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 15, 2020

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 15, 2020, management of Aclaris Therapeutics, Inc. (the "***Company***") will present a company overview at the virtual H.C. Wainwright & Co. 22nd Annual Global Investment Conference and at virtual one-on-one investor meetings. 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

Exhibit Number	Exhibit Description
99.1	Company Presentation.
104	The cover page from Aclaris Therapeutics, Inc.'s Form 8-K filed on September 15, 2020, 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/ Frank Ruffo
Frank Ruffo
Chief Financial Officer

Date: September 15, 2020

EMPOWERING PATIENTS THROUGH
KINOME INNOVATION

Company Overview

September 2020

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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," "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, **the uncertainty regarding the COVID-19 pandemic including its impact on the timing of Aclaris' regulatory and research and development activities**, 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, 2019, Aclaris' Quarterly Report on Form 10-Q for the quarter ended June 30, 2020 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.

Biotechnology Company Focused on the Kinome:
People + Platform + Pipeline

LEADERSHIP

Founded and Led by Physicians and Scientists

- World class ex-Pfizer (kinase) and ex-GSK (immunology) leadership
- Kinome experts skilled at developing kinase targeted medicines

KINect™ PLATFORM

Proprietary Kinase Discovery Engine

- Versatile platform
- Fully integrated discovery and development team
- Advancing small molecule drug candidates to parallel or exceed efficacy of high-value biologics

INNOVATIVE PIPELINE
(investigational drug candidates)

ATI-450 - MK2i

- Oral anti-TNFα, anti-IL1, anti-IL6

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

- Tissue specific therapy for the potential treatment of moderate-to-severe atopic dermatitis (AD)

ATI-2138 - ITK/TXK/JAK3i

- Oral dual inhibitor of T-cell and cytokine receptors

Development of Small Molecule Therapeutics for Immuno-inflammatory Diseases

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The Kinase Opportunity
Unlocking the Potential of the Kinome

Medically Important and Productive Target Class

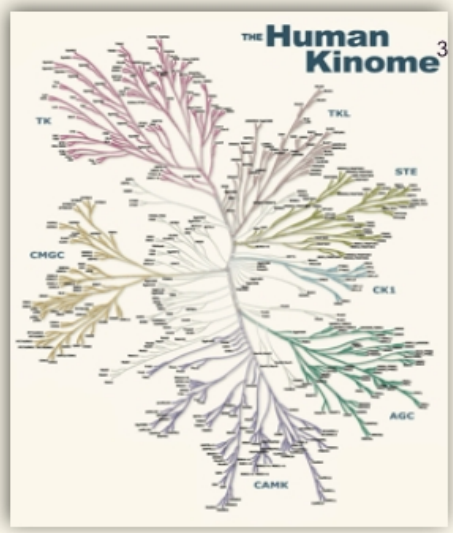
OFEV (nintedanib) capsules 150mg
Bosulif bosutinib
IBRANCE palbociclib
IRESSA
Inlyta axitinib
imbruvica (ibrutinib)
ZELBORAF (vemurafenib) tablets
ICLUSIG (ponatinib) tablets
COMETRIQ (cabozantinib)
gleevec (imatinib mesylate) tablets
Tarceva erlotinib
GILOTRIF (afatinib) tablets
ICLUSIG (ponatinib) tablets
Votrient pazopanib tablets 200 mg
Tykerb (lapatinib)
Jakafi ruxolitinib
SPRYCEL dasatinib
Zydelig (idelalisib) tablets
Caprelsa (vandetanib) tablets
Mekinist (trametinib)
XALKORI
Stivarga (regorafenib)
SUTENT sunitinib malate
ZYKADIA ceritinib
Nexavar (sorafenib) tablets
LENVIMA (lenvatinib) capsules
Tasigna nilotinib
XELJANZ (tofacitinib citrate)

~36 Marketed Drugs[1]

~$48B[1,2]

Annual Sales of Kinase Drugs

Most Members of the Kinome Remain Unexplored



518 Members

>90% of the Human Kinome remains undrugged[4]

Creating New Medicines Targeting Previously Inaccessible Kinome Targets

1. Data on file.
2. Oprea TI, et al. Unexplored opportunities in the druggable human genome. *Nature Rev Drug Discov*. Poster Jan. 2017.
3. Manning G, et al. *Science*. 2002;298(5600):1912-1934.
4. Oprea TI, et al. *Nat Rev Drug Discov*. 2018;17(5):317-332.

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Experienced R&D Leadership Team
Proven Track Record in Immunology and Inflammation

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

David Gordon
Chief Medical Officer

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

Joseph Monahan, PhD
EVP, R&D (Head of Discovery)

- 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

Walter Smith
SVP, R&D

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

Jon Jacobsen, PhD
VP, Chemistry

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

Paul Changelian, PhD
VP, Biology

- 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

David R Anderson, PhD *Sr. Director, Discovery, Early Development*

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

Gary DeCrescenzo
SVP, Pharm R&D

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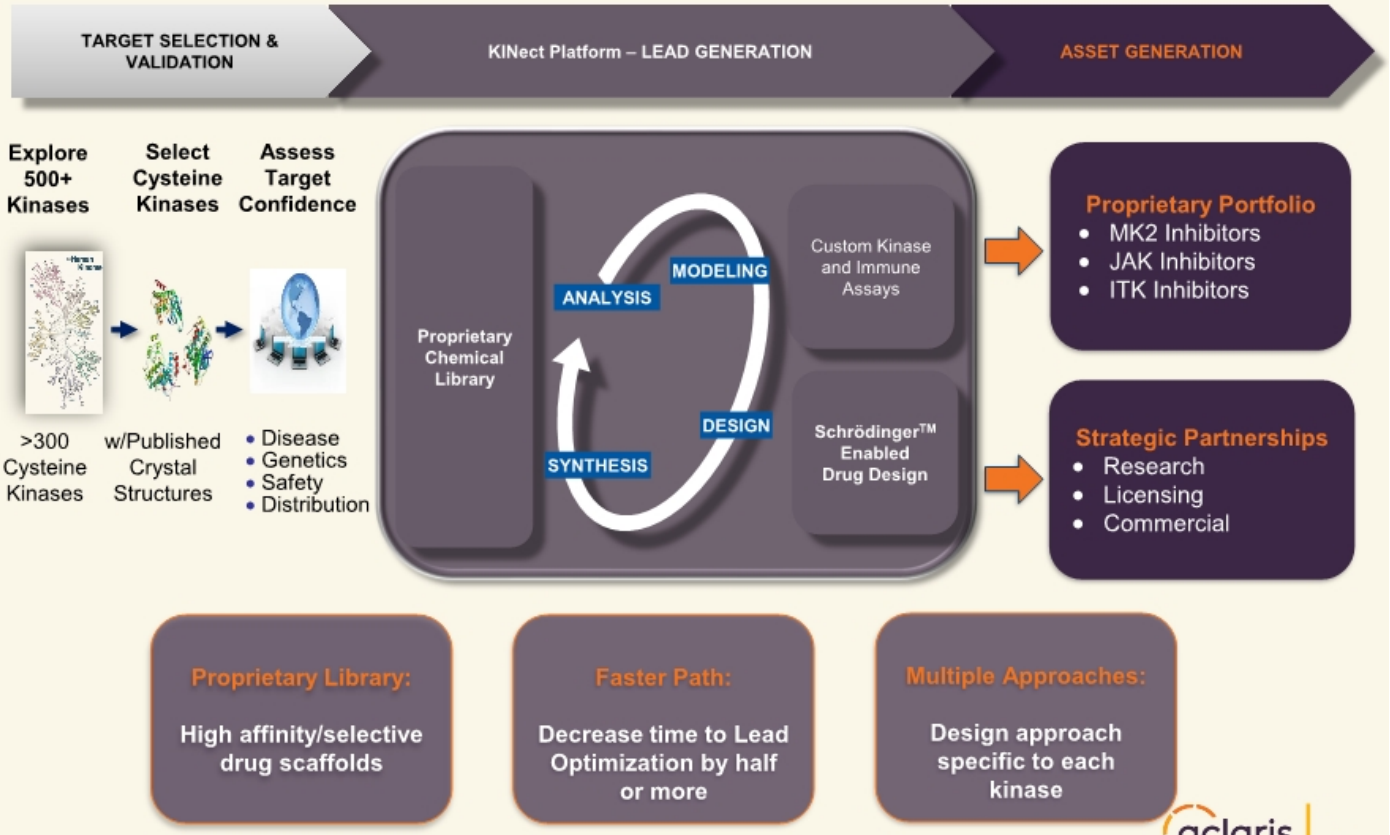
KINect™ Platform
Developing Kinase Drug Candidates Rapidly & Efficiently



Proprietary Library:
High affinity/selective drug scaffolds

Faster Path:
Decrease time to Lead Optimization by half or more

Multiple Approaches:
Design approach specific to each kinase

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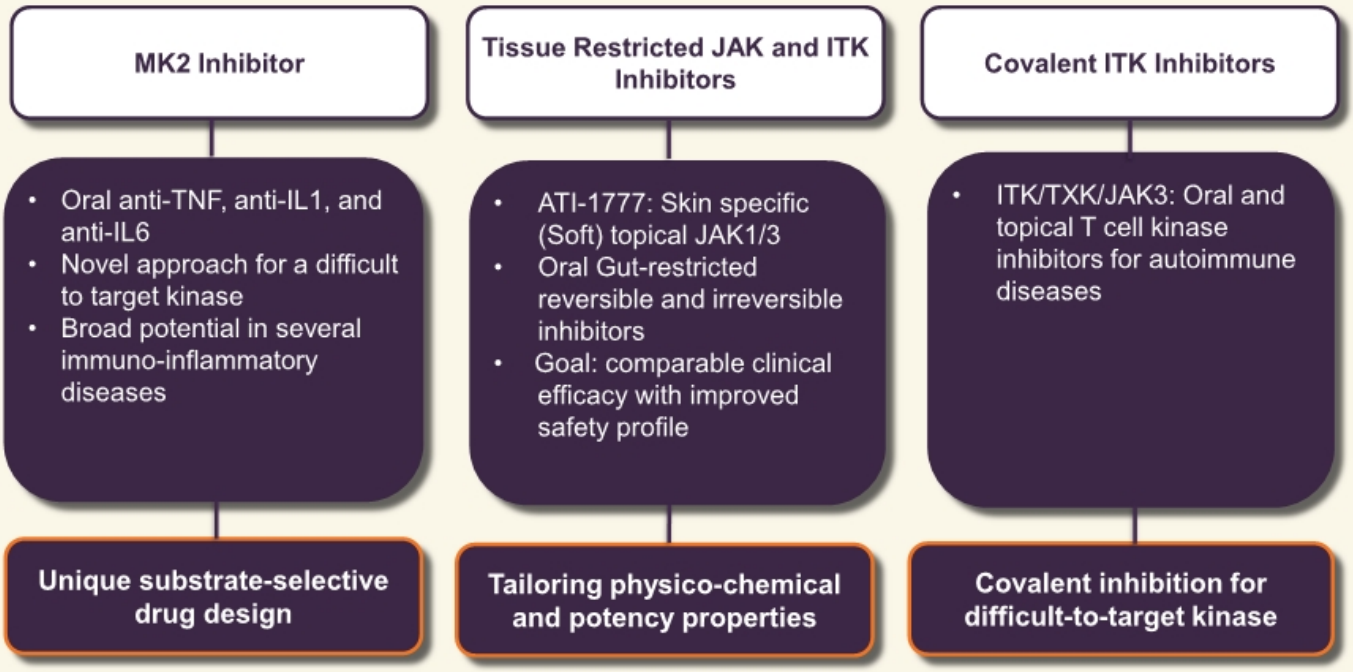
KINect™ Platform
Demonstrated Success in Reversible and Covalent MOA



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

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Pipeline

Program	Indication(s)	Preclinical	Phase 1	Phase 2	Phase 3
ATI-450 MK2 Inhibitor *Oral*	Rheumatoid Arthritis				
	COVID-19*				
	Cryopyrin-Associated Periodic Syndrome (CAPS)				
ATI-1777 JAK1/JAK3 Inhibitor *Soft Topical*	Atopic Dermatitis (moderate-to-severe)				
ATI-2138 ITK/TXK/JAK3 Inhibitor *Oral*	Psoriasis, Inflammatory Bowel Disease				
JAK1/JAK3 Inhibitor *Oral, gut-restricted*	Inflammatory Bowel Disease				
ITK/TXK/JAK3 Inhibitor *Oral, gut-restricted*	Inflammatory Bowel Disease				

* This is an investigator-initiated trial sponsored by the University of Kansas Medical Center.

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ATI-450: MK2 Inhibitor
(Investigational Drug Candidate)

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ATI-450: Small Molecule, Oral MK2 Inhibitor
Blocks the Same Targets as Broadly Used Biologics

MK2* drives pro-inflammatory cytokine expression

- Inhibiting MK2 blocks TNFα, IL1 and IL6, the targets of the following biologics:[1]
  - ✓ **anti-TNFα**: HUMIRA® (adalimumab), ENBREL® (etanercept), REMICADE® (infliximab)
  - ✓ **anti-IL1**: KINERET® (anakinra), ILARIS® (canakinumab), ARCALYST® (rilonacept)
  - ✓ **anti-IL6**: KEVZARA® (sarilumab), ACTEMRA® (tocilizumab)

ATI-450: Small molecule, oral MK2 inhibitor

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

* MK2 = Mitogen-activated protein kinase-activated protein kinase 2
1. Data on file.

** All trademarks are the property of their respective owners.

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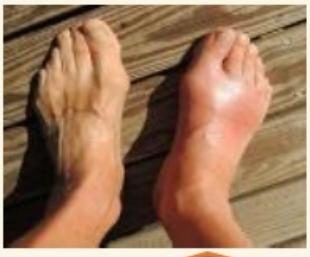
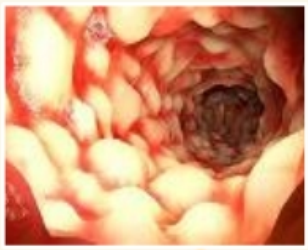
MK2-driven Cytokines are Central to Many Diseases*

TNFα, IL1, IL6 Are Mediators in Numerous Inflammatory Conditions

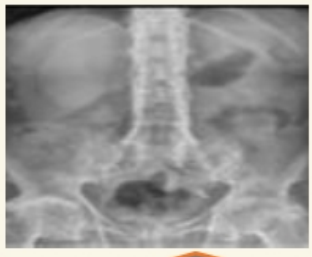
Rheumatoid arthritis/ Juvenile idiopathic arthritis



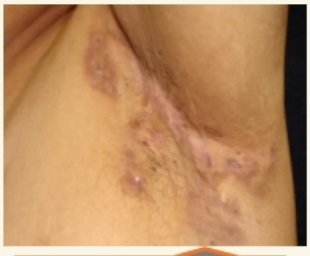
Gout



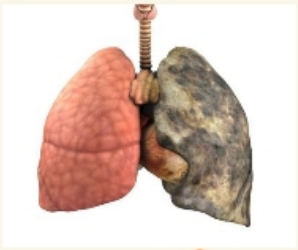
Inflammatory Bowel Disease



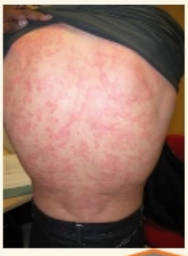
Ankylosing spondylitis



Neutrophilic Dermatoses (Hidradenitis Suppurativa)



COPD



CAPS

Cardiovascular/ Cerebrovascular Disease

*Singh RK, et al. *Pharmacol Reports*. 2017;69:746-756.

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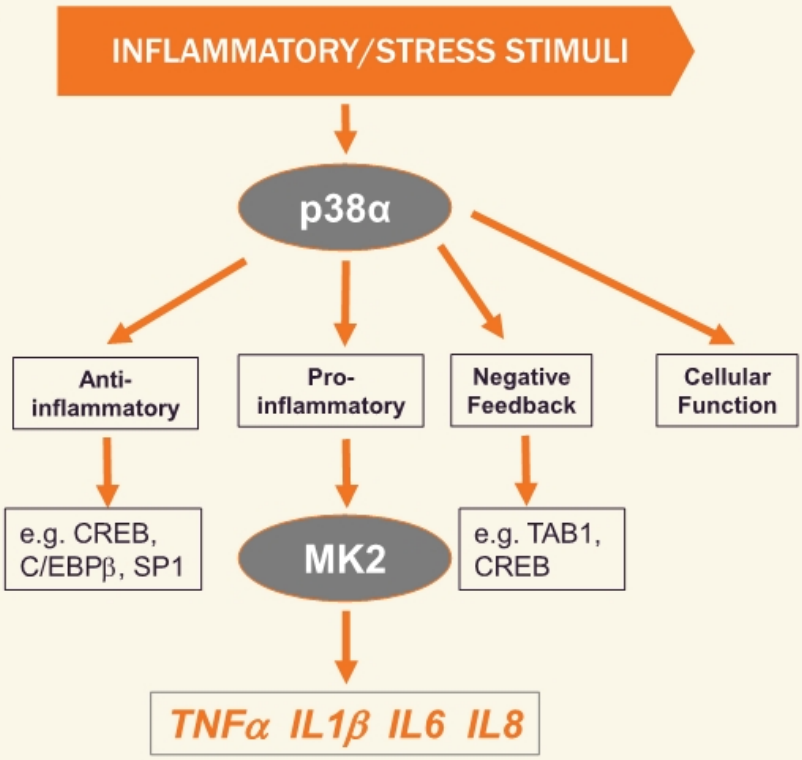
Evolution in Understanding a Well-Known Inflammatory Pathway
The Path From p38α to MK2

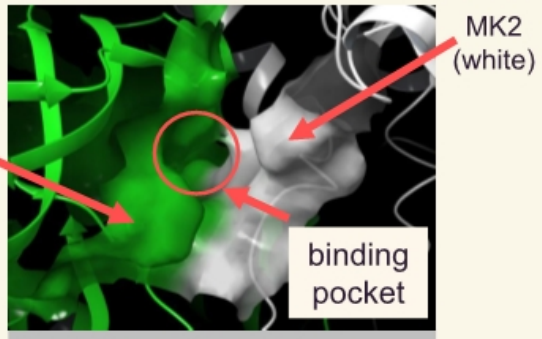
The relationship of p38α to MK2 is key to overcoming barriers for suppressing TNFα and other pro-inflammatory cytokines

- Global p38α inhibitors have exhibited toxicity and/or lack of sustained efficacy in RA and IBD
- p38α phosphorylates over 60 substrates - yet MK2 drives the proinflammatory node of this pathway
- MK2 has been a high priority therapeutic target since 1999 but has proven very difficult to drug

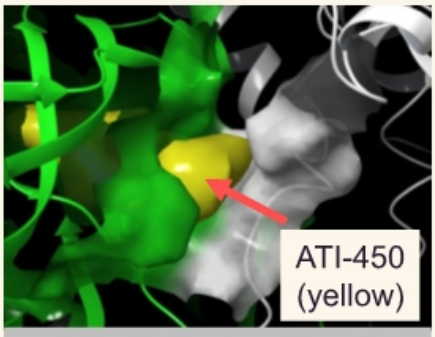


* Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.
* Cheung P, et al. *EMBO J*. 2003;22(21):5793-5805.
* Muniyappa H, et al. *Cell Signal*. 2008;20(4):675–683.
* Ma W, et al. *J Biol Chem*. 2001;276(17):13664-13674.

Novel Mechanism: Capturing MK2 in an Inactive State



Crystal structure of the p38α/MK2 complex



ATI-450 (yellow) docked in the pocket

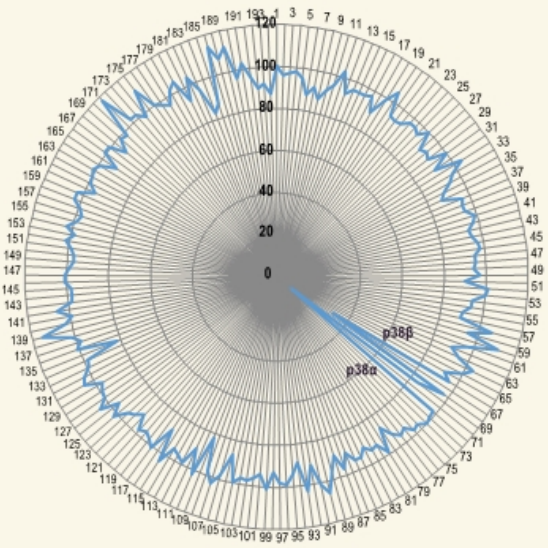
- In the nucleus, inactive MK2 and p38α dock in a high affinity complex that exhibits a binding pocket formed by juxtaposed walls of both proteins
- ATI-450 binds to both walls of the pocket, stabilizing the complex and preventing MK2 activation

ATI-450 locks MK2 in a catalytically inactive state – a unique MOA

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

ATI-450 Selectivity: Minimizing Off-Target Inhibition through High Affinity for the p38α/MK2 Complex

Human Kinome Selectivity[1]



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

MK2 Pathway Selectivity

ATI-450 is highly selective for the p38α/MK2 complex vs. other p38 substrates[1]

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

1. Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.
* Data on file.
** Optimized p38 peptide substrate

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

Therapeutic Area	Animal Model	Reference
Rheumatoid Arthritis/ Psoriatic Arthritis	Mouse Collagen-Induced Arthritis Model • Reduction in clinical arthritis score • Protection of joint histology Rat streptococcal cell wall arthritis model • Protection against bone deterioration • Protection against lethality Inhibition of cellular IL1β mRNA stability & translation	Data on file Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.
Inflammatory Bowel Disease	Adoptive transfer mouse model of colitis • Endoscopy scores show disease control • Decreased inflammatory infiltrate • Protected structural integrity of mucosa	Strasser S, et al. *Integrative Biology*. 2019;11(7):301-314.
Cryopyrin-Associated Periodic Syndromes (CAPS)	Murine NOMID (severe form of CAPS) transgenic model Human CAPS PBMC* IL1β modulation	Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.

* PBMC = Peripheral blood mononuclear cells

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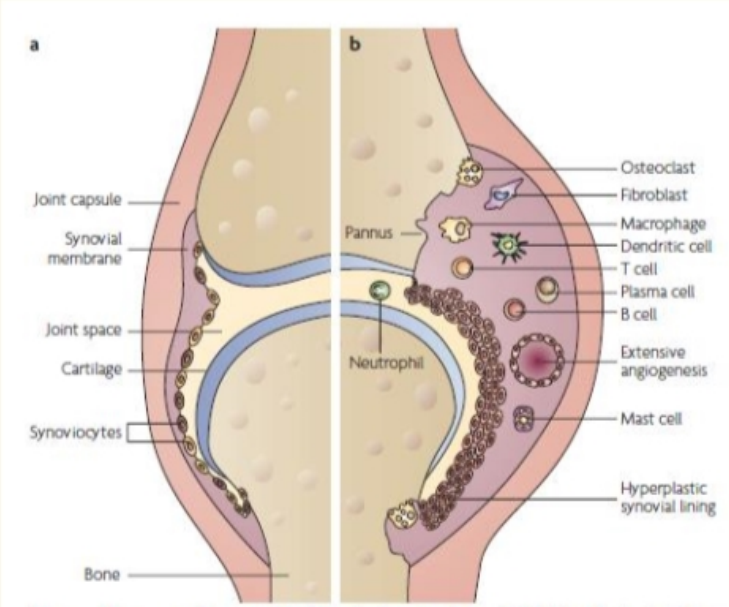
MK2 – Potential Effect in Rheumatoid Arthritis
ATI-450 regulates cells and cytokines involved in RA

Normal Joint

RA Joint



Strand V, et al. *Nat Rev Drug Discov.* 2007;6(Jan 2007):75-92.

Cells

Monocyte/Macrophage

Osteoclast

Epithelial Cells

RA Synovial Fibroblast

Chondrocytes

Cytokines

TNFα, IL1β, IL1α

IL6, IL8, IL18, RANKL

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

MK2 is a key regulator of pathogenic signals in chronic immuno-inflammatory diseases

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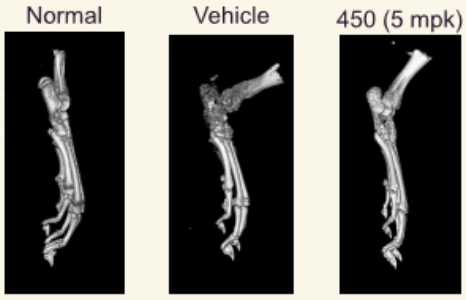
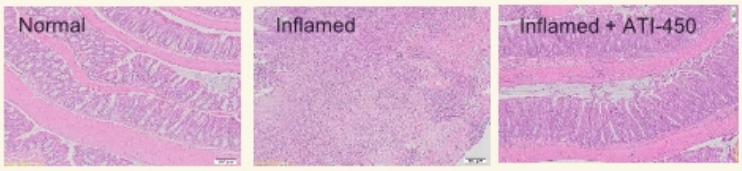
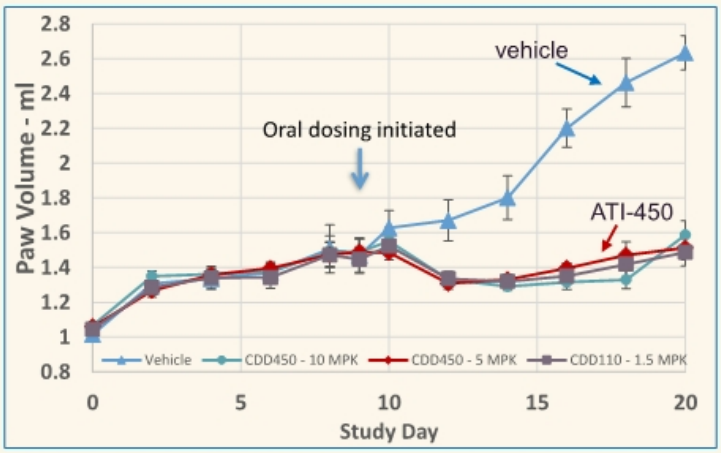
In Vivo Preclinical Data of MK2 Pathway Inhibitor ATI-450

Joint Protection in Rat Arthritis Model[1]

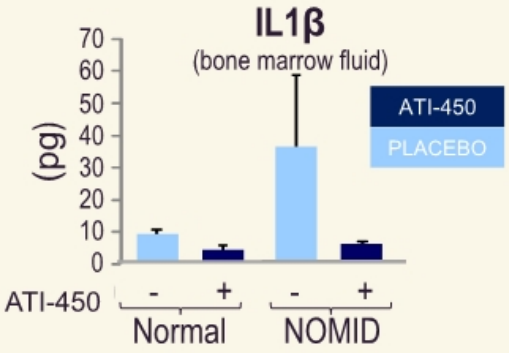


Blockade of Gut Inflammatory Infiltrate in Murine Adoptive Transfer Ulcerative Colitis Model[2]





Cytokine Modulation in Orphan Autoinflammatory Disease (CAPS)[1]



1. Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.
2. Strasser S, et al. *Integrative Biology*. 2019;11(7):301-314.

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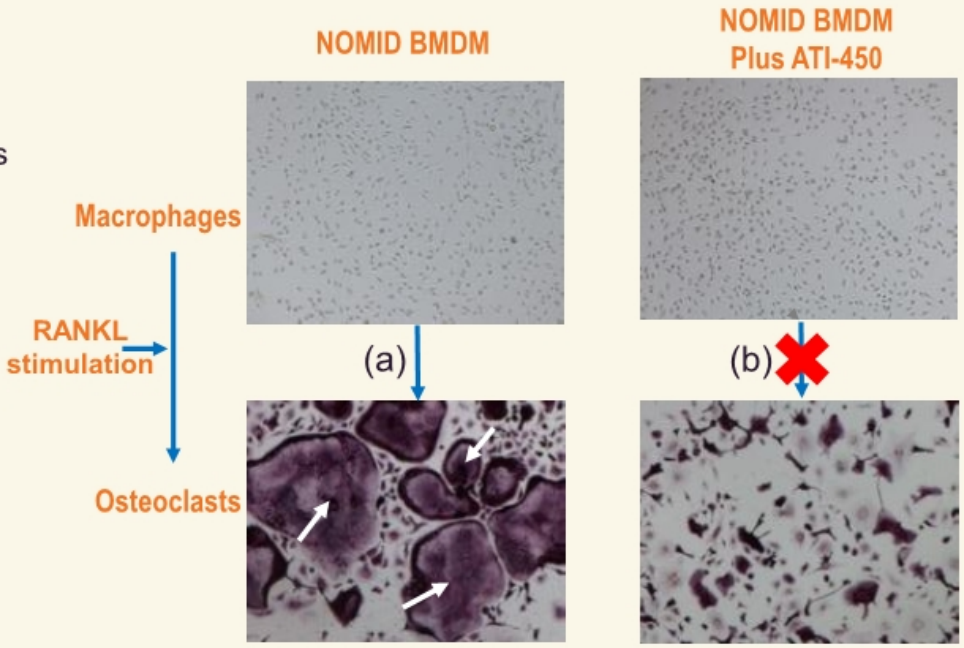
Mouse Model: ATI-450 Inhibits RANKL-stimulated Macrophage Differentiation into Osteoclasts (Osteoclastogenesis)

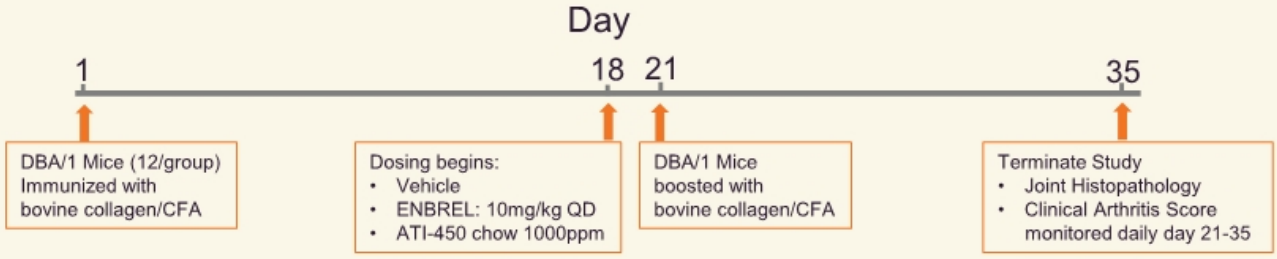
Bone marrow-derived macrophages (BMDM) from NOMID mice

- 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

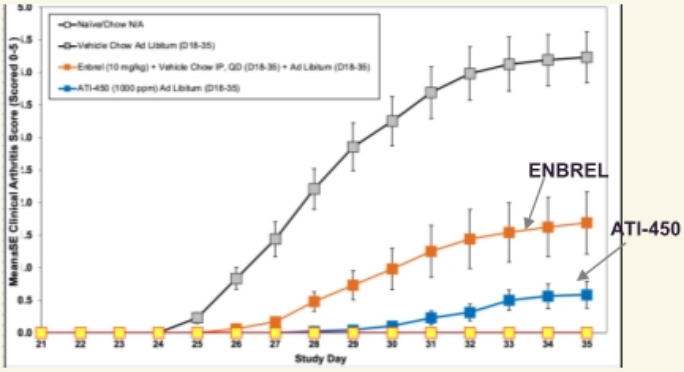


* Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.

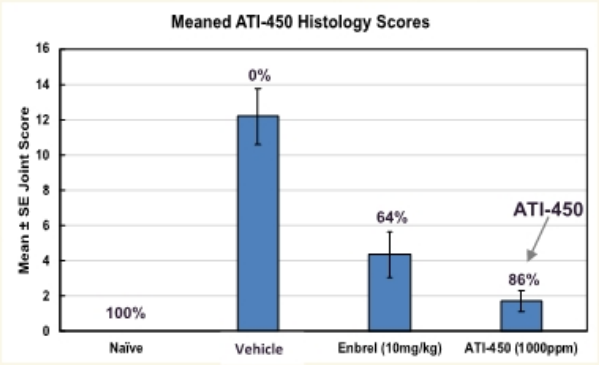
Mouse Model: ATI-450 is Efficacious in Murine Collagen-Induced Arthritis (mCIA)



Clinical Arthritis Score



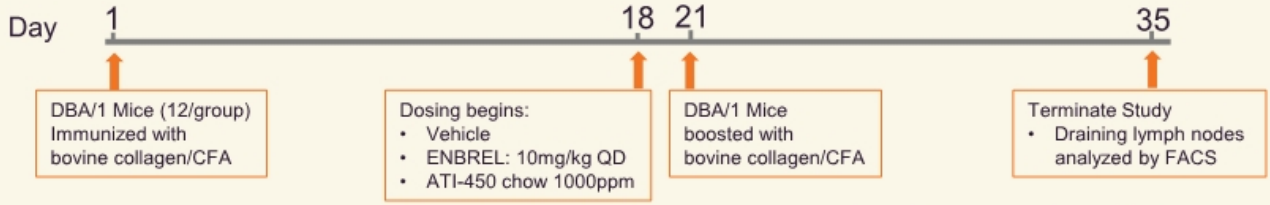
Joint Histology Score



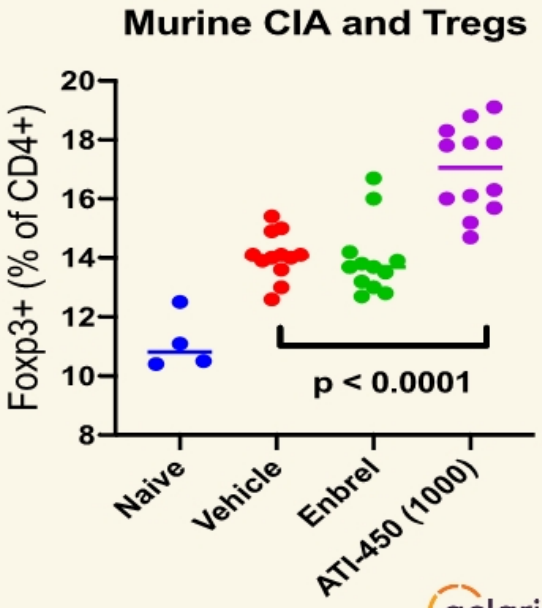
ATI-450 demonstrated broad efficacy in the gold standard mCIA model

* Data on file.

Mouse Model: ATI-450 Increases Regulatory T (Treg) Cells in mCIA



- The effect of ATI-450 treatment on T cell subsets was evaluated in the mCIA model
- A highly significant increase in Treg cells within the CD4+ population was observed with mice treated with ATI-450
- Treg cells are known to be involved in the maintenance of the immune response and have been shown to prevent autoimmune disease[1]



* Data on file.

1. Dominguez-Villar M, et al. *Nat. Immunol.* 2018;19:665-673.

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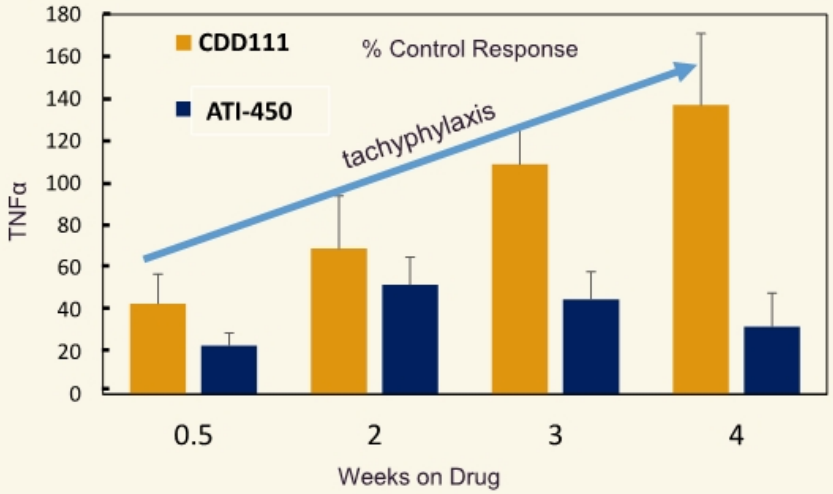
Mouse Model: LPS-Induced TNFα Production
ATI-450 demonstrated durable response (no tachyphylaxis)

- CDD-111 and 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 TNFα levels determined
- Global investigational p38 inhibitor CDD-111 lost inhibition over time



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

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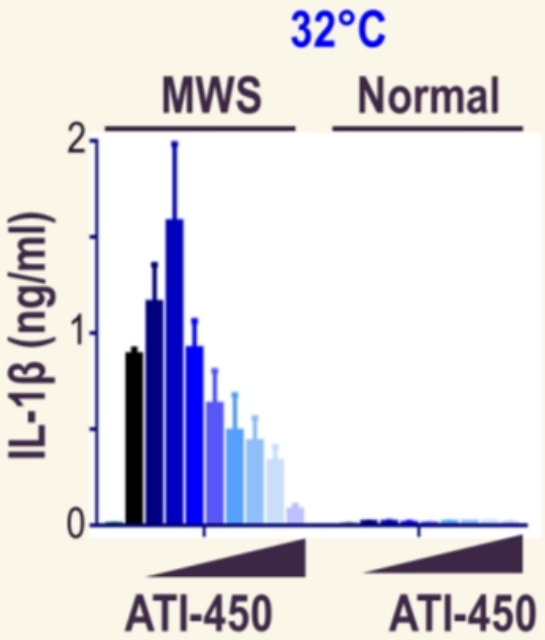
Ex Vivo Preclinical Data: ATI-450 Inhibits IL1β Expression in PBMCs from a Patient with CAPS



- PBMCs were isolated from patients with CAPS and healthy controls.
- In patients with CAPS (Muckle Wells Syndrome), IL1β expression is triggered by exposure to low temperatures.
- PBMCs from patients with CAPS spontaneously produced high amounts of IL1β at 32°C but not at 37°C.

ATI-450 blocks temperature stress induced IL1β production

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

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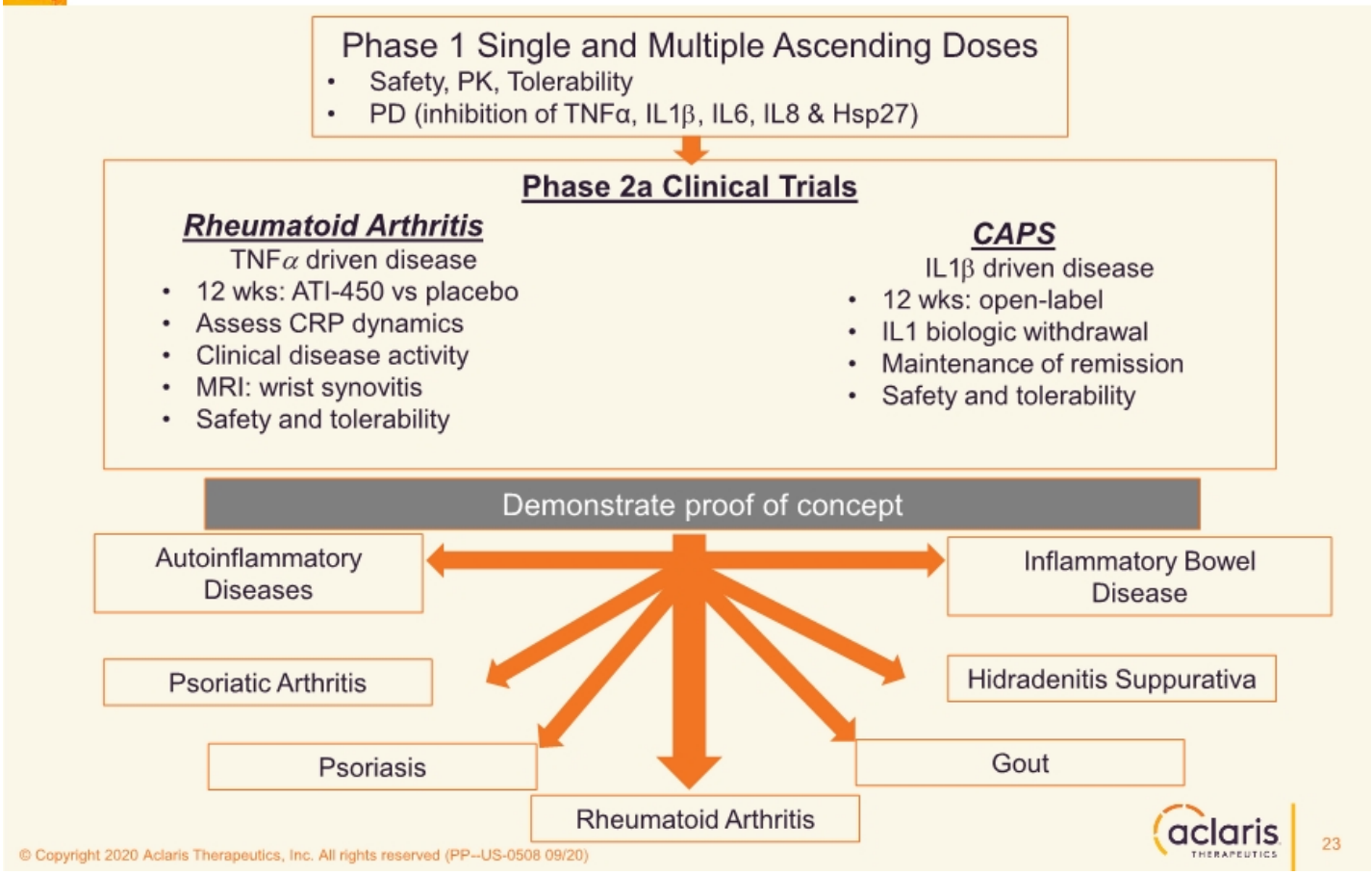
ATI-450 Clinical Development



ATI-450-PKPD-101
Trial Design and Demographics

Three-Part Study (77 Subjects)

Part A: single ascending dose (SAD) plus food effect (n=32)	**Part B:** multiple ascending dose (MAD) (n=30)	**Part C:** methotrexate (MTX) drug-drug interaction (DDI) (n=15)
• 4 cohorts: 10mg, 30mg, 50mg, 100mg (100mg repeated with high fat meal) • 8 subjects per cohort (6 active, 2 placebo). Single dose after overnight fast	• 3 cohorts: 10mg, 30mg, 50mg all BID for 7 days • 10 subjects per cohort (8 active, 2 placebo)	• 1 cohort: MTX day 1 and 8. ATI-450 on days 2-9 • All dosed with active

Demographics: (All dose groups, all parts):
- Age: Mean 34 years
- Gender: 44 female/33 male
- Race: White-40, Black-32, Other-5

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ATI-450-PKPD-101
Safety: ATI-450 Generally Well-Tolerated

Most Common Adverse Events (≥2 subjects in the trial)

SAD/MAD cohorts (blinded)

Preferred Term	ATI-450 n (%) (n=48)	Placebo n (%) (n=14)
Dizziness	6 (12.5)	0
Headache	10 (20.8)	2 (14.3)
Upper respiratory tract infection	3 (6.3)	1 (7.1)
Constipation	3 (6.3)	1 (7.1)
Nausea	2 (4.2)	1 (7.1)
Abdominal pain	2 (4.2)	0
Vomiting	0	2 (14.3)

DDI cohort (unblinded ATI-450 + MTX)

Preferred Term	ATI-450 n (%) (n=15)
Dizziness	7 (46.7)
Headache	1 (6.7)
Upper respiratory tract infection	1 (6.7)
Constipation	0
Nausea	0
Abdominal pain	0
Vomiting	0

- No serious adverse events or adverse events that led to discontinuation of study medication
- All adverse events were mild in severity and did not interfere with everyday activities
- A trend of a decrease in absolute neutrophil count was observed; no correlation with clinical sequelae
  - This effect is consistent with the pharmacodynamic profile of certain anti-TNF therapies[1]

1. Dillingh M, et al. *Front. Immunol.* 2016;7(508):1-9.
* Data on file.

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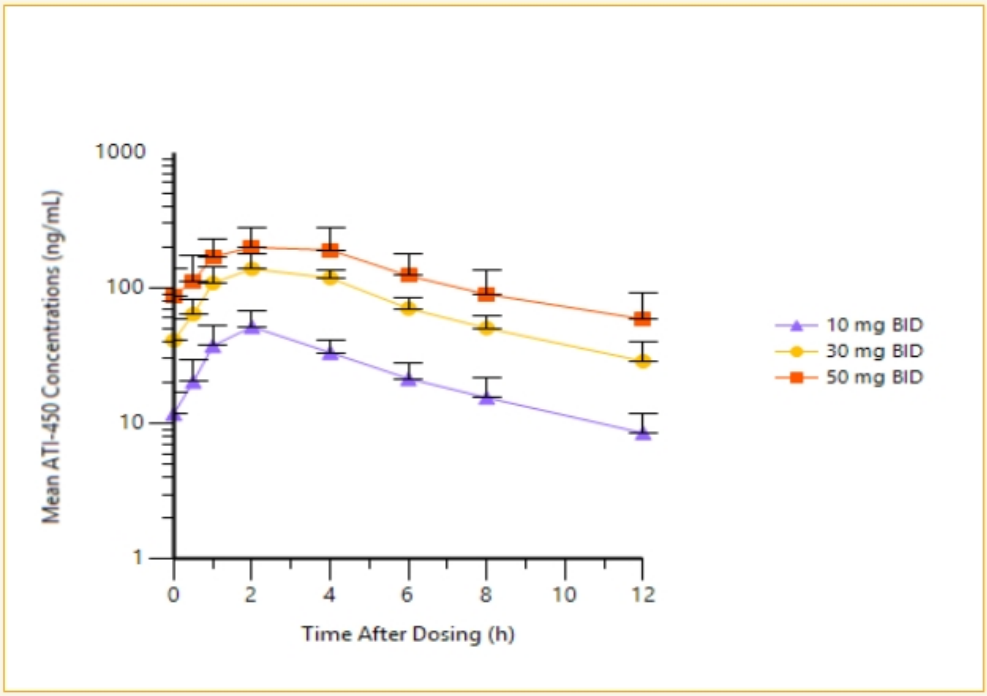
ATI-450-PKPD-101
MAD Pharmacokinetics: Dose Proportional PK

Mean (SD) plasma concentration-time profiles of ATI-450: Day 7



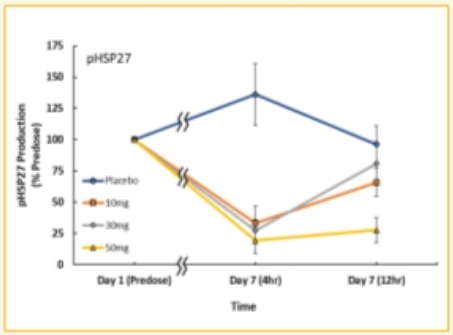
$t_{1/2}$ = 9-12 hours

* Data on file

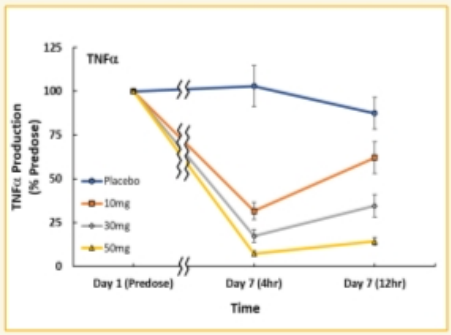
ATI-450-PKPD-101: Day 7 MAD PD Marker Time Dependence

Target Biomarker pHSP27 and Cytokines TNFα and IL1β

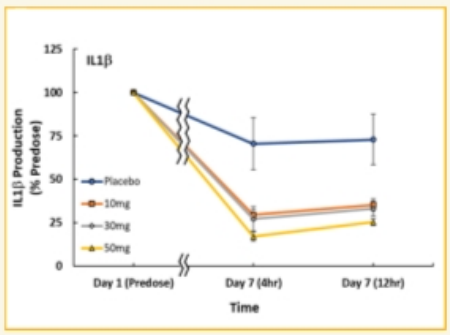
pHSP27



TNFα



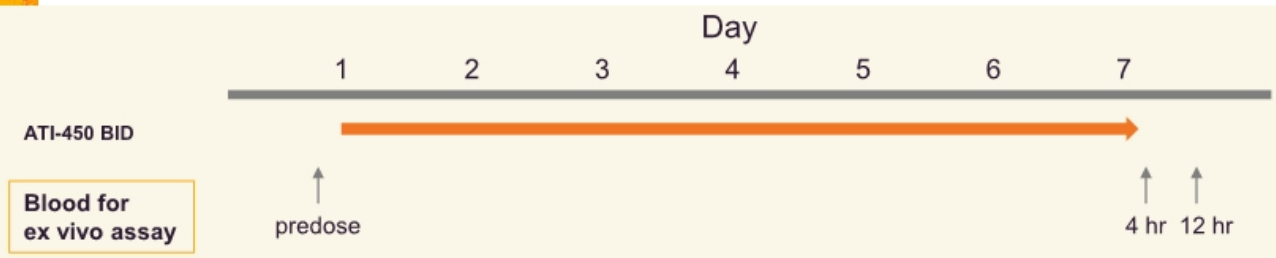
IL1β

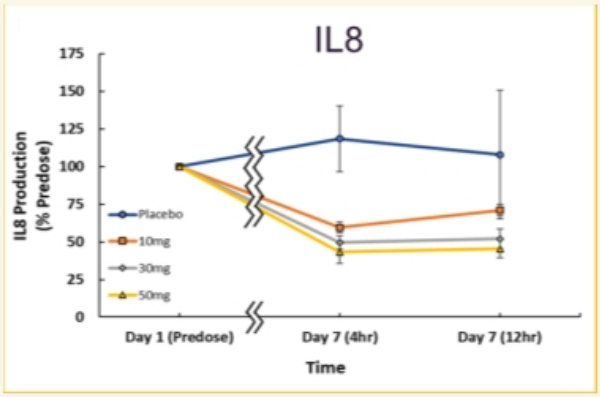


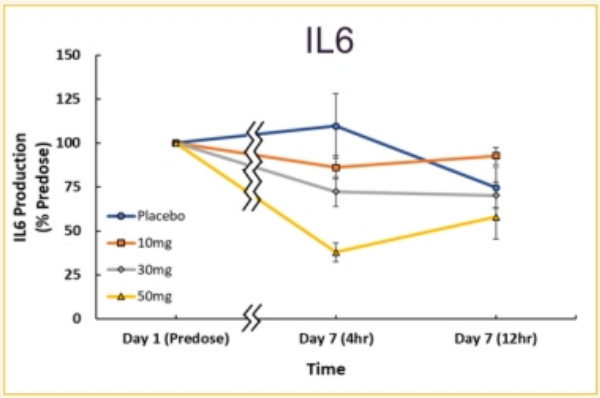
- ATI-450 dosed orally BID for 7 days in healthy subjects at doses of 10mg, 30mg and 50mg
- Day 1 (predose) is from blood taken on day 1 just prior to the first dose of ATI-450
- Samples ex vivo stimulated with LPS
- Data expressed as mean +/- SEM

* Data on file

ATI-450-PKPD-101: Day 7 MAD PD Biomarker Time Dependence
Cytokines IL8 and IL6







- ATI-450 dosed orally BID for 7 days in healthy subjects at doses of 10mg, 30mg and 50mg
- Day 1 (pre-dose) is from blood taken on day 1 just prior to the first dose of ATI-450
- Samples ex vivo stimulated with LPS
- Data expressed as mean +/- SEM

* Data on file

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ATI-450-PKPD-101
Multiples of Cytokine IC_{80} Across Dosing Interval

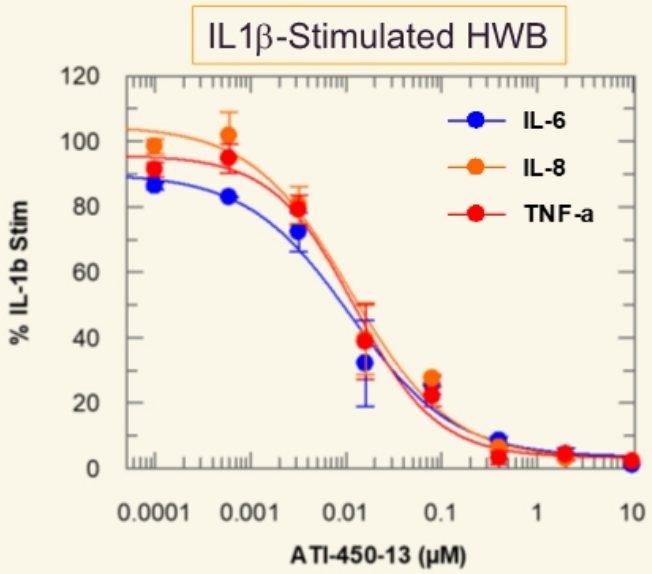
The MAD 50mg BID cohort achieved systemic drug concentrations in excess of IC_{80} for pHSP27, TNFα, IL1β and IL8 at C_{max} (3.5-6.0X) and C_{trough} (1.4-2.4X).

Biomarker	*IC_{80} ng/ml	**C_{trough} Multiple of IC_{80}	**C_{max} Multiple of IC_{80}
pHSP27	36.7	2.4x	6.0x
TNFα	62.6	1.4x	3.5x
IL1β	40.8	2.2x	5.4x
IL6	747.8	0.1x	0.3x
IL8	38.8	2.3x	5.6x

*IC_{80} values generated with all SAD/MAD exposure data using the E_{max} model in WinNonlin
** 50 mg BID MAD Cohort
50 mg BID C_{trough} = 87.9 ng/ml
50 mg BID C_{max} = 215 ng/ml

* Data on file.

In Vitro Model: *ATI-450 Inhibited IL1b-Stimulated Cytokines in Human Whole Blood*

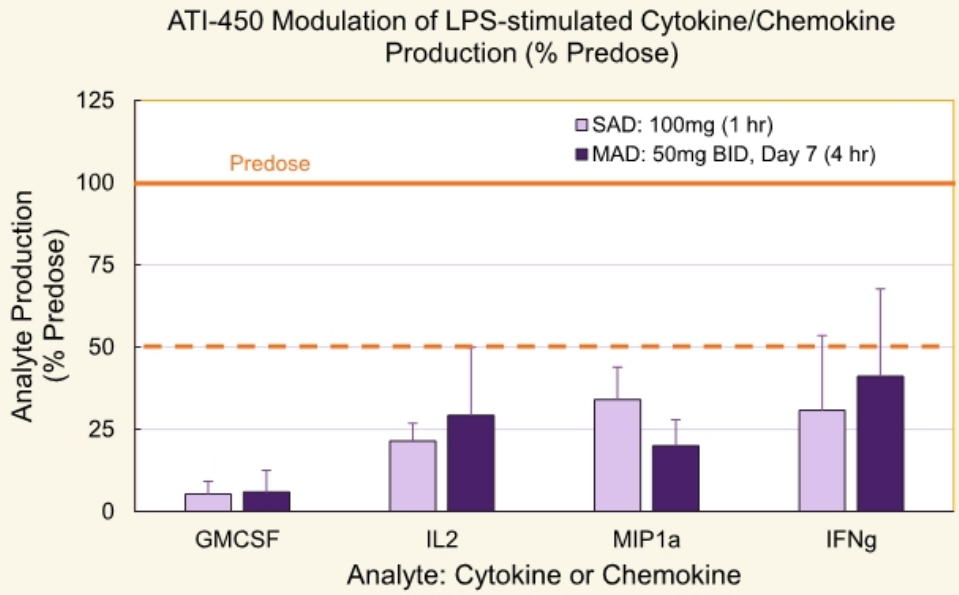


Cytokine	IC_{80} (ng/ml)
TNFα	31 ± 6
IL6	41 ± 20
IL8	40 ± 12

- ATI-450 was added to freshly isolated human whole blood for 1 hour and stimulated with IL1β (10 ng/ml) for 5 hours
- Cytokines were measured by Meso Scale Discovery technology.

* Data on file.
HWB = Human Whole Blood

ATI-450 Inhibited Additional CRS-Related Proteins in HWB
Ex Vivo LPS-Stimulated HWB from SAD/MAD Study



Marked Inhibition of CRS Cytokines by ATI-450 in Phase 1 Trial

*Data on file.

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

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Atopic Dermatitis Opportunity

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

- ✓ The prevalence rate for AD (US) is 10-12% in children and 0.9% 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]

Approach	Status
• Comparable efficacy to other topical JAKs but "soft" drug to minimize the potential for systemic immunosuppression • JAK1/3 selective to minimize JAK2 inhibition toxicity • Deliver in a patient-friendly formulation • Patients with moderate to severe AD	• IND allowed • Next key milestone: First In Human Trial - 2H2020 • Plan to study in patients with moderate to severe AD

1 https://emedicine.medscape.com/article/1049085-overview. Last accessed 5-26-20.
2 https://emedicine.medscape.com/article/1049085-overview#a8. Last accessed 5-26-20.
3 Auster M, et al. Something Big Is Getting 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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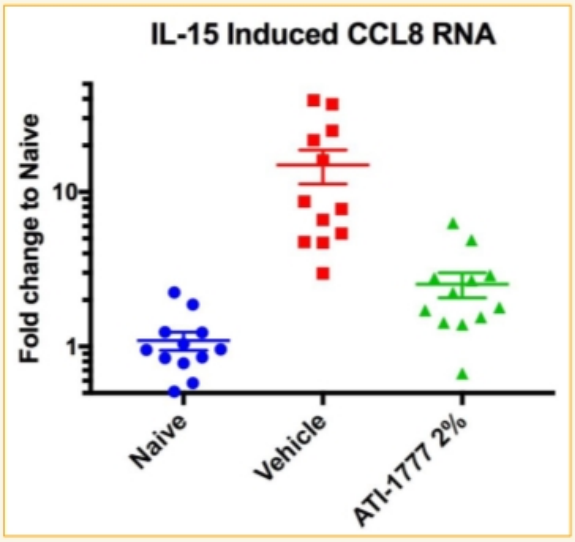
Porcine Model:
ATI-1777 Blocks IL15 Induced CCL8 mRNA in Skin

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 (JAK1/3) induced gene induction (CCL8).

* Data on file

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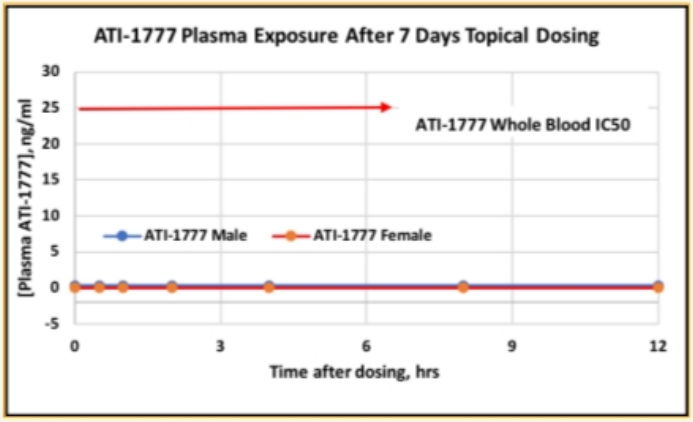
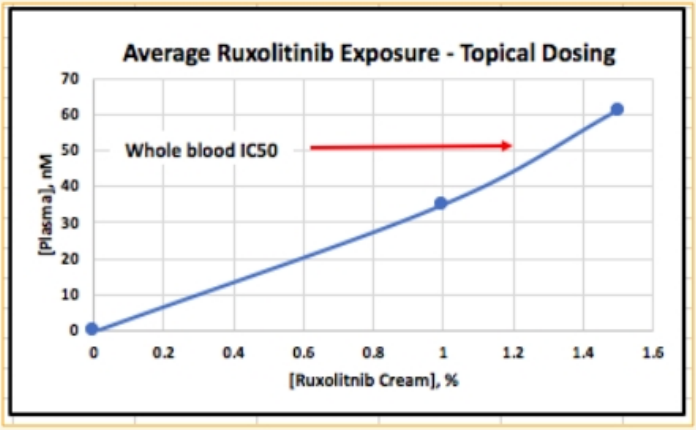
Minipig Model:
ATI-1777 Non-clinical Safety Program TK Data

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 IC_{50}



MINIPIG[1]



HUMAN[2,3]

1. Data on file.
2. Chen X, et al. *Clin Pharmacol Drug Dev.* 2013;3(1):34–42.
3. Purwani N, et al. *Br J Dermatol.* 2015;173:989–997.

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ATI-2138 (ITK/TXK/JAK3 Inhibitor)
(Investigational Drug Candidate)

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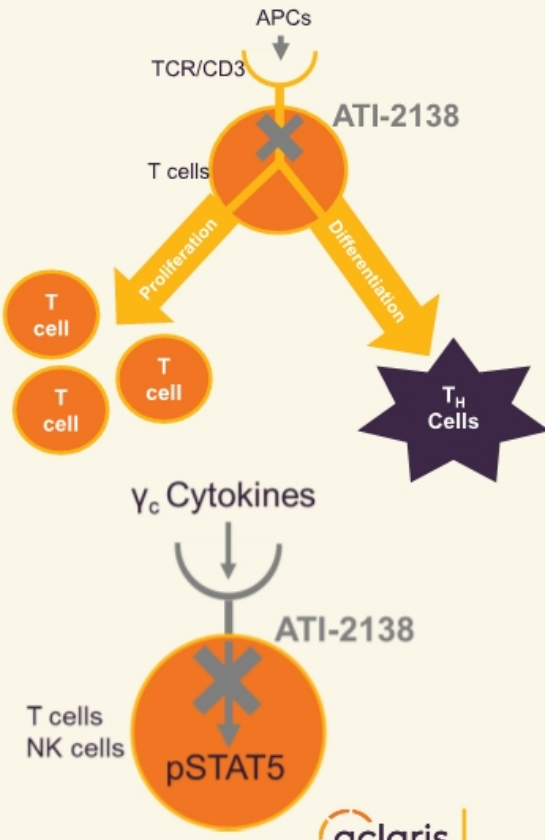
ATI-2138: Covalent ITK/TXK/JAK3 (ITJ) Inhibitor

- ATI-2138 covalently blocks ITK/TXK/JAK3[1]
  - ✓ Potential for synergistic efficacy
    - ITK/TXK required for T-cell receptor (TCR) signaling
    - JAK3 required for γc cytokines (IL-2/4/7/9/15/21)
  - ✓ PD effects persist after plasma clearance
- ATI-2138 is selective for T-cell signaling[2,3]
  - ✓ Drugs like cyclosporine (CsA) inhibit calcineurin which is widely expressed
  - ✓ ATI-2138 targets unique kinases expressed only in immune cells
- ATI-2138 may potentially treat T-cell mediated autoimmune diseases[4,5]



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.

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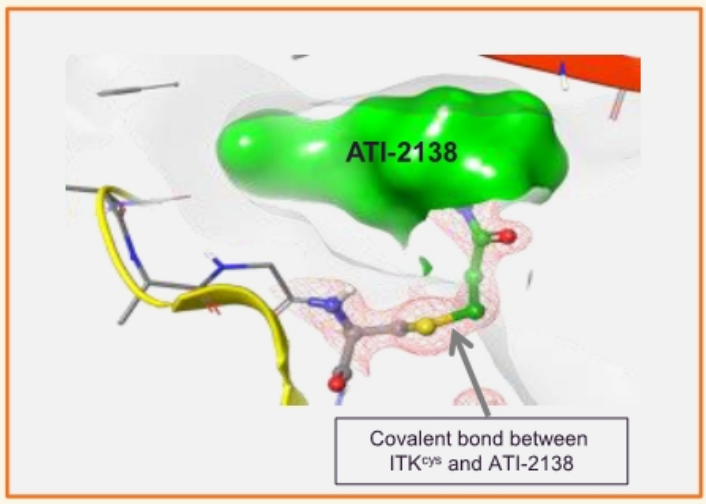
ATI-2138 is a Potent Covalent Inhibitor



Co-Crystal Structure of ATI-2138/ITK - shows ATI-2138 covalent binding to ITK

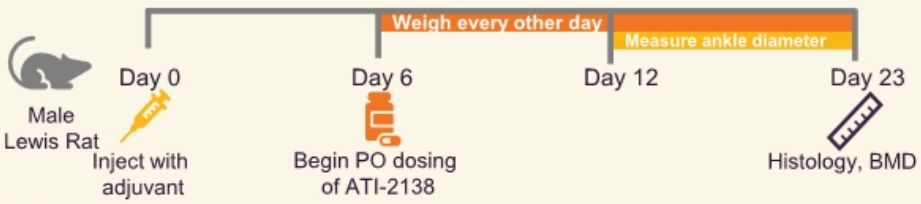
Cellular Inhibition of JAK and ITK/TXK

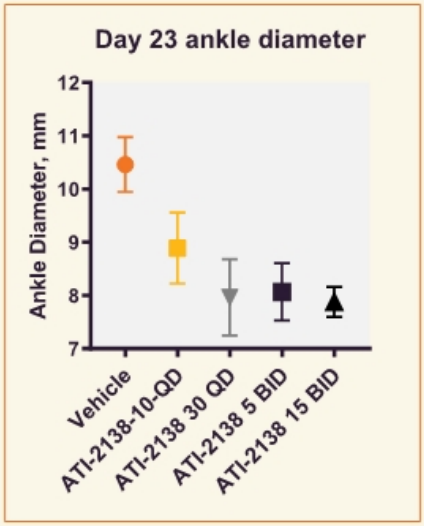
Assay Description	ATI-2138 IC_{50} (nM)	Assay
ITK/TXK activity	7	Jurkat pPLCγ-1
JAK1/3 activity	20	PBMC pSTAT-5
Both ITK/TXK and JAK3	13	HWB αCD3/IL15 IFNγ
BTK activity	52	Ramos pPLCγ-2

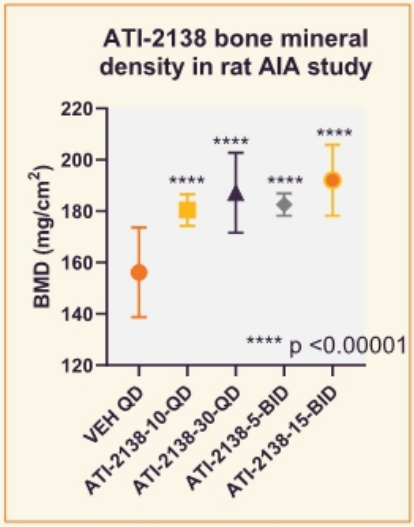
ATI-2138 potently inhibits ITK/TXK and JAK3 in cells and in whole blood

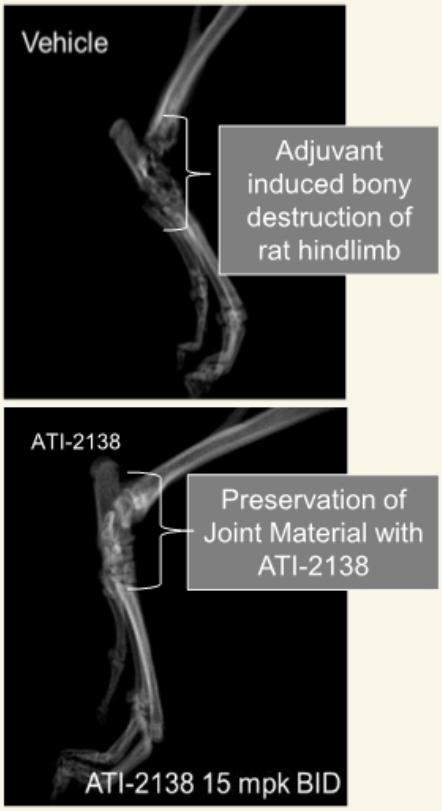
* Data on file

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









ATI-2138 reduced inflammation and bone mineral density loss

* Data on file

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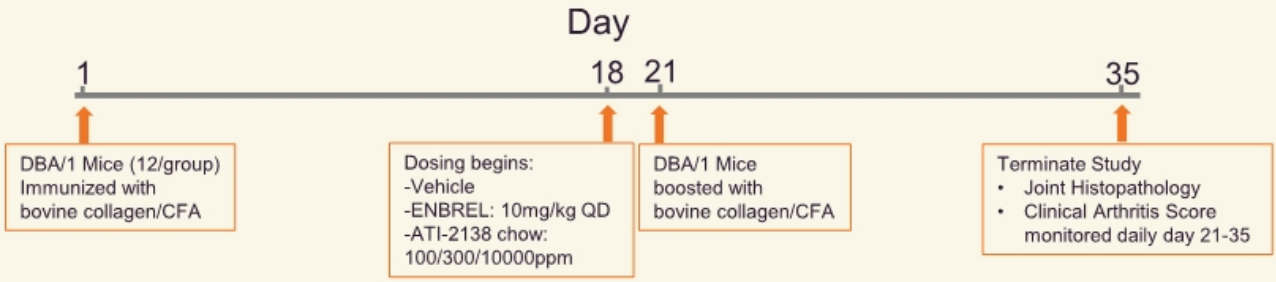
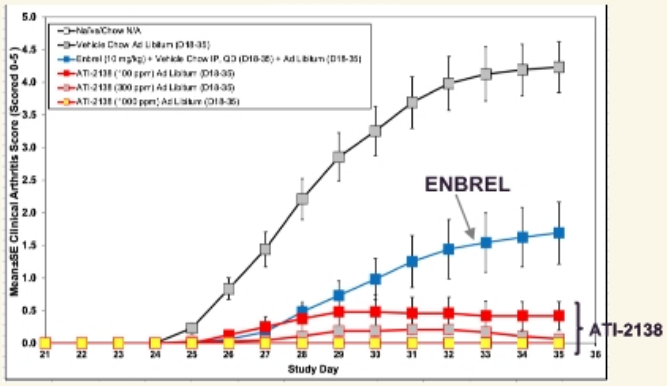
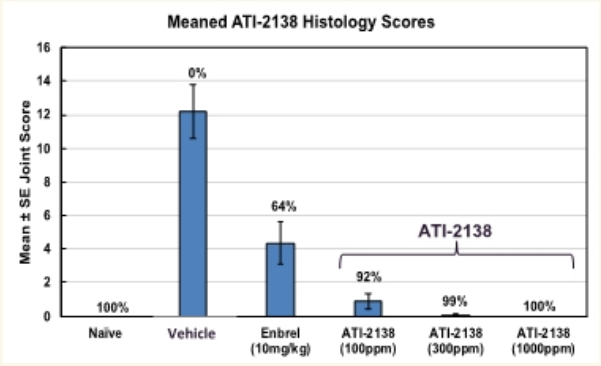
Mouse Model: ATI-2138 is Efficacious in mCIA



Clinical Arthritis Score



Joint Histology Score



In the gold standard mCIA model, ATI-2138 demonstrated efficacy superior to ENBREL

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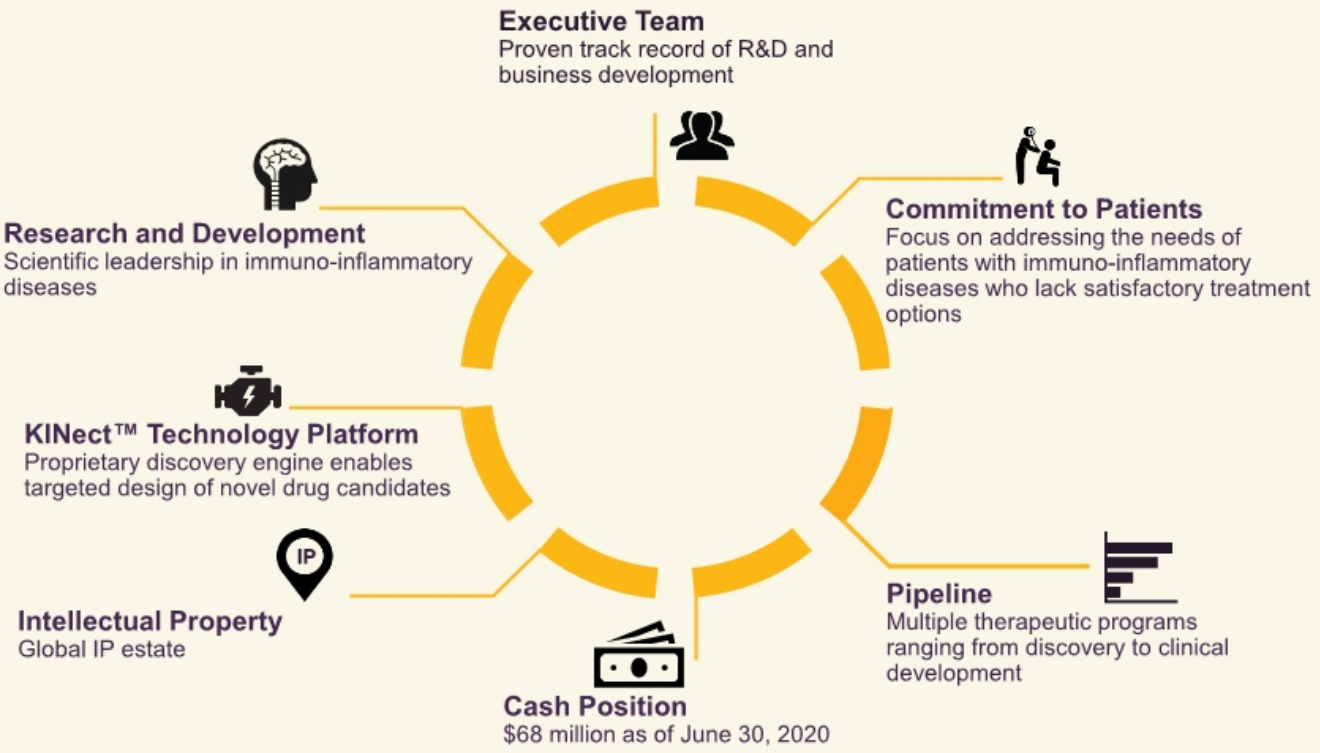
Empowering Patients Through Kinome Innovation



Key Milestones

Program/Milestone	2020				2021	
	1Q	2Q	3Q	4Q	1Q	2Q
ATI-450 (MK2 Inhibitor)						
Phase 1 Data (SAD/MAD)	✓					
Initiate Phase 2a Trial in Rheumatoid Arthritis	✓					
Phase 2a Data in Rheumatoid Arthritis						
Initiate Phase 2a Trial in CAPS						
ATI-1777 (Topical "Soft" JAK Inhibitor)						
Submit IND		✓				
Initiate Phase 2a Trial in Moderate to Severe Atopic Dermatitis						
ATI-2138 (ITK/TXK/JAK3 Inhibitor)						
Submit IND						

EMPOWERING PATIENTS THROUGH
KINOME INNOVATION

THANK YOU

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