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

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**FORM 8-K**

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**CURRENT REPORT**

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

**January 12, 2021**
Date of Report (Date of earliest event reported)

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# Aprea Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

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

| **535 Boylston Street**<br>**Boston, Massachusetts** | **02116** |
|---|---|
| (Address of principal executive offices) | (Zip Code) |

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

(Former name or former address, if changed since last report): Not applicable

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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))

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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 2.02 Results of Operations and Financial Condition**

As discussed below, in connection with participation in the 39th Annual J.P. Morgan Healthcare Conference, Aprea Therapeutics, Inc. (the "Company") updated its corporate presentation to include disclosure that the Company had $89.0 million of cash and cash equivalents (unaudited) as of December 31, 2020.

Because the Company's consolidated financial statements for the year ended December 31, 2020 have not yet been finalized or audited, the preliminary statement of the Company's cash and cash equivalents as of December 31, 2020 in this Item 2.02 is subject to change, and the Company's actual cash and cash equivalents as of December 31, 2020 may differ materially from this preliminary estimate. Accordingly, you should not place undue reliance on this preliminary estimate.

**Item 7.01 Regulation FD Disclosure**

Beginning on January 12, 2021, the Company will participate in the 39th Annual J.P. Morgan Healthcare Conference. The Company has updated its corporate presentation that it intends to use in connection with its presentation on Tuesday January 12, 2020 at 2:50 p.m. Eastern Time in meetings with investors. The updates primarily include updates on the Company's ongoing and planned clinical trials and disclosure regarding the Company's cash and cash equivalents as of December 31, 2020.

A copy of the Company's corporate presentation is attached hereto 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 |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**Aprea Therapeutics, Inc.**

Dated: January 12, 2021

By: /s/ Christian S. Schade
Name: Christian S. Schade
Title: Chairman and Chief Executive Officer

Exhibit 99.1

aprea therapeutics

The p53 Reactivation Company

# J.P. Morgan 39th Annual Healthcare Confere

January 2021

# Forward-Looking Statements

Certain information contained in this presentation includes "forward-looking statements", within the me
the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as ame
clinical trials and regulatory submissions. We may, in some cases use terms such as "predicts," "believes
"anticipates," "estimates," "expects," "plans," "intends," "may," "could," "might," "likely," "will," "should"
convey uncertainty of the future events or outcomes to identify these forward-looking statements. Our
statements are based on current beliefs and expectations of our management team that involve risks, p
circumstances, assumptions, and uncertainties. Any or all of the forward-looking statements may turn
affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Th
statements are subject to risks and uncertainties including risks related to the success and timing of our
studies and the other risks set forth in our filings with the U.S. Securities and Exchange Commission, inc
Report on Form 10-Q. For all these reasons, actual results and developments could be materially differe
in or implied by our forward-looking statements. You are cautioned not to place undue reliance on thes
statements, which are made only as of the date of this presentation. We undertake no obligation to pub
looking statements to reflect subsequent events or circumstances.

# Aprea Therapeutics

- The global leader in p53-targeted therapies for the treatment of cancer
  - Proof-of-concept and proof-of-principle demonstration of mutant p53 reactivation

## Presentation Agenda

- Update on Phase 3 MDS Clinical Study
- Development Pipeline
  - 1L AML
  - Post-transplant maintenance in MDS/AML
  - CLL / MCL
  - Advanced solid tumors
- Financial and Operational Highlights
- 2021 Milestones

# p53: The "Guardian of the Genome"

## p53 tumor suppressor

**The nexus and regulator of key anti-cancer network of signals**

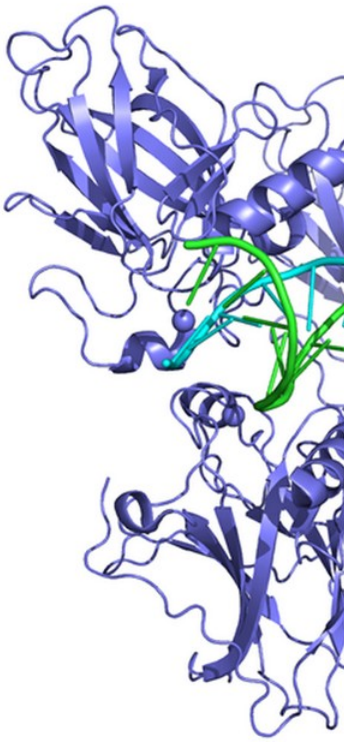
- Triggers cell cycle arrest and apoptosis in response to DNA damage and other cellular stresses

**The most frequently mutated gene in human cancers**

- Mutations in the *TP53* gene occur in approximately 50% of tumors
- p53 mutations destabilize the protein and lead to protein misfolding

**Mutations are associated with very poor prognosis**

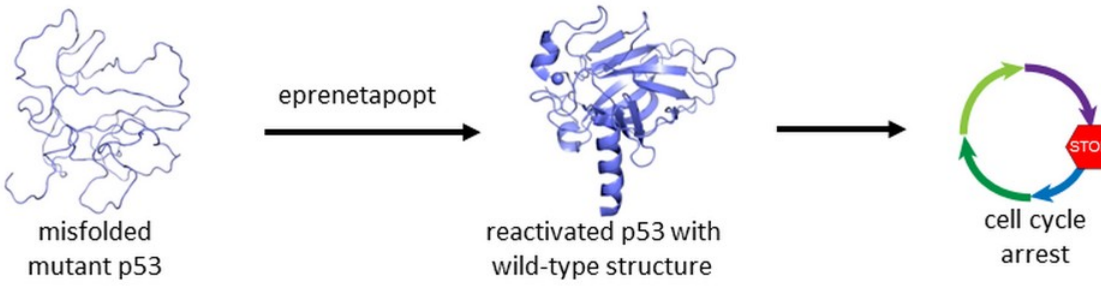
- *TP53* mutations compromise tumor suppressive function and can promote tumor growth and metastasis



# Reactivation of Mutant p53 Across Mutation Type

- p53 protein destabilization is a general and direct consequence of mutation
- Eprenetapopt MoA is agnostic to specific p53 mutation, capitalizes on principles of protein
  - ◊ Activity observed in nearly 100 different p53 mutations in preclinical studies across hot spots an
  - ◊ Clinical responses recorded in patients spanning more than 80 unique p53 mutations across hot mutations

**p53 reactivation**



aprea therapeutics
The p53 Reactivation Company

# Clinical Developmen

# Execution on Clinical Development

| Molecule | Indication | Preclinical | Phase 1 | Phase 2 |
|---|---|---|---|---|
| Eprenetapopt (APR-246) | 1L *TP53* Mutant MDS[1] | eprenetapopt + aza[3] | | |
| | 1L *TP53* Mutant MDS and AML (U.S. study)[2] | eprenetapopt + aza | | Publication |
| | 1L *TP53* Mutant MDS and AML (French study)[2] | eprenetapopt + aza | | Publication |
| | *TP53* Mutant MDS and AML Post-Transplant Maintenance | eprenetapopt + aza | | |
| | 1L and R/R *TP53* Mutant AML | eprenetapopt + ven[4] and/or aza | | |
| | R/R *TP53* Mutant CLL and MCL | eprenetapopt + ibrutinib or ven-R[5] | | |
| | Advanced Gastric, Bladder, NSCLC | eprenetapopt + pembrolizumab | | |
| APR-548 | 1L and R/R *TP53* Mutant MDS | APR-548 + aza | | |




[1]Trial did not achieve statistical significance
[2]Investigator-initiated trials; [3]azacitidine; [4]v

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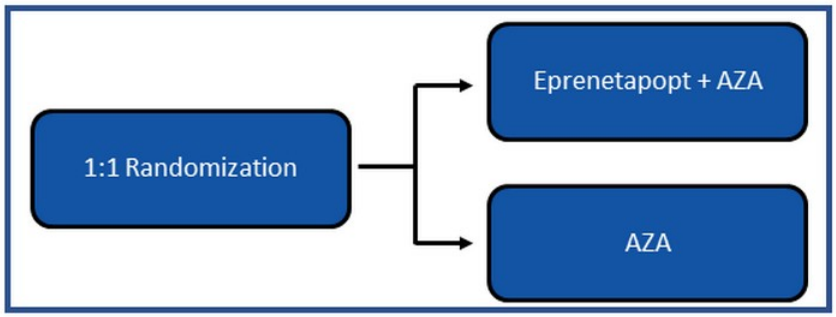
# Phase 3 MDS Review

# Randomized Phase 3 Trial in 1L *TP53* Mutant MDS

## Trial design




Powered at 90% to detec
- based on initial assumpti
eprenetapopt + AZA arm

Same eligibility criteria, t
as Phase 1b/2 trials

### Patients

- N = 154
- At least one *TP53* mutation
- Int/High/Very High IPSS-R
- ECOG performance status of 0, 1 or 2
- *De novo* and secondary MDS eligible
- HMA naïve

### Trial Endpoint

- Primary: CR rate
- Secondary: OS, ORR DoR, DoCR, PF
rate

# Recap of Results from Phase 3 Trial in *TP53* Muta

- Primary data cut (LPI + 6 months)
  - Failed to meet CR primary endpoint in ITT population
    - 33.3% in eprenetapopt + AZA arm vs. 22.4% in AZA alone arm (P = 0.13)
    - Primary endpoint did not reach statistical significance
      - CR rate was 53% higher in eprenetapopt + AZA arm
    - 24 patients on study treatment: 14 patients on eprenetapopt + AZA, 10 patients on AZA
  - Secondary endpoints
    - ORR and duration of responses appear to favor eprenetapopt + AZA arm but are not significantly different from AZA alone
    - Median OS was similar between arms
    - Preliminary analysis of clinical subsets based on demographics and disease characteristics (e.g., IPSS-R, bone marrow blast %, group significantly favoring the eprenetapopt + AZA arm
  - Combination of eprenetapopt + AZA appeared well-tolerated
    - Adverse event profile similar to Phase 2 US and French trials
  - Ongoing and future analyses
    - Mutation and pharmacokinetic data analyses
    - Other potential ad hoc analyses
    - Subsequent analyses to be performed at LPI + 9 months
  - Anticipate discussion of results with FDA in 1H 2021
  - Anticipate presentation of results at an upcoming scientific conference

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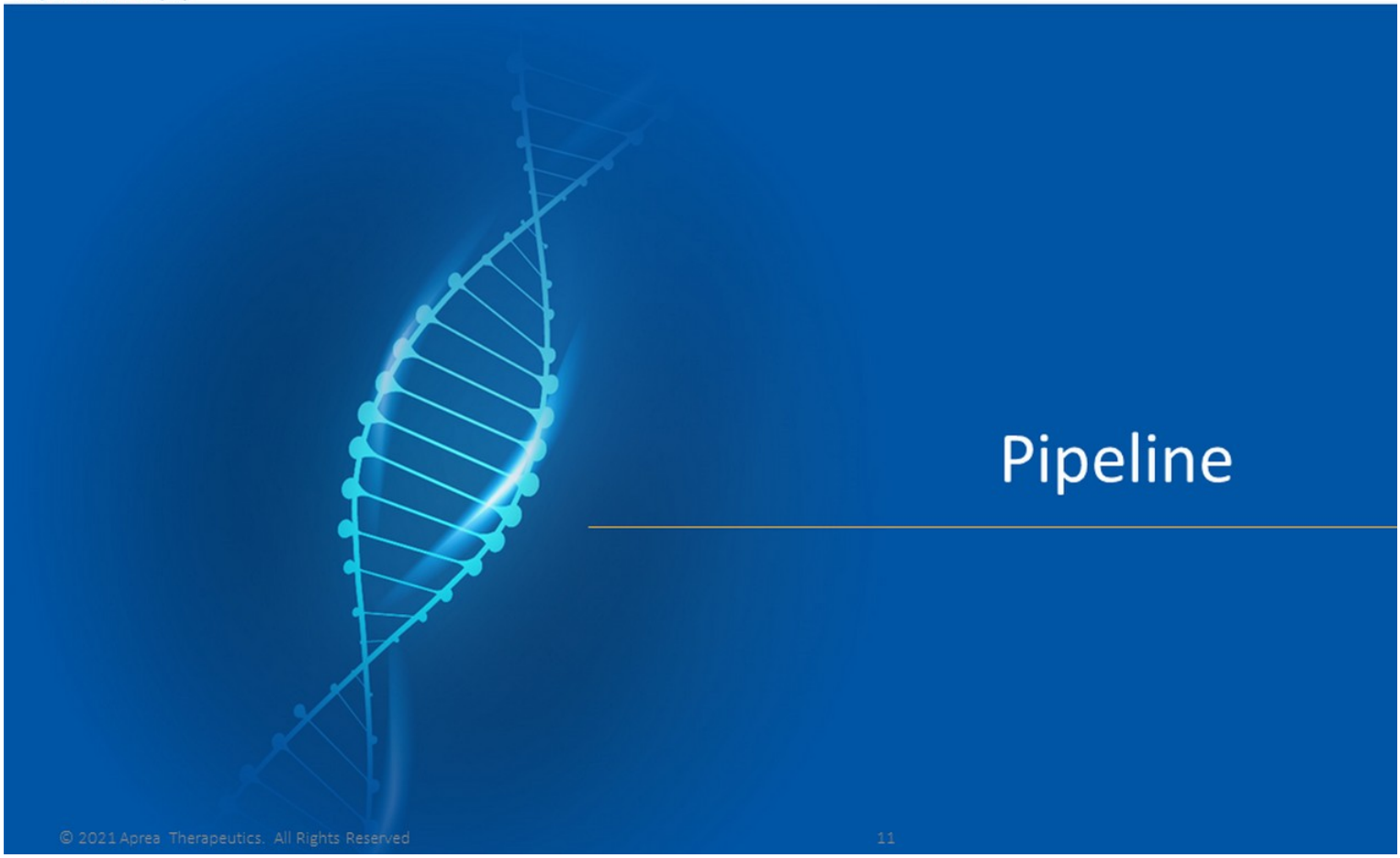
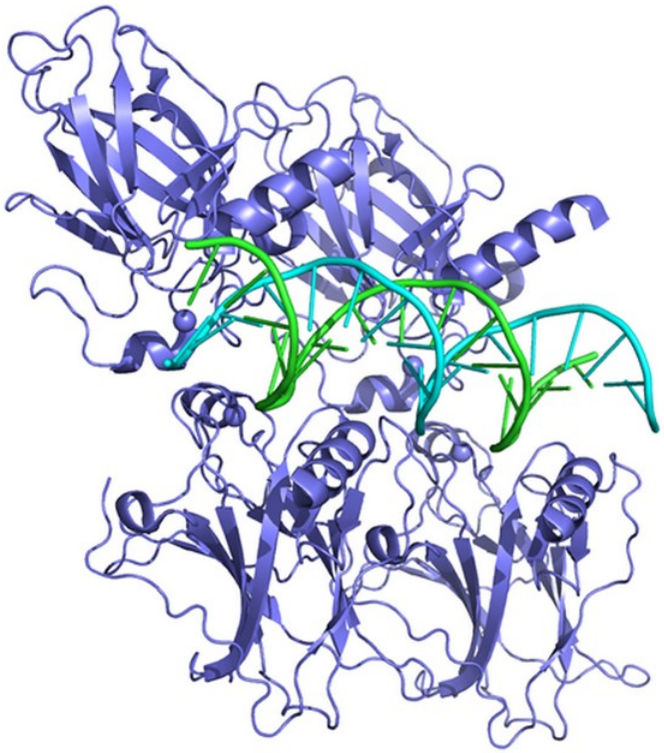


# Pipeline

# *TP53* Mutant AML is a Major Unmet Medical Need wit Treatment Options



## Incidence

**45,000** in 2019 in US/EU5/JP

## *TP53* mutation is common

**20-30%** *TP53* mutant

## Prognosis with available therapie

**0-20%** complete remission (CR)

**~6 months** overall survival (OS



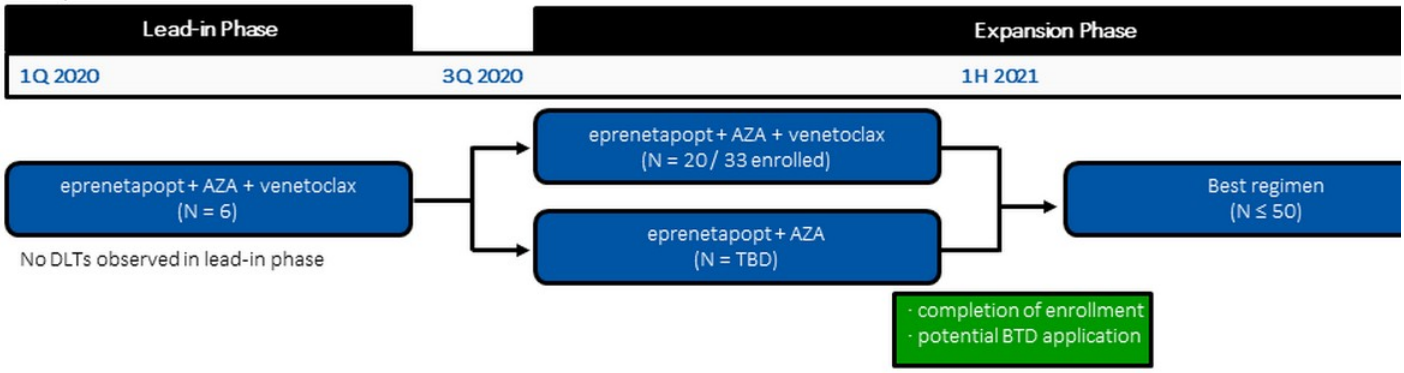

Global Data, "Acute Myeloid Leukemia Fore

# 1L *TP53* Mutant AML Trial

- Current Eprenetapopt Data and Therapeutic Benchmark

| | Phase 1/2 AML Trial[1] (Eprenetapopt + Ven + AZA) | Benchmark[2] |
|---|---|---|
| Evaluable[3] AML patients, n | 6 (lead-in) + 6 (expansion) | 38 (Ven-Aza: VIALE-A)<br>14 (Aza: VIALE-A) |
| Response rates | | |
| CR + CRi | 58% | 55% (Ven-Aza: VIALE-A)<br>0% (Aza: VIALE-A) |
| CR | 25% | ?[4] (Ven-Aza: VIALE-A)<br>0% (Aza: VIALE-A) |

- Phase 1/2 AML Trial Plan




[1]Phase 1/2 AML Trial as of December 31, 2020; [2]Dinardo et al, EHA 2020; Dinardo et al, I repeat bone marrow biopsy; [4]Aldoss et al, Br J Hematol, 2019, Dinardo et al, Blood, 202 patients receiving Ven-Aza

# Post-Transplant Maintenance Therapy in *TP53* Mutant

## Unmet Need

- Allo-HCT is currently the only potentially curative option for *TP53* mutant MDS/AML, however only 5
  to undergo transplantation
- Prognosis remains poor even in patients who undergo transplantation
  - 30% relapse free survival (RFS) at 1-year
  - ~8 mo median OS

## Development Status

- Phase 2 Trial of Post-Transplant Maintenance in *TP53* mutant MDS and AML
  - Eprenetapopt + AZA maintenance up to 12 months
  - Primary endpoints: relapse-free survival, tolerability
  - Secondary endpoints: OS, non-relapse mortality, PFS, LFS, GVHD, EFS
  - Trial fully enrolled with N = 33
  - 1-year RFS primary endpoint readout anticipated 2Q 2021




Lindsley et al, New England J Med, 2017, 5

# Eprenetapopt Combination in R/R Lymphoid Mali

## Unmet Need

| Incidence | *TP53* Mutation | |
|---|---|---|
| CLL: ~45,000 annually in US/EU5/JP | ~50% *TP53* mutant in R/R | 0-2 |
| MCL: ~7,000 annually in US/EU5/JP | | ≤ 12 |

- There is a lack of effective treatments for R/R *TP53* mutant CLL and MCL

## Rationale

- Preclinical data demonstrating synergistic activity of eprenetapopt + venetoclax, eprenetapopt + ibrutinib
- Encouraging clinical data in CLL from first-in-human trial with eprenetapopt monotherapy

## Development Status

- Phase 1 Trial in *TP53* mutant R/R CLL and MCL
  - Safety Lead-in
    - Eprenetapopt + ibrutinib in CLL (N ≈ 28)
    - Eprenetapopt + venetoclax-rituximab in CLL (N ≈ 28)
  - Expansion
    - Eprenetapopt + X in CLL (N ≈ 20) and MCL (N ≈ 40)
  - First patient anticipated 1Q 2021
  - Preliminary tolerability and efficacy data anticipated 2H 2021




Global Data, "Chronic Lymphocytic Leukemia: C
"B-Cell Non-Hodgkin's Lymphoma (NHL): Oppor

# Eprenetapopt Combination in Advanced Solid Tun

## Unmet Need

| Incidence | *TP53* Mutation | |
|---|---|---|
| **Gastric: ~185,000** annually in US/EU5/JP | **~50-80%** *TP53* mutant | 0-1 |
| **Bladder: ~225,000** annually in US/EU5/JP | | ≤ 12 |
| **NSCLC: ~500,000** annually in US/EU5/JP | | |

## Rationale

- APR-246 enhances effects of PD-1 blockade in murine melanoma and colorectal carcinoma models
- APR-246 induces pro-inflammatory tumor microenvironment and activity driven by tumor associated macro

## Development Status

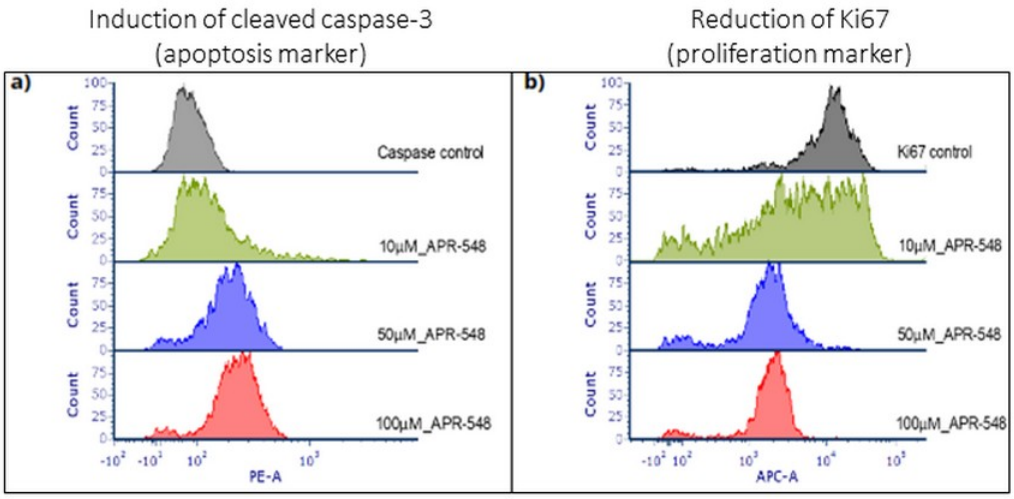
- Phase 1/2 Solid Tumor Trial Design
  - Safety Lead-in
    - Eprenetapopt + pembrolizumab in advanced solid tumors (N = 6)
  - Expansion
    - Advanced gastric (N ≈ 40), bladder (N ≈ 40), and NSCLC (N ≈ 20)
  - Safety lead-in cohort enrollment complete (N=6) and no DLTs
  - Expansion cohort enrollment ongoing
  - Preliminary tolerability and efficacy data anticipated 2H 2021

Global Data, "Gastric Cancer – Epidemiolog
Epidemiology Forecast to 2028"; "Non-Sma
to 2025"; Ghosh et al, 2019 AACR Annual M

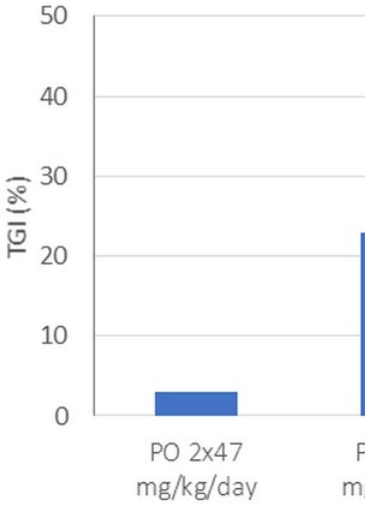
# APR-548: Next-Generation Oral p53 Reactivator

- APR-548 is converted to MQ, shares a similar mechanism of action to eprenetapopt
  - ◊ High oral bioavailability supportive of oral administration
  - ◊ Greater potency than eprenetapopt in preclinical studies
  - ◊ Faster conversion to MQ may provide for higher intra-tumoral drug levels

**Induction of Apoptosis and Reduction of Cell Proliferation in R248Q p53 mutant myeloid cells**




**Tumor Growth Inhibitic mutant Breast Ca**

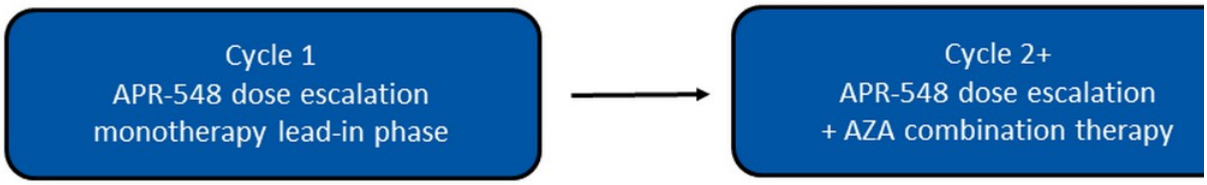



[1]Mice received APR-548 by twice daily oral
(five days on treatment, two days off treatr
MDA-MB-231 breast cancer cells

# First-in-Human Clinical Trial of APR-548 in *TP53* Mutant

## IND and protocol have been accepted by FDA

- Overview of FIH Trial




  - Provides opportunity to collect blood and bone marrow samples to study pharmacodynamics

- Status
  - FPI anticipated Q1 2021

- Following completion of FIH Phase 1, possibility to explore expansion in MDS, AML or othe

# Financial and Operational Highlights

- Financial
  - $89.0 million of cash and cash equivalents (unaudited) at December 31, 2020
  - No outstanding debt
  - Anticipated cash burn for 2021: $30 – 35 million
  - Existing cash should fund operations into 2023
  - Consider strategic alternatives

- Operational
  - 17 full-time employees
  - Clinical trials designed to efficiently reach preliminary efficacy readouts
    - Clinical data will drive decisions on further development and strategic options

# 2021 Anticipated Milestones

| Milestones |
| --- |
| **Phase 2 MDS / AML post-transplant maintenance** |
| Primary endpoint readout |
| **Phase 1/2 AML Trial** |
| Tolerability and efficacy data from cohort expansion |
| **Phase 1 NHL Trial** |
| Preliminary tolerability and efficacy data |
| **Phase 1/2 Solid Tumor I-O Trial** |
| Preliminary tolerability and efficacy data |
| **2nd Generation p53 reactivator, APR-548** |
| First patient enrolled in Phase 1 trial |