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

May 14, 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 May 14, 2024, Aprea Therapeutics, Inc. (the "Company") issued a press release announcing its financial results for the three months ended March 31, 2024, 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 May 14, 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 May 14, 2024.
99.2	Corporate Presentation (May 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: May 14, 2024

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

Exhibit 99.1

Aprea Therapeutics Reports First quarter 2024 Financial Results and Provides a Business Update

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 June 2024

First-in-class macrocyclic ATR inhibitor, ATRN-119, on track to complete dose escalation in ABOYA-119 clinical trial and potentially generate initial human efficacy data in 2H 2024

Company had four poster presentations at the AACR Annual Meeting, including updates on APR-1051 and ATRN-119

$32.4 million in cash and cash equivalents as of March 31, 2024

DOYLESTOWN, PA, May 14, 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 first quarter ended March 31, 2024, and provided a business update.

"During the first quarter of 2024, Aprea had a number of noteworthy achievements across clinical, regulatory and corporate fronts," said Oren Gilad, Ph.D., President and Chief Executive Officer of Aprea. "FDA clearance of the IND for APR-1051, our next-generation inhibitor of WEE1 kinase, was an important milestone and allows us to commence clinical trials with this exciting, differentiated and potentially best in class molecule. We look forward to evaluating its therapeutic activity in patients, focusing on Cyclin E overexpressing cancers, including ovarian and breast cancers amongst others. Enrollment continues in the dose escalation portion of our ABOYA-119 clinical trial evaluating ATRN-119 in patients with advanced solid tumors having mutations in defined DDR-related genes. We are encouraged by correlations of the preliminary signs of clinical benefit and genetic mutations. Importantly, Aprea has a strong balance sheet, and the closing of our successful private placement in March of this year provides us with the capital to fund both our lead programs through meaningful clinical milestones. As we progress, we are committed to leveraging our expertise in synthetic lethality in order to provide hope and new treatment options to cancer patients who urgently need them. We believe that our strategic initiatives and pipeline expansion have the potential to drive substantial value for shareholders."

Key Business Updates and Potential Upcoming Key Milestones

ABOYA-119: ATR inhibitor, ATRN-119, on track to complete monotherapy dose escalation end of the year

- 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.
- Enrollment continues in the open-label Phase 1/2a clinical trial of ABOYA-119 (study AR-276-01) as monotherapy in patients with advanced solid tumors having at least one mutation in a defined panel of DDR-related genes.
- An update on the ongoing trial was featured in a poster at the AACR Annual Meeting this past April. As of March 12, 2024, 16 patients were enrolled in the first five cohorts of the dose escalation stage (50 mg/day, 100 mg/daily, 200 mg/daily, 350 mg/daily, and 550 mg/daily). Based on data to date, ATRN-119 has been found to be safe and well tolerated. PK studies show ATRN-119 serum concentrations are entering the expected therapeutic range at the current highest dose level (550 mg). We have clearance up to 800 mg/daily and, on March 12, submitted an amendment to the FDA for the additional cohorts. Preliminary signs of clinical benefit have been observed with two patients achieving stable disease (SD) – one in the 50 mg/day cohort and a second patient who showed longer duration when treated at 200 mg/day. The latter patient at 200 mg/day had SD at Days 55, 112, and 168. For further details, including the status of all 16 patients enrolled to date, refer to the AACR poster here.
- Initial efficacy data from Part 1 of the study may potentially be announced in 2H 2024. At completion of Part 1, 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.
- For more information, please refer to clinicaltrials.gov NCT04905914.

ACESOT-1051: Oral WEE1 inhibitor, APR-1051, expected to enter Phase 1 clinical trial in June, 2024

- APR-1051 is a potent and selective small molecule that has been designed to potentially solve liabilities and achieve greater clinical activity than other WEE1 programs currently in development. Aprea is advancing APR-1051 as monotherapy in ovarian and breast cancers with Cyclin E over expression, amongst others. 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 is allowing Aprea to initiate the Phase 1 ACESOT-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 2Q 2024 with an update expected in 4Q 2024.
- APR-1051 was featured in two posters at the American Association of Cancer Research (AACR) annual meeting which took place in April 2024 in San Diego, which summarized the pre-clinical data supporting APR-1051 and the trial design for ASECOT-1051.

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 chemists and discovery team are developing a series of molecules that are selective and potent against it.
- A lead molecule is expected to be declared in 3Q 2024. This program may provide clinically meaningful differences for cancer patients that currently have limited therapies.
- An additional poster at AACR described a combination approach using Aprea's next-generation macrocyclic ATR inhibitor, ATRN-333, to sensitize glioblastoma (GBM) tumors to lomustine, an oral DNA alkylating agent. The results support further investigation and potential clinical implementation of ATRN-333 and other macrocyclic ATR inhibitors as chemosensitizers for glioblastoma.

Corporate

- In March 2024, Aprea announced a securities purchase agreement with new and existing healthcare institutional investors and certain Company insiders to raise up to $34.0 million in gross proceeds, including initial upfront gross funding of $16.0 million and up to an additional $18.0 million upon cash exercise of accompanying warrants at the election of the investors. The financing was led by Sphera Healthcare with participation from new and existing healthcare focused investors including Nantahala Capital, DAFNA Capital Management, Exome Asset Management and Stonepine Capital Management, among others, as well as certain Company insiders. The capital is being deployed for general working capital purposes and to fund the Phase 1 ACESOT-1051 clinical trial, as well as, continuation of patient enrollment in the dose expansion portion of the ABOYA-119 clinical trial evaluating ATRN-119.
- Appointed Nadeem Q. Mirza, M.D., M.P.H. as Chief Medical Officer (CMO), effective May 1, 2024. Dr. Mirza had been a consultant to Aprea since February, 2023 and has now assumed a more central role in leading the Company's development of its expanding clinical pipeline.

Select Financial Results for the First Quarter ended March 31, 2024

- As of March 31, 2024, the Company reported cash and cash equivalents of $32.4 million, compared to $21.6 million at December 31, 2023. The Company believes its cash and cash equivalents as of March 31, 2024 will be sufficient to meet its currently projected operating expenses and capital expenditure requirements into the third quarter of 2025.
- For the quarter ended March 31, 2024, the Company reported an operating loss of $3.1 million, compared to an operating loss of $4.6 million in the comparable period in 2023.
- Research and Development (R&D) expenses were $1.6 million for the quarter ended March 31, 2024, compared to $1.3 million for the comparable period in 2023. The increase in R&D expense was primarily related to IND enabling studies for APR-1051, the Company's small molecule WEE1 inhibitor, in preparation for enrollment of first patient into Phase 1 dose-escalation in the second quarter of 2024.
- General and Administrative (G&A) expenses were $1.9 million for the quarter ended March 31, 2024, compared to $3.4 million for the comparable period in 2023. The decrease in G&A expenses was primarily due to a decrease in personnel costs.
- The Company reported a net loss of $2.8 million ($0.67 per basic share) on approximately 4.2 million weighted-average common shares outstanding for the quarter ended March 31, 2024, compared to a net loss of $4.4 million ($1.34 per basic share) on approximately 3.3 million weighted average common shares outstanding for the comparable period in 2023.

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 Balance Sheets

	March 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 32,369,973	$ 21,606,820
Prepaid expenses and other current assets	698,864	914,275
Total current assets	33,068,837	22,521,095
Property and equipment, net	90,183	88,362
Restricted cash	40,986	40,717
Total assets	$ 33,200,006	$ 22,650,174
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,318,385	$ 1,670,369
Accrued expenses	1,498,286	2,186,262
Deferred revenue	148,405	528,974
Total current liabilities	2,965,076	4,385,605
Total liabilities	2,965,076	4,385,605
Commitments and contingencies		
Series A convertible preferred stock, $0.001 par value, 40,000,000 shares authorized; 56,227 shares issued and outstanding at March 31, 2024 and December 31, 2023, respectively.	1,311,063	1,311,063
Stockholders' equity:		
Common stock, $0.001 par value, 400,000,000 shares authorized, 5,430,215 and 3,736,673 shares issued and outstanding at March 31, 2024 and December 31, 2023, respectively.	5,430	3,736
Additional paid-in capital	350,438,045	335,644,204
Accumulated other comprehensive loss	(10,626,356)	(10,611,273)
Accumulated deficit	(310,893,252)	(308,083,161)
Total stockholders' equity	28,923,867	16,953,506
Total liabilities and stockholders' equity	$ 33,200,006	$ 22,650,174

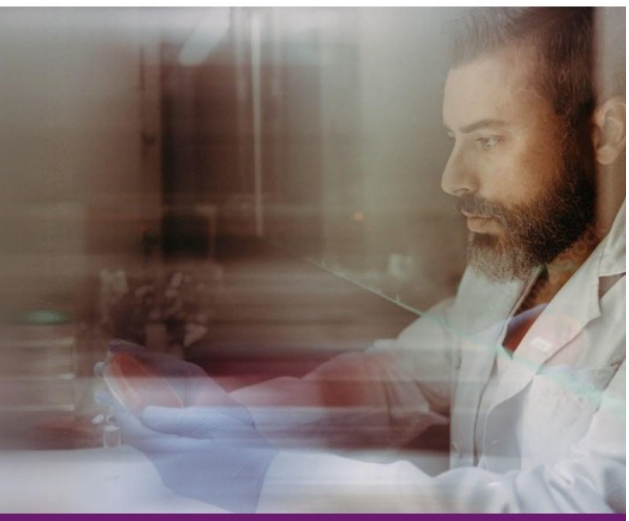
Aprea Therapeutics, Inc.

Consolidated Statements of Operations and Comprehensive Loss

	Three Months Ended March 31,	
	2024	**2023**
Grant revenue	$ 380,569	$ —
Operating expenses:		
Research and development	1,600,373	1,256,542
General and administrative	1,929,866	3,365,961
Total operating expenses	3,530,239	4,622,503
Loss from operations	(3,149,670)	(4,622,503)
Other income (expense):		
Interest income, net	283,403	256,410
Foreign currency gain (loss)	56,176	(13,797)
Total other income	339,579	242,613
Net loss	$ (2,810,091)	$ (4,379,890)
Other comprehensive (loss) gain:		
Foreign currency translation	(15,083)	61,956
Total comprehensive loss	(2,825,174)	(4,317,934)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.67)	$ (1.34)
Weighted-average common shares outstanding, basic and diluted	4,198,326	3,260,484

APREA THERAPEUTICS

Precision Oncology Through Synthetic Lethality



May 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
- 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
  - Minimal 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

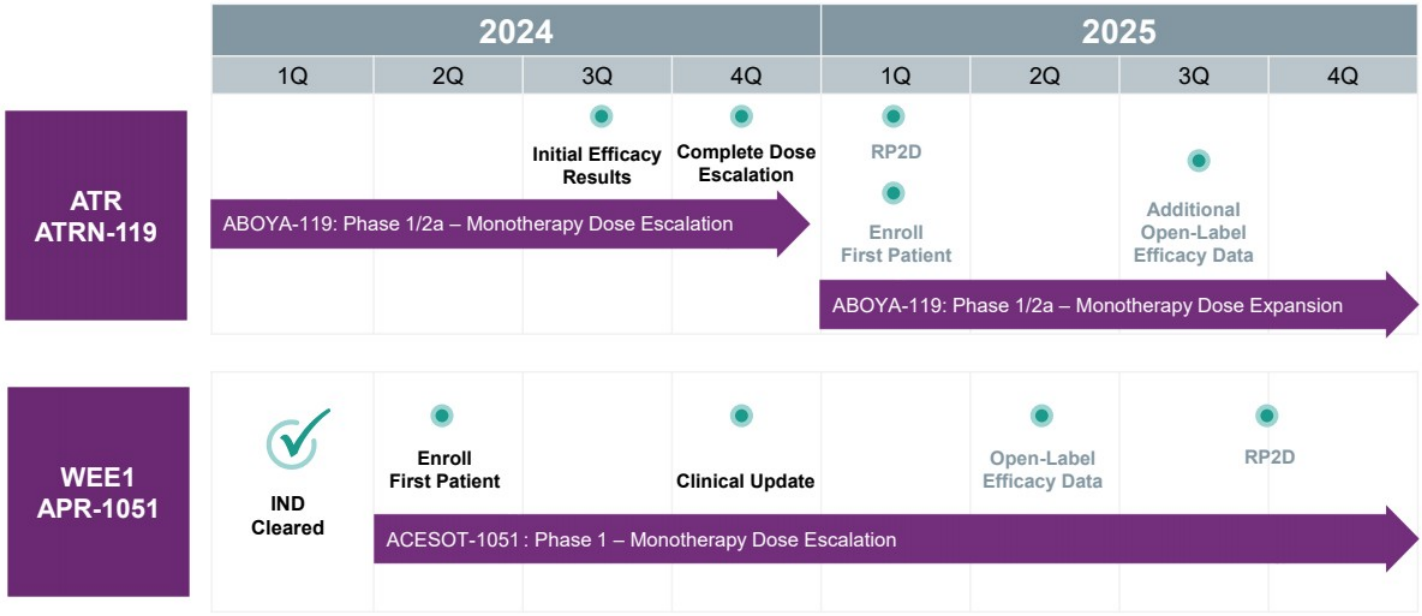
- Lead optimization
- Target identified from our RepliBior discovery platform

APREA THERAPEUTICS

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

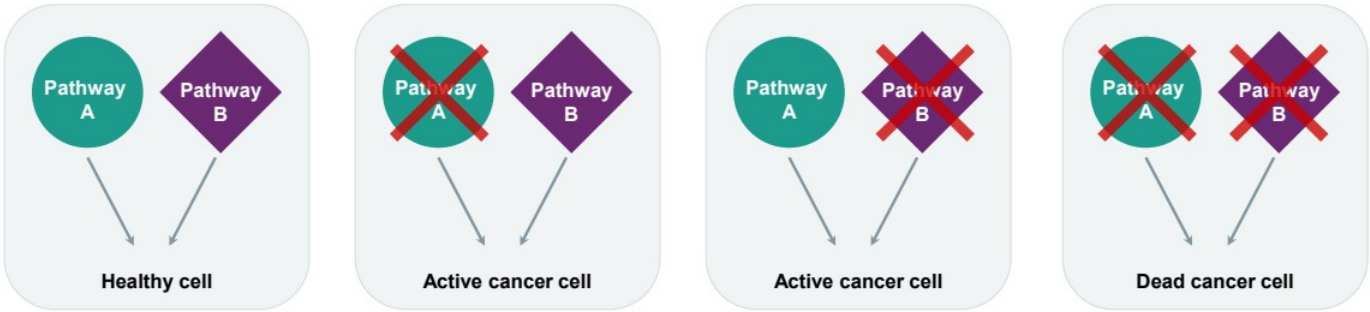
Robust DDR Development Pipeline Milestones

2024-2025 Anticipated Clinical Milestones



APREA THERAPEUTICS

Synthetic Lethality



- Cancer cell death only upon the loss of function of two codependent pathways
- 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 P. Hamill Sr. Vice President and CFO	Nadeem Q. Mirza, M.D., MPH Chief Medical Officer	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 Verastem Oncology TRIGR THERAPEUTICS abbvie sanofi	ATRIN Pharmaceuticals INTEC PHARMA pwc	iniphorm ATRIN Pharmaceuticals MERCK Bristol Myers Squibb presage MaYu PHARMA	Boston BioConsulting Gloucester Aventis

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

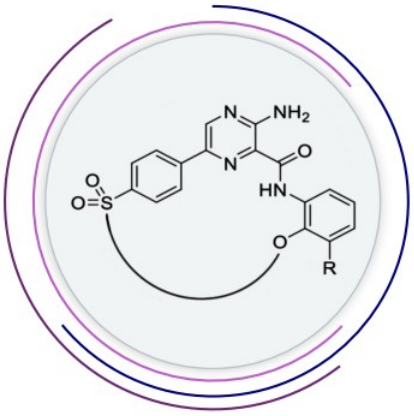
ATR Inhibitor: ATRN-119

A Potentially Differentiated ATRi

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)



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

Macrocycles restrict number of conformations formed for increased selectivity

Potential advantages for ATRN-119:

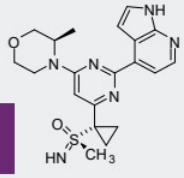
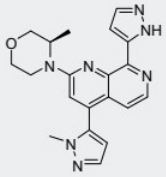
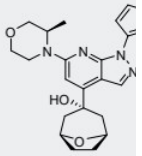
- Increased selectivity ⇢ Improved tolerability
- Improved tolerability ⇢ Further efficacious dosing

[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

Reported Challenges with Other ATR Inhibitors

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

	AstraZeneca AZD6738[1,2] 	Bayer BAY1895344[3] 	Repare RP-3500[4] 
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

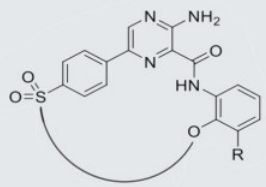
[2] Poster CT084: A Phase I dose-escalation study of ATR inhibitor monotherapy with AZD6738 in advanced solid tumors (PATRIOT Part A), AACR 2017

[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 Disco 2021;11:80-91 and 2019 ASCO Poster, De-Bono et al.

[4] Preliminary Phase 1 Data From Ongoing First-in-Human Phase 1/2 TRESR Study of RP-3500, AACR 2022

APREA THERAPEUTICS

ATRN-119: Potential Best-in-Class Oral ATR Inhibitor Structurally Differentiated Core, Backbone, and Toxicity Profile

	ATRN-119[1] 
Route of administration	**Oral**
Dosing regimen	**Continuous daily dosing (RP2D TBD in Phase 1)[1]**
Hematological toxicities in preclinical studies	• **Small magnitude and within normal range hematological changes in 28-day GLP tox dog study** • **Significantly less toxicity in head-to-head comparative tolerability study vs other clinical stage ATRI[2]**

ATRN-119 potentially the preferred ATRi both as a single agent and in combination with standard-of-care therapies

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[1] ATRN-119, Phase 1/2a Clinical Study Protocol
[2] Internal pre-clinical head-to-head tolerability study in male beagle dogs.

ATRN-119 Daily Dosing Supports Potential Continuous Tumor Suppression

Intermittent Dosing May Lead to Tumor Resistance

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ATR Inhibitor: ATRN-119

ABOYA-119: Clinical Proof-of-Concep

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ABOYA-119: 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

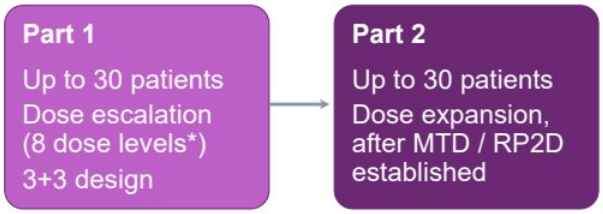
Patient enrollment:
Up to 60 patients in total

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

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



Objectives:

Primary

- Safety, MTD, RP2D
- Pharmacokinetics

Secondary

- Antitumor activity (RECIST/PCWG3)

Exploratory

- Association betwee identified mutations and clinical outcome

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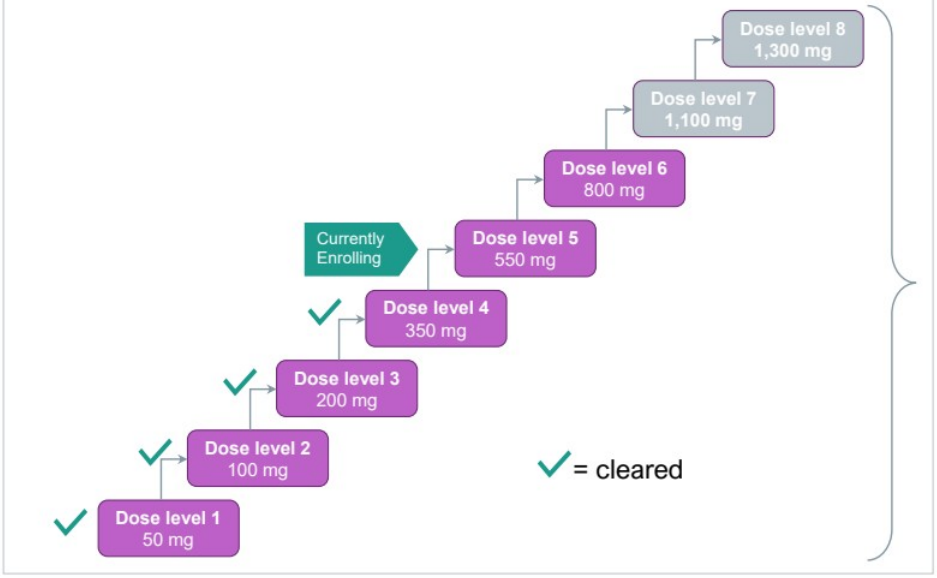
*Protocol amendment adding cohorts 7 and 8

ABOYA-119: Clinical Study Design

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

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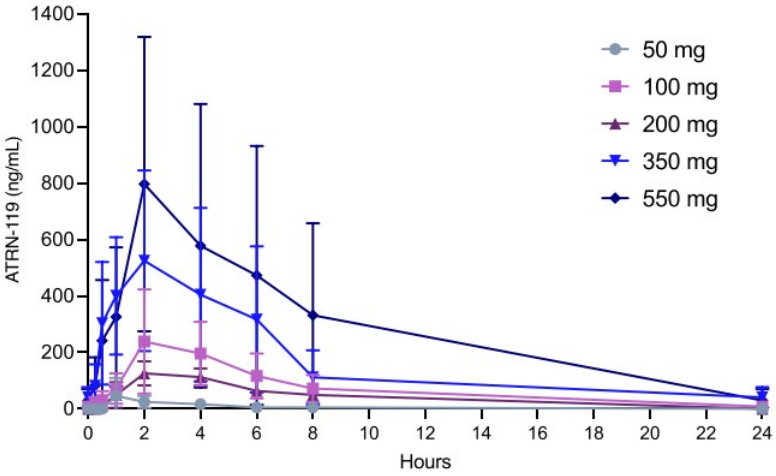
* protocol amendment adding cohorts 7 and 8 was filed on March 12, 2024

ATRN-119 Steady State Plasma Concentrations (Cycle 1 Day 7)

ATRN-119 Exhibits Near-dose Proportional Exposure Following Oral Administration



Dose Level mg, once daily	N	AUC 0-24hr (ng*h/mL)	C_{max} (ng/mL)	Half-lif (hours
		Mean (SD)	Mean (SD)	Mean (SI
50	3	180 (143)	94 (119)	1.4 (1.1
100	3	1771 (920)	305 (171)	4.6 (0.5
200	3	1024 (162)	179 (23)	4.3 (0.3
350	3	5252 (4362)	605 (358)	6 (0.7)
550	3	6899 (6058)	797 (522)	4.5 (0.7
800				
1100				
1300				

- T_{max} is approximately 2 hours and the half-life is estimated between 4-6 hours
- The duration of systemic exposure substantially increases with each dose level

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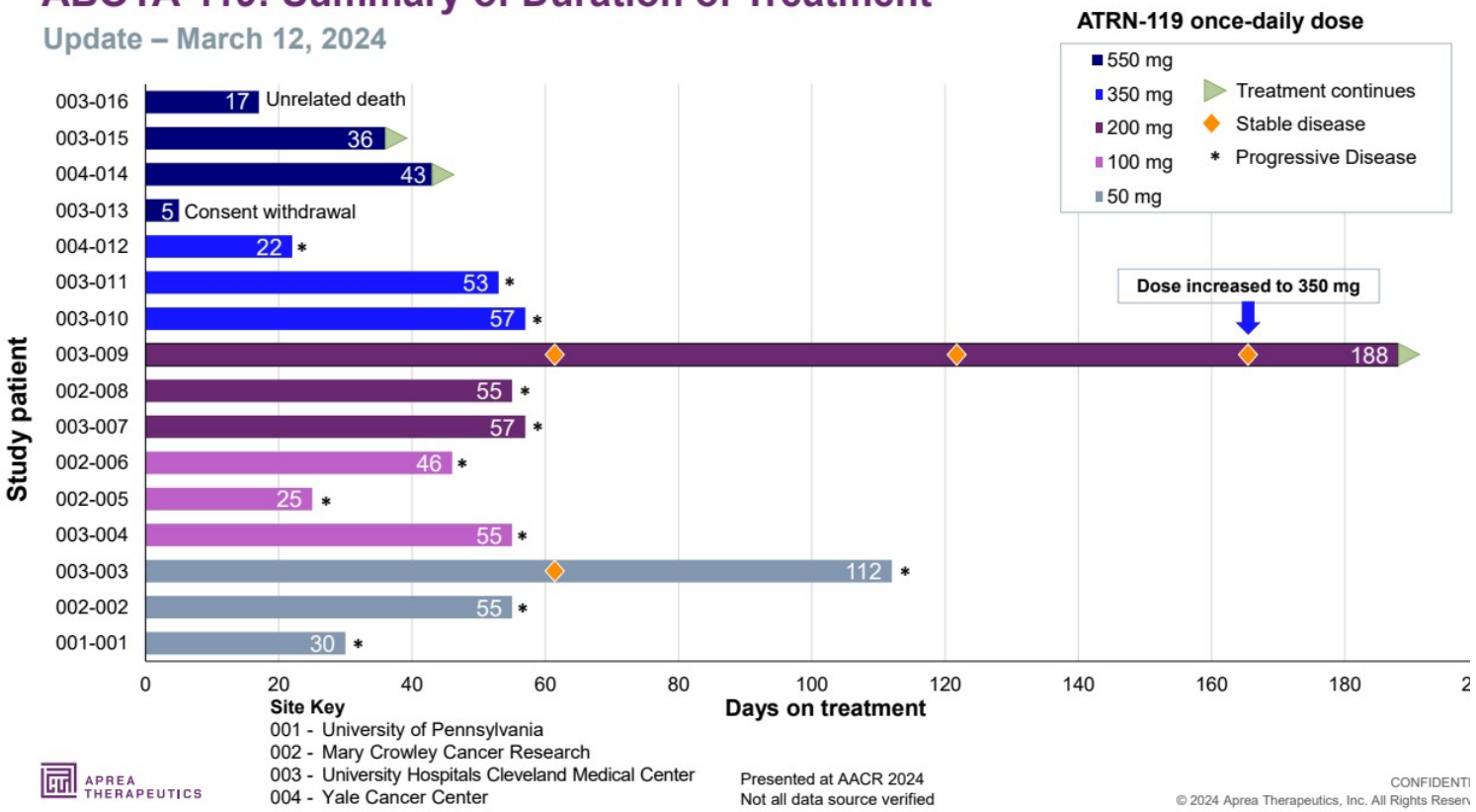
Presented at AACR 2024

ABOYA-119: Summary of Duration of Treatment

Update – March 12, 2024



Site Key

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

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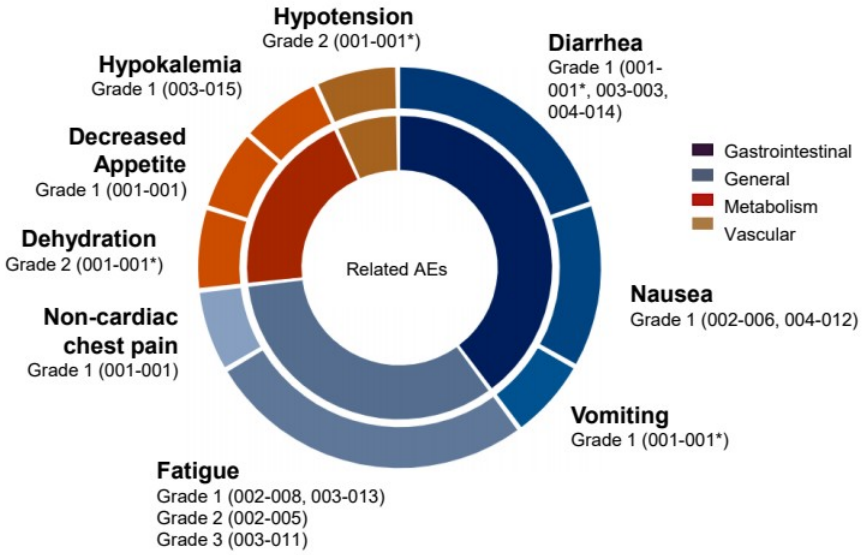
Presented at AACR 2024
Not all data source verified

ABOYA-119: Summary of Related Adverse Events

Update – March 12, 2024

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



*Resulted in treatment interruption
Presented at AACR 2024
Not all data source verified

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ATRN-119: Summary

First and only macrocyclic ATR inhibitor

- Differentiated from other ATR inhibitors in selectivity and toxicity profile, permitting continuous dosing
- Strong tumor control observed in vivo, including in challenging genetic backgrounds
- Daily oral dosing provides potential continuous tumor suppression

ABOYA-119: Ongoing Phase 1/2a Clinical Study (NCT04905914)

- Patients with advanced solid tumors harboring specific DDR mutations
- Well tolerated with no DLTs to date (550mg/daily)
- Near-dose proportional exposure following oral administration
- Preliminary signs of clinical benefit already observed at low doses
- Potential efficacy data readout in 2H 2024

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WEE1 Inhibitor: APR-1051

A Potentially Differentiated Wee1i

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WEE1 – Clinically Validated Target: An Unmet Medical Need

Multiple Phase 2 Studies Show Substantial Single-Agent Activity Of A WEE1 Inhibitor (Adavosertib[1])

Phase 2 Study	Indication	Evaluable Patients N	ORR		PFS
NCT03668340 [2]	Recurrent uterine serous carcinoma	34	**29.4%** 1 CR 9 PR		mPFS - 6.1 PFS6 – 16 Pt (47.1%)
IGNITE [3]	Recurrent high-grade, serous ovarian cancer with CCNE1 overexpression with (Cohort 1) and without (Cohort 2) gene amplification	79 Cohort 1 - 21 Cohort 2 - 58	Cohort 1: **38%** 7 PR 1 CA125	Cohort 2: **45%** 3 CR 18 PR 5 CA125	No PD for ≥ 18 weeks: Cohort 1: 53% Cohort 2: 48%
NCT03253679 [4]	Refractory solid tumors harboring *CCNE1* amplification	30 Ovarian - 14, Breast - 3, Uterine - 3, Other - 10	All Pt: Ovarian Pt:	**27%** (8 PR) **36%** (5 PR)	mPFS: All Pt: 4.1 Ovarian Pt: 6.3

WEE1 Inhibitors have been associated with significant Grade ≥3 hematological, GI and CV toxicities

The Need – a highly efficient WEE1 inhibitor with a good safety and tolerability profile

Examples for Phase 2 Studies with Adavosertib as monotherapy

1 AZD-1775. AstraZeneca announced in July 2022 the discontinuation of development of AZD-1775 due to its tolerability profile

2 Phase II Study of the WEE1 Inhibitor Adavosertib in Recurrent Uterine Serous Carcinoma, Liu et al, J Clin Oncol 2021;39:1531–9.

3 IGNITE: A phase II signal-seeking trial of Adavosertib targeting recurrent high-grade, serous ovarian cancer with cyclin E1 overexpression with and without gene amplification. Au-Yeung et Gynecol Cancer 2023;33(Suppl 4):A1–A278

4 Multicenter Phase II Trial of the WEE1 Inhibitor Adavosertib in Refractory Solid Tumors Harboring CCNE1 Amplification, Fu et al, J Clin Oncol. 2023 Mar 20; 41(9): 1725–1734.

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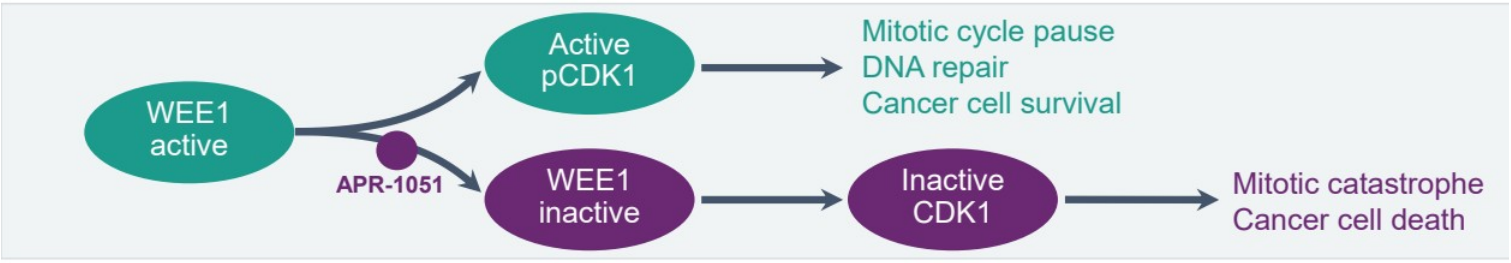
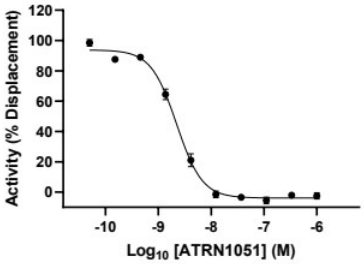
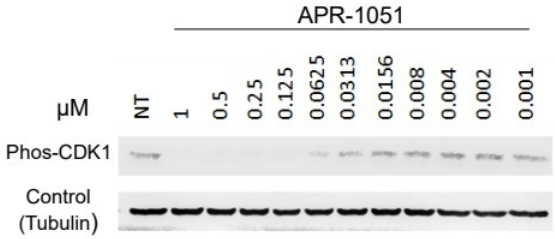
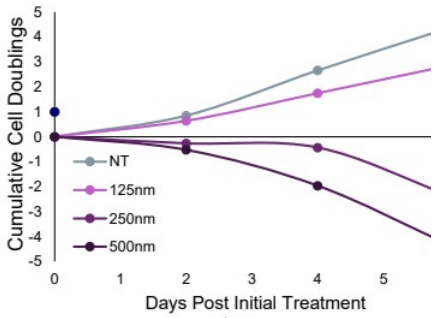
WEE1 Inhibitor – APR-1051
Mechanism of Action – Prevent CDK1 Phosphorylation by WEE1 Kinase









APR-1051 binds to WEE1

…inhibits its biological activity…

…and triggers mitotic catastrophe and cancer cell death

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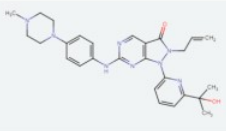
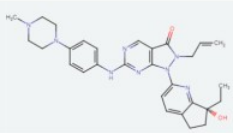
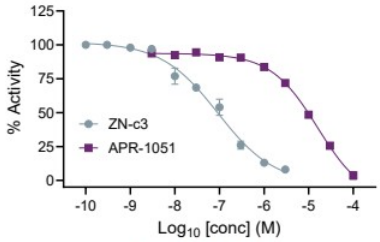
pCDK1- Phosphorylated Cyclin Dependent Kinase 1
Data on file

APR-1051 Potentially Best in Class WEE1 Inhibitor

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

		 AstraZeneca Adavosertib (AZD-1775)[1,2]	 Zentalis Azenosetrib (ZN-c3)[1]	 Undisclosed Aprea APR-1051
On-Target IC_{50} (nM)	**WEE1**	3.8	3.8	1.9

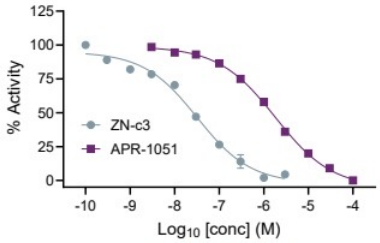
PLK1 IC_{50} Determination



ZN-c3 = 92.1 nM
APR-1051 = 15,900 nM

PLK1 Inhibition
IC50 values show >150-fold

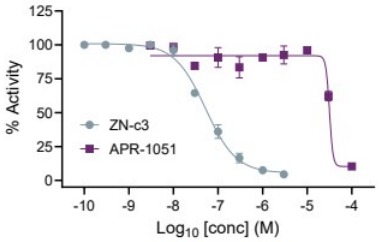
PLK2 IC_{50} Determination



ZN-c3 = 32.0 nM
APR-1051 = 1,800 nM

PLK2 Inhibition
IC50 values show >50-fold

PLK3 IC_{50} Determination



ZN-c3 = 52.2 nM
APR-1051 = 31,600 nM

PLK3 Inhibition
IC50 values show >600-fold

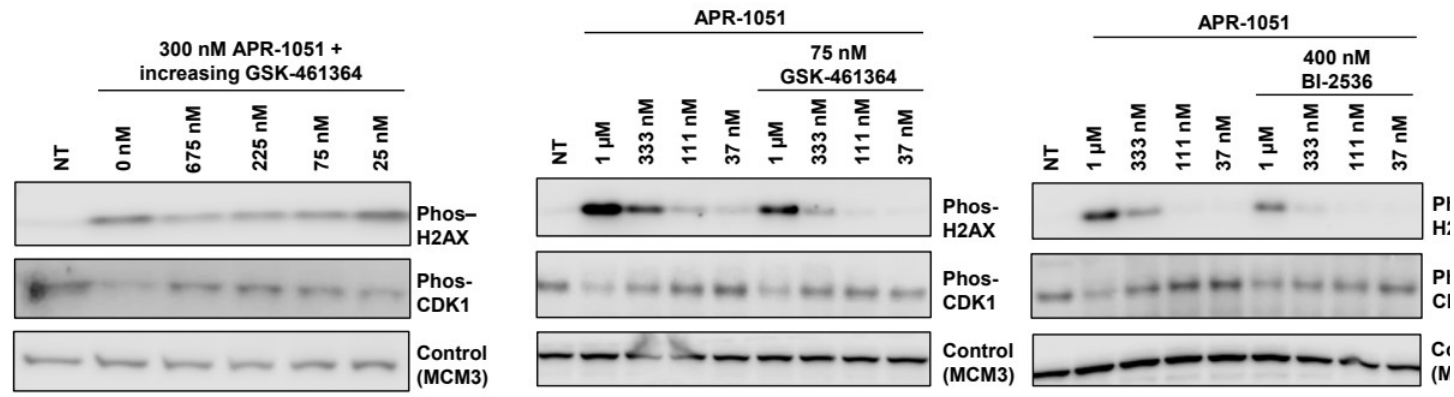
APREA THERAPEUTICS

[1]Huang et al, (2021) J Med Chem
[2]AstraZeneca announced in July 2022 the discontinuation of development of AZD-1775

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

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

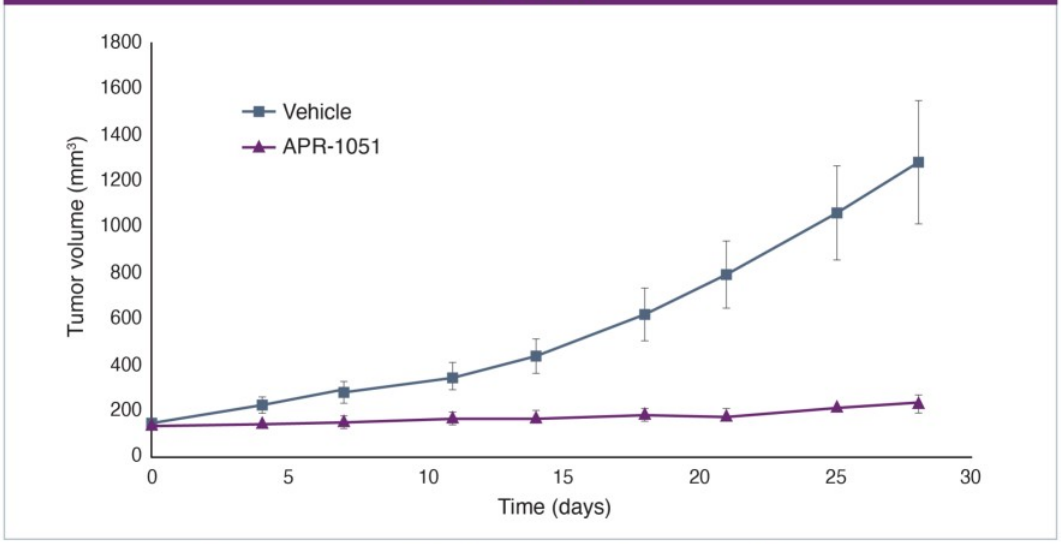
In vitro kinase assays IC50		Average WEE1 kinase IC50	hERG inhibition IC50		Average hERG IC50	Fold difference betw kinase IC50 and hE IC50
LanthaScreen (Thermo)	Hotspot (Reaction Biology)		HEK293 cells (Medicilon)	CHO cells (WuXi)		hERG inhibition over W kinase inhibition
2.2 nM	41.4 nM	**21.8 nM**	8,840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

No ECG changes related to APR-1051 were observed in IND enabling studies

APR-1051 Demonstrated Potentially Compelling Anti-tumor Activity In Pre-clinical Model

IND Cleared March 2024

Tumor Growth Inhibition
OVCAR-3



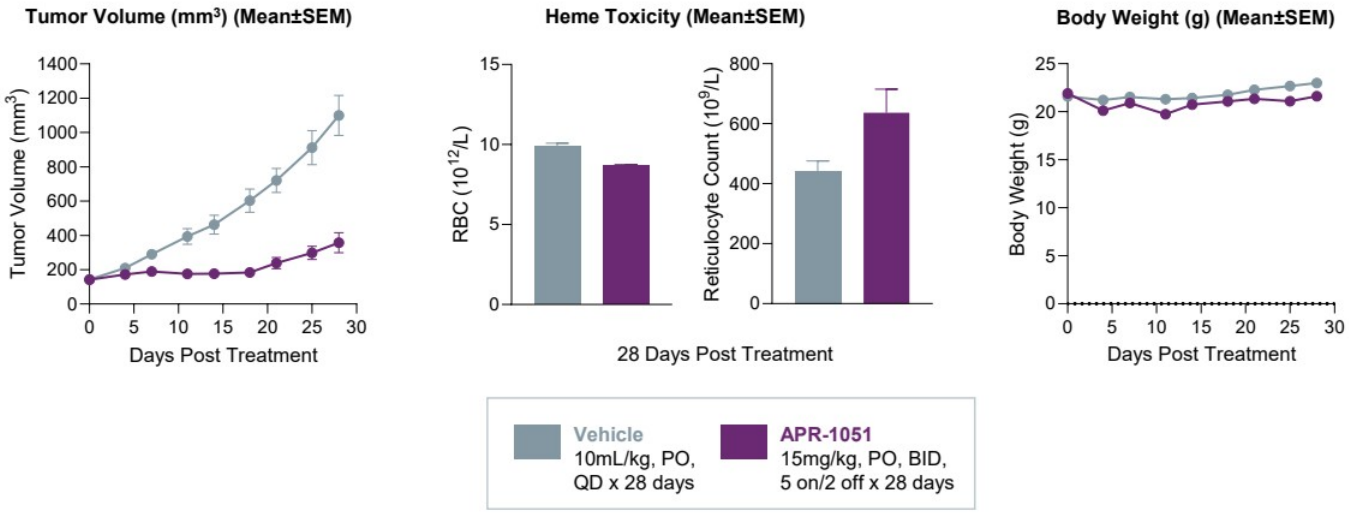
N=7 mice per group, APR-1051, exploratory formulation - 30 mg/kg/day

APREA THERAPEUTICS

Pre-clinical studies with APR-1051
Data on file

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

OVCAR Xenograft Tumor Model in Female Nude Mice



WEE1 Inhibitor: APR-1051

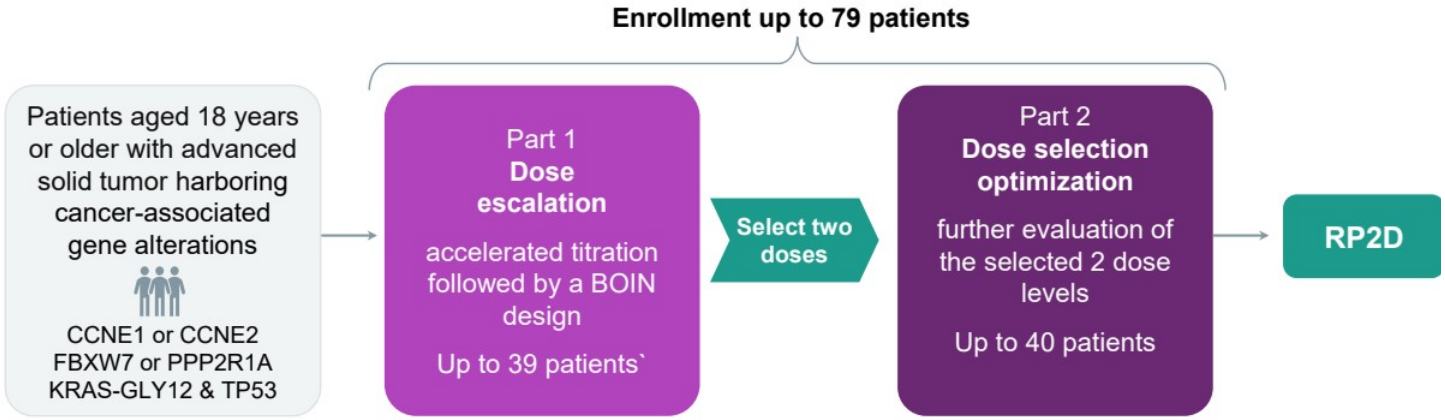
ACESOT-1051: Clinical Proof-of-Concep

APREA THERAPEUTICS

ACESOT-1051: Clinical Study Overview

Multi-center, Open-Label Phase1 Single-Agent Dose Escalation and Dose Selection Optimization

First patient to be enrolled in 1H 2024. Clinical update expected 4Q 2024



Oral APR-1051 will be administered once-daily for 28-day cycles

Primary objectives: Safety, DLT, MTD/MAD, RP2D

Secondary objectives: Pharmacokinetics, Antitumor activity (RECIST/PCWG3)

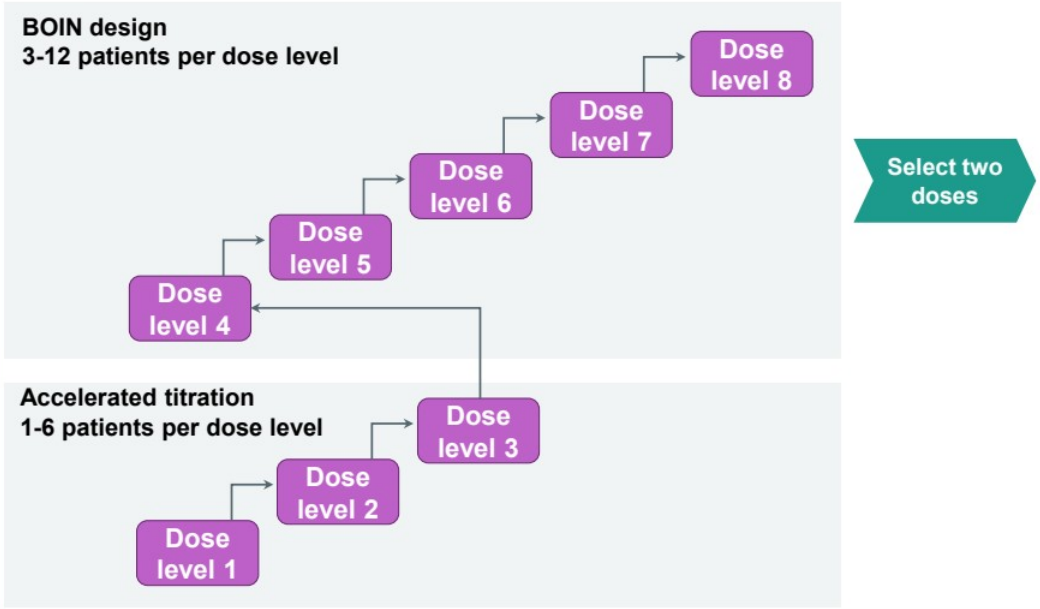
Exploratory objectives: Pharmacodynamics

APREA THERAPEUTICS

ACESOT-1051: Clinical Study Design

Part 1 - Single-agent APR-1051 Dose Escalation Study Schema

Up to 39 patients with advanced solid tumors harboring cancer-associated gene alterations:



APREA THERAPEUTICS

APR-1051: Summary

Potential best in class WEE1 inhibitor

- High potency for WEE1 inhibition in vitro
- Low off-target inhibition of the PLK family of kinases
- Suppresses growth of CCNE1-amplified HGSOC xenografted tumors and relatively well-tolerated in mice

ACESOT-1051: First-In-Human Study (NCT06260514)

- IND Cleared
- Biomarker-driven study in patients with advanced/metastatic solid tumors
- Targeted gene alterations include CCNE1, CCNE2, FBXW7, PPP2R1A, or KRASG12 with TP53
- First patient in (FPI) expected 1H 2024
- Clinical update expected 4Q 2024
- MD Anderson Cancer Center lead site, with up to 10 sites total in U.S

Aprea Therapeutics (NASDAQ: APRE)

Intellectual Property Portfol

Financial Summary & Capitalization

Investment Highlights

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 $32.4M as of March 31, 2024

Closed approximately $16.0M (before deducing placement agent fees and offering costs of approximately $1.3 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 May 14, 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	709,021
Restricted Stock Units	34,860
Fully Diluted Equivalents	8,904,072

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 (ATRN-119) and WEE1 (APR-1051) inhibitors
- Opportunities in ovarian, colorectal, prostate, and breast cancers
- Single agent and combination therapies

Near term catalysts

- 1H 2024 initiate APR-1051 Phase 1; clinical update 4Q 2024
- 2H 2024 potential efficacy ATRN-119; complete dose escalation 4Q 2024

Financed into 3Q 2025

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

APREA THERAPEUTICS