Aclaris Therapeutics Announces ATI-450 (MK2 pathway Inhibitor) publication in Journal of Experimental Medicine

WAYNE, Pa., March XXX, 2018 (GLOBE NEWSWIRE) -- Aclaris Therapeutics, Inc. (NASDAQ:ACRS), a dermatologist-led biopharmaceutical company committed to identifying, developing, and commercializing innovative therapies to address significant unmet needs in aesthetic and medical dermatology and immunology, today announced a publication in the Journal of Experimental Medicine

The title of the article is: "Selective inhibition of the p38α MAPK-MK2 axis inhibits inflammatory cues, including inflammasome priming signals".

ATI-450, an investigational drug formerly known as CDD-450, is a unique p38α MAPK–MK2 pathway selective inhibitor used to uncover the function of this protein complex in inflammasome priming signals. Importantly, ATI-450 is as efficacious as global p38α MAPK inhibitors in decreasing inflammation in disease models. Cryopyrin-Associated Periodic Syndrome (CAPS) and the most severe form of the disease, Neonatal-Onset Multisystem Inflammatory Disease (NOMID) result from dysregulated inflammasome generating elevated systemic levels of the cytokine IL-1β. As the article elucidates:

- Selective inhibition of p38α MAPK –MK2 decreases IL-1β, IL-6, and TNF-α production by promoting mRNA instability.
- ATI-450 attenuates NOMID-associated complications in a transgenic mouse model of CAPS.
- ATI-450 prevents bone destruction in CAPS mice.
- ATI-450 inhibits IL-1β in blood cells from CAPS patients
- ATI-450 prevents inflammation and joint destruction in inflammatory arthritis in rats.

ATI-450 selectively blocks p38α MAPK activation of the proinflammatory kinase MK2 while sparing p38α activation of other effectors such as PRAK and ATF2. Use of ATI-450 helped to reveal a critical role of the p38α MAPK –MK2 pathway in NLRP3 inflammasome priming. ATI-450 also inhibited other inflammatory pathways (e.g., TNF-α and IL-6), thus implying potential indications for this drug candidate beyond inflammasopathies. These findings may have potential clinical implications because ATI-450 is at least as efficacious as clinically evaluated global p38α MAPK inhibitors in suppressing inflammation in both animal disease models and patients' cells, and ATI-450's offers the potential lack of transient efficacy and safety issues associated with global p38α MAPK inhibitors which may result from their inhibition of non-MK2 substrates involved in anti-inflammatory and housekeeping functions.

This study was carried out by Aclaris Therapeutics, Inc. in collaboration with the laboratory of Gabriel Mbalaviele, Ph.D., at Washington University Medical School.

The article is available at http://jem.rupress.org/cgi/doi/10.1084/jem.20172063 and will appear in print form on May 7th.

About Aclaris Therapeutics, Inc.

Aclaris Therapeutics, Inc. is a dermatologist-led biopharmaceutical company committed to identifying, developing, and commercializing innovative therapies to address significant unmet needs in dermatology, both aesthetic and medical, and immunology. Aclaris' focus on market segments with no

FDA-approved medications or where treatment gaps exist has resulted in the first FDA-approved treatment for raised seborrheic keratoses and several clinical programs to develop medications for the potential treatment of common warts, alopecia areata, and vitiligo. For additional information, please visit www.aclaristx.com and follow Aclaris 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 "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 Aclaris' preclinical and clinical development of its drug candidates. 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, 2017 and other filings Aclaris makes with the U.S. Securities and Exchange Commission from time to time. These documents are available under the "Financial Information" 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.

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