UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of
The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 19, 2021

Aclaris Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-37581**	**46-0571712**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

640 Lee Road, Suite 200
Wayne, PA 19087
(Address of principal executive offices, including zip code)

(484) 324-7933
(Registrant's telephone number, including area code)

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class:	Trading Symbol(s)	Name of Each Exchange on which Registered
Common Stock, $0.00001 par value	ACRS	The Nasdaq Stock Market, LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On January 19, 2021, Aclaris Therapeutics, Inc. (the "***Company***") will hold a conference call to discuss preliminary topline data for its Phase 2a clinical trial of ATI-450, an investigational oral MK2 inhibitor, in subjects with moderate to severe rheumatoid arthritis (the "***Preliminary Topline Data***"), and related matters. A copy of the presentation that will accompany the conference call is furnished herewith as Exhibit 99.1 to this Current Report on Form 8-K.

In accordance with General Instruction B.2. of Form 8-K, the information in this Item 7.01 and Exhibit 99.1 hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "***Exchange Act***"), or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference in any of the Company's filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any incorporation language in such a filing, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On January 19, 2021, the Company issued a press release announcing the Preliminary Topline Data and related matters. A copy of this press release is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Company Presentation.
99.2	Press Release dated January 19, 2021.
104	The cover page from Aclaris Therapeutics, Inc.'s Form 8-K filed on January 19, 2021, formatted in Inline XBRL.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ACLARIS THERAPEUTICS, INC.

By: /s/ Frank Ruffo
Frank Ruffo
Chief Financial Officer

Date: January 19, 2021

EMPOWERING PATIENTS THROUGH
KINOME INNOVATION

ATI-450-RA-201
ATI-450-PKPD-102

January 2021

Preliminary Topline Analyses

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Cautionary Note Regarding Forward-Looking Statements

Any statements contained in this presentation 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 ATI-450 as a potential treatment for rheumatoid arthritis and the clinical development of ATI-450, including the further development at higher doses. 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, **the uncertainty regarding the COVID-19 pandemic including its impact on the timing of Aclaris' regulatory and research and development activities**, 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 http://www.aclaristx.com. Any forward-looking statements speak only as of the date of this presentation and are based on information available to Aclaris as of the date of this presentation, 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

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

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Biotechnology Company Focused on the Kinome:
People + Platform + Pipeline

LEADERSHIP

Founded and Led by Physicians and Scientists

- World class ex-Pfizer (kinase) and ex-GSK (immunology) leadership
- Kinome experts skilled at developing kinase targeted medicines

KINect™ PLATFORM

Proprietary Kinase Discovery Engine

- Versatile platform
- Fully integrated discovery and development team
- Advancing small molecule drug candidates designed to parallel or exceed efficacy of high-value biologics

INNOVATIVE PIPELINE
(investigational drug candidates)

ATI-450 - MK2i

- Oral anti-TNFα, anti-IL1, anti-IL6

ATI-1777 - Topical "Soft" JAK1/3i

- Tissue specific therapy for the potential treatment of moderate-to-severe atopic dermatitis (AD)

ATI-2138 - ITK/TXK/JAK3i

- Oral dual inhibitor of T-cell and cytokine receptors

Development of Small Molecule Therapeutics for Immuno-inflammatory Diseases

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Experienced R&D Leadership Team
Proven Track Record in Immunology and Inflammation

- Former SVP, R&D at GSK.
- Led discovery and development teams in Immuno-Inflammation and Dermatology leading to multiple successful NDAs, including NUCALA® & BENLYSTA®

David Gordon
Chief Medical Officer

- Former Executive Director, Pfizer Inflammation Research and Leader of Global Kinase Technology Team
- >95 publications and patents (>30 total on kinases)

Joseph Monahan, PhD
Chief Scientific Officer

- Former VP Research & Global Head, Pfizer Inflammation, co-leader of Pfizer Licensing Team
- Delivered 8 clinical candidates, 6 INDs and 1 NDA in inflammation and cancer

Walter Smith
Scientific & BD Consultant

- Former Research Fellow and Director, Pfizer Chemistry
- >100 publications and patents (15 total on kinases)
- Project Lead for PFE JAK Program

Jon Jacobsen, PhD
VP, Chemistry

- Immunologist/drug discovery leader at pharma (Pfizer & biotech)
- Validated JAK 1/3 as target for transplant/RA/psoriasis, leading to approval of XELJANZ®

Paul Changelian, PhD
VP, Biology

- Former research project leader at Pfizer. Director of Chemistry at Mnemosyne, Luc, Cadent.
- Inventor of 6 clinical candidates and author of 40 peer reviewed publications and patents

David R Anderson, PhD *Sr. Director, Discovery, Early Development*

- Former Exec. Director, Pfizer. Site Head for Medicinal & Structural Chemistry.
- >100 patents.
- Co-inventor of multiple drug candidates

Gary DeCrescenzo
SVP, Pharm R&D

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Strategic Focus

Leverage Kinome Target Discovery to Address Unmet Needs

Advance the process of identifying and targeting key kinome-based enzymes involved in chronic inflammation and autoimmune disease.

Model, elaborate and assess compounds through a unique combination of our proprietary chemical library of kinase inhibitors, our expertise in structure-based drug design, and our custom kinase assays.

Validate newly created drug candidates through pathophysiologically-relevant custom assays that effectively translate to human diseases.

Leverage research and commercial partnerships to accelerate the clinical evaluation and potential impact of discovery platforms.

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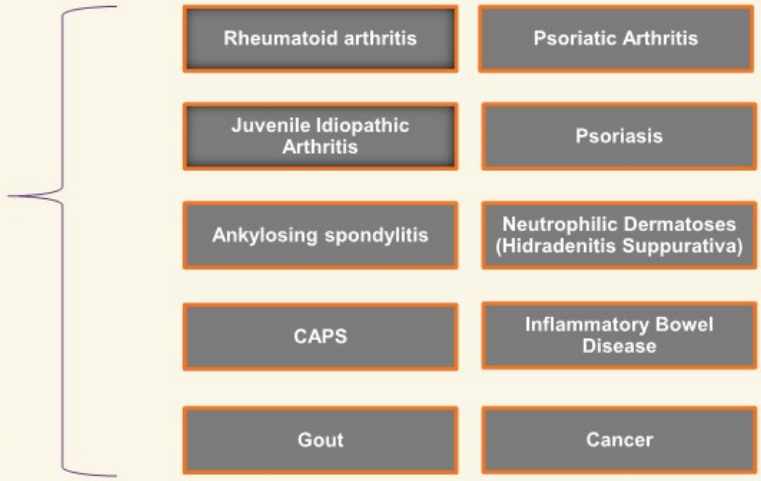
ATI-450: Investigational Small Molecule, Oral MK2 Inhibitor
Designed to Block the Targets of Broadly-Used Biologics

- **MK2* drives pro-inflammatory cytokine expression**
- **By inhibiting multiple cytokines, ATI-450 may be a potential treatment for multiple diseases**
- **Potential alternative to injectable, anti-cytokine biologics and JAK inhibitors for immuno-inflammatory diseases**

Inhibiting MK2 blocks TNFα, IL1α/β and IL6[1], the targets of commercially successful biologics



Global immunology market valued at >$77B in 2018[2]

* MK2 = Mitogen-activated protein kinase-activated protein kinase 2
1. Data on file.
2. Fortune Business Insights. Accessed January 18, 2021. https://www.fortunebusinessinsights.com/industry-reports/immunology-market-100657.

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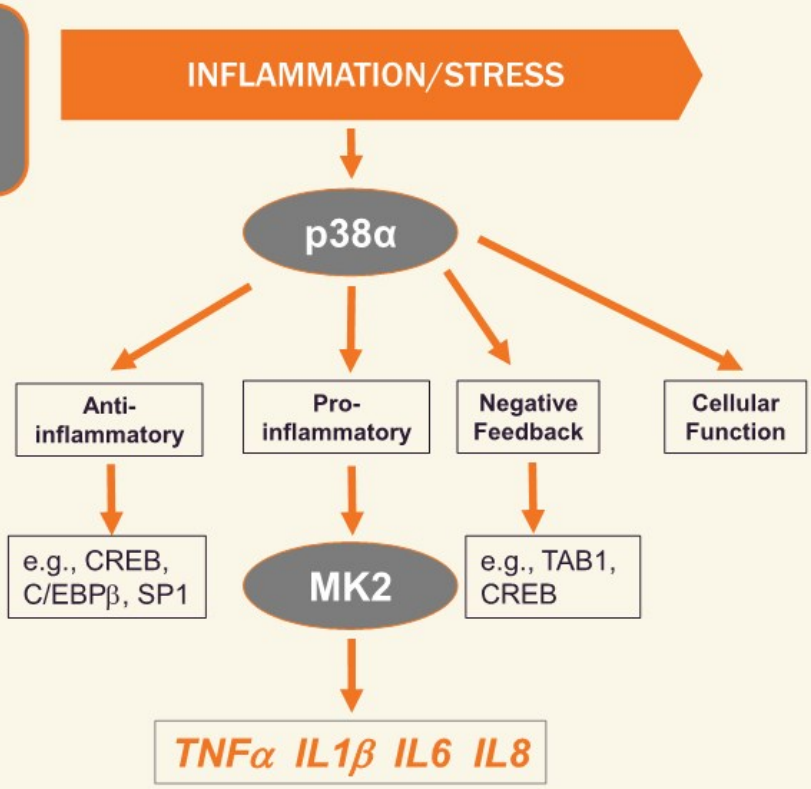
Evolution in Understanding a Well-Known Inflammatory Pathway
The Path From p38α to MK2

We believe MK2 is the optimal drug target in the p38 pathway to maximize anti-inflammatory efficacy and minimize toxicity

- Global p38α inhibitors have exhibited toxicity and/or lack of sustained efficacy in RA and IBD
  - Inability to dose escalate due to safety
  - Signaling network reprogramming
  - Downregulation of anti-inflammatory cytokines
- MK2 drives the proinflammatory node of this pathway while p38α phosphorylates over 60 substrates
- MK2 has been a high priority therapeutic target since 1999 but has proven very difficult to drug



* Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.
* Cheung P, et al. *EMBO J*. 2003;22(21):5793-5805.
* Muniyappa H, et al. *Cell Signal*. 2008;20(4):675–683.
* Ma W, et al. *J Biol Chem*. 2001;276(17):13664-13674.

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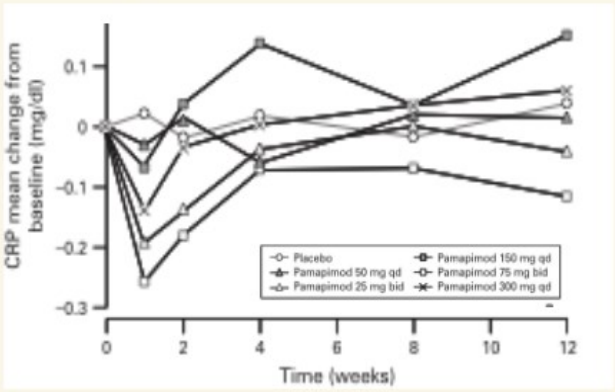
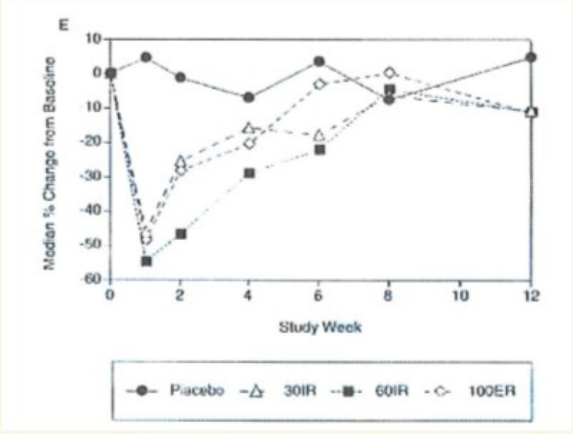
p38 Inhibitors: Tachyphylaxis in RA Clinical Trials
Transient CRP Reduction

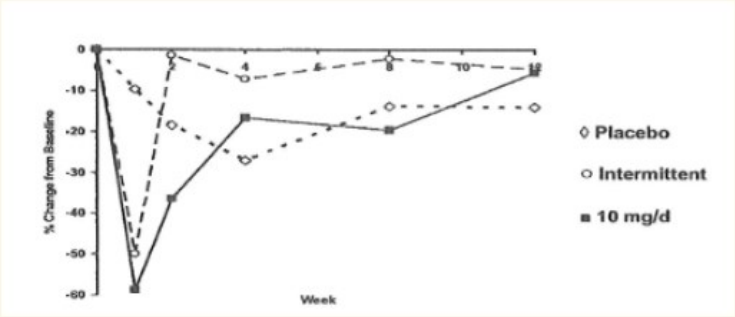
Pamapimod + MTX vs. Placebo + MTX[1]



SCIO-469 vs. Placebo[2]



304: VX-702 + MTX vs. Placebo + MTX[3]



Transient CRP reduction in multiple trials

1. Alten RE, et al. *Ann Rheum Dis.* 2010;69(2):364-367.
2. Genovese MC, et al. *J Rheumatol.* 2011;38(5):846-854.
3. Damjanov N, et al. *Arthritis Rheum.* 2009;60(5):1232-1241.

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Overview

- **ATI-450 development program consists of:**
  - Rheumatoid Arthritis
  - CAPS
  - COVID-19
  - MAD cohort extension (80mg BID, 120mg BID)

- **Today's update:**
  - Progress on RA-201: summary of topline data
  - MAD cohort extension (80mg and 120mg BID)

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ATI-450-RA-201
Preliminary Topline Data Analysis

Trial Design

- Diagnosis of adult-onset RA (ACR/EULAR classification criteria)
- DAS28-CRP ≥3.2 defined as moderate to high disease activity
- Moderately to severely active RA defined by at least 4/28 tender and 4/28 swollen joints
- hsCRP ≥5 mg/L at screening
- Definitive intra-articular synovitis or osteitis defined as a score of 1 or greater on a Hand-Wrist MRI (using RAMRIS)
- Stable MTX dose (defined as 7.5 mg to 25 mg weekly) for at least 4 weeks prior to the screening visit

RANDOMIZATION (3:1)

ARM 1
ATI-450, 50 mg BID + MTX

ARM 2
Placebo, BID + MTX

12 weeks

Primary Objective: Safety

N-25 (to get 15 completers)

Secondary Objectives

- % change from baseline in hsCRP
- Mean change from baseline in DAS28-CRP
- Proportion of patients with DAS28-CRP below 2.6
- Mean change in RAMRIS assessments of synovitis or osteitis
- Proportion of patients with ACR 20/50/70

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Key Demographics

Parameter	Placebo (n=3) Median (Min – Max)	ATI-450 (n=16) Median (Min – Max)
Age (years)	53 (50 – 63)	59.5 (32 – 65)
Gender	(F) 3/3 (100%) (M) 0/0 (0%)	(F) 11/16 (68.75%) (M) 5/16 (31.25%)
Weight (kg)	105.4 (82.2 - 109.2)	88.15 (52.7 - 141.5)
Duration of Disease	1.6 (0.3 - 20.6)	6.45 (0.3 - 33.4)
hsCRP (mg/L)	21.3 (12.6 - 31.2)	11.7 (2.6 - 29.5)
DAS-28	5.3 (5.3 - 6.7) Mean (SD): 5.77 (0.808)	5.65 (3.9 - 7.4) Mean (SD): 5.71 (0.937)

- 19 subjects randomized (16 ATI-450, 3 PBO)
- Broad range of disease duration 0.3 – 33.4 years
  - High hsCRP despite long history and multiple treatment options

- 2 Withdrawals
  - Placebo: subject required prohibited meds for musculoskeletal pain
  - ATI-450: subject evaluated for palpitations and elevated CPK – no cardiac event

* Data on file

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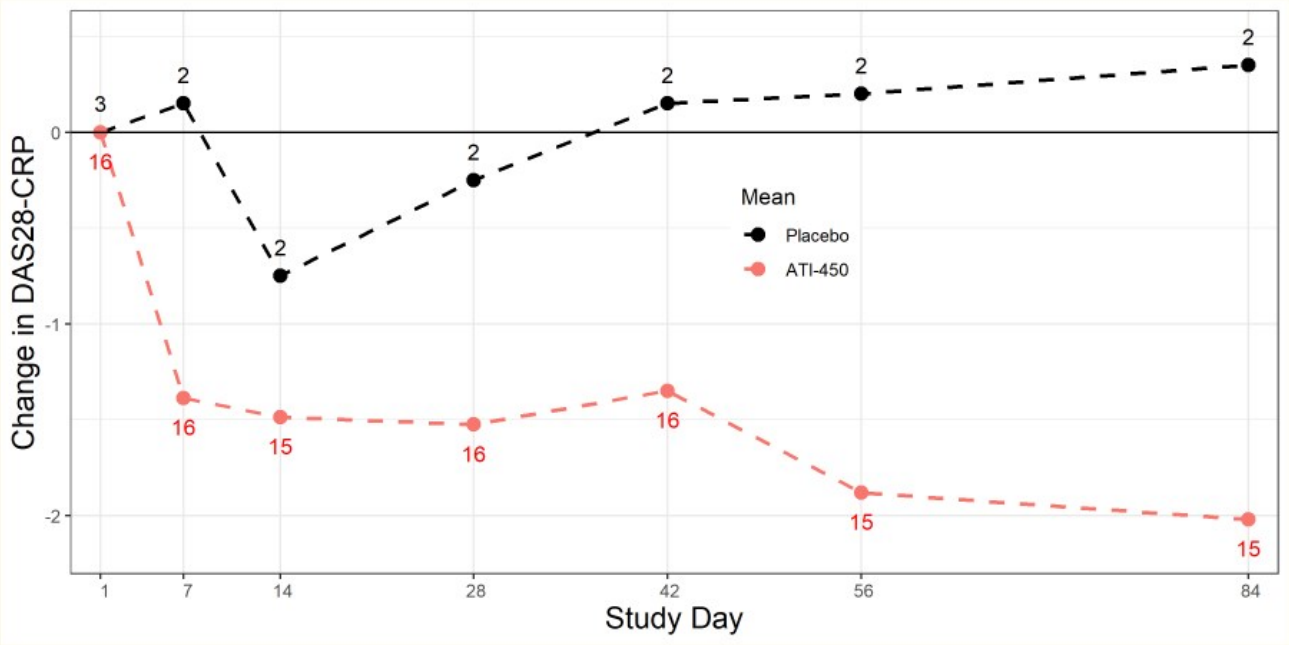
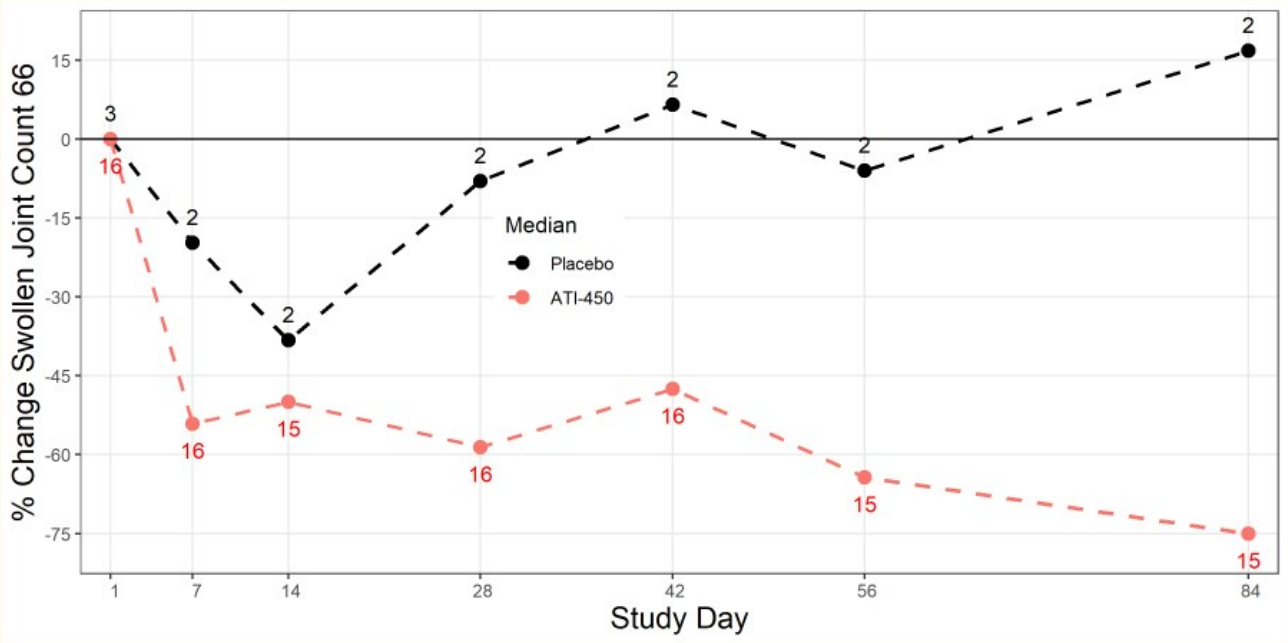
DAS28-CRP
Mean Change From Baseline



Numbers on lines = no. of subjects at each timepoint

* Data on file

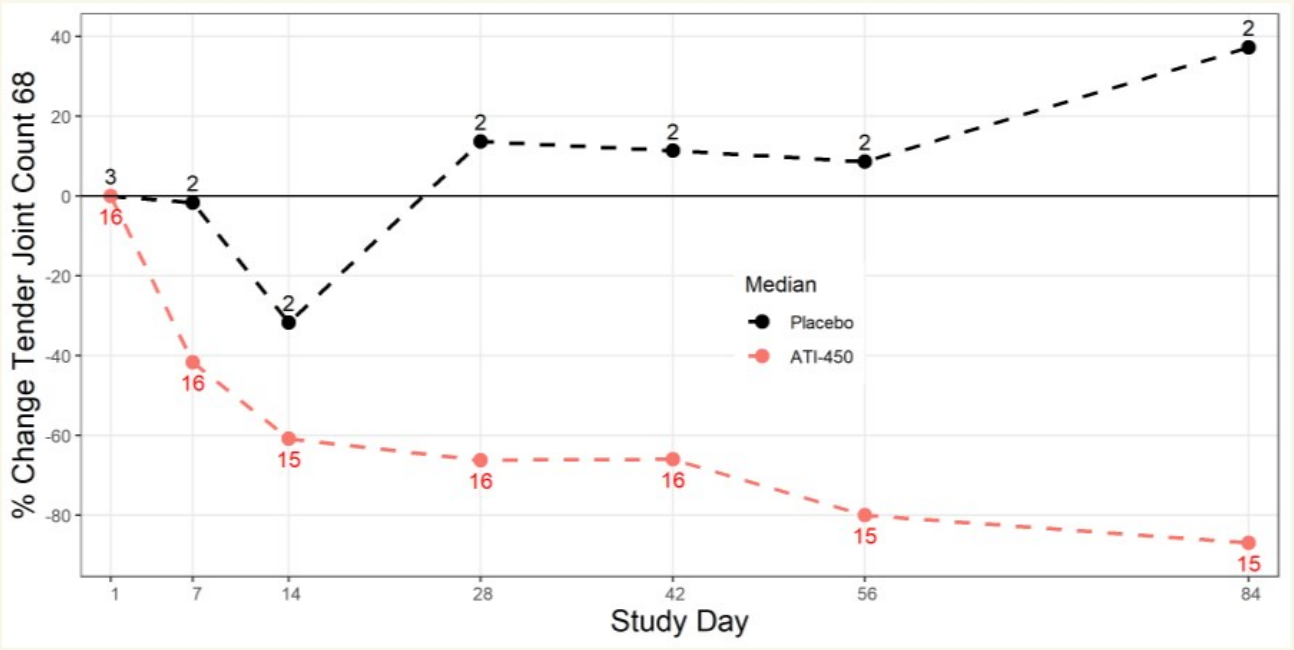
Swollen Joint Count
Median Percent Change From Baseline



Numbers on lines = no. of subjects at each timepoint

* Data on file

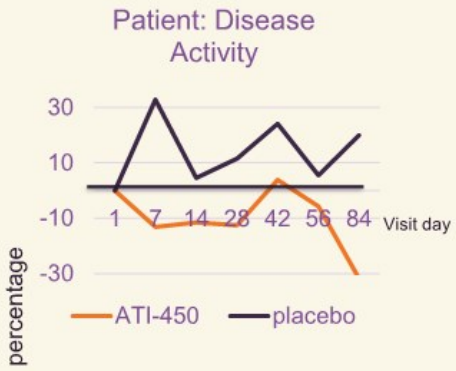
Tender Joint Count
Median Percent Change From Baseline

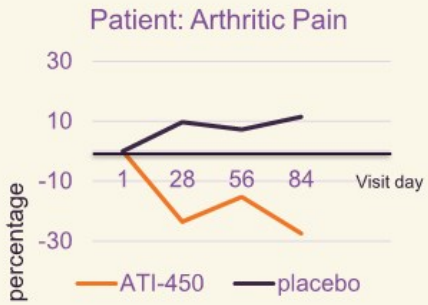


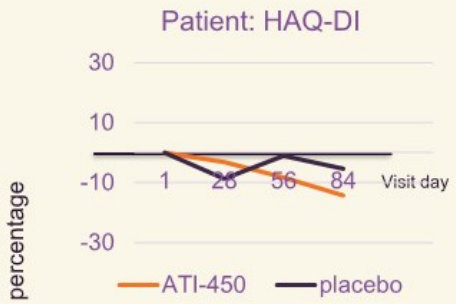
Numbers on lines = no. of subjects at each timepoint

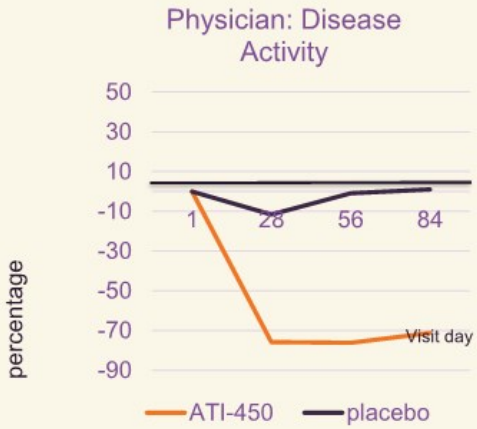
* Data on file

Subjective Physician & Patient VAS Scores
Median Percent Change









* Data on file

HAQ-DI = Health Assessment Questionnaire-Disability Index

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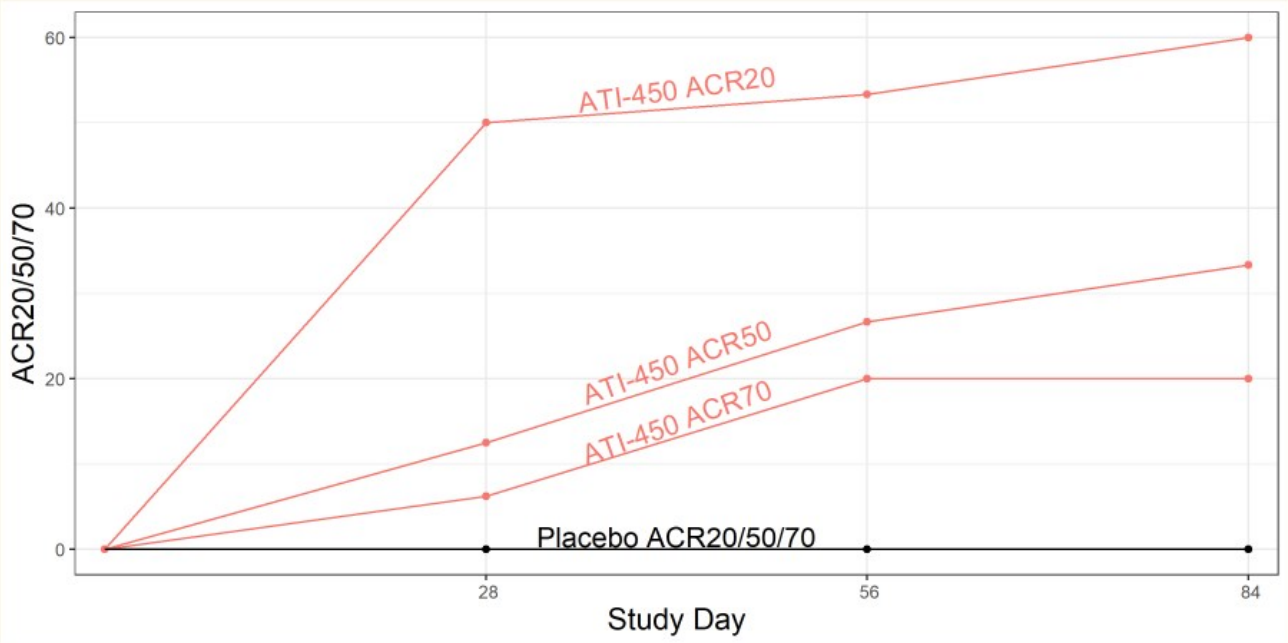
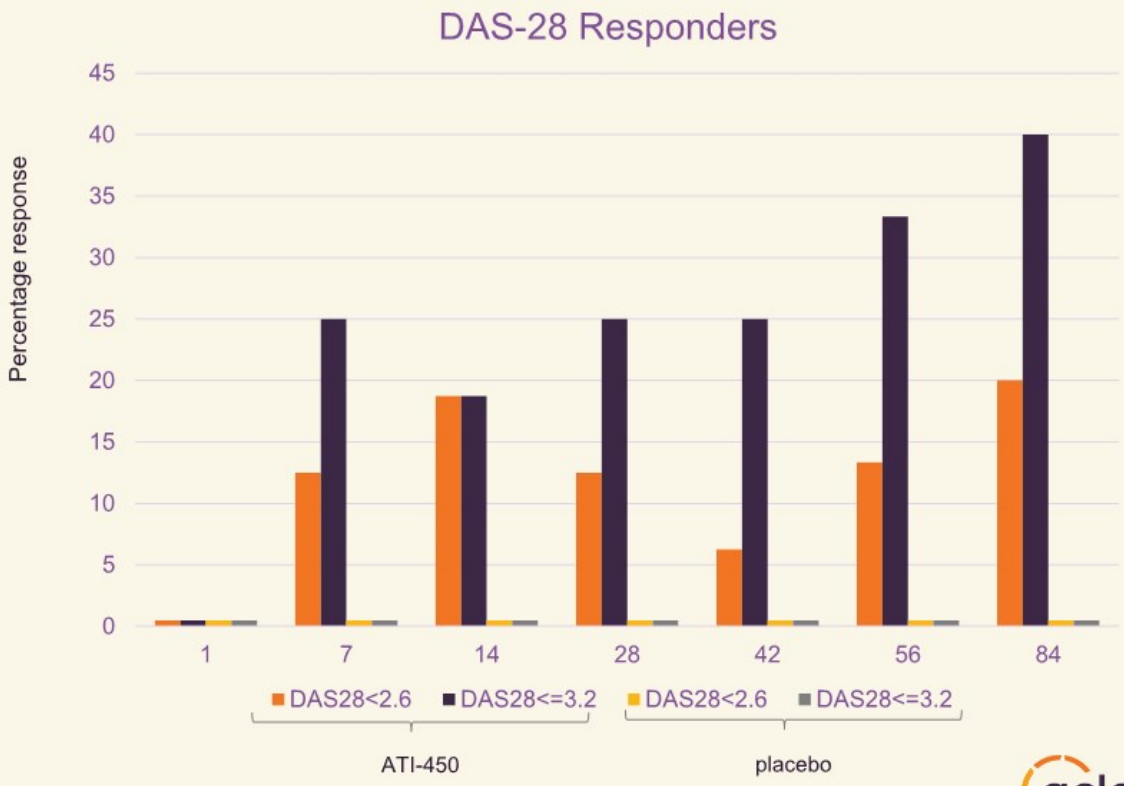
ACR20/50/70: *Responder Analysis over time*



* Data on file

DAS28-CRP: *Responder Analysis over time*



* Data on file

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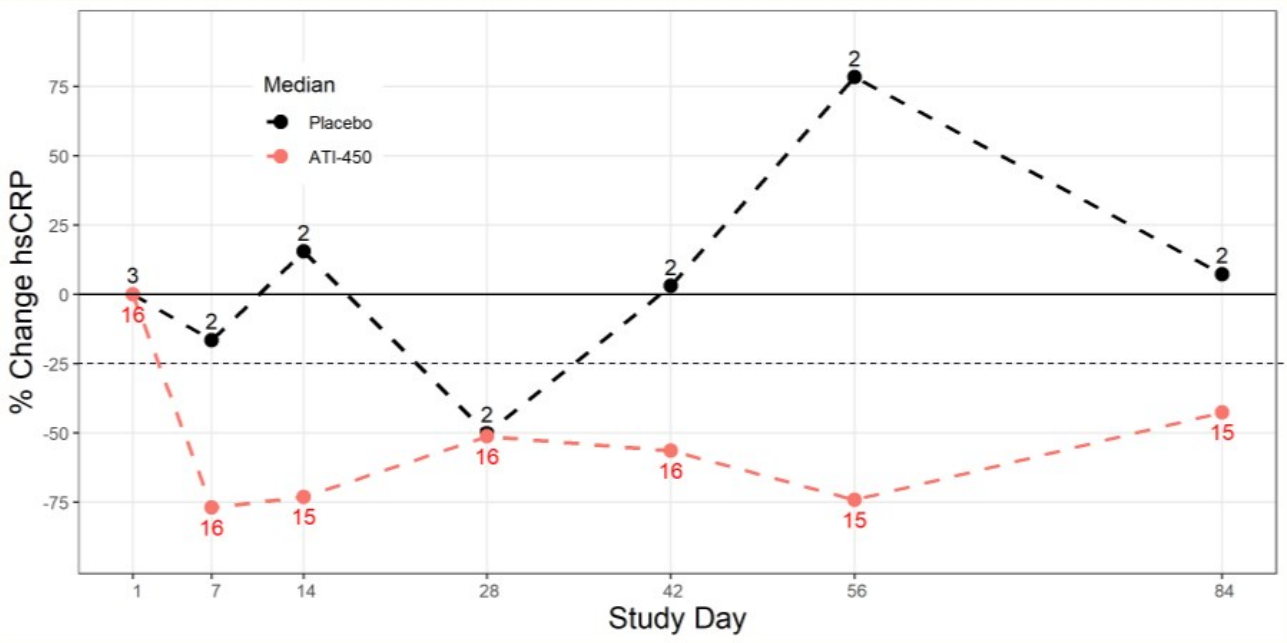
hsCRP (mg/L)
Median Percent Change From Baseline



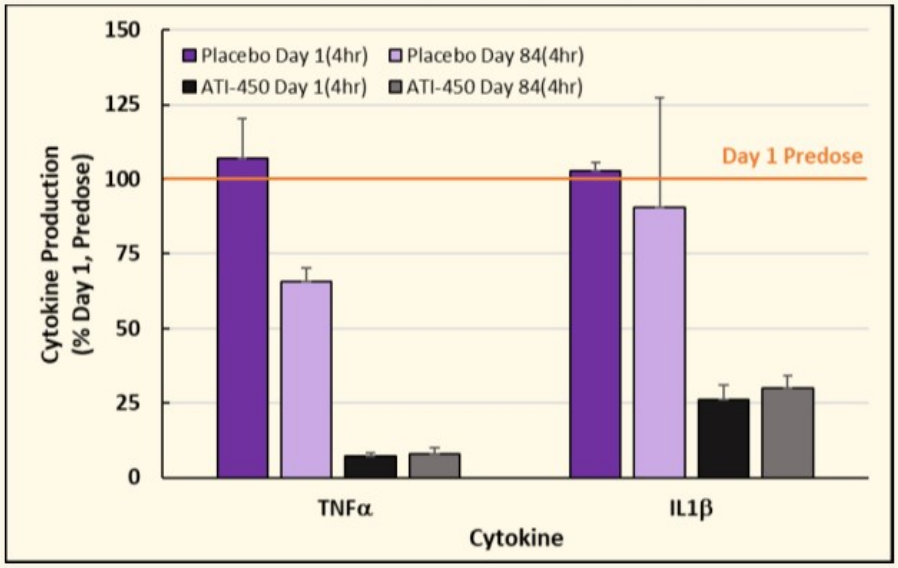
Numbers on lines = no. of subjects at each timepoint

* Data on file

RA Patients Treated with ATI-450 for 12 Weeks

Ex Vivo LPS-Stimulated Cytokines Day 1 vs Day 84

Hypothesis: p38 transient efficacy (tachyphylaxis) may be associated with feedback loops and pathway reprogramming. Selectively targeting MK2 inhibition circumvents these issues through selective downstream pathway blockade.



Durable Dependence on MK2 for Cytokine Production

Interim Data N=11 Active, 2 Pbo

* Data on file as of December 10, 2020.

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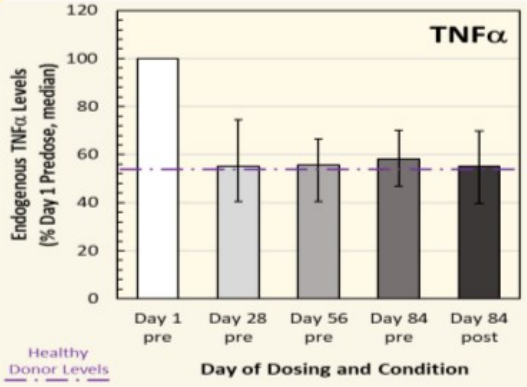
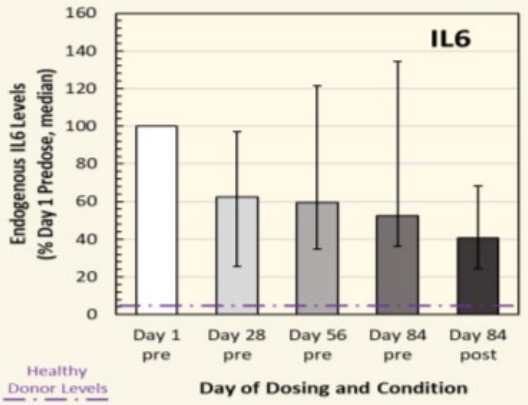
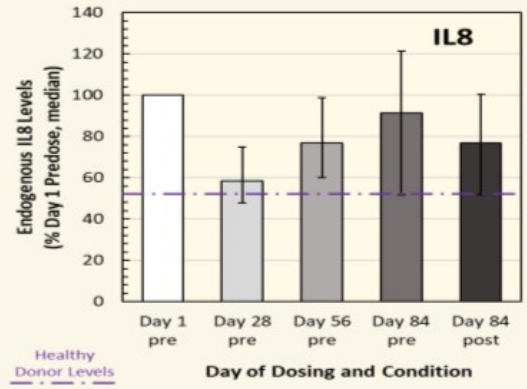
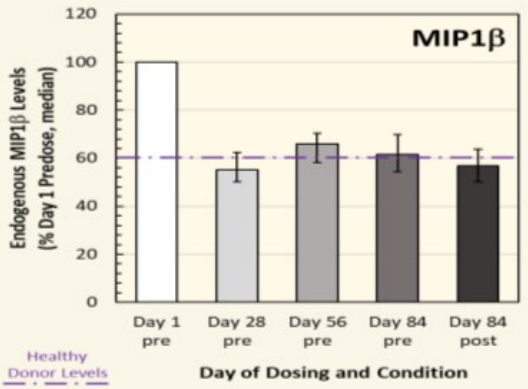
Impact of ATI-450 on Endogenous Plasma Cytokine Levels in RA-201

TNFα, IL6, IL8 and MIP1β









- Cytokines with endogenous levels <0.5 pg/ml predose:IL1β, IL10, IL4 and GM-CSF

* Data on file

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Adverse Events: Subjects with at least one event

Preferred Term	ATI-450 50 mg BID (N = 16)		Placebo (N = 3)	
	Mild n(%)	Moderate n(%)	Mild n(%)	Moderate n(%)
Blood cholesterol increased	1(6.25)	0		
Blood creatine phosphokinase increased	0	1(6.25)		
Constipation	1(6.25)	0		
Dental caries			1(33.33)	0
Ear infection	1(6.25)	0		
Electrocardiogram abnormal	1(6.25)	0		
Essential hypertension	0	1(6.25)		
Hyperlipidaemia	0	1(6.25)		
Hypokalaemia	0	1(6.25)		
Ligament sprain	1(6.25)	0		
Low density lipoprotein increased	1(6.25)	0		
Mouth ulceration	1(6.25)	0		
Muscle strain			0	1(33.33)
Palpitations	1(6.25)	0		
Rash erythematous	1(6.25)	0		
Sinusitis	0	1(6.25)		
Skin abrasion	1(6.25)	0		
Urinary tract infection	0	2(12.5)		
Ventricular extrasystoles	1(6.25)	0		
White blood cell count increased	1(6.25)	0		

- No Serious Adverse Events (SAE)
- No Severe Adverse Events
- ATI-450: one subject withdrew - evaluated for palpitations and elevated CPK – no cardiac event

* Data on file

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ATI-450-PKPD-102
Preliminary Topline Data Analysis

ATI-450-PKPD-102
Evaluation of Safety, PK and PD of Higher Doses

Background:

- ATI-450-PKPD-101: Phase 1 SAD/MAD trial in male and female healthy volunteers
  - No SAEs or AEs that led to discontinuation
  - All AEs were mild in severity and did not interfere with everyday activities
  - Trend of decrease in ANC observed; no correlation with clinical sequelae
  - Linear (dose-and time-independent) PK after multiple-dosing with terminal $t_{1/2}$ of ~9-12 hours; steady state by day 2
  - No meaningful impact on systemic exposure in the fed state
  - MTX PK was similar with or without ATI-450 exposure

- ATI-450-PKPD-102: Phase 1 MAD trial in male and female healthy volunteers
  - Same design to MAD portion of PKPD-101
  - 2 cohorts: 80mg, 120mg BID for 6.5 days
  - 10 subjects per cohort (8 active, 2 placebo)

* Data on file

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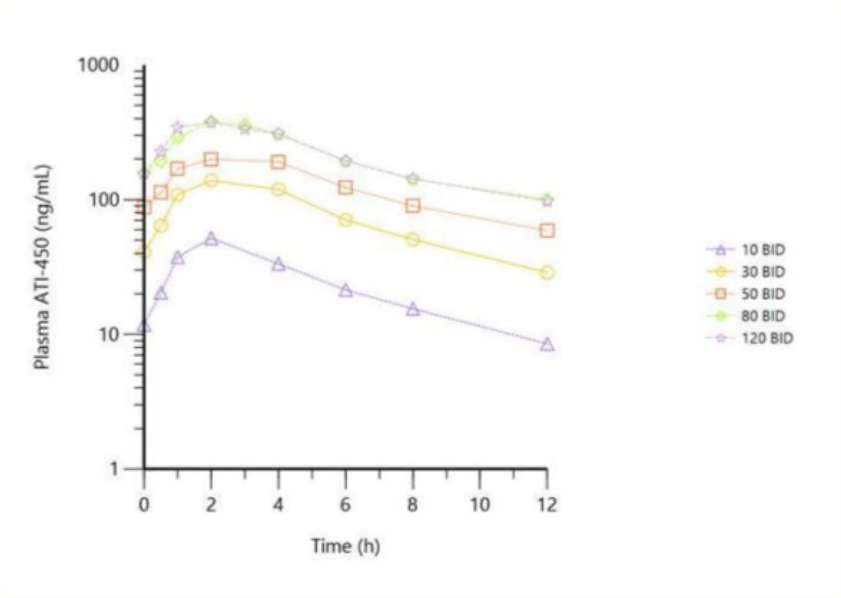
ATI-450-PKPD-101 & ATI-450-PKPD-102

Day 7 Steady State

- t½ 9-14 hours
- 80mg cohort dose proportional with previous cohorts
- No significant increased exposure in 120mg cohort



* Data on file

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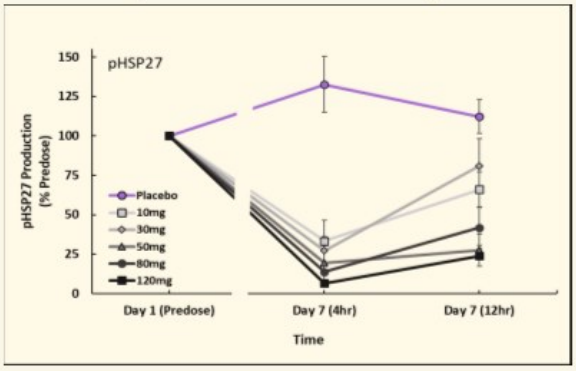
ATI-450-PKPD-101 & ATI-450-PKPD-102

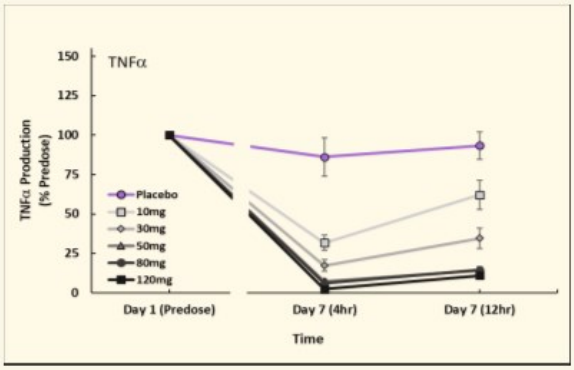
Ex vivo LPS stimulated pHSP27 and TNFα Day7 Peak and Trough

Day 7 Peak and Trough

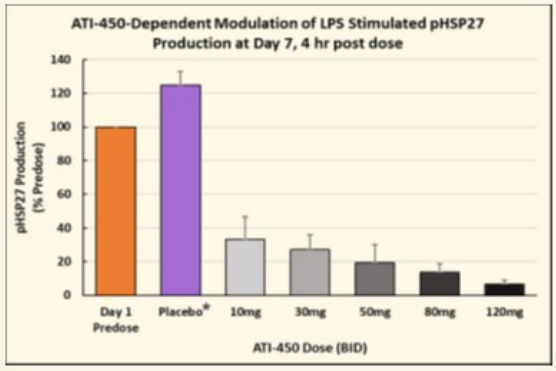
pHSP27

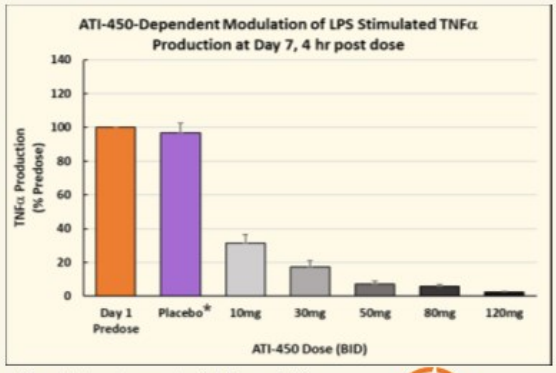


TNFα



Dose Response Day 7 Peak





(*) = All placebo samples (all time points)

* Data on file

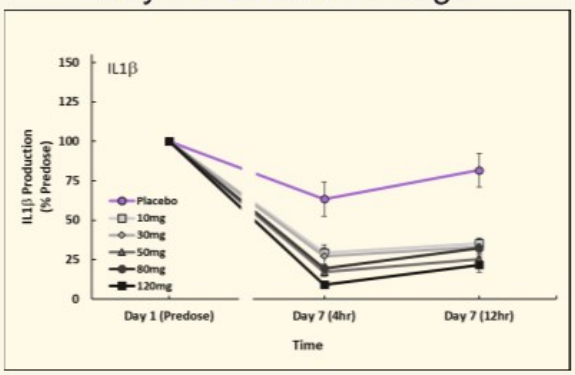
aclaris THERAPEUTICS

ATI-450-PKPD-101 & ATI-450-PKPD-102

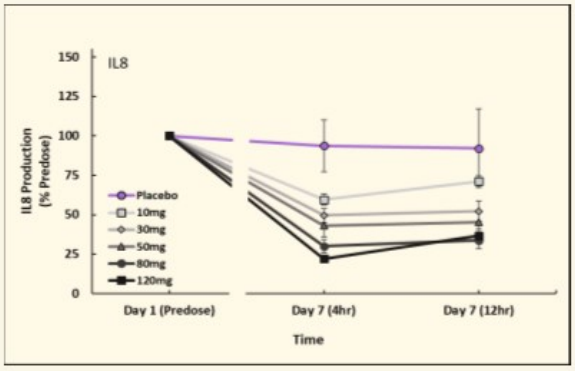
Ex vivo LPS stimulated IL1β and IL8 Day7 Peak and Trough

Day 7 Peak and Trough

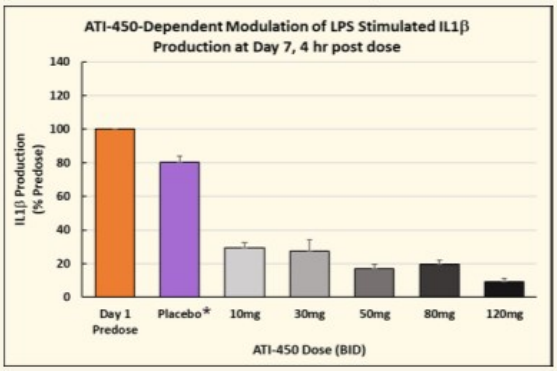
IL1β

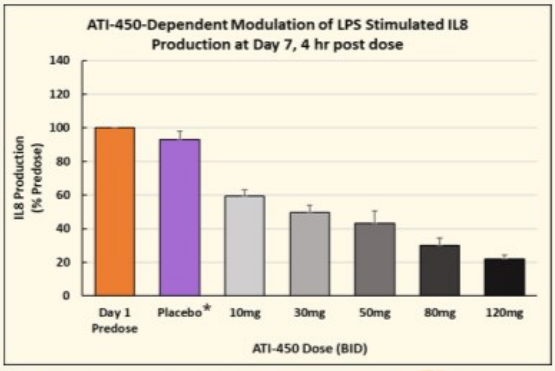


IL8



Dose Response Day 7 Peak





(*) = All placebo samples (all time points)

* Data on file

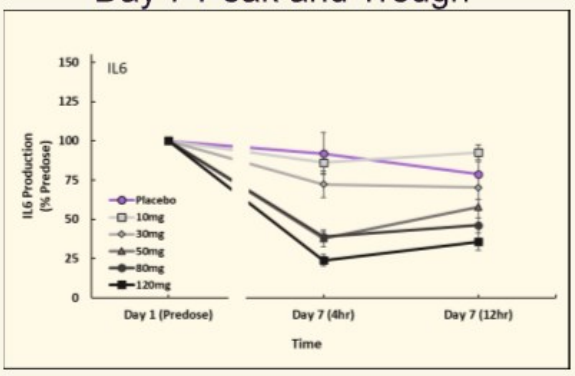
aclaris THERAPEUTICS

ATI-450-PKPD-101 & ATI-450-PKPD-102

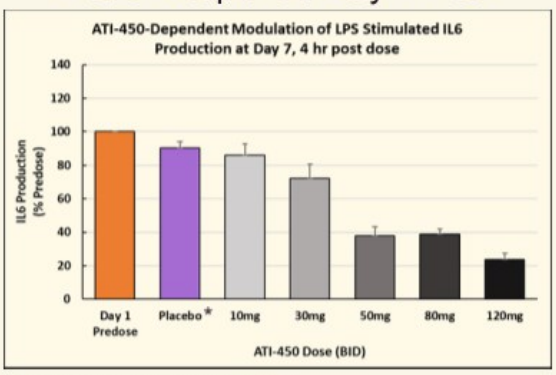
Ex vivo LPS stimulated IL6 Day7 Peak and Trough

IL6

Day 7 Peak and Trough



Dose Response Day 7 Peak

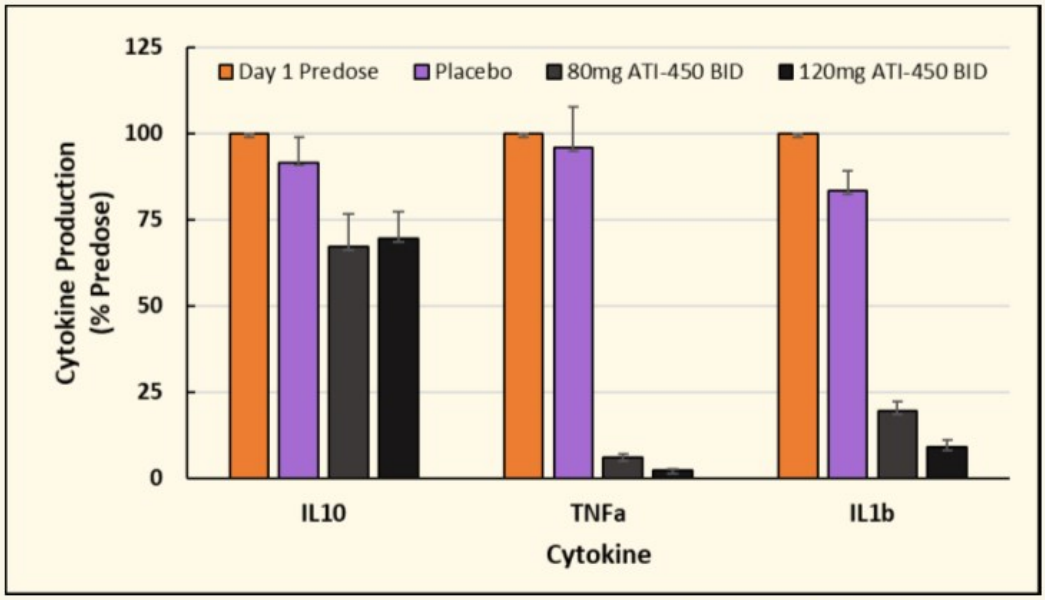


(*) = All placebo samples (all time points)

* Data on file

Phase 1 MAD Extension

Differential Modulation of Ex Vivo LPS-Stimulated IL10 vs. TNFα and IL1β by ATI-450 Day 7 (4 hr)



(*) = All placebo samples (all time points)

The anti-inflammatory cytokine, IL10, was only modulated approximately 30% at doses of ATI-450 that generated near maximal inhibition of proinflammatory cytokines (TNFα and IL1β)

* Data on file

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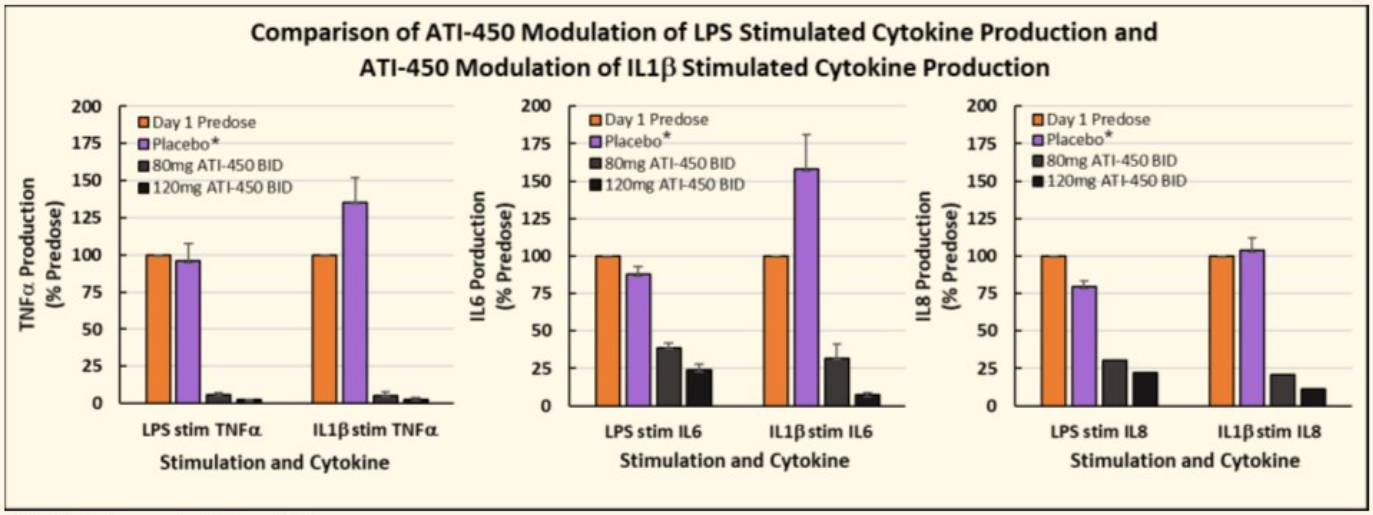
ATI-450 Phase 1 MAD Extension: 80mg and 120mg

Ex Vivo IL1β Stimulation of HWB Day 7 (4 hr)



(*) = All placebo samples (all time points)

ATI-450 potently inhibited ex vivo IL1β-induced proinflammatory cytokines, TNFα, IL6 and IL8

* Data on file

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ATI-450-PKPD-102
Adverse Events

	Cohort 1 80mg BID N=8	Cohort 1 Pbo N=2	Cohort 2 120mg BID N=8	Cohort 2 Pbo N=2	Severity
Total subjects with at least 1 AE	4 (50%)		8 (100%)	1 (50%)	
Headache#	2 (25%)		7 (88%)	1 (50%)	Mild
Dizziness+	2 (25%)		6 (75%)		Mild
Dry Skin*	1 (13%)		5 (63%)		Mild
Constipation	1 (13%)				Mild
Nausea			2 (25%)		Mild
Parasthesia			2 (25%)		Mild
Abdominal Pain			1 (13%)		Mild
Diarrhea			1 (13%)		Mild
Pharyngitis			1 (13%)		Mild

only 1st or 2nd day
+ 7 cases resolved on drug
* After stopping drug

- No SAEs
- No withdrawal for AEs
- No significant ECG, Laboratory findings

* Data on file

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Topline Analyses Summary

- **Main objectives of POC trial were achieved**
  - Potent and durable clinical activity with 50mg BID
    - Rapid reduction in median percentage of tender and swollen joint count, which persisted
    - DAS28-CRP reduction persisted
    - ACR20/50/70 observed in 60%/33%/20% of treatment arm
    - hsCRP reduction maintained
  - ATI-450 was generally well tolerated
- **Positive Phase 1 trial (80 and 120mg BID)**
  - No dose limiting toxicity in phase 1
  - Incremental inflammatory cytokine suppression
  - Pharmacokinetics data continue to support dosing flexibility (QD or BID)
  - Pharmacodynamic data provide rationale for evaluating activity at 80-120mg BID
- **Next steps**
  - Planning for Phase 2b program initiated

* Data on file

aclaris THERAPEUTICS

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

- ***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., January 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