

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)  
of the Securities Exchange Act of 1934

May 15, 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 May 15, 2023, Aprea Therapeutics, Inc. (the "Company") issued a press release announcing its financial results for the three months ended March 31, 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 May 15, 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 May 15, 2023.</a>
99.2	<a href="#">Corporate Presentation (May 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: May 15, 2023

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

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**Aprea Therapeutics Reports First Quarter 2023 Financial Results and Provides Update on Business Operations**

DOYLESTOWN, PA, May 15, 2023 (GLOBE NEWSWIRE) – Aprea Therapeutics, Inc. (Nasdaq: APRE) (“Aprea”, or the “Company”), a clinical stage biopharmaceutical company focused on developing novel synthetic lethality-based cancer therapeutics targeting DNA damage response (DDR) pathways, today reported financial results for the three months ended March 31, 2023 and provided a business update.

“We are excited about the strong start for 2023 as we focus on the execution of the pipeline development plan and continue enrollment in our Phase 1/2a dose escalation study of our ATR inhibitor, ATRN-119, in patients with biomarkers related to DDR mutations,” said Oren Gilad, Ph.D., President and Chief Executive Officer of Aprea. “Our cash position remains strong with a runway to carry us into the third quarter of 2024 and cross meaningful clinical milestones in our two lead inhibitor programs, ATR and WEE1. In February, we closed an underwritten public offering pursuant to which the Company received approximately \$4.9 million in net proceeds. In April, we participated in the American Association of Cancer Research Conference where we had the opportunity to share preclinical results pointing to the potential, groundbreaking benefits of combination therapy with ATRN-119 and ATRN-1051. Our IND-enabling studies continue to progress for our ATRN-1051 inhibitor program and anticipate filing an IND by the end of 2023.”

**Key Business and Financial Updates**

- *ATR inhibitor program: ATRN-119* – Enrollment continues in the Phase 1/2a trial of Aprea’s lead clinical candidate, ATRN-119, a potential best-in-class ATR inhibitor for treatment of advanced solid tumors harboring defined mutations in DDR pathways. ATRN-119 is an orally bioavailable, potent and selective macrocyclic small molecule inhibitor of ATR. ATR is one of several key regulators impacting response to defective DNA replication and DNA damage, which occurs more commonly in cancer cells than in normal cells. Primary endpoints of the Phase 1 dose escalation part of the study include safety, tolerability, pharmacokinetics and a recommended Phase 2 dose. The Company expects to report initial safety, tolerability, and pharmacokinetic data from the ongoing Phase 1 trial of ATRN-119 in the first quarter of 2024.
- *WEE1 inhibitor program: ATRN-1051* – ATRN-1051 is an orally-bioavailable, highly potent and selective small molecule inhibitor of WEE1, a key regulator of multiple phases of the cell cycle. The Company believes preclinical findings support potentially favorable drug selectivity and exposure. Investigational New Drug (IND) enabling studies with ATRN-1051 are under way, and the Company anticipates filing an IND by the end of 2023.
- Presented Preclinical data on pipeline programs at the American Association for Cancer Research (AACR) 2023 Annual Meeting, held April 14-19, 2023, in Orlando, Florida. In April 2023, the Company presented a poster, titled “*ATRN-119 and ATRN-W1051: Novel and potentially well tolerated ATR and WEE1 inhibitors for targeted cancer treatment,*” highlighting its lead program ATRN-119 and preclinical WEE1 inhibitor ATRN-1051. In *in vivo* models, ATRN-119 demonstrated anti-tumor efficacy, both as a monotherapy and in combination with PARP inhibitors. In xenograft models, ATRN-1051 demonstrated high potency, potentially favorable pharmacokinetic properties, and anti-tumor efficacy.
- Secured non-dilutive funding via a research grant from the National Cancer Institute (NCI) supporting development of DDR inhibitors. In February 2023, the Company announced that it received an award notification from the NCI for the development of a first-in-class combination of DNA damage response inhibitors for the treatment of high-grade serous ovarian cancer (HGSOC). HGSOC is a devastating disease responsible for the deaths of about 125,000 women worldwide each year and has low survival rates.
- Closed an underwritten public offering in February 2023 pursuant to which the Company received approximately \$4.9 million in net proceeds, after deducting underwriting discounts and offering expenses. Net proceeds from the public offering support the continuing development of ATRN-119 and ATRN-1051 as well as general corporate overhead.
- Appointed Gabriela Gruia, M.D., to the Board of Directors, strengthening the Company’s leadership. Dr. Gruia brings over 25 years of clinical, regulatory and life science leadership experience to Aprea, having worked for Novartis, Pfizer, Pharmacia, Aventis and Rhone Poulenc. Dr. Gruia received her M.D. from Bucharest Medical School in Romania and a Masters in Breast Pathology and Mammography from Rene Huguenin/Curie Institute Cancer Center in Paris, France.

## Select Financial Results for the First Quarter ended March 31, 2023

- As of March 31, 2023, the Company reported cash and cash equivalents of \$31.0 million.
- For the quarter ended March 31, 2023, the Company reported an operating loss of \$4.6 million, compared to an operating loss of \$8.1 million for the same period in 2022.
- Research and Development (R&D) expenses were \$1.3 million for the quarter ended March 31, 2023, compared to \$4.1 million for the same period in 2022. The decrease in R&D expense was related to lower clinical trial expense primarily due to the close out of legacy Aprea clinical trials, lower personnel costs for the former facility in Sweden, and lower non-cash stock-based compensation expense.
- General and Administrative (G&A) expenses were \$3.4 million for the quarter ended March 31, 2023, compared to \$4.0 million for the same period in 2022. The decrease in G&A expenses was due to a lower non-cash stock-based compensation and insurance premium expenses, partially offset by higher personnel costs in the quarter ended March 31, 2023 related to severance expenses for former executives.
- The Company reported a net loss of \$4.4 million (\$1.34 per basic share) on approximately 3.3 million weighted-average common shares outstanding for the quarter ended March 31, 2023, compared to a net loss of \$7.9 million (\$7.25 per basic share) on approximately 1.1 million weighted average common shares outstanding for the same period in 2022.

### About Aprea Therapeutics, Inc.

Aprea Therapeutics, Inc. is a clinical stage biopharmaceutical company headquartered in Doylestown, Pennsylvania, focused on developing novel synthetic lethality-based cancer therapeutics that target DNA damage response pathways. The Company's lead program is ATRN-119, a clinical-stage small molecule ATR inhibitor being developed for solid tumor indications. Our WEE1 inhibitor 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 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, 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.

Source: Aprea Therapeutics, Inc.

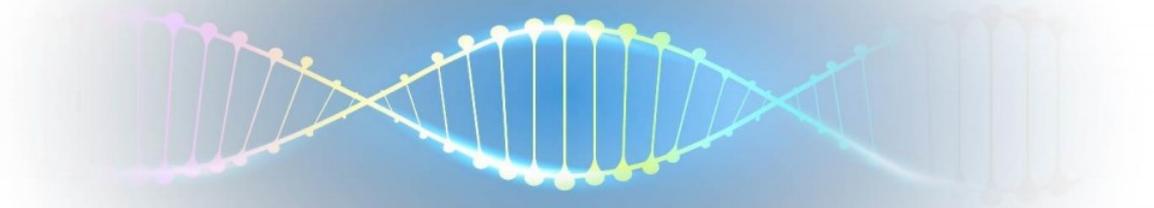
**Investors and Media:**  
[aprea@argotpartners.com](mailto:aprea@argotpartners.com)  
212-600-1902

Aprea Therapeutics, Inc.  
Condensed Consolidated Balance Sheets

	March 31, 2023	December 31, 2022
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 30,995,714	\$ 28,786,647
Prepaid expenses and other current assets	1,022,803	1,366,859
Total current assets	32,018,517	30,153,506
Property and equipment, net	1,912	2,321
Total assets	<u>\$ 32,020,429</u>	<u>\$ 30,155,827</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 826,027	\$ 842,754
Accrued expenses	3,401,361	2,358,332
Total current liabilities	4,227,388	3,201,086
Total liabilities	4,227,388	3,201,086
Commitments and contingencies (Note 8)		
Series A convertible preferred stock, \$0.001 par value, 40,000,000 shares authorized; 56,227 shares issued and outstanding at March 31, 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, 3,731,562 and 2,655,269 shares issued and outstanding at March 31, 2023 and December 31, 2022, respectively.	3,731	2,655
Additional paid-in capital	335,215,994	330,060,836
Accumulated other comprehensive loss	(10,561,452)	(10,623,408)
Accumulated deficit	(298,176,295)	(293,796,405)
Total stockholders' equity	26,481,978	25,643,678
Total liabilities and stockholders' equity	<u>\$ 32,020,429</u>	<u>\$ 30,155,827</u>

Aprea Therapeutics, Inc.  
Condensed Consolidated Statements of Operations and Comprehensive Loss

	Three Months Ended March 31,	
	2023	2022
Operating expenses:		
Research and development	\$ 1,256,542	\$ 4,089,577
General and administrative	3,365,961	3,985,298
Acquired in-process research and development	—	—
Total operating expenses	4,622,503	8,074,875
Other income (expense):		
Interest income, net	256,410	1,971
Foreign currency (loss) gain	(13,797)	136,211
Total other income	242,613	138,182
Net loss	\$ (4,379,890)	\$ (7,936,693)
Other comprehensive loss:		
Foreign currency translation	61,956	(65,505)
Total comprehensive loss	(4,317,934)	(8,002,198)
Net loss per share attributable to common stockholders, basic and diluted	\$ (1.34)	\$ (7.25)
Weighted-average common shares outstanding, basic and diluted	3,260,484	1,095,076



# Precision Oncology through Synthetic Lethality

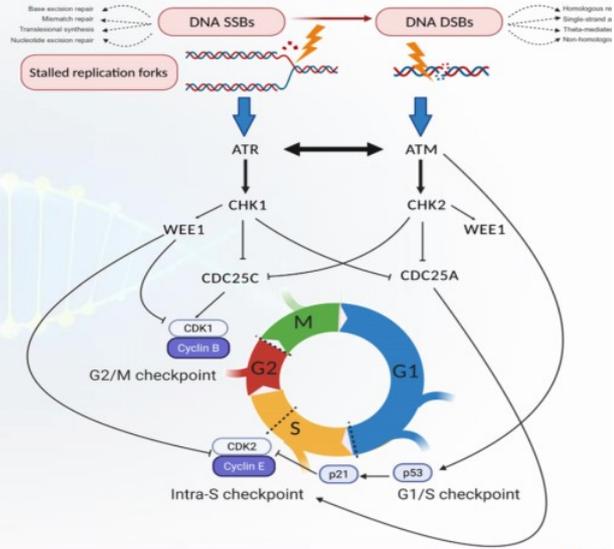
May 2023

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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 to anticipate,” “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 oncology company developing novel synthetic lethality-based therapeutics in areas of high unmet need
  - ◇ ATRN-119: ATR Inhibitor
  - ◇ ATRN-1051: WEE1 Inhibitor
  - ◇ Undisclosed DDR Inhibitor
- Synthetic lethality assets potentially differentiated from competitors
- Innovative platform technologies

### One Critical Pathway, Multiple Target

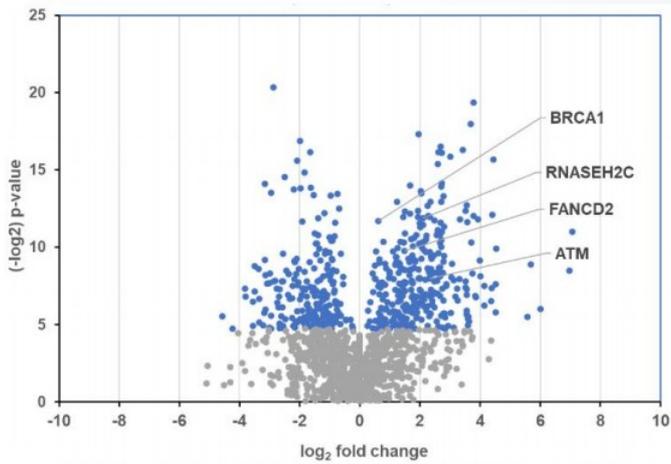


Capital-efficient model and near-term clinical milestones drive compelling investment opportunity

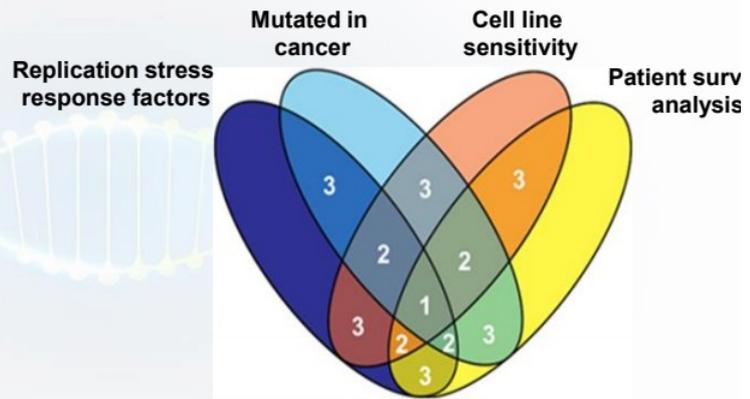
MOLECULE	TARGET	INDICATION	BIOMARKER	Preclinical	IND-Enabling	Phase 1	Anticipated Milestones
ATRN-119	ATR	Advanced solid tumors	Defined biomarkers	monotherapy			Q1 2024: Phase 1 tolerability, PK
		Ovarian, breast, prostate	BRCA1/2 + others	combination with PARPi			Q4 2023 / Q1 2024: Ph1 initiation
ATRN-1051	WEE1	Advanced solid tumors	CCNE amplification + others				End of 2023: IND submission
ATRN-354 <sup>1</sup>	ATR	Advanced solid tumors	Defined biomarkers				Second half of 2024: IND submission
APRE-DDRi	DDR Target	Advanced solid tumors	Defined biomarkers				Mid-2024: Development candidate

<sup>1</sup> ATRN-354 timeline and anticipated milestones subject to data from ATRN-119 clinical trial

## Drug response factor identification



## Biomarker prioritization



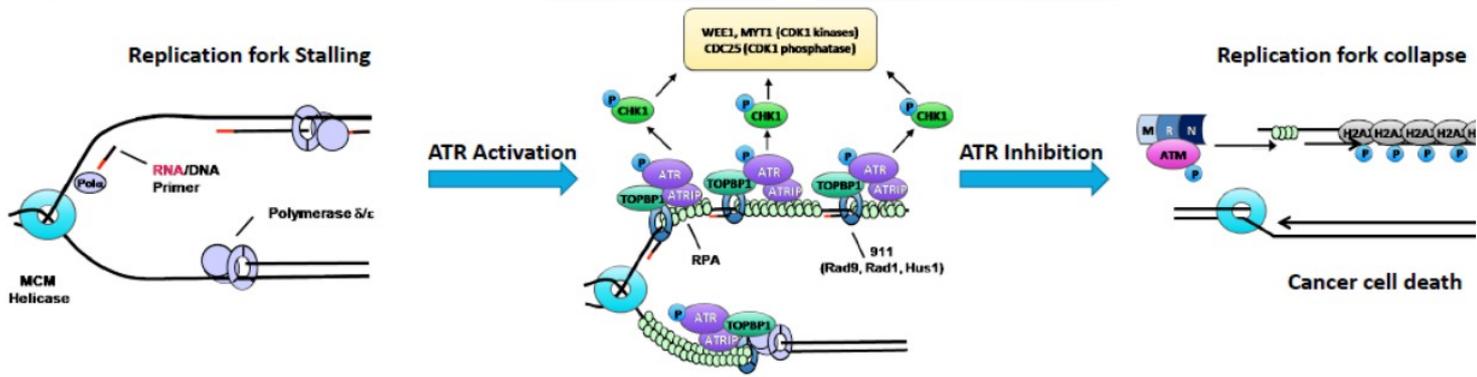
- Repli-Biom platform is designed to identify factors that respond to drug treatment at the mechanistic site of drug action, the replication fork
- Repli-Biom shows potential to identify candidate biomarkers of therapeutic benefit as well novel SL targets
- Combination SL may permit lower doses and decreased rates of acquired resistance, potentially leading to durable responses in cancers with specific mutations



# ATRN-119

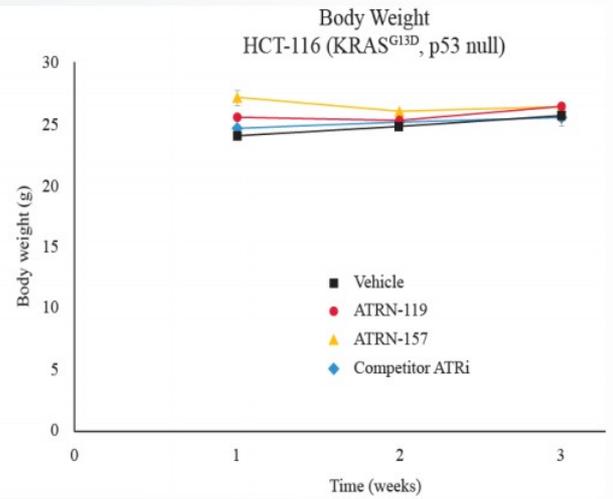
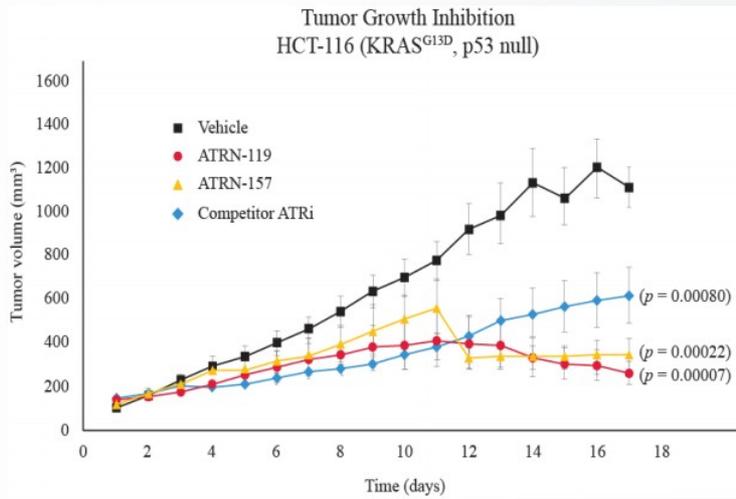
## ATR Inhibitor

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- Defects in DDR lead to compromised genomic instability and stalling of the replication fork
- ATR is activated by replication stress
- ATR Inhibition leads to replication fork collapse and cancer cell death
  - ◆ Cancer cells with dysfunctional and/or dysregulated DDR are particularly sensitive to ATR inhibition
  - ◆ Examples: Oncogenic RAS mutations, MYC overexpression, ATM mutations, BRCA1, BRCA2

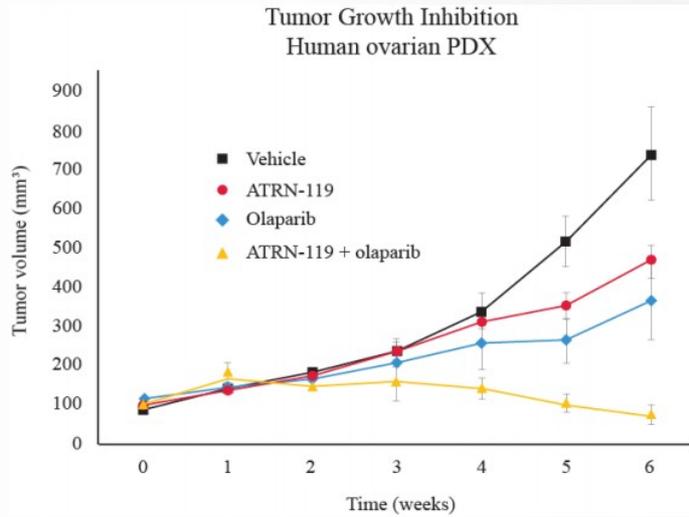
- Nanomolar potency *in vitro* across a broad spectrum of cancer cell lines
- Based on pre-clinical studies, strong tumor control observed *in vivo*, including in challenging genetic backgro



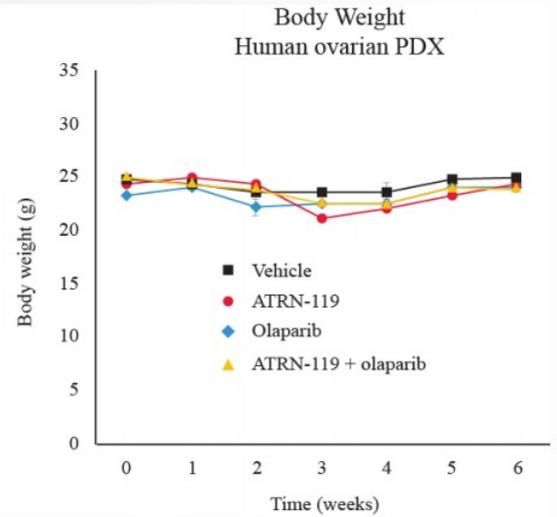
N=4 female mice per group, ATRN-119 - 100 mg/kg/day P.O, Competitor ATRi - 25 mg/kg/day P.O, ATRN-157 - 20 mg/kg/day SQ.

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

**These data are potentially supportive of future potential clinical trials to evaluate the combination of a PARP inhibitor and ATRN-1:**

- ATRN-119 has shown the potential to be highly potent with high selectivity to limit off-target toxicity

	On-Target Cellular IC <sub>50</sub> (nM)	Fold Difference in IC <sub>50</sub> for Off-Target PIKK Inhibition		
		ATM	DNA-PK	mTOR
Aprea: ATRN-119 <sup>(1)</sup>	4	> 600x	> 2000x	> 2000x
AstraZeneca: AZD-6738 <sup>(2)</sup>	74	> 400x	> 400x	70 – 310x
Bayer: BAY 1895344 <sup>(3)</sup>	36	39x	9x	61x
Repare/Roche: RP3500 <sup>(4)</sup>	0.33	> 20000x	> 20000x	30x

**Summary:**

- ATRN-119 is highly potent and selective to potentially limit off-target toxicity
- In pre-clinical studies, ATRN-119 has shown potential to have favorable tolerability profile

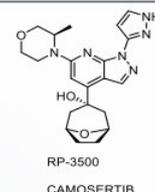
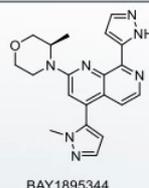
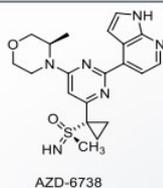
Note: Head-to-head studies with ATRN-119 have not been conducted

(1) Atrin data reported for HCT116 - Bcl/XL cell line;

(2) Foote et al (2018), J Med Chem;

(3) Lücking et al (2020), J Med Chem;

(4) Roulston et al (2022) Mol Cancer Ther



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> : Anemia (1/6, 17%)  Patriot 2, Expansion Phase <sup>(1)</sup> : Fatigue, anemia, nausea & thrombocytopenia (not differentiated) <sup>(1)</sup> : (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 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

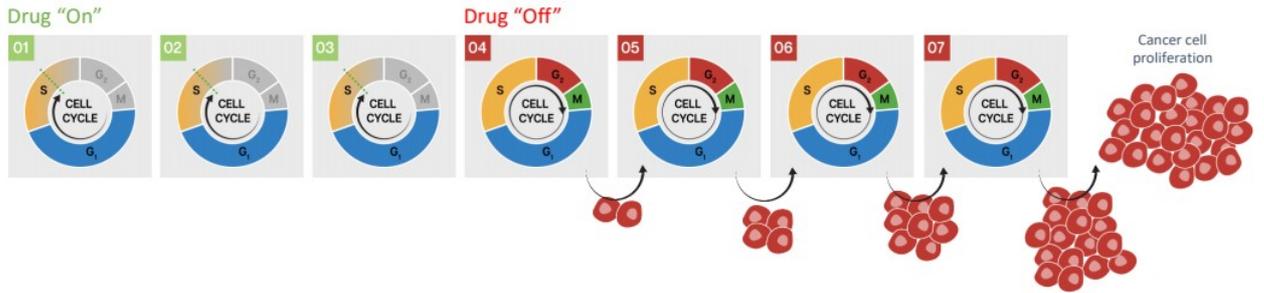
(2) Poster CT084-A Phase I dose-escalation study of ATR inhibitor monotherapy with AZD6738 in advanced solid tumors (PATRIOT Part A), AACR 2017

(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

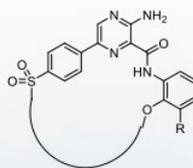
## Intermittent dosing



## Continuous dosing



Improved tolerability of an ATR inhibitor could potentially provide opportunities to expand the therapeutic window and administer higher doses on a continuous daily dosing schedule to potentially improve response rates and response duration



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>

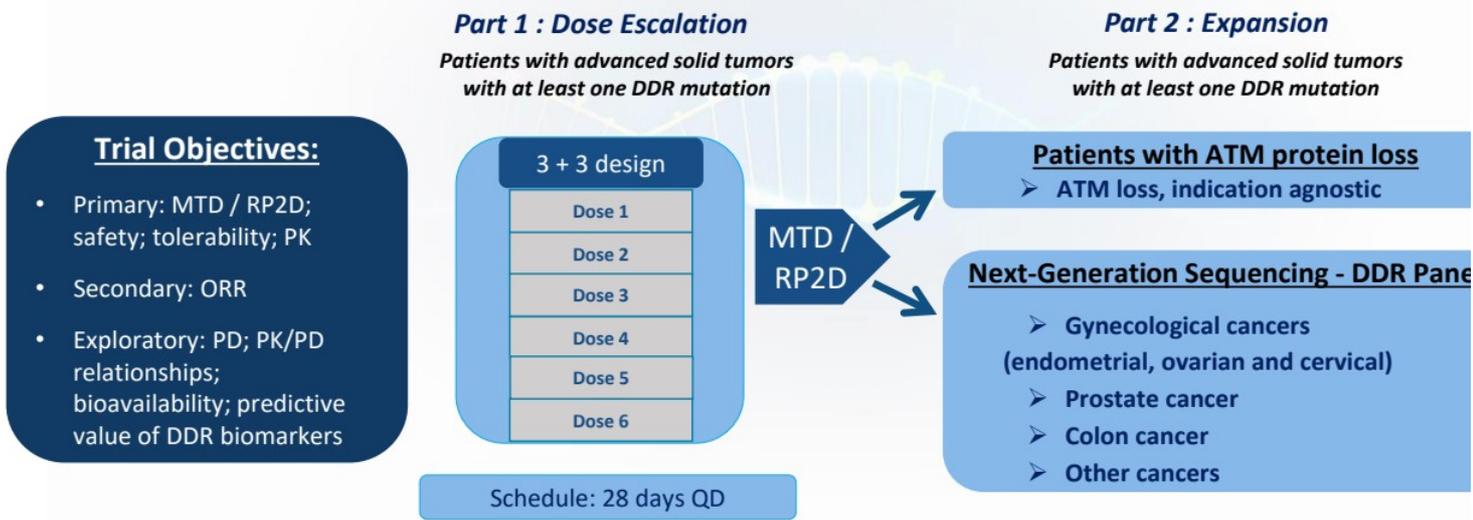
ATRN-119 potential for reduced toxicity could make it a preferred ATR inhibitor as a single agent, as well as a candidate for combination with standard-of-care therapies.

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%).

- NGS testing used to determine presence of DDR mutations/LOF
- Patient selection is critical - Subjects may be enrolled with advanced solid tumor with at least one DDR mutation
- Biomarkers with high likelihood for increased sensitivity to our lead drug candidate have been identified



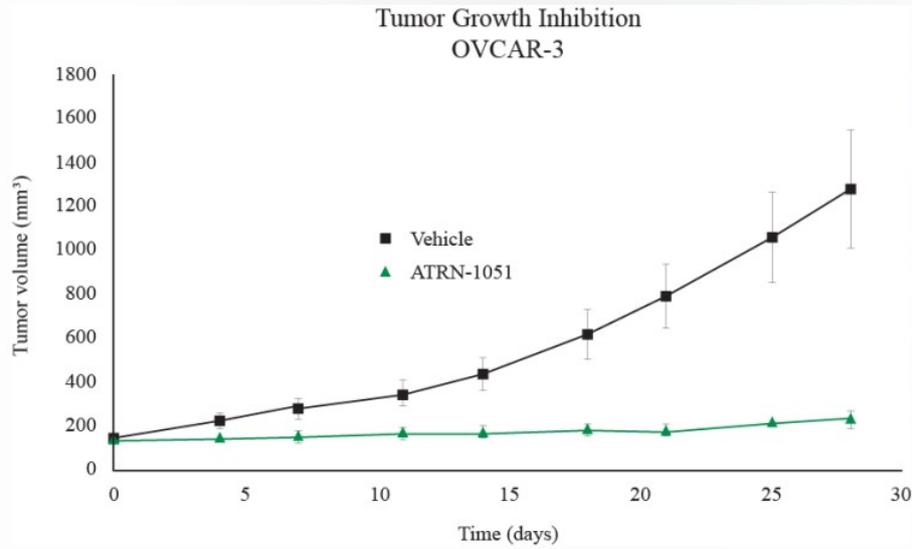


# ATRN-1051

## WEE1 Inhibitor

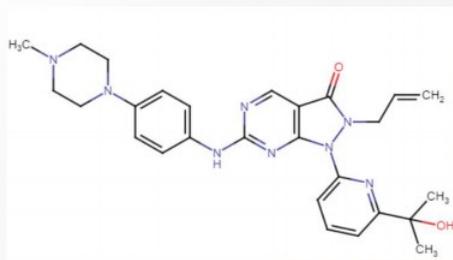
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- Nanomolar anti-proliferative potency in vitro against multiple cancer cell lines
- Potent anti-tumor activity observed in vivo in an ovarian cancer xenograft model (CCNE1-amplified cell line)

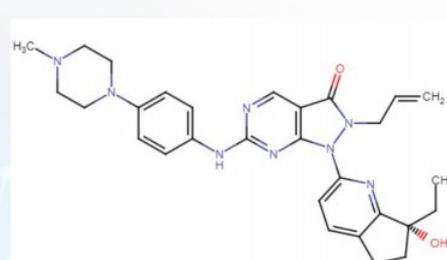


N=7 mice per group, ATRN-1051, exploratory formulation - 30 mg/kg/day

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



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



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: 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

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

	ATRN-1051 <sup>(1)</sup>	Zentalis ZN-c3 <sup>(2)</sup>			AstraZeneca AZD-1775 <sup>(2)</sup>		
Dose (mg/kg/d)	10	20	40	80	20	40	80
C <sub>max</sub> , ng/mL	1460	1167	1997	5100	635	2460	4703
T <sub>max</sub> , hr	2.7	1	1	1	1	1	1
AUC <sub>0-24</sub> , ng*hr/mL	16739	4863	17088	39722	1494	6313	13408

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



# Intellectual Property

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## Four issued US patents protecting lead molecule and analogs

- **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. 13<sup>th</sup>, 2015
  - Patents granted in AU, CA, CN, EP, IL, JP, MX. 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 & methods of use**
  - Carboxylic acid-containing macrocyclic ATR inhibitors, and prodrugs; methods of using these inhibitors to treat various cancers; filed Apr. 12<sup>th</sup>, 2017
  - *Issued on May 28, 2019 as U.S. Patent 10,301,324*
  
- **Family 3: ATR inhibitor Pharmaceutical Composition and Methods:**
  - Provisional application filed on Apr. 14<sup>th</sup>, 2022
  - Pharmaceutical formulation and composition of our lead molecule in the clinic
  
- **Family 4: WEE1 inhibitor Pharmaceutical Compositions and Methods:**
  - International Application filed on Jun. 3<sup>rd</sup>, 2022
  - Composition of our lead WEE1 inhibitor compounds



## Corporate Highlights & Milestones

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MOLECULE	TARGET	INDICATION	BIOMARKER	Preclinical	IND-Enabling	Phase 1	Anticipated Milestones
ATRN-119	ATR	Advanced solid tumors	Defined biomarkers	 monotherapy			Q1 2024: Phase 1 tolerability, PK
		Ovarian, breast, prostate	BRCA1/2 + others	 combination with PARPi			Q4 2023 / Q1 2024: Ph1 initiation
ATRN-1051	WEE1	Advanced solid tumors	CCNE amplification + others				End of 2023: IND submission
ATRN-354 <sup>1</sup>	ATR	Advanced solid tumors	Defined biomarkers				Second half of 2024: IND submiss
APRE-DDRi	DDR Target	Advanced solid tumors	Defined biomarkers				Mid-2024: Development candida

<sup>1</sup> ATRN-354 timeline and anticipated milestones subject to data from ATRN-119 clinical trial

## Robust synthetic lethality (SL) portfolio built in-house from foundational, proprietary DNA damage repair (DDR) platform

- ◇ Addressing critical unmet therapeutic needs for patients with genetically defined cancers.

- ATR Program: ATRN-119

- ◇ Lead clinical candidate ATRN-119 is a potential best-in-class oral ATR inhibitor for the treatment of advanced solid tumors harboring defined mutations in DDR pathways. Currently enrolling patients into Phase 1/2a. ATRN-119 is structurally differentiated and has shown in pre-clinical studies to be potentially highly selective and exhibit a favorable tolerability profile.

- WEE1 Program: ATRN-1051

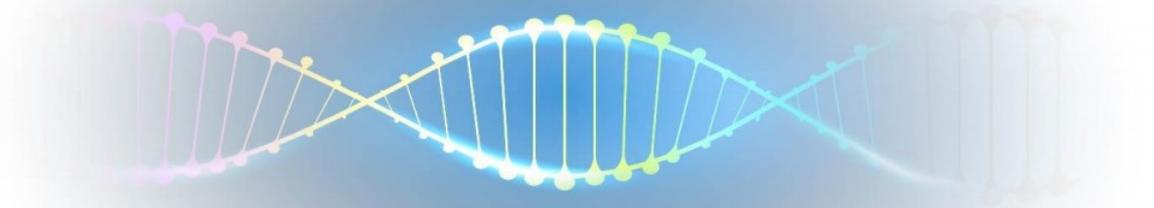
- ◇ ATRN-1051 is a highly potent WEE1 inhibitor currently in IND-enabling studies. Preclinical findings show potentially favorable drug selectivity and exposure.

- Pipeline

- ◇ Additional undisclosed synthetic lethality assets show promising potential in novel oncology targets.

- Cash & Equivalents of \$31.0 million as of March 31, 2023
- Closed \$4.9M (net) public offering in February 2023
- Obtained non-dilutive funding via research grant from National Cancer Institute (NCI)

Securities	Common Equivalents as of May 15, 2023
Preferred Stock (as converted)	28,112
Common Stock	3,731,571
Options	558,141
Restricted Stock Units	25,972
Fully Diluted Equivalents	4,343,796



# Precision Oncology through Synthetic Lethality

May 2023

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