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): May 8, 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.)

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 2.02 Results of Operations and Financial Condition.

On May 8, 2023, Aclaris Therapeutics, Inc. (the "***Registrant***") issued a press release announcing its financial results for the quarter ended March 31, 2023, as well as information regarding a conference call to discuss these financial results and business updates. A copy of this press release is furnished herewith as Exhibit 99.1 to this Current Report.

In accordance with General Instruction B.2. of Form 8-K, the information in this Item 2.02 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 Registrant's filings under the Securities Act of 1933, as amended (the "***Securities Act***"), 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 7.01 Regulation FD Disclosure.

On May 8, 2023, the Registrant will hold a conference call to discuss the financial results for the quarter ended March 31, 2023 and provide a corporate update. The conference call will include a slide presentation. A copy of the slide presentation that will accompany the conference call is furnished as Exhibit 99.2 to this Current Report.

In accordance with General Instruction B.2. of Form 8-K, the information in this Item 7.01 and Exhibit 99.2 hereto shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference in any of the Registrant's filings under the Securities Act 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 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Press Release, dated May 8, 2023.
99.2	Company Presentation.
104	The cover page from Aclaris Therapeutics, Inc.'s Form 8-K filed on May 8, 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
President and Chief Executive Officer

Date: May 8, 2023

Aclaris Therapeutics Reports First Quarter 2023 Financial Results and Provides a Corporate Update

- Management to Host Conference Call at 8:00 AM ET Today –

WAYNE, Pa., May 8, 2023 (GLOBE NEWSWIRE) -- Aclaris Therapeutics, Inc. (NASDAQ: ACRS), a clinical-stage biopharmaceutical company focused on developing novel drug candidates for immuno-inflammatory diseases, today announced its financial results for the first quarter of 2023 and provided a corporate update.

"The first quarter of 2023 represented another period of continued progress advancing our clinical stage development programs toward important data milestones," stated Doug Manion, M.D., Chief Executive Officer of Aclaris. "As we continue to move toward data catalysts for zunsemetinib in rheumatoid arthritis and psoriatic arthritis as well as ATI-1777 in atopic dermatitis, we also are making positive progress towards bringing our next potentially broadly applicable candidate, ATI-2138, into its first proof of concept trial in ulcerative colitis."

Continued Dr. Manion, "Regarding our proof-of-concept trial of zunsemetinib in hidradenitis suppurativa, which we reported in March, while we did not see positive efficacy results in this particularly challenging disease, we were able to strengthen our safety database and demonstrate mechanistically that our potentially first-in-class MK2 inhibitor performed as expected."

Research and Development Highlights:

Clinical Development Programs:

- **Zunsemetinib**, an investigational oral small molecule MK2 inhibitor:
  Currently being developed as a potential treatment for immuno-inflammatory diseases
    - **Rheumatoid Arthritis (ATI-450-RA-202)**: This Phase 2b dose ranging trial to investigate the efficacy, safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of multiple doses (20 mg and 50 mg twice daily) of zunsemetinib in combination with methotrexate in subjects with moderate to severe rheumatoid arthritis (RA) is ongoing. Based on the continued positive enrollment momentum, Aclaris is narrowing its timing guidance for topline data to the fourth quarter of 2023.
    - **Psoriatic Arthritis (ATI-450-PsA-201)**: This Phase 2a trial to investigate the efficacy, safety, tolerability, PK and PD of zunsemetinib (50 mg twice daily) in subjects with moderate to severe psoriatic arthritis (PsA) is ongoing. Based on a slower than anticipated study start up in Europe, the trial enrollment has taken longer than expected. Based on current enrollment trends and momentum, particularly in Poland, Aclaris now expects topline data in the first half of 2024, rather than year end 2023.
- **ATI-1777**, an investigational topical "soft" Janus kinase (JAK) 1/3 inhibitor:
  Currently being developing as a potential treatment for mild to severe atopic dermatitis (AD)

- **Atopic Dermatitis (ATI-1777-AD-202)**: This Phase 2b trial to determine the efficacy, safety, tolerability, and PK of multiple doses and application regimens of ATI-1777 in subjects with mild to severe AD is ongoing. In April 2023, Aclaris modified the protocol to expand the inclusion criteria for the trial to enroll patients with milder disease to broaden the drug's target indication potential and to further aide enrollment which was challenged by an unexpected milder winter season. As a result, Aclaris currently projects topline data in the second half of 2023, rather than mid-year 2023.

- **ATI-2138**, an investigational oral covalent ITK/JAK3 inhibitor:
  Currently being developed as a potential treatment for T cell-mediated autoimmune diseases

  - Aclaris has selected ulcerative colitis as the intended first clinical development target for ATI-2138. Aclaris is also exploring additional indications that are relevant to the mechanism of action.

  - **Healthy Volunteers (ATI-2138-PKPD-102)**: This Phase 1 MAD (multiple ascending dose) trial to investigate the safety, tolerability, PK and PD of ATI-2138 in healthy volunteers is ongoing. Aclaris continues to expect topline data in the second half of 2023.

Preclinical Development Program

- **ATI-2231**, an investigational oral MK2 inhibitor compound:
  Currently being explored as a potential treatment for pancreatic cancer and metastatic breast cancer as well as in preventing bone loss in patients with metastatic breast cancer

  - Second MK2 inhibitor generated from Aclaris' proprietary KINect® drug discovery platform and designed to have a long plasma half-life.

  - Aclaris expects clinical development activities to be initiated in 2023, which is expected to advance as a collaboration with an academic third party.

Financial Highlights:

Liquidity and Capital Resources

As of March 31, 2023, Aclaris had aggregate cash, cash equivalents and marketable securities of $204.4 million compared to $229.8 million as of December 31, 2022.

Additionally, in March 2023, Aclaris issued a placement notice to sell approximately 3.4 million shares under its ATM facility for aggregate net proceeds of $26.7 million. This transaction closed in April 2023.

Aclaris continues to anticipate that its cash, cash equivalents and marketable securities as of March 31, 2023 in combination with the $26.7 million in net proceeds from sales under the ATM facility subsequent to quarter end, will be sufficient to fund its operations through the end of 2025, without giving effect to any potential business development transactions or additional financing activities.

Financial Results

First Quarter 2023

- Net loss was $28.2 million for the first quarter of 2023 compared to $18.8 million for the first quarter of 2022.
- Total revenue was $2.5 million for the first quarter of 2023 compared to $1.5 million for the first quarter of 2022. The increase was driven primarily by higher licensing revenues from royalties earned on out-licensed intellectual property in the first quarter of 2023.
- Research and development (R&D) expenses were $22.6 million for the quarter ended March 31, 2023 compared to $14.3 million for the prior year period.
    - The $8.3 million increase was primarily the result of higher:
        - Zunsemetinib development expenses related to drug candidate manufacturing and costs associated with clinical activities for a Phase 2b trial for RA.
        - ATI-1777 development expenses related to costs associated with a Phase 2b clinical trial for AD.
        - ATI-2138 development expenses, including costs associated with a Phase 1 MAD trial and other preclinical activities.
        - Compensation-related expenses due to an increase in headcount.
- General and administrative (G&A) expenses were $8.8 million for the quarter ended March 31, 2023 compared to $6.1 million for the prior year period. The increase was primarily due to an increase in compensation-related expenses due to an increase in headcount.
- Licensing expenses were $1.1 million for the quarter ended March 31, 2023 resulting from separate third-party contractual obligations related to the non-exclusive patent license agreement with Lilly. There were no licensing expenses for the quarter ended March 31, 2022.
- Revaluation of contingent consideration resulted in a $0.8 million credit for the quarter ended March 31, 2023 compared to a credit of $1.2 million for the prior year period.

Conference Call and Webcast

As previously disclosed on May 2, 2023, management will host a conference call and webcast, with an accompanying slide presentation, at 8:00 AM ET today to provide a corporate update. 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.

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 the development of Aclaris’ drug candidates, including the timing of its clinical trials, availability of data from those trials, and regulatory filings, and its belief that its existing cash, cash equivalents and marketable securities will be sufficient to fund its operations through the end of 2025. 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 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 Therapeutics, Inc.

Condensed Consolidated Statements of Operations

(unaudited, in thousands, except share and per share data)

	Three Months Ended March 31,	
	2023	**2022**
Revenues:		
Contract research	$ 889	$ 1,221
Licensing	1,639	202
Other	—	30
Total revenue	2,528	1,453
Costs and expenses:		
Cost of revenue [1]	808	1,155
Research and development [1]	22,587	14,306
General and administrative [1]	8,790	6,099
Licensing	1,061	—
Revaluation of contingent consideration	(800)	(1,200)
Total costs and expenses	32,446	20,360
Loss from operations	(29,918)	(18,907)
Other income, net	1,758	118
Net loss	$ (28,160)	$ (18,789)
Net loss per share, basic and diluted	$ (0.42)	$ (0.31)
Weighted average common shares outstanding, basic and diluted	66,872,778	61,431,026

(1) *Amounts include stock-based compensation expense as follows:*

Cost of revenue	$ 299	$ 228
Research and development	2,602	(113)
General and administrative	3,905	2,231
Total stock-based compensation expense	$ 6,806	$ 2,346

Aclaris Therapeutics, Inc.

Selected Consolidated Balance Sheet Data

(unaudited, in thousands, except share data)

	March 31, 2023	December 31, 2022
Cash, cash equivalents and marketable securities	$ 204,405	$ 229,813
Total assets	$ 229,705	$ 254,596
Total current liabilities	$ 18,258	$ 21,938
Total liabilities	$ 52,895	$ 56,975
Total stockholders' equity	$ 176,810	$ 197,621
Common stock outstanding	67,206,025	66,688,647

Aclaris Therapeutics, Inc.
Selected Consolidated Cash Flow Data
(unaudited, in thousands)

	Three Months Ended March 31, 2023	Three Months Ended March 31, 2022
Net loss	$ (28,160)	$ (18,789)
Depreciation and amortization	198	208
Stock-based compensation expense	6,806	2,346
Revaluation of contingent consideration	(800)	(1,200)
Changes in operating assets and liabilities	(4,397)	(3,534)
Net cash used in operating activities	$ (26,353)	$ (20,969)

Aclaris Therapeutics Contact:

Robert A. Doody Jr.
Vice President, Investor Relations
484-639-7235
rdoody@aclaristx.com

Q1 2023 Investor Conference Call

May 8, 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," "may," "plan," "potential," "will," and similar expressions, and are based on Aclaris' current beliefs and expectations. These forward-looking statements include expectations regarding the development of Aclaris' drug candidates, including the timing of its clinical trials, availability of data from those trials, and regulatory filings, identification of novel development candidates through Aclaris' KINect discovery engine, and its belief that its existing cash, cash equivalents and marketable securities will be sufficient to fund its operations through the end of 2025. 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.

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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Agenda

Opening Remarks

Douglas Manion, Chief Executive Officer

Clinical Development Update and HS Trial

Gail Cawkwell, Chief Medical Officer

ATI-450 Pharmacodynamic Analysis

Joe Monahan, Chief Scientific Officer

Financial Results

Kevin Balthaser, Chief Financial Officer

Closing Remarks

Douglas Manion, Chief Executive Officer

Q&A Session

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Drug Development Pipeline

Drug Candidate/Program	Target	Route of Administration	Indication	Development Phase	Topline Dat Expected
Immuno-Inflammatory					
Zunsemetinib (ATI-450)	MK2 inhibitor	Oral	Rheumatoid arthritis (moderate to severe)	Phase 2b	Q4 2023
			Psoriatic arthritis (moderate to severe)	Phase 2a	H1 2024
ATI-1777	"Soft" JAK 1/3 inhibitor	Topical	Atopic dermatitis (mild to severe)	Phase 2b	H2 2023
ATI-2138	ITK/JAK3 inhibitor	Oral	T cell-mediated autoimmune diseases	Phase 1 Multiple Ascending Dose	H2 2023
Gut-Biased Program	JAK inhibitor	Oral	Inflammatory bowel disease	Discovery	
Oncology					
ATI-2231	MK2 inhibitor	Oral	Metastatic breast cancer	Preclinical	
			Pancreatic cancer		

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ATI-1777 (Topical “Soft” JAK Inhibitor) (Investigational Drug Candidate)

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Aiming to Develop an Effective and Safe Therapy for Atopic Dermatitis

Atopic dermatitis (AD) is a chronic, pruritic inflammatory skin condition[1]

- The U.S. prevalence of AD is reported to be 11.3–12.7% in children and 6.9–7.6% in adults[2]
- Market projected to be $8-12 billion at peak (moderate to severe AD)[3]
- Systemic and topical JAK inhibition has demonstrated promising results in AD clinical trials[4]

Goal

- Comparable efficacy to other topical JAKs but a "soft" drug to minimize the potential for systemic toxicities
- JAK1/3 selective to minimize JAK2 mediated hematopoietic effects
- Patients with mild to severe AD
- Deliver in a patient-friendly formulation

ATI-1777 (investigational compound)

- First-in-human Phase 2a trial in subjects with moderate to severe AD completed
- Phase 2a - 4-week trial in subjects with moderate to severe AD completed with primary endpoint of % change from baseline in mEASI
- Phase 2b dose ranging study underway in mild-severe, including children down to 12 years

1. Medscape. Accessed January 7, 2023. https://emedicine.medscape.com/article/1049085-overview. 2. Silverberg J. Dermatol Clin. 2017;Jul;35(3):283-289; 3. Auster M, et al. Something Big Is Ge
Bigger [research note]. Credit Suisse Equity Research; 2019; 4. Shreberk-Hassidim R, et al. J Am Acad Dermatol. 2017;Apr;76(4):745-753.

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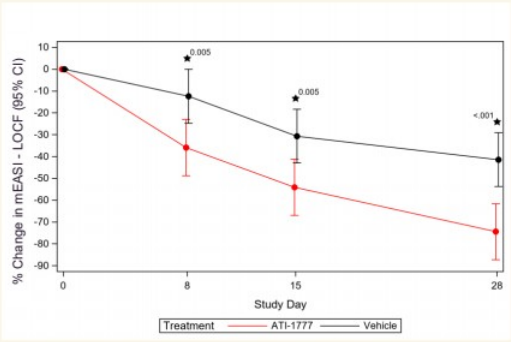
Positive Data Demonstrated in ATI-1777 Phase 2 Study in Atopic Dermatitis

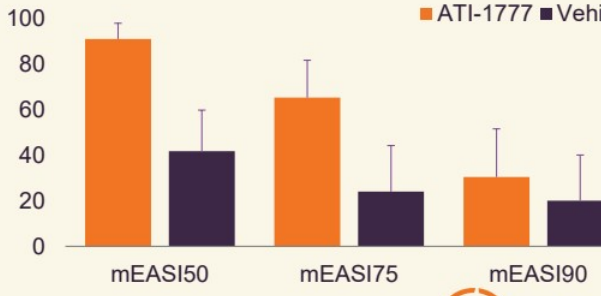
Phase 2a Trial Highlights

- ATI-1777 achieved statistically significant result in the primary efficacy endpoint at week 4
- Positive trends were observed in secondary endpoints including improvement of itch, percent of mEASI-50 responders, IGA responder analysis and reduction in BSA impacted by disease
- ATI-1777 was generally well tolerated

Primary Efficacy Endpoint: % Change in mEASI – LOCF (FAS)



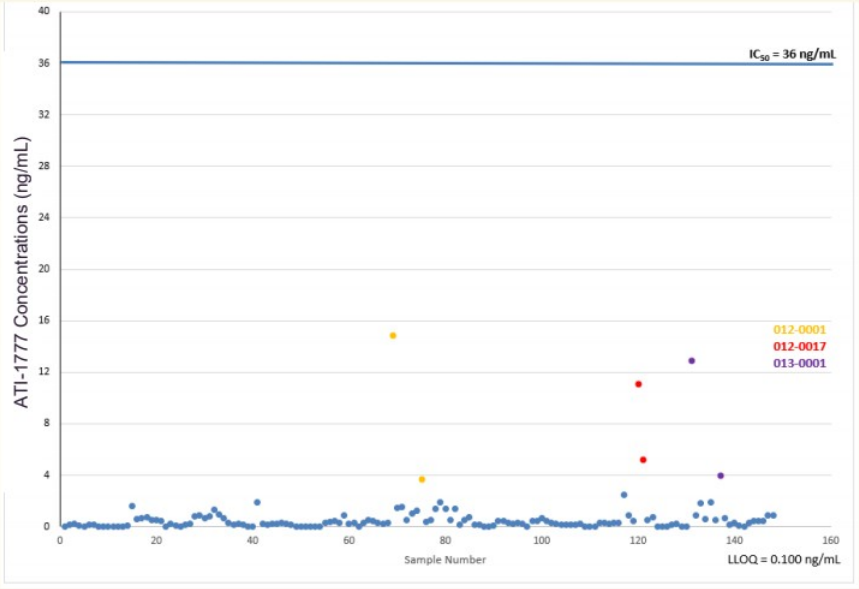
Secondary Efficacy Endpoint: mEASI50/75/90 at Day 28 (FAS)



Note: (FAS): Full Analysis Set

Low Plasma Levels of ATI-1777 Following Topical Application

PK Plasma Concentrations of ATI-1777 in Subjects



- >86% of samples tested following ATI-1777 administration exhibited blood levels below the detectable level
- Average concentration in subjects receiving ATI-1777 solution was never >5% the IC_{50}
- Only 3 subjects (6 out of 148 total samples) with concentrations > $1/10^{th}$ the IC_{50}

Note: Data on file

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Phase 2a Study of Zunsemetinib in Hidradenitis Suppurativa

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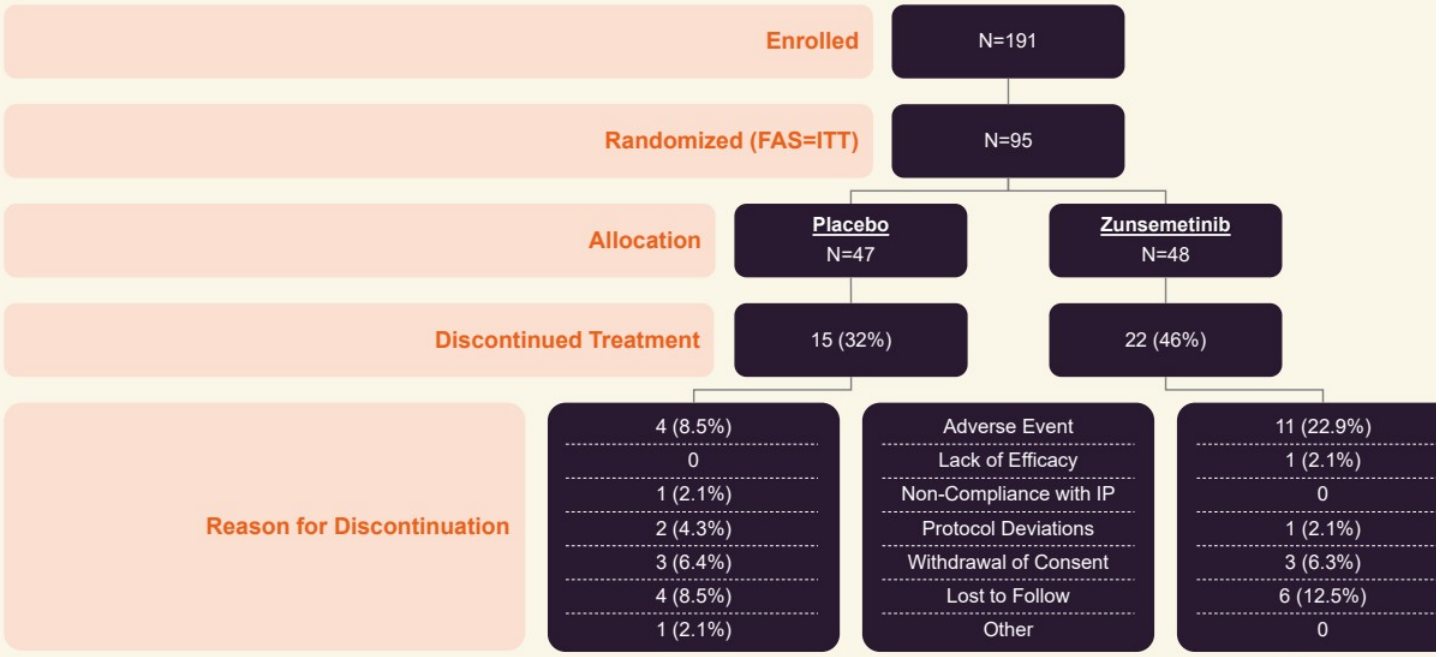
Subject Disposition and Discontinuations



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Demographics and Baseline Characteristics

		Placebo (N=47)	Zunsemetinib (N=48)
Age in years	Mean (SD)	36.6 (9.32)	35.1 (9.87)
Female (at birth)		40 (85.1%)	39 (81.3%)
White – African American - Other		57.4 - 42.6 - 0%	58.3 - 37.5 - 4.2%
Duration of HS in years	Mean (SD)	13.5 (9.97)	11.3 (8.28)
Baseline Inflammatory Nodule/Abscess Count (AN)	Mean(SD)	11 (10.2)	11 (6.4)
Baseline AN Count	Min, Max	5, 67	4, 31
Baseline HS-Physician's Global Assessment	Mean (SD)	4 (0.9)	4 (0.8)
Baseline Patient's Global Assessment of Skin Pain	Mean (SD)	5 (2.3)	5 (2.8)
Baseline Hurley Stage	Mild – Mod – Severe	6.4 - 74.5 - 19.1 %	10.4 - 62.5 - 27.1%

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TEAEs in >1 Patient on Either Treatment Arm

The most common TEAEs on zunsemetinib were dizziness, headache, diarrhea and acne

Treatment-Emergent Adverse Event Preferred Term	Placebo (N=47)	Zunsemetinib (N=48)
Dizziness	0	8 (16.7%)
Headache	2 (4.3%)	6 (12.5%)
Diarrhea	4 (8.5%)	6 (12.5%)
Acne	0	5 (10.4%)
Blood CK increased	0	4 (8.3%)
Mouth ulceration	0	3 (6.3%)
Fatigue	0	3 (6.3%)
Nausea	3 (6.4%)	2 (4.2%)
Vomiting	1 (2.1%)	2 (4.2%)
Abdominal pain	0	2 (4.2%)
Upper respiratory tract infection	1 (2.1%)	2 (4.2%)
Tremor	0	2 (4.2%)
Nasopharyngitis	5 (10.6%)	1 (2.1%)

Most TEAEs were mild or moderate

Overall Infections were evenly balanced (13 patients on placebo, 12 on zunsemetinib within infection grouping) – none serious or opportunistic

Headache and dizziness were generally mild-moderate, occurred early and generally resolved with continued treatment

3 patients had possibly/probably relate acne, confounded by known increase HS-acne comorbidity

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Discontinuations due to AEs

11 patients on zunsemetinib and 4 patients on placebo discontinued study treatment due to adverse events. Most of these:

- Were due to events that have been seen in other zunsemetinib clinical trials
- Occurred early in the course of the study
- Only one patient (on placebo) had serious adverse event of HS worsening

Discontinuations were generally individual events except:

- HS worsening, HS complications or HS co-morbidities led or were contributing TEAEs in 4 on zunsemetinib and 1 on placebo
- Diarrhea led to discontinuation in 2 on zunsemetinib and 1 on placebo

Of the 11 patients who discontinued on zunsemetinib due to TEAEs:

- AN count was no better or worse in most (7 of 11)
- Severity of TEAEs was mild-to-moderate in most (7 of 11)

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CK Elevations Were Common on Zunsemetinib and Placebo and all Were Without Muscle Symptoms

Maximum CK during the study at any point	ATI-450	Placebo
Grade 1 (>ULN - 2.5 x ULN)	7	5
Grade 2 (>2.5 x ULN - 5 x ULN)	3	0
Grade 3 (>5 x ULN - 10 x ULN)	2	1
Grade 4 (>10 x ULN)	1	0
CK increased before treatment (with reduction or no further increase during treatment)	2	5

- 26 patients had a CK elevation at some point during the study
  - 15 on zunsemetinib and 11 on placebo
- There were no adverse events of myalgia or weakness
- When fractionated, no evidence of cardiac involvement

- Many patients had CK elevations before treatment
- Randomly, more meaningful pre-treatment CK elevations observed in patients were on zunsemetinib

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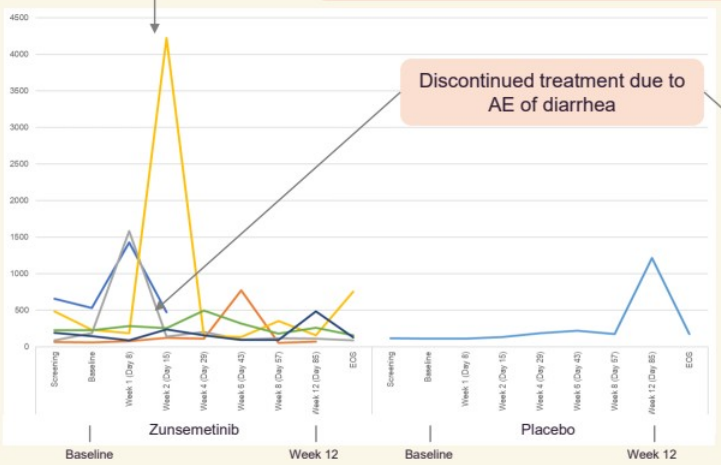
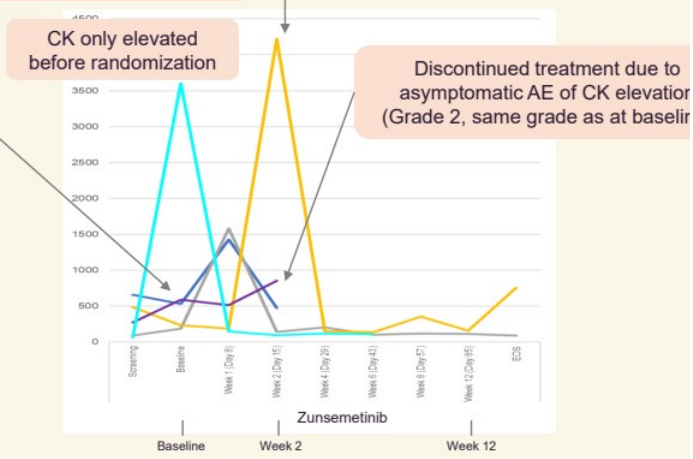
CK Elevations Generally Transient and Generally Resolved on Treatment

Subject noted intense exercise
CK increase assessed as unrelated to study treatment by the investigator





Treatment Emergent CK Elevations ≥Grade 2

Were generally transient and generally returned to baseline while continuing study treatment

CK Elevations Reported as AEs

5 originally reported corrected to 4,
as 1 was baseline only (pre-treatment)
3 of 5 continued treatment with subsequent normalization of CK

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Zunsemetinib in HS: Safety Profile was Generally Consistent with Previous Zunsemetinib Studies, while Efficacy was Not Demonstrated

- ATI-450-HS-201 50 mg BID did not demonstrate efficacy in the Hidradenitis Suppurativa study
- PK and PD were generally consistent with prior zunsemetinib studies
- No increased risk of infections and no serious or opportunistic infections occurred
- Discontinuation due to TEAEs were higher in active than placebo (11 vs 4)
- Lack of improvement or worsening AN in 7 (64%) of those who discontinued zunsemetinib due to a TEAE
- Adverse event profile was as expected
- The most common TEAEs (>10% on zunsemetinib) were dizziness, headache, diarrhea and acne
- Asymptomatic CK elevations were seen and generally resolved with continued treatment

Addition of 47 patients randomized to zunsemetinib 50 mg for 12-week treatment period meaningfully increases the safety database, with no meaningfully different findings identified

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Zunsemetinib HS-201 Exploratory PD Efforts – Looking toward RA2b

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HS-201: Exploratory Pharmacodynamic Analysis

Analysis of Cytokines in Ex vivo Stimulated Patient Blood

- Assay - **Ex vivo** LPS stimulated cytokine production in whole blood
- Samples from both placebo and Zunsemetinib treated HS patients plus healthy donor controls
- Small sample set – 5 patients total
- Cytokines – TNFα, IL1β, IL6 & IL8

Analysis of HS Patient Endogenous Plasma Cytokines

- Assay – Measurement of endogenous cytokines,chemokines and markers of inflammation in plasma from zunsemetinib or placebo treated HS patients
- All 95 patients in the study plus healthy donor controls
- Patient sample set = Days 1, 29, 57 & 85. Fifty-seven complete/thirty-eight partial sets.
- Analytes measured – IFNγ, IL-1α, IL-1β, IL-6, IL-8, IL-10, TNFα, IL-12/IL23p40, IL-1RA, IL-17A/F, IP10, MIP1β, SAA, CRP

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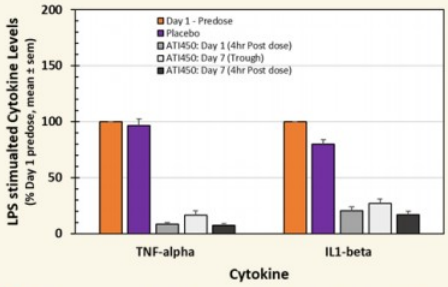
MK2 Pathway Cytokine Dependence and Response Durability

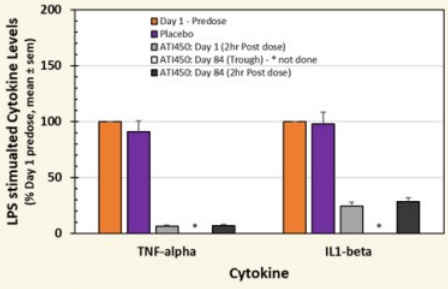
Ex vivo LPS-Stimulated Blood Analyses Across Zunsemetinib Studies

Phase 1 | **Phase 2a**

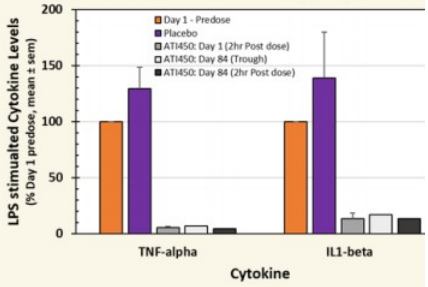
Phase 1 : MAD



Phase 2a : RA



Phase 2a : HS[1]



- Zunsemetinib potently inhibited TNFα and IL1β on day 1 suggesting that proinflammatory cytokine production in healthy subjects, RA and HS patients is dependent on the MK2 pathway
- Zunsemetinib potently inhibited TNFα and IL-1β following prolonged dosing (MAD: 7 days BID; RA 2a: 84 days BID; H 2a: 84 days BID) consistent with lack of pathway reprogramming and tachyphylaxis in all studies

1. Subset of patients

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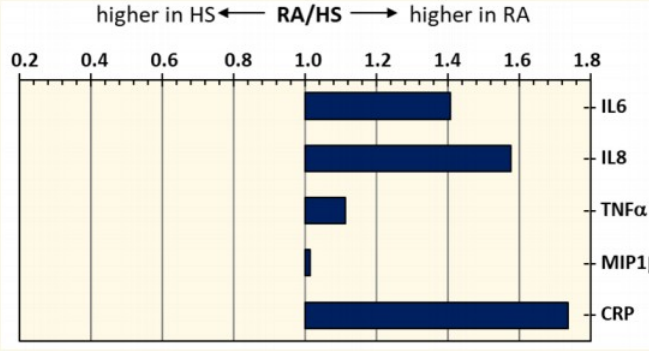
Lower Endogenous Plasma Cytokines Observed in HS vs in RA Phase 2a Studies

Median Cytokine Levels Pre-Dose

Cytokine	HS Patient Day 1 Levels		RA Patient Day 1 Levels	
	median (pg/ml)	Q1 ; Q3 (pg/ml)	median (pg/ml)	Q1 ; Q3 (pg/ml)
IL6	1.72	0.9; 2.79	2.42	1.27 ; 4.22
IL8	6.01	3.91 ; 9.77	9.47	6.39 ; 15.5
TNFa	1.06	0.79 ; 1.36	1.18	0.79 ; 1.44
MIP1b	54.67	41 ; 72.19	55.50	44.9 ; 78.61
CRP*	7.84	4.26 ; 14.01	13.60	6.23 ; 22.5

*CRP = mg/L

Ratio of RA/HS Cytokine Levels



Endogenous proinflammatory cytokines and CRP were lower in the HS phase 2a study compared with the RA phase 2a study consistent with a lower level of systemic inflammation

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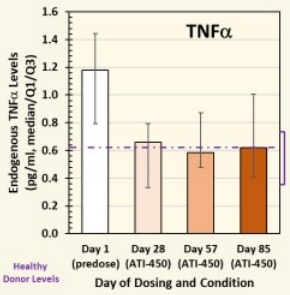
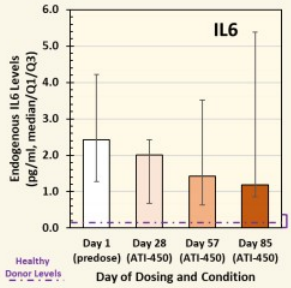
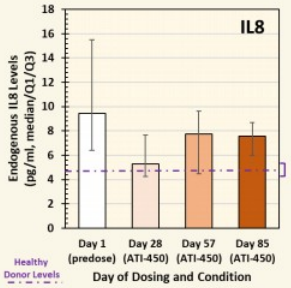
Zunsemetinib Modulation of Endogenous Cytokines

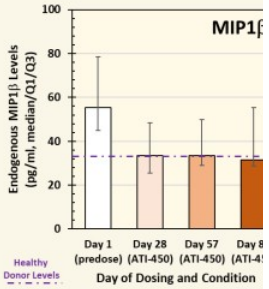
Comparison of RA and HS Phase 2a Studies

RA Study

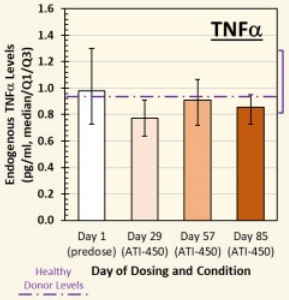


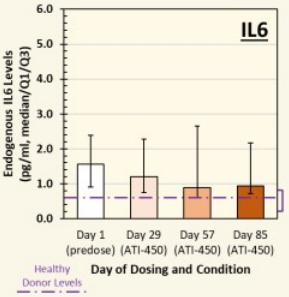


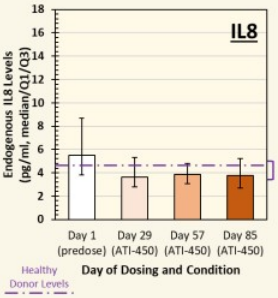


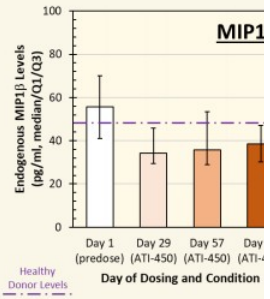


HS Study



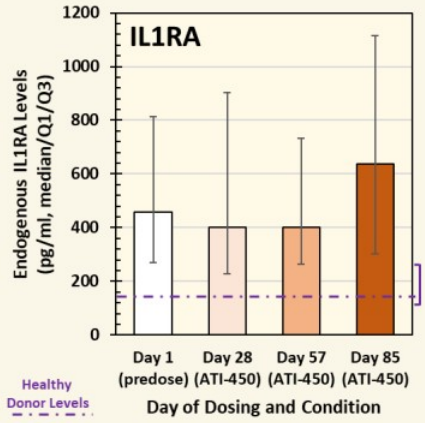




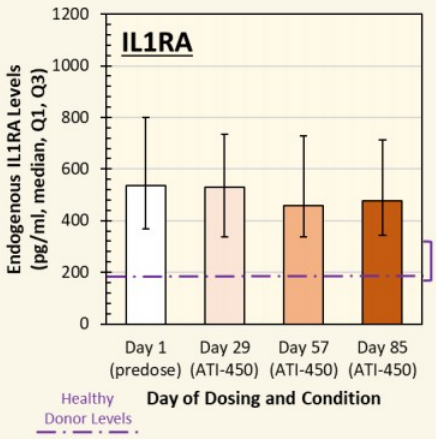


Zunsemetinib Did Not Inhibit the Anti-Inflammatory IL-1 Receptor Antagonist (IL-1RA) Cytokine in either HS or RA Phase 2a Studies

RA Phase 2a Study



HS Phase 2a Study



The anti-inflammatory cytokine IL-1RA was elevated in both HS and RA patients and was not inhibited by zunsemetinib in contrast to the proinflammatory cytokines

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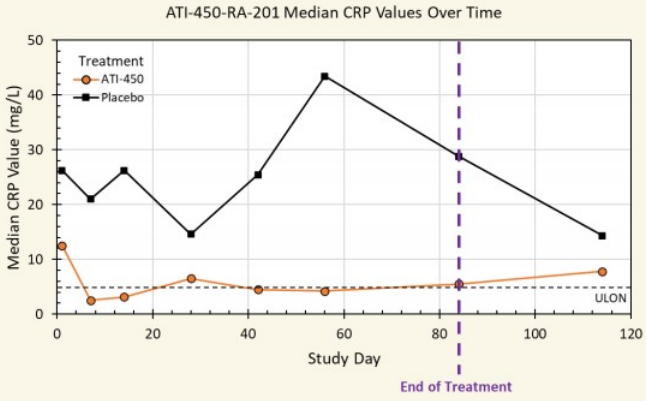
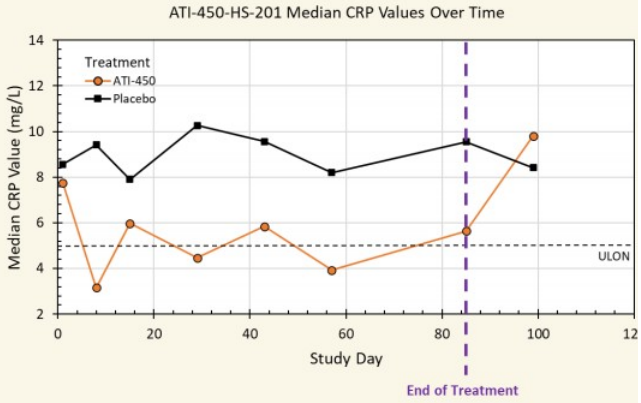
Zunsemetinib Treatment Resulted in a Sustained Inhibition of CRP in both RA-201 and HS-201 Studies

RA Phase 2a Study



HS Phase 2a Study



Sustained inhibition of plasma CRP in HS patients was observed with zunsemetinib treatment similar to that observed in the RA-201 Phase 2a study

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Summary and Conclusions

- **Ex vivo stimulated cytokine inhibition in whole blood**
  - Consistent results across three studies demonstrate marked and sustained inhibition of proinflammatory cytokines and no evidence of tachyphylaxis
- **Endogenous pharmacodynamic plasma biomarker analysis**
  - A subset of cytokines elevated in HS blood relative to healthy donor but to a lesser extent than observed in the RA-201 study
  - Zunsemetinib inhibition trends with proinflammatory cytokines were similar in both the HS and RA phase 2a studies
  - The elevated anti-inflammatory cytokine (IL1RA) was not modulated by zunsemetinib in either the HS or RA phase 2a studies
  - Acute phase systemic inflammation markers CRP and IL-6 were inhibited by zunsemetinib in both the HS and RA phase 2a studies
- **RA and HS phase 2a pharmacodynamic analyses demonstrate persistent systemic anti-inflammatory activity for zunsemetinib**

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Q1 2023 Financial Results Highlights

Q1 2023 total revenue of $2.5M, up 74% YoY

- Licensing revenue increased driven primarily by higher royalties from licensed IP

Q1 2023 net loss of $28.2M, up 50% YoY

- Research and development expense increased by $8.3M, driven by
  - Zunsemetinib clinical trials in RA
  - ATI-1777 in AD
  - ATI-2138 multiple ascending dose study
  - Personnel and stock-based compensation
- General and administrative expense increased by $2.7M, driven by
  - Personnel and stock-based compensation

Financial Strength – Cash runway through the end of 2025

- March 31, 2023 cash, cash equivalents and marketable securities balance of $204M
- Issued placement notice to sell 3.4M shares under at-the-market facility during the first quarter
  - Aggregate net proceeds of $26.7M
  - Transaction closed in April and therefore is not included in the March 31, 2023 cash balance

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Q&A Session

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