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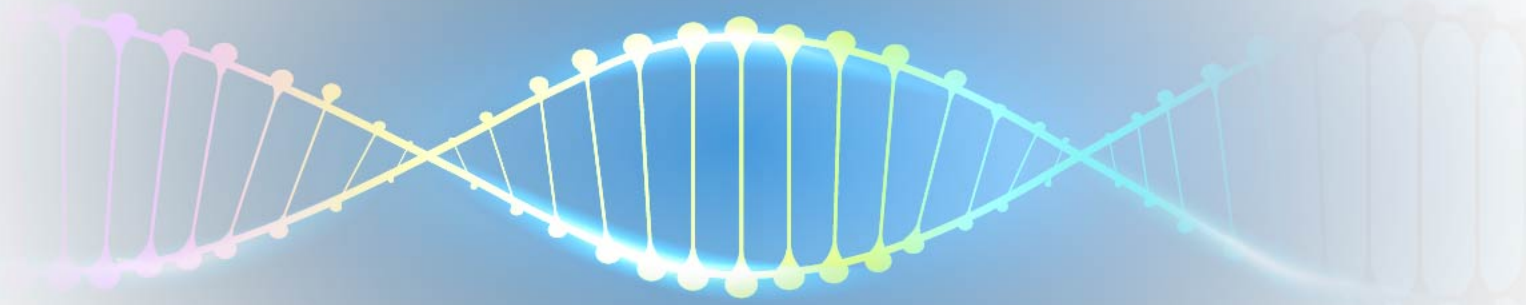


Aprea Therapeutics R&D Update

April 22, 2021

Forward-Looking Statements

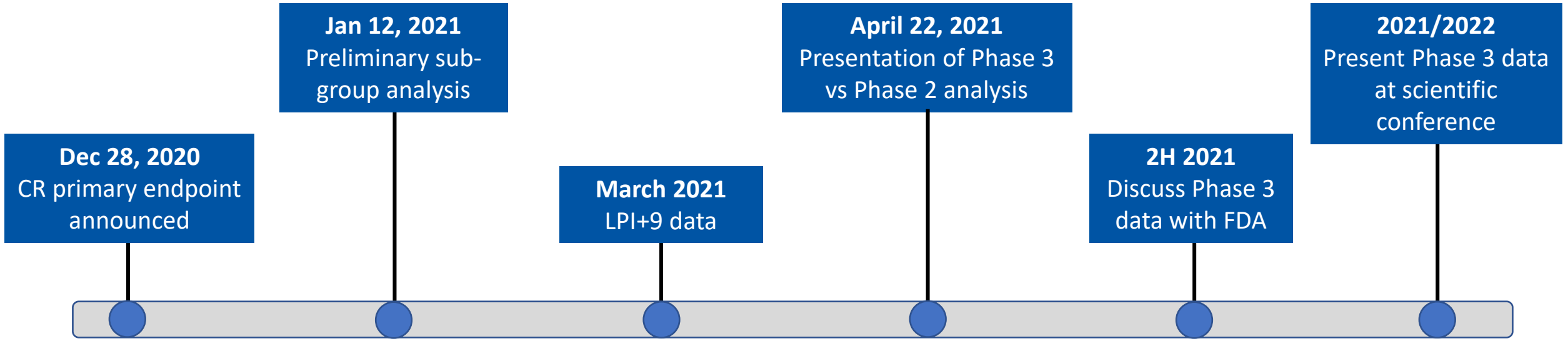
Certain information contained in this presentation includes “forward-looking statements”, within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, related to our clinical trials and regulatory submissions. We may, 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

Presentation Overview

- Latest Analysis of Phase 3 MDS Clinical Trial
  - Undertreatment in experimental arm negatively impacted efficacy in the Phase 3 study
- Current Clinical Pipeline Update
  - Compelling efficacy data in Phase 1/2 AML triplet therapy
  - Encouraging preliminary RFS and OS data in Phase 2 MDS/AML post-transplant maintenance trial
  - Enrollment proceeding in Phase 1 lymphoid malignancies trial and Phase 1/2 solid tumor trial
  - FIH APR-548 Orally-Bioavailable Next Generation Molecule – FPI Q2 2021
- R&D Update
  - Continue to explore emerging first-in-class oxidative stress and ferroptosis activities of eprenetapopt
  - Anticipate Phase 1 clinical study by end of 2021
- Milestones and Financial Update
  - Clinical milestones throughout 2021
  - Sufficient current resources

Conducted a Thorough and Methodical Analysis to Understand the Phase 3 Results



Was CR rate in Phase 3 with eprenetapopt + AZA lower than expected because of patient differences across arms?

Phase 3 Subgroup Analysis

- Demographics
- Baseline disease characteristics
- Genetic mutations
- Pharmacokinetics

Why was CR rate in Phase 3 with eprenetapopt + AZA different from Phase 2 results?

Phase 3 vs Phase 2 Analysis

- Demographics
- Baseline disease characteristics
- Adverse event profile
- COVID-19 impact
- **Dose exposure**

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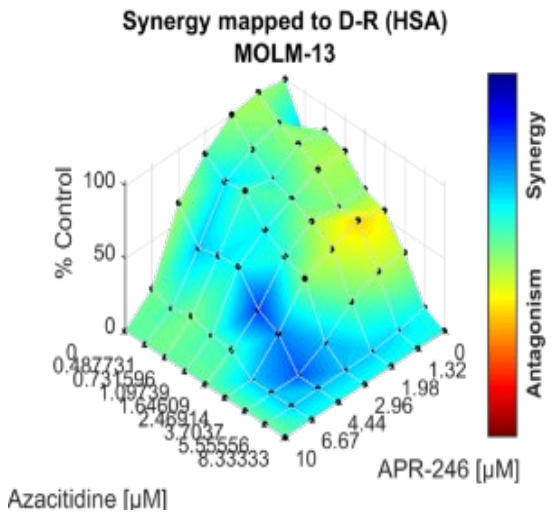
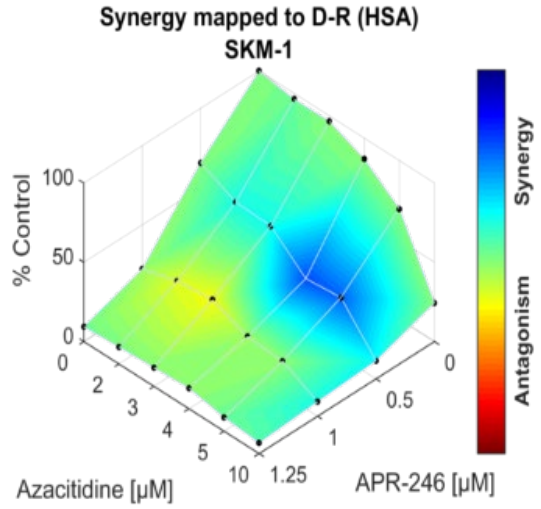
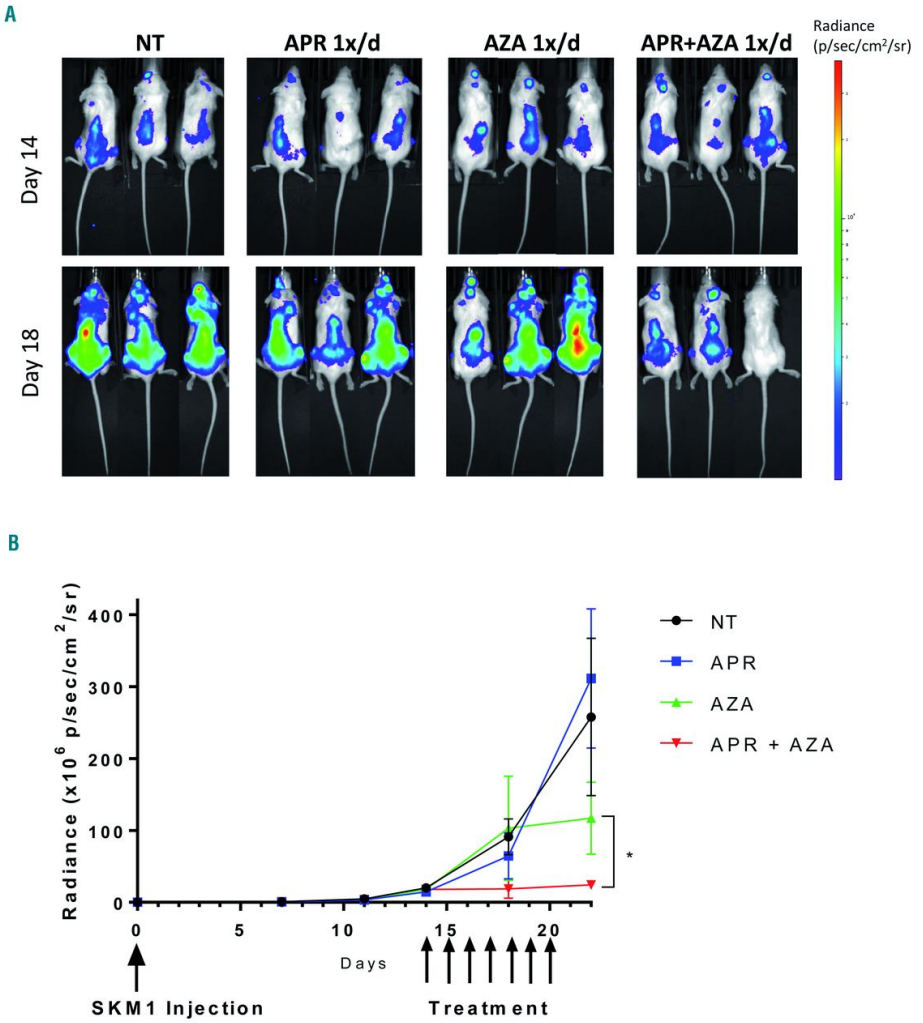
Phase 3 MDS Trial Results & Analysis

Eprenetapopt Interacts Synergistically with Standard of Care Agent AZA in Myeloid Malignancies

- Eprenetapopt interacts synergistically with AZA in AML and MDS-derived AML cells







[1]Aprea data; Maslah et al, Haematologica, 2020.

Results of U.S. and French Phase 2 Trials Published[1] in the *Journal of Clinical Oncology* in 1Q 2021

original reports

Eprenetapopt (APR-246) and Azacitidine in *TP53*-Mutant Myelodysplastic Syndromes

David A. Sallman, MD[1]; Amy E. DeZern, MD[2]; Guillermo Garcia-Manero, MD[3]; David P. Steensma, MD[4]; Gail J. Roboz, MD[5]; Mikkael A. Sekeres, MD, MS[6]; Thomas Cluzeau, MD, PhD[7]; Kendra L. Sweet, MD[1]; Amy McLemore, MS[1]; Kathy L. McGraw, PhD[1]; John Puskas, PhD[1]; Ling Zhang, MD[1]; Jiqiang Yao, PhD[8]; Qianxing Mo, PhD[8]; Lisa Nardelli, BS[1]; Najla H. Al Ali, MSc[1]; Eric Padron, MD[1]; Greg Korbel, PhD[9]; Eyal C. Attar, MD[9]; Hagop M. Kantarjian, MD[3]; Jeffrey E. Lancet, MD[1]; Pierre Fenaux, MD, PhD[10]; Alan F. List, MD[1]; and Rami S. Komrokji, MD[1]

original reports

Eprenetapopt Plus Azacitidine in *TP53*-Mutated Myelodysplastic Syndromes and Acute Myeloid Leukemia: A Phase II Study by the Groupe Francophone des Myélodysplasies (GFM)

Thomas Cluzeau, MD, PhD[1,2,3]; Marie Sebert, MD, PhD[3,4]; Ramy Rahmé, MD[3,4]; Stefania Cuzzubbo, MD, PhD[5]; Jacqueline Lehmann-Che, MD[6]; Isabelle Madelaine, PharmD[6]; Pierre Peterlin, MD[3,7]; Blandine Bève, PhD[3]; Habiba Attalah, PhD[3]; Fatiha Chermat, PhD[3]; Elsa Miekoutima, MD[4]; Odile Beyne Rauzy, MD, PhD[3,8]; Christian Recher, MD, PhD[3,8]; Aspasia Stamatoullas, MD[3,9]; Lise Willems, MD[3,10]; Emmanuel Raffoux, MD[3,4]; Céline Berthon, MD[3,11]; Bruno Quesnel, MD, PhD[3,11]; Michael Loschi, MD, PhD[1,2]; Antoine F. Carpentier, MD, PhD[5]; David A. Sallman, MD[12]; Rami Komrokji, MD[12]; Anouk Walter-Petrich, PhD[13]; Sylvie Chevret, PhD[13]; Lionel Ades, MD, PhD[3,4]; and Pierre Fenaux, MD, PhD[3,4]

understanding the pathway

Drugging the Master Regulator TP53 in Cancer: Mission Possible?

Giovanni Blandino, MD[1]

TP53 scores first in the landscape of human cancers both as the most frequent site for genetic alterations and as the most frustrating target for cancer therapy.[1] Somatic *TP53* mutations are common in human cancers, with a prevalence that varies among diverse cancer types and reaches 95% in advanced serous ovarian cancers. Germline *TP53* mutations are the basis of the rare Li-Fraumeni syndrome, which confers affected individuals with an exceptionally high risk of developing cancer.[2] Missense mutations comprise the vast majority of *TP53* mutations in human cancers. Although wild-type p53 has a short half-life and regulates the expression of a plethora of target genes, mutant p53 proteins typically have a longer half-life, accumulate in the cancer cells, and are unable to exert the tumor-suppressive functions of the wild-type p53 protein.

In the companion to this article, Cluzeau et al[3] report the results of a phase II study evaluating the safety and efficacy of targeting mutant p53 with eprenetapopt (APR-246) in combination with azacitidine in patients with myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Eprenetapopt, a first-in-class small molecule, is a prodrug spontaneously converted to methylene quinuclidinone (MQ), a Michael acceptor that binds covalently to cysteine residues in mutant p53 protein. This leads to thermostabilization of the p53 protein by shifting the equilibrium toward wt-p53 conformation, thereby restoring wt-p53 tumor suppressor activities in TP53-mutated cancer cells.[4-6]

The current study builds on the results of a prior phase Ib trial (ClinicalTrials.gov identifier: NCT03072043) that had demonstrated that eprenetapopt treatment induced p53 transcriptional activity with patients experiencing mostly grade 1 or 2 adverse events (AEs) and no dose-limiting toxicities.[7] *TP53* mutations occur in 5%-10% of patients with de novo MDS and AML and in 25%-40% of therapy-related MDS and AML. Approximately half of patients with MDS with complex karyotypes exhibit *TP53* mutations associated with biallelic mutation. The impact of *TP53* mutations in both MDS and AML is deleterious causing poor clinical outcomes with 6-12 months of median overall survival. In the present study, 52 TP53-mutant p53 patients (34 MDS and 18 AML) were enrolled (Fig 1). Overall response rate (ORR) was 62% and 33% in MDS and AML, respectively. Complete remission (CR) was 47% with a median duration of response of 10.4 months in MDS and 17% in AML with a median duration of response of 12.7 months. In patients with MDS and AML who received at least three cycles of combined treatment, ORR was 75% and 55%, respectively. Interestingly, 73% of the responders exhibited TP53 negativity with a variant allele frequency lower than 5%. Eprenetapopt plus azacitidine treatment was generally well-tolerated. All-grade AEs included febrile neutropenia (37%) and neurologic (40%) AEs that were grade 3 only in three patients (one acute confusion and two ataxia). The study conclusions indicate that the addition of eprenetapopt to azacitidine was safe and performed better than azacitidine alone in high-risk TP53-mutant patients with MDS and AML. These data are consistent with those achieved in another phase Ib/2 study (ClinicalTrials.gov identifier: NCT03072043)[7] and supported the development of an ongoing multicenter, randomized phase III study (ClinicalTrials.gov identifier: NCT03745716) that compares the rate of CR and duration of CR in patients with TP53-mutated MDS (n = 154) who receive either APR-246 plus azacitidine (experimental arm) or azacitidine alone (control arm).

Aprea Therapeutics publicly announced a few weeks ago that eprenetapopt plus azacitidine compared favorably with azacitidine alone in CR of patients with MDS but this effect did not reach statistical significance. Despite these disappointing results, this study has clearly paved the way to target therapeutically one of the most undruggable genetic alterations of human cancers and several other trials are planned or in progress. These include a phase Ib study of eprenetapopt in combination with carboplatin and pegylated liposomal doxorubicin in high-grade serous ovarian cancer (PISARRO trial, ClinicalTrials.gov identifier: NCT020983439), a phase I study that combines eprenetapopt with azacitidine and venetoclax in TP53-mutant myeloid malignancies (ClinicalTrials.gov identifier: NCT04214860), and a phase 1b study in which eprenetapopt in combination with pembrolizumab is tested in solid tumors (ClinicalTrials.gov identifier: NCT04383938).

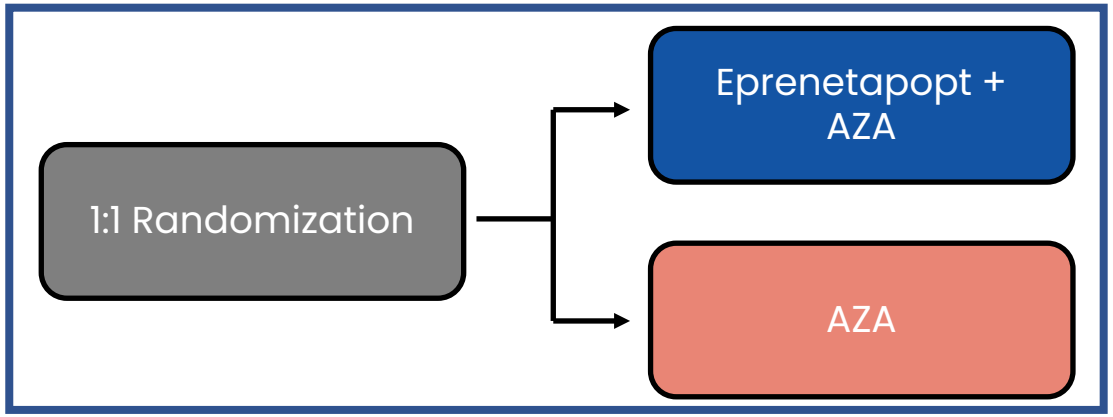
What do we need to further advance therapeutic targeting of *TP53* mutations in human cancers? One of the challenges remains our incomplete understanding of how the wide range of *TP53* mutations, which produce a plethora of diverse mutant p53 proteins, affect p53 function(s) in the specific context of each

ASSOCIATED CONTENT
See accompanying article doi: 10.1200/JCO.20.02342
Author affiliations and support information (if applicable) appear at the end of this article.
Accepted on February 25, 2021 and published at ascopubs.org/journal/jco on April 2, 2021: DOI https://doi.org/10.1200/JCO.21.00192

[1]Sallman et al, J Clin Oncol, 2021; Cluzeau et al, J Clin Oncol, 2021

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

Trial design



- Powered at 90% with 2-sided alpha of 0.05, based on initial assumptions of 50% CR in eprenetapopt + AZA arm vs. 25% CR in AZA arm (ITT populations)
- Same eligibility criteria and treatment as Phase 1b/2 trials
- No placebo in AZA control arm

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 in ITT population
- Secondary: OS, ORR DoR, DoCR, PFS, LFS, HSCT rate, TI rate

Efficacy Results from Phase 3 and Phase 2 Trials

- Phase 3 trial failed to meet CR primary endpoint in ITT population at LPI + 6 data cutoff
  - 53% more patients achieved CR in eprenetapopt + AZA arm
  - Primary CR endpoint missed p-value < 0.05 by a total of ~4 patients
  - 24 patients remained on study treatment: 14 patients on eprenetapopt + AZA, 10 patients on AZA
- ORR, duration of responses in ITT population favor eprenetapopt + AZA but not significantly different from AZA

Efficacy in MDS Patients	Phase 3 (LPI + 6 months)		Eprenetapopt + AZA Phase 2 Trials	
(ITT population)	Experimental Arm	Control Arm	U.S. Trial[1]	French Trial[2]
Response Rates, %				
CR	33.3 (P=0.13)	22.4	50	47
ORR	65.4	48.7	73	62
Duration of response, median, days				
CR	261	229	210	312
Overall	239	185	252	342

- LPI + 9 months data cut update
  - 34.6% CR rate in Experimental Arm vs 22.4% CR rate in Control Arm
  - 65.4% ORR in Experimental Arm vs 47.4% in Control Arm
  - 14 patients remained on study treatment: 9 patients on eprenetapopt + AZA, 5 patients on AZA

[1]Sallman et al, J Clin Oncol, 2021; [2]Cluzeau et al, J Clin Oncol, 2021

Similar Baseline Characteristics Between Phase 3 and Phase 2 Trials

Characteristic*	Phase 3 Trial: Eprenetapopt + AZA (N=78)	Phase 3 Trial: AZA (N=76)	Phase 2 U.S. Trial (N=40 MDS)	Phase 2 French Trial (N=34 MDS)
Age, median (range)	68 (34-90)	68 (29-86)	66 (34-80)	74 (46-87)
Female, %	46	38	43	56
ECOG 0-1, %	85	91	93	79
IPSS-R , %				
Int	14	9	10	12
High	24	22	20	15
Very High	62	68	70	74
Karyotype, %	90 abnormal	96 abnormal	90 complex	85 complex
Therapy-related, %	51	46	35	26

*Some categories may not add to 100% due to rounding.

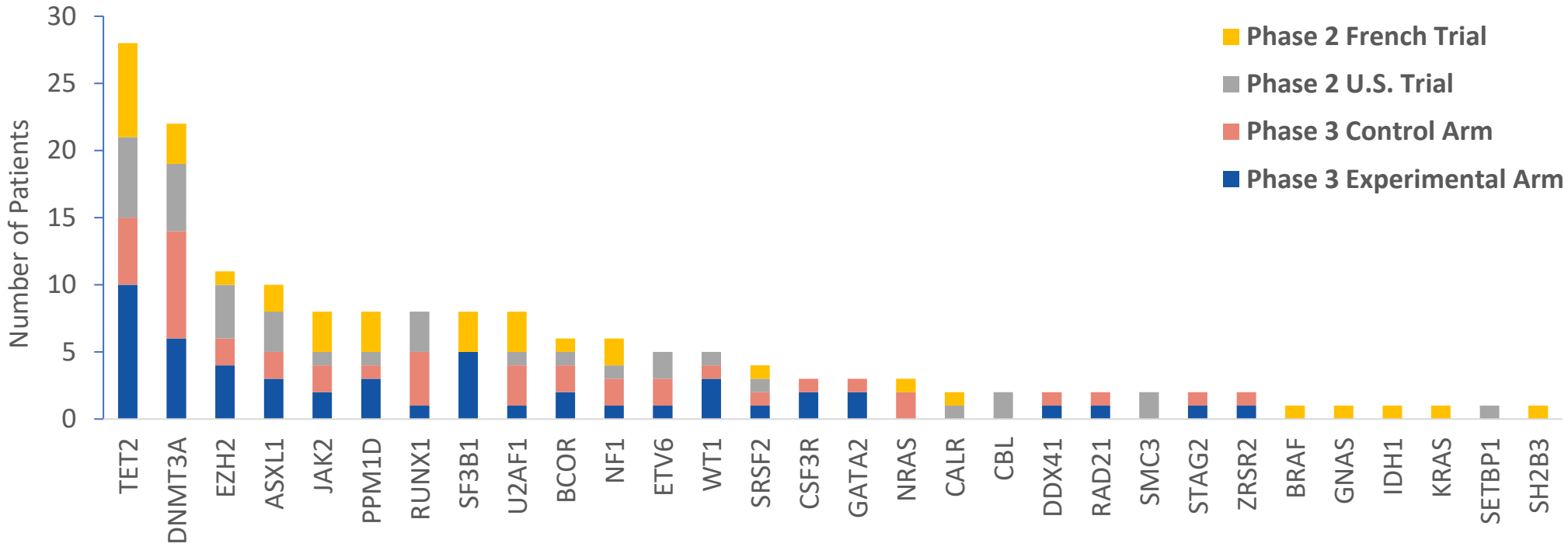
Similar *TP53* Mutations Between Phase 3 and Phase 2 Trials

Characteristic	Phase 3 Trial		Phase 2 U.S. Trial	Phase 2 French Trial
	Eprenetapopt + AZA (N=78)	AZA (N=76)	(N=40 MDS)	(N=34 MDS)
TP53 Mutations, %*				
Missense	82	87	75	68
Nonsense	10	8	8	6
Frameshift	15	9	8	3
Splice	8	8	5	15
TP53 VAF, %, median (range)	35 (4 - 95)	29 (1.5 - 84)	20 (1 - 72)	20 (0.1 - 83)
Patients with >1 *TP53* mutation, %	36	26	31	18

*Based on dominant baseline *TP53* mutation for patients with > 1 *TP53* mutation.

- Phase 3 experimental arm had highest rate of patients with therapy-related MDS, *TP53* VAF, and patients with > 1 *TP53* mutation
- No relationship observed between *TP53* mutation category and response in arms of Phase 3

Similar Profiles of Non-*TP53* Co-Mutations in Phase 3 and Phase 2 Trials



- Similar frequency of non-*TP53* co-mutations across Phase 3 and Phase 2 and no specific co-mutation associated with response

Phase 3 Experimental Arm AE Profile[1] Consistent with Phase 2 Studies

AE profile in control arm consistent with established AZA monotherapy profile

All Grade AEs ≥20% in Phase 3 Experimental Arm	Phase 3 Trial Eprenetapopt + AZA	Phase 2 U.S. Trial[2] Eprenetapopt + AZA	Phase 3 Trial AZA
Nausea	64	64	34
Constipation	62	42	52
Vomiting	53	45	13
Neutrophil count decreased	43	29	38
Anemia	41	15	43
Febrile neutropenia	41	33	26
White blood cell count decreased	39	31	31
Fatigue	38	44	33
Platelet count decreased	32	29	39
Dizziness	32	36	20
Headache	32	29	20
Diarrhea	29	33	30
Pyrexia	28	22	28
Edema peripheral	24	38	21
Thrombocytopenia	24	29	21
Hypokalemia	24	15	20
Injection site reaction	21	0	28
Neutropenia	21	29	28
Decreased appetite	21	24	18
Cough	21	27	16

[1]Safety population at LPI + 6 months data cutoff; [2]Similar AE profile observed in Phase 2 French trial by Cluzeau et al

Phase 3 Experimental Arm Patients had Fewer Treatment Cycles Compared to Patients on Control Arm and Phase 2 Trials

	Phase 3 Trial				
	Experimental Arm		Control Arm		
Characteristic	**Eprenetapopt**	**AZA**	**AZA**	**Phase 2 U.S. Trial**	**Phase 2 French Trial**
Median treatment cycles	4	4	5	5	6

- Given lower median treatment cycles in experimental arm we comprehensively analyzed dose exposure

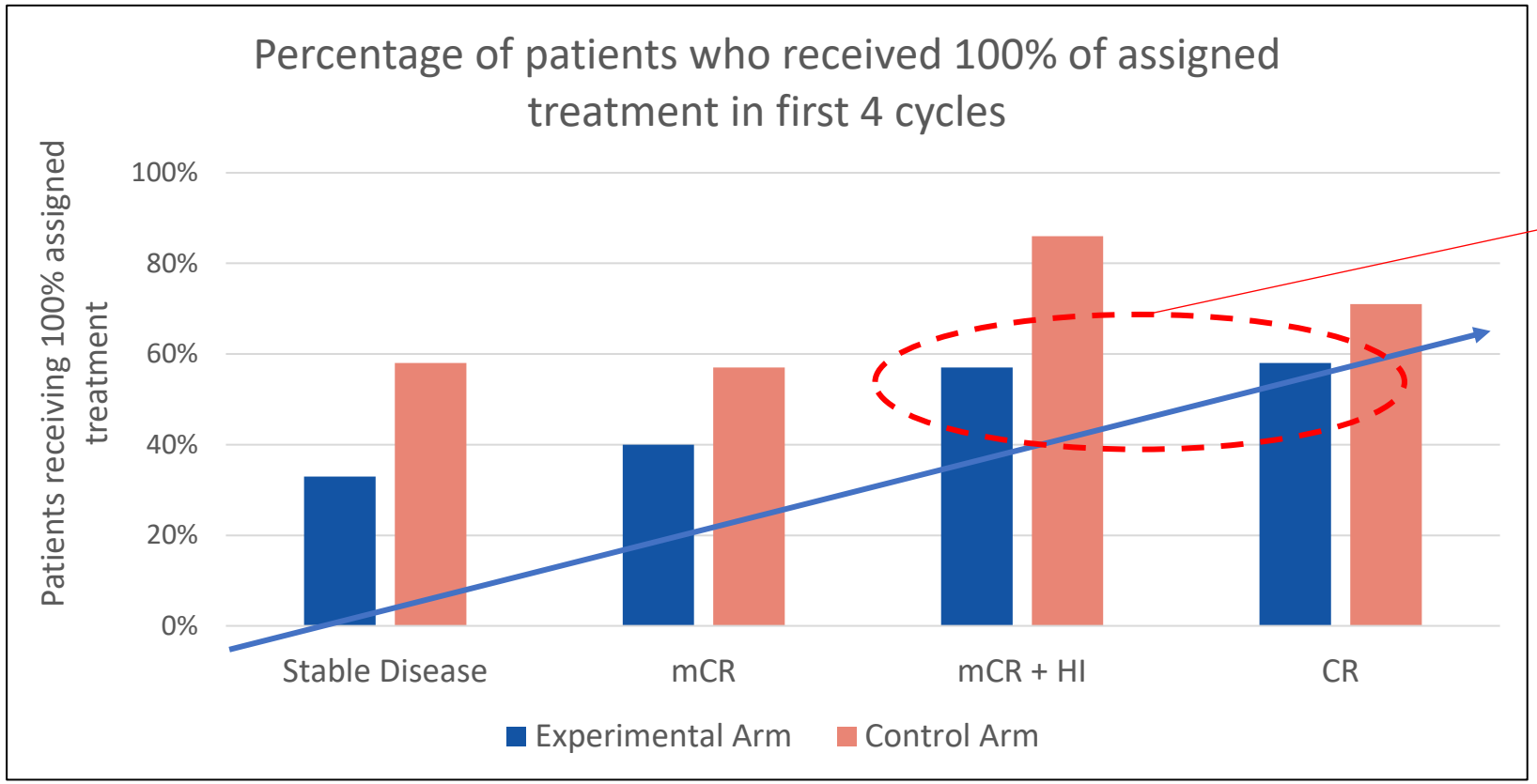
Phase 3 Experimental Arm had Higher Rate of AZA Dose Missing and Dose Reduction than Control Arm

Phase 2 Trials had no AZA dose reductions

	Phase 3 Trial		
	Experimental Arm		Control Arm
Patients, %	**Eprenetapopt**	**AZA**	**AZA**
Any dose missing	12	14	8
Any dose reduction	24	20	11

- In Phase 2 trials:
  - Eprenetapopt
    - U.S. Trial: 5% patients with any dose reduction
    - French Trial: 33% patients with any dose reduction; dose reductions correlated with increased age
  - **AZA**
    - **U.S. Trial: no dose reductions**
    - **French Trial: no dose reductions**

Percentage of Patients Receiving 100% of Assigned Dose was Lower in Phase 3 Experimental vs Control Arm

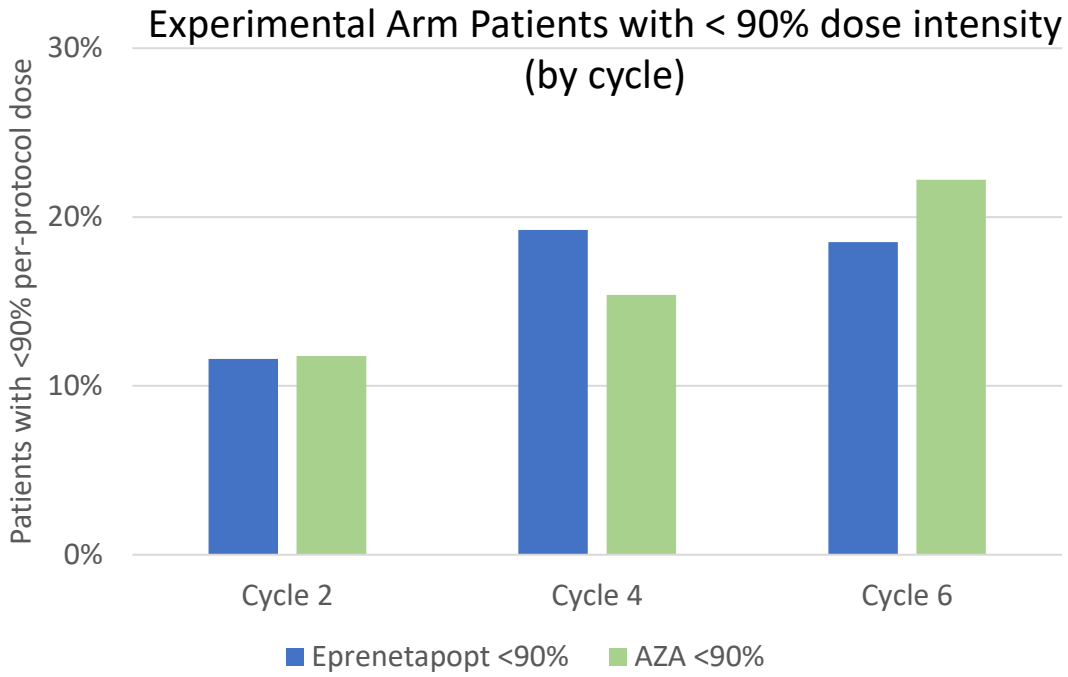


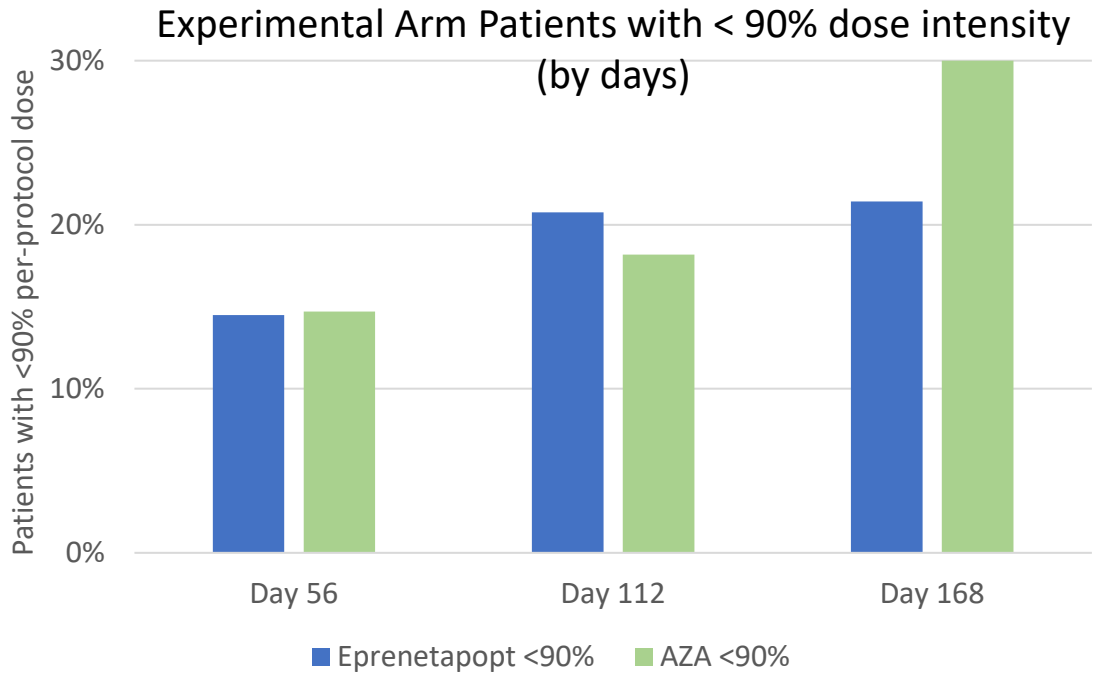
Higher rates of 100% dose intensity observed in experimental arm patients who have responses of mCR+HI and CR suggests dose intensity and synergy are related to improved response

- 100% dose intensity was significantly associated with CR in the experimental arm (p=0.048) but not in the control arm (p=0.154)

Undertreatment Negatively Impacted the Probability of CR in Phase 3

- By cycle 6 or Day 168, 18-30% of experimental arm patients received < 90% of assigned dose of eprenetapopt and AZA due to dose modifications.





- The impact of dose intensity on the probability of CR in the experimental arm:
  - **A 40-60% decrease in probability of CR for every 10% decrease in eprenetapopt exposure**
  - **A 50-80% decrease in probability of CR for every 10% decrease in AZA exposure**
- Though dose modifications were also observed in the control arm, the CR rate may have been more profoundly impacted in the experimental arm due to dose modifications of both agents, resulting in loss of synergy.

Despite Similar AE Profiles Across Studies, Dose Modifications in Phase 3 Experimental Arm Were More Frequent Than in Phase 2 US and French Trials

Reason for <100% Assigned Dose by Best Response Category

	Eprenetapopt + AZA						AZA					
	CR	mCR + HI	mCR	SD	PD	NE[1]	CR	mCR + HI	mCR	SD	PD	NE[1]
AE leading to treatment discontinuation, n	0	0	0	0	0	4	0	0	0	1	0	0
AE leading to dose modification, n	9	1	6	8	0	0	3	0	0	1	0	0

- AEs leading to dose modification and treatment discontinuation accounted for decreased dose exposure in the experimental arm of Phase 3

[1]NE: not evaluable for response

Treatment Dose Intensity is Important to Achieving Clinical Response in High Risk MDS

ORR Rates in Randomized SWOG S1117 (2017) Study were Lower than P2 Single Arm Studies Due to Undertreatment

	AZA	AZA + vorinostat	AZA + lenalidomide
Non-randomized Phase 2 ORR, %		73[1]	72[2]
Randomized Phase 2 (SWOG S1117) ORR, %	38	27	49
Nonprotocol-defined dose modifications, %	24	42	43
Discontinued for toxicity, %	8	20	19

- Impact of undertreatment in high-risk MDS populations in SWOG S1117[3]
  - Despite similarity in adverse events across arms, management of AEs, and in some cases early treatment discontinuation, led to differences in AZA dose intensity that may have resulted in undertreatment
  - *"Because underdosing may have been associated with compromised response and survival in combination arms, in most circumstances, patients with higher risk MDS should be treated without dose adjustment for induction phase of the first 4 months of therapy."*

[1]Silverman et al, *Blood*, 2013; [2]Sekeres et al, *Blood*, 2012; [3]Sekeres et al, *J Clin Oncol*, 2017;

Conclusions and Next Steps

- In Phase 3, dose modifications of eprenetapopt and azacitidine led to undertreatment in the experimental arm that negatively impacted efficacy, particularly the primary endpoint of CR rate
  - With a small sample size, minor changes in treatment compliance can impact study outcome
  - As in SWOG 1117, the Phase 3 eprenetapopt trial suggests that open-label AZA combination studies in high risk MDS without a placebo control are potentially vulnerable to undertreatment

- Anticipate discussion of data with FDA in 2H 2021
  - Do not expect registrational pathway for this Phase 3 study
  - Leverage eprenetapopt BTD (granted Jan 2020) in MDS for discussions around future possible pathway
    - Any decision on further development in MDS to balance considerations of time and resource allocation

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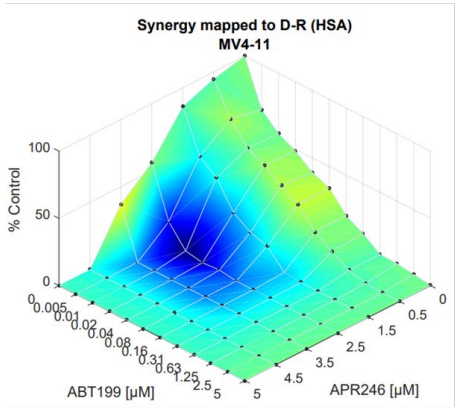
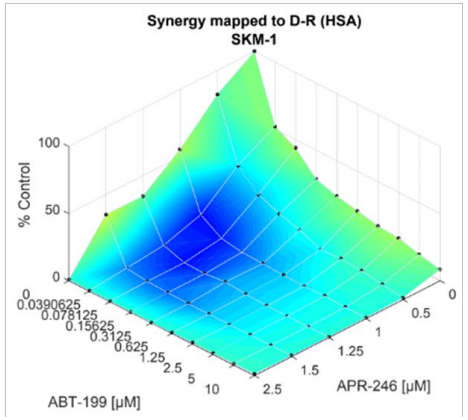
Pipeline Update

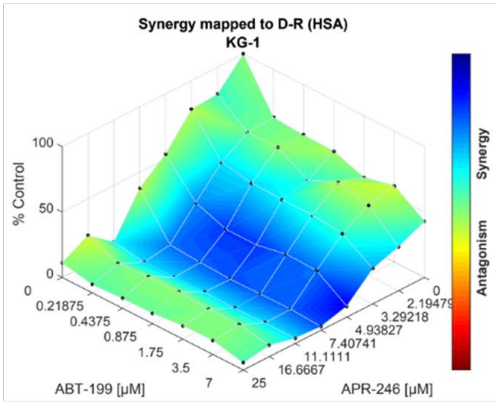
Phase 1/2 Trial of Eprenetapopt + Ven ± Aza in AML

FDA has granted Fast Track (Nov 2020) and Orphan (Apr 2021) designations for eprenetapopt in AML

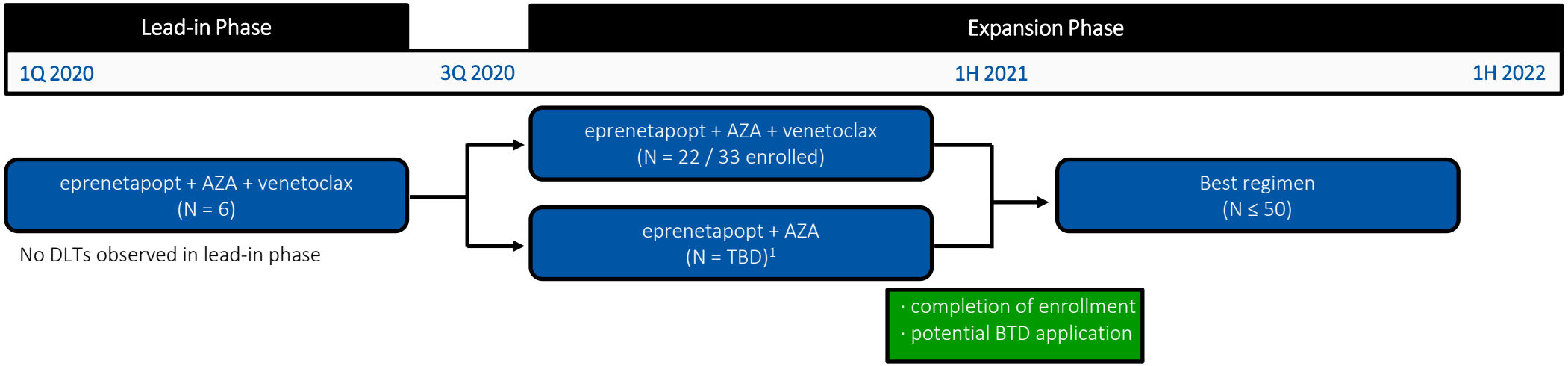
- Strong synergy observed in preclinical testing of eprenetapopt + Ven







- Concomitant dosing to maximize synergistic activities



[1]Not currently enrolling doublet arm

Triplet Eprenetapopt+Ven+AZA Responses Compare Favorably to Ven+AZA in 1L *TP53* Mutant AML

	Phase 1/2 AML Trial[1] Eprenetapopt + Ven + AZA	Dinardo et al, Blood, 2018 Ven + AZA	VIALE-A[2] Ven + AZA vs AZA
Patients, n	6 (lead-in) + 13 (expansion)	36	38 (Ven + AZA) 14 (AZA)
Response rates, %			
CR + CRi	63	47	55 (Ven + AZA) 0 (AZA)
CR	31	?[3]	?[3] (Ven + AZA) 0 (AZA)

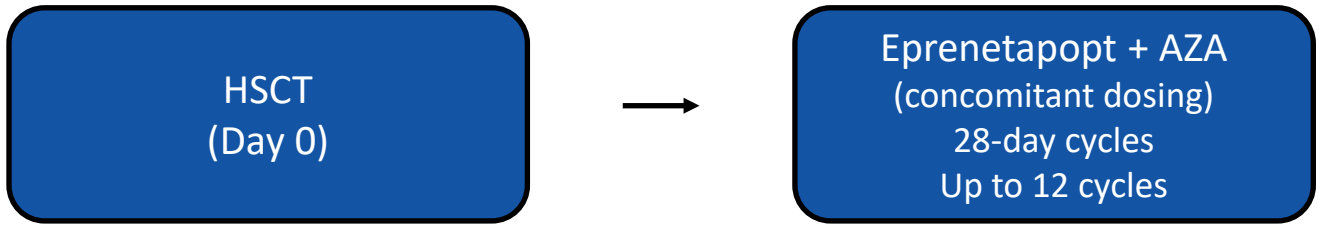
Out of 6 patients with CRi, 3 (50%) have discontinued study treatment to proceed to HSCT.

- Completion of enrollment in triplet arm anticipated in Q2 2021
- Preliminary response rate data in triplet arm anticipated in Q2 2021
- Regulatory pathway to be discussed with FDA subject to positive data

[1]Phase 1/2 AML Trial as of February 25, 2021; [2]Dinardo et al, EHA 2020; Dinardo et al, *N Engl J Med* 2020; 383:617-629; [3]Neither Dinardo et al, *Blood*, 2018 nor Viale-A reported CR rate; however, 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 of *TP53* Mutant MDS and AML with Eprenetapopt + AZA

- Phase 2 Post-Transplant Maintenance Trial Overview

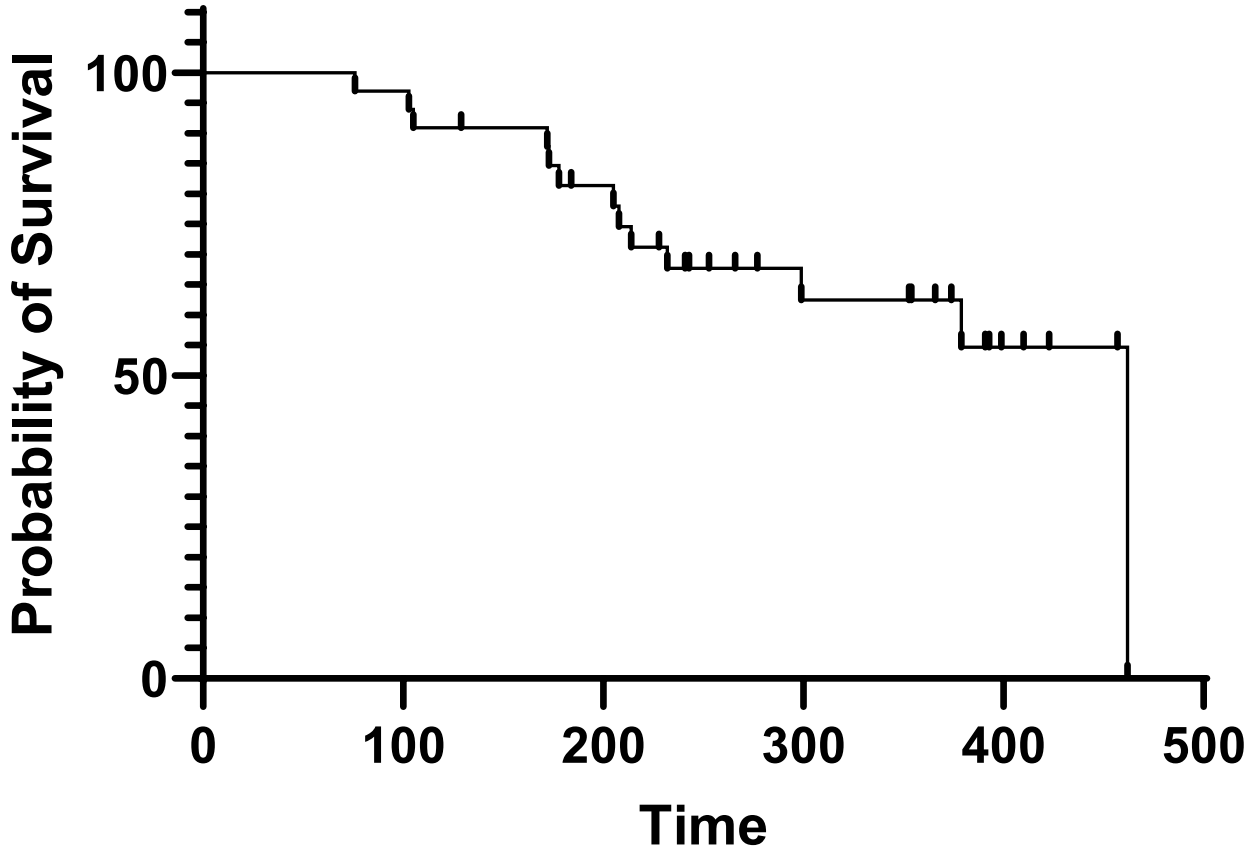


- Endpoints
  - Primary: 1-year RFS, tolerability
    - 90% power with 1-sided alpha of 0.1 to discern 1-year RFS >50% vs ≤30%
  - Secondary: OS, non-relapse mortality, PFS, LFS, GVHD, EFS

- Status
  - Enrollment complete (N = 33)
  - Initial availability of 1-year RFS data anticipated 2Q 2021

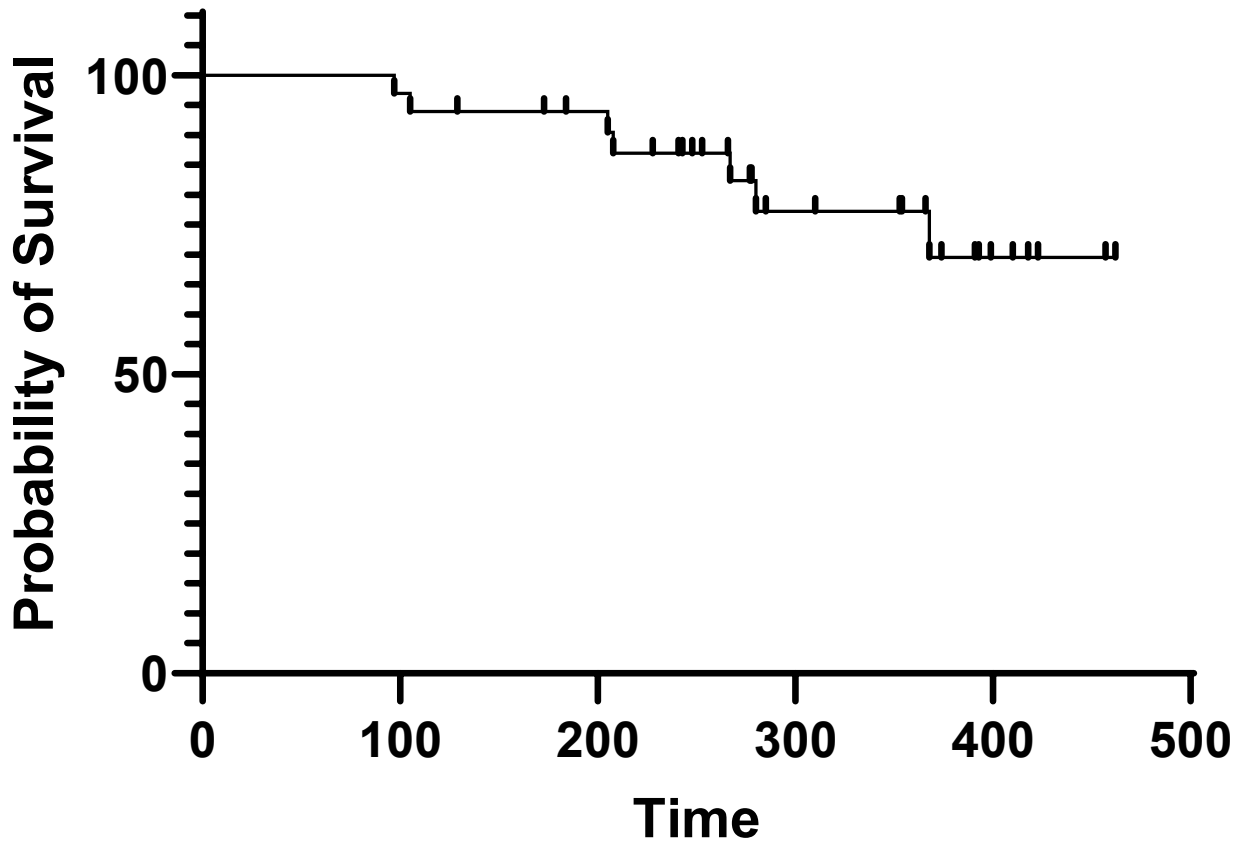
- Next steps
  - Continue discussions with Blood and Marrow Transplant Clinical Trials Network on further study
  - Potential discussion with FDA after results

Interim RFS from Day 0 HSCT in Days (cutoff: 02 April 2021)



1-year RFS = 62%
Median = 462 days

Interim OS from Day 0 HSCT (cutoff: 02 April 2021)



1-year OS = 77%
Median = not estimable

Phase 1 Trial of Eprenetapopt Combination Therapy in R/R *TP53* Mutant CLL and MCL

- Del17p / *TP53* mutations in CLL and MCL are associated with poor outcomes[1]
  - Shorter median PFS and OS
  - Increased risk of progression

- In large cancer cell databases, lymphoid cancer cell lines appear to be among the most sensitive to eprenetapopt[2]

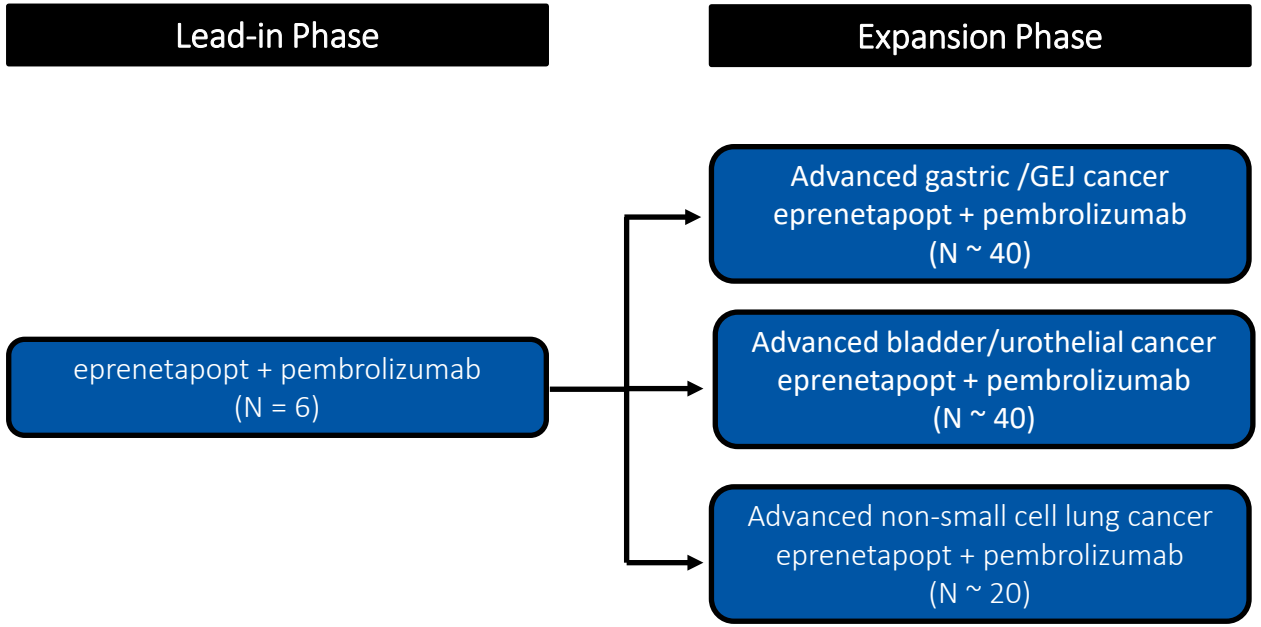
- Overview of Phase 1 Trial in R/R CLL and MCL

- Status
  - First patient enrolled 1Q 2021
  - Preliminary tolerability and efficacy data anticipated 2H 2021

[1] O'Brien et al (2019) *Blood*; Kater et al (2019) *J Clin Oncol*; Jain, et al. (2020), *J Clin Oncol*; [2]Aprea analysis of Broad Institute DepMap portal (www.depmap.org); Picco et al, *Nat Commun*, 2019.

Phase 1/2 Trial of Eprenetapopt + Pembrolizumab Combination in Advanced Solid Tumors

- Overview of Phase 1/2 Solid Tumor Trial

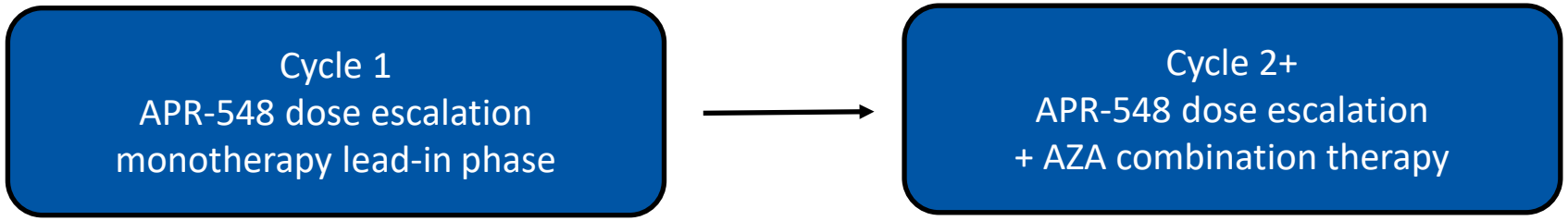


- Program update
  - No dose limiting toxicities in lead-in phase (N=6)
  - Enrollment ongoing, currently 15 patients enrolled across expansion arms
  - Trials-in-Progress presentation ASCO 2021 (abstract TPS3161)

First-in-Human Clinical Trial of APR-548 in MDS

APR-548 is being developed for oral administration

- Overview of FIH Trial



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

- Status
  - First patient anticipated early 2Q 2021

- Future Development
  - Following completion of FIH Phase 1, possibility to explore expansion in MDS, AML or other indications including solid tumors

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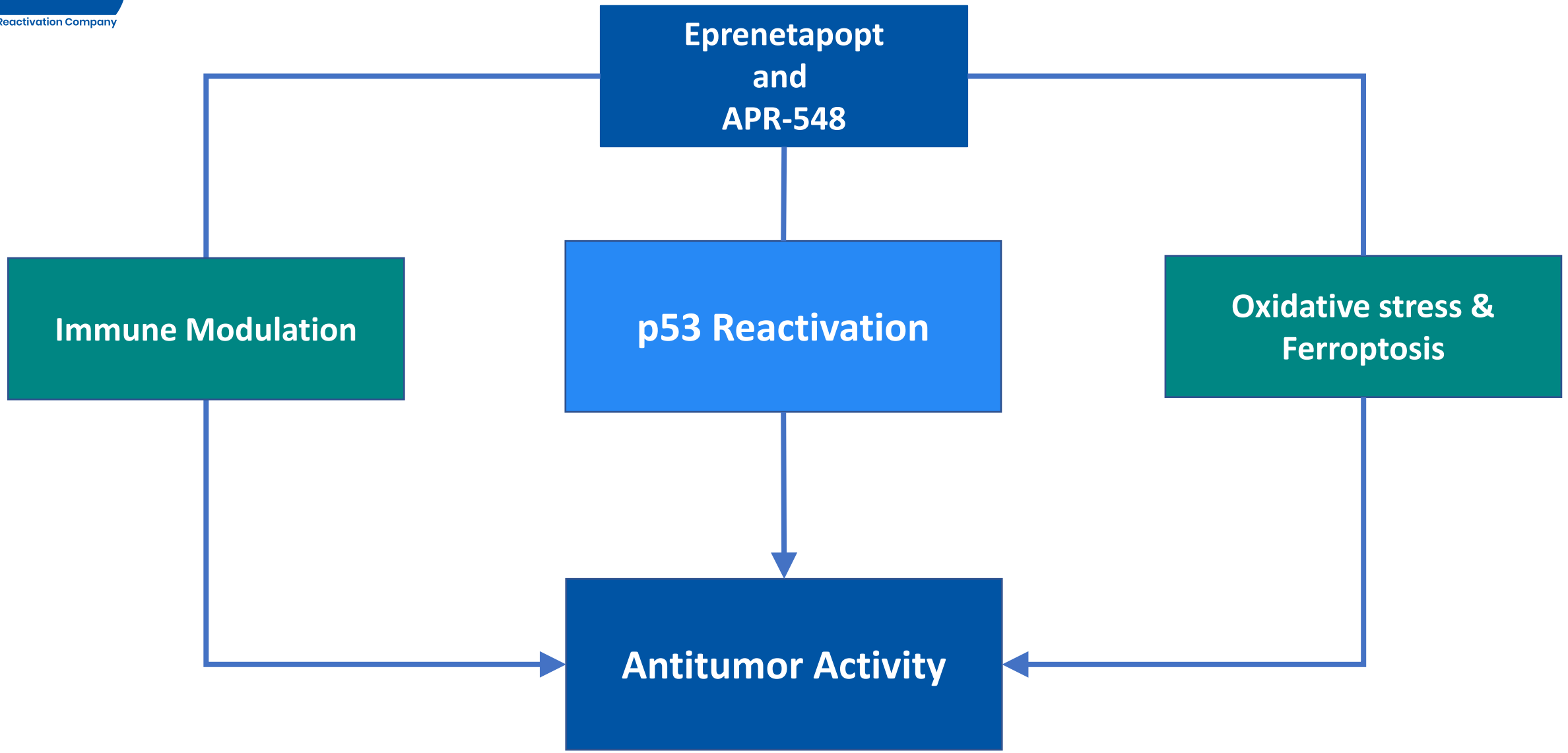
Development Strategy

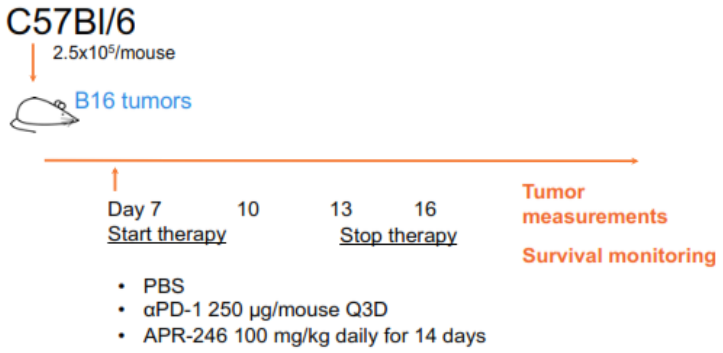
Multiple Pathways to Induce Antitumor Activity

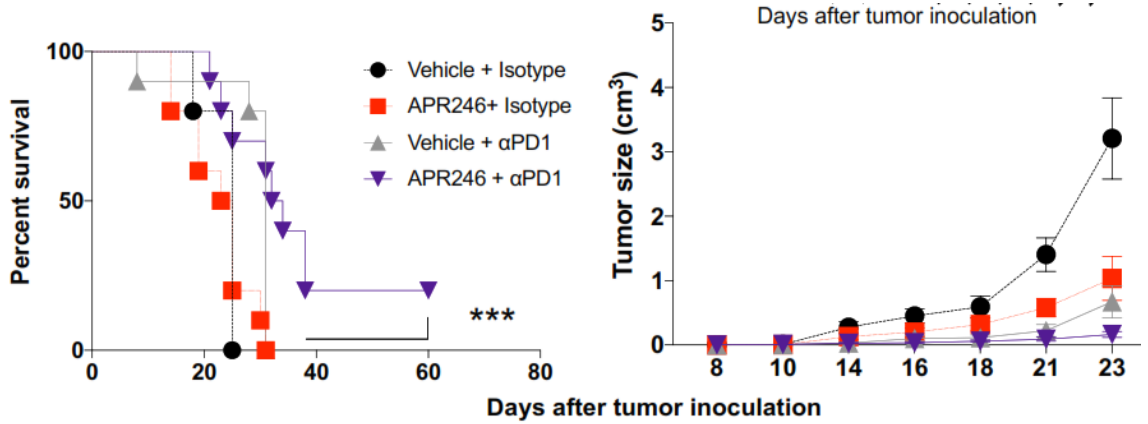


Eprenetapopt Modulates the Immune System

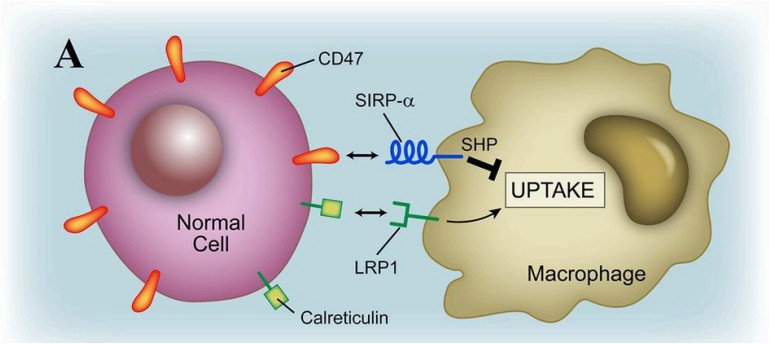
Enabling important opportunities for combination with immuno-oncology agents

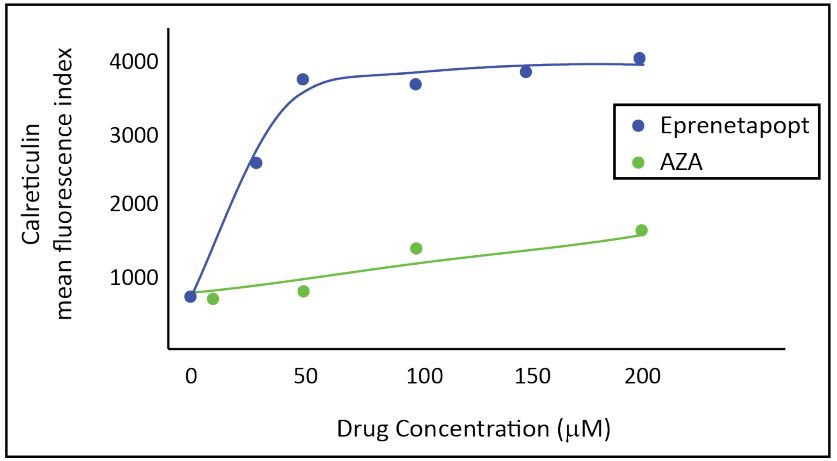
- Enhancement of p53 signaling in macrophages by eprenetapopt augments T-cell mediated anti-tumor activity in combination with anti-PD-1





- Eprenetapopt robustly induces calreticulin surface exposure, a critical mediator of anti-CD47 activity, in a dose-dependent manner

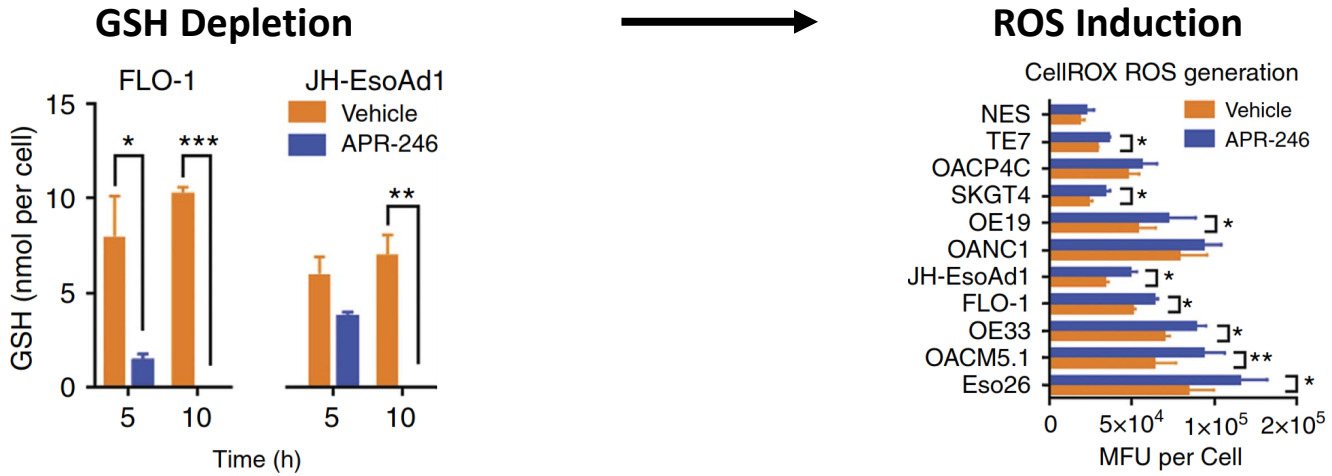




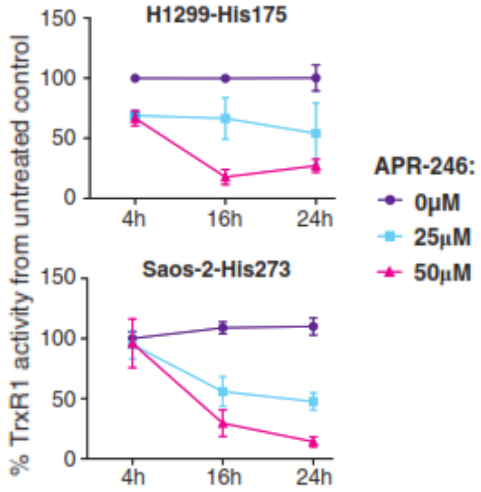
[1]Ghosh et al, 2019 AACR Annual Meeting, Abstract 4843; [2]Aprea data. Figure from [insert ref]

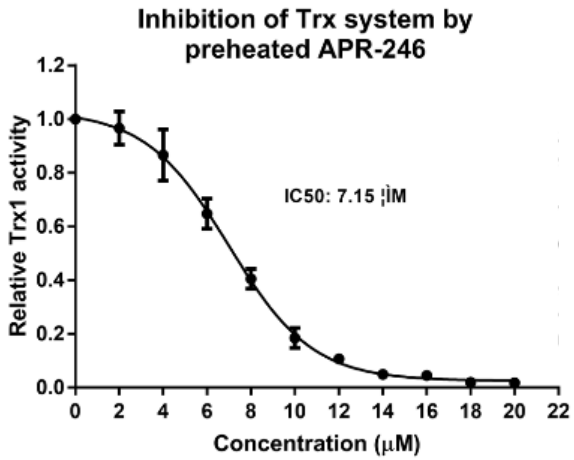
Eprenetapopt Depletes Glutathione and Increases Oxidative Stress

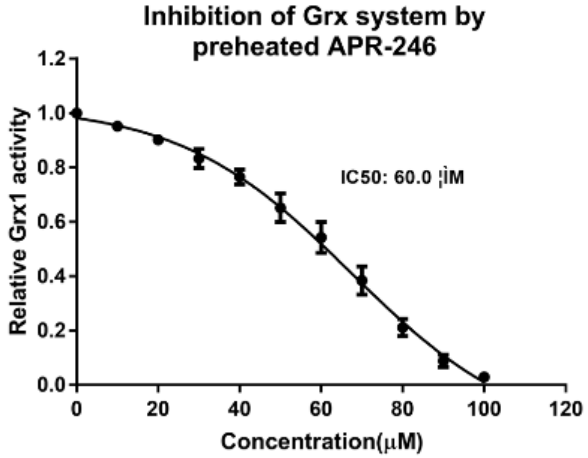
- Eprenetapopt depletes glutathione (GSH) levels and induces reactive oxygen species (ROS)[1]



- Eprenetapopt induces oxidative stress via inhibition of thioredoxin reductase[2], thioredoxin[3] and glutaredoxin[3]





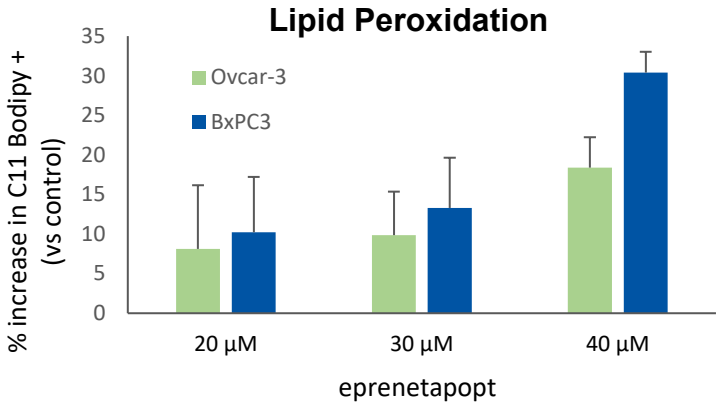


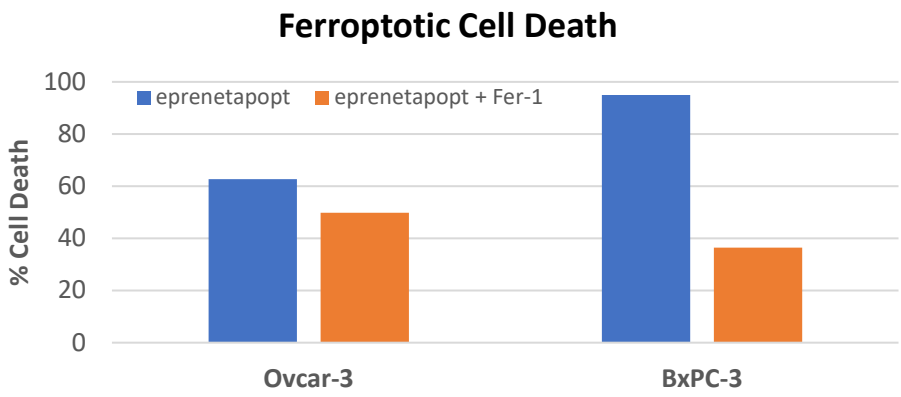
[1]Liu et al, *Gut*, 2017; [2]Peng et al, *Cell Death Dis*, 2013; [3]Haffo et al. *Sci Reports*, 2018

Eprenetapopt Induces Ferroptosis in Cancer Cells

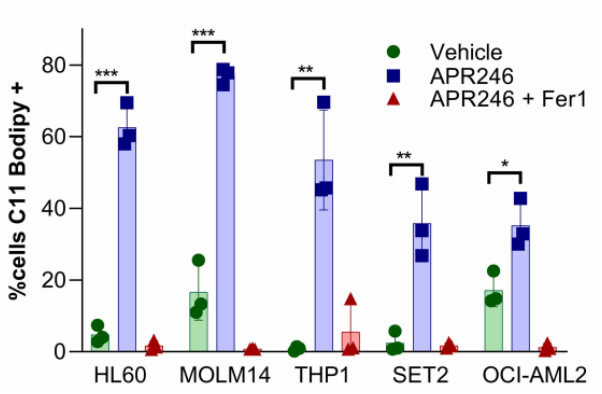
Ferroptosis is an important iron-dependent, non-apoptotic programmed cell death pathway characterized by lipid peroxidation

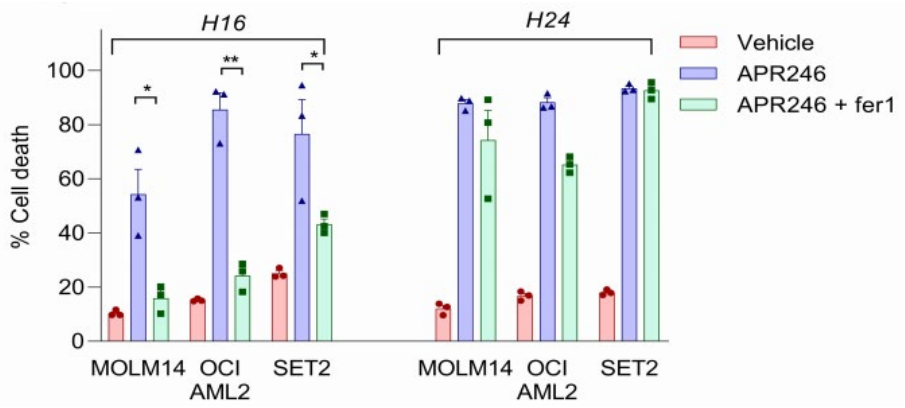
- We have demonstrated eprenetapopt-induced lipid peroxidation and ferroptosis in pancreatic and ovarian cancer cells[1]





- Academic collaborators have independently demonstrated eprenetapopt-induced ferroptosis in AML[2]





[1]Aprea data; [2]Birsen et al, *Haematologica*, 2021

Preclinical Research is Ongoing to Enable Future Clinical Trials

- Continued exploration of eprenetapopt/APR-548 mechanism of action yields important new anticancer therapeutic strategies

- We are conducting extensive *in vitro* and *in vivo* preclinical studies that continue to guide design and execution of future clinical trials to maximize effects on:
  - p53 reactivation
  - Immune modulation
  - Oxidative stress and ferroptosis

- We are collaborating with global ferroptosis thought leaders as a prelude to clinical studies
  - Completing preclinical studies of eprenetapopt with agents that trigger ferroptosis, such as sorafenib, to enable clinical trials in renal cell carcinoma, hepatocellular carcinoma and other malignancies
  - Goal is to commence Phase 1 clinical trials Q4 2021 or Q1 2022

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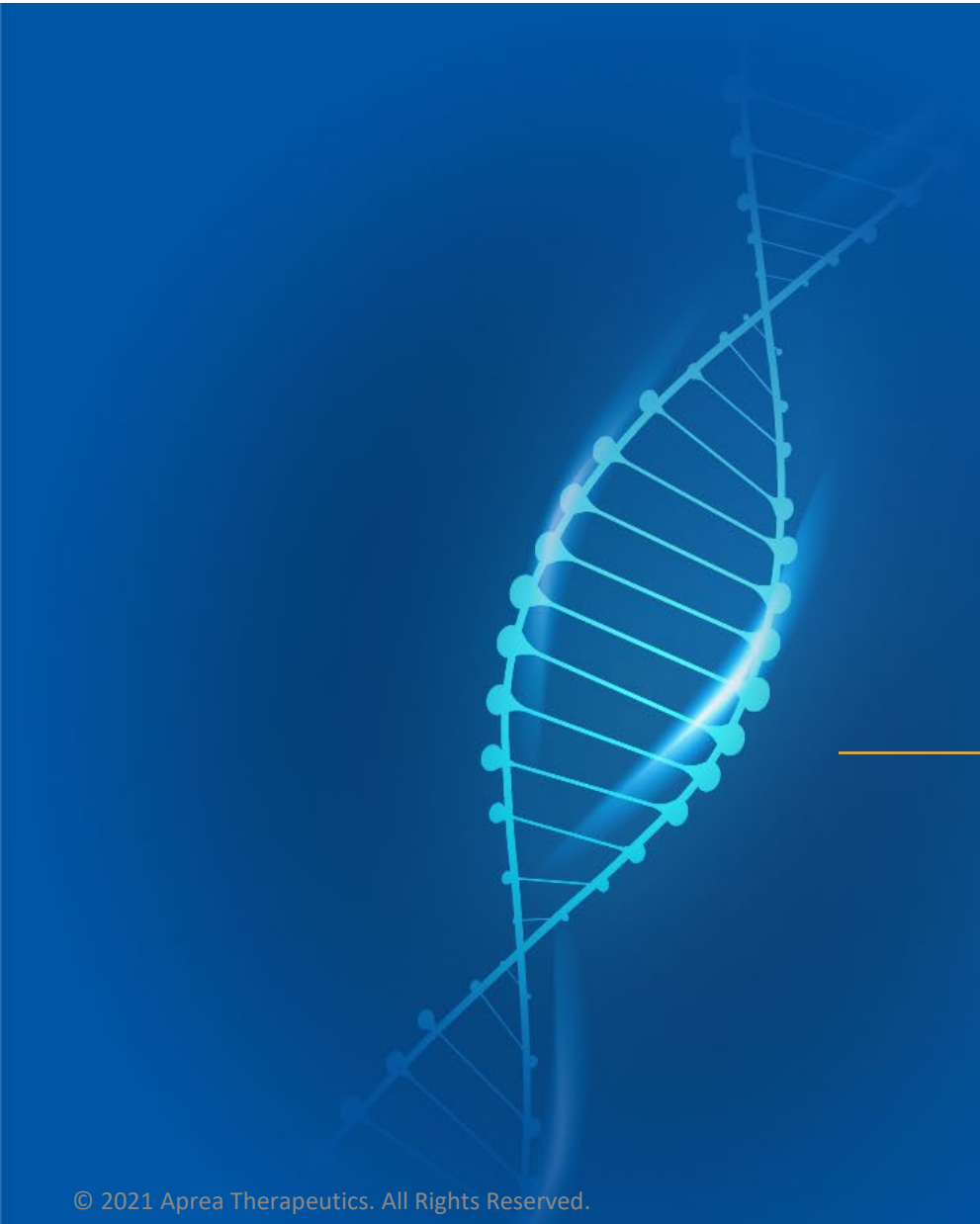

Q&A

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Wrap-Up

Wrap-up

- Milestones and Financial Update
  - YE 2020 cash balance ~$90 million
    - Anticipate 2021 burn ~$30-35 million and year-end cash ~$55-60 million
  - Continue to invest in clinical programs with near-term milestones
    - AML and post-transplant maintenance (Q2 2021)
    - Lymphoid malignancies (fully-enrolled by end of 2021)
    - APR-548 and solid tumor strategy (Q4 2021)
  - Sufficient current resources to invest in:
    - AML and post-transplant clinical development
    - FIH APR-548 and expansion of clinical indications
    - Phase 1 clinical studies of alternative mechanisms of action, including ferroptosis
- Summary
  - In Phase 3, dose modifications of eprenetapopt and azacitidine led to undertreatment in the experimental arm that negatively impacted efficacy, particularly the primary endpoint of CR rate
  - Strong progress in ongoing programs, particularly AML
  - Continued platform rollout of eprenetapopt and APR-548 with new indications and combinations