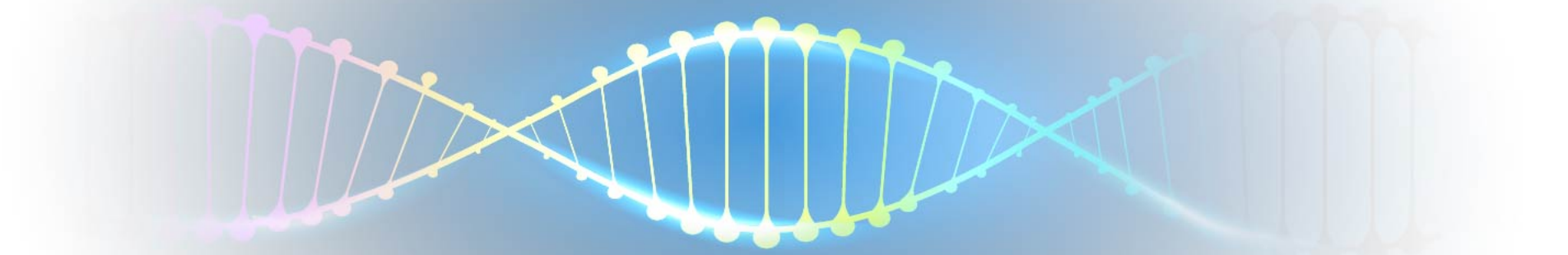
aprea therapeutics

The p53 Reactivation Company



J.P. Morgan 39th Annual Healthcare Conference

January 2021

Forward-Looking Statements

Certain information contained in this presentation includes “forward-looking statements”, within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, related to our clinical trials and regulatory submissions. 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. Our forward-looking statements are based on current beliefs and expectations of our management team that involve risks, potential changes in circumstances, assumptions, and uncertainties. Any or all of 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 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 Quarterly Report on Form 10-Q. 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 publicly update such forward-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

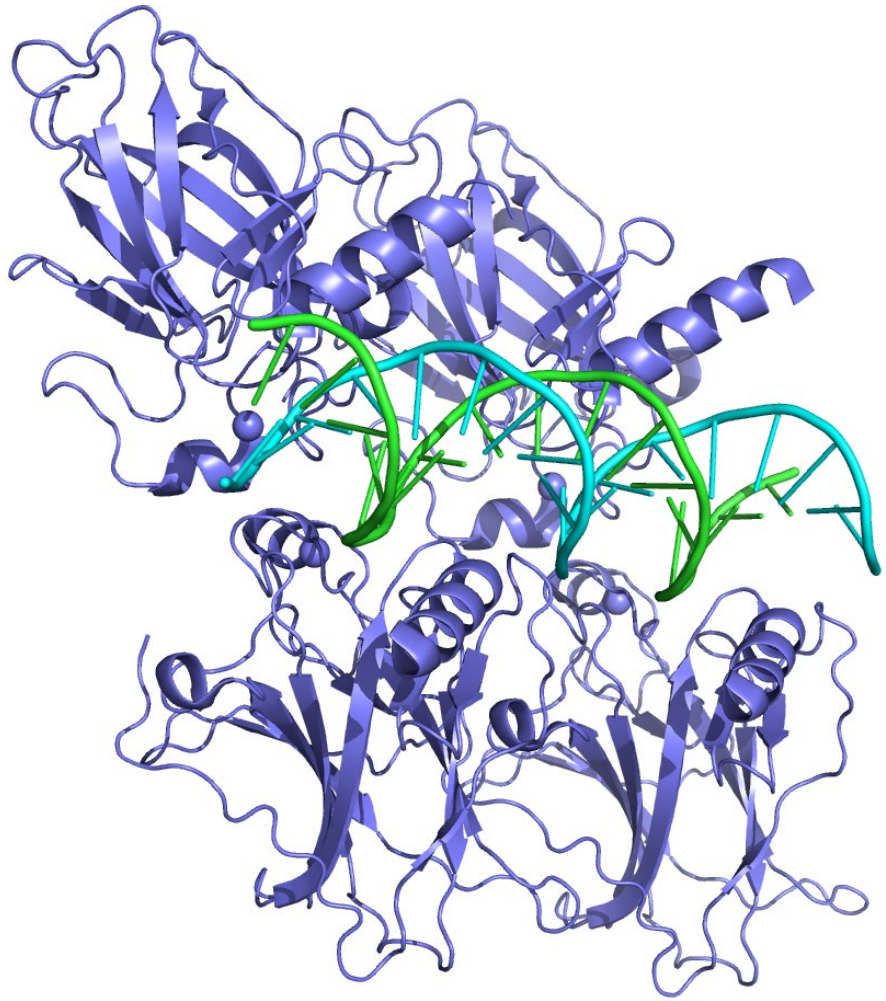
- Triggers cell cycle arrest and apoptosis in response to DNA damage and other cellular stresses

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

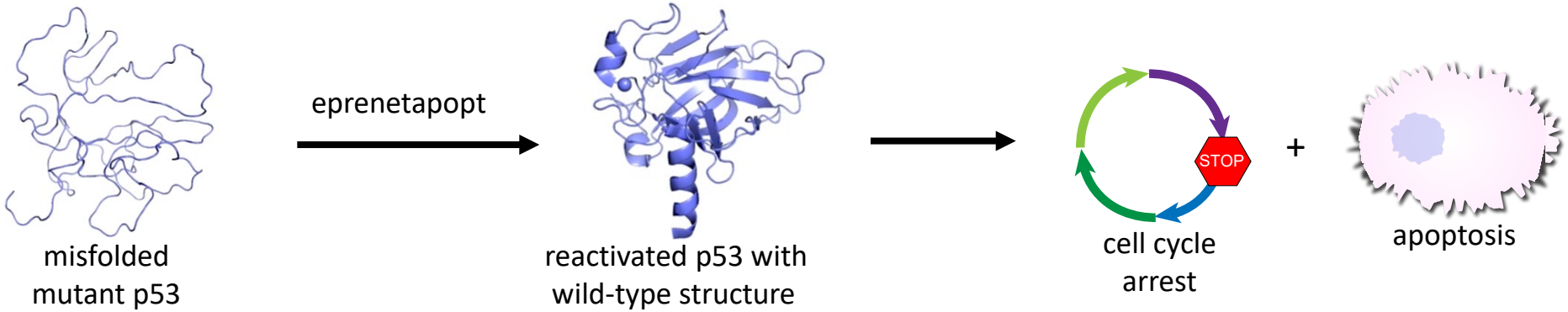
- *TP53* mutations compromise tumor suppressive function and can promote tumor growth and metastasis



Reactivation of Mutant p53 Across Mutation Types

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

p53 reactivation



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Clinical Development

Execution on Clinical Development

Molecule	Indication	Preclinical	Phase 1	Phase 2	Phase 3	
Eprenetapopt (APR-246)	1L *TP53* Mutant MDS[1]	eprenetapopt + aza[3]				
	1L *TP53* Mutant MDS and AML (U.S. study)[2]	eprenetapopt + aza				Publication pending
	1L *TP53* Mutant MDS and AML (French study)[2]	eprenetapopt + aza				Publication pending
	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 in primary endpoint of complete remission; [2]Investigator-initiated trials; [3]azacitidine; [4]venetoclax; [5]venetoclax + rituximab

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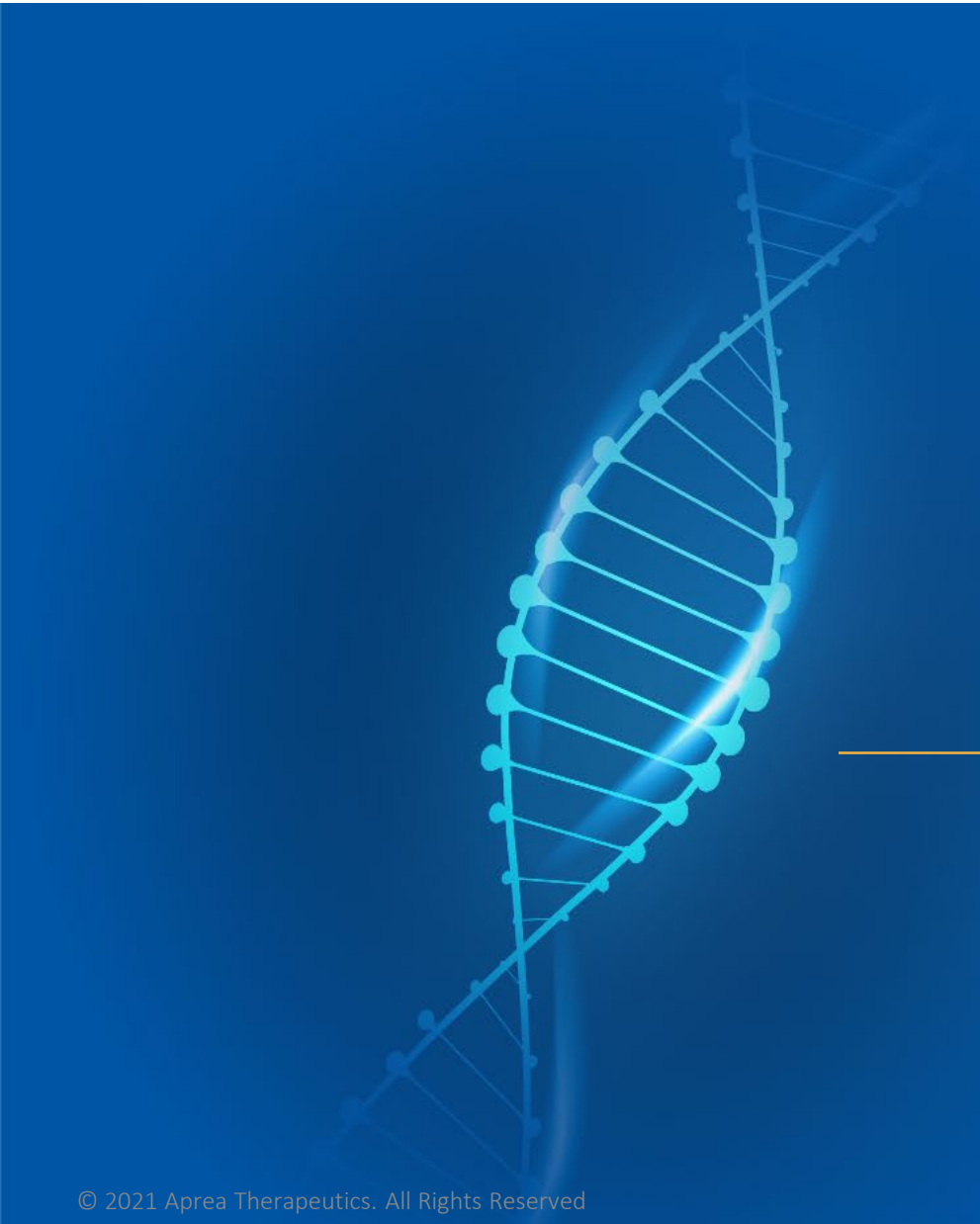
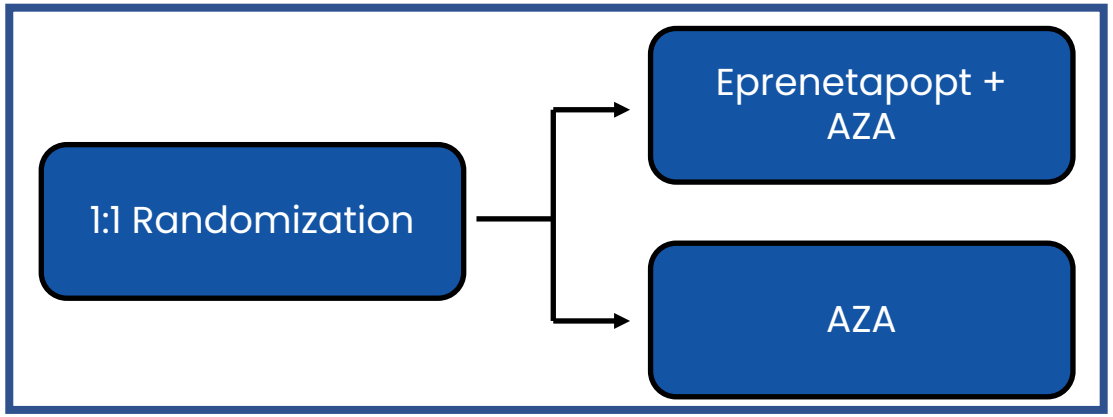


Phase 3 MDS Review

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

Trial design



Powered at 90% to detect 2-sided alpha of 0.05

- based on initial assumptions of 50% CR in eprenetapopt + AZA arm vs. 25% CR in AZA arm

Same eligibility criteria, treatment doses and sites 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 Endpoints

- Primary: CR rate
- Secondary: OS, ORR DoR, DoCR, PFS, LFS, HSCT rate, TI rate

Recap of Results from Phase 3 Trial in *TP53* Mutant MDS

- 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 %, prior therapy) has not identified a 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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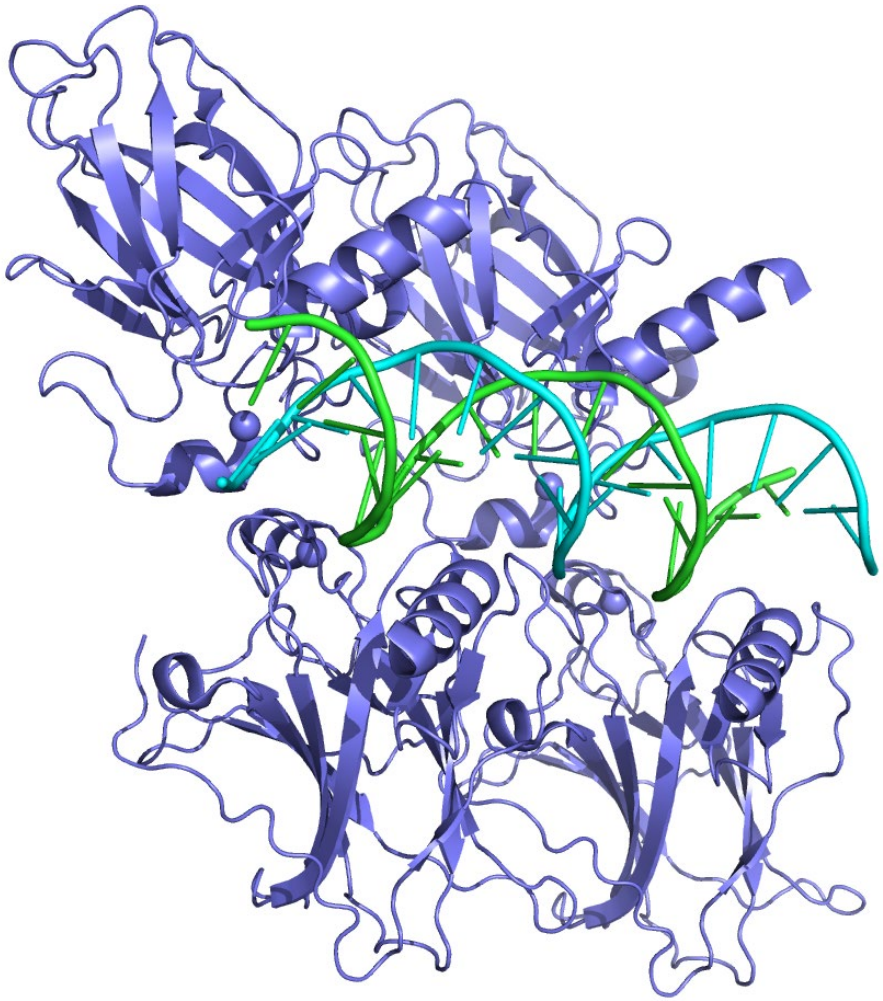
Pipeline

TP53 Mutant AML is a Major Unmet Medical Need with Limited Treatment Options



Incidence

45,000 in 2019 in US/EU5/JP

TP53 mutation is common

20-30% *TP53* mutant

Prognosis with available therapies

0-20% complete remission (CR)

~6 months overall survival (OS)

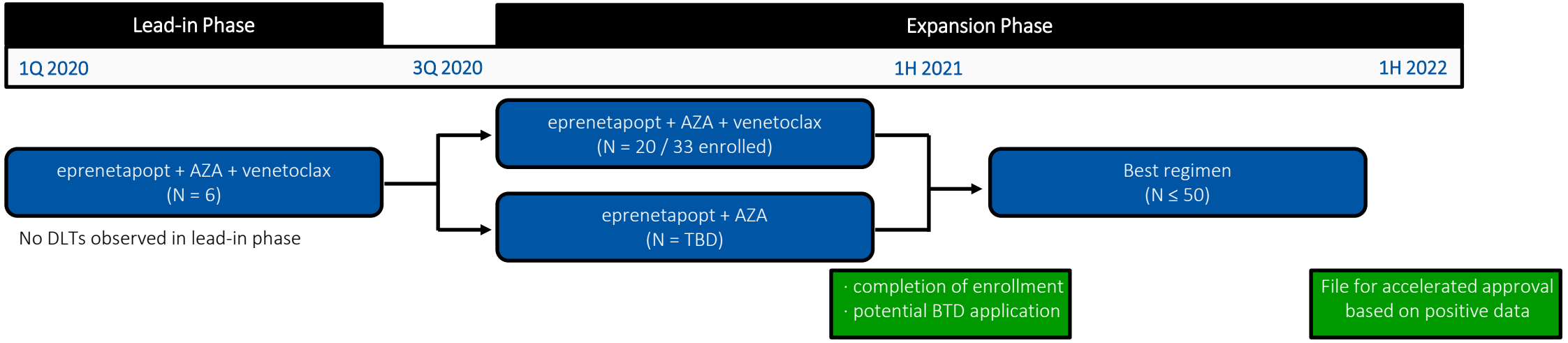
Global Data, "Acute Myeloid Leukemia Forecast to 2029"

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) 14 (Aza: VIALE-A)
Response rates		
CR + CRi	58%	55% (Ven-Aza: VIALE-A) 0% (Aza: VIALE-A)
CR	25%	?[4] (Ven-Aza: VIALE-A) 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, N Engl J Med 2020; 383:617-629; [3]Patients who have undergone repeat bone marrow biopsy; [4]Aldoss et al, Br J Hematol, 2019, Dinardo et al, Blood, 2020, have described CR rates of 23% and 22%, respectively, in AML patients receiving Ven-Aza

Post-Transplant Maintenance Therapy in *TP53* Mutant MDS and AML

Unmet Need

- Allo-HCT is currently the only potentially curative option for *TP53* mutant MDS/AML, however only 5-10% of patients are able 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, 536.

Eprenetapopt Combination in R/R Lymphoid Malignancies

Unmet Need

Incidence	*TP53* Mutation	Prognosis
CLL: ~45,000 annually in US/EU5/JP	~50% *TP53* mutant in R/R	0-20% complete remission (CR)
MCL: ~7,000 annually in US/EU5/JP		≤ 12 months overall survival (OS)

- 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: Opportunity Analysis and Forecasts to 2027"; "B-Cell Non-Hodgkin's Lymphoma (NHL): Opportunity Analysis and Forecasts to 2027"

Eprenetapopt Combination in Advanced Solid Tumors

Unmet Need

Incidence	*TP53* Mutation	Prognosis
Gastric: ~185,000 annually in US/EU5/JP	**~50-80%** *TP53* mutant	**0-10%** complete remission (CR)
Bladder: ~225,000 annually in US/EU5/JP		**≤ 12 months** overall survival (OS)
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 macrophages

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 – Epidemiology Forecast to 2024"; "Bladder Cancer: Epidemiology Forecast to 2028"; "Non-Small Cell Lung Cancer: Epidemiology Forecast to 2025"; Ghosh et al, 2019 AACR Annual Meeting, Abstract 4843

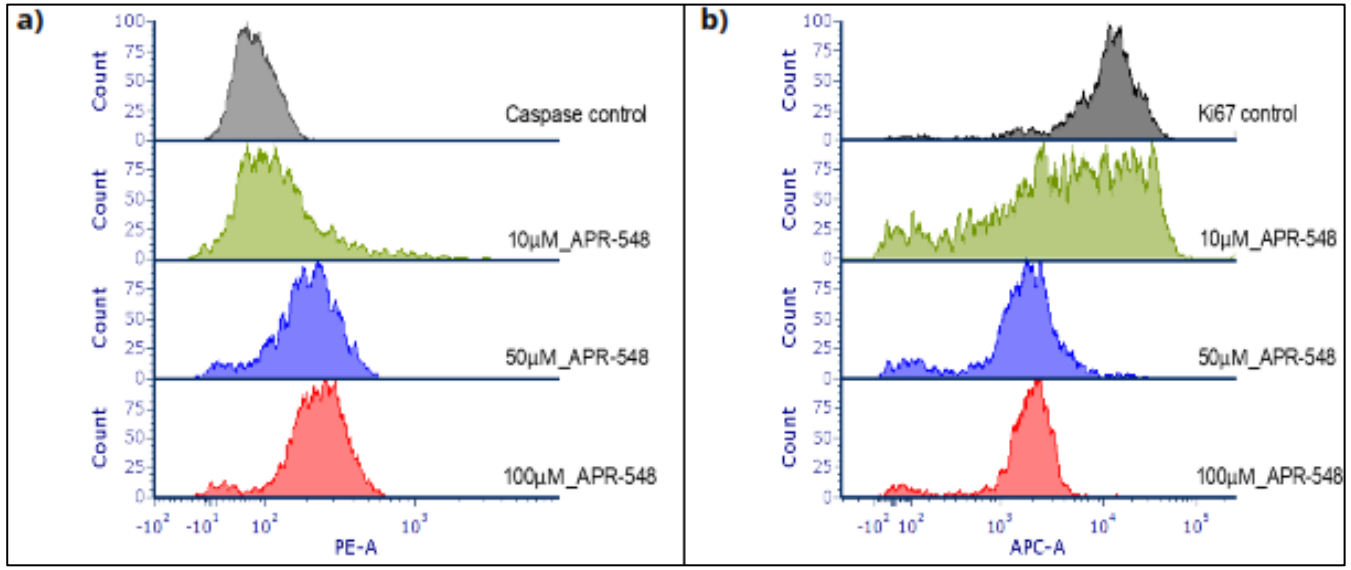
APR-548: Next-Generation Oral p53 Reactivator

- 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

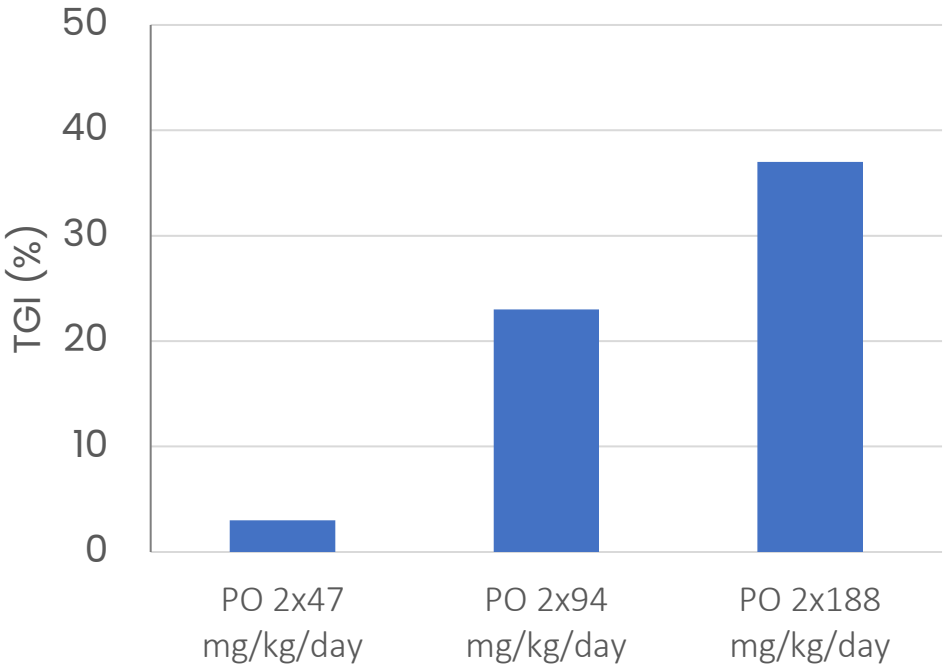
Induction of Apoptosis and Reduction of Cell Proliferation in R248Q p53 mutant myeloid cells

Induction of cleaved caspase-3 (apoptosis marker)

Reduction of Ki67 (proliferation marker)



Tumor Growth Inhibition (TGI) in R280K p53 mutant Breast Cancer Xenograft[1]

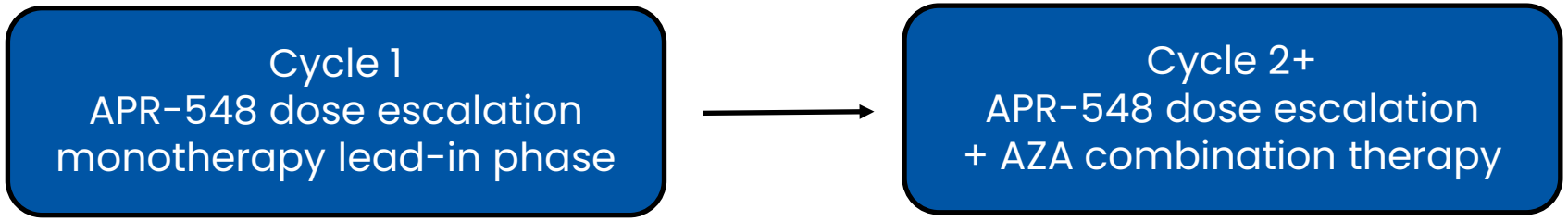


[1]Mice received APR-548 by twice daily oral administration for three consecutive cycles (five days on treatment, two days off treatment) starting on day 11 post-implant of MDA-MB-231 breast cancer cells

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

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 other indications

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	Timeline
Phase 2 MDS / AML post-transplant maintenance	
Primary endpoint readout	2Q 2021
Phase 1/2 AML Trial	
Tolerability and efficacy data from cohort expansion	2Q 2021
Phase 1 NHL Trial	
Preliminary tolerability and efficacy data	2H 2021
Phase 1/2 Solid Tumor I-O Trial	
Preliminary tolerability and efficacy data	2H 2021
2nd Generation p53 reactivator, APR-548	
First patient enrolled in Phase 1 trial	1Q 2021