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

January 13, 2025
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 January 13, 2025, Aprea Therapeutics, Inc. (the "Company") posted an updated corporate presentation slide deck (the "Corporate Presentation") to its website. In the Corporate Presentation, the Company disclosed that, as of December 31, 2024, it had a cash and cash equivalents balance of $22,800,000. The foregoing financial information is unaudited and preliminary, does not present all information necessary for an understanding of the Company's financial condition as of December 31, 2024, and remains subject to completion of the Company's financial statements for the fiscal year ended December 31, 2024.

A copy of the Corporate Presentation is furnished as Exhibit 99.1 to this Form 8-K and incorporated herein by reference.

The information included in Item 2.02 (including Exhibit 99.1) of this Form 8-K, shall not be deemed to be "filed" for 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 to be incorporated by reference in any Company filing under the Securities Act or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

The Company disclosed that, as of December 31, 2024, it had a cash and cash equivalents balance of $22,800,000. The foregoing financial information is unaudited and preliminary, does not present all information necessary for an understanding of the Company's financial condition as of December 31, 2024, and remains subject to completion of the Company's financial statements for the fiscal year ended December 31, 2024.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Corporate Presentation (January 2025).
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.

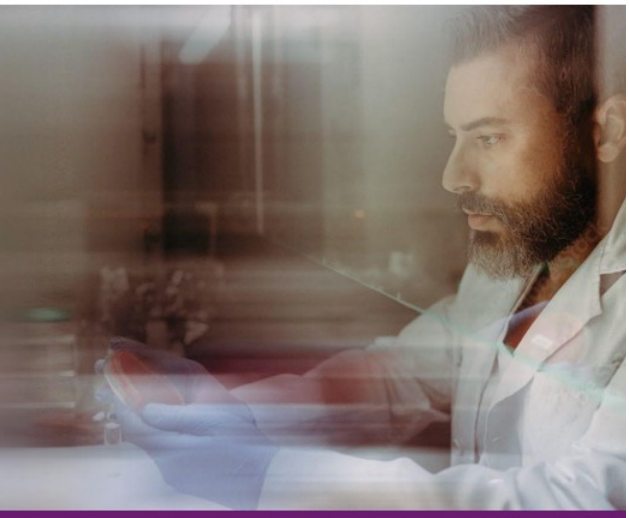
Aprea Therapeutics, Inc.

Dated: January 13, 2025

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

APREA THERAPEUTICS

Precision Oncology Through Synthetic Lethality



January 2025

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

WEE1 Inhibitor: APR-1051

- Best in class, next generation
- Well clinically validated target
- 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)
  - Favorable pharmacokinetics
- Phase 1 study – enrolling 4th cohort
- No hematologic toxicity observed
- Safety/efficacy data expected H1 2025

ATR Inhibitor: ATRN-119

- First macrocyclic ATR inhibitor
- Highly selective with continuous daily dosing
- Pre-clinical proof-of-principle
  - Anti-tumor activity at nanomolar concentration
  - Preserved hematologic safety profile
- Phase 1/2a – ongoing
  - Approaching therapeutic dose
  - No hematologic toxicity observed
  - BID regimen added
  - Readout H2 2025

DDR Inhibitor: Undisclosed

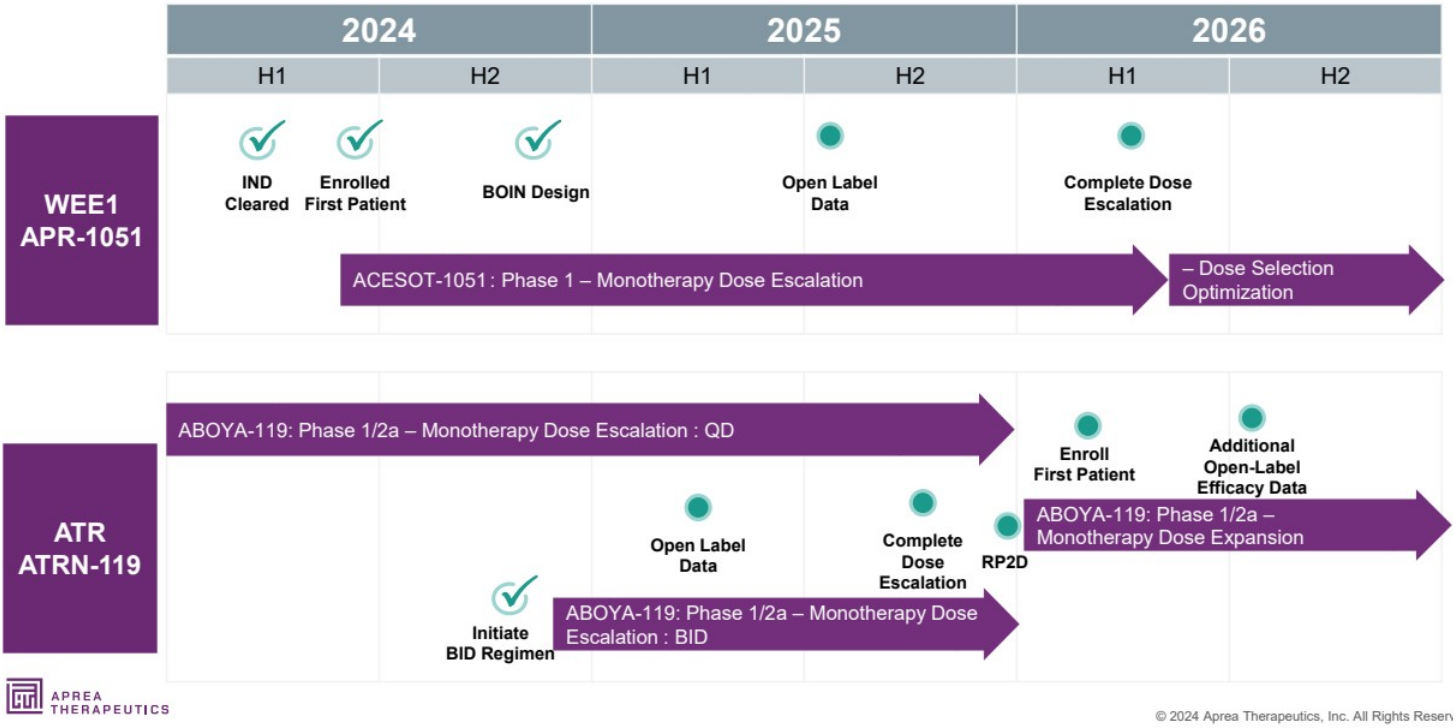
- Lead optimization
- Target identified from our RepliBior discovery platform
- Identify lead candidate by year-enc 2024

APREA THERAPEUTICS

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

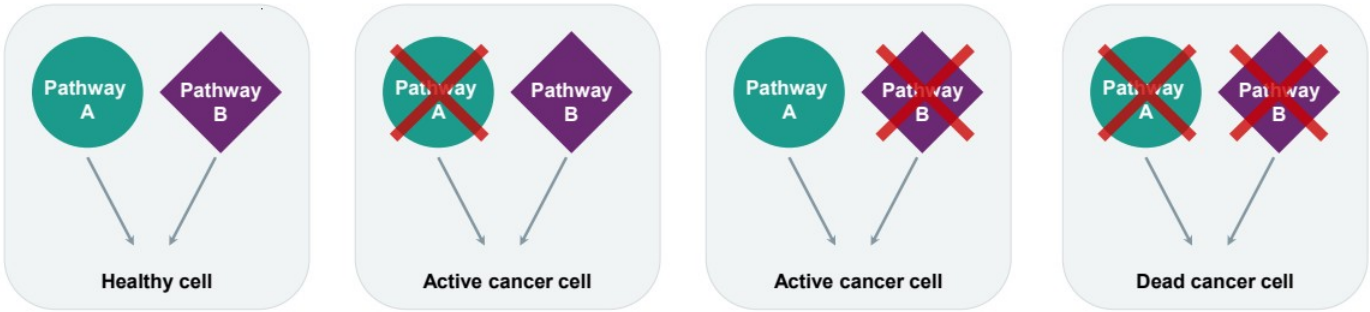
Robust DDR Development Pipeline Milestones

2024-2026 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) overcoming affected pathway
- 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.

Strong Drug Development and Commercial Expertise

Leaders in Synthetic Lethality and Targeted Therapy

Management

Oren Gilad, Ph.D. President and CEO	**John P. Hamill** Sr. Vice President and CFO	**Philippe Pultar, MD** Head of WEE1 Clinical Development	**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	zentalis NOVARTIS agennix ImClone Systems	ATRIN Pharmaceuticals INTEC PHARMA pwc	inipharm ATRIN Pharmaceuticals MERCK Bristol Myers Squibb presage MaYu PHARMA	Boston BioConsulting NewL Gloucester Celg Aventis MILLENN

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

WEE1 Inhibitor: APR-1051

Potentially Differentiated Clinical Stage WEE1i

APREA THERAPEUTICS

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 months 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 week 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 an improved 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.

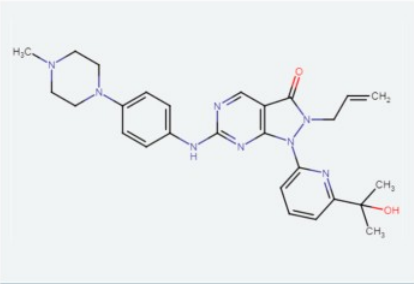
[3] IGNITE: A phase II signal-seeking trial of Adavosertib targeting recurrent high-grade, serous ovarian cancer with cyclin E1 overexpression with and without gene amplification. Au-Yeung et al, *Int J Gynecol Cancer* 2023;33(Suppl 4):A1–A278

[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.

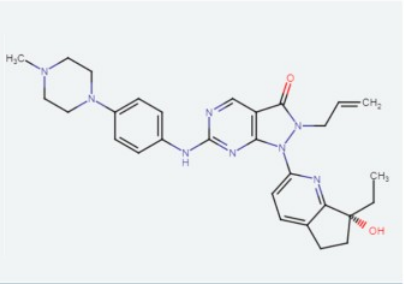
APREA THERAPEUTICS

APR-1051 Potentially Best in Class WEE1 Inhibitor

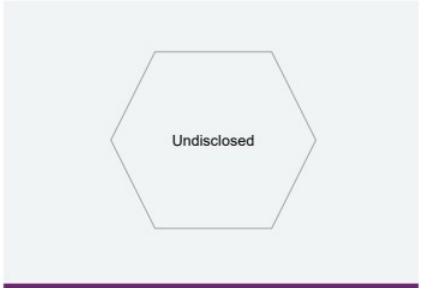
Potent and Structurally Differentiated, with High Selectivity to Limit Off-target Toxicity



AstraZeneca
Adavosertib (AZD-1775)



Zentalis
Azenosertib (ZN-c3)



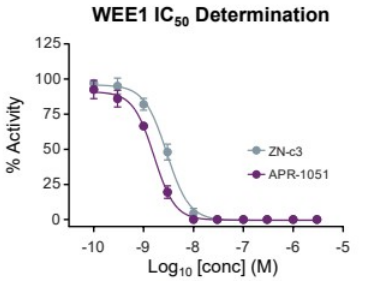
Aprea
APR-1051

APR-1051: Potentially Best-in-Class WEE1 Inhibitor

Potent WEE1i that Does Not Substantially Inhibit PLK1, PLK2 or PLK3

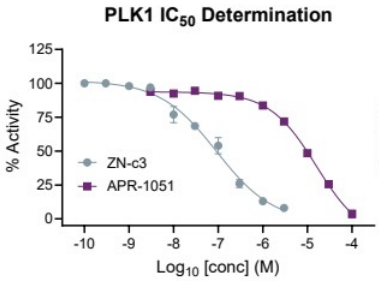
On-target WEE1 activity

Off-target inhibition of PLK1, PLK2 and PLK3



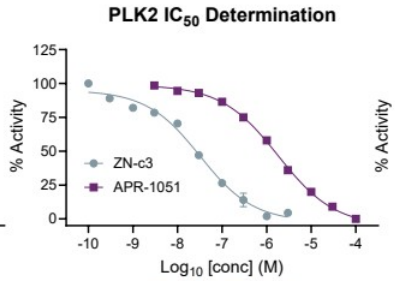
ZN-c3 = 2.9 nM
APR-1051 = 1.6 nM

WEE1 Inhibition
IC50 similar to ZN-c3



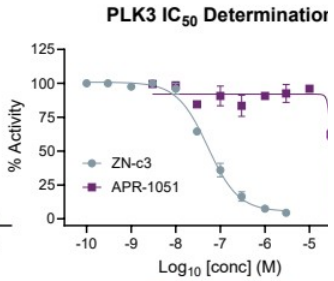
ZN-c3 = 92.1 nM
APR-1051 = 15,900 nM

PLK1 Inhibition
IC50 >150-fold difference



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

PLK2 Inhibition
IC50 >50-fold difference



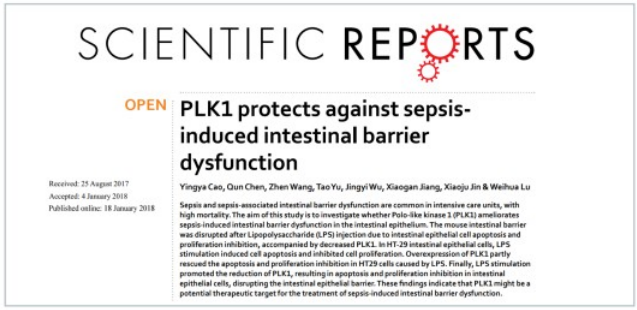
ZN-c3 = 52.2 nM
APR-1051 = 31,600 nM

PLK3 Inhibition
IC50 >600-fold difference

APREA THERAPEUTICS

AACR-NCI-EORTC Meeting, Poster B323, 20

Studies Show PLK1 Suppression is Associated with Sepsis-Induced Loss of Intestinal Barrier Function



SCIENTIFIC REPORTS

OPEN

PLK1 protects against sepsis-induced intestinal barrier dysfunction

Received: 25 August 2017
Accepted: 4 January 2018
Published online: 18 January 2018

Yingya Cao, Qun Chen, Zhen Wang, Tao Yu, Jingyi Wu, Xiaogan Jiang, Xiaoju Jin & Weihua Lu

Sepsis and sepsis-associated intestinal barrier dysfunction are common in intensive care units, with high mortality. The aim of this study is to investigate whether Polo-like kinase 1 (PLK1) ameliorates sepsis-induced intestinal barrier dysfunction in the intestinal epithelium. The mouse intestinal barrier was disrupted after Lipopolysaccharide (LPS) injection due to intestinal epithelial cell apoptosis and proliferation inhibition, accompanied by decreased PLK1. In HT-29 intestinal epithelial cells, LPS stimulation induced cell apoptosis and inhibited cell proliferation. Overexpression of PLK1 partly rescued the apoptosis and proliferation inhibition in HT29 cells caused by LPS. Finally, LPS stimulation promoted the reduction of PLK1, resulting in apoptosis and proliferation inhibition in intestinal epithelial cells, disrupting the intestinal epithelial barrier. These findings indicate that PLK1 might be a potential therapeutic target for the treatment of sepsis-induced intestinal barrier dysfunction.

Cao et al. Molecular Medicine (2022) 28:163
https://doi.org/10.1186/s10020-022-00597-z

Molecular Medicine

RESEARCH ARTICLE Open Access

PLK1 protects intestinal barrier function during sepsis by targeting mitochondrial dynamics through TANK-NF-κB signalling

Ying-Ya Cao[1,2†], Yuan Zhang[1†], Wuyun Gerile[1†], Yan Guo[1], Li-Na Wu[1], Li-Li Wu[1], Kai Song[1], Wei-Hua Lu[2] and Jian-Bo Yu[1*]

Contents lists available at ScienceDirect

Cytokine

journal homepage: www.elsevier.com/locate/cytokine

ELSEVIER

PLK1 protects intestinal barrier function in sepsis: A translational research

Ying-Ya Cao [a,b,1], Juan Li [c,1], Qun Chen [a,b,1], Yu-Peng Qi [a,b,1], Qian-Cheng Xu [a,b], Jia-Min He [a,b], Zhen Wang [d], Wei-Hua Lu [a,b,*]

[a] Department of Critical Care Medicine, The First Affiliated Hospital of Wannan Medical College (Yijishan Hospital of Wannan Medical College), Wuhu 241001, Anhui, China
[b] Anhui Province Clinical Research Center for Critical Respiratory Medicine, Wuhu 241001, Anhui, China
[c] Department of Nephrology, Wuhu Hospital, East China Normal University (The Second People's Hospital, Wuhu), Wuhu 241000, Anhui, China
[d] Department of General Practice, The First Affiliated Hospital of Wannan Medical College (Yijishan Hospital of Wannan Medical College), Wuhu 241001, Anhui, China

Received: 15 February 2021 | Revised: 25 April 2021 | Accepted: 16 May 2021
DOI: 10.1002/cbin.11633

RESEARCH ARTICLE

Cell Biology International WILEY

LncRNA DANCR improves the dysfunction of the intestinal barrier and alleviates epithelial injury by targeting the miR-1306-5p/PLK1 axis in sepsis

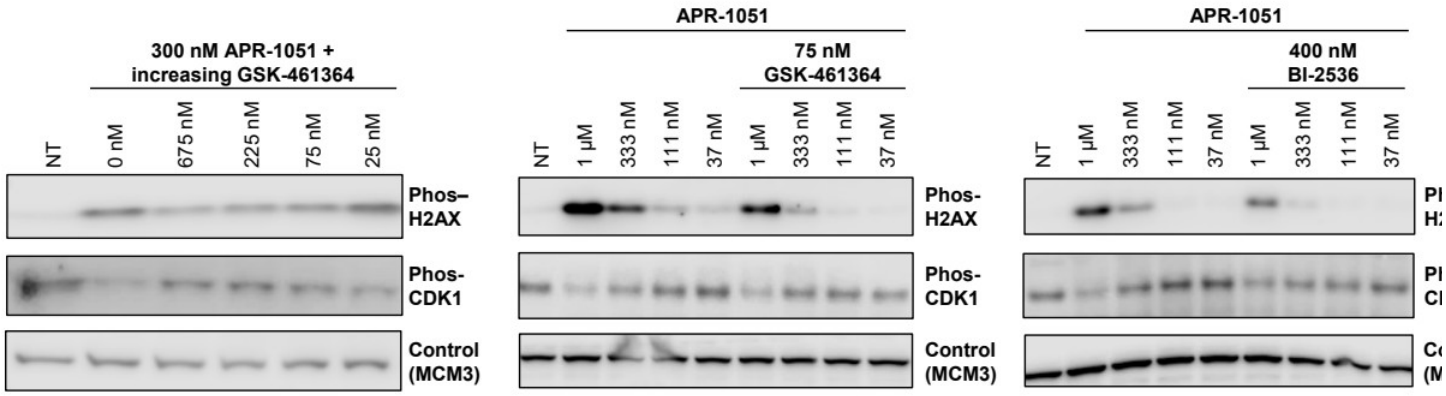
Zhen Wang[1] | Changshun Zhong[1] | Yingya Cao[1] | Hongzhen Yin[1] | Guanggui Shen[1] | Weihua Lu[1] | Wei Ding[2]

1 PLK1 protects against sepsis-induced intestinal barrier dysfunction, Cao et al, *Scientific Reports* (2018).
2 PLK1 protects intestinal barrier function in sepsis: A translational research, Cao et al, *Cytokine* (2023).
3 PLK1 protects intestinal barrier function in sepsis: A translational research, Cao et al, *Molecular Medicine* (2022).
4 LncRNA DANCR improves the dysfunction of the intestinal barrier and alleviates epithelial injury by targeting the miR-1306-5p/PLK1 axis in sepsis, Wang et al., *Cell Biology International* (2021).

APREA THERAPEUTICS

PLK1 Inhibition Reduces Cytotoxic Effects of WEE1 Inhibitors

Minimal PLK1 Co-inhibition Enables Full Therapeutic Potential Of 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 B323, 20

APR-1051 Preclinical Data Highlight Potentially Favorable PK Properti

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

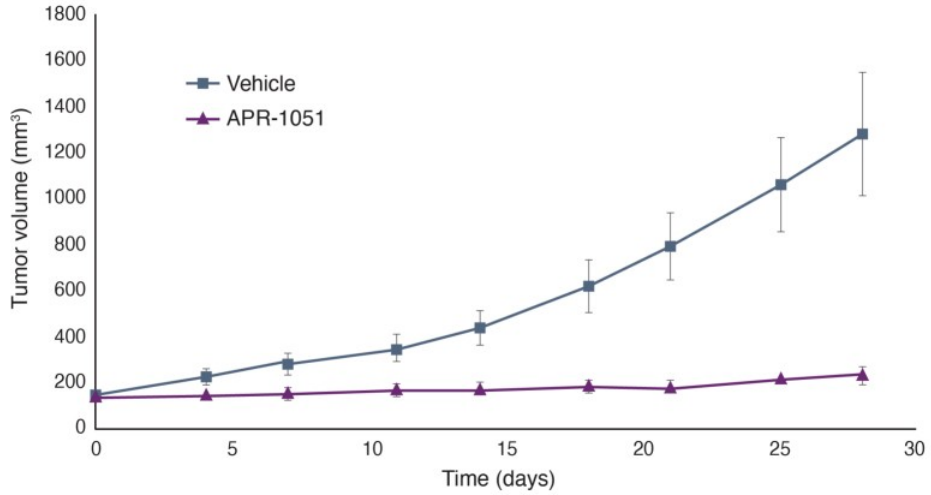
QT prolongation AEs were reported with some competitor WEE1 inhibitors

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



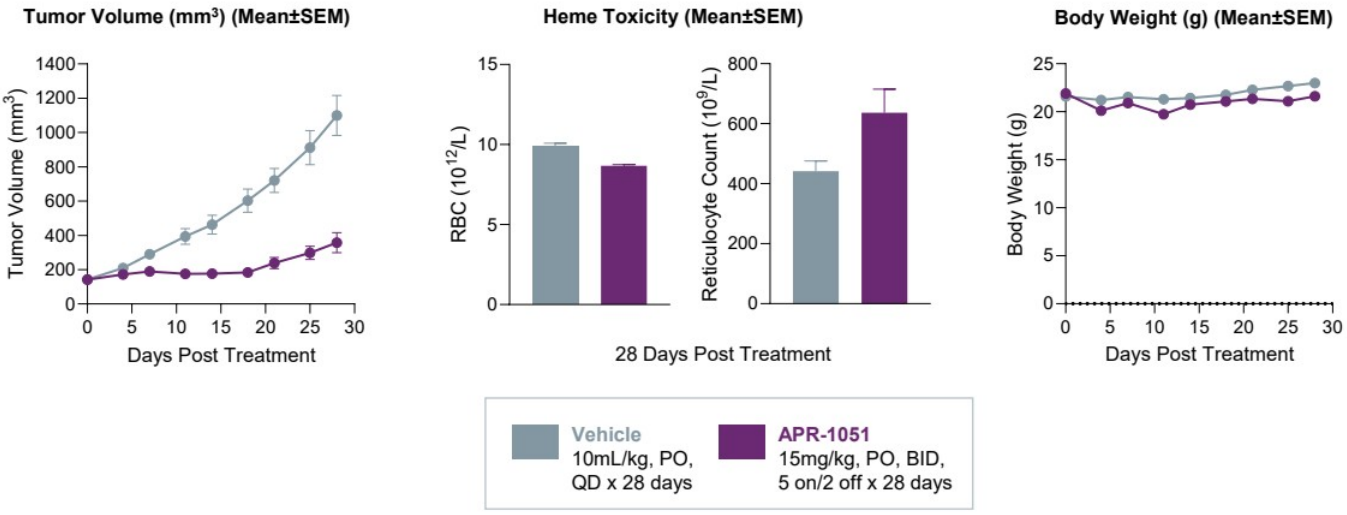
N=7 mice per group, APR-1051, 30 mg/kg/day

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



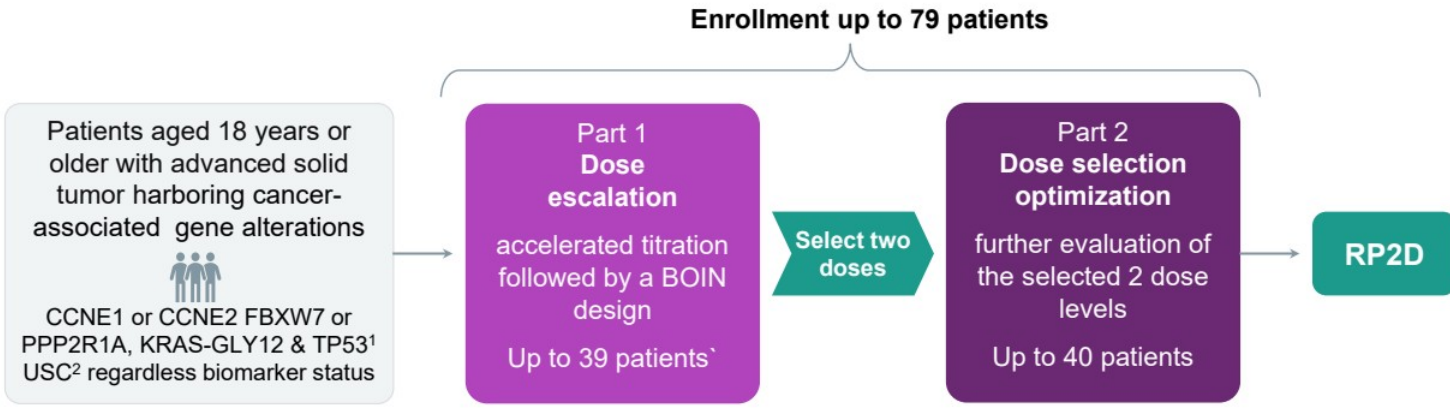
WEE1 Inhibitor: APR-1051

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



Oral APR-1051 is administered once-daily for 28-day cycles

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

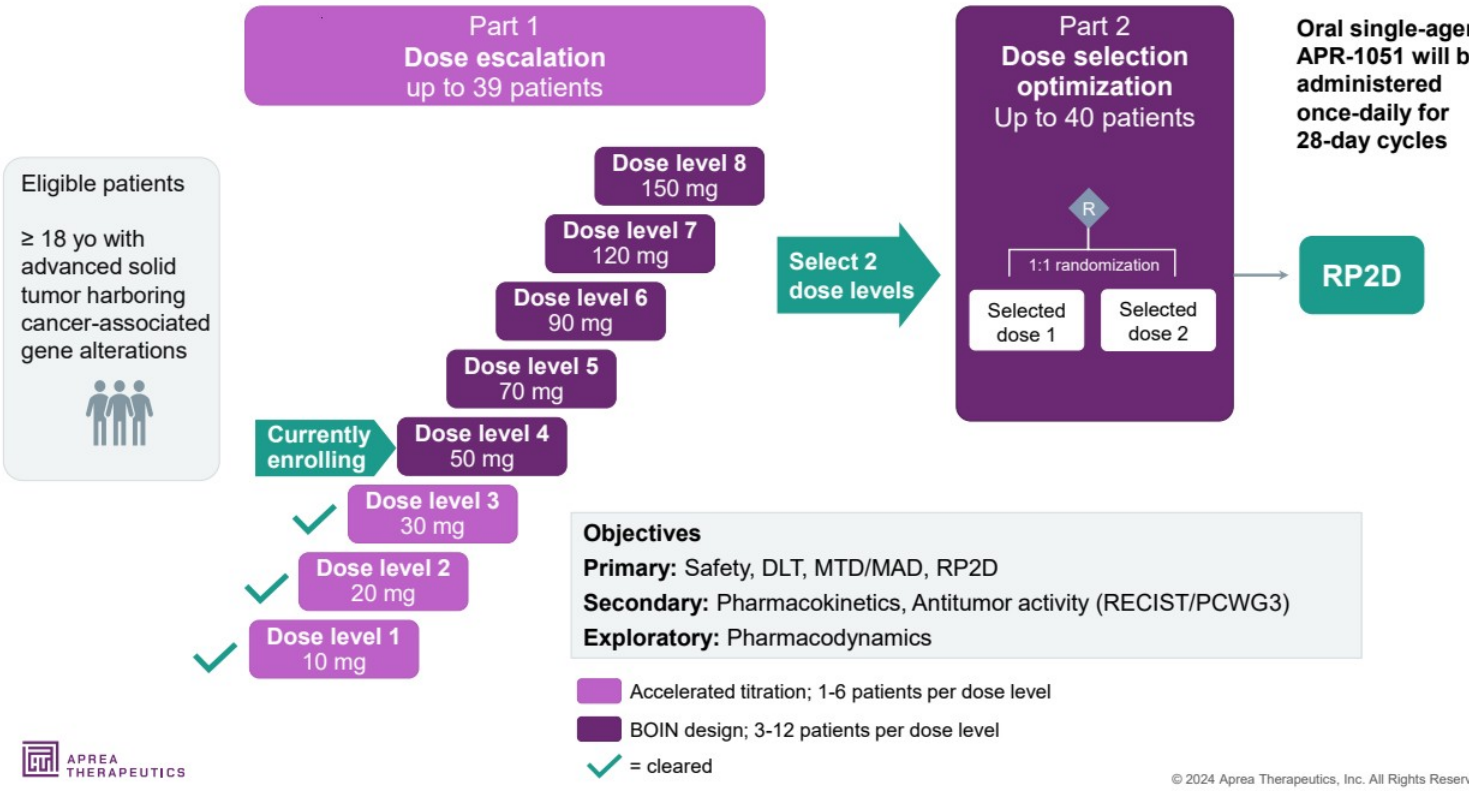
Secondary objectives: Pharmacokinetics, Antitumor activity (RECIST/PCWG3)

Exploratory objectives: Pharmacodynamics

APREA THERAPEUTICS

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

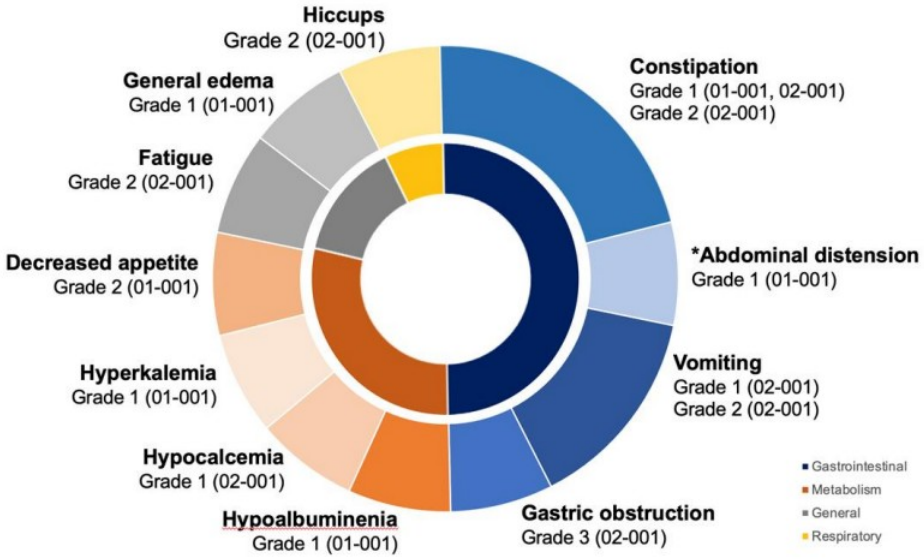
ACESOT-1051: Study Design



APREA THERAPEUTICS

ACESOT-1051: Summary of all-cause AEs

Update - October 7, 2024



APREA THERAPEUTICS

*One AE possibly related to APR-1051

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)

- Accelerated titration dose escalation completed, fourth cohort now enrolling
- Safe and well tolerated to date with no hematologic toxicity observed
- Biomarker-driven study in patients with advanced/metastatic solid tumors
- Targeted gene alterations include CCNE1, CCNE2, FBXW7, PPP2R1A, or KRAS-G12 with TP53
- Open label data expected H1 2025
- MD Anderson Cancer Center lead study site, with up to 10 sites in U.S.

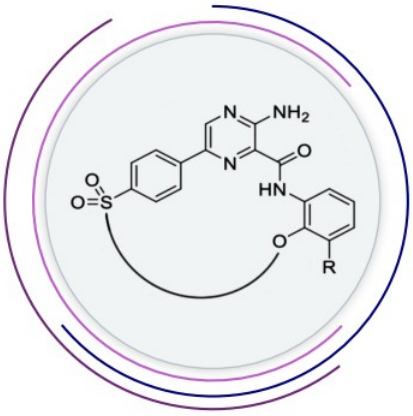
ATR Inhibitor: ATRN-119

Potentially Differentiate
Clinical Stage 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)[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:

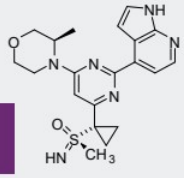
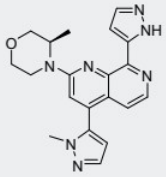
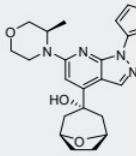
- Increased selectivity → Improved tolerability
- Improved tolerability → More efficacious dosing

[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

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** (25/95, 26%) **Neutrophil count decreased** (13/95, 14%) **Platelet count decreased** (7/95, 7%)

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, *Ann. Oncol*. 2019:30 (supplement 5), Pages v165-

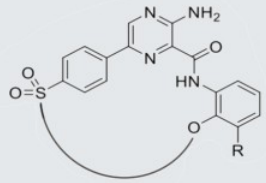
[2] Poster CT084: A Phase I dose-escalation study of ATR inhibitor monotherapy with AZD6738 in advanced solid tumors (PATRIOT Part A), AACR 2017

[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] Camonsertib in DNA damage response-deficient advanced solid tumors: phase 1 trial results, Yap et al. *Nature Medicine* 2023;29:1400-1411

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]**

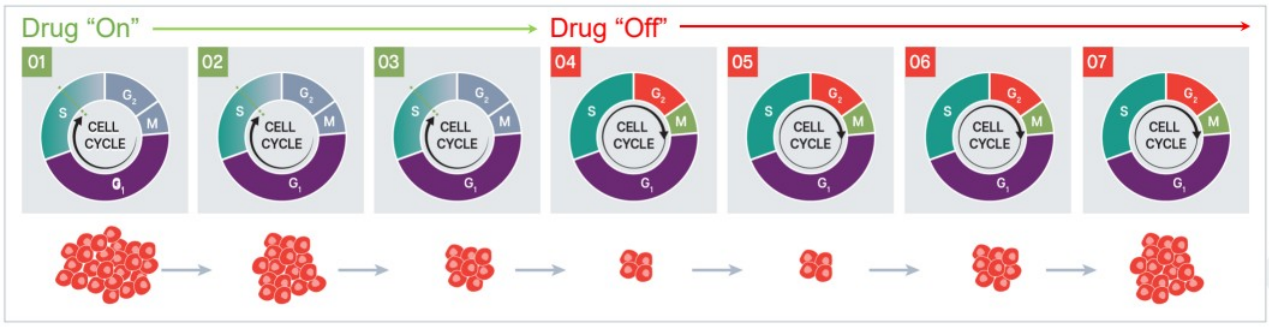
ATRN-119 potentially the preferred ATRi both as a single agent and in combination with standard-of-care therapies

APREA THERAPEUTICS

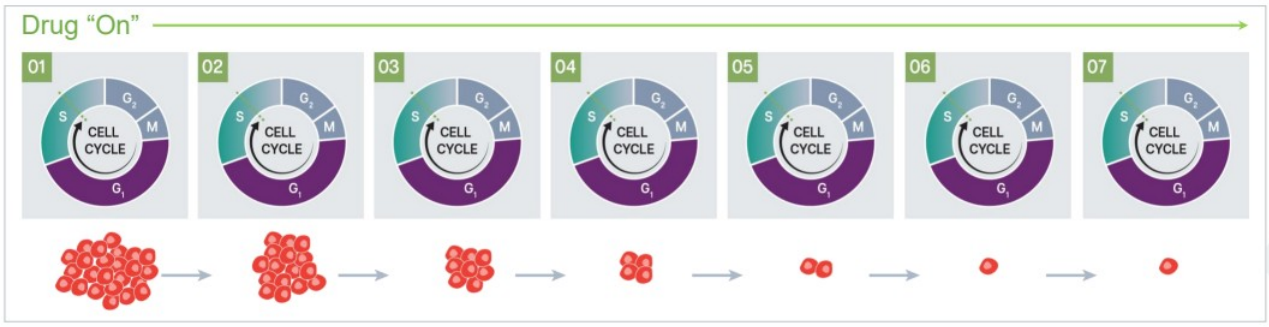
[1] ATRN-119, Phase 1/2a Clinical Study Protocol
[2] Internal pre-clinical head-to-head tolerability study in male beagle dogs

ATRN-119 Daily Dosing Supports Potential Continuous Tumor Suppressio

Intermittent Dosing May Lead to Tumor Resistance



Tumor reduc
and regrowth



Continuous
tumor reduct

APREA THERAPEUTICS

ATR Inhibitor: ATRN-119

ABOYA-119: Clinical Proof-of-Concep

APREA THERAPEUTICS

ABOYA-119: Phase 1/2a - Study Overview

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

Sites:

5 US sites for dose escalation

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

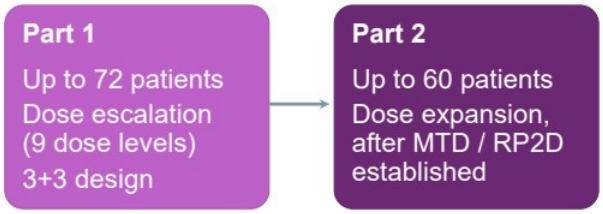
Patient enrollment:
Up to 132 patients in total

- Escalation phase: up to 72 patients
- Expansion phase: up to 60 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)

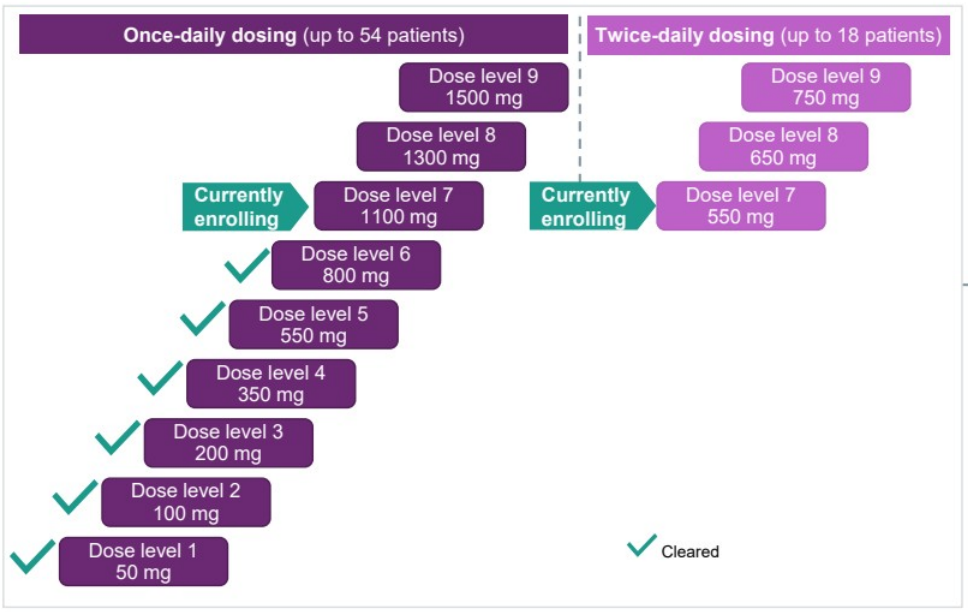
Exploratory

- Association betwee identified mutations and clinical outcome

APREA THERAPEUTICS

ABOYA-119: Clinical Study Design

Part 1. Dose escalation (up to 72 patients)



MTD/RP2D

Part 2. Dose expansion (up to 60 patients)

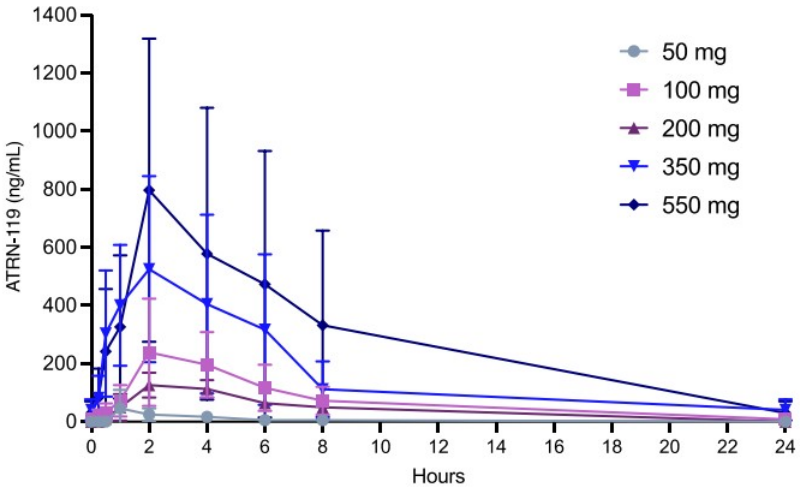
Single-agent ATRN-119 after MTD/RP2D is established

Potential indications: colorectal, prostate, gastric, endometrial

APREA THERAPEUTICS

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

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

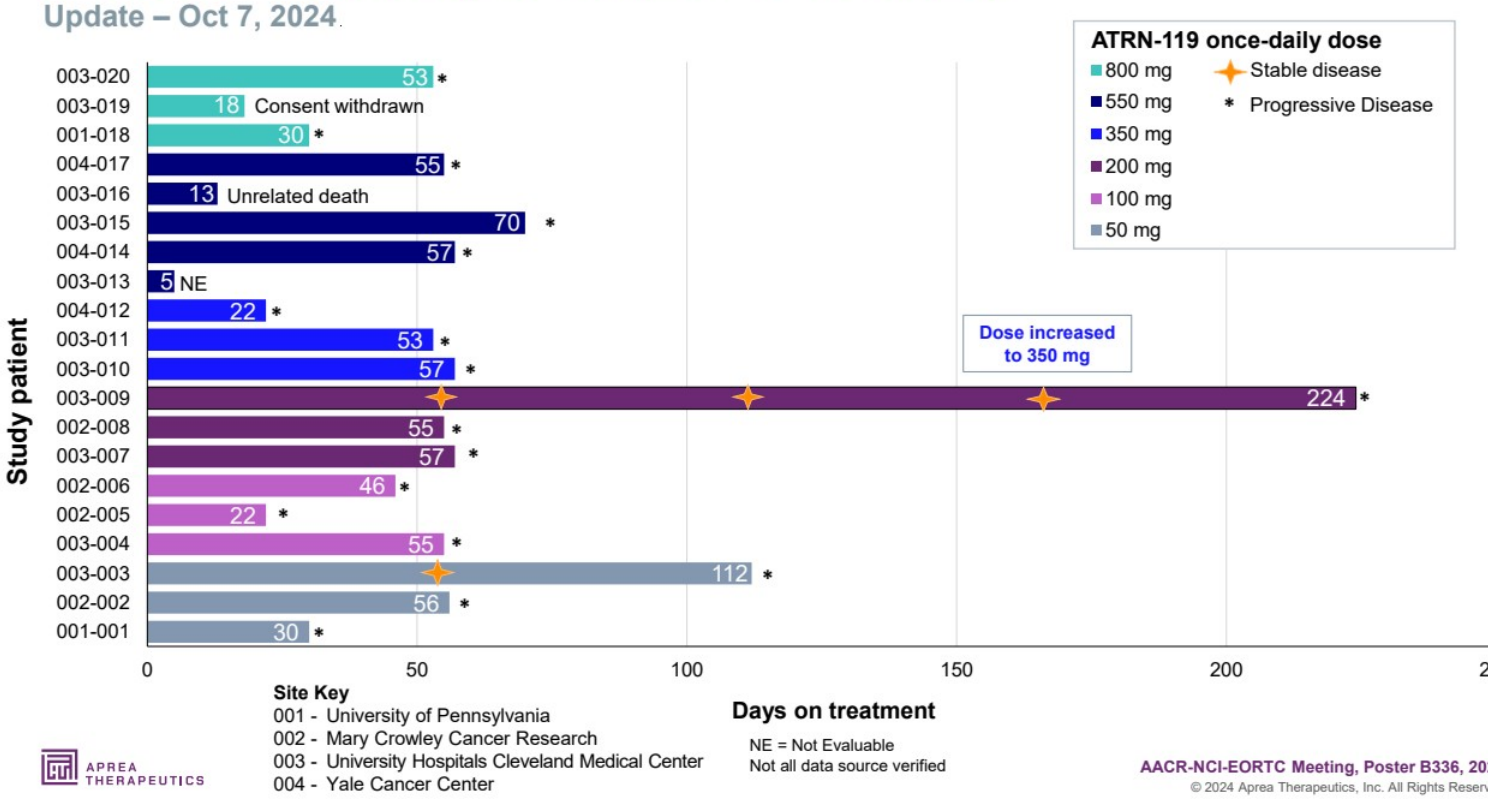


Dose Level mg, once daily	N	AUC 0-24hr (ng*h/mL)	C_{max} (ng/mL)	Half-life (hours)
		Mean (SD)	Mean (SD)	Mean (SD
50	3	180 (143)	57 (56)	2.1 (1.4
100	3	1771 (920)	277 (151)	3.8 (1.6
200	3	1024 (162)	149 (9.2)	3.2 (0.5
350	3	5252 (4362)	525 (320)	5.9 (0.5
550	3	6899 (6058)	797 (522)	5.5 (1.4

- 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

ABOYA-119 Summary of Duration of Treatment

Update – Oct 7, 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

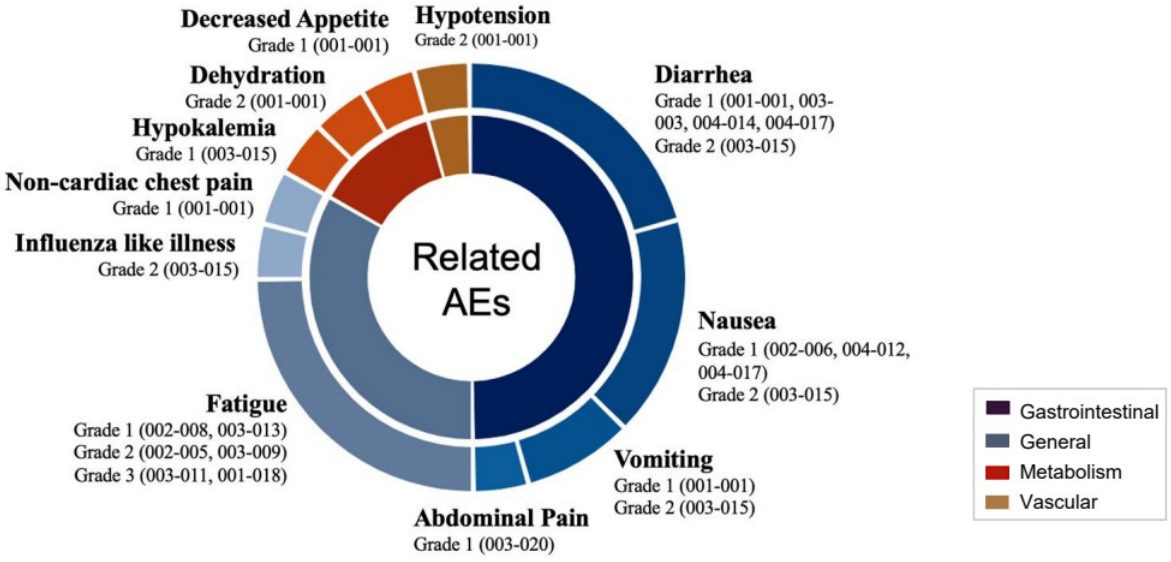
APREA THERAPEUTICS

AACR-NCI-EORTC Meeting, Poster B336, 20

ABOYA-119: Summary of Related Adverse Events

Update – October 2, 2024

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



APREA THERAPEUTICS

Not all data source verified

ATRN-119: Summary

First and only macrocyclic ATR inhibitor

- Potentially differentiated from other ATR inhibitors in selectivity and toxicity profile
- Continuous dosing provides increased drug exposure
- 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 hematologic toxicity reported
- Near-dose proportional exposure following oral administration
- Preliminary signs of clinical benefit already observed at low doses
- Potential efficacy data readout in H2 2025

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, BR, CA, CN, EP, IL, IN, JP, KR, MX, HK.
- 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
- Nationalizations pending for US, AU, BR, CA, CN, EA, EP, IL, IN, JP, KR, MX, NZ, PH, SG, ZA

Family 4: WEE1 Inhibitor Pharmaceutical Compositions and Methods

- International Application filed on Jun. 3rd, 2022
- Composition of our lead WEE1 inhibitor compounds
- Nationalizations in US, AU, BR, CA, CN, EP, IL, IN, JP, KR, MX, ZA

Family 5: Methods of Treating Cancer

- U.S. Provisional Application filed on Sep. 19th, 2024
- Clinical methods of treating advanced solid cancer tumors using lead molecule

Four issued US patents protecting lead molecule and analogs

Aprea Therapeutics (NASDAQ: APRE)
Financial Summary & Capitalization

Cash & Equivalents of ~$22.8M as of December 31, 2024

Closed approximately $16.0M (before deducting placement agent fees and offering costs of approximately $1.3M) from our private placement of our common stock in March 2024 with the potential to receive up to an additional $18.0M upon cash exercise of accompanying warrants at the election of the investors.

Securities	Common Equivalents as of December 31, 2024
Preferred Stock (as converted)	28,112
Common Stock	5,481,055
Warrants:	
Pre-Funded	507,076
Tranche A	1,097,394
Tranche B	1,097,394
Total	2,701,864
Options	715,620
Restricted Stock Units	29,712
Fully Diluted Equivalents	8,956,363

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

Near term catalysts

- H2 2025 open label data APR-1051; Complete dose escalation H1 2026
- H1 2025 open label data ATRN-119; Complete dose escalation H2 2025

Financed into Q4 2025

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

APREA THERAPEUTICS