Corporate Overview

November 2024

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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 “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 BSI-045B and BSI-502, to provide meaningful benefit to patients suffering from atopic dermatitis, COPD, asthma or other indications, the development of Aclaris’ drug candidates, including BSI-045B, BSI-502, 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 market opportunity for Aclaris’ drug candidates, including BSI-045B and BSI-502, in the indications they seek to target, the potential of BSI-045B to be dosed monthly, the PIPE financing and the expected net proceeds from such financing, 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.

Executive Summary

- **In-licensing two biologics from Biosion**
  - **BSI-045B –** anti-TSLP mAb (Phase 2)
  - **BSI-502 –** anti-TSLP/IL4R BsAb (IND enabling tox)

- **Broad Immunology-Focused Development Pipeline**
  - ✓ Two Phase 2 I&I assets, multiple preclinical programs, and proprietary kinase inhibitor discovery engine
    - **BSI-045B** – potential best-in-class clinical stage anti-TSLP mAb, including potential first-in-class in atopic dermatitis
      - – Ongoing Phase 2 in Severe Asthma and Phase 2 in Chronic Rhinosinusitis with Nasal Polyps in China (partner)
    - **ATI-2138** – oral inhibitor of ITK/JAK3
    - **BSI-502** – potential best-in-class anti-TSLP/IL4R BsAb
    - **ITK inhibitor** – oral selective ITK inhibitor
  - ✓ Rich catalyst calendar

- **Strong Balance Sheet**
  - ✓ Proforma cash, cash equivalents and marketable securities as of September 30, 2024 of $213M[1], is expected to fund company into 2028[2]
  - ✓ Cash runway expected to fund multiple catalysts across the pipeline, including with respect to BSI-045B Phase 2b in AD, BSI-502 Phase 1/1b, ATI-2138 Phase 2a in AD and Phase 2 in AA, and ITK Selective Phase 1/1b
    - Additional catalysts expected from the development of BSI-045B in China by other Biosion partner

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.

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Biotechnology Company Focused on Immuno-inflammatory Diseases with Large and Small Molecule Therapeutics

Pipeline + Platform + People

Innovative Pipeline
(investigational drug candidates)

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

BSI-502 – bispecific antibody targeting both TSLP and interleukin-4 receptor (IL4R)

ATI-2138 – oral inhibitor of ITK/JAK3

ITK inhibitor – oral selective ITK inhibitor

Discovery Engine/Expertise

Proprietary kinase small molecule discovery engine

Large molecule discovery and development expertise – leadership with over a dozen biologics approved

Leadership

Proven leadership team

World class small molecule and large molecule expertise

Large multinational and small biotech company experience

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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 including Aclaris, Vicept Therapeutics and Tricept Therapeutics
- 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 COO

- 35+ years in biologics development, clinical pharmacology, and business development
- Former roles at Frontage, GSK, 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
- Antares, Valeant, 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, Inc. and PwC
- Certified Public Accountant

Broad Immunology Development Pipeline

Program	Indication(s)	Preclinical	Phase 1	Phase 2	Phase 3
BSI-045B **TSLP mAb** *Subcutaneous*	Atopic Dermatitis (moderate-to-severe)				
ATI-2138 **ITK/JAK3 Inhibitor** *Oral*	Atopic Dermatitis (moderate-to-severe)				
BSI-502 **TSLP x IL4R BsAb** *Subcutaneous*	Respiratory/Dermatology				
Undisclosed **ITK Selective Inhibitor** *Oral*	Autoimmune				
Lepzacitinib (ATI-1777) **JAK1/JAK3 Inhibitor** *Soft Topical*	Atopic Dermatitis (moderate-to-severe)				Partnered in China and pursuing additional discussions
Zunsemetinib (ATI-450) **MK2 Inhibitor** *Oral*	Pancreatic cancer; Metastatic Breast Cancer				Investigator-initiated trials at Washington Univ, St. Louis

BSI-045B: Anti-TSLP Monoclonal Antibody Program

(Investigational Drug Candidate)

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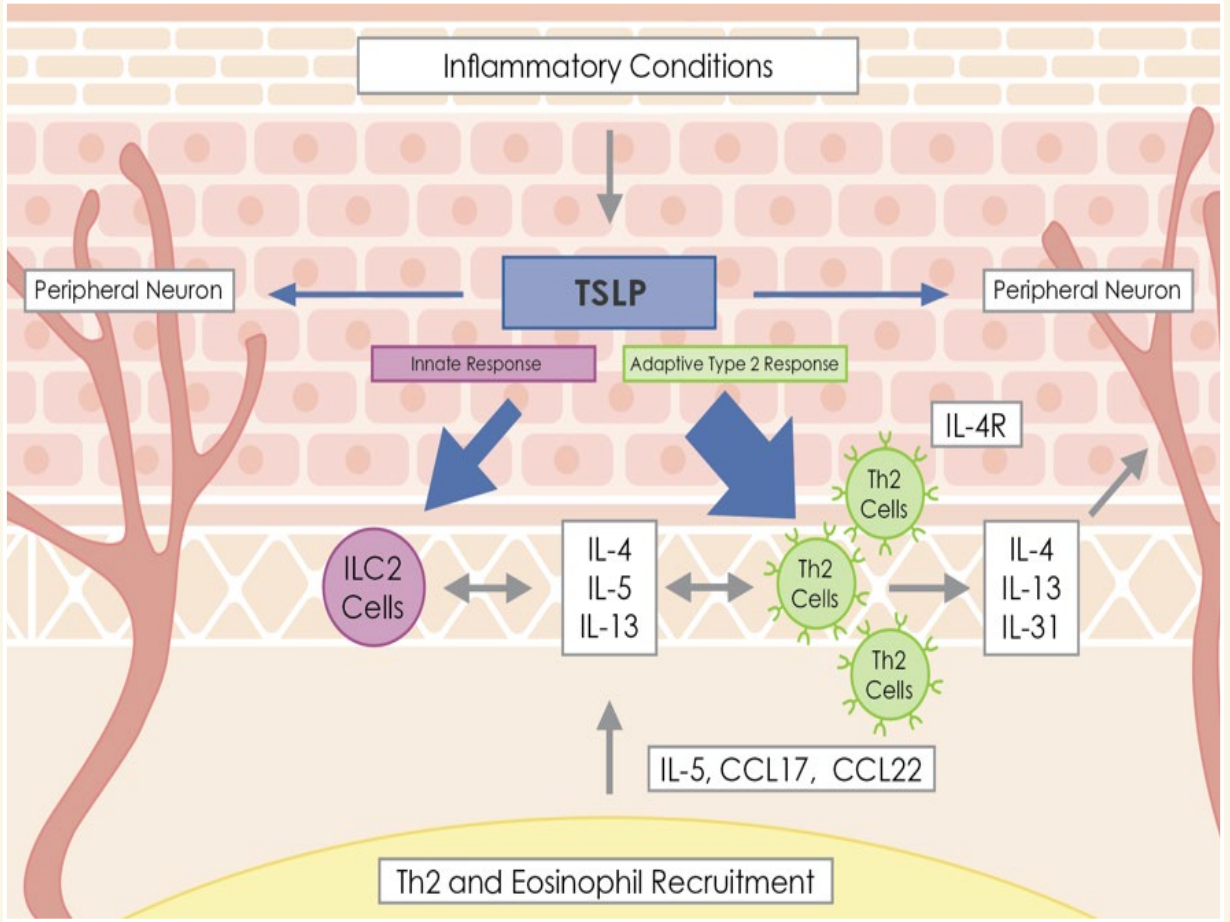
BSI-045B Overview

- BSI-045B is a humanized monoclonal antibody targeting thymic stromal lymphopoietin (TSLP)
- TSLP - master regulator of type 2 (Th2) immune responses at the barrier surfaces of skin and the respiratory/gastrointestinal tract.
- Proven biology - the expression of TSLP is elevated in individuals with atopic diseases such as atopic dermatitis (AD) and various respiratory diseases.
- TEZSPIRE® approved in severe asthma
  - Studied in COPD and AD
- Potential advantages of BSI-045B:
  - ✓ Potency versus tezepelumab and other assets in clinical development
  - ✓ Unique binding characteristics
  - ✓ Slow dissociation rate versus competitors
  - ✓ Opportunity for extended dosing



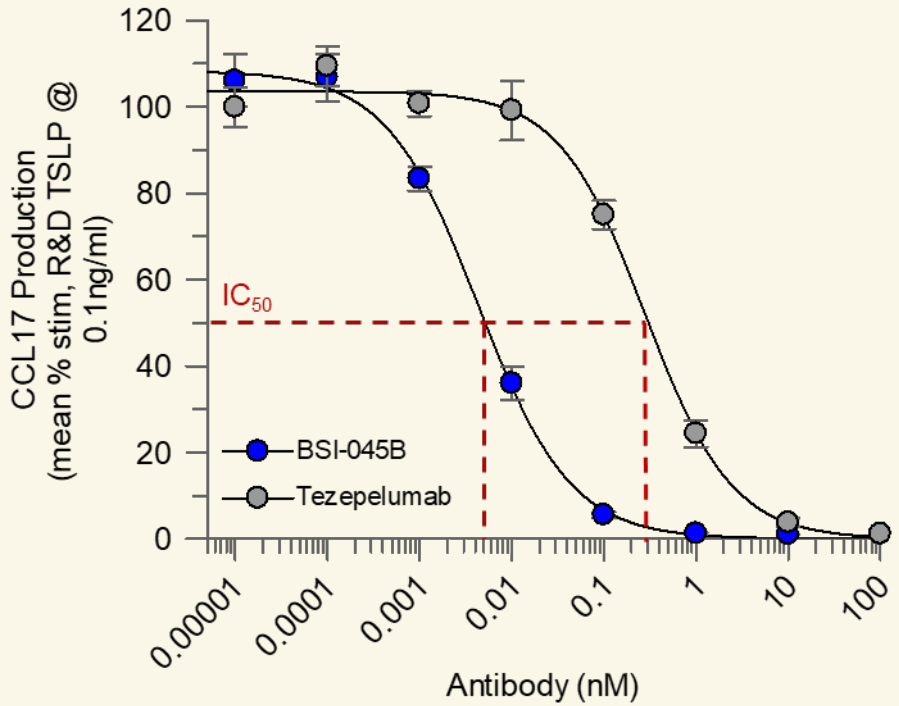
Adapted from Nakajima et al. Allergology International 2020

BSI-045B Key Properties

60x More Potent than Tezepelumab

Molecule	Human TSLP		
	ka (1/Ms)	kd (1/s)	K_D (M)
BSI-045B	2.16E+06	<1E-05*	<4.63E-12*

>60x hPBMC CCL17 Inhibition

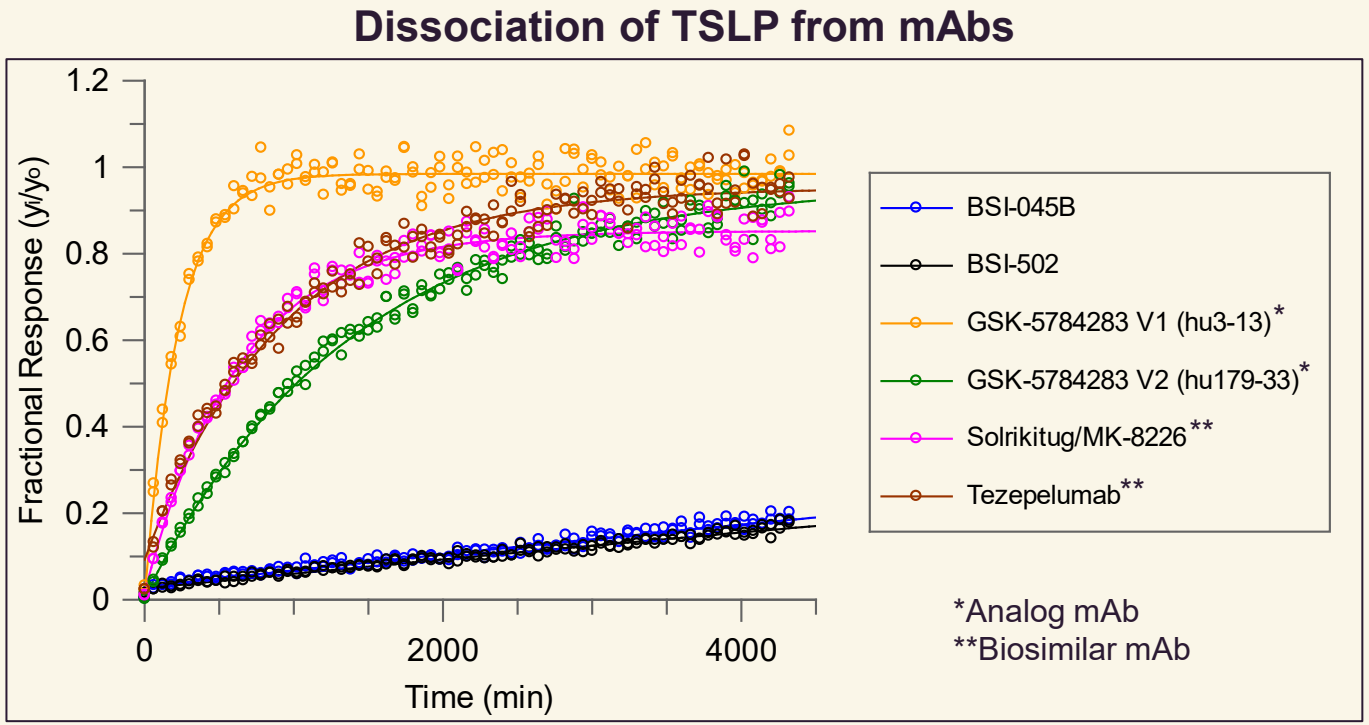


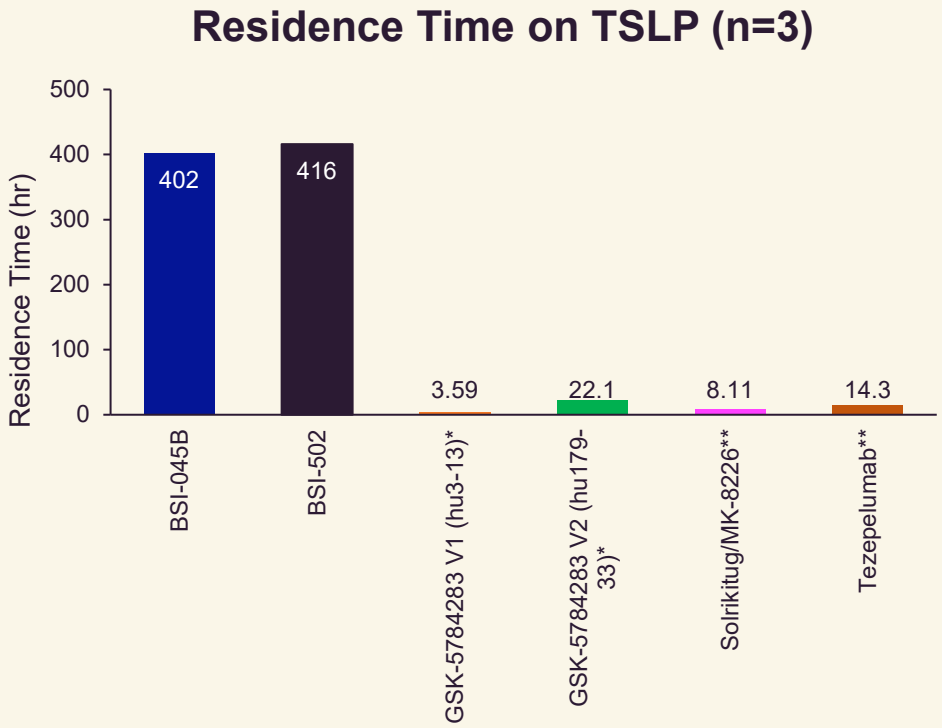
- Very high affinity to TSLP
- Extremely low dissociation rate from TSLP*, leading to long residence time and enhanced neutralization activity
- Very high potency
- Unique binding characteristics to TSLP
- ~23-day half-life that can potentially support an extended dosing interval (data not shown)

Data on file.

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

Dissociation Kinetics of TSLP Binding to anti-TSLP mAb using TR-FRET



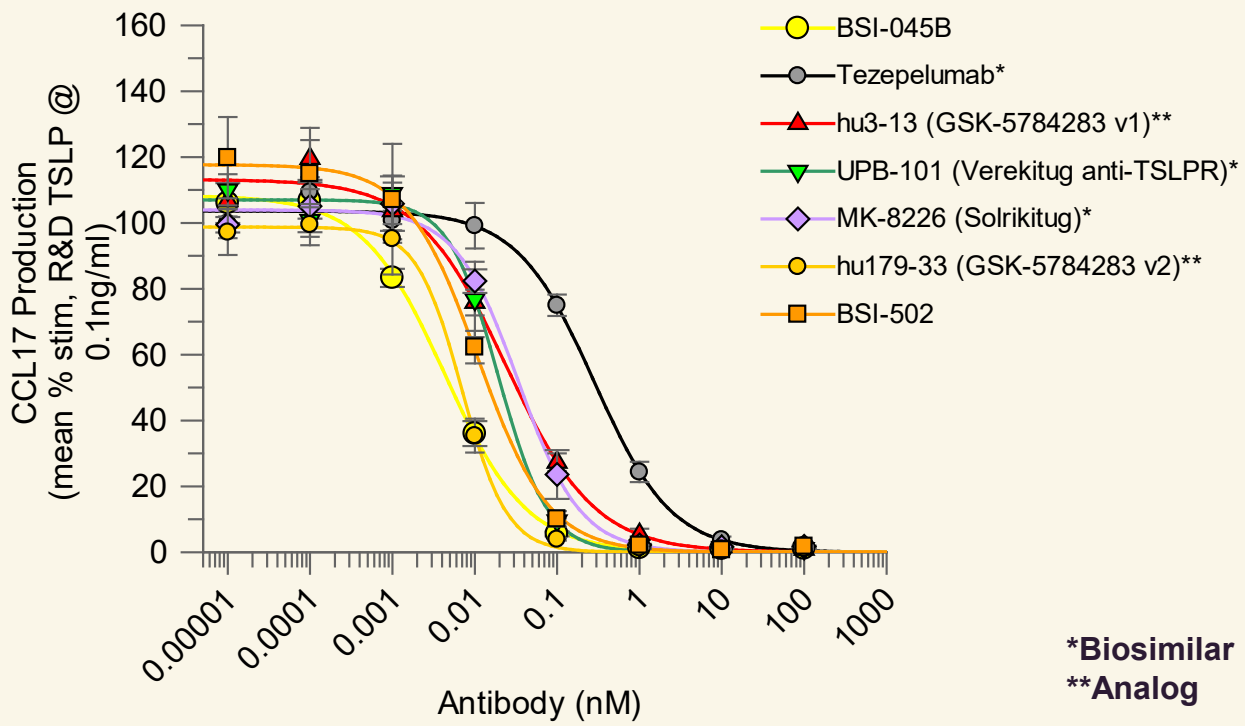


- BSI-045B and BSI-502 demonstrate very slow dissociation kinetics from TSLP relative to comparator antibodies
- The residence time for BSI-045B and BSI-502 is ~20-100x longer than comparator antibodies

Data on file.

BSI-045B Has Greater Potency Than Other TSLP/TSLPR Antibodies

TSLP Stimulated CCL17 Production from hPBMC (0.1ng/ml TSLP)



***Biosimilar**
****Analog**

Antibody	Antibody-dependent CCL17 Modulation		IC_{50} (XΔ) vs BSI-045B
	TSLP @ 0.1ng/ml (IC_{50} / IC_{90}), nM	n	
BSI-045B	0.004 / 0.059	10	**1X**
Tezepelumab*	0.282 / 3.158	10	**71X**
hu3-13 (GSK1)**	0.024 / 0.433	4	**6X**
UPB-101*	0.019 / 0.093	4	**5X**
MK-8226*	0.034 / 0.239	4	**9X**
hu179-33 (GSK2)**	0.007 / 0.028	4	**2X**
BSI-502	0.011 / 0.116	4	**3X**

- **BSI-045B is the most potent of the TSLP/TSLPR antibodies evaluated in blocking CCL17 production**
- **The bifunctional antibody, BSI-502, retains much of the potency for TSLP functional blockade compared with the parent BSI-045B**

Data on file.

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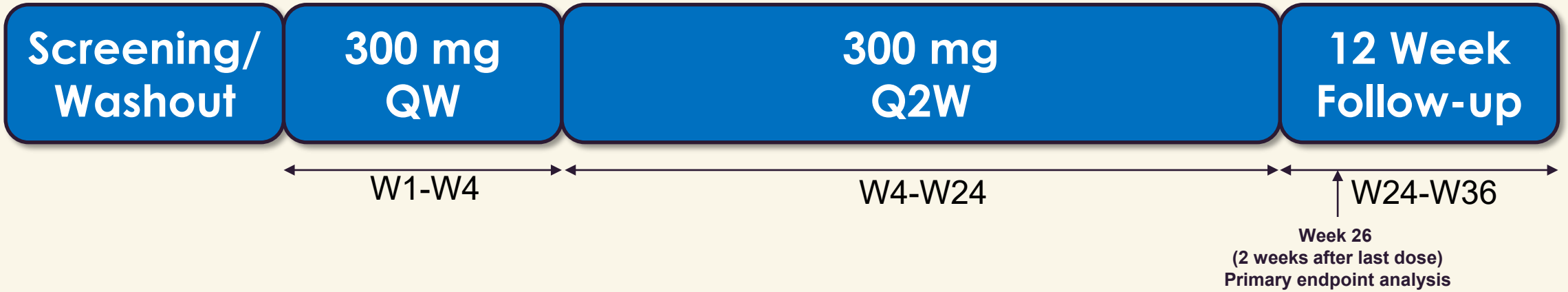
Clinical Translation: BSI-045B Phase 2a (US-Based) POC Monotherapy Study Summary



Primary Objectives

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

Secondary Objectives

- To evaluate the pharmacokinetics, immunogenicity and pharmacodynamic biomarkers of BSI-045B in subjects with moderate to severe AD

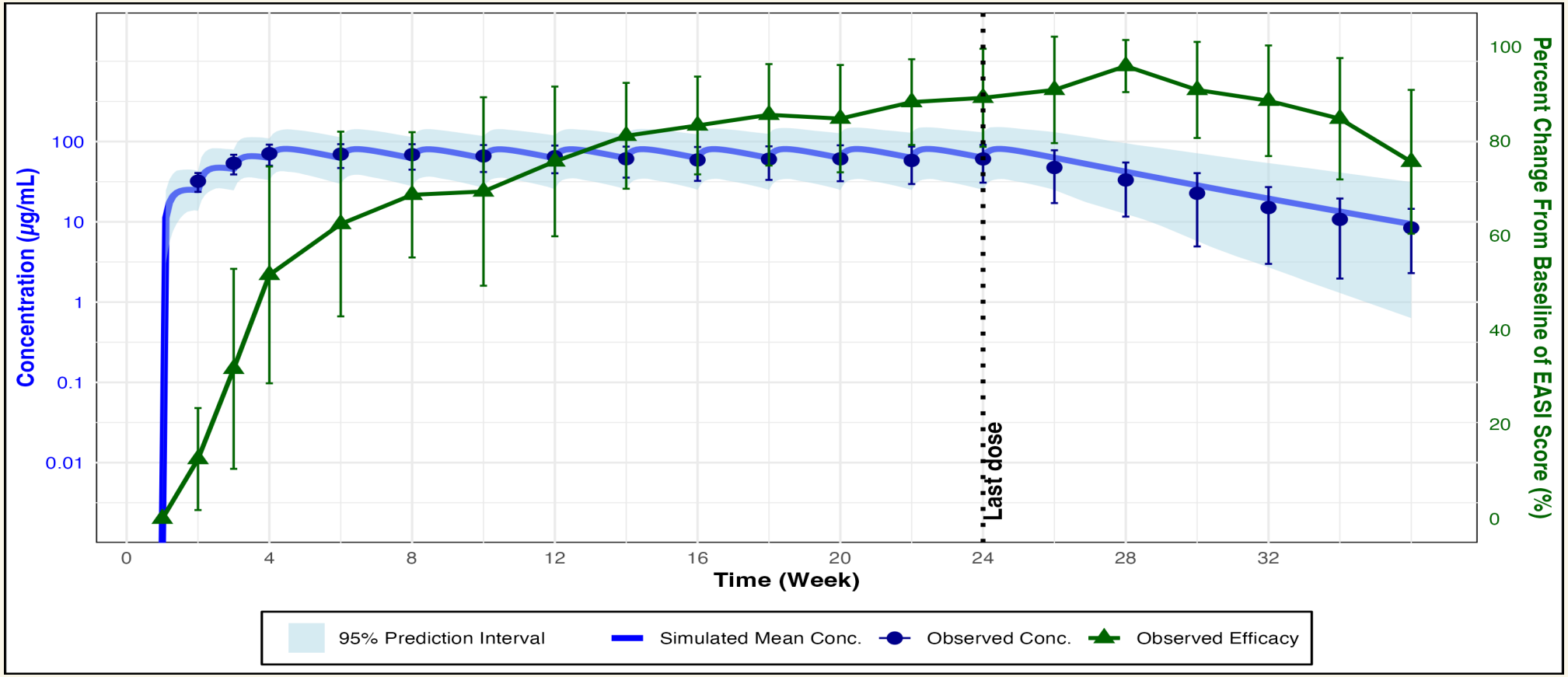
Enrolled: 22 subjects (17 completed treatment) at 7 US-based sites

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

BSI-045B 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



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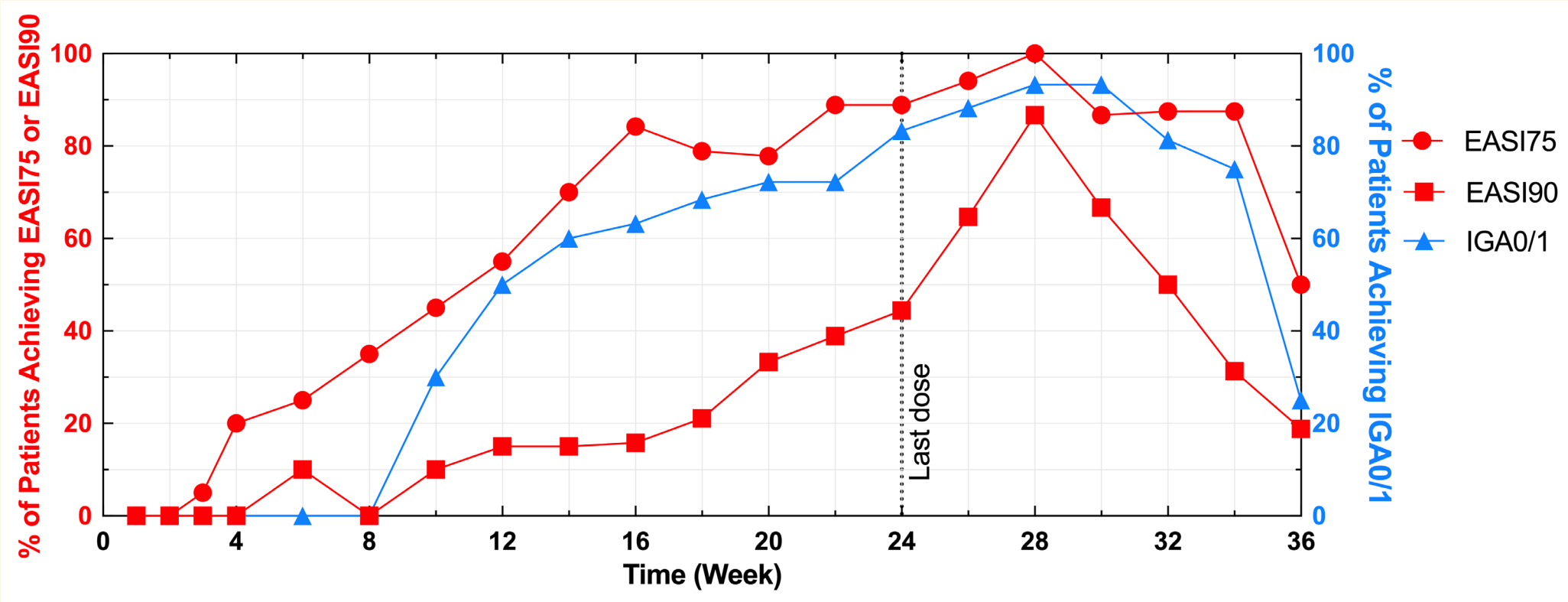
BSI-045B Demonstrated Improvement in Efficacy Measures (Week 26, N=17)

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



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BSI-045B Safety and Immunogenicity Profile in P2a POC

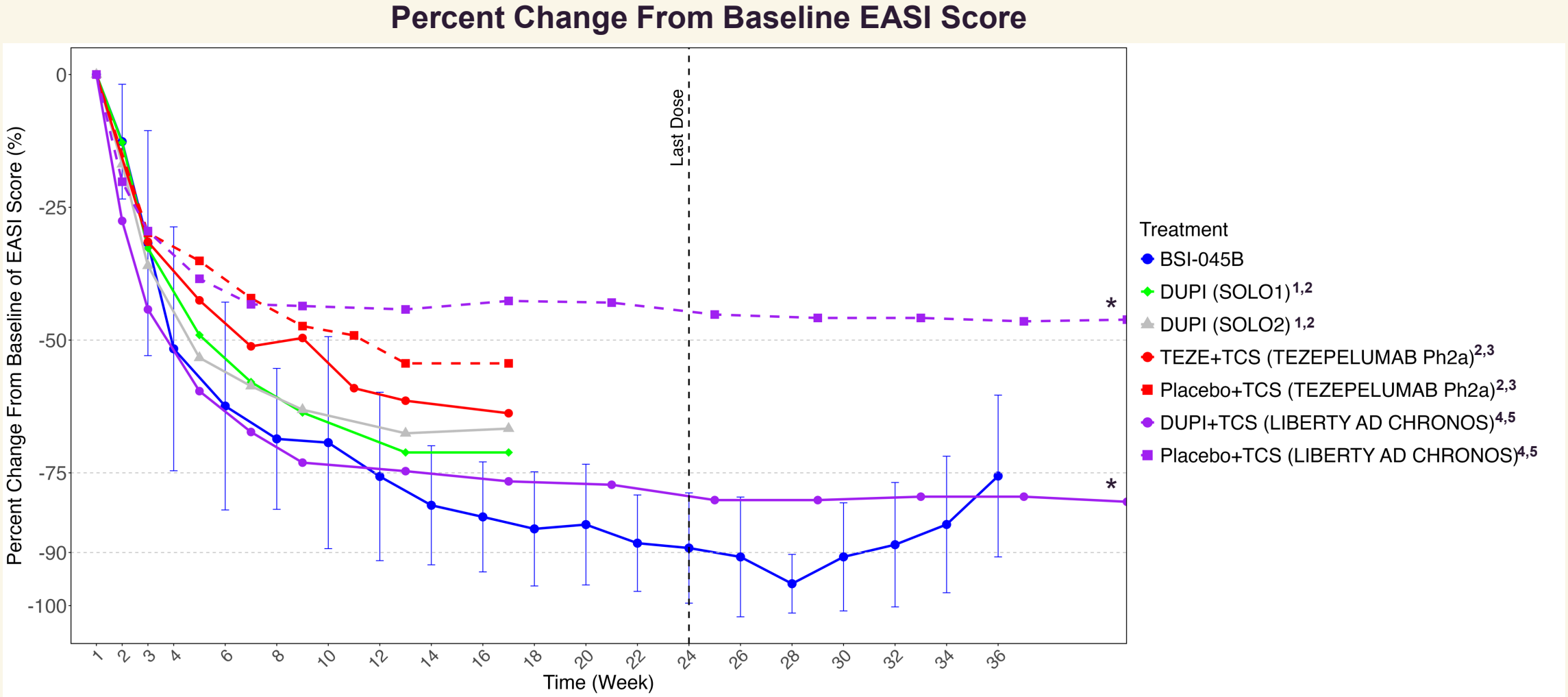
Safety

- A total of 13 (59.1%) participants had TEAEs, and 3 (13.6%) had treatment-related TEAEs
  - Among 13 participants with TEAEs, 2 participants had grade 2 TEAEs (neither treatment-related)
- No serious TEAEs, ≥Grade 3 TEAEs, or TEAEs leading to treatment interruption
- One (4.5%) participant had a non-treatment related TEAE leading to treatment withdrawal
- Headache was the most common TEAE (5/22, 22.7%)
- Most common type of injection site reaction was tenderness (11/22, 52.4%); all grade 1

Immunogenicity

- The occurrence of positive anti-drug antibodies (ADA) was low (4.5%). ADAs developed post-cessation of treatment and did not significantly impact the observed PK exposure.

Comparison to Dupilumab Mono, Combo, and Tezepelumab Combo Studies**
Percent Change from Baseline EASI Score



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 BSI-045B trial

**Not a head-to-head comparison

Significant Unmet Medical Needs Exist For Current Atopic Dermatitis Treatment

BSI-045B Has Best-in-class Potential Compared to Currently Approved Agents

Unmet Medical Need for AD Treatment		BSI-045B[1]	Dupilumab[2]	Tralokinumab[3]	Lebrikizumab[4]	Oral JAKi Upadacitinib[5] as example
Efficacy	**% of Patients Achieving EASI75/90**	✓ 94% / 65% mono-therapy	69% / 40% combo with TCS	56% / 33% combo with TCS	70% / 41% combo with TCS	60-80% / 43-66%
	% of Patients Achieving IGA 0 or 1 with ≥ 2-point Improvement	✓ 88% mono-therapy	39% combo with TCS	39% combo with TCS	41% combo with TCS	39-48%
	TCS Needed	✓ mono-therapy	Yes	Yes	Yes	✓ No
Safety	**No Box Warning**	✓ favorable safety profile with no SAE observed	✓	✓	✓	✗ Box warning
Dosing & Convenience	**Dosing Interval**	✓ Q2W with potential Q4W+ dosing	Q2W	Q2W	Q2W	Once daily
	Route of Administration	SC	SC	SC	SC	✓ Oral
Indication	**Other Atopic, Immunologic and Respiratory Indications**	✓ potential in asthma, CRSwNP, EoE, COPD	✓ approved for asthma, CRSwNP, EoE, COPD, PN	✗	✗	✓ approved for RA, UC, Crohn's disease

1. BSI-045B ph2a AD clinical trial (mono therapy at Week 26 N=17); 2. Dupilumab ph3 AD clinical trials CHRONOS at 16 weeks, q2w (Clinicaltrials.gov, NCT02260986)(Lancet. 2017; 389:2287); TCS = topical corticosteroid; 3. Tralokinumab ph3 AD clinical trial ECZTRA 3 at 16 weeks, q2w (Clinicaltrials.gov, NCT03363854); 4. Lebrikizumab ph3 AD clinical trial ADhere at 16 weeks, q2w (Clinicaltrials.gov, NCT04250337); 5. Upadacitinib ph3 AD clinical trials Measure Up 1 & 2 at 16 weeks (Clinicaltrials.gov, NCT03569293 & NCT03607422)

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BSI-045B Summary

- BSI-045B exhibits high affinity, slow dissociation and long residence time - results in very high potency

- BSI-045B's high potency and long half-life translated to a very high clinical response in subjects with moderate to severe atopic dermatitis in a US-based Phase 2a POC trial
  - ✓ 65% of subjects achieving 90% or greater reduction in EASI score
  - ✓ 88% of subjects achieving an IGA 0/1 at Week 26
  - ✓ Sustained EASI-75 responses post last dose

- BSI-045B currently in Phase 2 studies in China (partner)
  - ✓ Severe Asthma
  - ✓ CRS w/NP

- The pharmacodynamics, safety, and efficacy profile of BSI-045B
  - ✓ Provides strong confidence to conduct randomized, placebo-controlled Phase 2b clinical trials in atopic dermatitis, severe asthma, COPD, chronic rhinosinusitis with nasal polyps, and eosinophilic esophagitis
  - ✓ Forms the basis for confidence in the bispecific approach of BSI-502

BSI-502: Anti-TSLP x IL4R Bispecific Antibody Program

(Investigational Drug Candidate)

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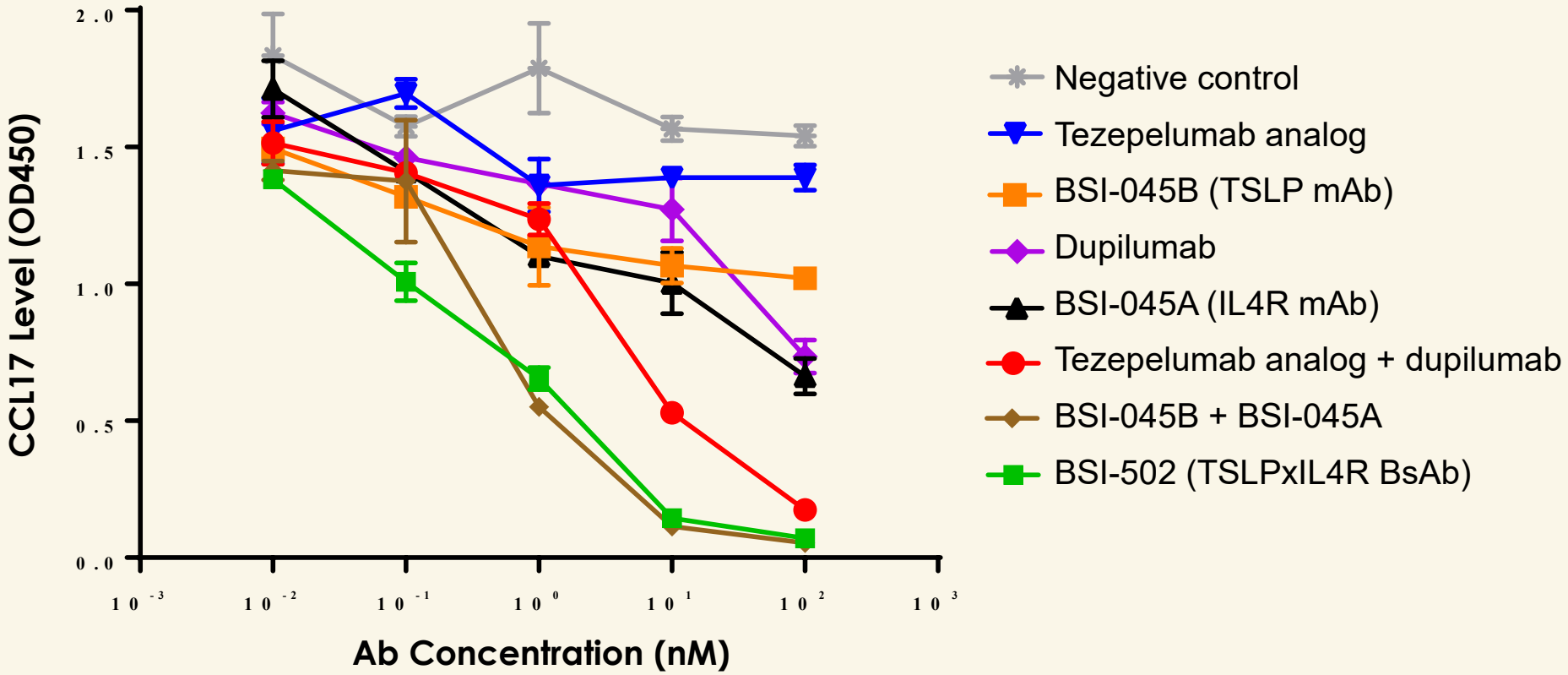
BSI-502 – Key Asset Highlights

- Exhibits **high binding affinity** to and **dual blockade** of both TSLP and IL4R
- 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

Data on file.

BSI-502 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**



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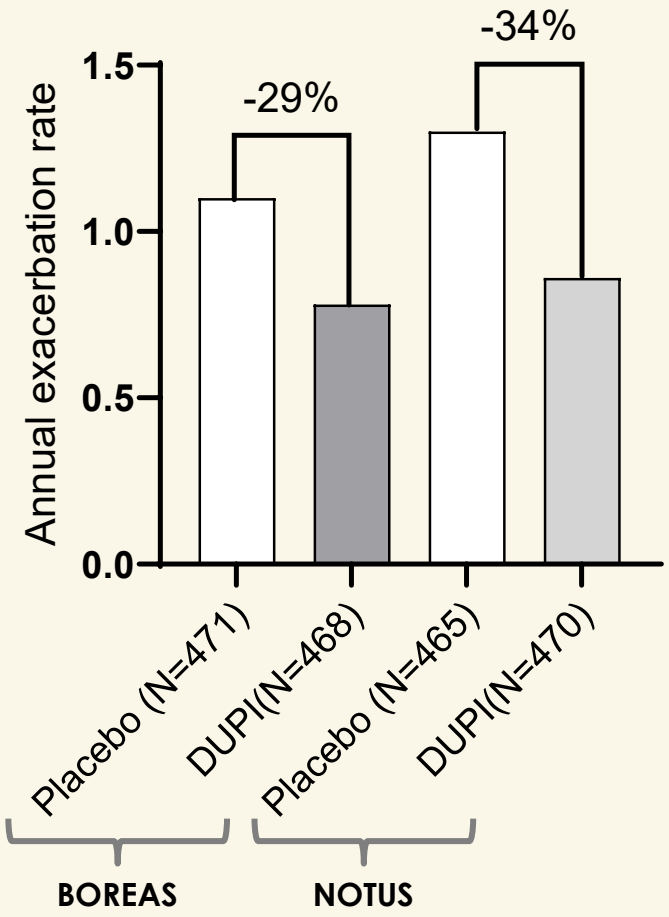
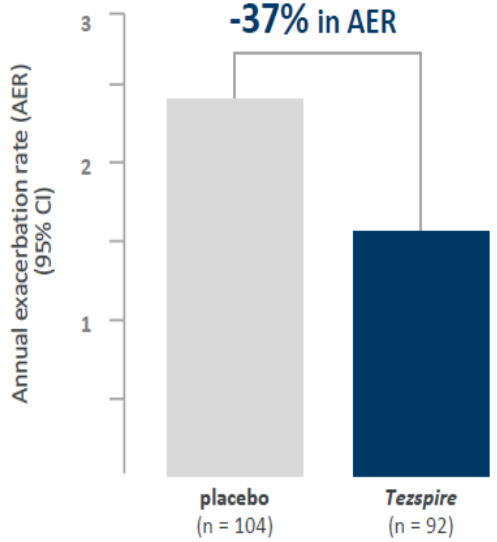
Bispecific Approach: Blocking both IL4R and TSLP Could Drive Enhanced Efficacy

Tezepelumab and Dupilumab Efficacy in COPD

DUPIXENT® Ph3 Trial BOREAS and NOTUS EOS>300 cells/µL[1]



Tezspire Phase IIa COURSE data in COPD[2]



Primary subgroup analysis: EOS >150 cells/µL

Missed primary endpoint of annual rate of moderate or severe exacerbations in ITT population (all-comers; 17% reduction vs. placebo)

37% reduction in AER (EOS >150, 95% CI: 7, 57)

Nominal p=0.0212

2. Singh et al, "Tezepelumab in adults with moderate to very severe chronic obstructive pulmonary disease (COPD): efficacy and definitions can be found in Glossary.

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1. https://clinicaltrials.gov/study/NCT03930732?cond=COPD&intr=dupilumab&aggFilters=phase:3&rank=2&tab=results; https://www.sanofi.com/assets/dotcom/pressreleases/2023/2023-11-27-06-30-00-2785836-en.pdf. 2. AstraZeneca Investor Day 2024 BioPharmaceuticals Presentation. https://www.astrazeneca.com/content/dam/az/Investor_Relations/events/ID/BioPharmaceuticals-presentation.pdf

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BSI-045B and BSI-502 Summary

BSI-045B -The Leading TSLP Program in Development for both Atopic Dermatitis and Severe Asthma

- Validated target – BSI-045B has demonstrated functional superiority in comparison with market leader TEZSPIRE® (tezepelumab)*
  - Comparative data shows greater potency, affinity, and neutralization*
- Completed Ph. 2a in Atopic Dermatitis in US
  - Positive POC single arm study that showed over 90% of subjects with moderate-to-severe atopic dermatitis achieved a 75% reduction in their disease (EASI-75 response)
- Ongoing Ph. 2 in Severe Asthma and Ph. 2 in Chronic Rhinosinusitis with Nasal Polyps in China (partner)
  - Parallel development program in China can potentially be leveraged to accelerate timeline for severe asthma – Potential best-in-class TSLP in severe asthma
- Potential for a maintenance dosing of once monthly (compared to once every two weeks for dupilumab)

BSI-502 - Follow-on Next-generation Bispecific TSLP x IL4R program – *Potential Best-in-Class*

- Next-gen approach based on proven targets - combining a novel TSLP Ab and IL4R Ab in a novel bispecific format
- Dual-blockade of 'Upstream' (TSLP) and 'Downstream' (IL4, IL13) signaling shows improved effect on the chemokine CCL17**
- Potential for competitive positioning in severe asthma, atopic dermatitis, and COPD

Immunology Franchise Portfolio Opportunity – A Pipeline Within Two Assets

- Combined assets have the potential to take advantage of significant market opportunities in Severe Asthma, COPD, Atopic Dermatitis, Chronic Rhinosinusitis, Allergy and other Th2 mediated diseases
- Expanded clinical development strategy with streamlined execution can serve as value multiplier for both programs

*Superior characteristics (potency, affinity, bioavailability, and bioactivity) in comparison to tezepelumab based on internal data
**Data on File

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

(Investigational Drug Candidate)

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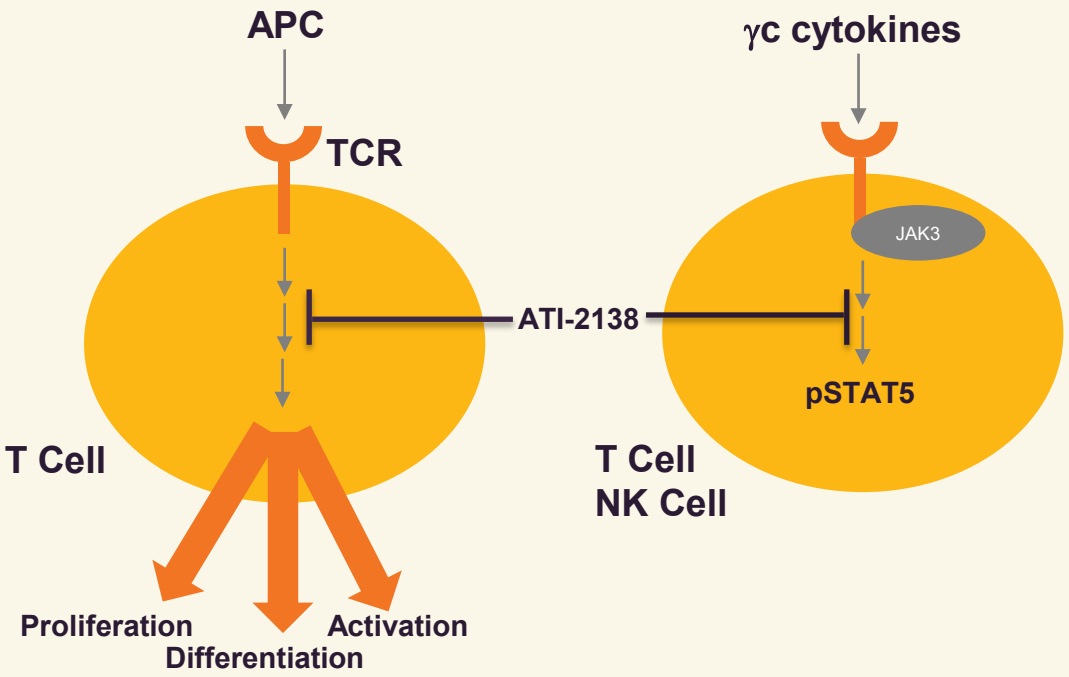
ATI-2138: Oral Small Molecule Covalent IL-2-Inducible Tyrosine Kinase (ITK) & JAK3 Inhibitor for Autoimmune Disease

- 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) and is designed to reduce T cell differentiation, proliferation and cytokine production
- ATI-2138 is differentiated from other kinase inhibitors as it 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

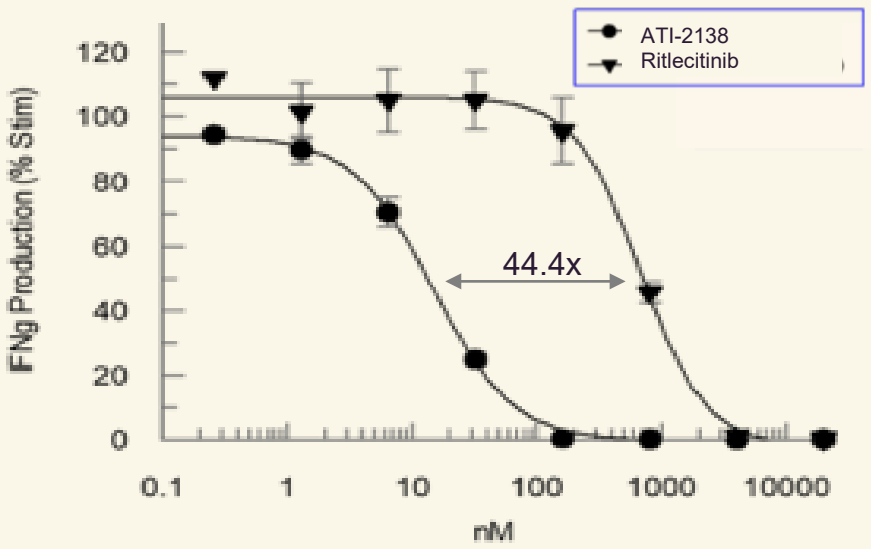


1. Data on file.

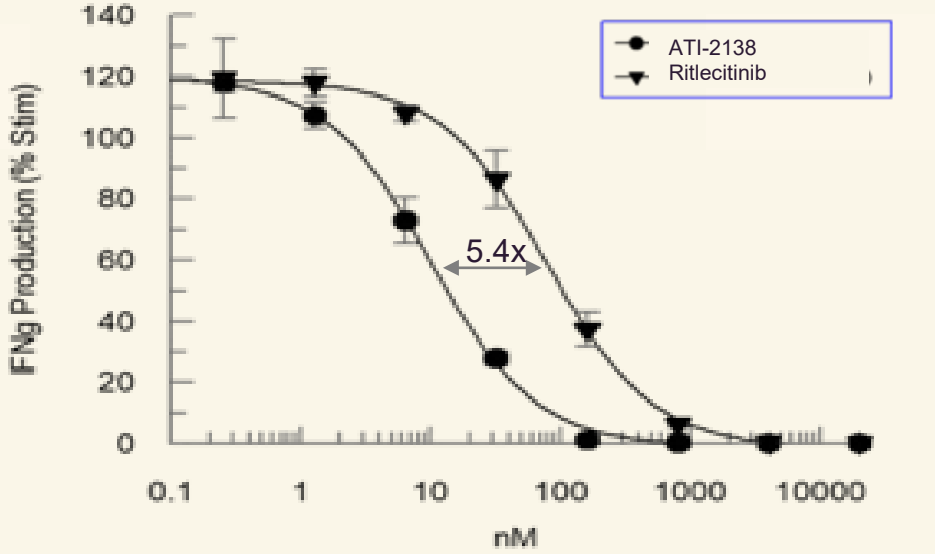
ATI-2138: Fast follower and Best-in-Class Potential vs Ritlecitinib

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

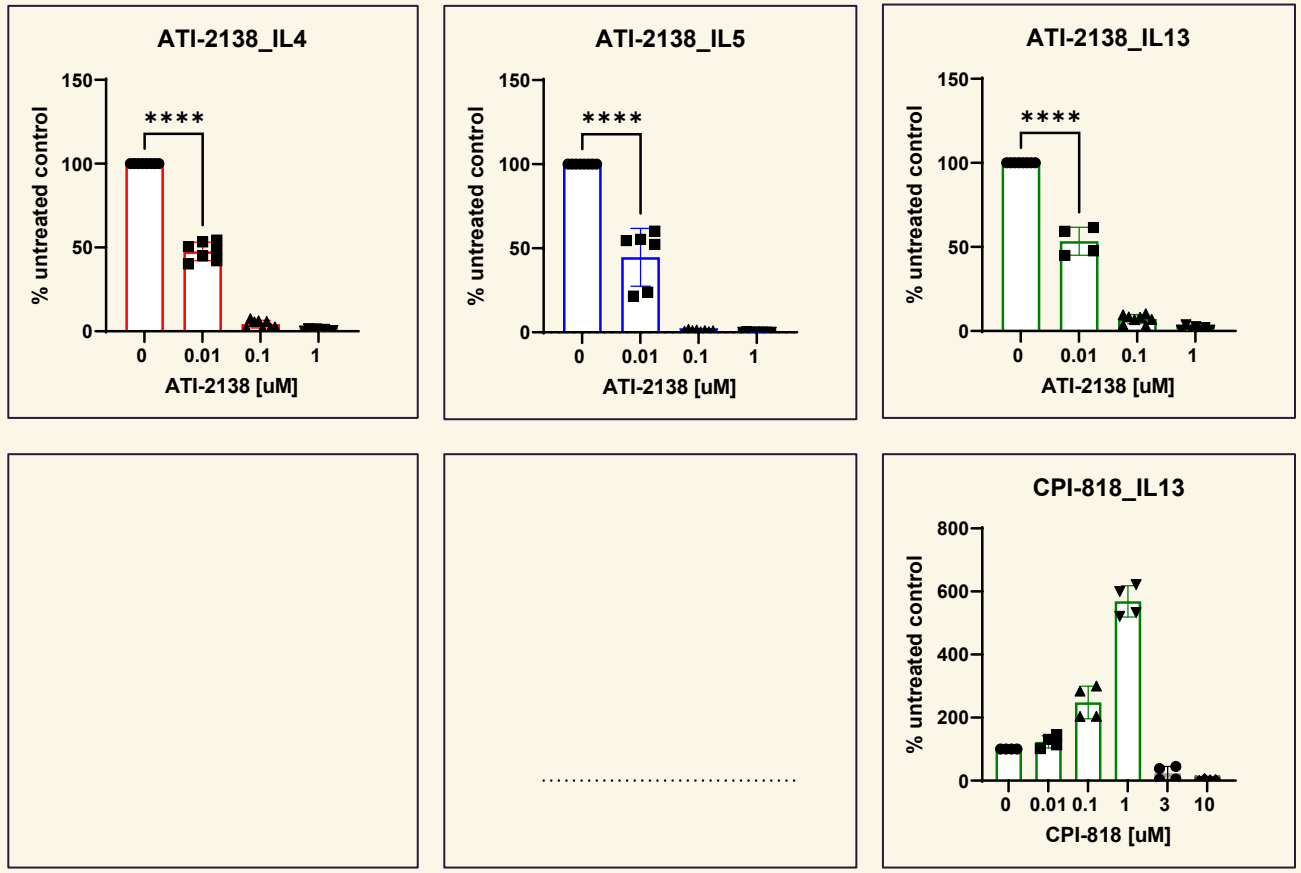
Data on file.

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

ITK Biochemical Enzyme Potency		
Compound	**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

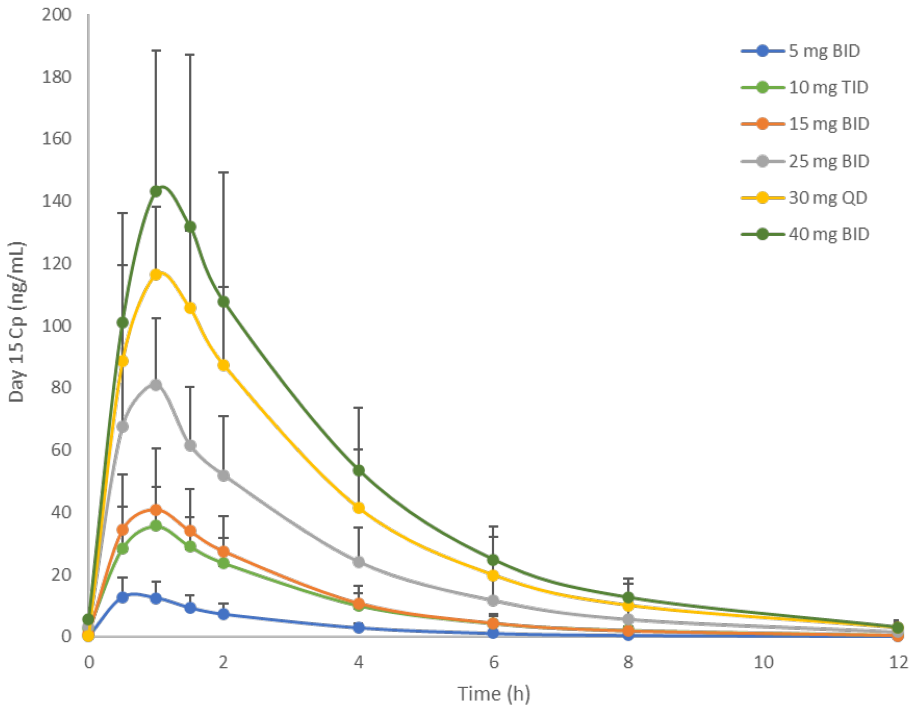


Data on file

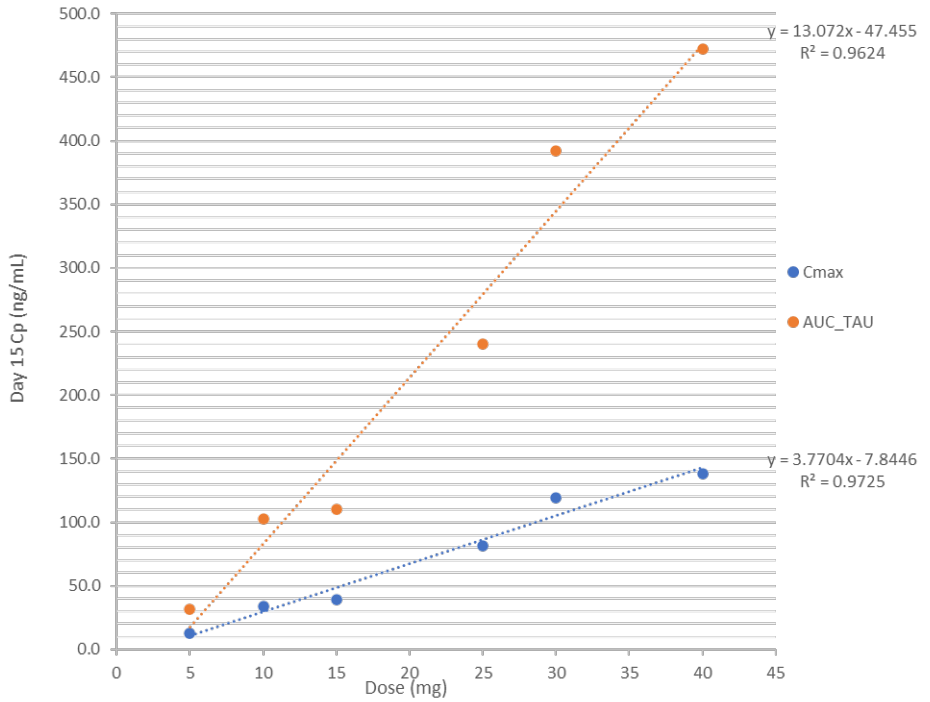
ATI-2138 Pharmacokinetic Analysis from MAD Study

Exhibited Linear PK and Targeted Exposure

ATI-2138 PK



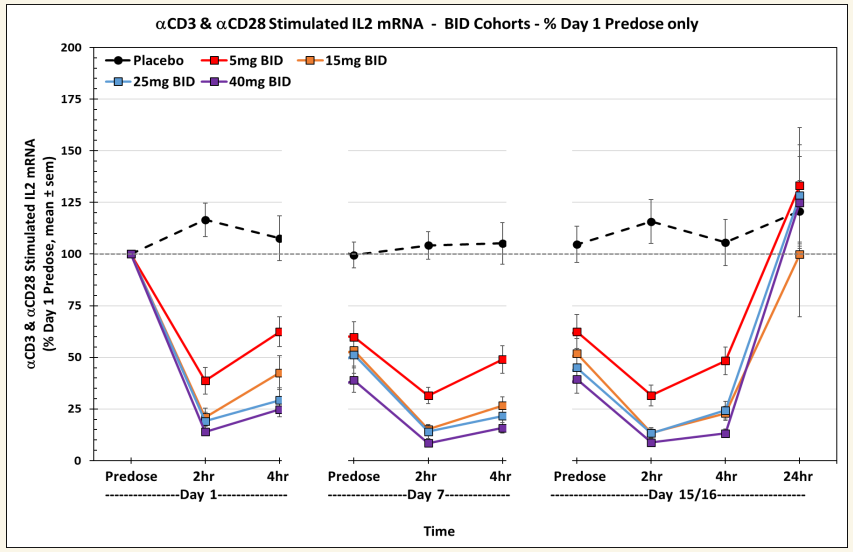
Steady State PK Dose Proportionality

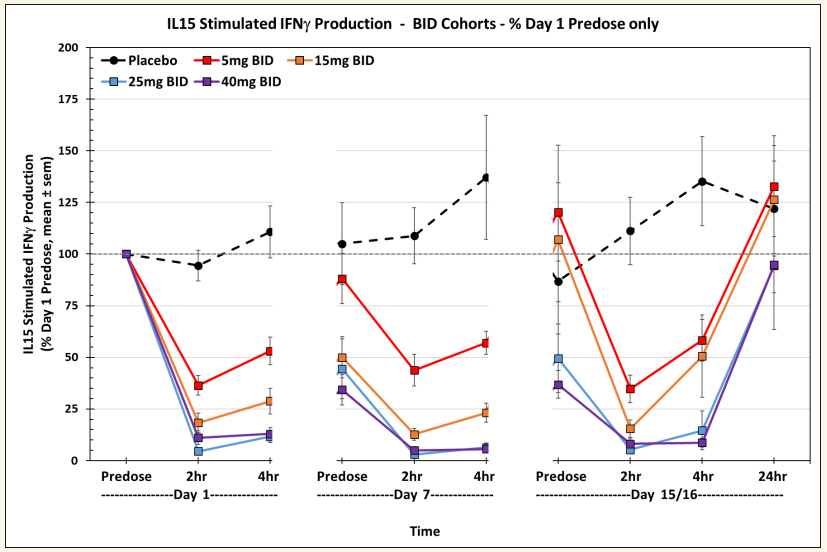


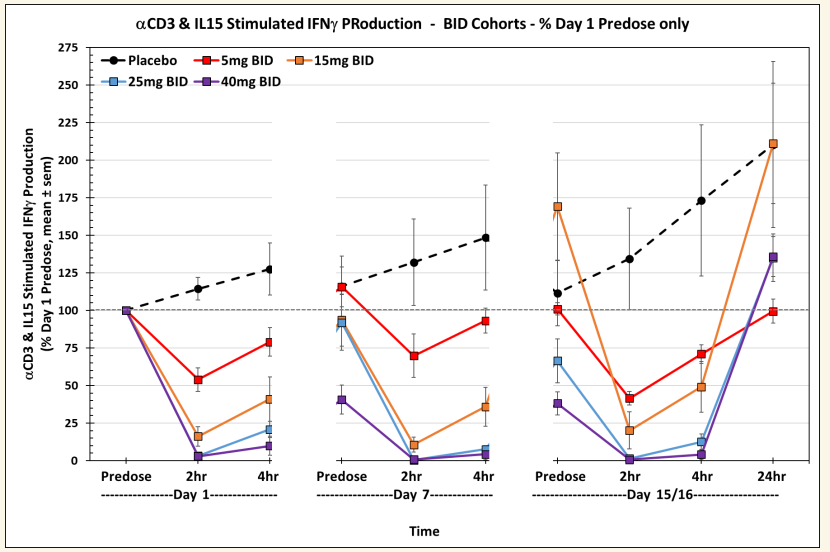
- Day 15 plasma concentration curves demonstrated linear PK for ATI-2138
- Targeted ATI-2138 average exposure over the dosing interval was achieved at doses of 10mg per day and above

ATI-2138 MAD Exploratory Pharmacodynamics

Dose Response Data (BID Cohorts)







- Pharmacodynamic biomarkers - Ex-vivo stimulation of whole blood taken from subjects before and after administration of ATI-2138 – BID cohorts
- Stimulation with anti-CD3 and anti-CD28 (readout IL-2 mRNA; T-cell activation), IL-15 (readout INFγ; JAK1/3 activation) and dual stimulation (readout INFγ; T-cell and cytokine stimulation)
- ATI-2138 showed dose and time dependent inhibition of all stimulation conditions

Data on file

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-IL4Rα) 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 γ-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

ATI-2138 Summary: Combined IL-2-Inducible Tyrosine Kinase (ITK) & JAK3 Inhibitor for Autoimmune Disease

- ATI-2138 is an oral compound which interrupts Th2 cell receptor (TCR) signaling by inhibiting ITK and JAK3 signaling of common γ chain cytokines in lymphocytes (including IL-2, IL-4 & IL-15)
- ATI-2138 potently and selectively inhibits ITK and JAK3
- ATI-2138 has demonstrated the prevention of inflammation in animal models of colitis and arthritis
- Safety, pharmacology and toxicology studies have been completed
- Phase 1 SAD and MAD studies in healthy volunteers have been completed
  - ✓ ATI-2138 was generally well tolerated, and no serious adverse events were reported
  - ✓ PK was dose proportional with adequate exposure to block ITK and JAK3 in PD biomarker assays
- Evaluating ATI-2138 for the potential treatment of numerous T cell-mediated autoimmune diseases
- A Phase 2a atopic dermatitis trial is under way with data expected in 1H 2025
  - PD to be assessed demonstrating the importance of ITK inhibition

The unique pharmacological profile of ATI-2138 provides opportunity for differentiation

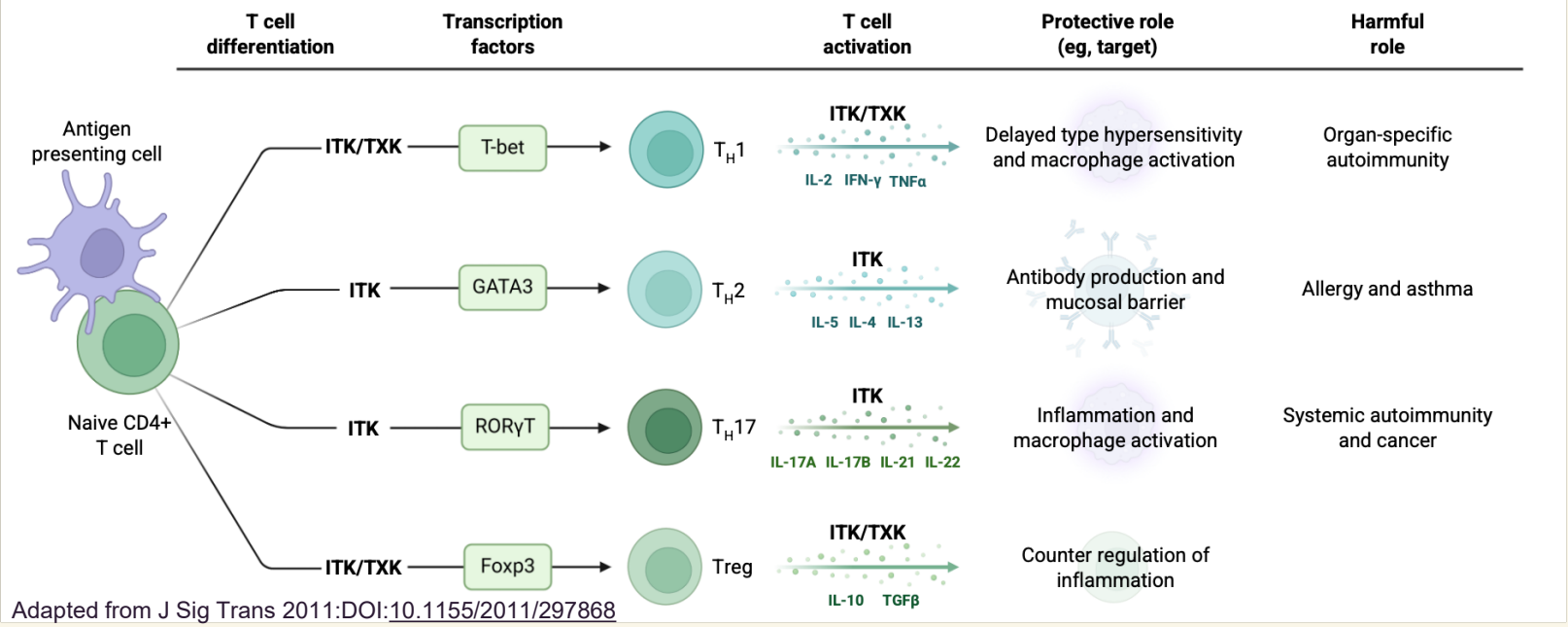
aclaris THERAPEUTICS

Next Generation Selective ITK Inhibitor

aclaris® THERAPEUTICS

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

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.

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