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): November 13, 2023

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.)

701 Lee Road, Suite 103
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 November 13, 2023, Aclaris Therapeutics, Inc. (the "***Company***") will hold a conference call to discuss top-line results for its Phase 2b clinical trial of zunsemetinib (ATI-450), an investigational oral MK2 inhibitor, in subjects with moderate to severe rheumatoid arthritis (the "***Top-line Results***"), 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 November 13, 2023, the Company issued a press release announcing the Top-line Results 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 November 13, 2023.
104	The cover page from Aclaris Therapeutics, Inc.'s Form 8-K filed on November 13, 2023, 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.

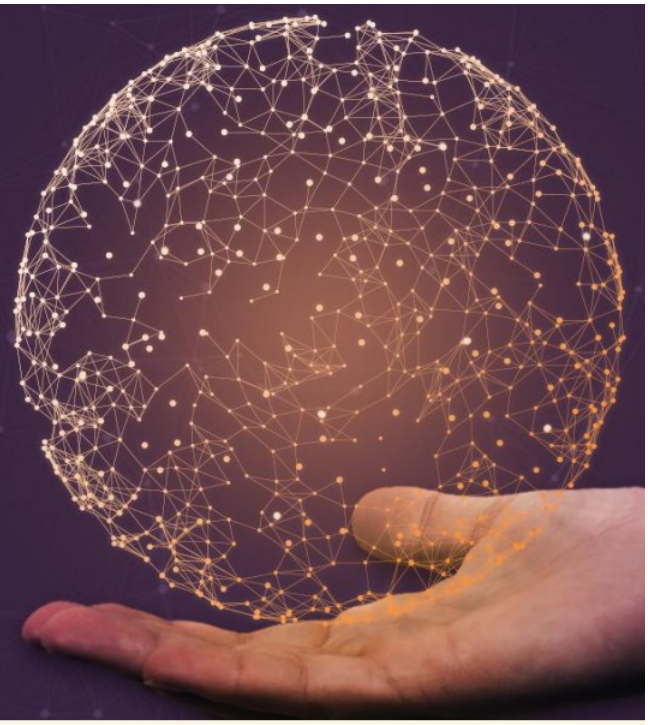
By: /s/ Douglas Manion
Douglas Manion
Chief Executive Officer and President

Date: November 13, 2023

EMPOWERING PATIENTS THROUGH KINOME INNOVATION

Zunsemetinib (ATI-450) Phase 2b Rheumatoid Arthritis Trial Top-line Results

November 13, 2023



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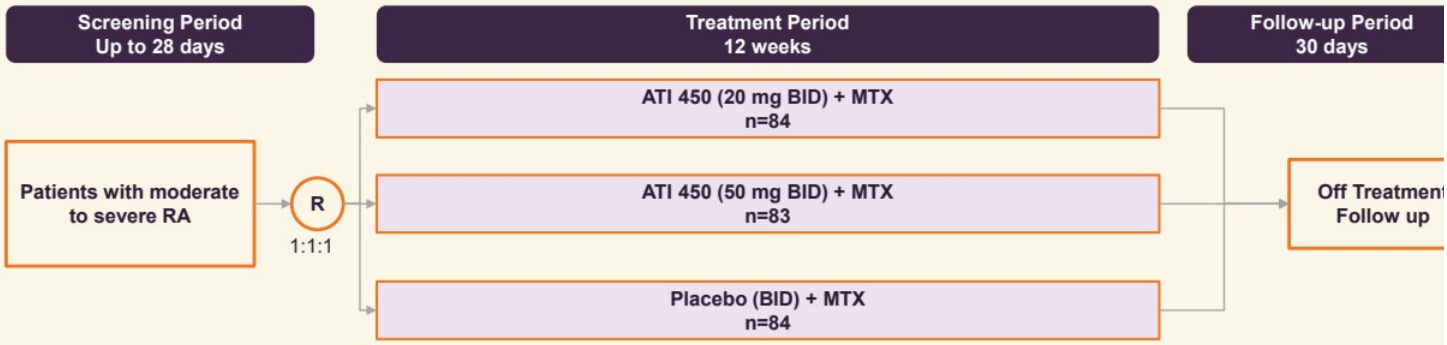
Cautionary Note Regarding Forward-Looking Statements

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,” “intend,” “anticipate,” “may,” “plan,” “potential,” “will,” and similar expressions, and are based on Aclaris’ current beliefs and expectations. These forward-looking statements include expectations regarding the future development of Aclaris’ drug candidates, including the timing of reporting results from trials for 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, 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, 2022, 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 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.

Trial Design



Assessment	Baseline	Week 1	Week 2	Week 4	Week 6	Week 8	Week 12
Tender and Swollen Joint Count	X	X	X	X	X	X	X
Patient Global Assessment	X	X	X	X	X	X	X
Physician Global Assessment	X	X	X	X	X	X	X
Patient pain, HAQ-DI	X			X		X	X
hsCRP	X	X	X	X	X	X	X
Pharmacodynamics (PD)	X			X		X	X

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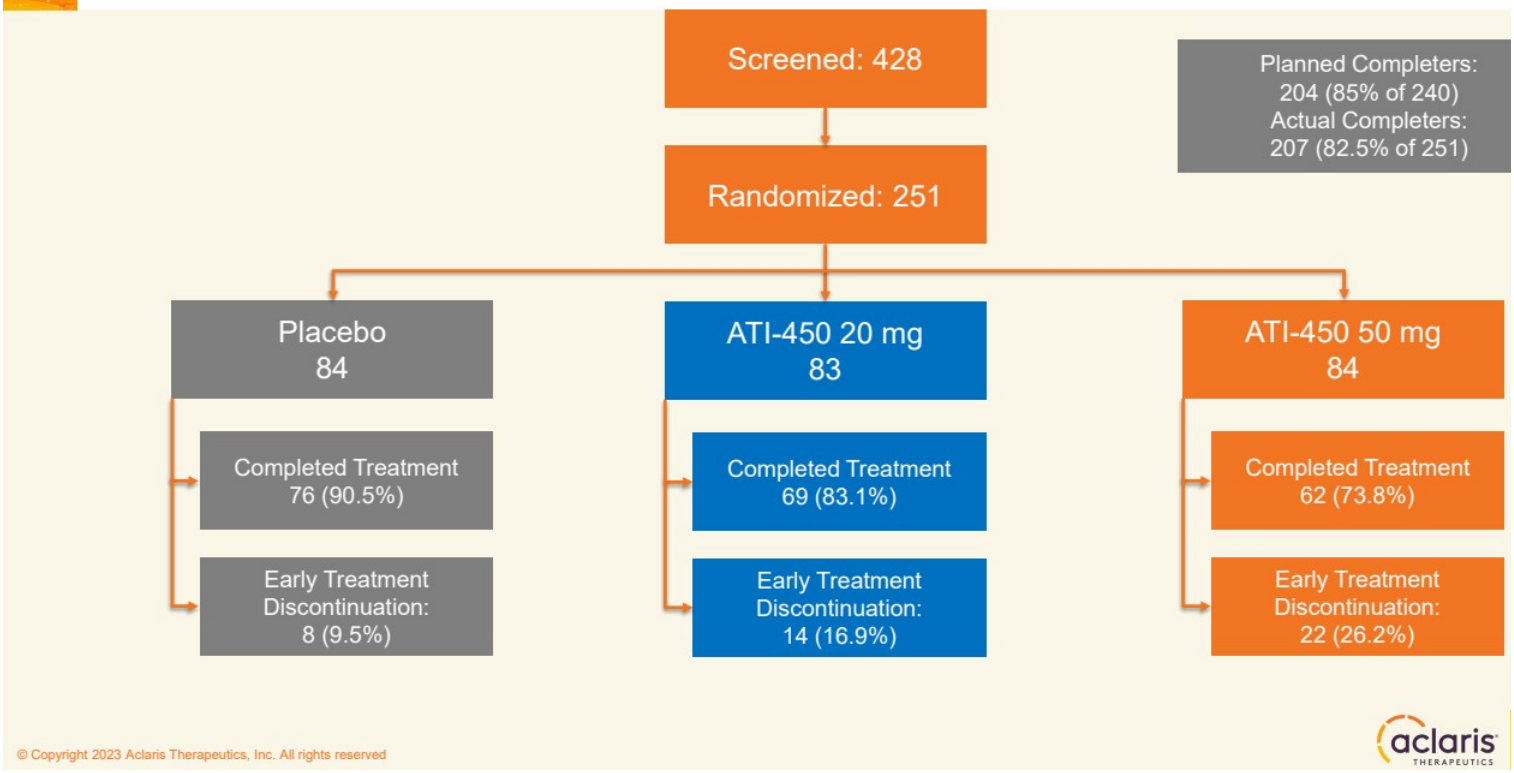
Patient Disposition: Treatment Arms Were Nearly Equal At Randomization with Higher Discontinuation Rate in Active Arms



Demographics: Arms Were Generally Balanced and Similar to Comparable Studies

Parameter	Placebo BID (N=84)	ATI-450 20 mg BID (N=83)	ATI-450 50 mg BID (N=84)
Age (mean)	55.5	55.9	55.8
Sex Male Female	 14.3% 85.7%	 25.3% 74.7%	 23.8% 76.2%
Race: White Black	 89.3% 3.6%	 91.6% 3.6%	 86.9% 2.4%
Weight (kg, Mean)	76.6	77.0	76.3
Height (cm, Mean)	164.3	166.1	165.9
BMI (Mean)	28.1	27.8	27.7

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Baseline Disease Characteristics Were Generally Balanced Across Treatment Arms and Generally Similar to Comparable Studies

Parameter	Placebo BID (N=84)	ATI-450 20 mg BID (N=83)	ATI-450 50 mg BID (N=84)
Duration of RA (years)	7.8	8.0	6.9
Tender Joint Count (out of 68)	20	19	20
Swollen Joint Count (out of 66)	14	14	12
hsCRP	7.8	9.6	13.3
DAS28-CRP	5.4	5.4	5.5
HAQ Disability Index	1.4	1.4	1.4
Pain VAS	64.4	66.2	64.2
Patient Global VAS	66.1	66.5	65.1
Physicians' Global VAS	65.9	65.7	62.3
DAS28-CRP (Moderate/Severe)	32% / 67%	32% / 68%	36% / 64%
Rheumatoid Factor or anti-CCP Positive	88%	89%	89%
Prior Biologic or JAKi treatment	20%	20%	21%

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High Discontinuation Rate with ATI-450 at the 50 mg Dose was Mainly Due to Adverse Events and Withdrawal of Consent

Reason	Placebo N = 84	ATI-450 20 mg N = 83	ATI-450 50 mg N = 84
All Causes	8 (9.5%)	14 (16.9%)	22 (26.2%)
Adverse Events	1 (1.2%)	5 (6.0%)	10 (11.9%)
Withdrawal of Consent	1 (1.2%)	5 (6.0%)	9 (10.7%)
Lack of Efficacy	5 (6.0%)	1 (1.2%)	0
Lost to Follow up	0	2 (2.4%)	2 (2.4%)
Other	1 (1.2%)	1 (1.2%)	0
Non-Compliance	0	0	1 (1.2%)

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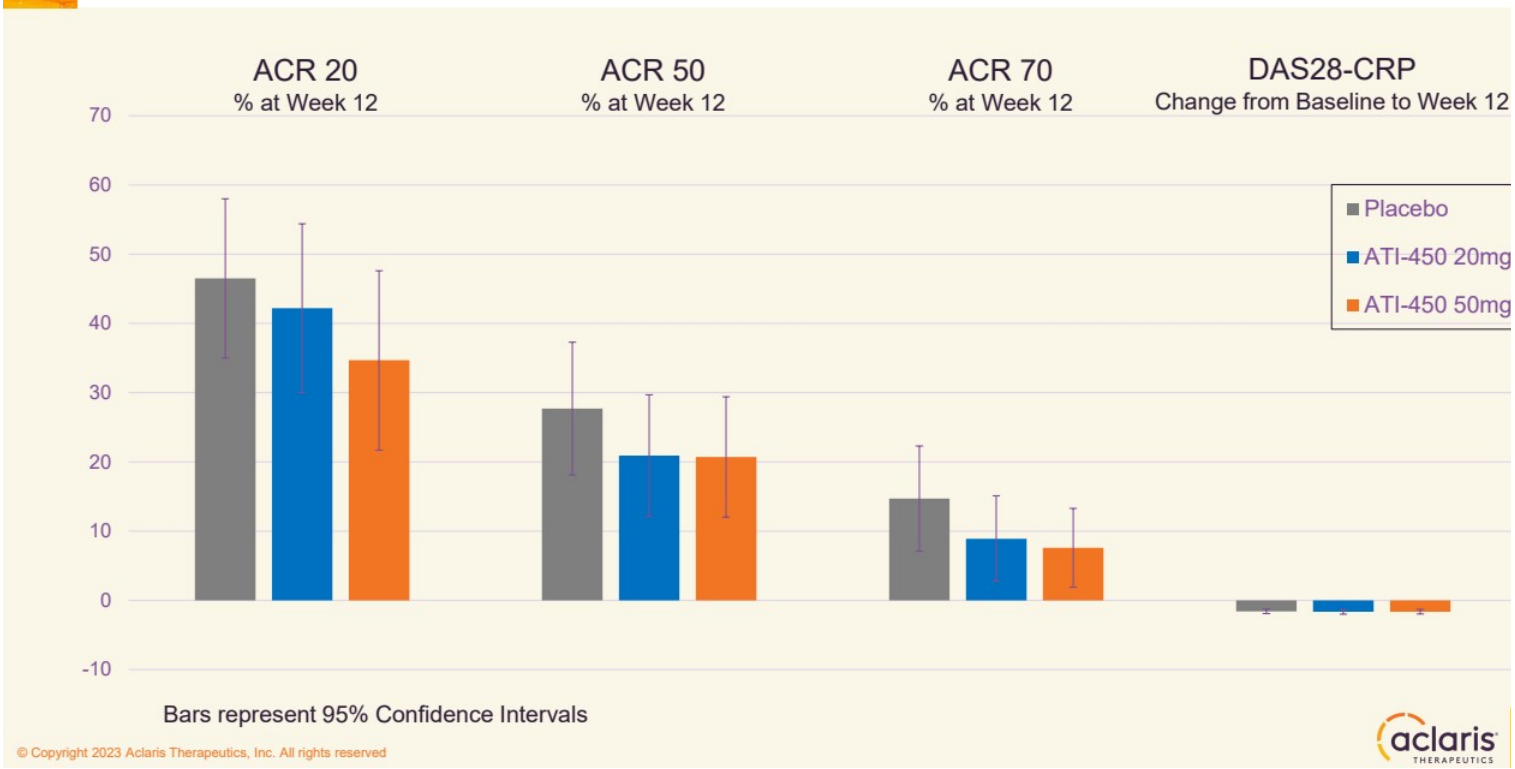
Primary and Key Secondary Efficacy Endpoints at Week 12 Failed to Differentiate from Placebo



Overall Summary of Adverse Events (AE): More Treatment Emergent Adverse Events (TEAE) and Discontinuations Due to AEs with Increasing Dose

Most TEAEs were Mild or Moderate

	Placebo (N=83)	ATI-450 20 mg (N=82)	ATI-450 50 mg (N=85)
Patients with any TEAE	24 (28.9%)	34 (41.5%)	44 (51.8%)
Patients with any Serious TEAE	1 (1.2%)	0	3 (3.5%)
Patients with any Mild TEAE	17 (20.5%)	21 (25.6%)	31 (36.5%)
Patients with any Moderate TEAE	10 (12.0%)	16 (19.5%)	21 (24.7%)
Patients with any Severe TEAE	1 (1.2%)	1 (1.2%)	3 (3.5%)
Patients with any Related TEAE	7 (8.4%)	14 (17.1%)	24 (28.2%)
Patients with any TEAE Leading to Discontinuation of Study Drug	1 (1.2%)	5 (6.1%)	10 (11.8%)
Patients with any Related TEAE Leading to Discontinuation of Study Drug	1 (1.2%)	4 (4.9%)	8 (9.4%)

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TEAEs Occurring in ≥ 2 Patients in 50 mg arm by Preferred Term

Most common TEAEs on 50 mg are Nausea, Nasopharyngitis, CK increased, and Diarrhea

Preferred Term	Placebo BID	ATI-450 20 mg BID	ATI-450 50 mg BID
Nausea	1(1.2%)	2(2.4%)	4(4.7%)
Nasopharyngitis	3(3.6%)	2(2.4%)	3(3.5%)
Creatine phosphokinase increased	1(1.2%)	2(2.4%)	3(3.5%)
Diarrhea	1(1.2%)	1(1.2%)	3(3.5%)
Upper respiratory tract infection	1(1.2%)	5(6.1%)	2(2.4%)
Urinary tract infection	1(1.2%)	2(2.4%)	2(2.4%)
Abdominal pain upper	0	2(2.4%)	2(2.4%)
Arthralgia	1(1.2%)	1(1.2%)	2(2.4%)
Alanine aminotransferase increased	1(1.2%)	0	2(2.4%)
Aspartate aminotransferase increased	1(1.2%)	0	2(2.4%)
Headache	1(1.2%)	0	2(2.4%)
Rash	0	1(1.2%)	2(2.4%)
Vomiting	0	1(1.2%)	2(2.4%)
Acne	0	0	2(2.4%)
Aphthous ulcer	0	0	2(2.4%)
Bronchitis	0	0	2(2.4%)
Influenza	0	0	2(2.4%)
Palpitations	0	0	2(2.4%)
Tremor	0	0	2(2.4%)
Vertigo	0	0	2(2.4%)

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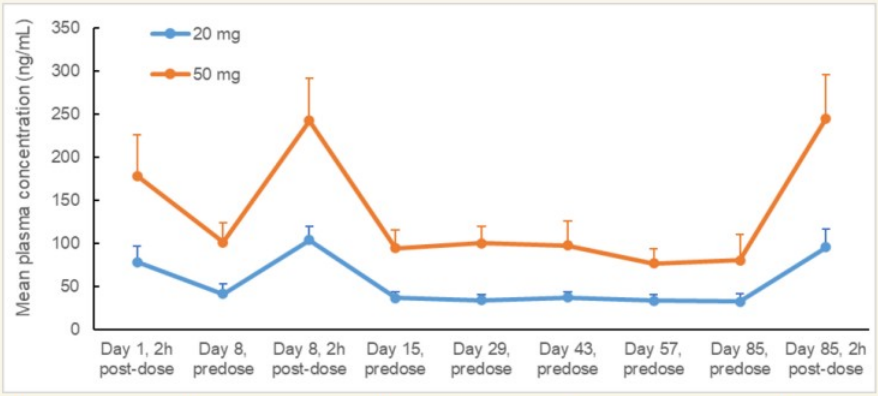
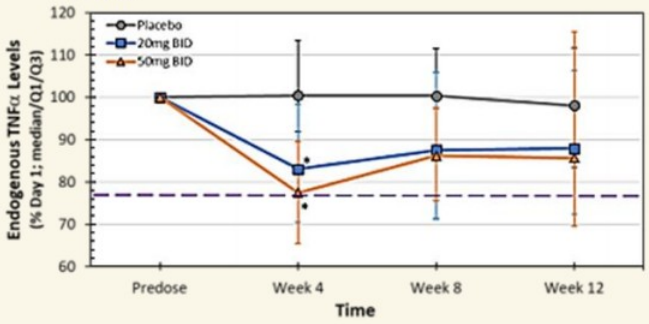
ATI-450 Plasma Concentrations



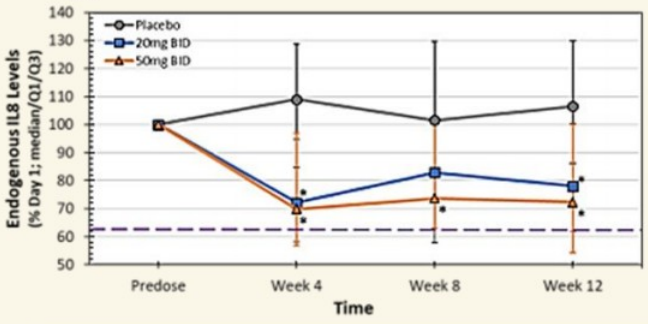
Mean ATI-450 Plasma Concentration 50 mg BID (ng/mL)	Co-Med	Day 1 2h postdose	Day 7/8 predose	Day 7/8 2h postdose	Day 84/85 predose	Day 84/85 2h postdose
Healthy Volunteers	-	178	88	200	-	-
RA-201 patients	MTX	226	164	-	125	293
HS-201 patients	-	148	102	208	104	242
RA-202 patients	MTX	179	101	242	80	245

Preliminary Exploratory Pharmacodynamic Analysis

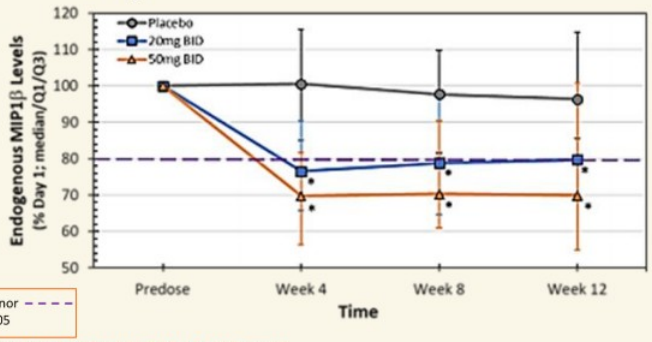
TNFα



IL8



MIP1β



Healthy Donor
(*) = p < 0.05

- Data calculated as percent Day 1 pre-dose by subject. Healthy donor levels expressed as percent of RA patient pre-dose levels
- An ATI-450 dependent, durable inhibition of the proinflammatory markers TNFα, IL8 and MIP1β was observed at both the 20 mg BID and 50 mg BID doses relative to placebo
- The IL1RA (anti-inflammatory cytokine) and IL6 were not inhibited at either dose (not shown)

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Summary of Results and Conclusions

- **Efficacy: ATI-450 20 mg BID and 50 mg BID did not differentiate from placebo in ACR20 and other measures**
  - Efficacy of ATI-450 20 mg BID, 50 mg BID and placebo were generally very similar at week 12 on all measures
  - Placebo response at higher end of the expected range
- **Safety: No meaningful safety findings**
  - More discontinuations due to AEs on ATI-450 (especially 50 mg BID) than placebo, although reasons are diverse
- **PK and PD**
  - PK dose proportional with exposure similar to HS-201 and healthy volunteer studies, while a little lower than RA-201
  - Proinflammatory PD biomarkers (TNFα, IL8 and MIP1β) performed as expected at both 20 and 50 mg BID relative to placebo while IL6 and the anti-inflammatory cytokine IL1RA were not inhibited at either dose

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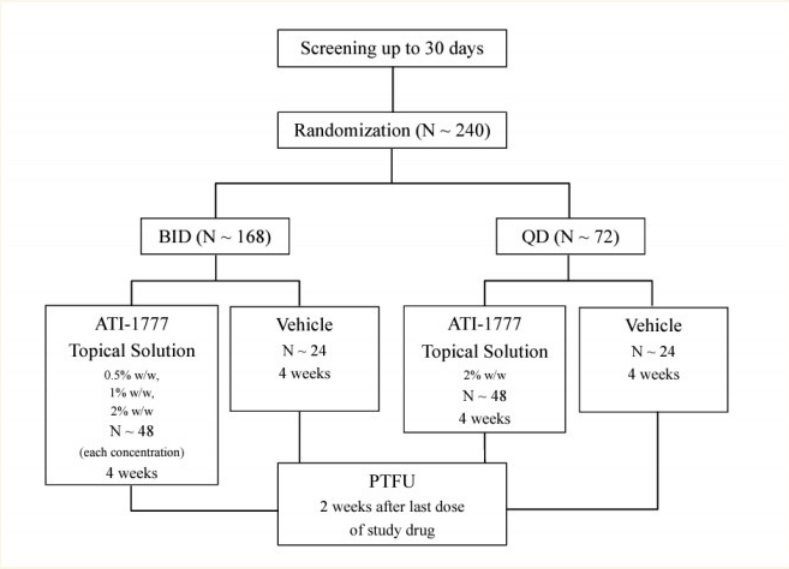
Phase 2b Trial of ATI-1777 in Atopic Dermatitis Results Expected Around Year End 2023

Phase 2b Multicenter, Randomized, Double-blind, Vehicle-controlled, Parallel-group Study to Determi the Safety, Tolerability, PK, and Efficacy of ATI-1777 in Patients 12-65 Years Old with Mild-Severe AD



Primary endpoint: % change from baseline to week 4 in EA

Secondaries include:

- EASI-50, -75, -90
- % achieving IGA-TS
- % change BSA
- Change in vIGA
- PP-NRS
- PGIC
- POEM
- DLQI and CDLQI

Unique spray on solution

- ATI-1777: 0.5% BID, 1% BID, 2% BID, and 2% once daily
- Vehicle: a BID and once-daily arm

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Drug Development Pipeline Fueled by the KINect® Platform Discovery Engine

Drug Candidate / Program	Target	Route of Administration	Indication	Development Phase
Immuno-Inflammatory Diseases				
ATI-1777	"Soft" JAK 1/3 inhibitor	Topical	Atopic dermatitis (mild to severe)	Phase 2b
ATI-2138	ITK/JAK3 inhibitor	Oral	T cell-mediated autoimmune diseases	Phase 2 Ready
Oncology				
ATI-2231	MK2 inhibitor	Oral	Metastatic breast cancer Pancreatic cancer	Phase 1a*

As of September 30, 2023, Aclaris had aggregate cash, cash equivalents and marketable securities of $187.0 million

* This is an investigator-initiated Phase 1a trial in patients with advanced solid tumor malignancies sponsored by Washington University.

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Aclaris Therapeutics Announces Top-line Results from 12-Week Phase 2b Trial of Oral Zunsemetinib (ATI-450) for Moderate to Severe Rheumatoid Arthritis and Provides Corporate Update

- **Study Did Not Meet Primary or Secondary Efficacy Endpoints in Rheumatoid Arthritis –**
- **Efficacy Results Do Not Support Further Development of Zunsemetinib –**
- **Company to Host Conference Call and Webcast Today at 8:00 AM ET –**

WAYNE, Pa., Nov. 13, 2023 (GLOBE NEWSWIRE) -- Aclaris Therapeutics, Inc. (NASDAQ: ACRS), a clinical-stage biopharmaceutical company focused on developing novel drugs for immuno-inflammatory diseases, today announced top-line results from a Phase 2b study of zunsemetinib (ATI-450), an investigational oral MK2 inhibitor, in subjects with moderate to severe rheumatoid arthritis (RA; ATI-450-RA-202).

ATI-450-RA-202 is a Phase 2b, randomized, multicenter, double-blind, placebo-controlled, dose-ranging study to investigate the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of two doses of zunsemetinib plus methotrexate (MTX) versus placebo plus MTX in patients with moderate to severe RA who have had an inadequate response to MTX alone. The study enrolled 251 patients across three treatment arms (ATI-450 20mg BID, ATI-450 50mg BID, Placebo BID) at approximately 40 trial sites in the United States, Poland, Bulgaria and Czech Republic. The primary efficacy endpoint is the proportion of patients achieving an ACR20 response following 12 weeks of treatment. Secondary efficacy endpoints included ACR50 response, ACR70 response, DAS28-CRP and other pertinent RA measures.

Results
In the trial, patients administered either the 20mg or 50mg dose did not meet the primary endpoint of ACR20 response or any of the secondary efficacy endpoints at 12 weeks, including ACR50 response, ACR70 response, and DAS28-CRP. There was no notable differentiation between zunsemetinib and placebo across any measures of efficacy at week 12. No meaningful safety findings were observed.

Based on the overall program results, Aclaris will discontinue further development of the ATI-450 program, including halting enrollment of Aclaris' ongoing Phase 2a trial of zunsemetinib in psoriatic arthritis.

"We are deeply disappointed with the results of this trial and for patients suffering from rheumatoid arthritis. We would like to thank the patients and investigators for their participation in the trial, and I am proud of our team for their commitment to its execution," stated Doug Manion, M.D., Aclaris' Chief Executive Officer. "Despite this setback, we continue to look forward to the upcoming results of our Phase 2b trial of ATI-1777 in atopic dermatitis and initiating our Phase 2 clinical development program for ATI-2138."

Additional Pipeline Updates

- **ATI-1777 (Topical "Soft" JAK1/3 Inhibitor)**: In June 2021, Aclaris announced positive results from its Phase 2a trial in patients with moderate to severe atopic dermatitis. ATI-1777 was designed to provide maximal activity against skin lesions whilst minimizing potential toxicities related to systemic exposure. Around the end of the year, Aclaris expects to provide the results of its 250 patient, 6-arm, Phase 2b study in patients with mild, moderate or severe atopic dermatitis, including adults and children as young as 12 years old, across approximately 30 clinical trial sites in the United States.

- **ATI-2138 (Oral Covalent ITK/JAK3 Inhibitor)**: Aclaris recently reported results of a multiple ascending dose study of ATI-2138 in healthy volunteers showing promising pharmacokinetic and pharmacodynamic properties that could positively impact T cell-mediated diseases. Aclaris anticipates beginning the Phase 2 program in early 2024 with ulcerative colitis as the initial indication, with other indications under consideration.

- **ATI-2231 (Oral MK2 Inhibitor)**: ATI-2231 is a potential treatment for pancreatic cancer and metastatic breast cancer as well as in preventing bone loss in patients with metastatic breast cancer. Aclaris is supporting Washington University in a first-in-human investigator-initiated Phase 1a trial of ATI-2231 in patients with advanced solid tumor malignancies. Aclaris is discontinuing its current efforts on ATI-2231 as a potential treatment for immuno-inflammatory diseases.

- **Confluence Discovery Technologies and KINect® Platform:** Aclaris' world class discovery team continues to innovate by targeting the human kinome to address areas of high unmet medical need.

- **Cash Position:** As of September 30, 2023, Aclaris had aggregate cash, cash equivalents and marketable securities of $187.0 million.

Conference Call and Webcast

Management will host a conference call and webcast, with an accompanying slide presentation of the data from the Phase 2b trial, at 8:00 AM ET today to review the results of the trial. 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 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.

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Aclaris Therapeutics Contact:

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