Aclaris Therapeutics Announces Positive Preliminary Topline Data from Phase 2a Trial of ATI-1777 for Moderate to Severe Atopic Dermatitis

June 8, 2021

- ***ATI-1777 Achieved Statistically Significant Result in the Primary Efficacy Endpoint at Week 4***
- ***Minimal Systemic Exposure Supports "Soft" Topical JAK Inhibitor Approach***
- ***ATI-1777 was Generally Well Tolerated***
- ***Data Support Progression to Phase 2b***
- ***Management to Host Conference Call at 8:00 AM ET Today***

WAYNE, Pa., June 08, 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 its first in human Phase 2a, multicenter, randomized, double-blind, vehicle-controlled, parallel-group clinical trial to evaluate the efficacy, safety, tolerability and pharmacokinetics of ATI-1777, an investigational topical "soft" JAK 1/3 inhibitor, in 50 subjects with moderate to severe atopic dermatitis (AD) (ATI-1777-AD-201). ATI-1777 is the second compound generated from Aclaris' proprietary KINect ® drug discovery platform to demonstrate positive proof of concept in clinical trials.

"We are very pleased that we achieved positive results in this trial of ATI-1777 in subjects with moderate to severe AD with minimal systemic exposure to drug," said Dr. David Gordon, Chief Medical Officer at Aclaris. "Our approach to treating patients with moderate to severe atopic dermatitis is particularly relevant in light of some of the potential safety concerns with oral therapies. We look forward to advancing ATI-1777 into the next phase of clinical development."

In the trial, which consisted of a 4-week treatment period and a 2-week follow-up period during which no treatment was given, 50 subjects with moderate to severe AD were randomized in a 1:1 ratio into one of two arms: ATI-1777 topical solution 2.0% w/w or vehicle applied twice daily. One of the key objectives of this first in human trial was to assess the "soft" aspect of this topical JAK inhibitor compound in subjects with moderate to severe atopic dermatitis. A preliminary analysis of pharmacokinetic plasma samples in the ATI-1777 arm showed greater than 86% of the plasma samples had concentrations below 1 ng/ml and mean drug levels in the ATI-1777 arm (as a group) were not greater than 5% of the IC50 of ATI-1777.

The primary efficacy endpoint of this trial was the percent change from baseline in the modified Eczema Area and Severity Index (mEASI) score at week 4. The mEASI is a modified measure of EASI which excludes evaluation of the body areas that were not treated in the trial (i.e., the head, palms of hands, soles of feet, groin, or genitalia). Only the primary efficacy endpoint was powered to detect a statistically significant outcome.

The Full Analysis Set (FAS), which was comprised of subjects randomized and documented to have received at least one dose of trial medication, was used for the primary endpoint. Two subjects in the ATI-1777 arm were excluded from the FAS analysis on the basis that they were lost to follow up after the baseline visit and did not have a formal record of having received at least one dose of trial medication. Key secondary efficacy endpoints, which were not powered for statistical significance, included the proportion of subjects who achieved 50% improvement in mEASI score (mEASI-50) within 4 weeks of the start of treatment, the change from baseline in the Investigator's Global Assessment (IGA) score at each trial visit, IGA responder analysis, change from baseline in Body Surface Area (BSA) affected by AD at each trial visit, and change from baseline in peak pruritus numerical rating scale (PP-NRS) score over time.

The FAS was comprised of 23 and 25 subjects in the ATI-1777 and vehicle arms, respectively. The trial achieved its primary endpoint with a high degree of statistical significance ($p<0.001$) (one-sided p-value), which corresponded to a 74.4% reduction in mEASI score from baseline at week 4 in subjects applying ATI-1777 compared to a 41.4% reduction in subjects applying vehicle. In addition, a post-hoc analysis which included the two randomized subjects not in the FAS, using their baseline mEASI score carried forward to day 28, was statistically significant ($p=0.002$) (one-sided p-value).

In addition, positive trends in favor of ATI-1777 were observed in key secondary efficacy endpoints, such as improvement in itch, percent of mEASI-50 responders, IGA responder analysis, and reduction in BSA impacted by disease.

ATI-1777 was generally well tolerated. Nine subjects in each arm reported treatment-emergent adverse events (9/23 and 9/25 in the ATI-1777 and vehicle arm, respectively). No serious adverse events were reported. One treatment-related adverse event (AE), application site pruritus, was reported in one subject in the ATI-1777 arm. The most common AEs (reported in ≥2 subjects in the trial) were increased blood creatinine phosphokinase and headache in subjects in the ATI-1777 arm and urinary tract infection (one each in the ATI-1777 and the vehicle arm); none of these AEs in the ATI-1777 arm were determined by the clinical trial investigators to be related to ATI-1777. There were no reports of thrombosis in the trial. In the FAS analysis, two subjects from the ATI-1777 arm withdrew from the trial (one lost to follow up, one withdrew consent), while seven subjects withdrew from the vehicle arm (three due to AEs and four withdrew consent).

Final trial results will be submitted for publication in a peer-reviewed scientific journal.

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 8990539. 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 Atopic Dermatitis

Atopic dermatitis (AD) is a chronic skin disease, affecting 11.3 to 12.7% of children and 6.9 to 7.6% of adults in the United States and is characterized by inflammation and intense itch. Signs and symptoms of AD include irritated and itchy skin that can cause red lesions that may ooze and crust.

About ATI-1777

ATI-1777 is an investigational topical “soft” Janus kinase (JAK) 1/3 inhibitor. “Soft” JAK inhibitors are designed to provide JAK inhibition at the site of application and be rapidly metabolized in systemic circulation. Aclaris plans to develop ATI-1777 as an emollient-containing spray formulation. Aclaris is developing ATI-1777 as a potential treatment for moderate to severe atopic dermatitis. ATI-1777 is currently in clinical development and its safety and efficacy has not been evaluated by regulatory authorities.

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 the potential benefits of ATI-1777 as a potential treatment for AD, the clinical development of ATI-1777, and the publication of the final trial results from the ATI-1777-AD-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, 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.

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Source: Aclaris Therapeutics, Inc.