

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 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 21, 2019

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:

<u>Title of Each Class:</u>	<u>Trading Symbol(s)</u>	<u>Name of Each Exchange on which Registered</u>
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 21, 2019, management of Aclaris Therapeutics, Inc. (the “*Company*”) will present a company overview at SVB Leerink’s 13th Annual POLARxPRESS Bus Tour in New York, New York. The presentation will include a slide presentation. A copy of this slide presentation 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 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 9.01 Financial Statements and Exhibits.

(d) Exhibits.

<u>Exhibit No.</u>	<u>Exhibit Description</u>
99.1	Company Presentation.

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: November 21, 2019

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

EMPOWERING PATIENTS THROUGH
KINOME INNOVATION

Company Overview

November 2019



Cautionary Note Regarding Forward-Looking Statements

Any statements contained in this presentation that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as "believe," "expect," "may," "plan," "potential," "will," and similar expressions, and are based on Aclaris' current beliefs and expectations. These forward-looking statements include expectations regarding Aclaris' development of its drug candidates, including the timing for initiation and completion of clinical trials, the availability of data from these trials and the timing of its regulatory submissions related to these 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, and other risks and uncertainties that are described in the Risk Factors section of Aclaris' Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, 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" section of the Investors page of Aclaris' website at <http://www.aclaristx.com>. Any forward-looking statements speak only as of the date of this presentation and are based on information available to Aclaris as of the date of this presentation, and Aclaris assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves 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.

Strategy: Development stage biotechnology company focused on immuno-inflammatory diseases



LEADERSHIP

- Physician/Scientist founded and led
- Kinome experts - combined 300+ years of R&D experience immunology and inflammation
- World class ex-Pfizer kinase and ex-GSK immunology R&D leadership

KINect™ PLATFORM Proprietary Discovery Engine

- Versatile platform with multiple approaches for difficult to drug kinases in precedent pathways
- Fully integrated discovery and development team
- Dedicated to the design of innovative, kinase targeted medicines for immuno-inflammatory diseases
- Positioning small molecule drug candidates to parallel or exceed efficacy of high value biologics

INNOVATIVE PIPELINE (investigational drug candidates)

ATI-450

- Oral Anti-TNF, IL1, IL6
- Novel target for the potential treatment of various inflammatory indications

ATI-1777-Topical Soft-JAK1/3i

- Innovative treatment limiting systemic exposure for the potential treatment of moderate-to-severe atopic dermatitis (AD)

ATI-2138 - ITK/TXK/JAK3i

- Dual inhibitor of T-cell and cytokine receptor for the potential treatment of auto-immune disease

R&D Leadership Team

Experienced team with deep scientific and operational experience

David Gordon

Chief Medical Officer

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

Joseph Monahan, PhD

Exec. VP R&D

(Head of Discovery)

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

Walter Smith

SVP, R&D

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

Jon Jacobsen, PhD

VP, Chemistry

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

Paul Changelian, PhD

VP, Biology

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

David R Anderson, PhD

Sr. Director, Discovery, Early Development

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

Gary DeCrescenzo

SVP, Pharm Dev

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

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Pipeline

Program	Indication(s)	Preclinical	Phase 1	Phase 2	Phase 3
ATI-450 MK2 Inhibitor <i>Oral</i>	Rheumatoid Arthritis + Additional Immuno-inflammatory Indication				
ATI-1777 JAK1/JAK3 Inhibitor <i>Soft Topical</i>	Atopic Dermatitis (moderate-to-severe)				
ATI-2138 ITK/TXK/JAK3 Inhibitor <i>Oral</i>	Psoriasis, Inflammatory Bowel Disease				
JAK1/JAK3 Inhibitor <i>Oral, gut-restricted</i>	Inflammatory Bowel Disease				
ITK/JAK3 Inhibitor <i>Oral, gut-restricted</i>	Inflammatory Bowel Disease				

The Kinase Opportunity and Challenge

Creating New Medicines Targeting Previously Inaccessible Kinome Targets

Medically Important and Productive Target Class

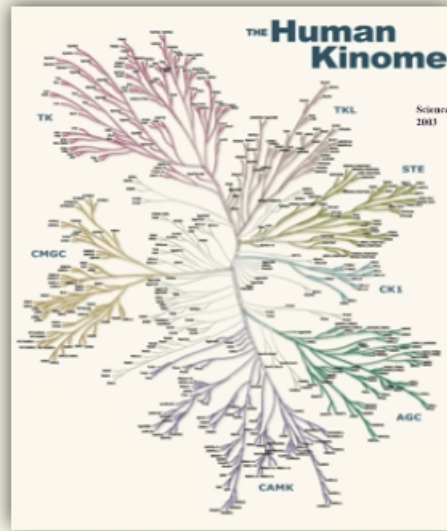


~36 Marketed Drugs

~\$48B*

Annual Sales of Kinase Drugs

Most Members of the Kinome Remain Unexplored



518 Members

>90% of the Human Kinome remains undrugged

These drugs target less than 5% of the kinome

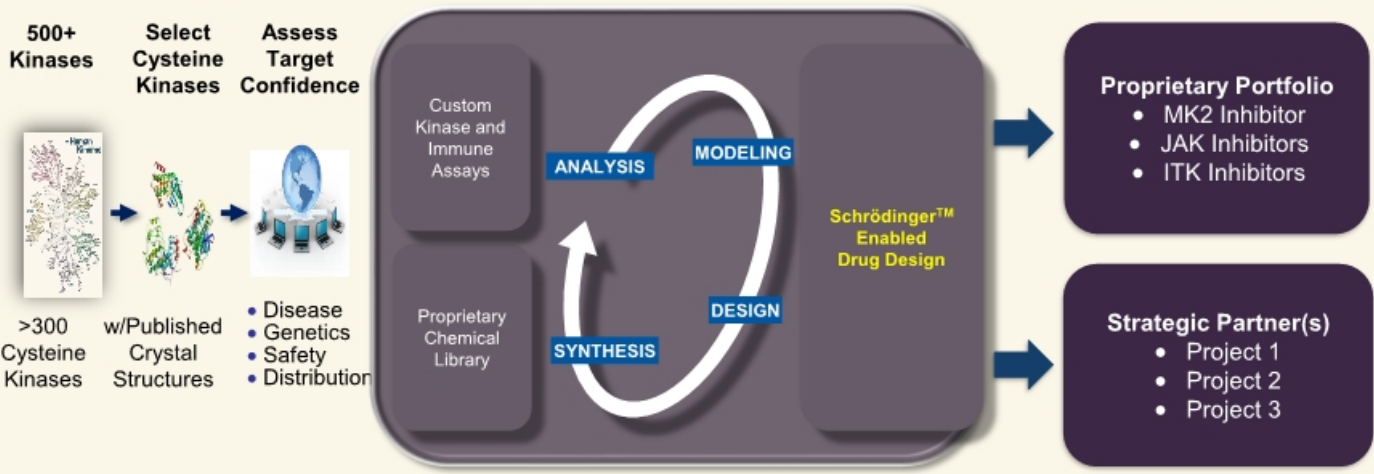
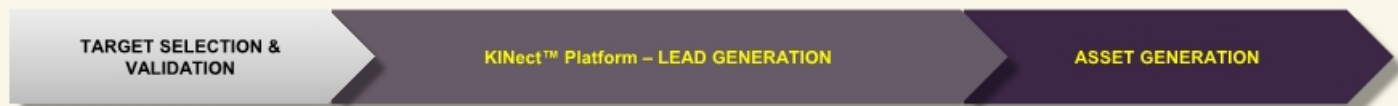
*Unexplored opportunities in the druggable human genome Nature Review Medicine

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KINect™ Platform

Developing Kinase Drug Candidates Rapidly & Efficiently



- Forward focus on the cysteinome with use of electrophilic warheads
- Leads are chemically tuned
- Multiple approaches for difficult to drug kinases
- Integrated system:
 - Structure-based drug design
 - Proprietary library of kinase inhibitor probes
 - Layers of validated translatable testing funnels
- Faster path to lead optimization
- Demonstrated success:
 - Substrate selective inhibitors
 - Tissue targeted reversible and irreversible kinase inhibitors
 - Covalent ITK inhibitors

KINect™ Platform Demonstrated Success

Reversible and Covalent

MK2 Inhibitor

Unique Substrate Selective Drug Design

- Oral anti-TNF, anti-IL1, and anti-IL6 MK2 kinase inhibitor drug
- Novel approach for a difficult to target kinase
- ATI-450 (investigational compound) currently in Phase 1 clinical trial

Tissue Restricted JAK and ITK Inhibitors

Tailoring physico-chemical and potency properties

- Potential approaches to achieve efficacy with improved safety
- ATI-1777 (investigational compound): Soft, topical drug for the potential treatment of moderate-to-severe AD
- Gut restricted inhibitor for the potential treatment for inflammatory bowel disease

Covalent ITK Inhibitors

Covalent Inhibition: for difficult to target kinase

- ITK T cell kinase inhibitors for autoimmune disease
- Reversible inhibition largely unsuccessful
- Oral and topical covalent drug candidates developed
- Oral: ATI-2138 (investigational compound) IND enabling work

Market Overview of Select Inflammatory Indications

	RA (moderate - severe)	Psoriasis (moderate - severe)	Ulcerative Colitis (moderate - severe)	Crohn's (moderate - severe)	Atopic Dermatitis (moderate - severe)
2018E WW Sales¹	~\$25B	~\$15B	~\$5B	~\$11B	~\$1B
Estimated Peak Market (WW)²	~\$25-30B	~\$20-25B	~\$8-12B	~\$15B	~\$8-12B
Prevalent US Moderate/Severe Population³	~1,000K+	~1,000-1,300K	~400-500K	~350-450K	~300-700K
Approved Agents (per target)	TNF-alpha: 5	TNF-alpha: 3	TNF-alpha: 2	TNF-alpha: 3	IgE: 1
	CD20: 1	IL-12 / IL-23: 2	Integrin α4β7: 1	IL-12 / IL-23: 1	IL-5: 3
	JAK: 2	IL-17A: 2	JAK: 1	Integrin α4β7: 1	IL-4R: 1
	Integrin α4β7: 1	PDE4: 1			
	Other: 3				
Agents in Clinic (per target)	BTK: 9	IL-23: 2	JAK/STAT: 4	JAK/STAT: 5	IL-33: 4
	JAK/STAT: 5	IL-17 / IL17R: 4	IL-23: 4	IL-23: 5	DP2 R: 2
	IL-6: 3	JAK/STAT: 2	S1P-R: 2	S1P Receptor: 3	TSLP: 1
	TNF-alpha: 1	Others: 7	Integrins: 2	Integrin α4β7: 1	IL-4R: 1
	T-cell Receptor: 1		Others: 12	Others: 12	IL-5: 1
	Others: 41				Others: 6
Opportunity for New Treatments	Orals, Improved risk/benefit, novel mechanism	Oral, novel mechanism, improved safety	Gut-restricted (improved safety)	Gut-restricted (Improved safety)	Improved risk/benefit, topical in moderate to severe

*Auster M., et al. Something Big Is Getting Bigger [research note]. New York, NY: Credit Suisse Equity Research; 2019.

(1) Estimates of total sales per indication from EvaluatePharma

(2) CS projections: based on US branded pricing

(3) Assumed peak treatable population with population with biologics/novel agents in the US: R 350-400k / Psoriasis 300-350k / Ulcerative

Colitis 225-275k / Atopic Dermatitis 150-200k / Asthma 275-325k

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ATI-450: MK2 Inhibitor

(Investigational Drug Candidate)



MK2 Inhibitor – Potential ORAL Alternative to Injectable, Anti-Cytokine Biologics and JAK Inhibitors for Immuno-Inflammatory Diseases

- MK2* is an attractive drug target because it drives pro-inflammatory cytokine expression
- The effects of inhibiting MK2 mirror the effects of anti-inflammatory biologics¹
 - **anti-TNF:** HUMIRA®, ENBREL®, REMICADE®
 - **anti-IL1:** KINERET®, ILARIS®, ARCALYST®
 - **anti-IL6:** KEVZARA®, ACTEMRA®
- ATI-450 inhibits MK2 via a novel MOA which involves binding to a drug “pocket” created in the p38 α /MK2 complex²

*MK2 = Mitogen-activated protein kinase-activated protein kinase 2

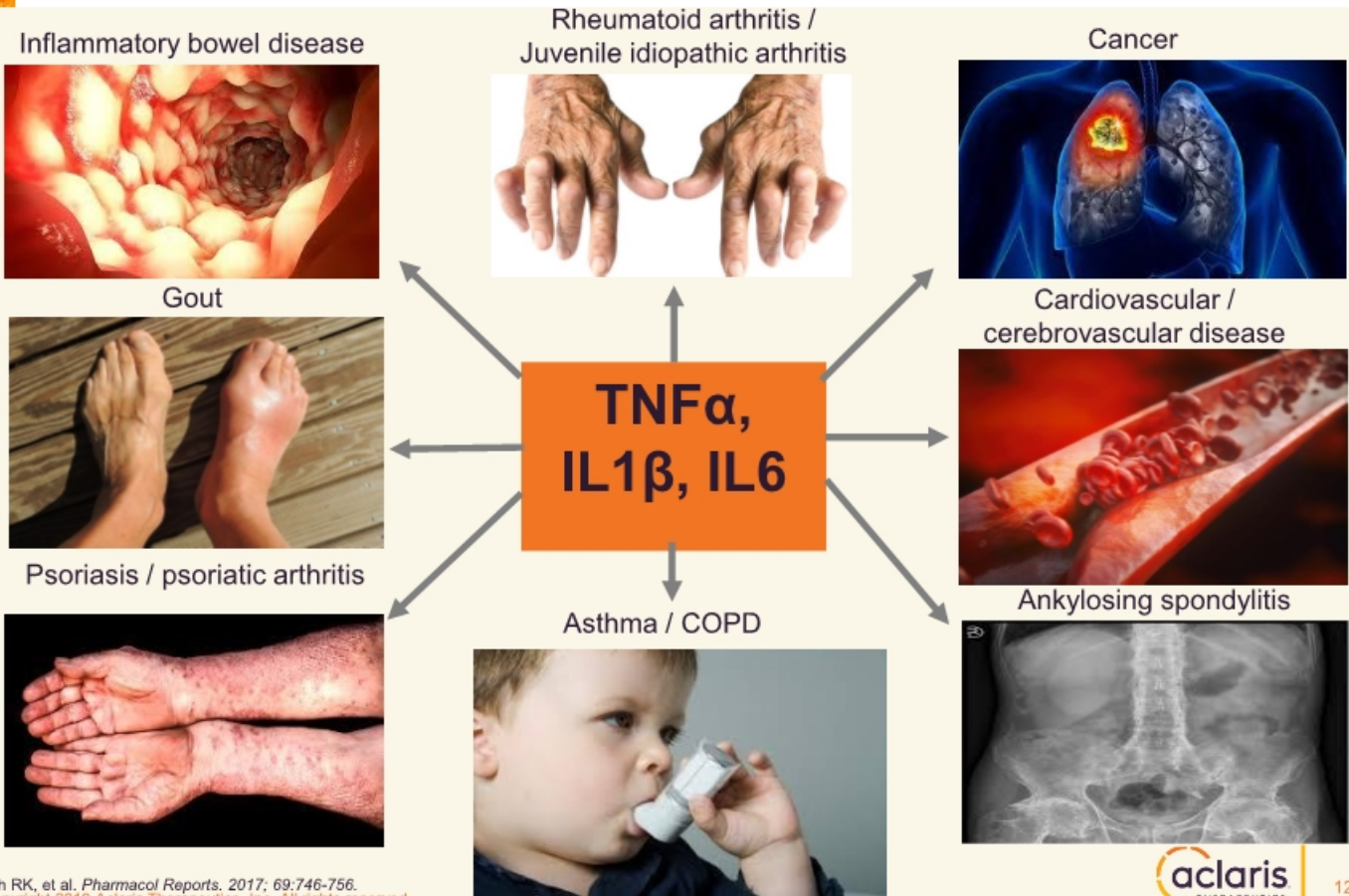
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1 Data on file

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

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MK2-driven Cytokines are Central to Many Diseases

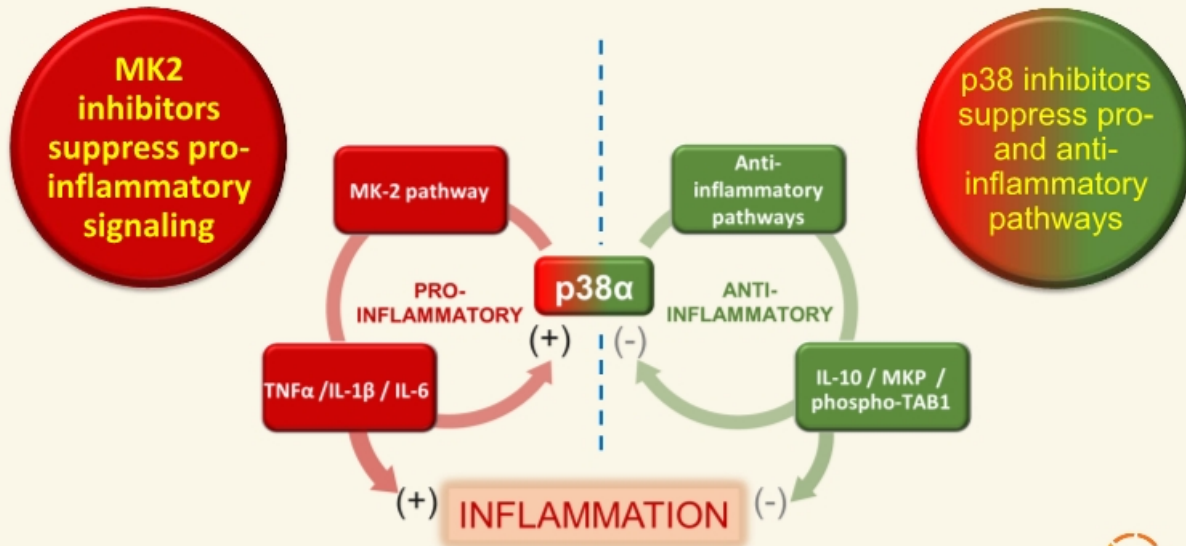


Evolution in Understanding of a Well-Known Path

The Path From p38 α to MK2

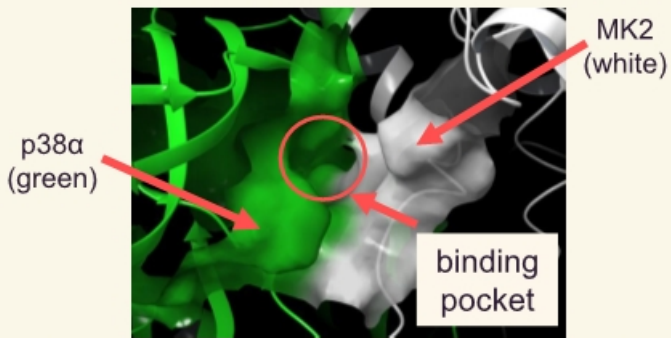
p38 α was the original therapeutic target for suppressing TNF α and other pro-inflammatory cytokines

- However, first generation p38 α inhibitors were not selective resulting in multiple safety issues including liver, kidney, GI, and skin toxicity.
- Second generation p38 α inhibitors demonstrated a lack of sustained activity in certain diseases such as RA and IBD and could not completely overcome toxicity.
- MK2 inhibitors became recognized as a more selective and targeted approach to this path.

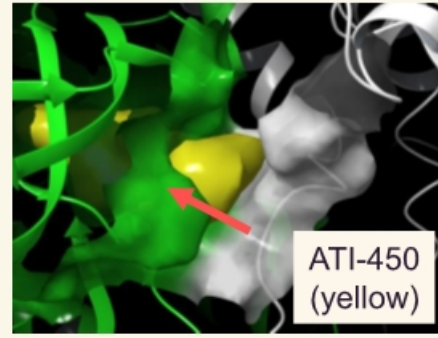


*Schindler et al. 2007. p38 pathway inhibitors as anti-inflammatory drug targets. J Dent Res. 2007;86(9): 800-811
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Capturing MK2 in an Inactive State



Crystal structure of the p38α/MK2 complex



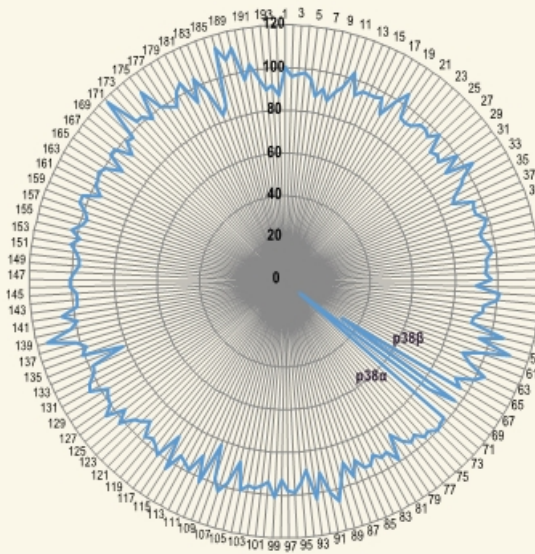
ATI-450 (yellow) docked in the pocket

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

Aclaris MK2 inhibitors lock MK2 in a catalytically inactive state – a unique MOA

ATI-450 selectivity

Human Kinome Selectivity¹



- ATI-450 (5μM) was tested vs 193 kinases
- >350-fold binding selectivity on all kinases in this panel except p38α and p38β

*Optimized p38 peptide substrate

** Data on file.

¹Wang C, et al. *J Exp Med.* 2018;215(5):1315-1325.

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MK2 Pathway Selectivity

ATI-450 is highly selective for the p38/MK2 complex vs. other p38 substrates¹

Assay	Fold Selective
p38α/MK2	1
p38α/ATF2	700
p38α/PRAK	750

ATI-450 binds to the p38α/MK2 complex with higher affinity than either p38 or MK2 alone^{**}

Assay	Fold Selective
p38α/MK2	1
p38α/p38tide*	51
MK2/HSP27	>550

Animal Models Supporting the Development of ATI-450 in Inflammatory Diseases

Therapeutic Area	Animal Model	Reference
Rheumatoid Arthritis / Psoriatic Arthritis	Rat streptococcal cell wall arthritis model <ul style="list-style-type: none"> • Protection against bone deterioration • Protection against lethality Inhibition of cellular IL1 β mRNA stability & translation	Wang C, et al. <i>J Exp Med.</i> 2018;215(5):1315-1325.
Inflammatory Bowel Disease	Adoptive transfer mouse model of colitis <ul style="list-style-type: none"> • Endoscopy scores show disease control • Decreased inflammatory infiltrate • Protected structural integrity of mucosa 	Strasser et al. <i>Integrative Biology</i> , in press - Substrate-based kinase activity inference identifies MK2 as driver of colitis.
Cryopyrin-Associated Periodic Syndromes (CAPS)	Murine NOMID (severe form of CAPS) transgenic model Human CAPS PBMC* IL1 β modulation	Wang C, et al. <i>J Exp Med.</i> 2018;215(5):1315-1325.

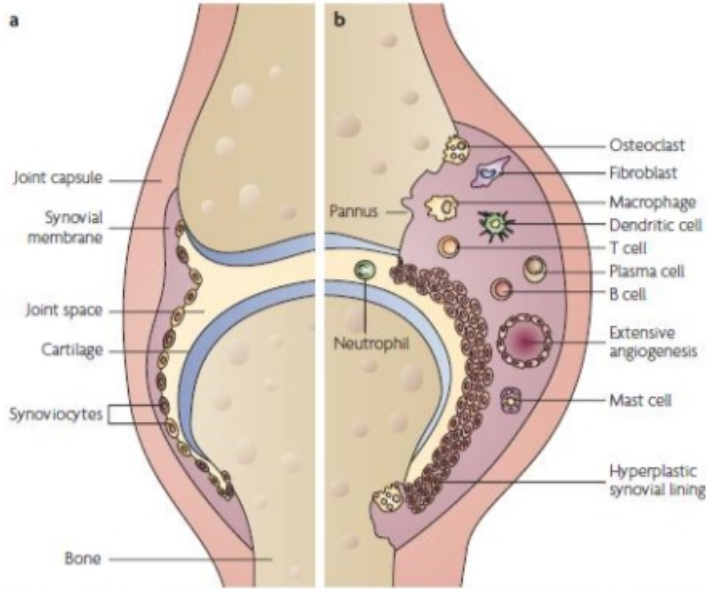
* PBMC = Peripheral blood mononuclear cells

ATI-450 Blocks MK2 – Potential Effect in Rheumatoid Arthritis

MK2 is a key regulator of essential pathogenic signals in chronic inflammatory and autoimmune diseases

Normal Joint

RA Joint



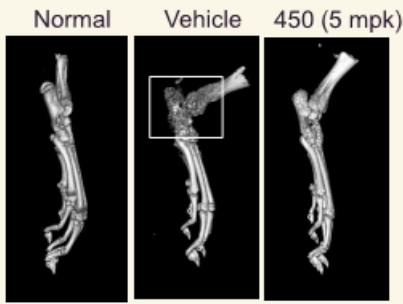
Nature Reviews Drug Discovery, Volume 6, 2007

Cells	Cytokines
Monocyte	TNFα
Macrophage	IL1β
Osteoclast	IL1α
Epithelial Cells	IL6
RA Syn Fibroblast	IL18
Chondrocytes	RANKL

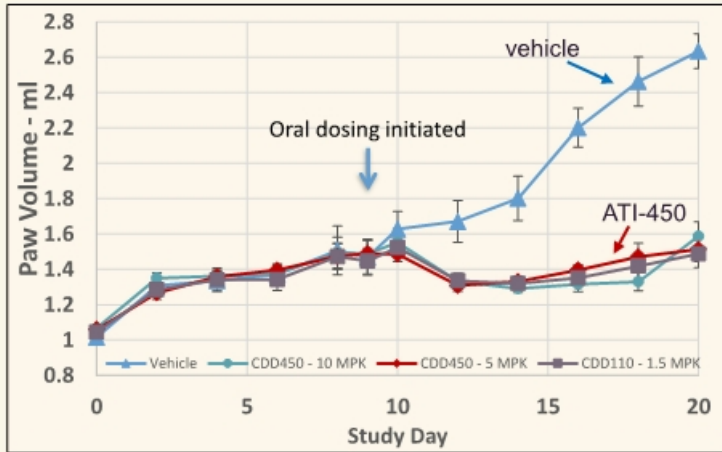
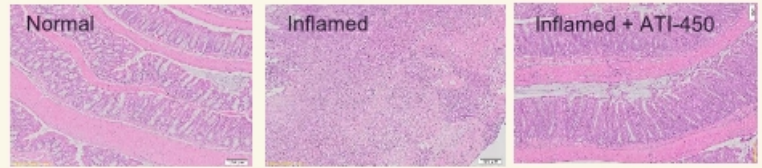
*ATI-450: for bold items above data on file and Wang C, et al. *J Exp Med.* 2018;215(5):1315-1325.

In vivo Preclinical Data of MK2 Pathway Inhibitor ATI-450

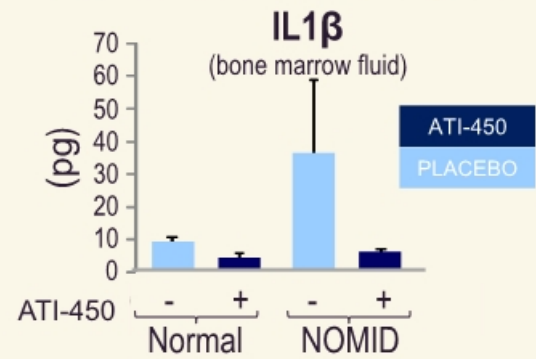
Joint Protection in Rat Arthritis Model¹



Blockade of Gut Inflammatory Infiltrate in Murine Adoptive Transfer Ulcerative Colitis Model²



Cytokine Modulation in Orphan Autoinflammatory Disease (CAPS)¹

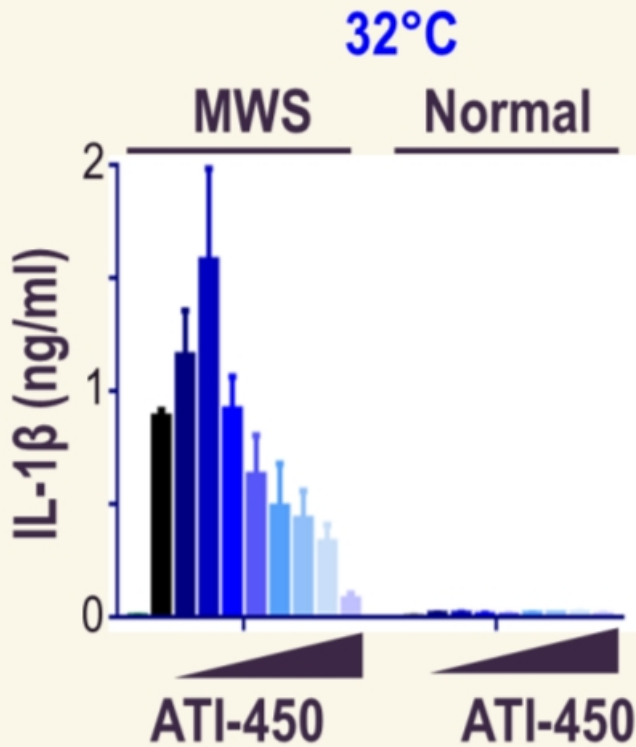


¹ Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.

² Strasser et al. *Integrative Biology*, in press - Substrate-based kinase activity inference identifies MK2 as driver of colitis.

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Ex vivo Preclinical Data: ATI-450 Inhibits IL1 β Expression in PBMCs from a CAPS Patient



- Peripheral blood mononuclear cells (PBMCs) were isolated from CAPS patients and healthy controls.
- In CAPS patients (Muckle Wells Syndrome; MWS), IL1 β expression is triggered by exposure to low temperatures.
- CAPS PBMCs spontaneously produced high amounts of IL1 β at 32°C but not at 37°C.
- ATI-450 blocks temperature stress induced IL1 β production.

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

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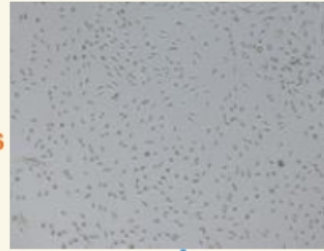
Mouse Model: ATI-450 Inhibits RANKL-induced Osteoclastogenesis

Bone marrow derived macrophages (BMDM) from NOMID mice

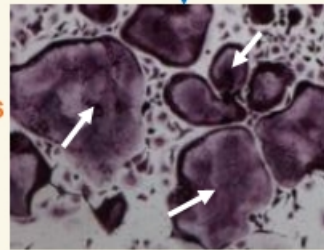
- In CAPS, osteoclastogenesis gives rise to low bone mass (osteopenia)
- (a) When bone marrow derived macrophages (BMDM) from NOMID mice are stimulated with RANKL (RANK ligand), they differentiate into osteoclasts
- (b) ATI-450 blocks this macrophage differentiation



NOMID BMDM



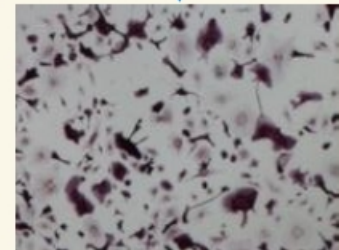
(a)



NOMID BMDM Plus ATI-450



(b) X



ATI-450 inhibits RANKL-stimulated macrophage differentiation into osteoclasts from NOMID mice

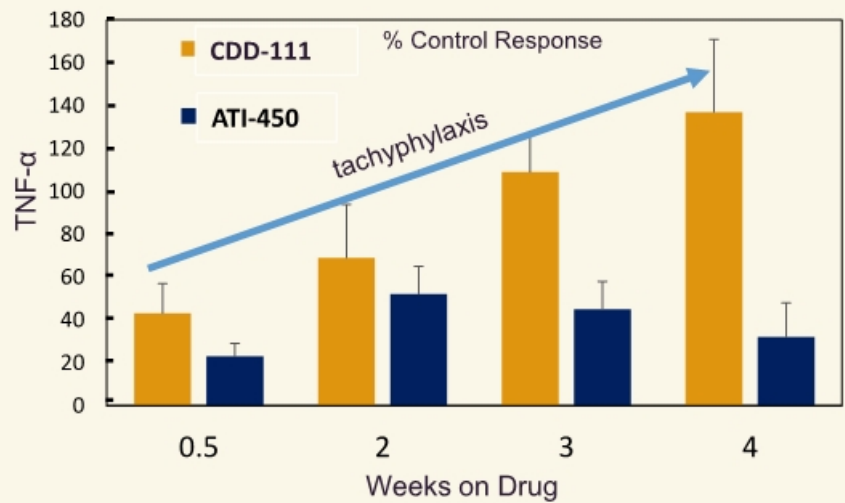
*Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.

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Mouse Model: LPS-Induced TNF α Production

ATI-450 demonstrated durable response (no tachyphylaxis)

- Global p38 inhibitor CDD-111 lost inhibition over time
- **MK2 inhibitor ATI-450 (investigational compound) demonstrated durable response (no tachyphylaxis)**



- Conventional p38 (CDD-111) and MK2i (ATI-450) administered to mice in feed starting day 1 and continuing through day 28
- At the time point indicated, mice were LPS challenged and blood TNF α levels determined

ATI-450 Clinical Development

Phase 1 Single and Multiple Ascending Doses

- Safety, PK, Tolerability
- PD (inhibition of $TNF\alpha$, $IL1\beta$, $IL6$, $IL8$ & $Hsp27$)

Rheumatoid Arthritis Phase 2 Clinical Trial

- 12 wks: ATI-450 vs placebo
- Assess CRP dynamics
- Clinical Disease Activity/PD Biomarkers
- MRI: wrist synovitis

Demonstrate proof of concept data

CAPS

Inflammatory Bowel Disease

Psoriatic Arthritis

Hidradenitis Suppurativa

Psoriasis

Gout

Rheumatoid Arthritis

MK2 inhibitor ATI-450 Summary

- Well-known pathway
- Discovered an approach to drug the target
- Novel mechanism designed to block inflammation
 - ✓ Multiple inflammatory cytokines impacted
 - ✓ Key RA inflammatory cell types impacted
 - ✓ Lock MK2 in a catalytically inactive state – a unique MOA
 - ✓ Broad IP issued or filed
- Oral option for numerous diseases currently treated by biologics
 - ✓ Robust efficacy in a range of inflammation and mouse cancer models^{1,2}
- Phase 1 study underway
- Proof of concept in RA trial expected to begin first half 2020
 - ✓ Demonstrate clear pharmacodynamic effect and no tachyphylaxis
 - ✓ Demonstrate early signs of efficacy in a well understood disease
- Other inflammatory indications under consideration

¹ Murali et al. 2018. Inhibition of the stromal p38MAPK/MK2 pathway limits breast cancer metastases and chemotherapy-induced bone loss. *Cancer Res* 78(19):1

² Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.

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ATI-1777 (Topical Soft-JAK Inhibitor)

(Investigational Drug Candidate)



ATI-1777 (Topical Soft-JAK Inhibitor)

Novel approach for moderate to severe Atopic Dermatitis

- Atopic dermatitis (AD) is a disease of unknown origin that usually starts in early infancy and is typified by pruritus, eczematous lesions, xerosis (dry skin), and lichenification on the skin (thickening of the skin and increase in skin markings).¹
 - ✓ Large and growing market – Projected to be \$8-12 billion at peak (moderate-to-severe AD)²
 - ✓ Unmet need for effective and safe topical treatment for AD
 - ✓ Systemic and topical JAK inhibition has demonstrated promising results in clinical trials for treating pruritus and inflammation in AD³
 - ✓ In AD, a compromised skin barrier means that a topically dosed JAK inhibitor might result in pharmacologically active systemic drug levels
- Topical soft-JAK inhibitor has potential to achieve efficacy with improved safety
 - ✓ Achieve efficacy in skin while minimizing systemic JAK inhibitor toxicity
 - ✓ JAK1/3 selectivity minimizes JAK2 toxicities given compromised skin barrier
- Topical formulations being optimized into a differentiated, patient-friendly emollient formulation (topical spray vs cream/ointment)
- First in human studies planned for second half 2020 in moderate-to-severe AD

¹ <https://emedicine.medscape.com/article/1049085-overview>

² Auster M., et al. Something Big Is Getting Bigger [research note]. New York, NY: Credit Suisse Equity Research; 2019.

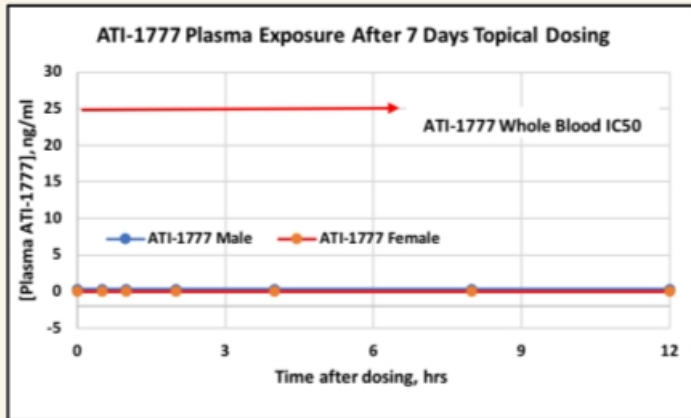
³ R Shreberk-Hassidim, Et Al Janus kinase inhibitors in dermatology: A systematic review, J Am Acad Dermatol. 2017 Apr;76(4):745-753.

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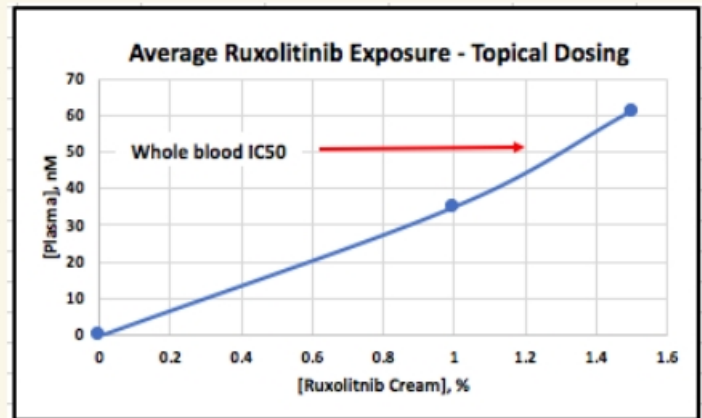
Minipig Model: ATI-1777 Nonclinical Safety Program TK Data

Tolerability/Toxicokinetic with 7-day dermal administration (non-GLP)

- No adverse effects noted (10% body surface area, QD)
- Bleeds at 0.5, 1, 2, 4, 8, 12, and 24 hours post-application: Days 1 and 6
- All plasma samples were below limit of quantification (<0.50 ng/mL) – well below cellular IC₅₀



MINIPIG¹



HUMAN^{2,3}

¹ Data on file
² Clinical Pharmacology in Drug Development 3(1) 34–42 © 2013
³ Punwani, N., et al. *British Journal of Dermatology* (2015) 173, 989–997
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Porcine Model: ATI-1777 Blocks IL15 Induced CCL8 mRNA



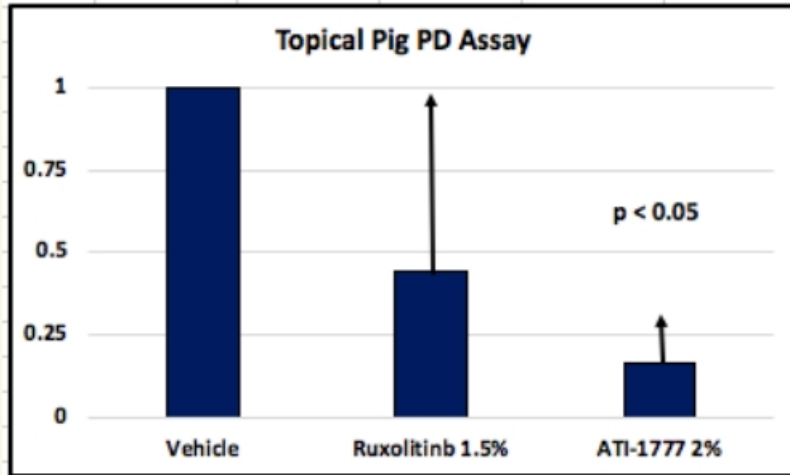
Apply formulation to back of pig, wait 1 hr



Intra-dermal Injection of porcine IL15, wait 3 hr



Harvest 6 mm biopsy, prepare RNA, measure CCL8 by qPCR



- Single application of 2% ATI-1777 development formulation significantly inhibits IL15 induced gene induction (CCL8).
- Clinical topical formulation of 1.5% ruxolitinib does not significantly inhibit IL15 (CCL8) induction.

*Data on file

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ATI-1777: Topical Soft-JAK Inhibitor to Target Moderate-to-Severe AD

Create topical atopic dermatitis therapy which meets the medical, aesthetic and compliance needs of patients and physicians

Approach

- Designed to be:
 - “Soft” drug to minimize the potential for systemic immunosuppression
 - JAK1/3 selective to minimize JAK2 inhibition toxicity
 - Delivered in a patient friendly formulation to clearly differentiate it from other topical therapies

Status

- Plan to study in patients with moderate-to-severe AD
- IND-enabling preclinical safety program initiated
- Next key milestone: First In Human - 2H2020

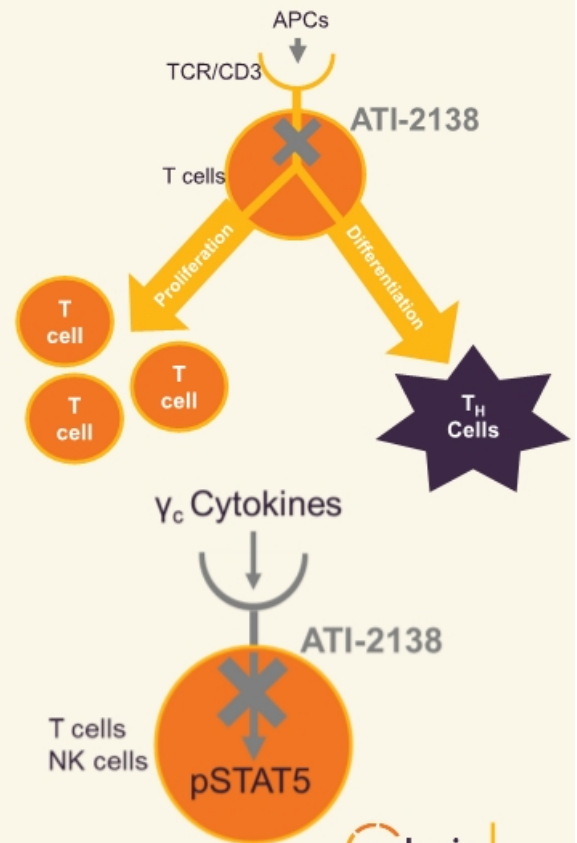
ATI-2138 (ITK/TKK/JAK3)

(Investigational Drug Candidate)



ATI-2138: Covalent ITK/TXK/JAK3 Inhibitor

- ATI-2138 covalently blocks ITK/TXK/JAK3
 - ✓ ITK/TXK required for T-cell receptor signaling
 - ✓ JAK3 required for γ_c cytokines (IL-2/4/7/9/15/21)
 - ✓ Targeting both with a single drug may produce synergistic efficacy - expected to have few off-target effects
 - ✓ PD effects persist after plasma clearance
 - ✓ Efficacy in rat arthritis and mouse colitis
- All T-cell mediated autoimmune diseases are potentially targetable
- Next milestones
 - ✓ IND submission in 4Q20/1Q21
 - ✓ First In Human - 1H 2021



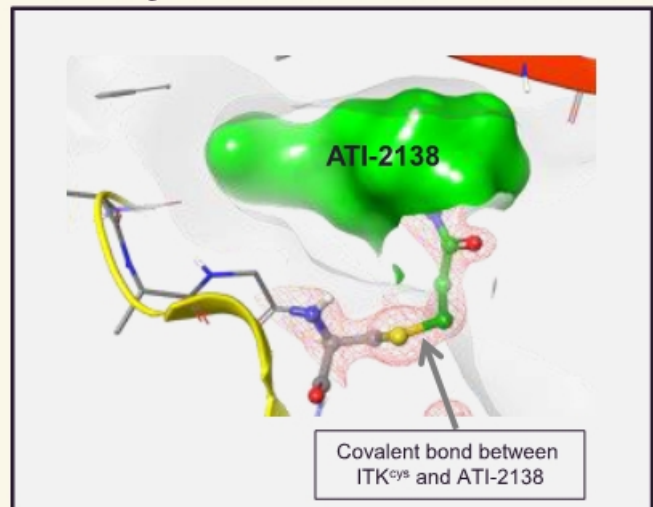
ATI-2138 is a Potent Covalent Inhibitor

Cellular Inhibition of JAK and ITK/TXK

Assay Description	ATI-2138 IC ₅₀ (nM)	Assay
ITK/TXK activity	7	Jurkat pPLCγ-1
JAK1/3 activity	20	PBMC pSTAT-5
BTK activity	52	Ramos pPLCγ-2
Both ITK/TXK and JAK3	13	HWB αCD3/IL15 IFNγ

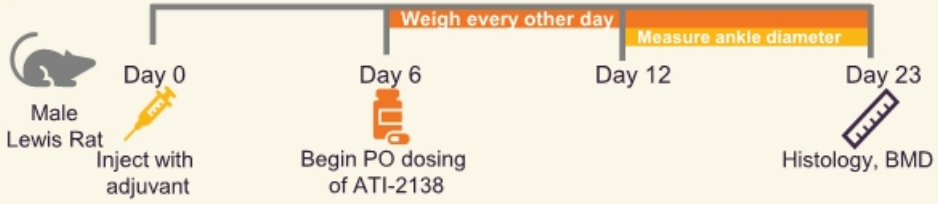
ATI-2138 potently inhibits ITK/TXK and JAK3 in cells and in whole blood

Co-Crystal Structure of ATI-2138/ITK

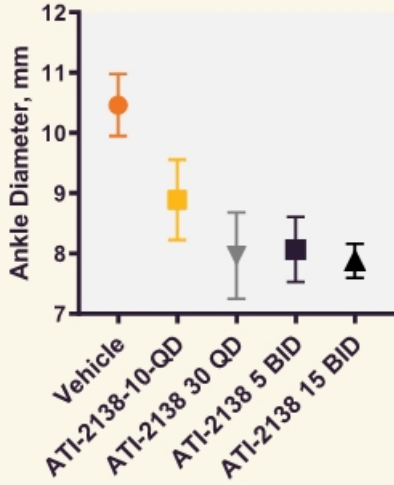


Crystal structure definitively shows ATI-2138 covalent binding to ITK

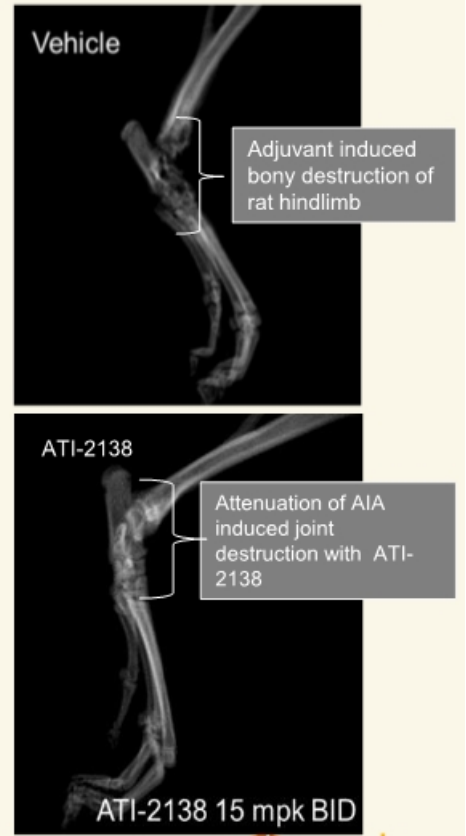
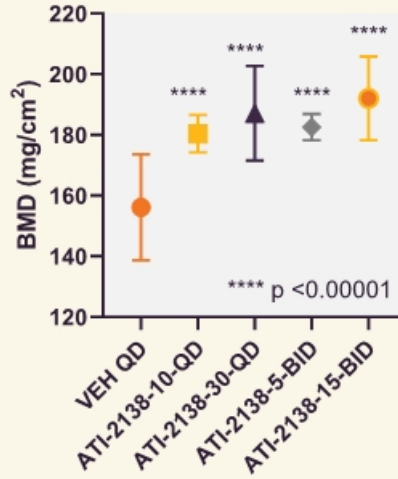
Rat Adjuvant Induced Arthritis (AIA) Model: ATI-2138 Reduced Inflammation and Protected Bone



Day 23 ankle diameter



ATI-2138 bone mineral density in rat AIA study



ATI-2138 reduced inflammation and bone mineral density loss

*Data on file
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Biopharmaceutical Company

Executive Team
Proven track record of R&D and business development



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

Research and Development
Scientific leadership in immuno-inflammatory diseases - innovative clinical and regulatory strategies



KINect™ Technology Platform
Proprietary discovery engine enables targeted design of novel drug candidates



Intellectual Property
Global IP estate - 43 issued patents and 29 pending applications on ATI-450 and earlier programs



Cash Position
\$91 million as of September 30, 2019



Pipeline
Multiple therapeutic programs ranging from discovery to Phase 3

Milestone	2019		2020			
	Q3	Q4	Q1	Q2	Q3	Q4
A-101 45% Common Warts						
Phase 3 Data (THWART-1, THWART-2)		✓				
Immuno-Inflammatory						
ATI-450 (MK2 Inhibitor) - Initiate Phase 1 Trial		✓				
ATI-450 (MK2 Inhibitor) - Phase 1 Data						
ATI-450 (MK2 Inhibitor) - Initiate Phase 2 Trial in Rheumatoid Arthritis						
ATI-450 (MK2 Inhibitor) - Phase 2 Data in RA						
ATI-1777 (Soft-JAK) – Submit IND						
ATI-1777 (Soft-JAK) – Initiate Phase 1/2 Trial						
ATI-2138 (ITK/JAK3) – Submit IND						

EMPOWERING PATIENTS THROUGH
KINOME INNOVATION

THANK YOU



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