Table of Contents

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

FORM 10-Q

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended June 30, 2020

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number 001-39069

Aprea Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**84- 2246769**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
535 Boylston Street **Boston, Massachusetts**	**02116**
(Address of principal executive offices)	(Zip Code)

(617) 463-9385
(Registrant's telephone number, including area code)

Not Applicable
(Former name, former address and former fiscal year, if changed since last report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol**	**Name of exchange on which registered:**
Common stock, par value $0.001 per share	APRE	NASDAQ Global Select Market

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a 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 13(a) of the Exchange Act. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

There were 21,186,827 shares of the registrant's common stock, $0.001 par value, outstanding as of August 11, 2020.

Aprea Therapeutics, Inc.
Quarterly Report on Form 10-Q
For the Quarter Ended June 30, 2020

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q includes statements that are, or may be deemed, "forward-looking statements." In some cases, these forward-looking statements can be identified by the use of forward-looking terminology, including the terms "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "designed," "would," "could," "might," "will," "should," "approximately" or, in each case, their negative or other variations thereon or comparable terminology, although not all forward-looking statements contain these words. They appear in a number of places throughout this Quarterly Report on Form 10-Q and include statements regarding our current intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned development, commercialization, and market uptake of APR-246 and our other potential product candidates, the strength and breadth of our intellectual property, our ongoing and planned clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, the legal and regulatory landscape impacting our business, the degree of clinical utility of our products, particularly in specific patient populations, expectations regarding clinical trial data, our development and validation of manufacturing capabilities, our results of operations, financial condition, liquidity, prospects, growth and strategies, the length of time that we will be able to continue to fund our operating expenses and capital expenditures, our expected financing needs and sources of financing, the industry in which we operate and the trends that may affect the industry or us.

By their nature, forward-looking statements involve risks and uncertainties because they relate to future events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. We caution you that forward-looking statements are not guarantees, or predictive, of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this Quarterly Report on Form 10-Q.

Some of the factors that we believe could cause actual results to differ from those anticipated or predicted include:

- estimates of our expenses, capital requirements and our needs for additional financing;
- business interruptions, including delays in enrollment, patient follow-up and data collection of clinical trials, resulting from the outbreak of the novel coronavirus, COVID-19;
- 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 generate sufficient or positive preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation of clinical trials of APR-548;
- 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 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.

Any forward-looking statements that we make in this Quarterly Report on Form 10-Q speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this Quarterly Report on Form 10-Q. You should also read carefully the factors described in the "Risk Factors" included in Part II, Item 1A of this Quarterly Report to better understand significant risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Quarterly Report on Form 10-Q will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all.

This Quarterly Report on Form 10-Q includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data.

We qualify all of our forward-looking statements by these cautionary statements. In addition, with respect to all of our forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

This Form 10-Q may include trademarks, tradenames, and service marks that are the property of other organizations. Solely for convenience, our trademarks and tradenames referred to in this Form 10-Q may appear without the ® and ™

symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and tradenames.

Aprea Therapeutics, Inc.
Part I – Financial Information

Item 1. Financial Statements

Aprea Therapeutics, Inc.
Condensed Consolidated Balance Sheets
(Unaudited)

	June 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 112,861,504	$ 130,088,869
Prepaid expenses and other current assets	1,475,223	2,955,878
Total current assets	114,336,727	133,044,747
Property and equipment, net	43,906	41,639
Right of use lease asset	408,794	521,392
Other noncurrent assets	29,368	107
Total assets	$ 114,818,795	$ 133,607,885
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 5,443,126	$ 2,176,852
Accrued expenses	8,827,860	6,642,553
Lease liability—current	241,527	242,329
Total current liabilities	14,512,513	9,061,734
Lease liability—noncurrent	185,926	302,621
Total liabilities	14,698,439	9,364,355
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Common stock, $0.001 par value, 400,000,000 shares authorized, 21,186,827 and 21,022,752 shares issued and outstanding at June 30, 2020 and December 31, 2019, respectively.	21,187	21,023
Additional paid-in capital	228,597,264	226,284,548
Accumulated other comprehensive loss	(12,201,648)	(11,533,778)
Accumulated deficit	(116,296,447)	(90,528,263)
Total stockholders' equity	100,120,356	124,243,530
Total liabilities and stockholders' equity	$ 114,818,795	$ 133,607,885

See accompanying notes to unaudited condensed consolidated financial statements.

Aprea Therapeutics, Inc.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Operating expenses:				
Research and development	$ 10,694,029	$ 4,319,826	$ 19,790,151	$ 7,998,270
General and administrative	3,786,886	1,618,589	6,563,354	2,347,915
Total operating expenses	14,480,915	5,938,415	26,353,505	10,346,185
Other income (expense):				
Interest income (expense)	2,678	(4,091)	227,120	(7,439)
Foreign currency (loss) gain	(1,889,690)	680,058	358,201	1,615,974
Total other income (expense)	(1,887,012)	675,967	585,321	1,608,535
Net loss	$ (16,367,927)	$ (5,262,448)	$ (25,768,184)	$ (8,737,650)
Other comprehensive income (loss):				
Foreign currency translation	1,756,783	44,508	(667,870)	(1,986,667)
Total comprehensive loss	(14,611,144)	(5,217,940)	(26,436,054)	(10,724,317)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.78)	$ (4.45)	$ (1.22)	$ (7.43)
Weighted-average common shares outstanding, basic and diluted	21,107,056	1,181,583	21,079,891	1,176,417

See accompanying notes to unaudited condensed consolidated financial statements.

Aprea Therapeutics, Inc.
Condensed Consolidated Statements of Convertible Preferred Stock and Stockholders' Deficit
(Unaudited)

	Convertible Preferred Stock											
	Series A		Series B		Series C		Common Stock		Additional Paid-in Capital	Other Comprehensive Loss	Accumulated Deficit	Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
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	—	—	—	—	—	—	—	—	97,946	—	—	97,946
Foreign currency translation	—	—	—	—	—	—	—	—	—	(2,031,175)	—	(2,031,175)
Net loss	—	—	—	—	—	—	—	—	—	—	(3,475,202)	(3,475,202)
Balance, March 31, 2019	612,446	$ 6,483,044	7,235,969	$ 49,742,942	5,179,877	$ 61,963,007	1,181,573	$ 129,974	$ 19,784,769	$ (10,792,500)	$ (65,943,658)	$ (56,821,415)
Stock-based compensation	—	$ —	—	$ —	—	$ —	—	$ —	$ 186,963	$ —	$ —	$ 186,963
Foreign currency translation	—	—	—	—	—	—	—	—	—	44,508	—	44,508
Net loss	—	—	—	—	—	—	—	—	—	—	(5,262,448)	(5,262,448)
Balance, June 30, 2019	612,446	$ 6,483,044	7,235,969	$ 49,742,942	5,179,877	$ 61,963,007	1,181,573	$ 129,974	$ 19,971,732	$ (10,747,992)	(71,206,106)	$ (61,852,392)
Balance, December 31, 2019	—	$ —	—	$ —	—	$ —	21,022,752	$ 21,023	$ 226,284,548	$ (11,533,778)	$ (90,528,263)	$ 124,243,530
Exercise of stock options	—	—	—	—	—	—	32,090	32	29,491	—	—	29,523
Stock-based compensation	—	—	—	—	—	—	—	—	905,471	—	—	905,471
Foreign currency translation	—	—	—	—	—	—	—	—	—	(2,424,653)	—	(2,424,653)
Net loss	—	—	—	—	—	—	—	—	—	—	(9,400,257)	(9,400,257)
Balance, March 31, 2020	—	$ —	—	$ —	—	$ —	21,054,842	$ 21,055	$ 227,219,510	$ (13,958,431)	$ (99,928,520)	$ 113,353,614
Exercise of stock options	—	$ —	—	$ —	—	$ —	131,985	$ 132	$ 121,294	$ —	$ —	$ 121,426
Stock-based compensation	—	—	—	—	—	—	—	—	1,256,460	—	—	1,256,460
Foreign currency translation	—	—	—	—	—	—	—	—	—	1,756,783	—	1,756,783
Net loss	—	—	—	—	—	—	—	—	—	—	(16,367,927)	(16,367,927)
Balance, June 30, 2020	—	$ —	—	$ —	—	$ —	21,186,827	$ 21,187	$ 228,597,264	$ (12,201,648)	$ (116,296,447)	$ 100,120,356

See accompanying notes to unaudited condensed consolidated financial statements.

Aprea Therapeutics, Inc.
Condensed Consolidated Statements of Cash Flows
(Unaudited)

	Six Months Ended June 30,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (25,768,184)	$ (8,737,650)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	7,866	4,739
Stock-based compensation	2,161,931	284,909
Amortization of right of use lease asset	108,164	51,853
Foreign currency gain	(358,201)	(1,615,974)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,480,655	19,721
Accounts payable	3,266,274	640,719
Accrued expenses and other liabilities	2,185,307	232,679
Lease liability	(263,750)	(53,815)
Net cash used in operating activities	(17,179,938)	(9,172,819)
Cash flows from investing activities:		
Purchases of property and equipment	(10,144)	(6,189)
Net cash used in investing activities	(10,144)	(6,189)
Cash flows from financing activities:		
Proceeds from the exercise of stock options	150,949	23,118
Deferred offering costs	—	(624,624)
Proceeds from issuance of Series C convertible preferred, net	—	5,598,362
Net cash provided by financing activities	150,949	4,996,856
Decrease in cash and cash equivalents	(17,039,133)	(4,182,152)
Effect of exchange rate changes on cash	(188,232)	(499,041)
Cash and cash equivalents—beginning of year	130,088,869	65,675,931
Cash and cash equivalents—end of year	$ 112,861,504	$ 60,994,738
Non-cash activities:		
Cumulative effect of change in accounting principle—ASC 842 adoption	$ —	$ 329,384

See accompanying notes to unaudited condensed consolidated financial statements.

Aprea Therapeutics, Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

1. Nature of business and basis of presentation

Nature of business—Aprea Therapeutics, Inc. (or 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 principal operations in 2006 and is headquartered in Boston, Massachusetts with research facilities in Stockholm, Sweden.

Corporate reorganization - In September 2019, the Company completed a corporate reorganization whereby Aprea Therapeutics AB became a wholly-owned subsidiary of the Company. In connection with the corporate reorganization, each issued and outstanding share of Series A, Series B and Series C convertible preferred stock of Aprea Therapeutics AB was exchanged on a one for one basis into shares of Series A, Series B and Series C convertible preferred stock of the Company.

Each share of common stock of Aprea Therapeutics AB ($0.11 par value) was also exchanged on a one for one basis into shares of common stock of the Company ($0.001 par value).

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 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 believes that the June 30, 2020 cash balance of approximately $112.9 million will be sufficient to fund the Company's operations into 2023. 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.

2. Summary of significant accounting policies

The Company's complete listing of significant accounting policies are described in Note 2 to the Company's audited consolidated financial statements as of December 31, 2019 included in its annual report on Form 10-K filed with the Securities and Exchange Commission (or the "SEC").

Principles of consolidation—The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries Aprea Therapeutics AB, 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 consolidated financial statements—The accompanying unaudited interim condensed consolidated financial statements have been prepared by the Company in accordance with U.S. GAAP for interim information and

Aprea Therapeutics, Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

pursuant to the rules and regulations of the SEC for reporting on Form 10-Q. Accordingly, certain information and footnote disclosure normally included in financial statements prepared in accordance with U.S. GAAP have been condensed or omitted pursuant to such rules and regulations. These unaudited condensed interim financial statements should be read in conjunction with the audited financial statements and related notes included in the Company's annual report on Form 10-K for the year ended December 31, 2019 filed with the SEC.

The unaudited interim consolidated financial 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 presentation of the financial information for the interim periods have been made. The results of operations for the three and six months ended June 30, 2020 are not necessarily indicative of the results to be expected for the full fiscal year or any future 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 stock-based compensation expense.

Foreign currency and currency translation—The functional currency for Aprea Therapeutics AB and 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. Operating 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' equity (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.

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.

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 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.

Aprea Therapeutics, Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

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.

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 are 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 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 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 ranged from approximately 3.0% to 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.

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.

Aprea Therapeutics, Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

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.

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, 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.

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,	
	2020	2019
Series A convertible preferred stock	—	612,446
Series B convertible preferred stock	—	7,235,969
Series C convertible preferred stock	—	5,179,877
Options to purchase common stock	3,755,959	2,761,794
Total shares of common stock equivalents	3,755,959	15,790,086

Recently issued accounting pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies that the Company adopts as of the specified effective date. Unless otherwise discussed below, the Company does not believe that the adoption of recently issued standards have or may have a material impact on our consolidated financial statements or disclosures.

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. ASU No. 2018-07 was adopted by the Company on January 1, 2020 and had no impact on the Company's financial condition or results of operations.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments ("ASU 2016-13"), which amends the impairment model by requiring entities to use a forward-looking approach based on expected losses rather than incurred losses to estimate credit losses on certain types of financial instruments, including trade receivables. ASU 2016-13 was adopted by the Company on January 1, 2020 and has no current impact on the Company as the Company does not have any financial instruments covered by the topic.

Management does not believe that any other recently issued, but not yet effective accounting pronouncements, if adopted, would have a material impact on the accompanying financial statements.

Aprea Therapeutics, Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

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 (see Note 2). The Company is party to two operating leases for office and 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. Rent expense for three and six months ended June 30, 2020 was $77,500 and $157,325, respectively. Rent expense for the three and six months ended June 30, 2019 was $31,831 and $69,524, respectively.

The Company has an operating lease in Boston, Massachusetts for office space. The lease will expire in December 2021 and does not have any renewal options. The Company also has an operating lease for office and laboratory space in Solna, Sweden that expires in June 2022.

Quantitative information regarding the Company's leases for the three and six months ended June 30, 2020 and 2019 is as follows:

	Three months ended June 30,		Six months ended June 30,	
Lease Cost	**2020**	**2019**	**2020**	**2019**
Operating lease cost	$ 27,265	$ 26,071	$ 54,223	$ 51,853
Other Information				
Operating cash flows paid for amounts included in the measurement of lease liabilities	$ 62,909	$ 30,409	$ 125,818	$ 60,818
Operating lease liabilities arising from obtaining right-of-use assets	$ —	$ —	$ —	$ —
Weighted average remaining lease term (years)	1.5 - 2.0	2.5	1.5 - 2.0	2.5
Weighted average discount rate	3.0 - 4.3%	3.0 - 4.3%	3.0 - 4.3%	3.0 - 4.3%

Future lease payments under noncancelable leases are as follows at June 30, 2020:

Future Lease Payments	**Operating Leases**
Remainder of 2020	$ 125,287
2021	252,870
2022	63,322
Total Lease Payments	$ 441,479
Less: Imputed Interest	(14,026)
Total Lease Liabilities	$ 427,453

As most of the Company's leases do not provide an implicit rate, the Company used its 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.

Aprea Therapeutics, Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

4. Accrued expenses

Accrued expenses consist of the following:

	June 30, 2020	December 31, 2019
Professional fees	$ 143,611	$ 207,917
Compensation and benefits	809,203	961,790
Research and development	6,528,641	4,992,311
Other	1,346,405	480,535
Total accrued expenses	$ 8,827,860	$ 6,642,553

5. Stockholders' equity (deficit)

The total number of shares of all classes of capital stock that the Company is authorized to issue is 440,000,000 shares, consisting 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.

Common Stock

The holders of common stock are entitled to one vote for each share of common stock. 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 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.

Stock-Based Compensation Expense

The Company recorded stock-based compensation expense of $1,256,460, and $2,161,931 for the three and six months ended June 30, 2020, respectively. The Company recorded stock-based compensation expense of $186,963 and $284,909 for the three and six months ended June 30, 2019, respectively.

6. Income Taxes

The Company has no income tax expense due to operating losses incurred for the three and six months ended June 30, 2020 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.

Realization of the future tax benefits is dependent on may 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 of 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's 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 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 June 30, 2020 and December 31, 2019, the Company had no uncertain tax positions or related interest and penalties accrued.

On March 27, 2020, the U.S. government enacted the Coronavirus Aid, Relief and Economic Security Act ("CARES Act") under which several restrictions for income tax purposes were relaxed, including with respect to, the limitation on business interest expense deductions, the ability to use net operating losses, and the acceleration of alternative minimum tax credits. Given the Company's history of losses, the CARES Act is not expected to have a material impact on income taxes.

7. Commitments and contingencies

The Company records a provision for contingent losses when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. As of June 30, 2020, the Company has not recorded a provision for any contingent losses.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with the unaudited financial information and notes thereto included in this Quarterly Report on Form 10-Q. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report, including information with respect to our plans and strategy for our business and related financing, including forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report, 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, or *eprenetapopt*, 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. Eprenetapopt has received orphan drug, fast track and breakthrough therapy designations from the FDA for MDS, and orphan drug designation from the European Commission for MDS, AML and ovarian cancer, and we believe eprenetapopt will be a first-in-class therapy if approved by applicable regulators. We recently completed enrollment of 154 patients in our pivotal Phase 3 trial of eprenetapopt with azacitidine for frontline treatment of *TP53* mutant MDS and expect top-line data from this trial by year-end 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.

We are currently enrolling a single-arm, open-label Phase 2 trial evaluating eprenetapopt with azacitidine as post-transplant maintenance therapy in *TP53* mutant MDS and AML patients who have received an allogenic stem cell transplant. We are also conducting a Phase 1 clinical trial in frontline and relapsed/refractory *TP53* mutant AML, assessing eprenetapopt with venetoclax with or without azacitidine.

Our second product candidate, APR-548, is a pre-clinical, next generation p53 reactivator with the potential for oral administration. APR-548 exhibits high oral bioavailability in preclinical testing and is being developed in an oral dosage form. We have completed Investigational New Drug, or IND, enabling preclinical studies of APR-548 and filed an IND with the FDA. However, based on feedback from the FDA, we will not be able to initiate human clinical trials of APR-548 until we are able to provide additional information necessary to address questions raised by the FDA.

Aprea Therapeutics AB, or Aprea AB, was originally incorporated in 2002 and commenced principal operations in 2006. We incorporated Aprea Therapeutics, Inc. (the "Company") in May 2019. In September 2019 we completed a corporate reorganization and, as a result, all of the issued and outstanding stock of Aprea AB was exchanged for common stock, preferred stock or options, as applicable, of the Company As a result of such transactions, Aprea AB became a wholly-owned subsidiary of the Company.

We have devoted substantially all of our resources to developing our product candidates, including eprenetapopt, 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 and the net proceeds received from the initial public offering (IPO) of our common stock. Through June 30, 2020, we had received net proceeds of approximately $223.9 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 $16.4 million and $25.8 million for the three and six months ended June 30, 2020 and $28.1 million, $15.5 million and $15.2 million for the years ended December 31, 2019, 2018 and

2017, respectively. As of June 30, 2020, we had an accumulated deficit of $116.3 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 eprenetapopt;
- 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 potential 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; and
- add operational, financial and management information systems and personnel, including personnel to support our drug development, any future commercialization efforts and our operation 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, 2020, we had cash and cash equivalents of $112.9 million. We believe that 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.”

The COVID-19 pandemic

The novel coronavirus outbreak (COVID-19) has been declared a "Public Health Emergency of International Concern" by the World Health Organization. COVID-19 has spread to many of the countries in which we, our suppliers, and our other business partners conduct business. Governments in affected regions have implemented, and may continue to implement or re-implement, safety precautions, including quarantines, travel restrictions, business closures, cancellations of public gatherings, and other measures they deem necessary. Like many other organizations and individuals, the Company and our employees are taking additional steps to avoid or reduce infection, including limiting travel and implementing remote work arrangements. We will continue to actively monitor the situation and may take further actions that could alter our business operations as may be required by national, state, or local authorities, or that we determine are in the best interests of our employees and stockholders.

As a result of the COVID 19 pandemic and policy responses to it, we did initially observe a decrease in both patient screening and patient enrollment in certain of our ongoing clinical trials. Recently, however, patient screening activity in many of the clinical sites has increased, resulting in a respective increase in the number of patients eligible for enrollment. Such patient screening and the number of patients eligible for enrollment in our clinical trials has returned to expected levels. Together with our investigators and clinical sites, we continue to assess the impact of the coronavirus pandemic on enrollment and the ability to maintain patients enrolled in our clinical trials and the corresponding impact on the timing of the completion of our ongoing clinical trials.

We have assessed both capacity and the current clinical supply chain associated with the production of eprenetapopt and have observed no disruptions to date in our clinical supply chain and our ability to provide supply for our on-going clinical trials. We will continue to monitor and assess the potential impact of the COVID-19 pandemic on our clinical trial supply chain.

There are many uncertainties regarding the COVID-19 pandemic, and we are closely monitoring the impact of the pandemic on all aspects of our business, including how it will impact our clinical trials, employees, suppliers, vendors and business partners. While the pandemic did not materially affect our financial results and business operations for the three and six months ended June 30, 2020, we are unable to predict the impact that COVID-19 will have on our financial position and operating results at this time due to numerous uncertainties such as the duration and spread of the outbreak. We will continue to assess the evolving impact of the COVID-19 pandemic and will make adjustments to our operations if necessary.

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 eprenetapopt 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 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 eprenetapopt, pursue later stages of clinical development of APR-246, initiate clinical trials for product candidates other than eprenetapopt 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 eprenetapopt, as well as of any future clinical trials of eprenetapopt 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 eprenetapopt: 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 *TP53* mutant MDS and AML with azacitidine, our Phase 2 trial of post-transplant maintenance therapy with azacitidine in *TP53* mutant MDS and AML, and our Phase 1b/2 trial for the treatment of *TP53* mutant AML with venetoclax. At this time, we cannot reasonably estimate the cost for initiating and completing other clinical trials or preclinical studies of eprenetapopt or other product candidates, 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 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 income consists of income earned on our cash and cash equivalents. Interest expense consists of bank charges and fees incurred on our cash and cash equivalents. Our interest income initially increased as our cash and cash equivalents were higher due to the cash proceeds received from our IPO. Such interest income is subsequently decreasing as our cash balance decreases as we continue to fund operations.

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 stockholders' equity and as other comprehensive loss on the consolidated statement of operations and comprehensive loss.

Income taxes

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.

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 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, 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, 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 (through October 2, 2019), there had been no public market for our common stock, 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-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 our common stock of $0.92 per share as of May 31, 2016, $1.01 per share as of October 2, 2017, $3.18 per share as of December 31, 2018 and $10.95 per share as of July 15, 2019.

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.

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 (EGC), 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 our IPO 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 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 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 three months ended June 30, 2020 and 2019

	Three months ended June 30,		
	2020	2019	Change
Operating expenses:			
Research and development	$ 10,694,029	$ 4,319,826	$ 6,374,203
General and administrative	3,786,886	1,618,589	2,168,297
Total operating expenses	14,480,915	5,938,415	8,542,500
Other income (expense):			
Interest income (expense)	2,678	(4,091)	6,769
Foreign currency (loss) gain	(1,889,690)	680,058	(2,569,748)
Total other income (expense)	(1,887,012)	675,967	(2,562,979)
Net loss	$ (16,367,927)	$ (5,262,448)	$ (11,105,479)

Research and development expenses

	Three months ended June 30,		
	2020	2019	Change
APR-246	$ 7,568,258	$ 3,575,419	$ 3,992,839
Other early-stage development programs	407,476	374,319	33,157
Unallocated research and development expenses	2,718,295	370,088	2,348,207
Total research and development expenses	$ 10,694,029	$ 4,319,826	$ 6,374,203

Research and development expenses for the three months ended June 30, 2020 were $10.7 million, compared to $4.3 million for the three months ended June 30, 2019. The increase of $6.4 million was primarily related to the advancement of our clinical product candidate, APR-246. In Q1 2019 we commenced a pivotal Phase 3 clinical trial of APR-246 with azacitidine for frontline treatment of *TP53* mutant MDS which completed enrollment in Q2 2020 and is supported by 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 addition, in Q1 2020, we continued to enroll patients in a Phase 2 post-transplant MDS/AML clinical trial and also began enrolling patients in a Phase 1 clinical trial in frontline and relapsed/refractory *TP53* mutant AML assessing APR-246 with venetoclax with or without azacitidine.

General and administrative expenses

General and administrative expenses for the three months ended June 30, 2020 were $3.8 million, compared to $1.6 million for the three months ended June 30, 2019. The increase of $2.2 million was primarily related to increases of $0.8 million in insurance expense, $0.5 million in non-cash stock-based compensation, $0.5 million in personnel related

costs and $0.4 million in commercial development expense. The increase in insurance expense was primarily related to costs associated with being a public company. The increase in non-cash stock-based compensation expense was primarily related to stock option grants made in October 2019 in connection with our IPO and in March 2020 in connection with the Company's annual compensation review.

Other income and expense

Foreign currency loss for the three months ended June 30, 2020 was $1.9 million compared to a foreign currency gain of $0.7 million for the three months ended June 30, 2019. The decrease of $2.6 million was primarily due to a weakening of the U.S. dollar against the Swedish Krona during the three months ended June 30, 2020. Interest income for the three months ended June 30, 2020 consisted of interest earned on our cash and cash equivalents.

Comparison of the six months ended June 30, 2020 and 2019

	Six months ended June 30,		
	2020	2019	Change
Operating expenses:			
Research and development	$ 19,790,151	$ 7,998,270	$ 11,791,881
General and administrative	6,563,354	2,347,915	4,215,439
Total operating expenses	26,353,505	10,346,185	16,007,320
Other income (expense):			
Interest income (expense)	227,120	(7,439)	234,559
Foreign currency gain	358,201	1,615,974	(1,257,773)
Total other income (expense)	585,321	1,608,535	(1,023,214)
Net loss	$ (25,768,184)	$ (8,737,650)	$ (17,030,534)

Research and development expenses

	Six months ended June 30,		
	2020	2019	Change
APR-246	$ 14,605,217	$ 6,314,584	$ 8,290,633
Other early-stage development programs	976,917	673,435	303,482
Unallocated research and development expenses	4,208,017	1,010,251	3,197,766
Total research and development expenses	$ 19,790,151	$ 7,998,270	$ 11,791,881

Research and development expenses for the six months ended June 30, 2020 were $19.8 million, compared to $8.0 million for the six months ended June 30, 2019. The increase of $11.8 million was primarily related to the advancement of our clinical product candidate, APR-246. In Q1 2019 we commenced a pivotal Phase 3 clinical trial of APR-246 with azacitidine for frontline treatment of *TP53* mutant MDS which completed enrollment in Q2 2020 and is supported by 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 addition, in Q1 2020, we continued to enroll patients in a Phase 2 post-transplant MDS/AML clinical trial and also began enrolling patients in a Phase 1 clinical trial in frontline and relapsed/refractory *TP53* mutant AML assessing APR-246 with venetoclax with or without azacitidine.

General and administrative expenses

General and administrative expenses for the six months ended June 30, 2020 were $6.5 million, compared to $2.3 million for the six months ended June 30, 2019. The increase of $4.2 million was primarily related to increases of $1.6 million in insurance expense, $1.0 million in non-cash stock-based compensation, $0.8 million in personnel related costs, $0.4 million in commercial development expense and $0.3 million in legal and consulting fees. The increase in insurance expense and legal and consulting fees was primarily related to costs associated with being a public company. The increase in non-cash stock-based compensation expense was primarily related to stock option grants made in October 2019 in connection with our IPO and in March 2020 in connection with our annual compensation review.

Other income and expense

Foreign currency gain for the six months ended June 30, 2020 was $0.4 million compared to $1.6 million for the six months ended June 30, 2019. The decrease of $1.2 million was primarily due to a weakening of the U.S. dollar against the Swedish Krona during the six months ended June 30, 2020. Interest income for the six months ended June 30, 2020 consisted of interest earned on our cash and cash equivalents.

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 and the net proceeds received from the initial public offering (IPO) of our common stock. Through June 30, 2020, we had received net proceeds of $223.9 million from our sales of preferred and common stock. As of June 30, 2020, we had cash and cash equivalents of $112.9 million.

Cash flows

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

	Six months ended June 30,	
	2020	2019
Net cash provided by (used in):		
Operating activities	$(17,179,938)	$ (9,172,819)
Investing activities	(10,144)	(6,189)
Financing activities	150,949	4,996,856
Net increase (decrease) in cash and cash equivalents	$(17,039,133)	$ (4,182,152)

Operating activities.

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 $17.2 million for the six months ended June 30, 2020 compared to $9.2 million for the six months ended June 30, 2019. The increase in cash used in operating activities of $8.0 million was primarily attributable to an increase in our net loss of $17.0 million, resulting from both increased research and development expenses and increased general and administrative expenses discussed previously partially offset by an increase in operating assets and liabilities of $5.8 million and an increase in non-cash stock-based compensation of $1.9 million.

Investing activities.

Cash used in investing activities for the six months ended June 30, 2020 and 2019, was $10,144 and $6,189, respectively. Cash used in investing activities for these periods represented the acquisition of property and equipment.

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

Financing activities.

Net cash provided by financing activities was $150,949 for the six months ended June 30, 2020 compared to $5.6 million for the six months ended June 30, 2019. The decrease in cash provided by financing activities was primarily attributable to the issuance of Series C convertible preferred stock in February 2019 for net proceeds of $5.0 million. Cash provided by financing activities for the six months ended June 30, 2020 represented proceeds received from the exercise of stock options.

Funding requirements

We expect our expenses to increase substantially in connection with our ongoing development activities related to eprenetapopt and other product candidates and programs which are still in the early stages of clinical development. In addition, we have incurred and continue 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 eprenetapopt;
- 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
- continue to operate as a public company.

As of June 30, 2020, we had cash and cash equivalents of $112.9 million. We believe that 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 eprenetapopt 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 eprenetapopt for our current targeted indications;
- the scope, progress, results and costs of drug discovery, preclinical research and clinical trials for eprenetapopt 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 impact of COVID-19 on the financial markets in general and on our business in particular;
- 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, ownership interests in our securities may be diluted, and the terms of these securities may include liquidation or other preferences and anti-dilution protections that could adversely affect the rights of our common stockholders. 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 existing 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

In August 2020, we entered into a companion diagnostics agreement with Invivoscribe, Inc. to collaborate on the development of an in vitro companion diagnostic test for eprenetapopt. Pursuant to the companion diagnostics agreement, Invivoscribe will develop a companion diagnostic assay for regulatory approval as a companion diagnostic for eprenetapopt in exchange for payments of up to $13.2 million in the aggregate, subject to the achievement of specified milestones and reimbursement of defined out-of-pocket expenses.

For additional details regarding our contractual obligations, see Note 3 “Leases” to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

Recent accounting pronouncements

See Note 2 to our condensed consolidated financial statements which discusses new accounting pronouncements.

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.

Item 3. 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, 2020, 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.

Item 4. Controls and Procedures

Disclosure Controls and Procedures

Our management, with the participation of our chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2020. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, mean controls and other procedures of a company that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms. Disclosure controls include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company on the reports that it files or submits under the Exchange Act is

accumulated and communicated to management, including, our principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure.

Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgement in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of June 30, 2020, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable level.

Changes in Internal Control

There has been no change in our internal control over financial reporting as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II: OTHER INFORMATION

Item 1. Legal Proceedings.

We are not currently subject to any material legal proceedings.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risk factors below together with the information contained elsewhere in this Quarterly Report on Form 10-Q, including Part I, Item 1 "Financial Statements" and Part I, Item 2. "Management's Discussion and Analysis of Financial Condition and Results of Operations," and in our other public filings in evaluating our business. 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 Quarterly Report, including our financial statements and the related notes. We believe the risks described below are the risks that are material to us as of the date of this Quarterly Report. 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 our stockholders may lose all or part of their 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 $16.4 million and $25.8 million for the three and six months ended June 30, 2020, and $28.1 million, $15.5 million and $15.2 million for the years ended December 31, 2019, 2018 and 2017, respectively. Our accumulated deficit was $116.3 million as of June 30, 2020 and $90.5 million as of December 31, 2019. 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 and the net proceeds received from the initial public offering (IPO) of our common 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 our stockholders to lose all or part of their 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, since the completion of our IPO, we have incurred and 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. The ongoing COVID-19 pandemic both in the United States and globally continues to cause uncertainty and volatility in financial markets which in turn may make raising additional funds even more difficult or impossible for us. 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 believe that our existing cash and cash equivalents as of June 30, 2020 will enable us to fund our operating expenses and capital expenditure requirements into 2023. Our estimate as to how long we expect 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 and 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, ownership interests in our securities may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect the rights of our common stockholders. 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;
- the impact of COVID-19 on our operations, ability to conduct clinical trials and on the ability of our regulators to review and approve APR-246;
- 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;
- successfully developing a companion diagnostic test on a timely and cost effective basis;
- 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. Additionally, COVID-19 may further negatively impact our ability to locate and enroll patients.

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;
- physicians' attitudes and practices with respect to clinical trial enrollment;
- 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. In the Phase 3 MDS Trial, serious adverse events, regardless of causality, reported for more than one patient as of July 31, 2020 were: febrile neutropenia (26%), pneumonia (10%), pyrexia (9%), sepsis (6%), muscle weakness (5%), confusional state (3%), respiratory failure (3%), cellulitis (2%), acute febrile neutrophilic dermatosis (1%), acute kidney injury (1%), acute respiratory distress syndrome (1%), anemia (1%), atrial flutter (1%), cardiac failure (1%), dyspnea (1%), encephalopathy (1%), fall (1%), headache (1%), hypotension (1%), hypoxia (1%), pericarditis (1%), platelet count decreased (1%), pneumonitis (1%), skin infection (1%), thrombocytopenia (1%), and urinary tract infection (1%). In the U.S. Phase 1b/2 MDS/AML Trial, serious adverse events, regardless of causality, reported for more than one patient as of July 31, 2020 were: febrile neutropenia (33%), pneumonia (25%), sepsis (11%), pyrexia (7%), dehydration (5%), embolism (5%), muscle weakness (5%), respiratory failure (5%), vomiting (5%), angina pectoris (4%), atrial fibrillation (4%), intracranial hemorrhage (4%) and multiple organ dysfunction syndrome (4%). In the French Phase 1b/2 MDS/AML Trial, serious adverse events, regardless of causality, reported for more than one patient as of July 31, 2020 were: febrile neutropenia (27%), device related infection (12%), pneumonia (8%), sepsis (8%), corona virus infection (6%), lung disorder (6%), ataxia (4%), cellulitis (4%), dizziness (4%), septic shock (4%), subdural hematoma (4%) and urinary tract infection (4%). In the Phase 2 MDS/AML post-transplant trial, serious adverse events, regardless of causality, reported for more than one patient as of July 31, 2020 were confusional state (9%) and pyrexia (9%). In the Phase 1 AML Trial, serious adverse events, regardless of causality, reported for more than one patient as of July 31, 2020 were: febrile neutropenia (40%), sepsis (13%) and subdural hematoma (13%). 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; there have been two deaths reported by an investigator as possibly related to both APR-246 and azacitidine, one death reported by an investigator as possibly related to APR-246 and four deaths reported by an investigator as possibly related to azacitidine. We believe that the deaths with any relation to APR-246 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 comparable foreign 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 comparable foreign regulatory authorities. 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 elsewhere to the satisfaction of 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;
- the impact of COVID-19 on patient screening and patient enrollment;
- 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 comparable foreign 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, and face legal and reputational risk. 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 frequently must defend against and respond to cybersecurity incidents and attacks and cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, compromises of personal information or confidential commercial information, other operationally significant 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. Third parties may also 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 post-market 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 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.

An epidemic or pandemic disease outbreak, including the 2019 novel coronavirus (COVID-19), could disrupt our business operations as well as the business or operations of our single third-party manufacturer, our CROs, clinical data management organizations, medical institutions and clinical investigators, or other third parties with whom we conduct business which may have a material adverse effect on our business, results of operations, financial condition and prospects.

An epidemic or pandemic disease outbreak, including the 2019 novel coronavirus (COVID-19), could severely disrupt our operations or the operations of third parties that we depend on, including our single third-party contract manufacturer, our CROs, clinical data management organizations, medical institutions and clinical investigators, and have a material adverse effect on our business, results of operations, financial condition and prospects. In addition, supply chain disruptions due to response to *COVID-19* or otherwise could have a material adverse effect on the availability or cost of materials for the API for APR-246. Quarantines, restrictions or bans in travel into and within the countries in which we operate, our manufacturer produces the API for APR-246 or where we conduct our clinical trials could impede, delay, limit or prevent the production or delivery or release of our product candidates to our trial sites, and trial investigators, patients or other critical staff could be restricted from traveling to our trial sites. In addition, some of our clinical sites could slow or cease patient recruitment, patient treatment and/or access to patient data. We had observed a decrease in both patient screening and patient enrollment as a result of the COVID-19 pandemic and such decreases may continue so in the future. Additionally, we and our employees are taking steps to avoid or reduce infection, including limiting travel and implementing remote work arrangements. It is possible that remote work arrangements will not be as efficient as physical operations, and this could adversely affect our business, operations and internal controls. Any or all of these factors could impede, delay, limit or prevent completion of our ongoing clinical trials, or require changes to our ongoing clinical trials, and ultimately lead to the delay or denial of regulatory approval of our product candidates, which would materially adversely affect our business, results of operations, financial conditions and prospects.

While there is significant uncertainty relating to the potential effect of the coronavirus on our business and operations, infections may become more widespread and travel restrictions may worsen, including in the United States, Sweden and other countries where our trials are conducted or the API for APR-246 is manufactured, any of which could have a material adverse effect our business, results of operations, financial conditions and prospects. Additionally, disruptions at the at FDA, the EMA and other regulators, caused by global health concerns, including the COVID-19 pandemic, including delays in inspections of clinical trial or manufacturing sites required as part of the drug application review process, could result in delays of reviews and approvals of our product candidate or our proposed clinical trials. For example, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products inspections of domestic manufacturing facilities through April 2020. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials. The FDA has since announced that it is working toward the goal of restarting on-site inspections, but it is currently unclear when or how this will be done. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic.

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 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 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 impact of COVID-19 on the facilities of our manufacturers and their supply lines;
- 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 comparable foreign 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, crystalline solid form, and combination therapy 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, which may be extended due to epidemic or pandemic disease outbreaks, such as COVID-19 or other public health situations,

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. In addition, extraneous factors, including an epidemic or pandemic disease outbreak such as COVID-19, or other public health situations, could impact the timeline for FDA and comparable foreign regulatory authorities to review an application for one of our product candidates. 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.

The vote on June 23, 2016 by the U.K. to exit the EU, or Brexit, has created uncertainty in the global financial markets, but the eventual effects of the U.K.'s withdrawal from the EU on our business or our investment portfolios are uncertain at this time. On March 29, 2017, the Prime Minister of the U.K. notified the European Council in accordance with Article 50 of the Treaty on European Union of the U.K.'s intention to withdraw from the EU, triggering a two-year period for the negotiation of the U.K.'s withdrawal from the EU. This period was further extended subsequently. The effect of Brexit on our business and investments is uncertain as negotiations commence to determine the future terms of the U.K. relationship with the EU. Furthermore, Brexit is likely to continue to adversely affect European and worldwide economic conditions and could contribute to greater instability in the global financial markets before and after the terms of the U.K.'s future relationship with the EU are settled. These effects could have an adverse effect on our business, investments and future operations in Europe. A withdrawal agreement and a political declaration were agreed at the European Council on October 17, 2019, on the terms of which the U.K. left the EU on January 31, 2020. A transition period is currently running, during which the U.K. is, with some exceptions, treated as a member of EU. After the transition period, which is expected to end on December 31, 2020, the relationship between the UK and the EU would be regulated by any agreement concluded during the transition period. A 'no-deal' Brexit scenario could therefore still occur if the U.K. and the EU do not conclude such an agreement. In a no-deal scenario, due to the U.K. leaving the single-market and in the absence of further transitional arrangements with the EU, there is a greater risk that trade

between UK and EU businesses will be materially adversely affected, particularly in relation to highly regulated products such as pharmaceuticals and products of animal-origin, due to the additional regulatory burdens that are likely to be imposed on exporters/importers which may affect the availability of these products.

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. 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 agreement in place on a future relationship 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 many 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 European Commission for MDS, 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 effectively 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 effectively. 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 (“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. While Congress has not enacted legislation to comprehensively repeal the PPACA, at least two bills affecting the implementation of certain provisions 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.” In December 2018, a federal district court in Texas ruled the individual mandate, without the penalty that was repealed effective January 1, 2019, 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. The Fifth Circuit Court of Appeals affirmed the district court's ruling that the individual mandate was unconstitutional, but it remanded the case back to the district court for further analysis of whether the mandate could be severed from the PPACA (i.e. whether the entire PPACA was therefore also unconstitutional). The Supreme Court of the United States granted certiorari on March 2, 2020, and the case is expected to be decided in 2021.

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. For example, 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.

Effective January 1, 2019, the Bipartisan Budget Act of 2018, among other things, further amended 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 must 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. In 2020, the CARES Act temporarily suspended the 2% cut in Medicare payments from May 1, 2020 through December 31, 2020, and it extended the cut through fiscal year 2030 to offset the cost of such temporary suspension. In addition, the American Taxpayer Relief Act of 2012, 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. 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 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 countries outside of the United States, 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.

Regulatory proposals have been made to allow the importation of prescription drugs into the United States that are approved for marketing in Canada, and potentially other countries. On July 24, 2020, President Trump issued an Executive Order directing the Secretary of the Health and Human Services to grant waivers of the prohibition of importation of prescription drugs to certain individuals and to complete the rulemaking process to allow the importation of certain prescription drugs from Canada. If such actions are implemented, and if APR-246 or another similar or equivalent drug product is approved in another ex-US jurisdiction, these regulatory proposals may impact the competition our product may face, if approved. 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.

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.

Although we have received breakthrough therapy designation for APR-246 for the treatment of patients with myelodysplastic syndrome having a susceptible *TP53* mutation, this does not ensure that we will receive marketing approval of that marketing approval will be granted within any particular timeframe.

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 payors, 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, to clarify that a person or entity need not have actual knowledge of this statute or specific intent to violate it. The Anti-Kickback Statute applies to arrangements between pharmaceutical manufacturers on the one hand and individuals, such as prescribers, patients, purchasers, and formulary managers on the other hand, including, for example, consulting/speaking arrangements, discount and rebate offers, grants, charitable contributions, and patient support offerings, among others. A conviction for violation of the Anti-Kickback Statute can result in criminal fines and/or imprisonment and requires mandatory exclusion from participation in federal health care programs. Exclusion may also be imposed if the government determines that an entity has committed acts that are prohibited by the Anti-Kickback Statute. 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 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, group purchasing organizations, 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 to 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 $11,665 to $23,331 per false claim or statement for penalties assessed after June 19, 2020, with respect to violations occurring after November 2, 2015. 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. There is also the Federal Criminal False Claims Act, which is similar to the Federal Civil False Claims Act and imposes criminal liability on those that make or present 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 healthcare benefits, items, or services.

- *HIPAA Criminal Federal Health Care Fraud Statute*—Enacted as part of HIPPA, makes it a crime to knowingly and willfully execute, or attempt to execute, a scheme or artifice to defend any health care benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any health care benefit program in connection with the delivery of or payment for 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 protected health information, including, among other requirements, to implement certain policies and procedures, to support certain substantive rights of patients, 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 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, Drug Price Transparency, 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, 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.

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 or disruptions to our IT systems, inappropriate use or disclosure of protected information, 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. Moreover, privacy and cybersecurity laws and regulations are evolving, and may continue to add additional compliance costs and legal risks. For example, the California legislature passed the California Consumer Protection Act (CCPA), which came into effect January 1, 2020. The CCPA requires companies doing business in California to disclose information regarding the collection and use of a consumer's personal data, and comply with certain qualified privacy rights requests, including rights to request deletion of or to stop the sale of their personal information. While the CCPA includes certain exemptions for data protected by HIPPA or in certain research contexts, the law covers a wide range of data we my process in other contexts. The CCPA also permits the imposition of civil penalties and expands existing state security laws by providing a private right of action for consumers in certain circumstances where consumer data is subject to a breach. Interpretations of the CCPA may continue to evolve with regulatory guidance and enforcement actions from the California Attorney General. Additionally, the CCPA may be further amended, including through a referendum called the California Privacy Rights Act, which has qualified to be on the ballot in California in November 2020. Several states are also considering similar legislation.

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.

Any clinical trial programs we conduct or research collaborations we enter into in the European Economic Area ("EEA")/UK may subject us to European data protection laws including, the EU General Data Protection Regulation 2016/679 ("GDPR").

We are subject to the GDPR (as implemented by countries in Europe), 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, 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. The GDPR also prohibits the international transfer of personal data from the EEA/UK to countries outside of the EEA/UK unless made to a country deemed to have adequate data privacy laws by the European Commission or a data transfer mechanism has been put in place. Until recently, one such data transfer mechanism was the EU-US Privacy Shield. However, in July 2020 the Court of Justice of the European

Union ("CJEU") declared the Privacy Shield to be invalid. The CJEU upheld the validity of the standard contractual clauses ("SCCs") as a legal mechanism to transfer personal data but companies relying on SCCs will – subject to additional guidance from regulators in the EEA/UK – need to evaluate and implement supplementary measures that provide privacy protections additional to those provided under SCCs. In turn, the findings of the CJEU will have significant implications for cross-border data flows.

Further, the GDPR provides that EU Member States (and the UK) 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 controllers and processors to maintain a record of their data processing activities and policies and procedures to demonstrate compliance with the GDPR. 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 stop or 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.

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 Financial 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.

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, 2019 were $19.7 million. Of that amount, $17.4 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 $19.7 million on our net deferred tax assets as of December 31, 2019, 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 Pub. L. 115-97, commonly known as the Tax Cuts and Jobs Act of 2017 (“TCJA”). Under the TCJA, as amended by the CARES Act, the amount of our net operating losses incurred in taxable years beginning after December 31, 2020 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. Under the CARES Act, net operating losses arising in taxable years beginning before January 1, 2021 are not subject to the 80% limitation.

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 the Company 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 the Company 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, the Company, 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 the Company 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 as of December 31, 2019, 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, we have not yet determined the amount of such earnings and profits and no assurance can be given that Aprea AB will not have any earnings and profits as of December 31, 2019.

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, the Company 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 and the COVID-19 pandemic and related travel restrictions may further limit our ability to reduce the risk of our foreign subsidiaries being treated as engaged in a U.S. trade or business. 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 some guidance has not yet been finalized. 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 proposed and final 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

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.

As of June 30, 2020, our executive officers and directors and our stockholders which own more than 5% of our outstanding common stock beneficially owned shares representing approximately 86.4 % of our common stock. 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 may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which common stockholders might otherwise receive a premium for our 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.

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

The trading market for our common stock is and will rely in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts who currently cover our business downgrade their evaluations of our business, or in the event we obtain additional coverage and one or more of the new analysts issues an adverse evaluation of our business, 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 has been and may continue to be volatile and fluctuate substantially.

Our stock price has been and is likely to continue 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, our stockholders may not be able to sell our common stock at or above the price they paid for it. 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.

In addition, the spread of COVID-19 has caused a broad impact globally. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, it has significantly disrupted global financial markets, and a recession or market correction resulting from the spread or continuation of COVID-19 could materially affect our business and the value of our common stock.

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 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, 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. 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 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 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 continue to 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 continue to 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 are 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.

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 may be investors’ 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 investors’ 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. As of June 30, 2020, we have outstanding 21,186,827 shares of common stock.

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 executed in connection with our IPO.

Our certificate of incorporation 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 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.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

Unregistered sales of equity securities

None, other than previously disclosed.

Use of proceeds from registered securities

On October 7, 2019, we completed our IPO, in which we sold 6,516,667 shares of common stock, $0.001 par value per share, which included the exercise in full by the underwriters of their option to purchase an additional 850,000 shares of common stock, at a price to the public of $15.00 per share. The offer and sale of the shares in the IPO was registered under the Securities Act pursuant to registration statements on Form S-1 (File No. 333-233662), which was filed with the SEC on September 6, 2019 and amended subsequently and declared effective on October 2, 2019, and Form S-1MEF, which was filed and declared effective with the SEC on October 2, 2019. The underwriters of the offering were J.P. Morgan Securities LLC, Morgan Stanley & Co. LLC and RBC Capital Markets, LLC.

Our registration statements relating to the IPO registered common stock with a maximum aggregate offering price of up to $103,500,005. We raised approximately $90.9 million in net proceeds after deducting underwriting discounts and commissions of $6.8 million but before deducting other offering expenses. No offering expenses were paid directly or

indirectly to any of our directors of officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

To date, we have not used any of the net proceeds from our IPO. There has been no material change in the planned use of proceeds from our IPO, as described in our final prospectus filed with the SEC on October 4, 2019 pursuant to Rule 424(b) under the Securities Act.

Repurchases of equity securities by the issuer

None.

Item 3. Defaults Upon Senior Securities

Not applicable.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

In August 2020, we entered into a companion diagnostics agreement with Invivoscribe, Inc. to collaborate on the development of an in vitro companion diagnostic test for eprenetapopt. Pursuant to the companion diagnostics agreement, Invivoscribe will develop a companion diagnostic assay for regulatory approval as a companion diagnostic for eprenetapopt in exchange for payments of up to $13.2 million in the aggregate, subject to the achievement of specified milestones and reimbursement of defined out-of-pocket expenses.

Item 6. Exhibits.

Exhibit Index

Exhibit Number	Description of Document
10.1†	Companion Diagnostic Agreement dated August 11, 2020, by and between Invivoscribe, Inc. and the Registrant.
31.1	Certification of the Registrant's Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of the Registrant's Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of the Registrant's Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of the Registrant's Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Taxonomy
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

† Portions of this exhibit (indicated by bracketed asterisks) have been omitted as the Registrant has determined that (i) the omitted information is not material and (ii) the omitted information would likely cause competitive harm to the Registrant if publicly disclosed.

* The certifications furnished in Exhibit 32.1 and Exhibit 32.2 hereto are deemed to accompany this Quarterly Report and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the registrant specifically incorporates it by reference.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: August 11, 2020

Aprea Therapeutics, Inc.

By: /s/ Christian S. Schade
Christian S. Schade
President and Chief Executive Officer (Principal Executive Officer)

Date: August 11, 2020

By: /s/ Scott M. Coiante
Scott M. Coiante
Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)

***Certain information, identified by [***], has been excluded from the exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.**

COMPANION DIAGNOSTICS AGREEMENT

This Companion Diagnostics Agreement (this "Agreement") dated August 11, 2020 (the "Effective Date"), by and between Invivoscribe, Inc., a California corporation with offices located at 10222 Barnes Canyon Rd., Building 1, San Diego, CA 92121 ("IVS"), and Aprea Therapeutics, Inc., a Delaware corporation ("APR") with offices located at 535 Boylston Street, Boston, MA 02116 (each a "Party" and collectively the "Parties").

RECITALS

WHEREAS, IVS, together with its Affiliates, is a diagnostics company with expertise and capability in research, development, manufacturing, marketing, and commercialization of *in vitro* diagnostics and companion diagnostics in relation to the pharmaceutical industry;

WHEREAS, APR, together with its Affiliates, is a pharmaceutical company with expertise in personalized healthcare engaged in the research, development, manufacture and commercialization of pharmaceutical products and methods to treat patients with pharmaceutical products; and

WHEREAS, IVS has been approached by APR to assist in the clinical validation of eprenetapopt (APR-246), an investigational therapeutic compound for frontline treatment of *TP53*-mutated patients; and

WHEREAS, the Parties hereby wish to establish this Agreement to collaborate on the development and commercialization of an in vitro companion diagnostic test for the APR Product (defined herein) on the terms and subject to the conditions set forth herein.

NOW THEREFORE, in consideration of the mutual covenants, agreements, representations and warranties set forth herein, the Parties agree as follows:

ARTICLE 1
DEFINITIONS

In this Agreement the following terms, when capitalized, shall have the following meanings:

1.1 "Activities" means the activities to be performed by any Party in connection with the Project, to the extent set forth in the Project Plan.

1.2 "Affiliate" means any Person that directly or indirectly Controls, is Controlled by, or is under common Control with, a Person. With respect to IVS, the term Affiliate shall include LabPMM, LabPMM GmbH, LabPMM GK, and Genection, Inc.

1.3 "Alliance Manager" shall have the meaning set forth in Section 2.6(a).

1.4 "Applicable Law" means all international, federal, state and local laws, rules, codes, regulations, including any rules, regulations, guidelines or guidances, or requirements of any Regulatory Authorities, government authorities, courts, tribunals, agencies other than Regulatory

Authorities, and legislative bodies that are in effect from time to time during the Term and applicable to a particular activity hereunder.

1.5 "Approved Development Budget" means the budget for the Development and Regulatory Approval of the Assay and the IVD Kit, as applicable, in the Territory, including, subject to Sections 7.2 and 10.3, all Pass-Through Expenses payable by APR to IVS under this Agreement. The Approved Development Budget is set forth in Schedule A, as may be amended from time to time solely in accordance with the terms and conditions of this Agreement.

1.6 "Approved Facilities" shall initially mean each of the following IVS facilities at which companion diagnostics testing for the APR Product with the Assay shall occur, and any additional IVS facilities as may be approved by the JSC during the Term: (1) IVS, in San Diego, California, (2) Laboratory for Personalized Molecular Medicine, LLC ("Lab PMM"), in San Diego, California, United States, (3) LabPMM GmbH, in Munich, Germany, and (4) LabPMM GK, located at Life Science & Environment Research Center (LiSE) 4th Floor, 3-25-13 Tonomachi, Kawasaki-ku, Kawasaki City, Kanagawa 210-0821, Japan.

1.7 "Approved Subcontractors" shall have the meaning set forth in Section 3.7.

1.8 "Assay" means IVS's Tumor protein p53 ("TP53") gene assay, an ***in vitro*** companion diagnostic test to detect mutations in human samples with the intent to select patients for treatment with the APR Product. The term "Assay" includes improved or subsequent versions of such companion diagnostic, associated reagents, procedures, instrumentation and/or software necessary to perform the Assay, but shall exclude any Samples.

1.9 "APR Product" means any pharmaceutical or over-the-counter preparation containing eprenetapopt (APR-246), an investigational therapeutic compound for frontline treatment of *TP53*-mutated myelodysplastic syndrome ("MDS") patients, in any formulation and/or dosage form. For clarity, "APR Product" includes an approved use of APR-246 in combination with another therapeutic ingredient or compound.

1.10 "APR Product IP" means any Background IP Controlled by APR that relates specifically to the composition of matter or use of the APR Product, including any Product Related Data.

1.11 "Background IP" means all Intellectual Property in existence and Controlled by a Party prior to the Effective Date or conceived, discovered, reduced to practice or writing, generated or developed by a Party or coming into Control of a Party during the Term independently of the Activities and conduct under the Project Plan and without the use of any Intellectual Property, Confidential Information, Project Data, Deliverables or Materials Controlled by the other Party. Background IP shall not include Joint Inventions, joint Know-How or Joint Patents.

1.12 "Background Patents" means those Patents Controlled by a Party prior to the Effective Date or during the Term, and any improvements thereof, that have been developed or obtained independently of this Agreement.

1.13 "Bridging Study" means the investigation of agreement between two methods generally requiring re-testing of all available clinical samples from a pivotal or phase 3 study in the

method to which the sponsor wishes to transition and requiring a high degree of concordance of results from the new method in comparison to the original method to be conducted in accordance with the Project Plan and the bridging study protocol developed by IVS and approved by APR.

1.14 "Budget" means the Approved Development Budget, as amended, supplemented or restated from time to time by mutual written agreement of the Parties.

1.15 "Business Day" means any day that is not a Saturday, a Sunday or a bank holiday in the United States, or in the local country where the Assay is performed.

1.16 "cGCP" means the current good clinical practice applicable to the clinical development of any APR Product or Assay or IVD Kit used in the Project under Applicable Laws, including the ICH guidelines.

1.17 "cGMP" means current Good Manufacturing Practices that apply to the manufacture of any APR Product or Assay or IVD Kit used in the Project, including the United States regulations set forth under Title 21 of the United States Code of Federal Regulations, parts 210,211 and 820 (as applicable), as may be amended from time-to-time, as well as all applicable guidance published from time-to-time by the FDA and the International Conference on Harmonisation ("ICH") Guidelines ICHQ7A Good Manufacturing Practice Guidance for API and/or the principles and guidelines of Good Manufacturing Practices for Medicinal Products as defined with EC Directive 2003/94/EC and associated EC Guide to Good Manufacturing Practice.

1.18 "Change of Control" means, with respect to IVS, the occurrence of any of the following events following the Effective Date: (i) any Person gains Control of IVS, directly or indirectly, by any means (including, but not limited to, acquisition of shares, share exchange or share transfer); (ii) IVS conveys, transfers, divests or leases (including, but not limited to, general succession and all types of corporate split) in one or more transactions to any corporation or other person or entity other than a wholly-owned subsidiary of IVS either: (x) all or substantially all of the assets of IVS or (y) all or substantially all of its assets that are material to the purpose of performance of its obligations hereunder; or (iii) IVS is involved in any merger, consolidation, corporate split or other similar transaction and the shareholders of IVS immediately prior to such transaction own fifty percent (50%) or less of the outstanding securities or ownership interests of the surviving or resulting entity immediately after such transaction.

1.19 "Commercialization" or "Commercialize" means all activities undertaken relating to the manufacture, marketing, pre-marketing, use, sale, pricing, reimbursement, importing, exporting, and distribution of the Assay and/or the IVD Kit. For clarity, Commercialization excludes all Development and Regulatory Approval activities.

1.20 "Commercially Reasonable Efforts" means, with respect to the efforts and resources to be expended by either Party with respect to any objective, such reasonable, diligent, and good faith efforts and resources as a similar party, similarly situated, would normally use to accomplish a similar objective under similar circumstances as expeditiously as possible, which in no event shall be less than the standard of care generally adhered to in the industry of such Party for the providing of such efforts.

1.21 "Confidential Information" means any and all information or material in any form, including any Project Data, Product Related Data, documents, notes, analyses, studies, samples, drawings, flowcharts, databases, models, plans and software (including source and object codes), which is disclosed by any Party or any of its agents or representatives (the "Disclosing Party") to any other Party or any of its agents or representatives (the "Receiving Party") pursuant to this Agreement, and which is of a confidential nature (including any information relating to business affairs, operations, products, processes, methodologies, testing processes, packaging and manufacturing techniques, formulae, plans, intentions, projections, know-how, intellectual property rights, trade secrets, market opportunities, suppliers, customers, marketing activities, sales, software, computer and telecommunications systems, costs and prices, wage rates, records, finances and personnel). For the avoidance of doubt, Personal Information is Confidential Information.

1.22 "Control" or "Controlled" means, (i) with respect to Intellectual Property, that a Party has the right directly or indirectly and whether by ownership, license or otherwise, to grant a license or sublicense to such Intellectual Property herein without violating the terms of any written agreement or arrangement with any Third Party or Applicable Laws and (ii) with respect to any Person, the possession, directly or indirectly, of at least fifty percent (50%) of the share or equity capital or voting rights or of the power to direct or cause the direction of the management and policies of such Person, whether through the ownership of voting securities, by contract or otherwise..

1.23 "Cover" means, with respect to any subject matter, the manufacture, use, sale, offering for sale, importation, exportation or other exploitation of such subject matter would (absent a license thereunder or ownership thereof) infringe a claim of a Patent at the time thereof. Cognates of the word "Cover" shall have correlative meanings.

1.24 "Data Breach" means any unauthorized Processing of or access to Personal Information, Confidential Information, or a Party's information technology assets or systems.

1.25 "Deliverables" shall mean the data and/or materials to be provided to APR by IVS under this Agreement.

1.26 "Develop" or "Development" means all activities undertaken relating to the research or development (including preclinical studies, clinical trials, and development activities) of the Assay or IVD Kit.

1.27 "Diagnostics Field"1.28 means the discovery, development, manufacture, and/or sale of laboratory developed tests, or in vitro diagnostic tests for research, clinical or medical use or as a diagnostic to identify the presence of a human disease or condition, predict development of a human disease or condition, monitor likelihood of patient response to an intervention or as a prognostic of a human disease or condition.

1.29 "Dispute" shall mean any dispute, controversy or claim between the Parties arising on or after the Effective Date out of or in connection with this Agreement (including the Project Plan and Budgets) or the Parties' activities hereunder (or thereunder).

1.30 "Effective Date" means the date first set forth above.

1.31 "Exclusivity Period" means the period of time commencing on the Effective Date and ending on the earliest of the following: (a) three (3) years after the Effective Date, (b) the date that this Agreement is terminated pursuant to Sections 11.3, 11.4 or 11.5, or (c) the date on which APR receives final notice (from which further appeal may not be taken) from a Regulatory Authority that the PMA for the Assay or IVD Kit for the APR Product will not receive Regulatory Approval.

1.32 "FDA" means the United States Food and Drug Administration and any successor agency.

1.33 "FD&C Act" means the United States Federal Food, Drug and Cosmetic Act, as amended.

1.34 "Final Study Report" means the document prepared at the end of the Bridging Study that describes the objectives, design, methodology, statistical analysis, results and conclusions of such Bridging Study.

1.35 "Independent Development" shall mean the undertaking of any and all development work that is: (a) not prohibited by this Agreement, and (b) undertaken without the aid, application or use of any of the other Party's Background IP, Inventions, Know-How, Confidential Information or the other Party's Project Data.

1.36 "Intellectual Property Rights" or "IPR" shall mean all intellectual property rights, including patent rights (pending or issued), Trade Secrets, utility models, registered designs, design rights (pending or issued), copyrights, copyright registrations, and similar intellectual property rights.

1.37 "Invention" means any and all inventions, discoveries, technology, know-how, materials, methods, processes and protocols, whether or not patentable, developed, generated, conceived and/or reduced to practice, during the course of and pursuant to the activities under this Agreement together with all Intellectual Property Rights (including applications) claiming such inventions, discoveries, technology, Know-How, materials, methods, processes and protocols. Inventions may rely upon or be developed based on Project Data, but for the purposes of this Agreement, Inventions shall not mean Project Data.

1.38 "IVD" or "*in vitro diagnostic*" means those reagents, instruments and systems intended for use in the diagnosis of disease or other conditions, including the state of health, in order to cure, mitigate, treat, or prevent or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.

1.39 "IVD Kit" means a kitted version of the Assay Developed by IVS pursuant to this Agreement, for Regulatory Approval as a companion diagnostic for the APR Product, to be distributed to its LabPMM laboratories and appropriate third party laboratories to enable LabPMM laboratories and appropriate third party laboratories to perform the IVD per applicable regulations. As used herein, "IVD Kit" shall include improved or subsequent versions of such test kit.

1.40 "IVS Know-How" means technologies Controlled by IVS in the areas of hardware, detection chemistry, computer software programs for bioinformatics, annotation, curation, image

analysis of biological systems, nucleic acid detection, automated anatomic pathology systems, assays, diagnostic assay development expertise, diagnostic test kits, statistical methodologies and other formulae and analytical techniques and laboratory services that (i) have been independently developed by IVS prior to the Effective Date or during the Term and relating to the Assay or the IVD Kit and the activities performed under the Project Plan, or (ii) are independently developed by IVS after the Effective Date apart from any activities under this Agreement and without reference to or the benefit of any information or Materials provided by or on behalf of APR.

1.41 "Joint Development Committee" or "JDC" shall have the meaning set forth in Section 2.5 below.

1.42 "Joint Steering Committee" or "JSC" means a group of persons established by the Parties to monitor and provide strategic oversight of the activities hereunder relating to the Development and Regulatory Approval of the Assay and IVD Kit and to facilitate communications between the Parties in relation thereto.

1.43 "Know-How" means all non-patented confidential and proprietary information or biological materials, including cells, cell lines, genes, gene fragments, gene sequences, probes, DNA, RNA, cDNA libraries, proteins, peptides, polypeptides, plasmids, vectors, expression systems, organisms, biological substances, and any constituents, progeny or replications thereof or therefrom, reagents, chemical compounds, inventions, whether or not patentable, improvements, practices, formula, Trade Secrets, techniques, methods, procedures, knowledge, skill, experience, results, test data (including pharmacological, toxicological and clinical test data), analytical and quality control data and any information regarding marketing, pricing, distribution, cost, sales or manufacturing. Know-How shall not include any Patents or Product Related Data.

1.44 "LDT" or "laboratory developed test" means a type of *in vitro* diagnostic test that is designed, manufactured and used within a single laboratory.

1.45 "Market Requirements Document" means a document prepared for the purpose of specifying customer needs and desires for a particular product or service.

1.46 "Materials" means Samples, biological materials, compounds, reagents, supplies, products and other goods that one Party delivers or causes to be delivered to the other Party.

1.47 "EMA" means the European Medicines Agency, or any successor to that agency.

1.48 "EU" means the member states of the European Union.

1.49 "NDA" means a New Drug Application, or its equivalent, and amendments thereto filed pursuant to the requirements of the FDA, for FDA approval of a product.

1.50 "Pass-Through Expenses" means and is limited to the following fees and expenses to the extent actually incurred by IVS: (i) submission fees for PMA and IRB review of the clinical protocol, (ii) Class C CDx submission and review, and ethics committee review of the clinical protocol in the European Union, (iii) licensing fees to run the assay on the [***] mode, if required, (iv) out-of-pocket expenses (including contingencies, travel and other expenses), and (v) any other expenses incurred by IVS under this Agreement or any Development Plan to the extent approved

in advance by the JSC, provided however, the sum of which fees and expenses set forth in clauses (i)-(iv) may not exceed $[***] in total unless any such overrun is approved by the JSC, provided however that the Parties acknowledge that such $[***] amount did not include the fees and expenses for a separate submission to the United Kingdom and so any such additional fees and expenses will need to be agreed upon by the JSC prior to any submission to the United Kingdom.

1.51 "Patents" means the issued patents and pending patent applications (including certificates of invention, applications for certificates of invention and priority rights) in any country or region, including all provisional applications, re-filings, substitutions, continuations, continuations-in-part, divisions, renewals, all letters patent granted thereon, and all reissues, re-examinations and patent term extensions thereof, and all international or foreign counterparts of any of the foregoing (including supplemental protection certificates, patents of addition and the like).

1.52 "Person" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture, or other similar entity or organization, including a government or political subdivision, department, or agency of a government.

1.53 "Personal Information" means (i) any information that identifies, relates to, describes, is reasonably capable of being associated with, or could reasonably be linked with a particular consumer or household; and (ii) "personal data," "personal information," "personal health information," "protected health information," "medical information," or similar terms, as those terms are defined in Privacy and Data Security Laws.

1.54 "Pharmaceutical Field" means the discovery, development, manufacture, use, and/or sale of biological or chemical substances for the medical cure, treatment, or prevention of diseases of human beings.

1.55 "PMA" means: (i) a U.S. pre-market approval application for a Class III medical device, including all information submitted with or incorporated by reference, and/or any new drug application for a medical device pursuant to section 520(1) of the FD&C Act, or (ii) any analogous application to those set forth in (i) that is filed with the relevant Regulatory Authority in another country. A supplemental PMA submission is referred to as an "sPMA".

1.56 "Pre-Submission" means a formal written request from an applicant/sponsor for feedback from FDA to be provided in the form of a formal written response or, if the manufacturer chooses, a face-to-face meeting or teleconference with FDA in which the feedback is documented in meeting minutes. A Pre-Submission is appropriate when FDA's feedback on specific questions is necessary to guide product development and/or application preparation.

1.57 "Privacy and Data Security Laws" means any and all applicable laws and regulations issued by any governmental authority relating to the Processing of Personal Information, including: (i) each law relating to the protection or Processing of Personal Information that is applicable to the Parties, including as applicable, but not limited to, the Federal Trade Commission Act, 15 U.S.C. § 45; the CAN-SPAM Act of 2003, 15 U.S.C. § 7701 et seq.; the Telephone Consumer Protection Act, 47 U.S.C. § 227; the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"); the Health Information Technology for Economic and Clinical Health Act ("HITECH"); the

California Confidentiality of Medical Information Act; the California Consumer Privacy Act ("CCPA"); the Electronic Communications Privacy Act, 18 U.S.C. §§ 2510-22; the Stored Communications Act, 18 U.S.C. § 2701-12; California Online Privacy Protection Act, Cal. Bus. & Prof. Code § 22575, et seq.; Massachusetts Gen. Law Ch. 93H, 201 C.M.R. 17.00; Nev. Rev. Stat. 603A; Cal. Civ. Code § 1798.82, N.Y. Gen. Bus. Law § 899-aa; the European Union's Directive on Privacy and Electronic Communications (2002/58/EC); the General Data Protection Regulation (2016/679); and all implementing regulations and requirements, and other similar laws.

1.58 "Processing", "Process" or "Processed", with respect to data or information technology systems or assets, means any collection, access, acquisition, storage, protection, use, re-use, disposal, disclosure, re-disclosure, destruction, transfer, modification, or any other processing (as defined by any applicable Privacy and Data Security Laws) of such data or information technology systems or assets.

1.59 "Project" means the project described in the Project Plan and performed under this Agreement, which project ultimately may result in the creation, Development, Regulatory Approval and subsequent Commercialization of a [***] Assay and [***] for use in the Target Countries for the APR Product under this Agreement.

1.60 "Project Data" means any information, records or other data developed in the course of the Project, including the results of the Assay and/or IVD Kit tests conducted thereunder and the results of the Bridging Study, if any. Project Data may be further identified as "IVS Project Data" or "APR Project Data" as set forth in Section 8.12.

1.61 "Project Plan" means the Plan for a [***] Assay, as shall be agreed upon in writing between the Parties, containing a list of Activities, Deliverables and other terms applicable to the Project.

1.62 "Product Related Data" means, only to the extent related to the APR Product, all Confidential Information: (a) supplied to IVS, its Affiliates or Approved Subcontractors by APR, its Affiliates or Approved Subcontractors, (b) generated by any Party in any clinical trial, (c) generated by the Approved Subcontractors in the course of any Project under this Agreement, (d) involving clinical outcomes of the APR Product, and/or (e) related to Commercialization of the APR Product. In addition to its obligations under Article 8, IVS shall use coded identifiers for such Product Related Data for additional security.

1.63 "QSR" or "Quality Systems Regulations" means the good manufacturing practices and design control requirements for medical devices set forth by Applicable Laws, including United States 21 C.F.R. Section 820.

1.64 "Regulatory Approval" means with respect to a regulatory jurisdiction, any and all approvals, product and/or establishment licenses, product listings, registrations or authorizations of any Regulatory Authority, necessary for the commercial manufacture, use, storage, import, export, transport, or Commercialization of a product in such regulatory jurisdiction, including, where applicable, (i) pricing and reimbursement approval in such regulatory jurisdiction, (ii) pre- and post-approval marketing authorizations (including any prerequisite manufacturing approval or authorization related thereto), (iii) labeling approval, and (iv) technical, medical and scientific licenses. For clarity, (x) with regard to an IVD, Regulatory Approval occurs upon registration and

product listing with FDA in connection with FDA approval of a PMA, granting a De Novo Classification, or FDA's clearance (or finding of substantial equivalence) in response to a premarket notification filed pursuant to §510(k) of the FD&C Act for the IVD and similar approvals of Regulatory Authorities in other countries, and (y) with regard to the APR Product, Regulatory Approval means NDA approval granted by the FDA, and similar approvals of Regulatory Authorities in other jurisdictions in the Territory outside of the United States.

1.65 "Regulatory Authority" means, as applicable, the FDA, the European Medicines Agency, and/or any other regulatory authority or agency in the Territory having responsibility for determining pharmaceutical product approvals, companion diagnostics approvals, packaging/labeling approvals, manufacturing standards, and/or approving the marketing, pricing and/or reimbursement, as applicable, of pharmaceutical products or companion diagnostics.

1.66 "Samples" means (i) human tissue samples, whether in blocks, slides, fresh or otherwise, (ii) human blood samples, bone marrow aspirates, extracted nucleic acid or other clinical isolate, bodily fluids, cells, organs, and human-derived waste or other similar specimen samples, and (iii) any data or information associated with such Samples.

1.67 "Target Countries" means the United States, the European Union and the United Kingdom.

1.68 "Territory" means the entire world.

1.69 "Term" shall have the meaning set forth in Section 11.1.

1.70 "TGA" means the Therapeutic Goods Administration.

1.71 "Third Party" means any individual or entity other than IVS, APR, or Affiliates of either IVS or APR.

1.72 "TP53" means the Tumor protein p53 (TP53) gene.

1.73 "Trade Secret" includes Know-How that is a trade secret, and trade secrets as defined under the Federal Defense of Trade Secrets Act.

1.74 "Working Group" shall have the meaning set forth in Section 2.6(b).

1.75 Construction. References herein to days means calendar days, unless the term "Business Days" is specified. References to a "country" shall be interpreted as referring to the applicable region or jurisdiction if the word "country" is not appropriate in that circumstance. The words "hereof", "herein" and "hereunder" and words of like import shall refer to this Agreement as a whole and not to any particular provision of this Agreement. The captions herein are included for convenience of reference only and shall be ignored in the construction or interpretation hereof. Any capitalized term used in any Project Plan but not otherwise defined therein shall have the meaning as defined in this Agreement. Any singular term in this Agreement shall be deemed to include the plural, and any plural term the singular, so long as the context supports such interpretation. Whenever the words "include", "includes" or "including" are used in this Agreement, they shall be deemed to be followed by the words "without limitation", whether or not

they are in fact followed by those words or words of like import. Ambiguities, if any, in this Agreement will not be construed against either Party, irrespective of which Party may be deemed to have authored the ambiguous provision. This Agreement will be fairly interpreted in accordance with its terms and without any strict construction in favor of or against either Party.

ARTICLE 2
PURPOSE AND GOVERNANCE

2.1 Plans. IVS and APR agree to collaborate to Develop and obtain Regulatory Approval of the Assay and/or the IVD Kit in accordance with this Agreement, and, as applicable, the Project Plan. The Project Plan and the accompanying Budget is for the Assay as a [***] assay [***], after Regulatory Approval of the Assay and for the Target Countries of the United States, the member states of the EU, and the United Kingdom. This Agreement shall govern the conduct of the Project Plan attached hereto, as amended, which may be approved by the JSC from time to time. IVS shall perform the Activities and provide the Deliverables as set forth in the Project Plan with the standards of care and skill to be reasonably expected in the field of Developing *in vitro* diagnostics and companion diagnostics, including adherence to applicable QSR and cGCP practices. The Parties shall cooperate in good faith to achieve the results contemplated in the Project Plan, including the Development of the Assay and IVD Kit.

2.2 Scope Changes. Changes to the Project Plan (including any additional Target Countries desired by APR), Activities or Deliverables shall be discussed at the JSC or a Working Group thereunder. Each time that the Parties agree that the Activities or Deliverables of the Project should be amended or additional Activities or Deliverables should be added to a Project, the Parties shall prepare a written amendment to the Project Plan for such Project, including a commensurate change in such Project Plan's Budget in response to such additions or deletions, and such amendment and changes must be agreed upon by the JSC. Upon APR's request to expand the scope of the Project, IVS shall: (i) not unreasonably withhold its consent to the relevant amendment provided that such change in scope does not jeopardize or put at risk any part of the business of IVS, and APR agrees to reasonable compensation and adjustment of timelines for the additional work, to the extent necessary and applicable, and (ii) reasonably discuss with APR in good faith the amendments to the Project Plan or Budget. The amended Plan and/or Budget shall have added to it a description of such new or amended Activities and/or Deliverables, provisions regarding the financial consideration, and other details regarding the new or amended Activities and/or Deliverables. A Party shall not vary from the Activities and Deliverables set out in the Project Plan until the Parties have agreed to do so in writing; provided that either Party can order a suspension of Activities if such Party identifies a material safety issue with respect to the Assay or IVD Kit.

2.3 Notification. Each Party agrees to promptly notify the other Party in writing of any actual or reasonably anticipated delays or other material problems in fulfilling any of its obligations under this Agreement or under any Plan. Such notification, however, shall not excuse any required performance under the Agreement. Moreover, each Party shall retain all of its rights under the Agreement should such delay or other material problem of the other Party be considered a breach under the terms of this Agreement.

2.4 Exclusivity.

(a) During the Exclusivity Period, APR agrees that it shall not work with a Third Party for the development of a *TP53* assay that tests for any *TP53* mutations for the APR Product for a Target Country for so long as IVS is not in breach of its obligations with respect to the Development of the Assay or IVD Kit hereunder, provided that in the event of such breach, APR must first notify IVS of such breach and provide IVS with the opportunity to cure pursuant to Section 11.4 of this Agreement.

(b) APR shall own and retain ownership of all rights, title and interest in and to the APR Product, shall be free to use the APR Product for any purpose, in combination with any product or service and in collaboration with any Third Party whatsoever, and will retain the right to perform Independent Development activities, including APR's rights to independently develop, utilize, or commercialize diagnostic tests, other than TP53 (including IVDs and LDTs) as described above in Section 2.4(a), in addition to the Assay or IVD Kit, whether alone or in collaboration with Third Parties.

(c) IVS shall own and retain ownership of all rights, title and interest in the Assay and the IVD Kit and shall be free to use the Assay and the IVD Kit for any purpose, in combination with any product or service and in collaboration with any Third Party, and will retain the right to perform Independent Development activities, including IVS's rights to independently develop, utilize, or commercialize the Assay or IVD Kit and other diagnostic tests, whether alone or in collaboration with Third Parties, for use either alone or in conjunction with the development or commercialization of any pharmaceutical products other than the APR Product; provided that IVS is bound by, and this Section 2.4(c) shall not modify, amend or limit, the license set forth in Section 10.2.

2.5 Governance.

(a) JSC. The Parties shall establish a Joint Steering Committee (the "JSC") to monitor and provide strategic oversight of the activities hereunder relating to the Development and Regulatory Approval of the Assay and IVD Kit and to facilitate communications between the Parties in relation thereto. Each Party shall initially appoint up to three (3) representatives to the JSC (which number need not be equal), with each representative having the requisite knowledge and expertise to oversee activities under this Agreement and sufficient seniority within the applicable Party or its Affiliates to make decisions arising with the scope of the JSC's responsibilities. The initial representatives for APR shall be Eyal Attar, Phill Gallacher and Lars Abrahmsen , and the initial representatives for IVS shall be Jeffrey Miller, Meghna Bhatnagar, and Jason Gerhold. In addition, each Party shall appoint one representative (the "Alliance Manager") who will not serve as a voting member of the JSC but who shall provide alliance management support for such Party for its activities hereunder. Each Party may replace any of its JSC representatives, or its Alliance Manager, at any time upon written notice to the other Party.

(b) Specific Responsibilities. The JSC shall have the following responsibilities with respect to the Project generally, the Project Plan, and to the Assay and the IVD Kit:

(i) Oversee the progress of the Activities under the Project and facilitate the exchange of information between the Parties during the Term;

(ii) Review quarterly progress reports under the Project and Project Plan, as well as quarterly updates on regulatory activities (including the Regulatory Approval process and timelines), communications and coordination. Each Party shall deliver such reports to JSC on a timely manner;

(iii) Review and approve any scope changes as described in Section 2.2 to the Project Plan and timelines therefor;

(iv) Maintain the list of Target Countries and make modifications thereto upon APR's notification and upon the appropriate adjustments in the Budget and Pass Through Expenses pursuant to Section 3.6. For clarity, Target Countries shall be determined by APR and not the JSC, but subject to agreement on the amended Budget as provided in Section 3.6;

(v) Align strategy and timing for the Regulatory Approval of the Assay and IVD Kit (including the labeling thereof) with the regulatory strategy and timing for the APR Product (including the labeling thereof); provided that the regulatory strategy for the APR Product (including the labeling thereof) shall be solely determined by APR, as set forth in Section 4.1;

(vi) Annually review and modify the Project Plan (including timelines) and Budget (including appropriate adjustments to reflect costs for Regulatory Approval of the Assay and/or the IVD Kit arising from newly identified and/or changes to Target Countries);

(vii) Establish, monitor and delegate duties to other committees, subcommittees, or directed teams (each a "Working Group") on an "as needed" basis to oversee particular projects or activities, including the Joint Development Committee (the "JDC"), which is described below;

(viii) Hear and resolve disputes of the Working Groups, including the JDC;

(ix) Approve all Pass-Through Expenses in excess of $[***] in total; and

(x) Taking such other actions as may be specifically allocated to the JSC by the Parties from time to time;

Each Party shall retain the rights, powers and discretion granted to it under this Agreement and no such rights, powers or discretion shall be delegated to or vested in the JSC unless such delegation or vesting of rights is expressly provided for in this Agreement or the Parties expressly so agree in writing. For the avoidance of doubt, APR shall be solely responsible for the performance of all clinical trials of the APR Product.

(c) Working Groups. Each Working Group shall be constituted and shall operate as the JSC determines. Working Groups may be established on an ad hoc basis for purposes of a specific project for the life of the APR Product, or on such other basis as the JSC may determine. Each Working Group and its activities shall be subject to the oversight, review and

approval of, and shall report to, the JSC. The authority of the Working Group cannot exceed that specified for the JSC in this Article 2. Each Party will bear the expense of its respective Working Group members' participation in Working Group meetings.

(d) Meetings. The JSC shall meet at least one (1) time per quarter, or at such other frequency as the Parties shall agree. The chairperson shall be appointed by APR. No later than ten (10) calendar days prior to any meeting of the JSC, the chairperson of the JSC, with input from the Alliance Managers, shall prepare and circulate an agenda for such meeting; provided, however, that either Party shall be free to propose additional topics to be included on such agenda, either prior to or in the course of such meeting. The JSC may meet in person, by videoconference, or by teleconference. In-person JSC meetings will be held at locations within the United States mutually agreed by APR and by IVS. The Parties aim to hold at least one (1) in-person meeting each year. Each Party will bear the expense of its respective JSC members' and Alliance Managers' participation in JSC meetings, provided that if APR requires more than one in person meeting each year that is not in San Diego, California, APR shall bear the expense of the JSC members's and Alliance Managers' participation in such meetings. Meetings of the JSC shall be effective only if at least one (1) voting representative of each Party is present or participating in such meeting. The chairperson of the JSC with the assistance of the Alliance Managers shall be responsible for keeping written minutes of all JSC meetings that reflect all decisions made and action items identified at such meetings, and the chairperson shall circulate draft minutes to the JSC members promptly after each meeting for review by each Party, each Party shall be entitled to submit suggested revisions, if any. Minutes will be officially endorsed and approved by the JSC at the next JSC meeting, or such approval may be obtained in writing (which may be via email) between the Parties. Additional representatives of the Parties may from time to time be invited to attend JSC meetings, subject to the other Party's prior consent which shall not be unreasonably withheld.

(e) JSC Actions. Subject to the remainder of this Section 2.6, the JSC shall act by unanimous vote, with each Party's representatives collectively having one vote. The JSC members shall use reasonable efforts to reach agreement on any and all matters. In the event that, despite such reasonable efforts, a Dispute cannot be solved by the JSC within ten (10) days after the JSC first meets to consider such matter, then, (a) any member of the JSC may refer such Dispute to the Parties' respective senior officers as further described (by title) on Schedule B (the "Senior Officers"), who shall promptly initiate discussions in good faith to resolve such Dispute and (b) if such Dispute is not resolved by the Senior Officers within ten (10) days after the date the Senior Officers first met to consider such Dispute or twenty one (21) days after the date the JSC first met to consider such Dispute, whichever is later, then, except as otherwise provided herein, (i) APR shall have final decision-making authority with respect to any Dispute that relates solely to the APR Product or that relates to development or commercialization of the APR Product, and (ii) IVS shall have final decision-making authority with respect to any Dispute that relates solely to the Assay and/or the IVD Kit and that does not have an adverse impact on the development or commercialization of the APR Product; provided that each Party shall only exercise such right in good faith after full consideration of the positions of the other Party. Notwithstanding anything to the contrary in this Agreement, any material change to the Project Plan and Approved Development Budget, shall be made by unanimous vote and shall not be subject to the final decision making authority of either Party. However, in no event shall the Parties, in exercising their final decision-making authority, have the right to determine any such resolution in a manner

that would conflict with the express terms and conditions of this Agreement, unless the Parties execute a corresponding amendment to this Agreement.

(f) Expenses. Each Party shall bear its own expenses for participation in the JSC and Working Group meetings (including the JDC and JCC), provided that IVS shall not be required to participate in more than one (1) in person meeting outside of San Diego, California, per Working Group, per year, unless APR agrees in advance to reimburse IVS for travel and lodging costs.

(g) Authority to Amend and Modify.

(i) No Authority. Notwithstanding anything herein to the contrary in this Agreement, neither the JSC nor any committee or team established hereunder will have any authority to amend, modify or waive compliance with this Agreement in any manner or any other agreement between the Parties.

(ii) Authority. The JSC shall have the authority to amend and modify provisions of the Project Plan and the Approved Development Budget from time to time as necessary, for example, pursuant to additional Target Countries identified by APR; provided, however, that the JSC may identify any decision as conditional on obtaining internal approvals.

2.6 Joint Development Committee. The JSC shall establish the JDC to monitor and provide strategic oversight of the Activities hereunder relating to the Development and Regulatory Approval of the Assay and IVD Kit. Such JDC shall be constituted and shall operate as the JSC determines.

2.7 Purpose. The explicit purpose of the Project ("Purpose") is to enable APR to market the APR Product together with the Assay as a companion diagnostic test for the APR Product. To this end, part of the Purpose of this Agreement is for IVS to pursue Regulatory Approval of the Assay and/or the IVD Kit in a timely manner using Commercially Reasonable Efforts with the intent of not causing delay to the launch of the APR Product in the Target Countries. This Purpose will inform the Parties' decision making under this Agreement, including but not limited to governance issues, financial decisions, and dispute resolution.

2.8 Financial Responsibilities.

(a) In-Scope Responsibilities. The Project is being performed on the basis for fees as set forth in the Approved Development Budget, including that APR will pay IVS the milestone amounts set forth in the Approved Development Budget upon achievement of the applicable milestone, and APR will pay IVS the Pass-Through Expenses as provided in this Agreement. Unless otherwise provided in this Agreement, IVS shall bear all costs and expenses in connection with the Project that are not Pass-Through Expenses, or which are not approved by the JSC, including cost overruns which do not result from changes to the initial Project Plan.

(b) Out of Scope Responsibilities. For any future work outside of the current scope of the Project Plan, or due to additional Target Countries identified by APR, which will necessitate an amendment to the Approved Development Budget, the Parties agree as follows:

(i) IVS will use good faith efforts to prepare a reasonable estimate of costs and expenses that will be incurred (or credited, as applicable).

(ii) IVS shall not be required to begin any work with respect thereto, and APR shall not be obligated to make any payments with respect thereto, until the JSC has reached agreement.

(iii) In the event that the JSC cannot reach agreement on modifications to the Approved Development Budget, the Parties will use Commercially Reasonable Efforts to identify a commercially reasonable resolution that supports the accomplishment of the Purpose of the Project.

(iv) The JSC shall review expenditures after the expenses are actually incurred to reconcile discrepancies between the estimated Pass-Through Expenses and the actual Pass-Through Expenses.

ARTICLE 3
DEVELOPMENT

3.1 Development of Assay and IVD Kit. IVS shall Develop the Assay and (as applicable) the IVD Kit as further described in the Project Plan using the IVS Know-How, software development, the technical validation and verification of the Assay, and clinical reproducibility studies of the Assay and the manufacturability of the Assay.

3.2 IVS Activities. Without limiting the generality of Section 3.1, IVS shall be responsible for the following with respect to Development of the Assay and the IVD Kit:

(a) Product Requirements Document. IVS shall Develop the Assay and (as applicable) the IVD Kit in a manner consistent with the market requirements document which will be prepared specifically for APR. IVS will be responsible for developing the Product Requirements Document with input and approval from APR and approved by the JSC, as the same may be amended from time to time by the JSC (the "PRD"). In the event of a change to the technical specifications in the PRD after the finalization of the Approved Development Budget, the JSC shall review the change and adjust the Approved Development Budget as appropriate.

(b) Validation. IVS shall perform analytical and clinical validation of the Assay (and, as applicable, the IVD Kit) as set forth in the Project Plan. In addition, IVS shall perform any additional validation (or other activities) that are required by the FDA or any other Regulatory Authority (as result of a Pre-Sub, similar foreign requirement or otherwise) in accordance with a mutually agreeable development plan (and related budget) set forth in an amendment to the Project Plan and/or an amendment to the Approved Development Budget.

3.3 Samples and other Materials.

(a) Privacy and Confidentiality. APR shall transfer necessary positive and negative clinical Samples to IVS under this Agreement and IVS shall receive, process, de-identify, track, store, transport, manipulate and (where appropriate) destroy all Samples under this Agreement in compliance with: (i) the terms and conditions of this Agreement, (ii) any applicable

requirements of an IRB/Ethics Committee and ethical standards, (iii) the terms of any applicable privacy policies, patient notices, patient authorizations and consents, and (iv) all Applicable Laws, including Privacy and Data Security Laws (collectively, (i), (ii), (iii) and (iv) referred to as "Sample Privacy Requirements"). Each Party shall develop and follow all of its documented policies and procedures to ensure the protection of the autonomy and confidentiality of the human subjects from whom the Samples are collected in compliance with the Sample Privacy Requirements. All Samples delivered under this Agreement shall be labeled clearly in accordance with the Sample Privacy Requirements.

(b) Ownership; Storage and Handling. All Samples belong to APR, and ownership of the Samples and the data and information they reflect remains with APR after transfer to IVS. IVS shall handle, store and use the Samples (and any other APR-provided Materials) in a secure environment in accordance with Applicable Laws, the relevant informed consent, the clinical trial protocol, any applicable documentation and labeling (including, for example, package inserts or legends reading "For Research Use Only" or "For Investigational Use Only"), and any written instructions of APR. IVS shall keep detailed records of the storage, use, handling and disposition of the Samples in accordance with the study protocol. IVS shall retain the Samples as specified in the Project Plan, unless APR requests their earlier or later return, and shall not further retain the Samples or information related to the Samples except to the extent required by Applicable Laws. At such time as APR requests the Samples' return, IVS shall promptly return the Samples to APR at APR's expense and in accordance with APR's instructions. Expenses for storage and maintenance of the Samples while in IVS's possession and control shall be at IVS's expense, provided that in the event APR requires additional storage or maintenance requirements over and above what is agreed to in the Approved Development Budget (*e.g.*, extended timeframe for storage to enable independent sample reanalysis), such additional requirements shall be at APR's cost and expense.

(c) Use, Retention, and Processing Restrictions. IVS agrees that it will only use and Process Materials provided to it by or on behalf of APR (including the Samples) for purposes of this Agreement and the Project Plan. IVS shall handle the Materials in accordance with any applicable documentation, reasonable handling procedures for similar materials, applicable common scientific standards of care, and APR's written instructions. IVS undertakes to use the Materials only in connection with the Activities described in the Project Plan and for no other purpose. None of the Materials shall be transferred or sold to Third Parties except to Approved Subcontractors. IVS shall not use the Materials for testing in or treatment of human subjects except to the extent described in the Project Plan.

3.4 Nature of Materials. The Materials are experimental in nature and may contain biohazards. APR shall not be liable for any loss, claim, damage or liability that may arise from IVS's or any of its Affiliates, Approved Subcontractors or Minor Subcontractors' use, storage or handling of the Materials.

3.5 Progress Reports. IVS shall keep APR reasonably informed of its progress and results in performing the Project during the Term, including by providing the JDC and the Working Groups, as appropriate, at least a monthly written report of the Activities performed, Deliverables and results achieved by IVS in the performance of its Activities under the Project.

3.6 Development for Additional Target Countries. In the event that APR designates additional Target Countries to be added to the Project Plan during the Term or revises the priority of Target Countries, IVS shall promptly prepare and propose an amendment to the Project Plan, the PRD and the Budgets to reflect the Development plan, specifications, costs and timelines for the Assay or (as applicable) the IVD Kit in such additional Target Countries for review and approval by APR, all under the supervision of the JSC and appropriate Working Groups. Any such amendment shall also include any changes to the Pass Through Expenses as are necessary. Any proposal for an Approved Development Budget for Development of the Assay in an additional Target Country shall be approved in accordance with Section 2.6.

3.7 Approved Third Party Contractors. Any involvement of Third Party contractors by any Party in the conduct of any Activities shall require the prior written consent of the other Party, such consent not to be unreasonably withheld (each, upon mutual approval, an "Approved Subcontractor"). The foregoing shall not apply to any Party's use of individual consultants or subcontracting of those minor, non-essential or routine portions of the Activities that it would customarily subcontract in the ordinary course of business (each consultant and subcontractor of minor, non-essential or routine portions of the Activities, shall be referred to as a "Minor Subcontractor"). To the extent that a Party utilizes Approved Subcontractors or Minor Subcontractors to perform tasks within the scope of the Project, such Party shall ensure all such Approved Subcontractors and/or Minor Subcontractors are obligated to: (a) treat the Disclosing Party's Confidential Information in accordance with the provisions of Article 8, (b) assign rights to any Inventions and Project Data so that such rights can be conveyed in accordance with the terms and conditions of Section 2.4, (c) comply with Applicable Laws in the conduct of Activities, and (d) with respect to IVS, that its Approved Subcontractors and Minor Subcontractors grant audits and inspection rights similar to the right set forth in this Agreement whereas the foregoing shall not limit IVS' audit and inspection responsibilities. Each Party shall be solely responsible and liable for compliance by its respective Approved Subcontractors and Minor Subcontractors with this Agreement and for the acts and omissions, performance and compensation of its respective Approved Subcontractors and Minor Subcontractors as if committed or omitted by the Party assigning such work. Cost overruns resulting from IVS's use of an Approved Subcontractor or Minor Subcontractor to conduct any Activities will be at IVS's expense.

3.8 Diligence. Each Party will use Commercially Reasonable Efforts to successfully complete the activities for which it is responsible under the Project Plan in accordance with applicable standards currently recognized by the Parties' profession or industry. Each Party shall also be responsible for the professional quality, training, and supervision of all its and its Affiliates' personnel who perform any activities under the Project Plan. IVS shall undertake its obligations in good faith, using Commercially Reasonable Efforts to diligently meet the milestones set forth in the Project Plan. The Parties recognize and acknowledge that IVS's obligation to perform its obligations and meet the milestones under this Agreement may be adversely affected as a result of APR's failure to perform any necessary APR action or a delay in critical performance on the part of APR or its Affiliates or Third Party agents.

3.9 Timelines for Performance. The Parties will use Commercially Reasonable Efforts to complete their respective obligations under the Project Plan within the timeframes specified in the Project Plan. Each Party will promptly inform the other Party in writing in the event that it anticipates or experiences a delay in the completion of such activities.

ARTICLE 4
REGULATORY

4.1 Regulatory Strategy. The Parties shall, through the JSC or any Working Group, work jointly on the regulatory strategy for the Regulatory Approval (including proposed labeling and/or labeling changes) of the Assay and (as applicable) the IVD Kit in every Target Country to ensure that the Assay and IVD Kit receives Regulatory Approval in sufficient time to secure a simultaneous market launch with the APR Product in each Target Country. The Parties shall consult, cooperate and assist each other reasonably in the Regulatory Approval process for the Assay and IVD Kit in the Target Countries, and reasonably coordinate and align their Regulatory Approval filings, or equivalents, and activities pertaining thereto, in the manner provided in this Agreement, the Project Plan, and the Approved Development Budget for such countries, which shall include the costs of obtaining Regulatory Approval for the Assay or the IVD Kit, as applicable, and including the manner in which the intended use statement and instructions for use for the Assay may reference the APR Product; provided that if the intended use statement references the APR Product, it shall be subject to the final approval of APR. If there are any issues related to the labeling of either the Assay, the IVD Kit or the APR Product, APR shall have sole decision-making authority for the APR Product and IVS will have sole decision-making authority for the Assay and IVD Kit; provided that the exercise of such decision making authority by IVS does not have any material adverse impact on the health authority approval and commercialization of the APR Product. IVS shall solicit and consider in good faith input from APR regarding the labeling of the Assay and IVD Kit. Notwithstanding anything to the contrary in this Agreement, APR shall solely control the regulatory strategy for the Regulatory Approval of the APR Product and IVS shall solely control the regulatory strategy for the Regulatory Approval of the Assay and IVD Kit, provided, however, that the regulatory strategy utilized for the Regulatory Approval of the Assay and IVD Kit cannot have an adverse impact on the APR Product and its approval.

4.2 Regulatory Approvals. APR shall be responsible for obtaining Regulatory Approvals for the APR Product. IVS shall be responsible for and shall prepare, file, obtain, own and maintain, in each Target Country, all Regulatory Approvals necessary or appropriate, in a timely fashion, (i) for use of the Assay and IVD Kit in the Bridging Study, and (ii) to ensure that the Assay and IVD Kit is commercially available for use with the APR Product in every Target Country. IVS shall ensure that the Assay and IVD Kit developed under the Agreement and the Project Plan complies, in each Target Country, with all Applicable Laws and fulfills all statutory requirements of the Regulatory Authorities, including the CE-marking in the European countries and requirements for comparable approvals in the other Target Countries. IVS shall comply with quality systems regulations ("QSR") design controls for the PMA submission, and any applicable foreign equivalents for comparable submissions in other countries. Such submissions shall be fully compliant with all requirements of the local Regulatory Authority(ies) and Applicable Laws.

4.3 Review of Submissions.

(a) **Until the submission of the Premarket Approval (PMA) application to the FDA Center for Devices and Radiological Health (CDRH) in the U.S. (or other equivalent submission to Regulatory Authorities in other Target Countries):** At least five (5) days prior to submission, IVS shall provide APR with a copy of any Clinical sections of any

1.

regulatory submissions involving the Assay and the IVD Kit impacting or referencing the APR Product (but with any commercially sensitive or proprietary information of IVS redacted in accordance with this Section 4.3). IVS shall give due consideration to any requests or written comments provided by APR. All such materials shall be provided to APR in English. IVS shall provide to APR a copy of final versions of any such clinical sections of such submissions (as filed, but with any commercially sensitive or proprietary information of IVS redacted in accordance with this Section 4.3), within five (5) Business Days of submission and a copy of such local language submission, if any, within ten (10) Business Days, and, upon request by APR and at the sole cost of APR, a copy of a certified English translation within thirty (30) calendar days of such request by APR.

(b) **The PMA application to the FDA Center for Devices and Radiological Health (CDRH) in the U.S. (or other equivalent submission to Regulatory Authorities in other Target Countries):** At least ten (10) days prior to submission by IVS to the Regulatory Authorities, IVS shall provide APR with a copy of any Clinical sections of any submissions involving the Assay and the IVD Kit impacting or referencing the APR Product (but with any commercially sensitive or proprietary information of IVS redacted in accordance with this Section 4.3). IVS shall give due consideration to any requests or written comments provided by APR. All such materials shall be provided to APR in English. IVS shall provide to APR a copy of final versions of the Clinical sections of any such submissions (as filed, but with any commercially sensitive or proprietary information of IVS redacted in accordance with this Section 4.3),including in connection with product life-cycle management, within five (5) Business Days of submission and a copy of such local language submission, if any, within ten (10) Business Days, and, upon request by APR and at the sole cost of APR, a copy of a certified English translation within thirty (30) calendar days of such request by APR.

In addition, APR may request a prior review of sections (for example only, any description of the TP53 expression profiles) that describe a link between the Assay and/or the IVD Kit and the APR Product and could impact the APR Product (redacted in accordance with this Section 4.3).

.

4.4 Regulatory Communications. IVS will handle all direct communications with the FDA Center for Devices and Radiological Health ("CDRH") in the U.S., the EMA in the EU, and other equivalent Regulatory Authorities in other Target Countries concerning the Assay and IVD Kit. Notwithstanding the foregoing, IVS shall (i) inform APR, in a timely manner, not to exceed five (5) Business Days if the communication relates to the APR Product or patient safety and not to exceed thirty (30) days for any other issue, before exchanging any information or material related to projects pertaining to the APR Product with any Regulatory Authority (other than in connection with routine correspondence relating to scheduling matters or confirmation of receipt of documents), (ii) promptly provide APR, no later than five (5) Business Days of receipt if the communication relates to the APR Product or patient safety and no later than thirty (30) days of receipt for any other issue, with a copy, via email, of any such information or material provided to the Regulatory Authority as well as with a copy of any and all correspondence or actions received from any Regulatory Authority promptly after receipt (and with a certified English translation if requested by APR (and for non-U.S. or EU Target Countries, such translations shall be prepared at the sole cost of APR), not to exceed five (5) Business Days if the communication relates to the APR Product or patient safety and not to exceed thirty (30) days for any other issue, and (iii) collaborate with APR to assist APR in understanding any requests or communications received by APR from

local Regulatory Authorities in relation to the Assay or IVD Kit for the APR Product in the Territory, and in developing a response thereto.

4.5 Participation in Meetings. Subject to any Third Party confidentiality obligations, at least two (2) representatives of APR may participate in material meetings and other material contacts with Regulatory Authorities pertaining to the obtaining of Regulatory Approvals for the Assay and IVD Kit to the extent that the subject of such meetings and contacts, or the applicable portions of such meetings or contacts, is the Assay or the IVD Kit each of which are being developed to be used specifically with the APR Product. In connection therewith, IVS shall provide APR with reasonable advance notice of all such meetings (but no less than fifteen (15) Business Day notice) and will supply advance copies of any documents (or portions thereof) that are reasonably necessary for APR's observations and comments to be meaningful. Except as permitted under this Agreement, under no circumstances is APR authorized to meet with or contact Regulatory Authorities in connection with any issue involving or related to the Assay or IVD Kit.

4.6 Regulatory Coordination. IVS shall work in good faith with APR during the Term to coordinate with APR on all regulatory matters relating to the Assay or the IVD Kit in the Territory, including in submissions with the FDA and other Regulatory Authorities. In the event of a conflict between the regulatory interests of APR and other IVS partners, IVS will inform APR and both Parties will work toward a mutually-agreeable resolution that is consistent with the business intent of this Agreement.

4.7 Right of Use and Reference. IVS hereby grants APR, APR's Affiliates, non-affiliated distributors, licensors and licensees, as well as, subject to APR's termination of the Agreement pursuant to Section 11.3, any Third Party designated by APR, a perpetual, irrevocable, exclusive, sublicensable, transferable and non-royalty bearing license to use any and all APR specific data and documentation included in, referenced in, or filed in support of any Regulatory Approval for the Assay or the IVD Kit in filings with Regulatory Authorities relating to the APR Product in the Territory, but excluding any asset development procedures or related data that are proprietary to IVS or another IVS client, provided that, for the avoidance of doubt, this license shall not imply IVS ownership of any data which would otherwise be owned by APR pursuant to this Agreement. As requested from time to time by APR, IVS shall provide to APR or its designee any appropriate letters or similar documentation necessary to cross-reference and rely upon any and all such data and documentation included in, referenced in, or filed in support of any Regulatory Approval for the Assay or the IVD Kit in regulatory filings relating to the APR Product in the Territory, but excluding any portion of such documentation that does not relate to the Project. The foregoing right of reference and use shall survive any expiration or termination of this Agreement.

4.8 Regulatory Fees. IVS shall pay all necessary fees to the Regulatory Authorities promptly as they become due when applying for, obtaining, or maintaining any Regulatory Approval for the Assay or IVD Kit in the Target Countries, and for any such countries other than the United States, and any such amounts shall be reimbursed by APR, unless such fees have been included in the Budget, or the parties agree otherwise, subject to Section 7.2.

4.9 Regulatory Changes. IVS shall notify APR in writing, which may be transmitted by electronic mail, of any change to its knowledge in Applicable Laws or in any publicly available FDA or similar guidance in the Territory. Such notice shall be given within thirty (30) Business Days of IVS becoming aware of such change (based on the local country where the change in

Applicable Law is taking place). In the event that regulatory requirements change during the Term, IVS shall make any additional submissions and take any other additional reasonable steps necessary to maintain the Assay and, as applicable, the IVD Kit as a viable commercial option to support the APR Product in each country in the Territory where APR is Commercializing the APR Product.

4.10 Regulatory Updates. IVS shall provide APR with (i) from time to time, at APR's request, information regarding its regulatory activities in the Territory related to the Assay or the IVD Kit; and (ii) an annual update within thirty (30) calendar days of the end of each calendar year setting forth all meetings held with Regulatory Authorities, expected date of Regulatory Approval, and such other information as APR may reasonably request.

4.11 Regulatory Inspections. IVS shall inform APR of any FDA or other Regulatory Authority audit or inspection of an Approved Facility (or other IVS-controlled site), if the audit or inspection relates to or may impact this Agreement, the Project or the APR Product, within two (2) Business Days of when an authorized agent of any Regulatory Authority notifies IVS that it intends to or does visit such facility. IVS will provide to APR all Regulatory Authority documents (e.g. Inspection Form 483) provided to it along with a report summarizing the audit by the Regulatory Authority within fourteen (14) days after completion of the audit, provided that should the report detail any issue related to patient safety such report shall be provided within five (5) Business Days. IVS shall provide copies to APR of all inspection observation reports and other regulatory communications that may affect the Project or the APR Product. IVS shall also provide copies of IVS's responses to such inspection observation reports or regulatory communications which relate to the Project or the APR Product promptly after their preparation (the inspection observation reports and IVS's responses and other regulatory communications are referred to collectively as "Regulatory Audit Materials"). APR will be allowed to review the Regulatory Audit Materials which directly relate to the Project or the APR Product. IVS shall promptly notify APR as to what corrective measure IVS is taking, whether before or following any regulatory inspection or audit, and keep APR informed on a regular, ongoing basis of related developments. Any audits pursuant to this Seciton 4.11 shall be performed at IVS' cost.

ARTICLE 5
COMMERCIALIZATION

5.1 Generally. The Parties agree that the ultimate goal of the Project conducted under this Agreement shall be the Commercialization of an Assay and IVD Kit as an IVD with the APR Product in the Target Countries, and acknowledge that availability of such Assay and IVD Kit as an IVD might be a condition for obtaining a Regulatory Approval for the APR Product. The determination of whether and to what extent and in which countries the APR Product shall be Commercialized shall be within APR's sole discretion.

5.2 Commercial Agreement. IVS shall Commercialize the Assay and IVD Kit in each Target Country in accordance with the terms of a Commercial Agreement to be negotiated in good faith by the Parties (the "Commercial Agreement"). The Commercial Agreement shall be for a [***] assay [***], after Regulatory Approval of the Assay. The Parties shall enter into negotiations for the Commercial Agreement before the earlier of (x) three (3) months after APR's payment of the milestone payment due in connection with positive top-level Phase III trial results or (y) the date that IVS files for Premarket Approval with the FDA. The Parties shall work together in good faith under the Commercial Agreement to determine launch sequencing in the Target Countries.

Initially, the Parties agree that the Assay would be launched in the United States and the Parties would work together to launch the Assay in the EU and the United Kingdom. IVS shall coordinate the launch of the Assay or the IVD Kit with the launch of the APR Product in each Target Country. The Commercial Agreement shall be an Addendum to this Agreement.

ARTICLE 6
COMPLIANCE WITH AGREEMENT

6.1 Records. IVS shall keep complete and accurate records in connection with the conduct of its Activities under this Agreement in conformity with generally accepted accounting procedures (for financial data) and scientific standards (for scientific and research data), which shall include a record of the IVS Project Data and any other Project Data that is not APR Project Data, records of information pertaining to the Project, and records of any Pass-Through Expenses, for a period of at least five (5) years from the creation of such records subject to compliance with any Applicable Laws in the Target Countries. IVS shall provide APR and Regulatory Authorities with reasonable access, on reasonable written notice and during regular business hours, to its IVS Project Data and other documentation, including Confidential Information related to the Assay, IVD Kit and the APR Product, to the extent necessary for APR to commercialize the APR Product. IVS will not destroy or discard any record described herein before notifying APR of such intent and upon receiving such notice APR may elect to have such records transferred, at its own cost, to its control for further retention, subject to APR record keeping policies.

6.2 Audit and Inspections by APR.

(a) Audit Rights. During the Term, and for a period of two (2) years after the expiration or termination of this Agreement, APR shall have the right to review, inspect and audit, or to designate an Affiliate, Approved Subcontractor or Minor Subcontractor to review, inspect and audit, IVS and the Approved Facilities for the purpose of confirming IVS's full compliance with the terms of this Agreement, including compliance with quality systems required to meet IVD requirements. Such audits will not exceed two (2) per year, absent a finding of error or breach which may substantiate the need for an additional audit(s). During the course of any such audit or inspection, APR, its Affiliate, Approved Subcontractor or Minor Subcontractor shall have access to the records, including only financial records necessary to verify compliance with this Agreement, and other documents and information applicable to the activities undertaken by IVS pursuant to this Agreement, to verify their accuracy and completeness and full compliance with the terms of this Agreement. IVS agrees that it shall cooperate in all respects with APR (and, if applicable, its Affiliates, Approved Subcontractors or Minor Subcontractors) to facilitate such audit, including making available such records and IVS personnel, as reasonably necessary. The provisions in this Section 6.2 shall survive any termination of this Agreement.

(b) Audit Procedures. Any audits or inspections by APR (or its Affiliates and Approved Subcontractors or Minor Subcontractors) hereunder shall be on at least ten (10) Business Days prior written notice during IVS's customary business hours (based on the location of the site being audited or inspected), and subject to reasonable obligations of confidentiality, security and safety generally applicable for auditors.

6.3 Corrective Actions. IVS agrees to promptly prepare a corrective action plan with respect to any audit findings, observations of non-compliance with this Agreement, any regulatory

issue that affects the Assay or IVD Kit. For any undisputed findings, IVS agrees to promptly implement such corrective actions to remove or address any of the defects. The JSC will review any disagreement regarding disputes over any audit findings or observations and necessary actions to address audit findings or observations by APR (or its Affiliates, Approved Subcontractors or Minor Subcontractors).

6.4 Regulatory Assistance. At the request and expense of APR, IVS (and/or its Affiliates and Approved Subcontractors or Minor Subcontractors) shall provide APR with information needed for regulatory filings for the APR Product.

ARTICLE 7
COMPENSATION

7.1 Up Front Fee; Execution Fee.

(a) Up Front Fee. APR has paid IVS a $[***] up front fee, which was payable upon execution of the Letter of Intent between the Parties dated June 1, 2020.

(b) Execution Fee. Within (15) days after the execution of this Agreement, APR shall pay to IVS an additional Up Front payment of $[***].

7.2 Pass Through Expenses. APR shall reimburse IVS for all Pass-Through Expenses in the Approved Development Budget, as may be modified and agreed to by the JSC, and for all costs and expenses for any Regulatory Approvals for the Assay and/or the IVD Kit as set forth in Section 4.8; provided that IVS shall use commercially reasonable efforts to minimize any such Pass-Through Expenses. The Pass-Through Expenses will be invoiced to APR on a monthly basis as such expenses are incurred.

7.3 Milestone Payments. In addition to the payments set forth in Section 7.1, APR will make the payments to IVS as set forth in the attached Schedule A for IVS Activities and Deliverables under this Agreement, contingent on the satisfaction of the obligations set forth in the proposed Project Plan, which milestone payments shall be made only once, regardless of the number of Assays or IVD Kits Developed, approved or Commercialized. If IVS is required to cease its activities under the Project Plan due to circumstances caused by any delay in the APR clinical trials or Regulatory Approvals, then APR shall pay to IVS the allocable portion of the next unpaid milestone to compensate IVS for work it has performed as of the date of such cessation.

7.4 Invoicing and Payments. IVS shall notify APR in writing promptly (and in any event within 30 days) upon achievement of any such milestones set forth in Section 7.3, and shall submit an invoice to APR thereafter, and payment in respect any undisputed invoice shall be due and payable by APR or any of its Affiliates within thirty (30) days of receipt of such invoice. IVS shall provide supporting documentation with respect to any Pass-Through Expenses in connection with any invoice that includes Pass-Through Expenses. APR may also request additional information with respect to achievement of any milestone if APR reasonably believe it has a reason to dispute such invoice, which request shall be in writing and shall be made within seven (7) business days of APR's receipt of IVS's notice of achievement of the milestone. If APR disputes any invoice or requests any additional information with respect to any invoice, payment shall not be due by APR until the dispute is resolved. All invoices may be sent by email, and shall be sent to:

1.

Aprea Therapeutics, Inc.
535 Boylston Street
Boston, Massachusetts 02116
Email: usfinance@aprea.com

7.5 Taxes.

(a) All agreed remunerations/fees are considered to be net of value added tax (hereinafter "VAT"), if applicable. VAT will be due additionally as legally owed to the applicable jurisdiction, payable after receipt of a proper invoice, which meets all legal requirements according to the applicable VAT-law.

(b) Each Party will be responsible for all taxes, fees, duties, levies or similar amounts imposed on its income, assets, capital, employment, personnel, and right or license to do business. To the extent that the goods or services to be provided hereunder are subject to any sales, use, rental, personal property, or any other transaction or indirect taxes under law, payment of said taxes is APR's responsibility, subject to any applicable exemption entitlement.

(c) Notwithstanding the foregoing, IVS shall inform APR in advance if any activities pursuant to this Agreement will be performed outside of the United States which may subject APR to paying any VAT.

(d) Any Party required to make a payment (hereinafter the "Paying Party") to the other Party (hereinafter the "Payee") under this Agreement shall be entitled to deduct and withhold from the amount payable the withholding tax for which the Paying Party is liable under any provisions of tax law. Any withheld tax shall be treated as having been paid by Paying Party to Payee for all purposes of this Agreement. Paying Party shall timely forward the tax receipts certifying the payments of withholding tax on behalf of Payee. In case Paying Party cannot deduct the withholding tax due to fulfillment completion of payment obligation by settlement or set-off, Payee will pay the withholding tax to Paying Party separately. If Paying Party failed to deduct withholding tax but is still required by tax law to pay withholding tax on account of Payee to the tax authorities, Payee shall assist Paying Party with regard to all procedures required in order to obtain reimbursement by tax authorities or, in case tax authorities will not reimburse withholding tax to Paying Party, Payee will immediately refund the tax amount. The Parties agree to reasonably cooperate with each other to proceed with exemptions from any double taxation.

7.6 Sunshine Act Reporting. Each Party shall report any reportable payments or transfers of value that it makes to covered recipients pursuant to §6002 of the Affordable Care Act of 2010 (the "ACA"). To avoid duplications in reporting any indirect payments or other transfers of value that APR makes through IVS to covered recipients under the ACA, pursuant to 42 CFR §403.908(d)(2), IVS shall either: (i) report to the Centers for Medicaid & Medicare Services ("CMS") such indirect payments or other transfers of value as required by the ACA and inform APR that IVS has made such report, or (ii) timely provide sufficient information to APR for APR to report to CMS such indirect payments or other transfers of value as required by the ACA. In the case of (i), above, APR shall refrain from making a duplicate report; in the case of (ii), above, IVS shall refrain from making a duplicate report.

ARTICLE 8
CONFIDENTIALITY

8.1 Non-Use, Non-Disclosure. Each Party shall use the Confidential Information of the other Party, its Affiliates and their respective representatives only for the purpose of performing its obligations under this Agreement (including under the Project Plan), and, except as otherwise provided for herein, no Party shall at any time (whether during the Term or, subject to Section 8.8, after its expiration or termination) use or otherwise Process the Confidential Information for such Party's own or any Third Party's benefit or purposes or disclose, publish or make available all or any portion of such Confidential Information to any other Third Party, without the prior written consent of the Disclosing Party.

8.2 Standard of Care. Each Party shall maintain and protect the confidentiality of Confidential Information of the other Party in accordance with all Applicable Laws, including without limitation the Privacy Laws and Data Security Requirements, and shall use at least the same degree of care to safeguard and to prevent unauthorized access to, loss of, alternation of, acquisition of, or disclosure of such Confidential Information as it employs with respect to its own confidential information (or information of its customers) of a similar nature, but at all times shall use at least reasonable care and administrative, technical, and organizational safeguards that satisfy at least industry standards with respect to protecting the confidentiality and security of such information. Without limiting the generality of the foregoing, each Party shall implement and maintain appropriate security measures to prevent unauthorized access to, or disclosure of Confidential Information. A Party's personnel and Approved Subcontractors shall have access to the relevant Confidential Information of the other Party only to the extent necessary for such person to perform his or her obligations under or with respect to this Agreement, provided that such access is not in violation of Applicable Law. Each Party shall remain fully responsible and liable for the acts or omissions of that party's subcontractors as if they were the Party's own personnel.

8.3 Required Disclosures. A Party shall be entitled to disclose Confidential Information to the extent required by Applicable Laws, a governmental authority, or court order on the condition that the Disclosing Party provides the Party whose Confidential Information is subject to disclosure with written notice that such Confidential Information is required to be disclosed sufficiently in advance of the disclosure so as to provide such Party with reasonable opportunity to seek to prevent the disclosure of or to obtain a protective order for the Confidential Information, in each case, to the extent allowed under Applicable Law; and provided further that the Disclosing Party makes any required disclosures in consultation with the non-Disclosing Party to the extent allowed under Applicable Law.

8.4 Exceptions to Confidentiality. Confidential Information shall not include information that (a) is, at the time of disclosure or becomes after disclosure, generally available to the public or within the industry to which such information relates other than as a result of a breach of this Agreement, (b) is already known by the Receiving Party at the time of disclosure as evidenced by the Receiving Party's written records, (c) becomes available to the Receiving Party on a non-confidential basis from a source that is entitled to disclose it on a non-confidential basis, or (d) was or is independently developed by or for the Receiving Party without reference to the Confidential Information of the Disclosing Party as evidenced by the Receiving Party's written records.

8.5 Notification. In the event the Receiving Party becomes aware or has knowledge of any reasonably suspected or confirmed Data Breach with respect to information or data Processed by or on behalf of Receiving Party under this Agreement, the Receiving Party shall notify the Disclosing Party of such Data Breach within 48 hours of becoming aware of it and, thereafter, shall take reasonable steps to assist the Disclosing Party in attempting to minimize any potential or actual damages or losses that result. Without limiting the generality of the foregoing, to the extent a reasonably suspected or confirmed Data Breach with respect to information or data Processed by or on behalf of Receiving Party under this Agreement may involve Personal Information of the Disclosing Party, the Receiving Party shall notify the Disclosing Party within 24 hours of becoming aware of it and shall promptly (i) investigate, mitigate, and respond to any such Data Breach (and keep Disclosing Party promptly informed of such investigation, mitigation and response, and all details thereof), (ii) take all reasonable steps to remedy any harm or potential harm caused by such Data Breach and its effects, and (iii) comply with all Applicable Laws regarding such Data Breach (including by providing legally required notices if requested to do so by Disclosing Party and with the Disclosing Party's approval of such notices), in each case (with respect to (i)-(iii)) at its own cost.

8.6 Return or Destruction. Except to the extent that Confidential Information is Personal Information, in which case Section 8.8 shall apply, upon receipt of a written request from the Disclosing Party, or upon termination of this Agreement, the Receiving Party shall promptly return to the Disclosing Party or destroy (and certify as to such destruction) all tangible Confidential Information and all Materials (including Samples), including all reproductions and copies thereof together with all internal material and documents generated by or on behalf of the Disclosing Party containing Confidential Information or references thereto and the Receiving Party shall delete all such Confidential Information and references thereto stored electronically, provided that such deletion obligations shall not extend to those files which (i) have been created pursuant to automatic archiving or back-up procedures on secured central storage servers, and (ii) are required to be maintained due to the Receiving Party's document retention programs subject to requirement of the Applicable Laws and/or agreements with governmental authorities. Notwithstanding the above, the Receiving Party may retain a single copy of any such Confidential Information as is reasonably necessary for regulatory or insurance purposes, and/or to assure compliance with this Agreement, subject to Receiving Party's obligations of confidentiality under this Agreement.

8.7 Public Announcements. The Parties may later agree that a press release is to be issued in the United States after the execution of this Agreement, or following FDA's acceptance and approval of the PMA (or sPMA, if relevant) filed by IVS for the Assay or in any of the Target Countries following regulatory acceptance and approval of the PMA (or sPMA, if relevant) filed by IVS for the IVD Kit (together the "Acceptance Releases"). The Acceptance Releases shall be mutually agreed by all the Parties to this Agreement, provided that each Party shall have a reasonable amount of time to review such releases and a Party's consent to such releases shall not be unreasonable withheld or delayed. No Party shall make any other press or other public announcement concerning any aspect of this Agreement unless the text of such announcement is first approved in writing by all the Parties to this Agreement.

8.8 Personal Information. APR shall comply with all Applicable Laws, including all Privacy and Data Security Laws, in providing or making available Personal Information to IVS. IVS shall Process Personal Information provided or made available to IVS (or those operating on

IVS's behalf) by APR in accordance with all Applicable Laws, including all Privacy and Data Security Laws. IVS shall Process Personal Information disclosed to it by APR, or made available to it by APR, only for the purpose of performing its obligations under this Agreement (including under the Project Plan) behalf of APR. Within ten (10) days of the termination of this Agreement, or within ten (10) days of any such request by APR, IVS shall securely return or permanently destroy all Personal Information provided or made available to IVS (or those operating on its behalf) under this Agreement. With respect to Personal Information provided or made available to IVS (or those operating on IVS's behalf) by APR, IVS represents and warrants that it will not undertake or attempt to: (i) "sell," as that term is defined under the CCPA, the Personal Information; (ii) retain, use, or disclose the Personal Information for any purpose, including any commercial purpose, other than those specified in the Agreement for performance of the services; or (iii) retain, use, disclose or otherwise Process the Personal Information outside of the direct business relationship between the IVS and APR. To the extent required by Applicable Laws, APR agrees to obtain a HIPAA authorization, IRB waiver, or foreign equivalent (or any combination thereof, as needed or required) prior to using or disclosing or making available such patients' or subjects' PHI to IVS under this Agreement. Each Party will only Process Personal Information obtained under this Agreement from the other Party in a manner consistent with any data subject's signed authorization or the IRB waiver. To the extent that IVS receives any requests from individuals relating to Personal Information IVS Processes about them on behalf of APR, IVS will notify APR of such requests within six (6) business days of receiving the request and shall provide APR with any information APR requires to respond to such request within ten (10) business days of receipt of APR's request. IVS represents and warrants that it has implemented and will at all times implement administrative, technical, and organizational safeguards sufficient to protect the Personal Information it Processes pursuant to this Agreement: (i) in accordance with all Applicable laws, notices, consents, authorizations, AVR and IVS privacy policies; (ii) in a manner that is at least as protective of the security, confidentiality, and integrity of the Personal Information as industry standard safeguards for information of comparable sensitivity; and (iii) in a manner that is reasonably designed to prevent Data Breaches with respect to the Personal Information to the greatest extent possible.

8.9 Duration of Confidentiality. All obligations of confidentiality and non-use imposed upon the Parties under this Agreement shall survive (a) for all Confidential Information which is not a Trade Secret, for ten (10) years after the expiration or earlier termination of this Agreement, (b) for all Confidential Information which is a Trade Secret, indefinitely as long as such Confidential Information remains a Trade Secret, (c) with respect tto any Personal Information, indefinitely and (d) with respect to the requirement to comply with Privacy Laws, for so long as required to comply with such provisions.

8.10 Equitable Relief. Each Party understands and agrees that money damages may not be a sufficient remedy for any breach of this Article 8 and that the non-breaching Party shall be entitled to seek specific performance, injunctive and/or equitable relief as a remedy for any such breach. Such remedy shall not be deemed to be the exclusive remedy for breach of this Article 8 but shall be in addition to any and all other remedies available at law or in equity.

8.11 Publication. Except with APR's prior written consent, IVS may not publish any paper or presentation relating to the performance of the Assay or of the IVD Kit in conjunction with the APR Product, and if such consent is provided, IVS agrees that it will provide APR with at least

thirty (30) days to review the proposed publication prior to publication and also that IVS will not include the Confidential Information of APR or any patentable subject matter.

8.12 Ownership.

(a) Background IP and Background Patents. Each Party shall own all right and title in and to its respective Background IP and Background Patents, including any improvements thereto.

(b) New Patents and Inventions. The determination of inventorship shall be made in accordance with United States patent law. Further, the Parties agree as follows:

(i) Joint Inventions. Subject to the exclusion of IVS Project Inventions set forth in Section 8.12(b)(ii), and APR Project Inventions set forth in Section 8.12(b)(iii) as between the Parties, any Invention arising under this Agreement shall be jointly owned by APR and IVS (each a "Joint Invention") and any Patent to the extent that it claims a Joint Invention arising under this Agreement shall be jointly owned by APR and IVS (each, a "Joint Patent"). Each Party retains an undivided one-half interest in and to any Joint Patents, and assigns to the other Party an undivided one-half interest in and to any Joint Patents.

(ii) IVS Project Inventions. Any Invention which is not an APR Project Invention and (1) is directed solely to the Assay or IVD Kit, including methods of making and/or using the Assay or IVD Kit, or (2) derives solely from the clinical validation of the Assay or the IVS Project Data, or (3) is conceived solely by employees or individuals working for IVS and/or its Affiliates during and in the course of performing this Agreement or in conducting the Project Plan, relating solely to Developing or Commercializing the Assay or the IVD Test without reference to or the use of any APR Project Data, APR Confidential Information, APR Background IP, or APR Background Patents, or (4) is in the Diagnostics Field and conceived solely by employees or individuals working for IVS and/or its Affiliates during and in the course of performing this Agreement or in conducting the Project Plan (each, an "IVS Project Invention") shall not be a Joint Invention, a Joint Patent, or an APR Project Invention, and shall be exclusively owned by IVS. APR hereby irrecovably assigns to IVS any and all right, title and interest it may have in any IVS Project Invention.

(iii) APR Project Inventions. Any Invention which (1) relates solely to the APR Product, including methods of making and/or using the APR Product, (2) is not related to the Diagnostics Field, or (3) derives from the any APR clinical trial, the Samples, or APR Project Data and is not related to the Diagnostics Field (each an "APR Project Invention") shall not be a Joint Invention, a Joint Patent, or an IVS Project Invention, and shall be owned by APR, provided however, that APR Project Inventions specifically does not include any data generated during the course of the Project that can be used to determine signal ratio test results for the Assay or the IVD Kit. IVS hereby irrevocably assigns to APR any and all right, title and interest it may have in any APR Project Invention.

(iv) Practice of Joint Patents. Either Party shall have the right to exercise its ownership rights in and to Joint Inventions and Joint Patents, for any field, including the right to license and sublicense or otherwise to exploit, transfer or encumber its ownership interest, without an accounting or obligation to, or consent required from, the other Party.

(c) Project Data. Subject to any other agreement between the Parties, all Project Data related to the analytical studies, clinical development and validation of the Assay (but not read-outs resulting from the use of the Assay or IVD Kit, including for eligibility of a patient for treatment with an APR Product) shall be designated as Confidential Information and owned by IVS ("IVS Project Data"). Project Data including (i) positive/negative assay data and (ii) read-outs resulting from the use of the Assay or IVD Kit, including for eligibility of a patient for treatment with an APR Product, shall be designated as Confidential Information and shall be owned by APR ("APR Project Data").

ARTICLE 9
INTELLECTUAL PROPERTY OWNERSHIP

9.1 Disclosure. During the Term, each Party shall fully and promptly disclose to the other Party all Inventions (whether or not patentable) that it conceives or reduces to practice in the course of its activities under the Project, regardless of ownership thereof.

9.2 Patent Prosecution.

(a) Definition. For purposes of this Section 9.2, "Prosecution and Maintenance" or "Prosecute and Maintain," with respect to a particular Patent, means the preparation, filing, prosecution and maintenance of such Patent, as well as re-examinations, reissues, applications for patent term extensions and the like with respect to that Patent, together with the conduct of interferences, the defense of oppositions and other similar proceedings with respect to that Patent.

(b) Patent Prosecution of Solely-Owned Patents. As between the Parties, IVS shall, at its sole discretion and expense, Prosecute and Maintain the IVS Background Patents and Patents covering IVS Project Inventions. As between the Parties, APR shall, at its sole discretion and expense, Prosecute and Maintain the APR Background Patents and Patents covering APR Project Inventions.

(c) Prosecution of Joint Inventions.

(i) APR and IVS shall select one or more mutually agreeable outside counsel (collectively, "Outside Patent Counsel") to be responsible for Prosecution and Maintenance of Joint Patents worldwide. The Outside Patent Counsel shall be instructed to (1) keep the Parties informed as to the Prosecution and Maintenance of such Patents, (including issues regarding (A) the countries in which to initiate or continue prosecution (including validation) or (B) the scope of, issuance of, rejection of, an interference involving, or an opposition to any such Patent application or resulting Patent such that each Party has sufficient time to review and comment upon any documents intended for submission to any patent office; (2) reasonably consider and incorporate comments of the Parties on documents filed

with any patent office. All applications for Joint Patents shall be filed in the name of APR and IVS as co-owners and assignees of such Joint Patent.

(ii) Decisions regarding the Prosecution and Maintenance of Joint Patents shall be mutually agreed by the Parties; provided if the Parties cannot agree, with the exception of provocation of an interference outlined below, IVS shall have the final decision on Inventions relating to the Diagnostics Field, and APR shall have the final decision on Inventions directed to any other field; provided further, if a Party elects not to participate in the Prosecution and Maintenance of a Joint Patent (whether worldwide or with respect to any particular country), including electing not to file a patent application with respect thereto or to allow a Joint Patent to lapse or become abandoned or unenforceable, then such Party shall promptly notify the other Party in writing at least thirty (30) calendar days prior to the lapse or abandonment of the Joint Patent. Thereafter, the other Party may, but is not required to, undertake, at its sole expense and in its sole discretion, the Prosecution and Maintenance of such Joint Patent, but for the avoidance of doubt each Party shall retain its undivided joint ownership interest therein. Except as provided above in this section, any costs and expenses incurred by the Parties in conducting such activities with respect such Joint Patents shall be equally shared by the Parties. Notwithstanding any other provision of this section, either Party may, with notification to the other Party, amend claims of a pending application in order to provoke interference. If such interference is not mutually agreed upon by both Parties, the Party provoking such interference may undertake the interference at its sole expense.

9.3 Assignment. Each Party hereby irrevocably makes the assignments necessary to accomplish the ownership provisions set forth in this Article 9, and each Party shall execute such further documentation as may be necessary or appropriate, and provide reasonable assistance and cooperation, to implement the provisions of this Article 9. In addition, each Party shall require all of its employees and any Third Parties working pursuant to this Agreement on its behalf, to assign to such Party any Patents and Know-How discovered, conceived and/or reduced to obtaining patent protection therefor. The Parties agree to reasonably cooperate with each other to effectuate ownership of any such Patents and Know-How as set forth herein, including by executing and recording documents.

9.4 Defense and Enforcement Rights for Infringement by Third Parties.

(a) Solely-Owned Patents.

(i) IVS Solely-Owned Patents. IVS shall have the sole right, but not the obligation, to control, at its own expense and discretion, the enforcement and defense of all IVS Background Patents and Patents covering IVS Project Inventions worldwide.

(ii) APR Solely-Owned Patents. APR shall have the sole right, but not the obligation, to control, at its own expense and discretion, the enforcement and defense of all APR Background Patents and Patents covering APR Project Inventions worldwide.

(b) Joint Patents. Subject to Section 9.4(c), both APR and IVS shall have the right, but not the obligation, to control, at their own expense and discretion, the enforcement and defense of all Joint Patents worldwide. If the enforcement or defense of any Joint Patent would, or would reasonably be expected to, have an impact on making or selling the APR Product, then APR shall have the first right (but not obligation) to control the enforcement and defense of such Joint Patent; provided that if APR declines to enforce such Joint Patent, then IVS shall have the right to control such enforcement or defense subject to the written consent of APR (which shall not be unreasonably withheld or delayed).

(c) Additional Rights and Obligations. With respect to Joint Patents:

(i) The other Party shall provide reasonable assistance to the enforcing/defending Party, at the enforcing/defending Party's expense.

(ii) The other Party shall have the right, at its own expense, to be represented in any such enforcement/defense by counsel of its own choice. If either Party is prohibited under Applicable Law from initiating or prosecuting such action solely in its own name, the other Party will join such action and will execute all documents necessary for the enforcing Party to initiate litigation to prosecute and maintain such action.

(iii) A settlement, consent judgment or other voluntary final disposition of a claim under Section 9.4(b) may be entered into without the consent of the other Party, provided that such settlement, consent judgment or other disposition would not adversely impact the other Party's rights or, impose a financial obligation upon the other Party.

Any recovery in connection with a claim involving such Patents shall be first applied towards the reimbursement of the Parties' costs and expenses associated with such claim (including attorneys' fees, expert witness fees, court costs and other litigation costs and expenses), and any remaining amount shall be shared equally between APR and IVS.

ARTICLE 10
LICENSES

10.1 APR License. APR hereby grants to IVS and its Affiliates a non-exclusive, fully-paid, royalty-free license in the Territory under the APR Background IP, APR Patents, APR Project Inventions and APR Project Data (in each case other than the Product Related Data or the APR Product IP) solely to the extent reasonably necessary to Develop the Assay and IVD Kit as a companion diagnostic for the APR Product in the Territory during the Term as provided in this Agreement (including the Project Plan), and to permit IVS to otherwise exercise its rights and carry out its obligations under this Agreement. IVS and its Affiliates shall treat the APR Project Data and the non-public portions of the APR Background IP, APR Know-How and APR Project Inventions as Confidential Information of APR and shall not, nor shall they assist or authorize any Third Party to, use the APR Background IP, Know-How Controlled by APR, APR Project Inventions or APR Project Data for any purpose except as specifically permitted herein. Such license is sublicensable by IVS solely in accordance with Sections 3.7 (Use of Third Party Contractors) and 15.3 (Use of

Affiliates). For clarity, IVS is granted no rights to the Product Related Data or the APR Product IP under this Section 10.1.

10.2 IVS License. So long as there exists an executed Commercial Agreement between IVS and APR, IVS hereby grants to APR and its Affiliates a non-exclusive, fully-paid, royalty-free, license in the Territory under IVS Background IP including IVS Patents, Patents claiming IVS Inventions, IVS Inventions, IVS Know-How and IVS Project Data solely to the extent reasonably necessary to (1) refer to the Assay and/or IVD Kit and/or otherwise using the Assay and/or IVD Kit in regulatory submissions, (2) refer to or recommend the Assay and/or the IVD Kit in product labeling and/or promotional materials for the APR Product, (3) use, market, and promote the Assay and/or the IVD Kit in connection with the APR Product, and (4) otherwise exercise APR's rights and carry out APR's obligations under this Agreement. Such license is sublicensable by APR solely in accordance with Section 3.7 (Use of Third Party Contractors) and 15.3 (Use of Affiliates). For clarity, apart from the rights granted herein, APR is granted no other rights to the Assay or the IVD Kit under this Section 10.2.

10.3 Third Party Licenses**.**

In the event the Parties determine, in the course of the Project, that Intellectual Property Controlled by a Third Party is necessary or advisable for the development, manufacture, use or commercialization of the APR Product (for example, any such Intellectual Property that is necessary or useful for the development, manufacture, use or commercialization of a APR Product, for the treatment of patients with a APR Product, or for the assessment of patient biomarker expression (in particular, assessment of TP53 mutations) for APR Product-related prognostic purposes or other clinical indication), APR shall decide, in its sole discretion and at its expense, whether or not it wants to obtain and/or maintain any licenses or other rights to access or use such other Intellectual Property Controlled by a Third Party that is necessary for the development, manufacture, use or commercialization of any APR Product.

(a) In the event the Parties determine, in the course of the Project, that Intellectual Property Controlled by a Third Party is necessary or advisable for the Development of the Assay or the IVD Kit, IVS shall be responsible, at its own expense, for obtaining and maintaining any licenses or other rights to access or use such other Intellectual Property Controlled by a Third Party that is necessary for the Development of the Assay or IVD Kit.

(b) Each Party shall regularly inform the other Party about the necessity of Third Party Intellectual Property necessary or advisable for the Development, manufacture, use, or Commercialization of the Assay and/or IVD Kit and the negotiation status of any agreement to license such Third Party Intellectual Property. Moreover, the Parties shall regularly consult with each other regarding the content of such Third Party Intellectual Property licenses. The negotiating Party shall reasonably take into account any comments from the other Party on the terms of the license agreements that are applicable to such Third Party Intellectual Property.

(c) IVS agrees to cooperate reasonably with APR to assist APR's acquisition of any licenses that it decides to obtain pursuant to Section 10.3(a); provided, however, that such cooperation shall not include the undertaking of any financial obligations such as the payment of royalties, milestones or the like, unless otherwise stipulated herein or otherwise agreed between the Parties.

(d) APR agrees to cooperate reasonably with IVS to assist IVS's acquisition of any licenses that it is obligated to obtain pursuant to Section 10.3(b); provided, however, that such cooperation shall not include the undertaking of any financial obligations such as the payment of royalties, milestones or the like, unless otherwise stipulated herein or otherwise agreed between the Parties.

10.4 No Implied License. Only the licenses granted or retained pursuant to the express terms of this Agreement shall be of any legal force or effect. No other license rights shall be created by implication, estoppel or otherwise.

ARTICLE 11
TERM AND TERMINATION

11.1 Term. The term of this Agreement commences upon the Effective Date, and shall continue until all of the Activities in the Project Plan, as amended, have been completed, and for as long as the APR Product is on the market as a commercialized product in any country in the Territory, unless this Agreement is earlier terminated in accordance with the terms hereof (the "Term").

11.2 Termination For Convenience. APR is entitled to terminate this Agreement in its entirety or on a country-by-country basis at any time during the Term for convenience upon ninety (90) days' written notice to IVS.

11.3 Termination after Phase III Trial. APR is entitled to terminate this Agreement after receiving the top line results of any Phase III study involving the IVD Kit and the APR Product. APR shall have the sole discretion to determine whether a Phase III study is positive or negative, and thus whether the Parties shall continue the Project pursuant to this Agreement after receiving such Phase III results. In the event of a negative outcome of the Phase III study and an APR decision not to move forward with any further work by IVS, any relevant work completed by IVS will be transferrable and, if appropriate, creditable, without further payment, to any future agreement between the Parties to complete a companion diagnostic assay. APR shall provide written notice to IVS if APR intends to terminate the Agreement pursuant to this Section 11.3. Upon receipt of such notice, IVS shall perform the activities required pursuant to Section 11.6(a) and then send APR an invoice for the applicable milestone payment as set forth in the Approved Development Budget, and for any Pass Through Expenses that are non-cancellable or have already been actually incurred by IVS as of the date of such termination under this Section 11.3. This Agreement shall terminate immediately upon APR's payment of such milestone payment and all such above-mentioned Pass Through Expenses. A termination by APR under this Section 11.3 shall not be deemed a Termination for Convenience under Section 11.2.

11.4 Termination for Cause. (a) Either Party is entitled to terminate this Agreement upon sixty (60) days' written notice if the other Party commits a material breach of this Agreement, and such breach is not cured by the breaching Party within such 60-day period, provided that if the nature of the breach is such that it cannot be cured within such 60-day period, and the breaching party initiates a cure within such period, and diligently pursues the cure, then the breaching Party will have such additional period (as determined by the JSC) as is reasonable under the circumstances to cure the breach, but in no event shall such cure period be longer than 180 days. If such non-cured breach relates solely to a particular country in the Territory, then the non-breaching

Party may only terminate that part of the Project Plan and Agreement which relates to such country by way of a written notice to the breaching Party. IVS may terminate the Agreement, on a country-by-country basis only, upon thirty (30) days written notice if IVS receives insufficient Project Data to reasonably support Regulatory Approval for the Assay and/or IVD Kit, as applicable, in a particular country.

(b) In addition, APR may terminate this Agreement upon ten (10) days written notice to IVS if APR has discontinued the development of the APR Product for all indications due to the feedback received from the FDA regarding the continuation of the their program, and this termination will be deemed to be a Termination for Cause for purposes of Section 11.6(c). A termination by APR under this Section 11.4 shall not be deemed a Termination for Convenience under Section 11.2. Subject to the terms of this Agreement, any relevant work completed by IVS will be, if appropriate, creditable, without further payment, to any future agreement between the Parties to complete a companion diagnostic assay to the extent such work can be used in such assay under the then applicable rules and regulations.

11.5 Termination for Bankruptcy. Either Party is entitled to terminate this Agreement immediately by written notice to the other Party, if the other Party makes or has made an assignment for the benefit of creditors, is the subject of proceedings in voluntary or involuntary bankruptcy instituted on behalf of or against it (except for involuntary bankruptcies which are dismissed within ninety (90) days) or has a receiver or trustee appointed for substantially all of its property. Regardless of which Party terminates under this Section 11.5, IVS shall cease performing all work not necessary for the orderly close-out of the Project Plan and for the fulfillment of any regulatory requirements. In the event that the Agreement is terminated for bankruptcy of IVS, then (unless otherwise agreed between the Parties) effective immediately on the tenth (10th) day thereafter, IVS shall promptly transfer the Regulatory Approval(s) for the Assay and IVD Kit and all Know-How related thereto, to APR or APR's designee, and APR or APR's designee shall have the right to have a royalty-free, fully-paid, non-exclusive license in the Territory to use any IVS Background IP, Patents claiming IVS Project Inventions, and IVS Project Data that is reasonably necessary for the Development, use manufacture and Commercialization of the Assay or the IVD Kit as a companion diagnostic for use in connection with the APR Product.

11.6 Effects of Termination.

(a) Close-Out of Project Plan. In addition to any other remedies either Party may have hereunder and under Applicable Law, in the event of any termination, in whole or in part, of this Agreement the Parties shall promptly meet to prepare a close-out of the Project Plan in the country(ies) being terminated, and IVS shall promptly (but in any event within thirty (30) days after termination) return all Samples to APR and use Commercially Reasonable Efforts to conclude as instructed by APR, as expeditiously as reasonably possible. The close-out of the Project Plan shall include activities relating to the execution of software validation, draft assay validation protocols and completion of process validation if APR terminates this Agreement pursuant to Section 11.3.

(b) Payments Due. APR shall pay IVS (i) a pro-rata portion of the next milestone payment, (ii) any Pass-Through Expenses already actually incurred, or any Pass-Through Expenses that are non-cancellable as of the date of termination of this Agreement, and (iii) any other non-refundable costs or expenses incurred or non-cancelable expenses committed

to be paid, in each case within the sixty (60) days following the date of termination of this Agreement; provided that such payments described in (iii) will not be due if such payments are solely due to a material breach by IVS pursuant to which APR terminated this Agreement pursuant to Section 11.4(a).

(c) Effect of Termination by APR for Cause. In the event of a termination by APR in accordance with Section 11.4, with regard to the Project that has been terminated in its entirety or that has been terminated solely in a particular country in the Territory:

(i) IVS shall cease performing all work not necessary for the orderly close-out of the applicable Activities or for the fulfilment of any regulatory requirements,

(ii) IVS shall use Commercially Reasonable Efforts to conclude the Project and to transfer such Project to APR or APR's designee in its entirety or in a particular country in the Territory, as the case may be, as instructed by APR, as expeditiously as reasonably possible and in accordance with all regulatory requirements,

(iii) any license granted by APR to IVS under under Section 10.1 for the terminated Project or for the terminated country in the Territory, as the case may be, shall terminate upon the effective date of such termination, and

(iv) IVS shall promptly transfer the Regulatory Approval(s) for the Assay and IVD Kit and all Know-How related thereto (including IVS Know-How), to APR, and APR shall, upon full payment of all amounts due to IVS under this Agreement pursuant to Section 11.6(b), have a royalty-free, fully-paid, non-exclusive license, with the right to sublicense, in the Territory to use any IVS Background IP, IVS Patents, Patents claiming IVS Project Inventions, and IVS Project Data that is reasonably necessary for the Development, use, manufacture and Commercialization of the Assay or the IVD Kit as a companion diagnostic for use in connection with the APR Product in the terminated country(ies) of the Territory until the APR Product is no longer being commercialized by APR, its Affiliates or its Approved Subcontractors in such Territory(ies).

(d) Effect of Termination by IVS For Cause. In the event of a termination by IVS in accordance with Section 11.4, with regard to the Project that has been terminated in its entirety or that has been terminated solely in a particular country in the Territory:

(i) IVS shall wind down the Project in accordance with all regulatory requirements,

(ii) IVS shall cease performing all work not necessary for the orderly close-out of the applicable Activities,

(iii) any license granted by IVS to APR under Section 10.2 for the terminated Project or for the terminated country in the Territory, as the case may be, shall terminate upon the effective date of such termination, and

(e) Effect of Termination by APR for Convenience. In the event of a termination by APR in accordance with Section 11.2, with regard to the Project that has been terminated in its entirety or that has been terminated solely in a particular country in the Territory:

(i) IVS shall cease performing all work not necessary for the orderly close-out of the applicable Activities or for the fulfilment of any regulatory requirements,

(ii) IVS shall use Commercially Reasonable Efforts to conclude the Project and to transfer such Project to APR or APR's designee in its entirety or in a particular country in the Territory, as the case may be, as instructed by APR, as expeditiously as reasonably possible and in accordance with all regulatory requirements,

(iii) APR shall pay [***] percent ([***] %) of the next milestone payment due as of such date, and [***] percent ([***] %) of any other unpaid milestone payments, as determined in Schedule A.

(iv) any license granted by APR to IVS under Section 10.1 for the terminated Project or for the terminated country in the Territory, as the case may be, shall terminate upon the effective date of such termination; and

(v) any license granted by IVS to APR under Section 10.2 for the terminated Project or for the terminated country in the Territory, as the case may be, shall terminate upon the effective date of such termination.

11.7 Survival. Termination or expiration of this Agreement will not relieve either Party of any liability which accrued hereunder prior to the effective date of such termination, nor preclude either Party from pursuing all rights and remedies it may have hereunder at law or in equity with respect to any breach of this Agreement, nor prejudice either Party's right to obtain performance of any obligation arising hereunder. Sections 4.7, 4.11, 6, 8, 9, 11, 13, 14, and 15 shall survive any termination or expiration of this Agreement, as the case may be.

ARTICLE 12
REPRESENTATIONS AND WARRANTIES

12.1 General Warranties. Each Party hereby represents and warrants to the other Party as of the Effective Date that: (i) it is a corporation duly organized, validly existing, and in good standing under Applicable Laws, (ii) it has obtained or will obtain by the applicable date all necessary consents, approvals and authorizations of all Regulatory Authorities and other persons required to be obtained by it in connection with this Agreement, (iii) the execution, delivery and performance of this Agreement have been duly authorized by all necessary corporate action on its part, and (iv) it has, to the best of its knowledge, the right to grant the applicable rights and licenses provided for under this Agreement and the right to perform under this Agreement.

12.2 Compliance with Laws. Each Party represents, warrants and covenants to the other Party that it and its Affiliates and permitted Approved Subcontractors and Minor Subcontractors shall perform their respective obligations under this Agreement in compliance with all Applicable

Laws, including, all applicable anti-bribery and antitrust laws. To the extent related to this Agreement, each Party represents and warrants that it has not made or provided, and will not make or provide, any payment or benefit, directly or indirectly, to government officials, customers, business partners, healthcare professionals or any other person in order to secure an improper benefit or unfair business advantage, affect private or official decision-making, affect prescription behavior, or induce someone to breach professional duties or standards.

12.3 No Inconsistent Agreements. Each of IVS and APR further hereby represents, warrants and covenants to the other Party that during the Term it will not grant or convey to any Third Party any right, license or interest in any Intellectual Property that is inconsistent with the rights and licenses expressly granted to the other Party under this Agreement.

12.4 No Debarment Nor Prohibited Payments. Each Party hereby certifies that it will not and has not employed or otherwise used in any capacity the services of any person debarred under Title 21 United States Code Section 335a in performing any activities under this Agreement. Each Party further represents and warrants that in connection with the subject matter of this Agreement: (i) none of its employees, agents, officers or directors is a Foreign Official as defined in the U.S. Foreign Corrupt Practices Act, (ii) it will not make, accept or request any payment, either directly or indirectly, of money or other assets to any Third Party where such payment would constitute violation of any law, including the U.S. Foreign Corrupt Practices Act and the UK Bribery Act 2010, (iii) regardless of legality, it shall neither make, accept nor request any such payment for the purpose of improperly influencing the decisions or actions of any Third Party, and (iv) it shall report any suspected or actual violation of this Section 12.4 to the other Party upon becoming aware of the same.

12.5 Non-Infringement. Each Party hereby represents, warrants and covenants to such Party's actual knowledge (without any further investigation) that (i) as of the Effective Date, it is not aware of any information or facts indicating, and has not received any notice (written or otherwise) from any Third Party asserting or alleging that the practice of its Background IP or the Background IP of its Affiliates that is contemplated to be utilized in the Project, infringes or misappropriates the Intellectual Property of such Third Party, and (ii), to its actual knowledge (without any further investigation), the performance of its respective obligations under this Agreement shall not infringe or misappropriate the Intellectual Property of any Third Party.

12.6 Additional Representations, Warranties, and Covenants of IVS. IVS represents, warrants that:

(a) IVS has not entered into any agreement with any Third Party that would limit or prohibit IVS's right to enter into this Agreement.

(b) IVS has and will maintain sufficient insurance policies in place to cover its obligations under this Agreement, including under Section 13.5.

(c) The Assay and the IVD Kit will be free from defects in design, materials and workmanship and will meet all specifications described in the PRD and Project Plan.

12.7 No Other Warranties. EXCEPT AS EXPRESSLY STATED IN THIS Article 12, (A) NO REPRESENTATION OR WARRANTY WHATSOEVER IS MADE OR GIVEN BY OR

ON BEHALF OF APR OR IVS; AND (B) ALL OTHER WARRANTIES WHETHER ARISING BY OPERATION OF LAW OR OTHERWISE ARE HEREBY EXPRESSLY EXCLUDED, INCLUDING ANY WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

ARTICLE 13
INDEMNIFICATION AND INSURANCE; LIMITATION OF LIABILITY

13.1 Indemnity by IVS. IVS will defend, indemnify, and hold harmless APR, its Affiliates, and their respective directors, officers, employees, agents and representatives (collectively, "APR Indemnitees"), at IVS's cost and expense, from and against any and all liabilities, losses, costs, damages, settlements, penalties, fines, fees or expenses (including reasonable legal expenses and attorneys' fees) payable to Third Parties (collectively, "Losses") arising out of any Third Party claims, suits, actions, demands or judgments (collectively, "Claims") brought against any APR Indemnitee to the extent such Claims and Losses result from: (a) the activities performed by IVS, its Affiliates or permitted Third Parties (or any employees, agents or representatives of any of them) under this Agreement or the the Project Plan; (b) a breach of any of IVS's representations or warranties in Article 12; (c) an IVS Indemnitees' gross negligence or willful misconduct; or (d) personal injury or death caused by the use or administration of the Assay or the IVD Kit. The indemnification obligations under this Section 13.1 (Indemnity by IVS) exclude Losses to the extent they arise from (a), (b), (c) or (d) below in Section 13.2 (Indemnity by APR).

13.2 Indemnity by APR. APR will defend, indemnify, and hold harmless IVS, its Affiliates, and their respective directors, officers, employees, agents and representatives (collectively, "IVS Indemnitees"), at APR's cost and expense, from and against any and all Losses arising out of any Claims brought against any IVS Indemnitee to the extent such Losses result from: (a) the activities performed by APR or its Affiliates (or any employees, agents or representatives of any of them) under this Agreement; (b) a breach of any of APR's representations or warranties in Article 12; (c) a APR Indemnitees' gross negligence or willful misconduct; or (d) personal injury or death caused by the use or administration of the APR Product. The indemnification obligations under this Section 13.2 (Indemnity by APR) exclude Losses to the extent they arise from (a), (b), (c) or (d) above in Section 13.1 (Indemnity by IVS).

13.3 Claim for Indemnification. Whenever any Claim or Loss arises for which a IVS Indemnitee or an APR Indemnitee (the "Indemnified Party") may seek indemnification under this Article 13 (Indemnification and Insurance), the Indemnified Party will promptly notify the indemnifying Party(ies) (the "Indemnifying Party(ies)") of the Claim or Loss; provided, that the failure by an Indemnified Party to give such notice will not relieve the Indemnifying Party(ies) of its (or their respective) indemnification obligations under this Agreement except and only to the extent that such Indemnifying Party is actually prejudiced as a result of such failure. The Indemnifying Party(ies) will have exclusive control of the defense and settlement of all Claims for which it is responsible for indemnification and will assume defense thereof at its own expense promptly upon notice of such Claim; provided, however, that counsel engaged by the Indemnifying Party is reasonably acceptable to the Indemnified Party. The Indemnified Party will have the right to employ separate counsel at the Indemnifying Party's expense and to control its own defense of the applicable Claim if: (i) there are or may be legal defenses available to the Indemnified Party that are different from or additional to those available to the Indemnifying Party; or (ii) in the reasonable opinion of counsel to the Indemnified Party, a conflict or potential conflict exists

between the Indemnified Party and Indemnifying Party(ies) that would make such separate representation advisable. In any event, the Indemnified Party shall cooperate reasonably with the Indemnifying Party and its legal representatives in connection with the investigation and defense of any Claim and/or Loss covered by this Section 13.3. Neither Party may enter into any settlement, consent judgment or other voluntary final disposition of any Claim and/or Loss for which an Indemnified Party seeks indemnification hereunder without the prior written consent of the other Party, if such settlement would: (a) impose any monetary obligation on the other Party or any of its Affiliates, (b) constitute an admission of guilt or wrong-doing by the other Party or any of its Affiliates, or (c) require the other Party or any of its Affiliates to submit to an injunction or otherwise limit the other Party's or any of its Affiliates' rights under this Agreement.

13.4 Defense of Claims. Except as otherwise provided in Section 13.3 (Claim for Indemnification), each Party (such Party referred to as the "Defending Party") will have the sole right, but not the obligation, to defend against any Claims made against it with respect to its activities hereunder at its sole cost and expense. Each Party will notify the other Party(ies) (the "Assisting Party(ies)") as promptly as practicable if any such Claim is commenced or threatened against it. The Assisting Party(ies) will reasonably assist the Defending Party and cooperate in any such litigation at Defending Party's reasonable request. Without limiting the foregoing, the Defending Party will keep the Assisting Party(ies) advised of all material communications, actual and prospective filings or submissions regarding such action, and will provide the Assisting Party(ies) copies of and an opportunity to review and comment on any such communications, filings and submissions. The Defending Party will control the defense and settlement of Claims. In the event that a Claim is brought against both Parties (a "Joint Claim"), then the Parties will determine whether to defend against such Joint Claim, which of the Parties should be the Defending Party or whether the Parties should jointly control such defense and the strategy for such defense.

13.5 Insurance. Each of the Parties will, at its own respective expense, procure and maintain during the Term, commercial general liability insurance with limits not less than $[***] and product liability insurance or clinical trial insurance, as applicable, with limits not less than $[***] per occurrence and $[***] in the aggregate, or the equivalent amount in self-insurance for bodily injury and property damage, including products and completed operations, contractual liability, personal and advertising liability and additional insureds, when required by contract. It is expressly understood that such insurance may not be adequate to protect a Party's interest and it will not create a limit to either Party's liability hereunder. All insurers utilized to confirm coverage within this Section 13.5 shall be rated A, Class IV or better by the latest edition of A.M. Best Company. At a minimum, each Party shall maintain the policy(ies) required hereunder for the entire term of this Agreement, plus an additional three years beyond termination. In any instance where such insurance is based upon a "claims made" policy, each Party shall secure an additional three year "extended reporting provision," beyond termination of the required coverage period. Certificates of insurance evidencing compliance with this provision shall be exchanged upon execution of this Agreement and on each policies subsequent renewals. Each Party will also maintain workers compensation insurance in accordance with the laws governing the states of operation.

13.6 Recalls; Field Corrections. In the event any Regulatory Authority having jurisdiction shall request or order, or if IVS shall reasonably determine to undertake, any corrective action with respect to the Assay or IVD Kit hereunder, including any seizure, recall, stock recovery, withdrawal

or field correction with respect thereto, and the cause or basis of such action is attributable to the Assay or IVD Kit and/or a breach by IVS of any of its warranties, guarantees, representations, obligations or covenants contained herein, IVS shall bear the reasonable costs and expenses of such seizure, recall, stock recovery, withdrawal, field correction or other corrective action. APR shall bear the reasonable costs and expenses for any recall based on circumstances, other than that listed in the preceding sentence, to the extent associated with the APR Product. Each Party shall cooperate to provide information and assistance as needed to facilitate performance of a recall or field correction regardless of the circumstances causing such recall. Depending upon the circumstances governing corrective action or a recall, the responsible Party shall maintain ultimate control of their respective product. Each Party agrees to provide written notification to the other, upon notice from a Regulatory Authority relating to the recall of the Assay, IVD Kit or APR Product, as applicable.

13.7 Mitigation of Loss. Each Indemnified Party will take and will procure that its Affiliates take such reasonable steps and action as are commercially reasonable to mitigate any claims or Losses (or potential losses or damages) under this Article 13. Nothing in this Agreement shall or shall be deemed to relieve any Party of any common law duty to mitigate any losses incurred by it.

13.8 Limitation of Liability. NEITHER PARTY WILL BE LIABLE TO THE OTHER FOR ANY INDIRECT, SPECIAL, EXEMPLARY, PUNITIVE OR OTHER SIMILAR DAMAGES (INCLUDING ANY CLAIMS FOR LOST PROFITS OR REVENUES) ARISING FROM OR RELATING TO THIS AGREEMENT; PROVIDED HOWEVER THAT THERE SHALL BE NO LIMITATION OF LIABILITY FOR BREACH OF ARTICLE 8 (CONFIDENTIALITY), WILLFUL MISCONDUCT OR FRAUD, OR WITH RESPECT TO THIRD PARTY CLAIMS FOR WHICH A PARTY PROVIDES INDEMNIFICATION UNDER THIS ARTICLE 13.

ARTICLE 14
DISPUTE RESOLUTION

14.1 Resolution of Disputes; General. It is the objective of the Parties to establish procedures to facilitate the resolution of Disputes arising under this Agreement in an expedient manner by mutual cooperation and without resort to litigation.

(a) All Disputes at the JSC shall be resolved as provided in Section 2.6(e), provided the issue in dispute is within the scope of the JSC's (or any Working Group thereunder) authority.

(b) All other Disputes shall be resolved as provided herein. The Parties shall meet and discuss in good faith a possible resolution of the Dispute. If the Dispute cannot be resolved within ten (10) days from the first date of such meeting, either Party may refer the Dispute to the Senior Officers, or their respective designees, for resolution through good faith negotiations. If the Dispute is not resolved by the Senior Officers within ten (10) days, either Party may proceed to binding arbitration as set forth below. To the extent that a Party's Senior Officer delegates his/her responsibility for resolution of a Dispute to another officer of such Party, such Party shall ensure that the designee has all necessary and appropriate authority to fully resolve the Dispute on behalf of such Party.

14.2 Arbitration. Except as otherwise expressly provided in this Agreement, any Dispute between the Parties arising in connection with this Agreement and/or their performance hereunder not resolved pursuant to Section 14.1(b) shall be finally resolved through binding arbitration. The arbitration shall be conducted by JAMS (formerly Judicial Arbitration and Mediation Services) ("JAMS") pursuant to the JAMS rules for commercial disputes and the applicable provisions of this Agreement.

14.3 Arbitration Panel. The arbitration shall be conducted by a panel of three (3) arbitrators. Within thirty (30) days after the initiation of the arbitration, each Party will nominate one person to act as an arbitrator, and the two arbitrators so named will then jointly appoint the third arbitrator within thirty (30) days of their appointment, who will serve as chairman of the arbitration panel. All three (3) arbitrators must be independent Third Parties having at least ten (10) years of dispute resolution experience (including judicial experience) and/or legal or business experience in the biotech or pharmaceutical industry. If any Party fails to timely nominate its arbitrator, or if the arbitrators selected by the Parties cannot agree on the person to be named as chairman within such thirty (30) day period, JAMS will make the necessary appointments for such arbitrator(s) or the chairman. Once appointed by a Party, such Party will have no ex parte communication with its appointed arbitrator.

14.4 Location and Proceedings. The place of arbitration will be New York, New York, or such other venue as the Parties may mutually agree. The arbitration proceedings and all communications with respect thereto will be in English. Except as otherwise stated herein, the arbitrators have the power to decide all matters in dispute, including any questions of whether or not such matters are subject to arbitration hereunder. The decisions of the arbitrators shall be final and binding on the Parties and shall not be subject to appeal. The parties hereby waive any right to a jury trial. The arbitrator shall have the discretion to award attorneys' fees to the party the arbitrator determines is the prevailing party in the arbitration. Nothing in this Agreement is intended to prevent either party from obtaining injunctive relief in court to prevent irreparable harm pending the conclusion of any such arbitration. Notwithstanding the foregoing, each party shall have the right to resolve any issue or dispute involving confidential, proprietary or trade secret information, or intellectual property rights, by Court action instead of arbitration. The parties shall instruct the arbitrators to render their decision no later than ninety (90) days after the submission of the dispute.

14.5 Limitation on Awards. The arbitrators shall have no authority to award any damages inconsistent with Section 13.8 (Limitation of Liability). The arbitrators shall not be authorized to award punitive damages with respect to any such claim or controversy, nor shall any party seek punitive damages relating to any matter under, arising out of, or relating to this Agreement in any other forum. Each Party shall bear its own costs and expenses (including attorneys' fees and expert or consulting fees) incurred in connection with the arbitration. The Parties shall equally (50:50) share the arbitrator's fees and any other administrative costs and expenses associated with the arbitration.

14.6 Confidentiality. Neither Party, nor any of the arbitrators, shall be permitted to disclose the existence, content or results of any arbitration proceedings pursuant to this Article 14, without the prior written consent of both Parties.

ARTICLE 15
MISCELLANEOUS

15.1 Governing Law. The formation, existence, performance, validity and all aspects of this Agreement shall be governed by and construed in all respects in accordance with the laws of the State of New York, without regard to its rules on conflicts of laws.

15.2 Use of Parties' Names. Neither Party shall make (or have made on its behalf) any oral or written release of any statement, press release, information, advertisement or publicity to promote this Agreement or the subject matter herein or which uses the other Party's name, symbols, or trademarks without the other Party's prior written approval.

15.3 Use of Affiliates. Each Party will perform its activities under this Agreement itself or through any of its Affiliates without notice to or consent from the other Party. Each Party will be responsible for compliance by its Affiliates with this Agreement and will be responsible for all acts and omissions of such Affiliates as if committed or omitted by the Party assigning such work. To the extent that a Party utilizes its Affiliates under this Agreement, such Party shall ensure all such Affiliates are obligated to: (i) treat the other Party's Confidential Information in accordance with the provisions of this Agreement, (ii) assign rights to any Inventions and results so that such rights can be conveyed in accordance with the terms and conditions of this Agreement, and (iii) with respect to IVS, that its Affiliates grant audits and inspection rights similar to the right set forth in this Agreement whereas the foregoing shall not limit IVS's audit and inspection responsibilities.

15.4 Change of Control. In the event of a Change of Control of IVS, such Change of Control shall not cause this Agreement to terminate and this Agreement shall remain in full force and effect. However, in the event of a Change of Control of IVS involving either (a) a company developing or commercializing a therapeutic product that is competitive to the APR Product or (b) a company developing or commercializing an assay or kit for use with a therapeutic product that is competitive to the APR Product, then IVS shall "firewall" all its activities and records under this Agreement so that they shall not be shared with or accessible to persons involved in the activities and records regarding such other therapeutic or diagnostic product of such competitor.

15.5 Assignment. Either Party may assign this Agreement or any of its rights and obligations hereunder without the other Party's consent to: (i) any Affiliate of such Party, or (ii) any successor in interest to all or substantially all of the assigning Party's assets, whether by reason of any merger, acquisition, reorganization, consolidation or other. Any attempt by either Party to effect any other assignment without the consent of the other Party will be void and without effect, and any other assignment of this Agreement shall require written notice to the non-assigning Party.

15.6 Counterparts. This Agreement may be signed in any number of counterparts (electronic transmission of scanned signatures included), each of which shall be deemed an original, but all of which shall constitute one and the same instrument. After electronic transmission of scanned signatures the Parties shall, upon one Party's request, execute and exchange documents with original signatures.

15.7 Entire Agreement. This Agreement, the Project Plan, and the Schedules hereto set out the entire agreement and understanding between the Parties regarding the subject matter of this

Agreement and supersedes all prior discussions, arrangements and agreements, whether oral or in writing or which may be inferred from the conduct of the Parties.

15.8 Agreement Precedence. In the event of conflict between the terms and conditions of this Agreement and the terms and conditions of the Project Plan, as amended, supplemented or restated from time to time by mutual written agreement of the Parties, this Agreement will take precedence.

15.9 Force Majeure. Neither Party shall be responsible to the other for any failure or delay in performing any of its obligations under this Agreement, or for other nonperformance hereunder, if such delay or nonperformance is caused by strike, stoppage of labor, lockout or other labor trouble, fire, flood, pandemic, earthquakes, accident, war, act of terrorism, act of God or of the government of any country or of any local government, or by cause unavoidable or beyond the control of any Party hereto (a "Force Majeure Event"). In the event any Party is unable to perform any of its obligations hereunder due to a Force Majeure Event, such Party shall promptly notify the other Party. In such event, the Party affected will use commercially reasonable efforts to promptly resume performance of its obligations. If the Force Majeure Event lasts for more than ninety (90) days, the non-affected Party may terminate this Agreement by written notice to the other Party.

15.10 Notice. All notices, consents, waivers, and other communications under this Agreement must be in writing and will be deemed to have been duly given when: (a) delivered by hand (with written confirmation of receipt); (b) sent by fax (with written confirmation of receipt), provided that a copy is immediately sent by an internationally recognized overnight delivery service (receipt requested); (c) when received by the addressee, if sent by an internationally recognized overnight delivery service (receipt requested), or (d) electronically by email, if confirmed by (a), (b) or (c) above, in each case to the appropriate addresses and fax numbers set forth below (or to such other addresses and fax numbers as a Party may designate by notice):

If to IVS:

Invivoscribe, Inc.
10222 Barnes Canyon Rd., Building 1
San Diego, CA 92121
Attn: Jeffrey E. Miller, CEO
Fax: (858) 224-6601

With a copy to (which shall not constitute notice):

Michael J. Kinkelaar, Esq.
Procopio, Cory, Hargreaves & Savitch LLP
525 B Street, Suite 2200
San Diego, CA 92101
Fax: (619) 744-5450

If to APR:

Aprea Therapeutics, Inc.
535 Boylston Street

Boston, Massachusetts 02116
Attn: Chris Schade, President

With a copy to (which shall not constitute notice):

General Counsel
Aprea Therapeutics, Inc.
_____
_____
Fax: _____

15.11 Relationship of the Parties. Each Party is an independent contractor under this Agreement. Nothing contained herein will be deemed to create an employment, agency, joint venture or partnership relationship between the Parties or any of their agents or employees, or any other legal arrangement that would impose liability upon one Party for the act or failure to act of the other Party. The Parties will operate their own businesses separately and independently and they will hold themselves out as, act as, and constitute independent contractors in all respects and not as principal and agent, partners or joint venturers. Neither Party will have any express or implied power to enter into any contracts or commitments or to incur any liabilities in the name of, or on behalf of, the other Party, or to bind the other Party in any respect whatsoever.

15.12 No Third Party Beneficiaries. Except as expressly set forth herein, no provision of this Agreement is intended to confer any rights, benefits, remedies, obligations or liabilities hereunder upon any person or entity other than the Parties hereto and their respective successors and assigns.

15.13 Validity/Severability. The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision which shall remain in full force and effect.

15.14 Waiver; Modification of Agreement. No waiver, amendment, or modification of any of the terms of this Agreement shall be valid unless in writing and signed by authorized representatives of both Parties. Failure by either Party to enforce any rights under this Agreement shall not be construed as a waiver of such rights nor shall a waiver by either Party in one or more instances be construed as constituting a continuing waiver or as a waiver in other instances.

15.15 Expanded Scope. In the event that APR notifies IVS in writing that it desires to expand the scope of the use of the IVS Assay for Regulatory submission for other indications not covered by this Agreement, IVS will review such expanded scope of work provided by APR, and IVS will then provide to APR an additional scope of work to be performed by IVS, along with the estimated budget for such work. Any analytical validation work performed and paid for by APR for this Assay under this Agreement, to the extent appropriate and applicable, will be creditable to any future agreement between the Parties for other indications of APR-246 using the same Assay.

IN WITNESS WHEREOF, IVS and APR, intending to be legally bound, have executed this Companion Diagnostic Agreement as of the Effective Date by their respective duly authorized representatives.

Aprea Therapeutics, Inc.		Invivoscribe, Inc.	
By:	/s/ Christian S. Schade	By:	/s/Jeffrey Miller
Name:	Christian S. Schade	Name:	Jeffrey Miller
Title:	Chief Executive Officer	Title:	Chief Scientific and Chief Executive Officer

Schedule A

Approved Development Budget

APR will make the following milestone payments to IVS for development milestones achieved:

	Estimated timelines*	**Milestone Payment Amount**
[***]	[***]	$[***]
[***]	[***]	$[***]
[***][1]	[***]	$[***]
[***]	[***]	$[***]
[***]	[***]	$[***]
[***]	[***]	$[***]
[***]	[***]	$[***]
[***]	[***]	$[***]
[***]	[***]	$[***]
[***]	[***]	$[***]
[***]	[***]	$[***]
[***]		$[***]
Total:		**$**[***]

[1] [***]

1.

Schedule B

Senior Officers of IVS and APR

For IVS:

Jeffrey Miller, Chief Executive Officer

Meghna Bhatnagar, Chief Financial Officer

For APR:

Chris Schade, President and Chief Executive Officer

Scott Coiante, Sr. Vice President and Chief Financial Officer

CERTIFICATION OF PERIODIC REPORT
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Christian S. Schade, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Aprea Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 11, 2020

/s/ Christian S. Schade
Christian S. Schade
Chief Executive Officer

CERTIFICATION OF PERIODIC REPORT PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Scott M. Coiante, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Aprea Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 11, 2020

/s/ Scott M. Coiante
Scott M. Coiante
Chief Financial Officer

STATEMENT OF CHIEF EXECUTIVE OFFICER OF
APREA THERAPEUTICS, INC.
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the quarterly report of Aprea Therapeutics, Inc. (the "Company") on Form 10-Q for the period ended June 30, 2020 as filed with the Securities and Exchange Commission (the "Report"), I, Christian S. Schade, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, based on my knowledge:

1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 11, 2020

/s/ Christian S. Schade
Christian S. Schade
Chief Executive Officer

STATEMENT OF CHIEF ACCOUNTING OFFICER OF
APREA THERAPEUTICS, INC.
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the quarterly report of Aprea Therapeutics, Inc. (the "Company") on Form 10-Q for the period ended June 30, 2020 as filed with the Securities and Exchange Commission (the "Report"), I, Scott M. Coiante, Chief Accounting Officer of the Company, certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, based on my knowledge:

1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 11, 2020

/s/ Scott M. Coiante
Scott M. Coiante
Chief Financial Officer