Aprea Therapeutics Provides Corporate Update and Announces Development Plans for 2024

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DOYLESTOWN, Pa., Jan. 04, 2024 (GLOBE NEWSWIRE) -- Aprea Therapeutics, Inc. (Nasdaq: APRE) ("Aprea", or the "Company"), a clinical-stage biopharmaceutical company focused on precision oncology through synthetic lethality, today provided a corporate update highlighting recent developments and plans for advancement of its pipeline of DNA Damage Response (DDR) anti-cancer agents in 2024.

"Having made substantial progress over the past twelve months, we are well positioned for ongoing success in 2024 as we execute on our mission to be a global leader in synthetic lethality," said Dr. Oren Gilad, President and CEO of Aprea. "We continue to advance towards achieving our milestones in the ongoing dose-escalation Phase 1 study of our novel macrocyclic ATR inhibitor, ATRN-119, and are finalizing submission of the IND for our next-generation, best-in-class WEE1 inhibitor, APR-1051. This IND is supported by a compelling pre-clinical package showing highly potent and selective anti-tumor activity, limited off-target effects, and favorable pharmacokinetics."

Update on Phase 1/2a Ongoing Trial of ATR Program, ATRN-119

Enrollment of patients continues in the dose escalation portion of the Phase 1/2a clinical trial (study AR-276-01) evaluating ATRN-119 in patients with advanced solid tumors having mutations in defined DDR-related genes. The primary objective of the Phase 1 part of this trial is evaluating the tolerability and pharmacokinetics of ATRN-119 when administered orally on a continuous, once-daily schedule. The daily dosing of ATRN-119 provides continuous ATR inhibition that may be preferable to intermittent dosing for both efficacy and safety, potentially supporting an important competitive advantage over the current class of ATR inhibitors. The secondary objective is the evaluation of antitumor efficacy.

The most recent analysis of the data cut (January 2, 2024) shows that two patients have achieved stable disease – one each in the 50 mg and 200 mg cohorts. Importantly, both these patients' tumors have mutations that have been predicted to confer sensitivity to ATR inhibition. The dose-limiting toxicity period for cohort 4 (350 mg) has been completed. The most recent patient with stable disease from cohort 3 (200mg), with a history of five prior lines of therapy is at approximately four months of treatment duration with ATRN-119, and, following clearance of the 350 mg cohort, is expected to be increased from 200 mg to 350 mg daily, as per the dose escalation trial protocol.

ATRN-119 is being developed as the first and only macrocyclic ATR inhibitor. Macrocycles restrict the number of conformations that a molecule can form, potentially resulting in increased potency and increased selectivity. These properties are expected to permit higher dosing that is potentially more effective with increased tolerability and decreased off-target activity. The company plans to amend the design of the ongoing study beyond the current 800 mg high-dose cohort to incorporate additional higher dose groups.

Upon the addition of the higher dose cohorts, Aprea expects to determine the recommended Phase 2 dose (RP2D) in the second half of 2024. Following dose escalation, the Phase 2a dose expansion part of the study may include patients with NSCLC, breast, colorectal, prostate, and ovarian cancers with selected genetic mutations.

Importantly, the potential for reduced hematologic toxicity from ATRN-119 suggests it may be an ideal DDR inhibitor for novel combination therapies. These potential combinations include ATRN-119 with PARP inhibitors, WEE1 inhibitors, and Antibody-Drug Conjugates (ADCs). The latter of these possibilities could provide a significant breakthrough for the use of ADCs linked to standard chemotherapies, as these promising biopharmaceuticals are often constrained by aberrant drug release and dose-limiting toxicities. Combination with ATRN-119 would potentially amplify the DNA-damaging effects of these ADCs in the targeted tumor cells, thus affording greater efficacy at lower ADC doses.

A more comprehensive dataset from the Phase 1 part of AR-276-01 will be submitted for presentation at a medical meeting in the first half of 2024. For more information, please refer to clinicaltrials.gov NCT04905914.

Investigational New Drug (IND) for WEE1 Program, APR-1051

Aprea completed IND-enabling studies and is finalizing the submission of the IND application with the FDA to begin clinical trials of APR-1051 in the first half of the year. APR-1051 is being developed as a next-generation, potential best-in-class inhibitor of WEE1 kinase with the following properties:

- APR-1051 has a different molecular structure from all other WEE1 inhibitors currently in development with improved selectivity for the target. The improved properties of APR-1051 relative to the other WEE1 inhibitors include its limited

effects on red blood cell counts, hERG inhibition, and body weight loss in pre-clinical studies.
- The selectivity of APR-1051 may solve a long-standing problem with WEE1 inhibitors. Preclinical studies have shown that APR-1051 is site-specific to WEE1 and does not significantly inhibit the PLK1, PLK2, and PLK3 family of kinases, potentially increasing the cancer-killing effects of WEE1i inhibition and reducing hematological toxicity caused by PLK off-targeting. PLK off-target activity has been a challenge for other WEE1 inhibitors. Recent studies indicate that PLK1 off-targeting partially counters the intracellular effects of WEE1 inhibition and could potentially contribute to the myelosuppression observed with other WEE1 inhibitors.
- Specific genetic mutations driving patient selection have been identified.

The company expects to receive FDA clearance on the IND during Q1 2024. Clinical development is in line with FDA requirements for a dose escalation trial to evaluate safety and pharmacokinetics. Leading institutions and a Principal Investigator have been identified for the trial.

Company to Participate in 2024 Corporate Access Event

Aprea will be hosting institutional investor and business development meetings at the Annual Corporate Access Event in San Francisco, hosted by our investor relations firm LifeSci Partners. Management will be available for meetings on Wednesday, January 10, 2024. To schedule a meeting, interested parties can register here or send an email to access@lifesciadvisors.com.

About Aprea
Aprea Therapeutics, Inc. is a clinical-stage biopharmaceutical company headquartered in Doylestown, Pennsylvania, focused on precision oncology through synthetic lethality. The Company's lead program is ATRN-119, a clinical-stage small molecule ATR inhibitor in development for solid tumor indications. Aprea completed all IND enabling studies and is moving towards the submission of an oral, small molecule WEE1 inhibitor, APR-1051. 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 Statement
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 study analyses, clinical trials, regulatory submissions, and projected cash position. We may, in some cases use terms such as "future," "predicts," "believes," "potential," "continue," "anticipates," "estimates," "expects," "plans," "intends," "targeting," "confidence," "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 and on information currently available to management that involve risks, potential changes in circumstances, assumptions, and uncertainties. All statements contained in this press release other than statements of historical fact are forward-looking statements, including statements regarding our ability to develop, commercialize, and achieve market acceptance of our current and planned products and services, our research and development efforts, including timing considerations and other matters regarding our business strategies, use of capital, results of operations and financial position, and plans and objectives for future operations. 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, without limitation, risks related to the success, timing, and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates, including statements regarding the timing of initiation, pace of enrollment and completion of the trials, futility analyses, presentations at conferences and data reported in an abstract, and receipt of interim or preliminary results (including, without limitation, any preclinical results or data), which are not necessarily indicative of the final results of our ongoing clinical trials, and the other risks, uncertainties, and other factors described under "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in the documents we file with the U.S. Securities and Exchange Commission. 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 update such forward-looking statements for any reason, except as required by law.

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