

**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): April 14, 2023

Aclaris Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of incorporation)

001-37581
(Commission File Number)

46-0571712
(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 April 14, 2023, Aclaris Therapeutics, Inc. (the “*Registrant*”) updated its company overview presentation, a copy of which is furnished 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 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

| <u>Exhibit Number</u> | <u>Exhibit Description</u> |
|-----------------------|--|
| 99.1 | Company Presentation |
| 104 | The cover page from Aclaris Therapeutics, Inc.’s Form 8-K filed on April 14, 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.

Date: April 14, 2023

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

EMPOWERING PATIENTS THROUGH KINOME INNOVATION

Corporate Overview

April 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 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, 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.

Biotechnology Company Focused on the Kinome

People + Platform + Pipeline

Leadership

Scientific Discovery led by World Class Kinase Expertise

- Kinome experts skilled at developing novel kinase targeted medicines

Proven Operational and Clinical Development Leadership Team in Place

KINect® Platform

Proprietary Kinase Discovery Engine

- Versatile discovery 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)

Zunsemetinib (ATI-450) - MK2i

- Oral anti-TNF α , anti-IL17, anti-IL1, anti-IL6

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

- Tissue specific therapy

ATI-2138 - ITK/JAK3i

- Oral dual inhibitor of T cell and cytokine receptors

Development of Small Molecule Therapeutics for Immuno-inflammatory Diseases

Note: KINect® is the registered trademark of Aclaris Therapeutics, Inc.

The Kinase Opportunity Unlocking the Potential of the Kinome

Medically Important and Productive Target Class

Oncology

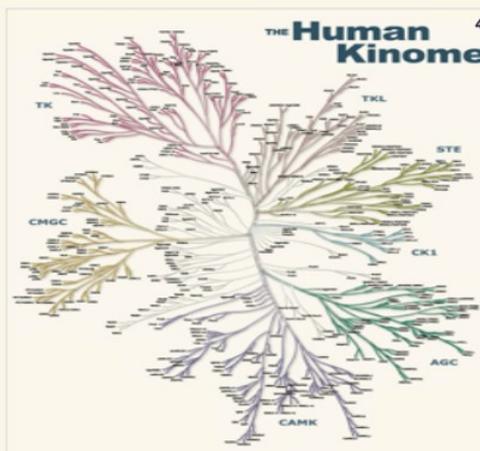


Non-Oncology



>70 Marketed Drugs¹ ~\$48B^{2,3}
Annual Sales of Kinase Drugs

Most Members of the Kinome Remain Unexplored



518 Members
>90% of the Hum:
Kinome remains
undrugged⁵

Creating New Medicines Targeting Previously Inaccessible Kinome Targets

Note: All trademarks are the property of their respective owners.

1. GoodRx. Accessed January 4, 2023. <https://www.goodrx.com/kinase-inhibitors/>; 2. Data on file; 3. Oprea TI, et al. Unexplored opportunities in the druggable human genome. Nature Rev Drug Disc Poster Jan. 2017; 4. Manning G, et al. Science. 2002;298(5600):1912-1934; 5. Oprea TI, et al. Nat Rev Drug Discov. 2018;17(5):317-332.

Precision Immunology with the KINect Platform

Demonstrated Success in Reversible and Covalent MOA

MK2 Inhibitors

- Zunsemetinib (ATI-450), ATI-2231: Oral anti-TNF, anti-IL17, anti-IL1, and anti-IL6
- Novel approach for a difficult to target kinase
- Broad potential in several immuno-inflammatory diseases

Unique kinase complex inhibitor

Tissue Restricted JAK Inhibitors

- ATI-1777: Skin specific (Soft) topical JAK1/3
- Oral Gut-biased JAK inhibitors
- Goal: Comparable clinical efficacy with improved safety profile

Tailoring physico-chemical and potency properties

Covalent ITK Inhibitors

- ATI-2138: ITK/JAK3 Oral T cell kinase inhibitor for autoimmune diseases

Covalent inhibition for difficult-to-target kinase

Small Molecule Therapeutics Targeting Multi-billion Dollar Immunology and Inflammation Markets

Drug Development Pipeline

| Drug Candidate / Program | Target | Route of Administration | Indication | Development Phase | Topline Data Expected |
|-------------------------------------|--------------------------|-------------------------|---|---------------------------------|---------------------------------|
| Immuno-Inflammatory Diseases | | | | | |
| Zunsemetinib (ATI-450) | MK2 inhibitor | Oral | Rheumatoid arthritis (moderate to severe) | Phase 2b | H2 2023 |
| | | | Hidradenitis suppurativa (moderate to severe) | Phase 2a | Topline Announcement March 2023 |
| | | | Psoriatic arthritis (moderate to severe) | Phase 2a | YE 2023 |
| ATI-1777 | "Soft" JAK 1/3 inhibitor | Topical | Atopic dermatitis (moderate to severe) | Phase 2b | Mid 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 | | |

Zunsemetinib (ATI-450): MK2 Inhibitor

(Investigational Drug Candidate)



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The Path From p38 α to MK2

p38 α was initially targeted for suppressing TNF α and other pro-inflammatory cytokines



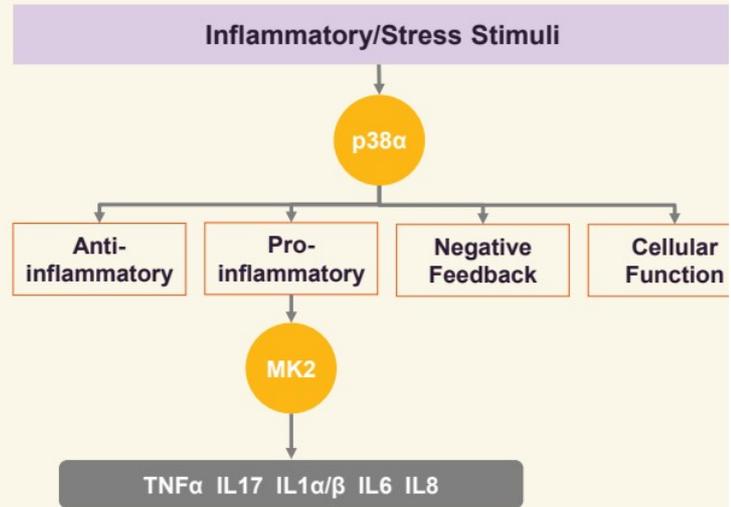
Global p38 α inhibitors have exhibited toxicity and/or lack of sustained efficacy “tachyphylaxis” in RA and IBD



p38 α phosphorylates over 60 substrates – yet MK2 drives the pro-inflammatory node of this pathway

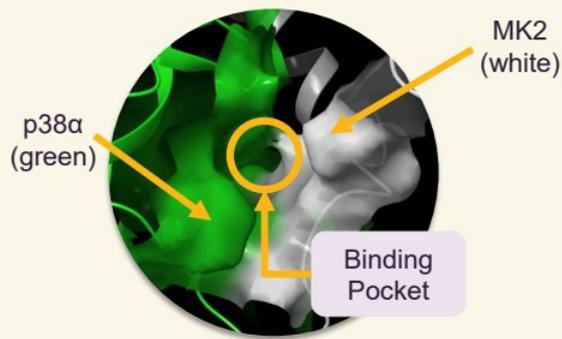


MK2 has been a high priority therapeutic target since 1999 but has proven very difficult to drug

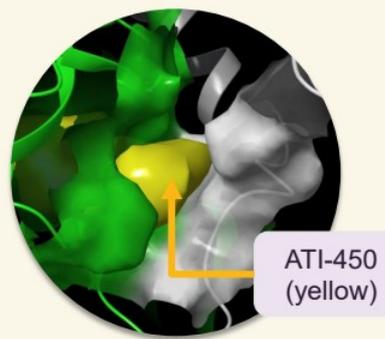


Note: Wang C, et al. J Exp Med. 2018;215(5):1315-1325; Cheung P, et al. EMBO J. 2003;22(21):5793-5805; Muniyappa H, et al. Cell Signal. 2008;20(4):675-683; Ma W, et al. J Biol Chem. 2001;276(17):13664-13674.

Novel Mechanism: Locking MK2 in an Inactive State



Crystal structure of the p38α/MK2 complex



Zunsemetinib (yellow) docked in the pocket

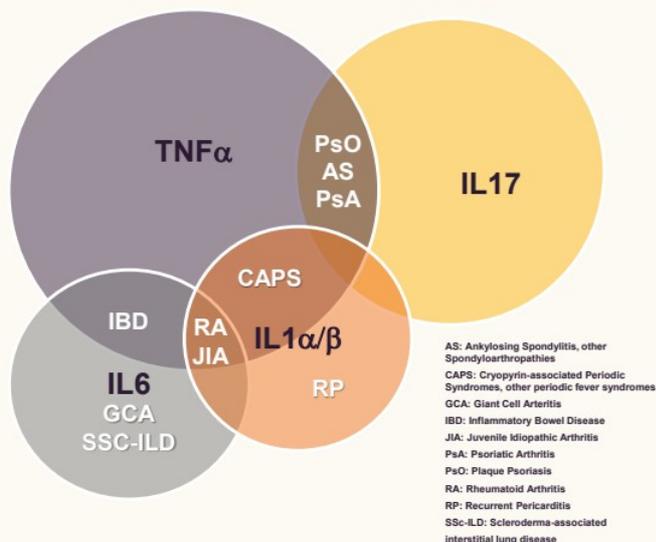
- In the nucleus, inactive MK2 and p38α dock in a high affinity complex that generates a binding pocket formed by juxtaposed walls of both proteins
- Zunsemetinib binds to both walls of the pocket, stabilizing the complex and preventing MK2 activation

Zunsemetinib locks MK2 in a catalytically inactive state – a unique MOA

Note: Wang C, et al. J Exp Med. 2018;215(5):1315-1325.

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

Inhibiting MK2 blocks $TNF\alpha$, IL17, IL1 α/β and IL6¹, the targets of commercially successful biologics



MK2 drives pro-inflammatory cytokine expression



By inhibiting multiple cytokines, zunsemetinib may be a potential treatment for multiple diseases



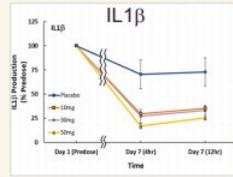
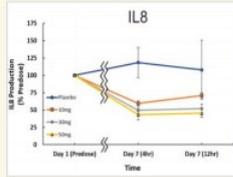
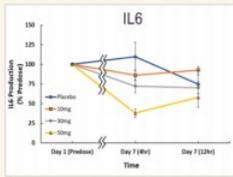
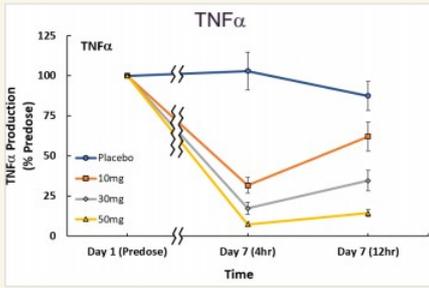
Potential alternative to injectable, anti-cytokine biologics and JAK inhibitors for immuno-inflammatory diseases

Global immunology market valued at >\$97B in 2021²

1. Data on file; 2. Fortune Business Insights. Accessed January 4, 2023. <https://www.fortunebusinessinsights.com/industry-reports/immunology-market-100657>;

Zunsemetinib Demonstrated Strong Inhibition Across Key Cytokines

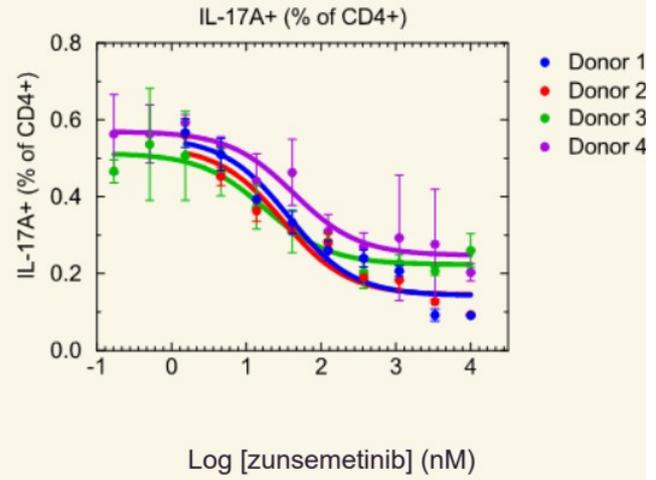
Zunsemetinib dosed orally BID for 7 days in healthy subjects at doses of 10, 30 or 50 mg in Phase 1



Note: Data on file

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hPBMc treated with antiCD3/28 for 72 hr in-vitro



aclaris
THERAPEUTICS

Zunsemetinib Phase 2a Trial in Rheumatoid Arthritis

Summary of Clinical Data

Potent and Durable Clinical Efficacy with 50mg

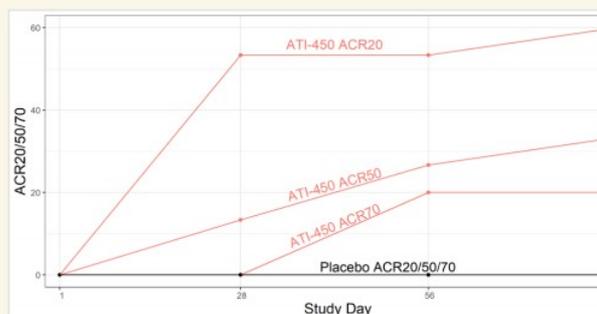
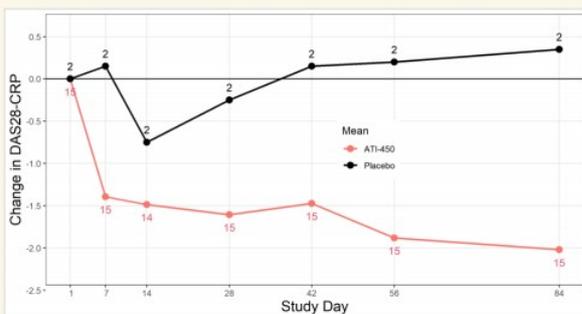
Main Objectives of POC Study were addressed

Potent and durable clinical efficacy with 50mg BID:

- DAS-28-CRP reduction persisted
- ACR effect comparable to other mechanisms
- hsCRP reduction maintained

Zunsemetinib was generally well tolerated

Summary of Efficacy Endpoints



Phase 2 Clinical Development: Zunsemetinib

Hidradenitis Suppurativa 12-week phase 2a randomized trial

Trial size: 95 subjects

Dose arms: Randomized 1:1 to
Zunsemetinib 50 mg BID
and placebo

Entry criteria:
Moderate-severe HS

Topline Data Announced:
March 2023

Rheumatoid Arthritis 12-week phase 2b randomized trial

Trial size: 240 subjects

Dose arms: Randomized 1:1:1
to Zunsemetinib 50 mg BID, 20
mg BID and placebo

Entry criteria: Moderate-severe
RA on methotrexate

Expected Topline Data:
2H 2023

Psoriatic Arthritis 12-week phase 2a randomized trial

Trial size: 70 subjects

Dose arms: Randomized 1:1 to
Zunsemetinib 50 mg BID
and placebo

Entry criteria: Moderate-severe
PsA unresponsive to ≥ 1 non-
biologic DMARD

Expected Topline Data:
YE 2023

Hidradenitis Suppurativa Phase 2a Preliminary Topline Data Summary

- Preliminary topline data announced in March 2023
 - ✓ Zunsemetinib in HS did not meet any primary or secondary efficacy endpoints
 - ✓ PD profile of zunsemetinib in trial demonstrated activity generally consistent to that observed in prior studies of zunsemetinib
 - In a subset of patients, *ex vivo* stimulated cytokines demonstrated knock-down consistent with prior RA trial at both Day 1 and Day 85 demonstrating no tachyphylaxis
 - Although endogenous cytokines in HS patients were, as expected, not significantly elevated relative to healthy donors, zunsemetinib reduced levels to near those of healthy donors
 - ✓ Safety profile of zunsemetinib bolstered
 - No serious adverse events, no serious or opportunistic infections, no end organ toxicity
 - Discontinuations due to adverse events were largely associated with lack of clinical efficacy
 - ✓ CPK elevations were relatively balanced (15 patients on zunsemetinib vs. 11 on placebo)
 - CPK elevations were either minor or generally transient in nature and resolved on continued treatment
 - None were accompanied by any related signs or symptoms (i.e.: muscle weakness, cardiac)
- Company expects to discuss more detailed trial results and learnings during upcoming corporate update call in May

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 condition¹

- The U.S. prevalence of AD is reported to be 11.3–12.7% in children and 6.9–7.6% in adults²
- 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 trials⁴

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 moderate 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
- 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

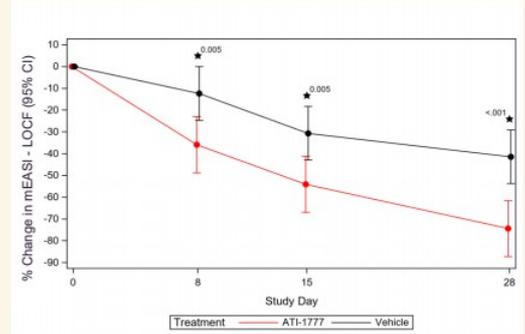
1. Medscape. Accessed January 7, 2023. <https://emedicine.medscape.com/article/1049085-overview>. 2. Silverberg J. Dermatol Clin. 2017;Jul;35(3):283-289; 3. Auster M, et al. Something Big Is Ge Bigger [research note]. Credit Suisse Equity Research; 2019; 4. Shreberk-Hassidim R, et al. J Am Acad Dermatol.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

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

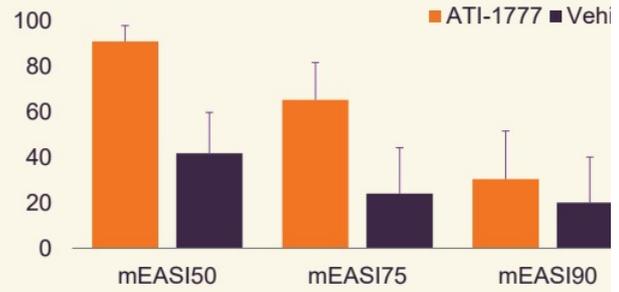
Phase 2a Trial Highlights

- 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)**



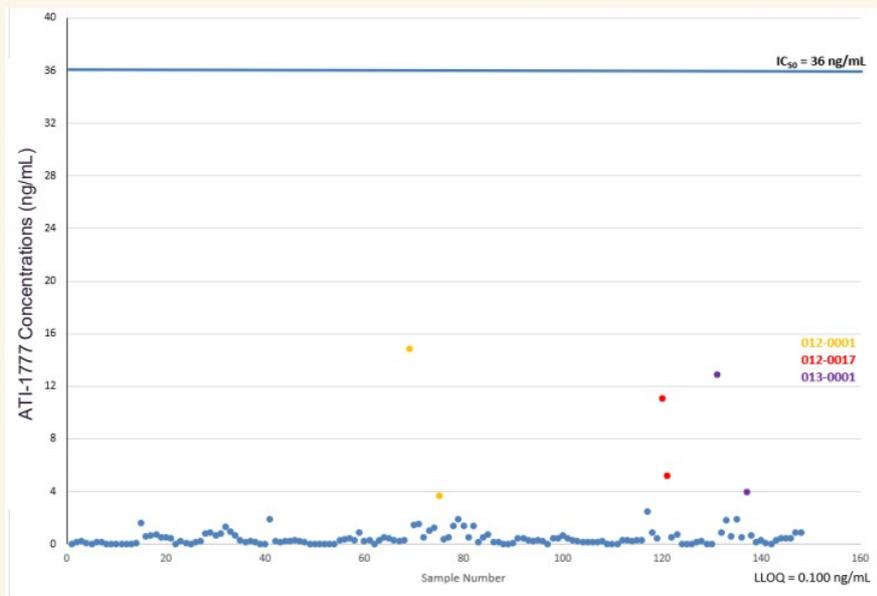
**Secondary Efficacy Endpoint:
mEASI50/75/90 at Day 28 (FAS)**



Note: (FAS): Full Analysis Set

Low Plasma Levels of ATI-1777 Following Topical Application

PK Plasma Concentrations of ATI-1777 in Subjects



Note: Data on file

- All concentrations < $\frac{1}{2}$ IC₅₀ (IC₅₀ = 36 ng/mL for JAK1/3)
- >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 IC₅₀
- Only 3 subjects (6 out of 148 total samples) with concentrations > 1/10th the IC₅₀



Positive Proof of Concept First in Human Study

- Moderate to Severe Atopic Dermatitis
 - ✓ Traditionally the domain of systemic therapy
- Rapid and continuing improvement over 4 weeks
- PK supports lack of systemic drug penetration
- Generally, well tolerated



Potential Positioning in Moderate to Severe Atopic Dermatitis

- Monotherapy
- Combination therapy with biologics to potentially drive improved efficacy¹



Licensing Agreement with Pediatrix Therapeutics for Greater China



Phase 2b Data Upcoming in Atopic Dermatitis (Expected Mid-Year 2023)

1. Reich, Teixeira, Bruin-Weller, Bieber, Lancet 397, Issue 10290, P2169-2181, June 5, 2021
Note: Data on file

ATI-2138 (ITK/JAK3 Inhibitor)

(Investigational Drug Candidate)



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ATI-2138: Covalent ITK/JAK3 Inhibitor with Potential for Ulcerative Colitis and other T Cell-Mediated Diseases

Background



- ATI-2138 covalently blocks ITK/JAK3¹
 - ✓ Potential for synergistic efficacy
 - ITK required for T cell receptor (TCR) signaling
 - JAK3 required for IL2R γ common cytokines (IL-2/4/7/9/15/21)
- JAK3 is the only JAK that is inhibited
- Tissue restricted expression could enhance safety
- ATI-2138 is selective for T cell signaling^{2,3}
- ATI-2138 has the potential to treat T cell-mediated autoimmune diseases^{4,5}

Status



- Phase 1 Single Ascending Dose Study successfully completed
- Phase 1 Multiple Ascending Dose Study initiated
- Phase 2a Proof of Concept study in Ulcerative Colitis under development

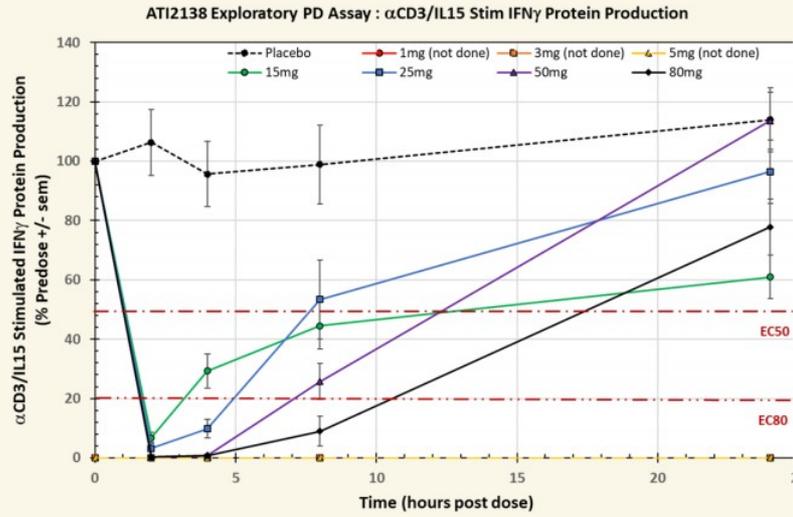
1. Data on file; 2. Graham RM. Cleve Clin J Med. 1994;61(4):308-313; 3. Siliciano JD, et al. Proc Natl Acad Sci U S A. 1992;89(23):11194-11198; 4. Robinson MF, et al. [published online ahead of print, 2020 May 18]. Arthritis Rheumatol. 2020; 5. Russell SM, et al. Science. 1995;270(5237):797-800

Simultaneous Stimulation of the ITK and JAK3 Pathways was Dose-Dependently Inhibited by ATI-2138

Phase 1 SAD Trial Highlights

- Safety Profile
 - ✓ ATI-2138 was generally well tolerated at all doses tested in the trial up to 80mg single dose
- PK
 - ✓ The PK data demonstrated dose-dependent exposure
 - ✓ Terminal half-life ranged from 1.5 – 2.5 hours
- PD
 - ✓ Dose-dependent inhibition of both ITK and JAK3 exploratory PD biomarkers was observed

Assesses modulation of both ITK and JAK3 via α CD3/IL-15-induced IFN γ protein production

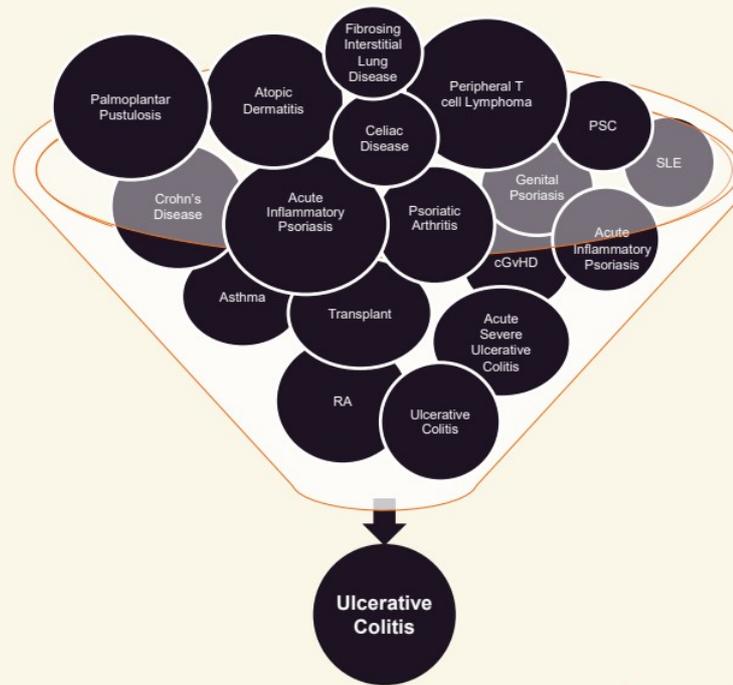


Pharmacodynamic Dual Stimulation Assay

Wide Array of Disease Targets for ATI-2138

Ulcerative Colitis Selected as First Indication for Proof of Concept

- Genetic linkage of the ITK locus to a murine model of disease¹
- Elevated expression of ITK in colonic mucosa of UC patients¹
- Similar T cell signaling of pathway of cyclosporine, a successful treatment for US that bears significant toxicity risks
- Continued need for new treatment approaches in UC, with increasing incidence and prevalence expected in the future²



1. Gastroenterology 2021; 161:1270-87; 2. Lancet GI&Hep, 2020. 5(1)17-30.

Corporate Highlights



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Empowering Patients Through Kinome Innovation



Executive Team

Proven track record of R&D, business development and scientific leadership in immuno-inflammatory diseases



KINect Technology Platform

Proprietary discovery engine enables targeted design of novel drug candidates



Pipeline

Multiple therapeutic programs ranging from discovery to clinical development



Intellectual Property

Global IP estate



Financial Strength

Ended Q4 2022 with \$230M of cash, cash equivalents and marketable securities and cash runway expected through end of 2025



Commitment to Patients

Focus on addressing the needs of patients with immuno-inflammatory diseases who lack satisfactory treatment options

Experienced Leadership Team



Douglas Manion
Chief Executive Officer

Over 25 years Pharmaceutical Industry Experience

Former EVP of R&D at Arena Pharmaceuticals

Former CEO of Kleo Pharmaceuticals

Former R&D leadership roles at BMS, GSK and DuPont Pharmaceuticals



Joseph Monahan
Chief Scientific Officer

Over 35 years pharmaceutical research experience

Lead Founder and Former CSO of Confluence Life Sciences

Former Pfizer Leader of Global Kinase Team

> 100 publications and patents (>30 total on kinases)



Matthew Rothman
General Counsel

Over a decade of legal leadership experience

Former corporate and securities group associate at Dechert LLP



Gail Cawkwell
Chief Medical Officer

Pediatric rheumatologist and epidemiologist with over 20 years of pharmaceutical development and medical affairs experience

Former SVP of Medical Affairs and Safety at Intercept Pharmaceuticals

Former leadership roles at Pfizer and other pharmaceutical companies



Kevin Balthaser
Chief Financial Officer

Over 13 years of financial leadership including 10 years in the pharmaceutical industry

Former accounting and finance roles at Lannett Company, Inc. and Pricewaterhouse Coopers, LLP.

Certified Public Accountant



James Loerop
Chief Business Officer

Over 30 years of pharmaceutical and biotech business development experience

Former EVP of Business Development at Anika Therapeutics

Former Business Development leadership roles at Alexion, GSK and Stifel Laboratories

Drug Development Pipeline

| Drug Candidate / Program | Target | Route of Administration | Indication | Partner | Development Phase |
|-------------------------------------|--------------------------|-------------------------|---|---|-------------------|
| Immuno-Inflammatory Diseases | | | | | |
| Zunsemetinib (ATI-450) | MK2 inhibitor | Oral | Rheumatoid arthritis (moderate to severe) | | Phase 2b |
| | | | Hidradenitis suppurativa (moderate to severe) | | Phase 2a |
| | | | Psoriatic arthritis (moderate to severe) | | Phase 2a |
| ATI-1777 | "Soft" JAK 1/3 inhibitor | Topical | Atopic dermatitis (moderate to severe) |  | Phase 2b |
| ATI-2138 | ITK/JAK3 inhibitor | Oral | T cell-mediated autoimmune diseases | | Phase 1 |
| Gut-Biased Program | JAK inhibitor | Oral | Inflammatory bowel disease | | Discovery |
| Oncology | | | | | |
| ATI-2231 | MK2 inhibitor | Oral | Metastatic breast cancer | | Preclinical |
| | | | Pancreatic cancer | | |

Note 1: In November 2022, Aclaris Therapeutics and Pediatrix Therapeutics Announced a License Agreement for ATI-1777 in Greater China
 2: All trademarks are the property of their respective owners.

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2023 Expected Data Readouts

