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 Society of Hematology (ASH) Annual Meeting in San Diego

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- 95% ORR (by IWG) in 20 evaluable patients
- 70% complete remission (CR) rate in 20 evaluable patients
- No dose-limiting toxicities to date

BOSTON, MA. and STOCKHOLM, SWEDEN, December 2, 2018 – Aprea Therapeutics presented results at the 2018 ASH Annual Meeting from its Phase Ib/II clinical study in MDS. The ongoing study is evaluating the safety and efficacy of APR-246 in combination with azacitidine for the treatment of *TP53* mutated MDS. The study is sponsored by the Moffitt Cancer Center with financial support from the MDS Foundation and the Aplastic Anemia and MDS International Foundation as administrator for the Evans MDS Clinical Research Consortium.

The overall response rate in 20 evaluable patients was 95%, with 14 (70%) patients achieving a complete remission (CR) at data cutoff. Relative to baseline, p53 immunohistochemistry positivity, mutant *TP53* variant allele frequency (VAF) and *TP53* minimal residual disease (MRD) were significantly decreased at time of disease assessment. No dose-limiting toxicities have been experienced to date and no exacerbation of the expected AZA-related safety profile has been observed.

“The expanding data set from this study is very encouraging,” said David Sallman, M.D., lead principal investigator of the clinical study from the Moffitt Cancer Center. “As of this latest data cutoff, responses have been achieved in nearly all patients, including a 70% complete remission rate, and accompanied by deep molecular remission in the majority of patients as assessed by serial *TP53* analysis. In addition, the overall safety experience indicates that the combination regimen of APR-246 and azacitidine is both safe and well-tolerated. Comparison of the current data set to historical AZA clinical experience suggests that combination of APR-246 with AZA may offer these patients a better potential treatment option than AZA alone.”

“The continued positive data from this clinical study has created the potential for a new treatment paradigm for patients with few therapeutic options,” said Christian S. Schade, President and Chief Executive Officer of Aprea. “As a result of this exciting progress, Aprea expects to soon begin enrolling a randomized, controlled Phase III clinical study of APR-246 in combination with AZA for the treatment of *TP53* mutated MDS.”

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). In the Phase Ib part of the clincal study, patients received 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. In the Phase II part of the clinical study, patients receive APR-246 as a 4,500 mg fixed dose IV daily (days 1-4) and AZA over 7 days (days 4-10 or 4-5 and 8-12) in 28-day cycles. Primary objective in Phase Ib part of the clinical study was safety, with AEs graded by CTCAE v4.03 and DLT assessment over 6 weeks. Secondary endpoints included 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. In the Phase II part of the clinical study the primary endpoint is response rate.

About Myelodysplastic Syndrome

Myelodysplastic syndromes (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.

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 MDS, AML, and ovarian cancer, 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/II 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 *TP53* 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 November 2018, Aprea completed a EUR 50 million Series C financing with an international syndicate led by the Redmile Group, with participation by new investor Rock Springs Capital and existing investors 5AM Ventures, Versant Ventures, HealthCap, Sectoral Asset Management and Karolinska Development AB (Nasdaq Stockholm: KDEV). For more information, please visit www.aprea.com.

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