EMPOWERING PATIENTS THROUGH
KINOME INNOVATION

Company Overview

February 2021

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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 availability of data from its clinical trials and the timing of its regulatory submissions. 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, risks and uncertainties associated with preliminary trial results varying from final results, 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, 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" page of the “Investors” section 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. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

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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 designed 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

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

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The Kinase Opportunity
Unlocking the Potential of the Kinome

Medically Important and Productive Target Class

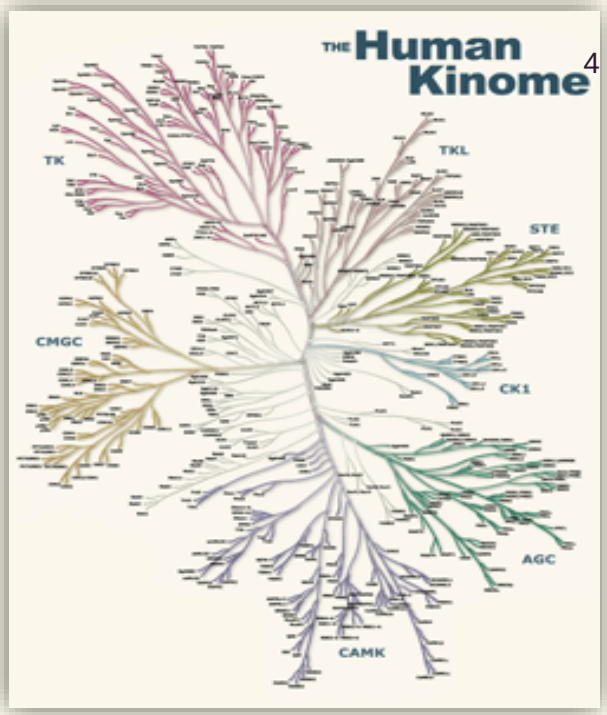
OFEV (nintedanib) capsules 150mg
Bosulif bosutinib
IBRANCE palbociclib
IRESSA
Inlyta axitinib
imbruvica (ibrutinib) 140mg capsules
ZELBORAF (vemurafenib) tablets
ICLUSIG (ponatinib) tablets 45 mg, 15 mg
COMETRIQ (cabozantinib) 80 mg and 20 mg capsules
gleevec (imatinib mesylate) tablets
RINVOQ upadacitinib
Votrient pazopanib tablets (200 mg)
GILOTRIF (afatinib) tablets
ICLUSIG (ponatinib) tablets 45 mg, 15 mg
XELJANZ (tofacitinib citrate)
Tykerb (lapatinib) 250 mg tablets
Jakafi ruxolitinib (tablets)
SPRYCEL dasatinib
Zydelig (idelalisib) tablets
Caprelsa (vandetanib) Tablets
Mekinist (trametinib)
XALKORI CRIZOTINIB
Stivarga (regorafenib) tablets
SUTENT capsules sunitinib malate
ZYKADIA ceritinib 150 mg capsules
Nexavar (sorafenib) tablets
LENVIMA (lenvatinib) capsules
Tasigna (nilotinib)
Tarceva erlotinib

>60 Marketed Drugs[1]

~$48B[2,3]

Annual Sales of Kinase Drugs

Most Members of the Kinome Remain Unexplored



518 Members

>90% of the Human Kinome remains undrugged[5]

Creating New Medicines Targeting Previously Inaccessible Kinome Targets

1. GoodRx. Accessed February 24, 2021. https://www.goodrx.com/kinase-inhibitors.
2. Data on file.
3. Oprea TI, et al. Unexplored opportunities in the druggable human genome. *Nature Rev Drug Discov*. Poster Jan. 2017.
4. Manning G, et al. *Science*. 2002;298(5600):1912-1934.
5. Oprea TI, et al. *Nat Rev Drug Discov*. 2018;17(5):317-332.

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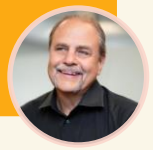
Experienced R&D Leadership Team
Proven Track Record in Immunology and Inflammation

- 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
Chief Scientific Officer



- 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
Scientific & BD Consultant

- 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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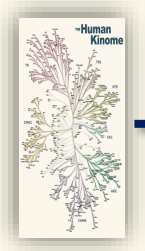
KINect® Platform
Developing Kinase Drug Candidates Rapidly & Efficiently

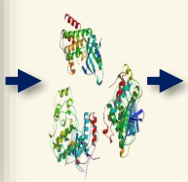
TARGET SELECTION & VALIDATION → **KINect Platform – LEAD GENERATION** → **ASSET GENERATION**

Explore 500+ Kinases



>300 Cysteine Kinases

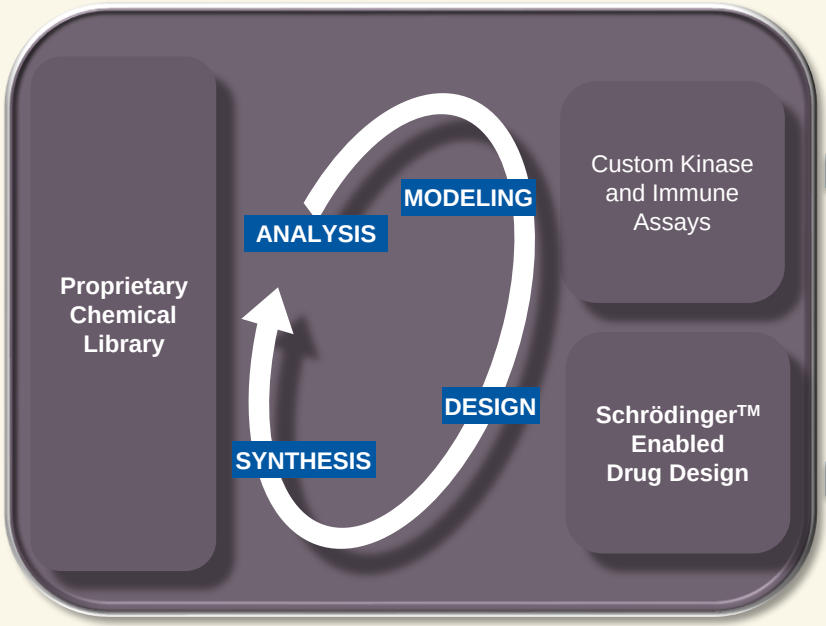
Select Cysteine Kinases



w/Published Crystal Structures

Assess Target Confidence

- Disease
- Genetics
- Safety
- Distribution



Proprietary Portfolio
- MK2 Inhibitors
- JAK Inhibitors
- ITK Inhibitors

Strategic Partnerships
- Research
- Licensing
- Commercial

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

MK2 Inhibitor	Tissue Restricted JAK and ITK Inhibitors	Covalent ITK Inhibitors
• Oral anti-TNF, anti-IL1, and anti-IL6 • Novel approach for a difficult to target kinase • Broad potential in several immuno-inflammatory diseases	• ATI-1777: Skin specific (Soft) topical JAK1/3 • Oral Gut-restricted reversible and irreversible inhibitors • Goal: comparable clinical efficacy with improved safety profile	• ITK/TXK/JAK3: Oral and topical T cell kinase inhibitors for autoimmune diseases
Unique substrate-selective drug design	**Tailoring physico-chemical and potency properties**	**Covalent inhibition for difficult-to-target kinase**

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

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Precision Immunology

Leverage Kinome Target Discovery to Address Unmet Needs

Advance the process of identifying and targeting key kinome-based enzymes involved in chronic inflammation and autoimmune disease.

Model, elaborate and assess compounds through a unique combination of our proprietary chemical library of kinase inhibitors, our expertise in structure-based drug design, and our custom kinase assays.

Validate newly created drug candidates through pathophysiologically-relevant custom assays that effectively translate to human diseases.

Leverage research and commercial partnerships to accelerate the clinical evaluation and potential impact of discovery platforms.

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Drug Development Pipeline

Drug Candidate / Program	Target	Route of Administration	Indication	Development Phase
Immuno-Inflammatory Diseases				
ATI-450	MK2 inhibitor	Oral	Rheumatoid arthritis (moderate to severe)	Phase 2
			Additional immuno-inflammatory diseases	Phase 2*
			COVID-19**	Phase 2
ATI-1777	"Soft" JAK 1/3 inhibitor	Topical	Atopic dermatitis (moderate to severe)	Phase 2
ATI-2138	ITK/TXK/JAK3 inhibitor	Oral	Psoriasis	Pre-IND
			Inflammatory bowel disease	
Undisclosed- Gut Restricted Program	JAK1/JAK3 inhibitor	Oral	Inflammatory bowel disease	Discovery
Undisclosed- Gut Restricted Program	ITK/TXK/JAK3 inhibitor	Oral	Inflammatory bowel disease	Discovery

* We are currently evaluating additional potential immuno-inflammatory indications which we expect to progress directly into Phase 2.
** 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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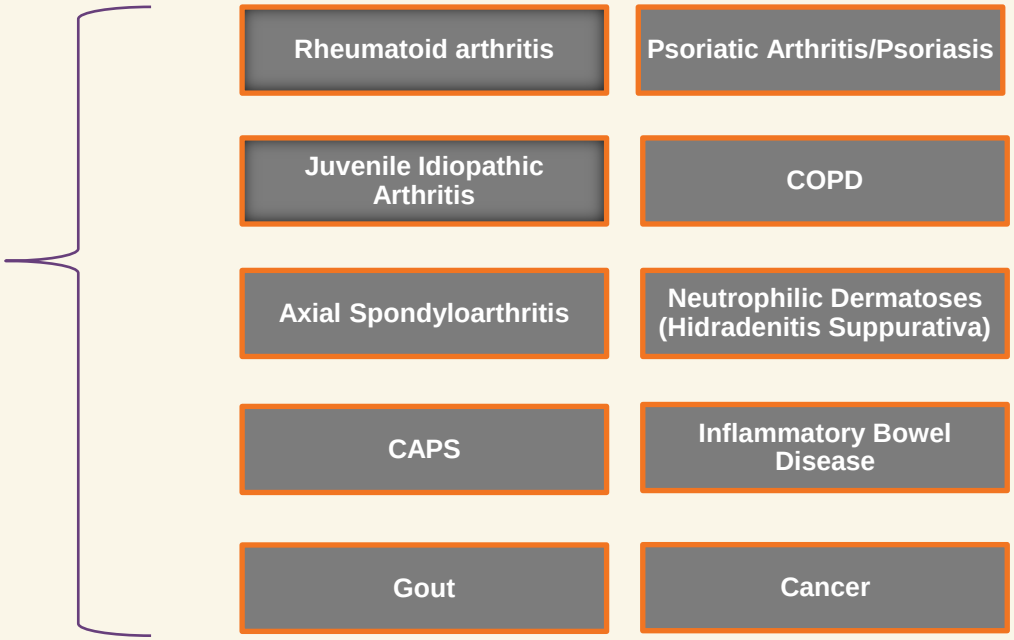
ATI-450: Investigational Small Molecule, Oral MK2 Inhibitor
Designed to Block the Targets of Broadly-Used Biologics

- **MK2* drives pro-inflammatory cytokine expression**
- **By inhibiting multiple cytokines, ATI-450 may be a potential treatment for multiple diseases**
- **Potential alternative to injectable, anti-cytokine biologics and JAK inhibitors for immuno-inflammatory diseases**

Inhibiting MK2 blocks TNFα, IL1α/β and IL6[1], the targets of commercially successful biologics



Global immunology market valued at >$77B in 2018[2]

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

1. Data on file.
2. Fortune Business Insights. Accessed February 22, 2021. https://www.fortunebusinessinsights.com/industry-reports/immunology-market-100657.

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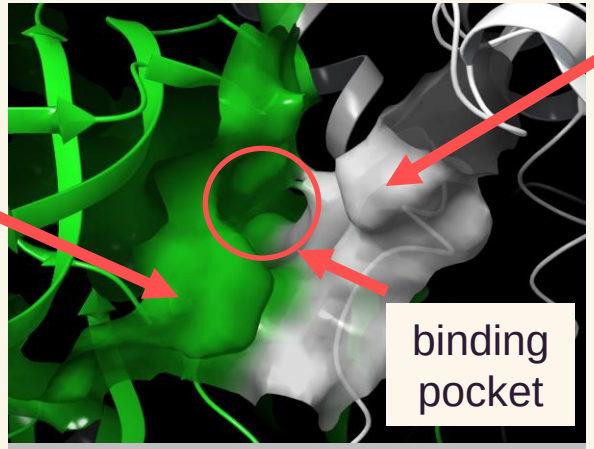
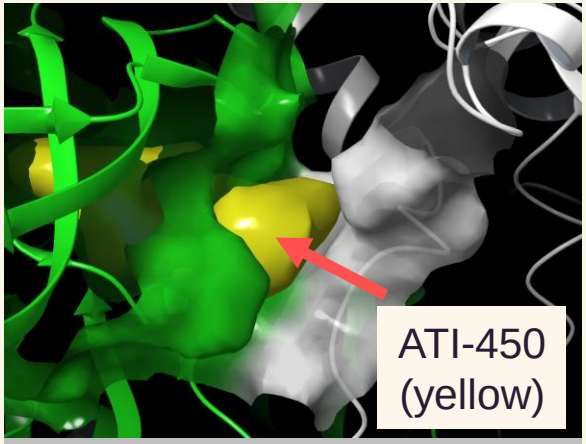
Novel Mechanism: Capturing MK2 in an Inactive State



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.

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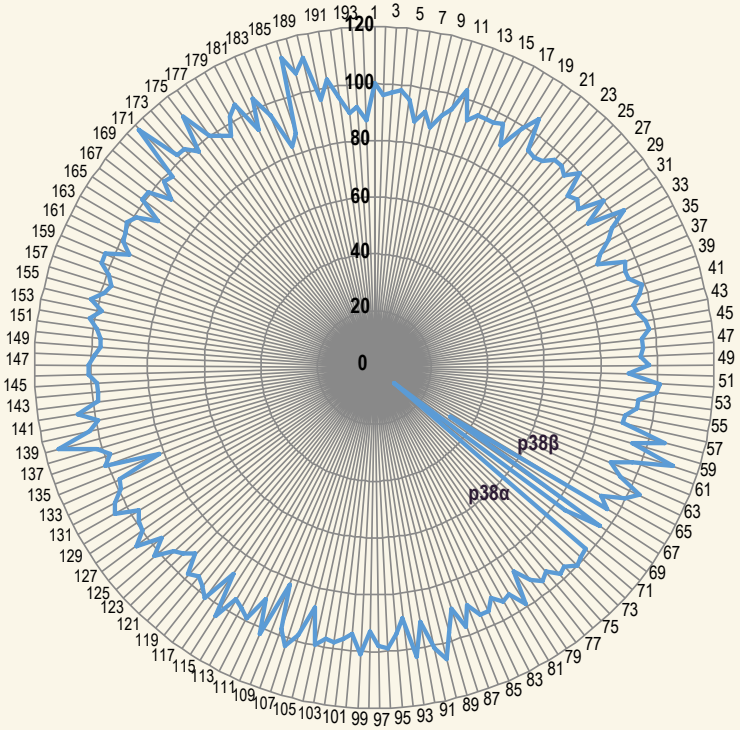
ATI-450 Selectivity: Minimizing Off-Target Inhibition through High Affinity for the p38α/MK2 Complex

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 Syndrome (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

ATI-450 Clinical Development

Phase 1 Single and Multiple Ascending Doses

- Safety, PK, Tolerability
- PD (inhibition of TNFα, IL1β, IL6, IL8 & Hsp27)

Phase 2a Clinical Trials

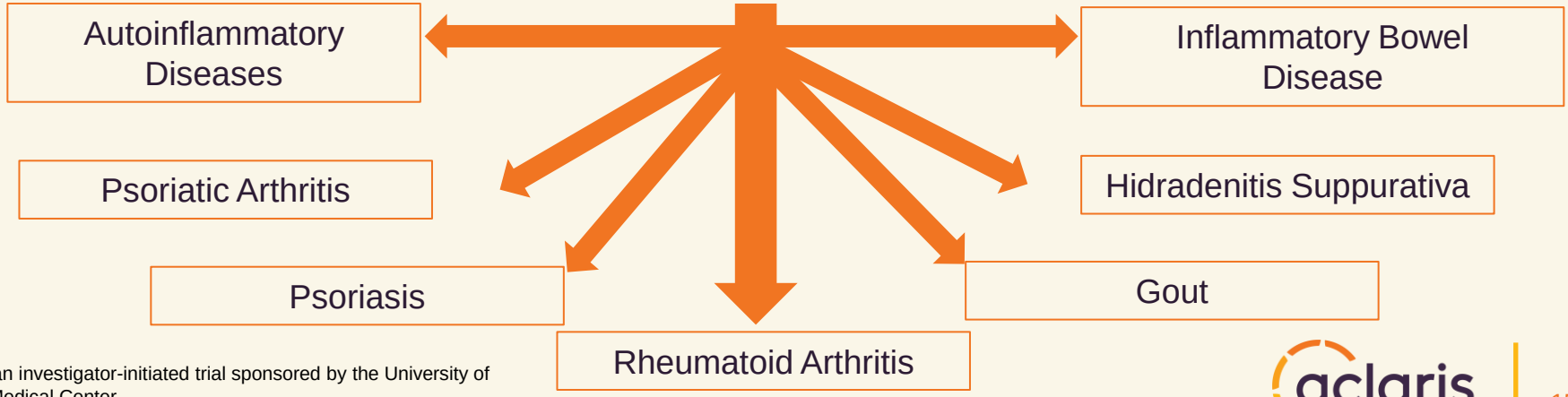
Rheumatoid Arthritis

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

COVID-19*

- 14 day: ATI-450 vs placebo
- Respiratory failure free
- Time of Hospitalization
- Time to intubation
- ARDS
- Safety and tolerability

Demonstrate proof of concept



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

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ATI-450-PKPD-101/102
Phase 1

ATI-450-PKPD-101 and -102
Safety, Tolerability, PK and PD in healthy volunteers

- ✓ **ATI-450-PKPD-101: Phase 1 SAD/MAD trial**
  - No serious adverse events (SAE) or adverse events (AE) that led to discontinuation
    - All AEs were mild in severity and did not interfere with everyday activities
  - Linear (dose-and time-independent) PK after multiple-dosing with terminal $t_{1/2}$ of ~9-12 hours; steady state by day 2
    - No meaningful impact on systemic exposure in the fed state
    - MTX PK was similar with or without ATI-450 exposure
  - Marked cytokine suppression

- ✓ **ATI-450-PKPD-102: Phase 1 MAD trial**
  - Same design to MAD portion of PKPD-101
    - 2 cohorts: 80mg, 120mg BID for 6.5 days (10 subjects/cohort (8 active, 2 placebo)
  - Generally well tolerated, all AEs mild in severity
    - Most common AEs (≥2 subjects who received ATI-450) were headache, dizziness, nausea, parasthesia and, in post-dosing safety follow-up phase of the trial, dry skin
  - Marked cytokine suppression at these higher doses

* Data on file

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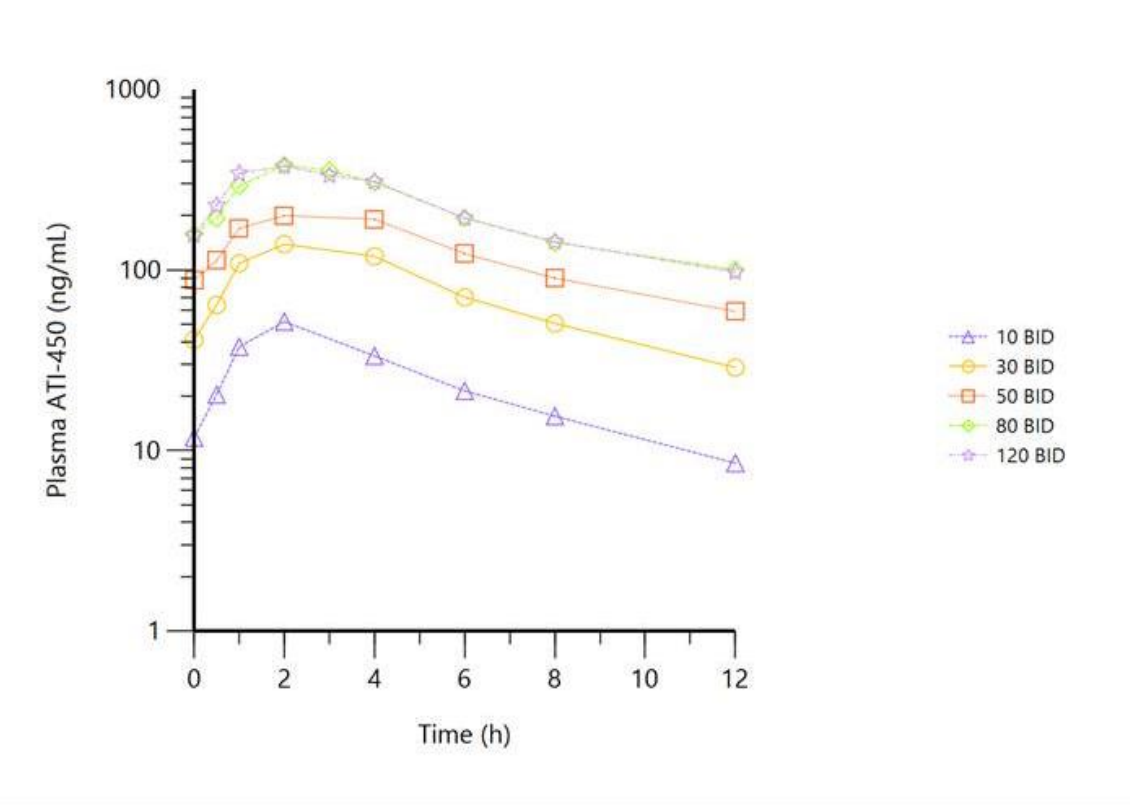
ATI-450-PKPD-101 & ATI-450-PKPD-102
Day 7 Steady State

- t½ 9-14 hours
- 80mg cohort dose proportional with previous cohorts
- No significant increased exposure in 120mg cohort



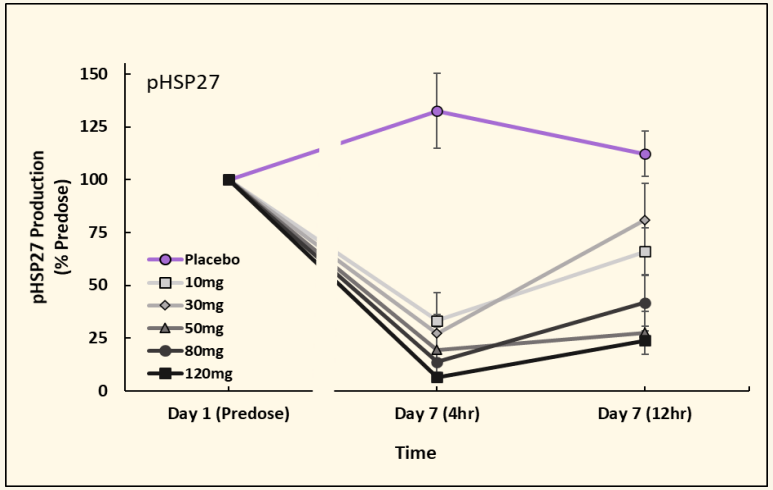
* Data on file

ATI-450-PKPD-101 & ATI-450-PKPD-102

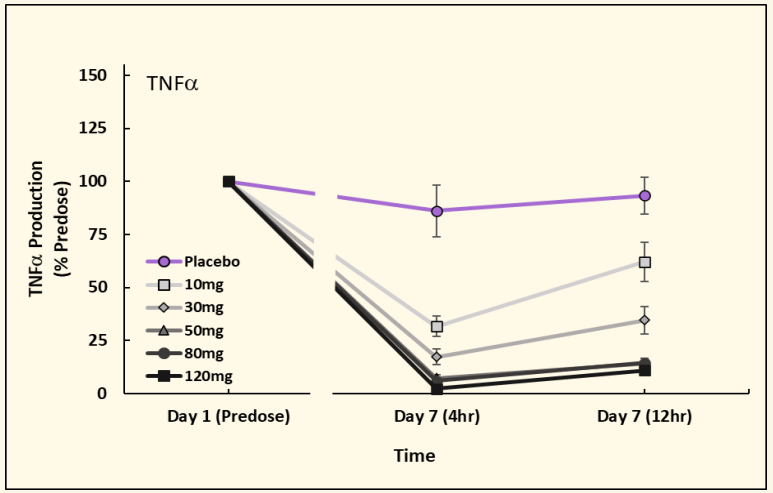
Ex vivo LPS stimulated pHSP27 and TNFα Day7 Peak and Trough

Day 7 Peak and Trough

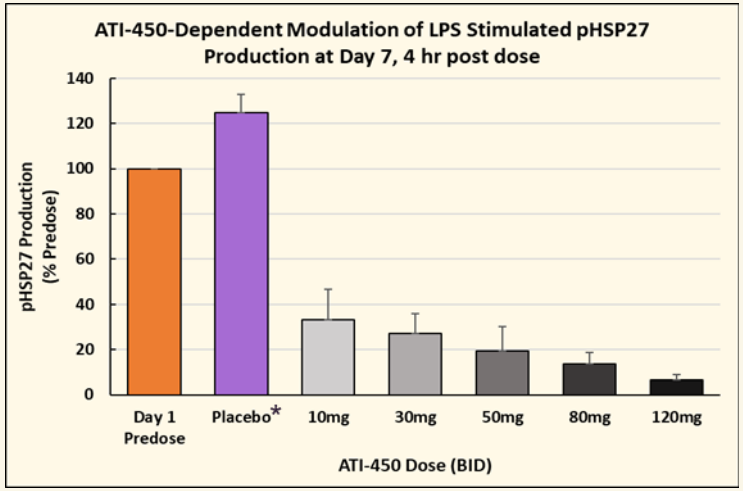
pHSP27

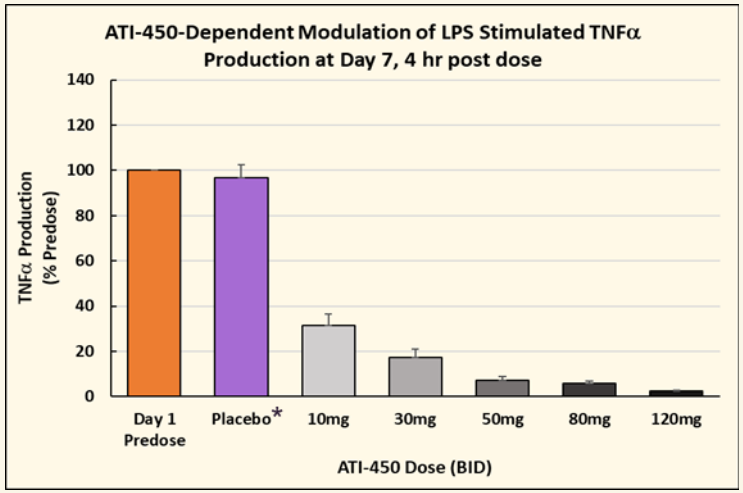


TNFα



Dose Response Day 7 Peak





(*) = All placebo samples (all time points)

* Data on file

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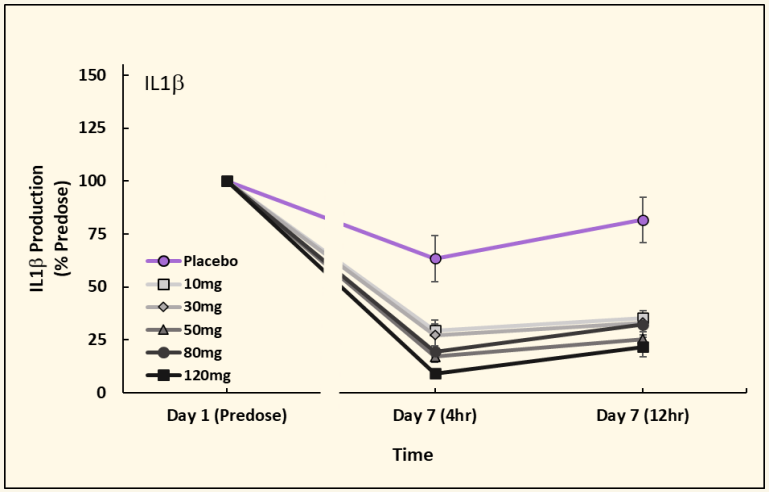
ATI-450-PKPD-101 & ATI-450-PKPD-102

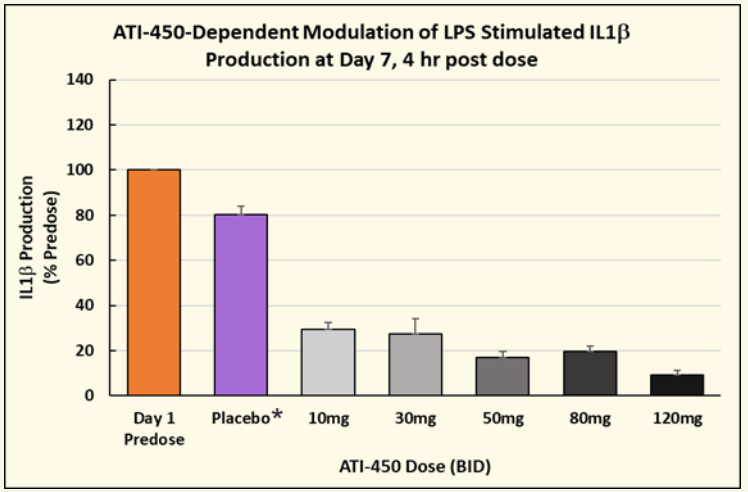
Ex vivo LPS stimulated IL1β and IL8 Day7 Peak and Trough

Day 7 Peak and Trough

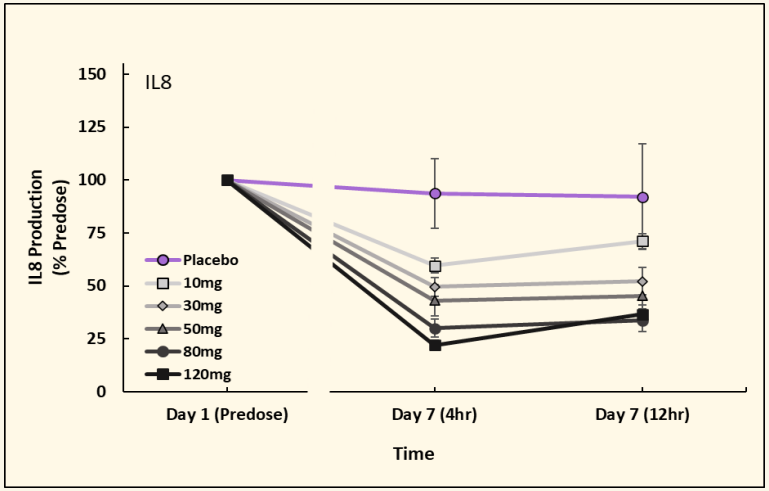
Dose Response Day 7 Peak

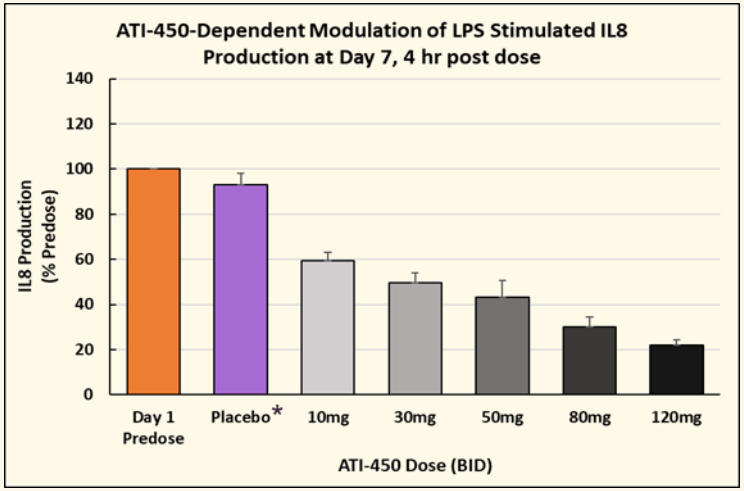
IL1β





IL8





(*) = All placebo samples (all time points)

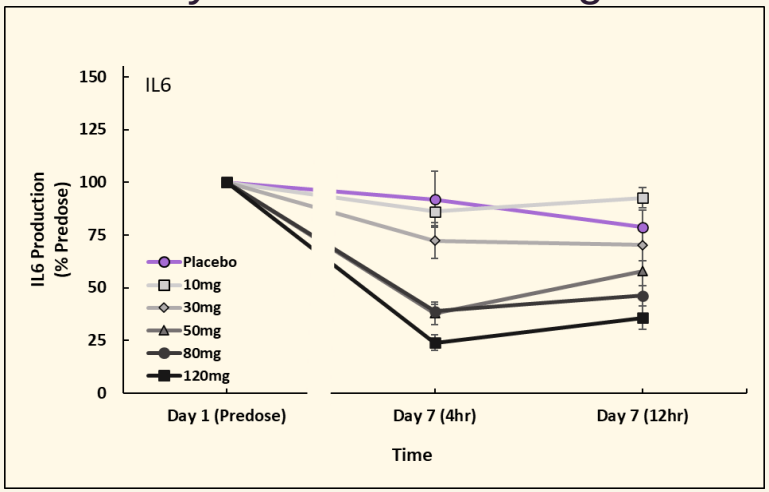
* Data on file

ATI-450-PKPD-101 & ATI-450-PKPD-102

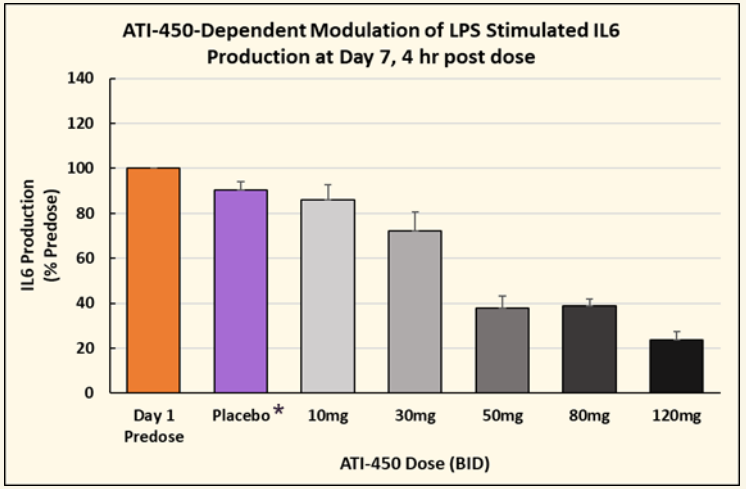
Ex vivo LPS stimulated IL6 Day7 Peak and Trough

IL6

Day 7 Peak and Trough



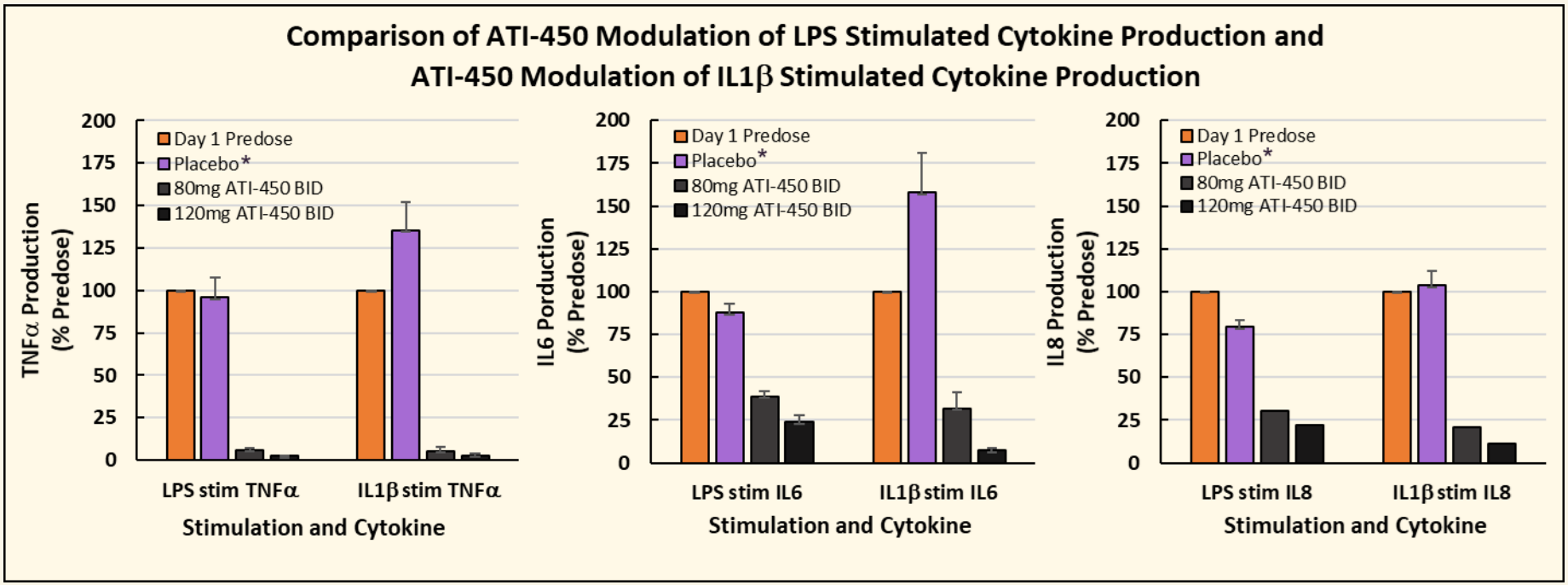
Dose Response Day 7 Peak



(*) = All placebo samples (all time points)

* Data on file

ATI-450 Phase 1 MAD Extension: 80mg and 120mg
Ex Vivo IL1β Stimulation of HWB Day 7 (4 hr)



(*) = All placebo samples (all time points)

ATI-450 potently inhibited ex vivo IL1β-induced proinflammatory cytokines, TNFα, IL6 and IL8

* Data on file

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ATI-450-RA-201
Preliminary Topline Data Analysis

Trial Design

- Diagnosis of adult-onset RA (ACR/EULAR classification criteria)
- DAS28-CRP ≥3.2 defined as moderate to high disease activity
- Moderately to severely active RA defined by at least 4/28 tender and 4/28 swollen joints
- hsCRP ≥5 mg/L at screening
- Definitive intra-articular synovitis or osteitis defined as a score of 1 or greater on a Hand-Wrist MRI (using RAMRIS)
- Stable MTX dose (defined as 7.5 mg to 25 mg weekly) for at least 4 weeks prior to the screening visit

RANDOMIZATION (3:1)

ARM 1
ATI-450, 50 mg BID + MTX

ARM 2
Placebo, BID + MTX

12 weeks

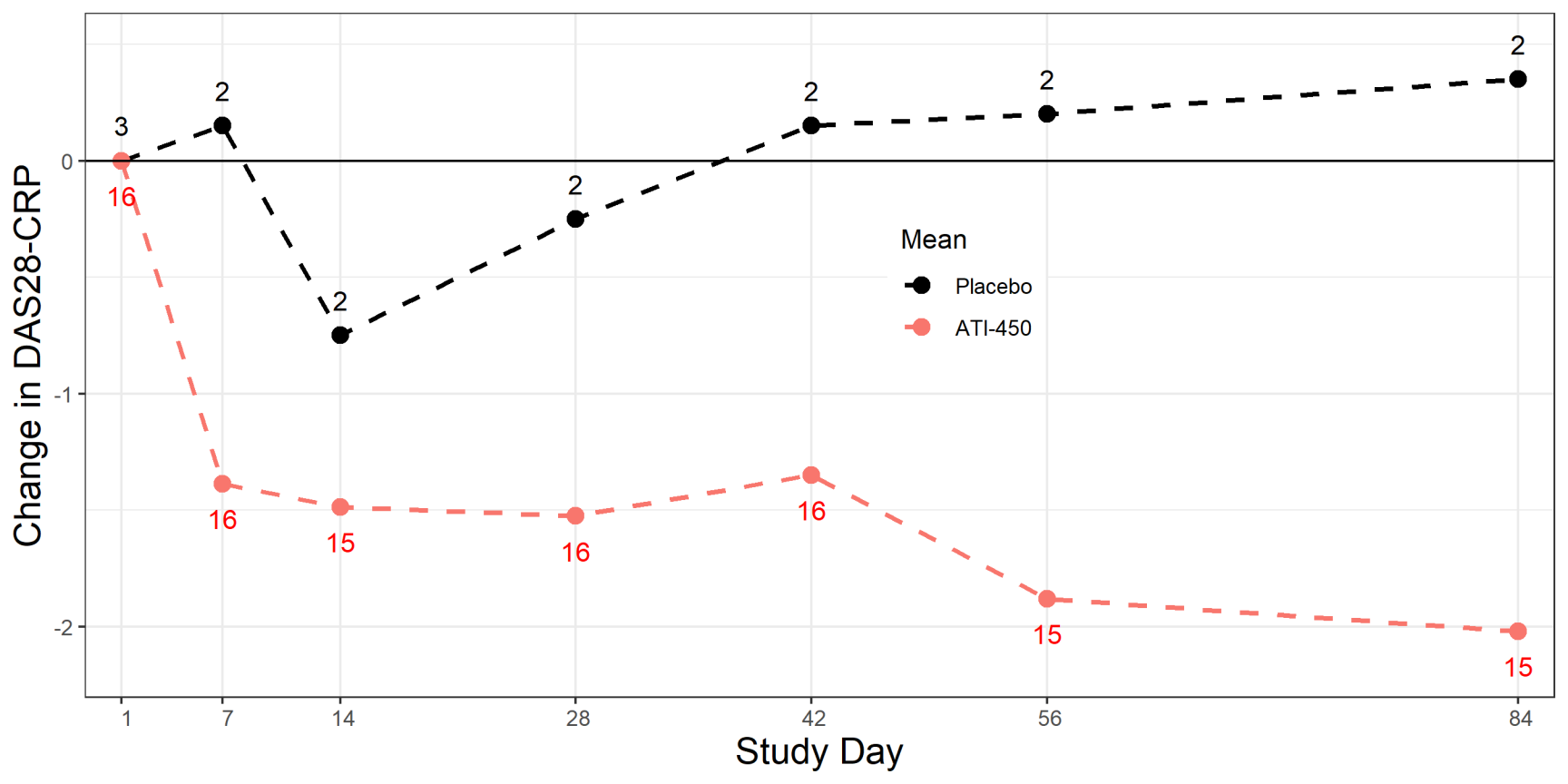
Primary Objective: Safety

N-25 (to get 15 completers)

Secondary Objectives

- % change from baseline in hsCRP
- Mean change from baseline in DAS28-CRP
- Proportion of patients with DAS28-CRP below 2.6
- Mean change in RAMRIS assessments of synovitis or osteitis
- Proportion of patients with ACR 20/50/70

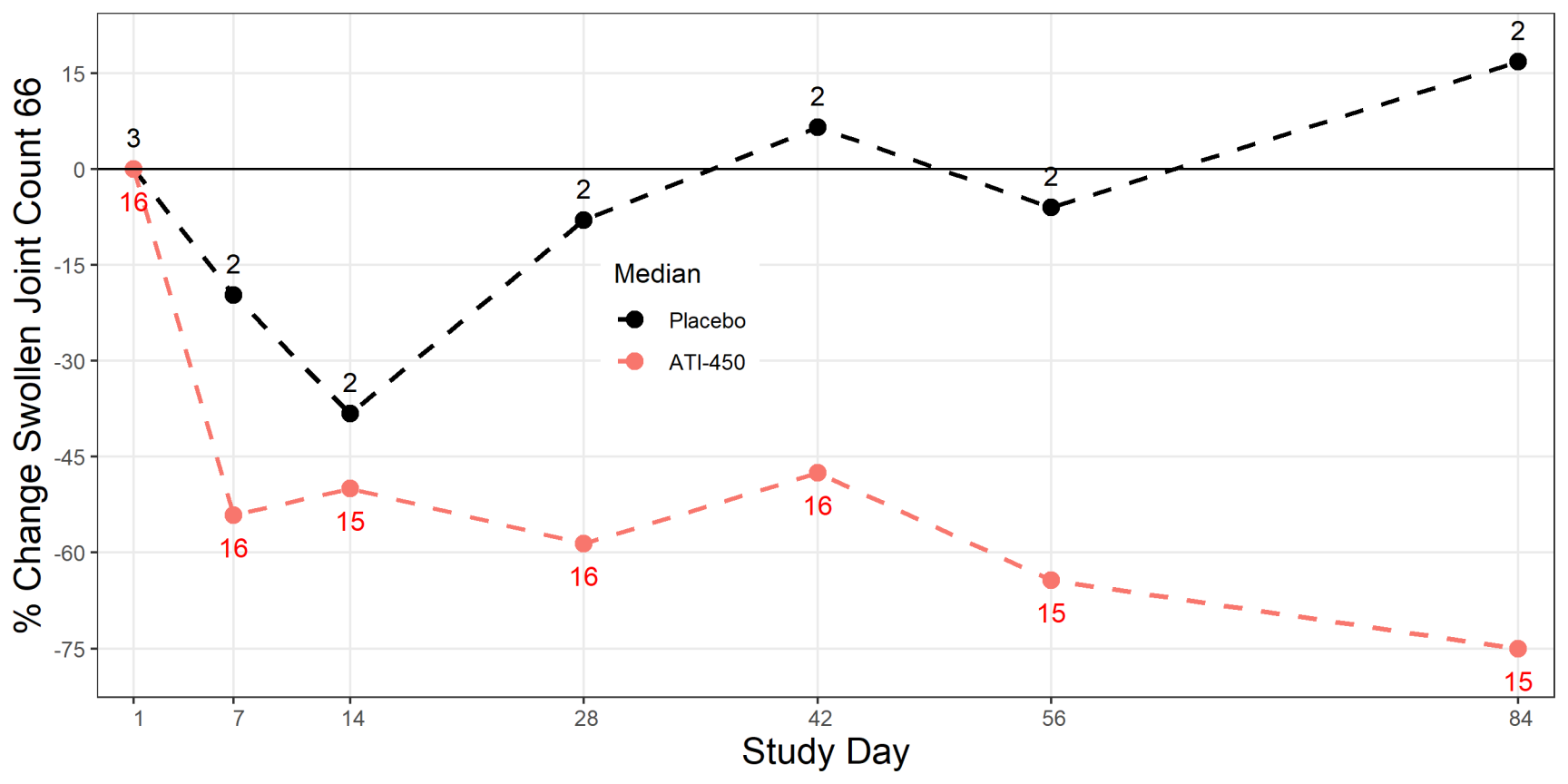
DAS28-CRP
Mean Change From Baseline



Numbers on lines = no. of subjects at each timepoint

* Data on file

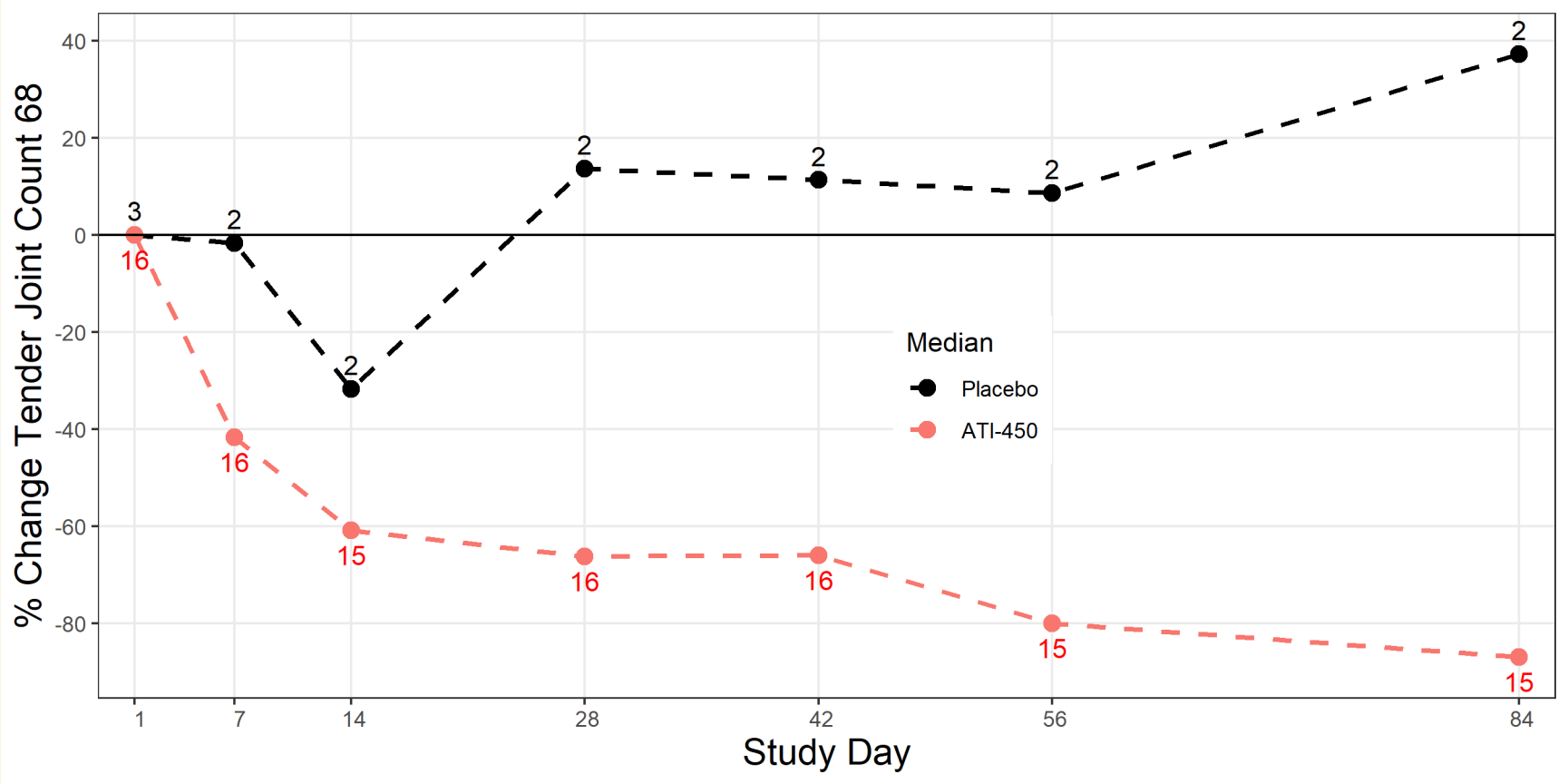
Swollen Joint Count
Median Percent Change From Baseline



Numbers on lines = no. of subjects at each timepoint

* Data on file

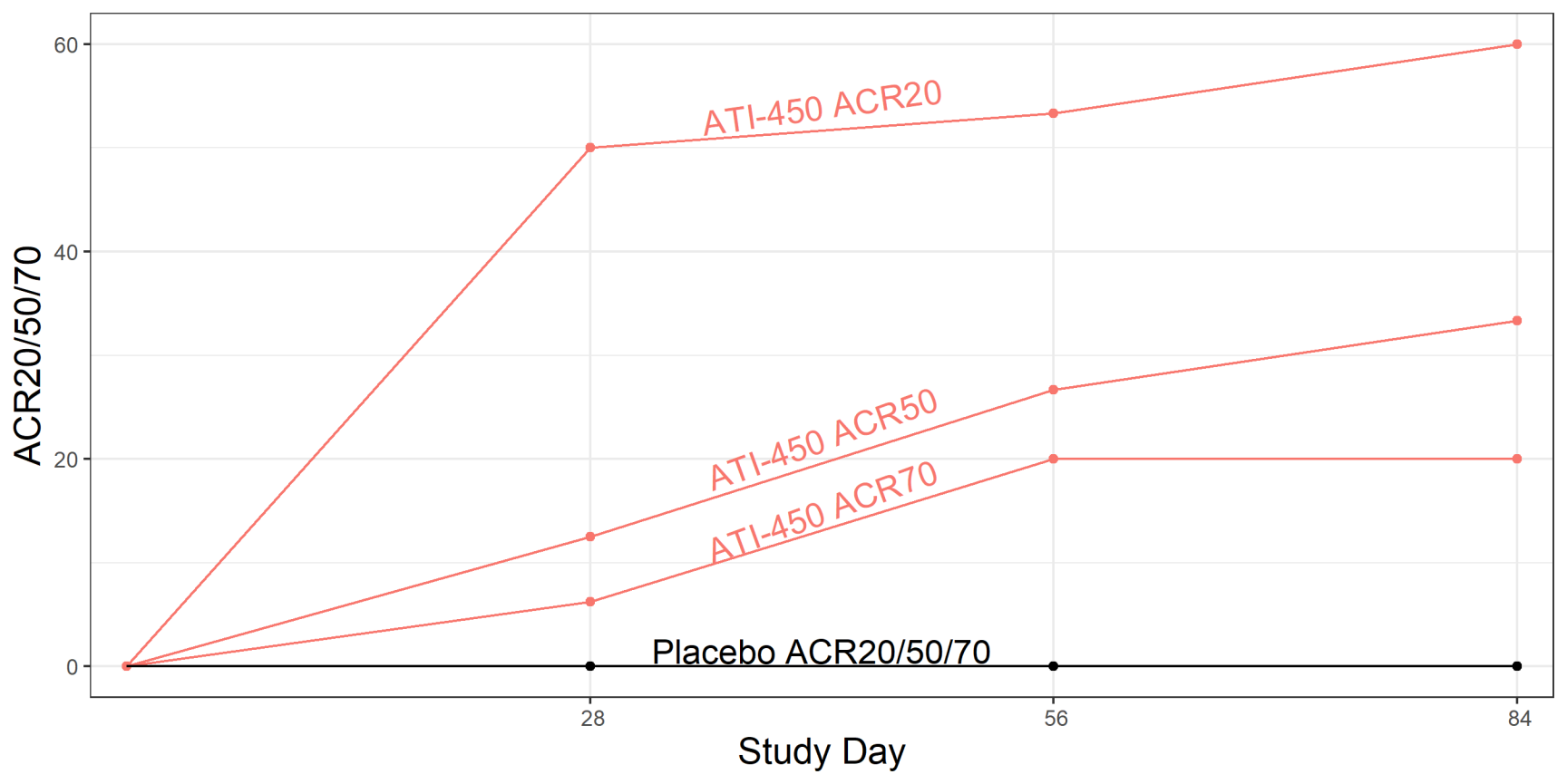
Tender Joint Count
Median Percent Change From Baseline



Numbers on lines = no. of subjects at each timepoint

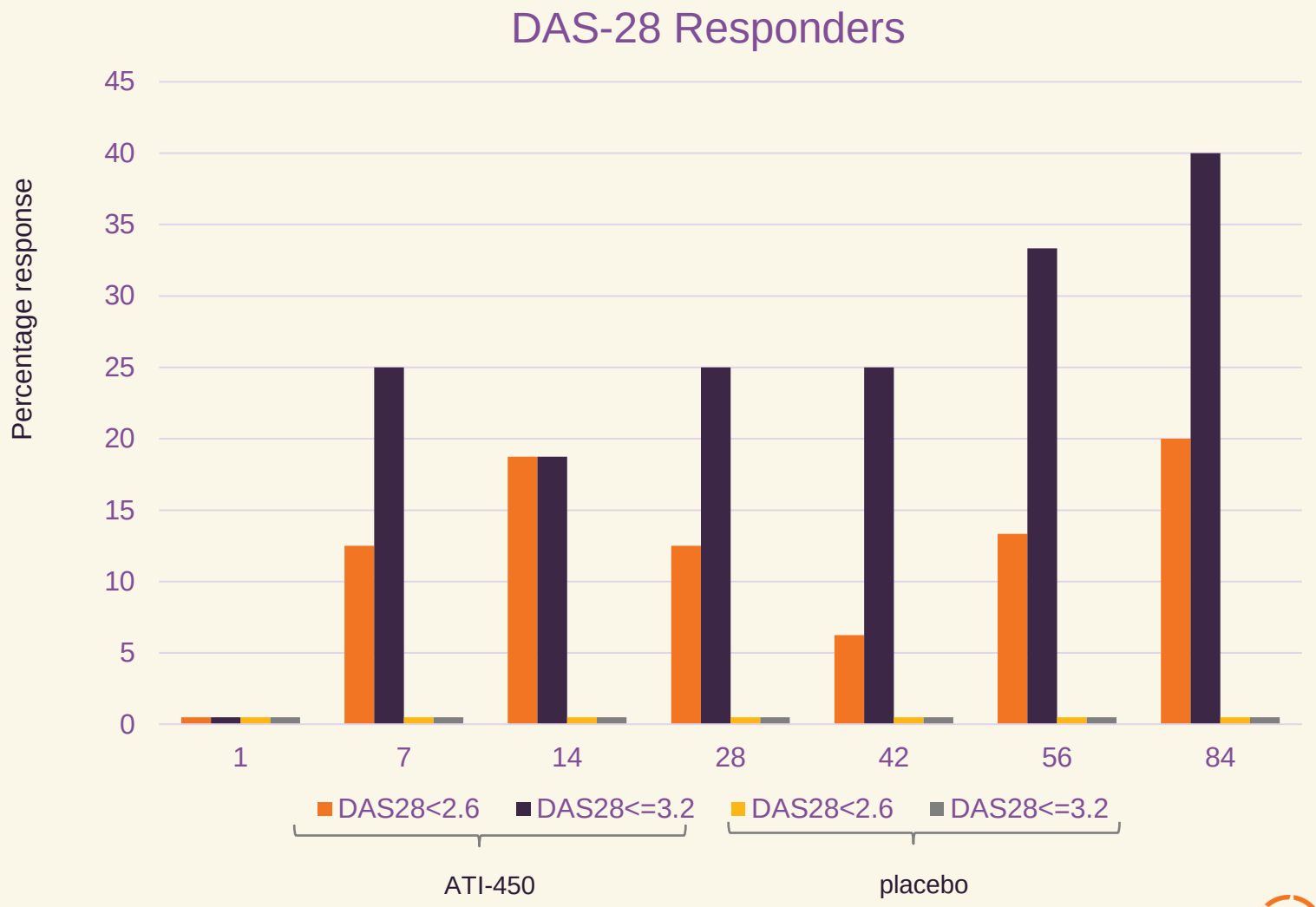
* Data on file

ACR20/50/70: *Responder Analysis over time*



* Data on file

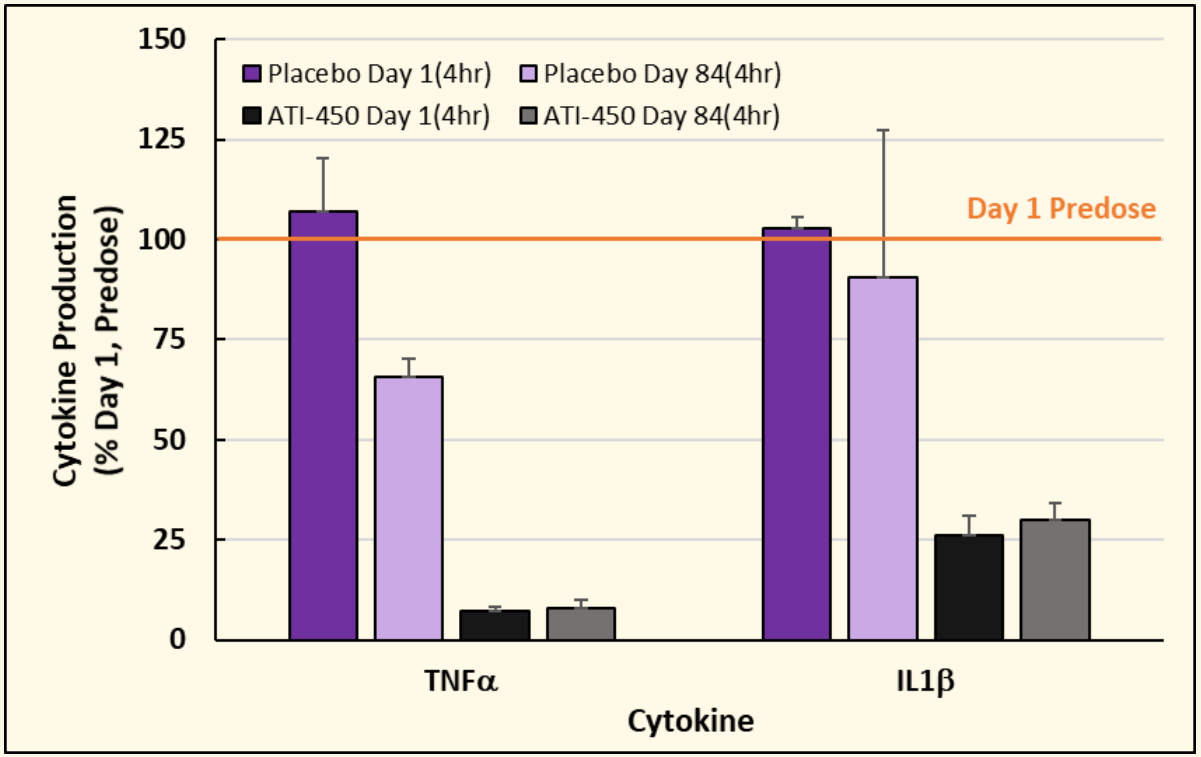
DAS28-CRP: *Responder Analysis over time*



* Data on file

RA Patients Treated with ATI-450 for 12 Weeks
Ex Vivo LPS-Stimulated Cytokines Day 1 vs Day 84

Hypothesis: p38 transient efficacy (tachyphylaxis) may be associated with feedback loops and pathway reprogramming. Selectively targeting MK2 inhibition circumvents these issues through selective downstream pathway blockade.



Durable Dependence on MK2 for Cytokine Production

Interim Data N=11 Active, 2 Pbo

* Data on file as of December 10, 2020.

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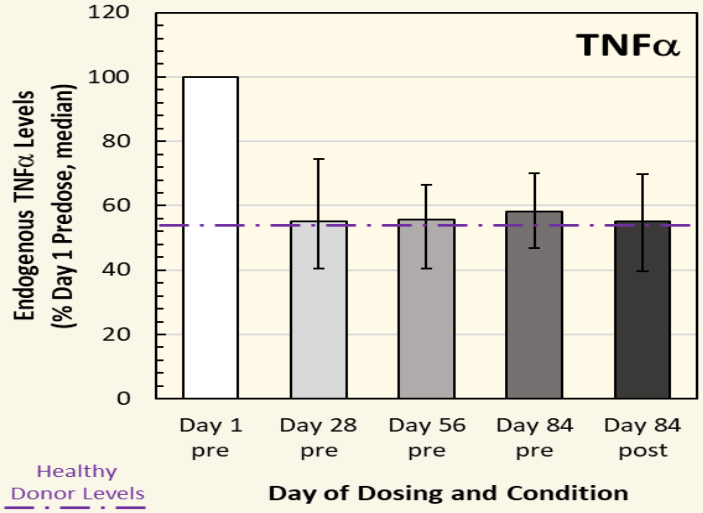
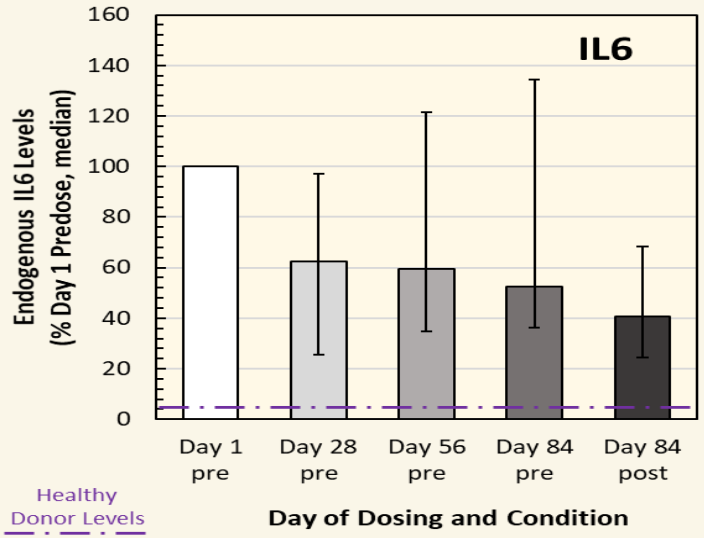
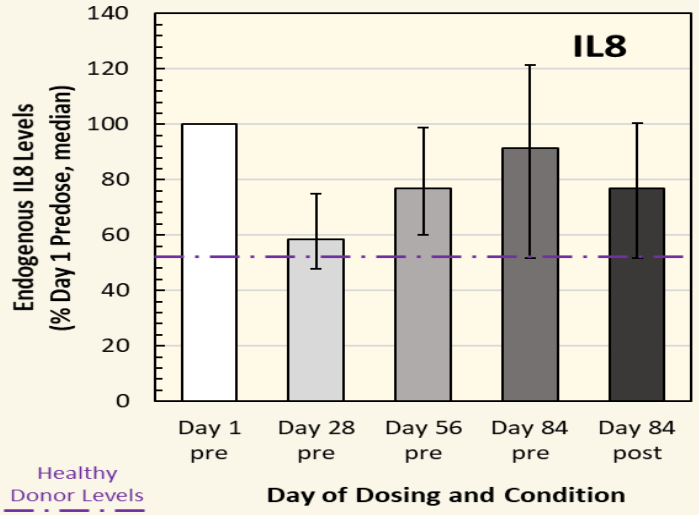
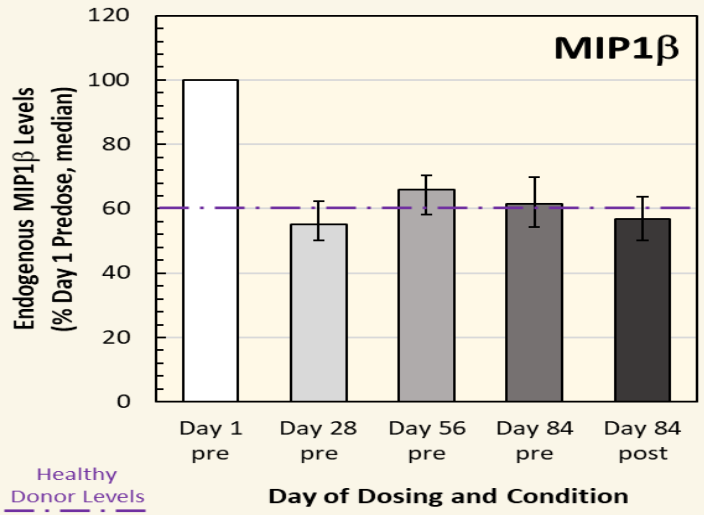
Impact of ATI-450 on Endogenous Plasma Cytokine Levels in RA-201

TNFα, IL6, IL8 and MIP1β









- Cytokines with endogenous levels <0.5 pg/ml predose:IL1β, IL10, IL4 and GM-CSF

* Data on file

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Adverse Events: Subjects with at least one event

	ATI-450 50 mg BID (N = 16)		Placebo (N = 3)	
Preferred Term	**Mild n(%)**	**Moderate n(%)**	**Mild n(%)**	**Moderate n(%)**
Blood cholesterol increased	1(6.25)	0		
Blood creatine phosphokinase increased	0	1(6.25)		
Constipation	1(6.25)	0		
Dental caries			1(33.33)	0
Ear infection	1(6.25)	0		
Electrocardiogram abnormal	1(6.25)	0		
Essential hypertension	0	1(6.25)		
Hyperlipidaemia	0	1(6.25)		
Hypokalaemia	0	1(6.25)		
Ligament sprain	1(6.25)	0		
Low density lipoprotein increased	1(6.25)	0		
Mouth ulceration	1(6.25)	0		
Muscle strain			0	1(33.33)
Palpitations	1(6.25)	0		
Rash erythematous	1(6.25)	0		
Sinusitis	0	1(6.25)		
Skin abrasion	1(6.25)	0		
Urinary tract infection	0	2(12.5)		
Ventricular extrasystoles	1(6.25)	0		
White blood cell count increased	1(6.25)	0		

- No SAEs during 12 week treatment phase
  - One treatment-unrelated SAE: COVID-19 reported during four week safety follow-up period while not on drug
- No Severe Adverse Events
- ATI-450: one subject withdrew - evaluated for palpitations and elevated CPK – no cardiac event

* Data on file

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Topline Analyses Summary

- **Main objectives of POC trial were achieved**
  - ✓ Potent and durable clinical activity with 50mg BID
    - Rapid reduction in median percentage of tender and swollen joint count, which persisted
    - DAS28-CRP reduction persisted
    - ACR20/50/70 observed in 60%/33%/20% of treatment arm
    - hsCRP reduction maintained
  - ✓ ATI-450 was generally well tolerated
- **Positive Phase 1 trials**
  - ✓ No dose limiting toxicity in phase 1
  - ✓ Marked inflammatory cytokine suppression
  - ✓ Pharmacokinetics data continue to support dosing flexibility (QD or BID)
  - ✓ Pharmacodynamic data provide rationale for evaluating activity up to 80-120mg BID
- **Next steps**
  - ✓ Planning for Phase 2b program initiated

* Data on file

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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

- 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

ATI-1777: Status

- Investigational Compound
- IND allowed
- First-in-human Phase 2a trial in patients with moderate or severe AD underway

1 Medscape. Accessed February 24, 2021. https://emedicine.medscape.com/article/1049085-overview.
2 Medscape. Accessed February 24, 2021. https://emedicine.medscape.com/article/1049085-overview#a8.
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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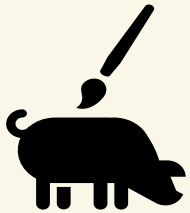
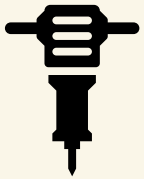
Porcine Model:
ATI-1777 Blocks IL15 Induced CCL8 mRNA in Skin

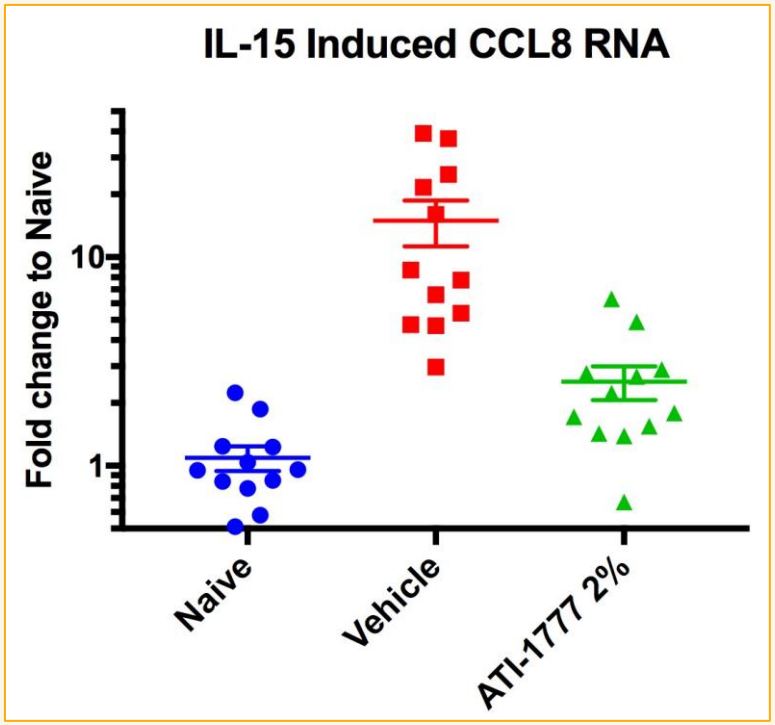


Apply formulation to back of pig, wait 1 hr

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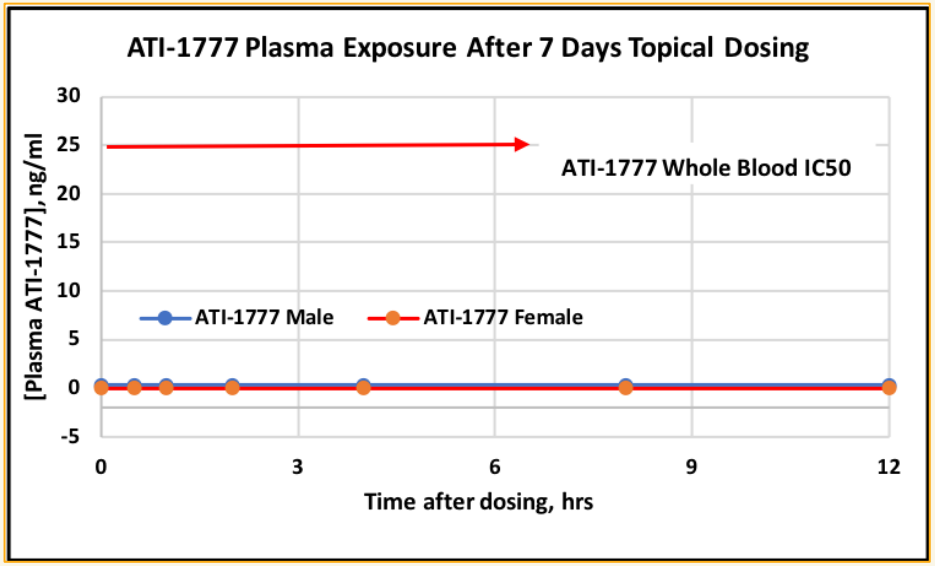
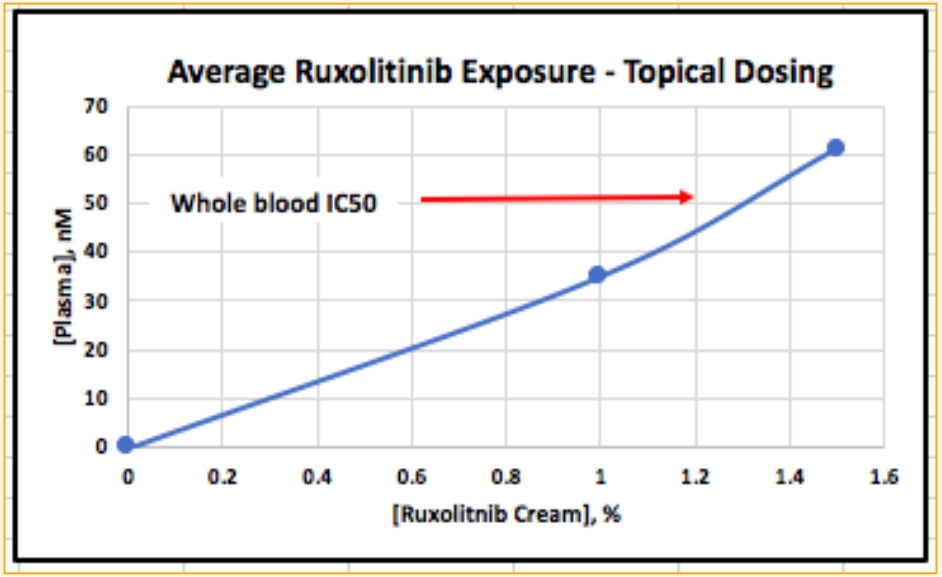
Minipig Model:
ATI-1777 Non-clinical Safety Program TK Data

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

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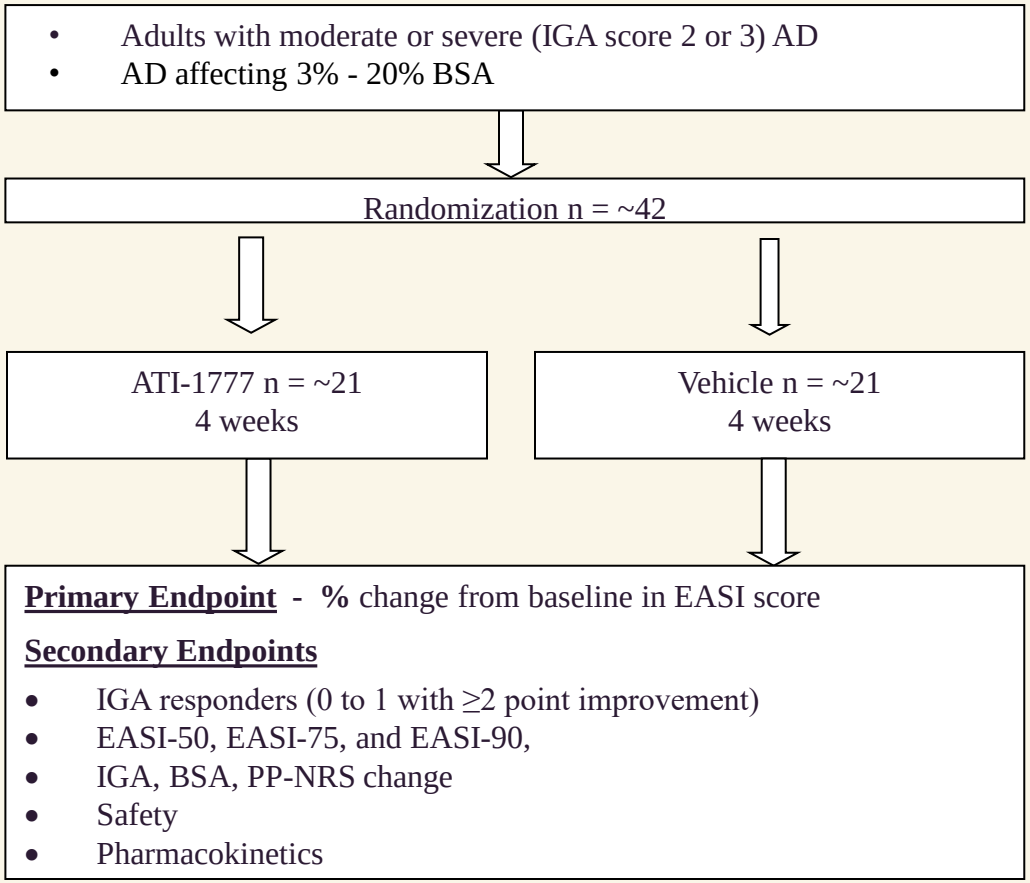
ATI-1777-AD-201
A Proof-of-Concept First-in-Human Trial

A Phase 2a, Multicenter, Randomized, Double-blind, Vehicle-controlled, Parallel-group Clinical Trial to Investigate the Efficacy, Safety, Tolerability and Pharmacokinetics of ATI-1777 in Subjects with Moderate to Severe Atopic Dermatitis



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

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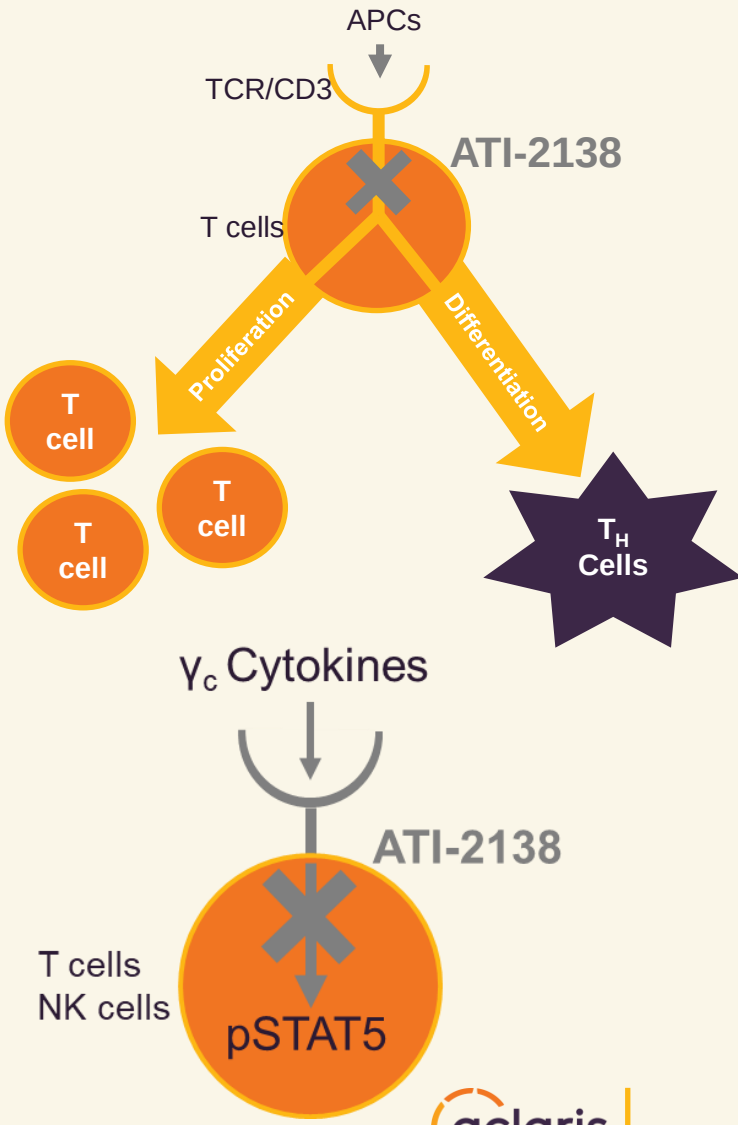
ATI-2138: Covalent ITK/TXK/JAK3 (ITJ) Inhibitor

- 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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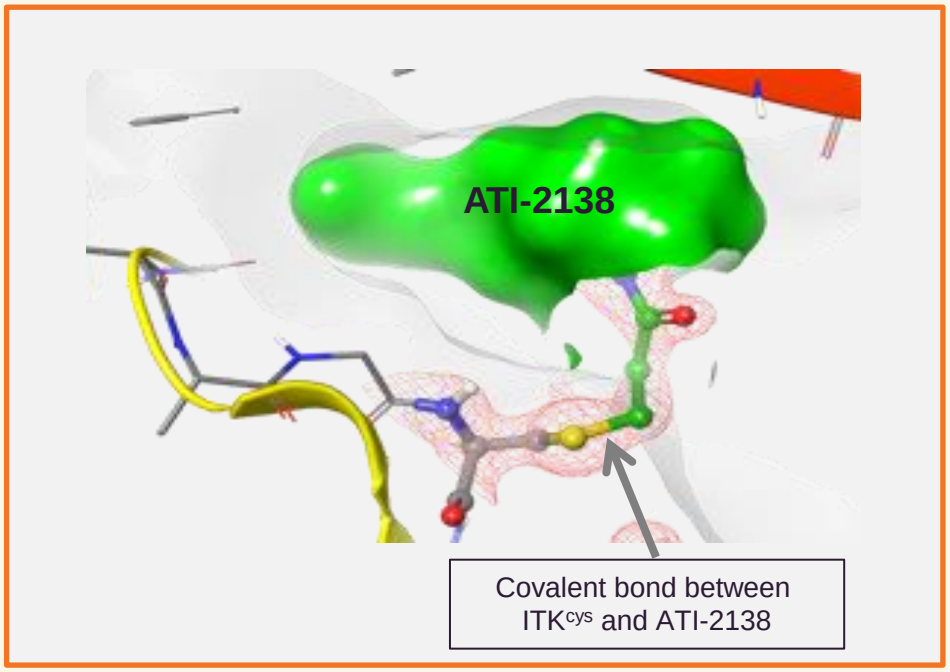
ATI-2138 is a Potent Covalent Inhibitor



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

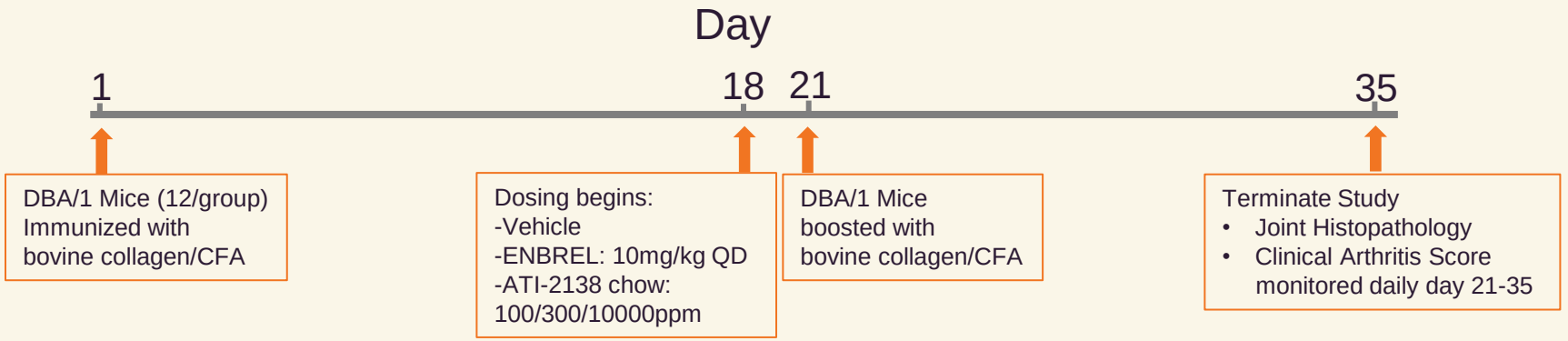
Cellular Inhibition of JAK and ITK/TXK

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

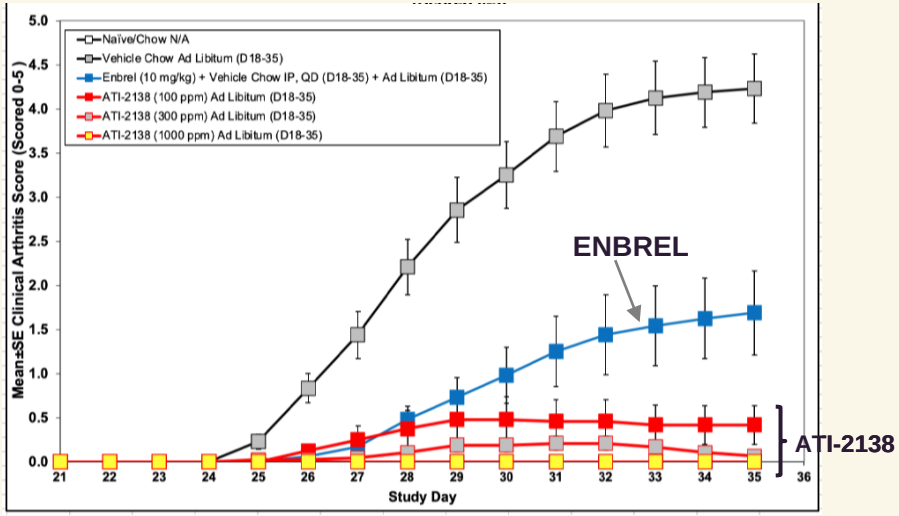
ATI-2138 potently inhibits ITK/TXK and JAK3 in cells and in whole blood

* Data on file

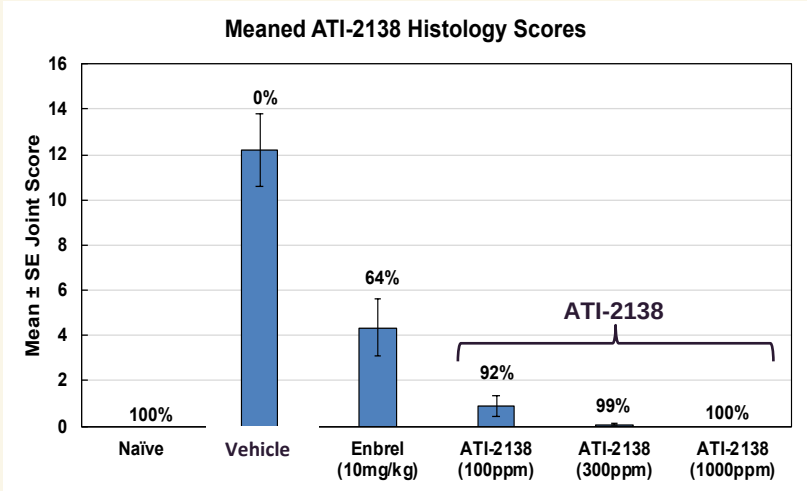
Mouse Model: ATI-2138 is Efficacious in mCIA



Clinical Arthritis Score



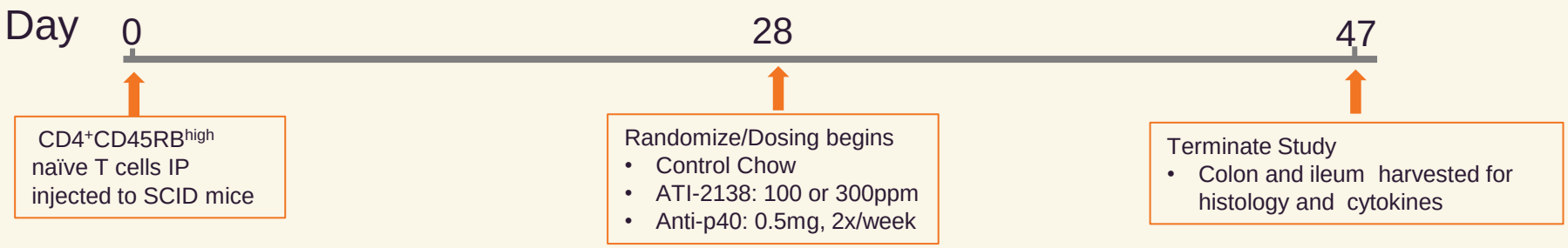
Joint Histology Score

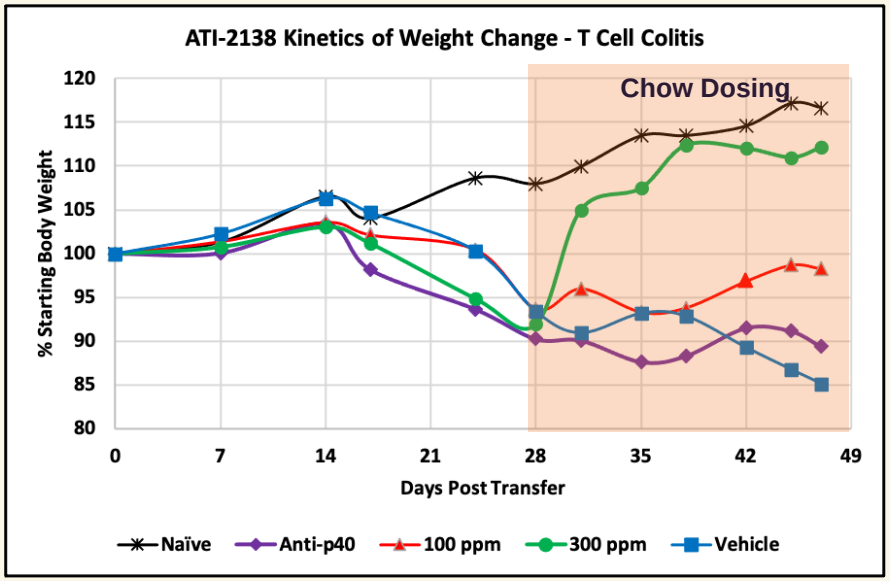


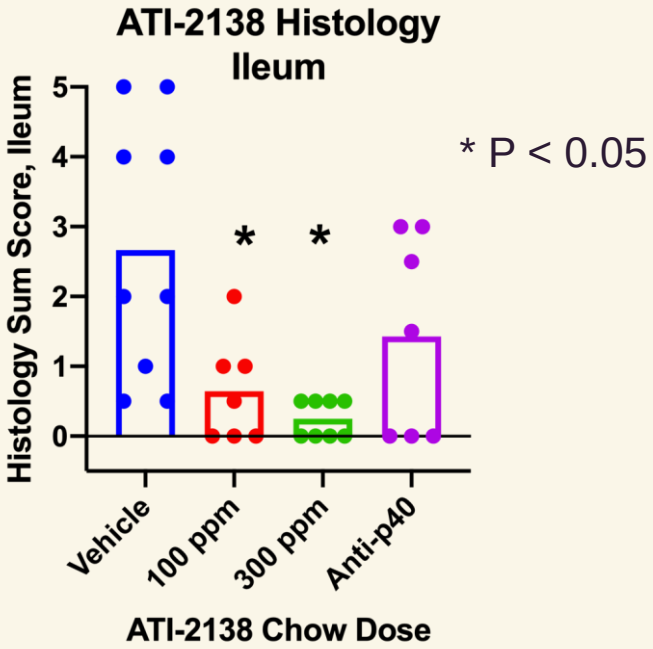
In the gold standard mCIA model, ATI-2138 demonstrated efficacy superior to ENBREL

* Data on file

Mouse Model: ATI-2138 - T Cell Transfer Colitis







- 300 ppm chow dose of ATI-2138 reversed weight loss trend in disease model to match naïve controls
- 100 and 300 ppm chow doses are effective in preventing tissue damage in the ileum by histology

* Data on file

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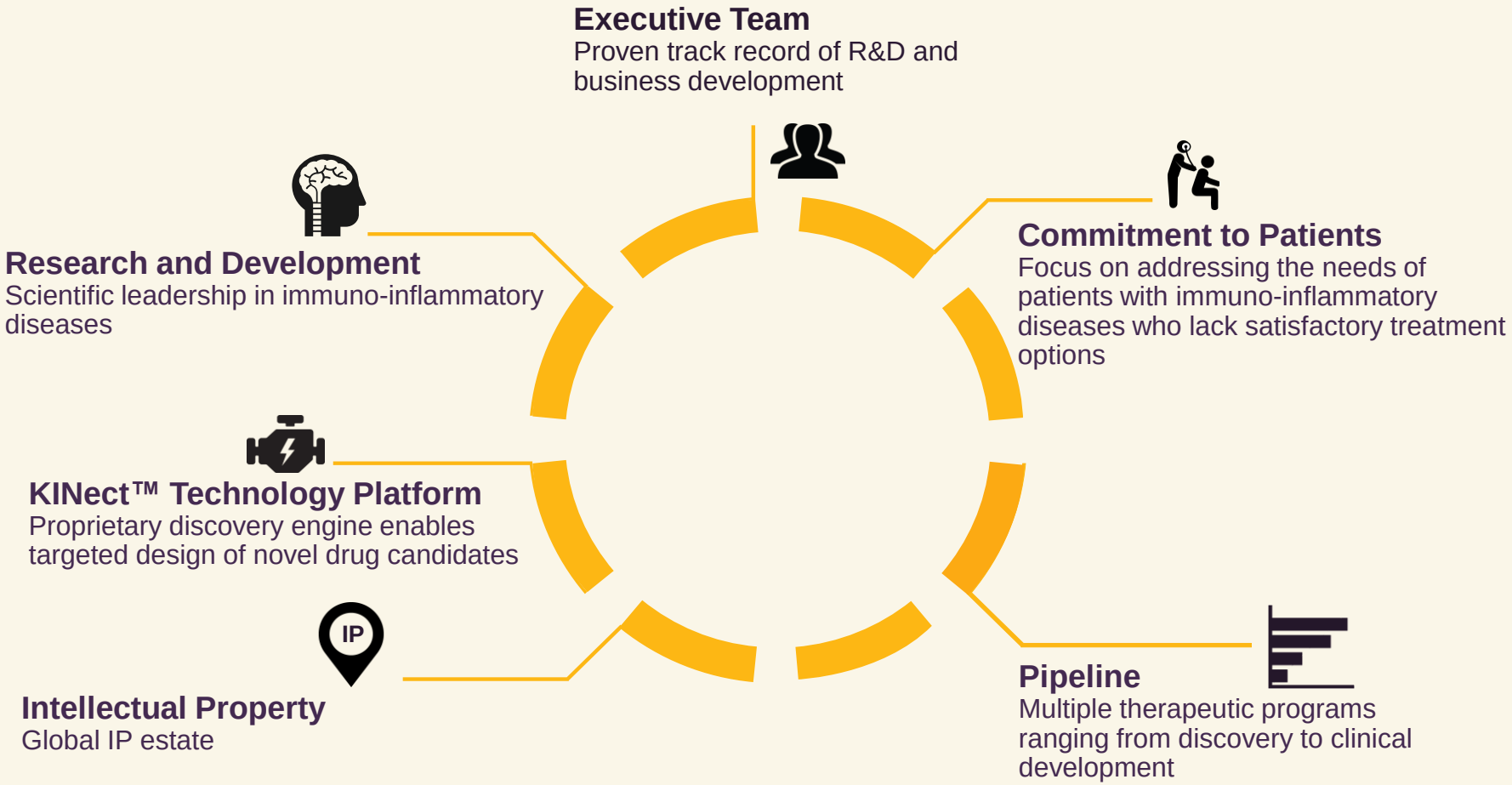
Empowering Patients Through Kinome Innovation



Key Milestones

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