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 press release. We undertake no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstances.
Aprea Therapeutics at a Glance

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

- p53 is a tumor suppressor protein considered to be “the Guardian of the Genome”
  - The TP53 gene is the most commonly mutated gene in human cancer

- Eprenetapopt (APR-246): First-in-class small molecule p53 reactivator
  - Broad opportunity to enhance potency of anti-cancer therapies; impact patient lives and treatment strategies

- Pivotal Phase 3 trial ongoing in myelodysplastic syndromes (MDS) with topline data by end of 2020
  - Breakthrough Therapy Designation from FDA in January 2020
  - NDA and MAA submissions planned in 2021
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 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
Eprenetapopt Selectively Reactivates 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
Eprenetapopt
Clinical Development
## Execution on Clinical Development

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Indication</th>
<th>Treatment Line</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eprenetapopt (APR-246)</strong></td>
<td><strong>TP53 Mutant MDS</strong></td>
<td>Frontline</td>
<td>eprenetapopt + aza&lt;sup&gt;2&lt;/sup&gt;</td>
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<tr>
<td></td>
<td><strong>TP53 Mutant MDS / AML</strong></td>
<td>Frontline (U.S. study)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>eprenetapopt + aza</td>
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<tr>
<td></td>
<td><strong>TP53 Mutant MDS / AML</strong></td>
<td>Frontline (French study)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>eprenetapopt + aza</td>
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</tr>
<tr>
<td></td>
<td><strong>TP53 Mutant MDS / AML</strong></td>
<td>Post-Transplant Maintenance</td>
<td>eprenetapopt + aza</td>
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<tr>
<td></td>
<td><strong>TP53 Mutant AML</strong></td>
<td>Frontline and Relapsed / Refractory</td>
<td>eprenetapopt + ven&lt;sup&gt;3&lt;/sup&gt; and/or aza</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>TP53 Mutant CLL / MCL</strong></td>
<td>Relapsed / Refractory</td>
<td>eprenetapopt + ibrutinib or ven-R&lt;sup&gt;4&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Gastric / Bladder / NSCLC</strong></td>
<td>Advanced</td>
<td>eprenetapopt + pembrolizumab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>APR-548</strong></td>
<td><strong>TP53 Mutant MDS</strong></td>
<td>Frontline and Relapsed / Refractory</td>
<td>APR-548 + aza</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

<sup>1</sup>Investigator-initiated trials; <sup>2</sup>azacitidine; <sup>3</sup>venetoclax; <sup>4</sup>venetoclax + rituximab
**TP53 Mutant MDS is a Major Unmet Medical Need with Dire Prognosis**

**Incidence**

50,000 – 87,000 in 2019 in US/EU5/JP

**TP53 mutation is common**

~20% of all MDS

30-40% in therapy-related & higher risk MDS

**Prognosis with available therapies**

15-20% complete remission (CR)

~7 months overall survival (OS)
Two parallel investigator-initiated trials evaluating eprenetapopt + AZA as frontline therapy

<table>
<thead>
<tr>
<th>Patient Demographics</th>
<th>U.S. Trial(^1)</th>
<th>French Trial(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (N=55)</td>
<td>MDS (N=40)</td>
</tr>
<tr>
<td>Age in years, median (range)</td>
<td>66 (34 – 85)</td>
<td>66 (34 – 80)</td>
</tr>
<tr>
<td>Disease type, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDS</td>
<td>40 (73)</td>
<td>34 (66)</td>
</tr>
<tr>
<td>IPSS-R: Intermediate</td>
<td>4 (7)</td>
<td>4 (10)</td>
</tr>
<tr>
<td>IPSS-R: High</td>
<td>8 (15)</td>
<td>8 (20)</td>
</tr>
<tr>
<td>IPSS-R: Very high</td>
<td>28 (51)</td>
<td>28 (70)</td>
</tr>
<tr>
<td>AML</td>
<td>11 (20)</td>
<td>18 (35)</td>
</tr>
<tr>
<td>MDS-MPN / CMML</td>
<td>4 (7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Complex karyotype, n (%)</td>
<td>47 (85)</td>
<td>36 (90)</td>
</tr>
</tbody>
</table>
Responses and Survival with Eprenetapopt + AZA in TP53 Mutant MDS Exceed Historical Experience with AZA Monotherapy

52% of evaluable MDS patients in U.S. trial were able to discontinue study treatment for transplant

Eprenetapopt + AZA combination regimen is well-tolerated and delivered in the outpatient setting

◊ Majority of adverse events were low grade (< 3) and associated with the underlying disease

<table>
<thead>
<tr>
<th></th>
<th>Evaluable Population</th>
<th>Intention-to-Treat Population</th>
<th>Historical AZA benchmark</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>U.S. Trial(^2)</td>
<td>French Trial(^3)</td>
<td>U.S. Trial(^2)</td>
</tr>
<tr>
<td><strong>Patients, n</strong></td>
<td>33</td>
<td>28</td>
<td>40</td>
</tr>
<tr>
<td><strong>Response rates</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORR</td>
<td>88%</td>
<td>75%</td>
<td>73%</td>
</tr>
<tr>
<td>CR</td>
<td>61%</td>
<td>57%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Median follow-up, months</strong></td>
<td>10.8</td>
<td>9.7</td>
<td></td>
</tr>
<tr>
<td><strong>Median DoR, months</strong></td>
<td>8.4</td>
<td>N/A(^5)</td>
<td>7.3</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>7.3</td>
<td>N/A(^5)</td>
<td></td>
</tr>
<tr>
<td>Median OS, months</td>
<td>10.4</td>
<td>12.1</td>
<td></td>
</tr>
</tbody>
</table>

Eprenetapopt Demonstrates Clinical Activity Across Multiple TP53 Mutations

- **U.S. Trial**¹,²

- **French Trial**¹,³

---

¹Data shown for all evaluable patients in each trial; ²Sallman et al, ASH 2019; ³Cluzeau et al, EHA 2020
**Randomized Phase 3 Trial in 1L TP53 Mutant MDS**

**Topline data by YE 2020**

**Trial Design**

- **1:1 Randomization**
  - Eprenetapopt + AZA (N = 77)
  - AZA (N = 77)

**Patients**
- N = 154
- At least one TP53 mutation
- Int/High/Very High IPSS-R

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

**Upcoming Milestones**
- **Topline CR data by YE 2020**
- NDA and MAA submissions planned in 2021

**Regulatory Designations**
- Breakthrough Therapy Designation for MDS granted by FDA in January 2020
- Fast Track Designation for MDS granted by FDA in April 2019
- Orphan Drug Designations for MDS granted by FDA in April 2019 and EMA in July 2019

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

**Incidence**

45,000 in 2019 in US/EU/JP

**TP53 mutation is common**

20-30% TP53 mutant

**Prognosis with available therapies**

0-20% complete remission (CR)

~6 months overall survival (OS)
1L TP53 Mutant AML Trial with Registration Potential

Current Eprenetapopt Data and Therapeutic Benchmark

<table>
<thead>
<tr>
<th>Evaluable AML patients, n</th>
<th>U.S. Trial¹ (Eprenetapopt + AZA)</th>
<th>French Trial² (Eprenetapopt + AZA)</th>
<th>Phase 1/2 AML Trial³ (Eprenetapopt + Ven + AZA)</th>
<th>Benchmark⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>11</td>
<td>6 (lead-in phase)</td>
<td>38 (Ven-Aza: VIALE-A)</td>
<td></td>
</tr>
<tr>
<td>Evaluable patients, n</td>
<td></td>
<td></td>
<td>14 (Aza: VIALE-A)</td>
<td></td>
</tr>
<tr>
<td>Response rates</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORR</td>
<td>88%</td>
<td>82%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>50%</td>
<td>27%</td>
<td>33%</td>
<td></td>
</tr>
</tbody>
</table>

Phase 1/2 AML Trial Plan

- No DLTs observed in lead-in phase
- eprenetapopt + AZA + venetoclax (N = 33)
- eprenetapopt + AZA (N = 33)
- Best regimen (N ≤ 50)

1Sallman et al, ASH 2019; 2Cluzeau et al, EHA 2020; 3Phase 1/2 AML Trial as of September 8, 2020; 4Dinardo et al, N Engl J Med 2020, 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

- 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

- Phase 2 Post-Transplant Maintenance Trial Design
  - Eprenetapopt + aza maintenance up to 12 months

- Endpoints
  - Primary: RFS, tolerability
  - Secondary: OS, non-relapse mortality, PFS, LFS, GVHD, EFS

- Status
  - Target enrollment (N = 31) reached
  - 1-year RFS primary endpoint readout anticipated mid-2021

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

- **Unmet Need**

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

- **Phase 1 CLL/MCL Trial Design**
  - 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)

- **Status**
  - Open and enrolling
  - Preliminary tolerability and efficacy data anticipated 2H 2021

---

**Incidence**
- CLL: ~45,000 annually in US/EU5/JP
- MCL: ~7,000 annually in US/EU5/JP

**TP53 Mutation**
- ~50% TP53 mutant in R/R

**Prognosis**
- 0-20% complete remission (CR)
- ≤ 12 months overall survival (OS)

---

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

- Unmet Need

- Incidence
  - Gastric: ~185,000 annually in US/EU5/JP
  - Bladder: ~225,000 annually in US/EU5/JP
  - NSCLC: ~500,000 annually in US/EU5/JP

- TP53 Mutation
  - ~50-80% TP53 mutant

- Prognosis
  - 0-10% complete remission (CR)
  - ≤ 12 months overall survival (OS)

- Rationale
  - APR-246 enhances effects of PD-1 blockade in murine melanoma and colorectal carcinoma models

- Phase 1/2 Solid Tumor Trial Design
  - Safety Lead-in
    - Eprenetapopt + pembrolizumab in advanced solid tumors (N ≈ 18)
  - Expansion
    - Advanced gastric (N ≈ 40), bladder (N ≈ 40), and NSCLC (N ≈ 20)

- Status
  - First patients enrolled August 2020
  - No DLTs in safety cohort (N=3); continued enrollment ongoing
  - Preliminary tolerability and efficacy data anticipated 2H 2021

APR-548: A Next-Generation p53 Reactivator Engineered for Oral Administration

- APR-548 is converted to MQ and thus shares a similar mechanism of action to eprenetapopt.

FACS analysis of R248Q p53 mutant myeloid cells treated with APR-548:
- Induction of cleaved caspase-3 (apoptosis marker)
- Reduction of Ki67 (proliferation marker)

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

1Mice 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 + AZA in TP53 Mutant MDS

IND and protocol have been accepted by FDA

- Overview of Trial
  
  APR-548 monotherapy lead-in phase followed by APR-548 + AZA combination therapy (N ~30)

- Status
  
  - Phase 1 trial anticipated to open enrollment in Q4 2020, FPI anticipated Q1 2021
  
  - Opportunities for accelerated path to commercialization (PK bridging to eprenetapopt, etc) will be explored in conjunction with tolerability and efficacy data
Financial Overview

» $101.1 million of cash and cash equivalents at September 30, 2020
» No outstanding debt
» Anticipated cash burn for 2020: $35.0 million – $40.0 million
» Existing cash should fund operations into 2023

Balance Sheet

» ~21.2 million common shares outstanding at September 30, 2020

Shares Outstanding

» 17 full-time employees at September 30, 2020

Other
Summary

- Continued strong execution of current eprenetapopt clinical development plan
  - Positive and concordant efficacy data in Phase 1b/2 trials for MDS/AML
  - CR endpoint readout in randomized Phase 3 trial for MDS by YE 2020
  - Target enrollment reached in Phase 2 trial for MDS/AML post-transplant maintenance
  - Expansion of cohorts underway in Phase 1/2 trial for AML

- Aggressively broadening pipeline with clinical trials in hematologic malignancies and solid tumors
  - Non-Hodgkins lymphomas (CLL, MCL)
  - Gastric cancer
  - Bladder cancer
  - Non-small cell lung cancer

- Next-generation, oral p53 reactivator APR-548 ready to enter clinical trials