Aclaris Therapeutics Announces Positive Preliminary Topline Data from 12-Week Phase 2a Trial of Oral ATI-450 for Moderate to Severe Rheumatoid Arthritis

January 19, 2021

- ***Durable Clinical Activity over 12 Weeks was Demonstrated***
- ***Data Support New Oral Approach for the Potential Treatment of Immuno-inflammatory Diseases, such as Rheumatoid Arthritis***
- ***ATI-450, an Investigational Oral MK2 Inhibitor, was Generally Well Tolerated***
- ***Data Support Progression to Phase 2b***
- ***Management to Host Conference Call at 8:00 AM ET Today***

WAYNE, Pa., Jan. 19, 2021 (GLOBE NEWSWIRE) -- Aclaris Therapeutics, Inc. (NASDAQ: ACRS), a clinical-stage biopharmaceutical company focused on developing novel drug candidates for immuno-inflammatory diseases, today announced positive preliminary topline results from a 12-week, Phase 2a, multicenter, randomized, investigator and patient-blind, sponsor-unblinded, parallel group, placebo-controlled clinical trial to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of ATI-450, an investigational oral MK2 inhibitor, in subjects with moderate to severe rheumatoid arthritis (RA) (ATI-450-RA-201). ATI-450 was developed internally utilizing Aclaris' proprietary KINect™ drug discovery platform.

In the trial, 19 subjects were randomized in a 3:1 ratio and received either ATI-450 at 50 mg twice daily or placebo, in combination with methotrexate, for 12 weeks. The primary endpoint was safety and tolerability. Key secondary and exploratory endpoints included the disease activity scores, DAS28-CRP and ACR20/50/70, and the change from baseline in high sensitivity C-reactive protein (hsCRP) and relevant endogenous cytokine levels. As this trial was designed to generate proof of concept, it was not powered to detect statistically significant outcomes on efficacy endpoints.

The mean DAS28-CRP score at baseline was 5.71 for the 16 subjects in the treatment arm and 5.77 for the three subjects in the placebo arm. Seventeen subjects (15 in the treatment arm and two in the placebo arm) completed 12 weeks of treatment.

In this trial, ATI-450 demonstrated durable clinical activity, as defined by a marked and sustained reduction in DAS28-CRP and evaluation of ACR20/50/70 responses over 12 weeks. The mean change from baseline in DAS28-CRP score at week 12 was a 2.0 reduction in the treatment arm compared to a 0.35 increase in the placebo arm. The proportion of subjects with a DAS28-CRP score at week 12 of ≤ 3.2 (low disease activity or remission) was 40% and 0% in the treatment and placebo arms, respectively, and the proportion of subjects with a DAS28-CRP score of < 2.6 (remission) was 20% and 0% in the treatment and placebo arms, respectively.

ACR20/50/70 was observed at week 12 in 60%, 33% and 20%, respectively, of the 15 subjects in the treatment arm, and in 0% of the two subjects in the placebo arm. The median reduction from baseline in hsCRP was >40% throughout the 12 weeks of the trial in the treatment arm. A sustained median reduction from baseline in hsCRP was not observed in the placebo arm. An interim analysis (11 treatment, two placebo) of *ex vivo* stimulated cytokines from blood samples taken from the treatment arm showed a marked and durable inhibition of TNFα, IL1β, IL6, and IL8 over the 12 week dosing period. Similarly, analysis of endogenous cytokines also demonstrated a marked and sustained inhibition of median concentrations of TNFα, IL6, IL8, and MIP1β in the treatment arm over the 12 week period.

ATI-450 was generally well tolerated. No serious adverse events were reported and all adverse events were mild to moderate. The most common adverse events (each reported in 2 subjects) were urinary tract infection (UTI), elevated lipids and ventricular extrasystoles, all of which were determined to be unrelated to treatment except for one UTI. Two subjects withdrew from the trial, one in the treatment arm and one in the placebo arm.

ATI-450 was also evaluated at higher doses in a separate Phase 1 clinical trial in healthy subjects (ATI-450-PKPD-102). In this placebo-controlled Phase 1 trial, one group of healthy subjects received 80 mg of ATI-450 twice daily and another group of healthy subjects received 120 mg of ATI-450 twice daily over 6.5 days. No dose-limiting toxicity was observed. *Ex vivo* analysis of blood samples from this Phase 1 trial showed that increased cytokine inhibition was achieved with these higher doses of ATI-450. A final analysis of this trial is underway.

Dr. David Gordon, Chief Medical Officer of Aclaris, said, "We're very pleased with these data which demonstrate that ATI-450 was generally well tolerated and showed durable clinical activity in RA over 12 weeks. We believe these data support our hypothesis that MK2 inhibition is an important novel target for the treatment of immuno-inflammatory diseases, such as rheumatoid arthritis, and we look forward to progressing ATI-450 to Phase 2b. We want to thank everyone who participated in these informative trials."

"Despite recent advances, rheumatoid arthritis continues to be a significant burden for large numbers of patients," said Stanley Cohen, MD, Clinical Professor in the Department of Internal Medicine and a Clinical Faculty Member in the Division of Rheumatology at UT Southwestern Medical School, and a Co-Director of the Division of Rheumatology at Presbyterian Hospital, Dallas. "These results are very encouraging and support further development of ATI-450 to treat rheumatoid arthritis with a new mechanism of action."

Aclaris expects to submit a full analysis of the Phase 2a data for publication in a peer-reviewed scientific journal. The full analysis will include data from other secondary and exploratory endpoints evaluated in the trial, including the four-week safety follow-up data and a full analysis of MRI, pharmacodynamic and pharmacokinetic data.

Conference Call and Webcast

Management will host a conference call and webcast with an accompanying slide presentation at 8:00 AM ET today to review these preliminary topline Phase 2a data and related matters. To participate in the live call, please dial (844) 776-7782 (domestic) or (661) 378-9535 (international) and reference conference ID 7166952. To access the live webcast of the call and the accompanying slide presentation, please visit the “Events” page of the “Investors” section of Aclaris’ website, www.aclaristx.com. The webcast will be archived for at least 30 days on the Aclaris website.

About ATI-450

ATI-450 is an investigational oral mitogen-activated protein kinase-activated protein kinase 2 (MK2) inhibitor. This mechanism potentially leads to the inhibition of multiple cytokines, chemokines, matrix metalloproteases and other inflammatory signals. Key inflammatory cytokines driven by this mechanism include tumor necrosis factor α (TNFα) and interleukin-1α, -1β, -6 and -8 (IL1α, IL1β, IL6 and IL8). Aclaris is developing ATI-450 as a potential treatment for rheumatoid arthritis and other immuno-inflammatory diseases.

About Aclaris Therapeutics, Inc.

Aclaris Therapeutics, Inc. is a clinical-stage biopharmaceutical company developing a pipeline of novel drug candidates to address the needs of patients with immuno-inflammatory diseases who lack satisfactory treatment options. The company has a multi-stage portfolio of drug candidates powered by a robust R&D engine exploring protein kinase regulation. For additional information, please visit www.aclaristx.com.

Cautionary Note Regarding Forward-Looking Statements

Any statements contained in this press release that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as “believe,” “expect,” “intend,” “may,” “plan,” “potential,” “will,” and similar expressions, and are based on Aclaris’ current beliefs and expectations. These forward-looking statements include expectations regarding ATI-450 as a potential treatment for RA, the clinical development of ATI-450, including the further development at higher doses, and the publication of the full analysis from the ATI-450-RA-201 trial. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Risks and uncertainties that may cause actual results to differ materially include uncertainties inherent in the conduct of clinical trials, risks and uncertainties associated with preliminary trial results varying from final results, Aclaris’ reliance on third parties over which it may not always have full control, Aclaris’ ability to enter into strategic partnerships on commercially reasonable terms, the uncertainty regarding the COVID-19 pandemic and other risks and uncertainties that are described in the Risk Factors section of Aclaris’ Annual Report on Form 10-K for the year ended December 31, 2019, Aclaris’ Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, and other filings Aclaris makes with the U.S. Securities and Exchange Commission from time to time. These documents are available under the “SEC Filings” page of the “Investors” section of Aclaris’ website at www.aclaristx.com. Any forward-looking statements speak only as of the date of this press release and are based on information available to Aclaris as of the date of this release, and Aclaris assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.

Aclaris Contact

investors@aclaristx.com

Source: Aclaris Therapeutics, Inc.