Aclaris Therapeutics Announces Positive Top-Line Results from Open-Label Phase 2a Trial of ATI-2138, a Potent and Selective Investigational Inhibitor of ITK and JAK3; Trial Achieves Primary and Key Secondary Endpoints

July 29, 2025

- Primary Endpoint Analysis Confirms Favorable Tolerability Profile of ATI-2138 Without Certain Risks Associated with Other Agents in the Class -

- Efficacy Results Show Comparable Outcomes to Approved Therapies with Potential for Improved Tolerability, Supporting Exploration of Higher Doses in Future Clinical Trials -

- Pharmacodynamic Results Validate Therapeutic Potential of ITK Inhibition and Corroborate Potential of Aclaris' ITK Franchise -

- Management to Host a Conference Call to Discuss Results Today at 5:00PM EDT -

WAYNE, Pa., July 29, 2025 (GLOBE NEWSWIRE) -- Aclaris Therapeutics, Inc. (NASDAQ: ACRS), a clinical-stage biopharmaceutical company focused on developing novel product candidates for immuno-inflammatory diseases, today announced positive top-line results from its open-label, single-arm Phase 2a trial of ATI-2138, a potent and selective investigational oral covalent inhibitor of interleukin-2-inducible T cell kinase (ITK) and Janus kinase 3 (JAK3), in 14 patients with moderate-to-severe atopic dermatitis (AD). Based on the growing body of supportive non-clinical and clinical evidence, Aclaris intends to further develop ATI-2138 in alopecia areata and is also exploring other indications relevant to the mechanism of action.

"These Phase 2a trial results represent a significant achievement for our ITK franchise by confirming the mechanism and corroborating our work on next-generation ITK selective compounds," said Dr. Neal Walker, Chief Executive Officer of Aclaris. "The objectives of this trial were to confirm the strong tolerability profile across multiple doses of ATI-2138 over 12 weeks, to test the mechanism in AD before initiating our work in other diseases including alopecia areata, and to further validate ITK as an important therapeutic target; we accomplished each of these. Consistent with prior results, ATI-2138 was shown to be well tolerated. The observed efficacy results across a variety of validated scoring tools – even at this low dose – suggest responses that are in line with, if not better than, that seen with approved therapies. And finally, the PD results confirmed the potential of targeting ITK, including strong downregulation of key ITK-dependent markers and an interesting antifibrotic effect."

The results observed in this trial include a favorable tolerability profile of ATI-2138, clinically meaningful improvements from baseline in assessments of disease severity including extent and severity of AD (Eczema Area and Severity Index (EASI)) and percent of patients experiencing a greater than or equal to four point improvement in worst itch in the last 24 hours (Peak Pruritus Numerical Rating Scale (PP-NRS)) in patients receiving low doses (10mg BID, 12 weeks) of ATI-2138, and PD results that validate ITK as a therapeutic target. Overall, these results provide evidence that the contribution of ITK has the potential to enable ATI-2138, even at low doses, to confer efficacy comparable to that observed in clinical trials of approved JAK and IL-4/13 inhibitors in moderate-to-severe AD, with improved tolerability and without the significant safety risks typically associated with JAK inhibition.

"Although this is a small study, the pharmacodynamic results are quite compelling; I'm excited about the anti-inflammatory activity we observed and the therapeutic potential for ATI-2138, and more broadly, ITK as a potential therapeutic target," said Emma Guttman, M.D., Ph.D., Waldman Professor of Dermatology and Immunology and Health System Chair of the Kimberly and Eric J. Waldman Department of Dermatology at the Icahn School of Medicine at Mount Sinai in New York City. "We observed strong downregulation of key inflammatory markers, including those associated with ITK including Th2 and Th1/Th17-related markers, as well as certain ITK pathway- and fibrosis-related markers. Overall, these are important results that define the potential of ATI-2138 and ITK inhibition to address Th2 and Th1/Th17 mediated diseases like alopecia areata, vitiligo, and atopic dermatitis."

Patient Demographics

Twenty-six (26) patients were screened for inclusion in this single-arm Phase 2a trial. Of the 14 that were enrolled, 12 completed treatment. Excluding two protocol violations, 10 patients were available for the per protocol analysis. The enrolled population was split evenly between male and female participants. Consistent with published demographics, half of the enrolled population self-identified as African American. Mean baseline EASI score was 22.7.

Primary Endpoint: Safety Results

ATI-2138 was very well tolerated in this Phase 2a trial. No severe adverse events (SAEs) or treatment-emergent adverse events (TEAEs) were observed. A majority of the adverse events were mild and resolved spontaneously during treatment; there were no discontinuations due to adverse events. Three patients experienced a combined total of four adverse events determined to be related to study drug (TRAE); all but one (moderate myalgia; starting on day 24 with no elevation in CPK) were mild, transient, and resolved during treatment. No safety signal over the extent of the trial was observed in chemistry, creatine phosphokinase (CPK), hematology (e.g., leukocytes, lymphocytes, neutrophils), lipids, electrocardiogram (ECG), ECG with corrected QT (ECG-QTcF), or vital signs.

Secondary Endpoints: Efficacy Results

Mean and median change from baseline in Eczema Area and Severity Score (EASI) over time:

The EASI score is a validated tool used to assess the severity of AD. It measures the extent and severity of lesional skin associated with AD across different body regions and assigns a composite score from 0 to 72, with higher scores indicating severe (21.1 to 50.0) or very severe (50.1 to 72.0) disease.

- At week 12 (end of treatment), the mean improvement in EASI score in patients receiving 10mg BID of ATI-2138 (n=10) was 60.5% (median improvement = 76.8%).
- Patients in the trial experienced a rapid and sustained response, with measurable improvements observed starting at the first (week 1) office visit. At week 4, the mean improvement in EASI score (n=10) was 70.5% (median improvement = 71.9%). At week 8, the mean improvement in EASI score (n=10) was 70.7% (median improvement = 76.3%).
- The week 12 results were skewed by a single patient who was identified by an independent lab as being a statistical molecular outlier by more than four standard deviations compared to others. This patient demonstrated systemic findings inconsistent with AD alone including significant non-lesional inflammation, based on various PD measures. In addition, this patient was not fully compliant with study drug administration. Excluding this patient, the mean improvement in EASI score at week 12 (end of treatment) was 77.1% (median improvement = 82.1%). At week 4, the mean improvement in EASI score was 77.3% (median improvement = 72.9%), and at week 8, the mean improvement in EASI score was 81.0% (median improvement = 77.1%).

All other assessed efficacy response curves showed similar mean and median improvements from baseline, starting at the first (week 1) office visit.

Percent of patients with a greater than or equal to four-point improvement in Peak Pruritus Numerical Rating Scale (PP-NRS):

The PP-NRS assesses the severity of itch at the worst moment during the previous 24 hours on a scale of 0 (“no itch”) to 10 (“worst itch imaginable”). A ≥4-point improvement in PP-NRS score is considered a clinically meaningful reduction in itch intensity and severity.

- At week 12 (n=8), 62.5% of patients experienced a ≥4-point improvement in PP-NRS.

Secondary Endpoint: Pharmacodynamic Results

The clinical activity was supported by pharmacodynamic analyses clearly demonstrating modulation of both the ITK and JAK3 pathways as evidenced by inhibition of ex vivo pathway-specific stimulation of patient whole blood. Near complete and sustained ITK target occupancy was observed across the dosing interval ranging from ~90% at peak to 60-70% at trough. Proteome and transcriptome lesional skin tape strip analyses (minimally invasive methods to study changes in gene expression in affected skin) measured at trough levels to better represent steady state showed significant ATI-2138-dependent reduction of multiple inflammatory pathways associated with ITK. Strong downregulation of key ITK-dependent markers including Th2, Th17, and TCR (ITK) pathways along with the Th1 pathway were observed at week 8 and week 12. Fibrosis-related markers were also shown to be strongly downregulated by ATI-2138. These tape strip data were confirmed with skin biopsies from a subset of patients.

Next Steps for ITK Franchise

Positive results from this Phase 2a single-arm, open-label trial help validate Aclaris’ ITK franchise. The Company intends to further develop ATI-2138 in alopecia areata and is also exploring other indications relevant to the mechanism of action. In addition, preclinical work is ongoing for next-generation ITK inhibitors, which Aclaris expects to provide the basis for new INDs starting in 2026.

About the Phase 2a Trial

The Phase 2a trial is an open-label, single-arm study designed to investigate the safety, tolerability, pharmacokinetics, efficacy, and pharmacodynamics of 10mg of ATI-2138 administered twice daily (BID) for 12 weeks in patients with moderate-to-severe AD. The primary endpoints were safety-related parameters. Secondary endpoints included pharmacodynamic assessments and efficacy as measured by scoring tools including the Eczema Area and Severity Index (EASI), Peak Pruritus Numerical Rating Scale (PP-NRS), and other pertinent efficacy related measures.

Webcast and Conference Call

Aclaris will host a webcast and conference call with slides at 5:00 p.m. EDT today to discuss the results of this Phase 2a trial. The live and archived webcast will be available on the Events page of the Company’s website: https://investor.aclaristx.com/events. The webcast will be archived on the same page for 30 days following the event. Please note the following process if you would rather access the call via telephone: To register and receive a dial in number and unique PIN to access the live conference call, please follow this link to register online. Upon registering you will receive the dial-in info and a unique PIN to join the call as well as an email confirmation with the details.

About ATI-2138

ATI-2138 is a highly potent and selective novel investigational pharmacologic agent that acts as a dual inhibitor of interleukin-2-inducible T cell kinase (ITK) and Janus kinase 3 (JAK3). ITK regulates T cell receptor signal transduction and inhibition of this kinase can affect T cell differentiation and activation. JAK3 is a key signal transduction kinase that forms a heterodimer with JAK1, modulates JAK1 phosphorylation of signal transducer and activator of transcription 5 (STAT5), and regulates cytokines that signal through the IL-2 receptor common gamma chain (IL-2_{Yc}) to affect lymphocyte proliferation and activation. The efficacy results exhibited in preclinical animal models of inflammation and autoimmune diseases, coupled with the favorable safety, PK, and PD profile in healthy human SAD and MAD studies and the top-line results of the Phase 2a trial in AD support the potential for ATI-2138 to affect several human inflammatory diseases and further investigation of this molecule in patients with atopic and autoimmune diseases that are dependent on T cell function and/or IL-2_{Yc} signaling.

About Aclaris Therapeutics, Inc.

Aclaris Therapeutics, Inc. is a clinical-stage biopharmaceutical company developing a pipeline of novel product candidates to address the needs of

patients with immuno-inflammatory diseases who lack satisfactory treatment options. The company has a multi-stage portfolio of product candidates powered by a robust R&D engine. For additional information, please visit www.aclaristx.com and follow Aclaris on X (formerly Twitter) at @AclarisTx and on LinkedIn.

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 “anticipate,” “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 its development plans for ATI-2138, and its next-generation ITK inhibitors, including plans to develop ATI-2138 in alopecia areata and potentially other indications and plans to have INDs in 2026 for its next-generation ITK inhibitors, and the therapeutic potential for ATI-2138 and its next-generation ITK inhibitors. 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, Aclaris’ ability to enter into strategic partnerships on commercially reasonable terms, the uncertainty regarding the macroeconomic environment 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, 2024, 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. No head-to-head clinical studies have been conducted against JAK or IL4/13 inhibitors. Differences exist between data and trial designs, and caution should be exercised when comparing data across studies. 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.