Aprea Therapeutics Presents Results From Phase Ib/II Clinical Study of APR-246 and Azacitidine (AZA) in Patients with TP53 Mutant Myelodysplastic Syndromes (MDS) at the 2018 American Association of Cancer Research (AACR) Annual Meeting in Chicago

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- ORR (by IWG) of 100% in all evaluable patients: 6 CR (75%) and 2 mCR (25%)
- All CR patients achieved complete cytogenetic response
- No responding patients have experienced relapse
- No treatment-related serious adverse events or dose-limiting toxicities to date

BOSTON, MA. and STOCKHOLM, SWEDEN, April 16, 2018 – Aprea Therapeutics today presented results at the 2018 AACR Annual Meeting from its ongoing Phase Ib/II clinical study in MDS. The ongoing study, sponsored by the Moffitt Cancer Center with financial support from the Evans MDS Clinical Research Consortium and the MDS foundation, evaluates the safety and efficacy of APR-246 in combination with azacitidine for the treatment of *TP53* mutated MDS.

The overall response rate in 8 evaluable patients was 100%, with 6 patients achieving a complete response (CR) and 2 patients achieving a marrow CR (mCR). Median progression free survival (PFS) and overall survival (OS) have not been reached, and no responding patients have experienced relapse. At data cutoff, 4 CR patients had complete cytogenetic response, with results of additional CR patients pending analysis. One CR patient achieved mCR and partial cytogenetic response after receiving four days of APR-246 monotherapy. Relative to baseline, p53 immunohistochemistry scores and mutant *TP53* variant allele frequency (VAF) were significantly decreased at time of disease assessment. Adverse events (AEs) during the APR-246 monotherapy lead-in phase were all grade 1. No dose-limiting toxicities have been experienced to date and no potentiation of the expected hypomethylating agent (HMA)-related safety profile has been observed.

David Sallman, M.D., lead principal investigator of the clinical study from the Moffitt Cancer Center, said, “Responses have been achieved in all patients, including a 75% complete response rate, and accompanied by deep molecular remissions. The emerging clinical data from this study are very encouraging, particularly given the dearth of current therapeutic options for *TP53* mutated MDS patients. Furthermore, the combination of APR-246 and azacitidine is well-tolerated, the maximum tolerated dose has not been reached and dose escalation in the study is ongoing.”

About the Clinical Study

Eligible patients in the Phase Ib/II clinical study include HMA naïve, *TP53* mutated MDS and oligoblastic acute myeloid leukemia (AML, ≤ 30% blasts). Patients receive APR-246 in a 3+3 dose escalation design (50, 75, 100 mg/kg lean body weight) IV daily over 4 days in a lead-in phase (days -14 to -10) followed by the same dose of APR-246 (days 1-4) and AZA 75 mg/m2 SC/IV over

7 days (days 4-10 or 4-5 and 8-12) in 28 day cycles. Primary objective of the clinical study is safety, with AEs graded by CTCAE v4.03 and DLT assessment over 6 weeks. Secondary endpoints include response rate by IWG 2006 criteria, PFS, OS, as well as serial next generation sequencing and p53 immunohistochemistry for evaluation of clonal suppression and depth of remission.

The design for Phase Ib portion of the study includes dose escalation cohorts, with 3 in dose-level 1 (DL1), 3 in DL2 and 6 in DL3. At baseline, all currently enrolled patients (12) had poor- or very poor risk cytogenetics (17% poor, 83% very poor) and intermediate risk or higher disease by IPSS-R (8% intermediate, 17% high, 75% very high). Baseline median bone marrow blast percentage was 13% (range: 1 – 30%). Eight of twelve patients enrolled were response evaluable at data cutoff, with one patient discontinuing treatment prior to first disease assessment and three patients whose treatment is ongoing but have not yet reached first disease assessment.

About Myelodysplastic Syndrome

Myelodysplastic syndrome (MDS) represents a spectrum of hematopoietic stem cell malignancies in which bone marrow fails to produce sufficient numbers of healthy blood cells. Approximately 30-40% of MDS patients progress to acute myeloid leukemia (AML) and mutation of the p53 tumor suppressor protein is thought to contribute to disease progression. Mutations in p53 are found in up to 20% of MDS and AML patients and are associated with poor overall prognosis.

About p53 and APR-246

The p53 tumor suppressor gene is the most frequently mutated gene in human cancer, occurring in approximately 50% of all human tumors. These mutations are often associated with resistance to anti-cancer drugs and poor overall survival, representing a major unmet medical need in the treatment of cancer. Some cancers, including melanoma, express wild-type p53 that is nonetheless inactivated and non-functional.

APR-246 has been shown to reactivate mutant and inactivated p53 protein – by restoring wild-type p53 conformation and function – and thereby induce programmed cell death in human cancer cells. APR-246 has demonstrated pre-clinical anti-tumor activity in a wide variety of solid and hematological (blood) tumors, including ovarian cancer, small cell lung cancer, esophageal cancer and acute myeloid leukemia (AML), among others. Additionally, strong synergy has been seen with both traditional anti-cancer agents, such as chemotherapy, as well as newer mechanism-based anti-cancer drugs and immuno-oncology checkpoint inhibitors. In addition to pre-clinical testing, a Phase I/Ib clinical program with APR-246 has been completed, demonstrating a favorable safety profile and both biological and confirmed clinical responses in hematological malignancies and solid tumors with mutations in the p53 gene.

About Aprea Therapeutics

Aprea Therapeutics is a Boston, Massachusetts- and Stockholm, Sweden-based biopharmaceutical company focused on the discovery and development of novel anticancer compounds that reactivate the tumor suppressor protein, p53. The Company's lead drug candidate is APR-246, a first-in-class small molecule in clinical development for platinum-sensitive high-grade serious ovarian cancer, platinum-resistant high-grade serious ovarian cancer; myelodysplastic syndrome (MDS); esophageal cancer; and melanoma. Aprea is also developing second generation p53 reactivators that have best-in-class potential. In March 2016, Aprea completed a EUR 46 million Series B financing with an international syndicate co-led by Versant Ventures and 5AM Ventures, with additional participation by Sectoral Asset Management, HealthCap, acting as local lead investor, and existing investor, Karolinska Development. For more information, please visit www.apreatherapeutics.com.

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