# Aclaris Therapeutics Announces Positive Results From Phase 1 Single and Multiple Ascending Dose Trial of ATI-450, an Investigational Oral MK2 Inhibitor

January 9, 2020

- **Oral small molecule showed marked inhibition of TNFα, IL1β, IL8, and IL6**
- **Preliminary data support progression to Phase 2a Proof of Concept Trials in Immuno-Inflammatory Diseases**

WAYNE, Pa., Jan. 09, 2020 (GLOBE NEWSWIRE) -- Aclaris Therapeutics, Inc. (NASDAQ: ACRS), a physician-led biopharmaceutical company focused on immuno-inflammatory diseases, today announced positive results from ATI-450-PKPD-101, a Single Ascending Dose and Multiple Ascending Dose (SAD/MAD) Phase 1 clinical trial of the investigational compound ATI-450. Preliminary data demonstrated that ATI-450:

- resulted in marked inhibition of TNFα, IL1β, IL8, and IL6;
- was generally well-tolerated at all doses tested in the trial;
- had dose proportional pharmacokinetics (PK) with a terminal half-life of 9-12 hours; and
- had no meaningful food effect or drug-drug interaction (DDI) with methotrexate.

ATI-450-PKPD-101 was a first-in-human, randomized, observer-blind, placebo-controlled Phase 1 clinical trial designed to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of orally administered ATI-450 in healthy subjects (n=77). The trial consisted of three parts:

- Single Ascending Dose (SAD) plus food effect (n=32, 8 subjects per dose cohort - 2 placebo, 6 active). A single dose of 10mg, 30mg, 50mg and 100mg was tested.
- Multiple Ascending Dose (MAD) (n=30, 10 subjects per dose cohort - 2 placebo, 8 active). 10mg BID, 30mg BID and 50mg BID doses were tested over 7 days of administration.
- Methotrexate DDI (n=15). Single 7.5-mg oral doses of methotrexate given alone or after ATI-450 50mg BID.

No serious adverse events or severe adverse events were reported, and no adverse events led to discontinuation of the study medication. The most common adverse events (reported by 2 or more subjects who received ATI-450) observed during the trial were dizziness, headache, upper respiratory tract infection, constipation, nausea, and abdominal pain. All adverse events were mild. A trend of a decrease in absolute neutrophil count (ANC) was observed without correlated clinical sequelae. This effect is consistent with the pharmacodynamic profile of certain anti-TNF therapies[1]. Other laboratory findings were generally unremarkable.

In this trial, ATI-450 had dose proportional pharmacokinetics with a terminal half-life of 9-12 hours in the MAD cohort on day 7. The PK profile was not meaningfully affected when taking ATI-450 with a high fat meal. Further, co-administration of ATI-450 with methotrexate had little impact on methotrexate pharmacokinetics.

The pharmacodynamics of ATI-450 were evaluated by investigating the potential to inhibit production of key cytokines in *ex vivo* stimulated blood samples collected from subjects. At the 50mg BID dose (the dose with the highest degree of inhibition) at day 7 (12 hours post last dose): the mean trough drug levels were above the IC80 for TNFα, IL1β and IL8; IL6 plasma levels were inhibited by more than 50% for part of the dosing interval; and the mean trough drug level was above the IC80 for phosphorylation of Heat Shock Protein 27, a downstream substrate of MK2 (and marker of inhibition of the MK2 target).

“We believe these data support the progression of ATI-450 into Phase 2 clinical development,” said Dr.  David Gordon, Chief Medical Officer of Aclaris. “The potential for an oral small molecule which suppresses multiple proinflammatory cytokines could be very meaningful for the treatment of a number of immuno-inflammatory diseases.”

Aclaris intends to initiate the first Phase 2 clinical trial in subjects with rheumatoid arthritis in the first half of 2020.

**About ATI-450**

ATI-450 is an investigational oral small molecule inhibitor of the p38α mitogen-activated protein kinase-activated protein kinase 2 (MK2) inflammatory signaling pathway. This pathway drives the expression of multiple cytokines, chemokines, matrix metalloproteases and other inflammatory signals. Key inflammatory cytokines driven by this pathway include tumor necrosis factor α (TNFα), interleukin-1α and -1β (IL1α and IL1β), and interleukin-6 (IL6). On the basis of this mechanism, Aclaris is developing ATI-450 as a potential treatment for immuno-inflammatory diseases.

**About Aclaris Therapeutics, Inc.**

Aclaris Therapeutics, Inc. is a physician-led biopharmaceutical company committed to addressing the needs of patients with immuno-inflammatory diseases who lack satisfactory treatment options. The company’s diverse and multi-stage portfolio includes one late-stage investigational drug candidate and a pipeline powered by a robust R&D engine exploring protein kinase regulation. For additional information, please visit www.aclaristx.com and follow Aclaris on LinkedIn or Twitter @aclaristx.

**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," "may," "plan," "potential," "will," and similar expressions, and are based on Aclaris' current beliefs and expectations. These forward-looking statements include

expectations regarding the development of Aclaris' drug candidates and the timing of the initiation of clinical trials. 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, Aclaris' reliance on third parties over which it may not always have full control, 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, 2018, Aclaris' Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, 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" section of the Investors page of Aclaris' website at http://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
Michael Tung, M.D.
Senior Vice President
Corporate Strategy/Investor Relations
484-329-2140
mtung@aclaristx.com

1 Dillingh M, et al. *Front. Immunol.* 2016;7(508):1-9.

Source: Aclaris Therapeutics, Inc.