
aclaris®
THERAPEUTICS
INVESTOR
PRESENTATION
Corporate
Overview
January 2025

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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 "anticipate," "believe," "expect," "intend," "may," "plan," "potential," "will," and similar expressions, and are based on Aclaris' current beliefs and expectations. These forward-looking statements include expectations regarding the therapeutic potential of Aclaris' drug candidates, including ATI-045, ATI-052 and ATI-2138, to provide meaningful benefit to patients suffering from atopic dermatitis, COPD, asthma and/or other indications, the development of Aclaris' drug candidates, including ATI-045, ATI-052, ATI-2138 and an undisclosed next generation selective ITK inhibitor, the timing of regulatory filings and initiation of clinical trials, the timing of selecting an ITK inhibitor drug candidate, the availability and timing of data from clinical trials, the potential of ATI-045 to have extended dosing, and Aclaris' cash runway. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Risks and uncertainties that may cause actual results to differ materially include uncertainties inherent in the conduct of clinical trials, Aclaris' reliance on third parties over which it may not always have full control, Aclaris' ability to enter into strategic partnerships on commercially reasonable terms, the uncertainty regarding the macroeconomic environment 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, 2023, and other filings Aclaris makes with the U.S. Securities and Exchange Commission from time to time. These documents are available under the "SEC Filings" page of the "Investors" section of Aclaris' website at www.aclaristx.com. Any forward-looking statements speak only as of the date of this 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 Immuno-inflammatory Diseases with Large and Small Molecule Therapeutics

All with best-in-class potential and proven biology

Innovative Pipeline
(investigational drug candidates)

ATI-045 – monoclonal antibody targeting thymic stromal lymphopoietin (TSLP)

ATI-052 – bispecific antibody targeting both TSLP and interleukin-4 receptor (IL4R)

ATI-2138 – oral inhibitor of ITK/JAK3

ITK inhibitor – oral selective ITK inhibitor

World Class Expertise/Capability

Small and large molecule discovery and development expertise – leadership with over a dozen biologics approved, and over 30 small molecules advanced into clinical development and 6 small molecules approved

Proprietary kinase small molecule discovery engine complemented by in-house multidisciplinary scientific team

Rich Catalyst Calendar

Strong balance sheet is expected to fund company into 2028

Cash runway is expected to fund **multiple catalysts per year**

Additional catalysts expected from the development of ATI-045 in severe asthma and CRSwNP by China partner

aclaris THERAPEUTICS

CRSwNP – Chronic Rhinosinusitis with Nasal Polyps

Experienced Leadership Team

DR. NEAL WALKER
Interim CEO & Chairman

25+ years life sciences experience

Successful serial entrepreneur; founder and leader of several life science companies

Board certified Dermatologist

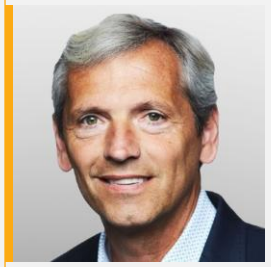
JOE MONAHAN, PHD
Chief Scientific Officer

35+ years pharmaceutical research experience

Lead Founder and Former CSO of Confluence Life Sciences

Former Pfizer Leader of Global Kinase Team

HUGH DAVIS, PHD
President and Chief Operating Officer



35+ years in biologics development, clinical pharmacology, and business development

Former roles at Frontage, GSK and Johnson & Johnson

Key team member for approval of REMICADE®, STELARA®, DARZALEX®

STEVEN KNAPP, PHARMD
EVP, Head of Regulatory & Quality

35+ years experience in in regulatory and quality

Former roles at Antares, Valeant and BMS

Key team member for approval of ERBITUX®

JAMES LOEROP
Chief Business Officer

30+ years of large pharma and biotech BD experience

Former Business Development leadership roles at Alexion, GSK. Stifel Laboratories and Anika Therapeutics

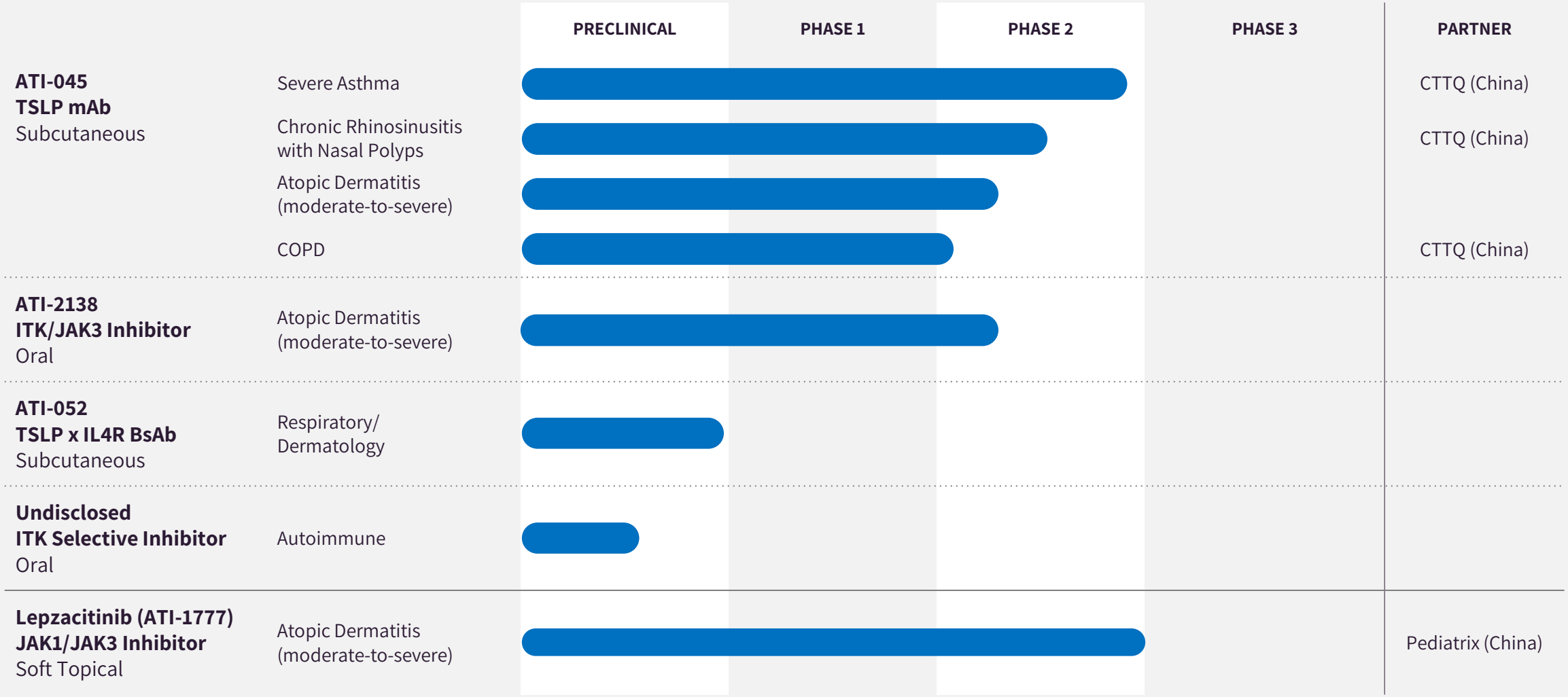
KEVIN BALTHASER
Chief Financial Officer

14+ years of financial leadership including over 10 years in the life sciences industry

Former accounting and finance roles at Lannett Company and PwC

Certified Public Accountant

Broad Immunology Development Pipeline

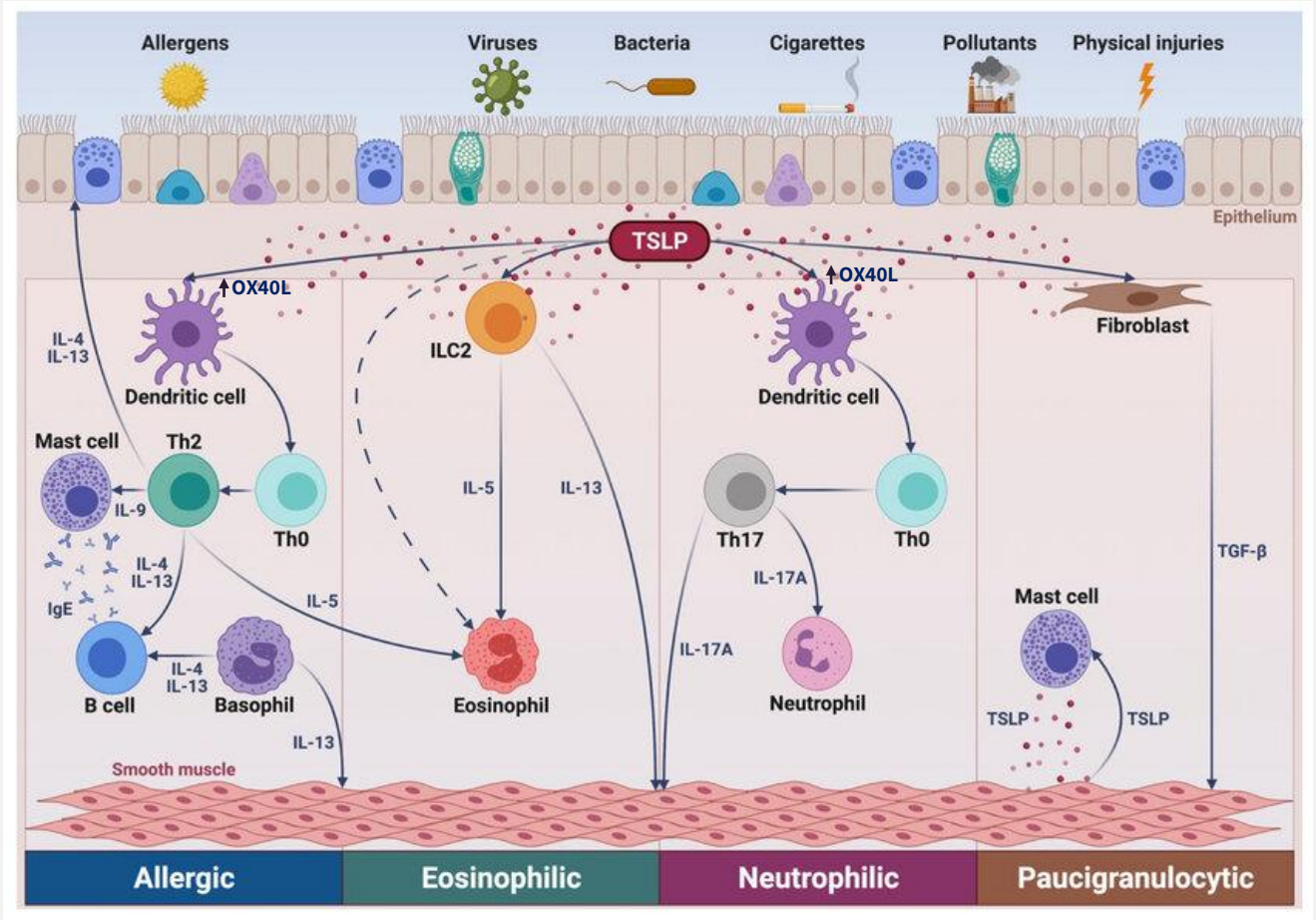


ATI-045: Anti-TSLP Monoclonal Antibody Program

Investigational Drug Candidate

TSLP Overview

- ATI-045 (Bosakitug) is a humanized monoclonal antibody targeting thymic stromal lymphopoietin (TSLP)
- TSLP - Pleiotropic and broad activity
  - Master regulator of type 2 (Th2) immune responses at the barrier surfaces of skin and the respiratory/ gastrointestinal tract
  - Drives eosinophilic and neutrophilic inflammation and acts on a wide variety of adaptive, innate, and structural cells
  - Involved in induction phase and effector phase as well as non-Th2 processes
  - Proven biology - the expression of TSLP is elevated in individuals with respiratory and skin disease
- TEZSPIRE® - first TSLP approved in severe asthma



Adapted from Int J Mol Sci. 2021 Apr 22;22(9):4369

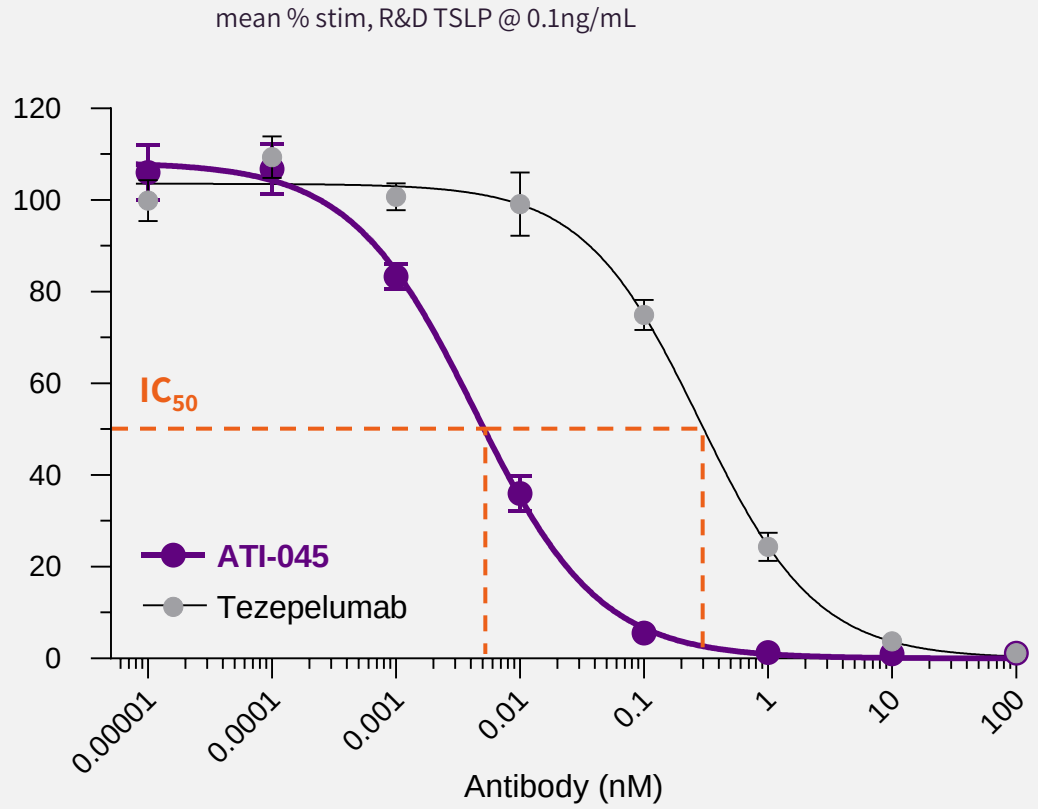
ATI-045 Unique Differentiation

Best-in-Class Potential

ATI-045 Key Properties

60x More Potent than Tezepelumab

>60x hPBMC CCL17 Inhibition



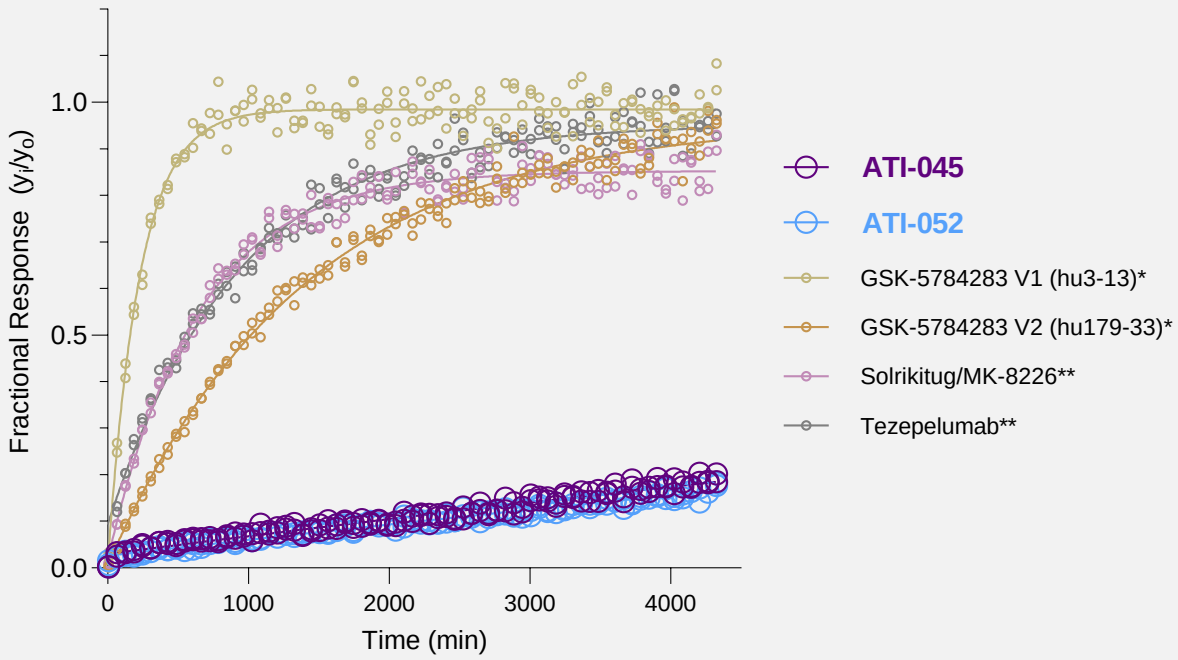
- Very high affinity to TSLP
- Extremely low dissociation rate from TSLP*, leading to long residence time and enhanced neutralization activity
- Very high potency
- Unique binding characteristics to TSLP
- ~23-day half-life that can potentially support an extended dosing interval (data not shown)

Human TSLP		
ka (1/Ms)	kd (1/s)	K_D (M)
2.16E+06	<1E-05*	<4.63E-12*

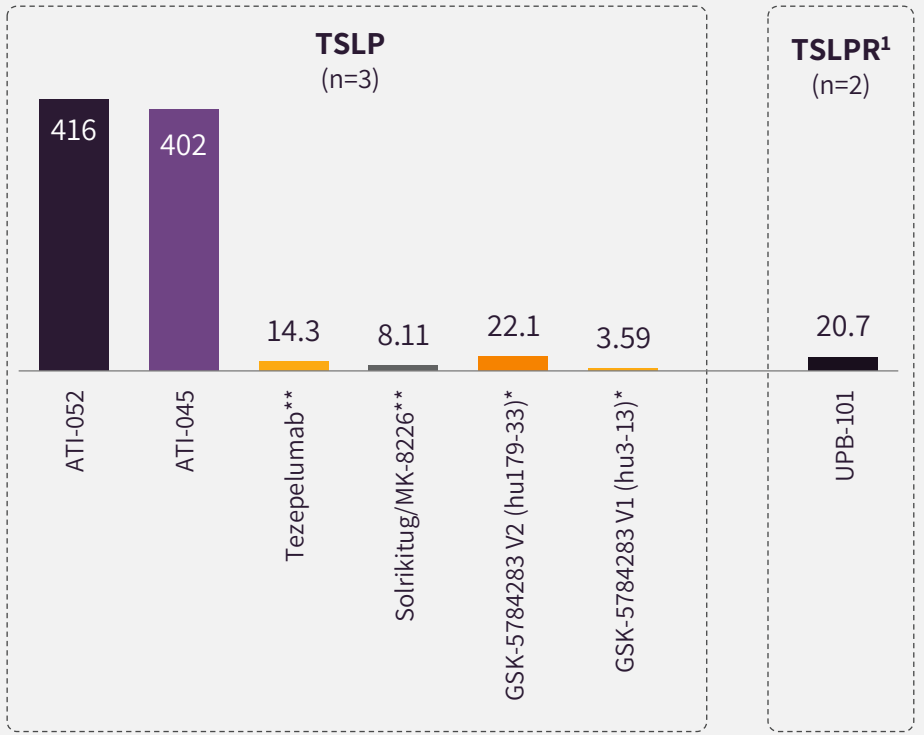
Data on file
* Quantification of dissociation rate limited by the surface plasmon resonance instrument sensitivity

Dissociation Kinetics and Residence Time

Dissociation of TSLP from mAbs (TR-FRET)



Residence Time
(hours)



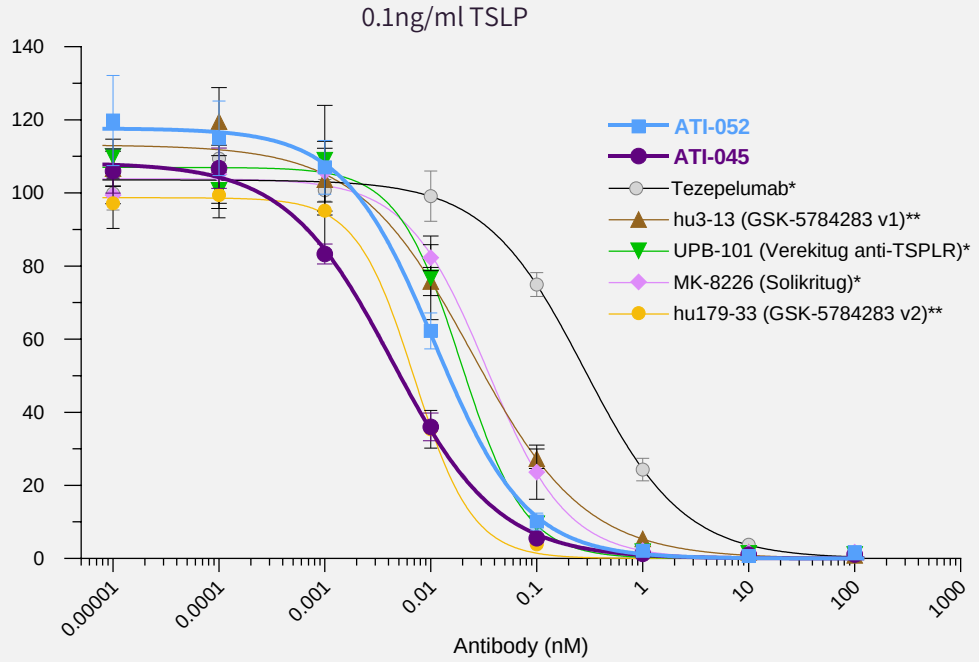
ATI-045 and ATI-052 demonstrate very slow dissociation kinetics from TSLP relative to comparator antibodies

The residence time for ATI-045 and ATI-052 is ~20-100x longer than comparator antibodies

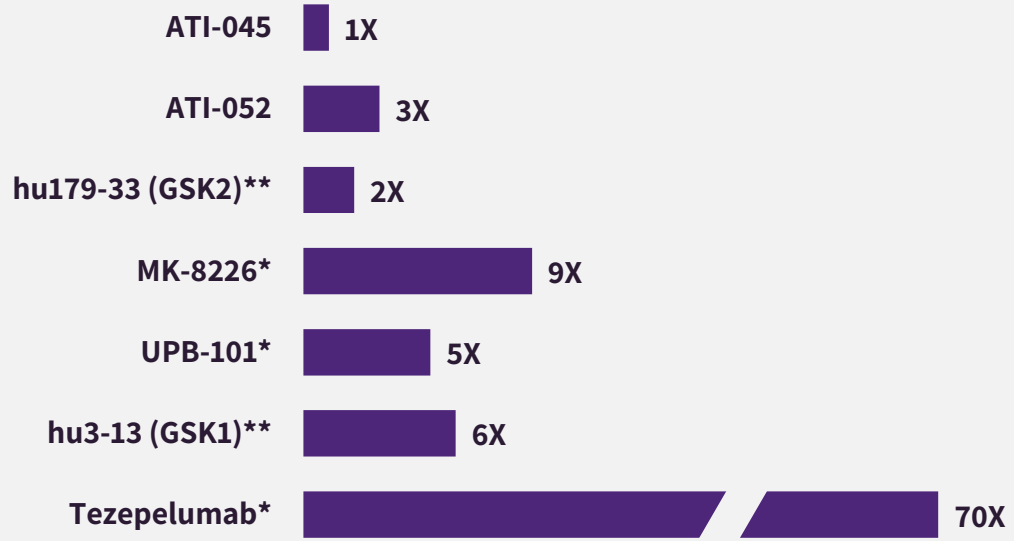
Data on file
1. SPR: Residence Time based on apparent kd using standard TSLPR immobilization density and bivalent fit; *Analog mAb; **Biosimilar mAb

ATI-045 Has Greater Potency Than Other TSLP/TSLPR Antibodies

TSLP Stimulated CCL17 Production from hPBMC



IC_{50} (XΔ) vs ATI-045



ATI-045 is the most potent of the TSLP/TSLPR antibodies evaluated in blocking CCL17 production

The bifunctional antibody, ATI-052, retains much of the potency for TSLP functional blockade compared with the parent ATI-045

Data on file
*Biosimilar; **Analog

ATI-045 Competitively Positioned as Potential Best-in-Class TSLP mAb

- Strong differentiation vs. tezepelumab and other clinical stage anti-TSLP mAbs
  - Slower dissociation rate
  - Very high residence time
  - Greater potency
- Unique binding characteristics
- Clinical translation:
  - Phase 2a atopic dermatitis study demonstrated 88% of protocol defined population exhibiting IGA 0/1 responses and 94% exhibiting at least 75% response in EASI score at week 26
- Opportunity for extended dosing

ATI-045 Respiratory Program

Partnered in China

Most Clinically Advanced Development-Stage TSLP mAb in Respiratory

Ongoing phase 2 clinical trials of ATI-045 (TQC2731) in multiple indications by CTTQ in China:

1

Severe Asthma[1]

- 220 participants
- 52-week primary endpoint
- 2 active dose groups vs Pbo
- 1H 2025 data anticipated*

2

Chronic Rhinosinusitis with Nasal Polyps[2]

- 80 participants
- 24-week primary endpoint
- 2 active dose groups vs Pbo
- 1H 2025 data anticipated*

3

Chronic Obstructive Pulmonary Disease[3]

- 258 participants
- 24-week primary and 52-week secondary endpoints
- 1 active dose group vs Pbo
- Recruiting

Parallel programs in China can potentially be leveraged to accelerate development timeline via data sharing with CTTQ

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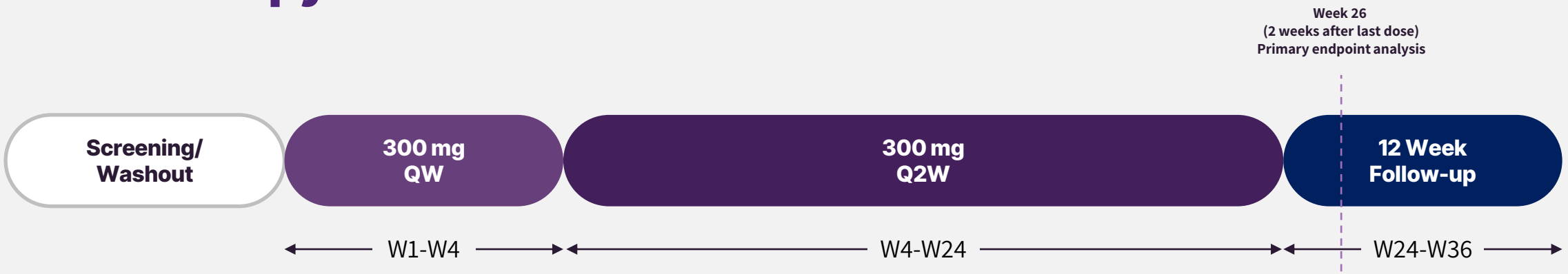
1. ClinicalTrials.gov Identifier: NCT05472324; 2. ClinicalTrials.gov Identifier: NCT06036927; 3. ClinicalTrials.gov Identifier: NCT06707883
*Partner data to inform internal development programs

ATI-045 Atopic Dermatitis Program

Potential First-in-Class TSLP mAb for AD

Clinical Translation: ATI-045 Phase 2a (US-Based) POC Monotherapy



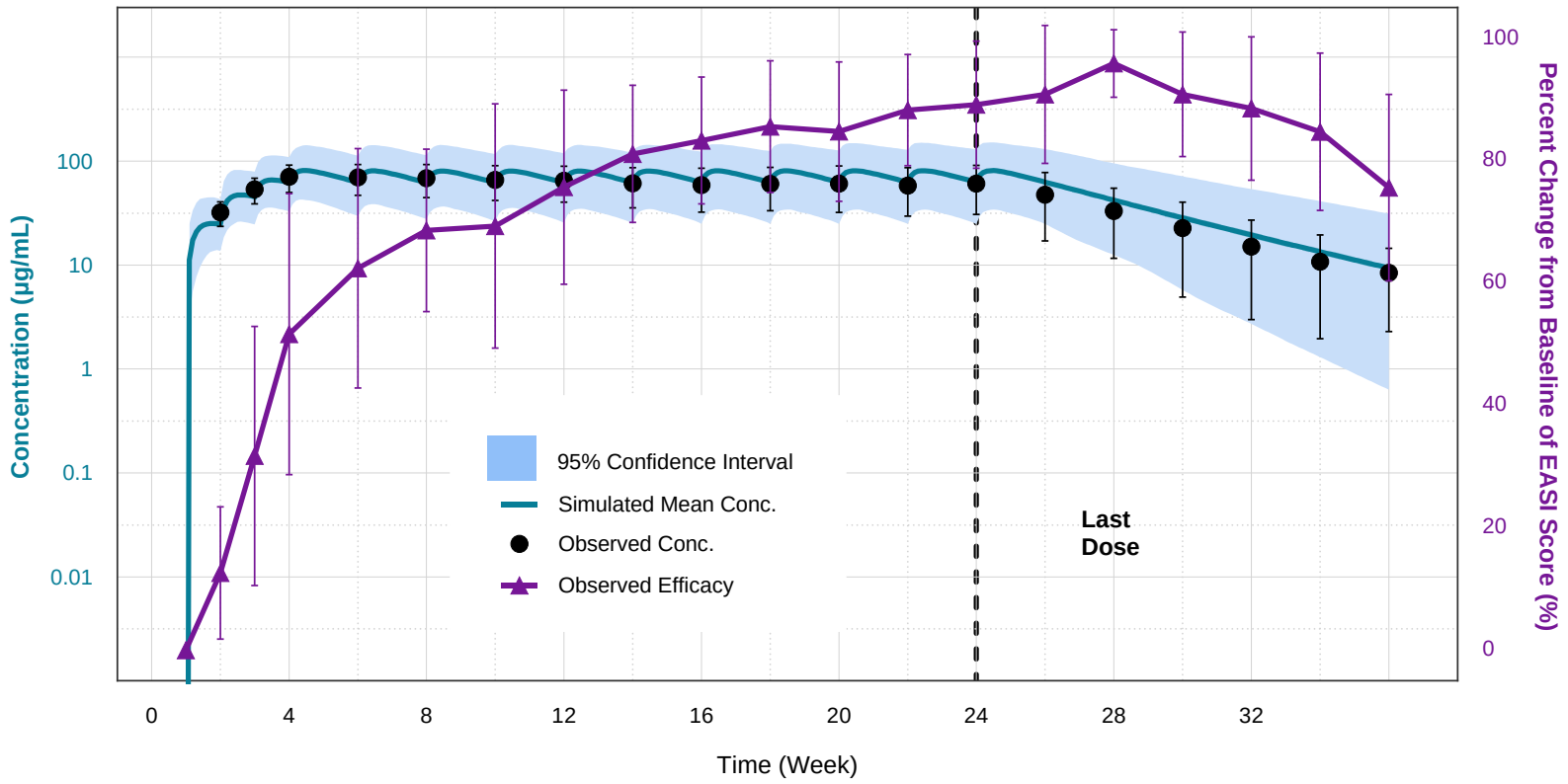
PRIMARY OBJECTIVES

- To evaluate the efficacy, safety and tolerability of ATI-045 as monotherapy in subjects with moderate to severe AD

SECONDARY OBJECTIVES

- To evaluate the pharmacokinetics, immunogenicity and pharmacodynamic biomarkers of ATI-045 in subjects with moderate to severe AD
- Enrolled: 22 subjects (17 completed treatment) at 7 US-based sites
- Eligibility: diagnosis of AD (present for at least 6 months); EASI ≥12; IGA ≥3; total AD BSA ≥10%
- Baseline Characteristics: Mean EASI of 17.6, Mean PP-NRS of 6.5; majority had prior medication prior to screening

ATI-045 Exposure and Efficacy Time Profile Demonstrated Sustained Clinical Response After the Last Dose

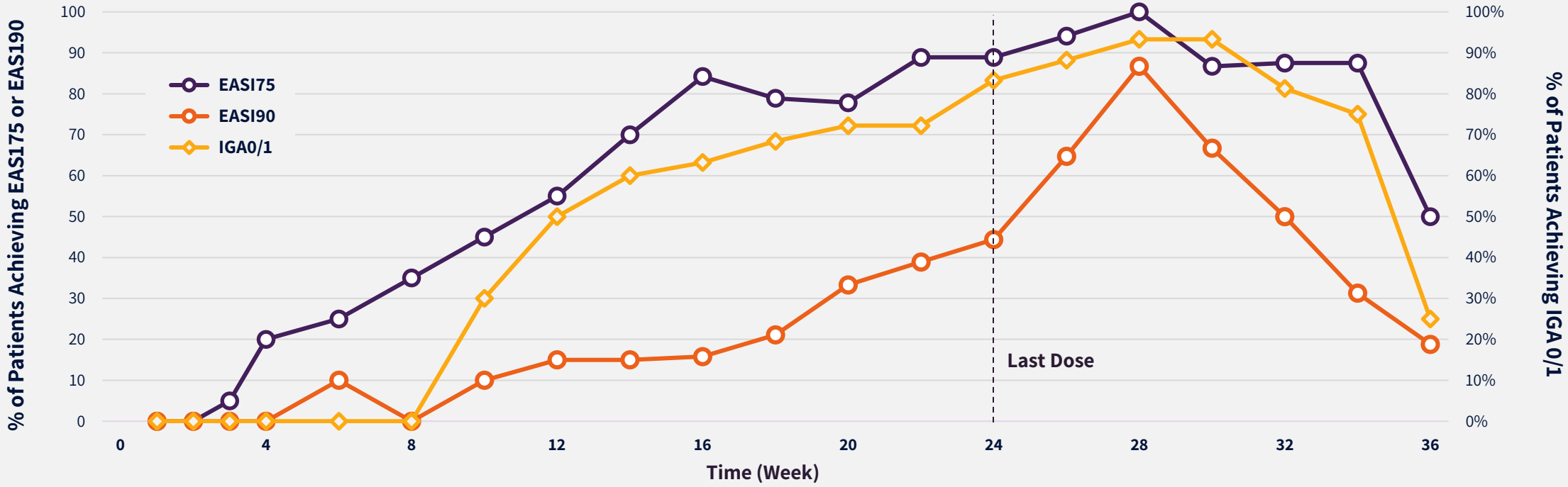


- A time lag in efficacy response relative to exposure was observed both while the drug was onboard and after the last dose
- EASI-75 sustained response after the last dose supports the possibility of longer dosing intervals
- Favorable safety and immunogenicity profile

Data on file

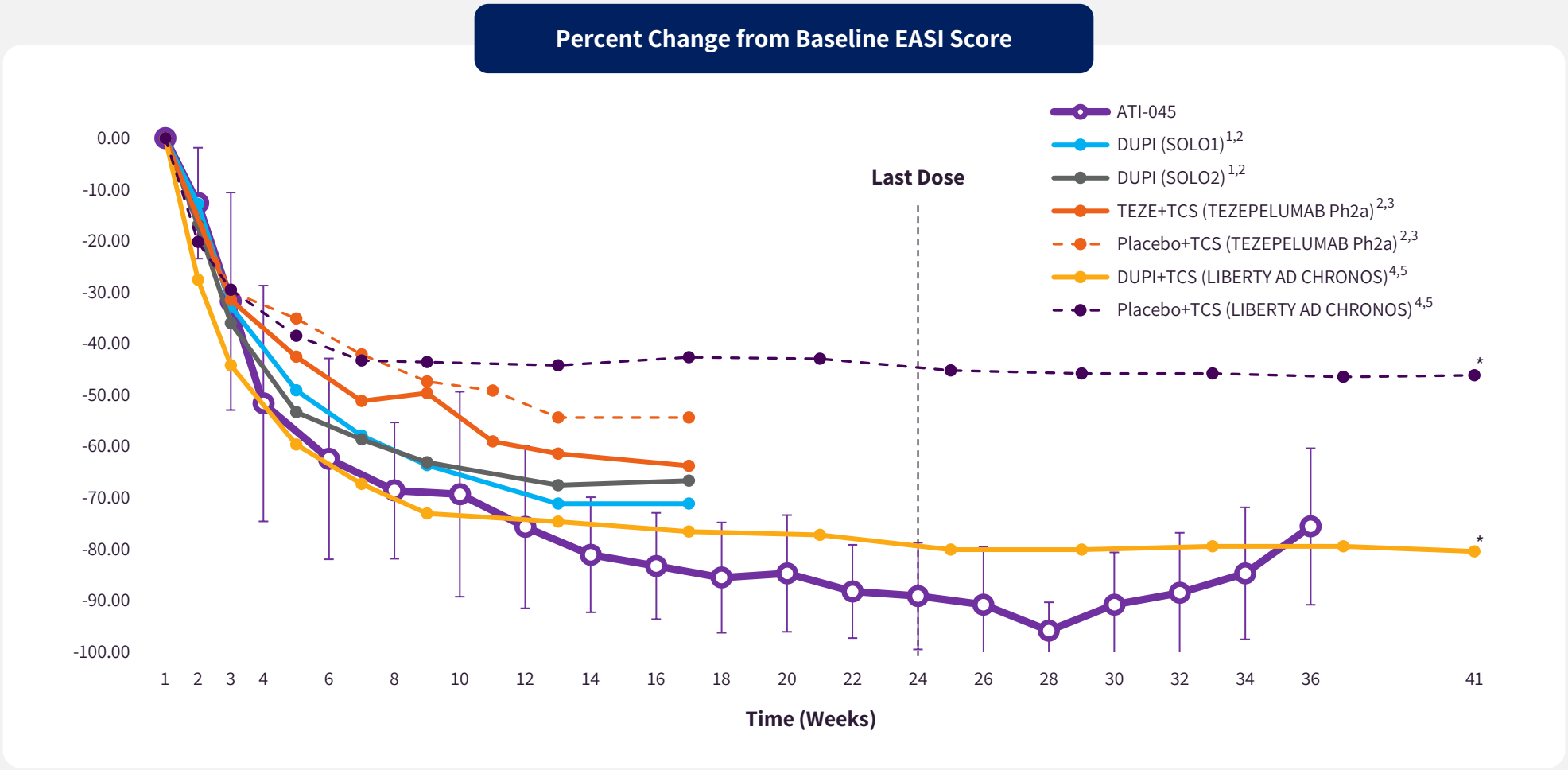
ATI-045 Demonstrated Improvement in Efficacy Measures (Week 26, N=17)

EASI 75 % @ Week 26	EASI 90 % @ Week 26	EASI 100 % @ Week 26	IGA 0/1 @ Week 26
94%	65%	24%	88%



Data on file

Comparison to Dupilumab Mono, Combo, and Tezepelumab Combo Studies**



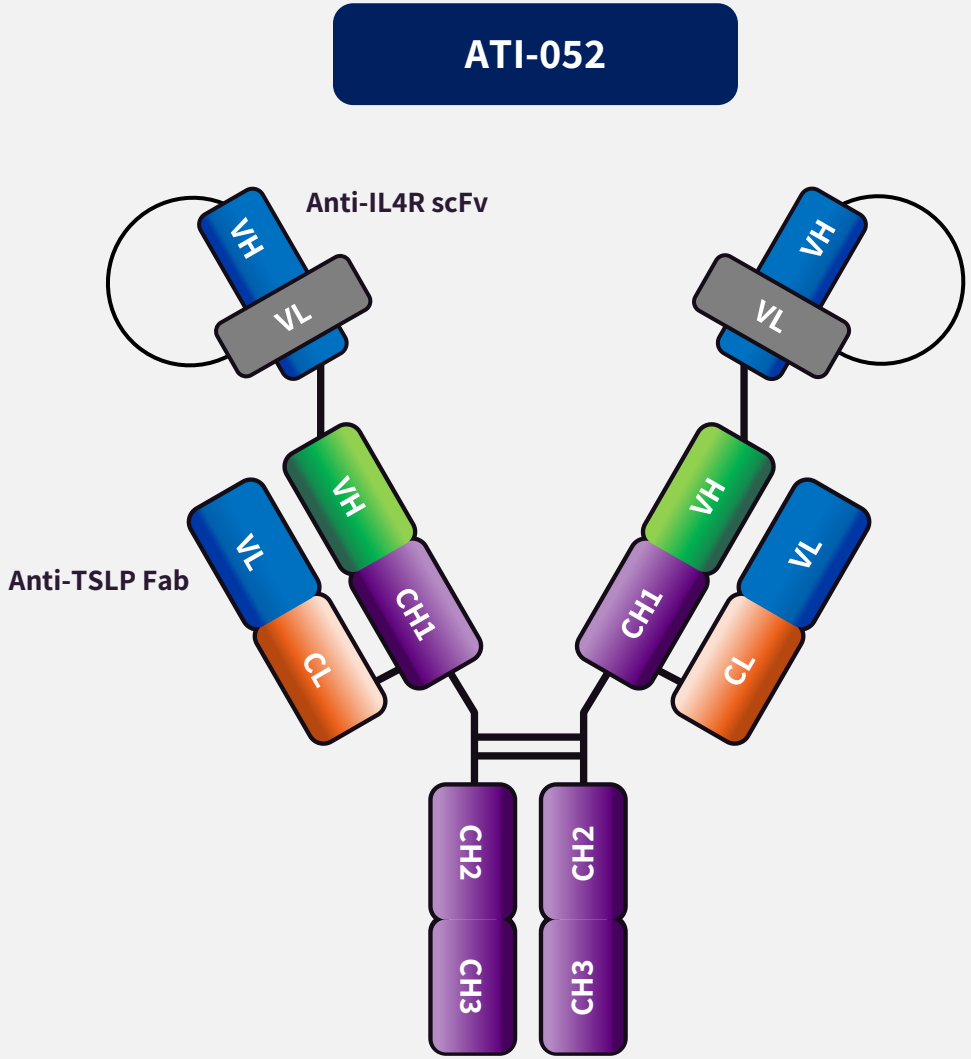
1. N Engl J Med. 2016 Dec 15;375(24):2335-2348. [SOLO1:NCT02277743; SOLO2:NCT02277769]; 2. 16-week study; 3. J Am Acad Dermatol. 2019 Apr;80(4):1013-1021. [NCT02525094]; 4. Lancet. 2017 Jun 10;389(10086):2287-2303. [NCT02260986]; 5*. LIBERTY AD CHRONOS was a 52-week study; data truncated to align with ATI-045 trial **Not a head-to-head comparison – differences exist between trial designs and caution should be exercised when comparing data across studies.

ATI-052: Anti-TSLP x IL4R Bispecific Antibody Program

Investigational Drug Candidate

ATI-052: Key Asset Highlights

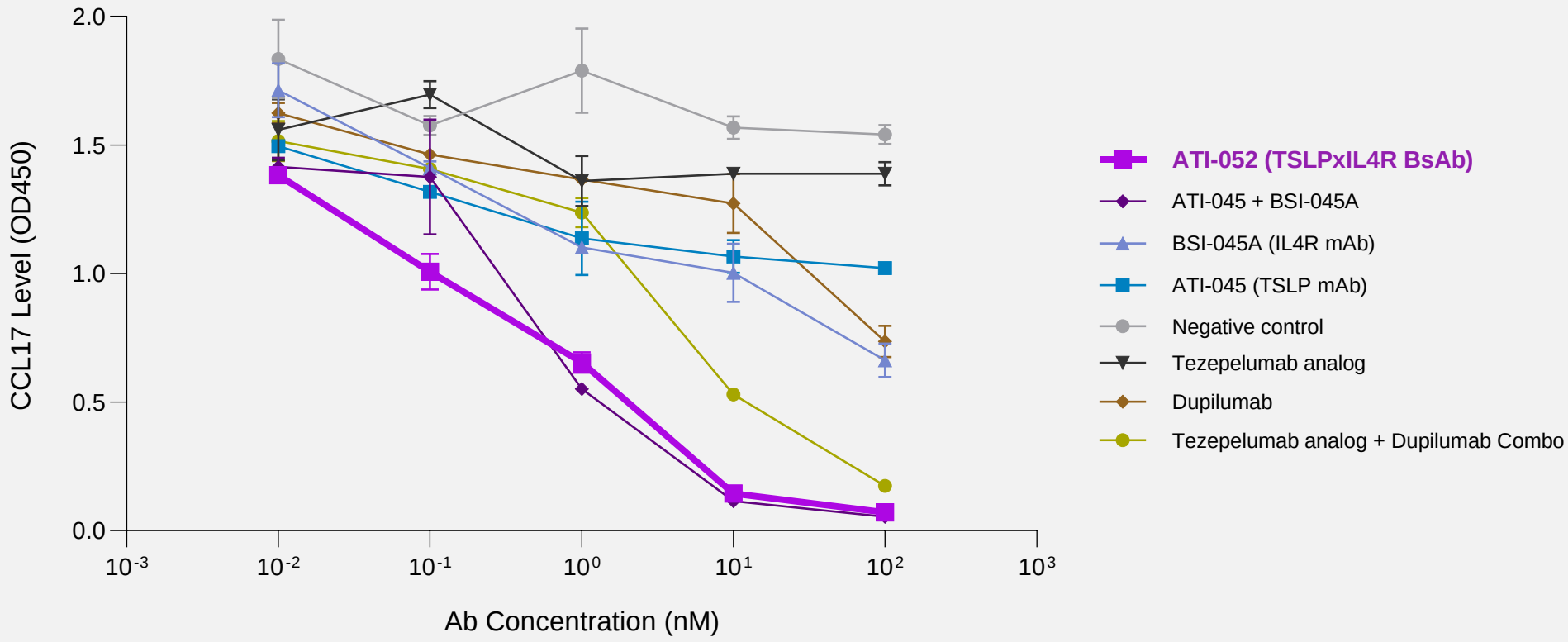
- Bispecific utilizing same antibody binding regions of ATI-045 combined with IL4R, inhibiting TSLP upstream and immune cells downstream of the Th2 cascade
- Anti-TSLP mAb component has Fc engineered to bind more tightly to FcRn, potentially extending half-life
- Exhibits greater cellular bioactivity on CCL17 release than the combination of tezepelumab and dupilumab, a key biomarker for atopic dermatitis
- Potential to show superior activity in AD, severe asthma and COPD compared to approved therapies
- IND submission planned for Q1 2025



ATI-052 Exhibits Greater Cellular Bioactivity than the Combination of Tezepelumab and Dupilumab on CCL17 Release

Effect on CCL17 Release Induced by 10 ng/mL IL4 plus 10 ng/mL TSLP

(*Ex vivo* PBMC assay)



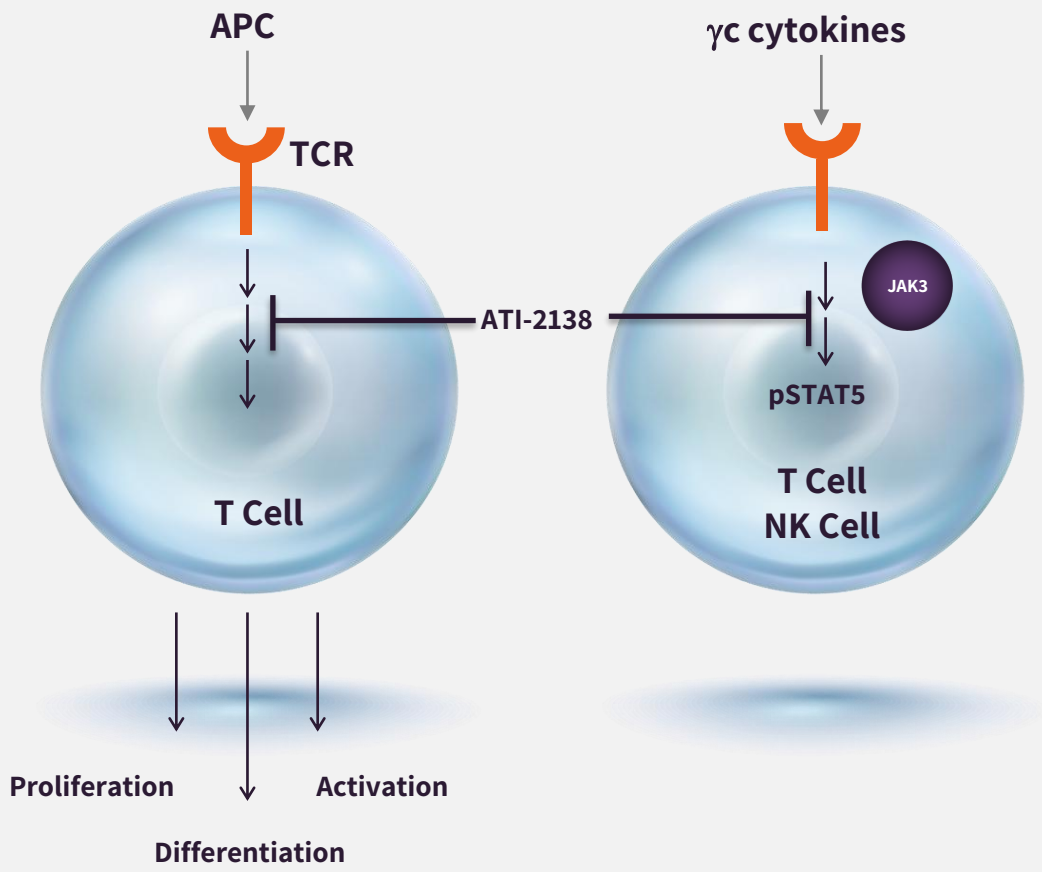
Data on file

ATI-2138: A First-Generation Novel ITK/JAK3 Inhibitor for T Cell-Mediated Diseases

Investigational Drug Candidate

ATI-2138: Oral Small Molecule Covalent IL-2-Inducible Tyrosine Kinase (ITK) & JAK3 Inhibitor for Autoimmune Disease

- ATI-2138 is an investigational oral compound which interrupts T cell receptor (TCR) signaling by inhibiting ITK and JAK3 signaling of common γ chain cytokines in lymphocytes (including IL-2 & IL-15)
- ATI-2138 is highly potent for both ITK and JAK3 (IC50: 0.2nM ITK; 0.5nM JAK3)[1]
- Positioned as fast follower to ritlecitinib – the only approved JAK3/TEC inhibitor
- SAD/MAD work completed demonstrating ATI-2138 was well tolerated[1]
- Currently enrolling POC study in Atopic Dermatitis
- Additional potential indications:
  - Alopecia Areata
  - Vitiligo
  - IBD

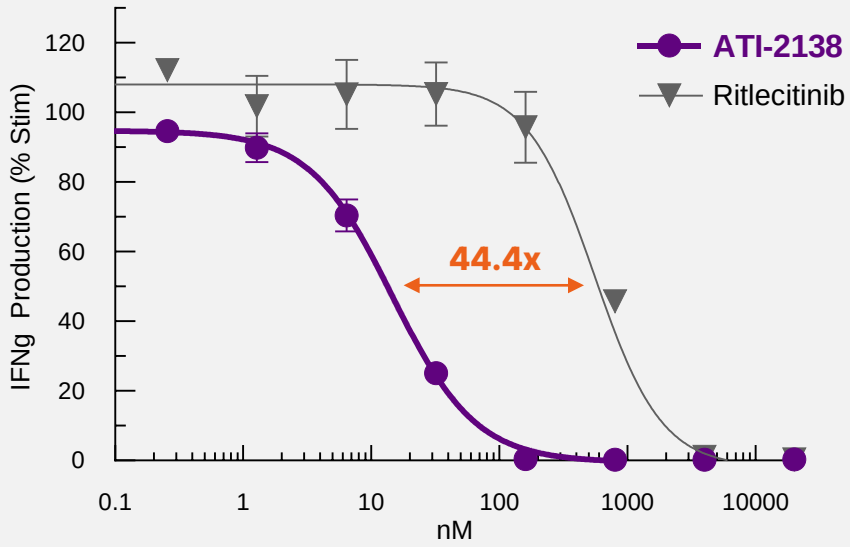


1. Data on file

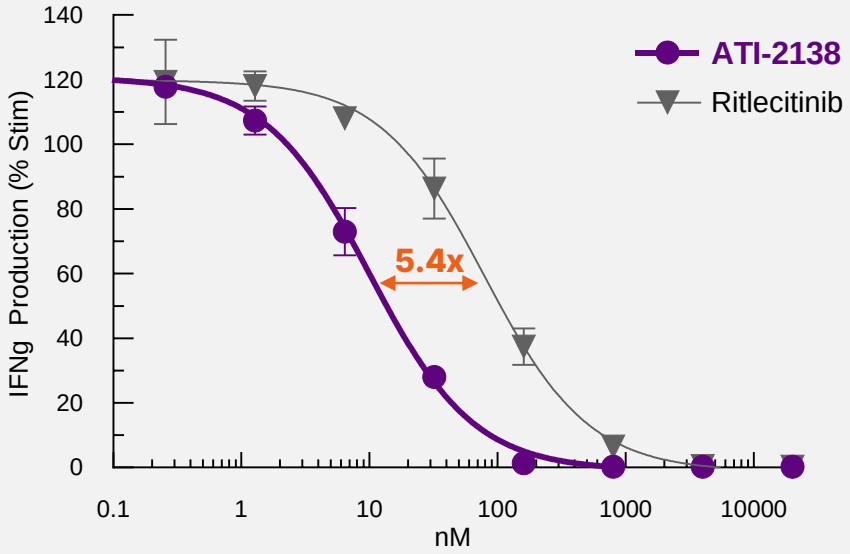
ATI-2138: Fast follower and Best-in-Class Potential vs Ritlecitinib

Dual ITK and JAK3 Inhibitors

ITK: HWB αCD3 Stimulated IFNγ Release



JAK3: HWB IL2 Stimulated IFNγ Release



- Ritlecitinib approved in Alopecia Areata
- ATI-2138 is 44.4x more potent than ritlecitinib for inhibiting αCD3 induced IFNγ production (ITK) and 5.4x more potent for inhibiting JAK3 dependent IL-2 induced IFNγ production in human whole blood
- At the FDA recommended 50 mg QD dose for alopecia areata, ritlecitinib plasma levels may not impact ITK (anti-CD3 /IFNγ) for any appreciable time
- In the ATI-2138 MAD study, the 5-40 mg BID doses inhibited up to 50%-90% of both ITK and JAK3 PD markers

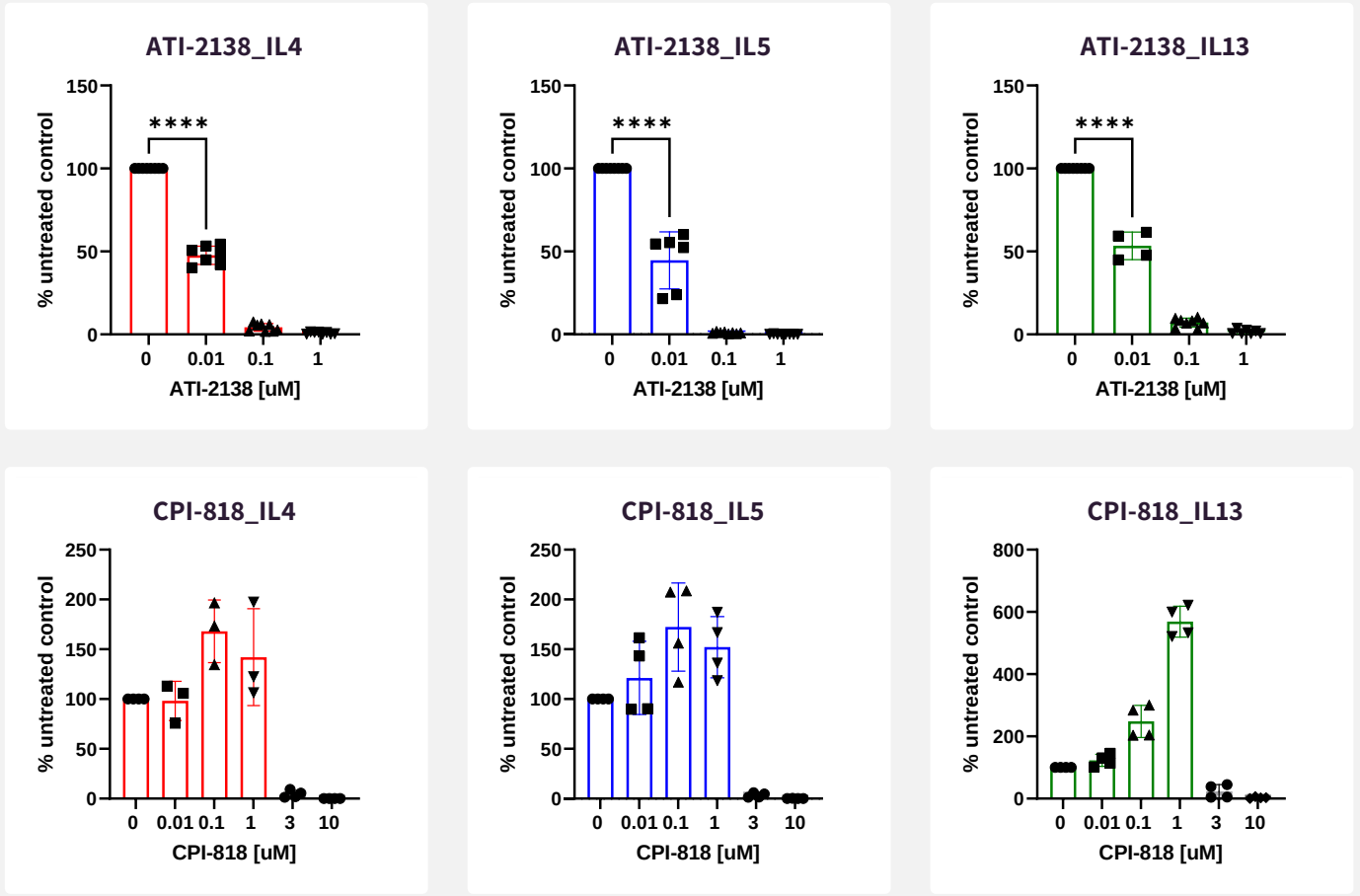
ATI-2138 and CPI-818 (Soquelitinib) Potency Comparison

ITK Biochemical Enzyme Potency

	ITK, IC50, nM	Kinact/Ki (uM-1s-1)
ATI-2138	0.25	0.34
CPI-818	9.5	0.022
Potency Ratio	**38x**	**15x**

- ATI-2138 is 15-38x more potent than CPI-818 in inhibiting the ITK enzyme activity
- ATI-2138 is significantly more potent than CPI-818 in blocking the Th2 derived cytokines, IL4, IL-5 and IL-13 (~100x)

Anti-CD3/CD28-Induced Cytokines from Human Th2 Cells



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Rationale for Dual Inhibition of ITK and JAK3

ATI-2138 in Atopic Dermatitis

ITK Inhibition

- Atopic dermatitis (AD) is a Th2 cell driven disease and ITK inhibition blocks Th2 cell differentiation/activation and production of IL-4 and IL-13
  - Dupilumab (anti-IL4Ra) and tralokinumab (anti-IL-13) are efficacious in AD
- Topical calcineurin inhibitors (TCI; tacrolimus and pimecrolimus) are effective in AD and function downstream of ITK
- T cells from AD patients have increased ITK expression[1]
- ITK polymorphisms are associated with increased atopy risk[2]
- ITK inhibitors are active in murine contact hypersensitivity[3]

JAK3 Inhibition

- JAK3 regulates g-common cytokines including IL-2 and IL-4
- JAK inhibitors (upadacitinib, abrocitinib and baricitinib) are efficacious in AD

1. Matsumoto Y., et al; Identification of Highly Expressed Genes in Peripheral Blood T Cells from Patients with Atopic Dermatitis. *Int Arch Allergy Immunol* 1 December 2002; 129 (4): 327–340; 2. Graves PE, et al. Association of atopy and eczema with polymorphisms in T-cell immunoglobulin domain and mucin domain-IL-2-inducible T-cell kinase gene cluster in chromosome 5 q 33. *J Allergy Clin Immunol*. 2005 Sep;116(3):650-6; 3. von Bonin, A., et al. (2011), Inhibition of the IL-2-inducible tyrosine kinase (Itk) activity: a new concept for the therapy of inflammatory skin diseases. *Experimental Dermatology*, 20: 41-47.

Phase 2a Trial Design of ATI-2138 in Atopic Dermatitis

Dosing Underway

Eligibility

- Moderate to Severe Atopic Dermatitis
- EASI ≥ 16
- vIGA 3-4
- BSA ≥ 10%
- 18-60 years
- Planned 15 patients

Treatment

- Open-label design
- Total 12 weeks treatment
- 10mg BID dosing

Endpoints

- Safety, PK
- PD: RNA analysis, proteomics, IHC to analyze specific pathway inhibition
- EASI-50, -75, -90, % change in EASI
- Change in vIGA, % achieving IGA-TS
- % change BSA, PP-NRS
- POEM, DLQI

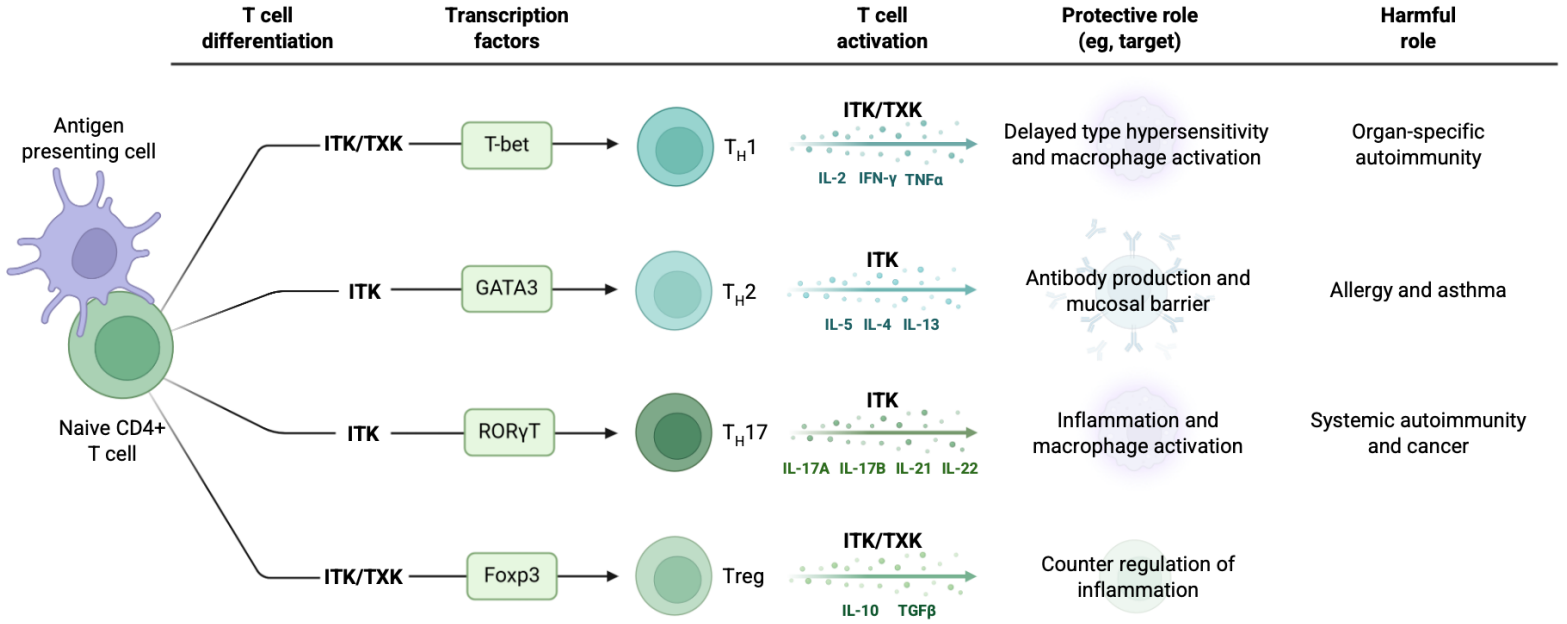
Wide Array of Disease Targets for ATI-2138

Areas of Current Focus:

Next-Generation Selective ITK Inhibitor

Selective ITK Inhibition Impacts Th2 Mediated Disease

ITK Skews T Helper Cell Differentiation Towards Th2 and Th17 Phenotypes



Adapted from J Sig Trans 2011:DOI:10.1155/2011/297868

- ITK has a nonredundant role in the differentiation and activation of T_H2 and T_H17 cells
- Blockade of T_H2 function inhibits production of IL-4 and IL-13, two cytokines with demonstrated importance in atopic and allergic diseases
- Goal of next generation ITK inhibitor is to eliminate crossover on JAK3 to minimize JAK safety concerns
- Selective targeting of ITK (T_H2 and T_H17 inhibition) and/or ITK/TXK (broad T cell inhibition) while sparing JAK3 should result in more specific T cell modulating drugs
- Actively progressing to candidate selection; planned IND submission 1H 2026

Rich Clinical Catalyst Calendar

2025

ATI-045
Severe Asthma Ph. 2 Data (CTTQ)
First Half 2025[1]

ATI-045
CRSwNP Ph. 2 Data (CTTQ)
First Half 2025[1]

ATI-2138
Atopic Dermatitis Ph. 2 Top Line Data
First Half 2025

ATI-052
IND Submission and Start of Ph. 1 Program
First Quarter 2025

2026

ATI-045
Atopic Dermatitis Ph. 2 Top Line Data

ATI-052
Phase 1/1b Top Line Data

ITK Selective Program
IND Submission and Start of Ph. 1 Program

All timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors.
1. Partner data to inform internal development programs

Company Summary

Executive Team

Proven track record of R&D, business development and scientific leadership in immuno-inflammatory diseases

KINect Technology Platform

Proprietary discovery engine enables targeted design of novel drug candidates

Pipeline

Multiple therapeutic programs ranging from discovery to clinical development

Intellectual Property

Global IP estate

Financial Strength

Proforma cash, cash equivalents and marketable securities as of Q3 2024 of $213M[1] and cash runway expected into 2028[2]

Commitment to Patients

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

1. After the upfront payment obligations under the Biosion license agreement and expected private placement net proceeds of $77M.
2. Without giving effect to additional business development transactions or financing activities.