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 26, 2024
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 26, 2024, Aprea Therapeutics, Inc. (the "Company") issued a press release announcing its financial results for the three and twelve months ended December 31, 2023, 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 8.01 Other Events.

On March 26, 2024, 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 26, 2024.
99.2	Corporate Presentation (March 2024).
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 26, 2024

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

Aprea Therapeutics Reports Fourth Quarter and Full Year 2023 Financial Results and Provides a Business Update

First-in-class macrocyclic ATR inhibitor, ATRN-119, on track to complete dose escalation and potentially generate human efficacy data in H2 2024

U.S. FDA cleared IND for APR-1051, a highly selective and potentially best-in-class oral WEE1 inhibitor; Company plans to initiate Phase 1 ACESOT-1051 clinical trial in H1 2024.

$21.6 million in cash and cash equivalents as of December 31, 2023

Private placement financing in March 2024 raised upfront gross proceeds of approximately $16 million

DOYLESTOWN, PA, Mar. 26, 2024 (GLOBE NEWSWIRE) – Aprea Therapeutics, Inc. (Nasdaq: APRE) ("Aprea", or the "Company"), a clinical-stage biopharmaceutical company focused on precision oncology through synthetic lethality, today reported financial results for the fourth quarter and full year ended December 31, 2023, and provided a business update.

"Aprea had a very productive 2023 with significant progress across our diversified pipeline of synthetic lethality-based cancer therapeutics. We are pleased to continue this positive momentum in 2024 and focus on the execution on our programs towards successfully delivering potentially safer and more effective therapies for cancer patients," said Oren Gilad, Ph.D., President and Chief Executive Officer of Aprea. "We continue to enroll and treat patients in the ongoing Phase 1/2a study of our novel macrocyclic ATR inhibitor, ATRN-119. ATRN-119 appears to be well tolerated with a manageable toxicity profile. Dose escalation will proceed throughout 2024 with potential for human efficacy data in the second half of the year. We are preparing to enter the clinic with our next generation inhibitor of WEE1 kinase, APR-1051, having received clearance from the FDA on our IND. Based on the unique characteristics of APR-1051 we believe it will be best in class."

Dr. Gilad continued "the closing of our recent private placement financing provides us with the capital to fund both of these lead programs through meaningful clinical milestones. I would like to thank our dedicated team, our academic collaborators, as well as existing and new investors who have supported our recent advancements. Our mission is to be a global leader in synthetic lethality and we see a great opportunity to help cancer patients in need and create value for our shareholders."

Key Business Updates and Potential Upcoming Key Milestones

ATR inhibitor, ATRN-119, on track to complete monotherapy dose escalation end of the year; initial efficacy data expected in second half of 2024

- ATRN-119 is a potent and highly selective first-in-class macrocyclic ATR inhibitor, designed to be used in patients with mutations in DDR-related genes. Cancers with mutation in DDR-related genes represent a high unmet medical need. Patients with DDR-related gene mutations have poor prognosis and, currently, have no effective therapies.
- In January 2023, enrollment commenced in an open-label Phase 1/2a clinical trial of ATRN-119 (study AR-276-010) as monotherapy in patients with advanced solid tumors having at least one mutation in a defined panel of DDR-related genes. In the ongoing monotherapy dose escalation phase (Part 1) of the trial, the primary endpoint is evaluating the tolerability and pharmacokinetics of continuous daily oral dosing of ATRN-119 using a 3+3 trial design in up to approximately 30 patients. A secondary endpoint is evaluating potential initial efficacy.
- An update from Part 1 of the trial was featured in a poster presentation at the AACR-NCI-EORTC International Conference in October 2023.
- As of January 2, 2024, 12 patients were enrolled to the first four cohorts of the Phase 1 escalation stage (50mg/day, 100mg/daily, 200mg/daily and 350mg/daily). ATRN-119 was found to be safe and well tolerated in all four cohorts, with no related adverse effects > grade 2. The most recent efficacy analysis conducted at that date shows that two patients achieved stable disease – one each in the 50 mg and 200 mg cohorts. Both these patients' tumors have mutations that have been predicted to confer sensitivity to ATR inhibition.
- As of March 26, 2024 four clinical sites have been activated in the US. At completion of Part 1 of the study, the company anticipates identification of a recommended Phase 2 dose (RP2D) that will be used in a Phase 2a cohort expansion (Part 2) to test the tolerability and potential efficacy of ATRN-119 monotherapy in approximately 30 additional patients. The Phase 1 dose

escalation is expected to be completed in 4Q 2024, and RP2D is to be determined in 1Q 2025. Enrollment in the Phase 2a cohort is expected to begin in 1Q 2025 with additional efficacy data expected in 3Q 2025.

- A more comprehensive dataset from Part 1 of the study has been accepted for presentation at the American Association of Cancer Research (AACR) annual meeting in April 2024.
- For more information, please refer to clinicaltrials.gov NCT04905914.

Oral WEE1 inhibitor, APR-1051, expected to enter Phase 1 clinical trial in the first half of 2024

- APR-1051 is a potent and selective small molecule that has the potential to avoid off target toxicity and achieve greater clinical activity than other WEE1 programs currently in development. Aprea is advancing APR-1051 as monotherapy in ovarian cancer with Cyclin E over expression. Cancers over expressing Cyclin E represent a high unmet medical need. Patients with Cyclin E over expression have poor prognosis and, currently, have no effective therapies.
- In March 2024, the U.S. FDA cleared the Investigational New Drug (IND) application (IND 169359) for APR-1051. Clearance of this IND will allow Aprea to initiate the Phase 1 ACESOT-1051 (**A** Multi-**C**enter **E**valuation of WEE1 Inhibitor in Patients with Advanced **S**olid **T**umors, APR-1051) trial. This dose escalation trial will evaluate the safety, tolerability, and preliminary efficacy of APR-1051. Enrollment of the first patient is expected in H1 2024 with an update expected in the Q4 2024.
- Preclinical data on APR-1051 were presented in a poster at the AACR-NCI-EORTC International Conference in October 2023. The data highlighted the selectivity of APR-1051 with low off-target activity against PLK1, PLK2 and PLK3, a family of kinases that promote M phase entry, a critical phase in the cell cycle. APR-1051 showed potentially favorable PK properties and appears to cause lower inhibition of hERG, a potential indication of low cardiotoxicity. At doses and scheduling that suppress tumor growth, APR-1051 causes little anemia. The selectivity of APR-1051 may solve a long-standing problem with other WEE1 inhibitors. Recent studies indicate that PLK1 off-targeting partially counters the intracellular effects of WEE1 inhibition and could potentially contribute to the myelosuppression observed with other WEE1 inhibitors.

Pipeline – lead candidate for a third synthetic lethality program to be selected in 2024

- Aprea's research and development team has identified a new target in synthetic lethality. Our discovery team is developing a series of molecules that are selective and potent against it.
- A lead molecule is expected to be declared in 2Q 2024.
- This program may provide clinically meaningful differences for cancer patients that currently have limited therapies.

KOL Event

- Hosted a Key Opinion Leader (KOL) event on October 31, 2023, highlighting the Company's portfolio of small molecules focused on Synthetic Lethality (SL) by targeting the DNA Damage Response (DDR) Pathways. The event featured Key Opinion Leaders Dr. Fiona Simpkins, Professor in the Division of Gynecology Oncology and Department of OB-GYN at the University of Pennsylvania, Dr. Timothy Yap, medical oncology physician-scientist and Professor at the University of Texas MD Anderson Cancer Center, Dr. Eric Brown, a consultant to Aprea and a Professor at the University of Pennsylvania and a member of the Abramson Family Cancer Research Institute, and Aprea's Dr. Nadeem Mirza, Senior Medical Advisor. The speakers, along with the management team, provided an overview of the Company's lead ATR inhibitor candidate, ATRN-119, and its WEE1 inhibitor candidate, APR-1051, and highlighted the addressable unmet clinical need and potential combination therapies using these programs. A replay of the event can be access on the Aprea corporate website here.

Select Financial Results for the Fourth Quarter ended December 31, 2023

- As of December 31, 2023, Aprea reported cash and cash equivalents of $21.6 million.
- For the quarter ended December 31, 2023, the Company reported an operating loss of $3.7 million, compared to an operating loss of $2.7 million in the fourth quarter of 2022.
- Research and Development (R&D) expenses were $2.0 million for the quarter ended December 31, 2023, compared to $0.5 million for the fourth quarter of 2022. The increase in R&D expense was primarily related to the Phase 1/2a clinical trial evaluating ATRN-119 which enrolled its first subject in Q1 2023 and IND enabling studies for APR-1051, the Company's small molecule WEE1 inhibitor.
- General and Administrative (G&A) expenses were $1.6 million for the quarter ended December 31, 2023, compared to $2.1 million for the comparable period in 2022. The decrease in G&A expenses was primarily due to a decrease in personnel costs and insurance premiums.
- The Company reported a net loss of $3.4 million ($0.92 per basic share) on approximately 3.7 million weighted-average common shares outstanding for the quarter ended December 31, 2023, compared to a net loss of $2.4 million ($0.92 per basic share) on approximately 2.6 million weighted average common shares outstanding for the comparable period in 2022.

Select Financial Results for the Year ended December 31, 2023

- As of December 31, 2023, the Company reported cash and cash equivalents of $21.6 million compared to $28.8 million as of December 31, 2022. The Company believes its cash and cash equivalents as of December 31, 2023, combined with the upfront gross proceeds of approximately $16.0 million received from the Company's private placement of common stock and warrants in March 2024, before deducting placement agent fees and offering costs of approximately $1.4 million, will be sufficient to meet its currently projected operating expenses and capital expenditure requirements into the third quarter of 2025.
- For the year ended December 31, 2023, the Company reported an operating loss of $15.5 million, compared to an operating loss of $113.4 million, which include $76.0 million for acquired in-process research and development, for the year ended December 31, 2022.
- Research and Development (R&D) expenses were $7.6 million for the year ended December 31, 2023, compared to $16.4 million for the year ended December 31, 2022. The decrease in R&D expense was primarily related to the close out of our clinical trials of eprenetapopt and APR-246, 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 2022 and personnel costs primarily related to the close out of our research facility in Sweden during 2022.
- General and Administrative (G&A) expenses were $8.4 million for the year ended December 31, 2023, compared to $21.0 million for the year ended December 31, 2022. The decrease in G&A expenses was primarily due to a decrease 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 2022 and insurance premiums.
- The Company reported a net loss of $14.3 million ($3.95 per basic share) on approximately 3.6 million weighted-average common shares outstanding for the year ended December 31, 2023, compared to a net loss of $112.7 million ($67.99 per basic share) on approximately 1.7 million weighted average common shares outstanding for the comparable period in 2022.

About Aprea

Aprea Therapeutics, Inc. is a clinical-stage biopharmaceutical company headquartered in Doylestown, Pennsylvania, focused on precision oncology through synthetic lethality. The Company's lead program is ATRN-119, a clinical-stage small molecule ATR inhibitor in development for solid tumor indications. Aprea has completed all IND enabling studies for its oral, small molecule WEE1 inhibitor, APR-1051, and recently received FDA clearance of its IND. 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, including timing considerations 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, without limitation, risks related to the success, timing, and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates, including statements regarding the timing of initiation, pace of enrollment and completion of the trials (including our ability to fully fund our disclosed clinical trials, which assumes no material changes to our currently projected expenses), futility analyses, presentations at conferences and data reported in an abstract, and receipt of interim or preliminary results (including, without limitation, any preclinical results or data), which are not necessarily indicative of the final results of our ongoing clinical trials, our understanding of product candidates mechanisms of action and interpretation of preclinical and early clinical results from its clinical development programs, and the other risks, uncertainties, and other factors described under "Risk Factors," "Management's Discussion

and Analysis of Financial Condition and Results of Operations" and elsewhere in the documents we file 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.

Investor Contact:

Mike Moyer
LifeSci Advisors
mmoyer@lifesciadvisors.com

Aprea Therapeutics, Inc.

Consolidated Statements of Operations and Comprehensive Loss

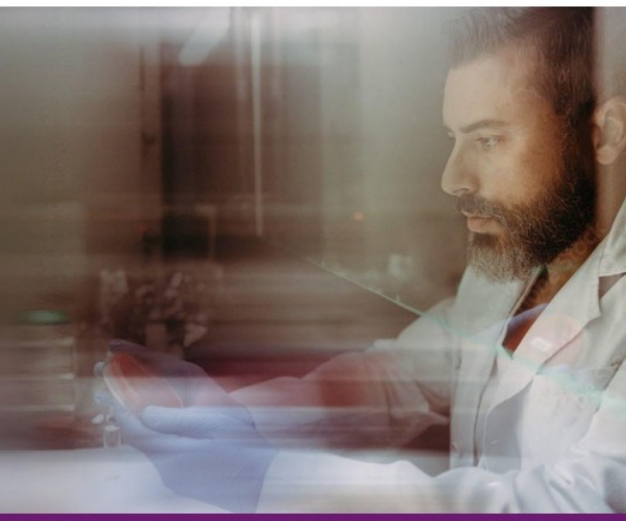
	Three Months Ended December 31,		Year Ended December 31,	
	2023	2022	2023	2022
	(Unaudited)			
Grant revenue	$ 14,075	$ —	$ 583,231	$ —
Operating expenses:				
Research and development	2,045,689	531,406	7,627,491	16,402,273
General and administrative	1,643,315	2,120,222	8,427,703	20,969,771
Acquired in-process research and development	—	—	—	76,020,184
Total operating expenses	3,689,004	2,651,628	16,055,194	113,392,228
Loss from operations	(3,674,929)	(2,651,628)	(15,471,963)	(113,392,228)
Other income:				
Interest income, net	310,287	243,082	1,224,133	448,667
Foreign currency gain (loss)	(78,612)	(33,596)	(38,926)	281,534
Total other income	231,675	209,486	1,185,207	730,201
Net loss	$ (3,443,254)	$ (2,442,142)	$ (14,286,756)	$ (112,662,027)
Other comprehensive gain (loss):				
Foreign currency translation	24,601	(382,763)	12,135	(264,452)
Total comprehensive loss	(3,418,653)	(2,824,905)	(14,274,621)	(112,926,479)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.92)	$ (0.92)	$ (3.95)	$ (67.99)
Weighted-average common shares outstanding, basic and diluted	3,736,673	2,649,349	3,617,607	1,657,055

Aprea Therapeutics, Inc.
Consolidated Balance Sheets

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 21,606,820	$ 28,786,647
Prepaid expenses and other current assets	914,275	1,366,859
Total current assets	22,521,095	30,153,506
Property and equipment, net	88,362	2,321
Restricted cash	40,717	—
Total assets	$ 22,650,174	$ 30,155,827
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,670,369	$ 842,754
Accrued expenses	2,186,262	2,358,332
Deferred revenue	528,974	—
Total current liabilities	4,385,605	3,201,086
Total liabilities	4,385,605	3,201,086
Commitments and contingencies		
Series A convertible preferred stock, $0.001 par value, 40,000,000 shares authorized; 56,227 shares issued and outstanding at December 31, 2023 and December 31, 2022, respectively.	1,311,063	1,311,063
Stockholders' equity:		
Common stock, $0.001 par value, 400,000,000 shares authorized, 3,736,673 and 2,655,269 shares issued and outstanding at December 31, 2023 and December 31, 2022, respectively.	3,736	2,655
Additional paid-in capital	335,644,204	330,060,836
Accumulated other comprehensive loss	(10,611,273)	(10,623,408)
Accumulated deficit	(308,083,161)	(293,796,405)
Total stockholders' equity	16,953,506	25,643,678
Total liabilities and stockholders' equity	$ 22,650,174	$ 30,155,827

APREA THERAPEUTICS

Precision Oncology Through Synthetic Lethality



March 2024

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 amend 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 ca use terms such as “predicts,” “believes,” “potential,” “continue,” “anticipates,” “estimates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “likely,” “will,” “should other words that convey uncertainty of the future events or outcomes to identify these forward-looking statements. The forward-looking statements are based current beliefs and expectations of our management team that involve risks, potential changes in circumstances, assumptions, and uncertainties. Any or all of 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 uncertainties. These forward-looking statements are subject to risks and uncertainties including, without limitation, risks related to the success and timing of our clin 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 Quarterly Reports on Form 10-Q. Forward-looking statements regarding our product candidates are also subject to additional risks and uncertainties, including with limitation, with respect to: our dependence on additional financing to fund our operations and complete the development and commercialization of our proc 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; limited history and preclinical status of the assets we acquired from Atrin Pharmaceuticals Inc.; our business plan or the likelihood of the successful implementatio 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 research and development programs and collaborations and the interpretation of the results and findings of such programs and collaborations and whether such res 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 candida the timing of initiation, futility analyses, data presentation, reporting and publication and receipt of interim results (including, without limitation, any preclinical result data); any statements about our understanding of product candidates mechanisms of action and interpretation of preclinical and early clinical results from its clin development programs and any collaboration studies; and other factors, including legislative, regulatory, political and economic developments not within our cont For all these reasons, actual results and developments could be materially different from those expressed in or implied by our forward-looking statements. You 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 obligatio 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 Novel Synthetic Lethality Therapeutics

All programs address significant unmet medical need, are synergistic with other anticancer therapies, and potentially differentiated in safety and tolerability

ATR Inhibitor: ATRN-119

- First macrocyclic ATR inhibitor
- Highly selective with continuous daily dosing targeted
- Phase 1/2a – Ongoing Dose Escalation
  - Readout 1Q 2025
  - Solid tumor with DDR mutation
- Pre-clinical proof-of-principle
  - Anti-tumor activity at nanomolar concentration
  - Preserved hematologic safety profile

WEE1 Inhibitor: APR-1051

- Best in class, next generation
- Pre-clinical proof-of-principle
  - Highly potent and selective anti-tumor activity
  - Limited off target effect
  - Ovarian cancer with Cyclin E over expression (OVCAR-3)
  - Stable hematologic function
  - Favorable pharmacokinetics
- IND cleared March 2024
- Phase 1 planned for 1H 2024

DDR Inhibitor: Undisclosed

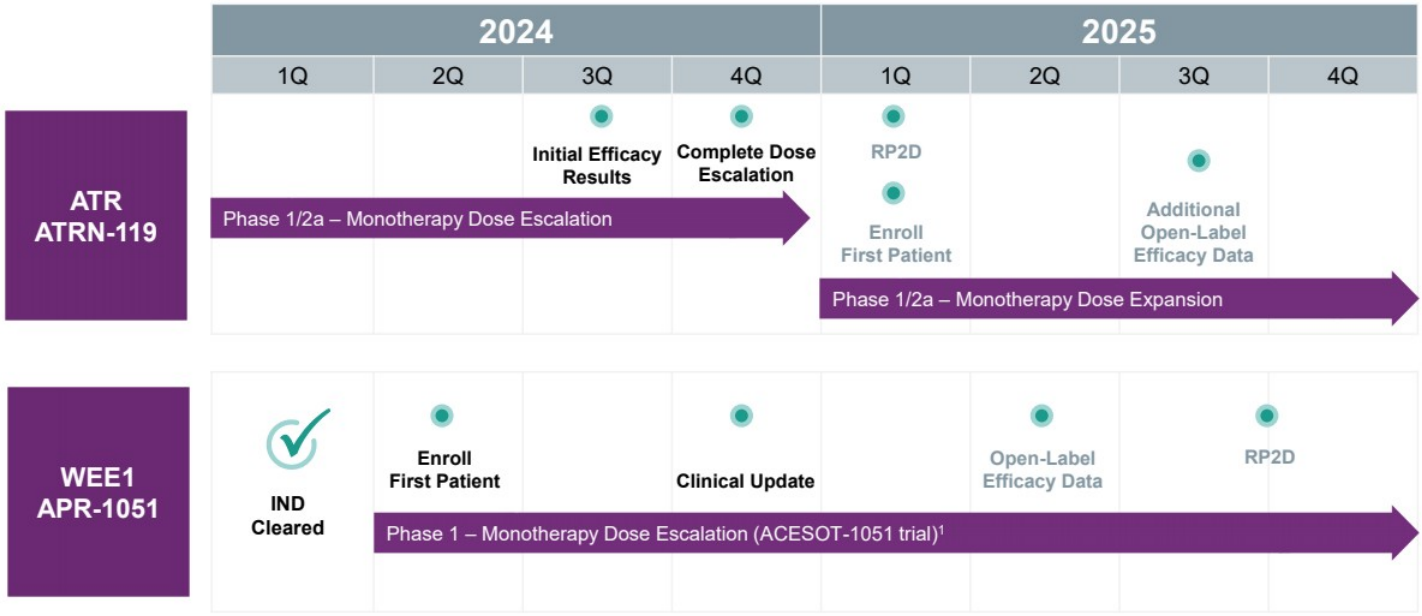
- Lead optimization
- Target identified from our RepliBior discovery platform

APREA THERAPEUTICS

ATR - Ataxia telangiectasia and Rad3-related
DDR – DNA Damage Response

Robust DDR Development Pipeline Milestones

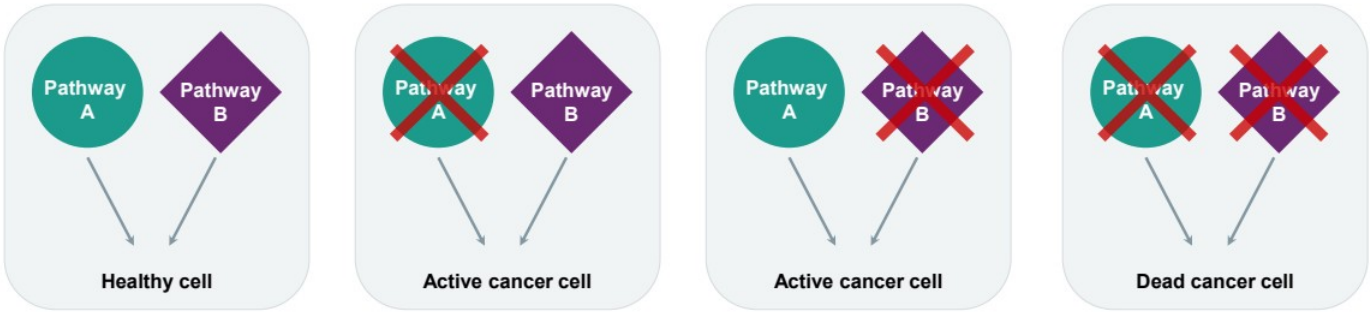
2024-2025 Anticipated Clinical Milestones



APREA THERAPEUTICS

1. **A** Multi-**C**enter **E**valuation of WEE1 Inhibitor in Patients with Advanced **So**lid **T**umors, APR-**1051**

Synthetic Lethality



- Cancer cell death only upon the loss of function of two codependent pathways
- Single pathway loss of function is inconsequential
- DNA Damage Response (DDR) allows cells to pause and self repair during replication (mitosis)
- Inhibition of DDR leads to mitotic catastrophe and cell death
- ATR and WEE1 inhibitors are integral to stopping DDR and are emerging targets for cancer cell death
- Builds on scientific innovation led by Aprea founder and key personnel[1]

APREA THERAPEUTICS

[1] Gilad et al, (2010) Cancer Res.

Leadership with Strong Drug Development and Commercial Expertise

Pioneers in Synthetic Lethality

Management

Oren Gilad, Ph.D. President and CEO	John Hamill Sr. Vice President and CFO	Nadeem Mirza, M.D., MPH Senior Medical Advisor	Ze'ev Weiss, CPA, B.Sc. Chief Business Advisor	Mike Carleton, Ph.D. Translational Medicine Advisor	Brian Wiley SVP, Corporate Strategy
ATRIN Pharmaceuticals Perelman School of Medicine	WINDTREE THERAPEUTICS Trevena SAVIENT PHARMACEUTICALS, INC. NephroGenex pharmanet	Salarius PHARMACEUTICALS TRIGR THERAPEUTICS Verastem Oncology abbvie sanofi	ATRIN Pharmaceuticals INTEC PHARMA pwc	inipharm MERCK Bristol Myers Squibb presage Mavu PHARMA	Boston BioConsulting Gloucester MILLENNIUM

Board of Directors

Richard Peters, M.D., Ph.D. Chairman of the Board	**Oren Gilad, Ph.D.** President and CEO	**Jean-Pierre Bizzari, M.D.** Director
Marc Duey Director	**Michael Grissinger** Director	**Gabriela Gruia, M.D.** Director
John Henneman Director	**Rifat Pamukcu, M.D.** Director	**Bernd R. Seizinger, M.D., Ph.D.** Director

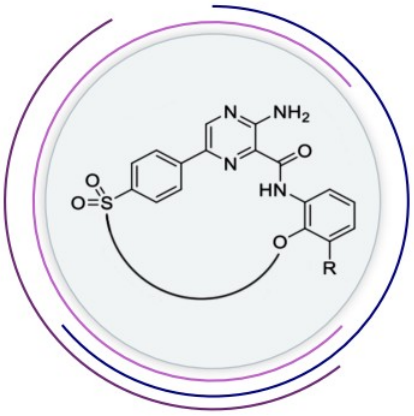
ATR Inhibitor: ATRN-119

Clinical Proof-of-Concept

APREA THERAPEUTICS

ATRN-119: First and Only Macrocyclic ATR Inhibitor[1]

Macrocycles: A Well-Evolved Approach for PIK-Related Kinase Inhibition (e.g., rapamycin and mTOR)[2]



Benefits of Unique Cyclic Skeleton Structure vs Competitors' First-Generation Acyclic Structure

Macrocycles restrict the number of conformations that can be formed, which can:

- Increase potency
- Increase selectivity

These effects can then promote:

- Increased tolerability by decreasing off-targeting
- Permit more efficacious dosing

[1] Based on company knowledge
[2] Brown, EJ et al, (1994) Nature
[3] Brown, EJ et al, (1995) Nature
[4] Brown, EJ and SL Schreiber, (1996) Cell

APREA THERAPEUTICS

AR-276-01: Aprea Phase 1/2a - Study Overview

A Phase 1/2a, Open-Label, Safety, Pharmacokinetic, and Preliminary Efficacy Study of Oral ATRN-119 in Patients with Advanced Solid Tumors

Sites:
4 US sites for dose escalation

- University of Pennsylvania
- Mary Crowley Cancer Research
- University Hospitals Cleveland Medical Center
- Yale Cancer Center

Patient enrollment:
60 patients in total

- Escalation phase: up to 30 patients
- Expansion phase: up to 30 patients

IMP: ATRN-119 is an oral ATR kinase inhibitor given daily

Patient Population:

Male or female subjects 12 years of age or older with solid tumors harboring specific DDR mutations per NGS

Part 1
Up to 30 patients
Dose escalation (8 dose levels*)
3+3 design

→

Part 2
Up to 30 patients
Dose expansion, after MTD / RP2D established

Primary objectives:

- Safety, MTD, RP2D
- Pharmacokinetics

Secondary objectives:

- Antitumor activity (RECIST/PCWG3)

Exploratory objectives:

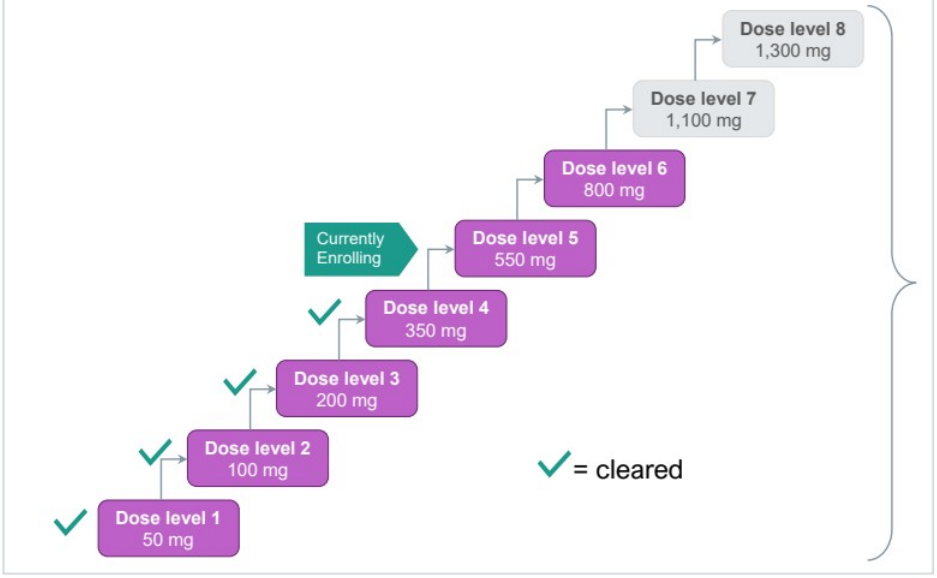
- Association between identified mutations and clinical outcomes

APREA THERAPEUTICS

*Planned protocol amendment adding cohorts 7 and 8

Aprea AR-276-01 Study

3+3 dose escalation with once-daily dosing (up to 30* patients)



MTD/RP2D

Dose expansion (up to 30 patients)

Potential indications
Colorectal
Prostate
Gastric
Endometrial

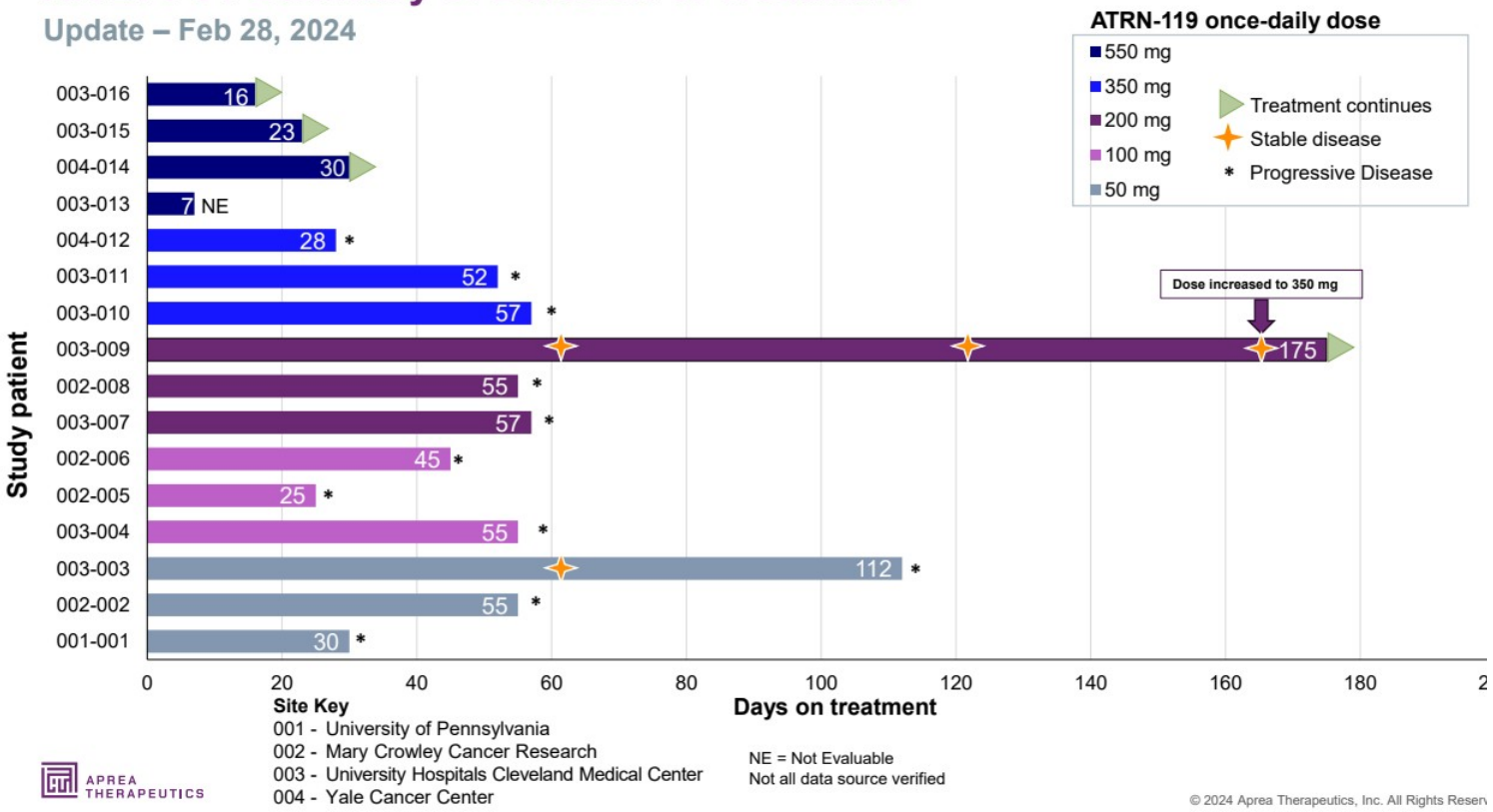
Mutations
Undisclosed RepliBion biomarkers

APREA THERAPEUTICS

*Planned protocol amendment adding cohorts 7 and 8

AR-276-01 Summary of Duration of Treatment

Update – Feb 28, 2024



Site Key

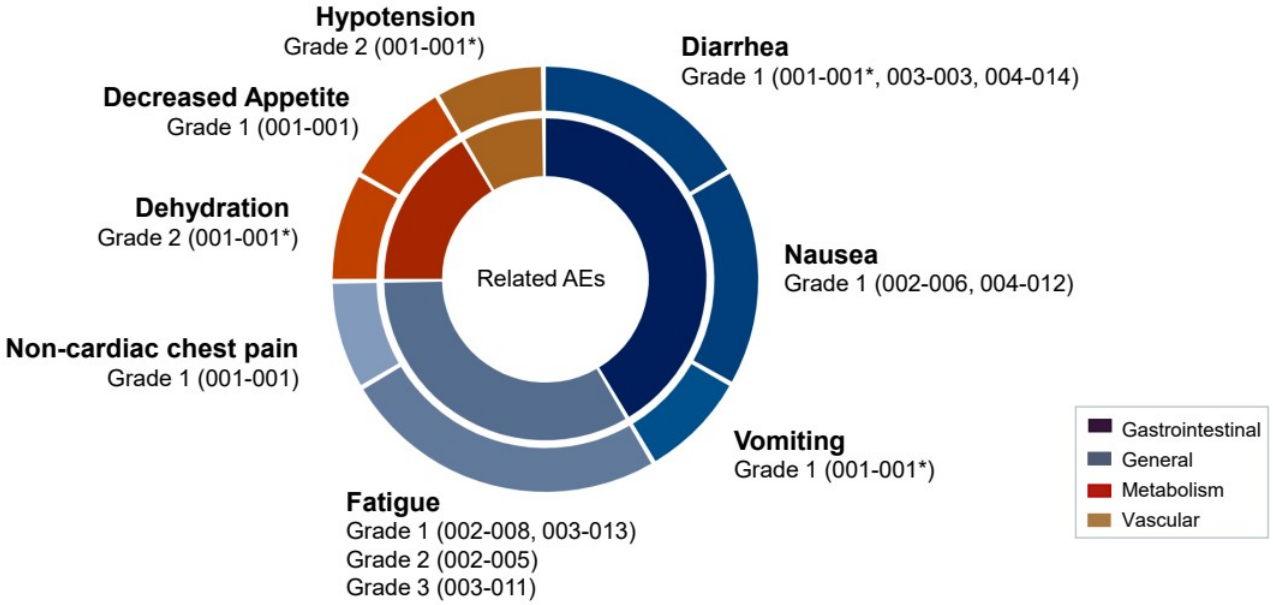
001 - University of Pennsylvania
002 - Mary Crowley Cancer Research
003 - University Hospitals Cleveland Medical Center
004 - Yale Cancer Center

NE = Not Evaluable
Not all data source verified

APREA THERAPEUTICS

No ATRN-119 Related SAE or Grade 4 Adverse Events Reported

As of February 23, 2024: Seven Of Fifteen Patients Experienced AEs# Possibly/probably Related to ATRN



APREA THERAPEUTICS

No grade 4 AEs were observed
* Resulted in treatment interruption
Not all data source verified

ATRN-119
2024-2025 Anticipated Clinical Milestones

Milestone	Timeline
Phase 1/2a – Monotherapy Dose Escalation	
Potential efficacy data	2H 2024
Complete Dose Escalation	4Q 2024
RP2D	1Q 2025
Phase 1/2a – Monotherapy Dose Expansion	
First Patient Enrolled	1Q 2025
Additional Open-Label Efficacy Data	3Q 2025

APREA THERAPEUTICS

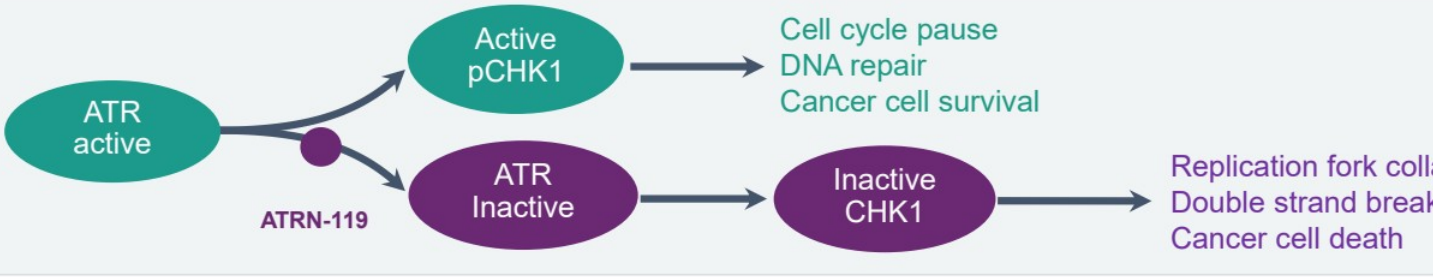
Planned protocol amendment adding cohorts 7 and 8 to monotherapy dose escalation 1Q2024

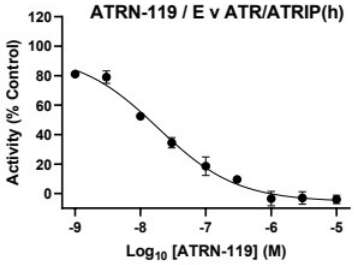
ATR Inhibitor: ATRN-119

Preclinical
Proof-of-Principal

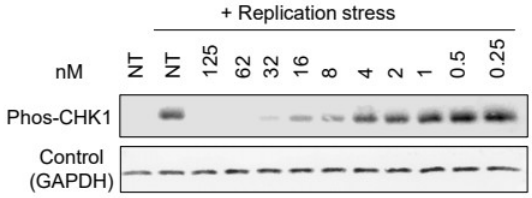
APREA THERAPEUTICS

ATR Inhibitor – ATRN-119
Mechanism of Action – Prevent CHK1 Phosphorylation by ATR Kinase



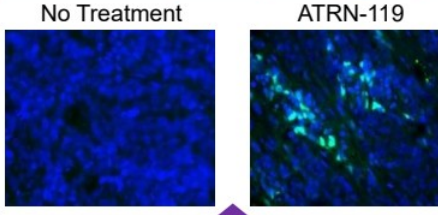


ATRN-119 binds to ATR



…inhibits its biological activity…

Tumor Samples
Pharmacodynamics - γH2AX (green)



…and triggers replication fork collapse and double-strand breaks (γH2AX)

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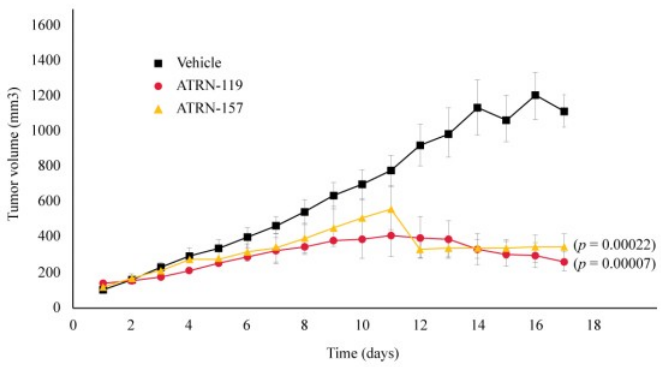
pCHK1 – Phosphorylated Checkpoint kinase 1
Data on file

ATRN-119 Preclinical Profile

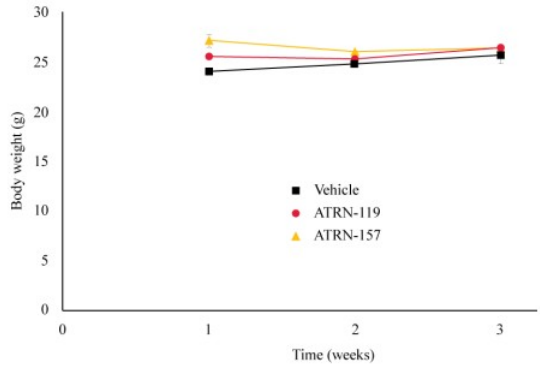
Nanomolar potency in vitro across a broad spectrum of cancer cell lines

Strong tumor control observed in vivo, including in challenging genetic backgrounds

Tumor Growth Inhibition
HCT-116 (KRAS^{G13D}, p53 null)



Body Weight
HCT-116 (KRAS^{G13D}, p53 null)

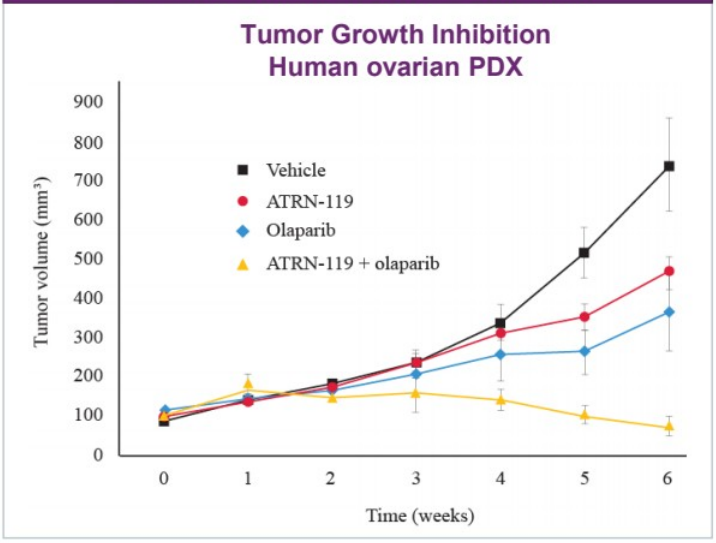


APREA THERAPEUTICS

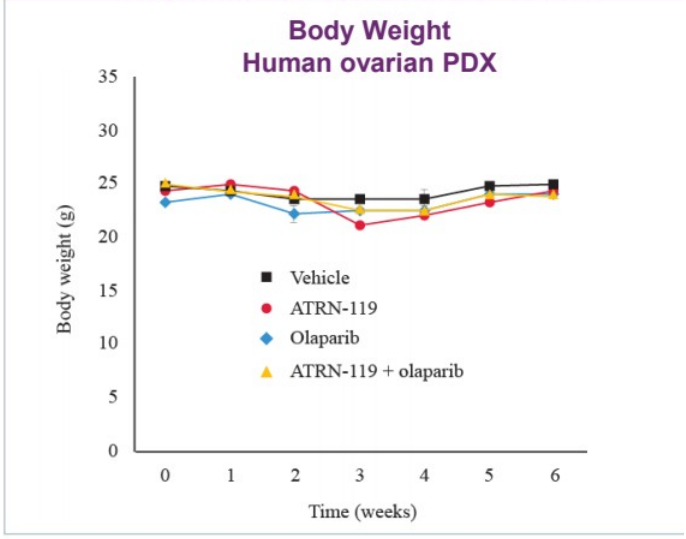
N=4 female mice per group, ATRN-119 - 100 mg/kg/day P.O, ATRN-157 - 20 mg/kg/day SQ.
ATRN-157 is an active metabolite identified in dogs receiving ATRN-119 P.O.. In vitro metabolism studies in dog and human hepatocytes and liver microsomes indicated formation of ATRN-157 in both species. Potency and selectivity of ATRN-157 was comparable to ATRN-119.
Pre-clinical studies with ATRN-119 and ATRN-157.

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



APREA THERAPEUTICS

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.
Pre-clinical studies with ATRN-119.
Data on file

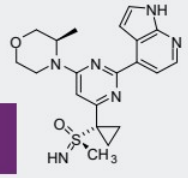
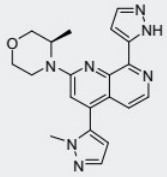
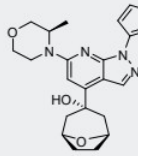
ATR Inhibitor: ATRN-119

A Potentially Differentiated ATRi

APREA THERAPEUTICS

Reported Challenges with Other ATR Inhibitors

First Generation Compounds Share Similar Core, Backbone, Toxicity, and Intermittent Dosing Schedu

Parameter	AstraZeneca AZD6738[1,2] 	Bayer BAY1895344[3] 	Repare / Roche[4] RP-3500[5] 
Route of Administration	**Oral**	**Oral**	**Oral**
MTD/RP2 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	Patriot 1, Escalation Phase, 160mg, BID[2]: **Anemia** (1/6, 17%) Patriot 2, Expansion Phase[1]: **Fatigue, anemia, nausea, and thrombocytopenia (not differentiated)** (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

APREA THERAPEUTICS

ATRN-119 Daily Dosing Means Continuous Tumor Reduction

Intermittent Dosing May Lead to Tumor Resistance

APREA THERAPEUTICS

Daily Dosing Is Clinically Superior Based on Other ATRi in Development

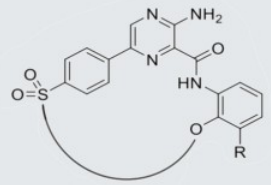
Artios ATR Inhibitor: ART0380
Initial Results From Phase 1 Dose Escalation[1]

Dose Escalation Phase	• 49 patients • Continuous dosing: QD; Range 200-400mg, (n=10) • Intermittent dosing: 3D on/4D off; Range 100 - 1,200mg, (n=39)
RP2D	• Continuous = 200mg • Intermittent dosing = 600mg
Efficacy Among Measurable Patients	• Continuous – **ORR 29%** (2/7). One of two responders treated at twice the RP2D. • Intermittent – **ORR 8%** (2/26). One of two responders treated at twice the RP2D.
Safety	• 36% Anemia Grade 3 at doses considered tolerable

APREA THERAPEUTICS

[1]ART0380-ESMO-Poster-2023

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 daily dosing (RP2D 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 and within normal ranges • 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.

APREA THERAPEUTICS

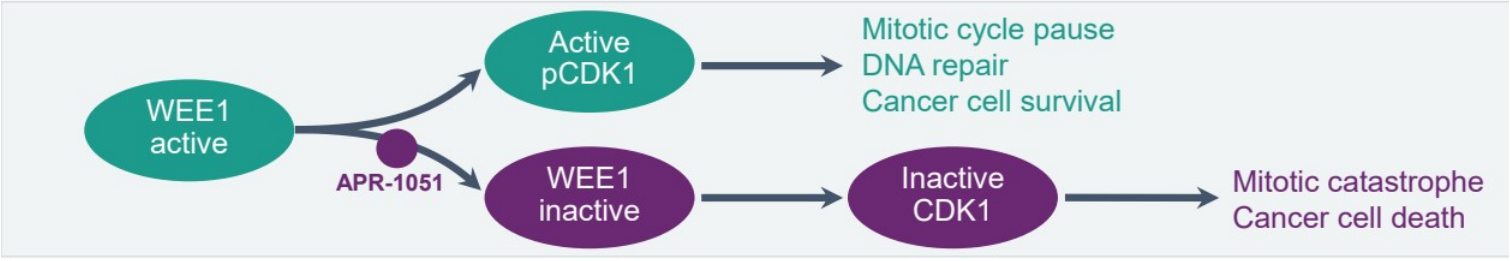
Note: ATRN-119 has not yet been tested clinically
[1] ATRN-119, Phase 1/2a Clinical Study Protocol
[2] Internal pre-clinical head-to-head tolerability study in male beagle dogs.

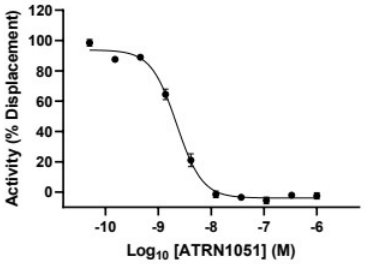
WEE1 Inhibitor: APR-1051

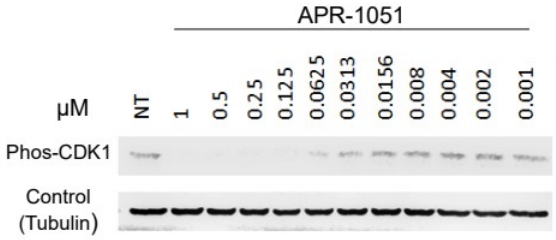
Preclinical Proof-of-Principle

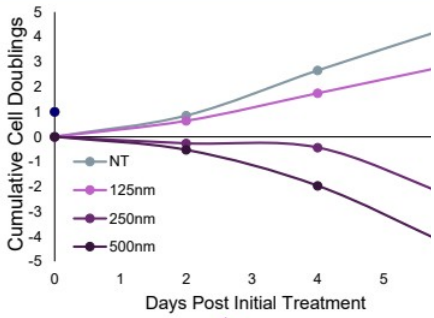
APREA THERAPEUTICS

WEE1 Inhibitor – APR-1051
Mechanism of Action – Prevent CDK1 Phosphorylation by WEE1 Kinas









APR-1051 binds to WEE1

…inhibits its biological activity…

…and triggers mitotic catastrophe and cancer cell death

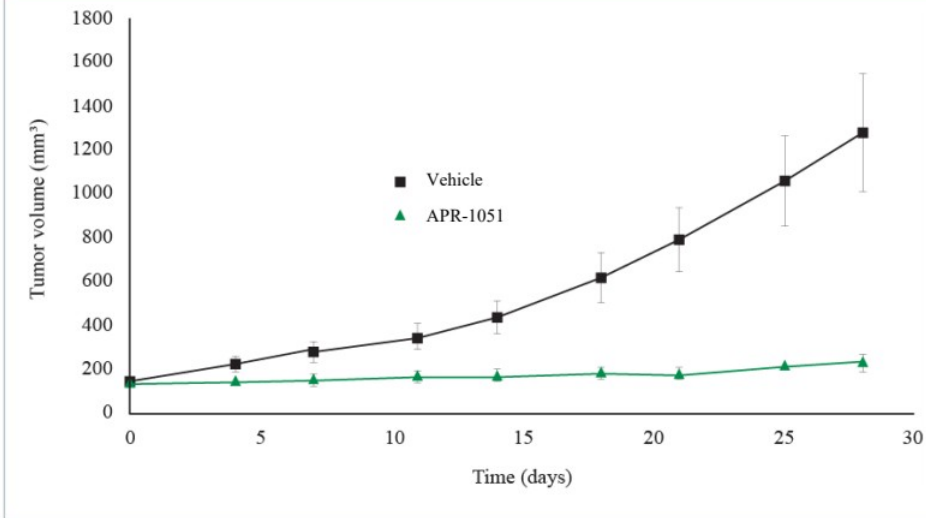
APREA THERAPEUTICS

pCDK1- Phosphorylated Cyclin Dependent Kinase 1
Data on file

APR-1051 Demonstrated Potentially Compelling Anti-tumor Activity

IND Cleared March 2024

Tumor Growth Inhibition
OVCAR-3



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

APREA THERAPEUTICS

Pre-clinical studies with APR-1051
Data on file

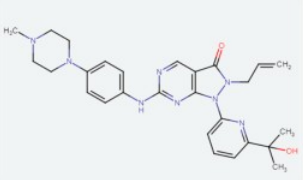
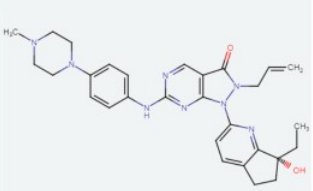
WEE1 Inhibitor: APR-1051

A Potentially Differentiated Wee1i

APREA THERAPEUTICS

APR-1051 Potentially Differentiated from Other WEE1 Inhibitors

APR-1051 Potent and Structurally Differentiated, with High Selectivity to Limit Off-target Toxicity

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

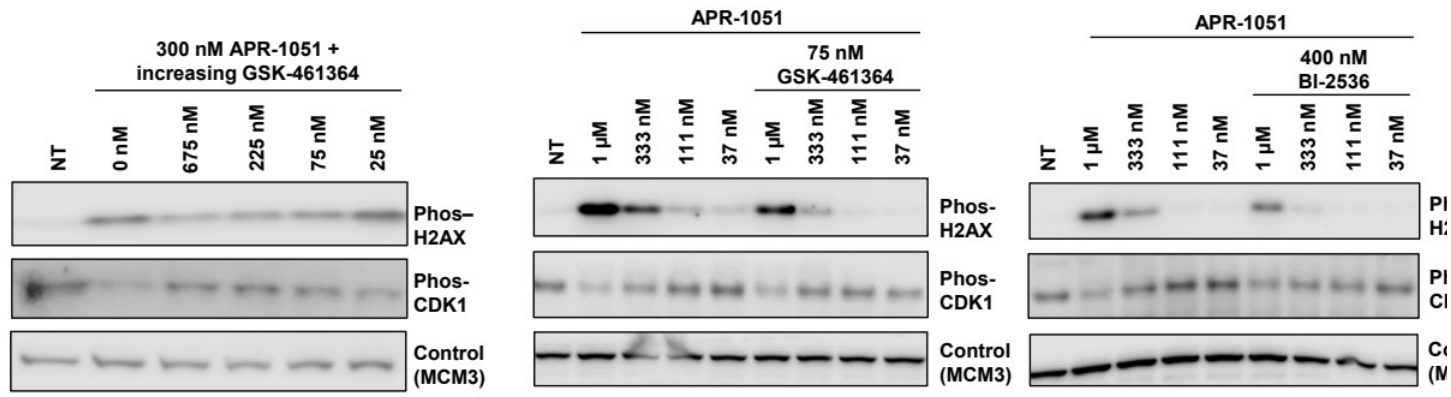
Note: Head-to-head studies have not been conducted
[1] Huang et al, (2021) J Med Chem
[2] AstraZeneca announced in July 2022 the discontinuation of development of AZD-1775

APREA THERAPEUTICS

AACR-NCI-EORTC Meeting, Poster C147, 20

PLK1 Inhibition Reduces Cytotoxic Effects of WEE1 Inhibitors

Minimal PLK1 Co-inhibition Enables Full Therapeutic Potential APR-1051



Dose range of PLK inhibitor GSK-461364 in combination with a single dose of APR-1051 in OVCAR-3 cells

PLK inhibitor, GSK-461364 interferes with the effects of APR-1051 in OVCAR-3 cells

PLK inhibitor, BI-2536, interferes with the effects of APR-1051 in OVCAR-3 cells

APREA THERAPEUTICS

AACR-NCI-EORTC Meeting, Poster C147, 20

APR-1051 Preclinical Data Highlight Potentially Favorable PK Properties

Based on Pre-clinical Studies, APR-1051 Shows Potentially Favorable Drug Exposure

	APR-1051[1]	Zentalis Azenosertib (ZN-c3)[2]			AstraZeneca Adavosertib (AZD-1775)[2]		
Dose (mg/kg/d)	**10**	20	**40**	80	20	40	**80**
C_{max} ng/ml	1,460	1,167	1,997	5,100	635	2,460	4,703
T_{max} hr	3	1	1	1	1	1	1
AUC_{0-24}, ng*hr/ml	**16,739**	4,863	**17,088**	39,722	1,494	6,313	**13,408**

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

[1] Data from an exploratory formulation of APR-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

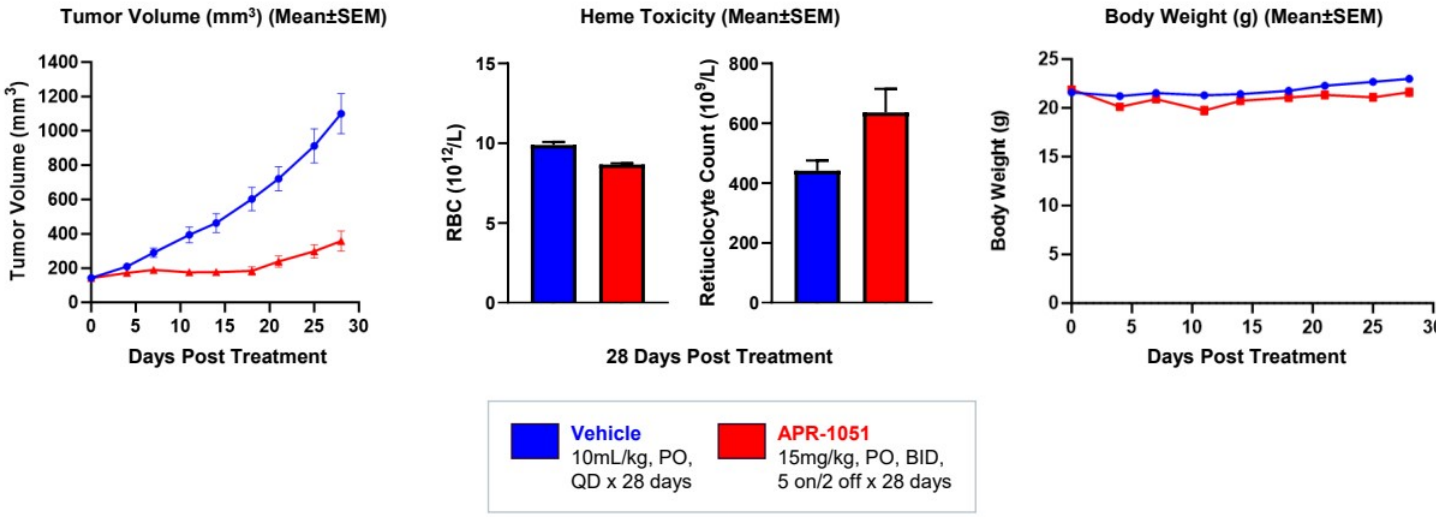
APR-1051 Shows Negligible Inhibition of hERG Channels

QT prolongation AEs were reported with some competitor WEE1 inhibitors

In vitro kinase assays IC50		Average WEE1 kinase IC50	hERG inhibition IC50		Average hERG IC50	Fold difference betw kinase IC50 and hE IC50
LanthaScreen (Thermo)	Hotspot (Reaction Biology)		HEK293 cells (Medicilon)	CHO cells (WuXi)		hERG inhibition over W kinase inhibition
2.2 nM	41.4 nM	**21.8 nM**	8,840 nM	660 nM	**4,750 nM**	**218-fold (range 16- to 3,946-fo**

APR-1051 Suppresses Tumor Growth While Causing Little Effect on RBCs and Body Weight

OVCAR Xenograft Tumor Model in Female Nude Mice



APR-1051
2024-2025 Anticipated Clinical Milestones

Milestone	Timeline
Phase 1 – Monotherapy Dose Escalation	
Enroll first patient	1H 2024
Clinical Update	4Q 2024
Open-Label Efficacy Data	2Q 2025
RP2D	2H 2025

APREA THERAPEUTICS

Strong Intellectual Property Portfolio

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, HK. 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 and 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 28th, 2019 as U.S. Patent 10,301,324

Family 3: ATR Inhibitor Pharmaceutical Composition and Methods

- International application filed on Apr. 14th, 2023
- 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

Family 5: Methods of Treating Cancer

- U.S. Provisional Application filed on Oct. 20th, 2023
- Clinical methods of treating advanced solid cancer tumors using lead molecule

Aprea Therapeutics (NASDAQ: APRE)
Financial Summary & Capitalization

Cash & Equivalents of $21.6M as of December 31, 2023

Closed approximately $16.0M (before deducing placement agent fees and offering costs of approximately $1.4 million) from our private placement of our common stock in March 2024 with the potential to receive up to an additional $18.0 million upon cash exercise of accompanying warrants at the election of the investors.

Securities	Common Equivalents as of March 26, 2024
Preferred Stock (as converted)	28,112
Common Stock	5,430,215
Warrants:	
Pre-Funded	507,076
Tranche A	1,097,394
Tranche B	1,097,394
Total	2,701,864
Options	596,466
Restricted Stock Units	18,040
Fully Diluted Equivalents	8,774,697

APREA THERAPEUTICS

Investment Highlights

Technology developed by pioneers in synthetic lethality

- Management with strong drug development and commercial expertise

Diversified portfolio with best in class, de-risked clinical and preclinical programs

- Highly potent and selective ATR and WEE1 inhibitors
- Opportunities in ovarian, colorectal, prostate, and breast cancers
- Single agent and combination therapies

Near term catalysts

- Phase 1/2a ATRN-119 potential efficacy 2H 2024; complete dose escalation 4Q 2024
- Initiate Phase 1 for APR-1051 1H 2024

Financed into 3Q 2025

- Reach short term inflection points and catalysts
- Evaluate optimal strategic partnerships

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