Recap and Update of Positive Data from Phase Ib/II Clinical Trials of APR-246 and Azacitidine (AZA) in Patients with TP53 Mutant Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML) Presented at the 2019 American Society of Hematology (ASH) An

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BOSTON, Dec. 12, 2019 (GLOBE NEWSWIRE) -- Lead investigators from US and French Phase Ib/II clinical trials of APR-246 and Azacitidine (AZA) in patients with *TP53* mutant MDS and AML, presented positive data on Monday at the 2019 ASH Annual Meeting. Both trials are evaluating the safety and efficacy of Aprea Therapeutics, Inc. (Nasdaq: APRE) lead product candidate, APR-246, in combination with azacitidine for the treatment of *TP53* mutant MDS and AML.

Dr. David Sallman of the Moffitt Cancer Center, the lead investigator on the US Trial, presented on 33 evaluable MDS patients as of the data cutoff, with an overall response rate (ORR) of 88%, and a 61% complete remission (CR) rate, by International Working Group (IWG) criteria. With a median duration of follow-up of 10.8 months, the median duration of response was 8.4 months and the median duration of CR was 7.3 months. Seventeen (52%) evaluable MDS patients discontinued therapy to pursue stem cell transplant. Median overall survival (OS) for all enrolled patients (n=55) was 10.8 months. Median OS in responding patients versus non-responders was 13.7 vs. 3.9 months. Adverse events, regardless of causality, were mostly grade 1/2. Grade 3+ adverse events occurring in ≥20% of patients were limited to cytopenias and infection, consistent with underlying hematopoietic malignancies, and no exacerbation of the expected AZA-related safety profile has been observed.

Prof. Thomas Cluzeau reported preliminary data for 24 evaluable MDS patients enrolled before June 2019 in the French trial being conducted by the Groupe Francophone des Myélodysplasies, which is led by Prof. Pierre Fenaux and who is also the lead investigator of the French trial. Following the oral presentation, the GFM informed Aprea that the analysis presented and previously reported included three MDS patients who achieved a complete remission (CR) but were enrolled after May 2019 and therefore should not have been included among the 24 evaluable patients under the specified enrollment cutoff. In addition, there were two additional MDS patients enrolled before June 2019 who had responded. The updated data for 24 evaluable MDS patients enrolled before June 2019 are overall response rate (ORR) of 71% and complete remission (CR) rate of 54% by IWG criteria. Inclusive of the CRs in 3 MDS patients enrolled after May 2019, the updated data for 27 evaluable MDS patients are ORR of 74% and CR rate of 59%. With a median duration of follow-up of 6.4 months, the median overall survival (OS) for all enrolled patients (n=53) had not been reached. In addition, all responding patients were alive at data cutoff. Relative to baseline, mutant *TP53* variant allele frequency (VAF) was significantly decreased in responding patients and undetectable in all patients who achieved a CR.

Updated summary information on both trials can be found on the Company's investor relations website at https://ir.aprea.com.

About the US Clinical Trial

Eligible patients in the Phase Ib/II clinical trial include HMA-naïve, TP53 mutated MDS, oligoblastic acute myeloid leukemia (AML, ≤ 30% blasts), MDS-myeloproliferative neoplasm (MDS-MPN) overlap and chronic myelomonocytic leukemia (CMML). In the Phase Ib part of the clinical trial, 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 daily for 7 days (days 4-10 or 4-5 and 8-12) in 28-day cycles. In the Phase II part of the clinical trial, patients receive APR-246 as a 4,500 mg fixed dose IV daily (days 1-4) and AZA daily for 7 days (days 4-10 or 4-5 and 8-12) in 28-day cycles. Primary objective in Phase Ib part of the clinical trial 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 trial the primary endpoint is CR rate.

About the French Clinical Trial

Eligible patients in the Phase Ib/II clinical trial include HMA naïve, *TP53* mutated MDS and acute myeloid leukemia (AML). All enrolled patients were to 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. The primary endpoint of the trial is CR 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 is a small molecule that has demonstrated reactivation of mutant and inactivated p53 protein – by restoring wild-type p53 conformation and function – and thereby induce programmed cell death in human cancer cells. Pre-clinical anti-tumor activity has been observed with APR-246 in a wide variety of solid and hematological cancers, 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.

A pivotal Phase 3 clinical trial of APR-246 and azacitidine for frontline treatment of *TP53* mutant MDS is ongoing. APR-246 has received Orphan Drug and Fast Track designations from the FDA for MDS, and Orphan Drug designation from the EMA for MDS, AML and ovarian cancer.

About Aprea Therapeutics

Aprea Therapeutics Inc., (NASDAQ: APRE) is a biopharmaceutical company headquartered in Boston, Massachusetts with research facilities in Stockholm, Sweden, focused on developing and commercializing novel cancer therapeutics that reactivate the mutant tumor suppressor protein p53. The Company's lead product candidate is APR-246, a small molecule in clinical development for hematologic malignancies, including myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). For more information, please visit the company website at www.aprea.com.

The Company may use, and intends to use, its investor relations website at https://ir.aprea.com as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD.

Forward-Looking Statements

Certain information contained in this press release 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.

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