

EMPOWERING PATIENTS THROUGH
KINOME INNOVATION

Company Overview

January 2020



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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 inprecedented 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, anti-IL1, anti-IL6
- Novel target for the potential treatment of various immuno-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 immuno-inflammatory diseases

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 R&D

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

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/TKK/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

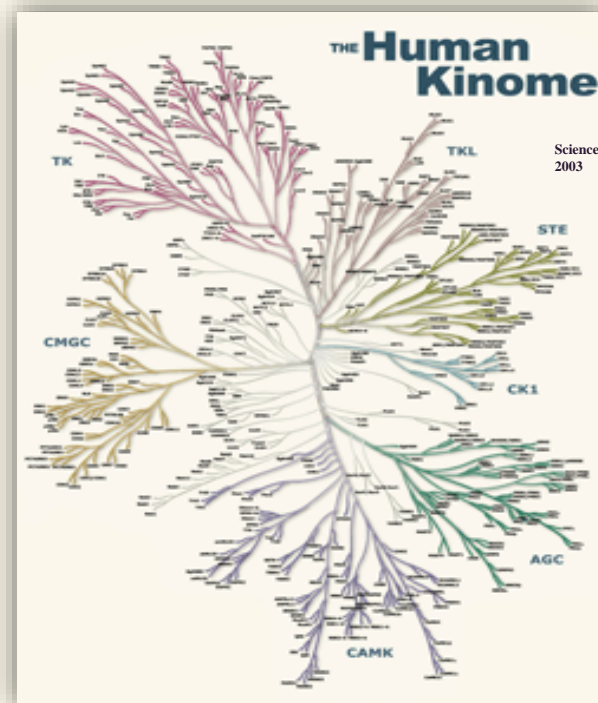


~36 Marketed Drugs

~\$48B*

Annual Sales of Kinase Drugs

Most Members of the Kinome Remain Unexplored



518 Members

>90% of the Human Kinome
remains undrugged

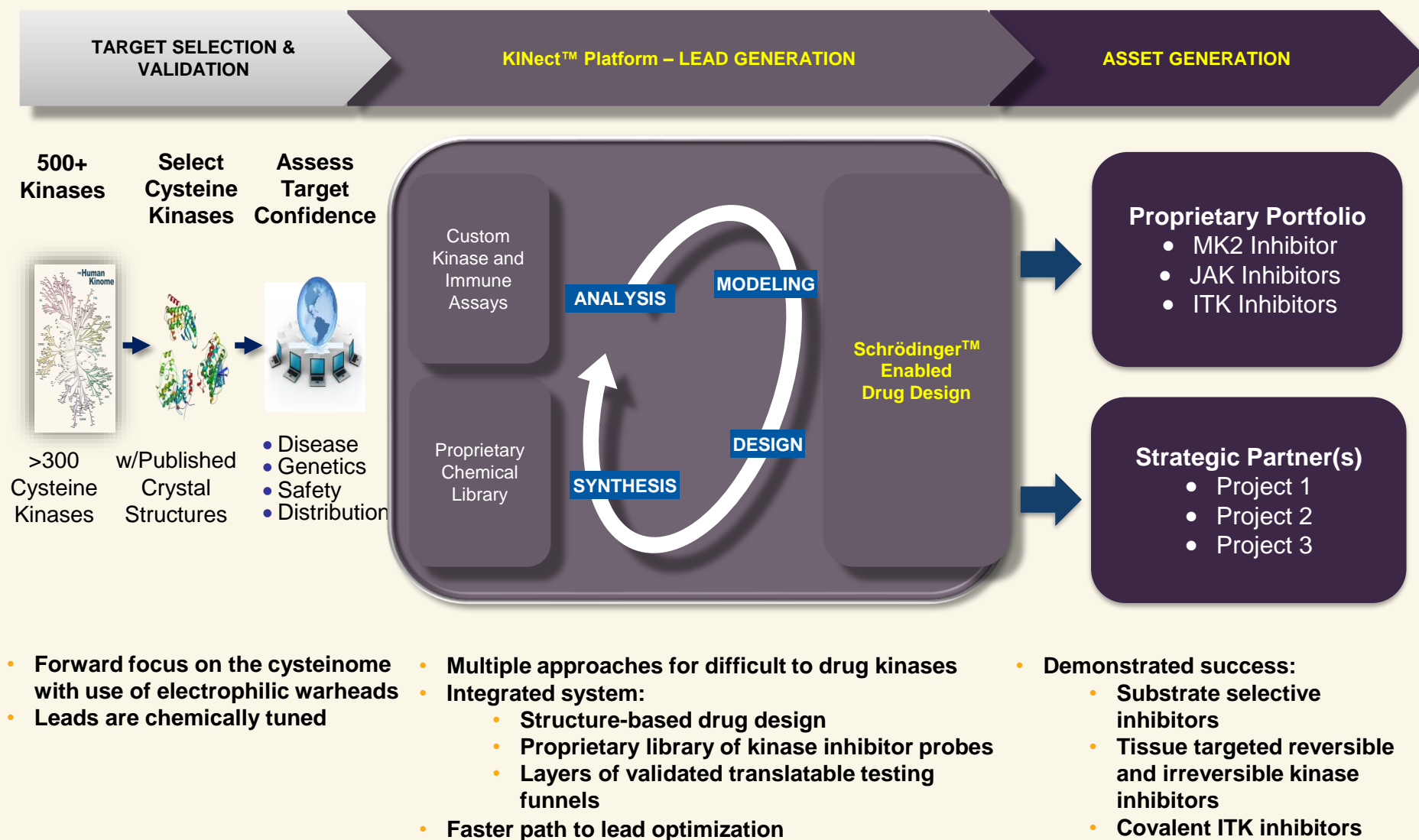
These drugs target less than 5% of the kinome

* Bologa C, et al. Unexplored opportunities in the druggable human genome. *Nat Rev Drug Discov.* 2018.

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KINect™ Platform

Developing Kinase Drug Candidates Rapidly & Efficiently



KINect™ Platform Demonstrated Success

Reversible and Covalent

MK2 Inhibitor

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

Tissue Restricted JAK and ITK Inhibitors

- 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

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

Unique Substrate Selective Drug Design

Tailoring physico-chemical and potency properties

Covalent Inhibition: for difficult to target kinase

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	IL-4R: 1
	CD20: 1	IL-12 / IL-23: 2	Integrin $\alpha 4\beta 7$: 1	IL-12 / IL-23: 1	
	JAK: 2	IL-17A: 2	JAK: 1	Integrin $\alpha 4\beta 7$: 1	
	Integrin $\alpha 4\beta 7$: 1	PDE4: 1			
	Other: 3				
Agents in Clinic (per target)	BTK: 9	IL-23: 2	JAK/STAT: 4	JAK/STAT: 5	JAK/STAT: 4
	JAK/STAT: 5	IL-17 / IL17R: 4	IL-23: 4	IL-23: 5	IL-33: 2
	IL-6: 3	JAK/STAT: 2	S1P-R: 2	S1P Receptor: 3	IL-13: 2
	TNF-alpha: 1	Others: 7	Integrins: 2	Integrin $\alpha 4\beta 7$: 1	IL-31: 2
	T-cell Receptor: 1		Others: 12	Others: 12	OX40: 2
	Others: 41				Others: 8
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 biologics/novel agents in the US: RA 350-400k / Psoriasis 300-350k / Ulcerative Colitis 225-275k / Crohn's 225-275k / Atopic Dermatitis 150-200k.

ATI-450: MK2 Inhibitor

(Investigational Drug Candidate)



MK2 Inhibitor – Potential 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[®] (adalimumab), ENBREL[®] (etanercept), REMICADE[®] (infliximab)
 - **anti-IL1:** KINERET[®] (anakinra), ILARIS[®] (canakinumab), ARCALYST[®] (rilonacept)
 - **anti-IL6:** KEVZARA[®] (sarilumab), ACTEMRA[®] (tocilizumab)
- ATI-450, an oral small molecule that 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

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

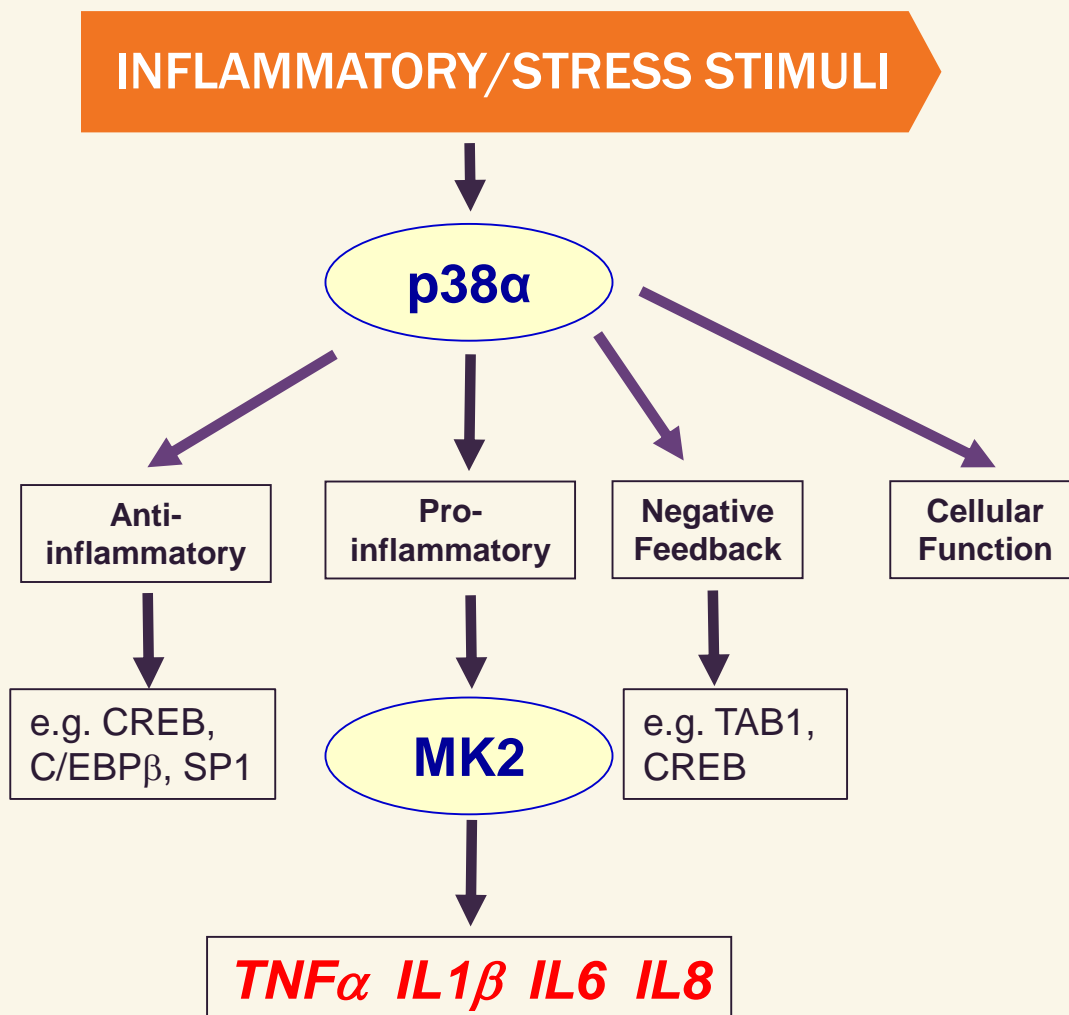


Evolution in Understanding of a Well-Known Path

The Path From p38 α to MK2

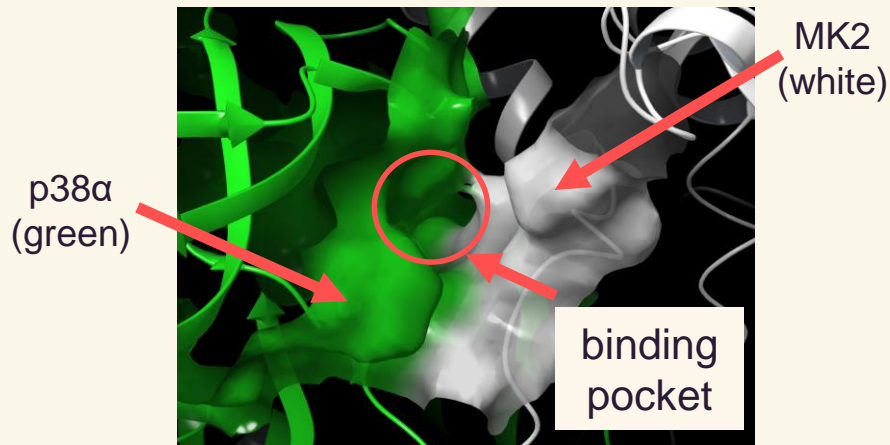
p38 α was initially targeted for suppressing TNF α and other pro-inflammatory cytokines

- Global p38 α inhibitors have exhibited toxicity and/or lack of sustained efficacy in RA and IBD
- p38 α 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
- ATI-450 locks MK2 in a catalytically inactive state – a unique MOA – which may be a viable approach to target MK2

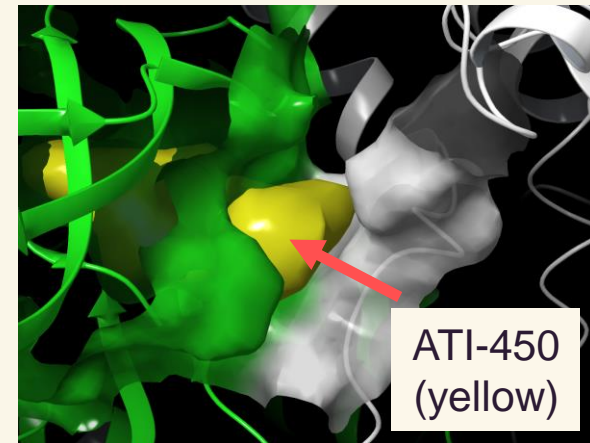


* Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.
* Cheung P, et al. *EMBO J*. 2003;22(21):5793-5805.
* Muniyappa H, et al. *Cell Signal*. 2008;20(4):675-683.
* Ma W, et al. *J Biol Chem*. 2001;276(17):13664-13674.

Capturing MK2 in an Inactive State



Crystal structure of the p38α/MK2 complex



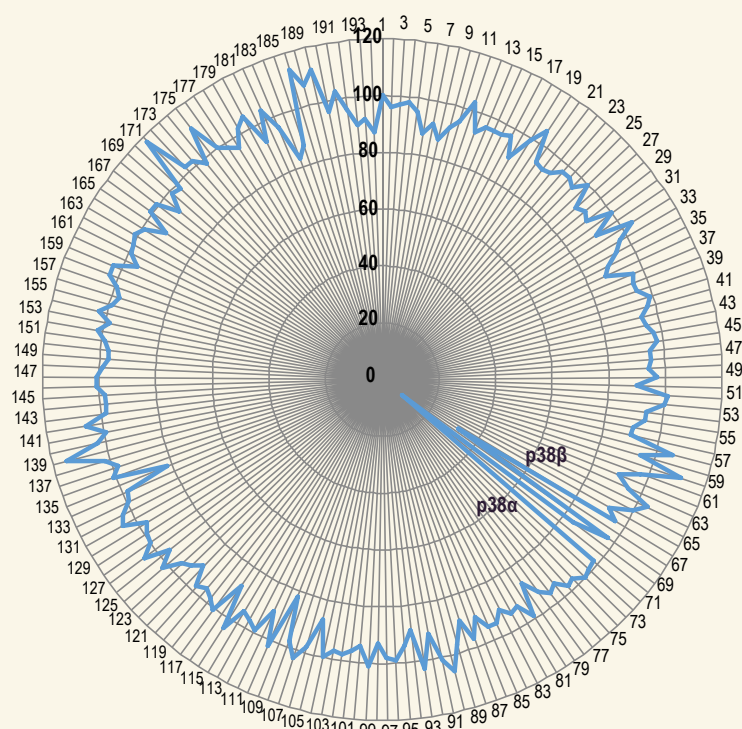
ATI-450 (yellow) docked in the pocket

- 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

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

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

* Optimized p38 peptide substrate

** Data on file.

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

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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	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 S, et al. <i>Integrative Biology.</i> 2019;11(7):301-314.
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.

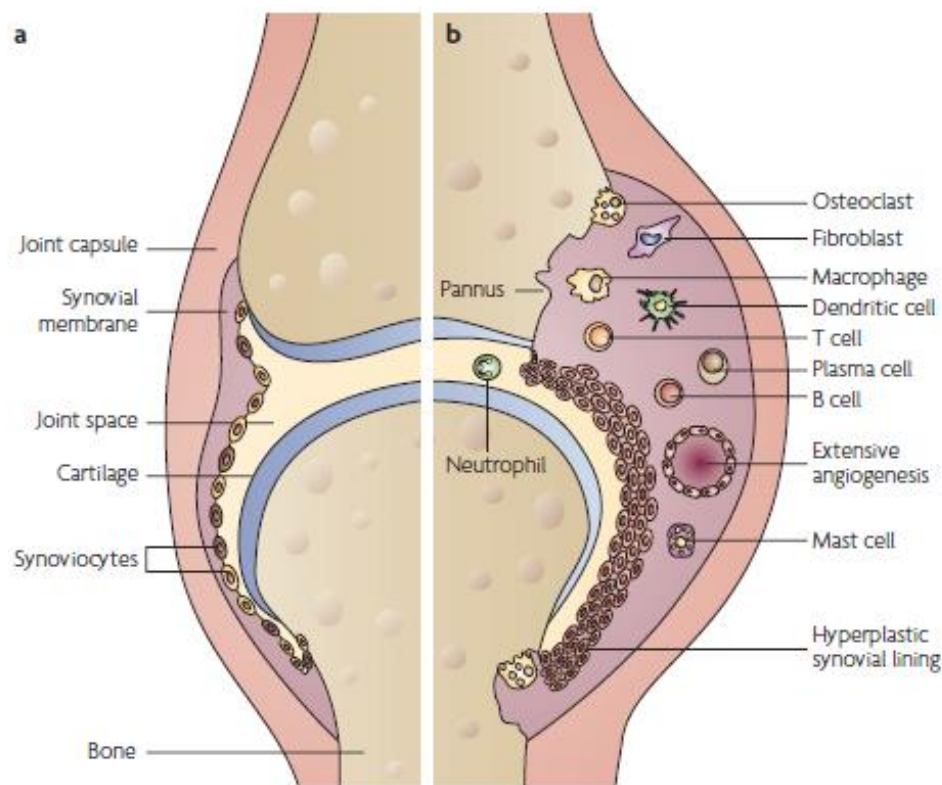
* PBMC = Peripheral blood mononuclear cells

ATI-450 Blocks MK2 – Potential Effect in Rheumatoid Arthritis

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

Normal Joint

RA Joint



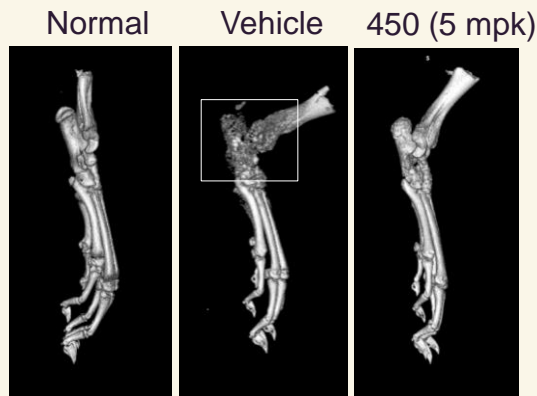
Strand V, et al. *Nat Rev Drug Discov.* 2007;6(Jan 2007):75-92.

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

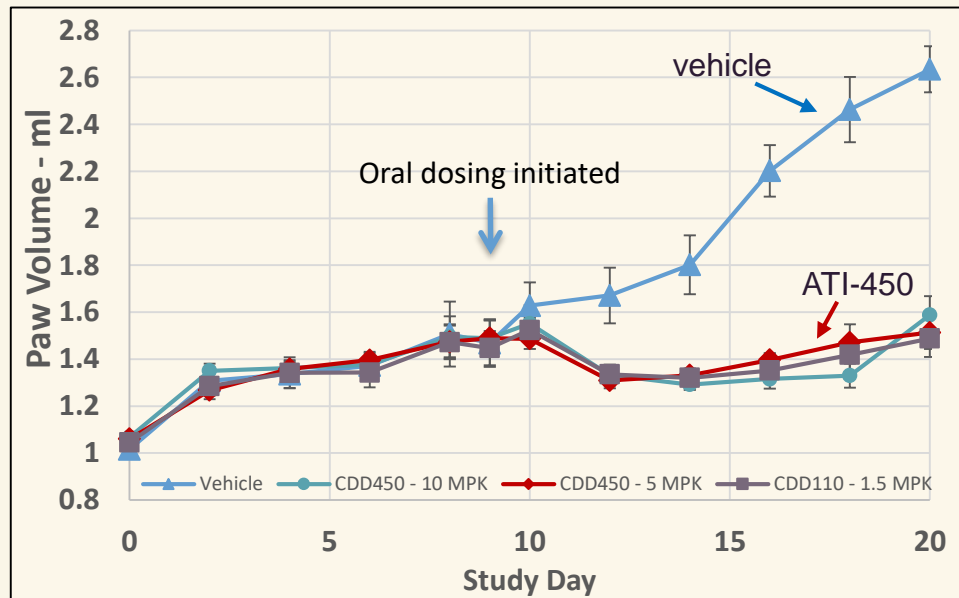
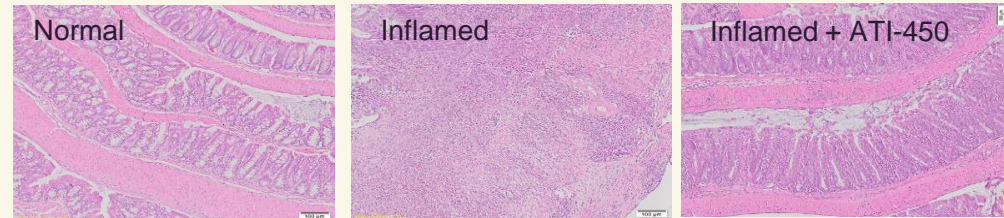
ATI-450: for bold items above data on file and Wang C, et al. *J Exp Med.* 2018;215 (5):1315-1325.

In vivo Preclinical Data of MK2 Pathway Inhibitor ATI-450

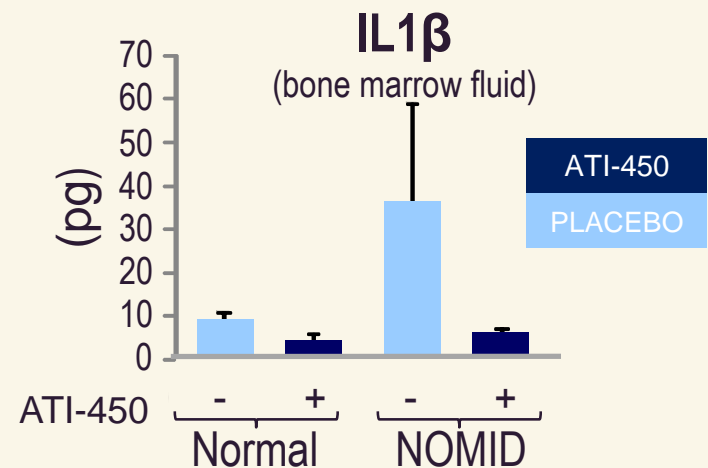
Joint Protection in Rat Arthritis Model¹



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



Cytokine Modulation in Orphan Autoinflammatory Disease (CAPS)¹

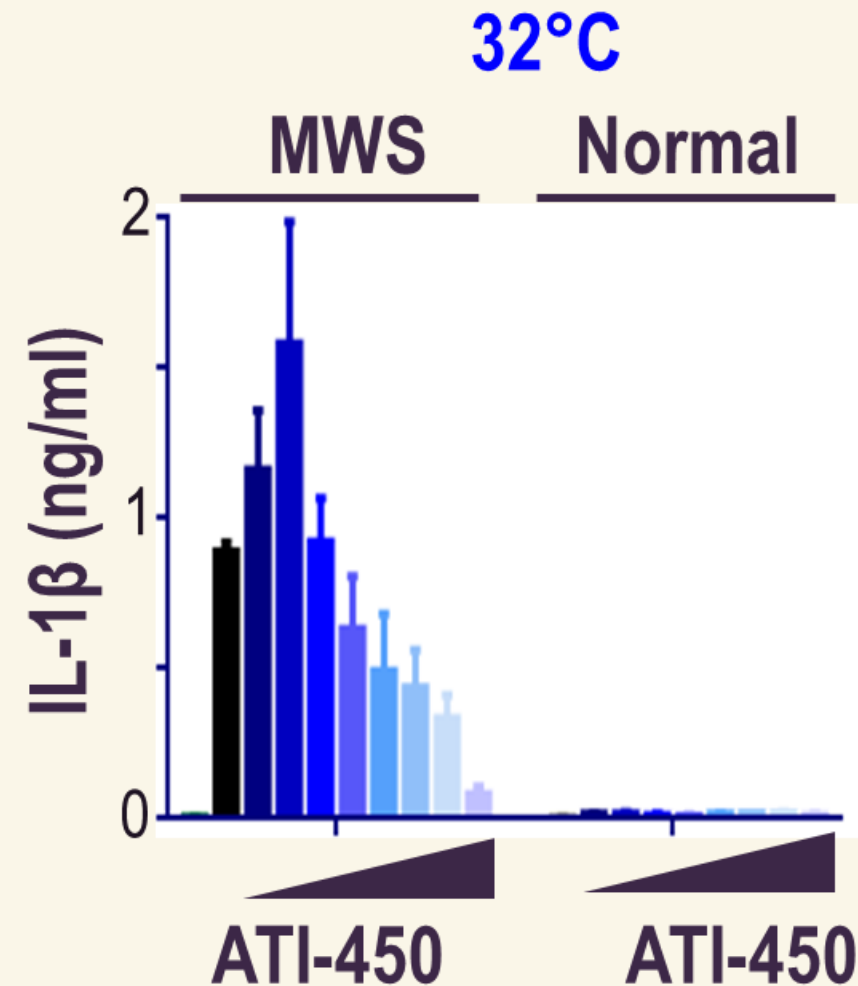


¹ Wang C, et al. *J Exp Med*. 2018;215(5):1315-1325.

² Strasser S, et al. *Integrative Biology*. 2019;11(7):301-314.

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



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

Mouse Model: ATI-450 Inhibits RANKL-induced Osteoclastogenesis

Bone marrow derived macrophages (BMDM) from NOMID mice

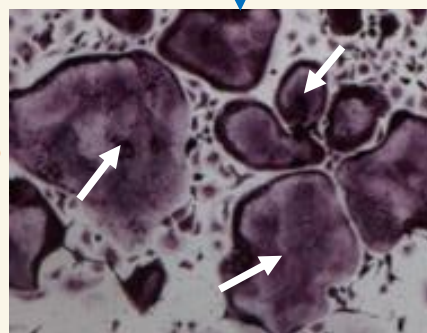
- In CAPS, osteoclastogenesis gives rise to low bone mass (osteopenia)
- (a) When bone marrow derived macrophages (BMDM) from NOMID mice are stimulated with RANKL (RANK ligand), they differentiate into osteoclasts
- (b) ATI-450 blocks this macrophage differentiation



NOMID BMDM



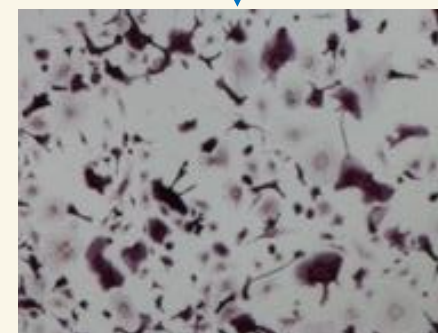
(a)



**NOMID BMDM
Plus ATI-450**



(b)

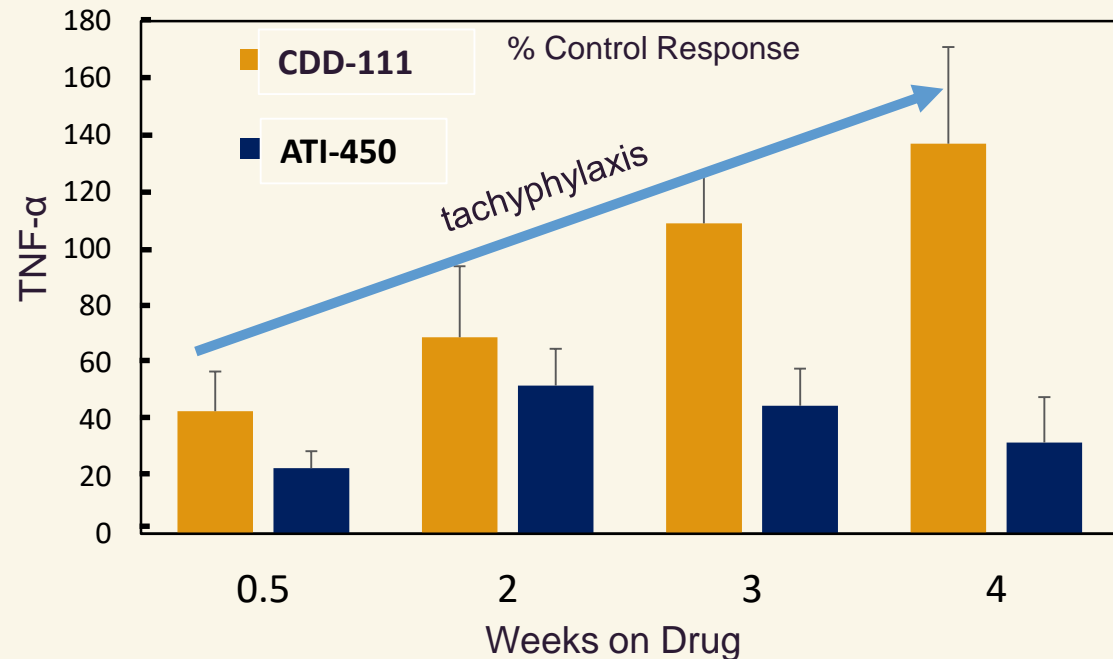


ATI-450 inhibits RANKL-stimulated macrophage differentiation into osteoclasts from NOMID mice

Mouse Model: LPS-Induced $\text{TNF}\alpha$ Production

ATI-450 demonstrated durable response (no tachyphylaxis)

- Global investigational p38 inhibitor CDD-111 lost inhibition over time
- MK2 inhibitor ATI-450 (investigational compound) 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 $\text{TNF}\alpha$ levels determined

ATI-450 Clinical Development

Phase 1 Single and Multiple Ascending Doses

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

Preliminary Data Analysis Available

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

ATI-450-PKPD-101 SAD/MAD Phase 1 Trial

Preliminary Data

- First-in-human, randomized, observer-blind, placebo-controlled trial
 - ✓ Single Ascending Doses and Multiple Ascending Doses (SAD/MAD)
- Objectives:
 - ✓ Primary
 - To assess the safety, tolerability, and pharmacokinetics (PK) profile of ATI-450, an investigational oral MK2* inhibitor compound
 - ✓ Secondary
 - To assess the effect of food on the PK of ATI-450
 - To explore the pharmacodynamics (PD) of ATI-450
 - To evaluate the potential for an interaction with methotrexate

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

ATI-450-PKPD-101

Trial Design and Demographics

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

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

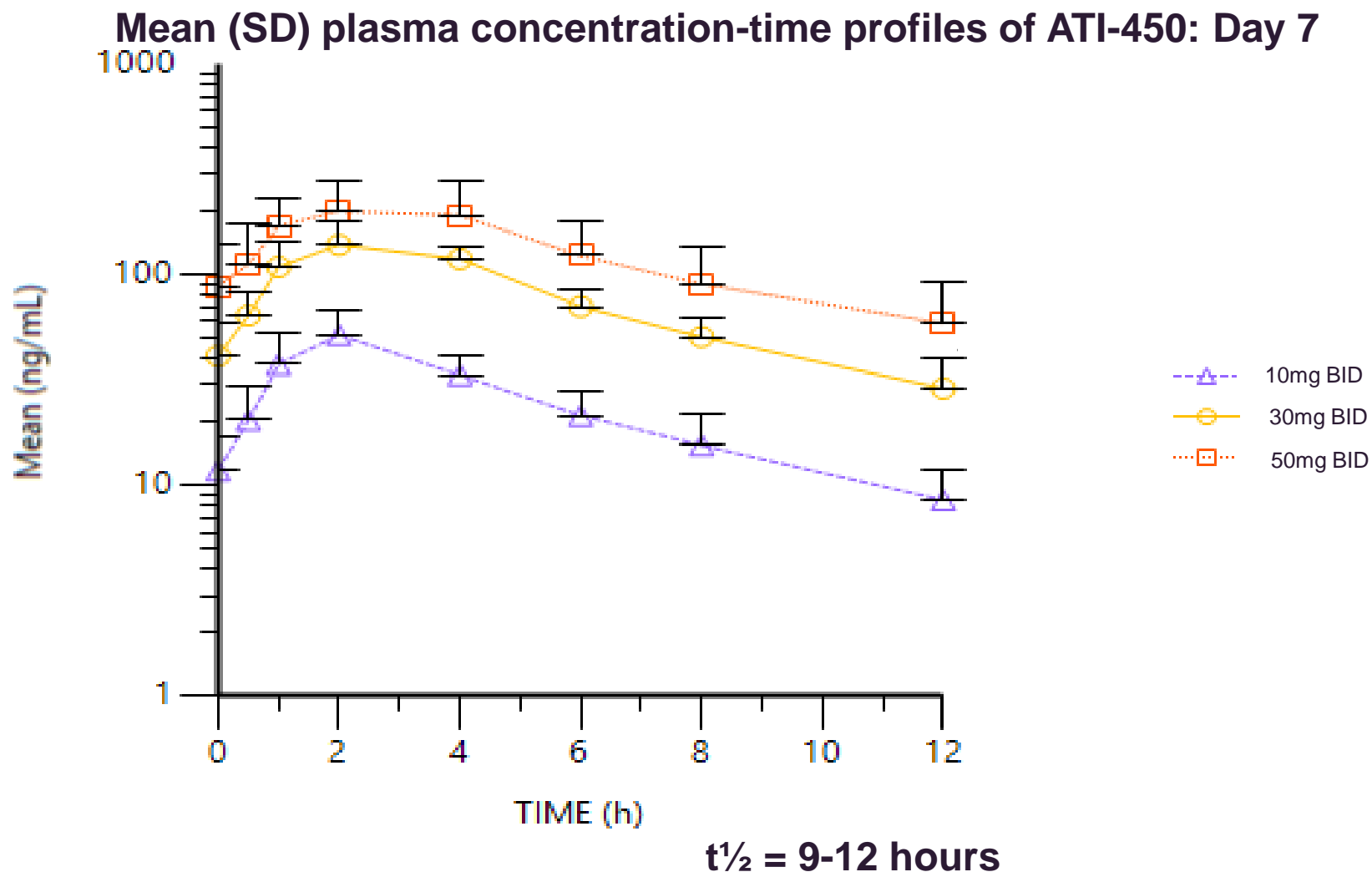
- No serious adverse events
- No adverse events led to discontinuation of study medication
- All adverse events were mild in severity - dizziness and other adverse events caused minimal discomfort, and did not interfere with everyday activities
- A trend of a decrease in absolute neutrophil count was observed
 - ✓ No correlation with clinical sequelae
 - ✓ This effect is consistent with the pharmacodynamic profile of certain anti-TNF therapies¹

¹ Dilling M, et al. *Front. Immunol.* 2016;7(508):1-9.

* Data on file.

ATI-450-PKPD-101

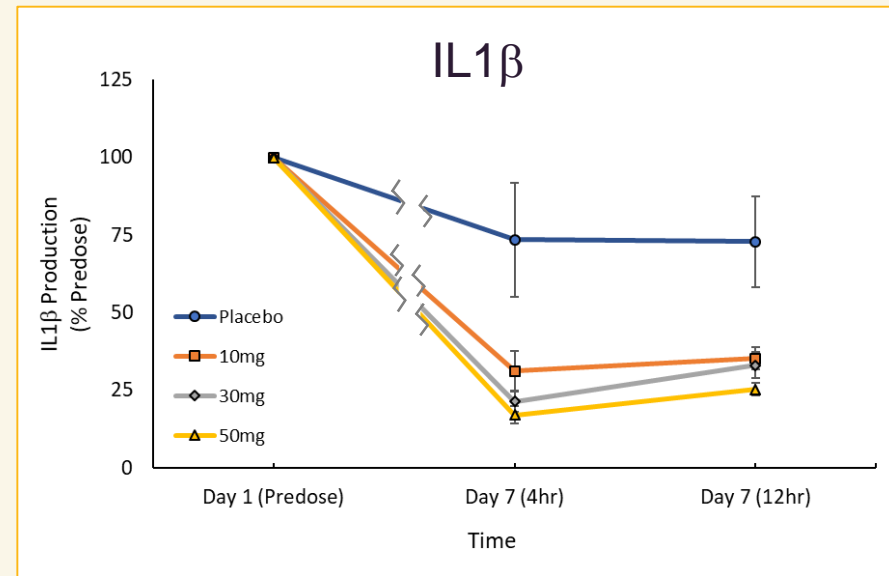
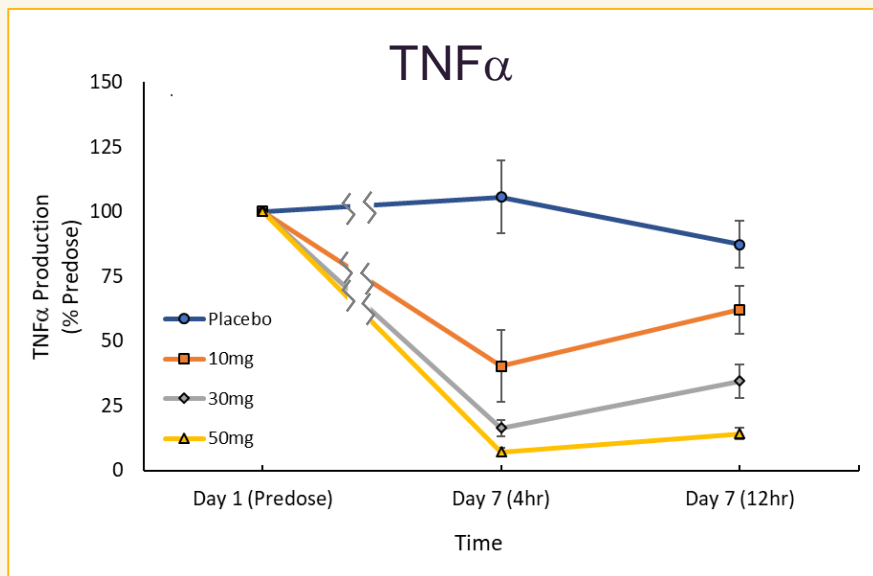
MAD Pharmacokinetics: Dose Proportional PK



* Data on file

ATI-450-PKPD-101

ATI-450 PD: Day 7 MAD PD Marker Time Dependence Cytokines $TNF\alpha$ and $IL1\beta$

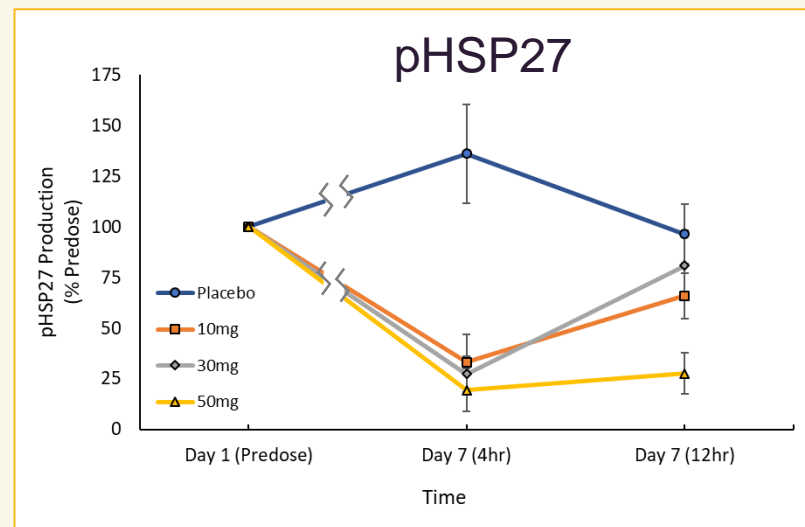
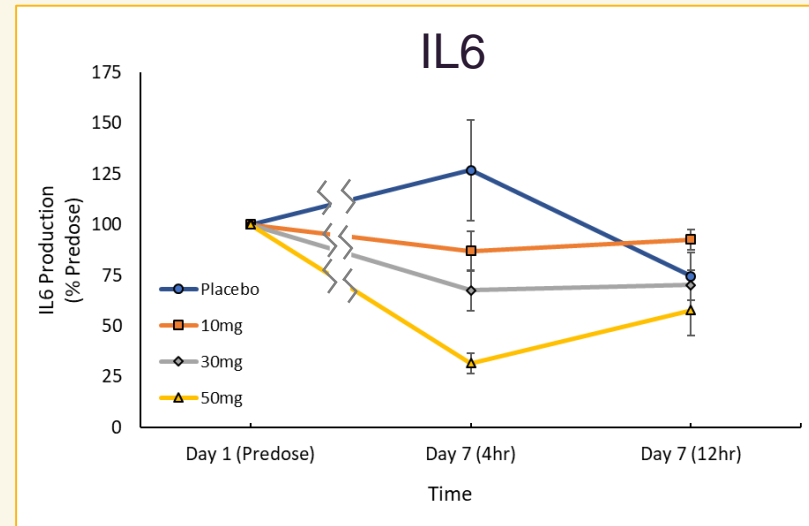
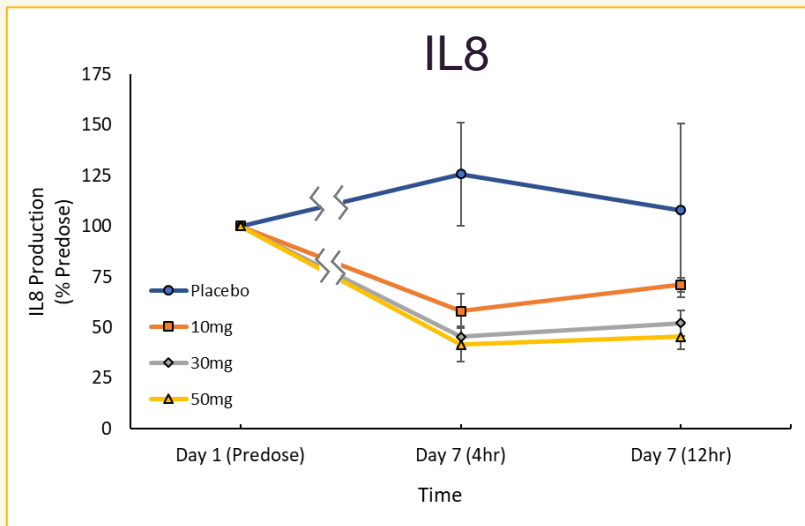


- ATI-450 dosed in subjects orally at doses of 10mg, 30mg and 50mg BID for 7 days
- Day 1 (pre-dose) levels are from blood taken on day 1 just prior to the first dose of ATI-450
- Blood samples drawn on day 7 at 4hr and 12hr post-dose
- Samples *ex vivo* stimulated with LPS
- Data expressed as mean +/- SEM

* Data on file

ATI-450-PKPD-101

ATI-450 PD: Day 7 MAD PD Marker Time Dependence Cytokines IL6 and IL8 and Target Biomarker pHSP27



- ATI-450 dosed in subjects orally at doses of 10mg, 30mg and 50mg BID for 7 days
- Day 1 (pre-dose) levels are from blood taken on day 1 just prior to the first dose of ATI-450
- Blood samples drawn on day 7 at 4hr and 12hr post-dose
- Samples *ex vivo* stimulated with LPS
- Data expressed as mean +/- SEM

ATI-450-PKPD-101

Plasma Levels Greater Than IC₈₀ Throughout Dosing Interval for 4 Key PD Markers at 50mg BID Dose

ATI-450 C_{trough} and C_{max} fold above IC₈₀ by dose

Analyte	Dose Level (mg BID)	Parameter	Ctrough	Cmax
IL1b	10	Fold IC80	0.3	1.5
IL6	10	Fold IC80	0.0	0.1
IL8	10	Fold IC80	0.3	1.5
pHsp27	10	Fold IC80	0.3	1.4
TNFa	10	Fold IC80	0.2	0.9
IL1b	30	Fold IC80	1.2	4.2
IL6	30	Fold IC80	0.1	0.2
IL8	30	Fold IC80	1.2	4.1
pHsp27	30	Fold IC80	1.1	4.0
TNFa	30	Fold IC80	0.7	2.4
IL1b	50	Fold IC80	2.5	6.4
IL6	50	Fold IC80	0.1	0.3
IL8	50	Fold IC80	2.5	6.2
pHsp27	50	Fold IC80	2.4	6.0
TNFa	50	Fold IC80	1.4	3.6

ATI-450 dosed at 50mg BID resulted in exposures 1.4-2.5x greater than those needed to inhibit 4 key PD markers (pHSP27, TNF α , IL1 β and IL8) at an IC₈₀

TNF α , IL1, and IL6: Validated Targets in Immuno-Inflammatory Diseases - *Opportunity for an Oral with Profile of ATI-450*

Injectables: Monoclonal antibodies (MAbs)

- MAbs with high degree of specificity against single cytokines approved in immuno-inflammatory diseases:
 - **anti-TNF:** HUMIRA[®] (adalimumab), ENBREL[®] (etanercept), REMICADE[®] (infliximab)
 - **anti-IL1:** KINERET[®] (anakinra), ILARIS[®] (canakinumab), ARCALYST[®] (rilonacept)
 - **anti-IL6:** KEVZARA[®] (sarilumab), ACTEMRA[®] (tocilizumab)

Oral: Small molecule MK2 inhibitor

- ATI-450 showed marked inhibition of TNF α , IL1 β , IL8 and IL6 in *ex vivo* stimulated blood samples collected from healthy volunteers in Phase 1*

* Data on file

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MK2 inhibitor ATI-450 Summary

- Discovered an approach to drug the target
 - ✓ Lock MK2 in a catalytically inactive state – a unique MOA
 - ✓ Multiple relevant inflammatory cytokines impacted
- Potential oral option for numerous diseases currently treated by biologics
 - ✓ Robust efficacy in a range of inflammation and mouse cancer models^{1,2}
- Phase 1 trial – Preliminary Data Available*
 - ✓ Generally well-tolerated at all doses
 - ✓ Dose proportional pharmacokinetics and a half-life supporting BID, and potentially QD, dosing
 - ✓ Inhibits key cytokines and biomarkers in a dose-dependent way
- Proof of concept Phase 2 trial in RA expected to begin first half 2020
 - ✓ To demonstrate clear pharmacodynamic effect and no tachyphylaxis
 - ✓ To demonstrate early signs of efficacy in a well understood disease
 - ✓ To assess safety and tolerability
- IL1 inflammatory indications under consideration

* Data on file

1 Murali B, et al. *Cancer Res.* 2018;78(19):1-13.

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
- 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>. Last accessed 11-1-19.

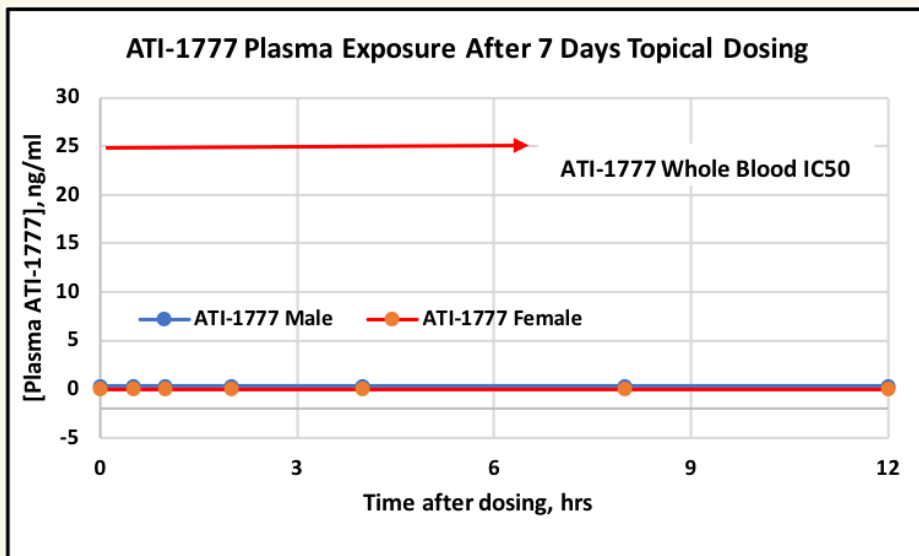
² Auster M, et al. Something Big Is Getting Bigger [research note]. *Credit Suisse Equity Research*; 2019.

³ Shreberk-Hassidim R, et al. *J Am Acad Dermatol*. 2017;Apr;76(4):745-753.

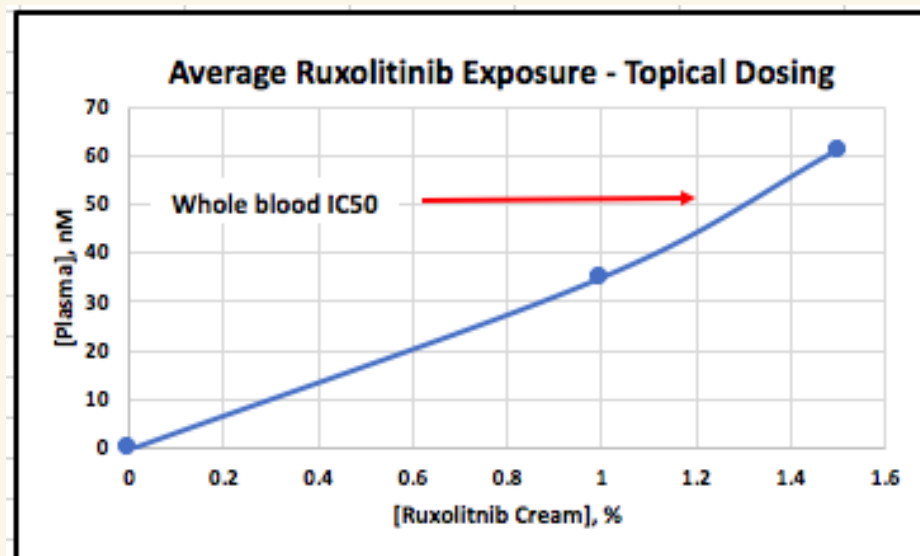
Minipig Model: ATI-1777 Nonclinical Safety Program TK Data

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}

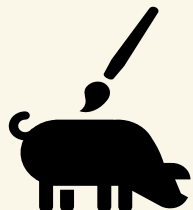
¹ Data on file.

² Chen X, et al. *Clin Pharmacol Drug Dev.* 2013;3(1):34–42.

³ Punwani N, et al. *Br J Dermatol.* 2015;173:989–997.

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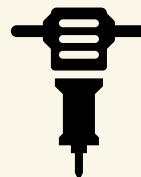
Porcine Model: ATI-1777 Blocks IL15 Induced CCL8 mRNA



Apply
formulation to
back of pig,
wait 1 hr



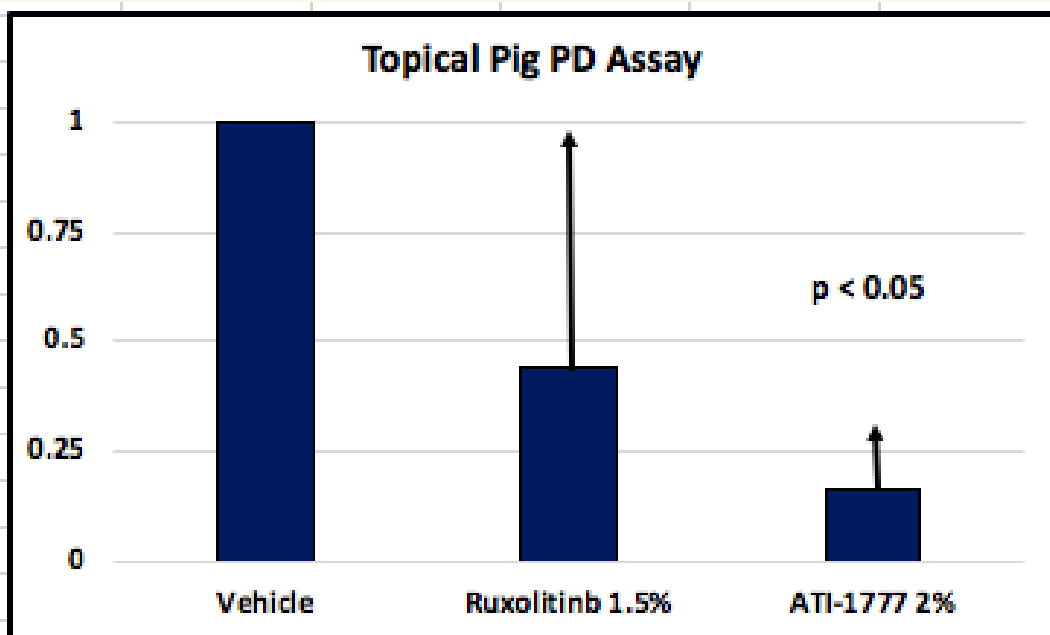
Intra-dermal
Injection of
porcine IL15,
wait 3 hr



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



Topical Pig PD Assay



- 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.

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

Formulate a topical therapy for atopic dermatitis 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

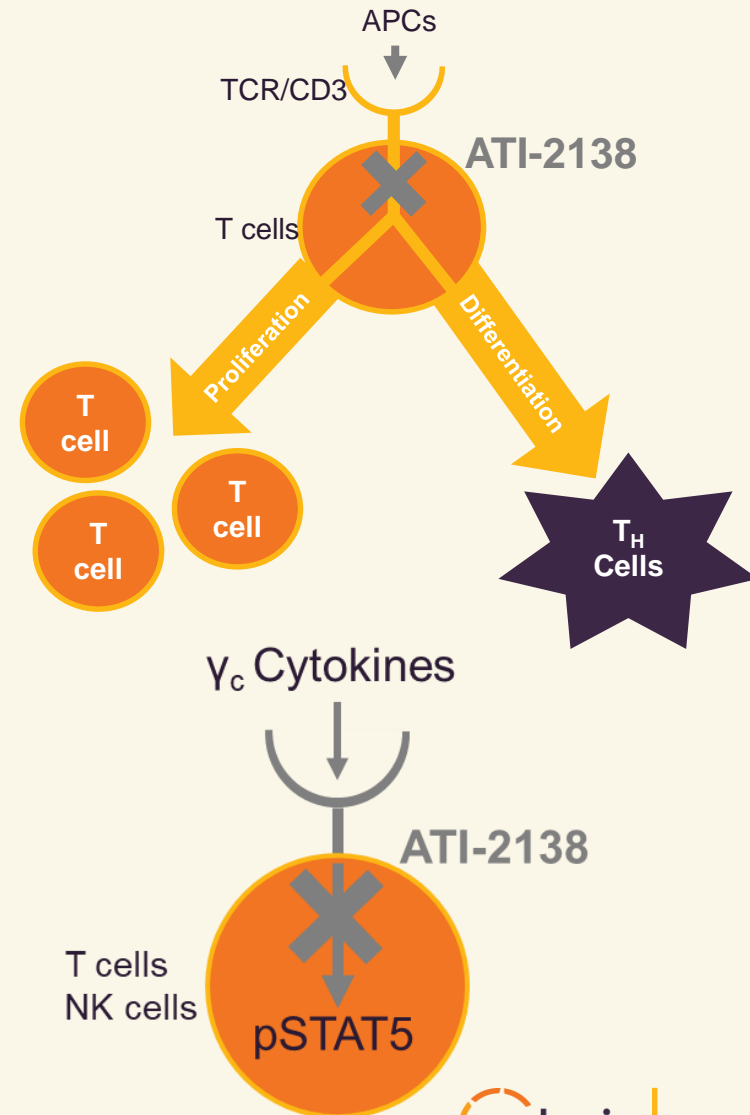
ATI-2138 (ITK/TXK/JAK3)

(Investigational Drug Candidate)

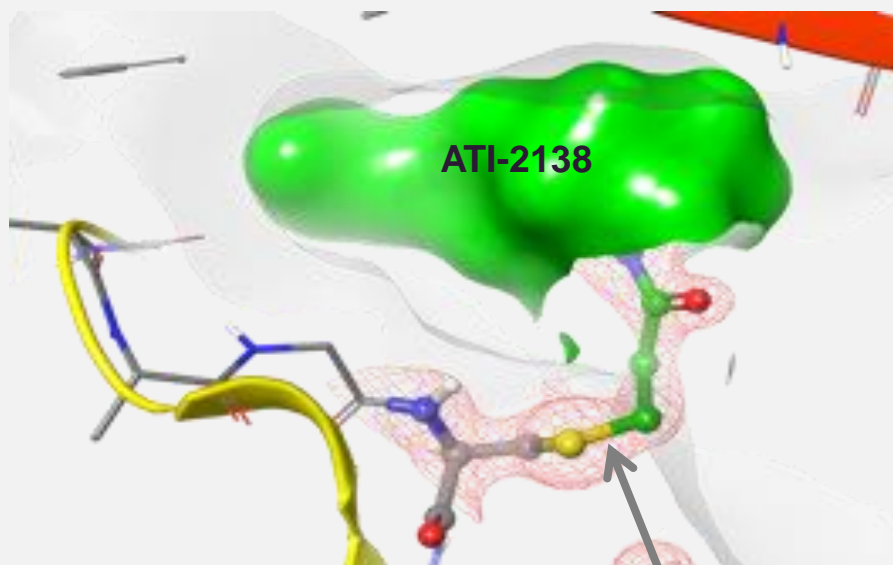


ATI-2138: Covalent ITK/TXK/JAK3 Inhibitor

- ATI-2138 (investigational compound) 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 planned milestones
 - ✓ IND submission in 4Q20/1Q21
 - ✓ First In Human - 1H 2021



ATI-2138 is a Potent Covalent Inhibitor



Covalent bond between
ITK^{Cys} and ATI-2138

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

Cellular Inhibition of JAK and ITK/TXK

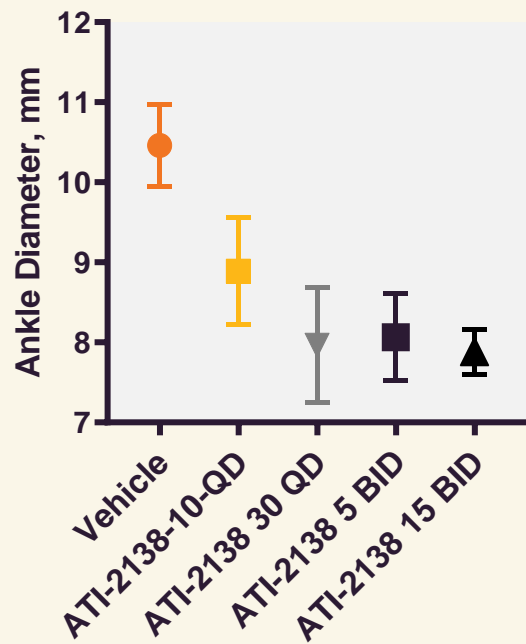
Assay Description	ATI-2138 IC ₅₀ (nM)	Assay
ITK/TXK activity	7	Jurkat pPLCγ-1
JAK1/3 activity	20	PBMC pSTAT-5
Both ITK/TXK and JAK3	13	HWB αCD3/IL15 IFNγ
BTK activity	52	Ramos pPLCγ-2

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

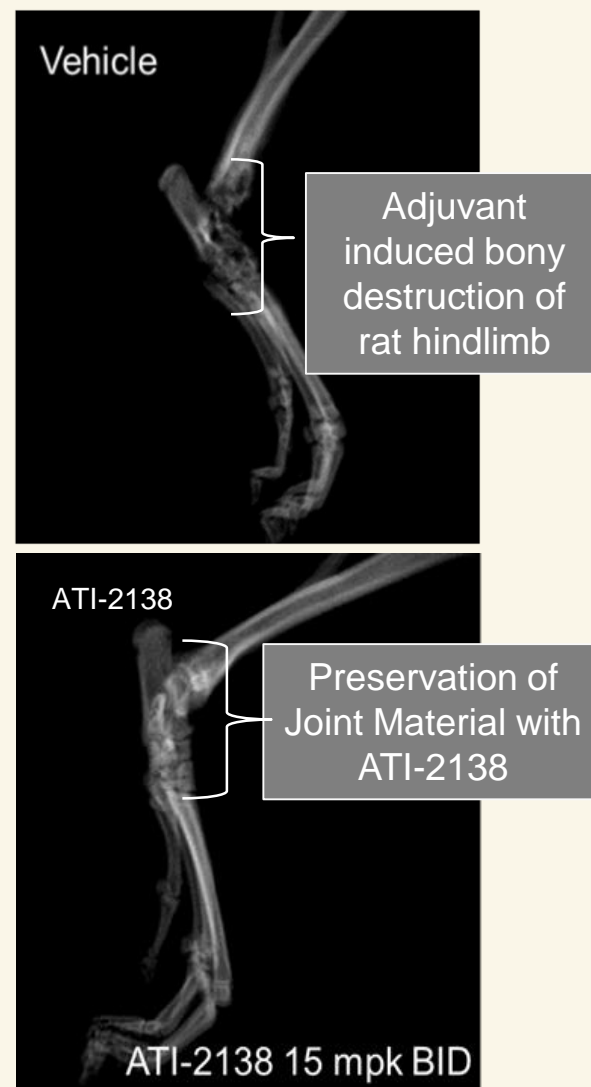
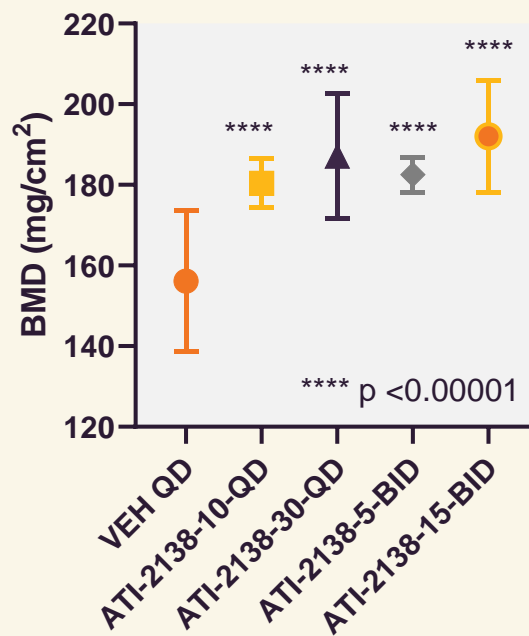
Rat Adjuvant Induced Arthritis (AIA) Model: ATI-2138 Reduced Inflammation and Protected Bone



Day 23 ankle diameter

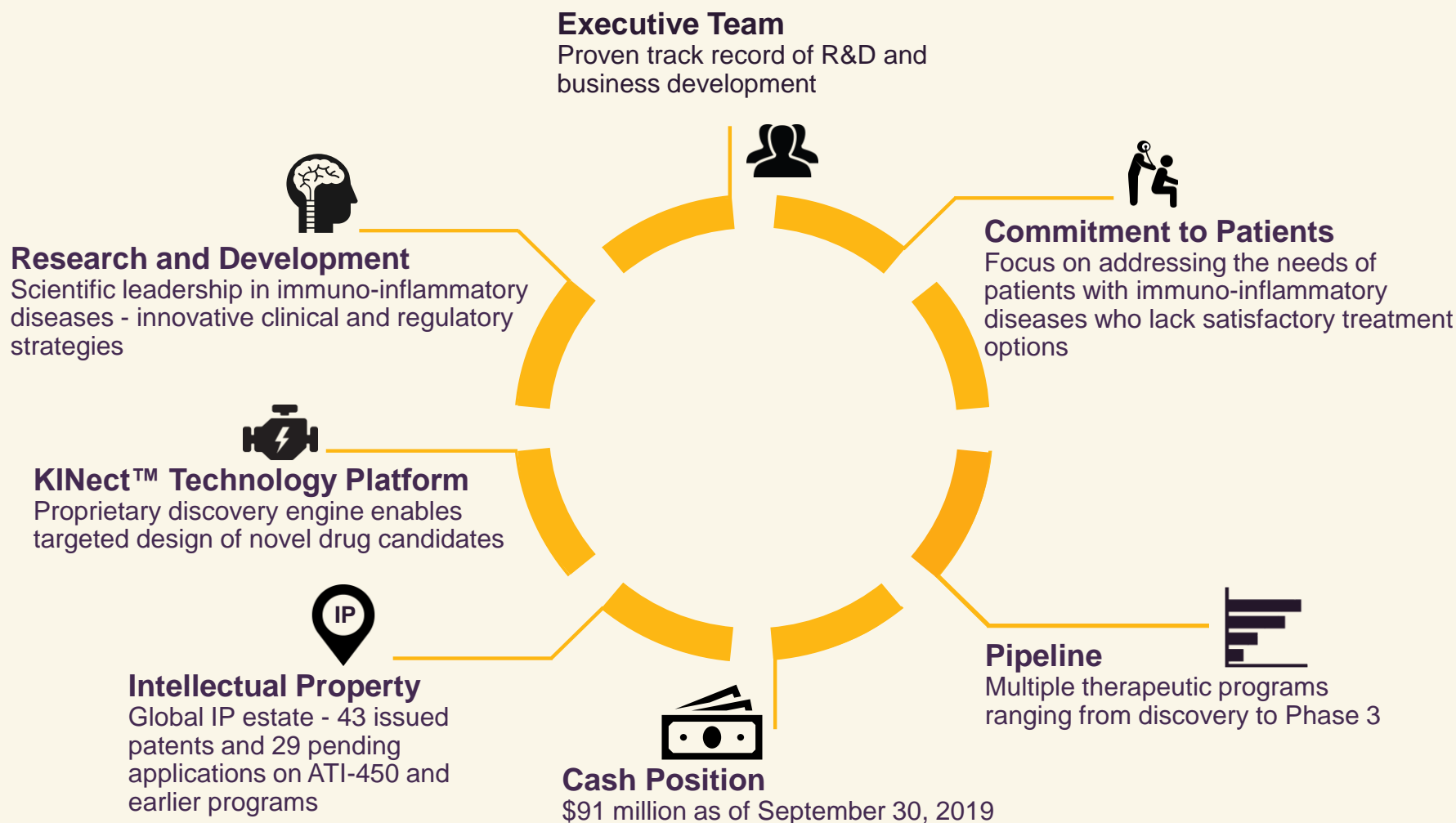


ATI-2138 bone mineral density in rat AIA study



ATI-2138 reduced inflammation and bone mineral density loss

Biopharmaceutical Company



Catalysts

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

