Aprea Announces Preclinical Data Supporting Highly Differentiated WEE1 Inhibitor, ATRN-1051, Relative To Other WEE1 Inhibitors

September 11, 2023

Demonstrating potential safety and efficacy of WEE1 inhibitor, ATRN-1051, in the treatment of ovarian cancer

Company anticipates submitting an IND by the end of 2023

Data to be presented at an upcoming 2023 scientific conference, with KOL event planned for the fall

DOYLESTOWN, Pa., Sept. 11, 2023 (GLOBE NEWSWIRE) -- Aprea Therapeutics, Inc. (Nasdaq: APRE) ("Aprea", or the "Company"), a clinical stage biopharmaceutical company focused on precision oncology through synthetic lethality, today announced updated preclinical data supporting development of the Company's WEE1 inhibitor candidate, ATRN-1051, for the treatment of ovarian cancer.

The preclinical and in vitro data suggest that the selective properties of ATRN-1051 may make it a more efficacious cancer therapy than the other WEE1 inhibitors in development. Importantly, ATRN-1051 is a highly potent and selective inhibitor of WEE1 that does not significantly affect off-target PLK1, PLK2 and PLK3, a family of kinases that promote M phase entry, a critical phase in the cell cycle. Such off-targeting of the PLK family has been a challenge to other WEE1 inhibitors in the class. Evidence generated by Aprea suggests that off-target inhibition of PLK1 substantially limits the ability of WEE1 inhibitors to cause genotoxicity, the proposed mechanism by which WEE1 inhibitors act as cancer therapeutics.

The preclinical research of ATRN-1051 in ovarian cancer also shows an increased expression of cyclin E1, or CCNE1. CCNE1 amplification, which is associated with platinum resistance and poor survival, has been shown to be a reliable predictive biomarker of response to WEE1 inhibition. As part of the preclinical studies with ATRN-1051, the Company conducted cell culture and CDX mouse model studies using the CCNE1-normal and CCNE1-amplified ovarian cancer cell lines to show that low doses of ATRN-1051 completely suppress the growth of CCNE1-amplified ovarian cancer cells and tumors. In addition to the anti-tumor activity, the preclinical studies of ATRN-1051 indicate improved AUC pharmacokinetic properties compared to other WEE1 inhibitors, with the low dose of ATRN-1051 showing a similar AUC as higher doses of other WEE1 inhibitors.

Table 1

	ATRN 1051 (1)	**Zentalis ZN-c3 (2)**			**AstraZeneca AZD-1775 (2)**		
Dose (mg/kg/d)	**10**	**20**	**40**	**80**	**20**	**40**	**80**
C_{max} ng/ml	**1,460**	**1,167**	**1,997**	**5,100**	**635**	**2,460**	**4,703**
T_{max} hr	**3**	**1**	**1**	**1**	**1**	**1**	**1**
AUC_{0-24}, ng*hr/ml	**16,739**	**4,863**	**17,088**	**39,722**	**1,494**	**6,313**	**13,408**

Note: Head-to-head studies have not been conducted

(1) Data from an exploratory formulation of ATRN-1051 administered to fasted Balb/c mice

(2) Data from study in A-427 NSCLC xenograft model as reported in Zentalis Corporate Overview, March 2022

"We are very excited and encouraged by these positive findings that demonstrate ATRN-1051's promise as a clinical agent based on its preclinical in vivo activity and safety profile," said Dr. Oren Gilad, President and CEO of Aprea. "We look forward to presenting the full data set at an upcoming 2023 scientific conference and to filing an IND for ATRN-1051 by the end of 2023. We believe these findings support the further development of this potentially substantial and clinically important agent. We also look forward to hosting a key opinion leader (KOL) event this fall highlighting these exciting data and outlining our development plan."

WEE1 kinase is a key regulator of multiple phases of the cell cycle, most prominently in progression from G1 to S phase and S to M phase through inhibitory phosphorylation of CDK2 and CDK1, respectively. Thus, when WEE1 is inhibited, both G1-S and S-M checkpoints are abrogated, leading to premature S-phase and M-phase entry. Notably, the replication stress caused by CCNE1 overexpression is transformed into toxic levels of double stranded breaks and cancer cell death when WEE1 is inhibited. The Company believes that *CCNE1* gene amplification or high CCNE1 protein expression is a potential predictive biomarker of ATRN-1051 efficacy.

About ATRN-1051

The Company is targeting the WEE1 kinase, a key regulator of multiple phases of the cell cycle, with its lead WEE1 inhibitor product candidate, ATRN-1051. ATRN-1051 is an orally bioavailable small molecule inhibitor of WEE1 that is highly potent and selective. ATRN-1051 is distinct from other WEE1 inhibitors based on its potentially superior pharmacokinetic properties and selectivity. The company anticipates filing an IND for ATRN-1051 by the end of 2023.

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 being developed for solid tumor indications. Our WEE1 inhibitor is being advanced to IND submission. 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 submits 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 statement for any reason, except as required by law.

Investor Contact:
Mike Moyer
LifeSci Advisors
mmoyer@lifesciadvisors.com

Source: Aprea Therapeutics, Inc.