

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

February 6, 2024

Date of Report (Date of earliest event reported)

Aprea Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-39069
(Commission
File Number)

84-2246769
(IRS Employer
Identification No.)

3805 Old Easton Road
Doylestown, PA
(Address of principal executive offices)

18902
(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 February 6, 2024, Aprea Therapeutics, Inc. updated its corporate presentation slide deck. A copy of the corporate presentation slide deck is filed as Exhibit 99.1 hereto and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Corporate Presentation (February 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: February 6, 2024

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



Precision Oncology Through Synthetic Lethality

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

Aprea Therapeutics (NASDAQ: APRE)

Precision Oncology via Novel Synthetic Lethality Therapeutics

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

ATR Inhibitor: ATRN-119

- First macrocyclic ATR inhibitor
- Highly selective with continuous daily dosing targeted
- Phase 1/2a – Ongoing Dose Escalation
 - Readout 4Q2024
 - 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
- IND Clearance 1Q2024
- Pre-clinical proof-of-principle
 - Highly potent and selective anti-tumor activity
 - Limited off target effect
 - Ovarian cancer with Cyclin E over expression (OVCAR-3)
 - Stable hematologic function
 - Favorable pharmacokinetics

DDR Inhibitor: Undisclosed

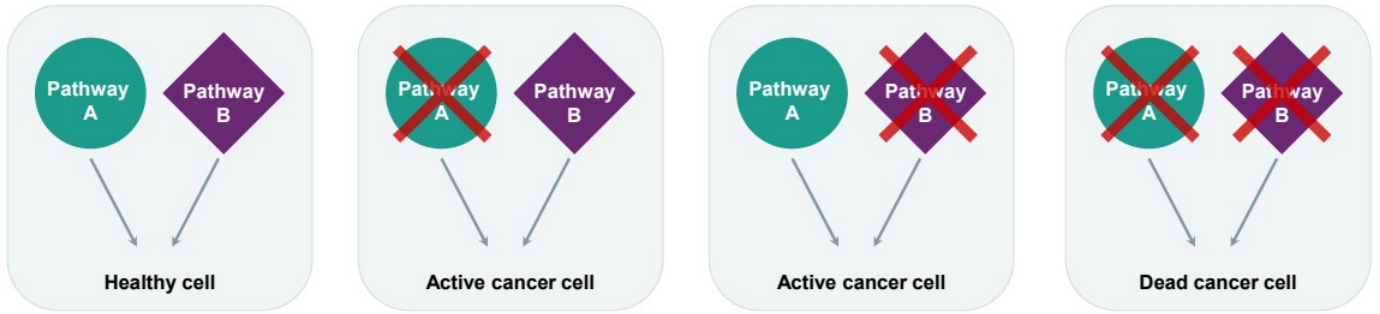
- Lead optimization
- Target identified from our RepliBior discovery platform



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

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Synthetic Lethality



- Cancer cell death only upon the loss of function of two codependent pathways
- Single pathway loss of function is inconsequential
- DNA Damage Response (DDR) allows cells to pause and self repair during replication (mitosis)
- Inhibition of DDR leads to mitotic catastrophe and cell death
- ATR and WEE1 inhibitors are integral to stopping DDR and are emerging targets for cancer cell death
- Builds on scientific innovation led by Aprea founder and key personnel¹

Leadership with Strong Drug Development and Commercial Expertise

Pioneers in Synthetic Lethality

Management

Oren Gilad, Ph.D. President and CEO	John Hamill CFO	Nadeem Mirza, M.D., MPH Senior Medical Advisor	Ze'ev Weiss, CPA, B.Sc. Chief Business Advisor	Mike Carleton, Ph.D. Translational Medicine Advisor	Brian Wiley SVP, Corporate Strategy

Board of Directors

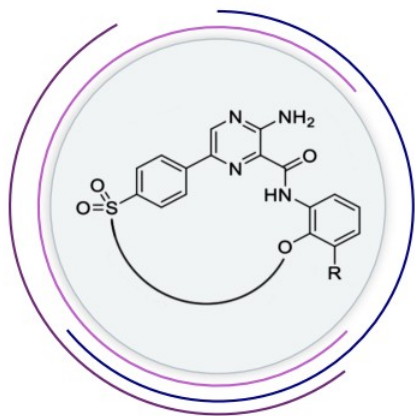
Richard Peters, M.D., Ph.D. Chairman of the Board	Oren Gilad, Ph.D. President and CEO	Jean-Pierre Bizzari, M.D. Director
Marc Duey Director	Michael Grissinger Director	Gabriela Gruia, M.D. Director
John Henneman Director	Rifat Pamukcu, M.D. Director	Bernd R. Seizinger, M.D., Ph.D. Director

ATR Inhibitor: ATRN-119

Clinical Proof-of-Concept

ATRN-119: First and Only Macrocyclic ATR Inhibitor¹

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



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

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

- Increase potency
- Increase selectivity

These effects can then promote:

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

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

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

Sites:

4 US sites for dose escalation

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

Patient enrollment:

60 patients in total

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

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

Patient Population:

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

Part 1

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



Part 2

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

Primary objectives:

- Safety, MTD, RP2D
- Pharmacokinetics

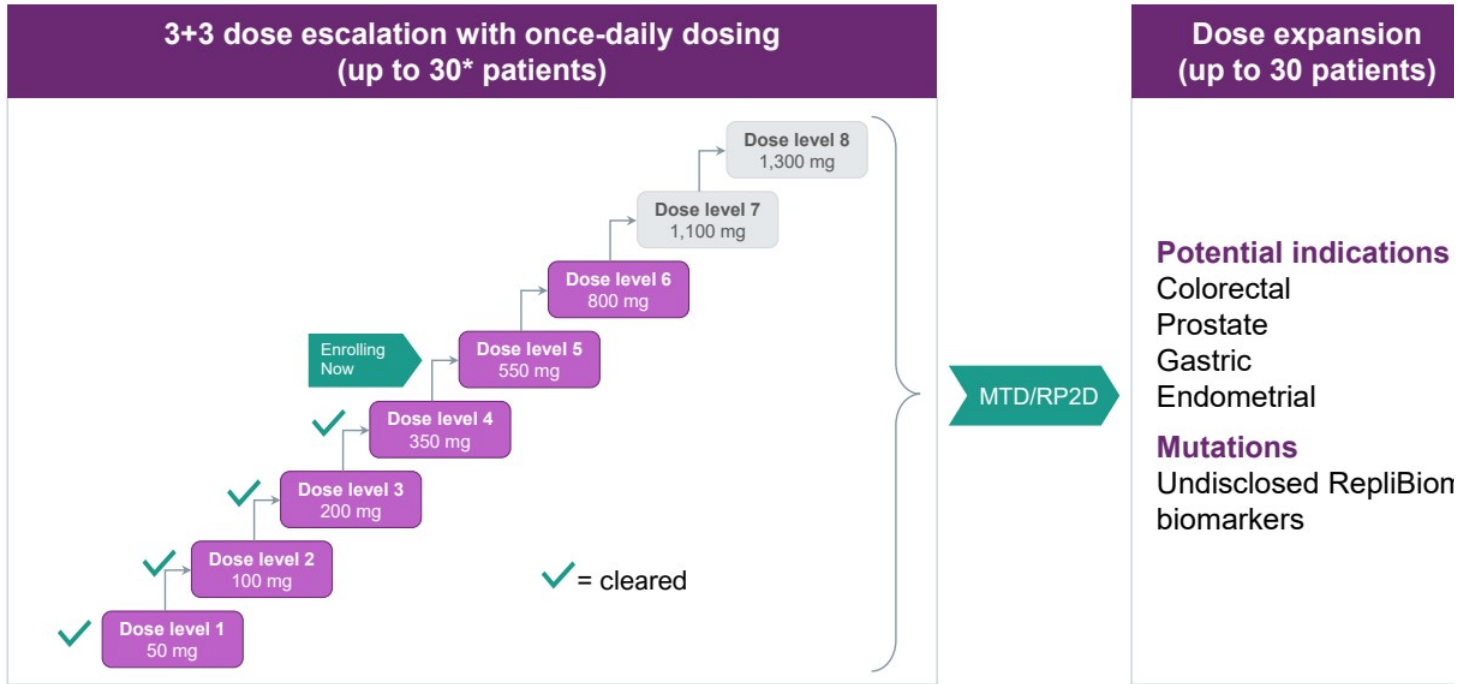
Secondary objectives:

- Antitumor activity (RECIST/PCWG3)

Exploratory objectives:

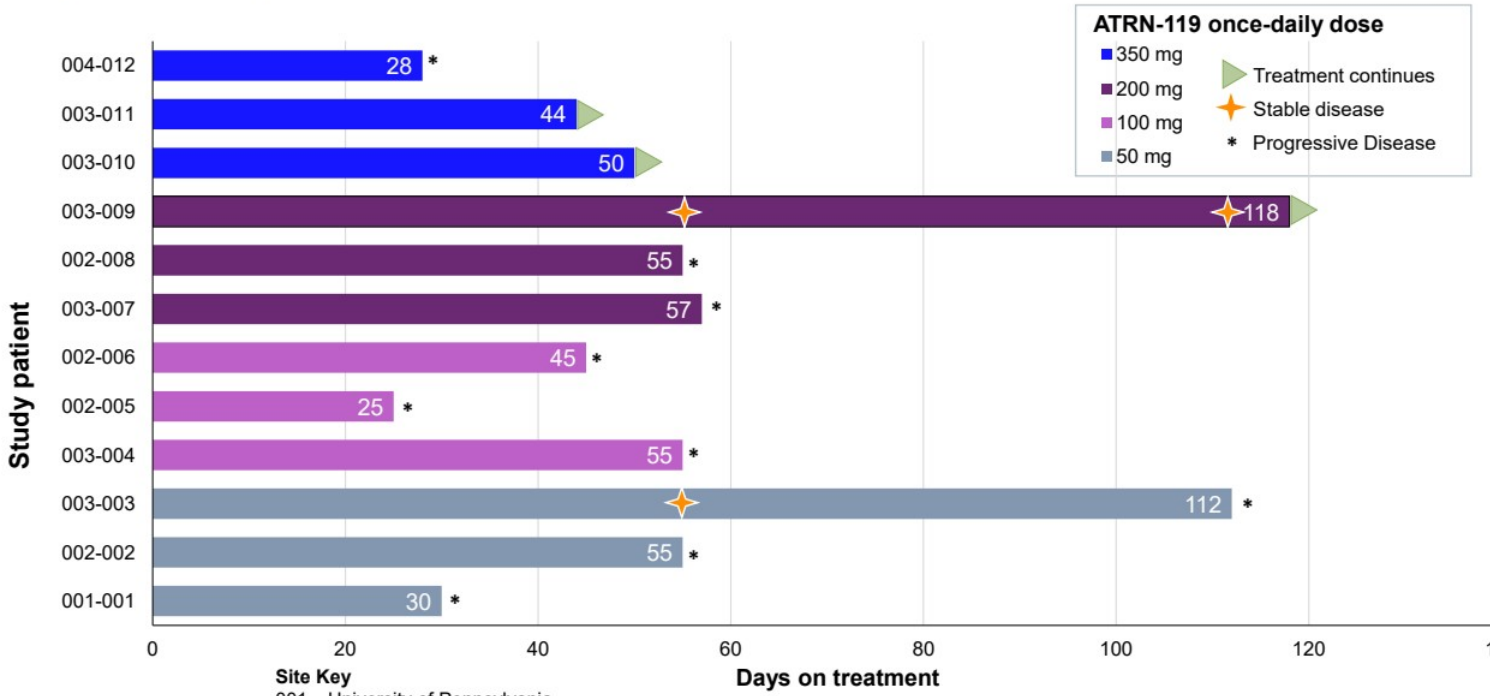
- Association between identified mutations and clinical outcomes

Aprea AR-276-01 Study Status



AR-276-01 Summary of Duration of Treatment

Update – Jan 2, 2024



Site Key

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

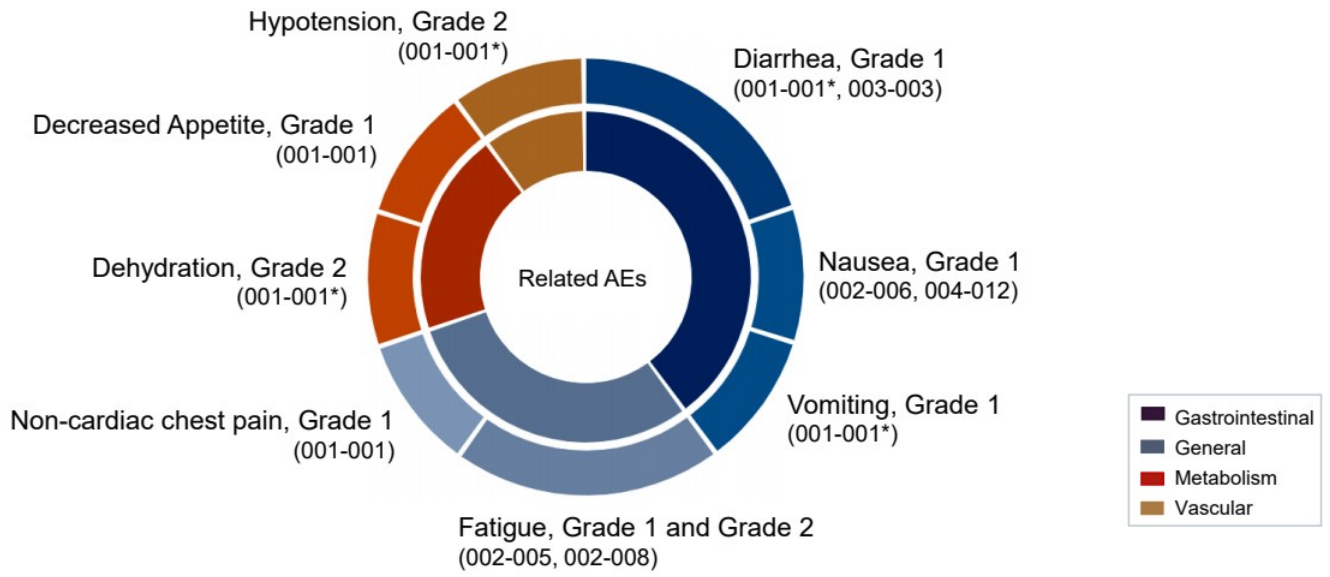


Not all data source verified

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No ATRN-119 Related Grade 3 or 4 Adverse Events Reported

As of January 2, 2024: Six Of Twelve Patients Experienced AEs# Possibly/probably Related to ATRN-119



No grade 3 or 4 AEs were observed
* Resulted in treatment interruption
Not all data source verified

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ATRN-119

2024-2025 Anticipated Clinical Milestones

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



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

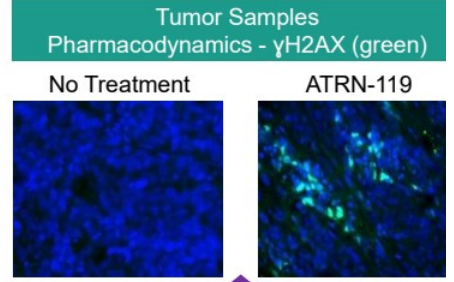
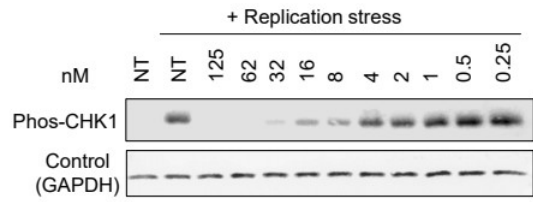
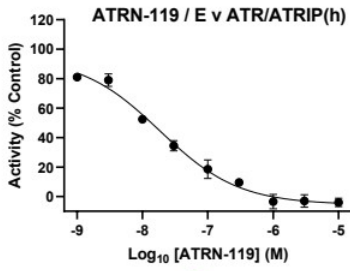
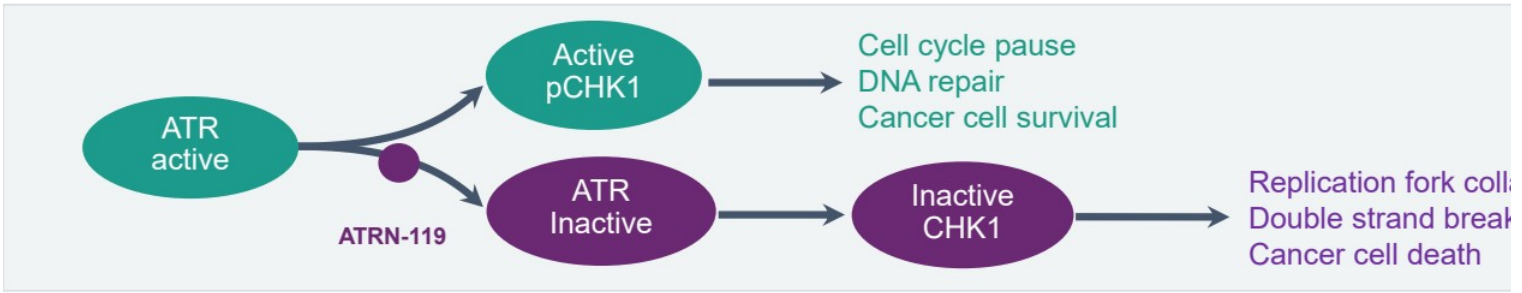
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ATR Inhibitor: ATRN-119

Preclinical Proof-of-Principal

ATR Inhibitor – ATRN-119

Mechanism of Action – Prevent CHK1 Phosphorylation by ATR Kinase



ATR-119 binds to ATR

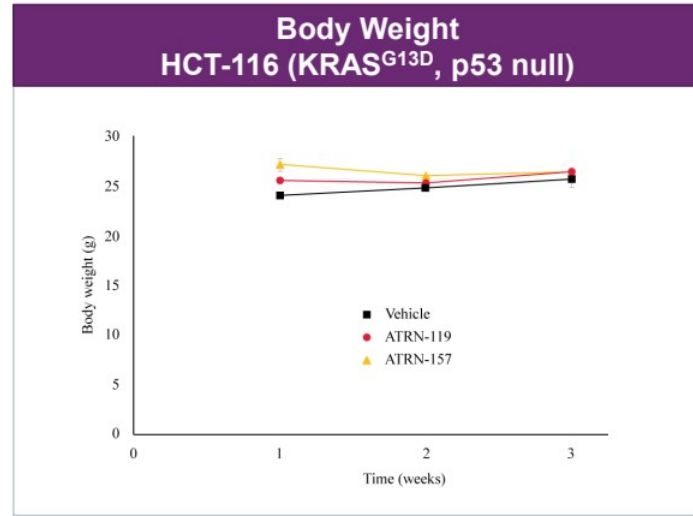
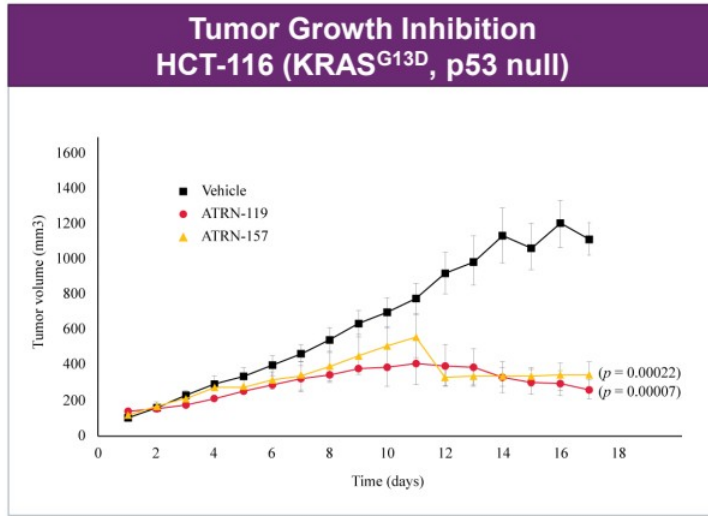
...inhibits its biological activity...

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

ATRN-119 Preclinical Profile

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

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

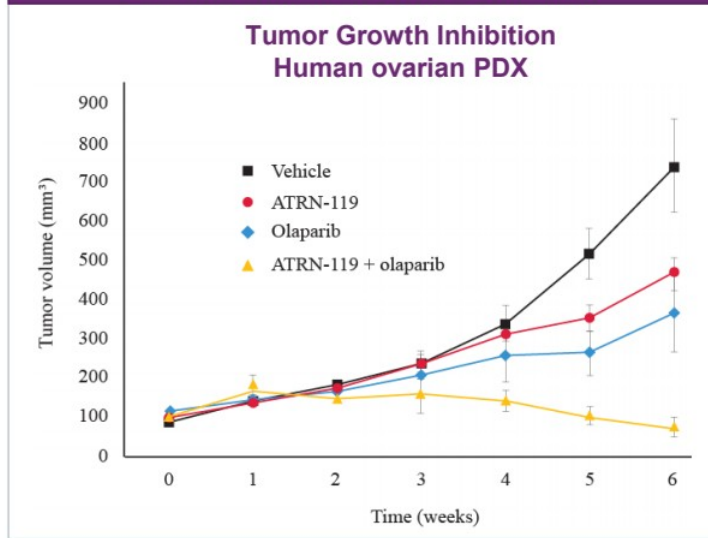


N=4 female mice per group, ATRN-119 - 100 mg/kg/day P.O., ATRN-157 - 20 mg/kg/day SQ.
ATRN-157 is an active metabolite identified in dogs receiving ATRN-119 P.O.. In vitro metabolism studies in dog and human hepatocytes and liver microsomes indicated formation of ATRN-157 in both species. Potency and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

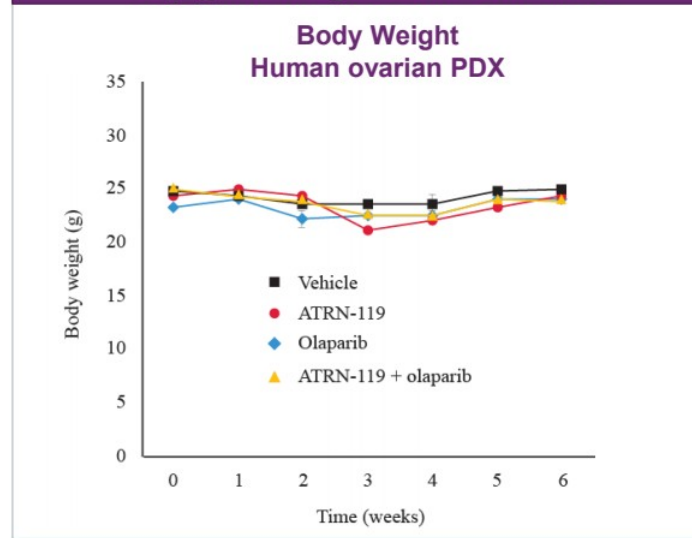
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ATRN-119 + Olaparib: Regression of BRCA2-Deficient Ovarian (HGSOC) Tumors

ATRN-119 + Olaparib Inhibits Ovarian Tumor Growth Over Time



ATRN-119 + Olaparib Shows Negligible Weight Loss Over Time



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

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ATR Inhibitor: ATRN-119

A Potentially
Differentiated ATRi

Reported Challenges with Other ATR Inhibitors

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

Parameter	AstraZeneca AZD6738 ^{1,2}	Bayer BAY1895344 ³	Repare / Roche ⁴ RP-3500 ⁵
Route of Administration	Oral	Oral	Oral
MTD/RP2 Dose Schedule	160mg BID, 2-weeks-on, 2-weeks-off, or: Continuous dosing ¹	40mg BID, 3-days-on/4-days-off	160mg QD, 3-days-on/4-days-off
Main Grade ≥3 Hematological toxicities	Patriot 1, Escalation Phase, 160mg, BID ² : Anemia (1/6, 17%) Patriot 2, Expansion Phase ¹ : Fatigue, anemia, nausea, and thrombocytopenia (not differentiated) (4/6, 67%) with continuous dosing (3/15, 20%) with 2-week-on, 2-week-off	Anemia (2/2, 100%) Neutropenia (1/2, 50%)	Anemia (23/95, 24%) Neutrophil count decreased (10/95, 11%) Platelet count decreased (5/95, 5%)

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

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

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

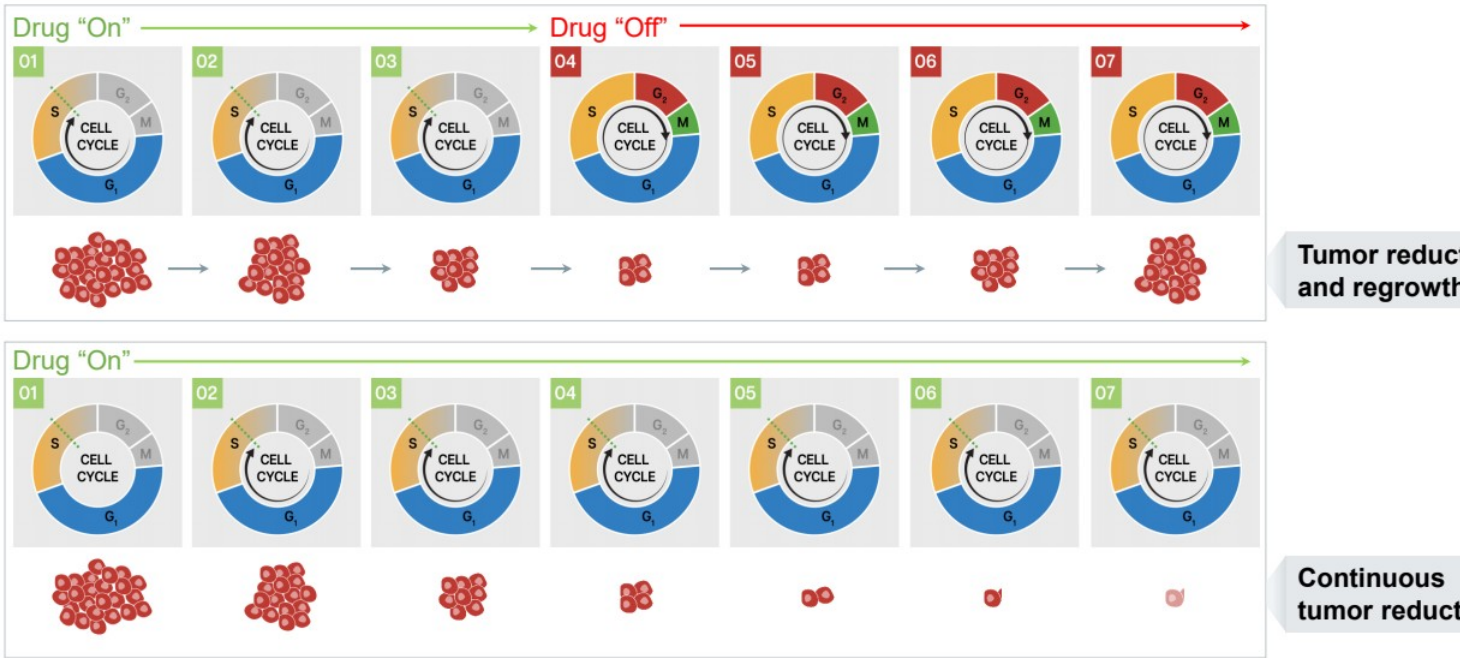
³ First-in-Human Trial of the Oral Ataxia Telangiectasia and RAD3-Related (ATR) Inhibitor BAY 1895344 in Patients with Advanced Solid Tumors, Yap et al, Cancer Discov 2021;11:80-91 and 2019 ASCO Poster, De-Bono et al.

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

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

ATRN-119 Daily Dosing Means Continuous Tumor Reduction

Intermittent Dosing May Lead to Tumor Resistance



Daily Dosing Is Clinically Superior Based on Other ATRi in Development

Artios ATR Inhibitor: ART0380

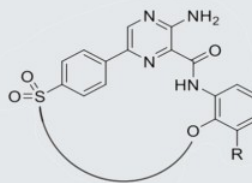
Initial Results From Phase 1 Dose Escalation¹

Dose Escalation Phase	<ul style="list-style-type: none">• 49 patients• Continuous dosing: QD; Range 200-400mg, (n=10)• Intermittent dosing: 3D on/4D off; Range 100 - 1,200mg, (n=39)
RP2D	<ul style="list-style-type: none">• Continuous = 200mg• Intermittent dosing = 600mg
Efficacy Among Measurable Patients	<ul style="list-style-type: none">• Continuous – ORR 29% (2/7). One of two responders treated at twice the RP2D.• Intermittent – ORR 8% (2/26). One of two responders treated at twice the RP2D.
Safety	<ul style="list-style-type: none">• 36% Anemia Grade 3 at doses considered tolerable

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

Parameter

ATRN-119 ⁽¹⁾



Route Of Administration

Oral

Clinical Studies Chosen (MTD/RP2D), Dose Schedule

Continuous daily dosing (RP2D TBD in Phase 1)¹

Hematological toxicities in preclinical studies

Pre-Clinical, Toxicology Studies:

- In 28-day GLP tox study in dogs, hematological changes were of small magnitude and within normal ranges
- In a head-to-head comparative tolerability study, ATRN-119 demonstrated significantly less toxicity than another oral ATRi that is currently in clinical development²

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



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

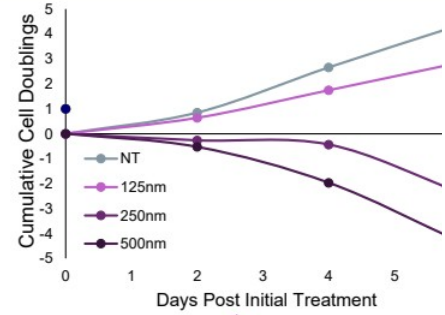
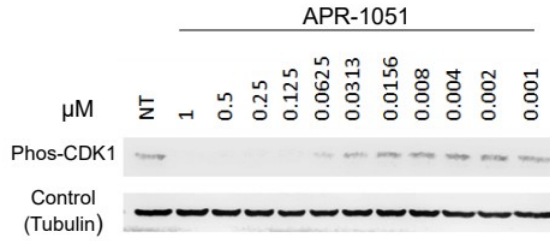
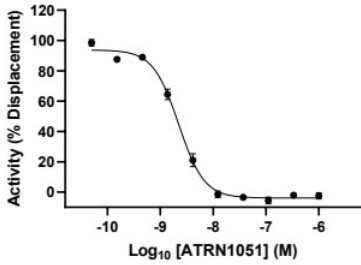
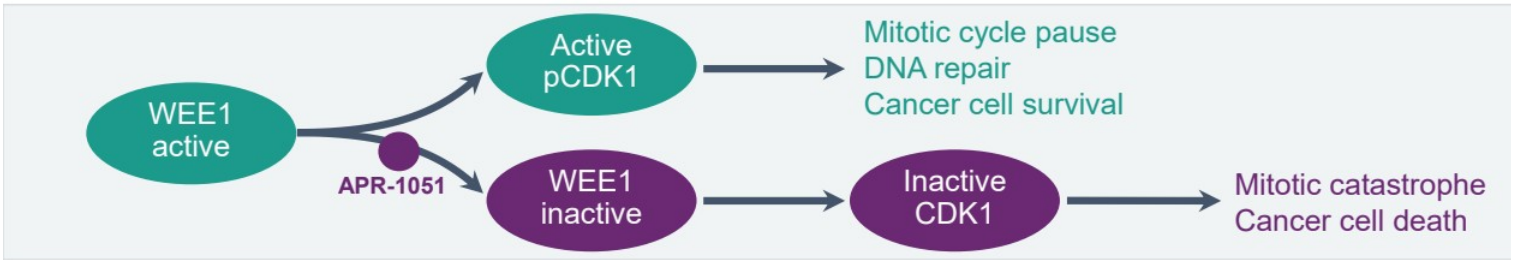
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WEE1 Inhibitor: APR-1051

Preclinical Proof-of-Principle

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

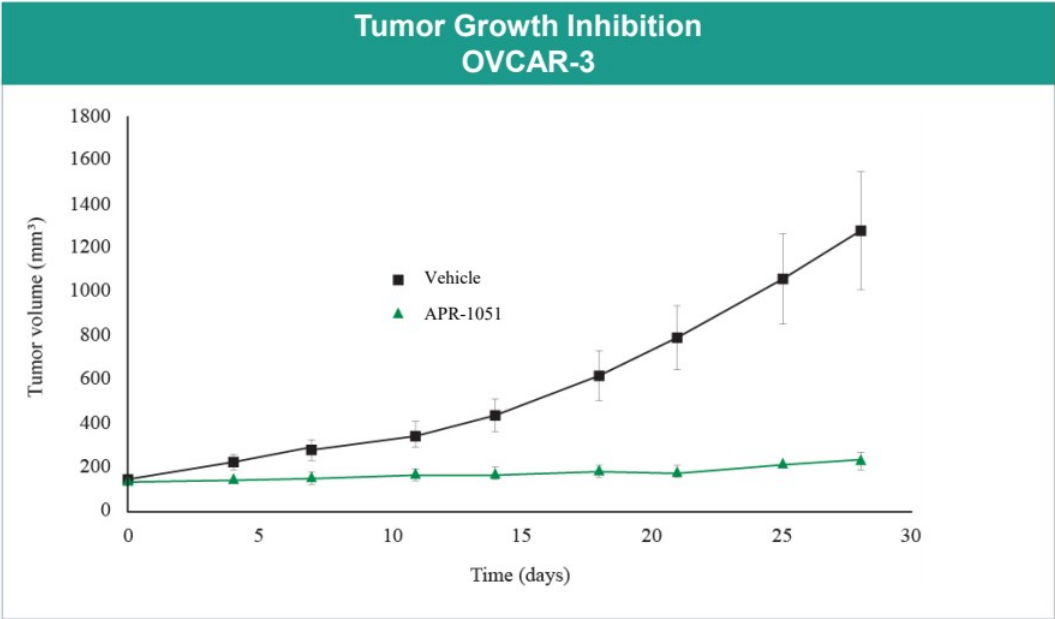


pCDK1- Phosphorylated Cyclin Dependent Kinase 1
Data on file

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APR-1051 Demonstrated Potentially Compelling Anti-tumor Activity

IND Clearance 1Q2024



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



Pre-clinical studies with APR-1051
Data on file

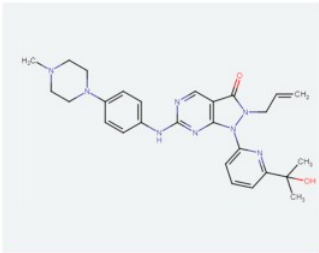
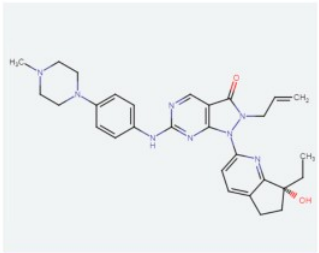

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WEE1 Inhibitor: APR-1051

A Potentially
Differentiated Wee1i

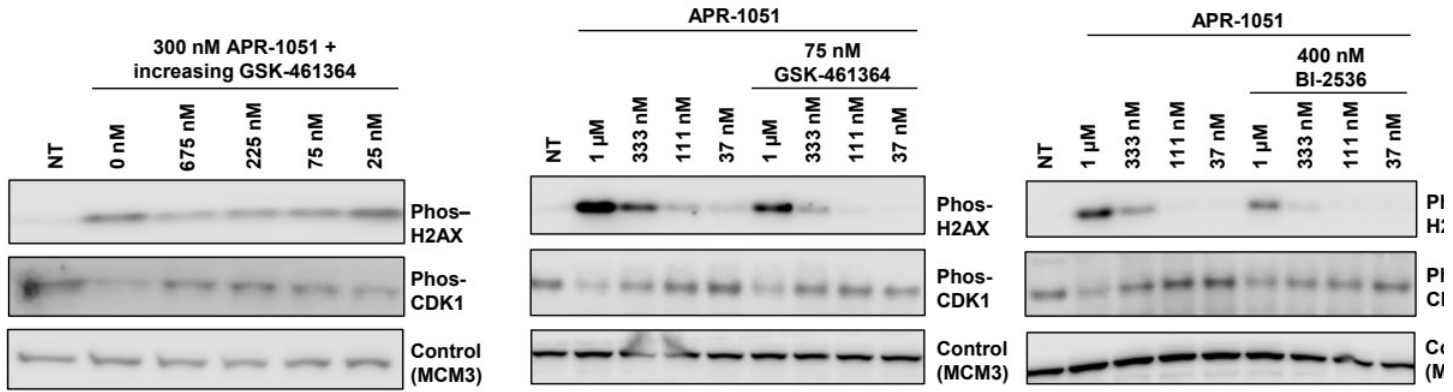
APR-1051 Potentially Differentiated from Other WEE1 Inhibitors

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	2.2
Off-Target Inhibition at 1 μM (%)	PLK1	70	79	17
	PLK2	101	96	33
	PLK3	91	92	12

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

AACR-NCI-EORTC Meeting, Poster C147, 20

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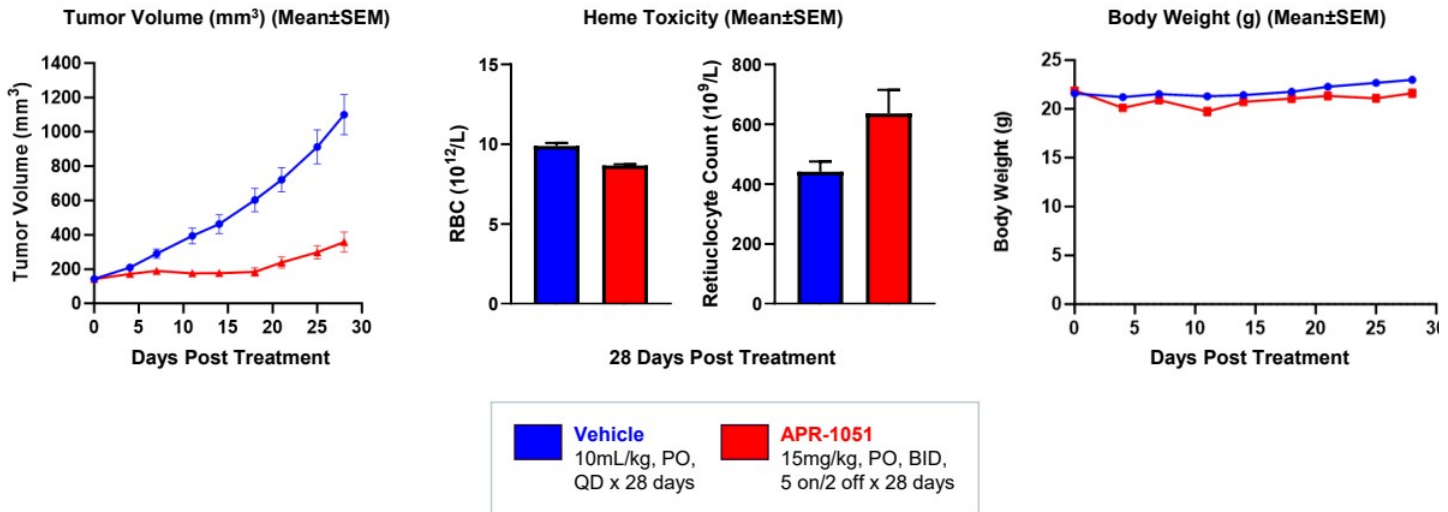
APR-1051 Shows Negligible Inhibition of hERG Channels

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 between kinase IC50 and hERG 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-fold)

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

OVCAR Xenograft Tumor Model in Female Nude Mice



APR-1051

2024-2025 Anticipated Preclinical and Clinical Milestones

Milestone	Timeline
<u>IND</u>	
Clearance	1Q 2024
<u>Phase 1/2a – Monotherapy Dose Escalation</u>	
First Patient Enrolled (subject to funding)	1H 2024
Open-Label Efficacy Data	2Q 2025
RP2D	2H 2025

Strong Intellectual Property Portfolio

Family 1: Ataxia Telangiectasia 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



Four issued US patents protecting lead molecule and analogs

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Aprea Therapeutics (NASDAQ: APRE) Financial Summary & Capitalization

Cash & Equivalents of \$25.4M as of
September 30, 2023

Closed \$5.5M (\$4.9M, net) public
offering in February 2023

Obtained \$2.0M non-dilutive
funding via research grant from
National Cancer Institute (NCI)

Securities	Common Equivalents as of Nov. 9, 2023
Preferred Stock (as converted)	28,112
Common Stock	3,736,673
Options	586,466
Restricted Stock Units	23,870
Fully Diluted Equivalents	4,375,121

Investment Highlights



Technology developed by pioneers in synthetic lethality

- Management with strong drug development and commercial expertise



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

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



Near term catalysts

- Phase 1/2a dose escalation ATRN-119 readout 4Q 2024
- IND clearance APR-1051 1Q2024



Financed through end of 2024

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