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

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

March 30, 2023
Date of Report (Date of earliest event reported)

Aprea Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-39069**	**84-2246769**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

3805 Old Easton Road **Doylestown, PA**	**18902**
(Address of principal executive offices)	(Zip Code)

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

(Former name or former address, if changed since last report): Not applicable

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, par value $0.001 per share	APRE	The NASDAQ Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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. ☒

Item 2.02 Results of Operations and Financial Condition.

On March 30, 2023, Aprea Therapeutics, Inc. (the "Company") issued a press release announcing its financial results for the quarter and fiscal year ended December 31, 2022, and provided an update on the Company's operations for the same period. The Company is furnishing a copy of the press release, which is attached hereto as Exhibit 99.1.

In accordance with General Instruction B.2 of Form 8-K, the information included in this Item 2.02, including Exhibit 99.1 hereto, shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any filing made by the Company under the Exchange Act or Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such a filing.

Item 7.01 Regulation FD Disclosure.

As previously disclosed in Item 7.01 of the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 13, 2023, the Company held its cash, cash equivalents, and short-term investments with Silicon Valley Bank ("SVB"). Beginning on Monday, March 13, 2023, the Company moved the majority of its cash, cash equivalents, and short-term investments held at SVB to other financial institutions. At present, the Company holds less than 0.05% of its cash, cash equivalents, and short-term investments with SVB. Therefore, the Company believes it does not have exposure to any liquidity concerns at SVB.

The information furnished under this Item 7.01 shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or subject to the liabilities of that section. The information shall not be deemed incorporated by reference into any other filing with the Securities and Exchange Commission made by the Company, regardless of any general incorporation language in such filing.

Forward-Looking Statements

This Current Report on Form 8-K may contain "forward-looking statements", within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Exchange Act, related to our study analyses, clinical trials, regulatory submissions, and projected cash position. We may, in some cases use terms such as "future," "predicts," "believes," "potential," "continue," "anticipates," "estimates," "expects," "plans," "intends," "targeting," "confidence," "may," "could," "might," "likely," "will," "should" or other words that convey uncertainty of the future events or outcomes to identify these forward-looking statements. The Company's forward-looking statements are based on current beliefs and expectations of the Company's management team that involve risks, potential changes in circumstances, assumptions, and uncertainties. Any or all of the forward-looking statements may turn out to be wrong or be affected by inaccurate assumptions the Company might make or by known or unknown risks and uncertainties. These forward-looking statements are subject to risks and uncertainties including, risks related to the success and timing of the Company's clinical trials or other studies, the possibility that the Company may be adversely affected by geopolitical and other economic, business and/or competitive factors, the Company's estimates of its financial performance, and the other risks set forth in the Company's filings with the U.S. Securities and Exchange Commission. For all these reasons, actual results and developments could be materially different from those expressed in or implied by our forward-looking statements. You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this press release. The Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstances.

Item 8.01 Other Events.

On March 30, 2023, the Company updated its corporate presentation slide deck. A copy of the corporate presentation slide deck is filed as Exhibit 99.2 hereto and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press release issued by Aprea Therapeutics, Inc. dated March 30, 2023.
99.2	Corporate Presentation (March 2023).
104	Cover Page Interactive Data File (embedded within the inline XBRL document).

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 hereunto duly authorized.

Aprea Therapeutics, Inc.

Dated: March 30, 2023

By: /s/ Oren Gilad
Name: Oren Gilad, Ph.D.
Title: President and Chief Executive Officer

Exhibit 99.1

Aprea Therapeutics Reports Fourth Quarter and Full Year 2022 Financial Results and Provides Update on Business Operations

DOYLESTOWN, PA, March 30, 2023 (GLOBE NEWSWIRE) – Aprea Therapeutics, Inc. (Nasdaq: APRE) ("Aprea", or the "Company"), a clinical stage biopharmaceutical company focused on developing novel synthetic lethality-based cancer therapeutics targeting DNA damage response (DDR) pathways, today reported financial results for the three months and year ended December 31, 2022 and provided a business update.

"2022 has been another transformational year for Aprea with progress on multiple fronts," said Oren Gilad, Ph.D., President and Chief Executive Officer of Aprea. "With the initiation of the Phase 1/2a clinical trial of our ATR inhibitor, ATRN-119, we remain on track to provide an update on clinical data later this year. Following this important achievement, we further strengthened our cash position with the closing of a public offering pursuant to which we received approximately $5.5 million in gross proceeds, allowing us to extend our cash runway into the third quarter of 2024. We believe our current cash runway will allow us to cross meaningful clinical milestones for our two lead programs. Additionally, we announced a non-dilutive SBIR award from the National Cancer Institute and welcomed John Hamill to the Aprea team. We look forward to his contribution as Chief Financial Officer as we advance our clinical pipeline of synthetic lethality-based cancer therapeutics targeting DDR pathways."

Key Business and Financial Updates

- *ATR inhibitor program: ATRN-119* – Significant progress made on the development of our lead ATR inhibitor program. Our lead clinical candidate, ATRN-119, is a potential best-in-class oral ATR inhibitor for treatment of advanced solid tumors harboring defined mutations in DDR pathways. The Phase 1/2a trial continues to enroll patients with biomarkers related to DDR mutations. ATRN-119 is an orally bioavailable, potent and selective macrocyclic small molecule inhibitor of ATR, a protein with key roles in response to DNA damage. The primary endpoint of the Phase 1 dose escalation part of the study is to assess safety/tolerability, pharmacokinetics and recommended Phase 2 dose. The Phase 2a expansion part of the study is designed to further evaluate tolerability and preliminary efficacy of ATRN-119 monotherapy in advanced solid tumors.
- *WEE1 inhibitor program: ATRN-1051* – ATRN-1051 is an orally-bioavailable, highly potent and selective small molecule inhibitor of WEE1, a key regulator of multiple phases of the cell cycle. The Company believes that preclinical findings show potentially favorable drug selectivity and exposure. IND-enabling studies with ATRN-1051 are under way and the Company anticipates filing of an IND with the FDA by the end of 2023.
- An abstract on combination of ATRN-119 and ATRN-1051 was selected for presentation as a poster at the American Association for Cancer Research (AACR) 2023 Annual Meeting, being held April 14-19, 2023, in Orlando, Florida.
- Obtained non-dilutive funding via a research grant from the National Cancer Institute (NCI) supporting development of DDR inhibitors. The Company announced that it received an award notification from the NCI for the development of a first-in-class combination of DNA damage response inhibitors for the treatment of high-grade serous ovarian cancer (HGSOC). HGSOC is a devastating disease responsible for the deaths of about 125,000 women worldwide each year and has low survival rates.
- Announced the Company had regained compliance with Nasdaq's minimum bid price requirement for continued listing on the Nasdaq Global Select Market.
- Closed an underwritten public offering in Q1 of 2023 pursuant to which we received approximately $5.5 million in gross proceeds. The net proceeds received from the public offering will enable the Company to continue developing its clinical asset, ATRN-119, its pre-clinical asset ATRN-1051 and for general corporate purposes.

Select Financial Results for the Fourth Quarter ended December 31, 2022

- As of December 31, 2022, the Company reported cash and cash equivalents of $28.8 million.
- For the fourth quarter ended December 31, 2022, the Company reported an operating loss of $2.7 million, compared to an operating loss of $7.8 million in the fourth quarter of 2021.
- Research and Development (R&D) expenses were $0.5 million for the quarter ended December 31, 2022, compared to $4.5 million for the fourth quarter of 2021. The decrease in R&D expense was primarily related to the wrap up and close out of legacy Aprea clinical trials which were largely completed by the fourth quarter 2022. Aprea only had one active clinical trial in the 4th quarter of 2022 compared to six active clinical trials in the 4th quarter of 2021.

- General and Administrative (G&A) expenses were $2.1 million for the quarter ended December 31, 2022, compared to $3.4 million for the comparable period in 2021. The decrease in G&A expenses was primarily due to a decrease in non-cash stock-based compensation.
- The Company reported a net loss of $2.4 million ($0.92 per basic share) on approximately 2.6 million weighted-average common shares outstanding for the quarter ended December 31, 2022, compared to a net loss of $7.8 million ($7.20 per basic share) on approximately 1.1 million weighted average common shares outstanding for the comparable period in 2021.

Select Financial Results for the Year ended December 31, 2022

- As of December 31, 2022, the Company reported cash and cash equivalents of $28.8 million compared to $53.1 million as of December 31, 2021. The Company believes its cash and cash equivalents as of December 31, 2022, combined with the gross proceeds received from the Company's $5.5 million public offering of common stock in February 2023 will be sufficient to meet its current projected operating requirements into the third quarter of 2024.
- For the year ended December 31, 2022, the Company reported an operating loss of $113.4 million, which include $76.0 million for acquired in-process research and development, compared to an operating loss of $37.4 million for the year ended December 31, 2021**.**
- Research and Development (R&D) expenses were $16.4 million for the year ended December 31, 2022, compared to $23.9 million for the year ended December 31, 2021. The decrease in R&D expense was primarily related to the wrap up and close out of legacy Aprea clinical trials which were largely completed by the fourth quarter of 2022.
- General and Administrative (G&A) expenses were $21.0 million for the year ended December 31, 2022, compared to $13.6 million for the year ended December 31, 2021. The increase in G&A expenses was primarily due to an increase in non-cash stock-based compensation from the acceleration of vesting of all outstanding stock options and restricted stock units in connection with the acquisition of Atrin Pharmaceuticals Inc. in May 2022.
- The Company reported a net loss was of $112.7 million ($67.99 per basic share) on approximately 1.7 million weighted-average common shares outstanding for the year ended December 31, 2022, compared to a net loss of $37.1 million ($34.88 per basic share) on approximately 1.1 million weighted average common shares outstanding for the same period in 2021.

About Aprea Therapeutics, Inc.

Aprea Therapeutics, Inc. is a clinical stage biopharmaceutical company headquartered in Doylestown, Pennsylvania, focused on developing and commercializing novel synthetic lethality-based cancer therapeutics targeting a critical pathway and some of the most central targets in DDR and cancer progression. The Company's lead program is ATRN-119, a clinical-stage small molecule ATR inhibitor being developed for solid tumor indications. Our WEE1 inhibitor is being advanced to IND submission. For more information, please visit the company website at www.aprea.com.

The Company may use, and intends to use, its investor relations website at https://ir.aprea.com/ as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD.

Forward Looking Statement

Certain information contained in this press release includes “forward-looking statements”, within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, related to our study analyses, clinical trials, regulatory submissions, and projected cash position. We may, in some cases use terms such as “future,” “predicts,” “believes,” “potential,” “continue,” “anticipates,” “estimates,” “expects,” “plans,” “intends,” “targeting,” “confidence,” “may,” “could,” “might,” “likely,” “will,” “should” or other words that convey uncertainty of the future events or outcomes to identify these forward-looking statements. Our forward-looking statements are based on current beliefs and expectations of our management team and on information currently available to management that involve risks, potential changes in circumstances, assumptions, and uncertainties. All statements contained in this press release other than statements of historical fact are forward-looking statements, including statements regarding our ability to develop, commercialize and achieve market acceptance of our current and planned products and services, our research and development efforts, and other matters regarding our business strategies, use of capital, results of operations and financial position, and plans and objectives for future operations. Any or all of the forward-looking statements may turn out to be wrong or be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. These forward-looking statements are subject to risks and uncertainties including risks related to the success and timing of our clinical trials or other studies, risks associated with the coronavirus pandemic and the other risks set forth in our filings with the U.S. Securities and Exchange Commission. For all these reasons, actual results and developments could be materially different from those expressed in or implied by our forward-looking statements. You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this press release. We undertake no obligation to update such forward-looking statements for any reason, except as required by law.

Source: Aprea Therapeutics, Inc.

Investors and Media:

aprea@argotpartners.com
212-600-1902

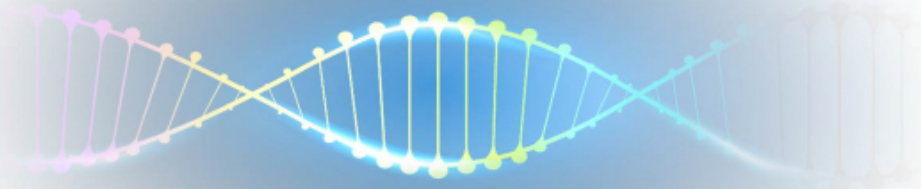
Aprea Therapeutics, Inc.
Condensed Consolidated Balance Sheets

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 28,786,647	$ 53,076,052
Prepaid expenses and other current assets	1,366,859	3,508,358
Total current assets	30,153,506	56,584,410
Property and equipment, net	2,321	23,870
Right of use lease and other noncurrent assets	--	215,183
Total assets	$ 30,155,827	$ 56,823,463
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 842,754	$ 1,773,032
Accrued expenses	2,358,332	5,352,996
Lease liability—current	--	190,471
Total current liabilities	3,201,086	7,316,499
Lease liability—noncurrent	--	--
Total liabilities	3,201,086	7,316,499
Commitments and contingencies		
Preferred stock, par value $0.001; 56,227 and 0 shares issued and outstanding at December 31, 2022 and 2021, respectively	1,311,063	--
Stockholders' equity:		
Common stock, par value $0.001; 2,655,269 and 1,092,967 shares issued and outstanding at December 31, 2022 and 2021, respectively	2,655	1,092
Additional paid-in capital	330,060,836	240,999,206
Accumulated other comprehensive loss	(10,623,408)	(10,358,956)
Accumulated deficit	(293,796,405)	(181,134,378)
Total stockholders' equity	25,643,678	49,506,964
Total liabilities and stockholders' equity	$ 30,155,827	$ 56,823,463

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

	Three Months Ended December 31, (Unaudited)		Year Ended December 31,	
	2022	**2021**	**2022**	**2021**
Operating expenses:				
Research and development	$ 531,406	$ 4,462,154	$ 16,402,273	$ 23,895,875
General and administrative	2,120,222	3,366,525	20,969,771	13,550,478
Acquired in-process research and development	--	--	76,020,184	--
Total operating expenses	2,651,628	7,828,679	113,392,228	37,446,353
Other income (expense):				
Interest income	243,082	3,326	448,667	1,648
Foreign currency gain (loss)	(33,596)	70,169	281,534	317,402
Total other income	209,486	73,495	730,201	319,050
Net loss	$ (2,442,142)	$ (7,755,184)	$ (112,662,027)	$ (37,127,303)
Other comprehensive income (loss):				
Foreign currency translation	(382,763)	95,743	(264,452)	(321,695)
Total comprehensive loss	(2,824,905)	(7,659,441)	(112,926,479)	(37,448,998)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.92)	$ (7.20)	$ (67.99)	$ (34.88)
Weighted-average common shares outstanding, basic and diluted	2,649,349	1,076,940	1,657,055	1,064,325

Exhibit 99.2



Precision Oncology through Synthetic Lethality

March 2023

Forward-Looking Statements

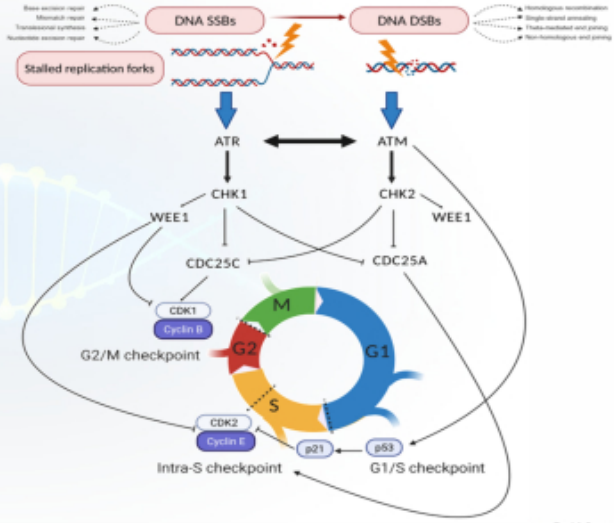
Certain information contained in this presentation includes "forward-looking statements", within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, related to our clinical trials, regulatory submissions and strategic plans. We may, in some cases use terms such as "predicts," "believes," "potential," "continue," "anticipates," "estimates," "expects," "plans," "intends," "may," "could," "might," "likely," "will," "should" or other words that convey uncertainty of the future events or outcomes to identify these forward-looking statements. The forward-looking statements are based on current beliefs and expectations of our management team that involve risks, potential changes in circumstances, assumptions, and uncertainties. Any or all of the forward-looking statements may turn out to be wrong or be affected by inaccurate assumptions our management team might make or by known or unknown risks and uncertainties. These forward-looking statements are subject to risks and uncertainties including, without limitation, risks related to the success and timing of our clinical trials or other studies and the other risks set forth in our filings with the U.S. Securities and Exchange Commission, including our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q. Forward-looking statements regarding our product candidates are also subject to additional risks and uncertainties, including without limitation, with respect to: our dependence on additional financing to fund our operations and complete the development and commercialization of our product candidates, and the risks that raising such additional capital may restrict our operations or require us to relinquish rights to our technologies or product candidates; our limited history and preclinical status of the assets we acquired from Atrin Pharmaceuticals Inc.; our business plan or the likelihood of the successful implementation of such business plan; the timing of initiation of planned clinical trials for our product candidates; the future success of such trials; the successful implementation of our research and development programs and collaborations and the interpretation of the results and findings of such programs and collaborations and whether such results are sufficient to support the future success of our product candidates; the success, timing and cost of our anticipated clinical trials for our current product candidates; the timing of initiation, futility analyses, data presentation, reporting and publication and receipt of interim results (including, without limitation, any preclinical results or data); any statements about our understanding of product candidates mechanisms of action and interpretation of preclinical and early clinical results from its clinical development programs and any collaboration studies; and other factors, including legislative, regulatory, political and economic developments not within our control. For all these reasons, actual results and developments could be materially different from those expressed in or implied by our forward-looking statements. You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this presentation. We undertake no obligation to update such forward-looking statements to reflect subsequent events or circumstances, except to the extent required by law or regulation.

Aprea Therapeutics (NASDAQ: APRE)

Precision Oncology via Synthetic Lethality in Defined Patient Populations

- Clinical stage precision oncology company developing novel synthetic lethality-based therapeutics in areas of high unmet need
  - ◊ ATRN-119: ATR Inhibitor
  - ◊ ATRN-1051: WEE1 Inhibitor
  - ◊ Undisclosed DDR Inhibitor
- Synthetic lethality assets potentially differentiated from competitors
- Innovative platform technologies

One Critical Pathway, Multiple Targets



Capital-efficient model and near-term clinical milestones drive compelling investment opportunity

Robust DDR Development Pipeline

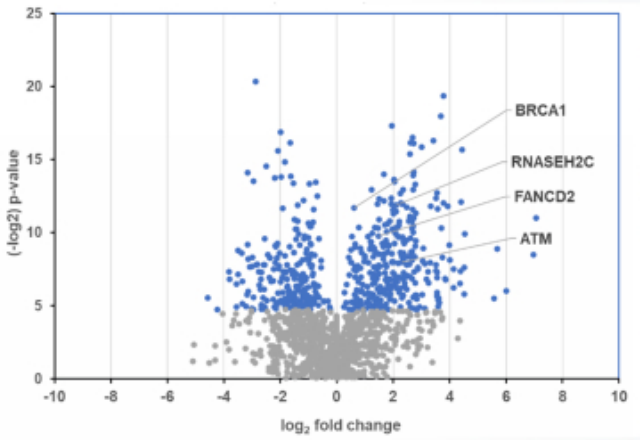
MOLECULE	TARGET	INDICATION	BIOMARKER	Preclinical	IND-Enabling	Phase 1	Anticipated Milestones
ATRN-119	ATR	Advanced solid tumors	Defined biomarkers	monotherapy			Q1 2024: Phase 1 tolerability, PK
		Ovarian, breast, prostate	BRCA1/2 + others	combination with PARPi			Q4 2023 / Q1 2024: Ph1 initiation
ATRN-1051	WEE1	Advanced solid tumors	CCNE amplification + others				End of 2023: IND submission
ATRN-354[1]	ATR	Advanced solid tumors	Defined biomarkers				Second half of 2024: IND submission
APRE-DDRi	DDR Target	Advanced solid tumors	Defined biomarkers				Mid-2024: Development candidate

[1] ATRN-354 timeline and anticipated milestones subject to data from ATRN-119 clinical trial

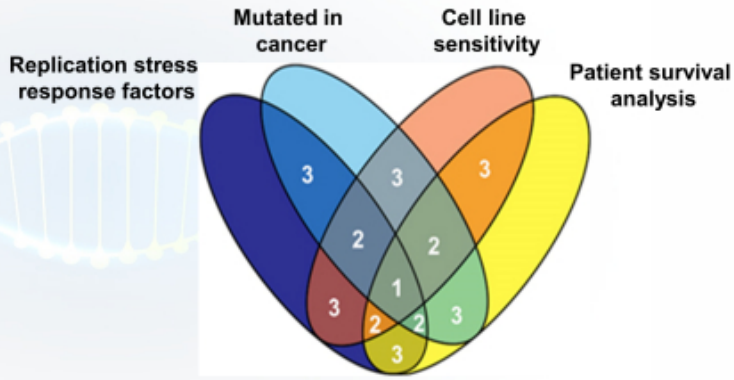
Repli-Biom Proprietary Platform and Combination Approaches

An Integrated Platform for Discovery of Novel SL Targets and Biomarkers

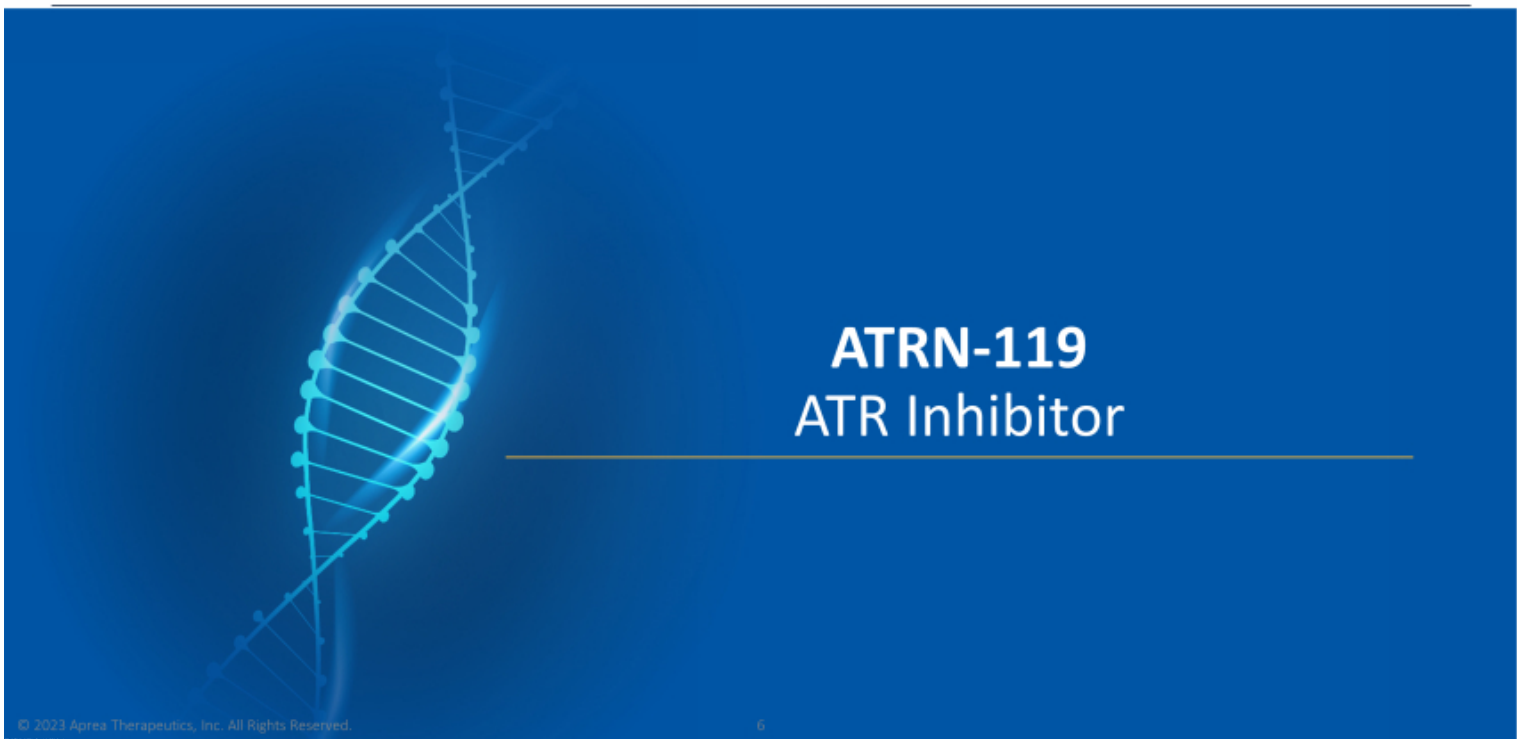
Drug response factor identification



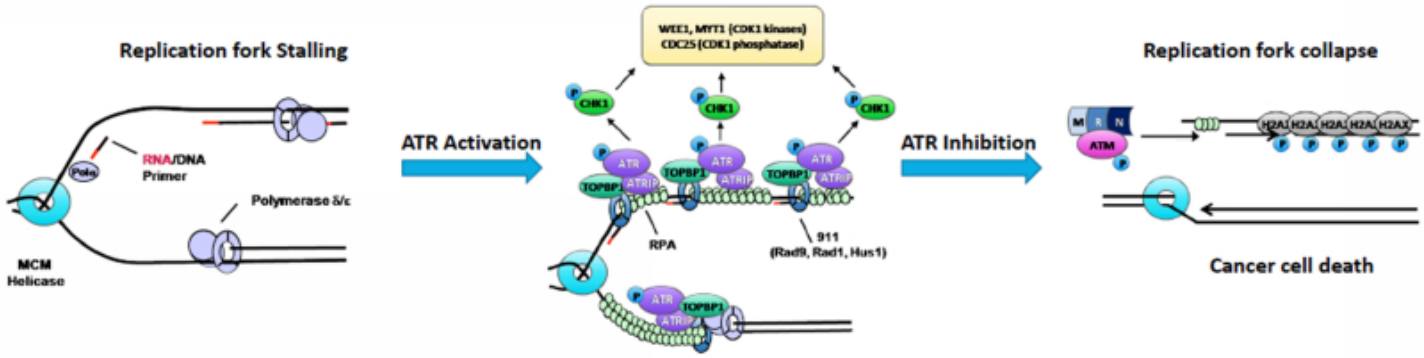
Biomarker prioritization



- Repli-Biom platform is designed to identify factors that respond to drug treatment at the mechanistic site of drug action, the replication fork
- Repli-Biom shows potential to identify candidate biomarkers of therapeutic benefit as well novel SL targets
- Combination SL may permit lower doses and decreased rates of acquired resistance, potentially leading to durable responses in cancers with specific mutations



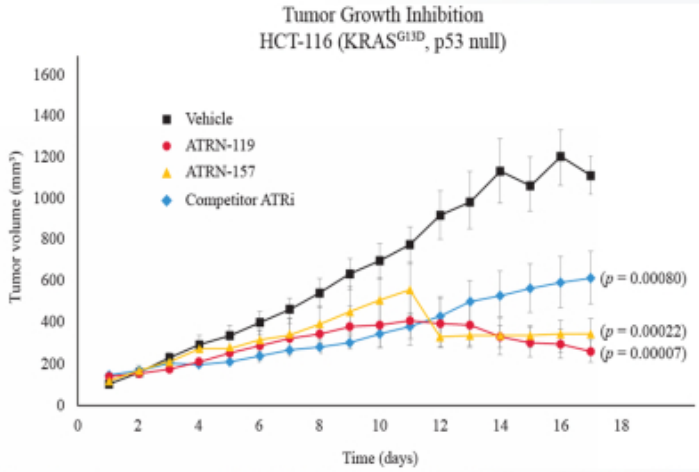
ATR is the Master Regulator of DDR

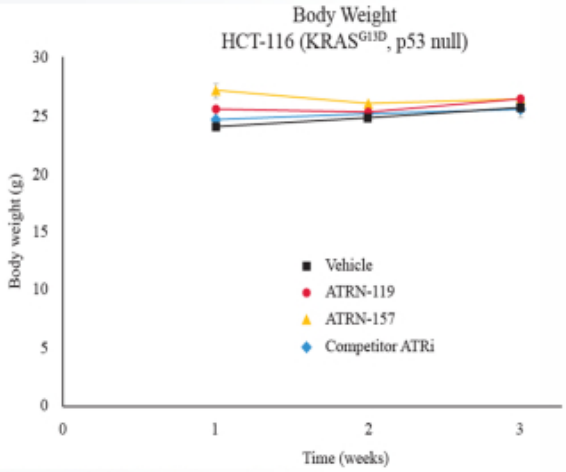


- Defects in DDR lead to compromised genomic instability and stalling of the replication fork
- ATR is activated by replication stress
- ATR Inhibition leads to replication fork collapse and cancer cell death
  - ◊ Cancer cells with dysfunctional and/or dysregulated DDR are particularly sensitive to ATR inhibition
  - ◊ Examples: Oncogenic RAS mutations, MYC overexpression, ATM mutations, BRCA1, BRCA2

ATRN-119 Preclinical Profile

- Nanomolar potency *in vitro* across a broad spectrum of cancer cell lines
- Based on pre-clinical studies, strong tumor control observed *in vivo*, including in challenging genetic backgrounds



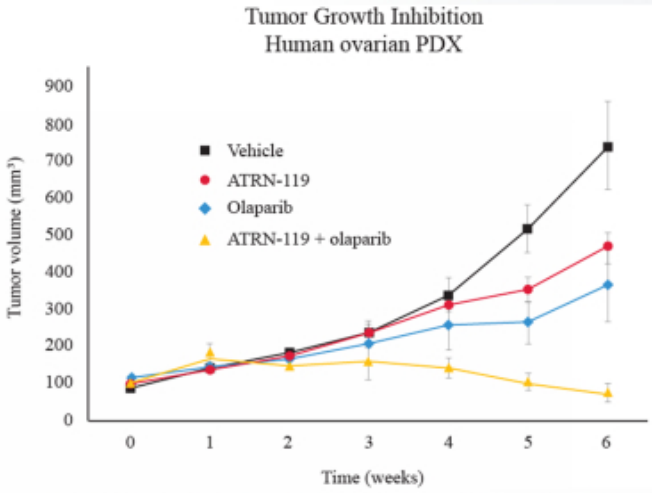


N=4 female mice per group, ATRN-119 - 100 mg/kg/day P.O, Competitor ATRi - 25 mg/kg/day P.O, ATRN-157 - 20 mg/kg/day SQ.

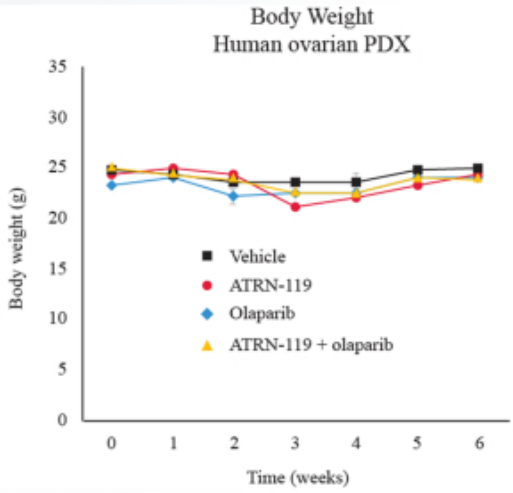
ATRN-157 is an active metabolite identified in dogs receiving ATRN-119 P.O.. In vitro metabolism studies in dog and human hepatocytes and liver microsomes indicated formation of ATRN-157 in both species. Potency and selectivity of ATRN-157 was comparable to ATRN-119.

ATRN-119 + Olaparib: Regression of BRCA2-Deficient Ovarian (HGSOC) Tumors

ATRN-119 + Olaparib Inhibits Ovarian Tumor Growth Over Time



ATRN-119 + Olaparib Shows Negligible Weight Loss Over Time



N=6-8 mice per group, ATRN-119 - 90 mg/kg P.O BID, Olaparib - 50 mg/kg/day P.O, ATRN-119+Olaparib at the same doses and schedules

These data are potentially supportive of future potential clinical trials to evaluate the combination of a PARP inhibitor and ATRN-119

ATRN-119 is Potentially Differentiated from Other ATR Inhibitors

- ATRN-119 has shown the potential to be highly potent with high selectivity to limit off-target toxicity

	On-Target Cellular IC_{50} (nM)	Fold Difference in IC_{50} for Off-Target PIKK Inhibition		
	ATR	ATM	DNA-PK	mTOR
Aprea: ATRN-119 [1]	4	> 600x	> 2000x	> 2000x
AstraZeneca: AZD-6738 [2]	74	> 400x	> 400x	70 – 310x
Bayer: BAY 1895344 [3]	36	39x	9x	61x
Repare/Roche: RP3500 [4]	0.33	> 20000x	> 20000x	30x

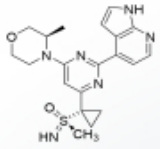
Summary:

- ATRN-119 is highly potent and selective to potentially limit off-target toxicity
- In pre-clinical studies, ATRN-119 has shown potential to have favorable tolerability profile

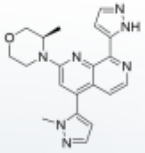
Note: Head-to-head studies with ATRN-119 have not been conducted
(1) Atrin data reported for HCT116 - Bcl/XL cell line;
(2) Foote et al (2018), J Med Chem;
(3) Lücking et al (2020), J Med Chem;
(4) Roulston et al (2022) Mol Cancer Ther

ATR Landscape Drives Potential Competitive Advantage for ATRN-119

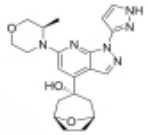
Current ATRs Structurally Similar in Core, Backbone, and Toxicity Profile



AZD-6738



BAY1895344



RP-3500

CAMOSERTIB

Parameter	AstraZeneca AZD6738 [1][2]	Bayer BAY1895344 [3]	Repare / Roche[4] RP-3500 [5]
Route Of Administration	Oral	Oral	Oral
Clinical Studies Chosen (MTD/RP2D), Dose Schedule	160mg BID, 2-weeks-on, 2-weeks-off, or: Continuous dosing [1]	40mg BID, 3-days-on/4-days-off	160mg QD, 3-days-on/4-days-off
Main Grade ≥3 Hematological toxicities reported at Chosen Dose Schedule (MTD/RP2D), in clinical studies	Patriot 1, Escalation Phase, 160mg, BID [2]: Anemia (1/6, 17%) Patriot 2, Expansion Phase [1]: Fatigue, anemia, nausea & thrombocytopenia (not differentiated) [1]: (4/6, 67%) with continuous dosing (3/15, 20%) with 2-week-on, 2-week-off	Anemia (2/2, 100%) Neutropenia (1/2, 50%)	Anemia (23/95, 24%) Neutrophil count decreased (10/95, 11%) Platelet count decreased (5/95, 5%)

Note: Head-to-head studies with ATRN-119 have not been conducted

(1) Phase I study of ATR inhibitor, AZD6738, as monotherapy in advanced solid tumors (PATRIOT part A, B), Dillon et al, Volume 30, October 2019, Pages v165-v166

(2) Poster CT084: A Phase I dose-escalation study of ATR inhibitor monotherapy with AZD6738 in advanced solid tumors (PATRIOT Part A), AACR 2017

(3) First-in-Human Trial of the Oral Ataxia Telangiectasia and RAD3-Related (ATR) Inhibitor BAY 1895344 in Patients with Advanced Solid Tumors, Yap et al, Cancer Discov 2021;11:80-91 and 2019 ASCO Poster, De-Bono et al.

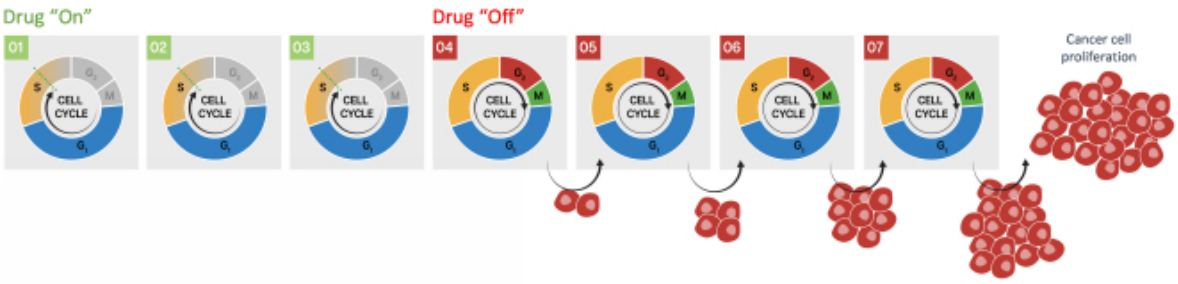
(4) Repare announced a worldwide license and collaboration agreement with Roche on June 1, 2022

(5) Preliminary Phase 1 Data From Ongoing First-in-Human Phase 1/2 TRESR Study of RP-3500, AACR 2022

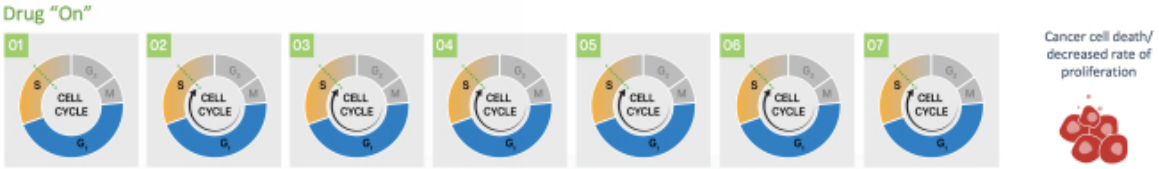
ATRN-119 Daily dosing Is Desirable

Lack of daily dosing may contribute to formation of resistance

Intermittent dosing



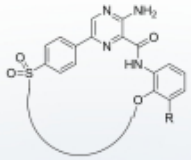
Continuous dosing



Improved tolerability of an ATR inhibitor could potentially provide opportunities to expand the therapeutic window and administer higher doses on a continuous daily dosing schedule to potentially improve response rates and response duration

ATRN-119: Potential Best-in-Class Oral ATR Inhibitor

With Structurally Differentiated Core, Backbone, and Toxicity Profile



Parameter	ATRN-119 (1)
Route Of Administration	Oral
Clinical Studies Chosen (MTD/RP2D), Dose Schedule	continuous once-daily dosing (dose TBD in Phase 1) (1)
Hematological toxicities in preclinical studies	**Pre-Clinical, Toxicology Studies:** • In 28-day GLP tox study in dogs, hematological changes were of small magnitude with complete recovery • In a head-to-head comparative tolerability study, ATRN-119 demonstrated significantly less toxicity than another oral ATRi that is currently in clinical development (2)

ATRN-119 potential for reduced toxicity could make it a preferred ATR inhibitor as a single agent, as well as a candidate for combination with standard-of-care therapies.

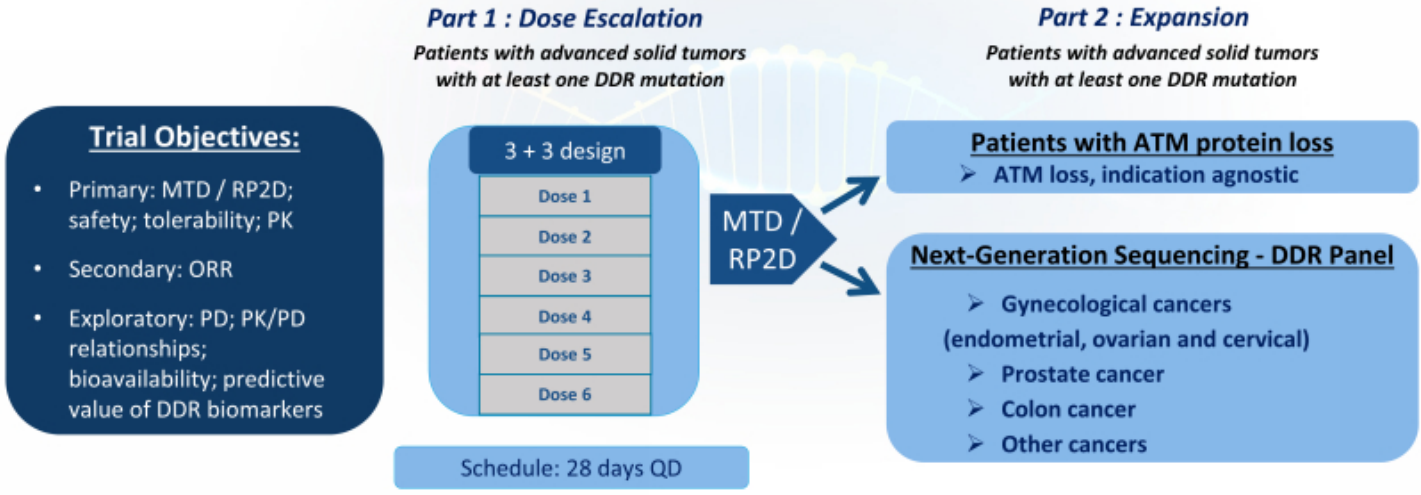
Note: ATRN-119 has not yet been tested clinically

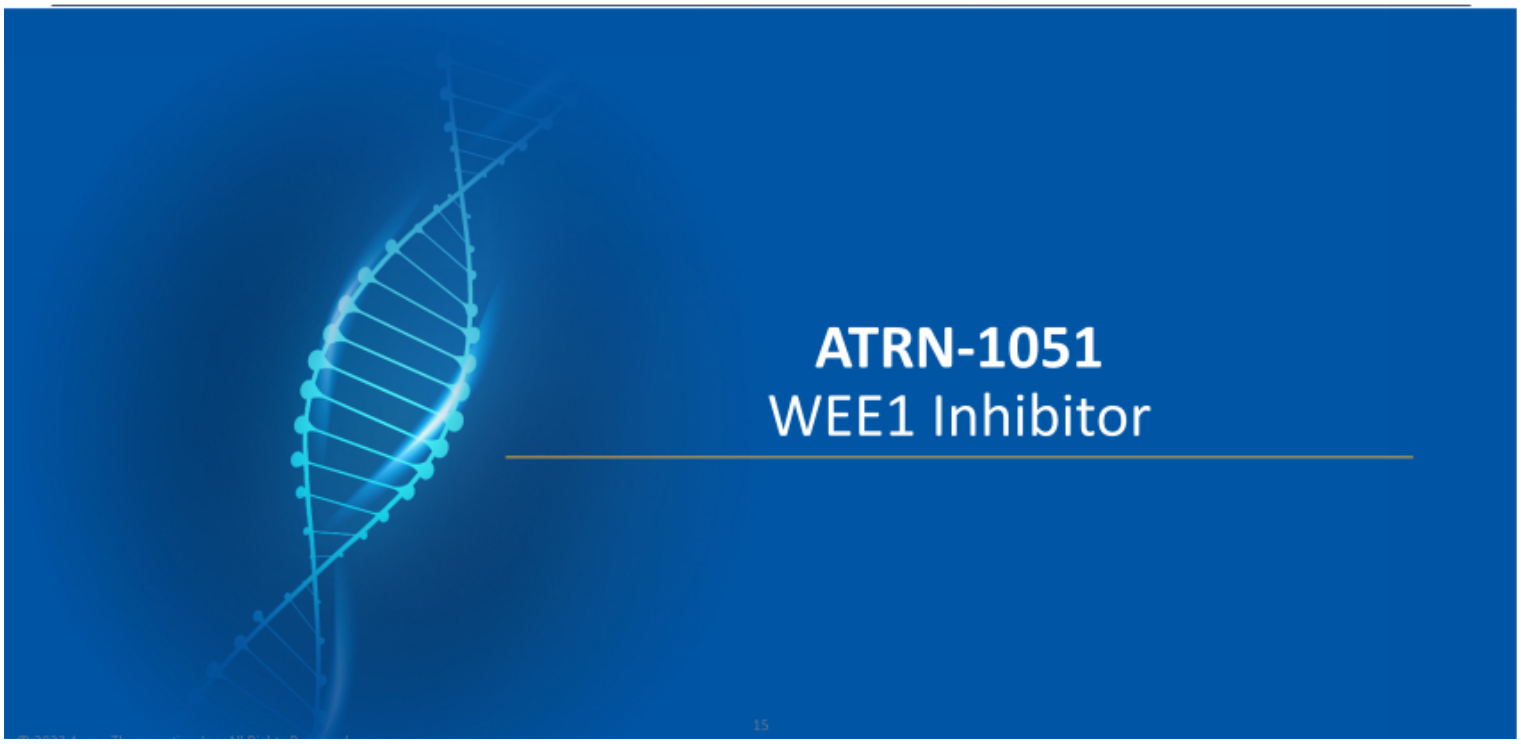
(1) ATRN-119, Phase 1/2a Clinical Study Protocol

(2) Internal pre-clinical head-to-head tolerability study in male beagle dogs. ATRN-119 - 20 mg/kg/day for 7 days, followed by 40 mg/kg/day for 7 days and finally 50 mg/kg/day for 7 days, all P.O. Competitor ATRi- administered at a clinically equivalent dose range during 21 days, P.O. By day 4 of dosing, the dog receiving the competitor ATRi exhibited severe reduction in multiple blood cell lineages including reticulocytes. Continued dosing of competitor ATRi for three weeks resulted in significant reduction of white blood cells, red blood cells and hemoglobin levels, and was accompanied by severe body weight loss (-15%). For the dog receiving ATRN-119, reduced levels of reticulocytes and neutrophils were noted with prolonged treatment but remained within normal ranges and body weight changes were negligible (-2% to +4%).

ATRN-119 Phase 1/2a Clinical Trial

- NGS testing used to determine presence of DDR mutations/LOF
- Patient selection is critical - Subjects may be enrolled with advanced solid tumor with at least one DDR mutation
- Biomarkers with high likelihood for increased sensitivity to our lead drug candidate have been identified

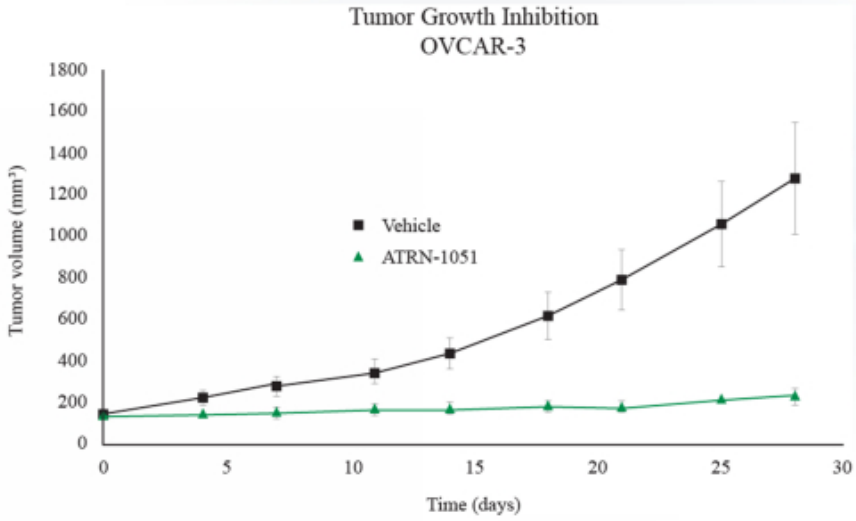



ATRN-1051
WEE1 Inhibitor
15

ATRN-1051 Has Demonstrated Potentially Compelling Anti-tumor Activity

IND filing targeted by the end of 2023

- Nanomolar anti-proliferative potency in vitro against multiple cancer cell lines
- Potent anti-tumor activity observed in vivo in an ovarian cancer xenograft model (CCNE1-amplified cell line)

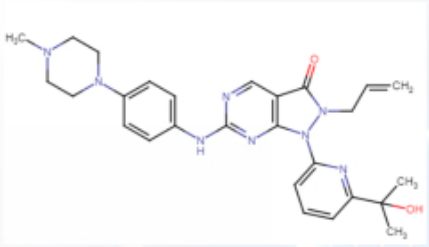


N=7 mice per group, ATRN-1051, exploratory formulation - 30 mg/kg/day

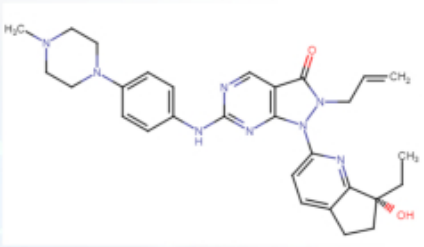
Pre-clinical studies with ATRN-1051

ATRN-1051 is Potentially Differentiated from Other WEE1 Inhibitors

ATRN-1051 shows potential to be potent and structurally differentiated, with high selectivity to limit off-target toxicity



AZD-1775[1]



ZN-c3

	On-Target IC_{50} (nM)	Off-Target Inhibition at 1 μM (%)		
	WEE1	PLK1	PLK2	PLK3
Aprea: ATRN-1051	2.2	17	33	12
Zentalis: ZN-c3 [1]	3.8	79	96	92
AstraZeneca: AZD-1775 [1][2]	3.9	70	101	91

Note: Head-to-head studies have not been conducted

(1) Huang et al, (2021) J Med Chem

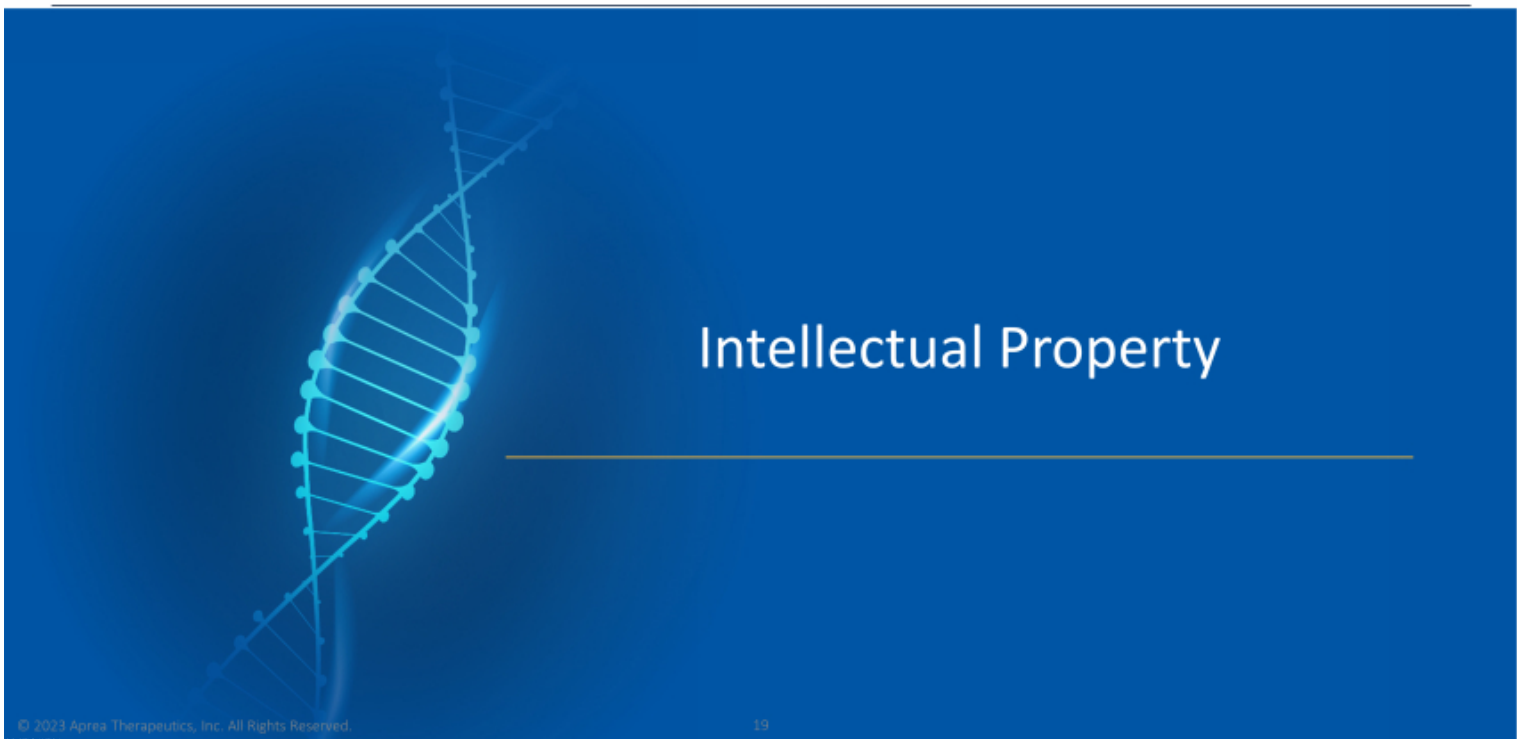
(2) AstraZeneca announced in July 2022 the discontinuation of development of AZD-1775

ATRN-1051 Preclinical Data Highlight Potentially Favorable PK Properties

Based on pre-clinical studies, ATRN-1051 shows potentially favorable drug exposure:

	ATRN-1051 (1)	Zentalis ZN-c3 (2)			AstraZeneca AZD-1775 (2)		
Dose (mg/kg/d)	10	20	40	80	20	40	80
C_{max}, ng/mL	1460	1167	1997	5100	635	2460	4703
T_{max}, hr	2.7	1	1	1	1	1	1
AUC_{0-24}, ng*hr/mL	16739	4863	17088	39722	1494	6313	13408

Note: Head-to-head studies have not been conducted
(1) Data from an exploratory formulation of ATRN-1051 administered to fasted Balb/c mice
(2) Data from study in A-427 NSCLC xenograft model as reported in Zentalis Corporate Overview, March 2022



Intellectual Property Portfolio Of DDR Inhibitors

Four issued US patents protecting lead molecule and analogs

- Family 1: Ataxia Telengiectasia And Rad3-Related (ATR) Protein Kinase Inhibitors
  - Macrocyclic inhibitors of ATR & methods of using them to treat various cancers, filed on Oct. 13th, 2015
  - Patents granted in *AU, CA, CN, EP, IL, JP, MX*. National phase examinations ongoing in BR, IN, KR
  - 1.1: *Issued on May 30, 2017 as U.S. Patent 9,663,535*
  - 1.2: *Issued on May 29, 2018 as U.S. Patent 9,981,989*
  - 1.3: *Issued on Feb. 5, 2019 as U.S. Patent 10,196,405*

- Family 2: ATR inhibitors & methods of use
  - Carboxylic acid-containing macrocyclic ATR inhibitors, and prodrugs; methods of using these inhibitors to treat various cancers; filed on Apr. 12th, 2017
  - *Issued on May 28, 2019 as U.S. Patent 10,301,324*

- Family 3: ATR inhibitor Pharmaceutical Composition and Methods:
  - Provisional application filed on Apr. 14th, 2022
  - Pharmaceutical formulation and composition of our lead molecule in the clinic

- Family 4: WEE1 inhibitor Pharmaceutical Compositions and Methods:
  - International Application filed on Jun. 3rd, 2022
  - Composition of our lead WEE1 inhibitor compounds

Corporate Highlights & Milestones

Robust DDR Development Milestones

MOLECULE	TARGET	INDICATION	BIOMARKER	Preclinical	IND-Enabling	Phase 1	Anticipated Milestones
ATRN-119	ATR	Advanced solid tumors	Defined biomarkers	monotherapy			Q1 2024: Phase 1 tolerability, PK
		Ovarian, breast, prostate	BRCA1/2 + others	combination with PARPi			Q4 2023 / Q1 2024: Ph1 initiation
ATRN-1051	WEE1	Advanced solid tumors	CCNE amplification + others				End of 2023: IND submission
ATRN-354[1]	ATR	Advanced solid tumors	Defined biomarkers				Second half of 2024: IND submission
APRE-DDRi	DDR Target	Advanced solid tumors	Defined biomarkers				Mid-2024: Development candidate

[1] ATRN-354 timeline and anticipated milestones subject to data from ATRN-119 clinical trial

Corporate Summary and Recent Highlights

Robust synthetic lethality (SL) portfolio built in-house from foundational, proprietary DNA damage repair (DDR) platform

- Addressing critical unmet therapeutic needs for patients with genetically defined cancers.

- ATR Program: ATRN-119
  - Lead clinical candidate ATRN-119 is a potential best-in-class oral ATR inhibitor for the treatment of advanced solid tumors harboring defined mutations in DDR pathways. Currently enrolling patients into Phase 1/2a. ATRN-119 is structurally differentiated and has shown in pre-clinical studies to be potentially highly selective and exhibit a favorable tolerability profile.
- WEE1 Program: ATRN-1051
  - ATRN-1051 is a highly potent WEE1 inhibitor currently in IND-enabling studies. Preclinical findings show potentially favorable drug selectivity and exposure.
- Pipeline
  - Additional undisclosed synthetic lethality assets show promising potential in novel oncology targets.

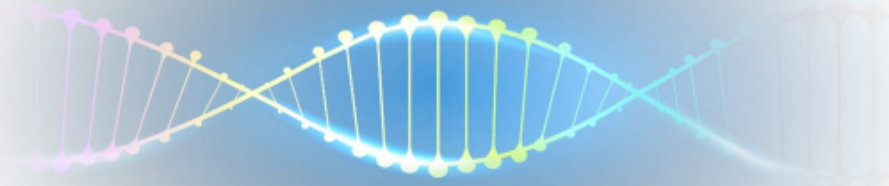
Aprea Therapeutics (NASDAQ: APRE)

Financial Summary & Capitalization

- Cash & Equivalents of $28.8 million as of December 31, 2022
- Closed $5.5M (gross) public offering February 2023
- Obtained non-dilutive funding via research grant from National Cancer Institute (NCI)

Securities	Common Equivalents as of March 30, 2023
Preferred Stock (as converted)	28,112
Common Stock	3,731,570
Options	552,511
Restricted Stock Units	30,227
Fully Diluted Equivalents	4,342,420

aprea therapeutics



Precision Oncology through Synthetic Lethality

March 2023