

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

November 9, 2023

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 2.02 Results of Operations and Financial Condition.**

On November 9, 2023, Aprea Therapeutics, Inc. (the "Company") issued a press release announcing its financial results for the three and nine months ended September 30, 2023, and provided an update on the Company's operations for the same period. The Company is furnishing a copy of the press release, which is attached hereto as Exhibit 99.1.

In accordance with General Instruction B.2 of Form 8-K, the information included in this Item 2.02, including Exhibit 99.1 hereto, shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any filing made by the Company under the Exchange Act or Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such a filing.

**Item 8.01 Other Events.**

On November 9, 2023, 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.

<b>Exhibit Number</b>	<b>Description</b>
99.1	<a href="#">Press release issued by Aprea Therapeutics, Inc. dated November 9, 2023.</a>
99.2	<a href="#">Corporate Presentation (November 2023).</a>
104	Cover Page Interactive Data File (embedded within the inline XBRL document).

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**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: November 9, 2023

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

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## Aprea Therapeutics Reports Third Quarter 2023 Financial Results and Provides a Business Update

DOYLESTOWN, PA, Nov. 9, 2023 (GLOBE NEWSWIRE) – Aprea Therapeutics, Inc. (Nasdaq: APRE) (“Aprea”, or the “Company”), a clinical-stage biopharmaceutical company focused on precision oncology through synthetic lethality, today reported financial results for the three and nine months ended September 30, 2023, and provided a business update.

“We are very pleased by the progress of our diversified programs this past quarter. Importantly, we presented initial clinical data from our Phase 1/2a study of our ATR inhibitor, ATRN-119, in solid tumors in a poster at the recent AACR-NCI-EORTC International Conference. To date, ATRN-119 has demonstrated an ability to be a very compelling molecule, appearing to be well tolerated with no reports of dose-limiting toxicities and ongoing daily dosing may result in persistent tumor-reducing effect,” said Oren Gilad, Ph.D., President and Chief Executive Officer of Aprea. “We are continuing with patients in the dose escalation portion of the study, and the dose expansion cohort is on track to be initiated in 2Q 2024. In our WEE1 inhibitor, ATRN-1051, program we are on track to file an IND with the FDA by the end of 2023, and plan to begin clinical testing in the first half of 2024. Our strong balance sheet continues to support our strategy and plans through our near-term milestones in both our ATR and WEE1 programs, with a cash runway through the end of the fourth quarter of 2024. We look forward to providing more updates as we make progress and reach important milestones in the coming weeks and months.”

**Key Business and Financial Updates**

- Hosted a Key Opinion Leader (KOL) event on October 31, 2023, highlighting the Company’s portfolio of small molecules focused on Synthetic Lethality (SL) by targeting the DNA Damage Response (DDR) Pathways. The event featured Key Opinion Leaders Dr. Fiona Simpkins, Professor in the Division of Gynecology Oncology and Department of OB-GYN at the University of Pennsylvania, Dr. Timothy Yap, medical oncology physician-scientist and Professor at the University of Texas MD Anderson Cancer Center, Dr. Eric Brown, a consultant to Aprea and a Professor at the University of Pennsylvania and a member of the Abramson Family Cancer Research Institute, and Aprea’s Dr. Nadeem Mirza, Senior Medical Advisor. The speakers, along with the management team, provided an overview of the Company’s lead ATR inhibitor candidate, ATRN-119, and its WEE1 inhibitor candidate, ATRN-1051, and highlighted the addressable unmet clinical need and potential combination therapies using these programs.
  - Presented initial clinical data on the Company’s ATR inhibitor, ATRN-119, and preclinical data on its WEE1 inhibitor, ATRN-1051, at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics on October 14, 2023. The first poster included initial data from the Company’s first-in-human Phase 1/2a dose escalation trial of ATRN-119 in solid tumors. The trial is being conducted to determine the recommended Phase 2 dose, with a daily dosing administration over a 56-day cycle. The Company is actively enrolling cohort 4 at 350mg, with subsequent 550mg cohort 5 and 800mg cohort 6 planned. The Company anticipates enrolling the first patient in the dose expansion portion of the study in Q2 2024.
  - The second poster presented preclinical data from the Company’s WEE1 inhibitor program that demonstrated the potential safety and efficacy of its highly differentiated WEE1 inhibitor, ATRN-1051, in the treatment of ovarian cancer. The data showed ATRN-1051 to be a highly potent and selective inhibitor of WEE1 that does not significantly affect the off-target PLK1, PLK2, and PLK3 family of kinases. ATRN-1051 shows potentially favorable PK properties and appears to cause lower inhibition of hERG, a potential indication of low cardiotoxicity. Importantly, at doses and scheduling that suppress tumor growth, ATRN-1051 causes little anemia. These findings have justified IND-enabling studies for clinical development of ATRN-1051. Evidence generated by Aprea suggests such off-targeting of the PLK family, which has been a challenge for other WEE1 inhibitors in the class, substantially limits the ability of WEE1 inhibitors to cause cell death.
  - Appointed Dr. Jean-Pierre Bizzari to its Board of Directors. Dr. Bizzari has been responsible for numerous global approvals of several billion-dollar therapies, has been involved in acquisition and licensing agreements with several major pharmaceutical companies, and is a member and leader on many scientific committees. The Company also named Dr. Richard Peters as Chairman of the Board; Dr. Peters has served as a member of the Board since June 2020 bringing over 2 decades of experience in developing new therapies for difficult-to-treat diseases.
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## Potential Upcoming Key Milestones

### ATR Inhibitor Clinical Program (ATRN-119)

- Phase 1/2a Monotherapy Dose Escalation study
  - 1Q 2024 Complete dose escalation
- Phase 1/2a Monotherapy Dose Expansion study
  - 2Q 2024 First patient enrolled

### WEE1 Inhibitor Program (ATRN-1051)

- IND
  - 4Q 2023 IND Submission
  - 1Q 2024 IND Clearance
- Phase 1/2a Monotherapy Dose Escalation Study
  - 1H 2024 First patient enrolled

## Select Financial Results for the Third Quarter ended September 30, 2023

- As of September 30, 2023, the Company reported cash and cash equivalents of \$25.4 million.
- For the quarter ended September 30, 2023, the Company reported an operating loss of \$3.5 million, compared to an operating loss of \$4.2 million for the same period in 2022.
- Research and Development (R&D) expenses were \$2.1 million for the quarter ended September 30, 2023, compared to \$1.1 million for the same period in 2022. The increase in R&D expense was related to IND enabling studies for ATRN-1051, the Company's small molecule WEE1 inhibitor, offset in part by a decrease in personnel costs related to the former facility in Sweden.
- General and Administrative (G&A) expenses were \$1.7 million for the quarter ended September 30, 2023, compared to \$3.1 million for the same period in 2022. The decrease in G&A expenses was due to a decrease in professional fees primarily associated with post-acquisition activities during 2022, a decrease in insurance premiums, and a decrease in personnel costs related to the former facility in Sweden.
- The Company reported a net loss of \$3.2 million (\$0.86 per basic share) on approximately 3.7 million weighted-average common shares outstanding for the quarter ended September 30, 2023, compared to a net loss of \$4.0 million (\$2.32 per basic share) on approximately 1.7 million weighted average common shares outstanding for the same period in 2022.

## About Aprea

Aprea Therapeutics, Inc. is a clinical-stage biopharmaceutical company headquartered in Doylestown, Pennsylvania, focused on precision oncology through synthetic lethality. The Company's lead program is ATRN-119, a clinical-stage small molecule ATR inhibitor in development for solid tumor indications. Its oral, small molecule WEE1 inhibitor, ATRN-1051, is being advanced to IND submission. For more information, please visit the company website at [www.aprea.com](http://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

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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, 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, 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

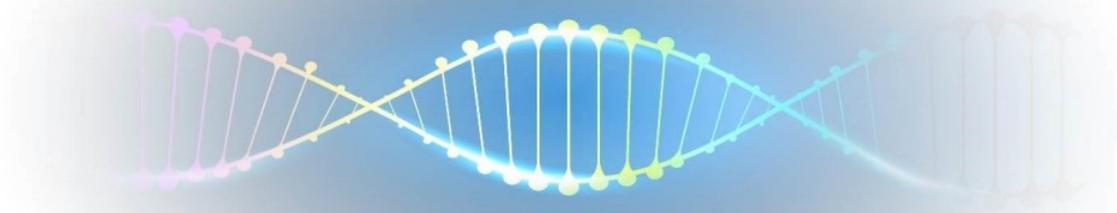
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**Aprea Therapeutics, Inc.**  
**Condensed Consolidated Balance Sheets**  
**(Unaudited)**

	September 30, 2023	December 31, 2022
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 25,353,513	\$ 28,786,647
Prepaid expenses and other current assets	286,263	1,366,859
Total current assets	25,639,776	30,153,506
Property and equipment, net	86,198	2,321
Restricted cash	40,449	—
Total assets	<u>\$ 25,766,423</u>	<u>\$ 30,155,827</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 862,552	\$ 842,754
Accrued expenses	3,303,510	2,358,332
Total current liabilities	4,166,062	3,201,086
Total liabilities	4,166,062	3,201,086
Commitments and contingencies		
Series A convertible preferred stock, \$0.001 par value, 40,000,000 shares authorized; 56,227 shares issued and outstanding at September 30, 2023 and December 31, 2022, respectively.	1,311,063	1,311,063
Stockholders' equity:		
Common stock, \$0.001 par value, 400,000,000 shares authorized, 3,736,673 and 2,655,269 shares issued and outstanding at September 30, 2023 and December 31, 2022, respectively.	3,736	2,655
Additional paid-in capital	335,561,343	330,060,836
Accumulated other comprehensive loss	(10,635,874)	(10,623,408)
Accumulated deficit	(304,639,907)	(293,796,405)
Total stockholders' equity	20,289,298	25,643,678
Total liabilities and stockholders' equity	<u>\$ 25,766,423</u>	<u>\$ 30,155,827</u>

**Aprea Therapeutics, Inc.**  
**Condensed Consolidated Statements of Operations and Comprehensive Loss**  
**(Unaudited)**

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Grant revenue	\$ 319,468	\$ —	\$ 569,156	\$ —
Operating expenses:				
Research and development	2,122,603	1,117,576	5,581,802	15,870,867
General and administrative	1,719,715	3,082,618	6,784,388	18,849,549
Acquired in-process research and development	—	—	—	76,020,184
Total operating expenses	3,842,318	4,200,194	12,366,190	110,740,600
Loss from operations	(3,522,850)	(4,200,194)	(11,797,034)	(110,740,600)
Other income:				
Interest income, net	321,215	151,123	913,846	205,585
Foreign currency gain (loss)	(2,880)	24,353	39,686	315,130
Total other income	318,335	175,476	953,532	520,715
Net loss	\$ (3,204,515)	\$ (4,024,718)	\$ (10,843,502)	\$ (110,219,885)
Other comprehensive loss:				
Foreign currency translation	(1,002)	26,161	(12,466)	118,311
Total comprehensive loss	(3,205,517)	(3,998,557)	(10,855,968)	(110,101,574)
Net loss per share attributable to common stockholders, basic and diluted	\$ (0.86)	\$ (2.32)	\$ (3.03)	\$ (83.33)
Weighted-average common shares outstanding, basic and diluted	3,735,176	1,732,783	3,577,482	1,322,652



# Precision Oncology Through Synthetic Lethality

November 2023

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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 trial 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, uncertainties. Any or all of the 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 without limitation, 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; our 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 our 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, utility analyses, data presentation, reporting and publication and receipt of interim results (including, without limitation, any preclinical results or 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.

- Clinical stage precision medicine via novel synthetic lethality (SL) - based therapeutics
- All programs addressing significant unmet medical need
  
- ATR Inhibitor: ATRN-119
  - ◇ Clinical proof-of-concept
    - ◇ Phase 1/2a – Ongoing Dose Escalation
      - ◇ Patients 12 years of age or older with solid tumors harboring DDR mutation
      - ◇ Primary objective : Safety, MTD, RP2D and PK profile
  - ◇ Pre-clinical proof-of-principle
    - ◇ Demonstrated anti-tumor activity
    - ◇ Synergistic with anti-cancer therapies, including PARP inhibitors
  - ◇ Potential differentiation in safety and tolerability

- WEE1 Inhibitor: ATRN-1051
  - ◇ IND enabling studies
    - ◇ Anticipate submitting an IND by the end of 2023
  - ◇ Pre-clinical proof-of-principle
    - ◇ Demonstrated anti-tumor activity
    - ◇ Ovarian cancer with Cyclin E over expression
    - ◇ Synergistic with anti-cancer therapies, including ATR inhibitor
  - ◇ Potential differentiation in safety and tolerability
  
- DDR Inhibitor: Undisclosed
  - ◇ Lead optimization
    - ◇ Target identified from our RepliBiom discovery platform

## Management

<b>Oren Gilad, Ph.D.</b> President and CEO	<b>John Hamill</b> CFO	<b>Nadeem Mirza, M.D., MPH</b> Senior Medical Advisor	<b>Ze'ev Weiss, CPA, B.Sc.</b> Chief Business Advisor	<b>Mike Carleton, Ph.D.</b> Translational Medicine Advisor

## Board of Directors

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



## ATR Inhibitor : ATRN-119

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ATR Inhibitor :  
ATRN-119

Clinical  
Proof-Of-Concept

**AR-276-01:** 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:** 48 patients in total

- Escalation phase: up to 18 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 any DDR mutation per NGS

**Part 1** (up to 18 patients)  
Dose escalation (6 dose levels)  
3+3 design



**Part 2** (up to 30 patients)  
Dose expansion, after MTD /  
RP2D established

## **Primary objectives:**

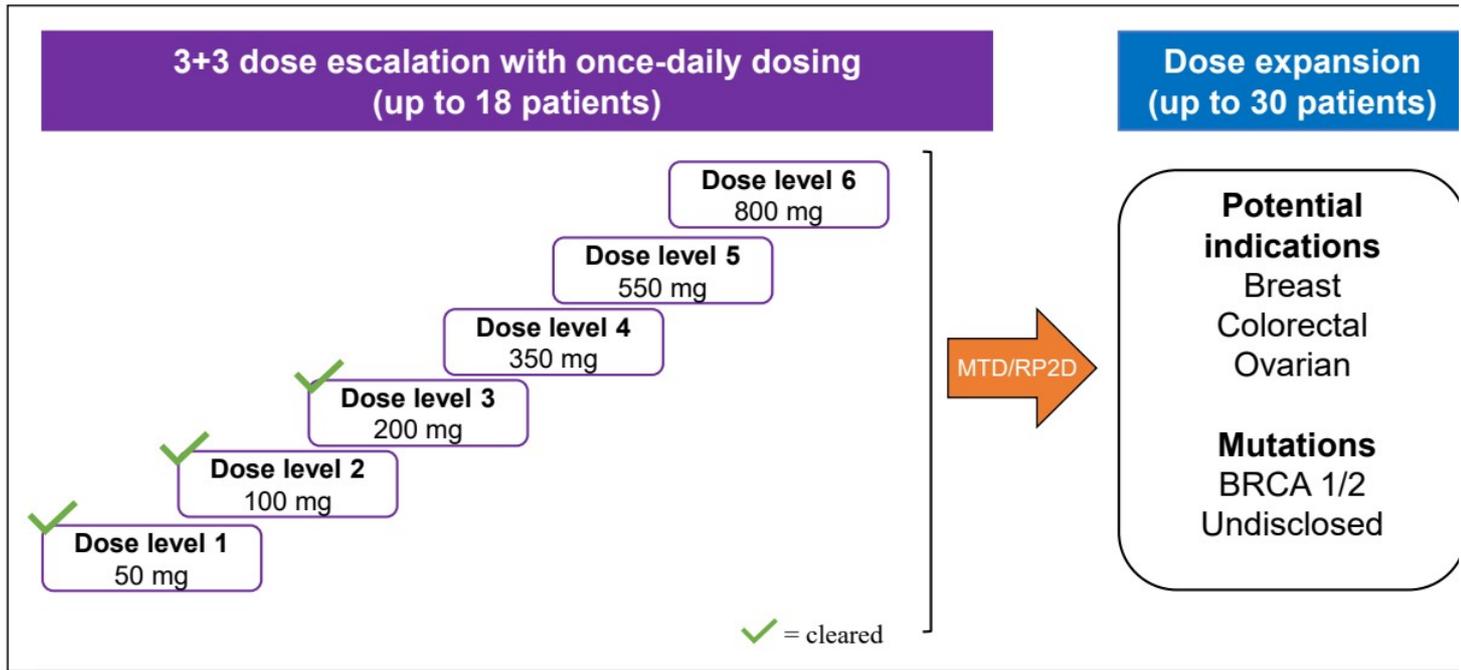
- Safety, MTD, RP2D
- Pharmacokinetics (PK profile of oral ATRN-119 and its active metabolite ATRN-157)

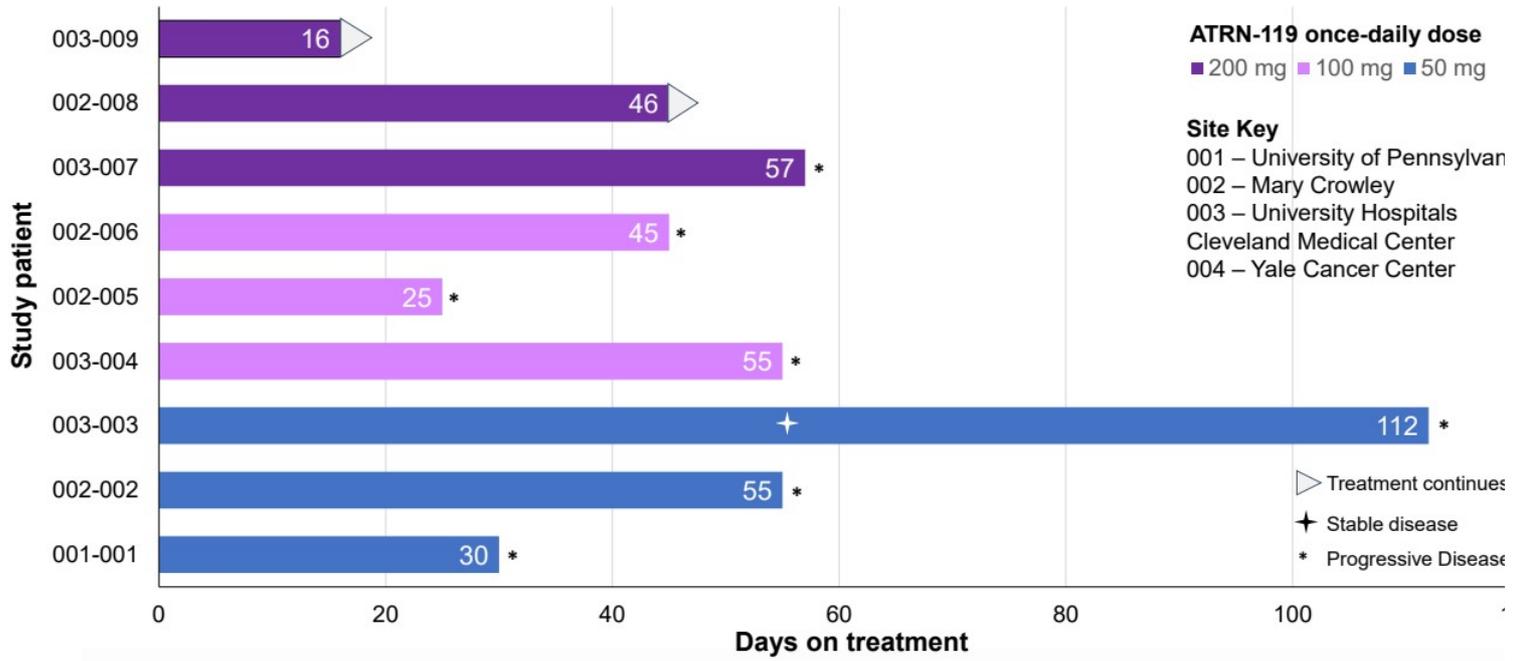
## **Secondary objectives:**

- Antitumor activity (RECIST/PCWG3)

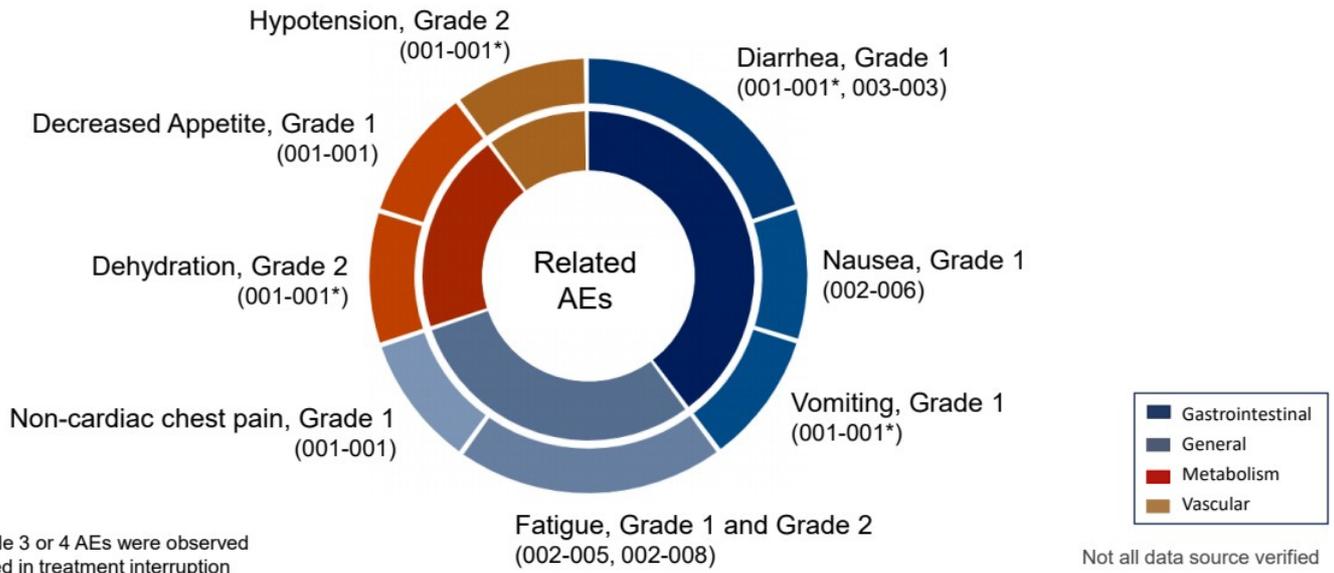
## **Exploratory objectives:**

- Association between identified mutations and clinical outcomes





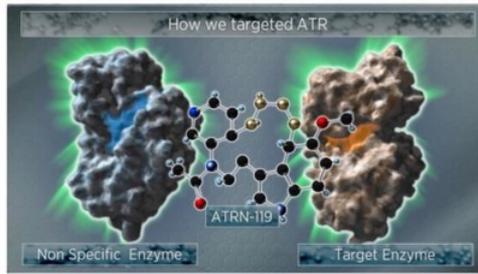
As of Sept 20, 2023: Five out of nine study patients have experienced AEs; assessed to be possibly/probably related to ATRN-119



Milestone	Timeline
Phase 1/2a – Monotherapy Dose Escalation	
Complete Dose Escalation	1Q 2024
Phase 1/2a – Monotherapy Dose Expansion	
First Patient Enrolled	2Q 2024
Last Patient Enrolled	2Q 2025

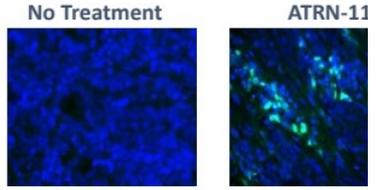
ATR Inhibitor :  
ATRN-119

Preclinical  
Proof-Of-Principal

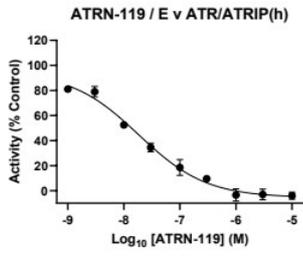


Replication fork collapse  
+ Double Strand Breaks

### Tumor Samples Pharmacodynamics - $\gamma$ H2A



...and triggers replication fork collapse and Double Strand Breaks

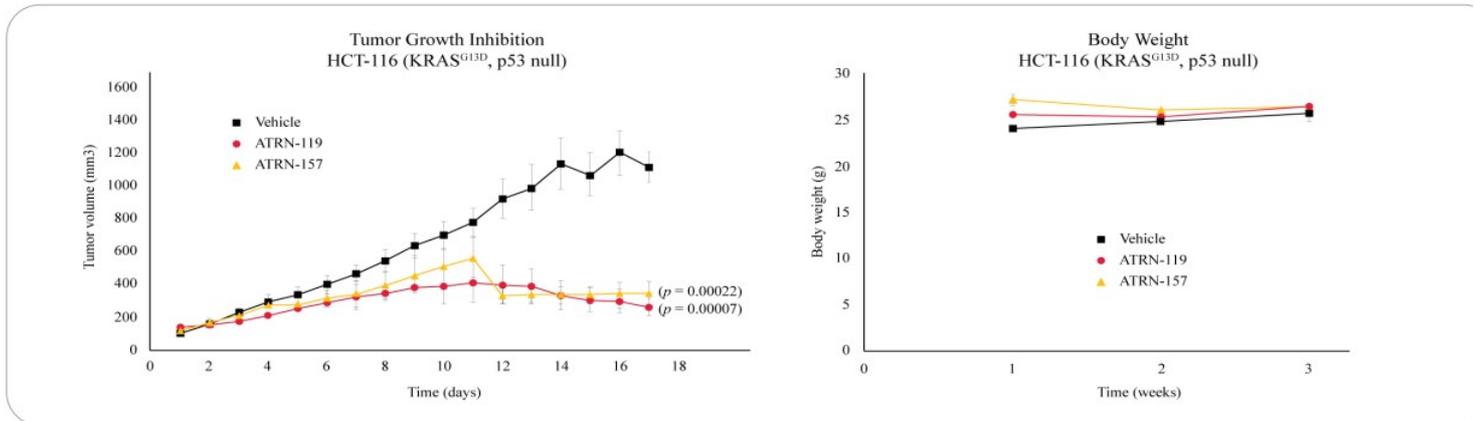


ATR-119 binds to ATR



...inhibits its biological activity...

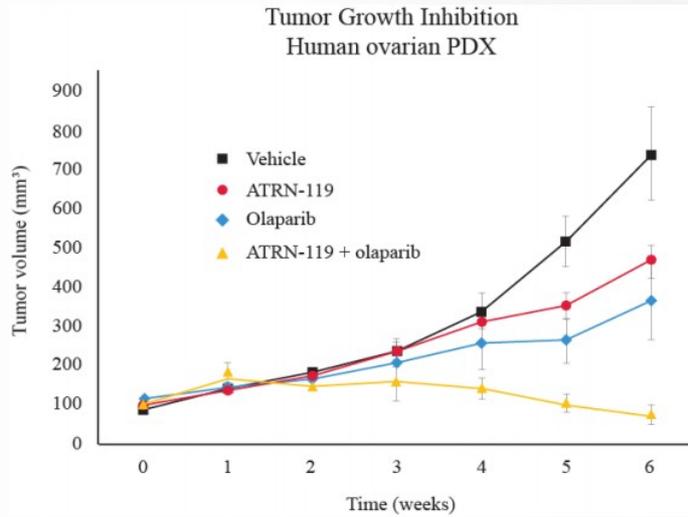
- Nanomolar potency in vitro across a broad spectrum of cancer cell lines
- Strong tumor control observed in vivo, including in challenging genetic backgrounds



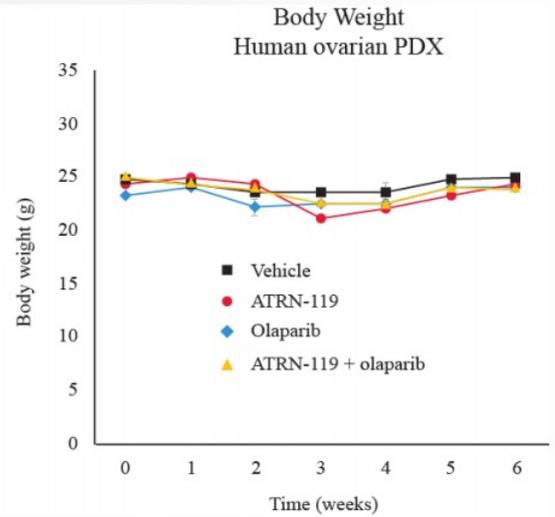
N=4 female mice per group, ATRN-119 - 100 mg/kg/day P.O, ATRN-157 - 20 mg/kg/day SQ.

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.

## ATRN-119 + Olaparib Inhibits Ovarian Tumor Growth Over Time



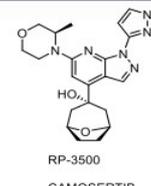
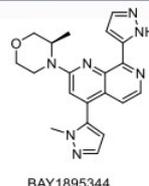
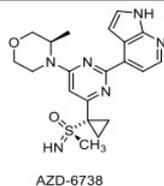
## ATRN-119 + Olaparib Shows Negligible Weight Loss Over Time



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

ATR Inhibitor :  
ATRN-119

Potential Differentiation



Parameter	AstraZeneca AZD6738 <sup>(1)(2)</sup>	Bayer BAY1895344 <sup>(3)</sup>	Repare / Roche <sup>(4)</sup> RP-3500 <sup>(5)</sup>
Route Of Administration	Oral	Oral	Oral
Clinical Studies Chosen (MTD/RP2D), Dose Schedule	160mg BID, 2-weeks-on, 2-weeks-off, or: Continuous dosing <sup>(1)</sup>	40mg BID, 3-days-on/4-days-off	160mg QD, 3-days-on/4-days-off
Main Grade ≥3 Hematological toxicities reported at Chosen Dose Schedule (MTD/RP2D), in clinical studies	Patriot 1, Escalation Phase, 160mg, BID <sup>(2)</sup> : <b>Anemia</b> (1/6, 17%)  Patriot 2, Expansion Phase <sup>(1)</sup> : <b>Fatigue, anemia, nausea &amp; thrombocytopenia (not differentiated) <sup>(1)</sup>:</b> (4/6, 67%) with continuous dosing (3/15, 20%) with 2-week-on, 2-week-off	<b>Anemia</b> (2/2, 100%)  <b>Neutropenia</b> (1/2, 50%)	<b>Anemia</b> (23/95, 24%)  <b>Neutrophil count decreased</b> (10/95, 11%)  <b>Platelet count decreased</b> (5/95, 5%)

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

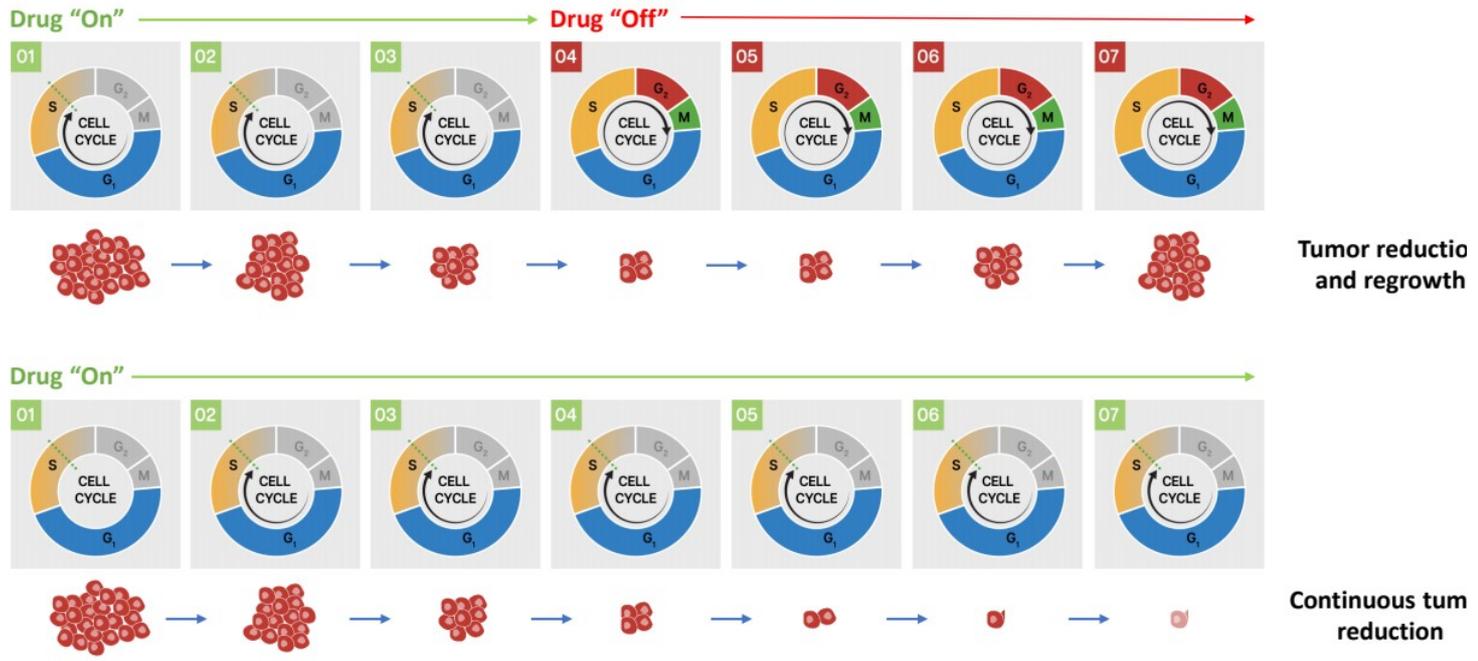
(1) Phase 1 study of ATR inhibitor, AZD6738, as monotherapy in advanced solid tumors (PATRIOT part A, B), Dillon et al, Volume 30, October 2019, Pages v165-v166

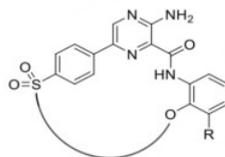
(2) Poster CT084: A Phase 1 dose-escalation study of ATR inhibitor monotherapy with AZD6738 in advanced solid tumors (PATRIOT Part A), AACR 2017

(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





Parameter	ATRN-119 <sup>(1)</sup>
Route Of Administration	Oral
Clinical Studies Chosen (MTD/RP2D), Dose Schedule	continuous once-daily dosing (dose TBD in Phase 1) <sup>(1)</sup>
Hematological toxicities in preclinical studies	<p><b>Pre-Clinical, Toxicology Studies:</b></p> <ul style="list-style-type: none"> <li>In 28-day GLP tox study in dogs, hematological changes were of small magnitude with complete recovery</li> <li>In a head-to-head comparative tolerability study, ATRN-119 demonstrated significantly less toxicity than another oral ATRi that is currently in clinical development <sup>(2)</sup></li> </ul>

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

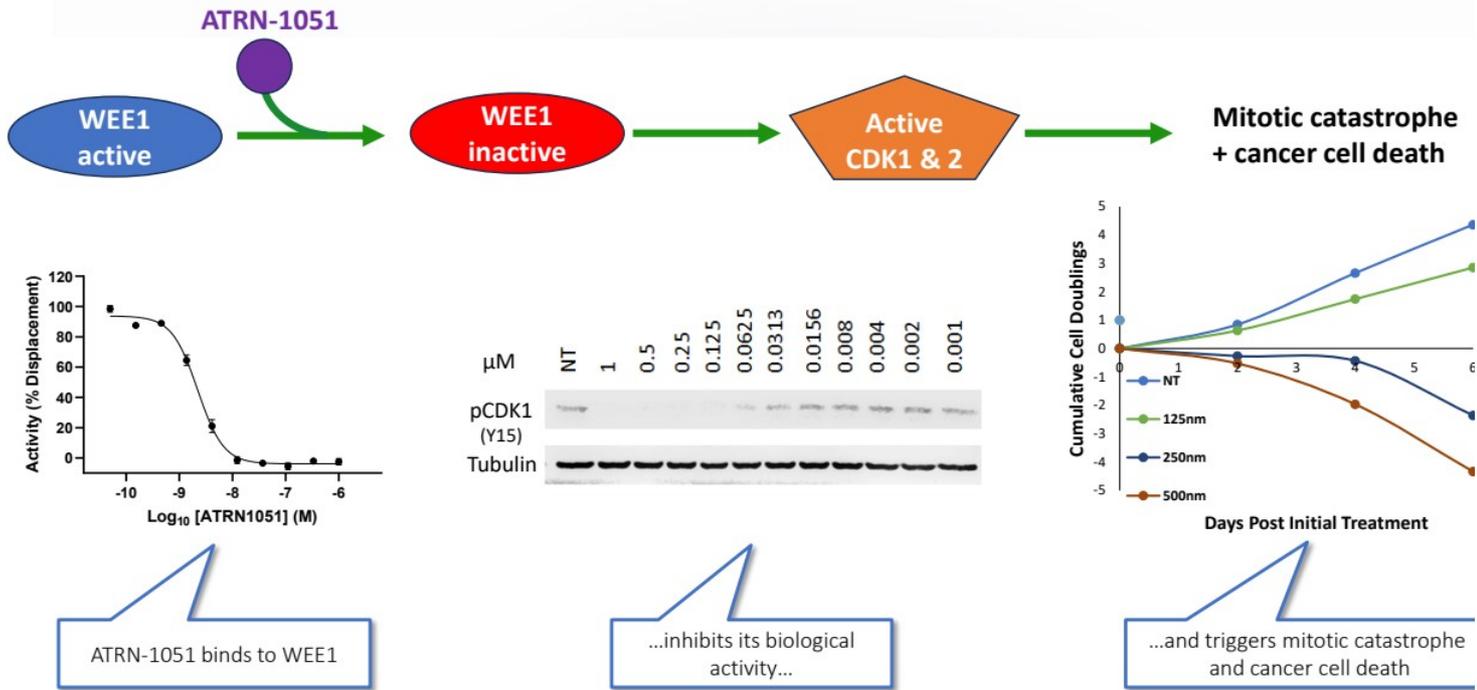
(1) ATRN-119, Phase 1/2a Clinical Study Protocol

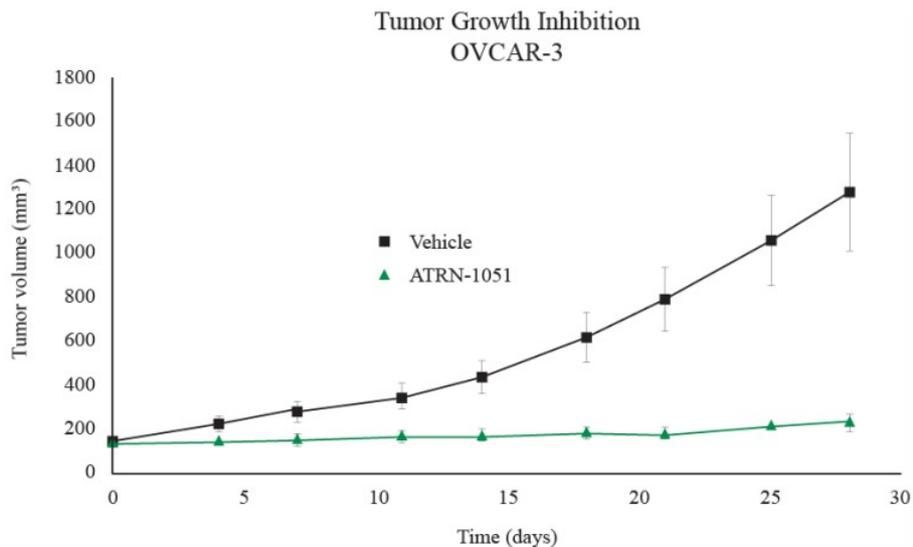
(2) Internal pre-clinical head-to-head tolerability study in male beagle dogs. ATRN-119 - 20 mg/kg/day for 7 days, followed by 40 mg/kg/day for 7 days and finally 50 mg/kg/day for 7 days, all P.O. Competitor ATRi- administered at a clinically equivalent dose range during 21 days, P.O. By day 4 of dosing, the dog receiving the competitor ATRi exhibited severe reduction in multiple blood cell lineages including reticulocytes. Continued dosing of competitor ATRi for three weeks resulted in significant reduction of white blood cells, red blood cells and hemoglobin levels, and was accompanied by severe body weight loss (-15%). For the dog receiving ATRN-119, reduced levels of reticulocytes and neutrophils were noted with prolonged treatment but remained within normal ranges and body weight changes were negligible (-2% to +4%).



## WEE1 Inhibitor : ATRN-1051 Preclinical proof-of-principle

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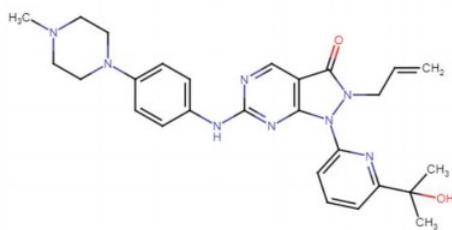


N=7 mice per group, ATRN-1051, exploratory formulation - 30 mg/kg/day

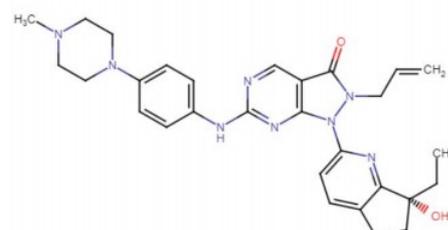
# WEE1 Inhibitor : ATRN-1051

## Potential Differentiation

ATRN-1051 shows potential to be potent and structurally differentiated, with high selectivity to limit off-target toxic



AZD-1775<sup>(1)</sup>



Azenosertib (ZN-c3)

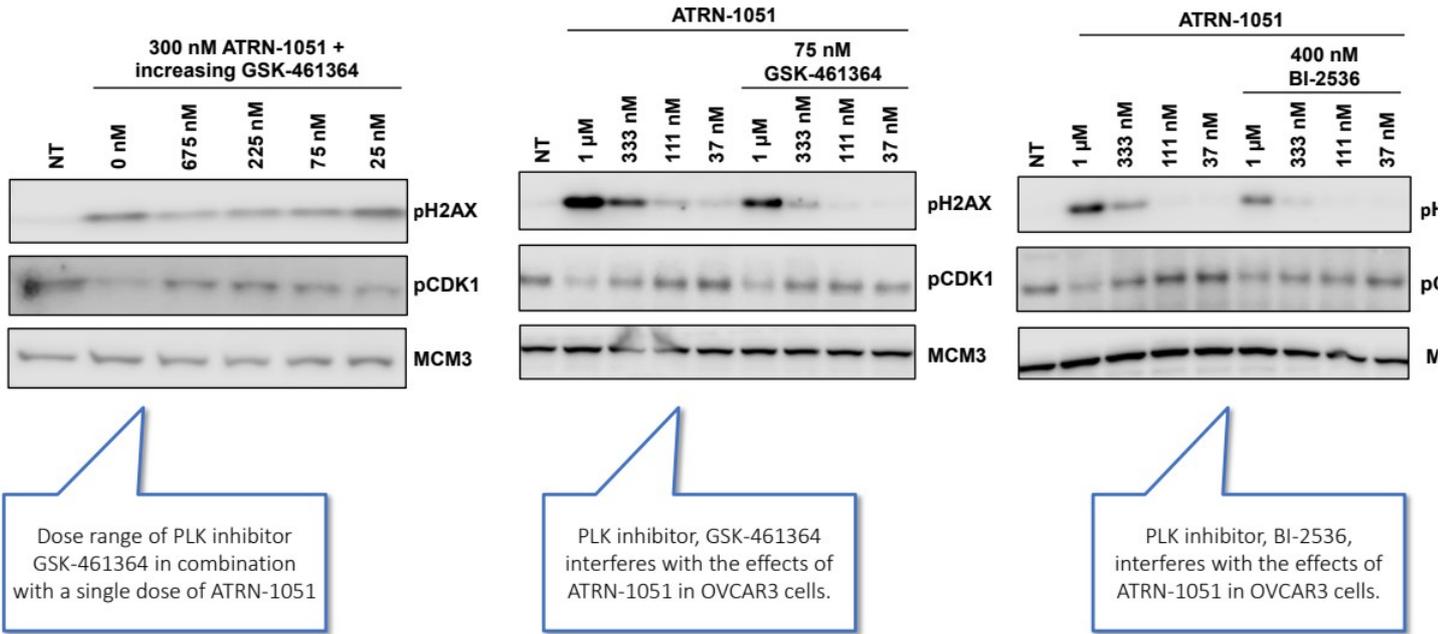
	On-Target IC <sub>50</sub> (nM)	Off-Target Inhibition at 1 μM (%)		
	WEE1	PLK1	PLK2	PLK3
Aprea: ATRN-1051	2.2	17	33	12
Zentalis: Azenosertib (ZN-c3) <sup>(1)</sup>	3.8	79	96	92
AstraZeneca: AZD-1775 <sup>(1)(2)</sup>	3.9	70	101	91

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

(1) Huang et al, (2021) J Med Chem

(2) AstraZeneca announced in July 2022 the discontinuation of development of AZD-1775

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Based on pre-clinical studies, ATRN-1051 shows potentially favorable drug exposure:



	ATRN 1051 <sup>(1)</sup>	Zentalis Azenosertib (ZN-c3) <sup>(2)</sup>			AstraZeneca AZD-1775 <sup>(2)</sup>		
Dose (mg/kg/d)	<b>10</b>	20	<b>40</b>	80	20	40	<b>80</b>
C <sub>max</sub> ng/ml	1,460	1,167	1,997	5,100	635	2,460	4,703
T <sub>max</sub> hr	3	1	1	1	1	1	1
AUC <sub>0-24</sub> ng*hr/ml	<b>16,739</b>	4,863	<b>17,088</b>	39,722	1,494	6,313	<b>13,408</b>

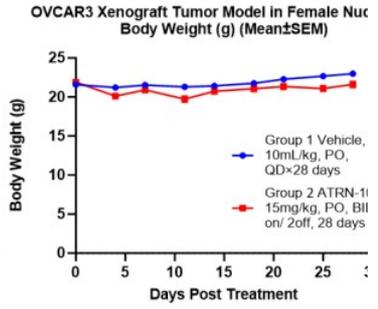
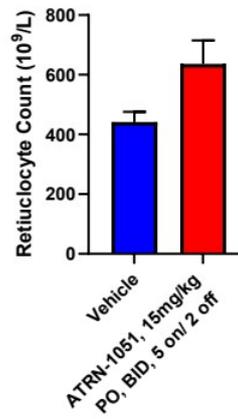
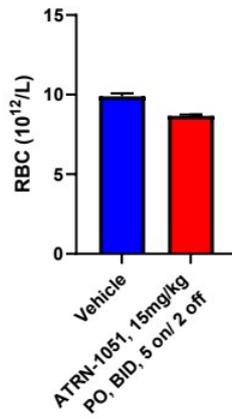
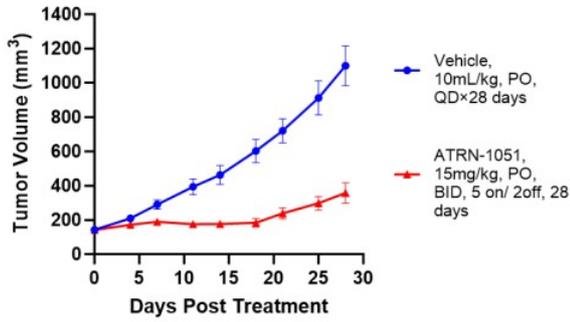
Note: Head-to-head studies have not been conducted

(1) Data from an exploratory formulation of ATRN-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

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## OVCAR3 Xenograft Tumor Model in Female Nude Mice Tumor Volume (mm<sup>3</sup>) (Mean±SEM)



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

Milestone	Timeline
IND	
Submission	4Q 2023
Clearance	1Q 2024
Phase 1/2a – Monotherapy Dose Escalation	
First Patient Enrolled	1H 2024
Last Patient Enrolled	2H 2025



## Summary

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- Cash & Equivalents of \$25.4 million as of September 30, 2023
- Closed \$4.9M (net) public offering in February 2023
- Obtained \$2.0 million 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

- Diversified portfolio with de-risked clinical and preclinical plans underway
  
- Opportunities in ovarian, CRC, prostate and breast cancers
  - ◇ Single agent and combination therapies
  
- Supportive follow-on strategy
  - ◇ IND submission by end of 2023
  - ◇ Undisclosed DDR asset
  
- Financed through the end of Q4 2024
  - ◇ Reach short term inflection points and catalysts
  - ◇ Evaluate optimal strategic partnerships