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

June 17, 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 8.01 Other Events.

On June 17, 2024, Aprea Therapeutics, Inc. (the "Company") issued a press release announcing that the first patient was dosed in the ACESOT-1051 Phase 1 trial evaluating oral WEE1 inhibitor APR-1051. A copy of the press release is filed as Exhibit 99.1 hereto and incorporated herein by reference.

On June 17, 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 June 17, 2024
99.2	Corporate Presentation (June 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: June 17, 2024

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

Aprea Therapeutics Announces First Patient Dosed in ACESOT-1051 Phase 1 Trial Evaluating Oral WEE1 Inhibitor APR-1051

APR-1051 is a highly selective and potentially best-in-class oral WEE1 inhibitor

Phase 1 ACESOT-1051 clinical trial is evaluating APR-1051 as monotherapy treatment in patients with significant unmet medical need

Dosing of the first patient in the ACESOT-1051 study represents a key advancement in Aprea's clinical pipeline

DOYLESTOWN, PA, June 17, 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 announced that the first patient has been dosed in the ACESOT-1051 Phase 1 study evaluating daily oral WEE1 inhibitor APR-1051 as monotherapy in advanced solid tumor patients with unmet medical need.

APR-1051 was discovered and preclinically evaluated by Aprea's team of chemists and scientists. APR-1051 is a potent and highly selective small molecule designed to limit off-target toxicity that may provide good safety and tolerability and has shown a potentially favorable drug exposure in pre-clinical models.

APR-1051 targets WEE1 kinase, an enzyme involved in the DNA damage response pathway. Based on preclinical studies, we believe APR-1051 may solve liabilities associated with other WEE1 inhibitors and is differentiated based on: 1) molecular structure; 2) selectivity for WEE1 versus off-target inhibition of the polo-like kinase, or PLK, family of kinases; 3) potentially improved pharmacokinetic (PK) properties; and 4) potential absence of QT prolongation at doses that significantly inhibit WEE1. No head-to-head studies with APR-1051 have been conducted.

ACESOT-1051 is a focused biomarker-driven study with advanced/metastatic solid tumors harboring the following cancer-associated gene alterations:

▪ Amplification/overexpression of CCNE1 or CCNE2 regardless of tumor type, or

▪ Deleterious mutations in FBXW7 or PPP2R1A regardless of tumor type, or

▪ Colorectal cancer with KRAS-GLY12 and TP53 co-mutation, or

▪ Uterine serous carcinoma regardless of biomarker status

"Dosing of the first patient in the ACESOT-1051 study is an important milestone in our APR-1051 development program and represents a key advancement of our clinical pipeline," said Oren Gilad, Ph.D., President and Chief Executive Officer of Aprea. "Adding a second clinical program enriches our asset portfolio. We are initially evaluating single agent activity of APR-1051 to provide the basis for future rational combination treatments. We hope to confirm APR-1051's safety profile in this Phase 1 study and generate the necessary data that will help us understand how it can be best utilized to treat patients. We plan to provide a clinical update by year-end 2024 and generate preliminary efficacy data during 2025."

The first patient was enrolled at NEXT Oncology, San Antonio, Texas. Additional centers, including The University of Texas MD Anderson Cancer Center, are expected to participate.

Anthony Tolcher M.D., Founder of Next Oncology commented, “NEXT Oncology is committed to exploring new treatment options for cancer patients and we are pleased to begin this important clinical trial. Cancers that over express Cyclin E (CCNE1 and CCNE2) represent a high unmet medical need, and patients with Cyclin E over expression have poor prognosis and no effective therapies. WEE1 kinase is a validated oncology target and we look forward to the results of this study.”

ACESOT-1051 Study Design

ACESOT-1051 (**A** Multi-**C**enter **E**valuation of WEE1 Inhibitor in Patients with Advanced **So**lid **T**umors, APR-1051) is designed to assess the safety, pharmacokinetics, pharmacodynamics, and preliminary efficacy of single-agent APR-1051 in advanced solid tumors harboring cancer-associated gene alterations. Oral APR-1051 will be administered once daily for 28-day cycles. The study consists of two parts: Part 1 is dose escalation and is expected to enroll up to 39 patients with advanced solid tumors. The first three dose levels will use accelerated titration followed by Bayesian Optimal Interval (BOIN) design for the remaining dose levels; Part 2 (up to 40 patients) is designed for dose optimization, with the goal of selecting the Recommended Phase 2 Dose (RP2D).

The primary objectives of the study are to measure safety, dose-limiting toxicities (DLTs), maximum tolerated dose or maximum administered dose (MTD/MAD), and RP2D; secondary objectives are to evaluate pharmacokinetics, preliminary efficacy according to RECIST or PCWG3 criteria; pharmacodynamics is an exploratory objective. The University of Texas MD Anderson Cancer Center is the lead site, and the study will be performed at between 3 and 10 sites in the U.S.

The ACESOT-1051 design was featured in a poster at the American Association of Cancer Research (AACR) annual meeting which took place in April 2024 in San Diego. A copy of the poster can be found here. For more information, refer to ClinicalTrials.gov NCT06260514.

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. APR-1051, an oral, small molecule WEE1 inhibitor, recently entered the clinic. 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

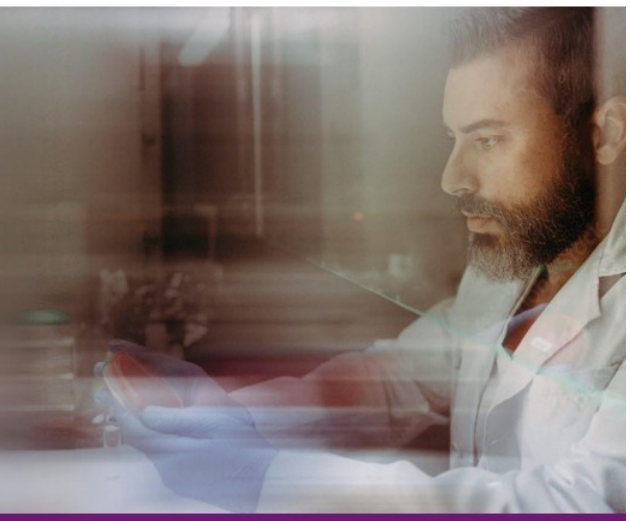
statements regarding our ability to develop, commercialize, and achieve market acceptance of our current and planned products and services, our research and development efforts, including timing considerations and other matters regarding our business strategies, use of capital, results of operations 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

Precision Oncology Through Synthetic Lethality



June 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
- First patient dosed June 2024
- Study update 4Q 2024

DDR Inhibitor: Undisclosed

- Lead optimization
- Target identified from our RepliBior discovery platform

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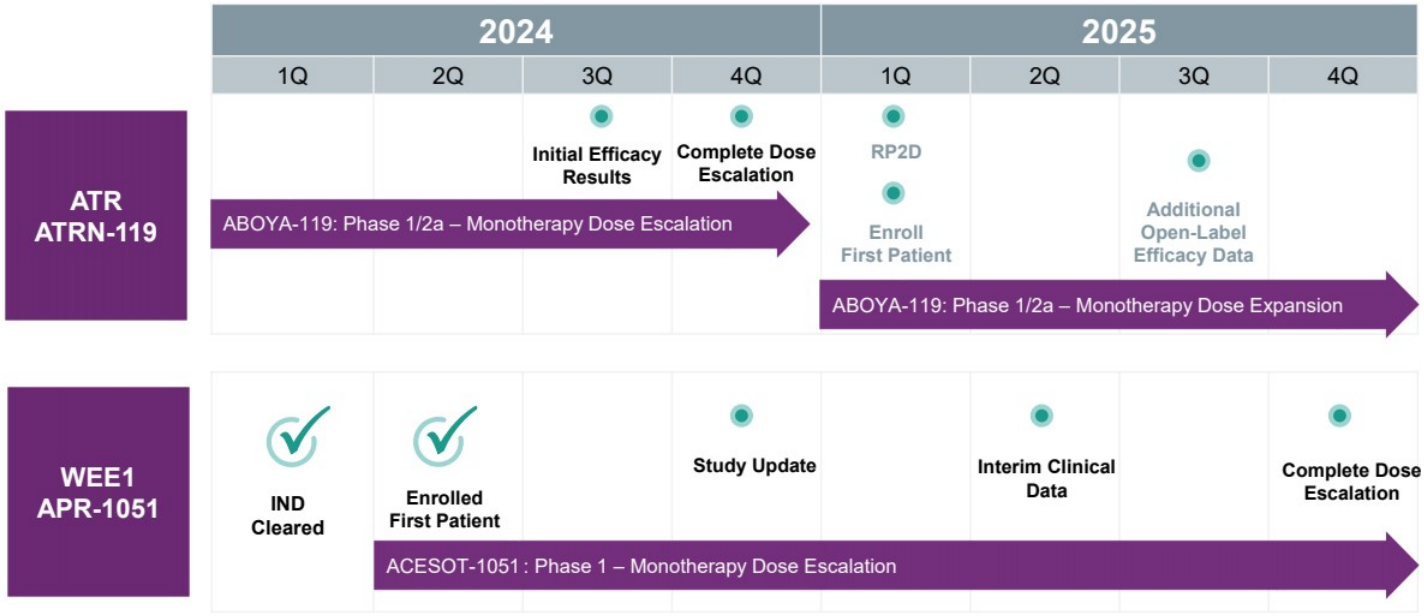
ATR - Ataxia telangiectasia and Rad3-related
DDR – DNA Damage Response

Robust DDR Development Pipeline Milestones

2024-2025 Anticipated Clinical Milestones



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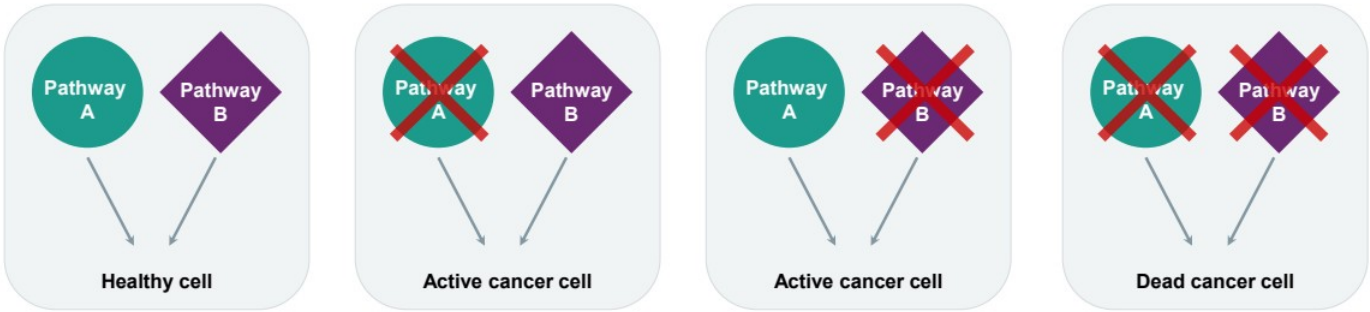
Synthetic Lethality



- 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]

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[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 Differentiated Clinical Stage ATRi

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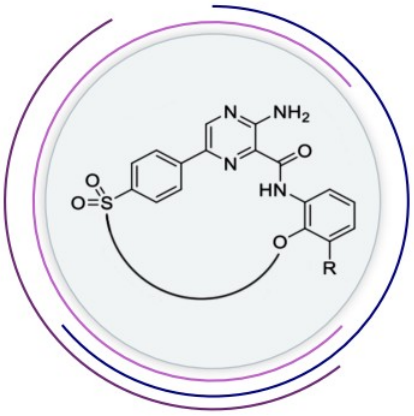
ATRN-119: First and Only Macrocyclic ATR Inhibitor[1]

Macrocycles: A Well-Evolved Approach for PIK-Related Kinase Inhibition (e.g., rapamycin and mTOR)[2-4]



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

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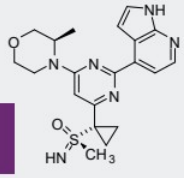
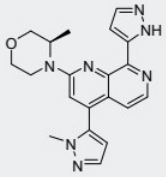
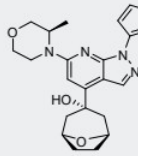
Reported Challenges with Other ATR Inhibitors

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

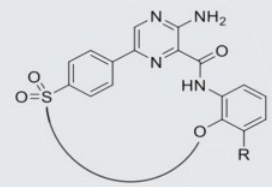
[2] Poster CT084: A Phase I dose-escalation study of ATR inhibitor monotherapy with AZD6738 in advanced solid tumors (PATRIOT Part A), AACR 2017

[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

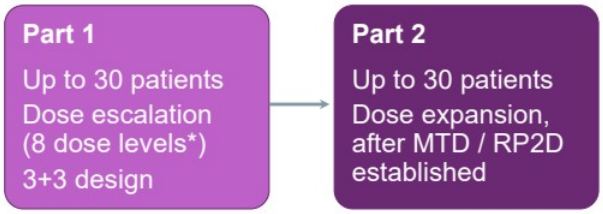
Patient enrollment:
Up to 60 patients in total

- 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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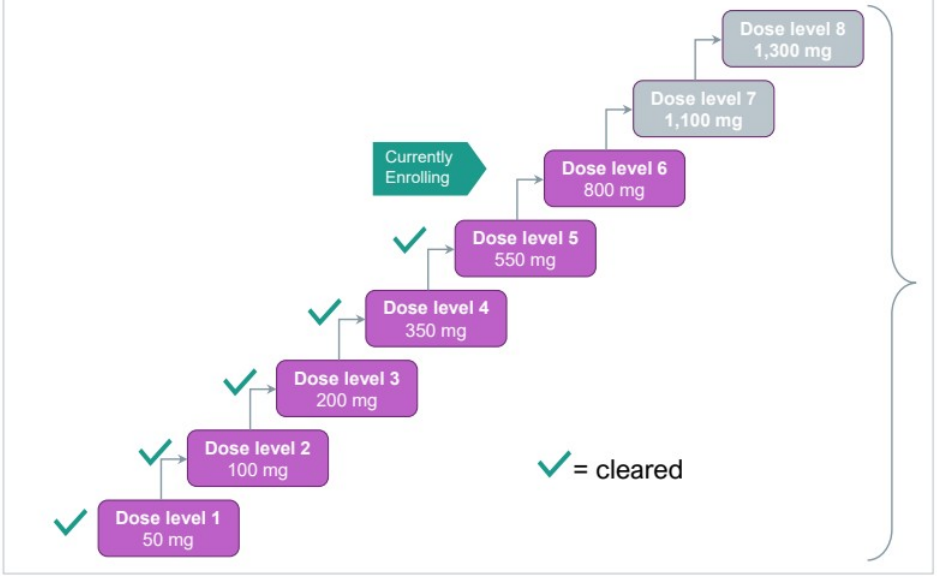
*Protocol amendment adding cohorts 7 and 8

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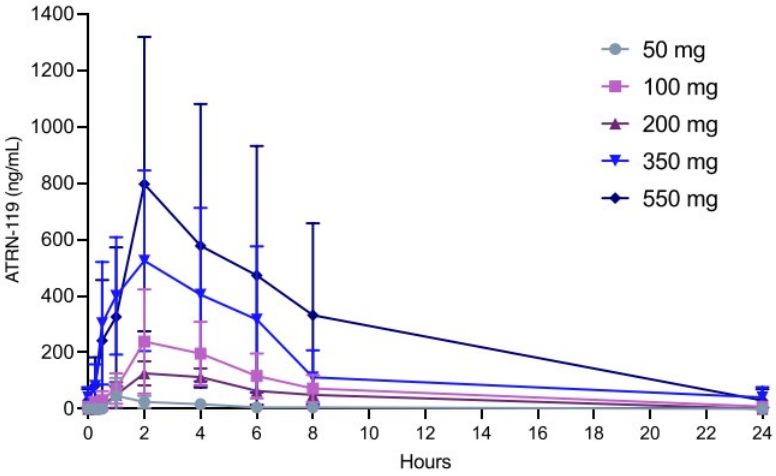
ATRN-119 Steady State Plasma Concentrations (Cycle 1 Day 7)

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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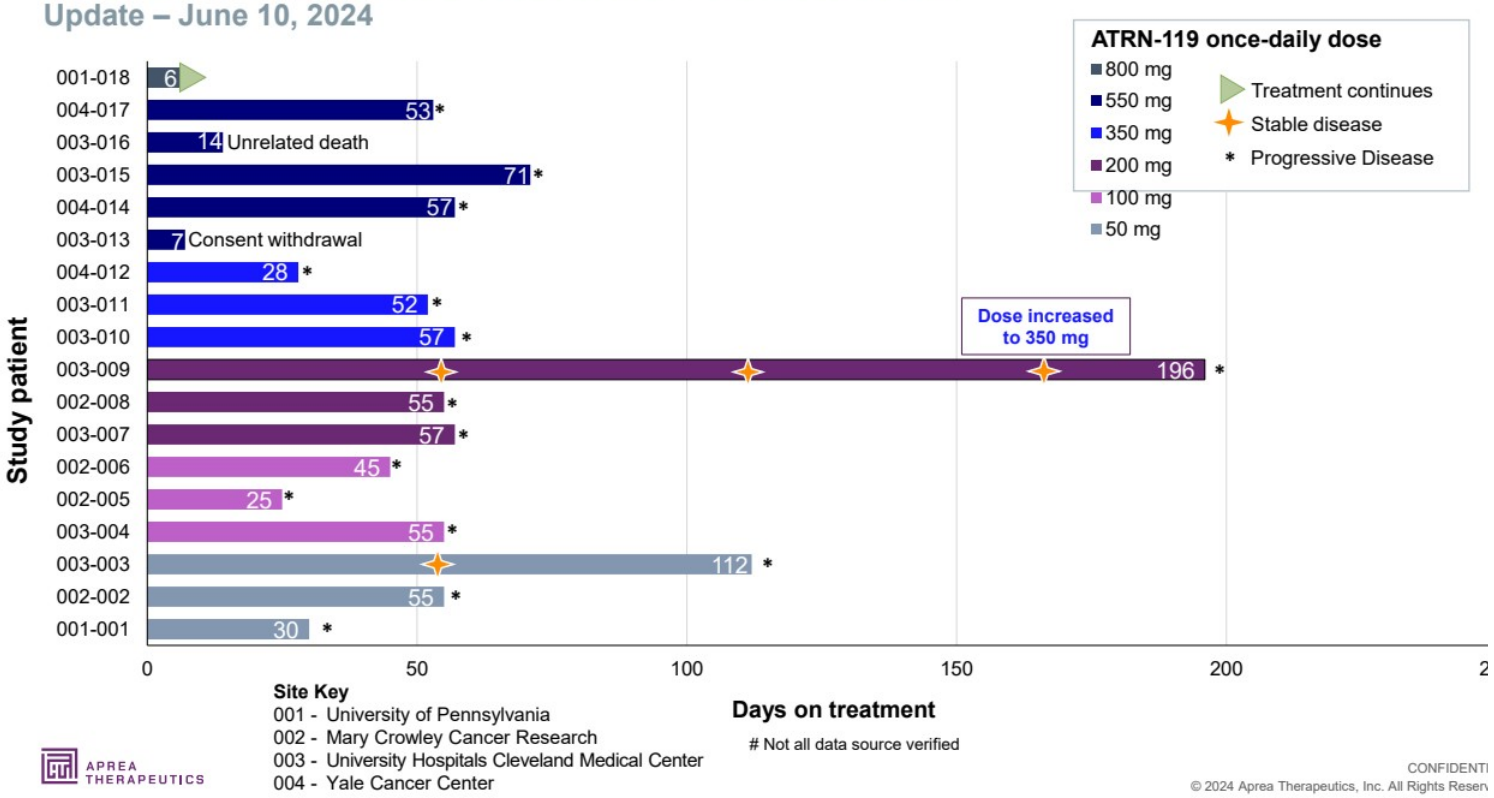
Presented at AACR 2024

ABOYA-119: Summary of Duration of Treatment#

Update – June 10, 2024



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

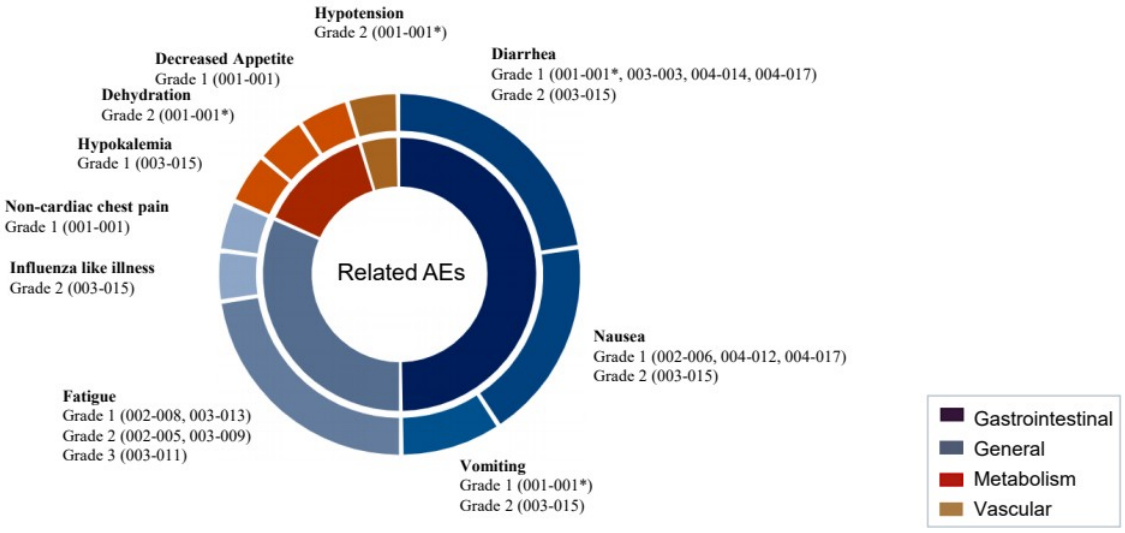
Not all data source verified

APREA THERAPEUTICS

ABOYA-119: Summary of Related Adverse Events

Update - June 10, 2024

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



* Resulted in treatment interruption
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 Differentiated Clinical Stage 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

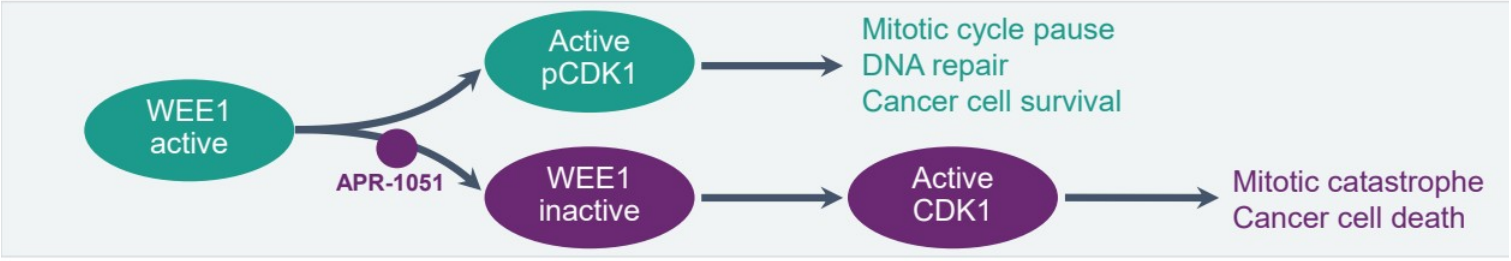
2 Phase II Study of the WEE1 Inhibitor Adavosertib in Recurrent Uterine Serous Carcinoma, Liu et al, J Clin Oncol 2021;39:1531–9.

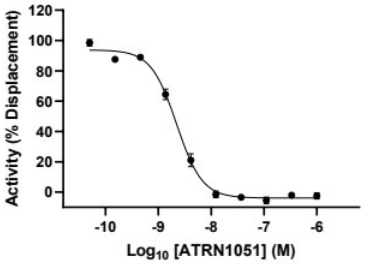
3 IGNITE: A phase II signal-seeking trial of Adavosertib targeting recurrent high-grade, serous ovarian cancer with cyclin E1 overexpression with and without gene amplification. Au-Yeung et Gynecol Cancer 2023;33(Suppl 4):A1–A278

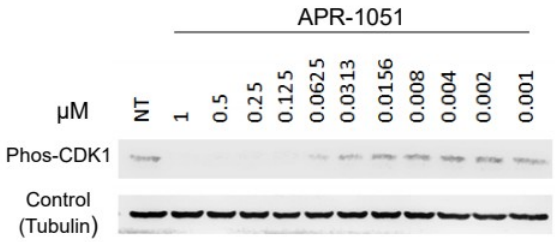
4 Multicenter Phase II Trial of the WEE1 Inhibitor Adavosertib in Refractory Solid Tumors Harboring CCNE1 Amplification, Fu et al, J Clin Oncol. 2023 Mar 20; 41(9): 1725–1734.

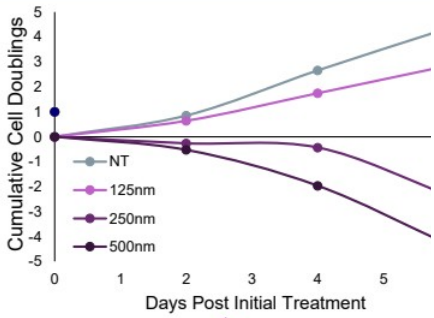
APREA THERAPEUTICS

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









APR-1051 binds to WEE1

…inhibits its biological activity…

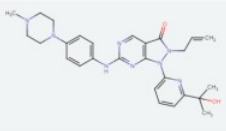
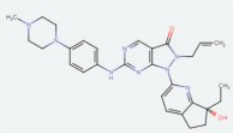
…and triggers mitotic catastrophe and cancer cell death

APREA THERAPEUTICS

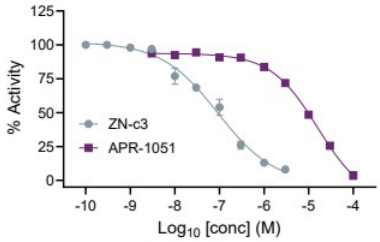
pCDK1- Phosphorylated Cyclin Dependent Kinase 1
Data on file

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]	 Aprea APR-1051
On-Target IC_{50} (nM)	**WEE1**	3.8	3.8	1.9

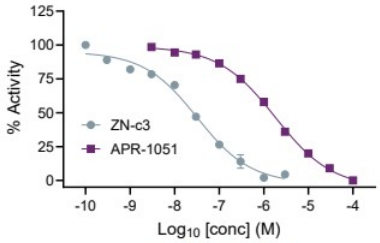
PLK1 IC_{50} Determination



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

PLK1 Inhibition
IC50 values show >150-fold

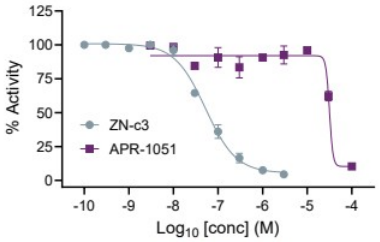
PLK2 IC_{50} Determination



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

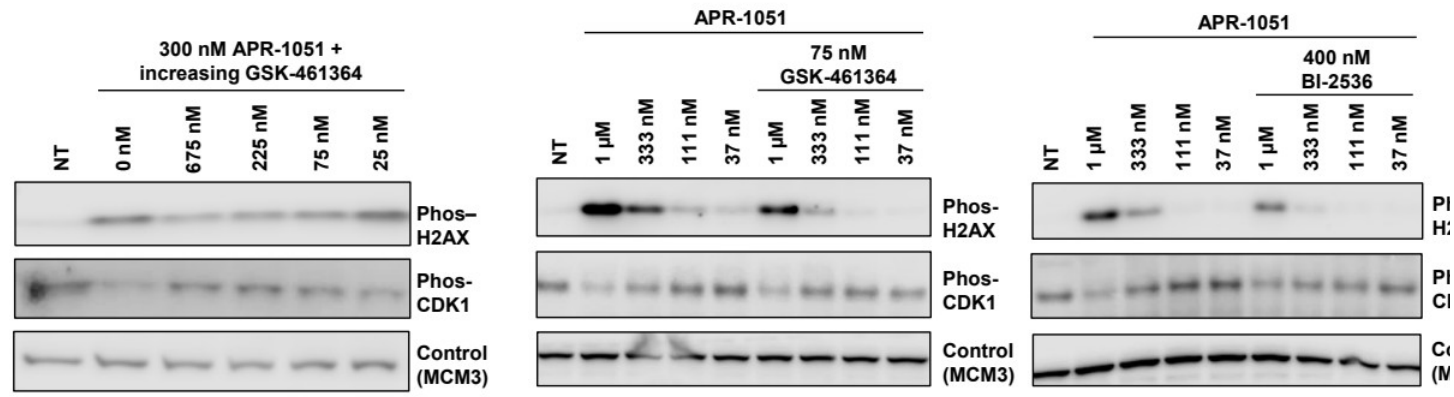
APREA THERAPEUTICS

[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

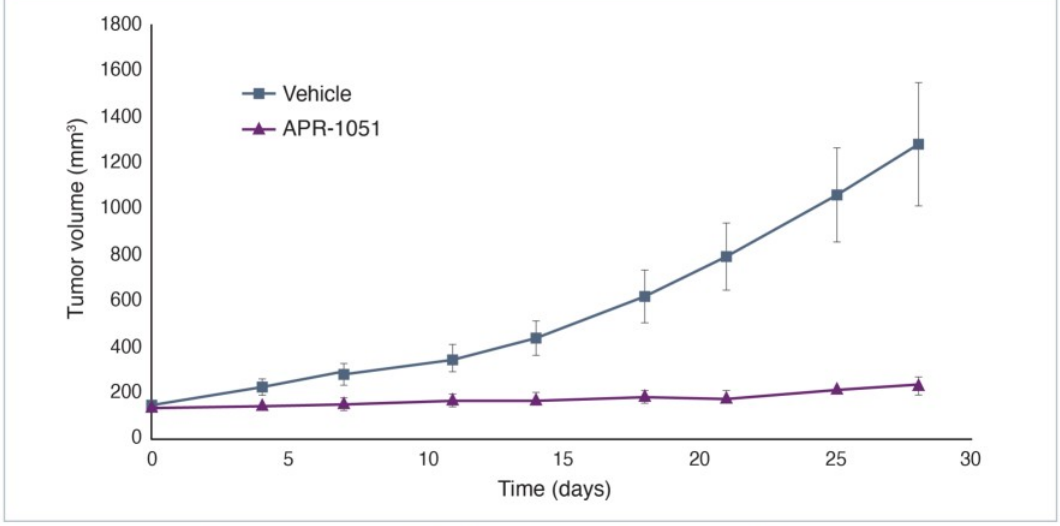
QT prolongation AEs were reported with some competitor WEE1 inhibitors

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
Potential absence of QT prolongation at doses that significantly inhibit WEE1

APR-1051 Demonstrated Potentially Compelling Anti-tumor Activity

Preclinical Tumor Growth Inhibition
OVCAR-3



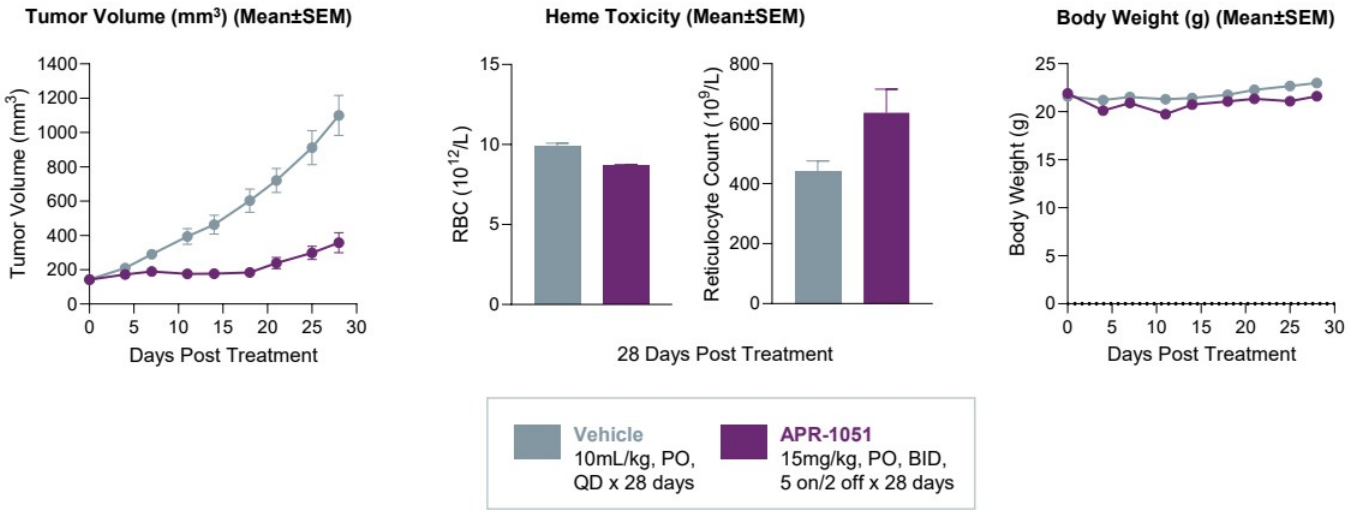
N=7 mice per group, APR-1051, exploratory formulation - 30 mg/kg/day

APREA THERAPEUTICS

Pre-clinical studies with APR-1051
Data on file

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

OVCAR Xenograft Tumor Model in Female Nude Mice



WEE1 Inhibitor: APR-1051

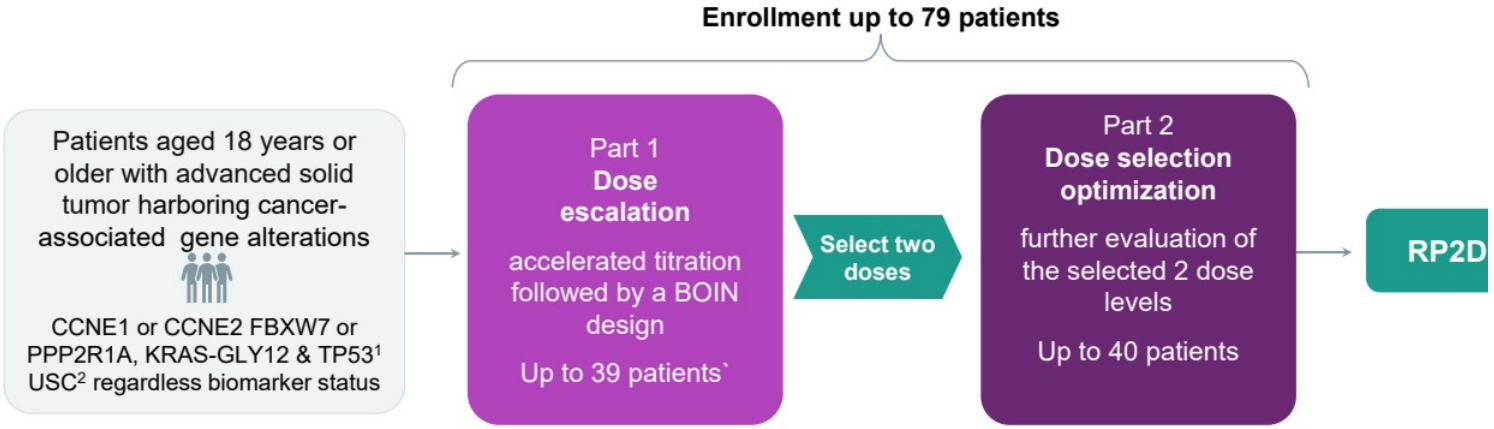
ACESOT-1051: Clinical Proof-of-Concep

APREA THERAPEUTICS

ACESOT-1051: Clinical Study Overview

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

First patient dosed in June 2024. Study 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

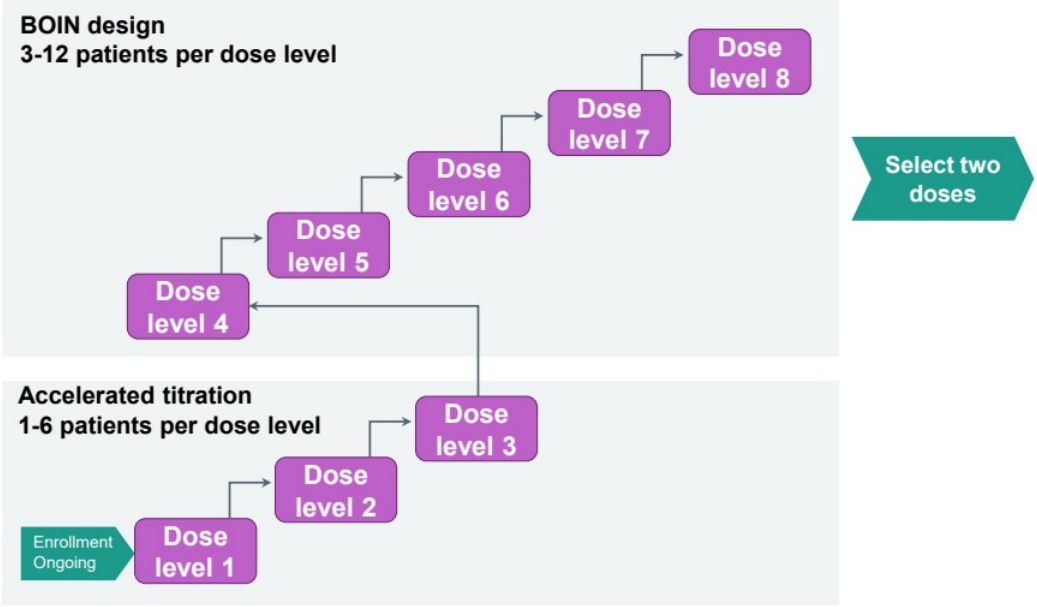
APREA THERAPEUTICS

[1] Colorectal cancer patients
[2] Uterine serous carcinoma patients

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)

- First patient dosed June 2024
- Biomarker-driven study in patients with advanced/metastatic solid tumors
- Targeted gene alterations include CCNE1, CCNE2, FBXW7, PPP2R1A, or KRAS-G12 with TP53
- Study update expected 4Q 2024
- MD Anderson Cancer Center lead study site, with up to 10 sites 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

- 4Q 2024 study update APR-1051 Phase 1
- 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