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): September 18, 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 7.01 Regulation FD Disclosure.

On September 18, 2023, Aclaris Therapeutics, Inc. (the "***Company***") issued a press release announcing positive preliminary results from its Phase 1 multiple ascending dose trial of ATI-2138, an investigational oral covalent ITK/JAK3 inhibitor (the "***ATI-2138 Phase 1 Results***"). Based on these results, the Company will progress this program into a Phase 2a proof of concept study in patients with ulcerative colitis, its previously announced intended first clinical development target, and anticipates initiation of the trial in early 2024. A copy of this press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Additionally, on September 18, 2023, the Company posted a slide presentation on its website regarding the ATI-2138 Phase 1 Results. A copy of this slide presentation is furnished as Exhibit 99.2 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, Exhibit 99.1 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 Company'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 September 18, 2023.
99.2	Company Presentation.
104	The cover page from Aclaris Therapeutics, Inc.'s Form 8-K filed on September 18, 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: September 18, 2023

Exhibit 99.1

Aclaris Therapeutics Announces Positive Results from Phase 1 Multiple Ascending Dose Trial of ATI-2138, an Investigational Oral Covalent ITK/JAK3 Inhibitor

- Preliminary Data Support Progression to Phase 2a Proof of Concept Trials in T cell-mediated Autoimmune Diseases -

WAYNE, Pa., Sep. 18, 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 positive results from ATI-2138-PKPD-102, a Phase 1 Multiple Ascending Dose (MAD) trial of the investigational compound ATI-2138.

Preliminary data from the MAD trial demonstrated:

- that ATI-2138 was generally well tolerated at all doses tested in the trial;
- that ATI-2138 had dose proportional pharmacokinetics (PK); and
- a dose-dependent inhibition of both ITK and JAK3 exploratory pharmacodynamic (PD) biomarkers, with near maximal inhibition achieved at the 30 mg total daily dose.

Based on these results, Aclaris will progress this program into a Phase 2a proof of concept study in patients with ulcerative colitis, its previously announced intended first clinical development target, and anticipates initiation of the trial in early 2024. Aclaris is also exploring the potential of conducting a second proof of concept trial in an additional T cell-mediated autoimmune disease.

ATI-2138-PKPD-102 was a two-week Phase 1 MAD trial to investigate the safety, tolerability, PK and PD of ATI-2138 in healthy volunteers. The study enrolled 60 healthy subjects across 6 dosing cohorts ranging from 10 to 80 mg of total daily doses, with 8 active/2 placebo controlled per arm. No serious adverse events were reported. The most common adverse events in subjects treated with ATI-2138, and the only events occurring in more than 1 subject, were headache (assessed as mild, 2 subjects on 5 mg BID, 1 on 40 mg BID) and diarrhea (assessed as mild, 2 subjects on 5 mg BID).

“The advancement of ATI-2138 to proof-of-concept stage of development marks yet another example of the strength of our world class discovery group and the KINect® platform,” stated Doug Manion, M.D., Aclaris’ Chief Executive Officer. “It is a rarity for a biotech company of our size to be armed with a productive discovery engine and expertise that rivals larger pharmaceutical companies.”

Continued Manion, “With so much unmet medical need remaining in immuno-inflammatory diseases such as ulcerative colitis, it is gratifying for all of us at Aclaris to progress the development of ATI-2138 for patients who remain underserved by the existing treatment options for the disease. Additionally, we look forward to the data from our two most advanced programs – zunsemetinib (ATI-450) in rheumatoid arthritis and ATI-1777 in atopic dermatitis – expected later this year.”

Aclaris has made available a related presentation for the ATI-2138 MAD trial data which can be found on the “Investors” section of its website, www.aclaristx.com.

About ATI-2138

ATI-2138 is an investigational oral covalent ITK/JAK3 inhibitor that is being developed as a potential therapeutic option across a variety of T cell-mediated diseases. ITK is a T cell receptor activated kinase involved in driving T cell effector functions while JAK3 is a non-receptor tyrosine kinase responsible for the signal transduction of common gamma receptor cytokines, IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21. In blocking both T cell receptor function and cytokine signaling, ATI-2138 has potential utility in T cell driven diseases. ATI-2138 is currently in clinical development and its safety and efficacy has not been evaluated by regulatory authorities.

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 “anticipate,” “believe,” “expect,” “intend,” “may,” “plan,” “potential,” “will,” and similar expressions, and are based on Aclaris’ current beliefs and expectations. These forward-looking statements include Aclaris’ expectations regarding the timing of the Phase 2a trial of ATI-2138 in ulcerative colitis as well the potential future opportunities for the clinical development of ATI-2138, and the timing of reporting results from other clinical trials. 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 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 Contact:

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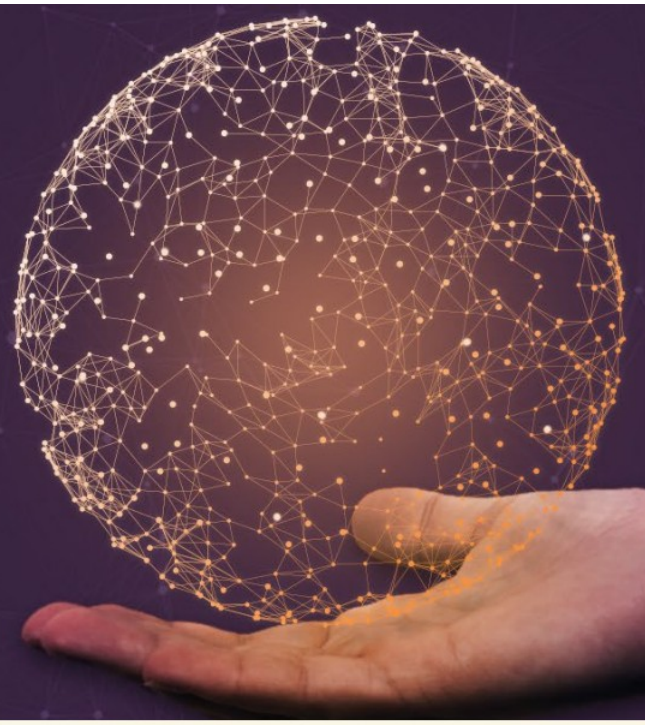
rdoody@aclaristx.com

EMPOWERING PATIENTS THROUGH
KINOME INNOVATION

ATI-2138: An Investigational Novel Covalent ITK-JAK3 Inhibitor for T-Cell Mediated Diseases



18 Sep 2023

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Cautionary Note Regarding Forward-Looking Statements

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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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ATI-2138: Combined IL-2-Inducible Tyrosine Kinase (ITK) & JAK3 Inhibitor for Autoimmune Disease

- ATI-2138 is an oral compound which interrupts T cell receptor (TCR) signaling by inhibiting ITK and JAK3 signaling of common γ chain cytokines in lymphocytes (including IL-2 & IL-15)
- ATI-2138 potently and selectively inhibits ITK and JAK3 (with some activity at TXK)
- ATI-2138 has demonstrated the prevention of inflammation in animal models of colitis and arthritis
- Safety, pharmacology and toxicology studies have been completed and support further development
- Phase 1 SAD and MAD studies in healthy volunteers have been completed
  - ✓ ATI-2138 was generally well tolerated and no serious adverse events were reported
  - ✓ PK was dose proportional with adequate exposure to block ITK and JAK3 in PD biomarker assays
- Aclaris is evaluating ATI-2138 for the potential treatment of a number of T cell-mediated autoimmune diseases
- A Phase 2a ulcerative colitis trial is in protocol development and operational preparations are under way

The unique pharmacological profile of ATI-2138 provides opportunity for differentiation

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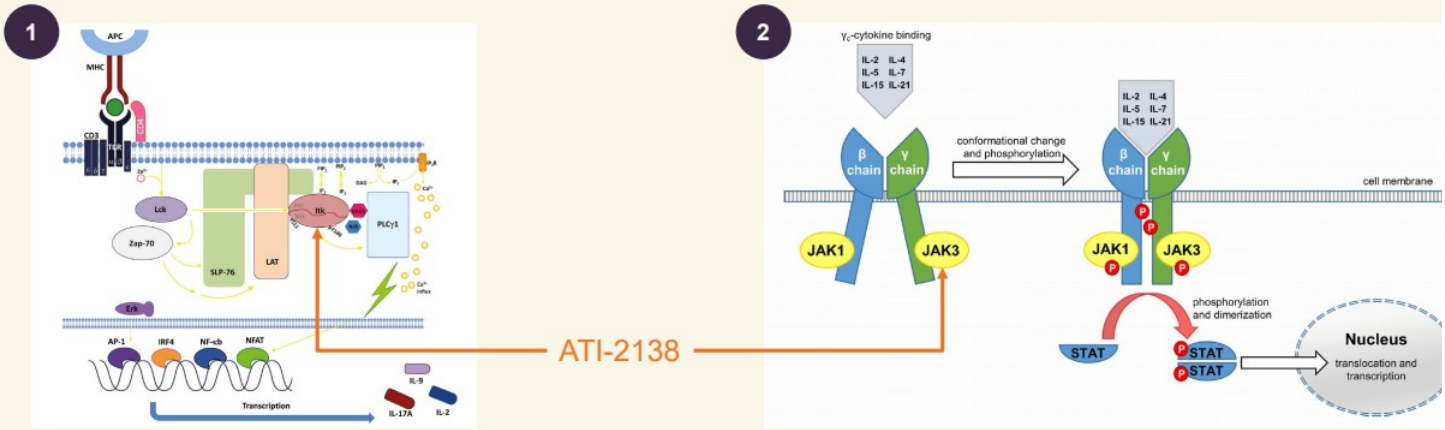
ATI-2138 is a Combined Covalent IL-2-Inducible Tyrosine Kinase (ITK) & JAK3 Inhibitor for Autoimmune Disease



- ATI-2138 is an investigational oral compound which interrupts T cell receptor (TCR) signaling by inhibiting ITK and JAK3 signaling of common γ chain cytokines in lymphocytes (including IL-2 & IL-15) and is designed to reduce T cell differentiation, proliferation and cytokine production
- ATI-2138 is differentiated from other kinase inhibitors as it is highly potent for both ITK and JAK3 (IC50: 0.2nM ITK; 0.5nM JAK3)[3]
- Aclaris is evaluating ATI-2138 for the potential treatment of a number of T cell mediated autoimmune diseases including ulcerative colitis

1. Lechner KS, Neurath MF, Weigmann B. Role of the IL-2 inducible tyrosine kinase ITK and its inhibitors in disease pathogenesis. J Mol Med (Berl). 2020 98(10):1385-1395; 2. Forster M, Gehringe Laufer SA. Recent advances in JAK3 inhibition: Isoform selectivity by covalent cysteine targeting. Bioorg Med Chem Lett. 2017 15;27(18):4229-4237.; 3. Study Report SR03001

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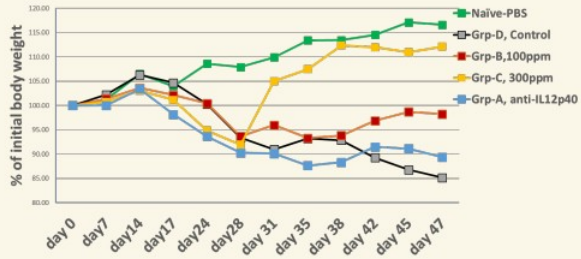
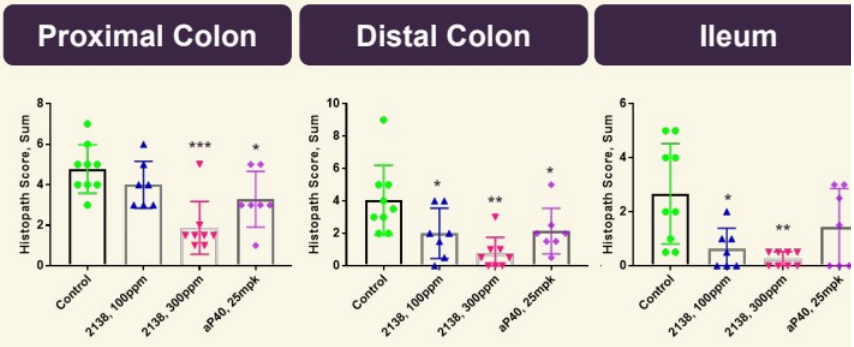
ATI-2138 Dose-Dependently Inhibited Inflammation in the Mouse T Cell Transfer Model of Inflammatory Bowel Disease





ATI-2138 inhibited colitis in the mouse T cell transfer model[1,2,3]

ATI-2138 dose-dependently decreased inflammation in proximal and distal colon, and ileum

Greater effect than anti-IL12 (P40) that significantly decreased inflammation in the proximal and distal colon

1. Study report SR03048; 2. CD4+CD45RB high naïve T cells injected to SCID mice; 3. *p<0.05, **p<0.01, ***p<0.001, vs Control group

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ATI-2138 Phase 1 Multiple Ascending Dose Study Design

N=60 | **5 Cohorts** | **2 Weeks of Treatment** | **8 Active and 2 Placebo Subjects per Arm**

Eligibility

- Healthy subjects age ranging between 18 and 55 years of age, inclusive at screening
- Minimum weight of 50 kg
- Body mass index of 18 to 32 kg/m2, inclusive

Cohort	No. Subjects	Dose
1	10	5 mg BID
2	10	15 mg BID
3a	10	30 mg QD[1]
3b	10	10 mg TID[1]
4	10	25 mg BID
5	10	40 mg BID

Objectives

- Primary
  - ✓ To assess the safety and tolerability of ATI-2138 following multiple oral doses ATI-2138 in healthy participants
- Secondary
  - ✓ To explore the pharmacokinetic (PK) profile of ATI-2138 following multiple or doses of ATI-2138 in healthy participan
- Exploratory
  - ✓ To explore the pharmacodynamic (PD) response to ATI-2138 following multiple oral doses of ATI-2138 in healthy participants

1. Not part of dose escalation

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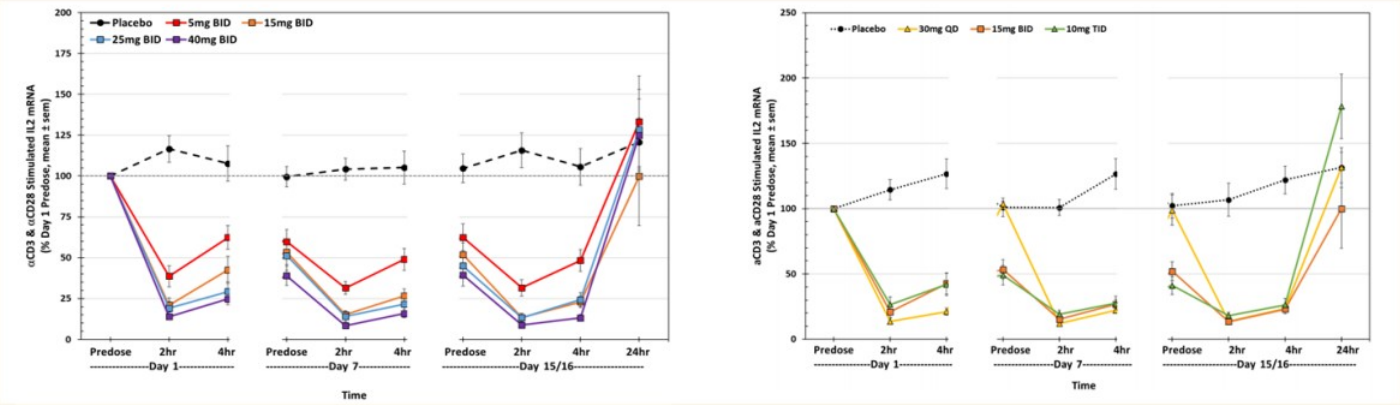
Dose-dependent Inhibition of Both ITK and JAK3 Exploratory PD Biomarkers was Observed in MAD Study

Anti-CD3 & anti-CD28 Stimulated IL-2 mRNA Expression (BID Cohorts left; 30mg Daily Cohorts right)



- Pharmacodynamic biomarkers - Ex-vivo stimulation of whole blood taken from subjects before and after administration of ATI-2138
- Stimulation with anti-CD3 and anti-CD28 (readout IL-2 mRNA; T-cell activation) – shown above, IL-15 (readout IFNγ; JAK1/3 activation) – not shown, and dual stimulation (readout IFNγ; T-cell and cytokine stimulation) – not shown
- ATI-2138 showed dose and time dependent inhibition of all stimulation conditions
- ATI-2138 30-80mg daily doses inhibited biomarker readouts by ~50-90% across the dosing intervals

Source – Data on file

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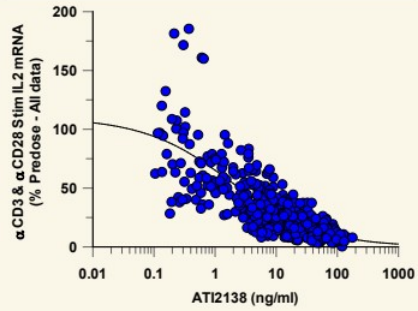
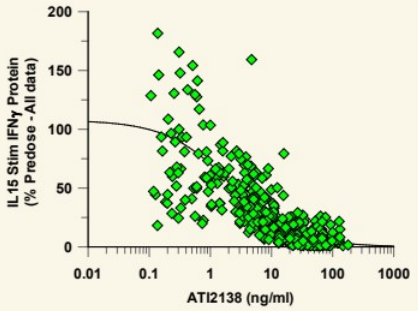
High Potency of ATI-2138 for ITK and JAK3 Observed in Preclinical Studies is Maintained in the SAD/MAD Clinical Study

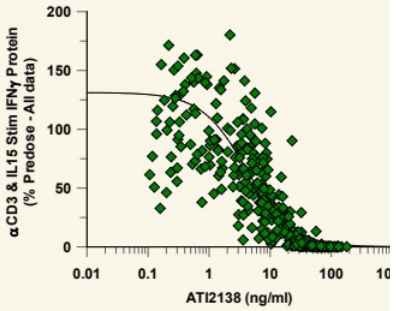
αCD3 & αCD28 stim IL-2 mRNA



IL15 stim IFNγ protein



αCD3 & IL15 stim IFNγ protein



MAD EC_{50} :	1.9ng/ml / 5.3nM	2.2ng/ml / 6.1nM	4.1ng/ml / 11.4nM
SAD EC_{50} :	5.5ng/ml / 15.2nM	(not done)	2.6ng/ml / 7.3nM
Preclinical IC_{50}* :	7.7ng/ml / 21.3nM	2.9ng/ml / 8.0nM	3.6ng/ml / 10.1nM

- Exposure response data in Phase 1 SAD and MAD clinical studies
- ATI-2138 potency comparison to preclinical cell assay data
- No significant change when comparing Day 1, 7 & 15 EC_{50} values

1. Assay configured slightly different from clinical assay

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ATI-2138 Multiple Ascending Dose: Preliminary Data Summary

Safety

- ATI-2138 was generally well tolerated at all doses tested in the trial.
- No serious adverse events were reported.
- The most common adverse events in subjects treated with ATI-2138, and the only events occurring in more than 1 subject, were headache (2 subjects on 5 mg BID, 1 on 40 mg BID, all mild, resolved) and diarrhea (2 subjects on 5 mg BID– both single episodes, both mild).

Pharmacokinetics

- ATI-2138 was rapidly absorbed and cleared from the human body.
- Multiple doses ranging from 10 to 80 mg daily over two weeks in healthy volunteers showed linear PK and dose-dependent increases in exposure.
- At 30 mg daily, ATI-2138 plasma concentration reached the targeted level established using preclinical data.

Pharmacodynamics

- Dose-dependent inhibition of both ITK and JAK3 exploratory PD biomarkers was observed.
- Near complete inhibition of the dual ITK and JAK3-stimulated IFNγ protein production was observed at 15 mg BID, with minimal incremental benefit at higher doses.

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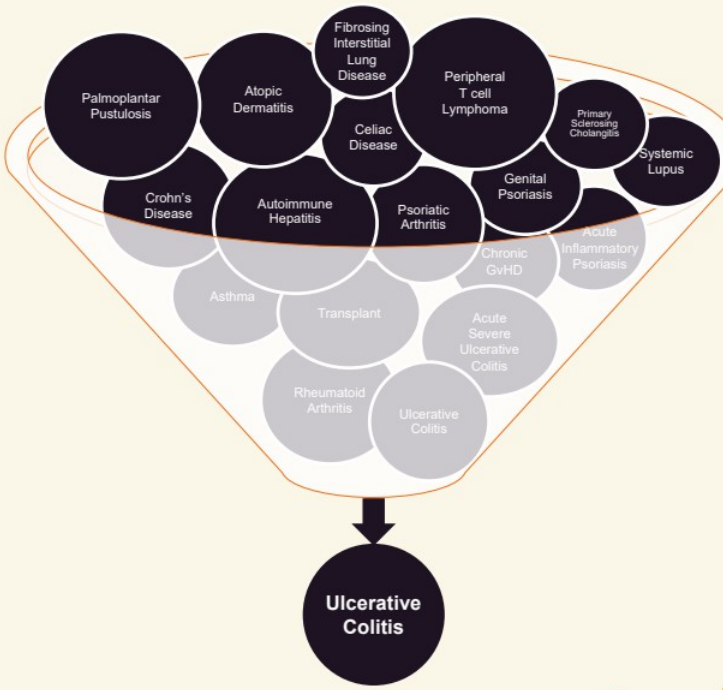
Initial Proof of Concept Trial in Ulcerative Colitis is Planned

- Cyclosporin A (CsA) is approved to treat UC and the mechanism of action is potentially related to inhibition of ITK in mucosal CD4+ T cells in animal models[1]
- The capacity of CsA to reduce experimental colitis may be dependent on ITK[1]
- Genetic inactivation of ITK prevented experimental colitis in 3 separate IBD models[1]
- ATI-2138 treatment suppressed established colitis in the mTCT model[2]



1. Lechner K et al. 2021. Gastroenterology;161(4):1270-1287.e19; 2. Study Report SR03048