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 10, 2023
Date of Report (Date of earliest event reported)

Aprea Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-39069**	**84-2246769**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

3805 Old Easton Road **Doylestown, PA**	**18902**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(617) 463-9385**

(Former name or former address, if changed since last report):

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	NASDAQ Global Select Market

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 10, 2023, Aprea Therapeutics, Inc. (the "Company") updated its corporate presentation that it intends to use in meetings with investors from time to time.

A copy of the Company's corporate presentation is filed herewith as Exhibit 99.1 and is hereby incorporated by reference herein.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Aprea Therapeutics, Inc. Presentation (February 2023)
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.

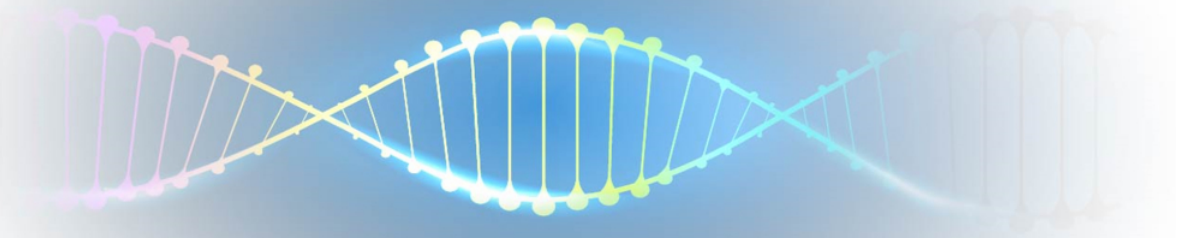
Aprea Therapeutics, Inc.

Dated: February 10, 2023

By: /s/ Oren Gilad
Name: Oren Gilad
Title: President and Chief Executive Officer

Exhibit 99.1

aprea therapeutics



Precision Oncology through Synthetic Lethality

February 2023

Forward-Looking Statements

Certain information contained in this presentation includes “forward-looking statements”, within the meaning of Se
Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, related to
regulatory submissions and strategic plans. We may, in some cases use terms such as “predicts,” “believes,” “potent
“anticipates,” “estimates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “likely,” “will,” “should” or other wo
uncertainty of the future events or outcomes to identify these forward-looking statements. The forward-looking sta
on current beliefs and expectations of our management team that involve risks, potential changes in circumstances,
uncertainties. Any or all of the forward-looking statements may turn out to be wrong or be affected by inaccurate as
management team might make or by known or unknown risks and uncertainties. These forward-looking statements
risks and uncertainties including, without limitation, risks related to the success and timing of our clinical trials or ot
the other risks set forth in our filings with the U.S. Securities and Exchange Commission, including our Annual Repor
and Quarterly Reports on Form 10-Q. Forward-looking statements regarding our product candidates are also subjec
risks and uncertainties, including without limitation, with respect to: our dependence on additional financing to fun
and complete the development and commercialization of our product candidates, and the risks that raising such ad
may restrict our operations or require us to relinquish rights to our technologies or product candidates; our limited
preclinical status of the assets we acquired from Atrin Pharmaceuticals Inc.; our business plan or the likelihood of th
implementation of such business plan; the timing of initiation of planned clinical trials for our product candidates; th
of such trials; the successful implementation of our research and development programs and collaborations and the
the results and findings of such programs and collaborations and whether such results are sufficient to support the
our product candidates; the success, timing and cost of our anticipated clinical trials for our current product candida
initiation, futility analyses, data presentation, reporting and publication and receipt of interim results (including, wit
any preclinical results or data); any statements about our understanding of product candidates mechanisms of actio
interpretation of preclinical and early clinical results from its clinical development programs and any collaboration st
factors, including legislative, regulatory, political and economic developments not within our control. For all these re
results and developments could be materially different from those expressed in or implied by our forward-looking s
cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of
We undertake no obligation to update such forward-looking statements to reflect subsequent events or circumstanc
extent required by law or regulation.

Aprea Therapeutics (NASDAQ: APRE)

Precision Oncology via Synthetic Lethality in Defined Patient Populations

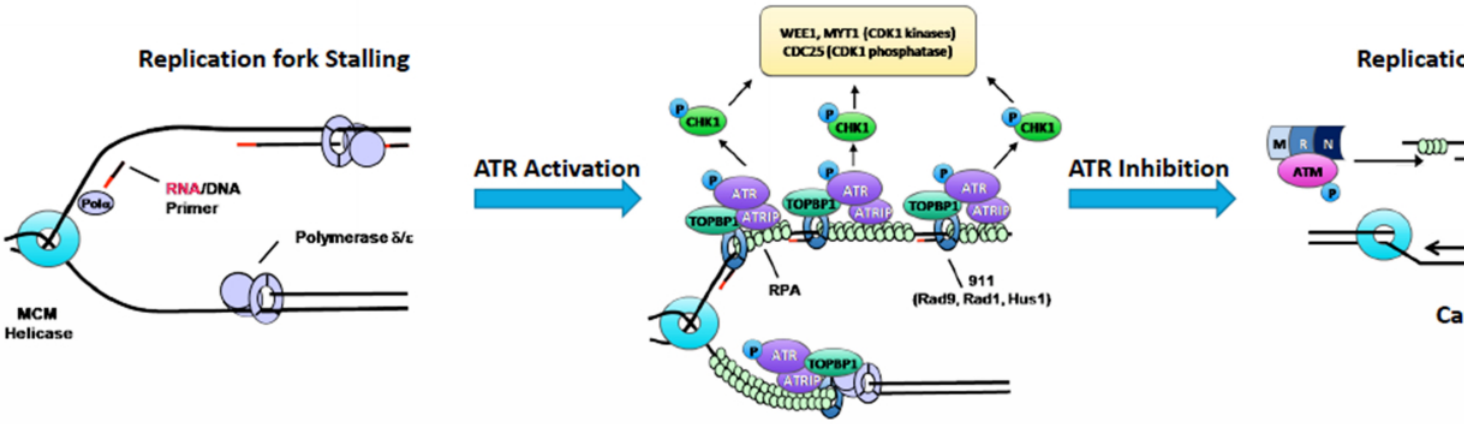
- Clinical stage precision oncology company developing novel synthetic lethality-based therapeutics in areas of high unmet need
  - ◊ ATRN-119: ATR Inhibitor
  - ◊ ATRN-W1051: WEE1 Inhibitor
  - ◊ Undisclosed DDR Inhibitor
- Synthetic lethality assets potentially differentiated from competitors
- Innovative platform technologies

Capital-efficient m
near-term clinical
drive compelling i
opportuni

Robust DDR Development Pipeline

*ATR = Timeline and capital allocation will be adjusted upon clinical data from lead ATR program.

ATR is the Master Regulator of DDR

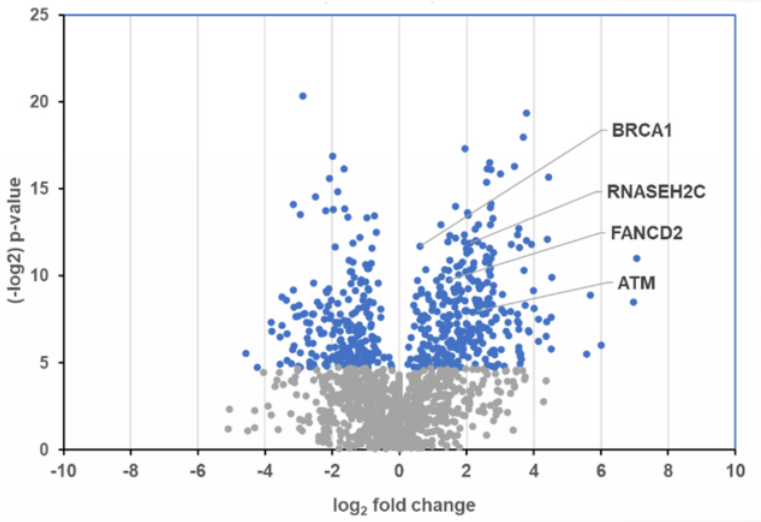


- Defects in DDR lead to compromised genomic instability and stalling of the replic
- ATR is activated by replication stress
- ATR Inhibition leads to replication fork collapse and cancer cell death
  - ◊ Cancer cells with dysfunctional and/or dysregulated DDR are particularly sensitive to ATR inhi
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

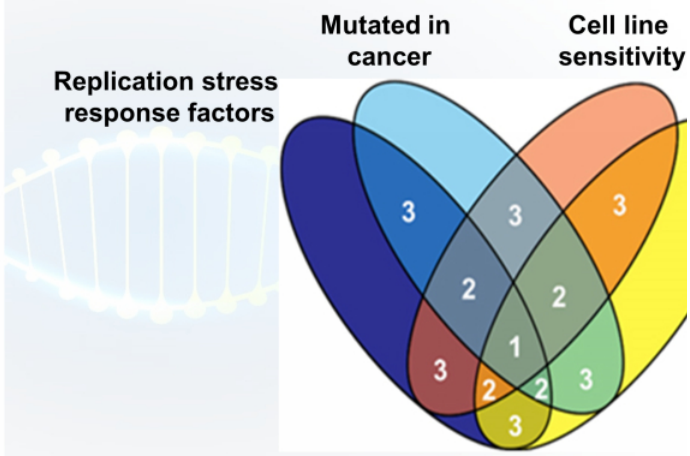
Repli-Biom Proprietary Platform and Combination Approache

An Integrated Platform for Discovery of Novel SL Targets and Biomarkers

Drug response factor identification



Biomarker prioritization



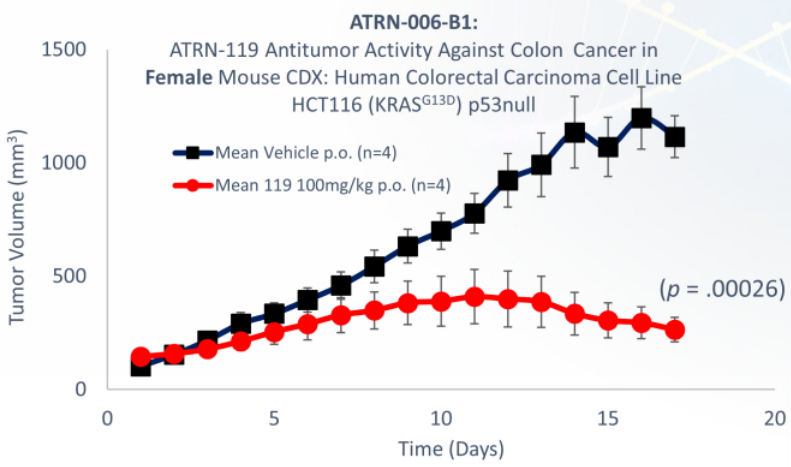
- Repli-Biom platform is designed to identify factors that respond to drug treatment at the mechanistic site of drug action, the re
- Repli-Biom shows potential to identify candidate biomarkers of therapeutic benefit as well novel SL targets
- Combination SL may permit lower doses and decreased rates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

ATRN-119
ATR Inhibitor

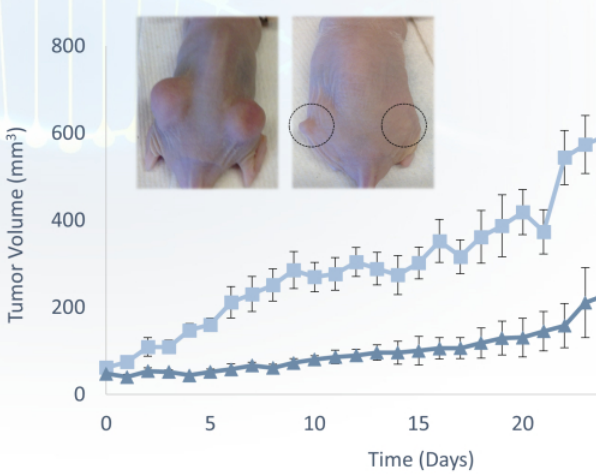
ATRN-119 Preclinical Profile

- 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 gen

HCT-116 p53 null (KRAS^{mut}, p53)



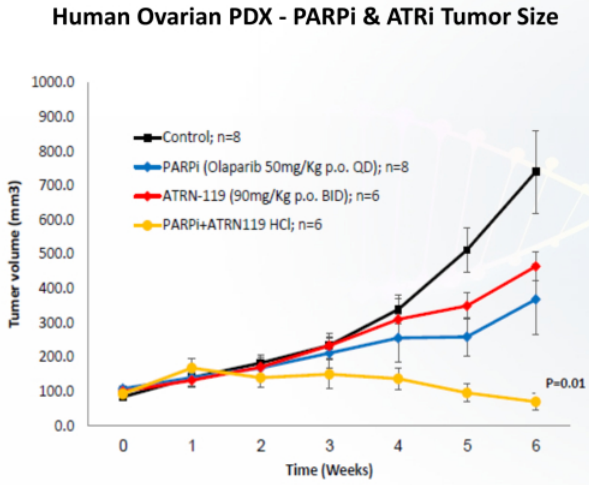
Pancreatic (CAPAN-1) (KRAS^{mut}, BRCA2)



Pre-clinical studies with ATRN-119

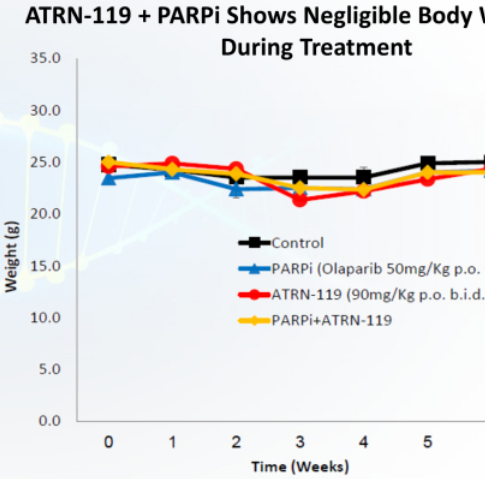
ATRN-119 + Olaparib (Lynparza®): Regression of BRCA2-Deficient Ovarian (HGSOC) Tumors

ATRN-119 + PARPi Inhibits Ovarian Tumor Growth Over Time



Based on pre-clinical results to date, the combination of ATRN-119 and PARPi has shown potentially compelling tumor growth inhibition

ATRN-119 + PARPi Shows Negligible Weight Loss Over Ti



Based on pre-clinical results to
combination of ATRN-119 and PAR
appears to be well tolera

Pre-clinical studies with ATRN-119

ATRN-119 is Potentially Differentiated from Other ATR Inhibit

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

	On-Target Cellular IC_{50} (nM)	Fold Difference in IC_{50} for Off-Target PIKK	
	ATRi	ATM	DNA-PK
Aprea: ATRN-119 (1)	4	> 600x	> 2000x
Merck KGaA: Berzosertib (1)	61	31x	> 200x
AstraZeneca: AZD-6738 (2)	74	> 400x	> 400x
Bayer: BAY 1895344 (3)	36	39x	9x
Repare/Roche: RP3500 (4)	0.33	> 20000x	> 20000x

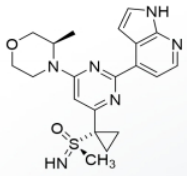
Conclusions:

- ATRN-119 is highly potent and selective to potentially limit off-target toxicity
- In pre-clinical studies, ATRN-119 has shown potential to have lower hematological toxicity than other ATRi

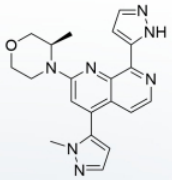
Note: Head-to-head studies with ATRN-119 have not been conducted
(1) Atrin data reported for HCT116 - Bcl/XL cell line;
(2) Foote et al (2018), J Med Chem;
(3) Lücking et al (2020), J Med Chem;
(4) Roulston et al (2022) Mol Cancer Ther

ATR Landscape Drives Potential Competitive Advantage for A

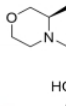
Current ATRs Structurally Similar in Core, Backbone, and Toxicity Profile



AZD-6738



BAY1895344



Parameter	AstraZeneca AZD6738 (1)(2)	Bayer BAY1895344 (3)	Repare / RP-35
Route Of Administration	Oral	Oral	Or
Clinical Studies Chosen (MTD/RP2D), Dose Schedule	160mg BID, 2-weeks-on, 2-weeks-off, or: Continuous dosing (1)	40mg BID, 3-days-on/4-days-off	160m 3-days-on/
Main Grade ≥3 Hematological toxicities reported at Chosen Dose Schedule (MTD/RP2D), in clinical studies	Patriot 1, Escalation Phase, 160mg, BID (2): **Anemia** (1/6, 17%) Patriot 2, Expansion Phase (1): **Fatigue, anemia, nausea & thrombocytopenia (not differentiated)** (1): (4/6, 67%) with continuous dosing (3/15, 20%) with 2-week-on, 2-week-off	**Anemia** (2/2, 100%) **Neutropenia** (1/2, 50%)	Ane (23/95 Neutrophil co (10/ Platelet cou (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

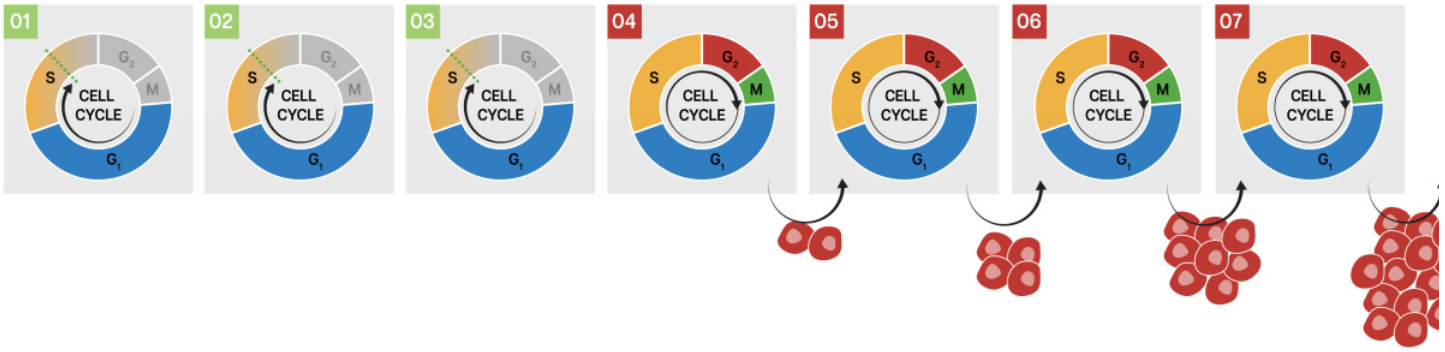
ATRN-119 Daily dosing Is Desirable

Lack of daily dosing may contribute to formation of resistance

Competitors (AstraZeneca, Bayer and Repare) intermittent dosing

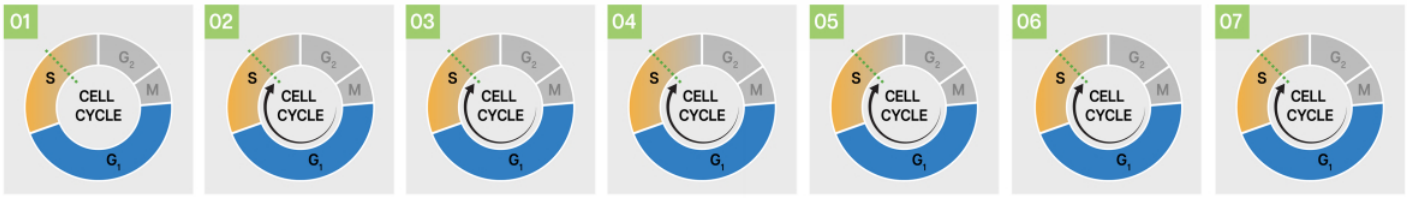
Drug “On”

Drug “Off”



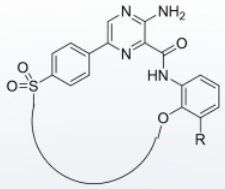
ATRN-119 Continuous dosing

Drug “On”



ATRN-119: Potential Best-in-Class Oral ATR Inhibitor

With Structurally Differentiated Core, Backbone, and Toxicity Profile



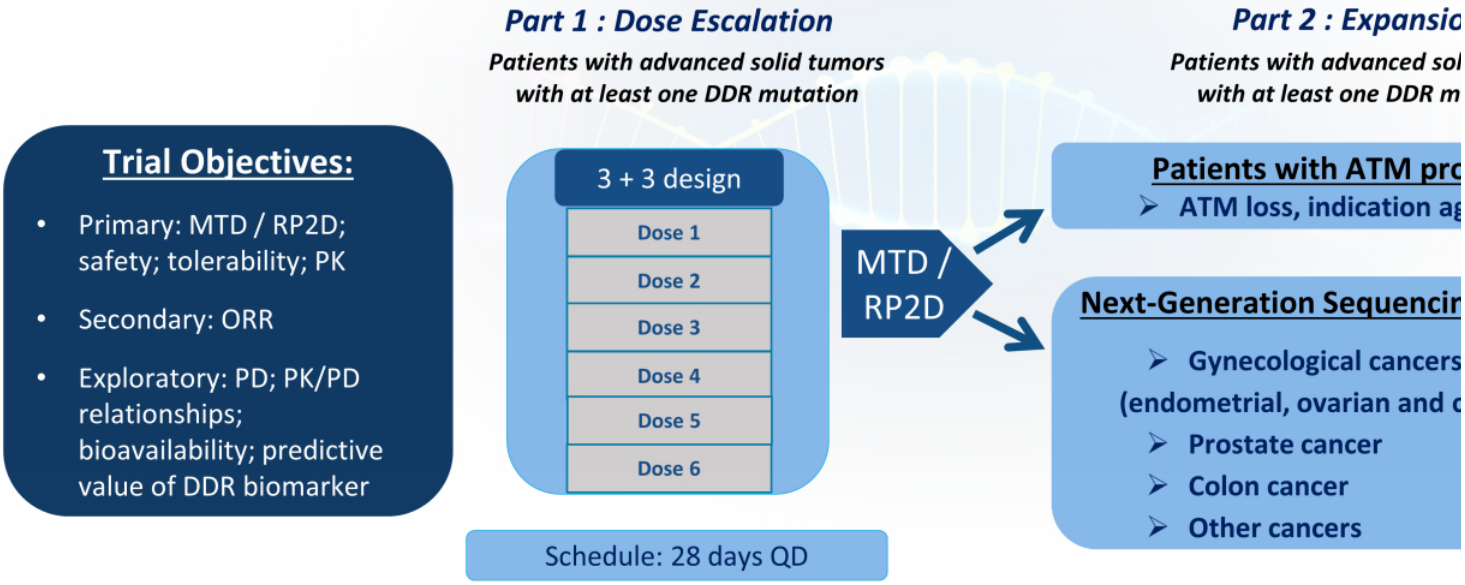
Parameter	ATRN-119 (1)
Route Of Administration	Oral
Clinical Studies Chosen (MTD/RP2D), Dose Schedule	continuous once-daily dosing (dose TBD in Phase 1) (1)
Hematological toxicities in preclinical studies	**Pre-Clinical, Toxicology Studies:** • In 28-day GLP tox study in dogs, hematological changes were of small magnitude with comp • In a head-to-head comparative tolerability study, ATRN-119 demonstrated significantly less t another oral ATRi that is currently in clinical development

ATRN-119 potential for reduced toxicity could make it a preferred ATR inhibitor as a single agent, as well a 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

ATRN-119 Phase 1/2a Clinical Trial Design

- 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 m
- Biomarkers with high likelihood for increased sensitivity to our lead drug candidate have been characteriz

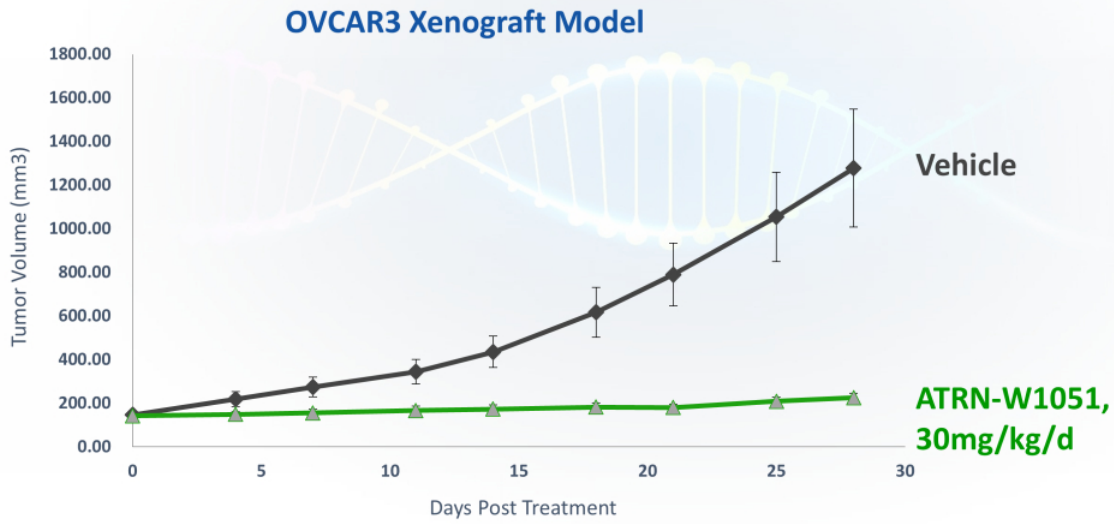


ATRN-W1051
WEE1 Inhibitor

ATRN-W1051 Has Demonstrated Potentially Compelling Anti-tum

IND targeted 4Q 2023

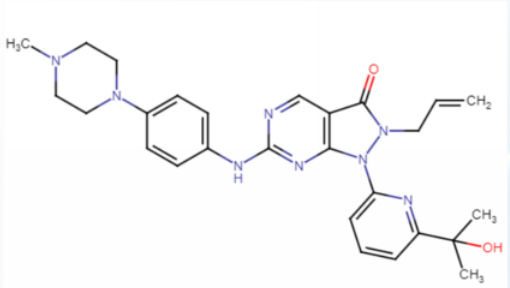
- Nanomolar anti-proliferative potency in vitro against multiple cancer cell lines
- Potent anti-tumor activity observed in vivo in an ovarian cancer xenograft model



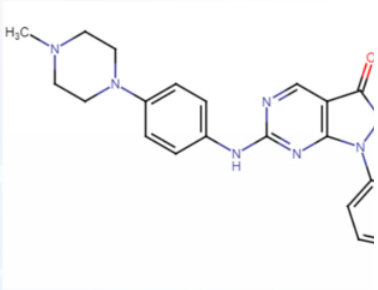
Pre-clinical studies with ATRN-W1051

ATRN-W1051 is Potentially Differentiated from Other WEE1 I

ATRN-W1051 shows potential to be potent and structurally differentiated, with high selectivity to limit



AZD-1775[1]



ZN-c3

	On-Target IC_{50} (nM)	Off-Target Inhibition at 1 μM (%)	
	WEE1	PLK1	PLK2
Aprea: ATRN-W1051	2.2	17	33
Zentalis: ZN-c3 [1]	3.8	79	96
AstraZeneca: AZD-1775 [1]	3.9	70	101

Note: Head-to-head studies have not been conducted
(1) Huang et al, (2021) J Med Chem

ATRN-W1051 Preclinical Data Highlight Potentially Favorable PK Prop

Based on pre-clinical studies, ATRN-W1051 shows potentially favorable drug exposure and tumor

	ATRN-W1051 (1)	Zentalis ZN-c3 (2)			AstraZe AZD-17	
Dose (mg/kg/d)	10	20	40	80	20	40
C_{max}, ng/mL	1219	1167	1997	5100	635	246
T_{max}, hr	2	1	1	1	1	1
AUC_{0-24}, ng*hr/mL	14211	4863	17088	39722	1494	631
Tumor concentration, ng/mL	9000 ng/gr (@ 15 mg/kg/d)	10.5	48	811	BQL	BQ

Note: Head-to-head studies have not been conducted
(1) Data from study in normal mice
(2) Data from study in A-427 NSCLC xenograft model as reported in Zentalis Corporate Overview, March 2022

Intellectual Property

Intellectual Property Portfolio

Four issued US patents protecting lead molecule and analogs

- Family 1: Ataxia Telengiectasia And Rad3-Related (ATR) Protein Kinase Inhibitors
  - Macrocyclic inhibitors of ATR & methods of using them to treat various cancers, filed on Oct. 13th, 2015
  - Patents granted in *AU, CA, CN, EP, IL, JP, MX*. 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*

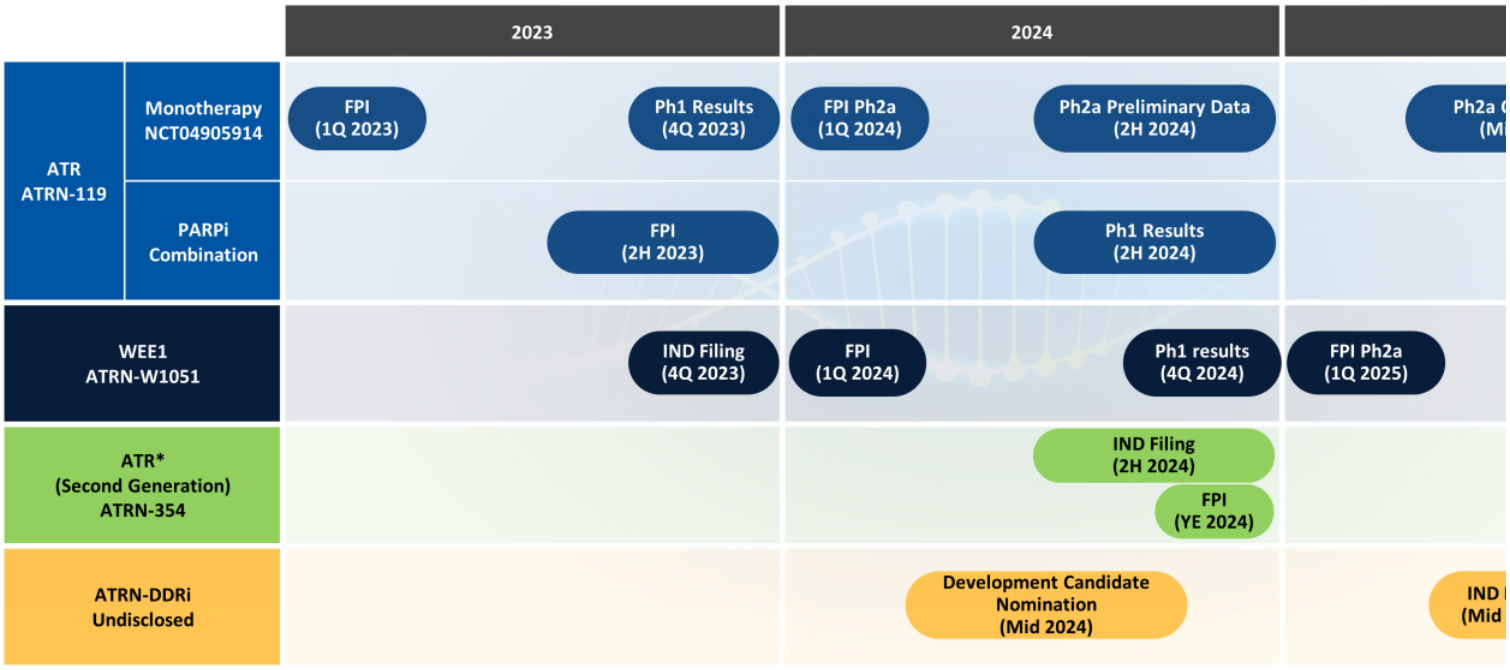
- Family 2: ATR inhibitors & methods of use
  - Carboxylic acid-containing macrocyclic ATR inhibitors, and prodrugs; methods of using these inhibitors to treat vario
    Apr. 12th, 2017
  - *Issued on May 28, 2019 as U.S. Patent 10,301,324*

- Family 3: ATR inhibitor Pharmaceutical Composition and Methods:
  - Provisional application filed on Apr. 14th, 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. 3rd, 2022
  - Composition of our lead WEE1 inhibitor compounds

Corporate Highlights & Milestones

Robust DDR Development Milestones



*ATR = Timeline and capital allocation will be adjusted upon clinical data from lead ATR program.

Aprea Therapeutics (NASDAQ: APRE)

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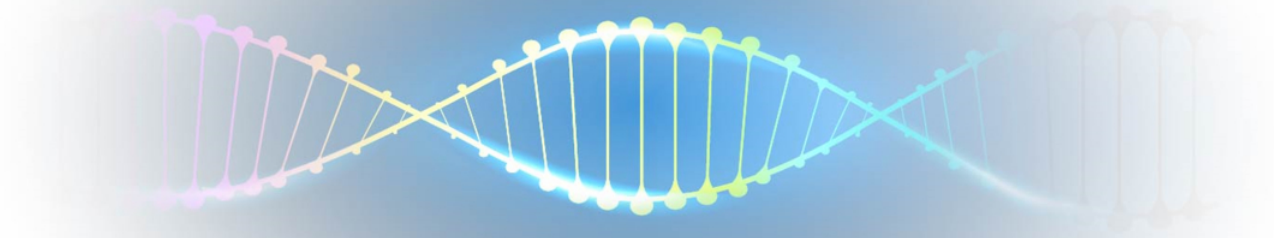

Precision Oncology through Synthetic Lethality

February 2023