executive's direction during the period of Executive's employment. Executive acknowledges that all work performed by Executive is on a "work for hire" basis, and Executive hereby does assign and transfer and, to the extent any such assignment cannot be fully made at present, will assign and transfer, to the Company and its successors and assigns all Executive's right, title and interest in all Developments that (i) relate to the business of the Company or any customer of or supplier to the Company or any of the products or services being researched, developed, manufactured, commercialized, marketed or sold by the Company or that may be used with such products or services; or (ii) result from tasks assigned to Executive by the Company; or (iii) result from the use of premises or personal property (whether tangible or intangible) owned, leased or contracted for by the Company ("**Company-Related Developments**"), and all related patents, patent applications, trademarks and trademark applications, copyrights and copyright applications, and other intellectual property rights in all countries and territories worldwide and under any international conventions ("**Intellectual Property Rights**"). To preclude any possible uncertainty, Executive has provided on **Exhibit A** to this Agreement a complete list of Developments that Executive has, alone or jointly with others, conceived, developed or reduced to practice prior to the commencement of Executive's employment with the Company that Executive considers to be Executive's property or the property of third parties and that Executive wishes to have excluded from the scope of this Agreement ("**Prior Inventions**"). Executive has also listed on **Exhibit A** all patents and patent applications in which Executive is named as an inventor, other than those that have been assigned to the Company, ("**Other Patent Rights**"). If no such disclosure is set forth on **Exhibit A**, Executive represents that there are no Prior Inventions or Other Patent Rights. If, in the course of Executive's employment with the Company, Executive incorporates a Prior Invention into a Company product, process or machine or other work done for the Company, Executive hereby grants to the Company a nonexclusive, royalty-free, irrevocable, worldwide license (with the full right to sublicense) to make, have made, modify, use and sell such Prior Invention. Notwithstanding the foregoing, Executive will not incorporate, or permit to be incorporated, Prior Inventions in any Company-Related Development without the Company's prior written consent. This Agreement does not

obligate Executive to assign to the Company any Development that, in the sole judgment of the Company, reasonably exercised, is developed entirely on Executive's own time and does not relate to the business efforts or research and development efforts in which, during the period of Executive's employment, the Company actually is engaged or reasonably would be engaged, and does not result from the use of premises or equipment owned or leased by the Company. However, Executive will also promptly disclose to the Company any such Developments for the purpose of determining whether they qualify for such exclusion. Executive understands that to the extent this Agreement is required to be construed in accordance with the laws of any state that precludes a requirement in an employee agreement to assign certain classes of inventions made by an employee, this Section 5(c) will be interpreted not to apply to any invention which a court rules and /or the Company agrees falls within such classes. Executive also hereby waives all claims to any moral rights or other special rights which Executive may have or accrue in any Company-Related Developments.

(d) **Enforcement of Agreement; Relief.** Executive acknowledges and agrees that the Restrictive Covenant Agreements and all other provisions of this Agreement that are intended to endure beyond the terms of Executive's employment shall survive the termination of Executive's employment and that any violation of any of the Restrictive Covenant Agreements will cause immediate and irreparable damage to the Company, entitling it to specific performance, injunctive relief and other equitable remedies. Executive specifically consents to the issuance of temporary, preliminary, and permanent injunctive relief to enforce the terms of this Agreement. In addition to injunctive relief, the Company is entitled to all money damages available under the law. If Executive breaches any of the covenants contained in the Restrictive Covenant Agreements, in addition to the Company's other legal and equitable remedies, the Company may cease any termination benefits to which Executive might otherwise be entitled. Any such termination of the termination benefits by the Company in the event of a breach by Executive shall not affect Executive's ongoing obligations to the Company including pursuant to the Release.

(e) **Notice of Intent to Resign.** In the event Executive wishes to voluntarily terminate Executive's employment, Executive agrees to provide the Company with four (4) weeks advance written notice (the "**Notice Period**") of Executive's intent to do so, and, if Executive intends or contemplates alternative employment, Executive also agrees to provide the Company with accurate information concerning such alternative employment in sufficient detail to allow the Company to meaningfully exercise its rights under this Section 5. After receipt of such notice, the Company, in its sole, absolute and unreviewable discretion, may (i) require Executive to continue working during the Notice Period, (ii) relieve Executive of some or all of his work responsibilities during the Notice Period, or (iii) shorten the Notice Period and make Executive's voluntary termination of employment effective immediately. Notwithstanding the foregoing, if Executive provides notice of resignation, in no event shall Executive's separation of employment be considered an involuntary termination by the Company, even if the effective date of termination is accelerated by the Company.

(f) **Non-Disparagement.** Executive agrees during and following the Term not to make, or cause to be made, any statement, observation, or opinion, or communicate any information (whether oral or written, directly or indirectly) that (i) accuses or implies that the Company or its Affiliates engaged in any wrongful, unlawful or improper conduct, whether relating to Executive's employment (or the termination thereof), the business or operations of the Company or its

Affiliates, or otherwise or (ii) disparages, impugns, or in any way reflects adversely upon the business or reputation of the Company or its Affiliates. Nothing herein will be deemed to preclude Executive from providing truthful testimony or information pursuant to subpoena, court order, or similar legal process, instituting and pursuing legal action, or engaging in other legally protected speech or activities.

(g) **Protected Rights.** Notwithstanding anything in this Agreement to the contrary, Executive understands that nothing contained in this Agreement limits the Executive's ability to report possible violations of law or regulation to or file a charge or complaint with the Securities and Exchange Commission, the Equal Employment Opportunity Commission, the National Labor Relations Board, the Occupational Safety and Health Administration, the Department of Justice, the Congress, any Inspector General, or any other federal, state or local governmental agency or commission or regulatory authority (collectively, "**Government Agencies**"). Executive further understands that this Agreement does not limit his ability to communicate with any Government Agencies or otherwise participate in any investigation or proceeding that may be conducted by any Government Agency, including providing documents or other information, without notice to the Company. Furthermore (i) Executive shall not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that: (A) is made (x) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney; and (y) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal, and (ii) if Executive files a lawsuit for retaliation by the Company for reporting a suspected violation of law, Executive may disclose a trade secret to his or her attorney and use the trade secret information in the court proceeding, if Executive files any document containing the trade secret under seal and does not disclose the trade secret except pursuant to court order.

(h) **Breach.** Executive acknowledges that the restrictions contained in this Agreement are fair, reasonable, and necessary for the protection of the legitimate business interests of the Company, that the Company will suffer irreparable harm in the event of any actual or threatened breach by Executive, and that it is difficult to measure in money the damages which will accrue to the Company by reason of a failure by Executive to perform any of Executive's obligations under this **Section 5**. Accordingly, if the Company or any of its Affiliates institutes any action or proceeding to enforce their rights under this **Section 5**, to the extent permitted by applicable law, Executive hereby waives the claim or defense that the Company or its Affiliates has an adequate remedy at law, Executive shall not claim that any such remedy at law exists, and Executive consents to the entry of a restraining order, preliminary injunction, or other preliminary, provisional, or permanent court order to enforce this Agreement, and expressly waives any security that might otherwise be required in connection with such relief. Executive also agrees that any request for such relief by the Company shall be in addition and without prejudice to any claim for monetary damages and/or other relief which the Company might elect to assert. In the event Executive violates any provision of this **Section 5**, the Company shall be entitled to recover all costs and expenses of enforcement, including reasonable attorneys' fees, and the time periods set forth above shall be extended for the period of time Executive remains in violation of the provisions.

(i) **Release.** Executive's execution of a complete and general release of any and all of Executive's potential claims (other than for benefits and payments described in this Agreement or

any other vested benefits with the Company and/or its Affiliates) against the Company, any of its Affiliates, and their respective successors and any officers, employees, agents, directors, attorneys, insurers, underwriters, and assigns of the Company or its Affiliates and/or successors, is an express condition of Executive's right to receive termination payments and benefits under this Agreement. Executive shall be required to execute within 45 days after Executive's termination of employment (or such shorter period of time as specified by the Company) the Company's standard form of general waiver and release agreement which documents the release required under this [Section 5](#).

6. **Survival.** [Sections 5, 6, 8, 10, and 12 - 17](#), and such other provisions hereof as may so indicate shall survive and continue in full force and effect in accordance with their respective terms, notwithstanding any termination of the Term.

7. **Notices.** Any notice provided for in this Agreement shall be in writing and shall be delivered (i) personally, (ii) by certified mail, postage prepaid, (iii) by Federal Express or other reputable courier service regularly providing evidence of delivery (with charges paid by the party sending the notice), or (iv) by facsimile or a PDF or similar attachment to an email, provided that such telecopy or email attachment shall be followed within one (1) business day by delivery of such notice pursuant to clause (i), (ii) or (iii) above. Any such notice to a party shall be addressed at the address set forth below (subject to the right of a party to designate a different address for itself by notice similarly given):

If to the Company:

APREA THERAPEUTICS, INC.
535 Boylston Street
Boston, MA 02116
Attention: Chief Executive Officer

If to Executive:

Scott M. Coiante
At the most recent address on file with the Company

With a copy to:

Sidley Austin LLP
Attn: Geoffrey W. Levin, Esq.
787 Seventh Avenue
New York, NY 10019

8. **Indemnification.** During the Term, the Company agrees that it shall indemnify Executive and provide Executive with Directors & Officers liability insurance coverage to the same extent that it indemnifies and/or provides such insurance coverage to Board members and other most senior executive officers of the Company

9. **Entire Agreement.** This Agreement constitutes the entire agreement and understanding between the parties with respect to the subject matter hereof and supersedes and preempts any prior understandings, agreements or representations by or between the parties, written or oral,

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which may have related in any manner to the subject matter hereof, including, without limitation, the Prior Agreement.

10. **No Conflict.** Executive represents and warrants that Executive is not bound by any employment contract, restrictive covenant, or other restriction preventing Executive from carrying out Executive's responsibilities for the Company, or which is in any way inconsistent with the terms of this Agreement. Executive further represents and warrants that Executive shall not disclose to the Company or induce the Company to use any confidential or proprietary information or material belonging to any previous employer or others.

11. **Successors and Assigns.** This Agreement shall inure to the benefit of and be enforceable by Executive and his heirs, executors and personal representatives, and the Company and its successors and assigns. Any successor or assignee of the Company shall assume the liabilities of the Company hereunder.

12. **Governing Law.** This Agreement shall be governed by the internal laws (as opposed to the conflicts of law provisions) of the State of Delaware.

13. **Amendment and Waiver.** The provisions of this Agreement may be amended or waived only with the prior written consent of the Company and Executive, and no course of conduct or failure or delay in enforcing the provisions of this Agreement shall affect the validity, binding effect or enforceability of this Agreement.

14. **Withholding.** All payments and benefits under this Agreement are subject to withholding of all applicable taxes and other required deductions.

15. **Clawbacks.** The payments to Executive pursuant to this Agreement are subject to forfeiture or recovery by the Company or other action pursuant to any clawback or recoupment policy which the Company may adopt from time to time, including without limitation any such policy or provision that the Company has included in any of its existing compensation programs or plans or that it may be required to adopt under the Dodd-Frank Wall Street Reform and Consumer Protection Act and implementing rules and regulations thereunder, or as otherwise required by law.

16. **Company Policies.** Executive shall be subject to additional Company policies as they may exist from time-to-time, including policies with regard to stock ownership by senior executives and policies regarding trading of securities.

17. **Code Section 409A.** This Agreement is intended to comply with the requirements of Section 409A of the Code, and shall be interpreted and construed consistently with such intent. The payments to Executive pursuant to this Agreement are also intended to be exempt from Section 409A of the Code to the maximum extent possible, under either the separation pay exemption pursuant to Treasury regulation §1.409A-1(b)(9)(iii) or as short-term deferrals pursuant to Treasury regulation §1.409A-1(b)(4), and for such purposes, each payment to Executive under this Agreement shall be considered a separate payment. In the event the terms of this Agreement would subject Executive to taxes or penalties under Section 409A of the Code ("[409A Penalties](#)"), the Company and Executive shall cooperate diligently to amend the terms of the Agreement to avoid such 409A Penalties, to the extent possible. To the extent any amounts under this Agreement

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are payable by reference to Executive's "termination of employment" such term and similar terms shall be deemed to refer to Executive's "separation from service," within the meaning of Section 409A of the Code. Executive hereby agrees to be bound by the Company's determination of its "specified employees" (as such term is defined in Section 409A of the Code) provided such determination is in accordance with any of the methods permitted under the regulations issued under Section 409A of the Code. Notwithstanding any other provision in this Agreement, to the extent any payments made or contemplated hereunder constitute nonqualified deferred compensation, within the meaning of Section 409A, then (i) each such payment which is conditioned upon Executive's execution of a release and which is to be paid or provided during a designated period that begins in one taxable year and ends in a second taxable year, shall be paid or provided in the later of the two taxable years and (ii) if Executive is a specified employee (within the meaning of Section 409A of the Code) as of the date of Executive's separation from service, each such payment that is payable upon Executive's separation from service and would have been paid prior to the six-month anniversary of Executive's separation from service, shall be delayed until the earlier to occur of (A) the first day of the seventh month following Executive's separation from service or (B) the date of Executive's death. Any reimbursement payable to Executive pursuant to this Agreement shall be conditioned on the submission by Executive of all expense reports reasonably required by Employer under any applicable expense reimbursement policy, and shall be paid to Executive within 30 days following receipt of such expense reports, but in no event later than the last day of the calendar year following the calendar year in which Executive incurred the reimbursable expense. Any amount of expenses eligible for reimbursement, or in-kind benefit provided, during a calendar year shall not affect the amount of expenses eligible for reimbursement, or in-kind benefit to be provided, during any other calendar year. The right to any reimbursement or in-kind benefit pursuant to this Agreement shall not be subject to liquidation or exchange for any other benefit. To the extent that the Severance Payment payable hereunder is deemed to be a substitute for a payment provided under another agreement with the Executive, then the Severance Payment payable hereunder shall be paid at the same time and in the same form as such substituted payment to the extent required to comply with Section 409A of the Code.

APREA THERAPEUTICS, INC.

By: /s/ Christian S. Schade

Name: Christian S. Schade
Title: President and Chief Executive Officer

EXECUTIVE

By: /s/ Scott M. Coiante

Name: Scott M. Coiante
Title: Senior Vice President, Chief Financial Officer

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated August 20, 2019 (except for the retroactive effect of the 1-for-1.6045 stock split of the Company's common stock as described in Note 1, as to which the date is September 27, 2019), with respect to the balance sheet as of July 11, 2019 of Aprea Therapeutics, Inc., and our report dated August 20, 2019 (except for the retroactive effect of the 1-for-1.6045 stock split of the Company's preferred and common stock as described in Note 1, as to which the date is September 27, 2019), with respect to the consolidated financial statements of Aprea Therapeutics AB for the years ended December 31, 2017 and 2018, in the Registration Statement (Form S-1 No. 333-233662) and related Prospectus of Aprea Therapeutics, Inc., for the registration of shares of its common stock.

/s/ Ernst & Young AB

Stockholm, Sweden

September 27, 2019

QuickLinks

[Exhibit 23.1](#)

[Consent of Independent Registered Public Accounting Firm](#)