aclaris® THERAPEUTICS

Patient *Focused Innovation*

Developing Therapeutic Franchises to Address Gaps in Important I&I Diseases

2025 R&D Day

October 14, 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' product candidates, including bosakitug (ATI-045), ATI-052, ATI-2138, next generation ITK selective inhibitors, and next generation bispecific and multispecific antibodies, including the potential for such product candidates to be first-in-class and/or best-in-class, the potential to increase the efficacy ceiling and show superior activity compared to other therapies, the potential for bosakitug to have extended dosing, and the potential for the next-generation ITK inhibitors to have once-per-day dosing, the development of such product candidates, including the potential targets and indications Aclaris may pursue, the timing and number of regulatory filings, the design of future clinical trials, the timing for the initiation of clinical trials, and the availability and timing of data from clinical trials, and Aclaris' cash runway, including potential to extend the cash runway through non-dilutive opportunities. 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, 2024, 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.

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All future development, clinical, and regulatory timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors.

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Today's Agenda

Patient *Focused Innovation*

Dr. Neal Walker
Chief Executive Officer
Introduction to Aclaris

Roland Kolbeck, Ph.D.
Chief Scientific Officer
World Class Development Engine

Joe Monahan, Ph.D.
Special Scientific Advisor
Founder, Confluence Discovery Technologies
Developing the Leading ITK Franchise

Hugh Davis, Ph.D.
President & Chief Operating Officer
The Science of Antibody Development

Jesse Hall, M.D.
Chief Medical Officer
Efficient Clinical Trial Execution and Milestones

Zuzana Diamant, M.D, Ph.D., FERS
SAB member; Pulmonologist & Clinical Pharmacologist, Department of Clinical Pharmacy & Pharmacology, University Medical Center Groningen, Netherlands

Michael Cameron, M.D., FAAD
Assistant Clinical Professor, Department of Dermatology, Mount Sinai, New York

Aclaris Therapeutics

Developing Therapeutic Franchises to Address Gaps in Important I&I Diseases

Dr. Neal Walker
Chief Executive Officer

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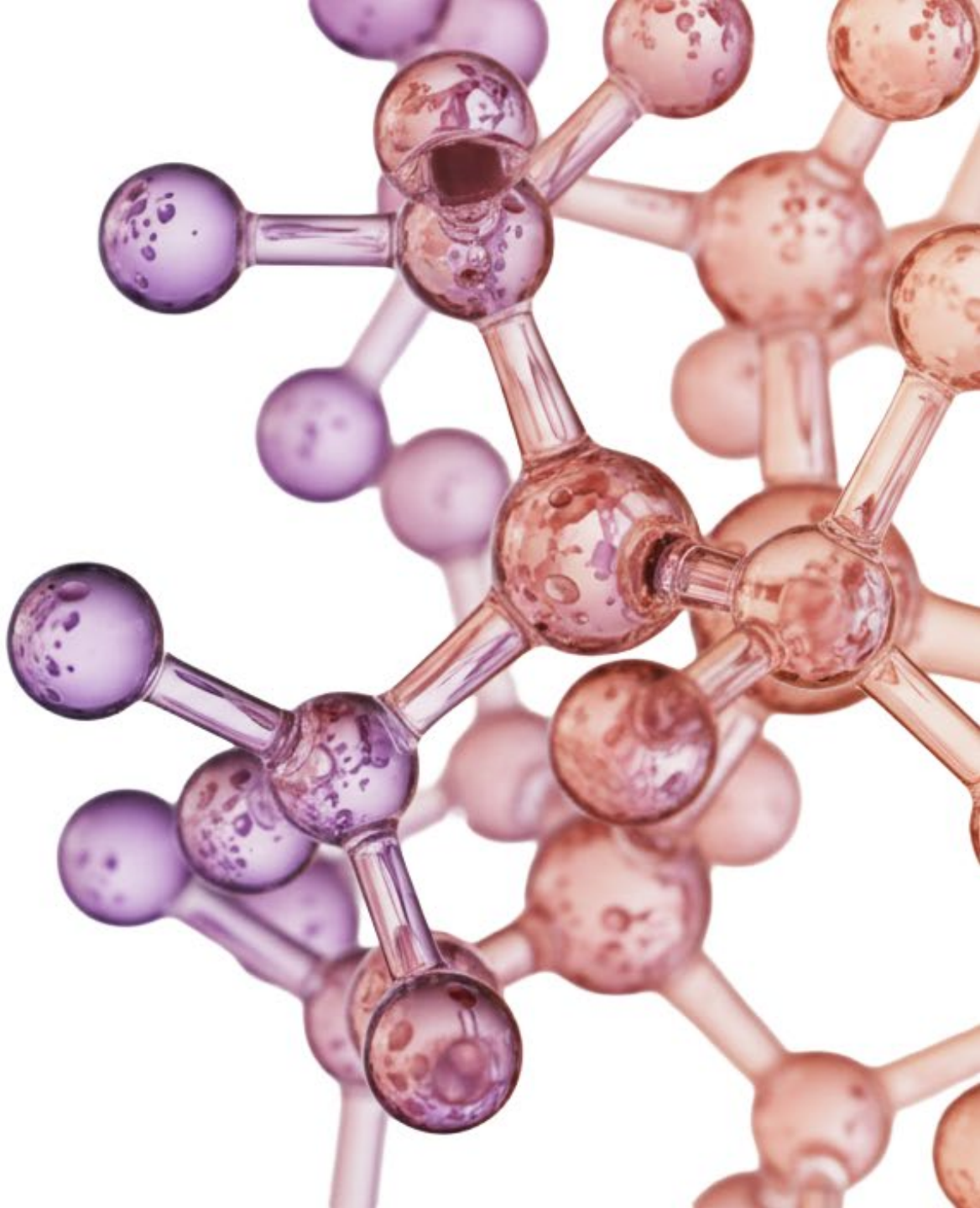
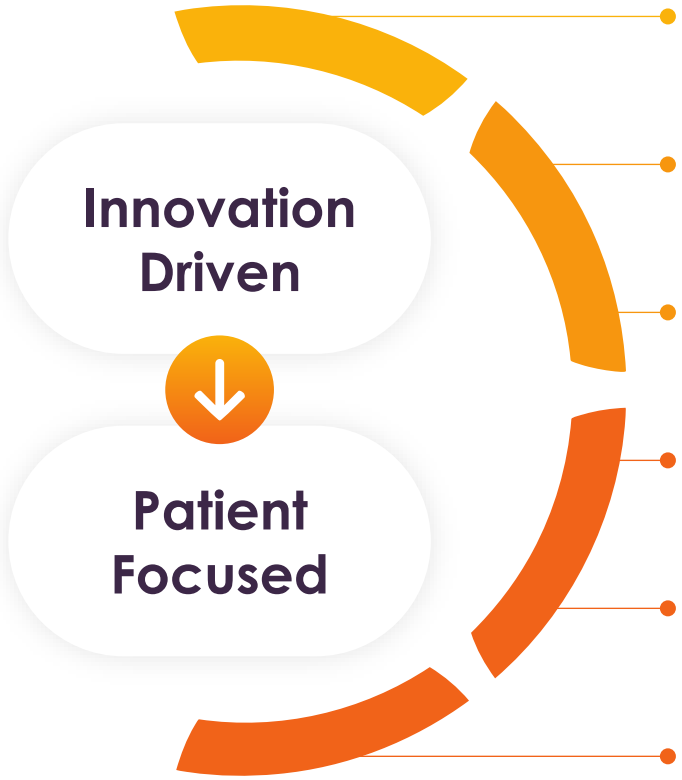


Aclaris Therapeutics



- **2026 is an important year** for Aclaris with four anticipated inflection points
- **Three clinical programs in 2025; four anticipated in 2026**
- **Validated targets**; positioned in the oral and antibody space
- Bispecific and ITK oral programs could be **potential game changers in multiple indications**
- **Prudent capital management** with a cash runway expected into second half of 2028
- Underpinned by **state-of-the-art scientific platform and world class people**

Advancing potential industry-leading inhibitors designed to address validated, therapeutically-relevant immune targets

Aclaris: Positioned for Significant Growth

Potential Best-in-Class Clinical Assets

- **Bosakitug (ATI-045):** Uniquely potent monoclonal antibody targeting TSLP
- **ATI-052:** Bispecific antibody (BsAb) targeting both TSLP and IL-4Rα
- **ATI-2138:** Potent and selective oral inhibitor of ITK/JAK3
- Discovery/preclinical lead candidate selection ongoing for **novel ITK inhibitors and BsAbs**

Continued Business Execution

- **ATI-2138:** Phase 2a OL trial achieved primary and key secondary endpoints in AD; further validated ITK as a therapeutic target
- **Bosakitug:** Dosing in two-arm placebo-controlled Phase 2 trial ongoing
- **ATI-052:** Phase 1a/1b SAD MAD program ongoing; dosing ongoing
- **New INDs starting in 2026** expected from discovery engine

World Class Expertise/Capability

- **World class development expertise**
- **Proprietary kinase small molecule discovery engine** complemented by in-house multidisciplinary team
- **Innovative biologic discovery program** incorporating dual-targeting strategies addressing validated pathways

Well Financed with Three-Year Cash Runway

- **Strong balance sheet** expected to fund operations into the second half of 2028
- Current cash runway expected to **fully fund preclinical and clinical development plans**
- Potential opportunities for additional **non-dilutive financing and development partners**

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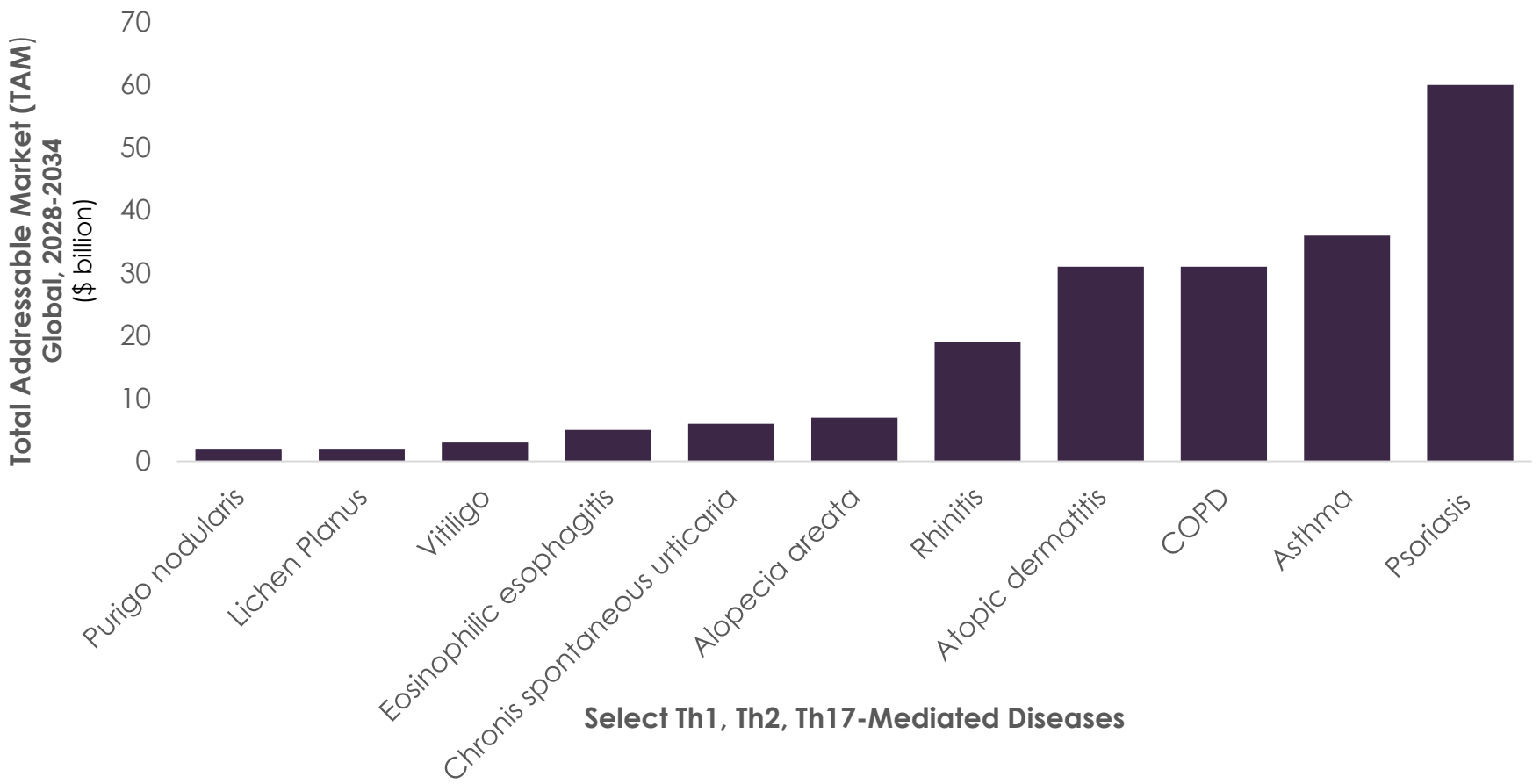
The Future Value of Drug Development

Addressing Th1, Th2 and Th17-Mediated Disorders



Significant opportunity for new innovative therapeutics for Th1, Th2, and Th17-mediated dermatological and respiratory diseases including potent and well tolerated biologics and oral inhibitors

Sources: Eczema stats: National Eczema Association (accessed 07/31/25); National Alopecia Areata Foundation (Accessed 07/31/25); Vitiligo Facts: Global Vitiligo Foundation (accessed 07/31/25); Precedence Research; Forbes Business Insights; American Medical Association; American Lung Association; Global Initiative for Asthma; World Health Organization; The Centers for Disease Control and Prevention (CDC); Business Research Company; peer research; Delveinsight; Cowen Categories Outlook 2024

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Opportunities in the I&I Space

Potential to Address Significant Gaps in Unsatisfied I&I Indications

Opportunities for Orals

- Faster onset, durable, consistent effect
- Broader efficacy across heterogenous populations
- Optimize symptom control: anti-itch effect, FEV1
- Potential anti-fibrotic effect
- Convenience of oral
- Improved tolerability profile

Opportunities for Antibodies

- Raise efficacy ceiling
  - Faster onset, durable, deeper, and more consistent effect
- Improved tolerability
- Improved convenience and practical dosing schedule

Aclaris Today

Patient *Focused Innovation*

- Unique **State-of-the-Art R&D capabilities and World Class Scientists**
- **Four potential Best-in-Class clinical stage assets** in 2026 targeting validated and therapeutically-relevant immune targets highlighted by a **potential Best-in-Class bispecific and oral ITK inhibitor**
- **Rich calendar of data events** expected throughout 2026 and 2027
- A cash runway expected to provide **approximately three years of capital**

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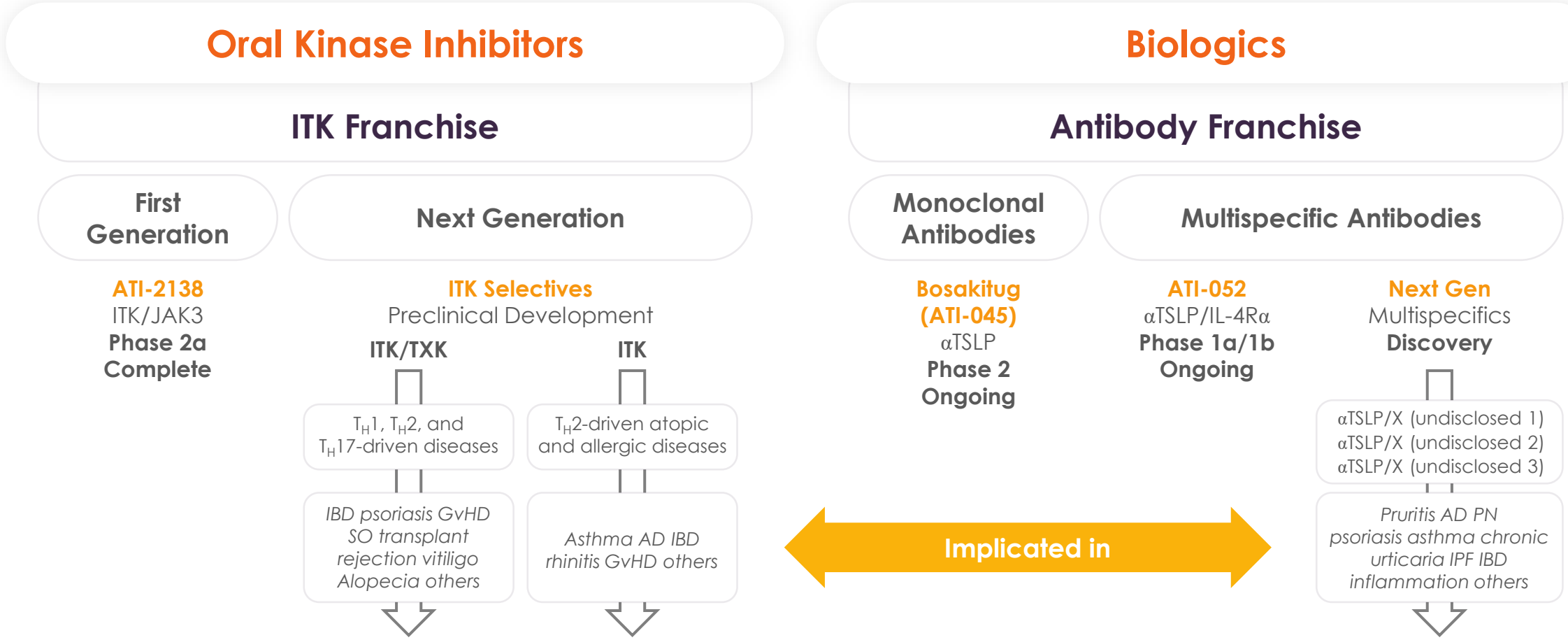
Broad Clinical and Preclinical I&I Pipeline

Potential Best-in-Class Inhibitors of Immunoinflammatory Cascade



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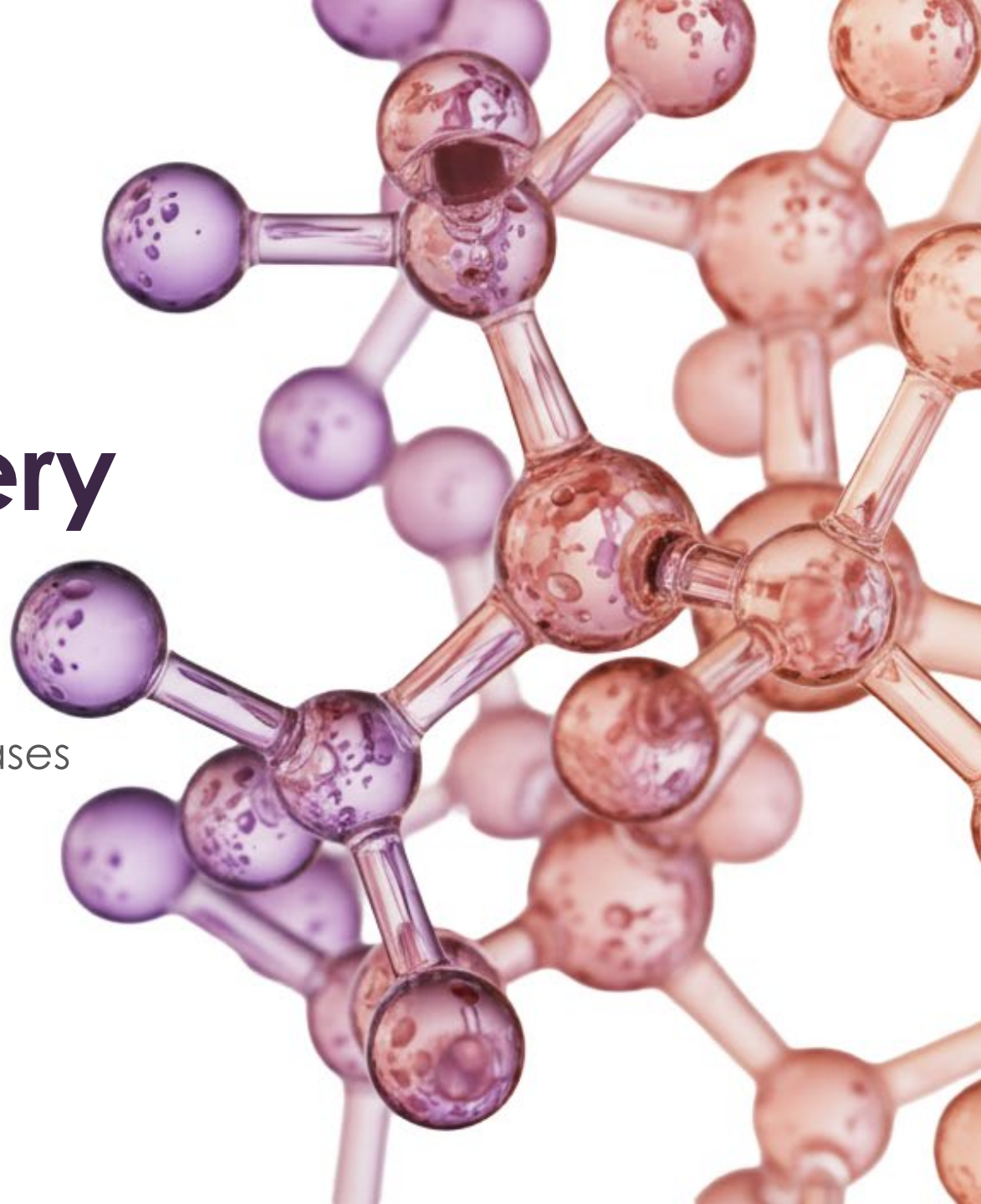
World-Class Discovery Engine

Leading Kinase and Antibody Innovation for the Treatment of Autoimmune & Inflammatory Diseases

Roland Kolbeck, Ph.D.
Chief Scientific Officer

Patient *Focused Innovation*



What Makes Aclaris Stand Out

- **Oral compounds targeting previously inaccessible parts** of the Kinome
- **Injectable potential best-in-class multi-specific antibodies** designed to address unmet clinical need and raise the efficacy ceiling
- **World-class track record** in drug discovery and development
- **State-of-the-Art** R&D capabilities
- **Seamless execution** by experienced drug developers

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The Kinase Opportunity

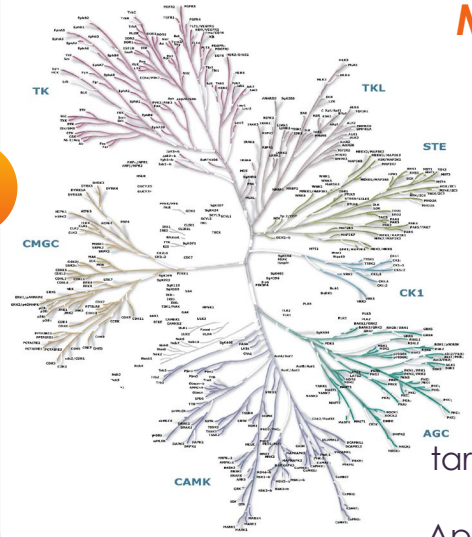
Medically Important and Productive Target Class

$62.8B
Annual Sales of Kinase Drugs in 2024

$88.6B
Market Opportunity in 2029

Most Members of the Kinome Remain Unexplored

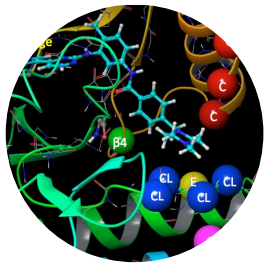
The Human Kinome



500 Members
2% of the Human Genome

<10%
of Kinome targeted by the 80+ FDA Approved Drugs

The Aclaris Solution



KINect® Technology Platform

Proprietary chemical library and integrated capabilities for interrogating 60% of the Kinome

Challenges with Difficult to Drug Kinases
Selectivity
Biochemical efficiency

100s More to be Explored

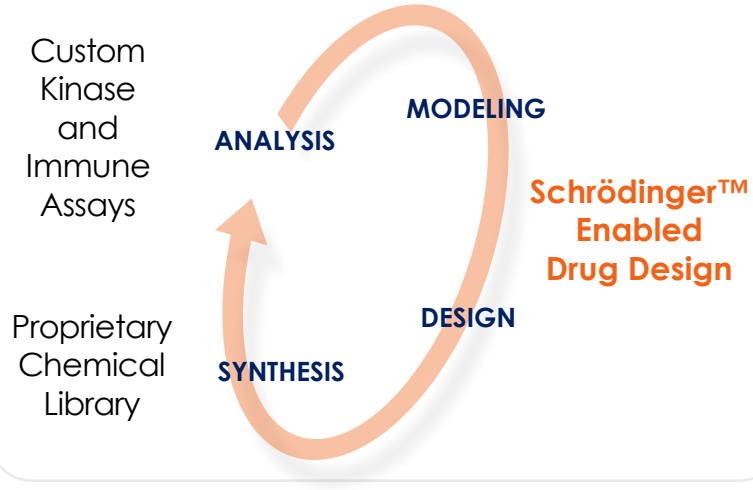
Sources: Kinase Inhibitors Market Overview (The Business Research Company);

KINect Platform

Rapid and Efficient Development of Kinase Drug Candidates

Proprietary Chemical Library + **Design Specific to Each Kinase** → **Faster Path to High Quality Assets**

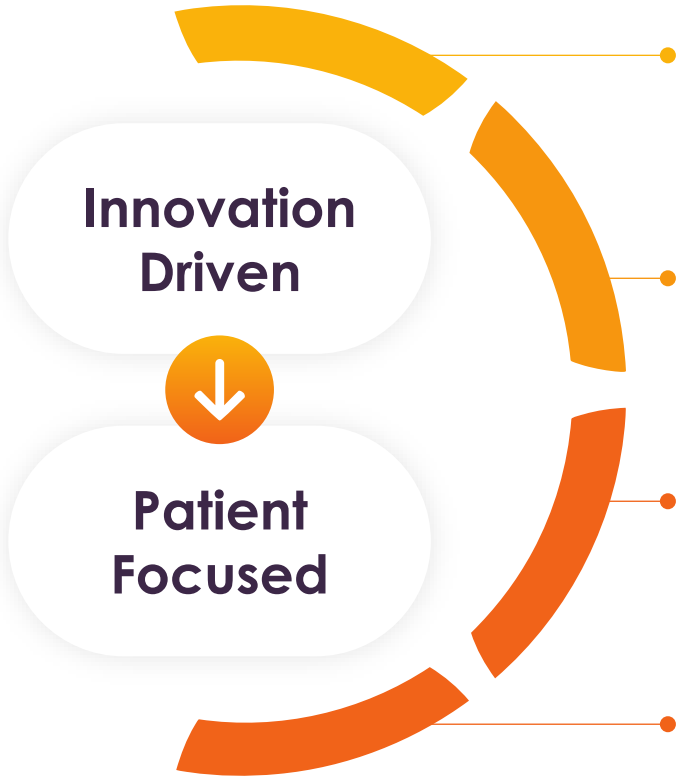
- **Expands druggable Kinome:** Targets Type 1 (215 kinases), Type 1.5 (68 kinases) and Type 2 (128 kinases) kinases. Competitors target subgroups of Type 1 kinases
- **Solves Class Challenges:** High affinity/selective drug scaffolds



- **Significantly decreases time to Lead Optimization**
- **Proprietary Portfolio of Inhibitors** in development
- **Expansion of target opportunities**

New Frontiers in Drug Discovery

Small Molecule Innovation



Covalent kinase inhibitors
Small molecules inhibiting kinases by forming irreversible bonds with a cysteine at the active site

Molecular glues
Small molecules that stabilize kinases in an inactive confirmation or set them up for degradation

Tissue specific inhibitors
Small molecules that inhibit kinases in target tissues with minimal systemic exposure

Protein degraders (PROTACs)
Small molecules that trigger the degradation of specific kinases by the ubiquitin/proteasome pathway

"Drugging the Undruggable"

Our approaches allow us to target previously inaccessible parts of the kinome and beyond

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The Multi-Specific Antibody Opportunity

Multi-specific Antibodies are a Successful Class of Medicines for Cancers

18 Number of Multi-Specific Antibodies Approved

$12.6B
Annual Sales of Multi-Specific Antibodies in 2024

Opportunity:
Best-In-Class Multi-Specific Antibodies for Autoimmune and Inflammatory Diseases

Increasing Health Burden
Over 100 autoimmune diseases; 50 million Americans affected; Prevalence rising

Unmet Clinical Need
Partial response; unresponsive disease; refractory disease; waning efficacy; safety; frequent administrations

$215B
Global health care spending in autoimmune diseases in 2024

$396B
Global AI disease therapeutics market opportunity by 2030

Sources: Kuick Research Report: Global Multispecific Antibodies Market, Drug Sales, Dosage, Price and Clinical Trials Insights; Autoimmune Disease Therapeutics Market – Global Forecast 2025-2032

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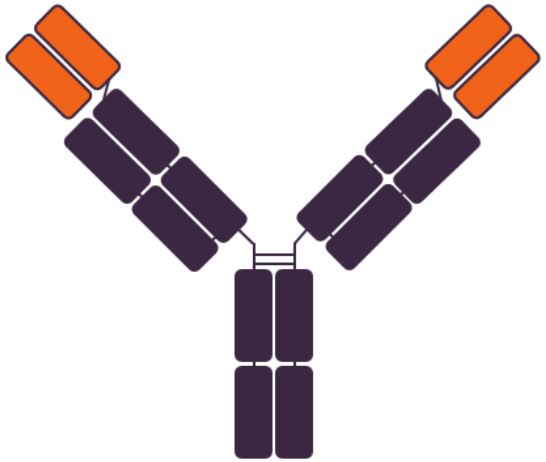
Developing Multi-Specific Antibodies

for Autoimmune Diseases

- Superior target affinity, specificity, potency
- Combinations of 2 or more clinically validated targets with non-overlapping biology
- Combinations of clinically validated targets with novel biology
- Synergistic target combinations: when one is not enough

Format
- Fit-for-purpose multi-specific format
- Fully human/humanized

Developability
- High expression
- Stability
- Aggregation



Multi-Specificity/Potency
- High affinity
- Cellular potency

Fc Modifications
- Enhanced or reduced effector function
- T1/2 extension

Working with world-class scientific partners to identify opportunities and best-in-class technologies

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Proven Track Record of Discovery and Development

Small Molecules

Covalent ITK/JAK3 Inhibitors (ATI-2138)

Dual ITK and JAK3 inhibition

ITK is downstream of the T cell receptor and impacts T cell function and differentiation

JAK3 is necessary for signaling from γ_c cytokines like IL-2

Covalently modifying both targets interrupts these pathways simultaneously impacting T cell survival, function and differentiation.

Next Generation ITK Inhibitors

Selective inhibition of ITK

Next generation compounds inhibit ITK without JAK3 crossover

Compounds designed to achieve sustained ITK inhibition at trough with QD dosing

Compounds with different degrees of TXK (RLK) selectivity are under evaluation

Antibodies

Bosakitug (ATI-045) Anti-TSLP mAb

Uniquely differentiated mAb

Very high affinity to TSLP

70x more potent than tezepelumab

Extremely low dissociation rate from TSLP, leading to long residence time and enhanced neutralization activity

~23-day T1/2 potentially supporting extended dosing interval

ATI-052 Anti-TSLP/IL4Rα BsAb

Potential for Best-in-Class bispecific antibody

Bosakitug, combined with anti-IL-4Rα

More potent than combination of tezepelumab + dupilumab

Engineered for extended T1/2

Potential for superior activity compared with monotherapy

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State of the Art R&D Capabilities

Expertise in Small Molecules and Antibodies R&D

Biochemistry & Enzymology

- Mechanistic Enzymology
- Compound - Target Interaction
- Enzyme Inhibitor Mechanisms
- Direct Binding Kinetics
- High Throughput Screening

Bioanalytical Chemistry

- Non-GLP Analytical
- Bioanalytical Method Development
- Bioanalytical Method Validation
- Pharmacokinetic / Toxicokinetic Analysis
- Ab Solubility and Aggregation

Computational & Medicinal Chemistry

- Schrödinger ™ Enabled Structure Based Drug Design
- AI Augmented Molecular Modeling
- In Silico Antibody Engineering
- Scale-Up and Route Optimization

Translational Research

- Biomarker Assay Development
- Clinical Biomarker Assessment
- Release Assay Validation

Immunology

- Cytokine Expression
- Th Cell Differentiation / Activation
- CTL Differentiation / Function
- B Cell and NK Cell Function
- Ag Specific Cell Activation
- HWB/PBMC/Monocyte Assays

In Vivo Pharmacology & PK

- Inflammation Models (Mouse & Rat)
- Immune Cell Phenotyping
- Cytokine Profiling
- Transcriptomics
- PK/PD Relationship

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World Class Discovery Engine

Summary

- Oral compounds targeting previously inaccessible parts of the Kinome with **proprietary KINect platform**
- Designing injectable multi-specific antibodies with superior target coverage and potency to **raise the efficacy ceiling**
- **Unique expertise** in small and large molecule development
- State-of-the-Art R&D capabilities with broad unique **expertise across spectrum of drug design and development**
- Seamless execution by experienced drug developers; anticipate **new INDs starting in 2026**

Leading Kinase and Antibody Innovation for the Treatment of Autoimmune & Inflammatory Diseases

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Developing the Leading ITK Franchise

Innovation Through ITK Inhibition

Joe Monahan, Ph.D.
Special Scientific Advisor
Founder, Confluence Discovery Technologies

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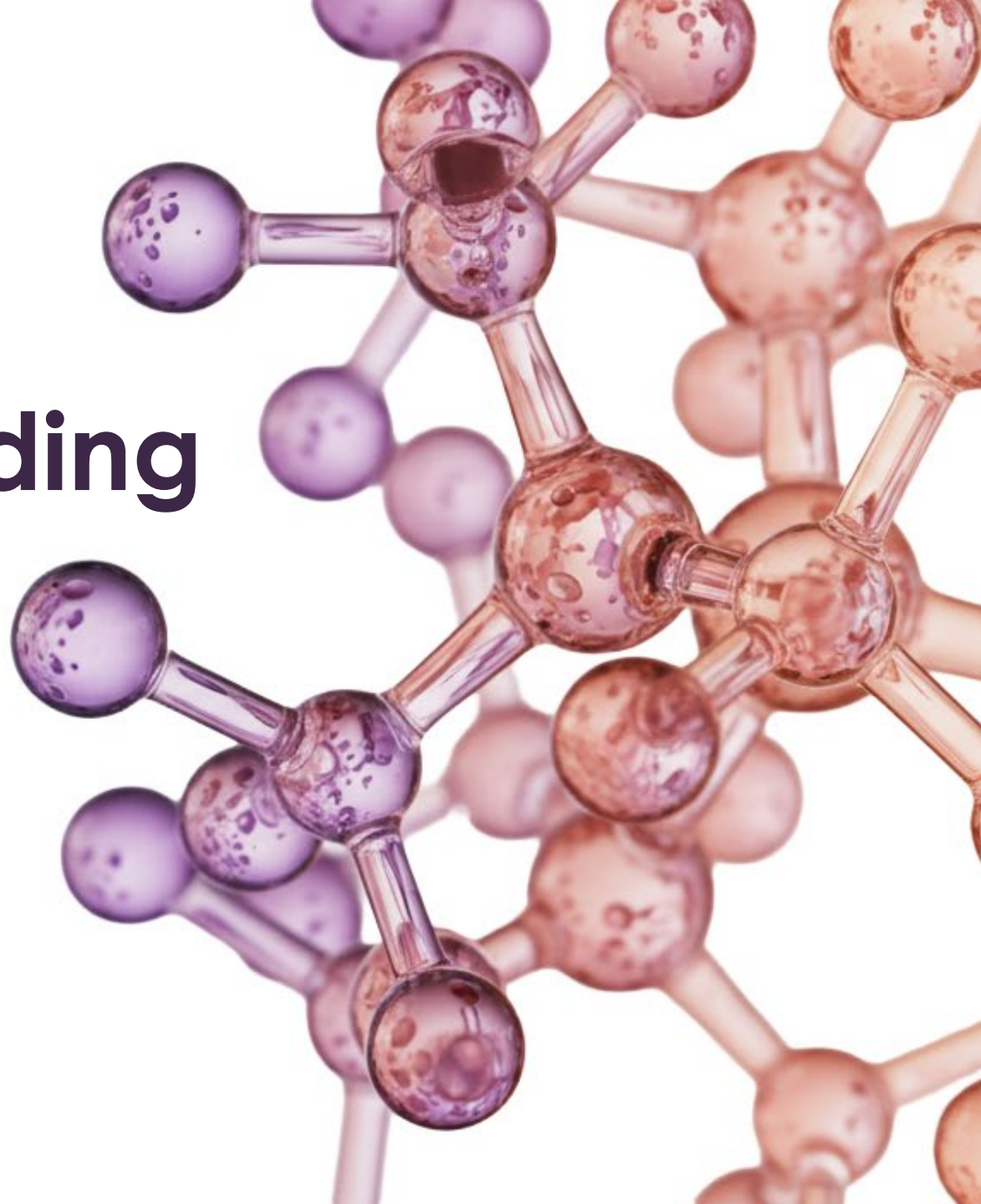


Broad Clinical and Preclinical I&I Pipeline

Potential Best-in-Class Inhibitors of Immunoinflammatory Cascade

Oral Kinase Inhibitors

ITK Franchise

First Generation

ATI-2138
ITK/JAK3
Phase 2a Complete

Next Generation

ITK Selectives
Preclinical Development

ITK/TXK
T_H1, T_H2, and T_H17-driven diseases

ITK
T_H2-driven atopic and allergic diseases

Biologics

Antibody Franchise

Monoclonal Antibodies

Bosakitug (ATI-045)
αTSLP
Phase 2

Multispecific Antibodies

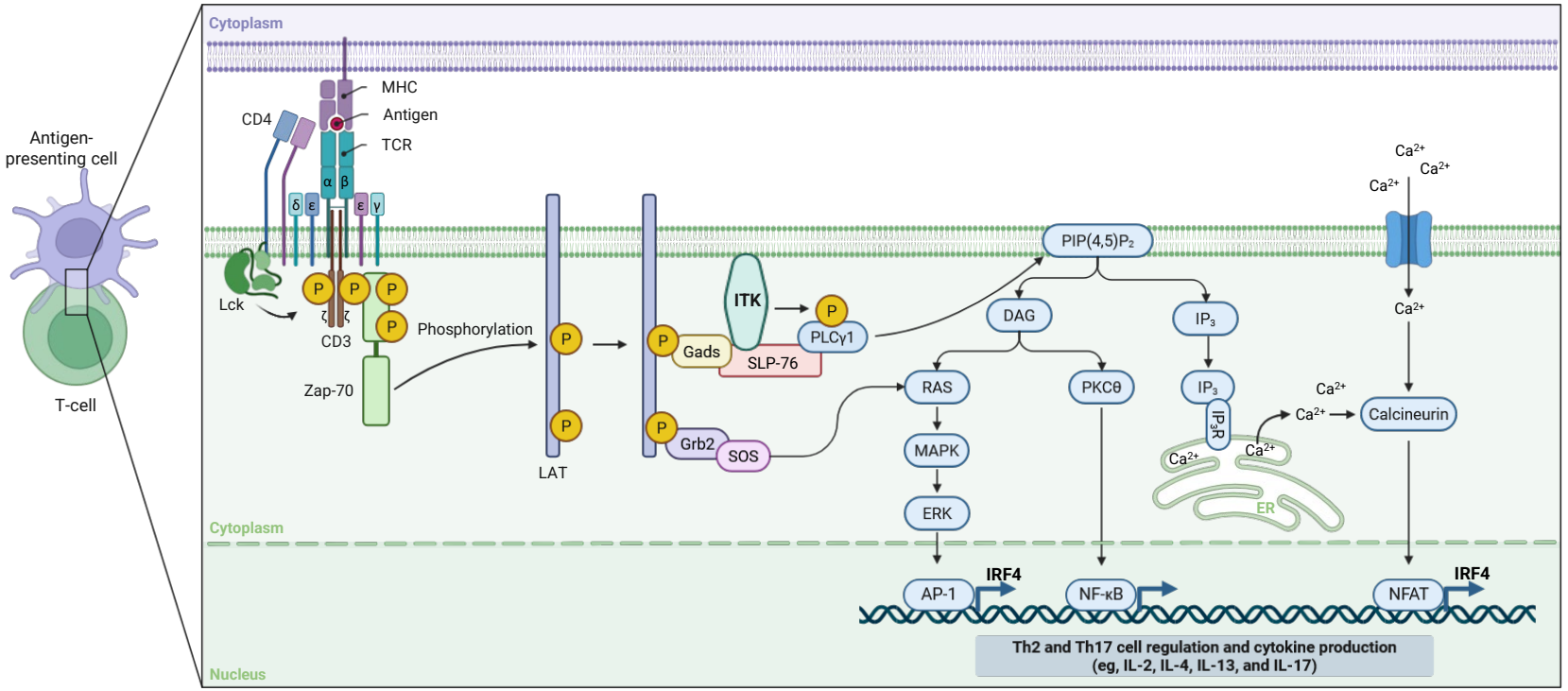
ATI-052
αTSLP/IL-4Rα
Phase 1a/1b

Next Gen
Multispecifics
Discovery

αTSLP/X(undisclosed 1)
αTSLP/X(undisclosed 2)
αTSLP/X(undisclosed 3)

T Cell Receptor (TCR) Pathway

Interleukin-2-inducible T-cell kinase (ITK) is a Key Kinase Involved in TCR Signaling



- TCR activation is critical for T lymphocyte differentiation, proliferation and activation
- TCR signaling proceeds through a complex intracellular pathway resulting in the activation of key transcription factors and production of cytokines
- Central to TCR signaling is the kinase ITK

Inhibiting/downregulating ITK shuts down TCR signaling under inflamed/allergic conditions and impacts disease

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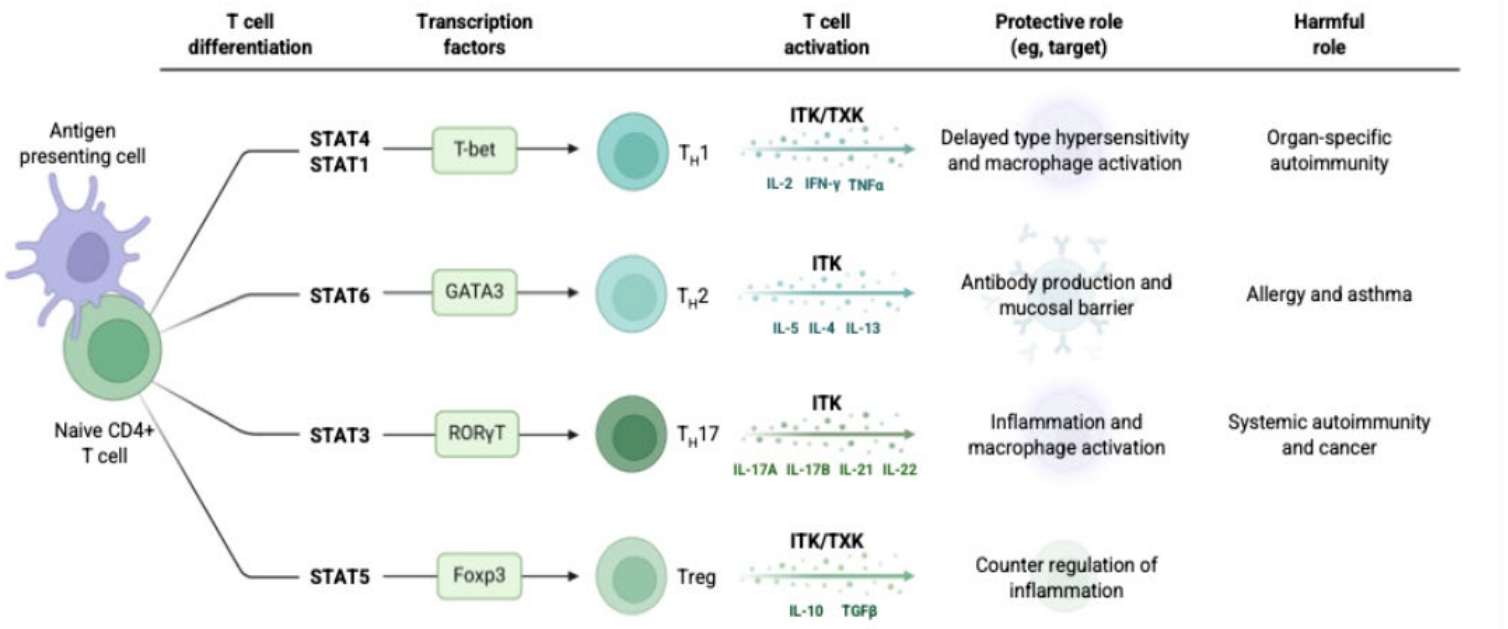
ITK Modulates T Cell Differentiation and Activation

Skews T Helper Cell Differentiation Towards Th2 and Th17 Phenotypes

- ITK has a nonredundant role in the differentiation, proliferation and activation of T_H2 and T_H17 cells
- ITK and the Tec kinase TXK are both required for Th1 function



Selective blockade of ITK impacts allergy and asthma

Dual blockade of ITK/TXK also impacts autoimmunity

Comparative Impact of ITK Inhibition

Broad Applicability in Inflammatory/Allergic Pathways

	Th2				Th17			ILC2		Th1	
	IL4	IL5	IL13	IL31	IL17	IL21	IL22	IL5	IL13	IFN γ	IL2
ITK Inhibitor	✓	✓	✓	✓	✓	✓	✓	✓	✓		
ITK/TXK Inhibitor	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
αIL-4R	✓		✓						✓		
αIL-13			✓						✓		
αIL-17					✓						
αIL-31R				✓							
JAK1	✓	✓	✓	✓		✓		✓	✓	✓	✓
JAK3	✓					✓					✓
STAT6 Inhibitor	✓		✓						✓		

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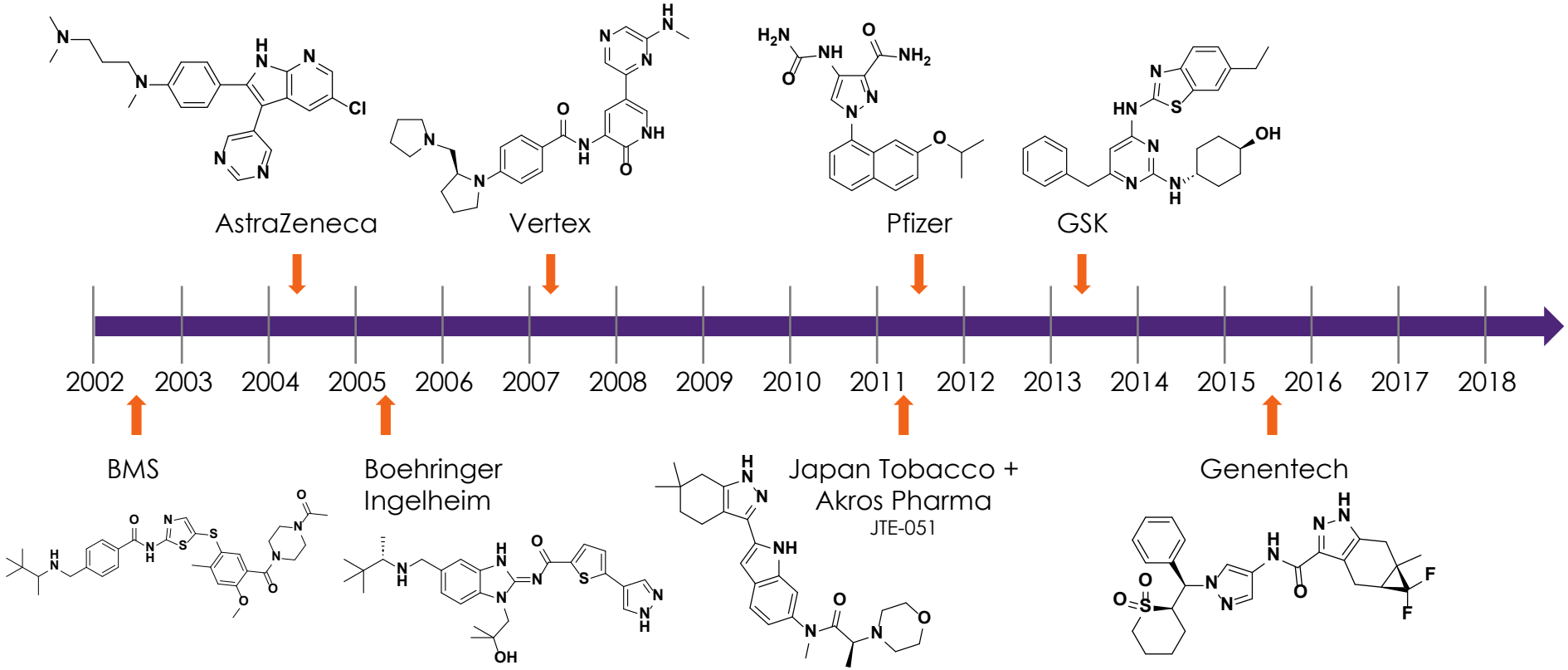
ITK is Therapeutically Relevant

But Historically Difficult to Drug

Reversible ATP Competitive Inhibitors Discontinued for Weak Cellular Potency, Poor ADME



Compounds targeting the ATP site of ITK have been pursued since the early 2000s

Only JTE-051 reached development and was discontinued

Issues with ATP Competitive ITK Inhibitors

- Generally large, lipophilic molecules with poor physicochemical properties
- Poor pharmacokinetic properties in most series
- Reactive metabolites with gene tox issues
- Variable selectivity against kinome
- Ambiguous mechanisms of action in cells
- Large shift in potency between enzyme and cell
- Low biochemical efficiency

Known concerns require alternative to ATP Competitive inhibitors

Covalent Kinase Inhibitors

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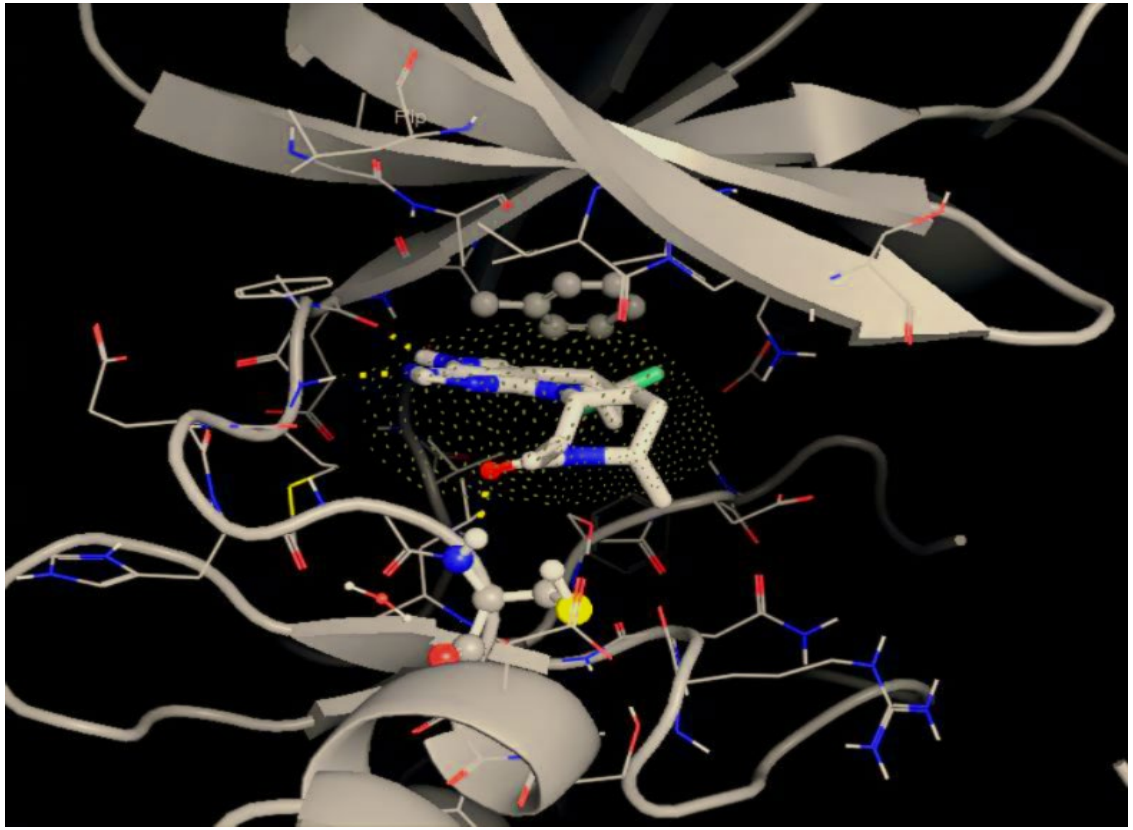
Covalent ITK Inhibition

Overcoming Issues with Biochemical Efficiency

Structure of ITK: Inhibitor Complex



- Design guided by modeling and proprietary crystal structures
- Crystal structure to confirm covalent binding characteristics
  - Designed to interact with the ATP site and covalently modifies CYS442 in ITK
- Maximize reversible affinity and minimize electrophile reactivity
- Approach overcomes issues with biochemical efficiency and enhances kinase selectivity

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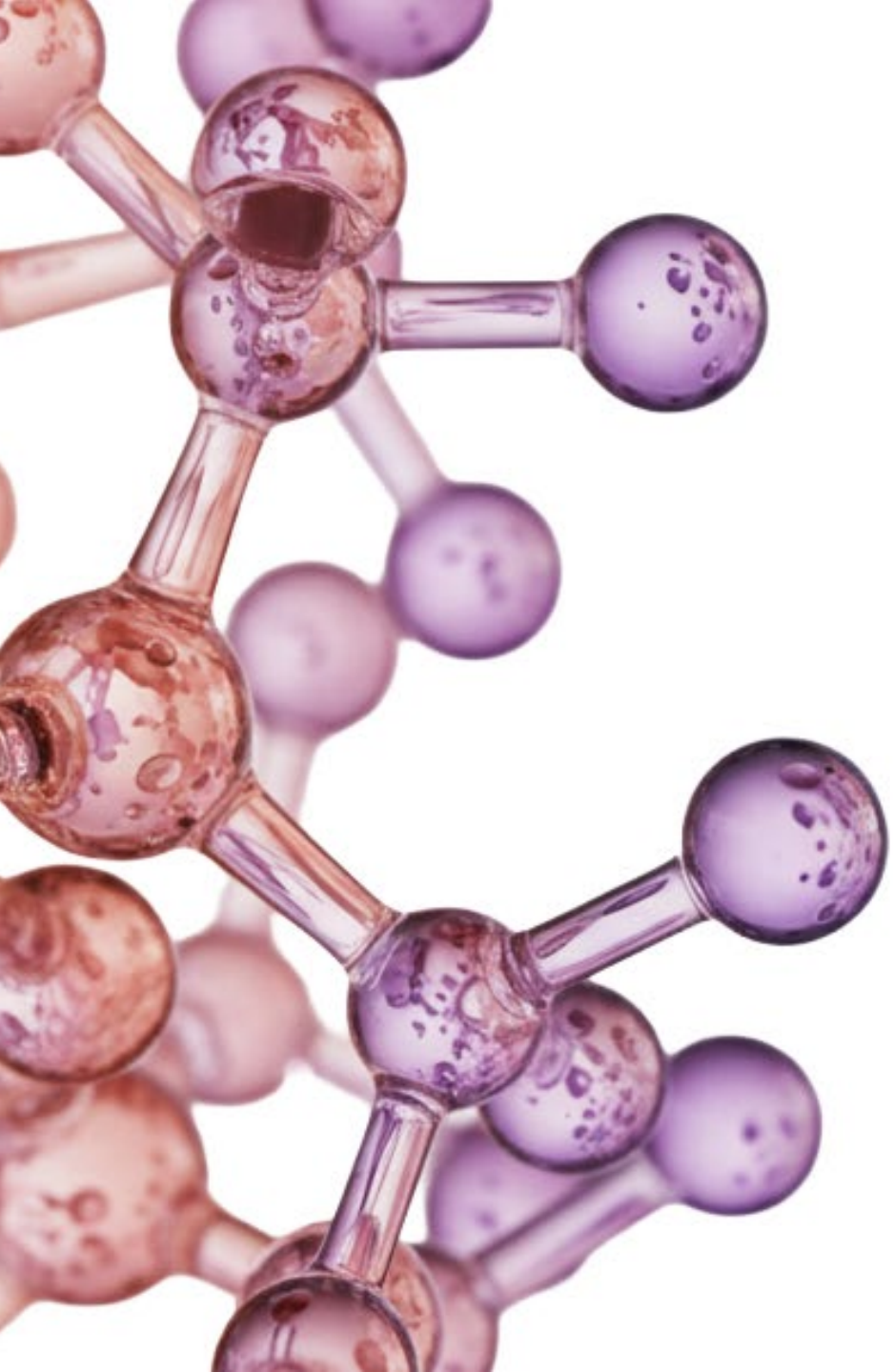

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ATI-2138: A First Generation Novel ITK/JAK3 Inhibitor for T Cell-Mediated Diseases

Potent and Selective Investigational Drug Candidate with Strong Tolerability Profile

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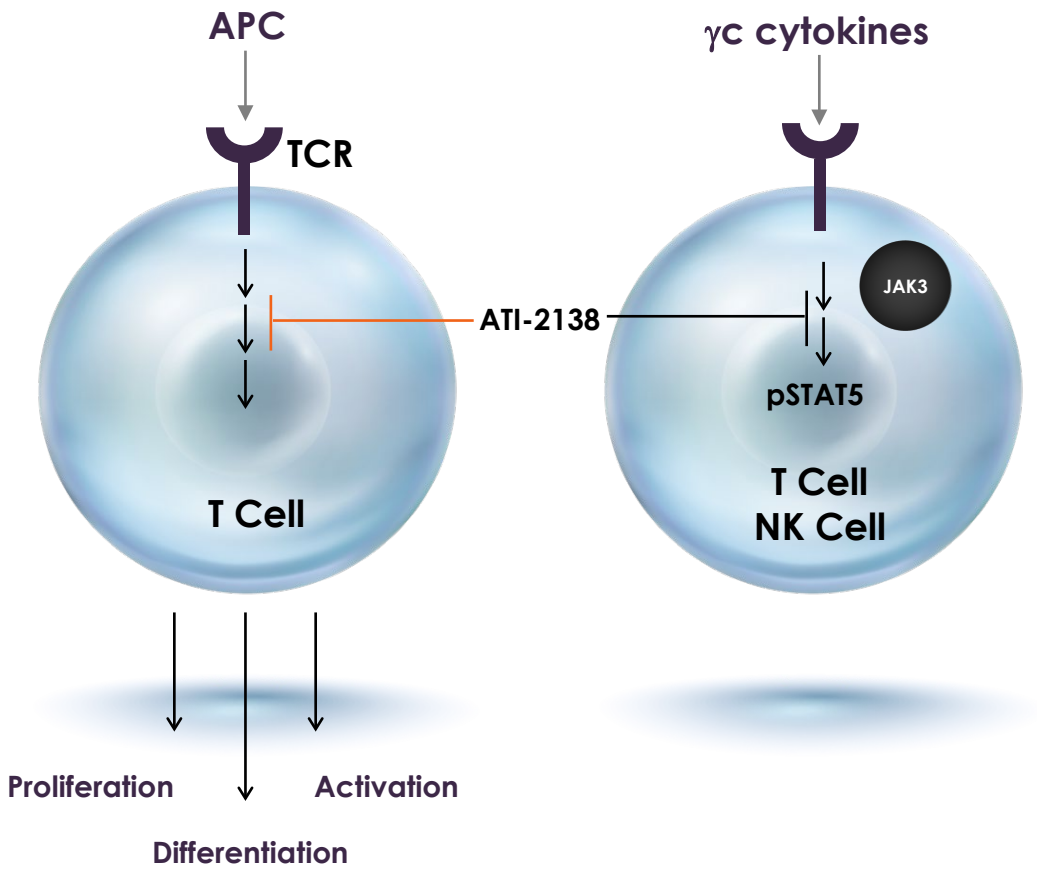
ATI-2138

Oral Small Molecule Covalent ITK & JAK3 Inhibitor for I&I Disease

- 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)
- Highly potent for both ITK and JAK3 (IC_{50}: 0.2nM ITK; 0.5nM JAK3)
- Highly selective against other JAK isoforms
- Unique dual pharmacology; best-in-class potential
- Clinical data thus far demonstrate good safety and PK characteristics; positive readout in a phase 2A AD study



Why this Molecule is Unique

Unique Dual Pharmacology of ATI-2138 Provides Best-in-Class Potential

High potency for inhibiting both ITK and JAK3

Regulation of T cell development and function both upstream (ITK) and downstream (JAK3)

Inhibiting both pathways may provide a **more potent and complete anti-inflammatory response**

As both targets are restricted in expression to immune cells, inhibitors have the **potential for a favorable safety profile**

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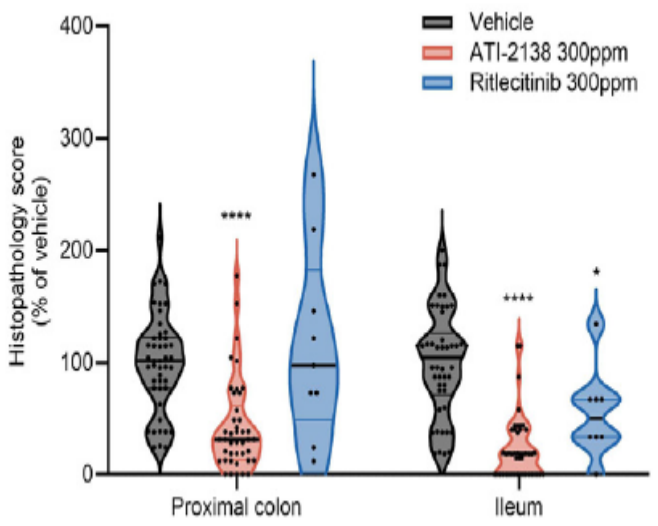
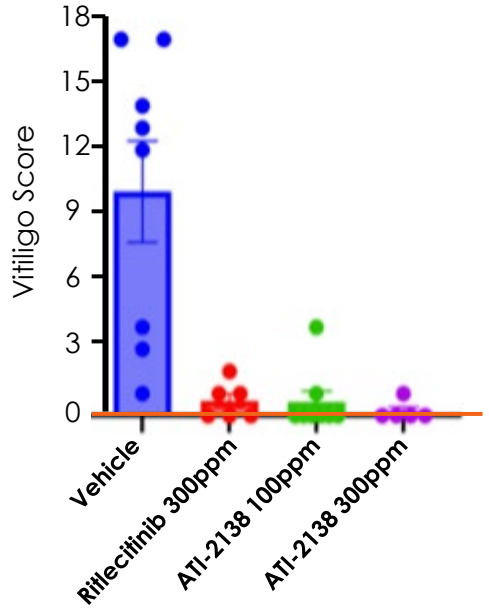
ATI-2138

Anti-inflammatory Activity in Mouse Models

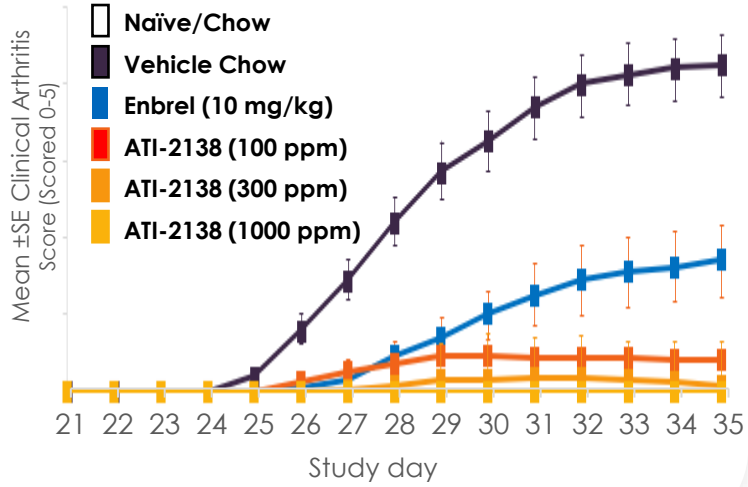
IBD
Mouse T Cell Transfer



Vitiligo
Mouse T Cell Transfer



Rheumatoid Arthritis
Mouse CIA Model



ATI-2138 has demonstrated robust anti-inflammatory activity in mouse models of disease:
Inflammatory Bowel Disease, Vitiligo, and Rheumatoid Arthritis

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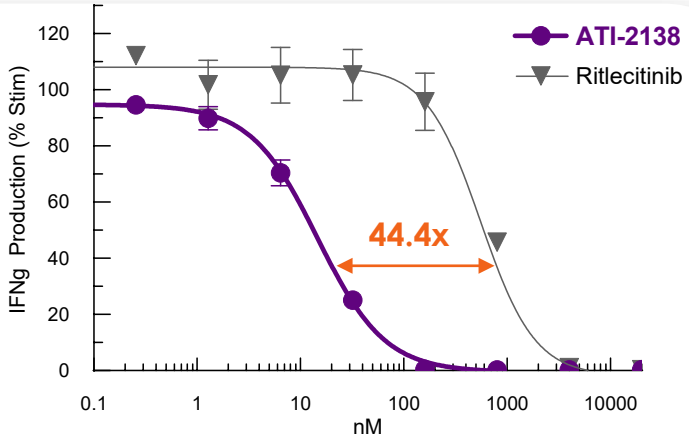
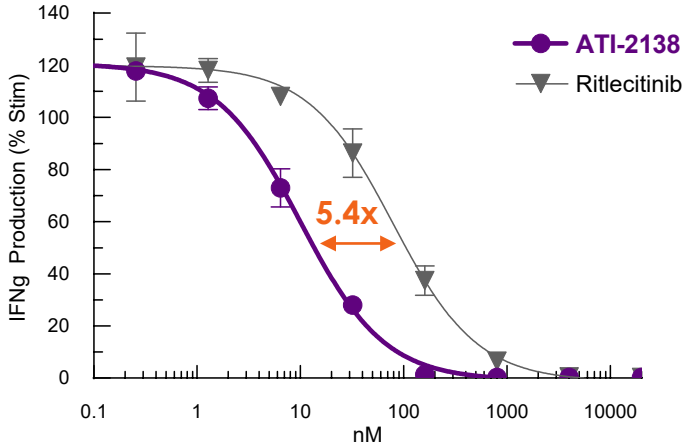
ATI-2138

Unique Dual Pharmacology and Best-in-Class JAK3 Inhibitor Potential

ITK: HWB αCD3 Stimulated IFNγ Release



JAK3: HWB IL2 Stimulated IFNγ Release



- **ATI-2138 is 44.4x more potent than ritlecitinib** for inhibiting anti-CD3 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

ATI-2138 and CPI-818 (Soquelitinib)

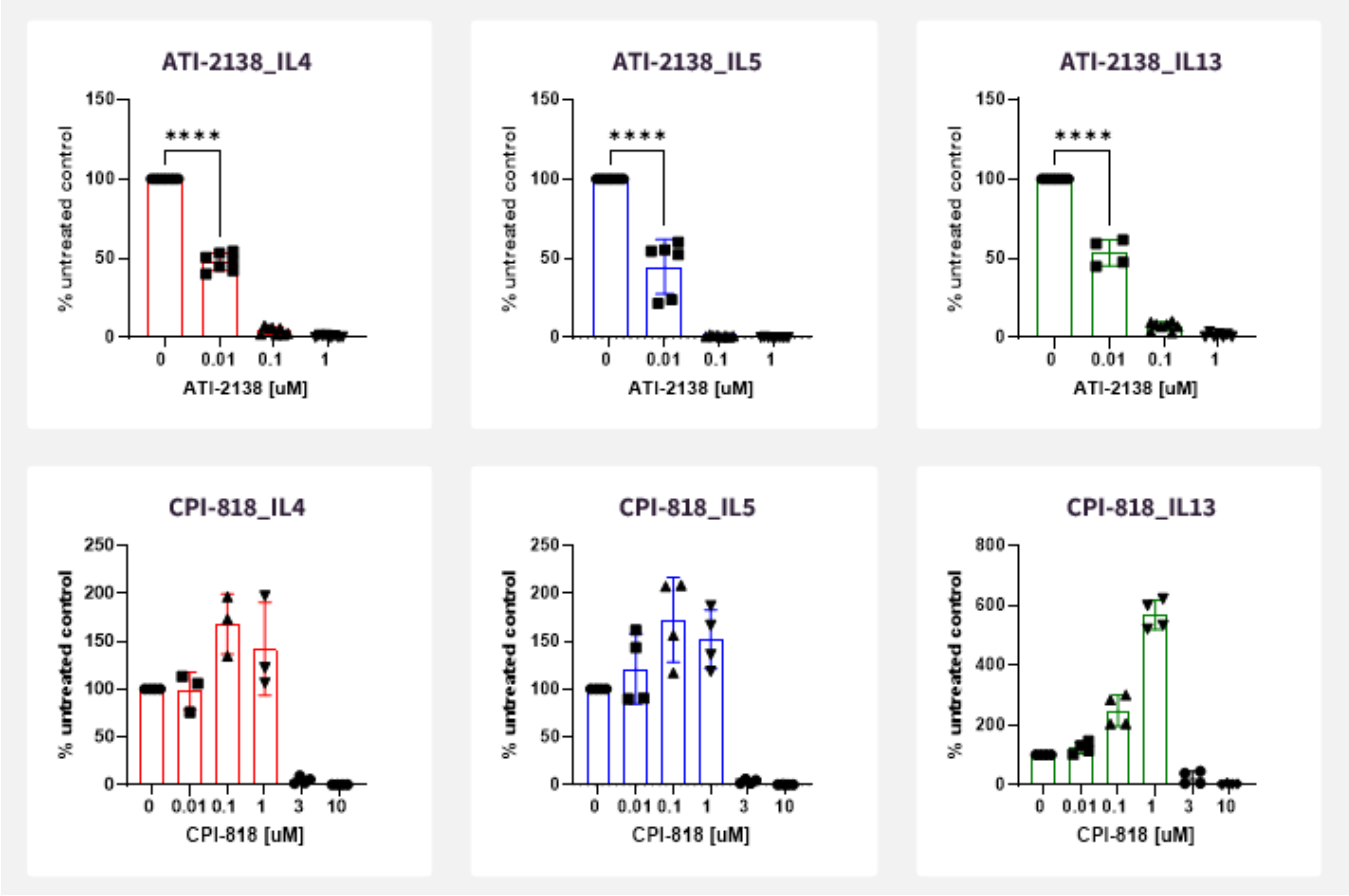
Best-in-Class ITK Inhibitor Potential

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, IL-4, IL-5 and IL-13 (30-100x)

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



ATI-2138

Single and Multiple Ascending Dose (SAD/MAD) Studies: Summary

Safety

- ATI-2138 was generally well tolerated at all doses tested in the trial
- No serious adverse events were reported

Pharmacokinetics

- ATI-2138 was rapidly absorbed
- Multiple doses ranging from 10 to 80 mg daily over two weeks in healthy volunteers showed linear PK and dose-dependent increases in exposure
- At 10-30 mg daily, ATI-2138 plasma concentration reached the targeted level established using preclinical data

Pharmacodynamics

- Time, dose and concentration-dependent inhibition of both the ITK and JAK3 pathways was observed with ATI-2138
- PD markers were inhibited across the dosing interval with the 5-40 mg BID doses inhibiting up to 50%-90% of both ITK and JAK3 functional markers

Phase 2a Trial in Atopic Dermatitis

- Twelve-week, open-label study with ATI-2138 (10mg BID) in moderate to severe AD patients
- Favorable safety profile
- Efficacy observed across multiple measures comparable to drugs approved for AD
- Exposure similar to or slightly higher than predicted from MAD study
- Efficacy and PD results validate therapeutic potential of targeting ITK:
  - Near complete and sustained inhibition and occupancy of ITK
  - Downregulation of multiple ITK-dependent immune pathways in the skin

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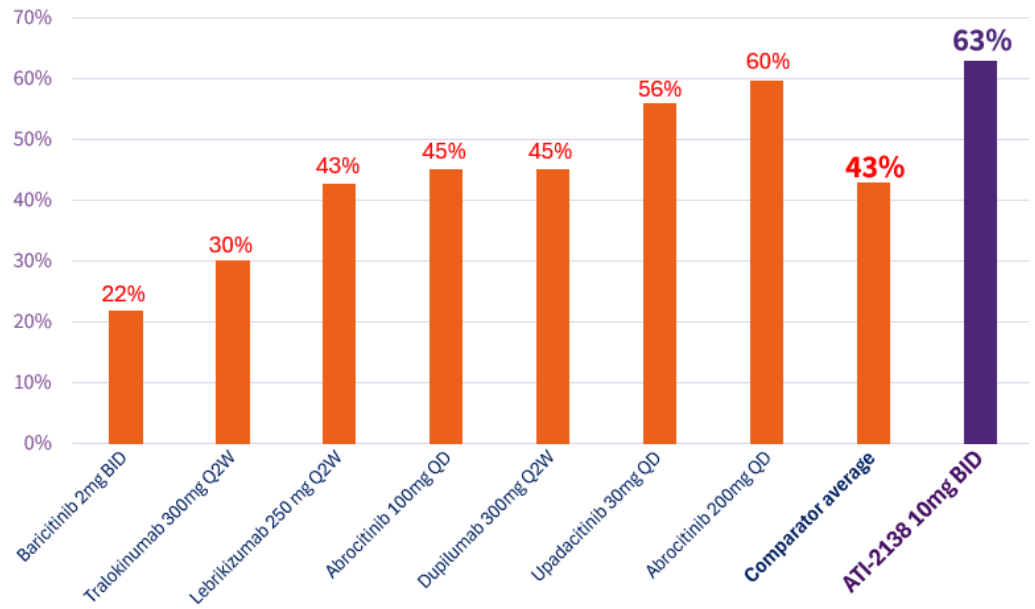
Phase 2a Trial in Atopic Dermatitis

A ≥4-point improvement in PP-NRS score is considered a clinically meaningful result

PP-NRS: % of Pts with ≥4 Point Improvement in Worst Itch over Prior 24 Hours



At week 12, **63%** of patients receiving a low dose (10mg BID) of ATI-2138 experienced a ≥4-point improvement worst itch in the past 24 hours

After four weeks of treatment

- **BSA** decreased by 63.9%
- **EASI** scores dropped by 77.3%
- **PP-NRS** decreased by 44.7%
- These changes were statistically significant and sustained through study conclusion (W12)

Molecular and Clinical Effects of oral ATI-2138, an ITK/JAK3 inhibitor, in Moderate-to-Severe Atopic Dermatitis: Sub-study of a Phase 2a Open-Label, Single-Arm Trial. Beaziz-Tordjman, Jessica *et al.* European Academy of Dermatology and Venereology, September 17, 2026.

Efficacy Results Show Strong Consistent Response to ATI-2138

Each other compound efficacy is the average percent improvement from multiple studies, at week 12 or 16 data from Phase 2 and Phase 3 published sources; head-to-head clinical studies have not been conducted. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies. Data collected on 8 of 10 PP patients.

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Phase 2a Trial in Atopic Dermatitis

Pharmacodynamic Assessment

Conducted to Assess **Target, Pathway, and Disease Markers** to Support Mechanism of Action

Understanding PK/PD

- **ITK Assay**
  - αCD3/aCD28 ex vivo stim mRNA (IL-2 and IFN γ) production
- **ITK Target Occupancy**
- **JAK3 Assay**
  - IL-15 ex vivo stim IFNg protein production
- **Immunophenotyping**

Relating PD to Efficacy

- **Punch Biopsy Analysis**
  - Immunohistochemistry
  - RNAseq Analysis (>16,000 genes)
- **Tape Strip Analysis**
  - RNAseq Analysis (>16,000 genes)
  - Olink Proteomics (300+ analytes)
- **Endogenous Biomarkers in Plasma**
  - OLink Proteomics (300+ analytes)

ATI-2138 is Mechanistically Unique and PD Supports Observed Clinical Efficacy

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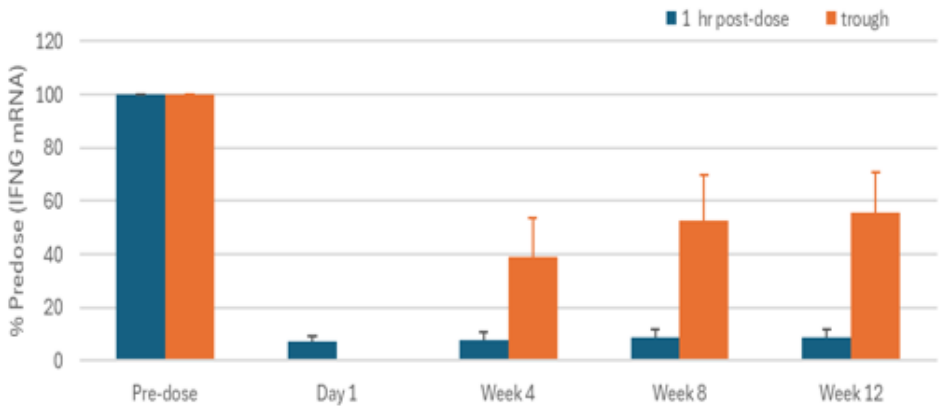
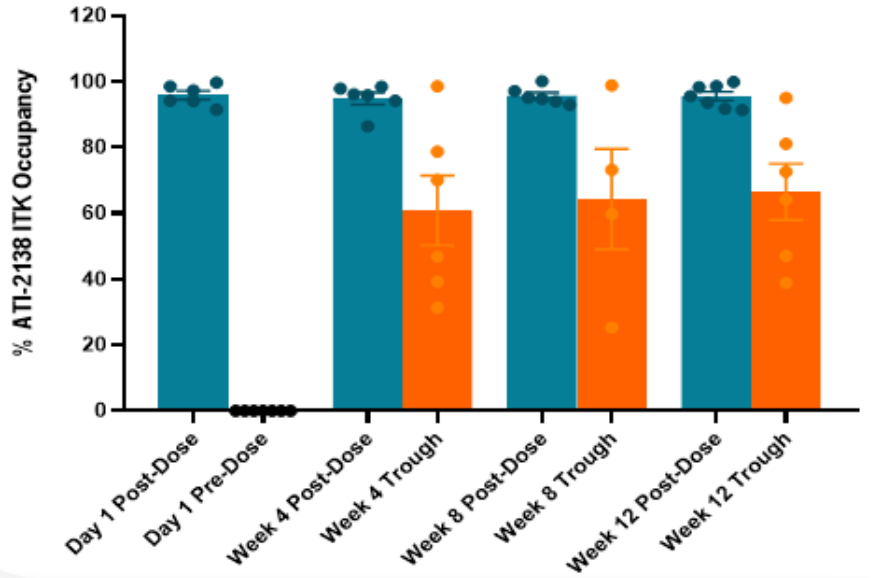
Phase 2a Trial in Atopic Dermatitis

Marked and Sustained ITK Inhibition Observed

ITK: Ex vivo Functional Assay



ITK: Target Occupancy



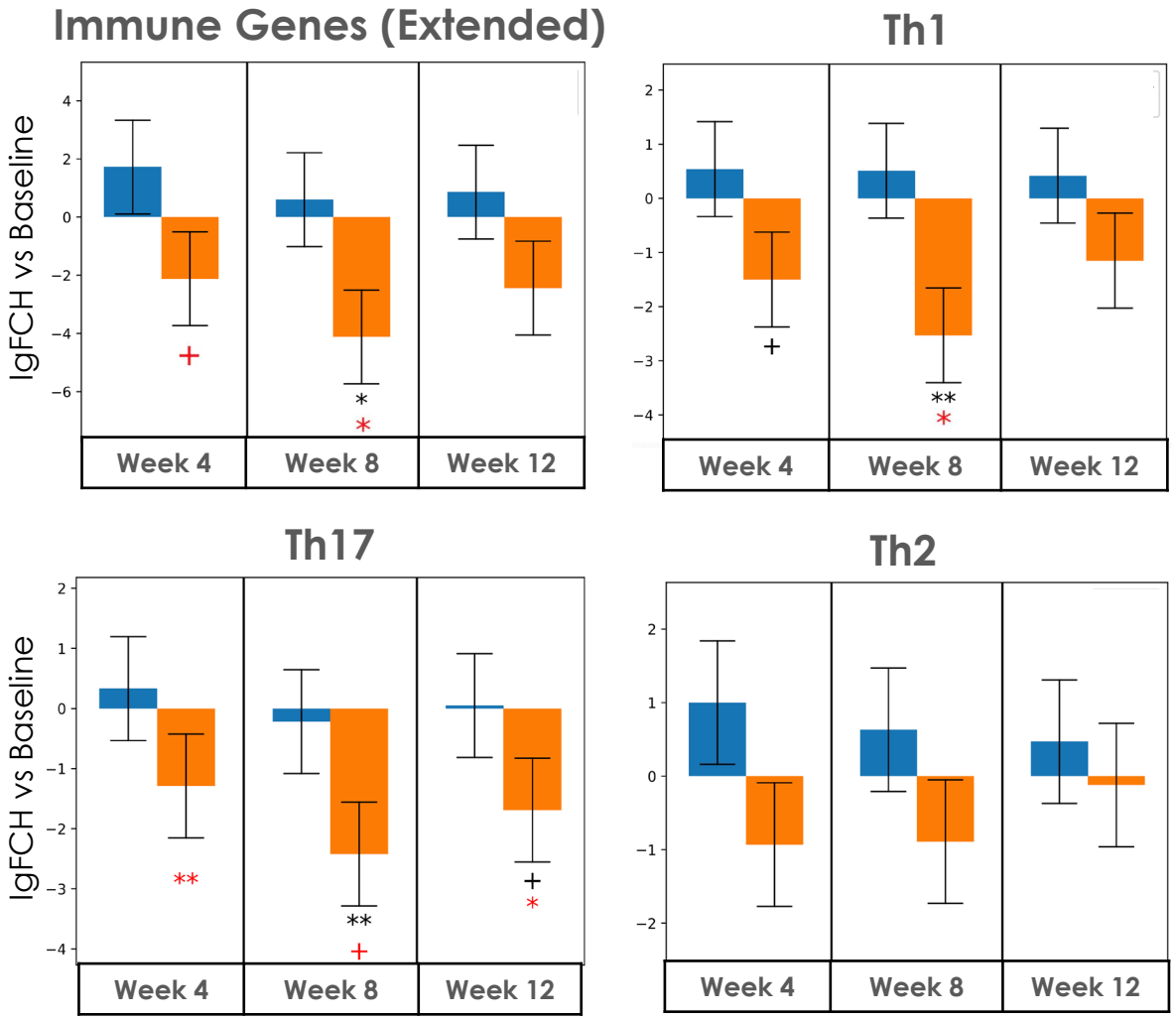
Functional inhibition and target occupancy retained across the dosing interval;

>90% inhibition IFNγ mRNA and near complete target occupancy observed 1 hour post dose

Data collected on 8 of 10 per protocol patients

Gene Set Variation Analysis (GSVA)

Tape Strip Proteomics Data



- Proteomic results corroborate genomics findings
- Immune-related gene or protein profile improved over time, with reduction of inflammation
- Variability between weeks 8 and 12 may be attributed to noncompliance by two patients

Black stars: significance vs baseline
Red stars: significance between change in lesional vs. change in non-lesional

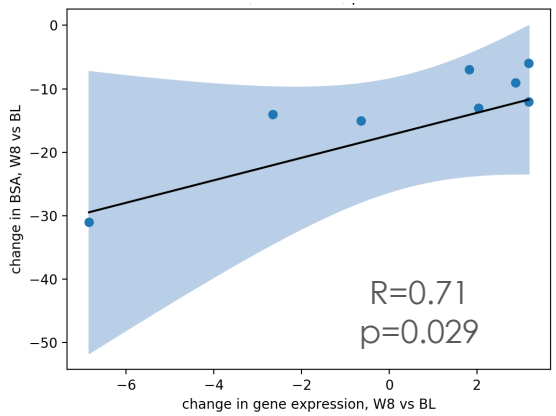
Non-lesional Lesional

Data collected on 8 of 10 per protocol patients

Correlation B/W Change in Clinical Scores & in Key Gene Expression

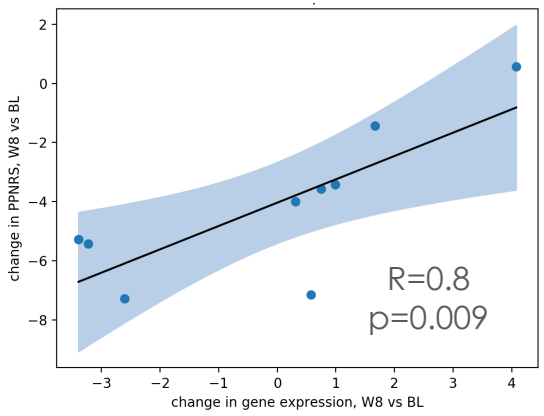
GENERAL INFLAMMATION

CXCL12



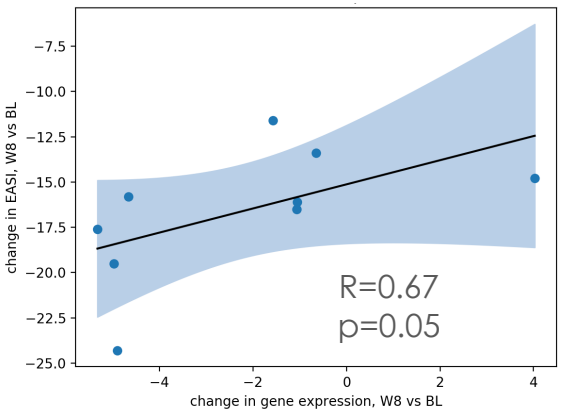
Th2

TSLP



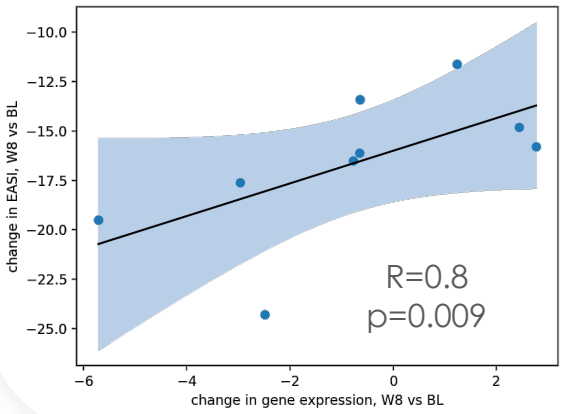
Th17

CCL21

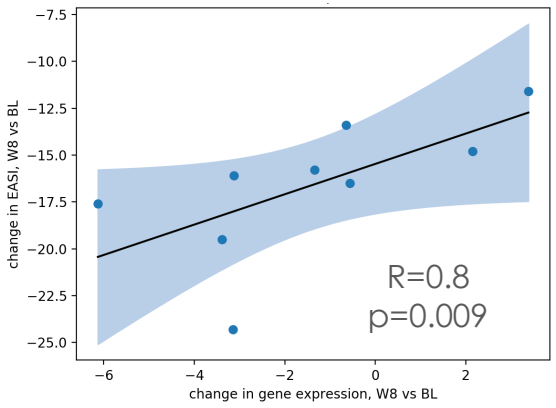


FIBROSIS

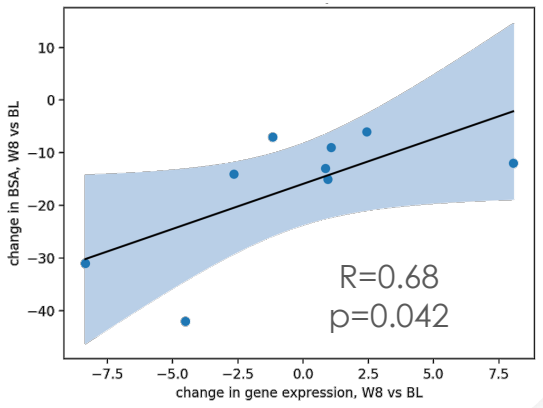
SPON1



LUM



ELN



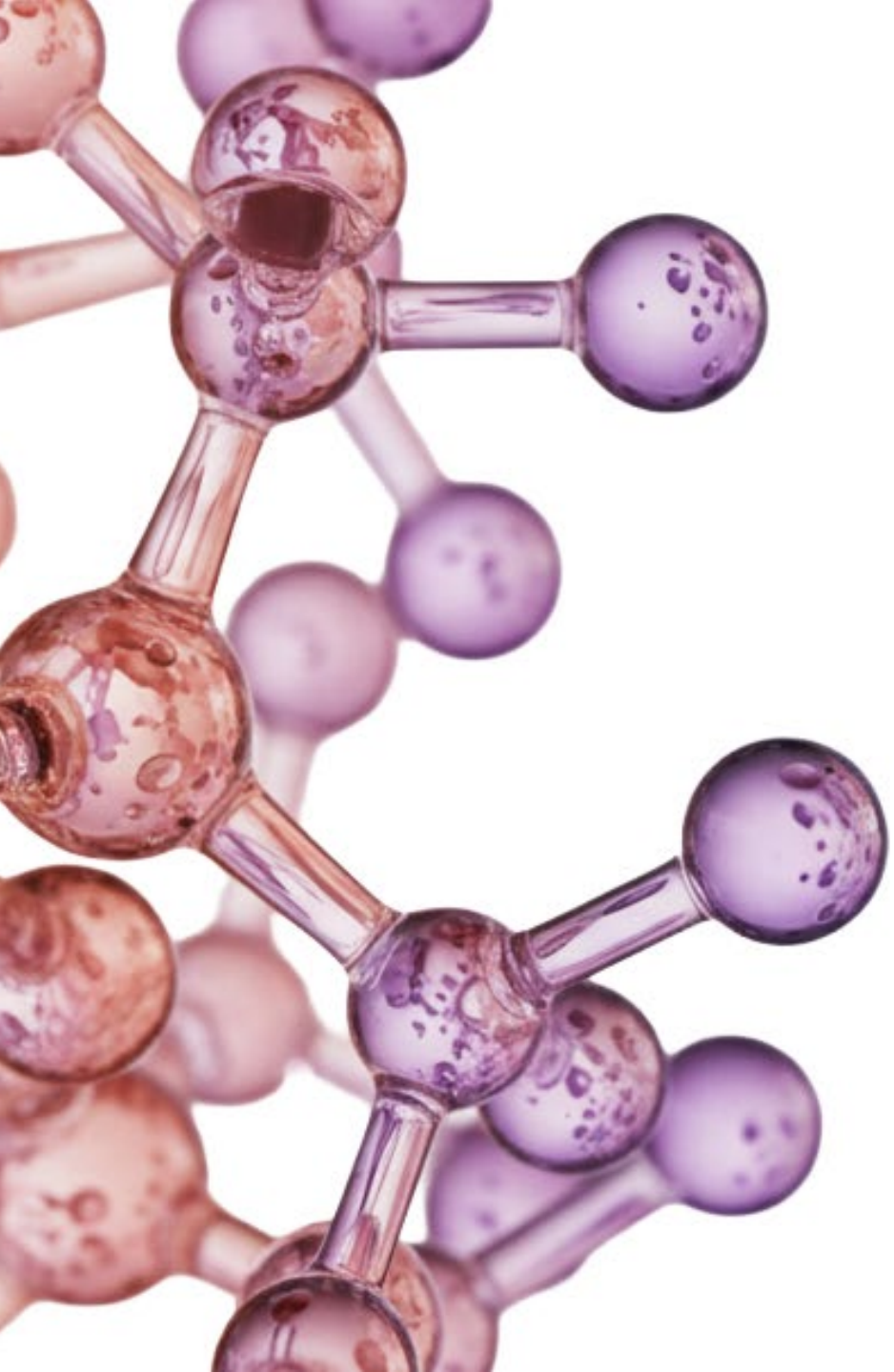
Decreases in inflammatory and fibrosis-related markers positively and strongly correlated with improvements in clinical scores

Data collected on 8 of 10 per protocol patients

Phase 2a Trial in Atopic Dermatitis

ITK Pathway Mediated Anti-Inflammatory Activity in Skin and Plasma

- ATI-2138 significantly downregulated multiple immune pathways in skin and plasma
- Strong downregulation of key ITK dependent pathway markers such as:
  - Th2 (e.g., CCL17, CCL24, IL13, TSLP)
  - Th17 (e.g., CXCL1, IL17A, IL6R)
  - TCR (ITK) Pathway (e.g., ITK, IL-13, CD3, ZAP70, LCK, PLCg1)
  - Th1 (e.g., CXCL11, CXCL9, IL2RA, TNF)
  - Fibrosis related markers (e.g., MMP9, TNFRSF9)
- Safety profile and expected incremental increase in PD with greater exposure may support higher dosing in subsequent studies



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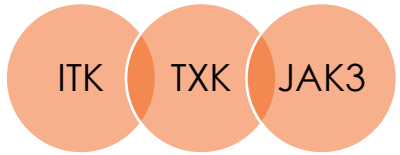
Next Generation ITK Inhibitors

Novel ITK and ITK/TXK Selective Inhibitors
Designed to Limit JAK Inhibitory Activity

Patient *Focused Innovation*

Aclaris ITK Inhibitor Program Status Summary

1st Generation



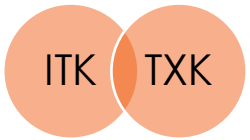
ATI-2138

Phase 2a AD study met primary and secondary key endpoints

Well tolerated at all doses

Validated ITK MOA and corroborates our work on next-generation ITK selective compounds

Next Generation Inhibitors



ACRS-1

ACRS-2

Highly potent ITK/TXK dual inhibitors

Extended half-life

Translatable JAK3 Selectivity

Low dose for total ITK occupancy

ACRS-3

Potent ITK-selective inhibitor

Extended half-life

JAK3 and TXK selectivity

Total ITK occupancy demonstrated in vivo

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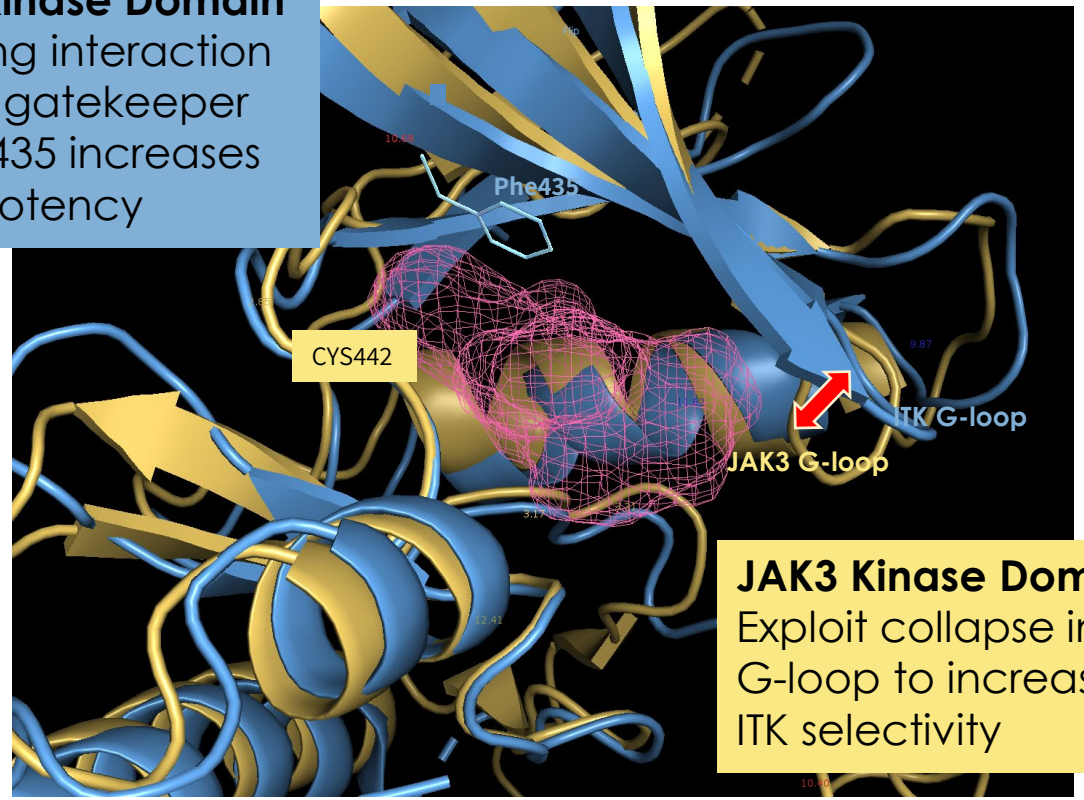
Next Generation ITK Inhibitors

Designing ITK Potency and JAK3 Selectivity

ITK Kinase Domain
Strong interaction with gatekeeper Phe435 increases ITK Potency



JAK3 Kinase Domain
Exploit collapse in G-loop to increase ITK selectivity

ACRS-2 modeled into ITK kinase domain 3QGY and JAK3 kinase domain 5TOZ SP covalent dock

- Aclaris compounds designed to form strong interactions in the ITK kinase domain with gatekeeper Phe435 leading to an increase in potency for ITK (Ki)
- The position and orientation of the G-loop is different between the ITK and JAK3 Kinase domains
- ACRS Next Generation compounds designed to take advantage of these structural differences to decrease potency for JAK3 compared to ITK

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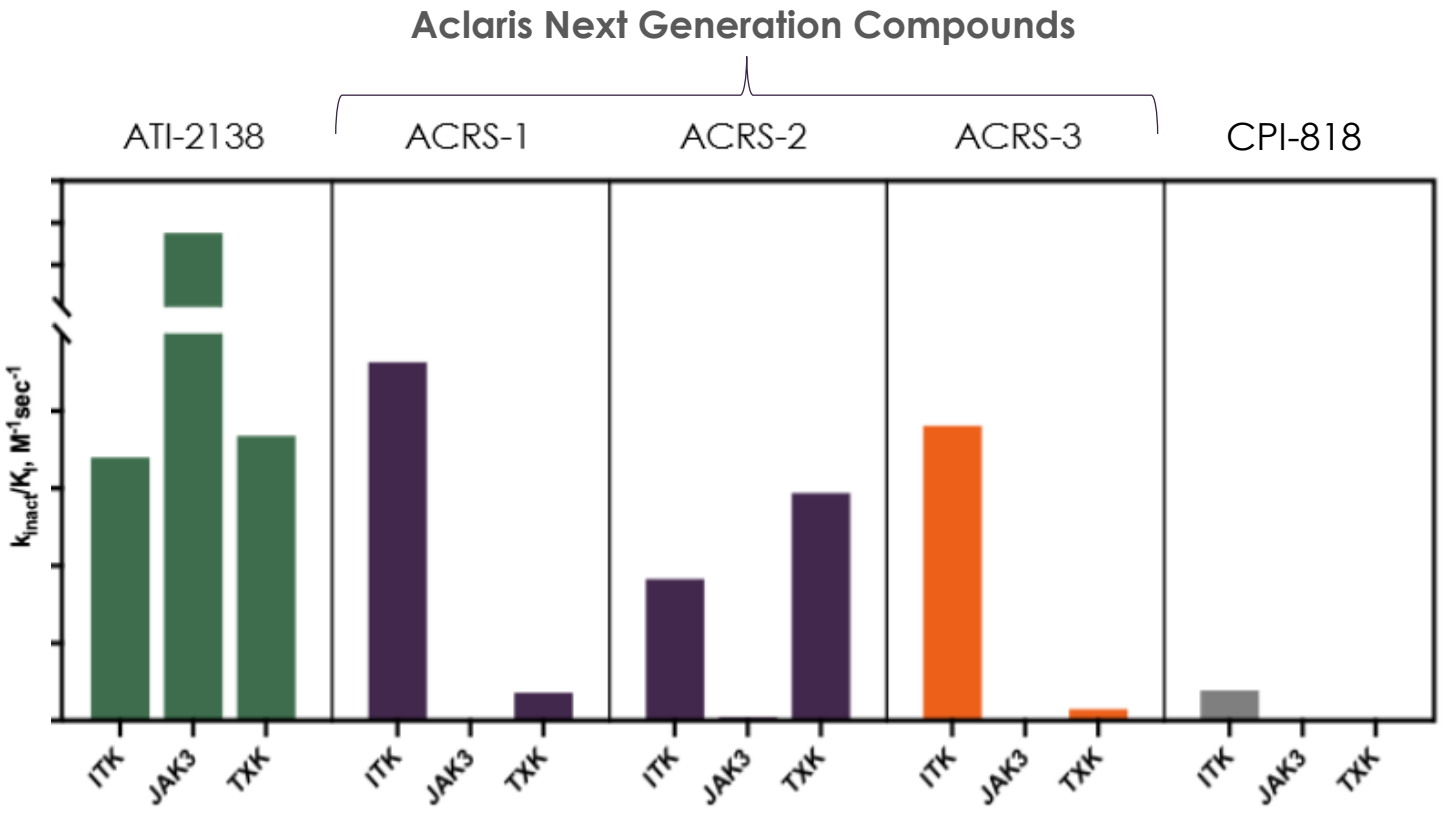
Efficiency and Selectivity in Enzyme-Based Assays



- Next Generation compounds have **decreased efficiency against JAK3 and variable efficiency against TXK**
- Aclaris compounds are **significantly more efficient inactivators of ITK** as compared to CPI-818

Potency, Occupancy and Selectivity

In Human Primary Cells

		Human PBMC Cell Data			Human Whole Blood Data
Compound	**Target**	**ITK Occupancy (OC_{90})**	**aCD3 stim IL-2 (IC_{50})**	**ITK/JAK3 (IC_{50} *Ratio*)**	**HWB ITK IC_{50} CD3/CD28 stim IL-2 mRNA**
ATI-2138	ITK/TXK/JAK3 1st Generation	17 nM	10 nM	*0.1x*	17 nM
ACRS-1	ITK/TXK	7 nM	7 nM	*79x*	51 nM
ACRS-2		69 nM	34 nM	*95x*	33 nM
ACRS-3	ITK	16 nM	16 nM	*109x*	61 nM
CPI-818	Corvus ITK-selective	117 nM	167 nM	*>40x*	408 nM

Aclaris compounds show significant increase in cell potencies for ITK as compared to CPI-818

Next Generation compounds show limited inhibition of JAK3

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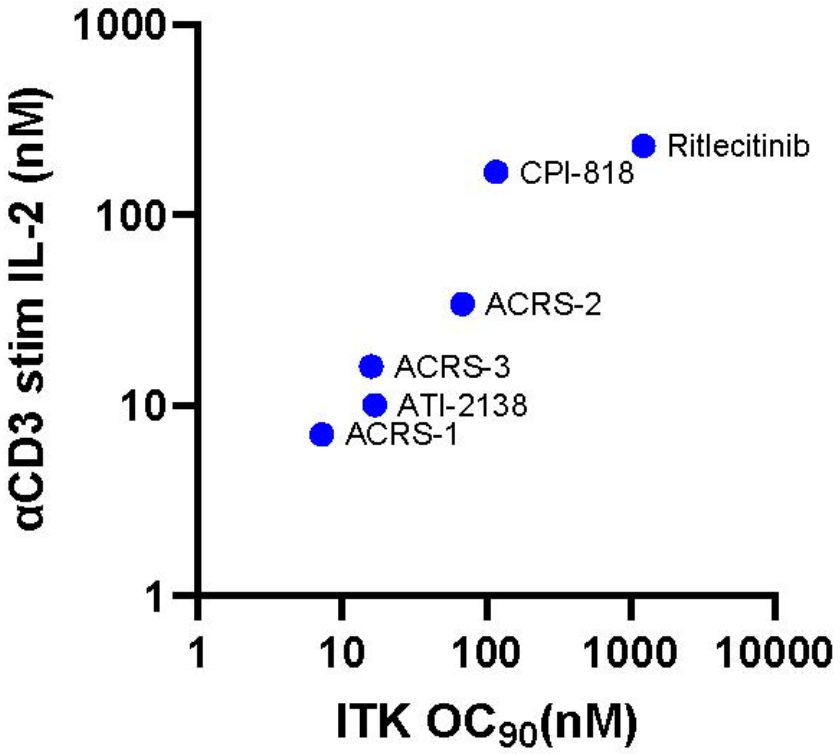
Correlation B/W Occupancy & Functional Inhibition in PBMC



Good correlation between functional ITK inhibition and target occupancy

Demonstrates potency and occupancy superiority for the ACRS ITK inhibitors vs competitors

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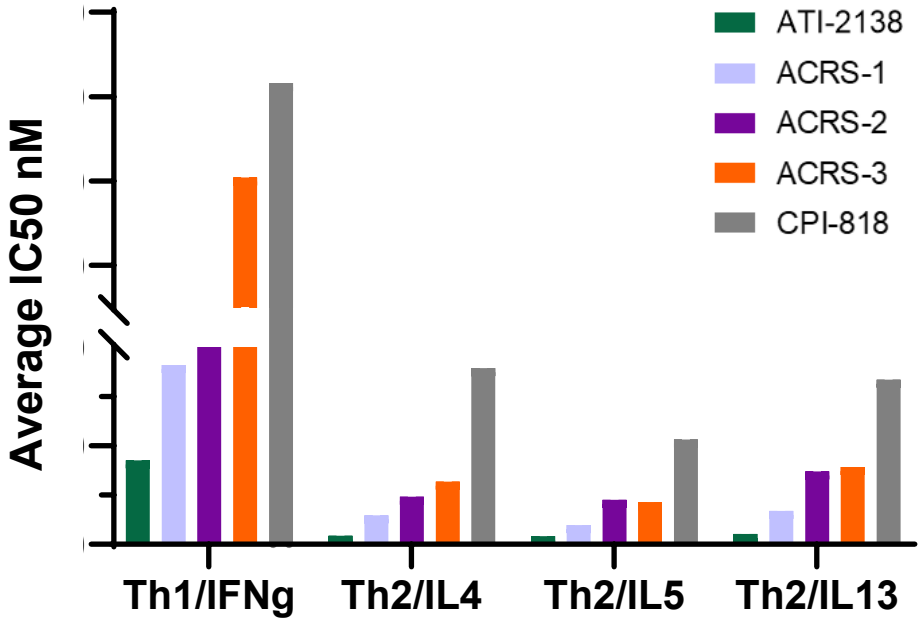
Differential Inhibitor Impact

Th1 and Th2 Cell Function

- Impact of inhibitors on canonical cytokines from human differentiated Th1 and Th2 cells
- ACRS 1 and ACRS 2 block Th1 and Th2 responses through dual inhibition of ITK and TXK
- ACRS 3 blocks Th2 responses and spares Th1 through selective inhibition of ITK



Next generation inhibitors potently block Th2 function and differentially modulate Th1 activation

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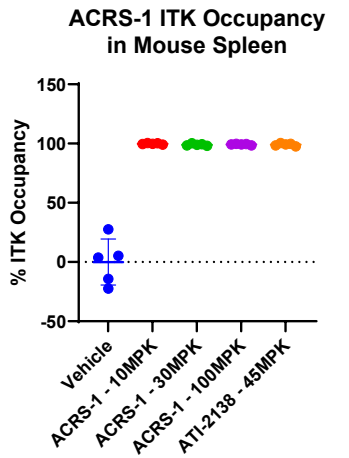
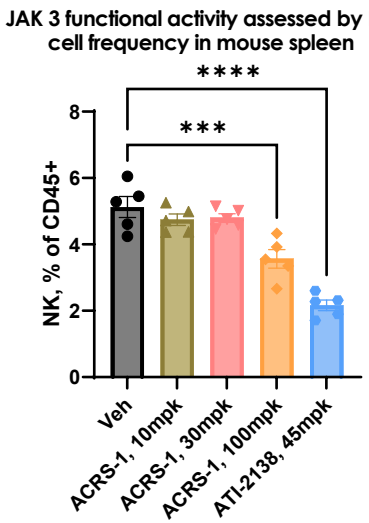
Why is Potency Important with Covalent Drugs?

- Enzyme inactivation efficiency drives drug potency
- Higher potency results in lower and less frequent dosing
- Lower and less frequent dosing decreases drug burden
- Lower drug burden increases selectivity and supports a superior safety profile
- Covalent drugs contain reactive electrophiles:
  - Low potency covalent inhibitors require high drug levels in blood and tissue
  - High drug concentrations increase probability of the electrophile reacting with non-target proteins, potentially increasing safety liabilities

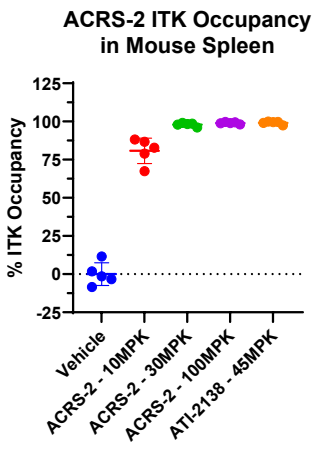
Next Gen ITK Inhibitors Demonstrate JAK3 Selectivity in Vivo

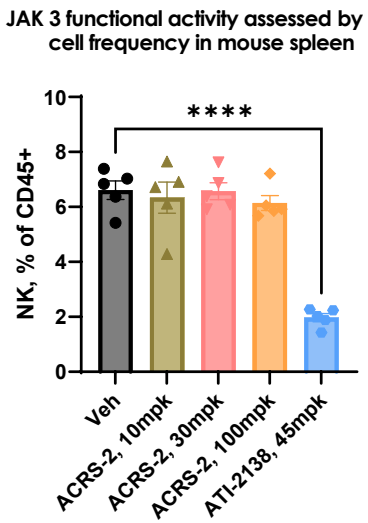
ACRS-1



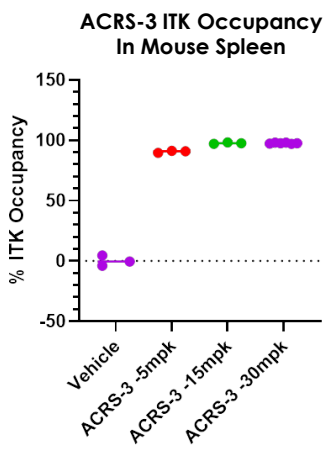


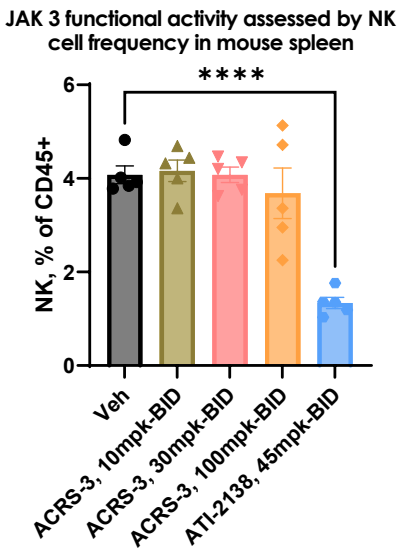
ACRS-2





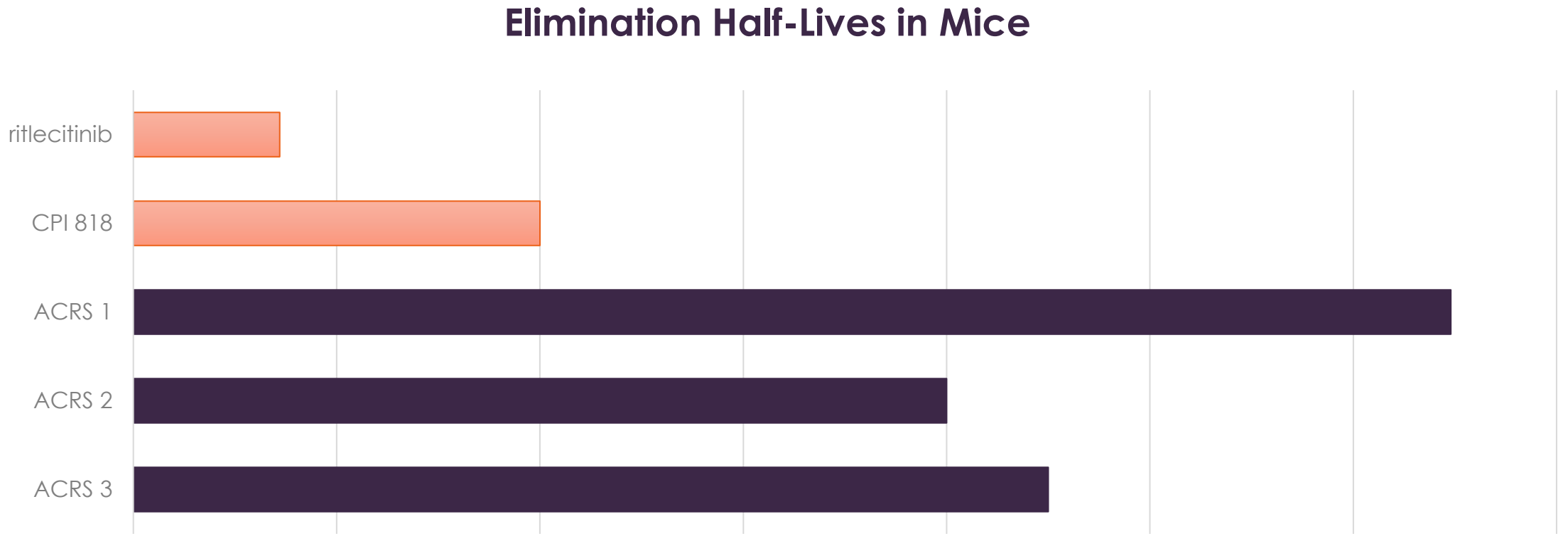
ACRS-3





Complete ITK occupancy achieved without impacting JAK3 function

Half-Life Comparison of Compounds



Aclaris Next Generation compounds demonstrate a significant increase in half-lives in mice as compared to ritlecitinib and CPI-818

More amenable to once-per-day dosing

Profiling of Next Generation Compounds

		ACRS-1	ACRS-2	ACRS-3
Pharmacology	Biochemical IC50 and kinact/Ki (ITK, TXK, BTK, and JAK3)	✓	✓	✓
	hPBMC Cell-Based Assays (Functional and Occupancy) ITK and JAK3	✓	✓	✓
	ITK Cell Cytotox IC50	✓	✓	✓
	HWB Translatable Functional Biomarker IC50 (ITK and JAK3)	✓	✓	✓
DMPK	Solubility in Biorelevant Media	✓	✓	✓
	Permeability and Efflux	✓	✓	✓
	Cross-species Stability (Liver, Hepatocytes, Blood, and Plasma)	✓	✓	✓
	Cross-species Plasma Protein Binding and Blood-to-Plasma Ratio	✓	✓	✓
	In vivo Pharmacokinetics in Rodent and Non-rodent Species	✓	✓	✓
	Human PK Projections (PBPK)	✓	✓	✓
Safety	hERG, and CEREP Panel	✓	✓	✓
	Kinase Selectivity	✓	✓	✓
	CYP (Inhibition, TDI, and Induction)	✓	✓	✓
	Transporter Inhibition	✓	✓	✓

Patent applications have been filed on Next Generation compounds

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Aclaris ITK Inhibitor Program

Summary

- Successfully generated a portfolio of covalent ITK inhibitors with differentiated pharmacological properties and selectivity profiles
- These inhibitors expected to differentially modulate T cell biology across a broad range of disease indications and have best-in-class/first-in-class potential
- ATI-2138 has demonstrated:
  - Favorable safety profile
  - Clear understanding of PK and PD
  - ITK pathway and T cell modulation
  - Early signs of efficacy in a 12-week AD study
- Next Generation JAK-sparing compounds progressing toward initial IND in 2026

Aclaris Next Generation ITK Inhibitor Program

	Potential Indications	Approved Inhibitors	TAMs*
ITK/TXK Potentially beneficial in Th1, Th2, and Th17-driven diseases	• IBD • Psoriasis • Chronic GvHD • SO Transplant Rejection • Vitiligo • Alopecia • Celiac disease • Eosinophilic esophagitis • Prurigo nodularis • Others	IL-4R: Dupixent® (dupilumab) IL-31R: Nemluvio® (nemolizumab) IL-17A: Cosentyx® (secukinumab) Taltz® (ixekizumab) Bimzelx® (bimekizumab) Siliq® (brodalumab) JAK1: Oluminant® (baricitinib) JAK1/2: Opzelura® (ruxolitinib) JAK3: Litfulo® (ritlecitinib)	**Alopecia areata: $7B** **Vitiligo: $3B** **Psoriasis: $60B** **EoE: $5B** **Prurigo nodularis: $2B** **COPD: $31B**
ITK Potentially beneficial in Th2-driven atopic and allergic diseases	• Asthma • Atopic Dermatitis • Rhinitis • COPD • CSU • Others	IL-4R: Dupixent® (dupilumab) IL-13: Ebglyss® (lebrikcizumab) Adbry® (tralokinumab) IL-31R: Nemluvio® (nemolizumab) JAK1: Rinvoq® (upadacitinib) Cibinqo® (abrocitinib)	**Asthma: $36B** **Atopic dermatitis: $31B** **Rhinitis: $19B** **CSU: $6B**

*TAM=Total Addressable Markets: Estimates, 2028-2034

Sources: Eczema stats: National Eczema Association (accessed 07/31/25); National Alopecia Areata Foundation (Accessed 07/31/25); Vitiligo Facts: Global Vitiligo Foundation (accessed 07/31/25); Precedence Research; Forbes Business Insights; American Medical Association; American Lung Association; Global Initiative for Asthma; World Health Organization; The Centers for Disease Control and Prevention (CDC); Business Research Company; peer research; Delveinsight; Cowen Categories Outlook 2024

Broad Clinical and Preclinical I&I Pipeline

Potential Best-in-Class Inhibitors of Immunoinflammatory Cascade

Oral Kinase Inhibitors

ITK Franchise

First Generation

ATI-2138
ITK/JAK3
Phase 2a Complete

Next Generation

ITK Selectives
Preclinical Development
ITK | ITK/TXK

Next Gen IND: 2H 2026

Biologics

Antibody Franchise

Monoclonal Antibodies

Bosakitug (ATI-045)
αTSLP
Phase 2

Multispecific Antibodies

ATI-052
αTSLP/IL-4Rα
Phase 1a/1b

Next Gen
Multispecifics
Discovery

αTSLP/X(undisclosed 1)
αTSLP/X(undisclosed 2)
αTSLP/X(undisclosed 3)

All future development, clinical, and regulatory timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors

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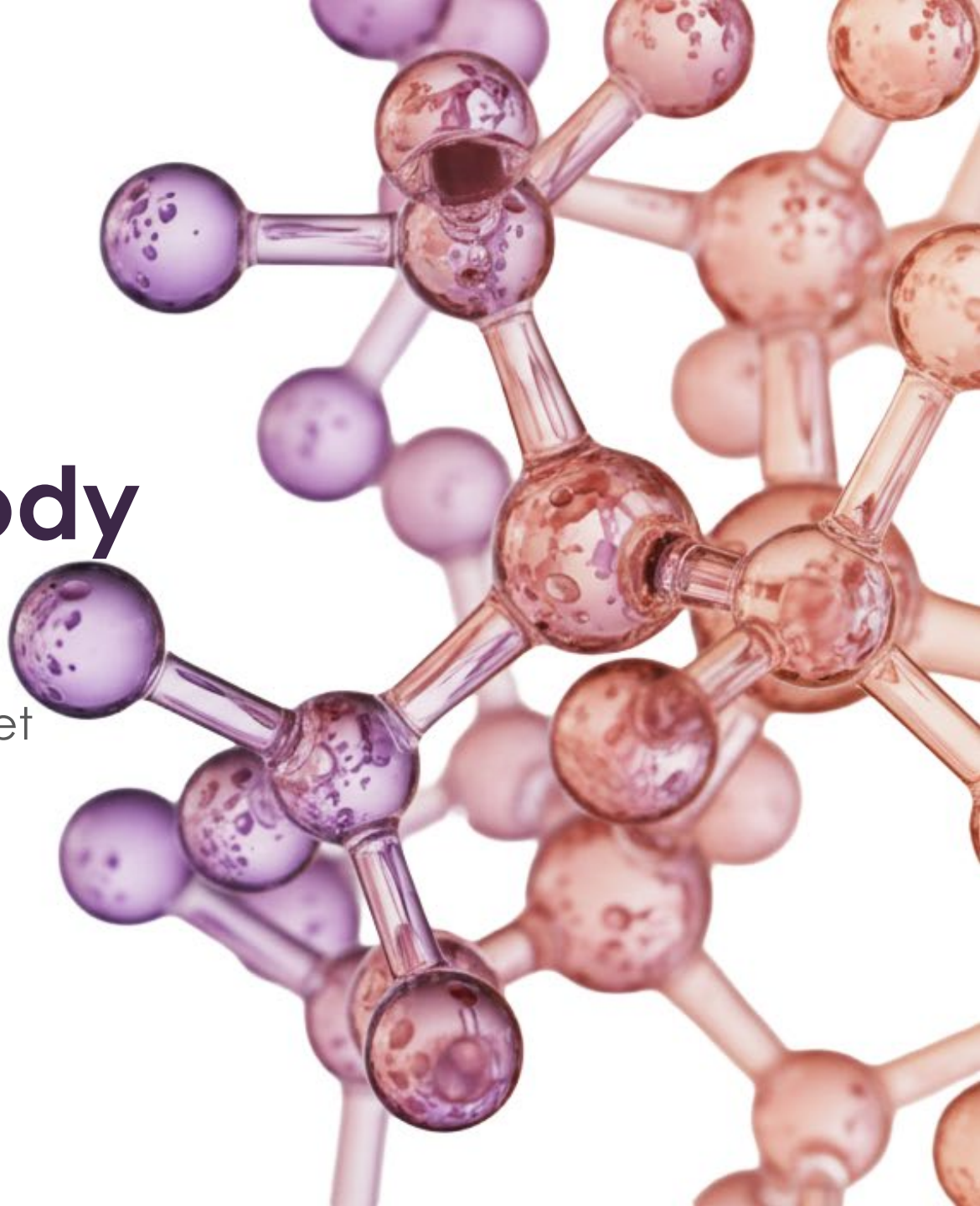
The Science of Antibody Development

Validating TSLP as an Effective Therapeutic Target

Hugh Davis, Ph.D.
President and Chief Operating Officer

Patient *Focused Innovation*



Broad Clinical and Preclinical I&I Pipeline

Potential Best-in-Class Inhibitors of Immunoinflammatory Cascade

Oral Kinase Inhibitors

ITK Franchise

First Generation

ATI-2138
ITK/JAK3
Phase 2a Complete

Next Generation

ITK Selectives
Preclinical Development
ITK | ITK/TXK

Next Gen IND: 2H 2026

Biologics

Antibody Franchise

Monoclonal Antibodies

Bosakitug (ATI-045)
αTSLP
Phase 2 Ongoing

Multispecific Antibodies

ATI-052
αTSLP/IL-4Rα
Phase 1a/1b Ongoing

Next Gen
Multispecifics
Discovery

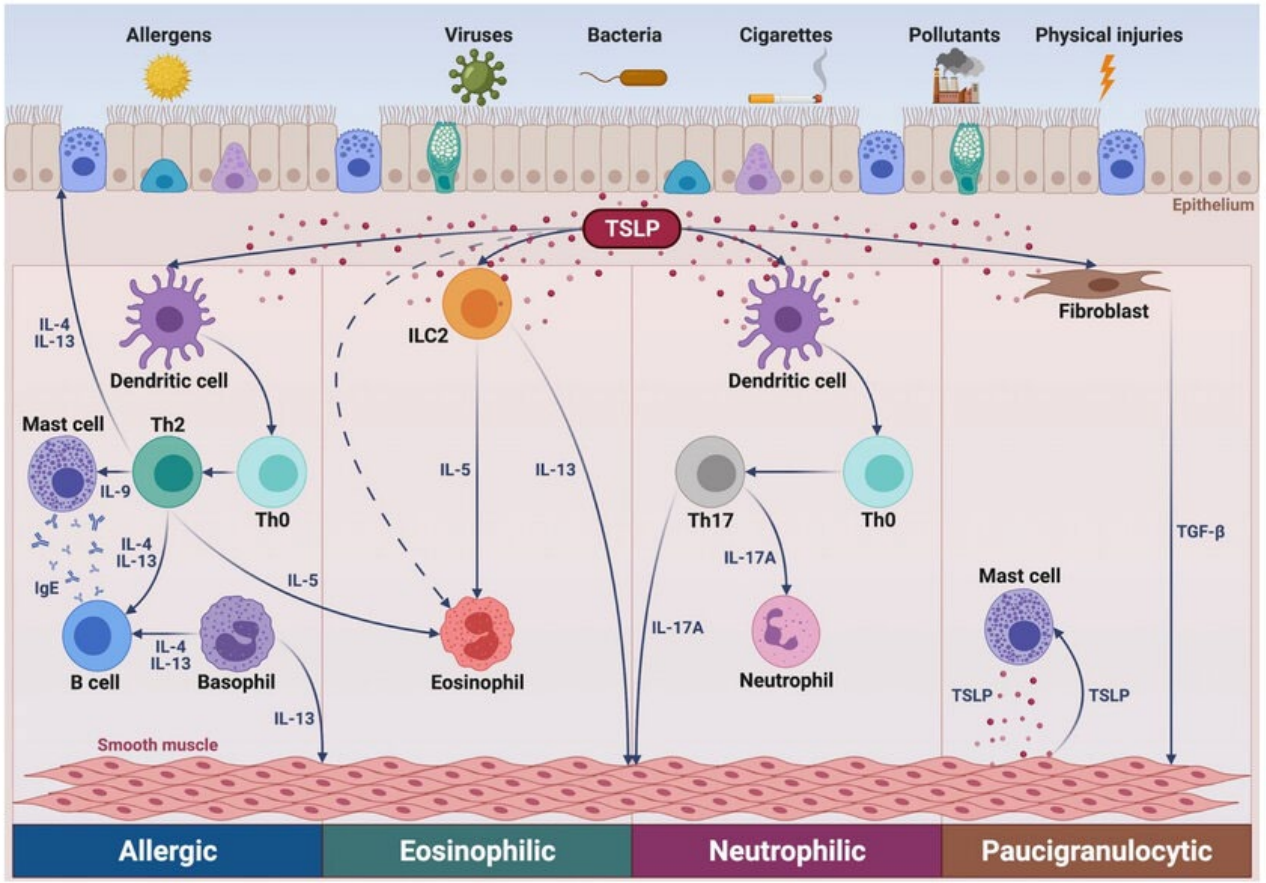
αTSLP/X(undisclosed 1)
αTSLP/X(undisclosed 2)
αTSLP/X (undisclosed 3)

All future development, clinical, and regulatory timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors

Targeting Thymic Stromal Lymphopoietin (TSLP)

Therapeutically Relevant Immune Target

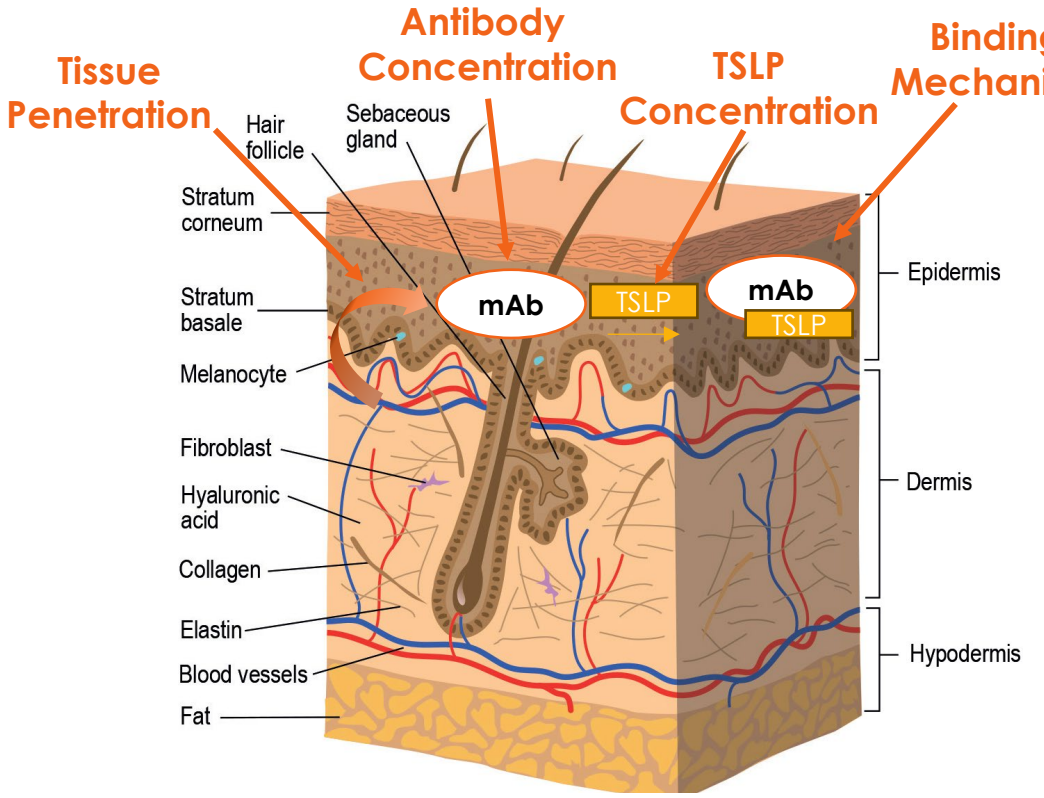
- Pleiotropic and broad activity
  - **Master regulator of type 2 (Th2) immune responses** at the barrier surfaces of skin and the respiratory/ gastrointestinal tract
  - **Drives eosinophilic and neutrophilic inflammation** and acts on a wide variety of adaptive, innate, and structural cells
  - **Broad activity:** 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



Adapted from Pelia *et al.*, Int J Mol Sci. 2021 Apr 22;22(9):4369

Driving High Efficacy in Dermatological Disease

High Potency Therapeutics are Key to Effectiveness



Adapted from Lavers *et al.*, Int J Aes Nursing 2017

- Abs must engage ligands at the site of action
- Key variables related to efficacy
  - TSLP concentration at site of lesion
  - Antibody concentration at site of lesion
    - Concentration of mAb in general circulation
    - Skin penetration of mAb
    - Dose
    - Potency
  - Binding Mechanism of mAb to TSLP
    - Binding affinity
    - Residence Time
  - Degree of TSLP reduction needed at site of lesion

Only 15% of mAb serum levels reach skin/site of lesion: Potency is Key to Efficacy

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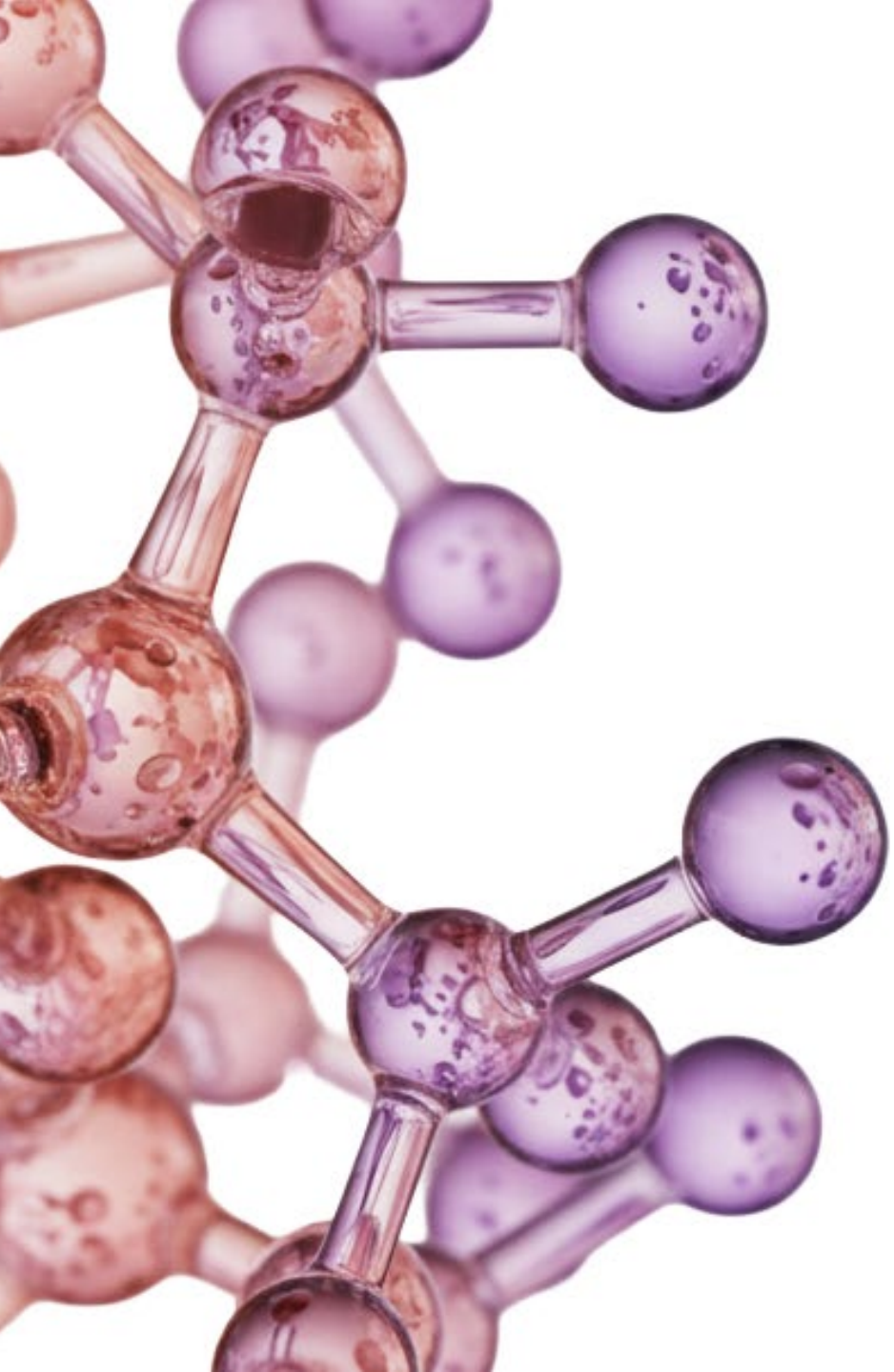

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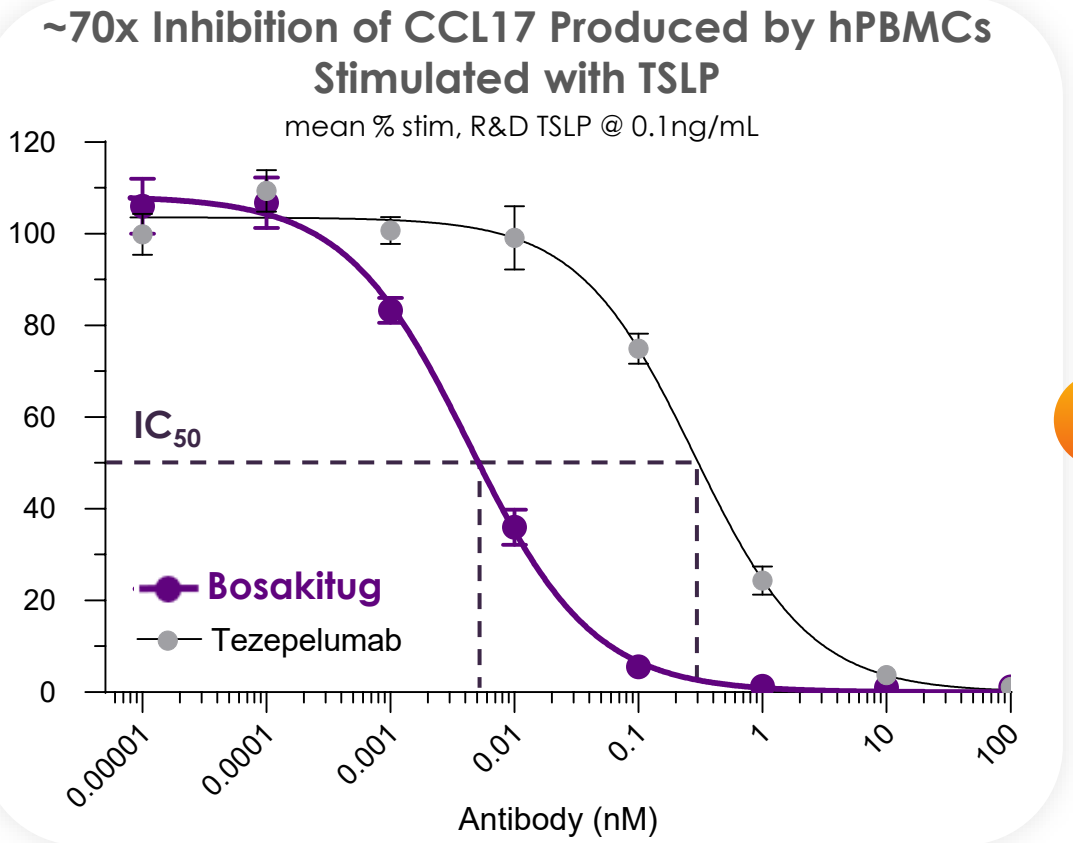
Bosakitug (ATI-045): Highly Differentiated Anti-TSLP Antibody Backbone

Best-in-Class Potential

Patient *Focused Innovation*

Bosakitug Key Properties



- 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 of up to 3 months

Bosakitug is ~70x More Potent than Tezepelumab, the Only Marketed Anti-TSLP mAb

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

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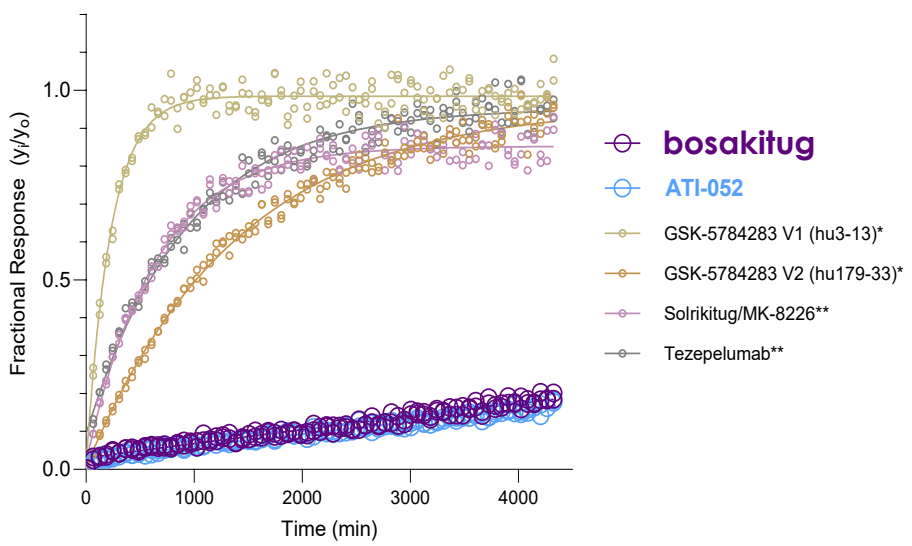
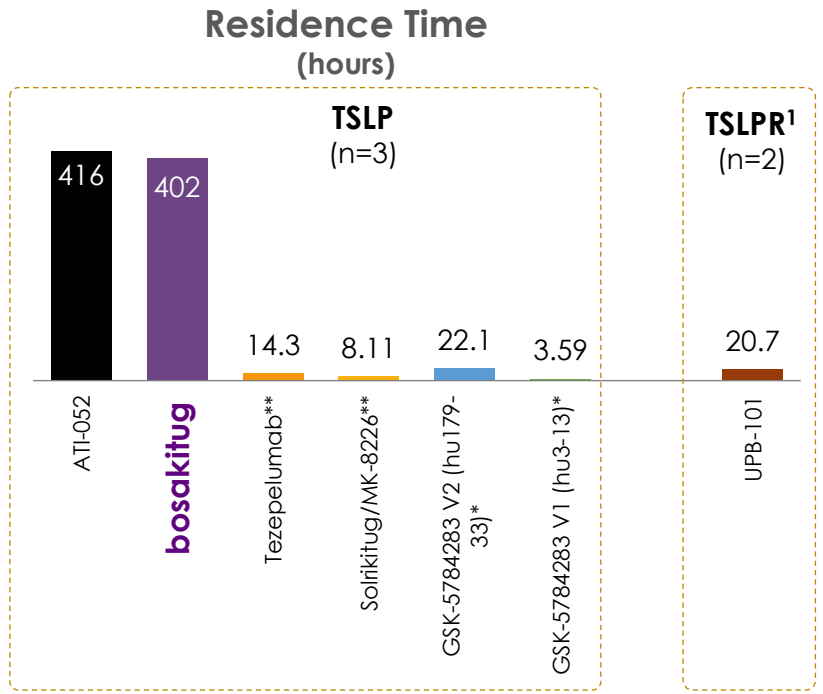
Bosakitug Key Properties

Lower Dissociation Rate = Longer Residence Time





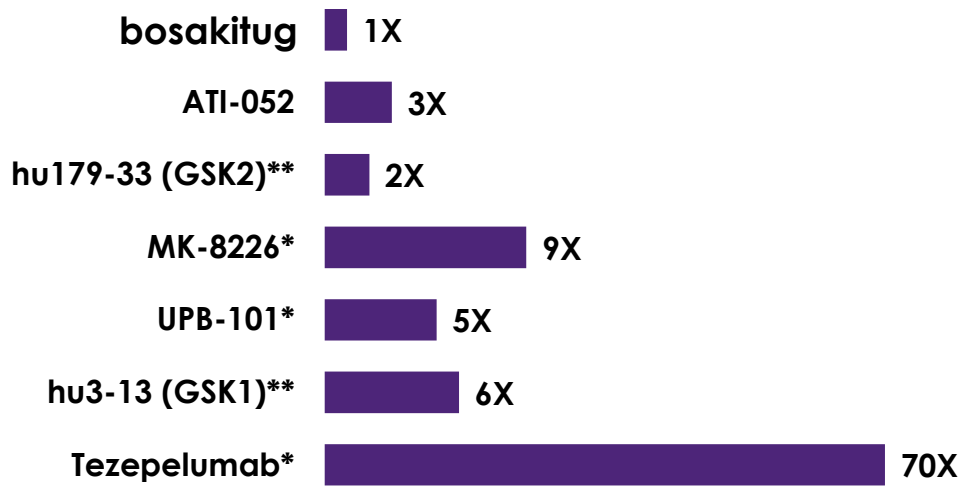
Bosakitug (and ATI-052) demonstrates very slow dissociation kinetics from TSLP

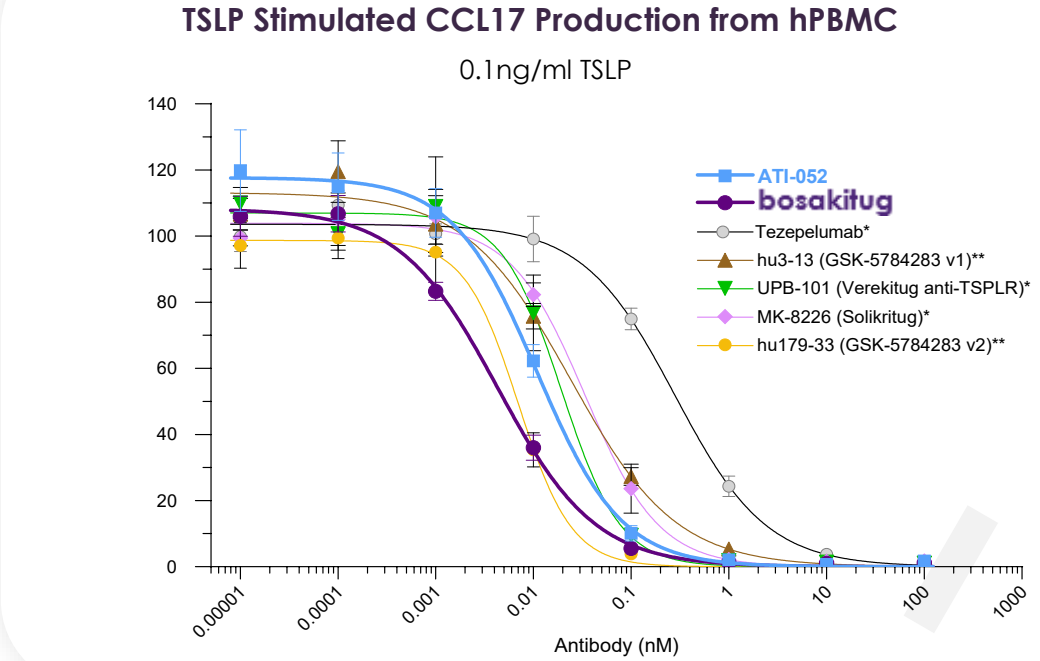
Residence time for Bosakitug (and ATI-052) is ~20-100x longer than comparator antibodies

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

Bosakitug Key Properties

Greater Potency Than Other TSLP/TSLPR Antibodies



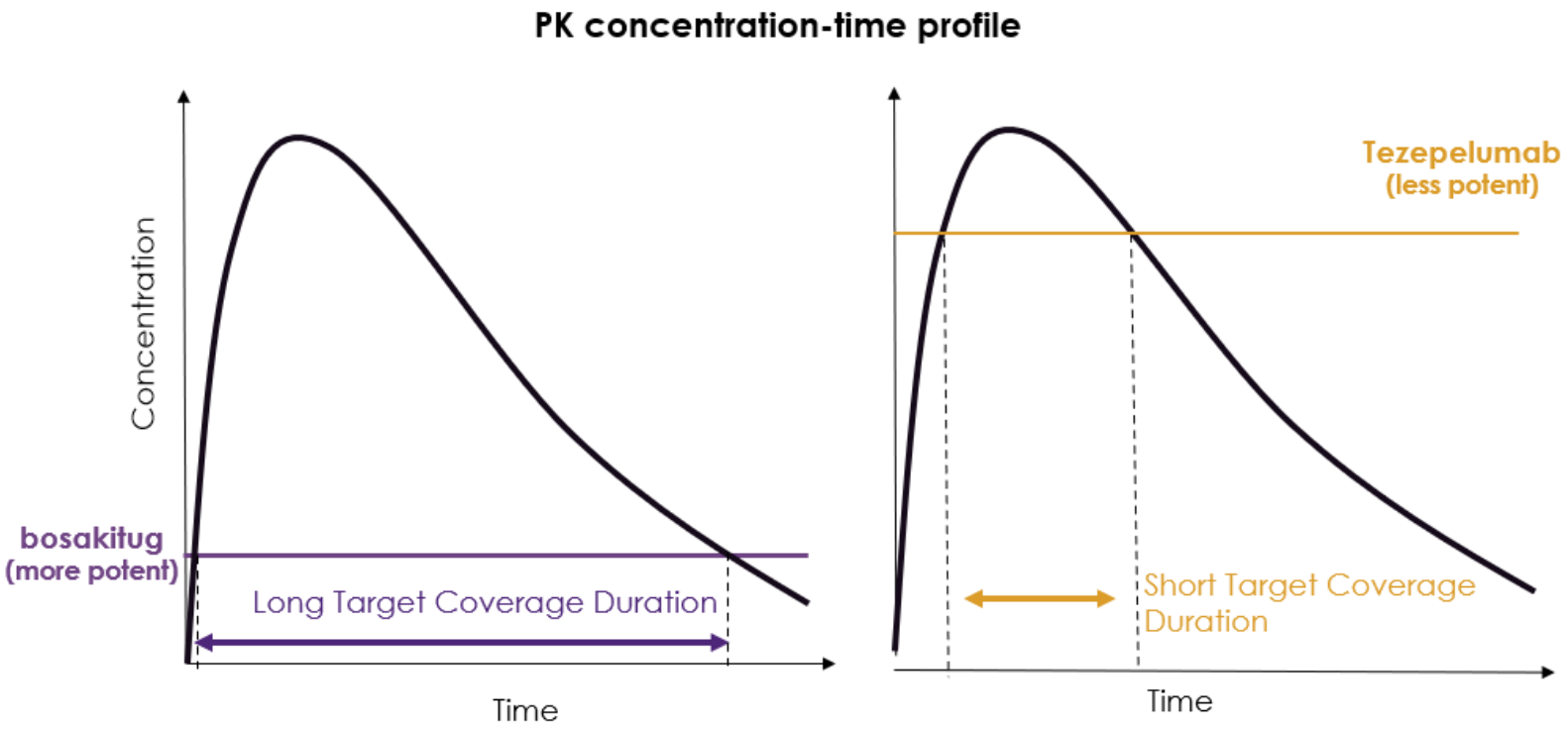


Bosakitug is the most potent of the TSLP/TSLPR antibodies evaluated in blocking CCL17 production

ATI-052 retains much of the potency for TSLP functional blockade

*Biosimilar; **Analog

Greater Potency Requires Lower Concentration to Exhibit the Same Effect



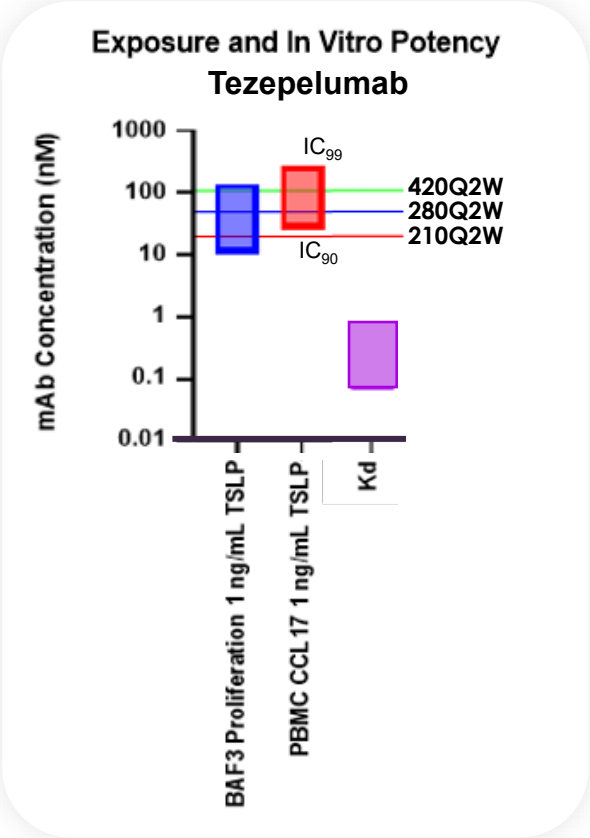
Bosakitug

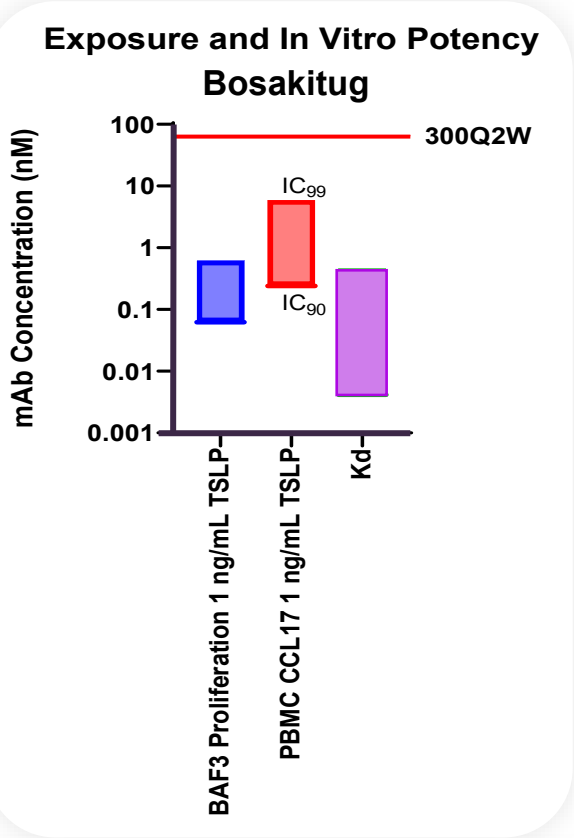
High affinity, long residence time, high potency

Best-in-Class Potential

Tezepelumab vs Bosakitug

Relationship of Potency and Exposure to Extent of TSLP Inhibition





- The highest dose of Tezepelumab may not cover the IC99 for TSLP at the site of action based on in vitro potency
- Bosakitug is expected to cover multiples over the concentration needed for 99% inhibition of TSLP at the site of action based on its in vitro potency

Bosakitug Potency Allows for Substantial Exposure Above 99% Inhibition of TSLP

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Bosakitug Key Properties

Uniquely Binds Both the N- and C-Terminus of TSLP

TSLP AA Sequence

N-Terminus

MKCLGQSKKEEVSFRKIFILQLVGLVLT[28]YDFTNCDFEKIKAAYLSTISKDLITYMSGTKSTEFNNTVSCSNRPHCLTEI
QSLTFNPTAGCASLAKEMFAMKTKAALAIWCPGYSETQINATQAMKKRRKRKVTTNKCLEQVSQLQGLWRRFNRPLLKQQ[159]

C-Terminus

Signal peptide
TSLP binding AA to TSLPR
TSLP Hot spot($R^{149/150/153}L^{156}$) to TSLPR
Projected Bosakitug(ATI-045)binding site
Tezepelumab binding site

The high affinity and low dissociation observed with Bosakitug/TSLP is a result of biparatopic binding that includes an N-terminal recognition site not observed with tezepelumab

Dual Binding Provides High Avidity and Low Dissociation

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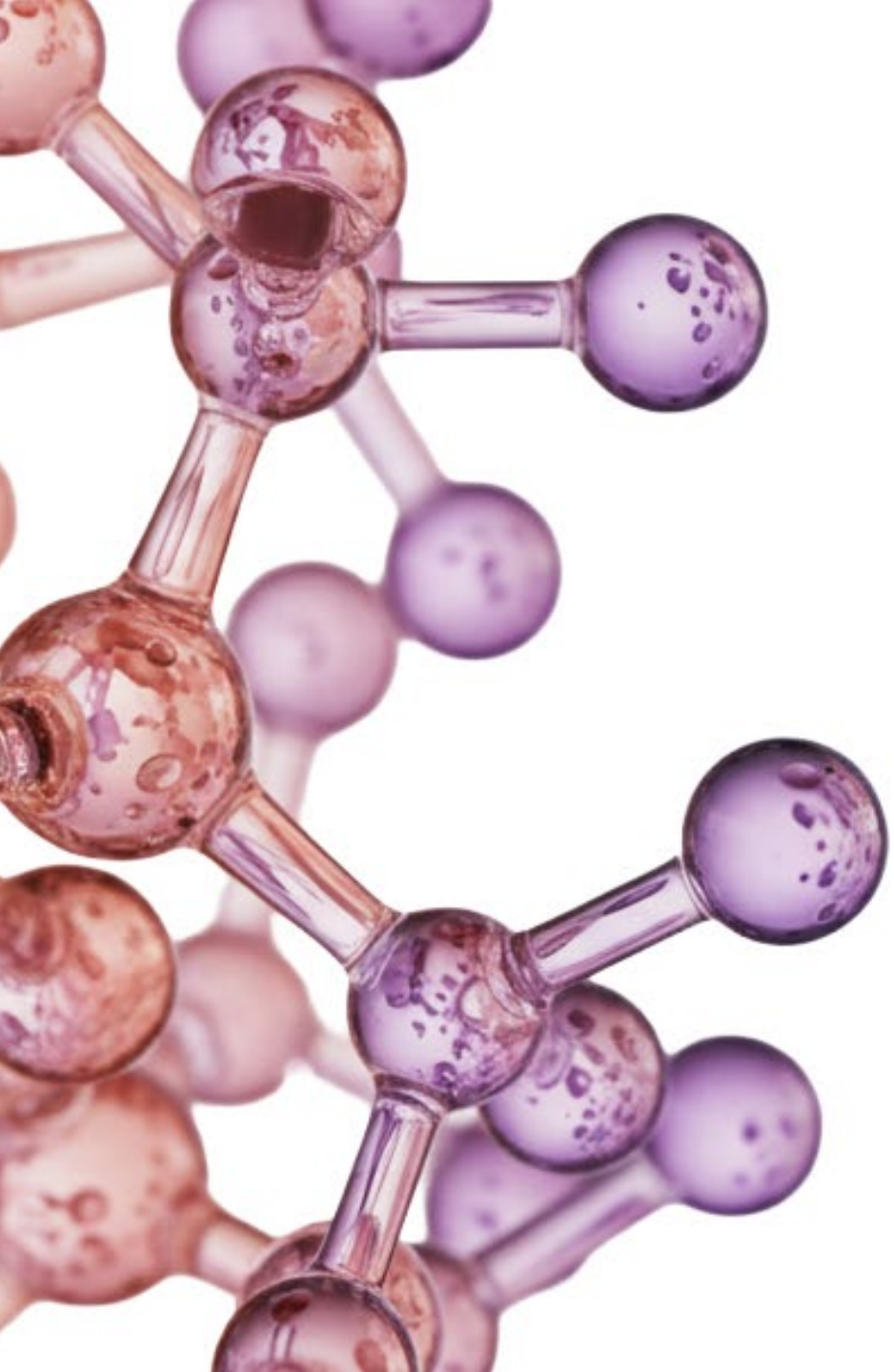
Bosakitug

Potential Best-in-Class Anti-TSLP Antibody

- Key properties support best-in-class potential
  - Greater potency than other TSLP/TSLPR antibodies
  - High affinity anti-TSLP mAb with long, natural half-life of 23 days
  - Unique binding mechanism, providing very low dissociation from TSLP
  - Very high residence time on TSLP, allowing for more sustained neutralization of TSLP
- In Vitro potency translated to substantial clinical activity in Phase 2a open label AD trial
- Clinically derisked: Data generated to date reinforce clinical confidence
  - Sustained clinical response after last dose
  - Pharmacokinetic (PK) data indicates long half-life; could support an extended dosing interval
  - Consistently strong safety and tolerability profile

ATI-052 utilizes the same Bosakitug anti-TSLP binding regions



ATI-052: Anti-TSLP x IL-4Rα First Generation Bispecific Antibody Program

Highly Potent and Bioactive Investigational Product Candidate

Patient *Focused Innovation*

Advantages of Multispecific Antibodies

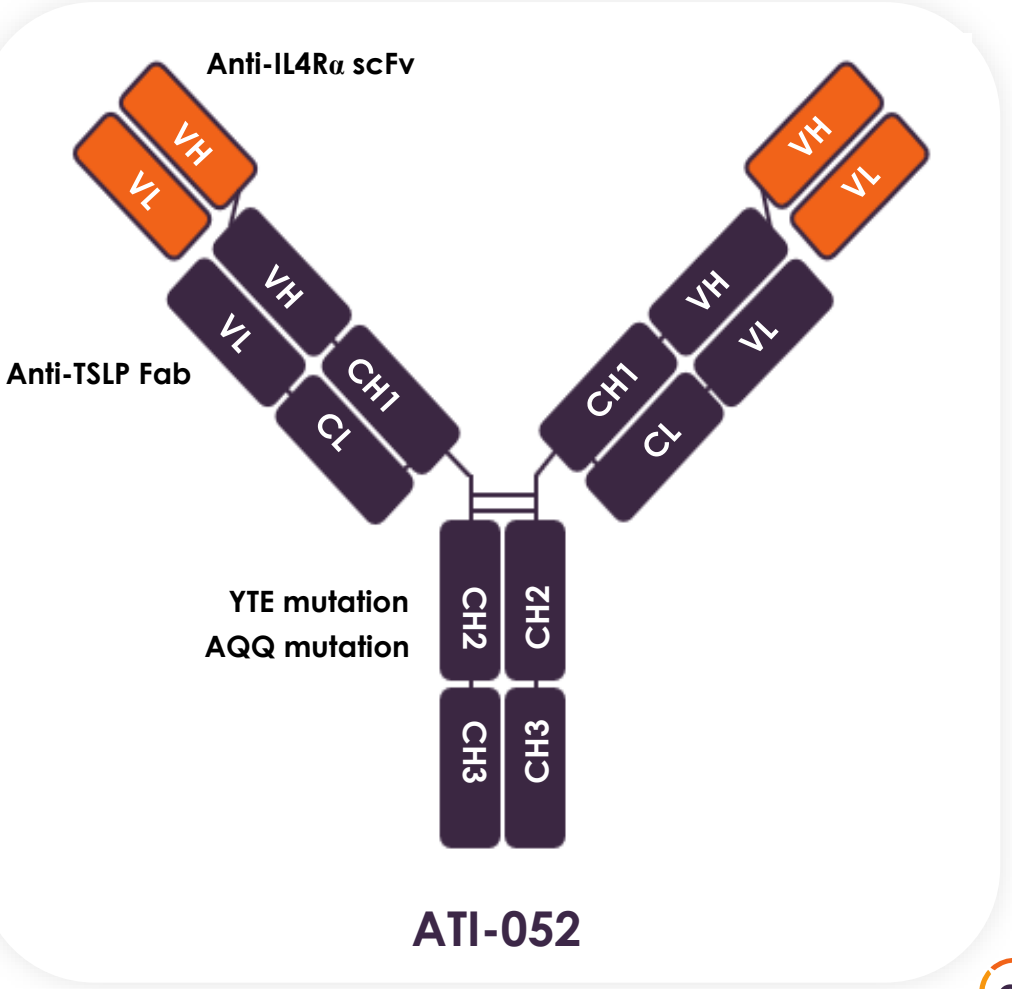
- **Increased efficacy ceiling** via multi-target engagement
- **Superior therapeutic window:** Enhanced efficacy with favorable safety profile
- **Reduced therapy resistance**
- **Extended dosing regimens** drive simplified treatment protocols
- Access to a projected BsAb **global market of $112 billion** (2030*)

*Precedence Research

ATI-052: Key Asset Highlights

Potential Best-in-Class Bispecific Anti-TSLP/IL-4Rα mAb

- Bispecific **utilizing same antibody binding regions of Bosakitug** combined with anti-IL-4Rα, inhibiting TSLP upstream and immune cells downstream of the Th2 cascade
  - Retains dissociation kinetics, residence time, and potency advantages of bosakitug over comparator Abs
- Anti-TSLP mAb component has Fc engineered to bind more tightly to FcRn, potentially extending half-life
- The AQQ mutation in the Fc silences effector functionality, thereby reducing off-target binding and potential toxicity
- Potential to show superior activity in certain dermatological and respiratory I&I disorders compared to approved therapies



ATI-052

Bispecific Binding Attributes ➞ Clinical Opportunity

Multispecific Binding → **Potential Clinical Efficacy**

Effective Binding of TSLP and IL-4Rα
ATI-052 binds both targets effectively; high affinity of either ligand is not altered by the binding of the other

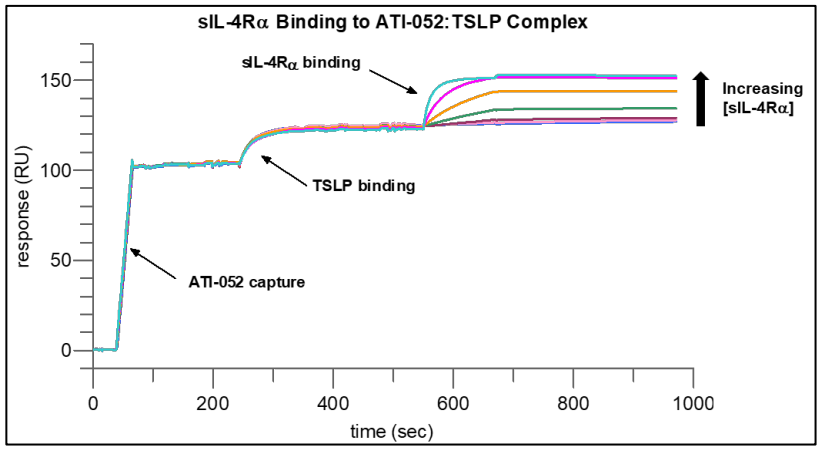
Simultaneous Binding of TSLP and IL-4Rα
High affinity to both ligands simultaneously: ATI-052 binds two molecules of TSLP and sIL4Rα

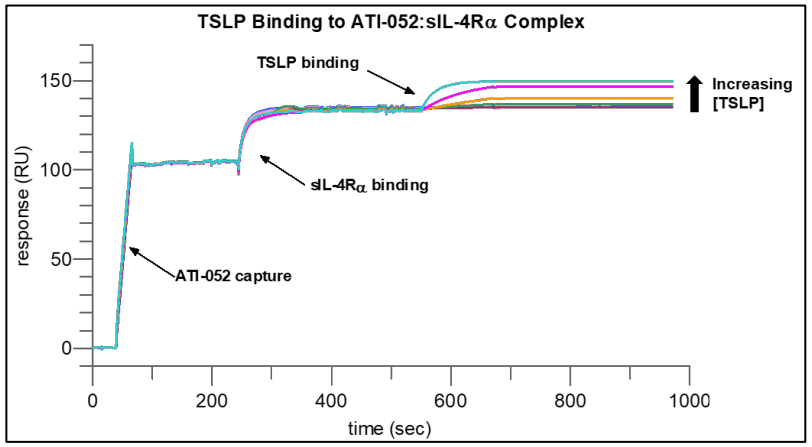
Higher Potency than Competitor Antibodies
Exhibits greater cellular bioactivity on CCL17 release than the combination of Tezepelumab and Dupilumab

Effective Blockade of IL-4 and IL-13
ATI-052 antagonism of IL4Rα blocks signaling of both IL-4 and IL-13

Concurrent Binding of TSLP and sIL4Rα to ATI-052

High Affinity to Both TSLP and IL-4Rα





Comparison of Affinity for sIL-4Rα Binding to ATI-052 or ATI-052:TSLP Complex

Parameter	ATI-052	ATI-052:TSLP
K_D (pM)	348	215

Comparison of Affinity for TSLP Binding to ATI-052 or ATI-052:sIL-4Rα Complex

Parameter	ATI-052	ATI-052:sIL-4Rα
K_D (pM)	41.2	33.9

ATI-052 Binds Both Targets Effectively

High affinity of either ligand is not altered by the binding of the other

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Concurrent Binding of TSLP and sIL4Rα to ATI-052

Simultaneous Binding of TSLP and IL-4Rα

Binding Sequence	TSLP:ATI-052 Stoichiometry*	sIL-4Rα:ATI-052 Stoichiometry*
ATI-052 capture / sIL-4Rα dose-response	n/a	2.25
ATI-052 capture / TSLP load / sIL-4Rα dose-response	1.82	2.10
ATI-052 capture / TSLP dose-response	2.04	n/a
ATI-052 capture / sIL-4Rα load / TSLP dose-response	1.82	1.97

** determined using molecular weights based on AA sequence, does not account for glycosylated species*

- ~2 molecules of sIL-4Rα bound to ATI-052 in the absence (2.25:1) and presence (2.10:1) of TSLP
- ~2 molecules of TSLP bound to ATI-052 in the absence (2.04:1) and presence (1.82:1) of sIL-4Rα

High Affinity to Both Ligands Simultaneously:

ATI-052 binds two molecules of TSLP and sIL4Rα

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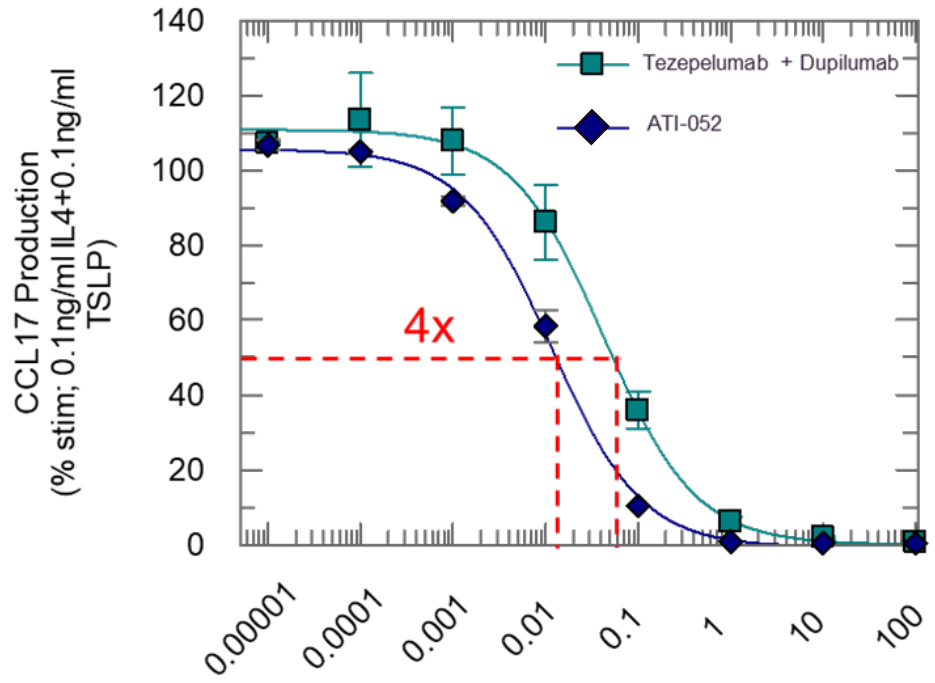
Comparison of ATI-052 vs Dupilumab + Tezepelumab

ATI-052 Demonstrates Greater Potency than the mAb Combination



mAb Concentration [nM]	
Antibody	**IC50 (nM)**
ATI-052	0.016
Dupilumab + Tezepelumab	0.069
Fold change	4.3

ATI-052 is Significantly More Potent than the Combination of Dupilumab and Tezepelumab

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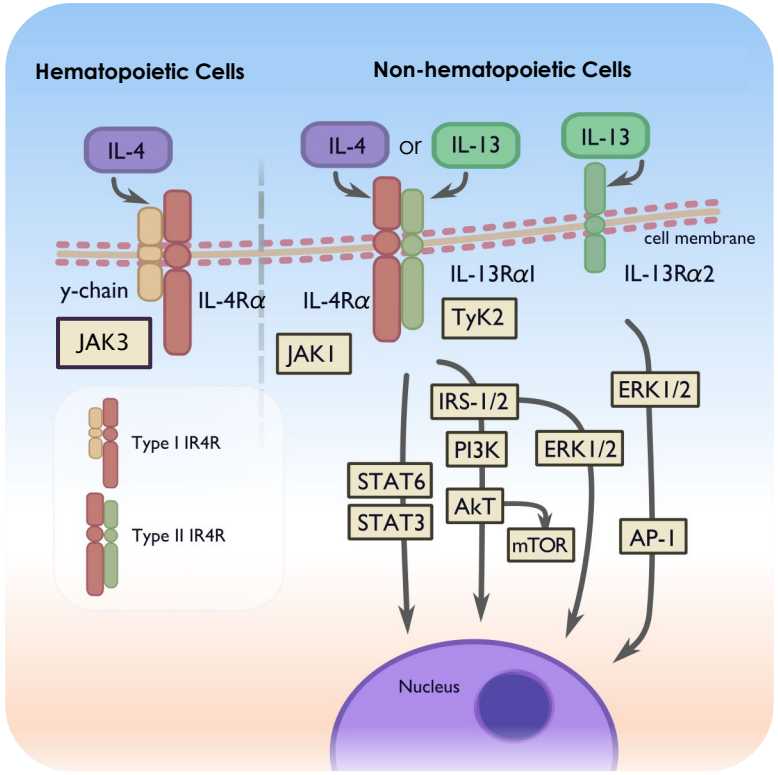
Impact of ATI-052 on IL-4 and IL-13 Receptor Activation



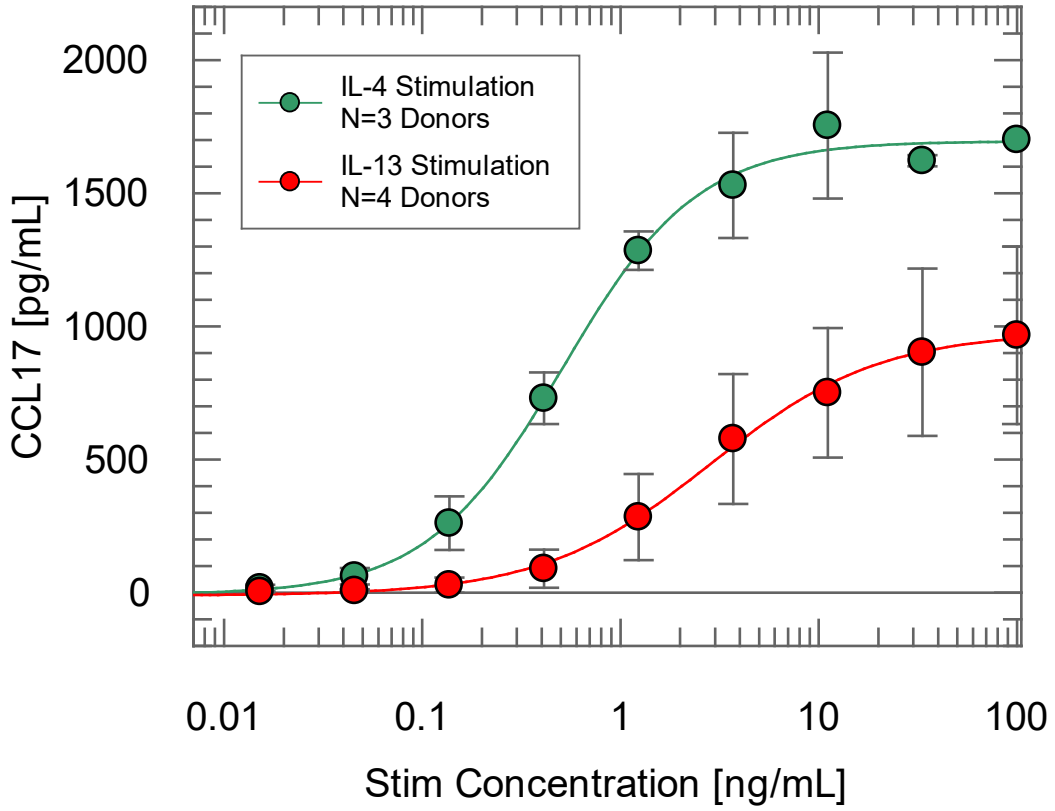
Adapted from Shi *et al.*, nt. J. Mol. Sci. 2021, 22(6), 2998

- IL-4 and IL-13 both bind to a receptor complex composed of the IL-4Rα and IL-13Rα1
- IL-4 also signals through the IL-4Rα and common gamma-chain (γc)
- Upon binding, the receptor complex activates the receptor-associated kinases (JAK1 and Tyk2), leading to the recruitment and phosphorylation of STAT6

Hypothesis:

If IL-4Rα is required for both IL-4 and IL-13 mediated signaling, then ATI-052 antagonism of the IL4Rα should block signaling of both IL-4 and IL-13

Comparison of CCL17 Levels Induced by IL-4 or IL-13



- IL-4 is ~10 fold more potent than IL-13 in stimulating CCL17 production from PBMCs (EC80 of ~1.5 ng/mL for IL-4 compared to 11.1 ng/mL for IL-13)
- IL-4 elicits consistently high concentration of CCL17 whereas IL-13 exhibits lower and greater subject-to-subject variability

IL-4 Appears to be a More Dominant and Consistent Driver of Downstream Chemokine Activation Compared to IL-13

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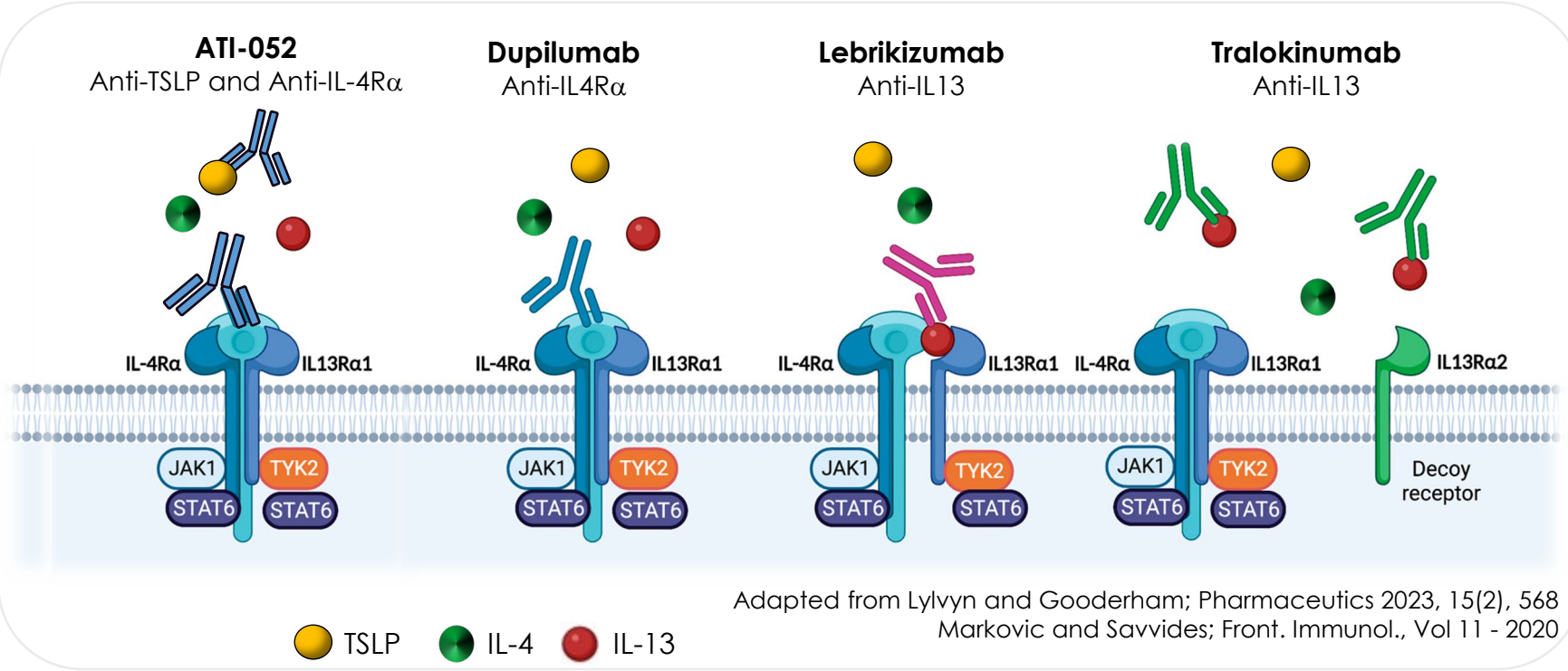
Comparison to Marketed Biologics that Inhibit IL-4 +/- IL-13 Signaling

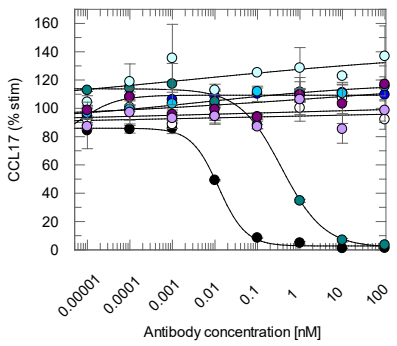


Adapted from Lylvyn and Gooderham; Pharmaceutics 2023, 15(2), 568
Markovic and Savvides; Front. Immunol., Vol 11 - 2020

Data Support the Need for Inhibition of Both IL-4 and IL-13 to be Effective in Respiratory Indications

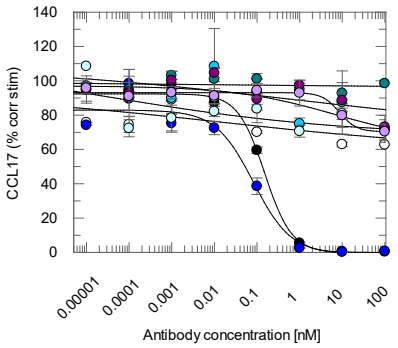
Comparison of IL-4/IL-13 Monoclonal Antibodies

TSLP-induced CCL17 release



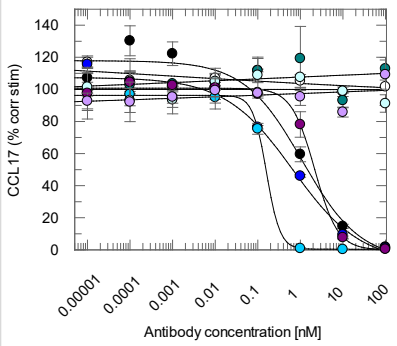
Antibody	IC50 [nM]
ATI-052	0.0077
Dupilumab	>100
Lebrikizumab	>100
Tezepelumab	0.4083
Tralokinumab	>100

IL-4-induced CCL17 release



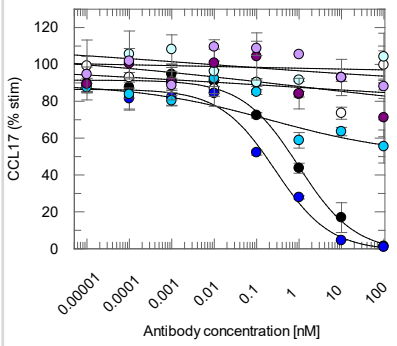
Antibody	IC50 [nM]
ATI-052	0.18
Dupilumab	0.09
Lebrikizumab	>100
Tezepelumab	>100
Tralokinumab	>100

IL-13-induced CCL17 release



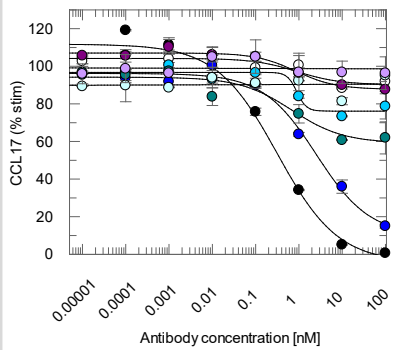
Antibody	IC50 [nM]
ATI-052	0.74
Dupilumab	0.57
Lebrikizumab	0.55
Tezepelumab	>100
Tralokinumab	1.83

IL-4+IL-13-induced CCL17 release



Antibody	IC50 [nM]
ATI-052	0.97
Dupilumab	0.27
Lebrikizumab	>100
Tezepelumab	N/A
Tralokinumab	>100

TSLP/IL-4/IL-13-induced CCL17 release



Antibody	IC50 [nM]
ATI-052	0.3625
Dupilumab	2.0217
Lebrikizumab	>100
Tezepelumab	>100
Tralokinumab	>100

- **ATI-052**
- Dupilumab
- Tezepelumab
- Tralokinumab
- Lebrikizumab
- IgG1
- IgG4k
- IgG4l

ATI-052 Exhibits Broadest Activity Among the Biologics Tested

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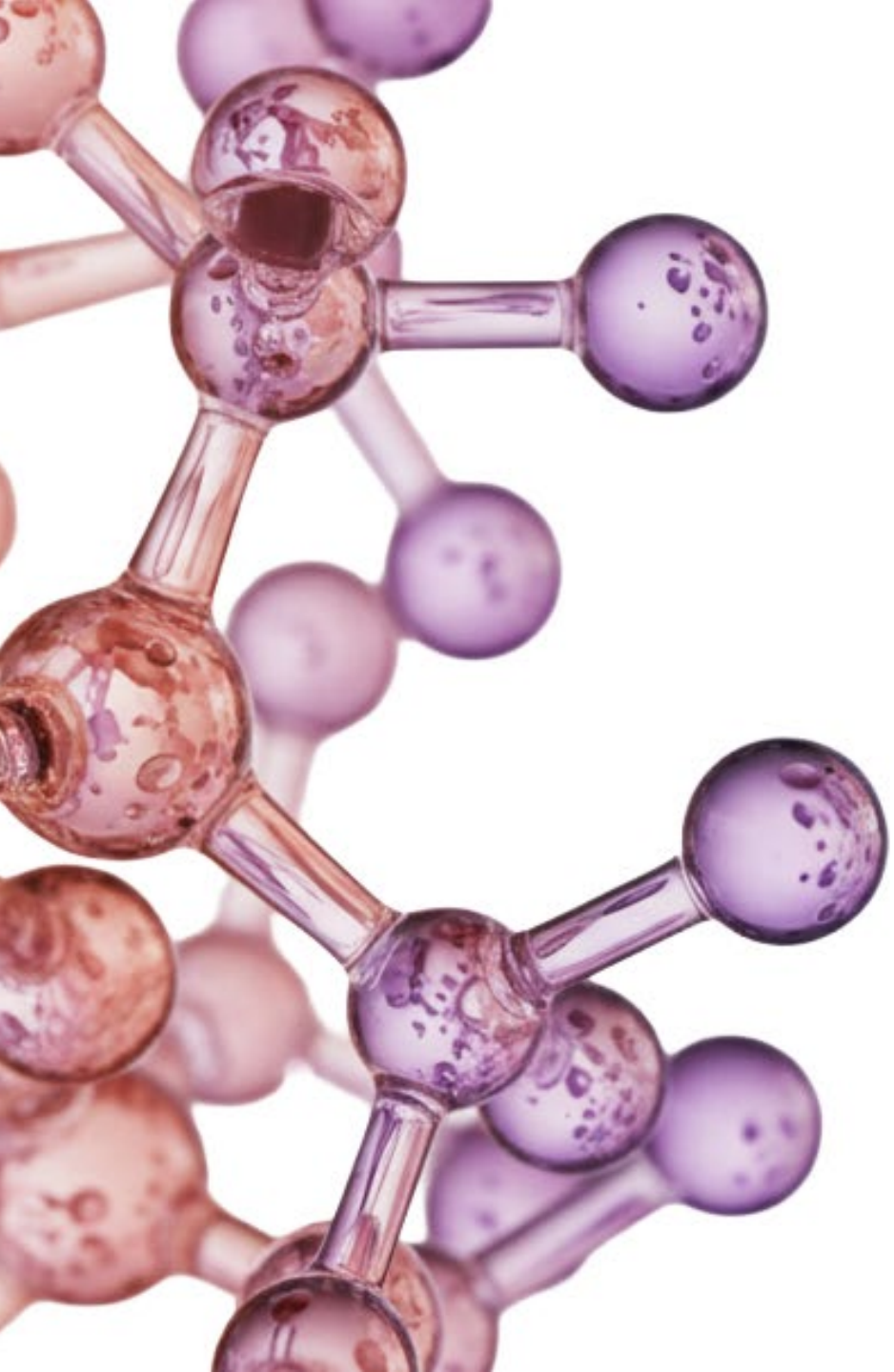
ATI-052

Summary

- Bispecific antibodies are engineered to have two distinct binding domains that can efficiently bind to two targets simultaneously
  - ATI-052 has two distinct binding domains that independently bind both TSLP and IL-4Rα with high affinity, efficiency and completeness
- YTE mutation in the Fc to allow for enhanced half-life
- AQQ mutation in the Fc silences effector functionality, reducing off-target binding and potential toxicity
- Inhibits TSLP and antagonism of IL-4Rα also blocks the signaling of both IL-4 and IL-13
- Highly potent; more potent than the combination of Tezepelumab and Dupilumab in inhibiting CCL17 production from the combination of TSLP and IL-4 treated PBMCs



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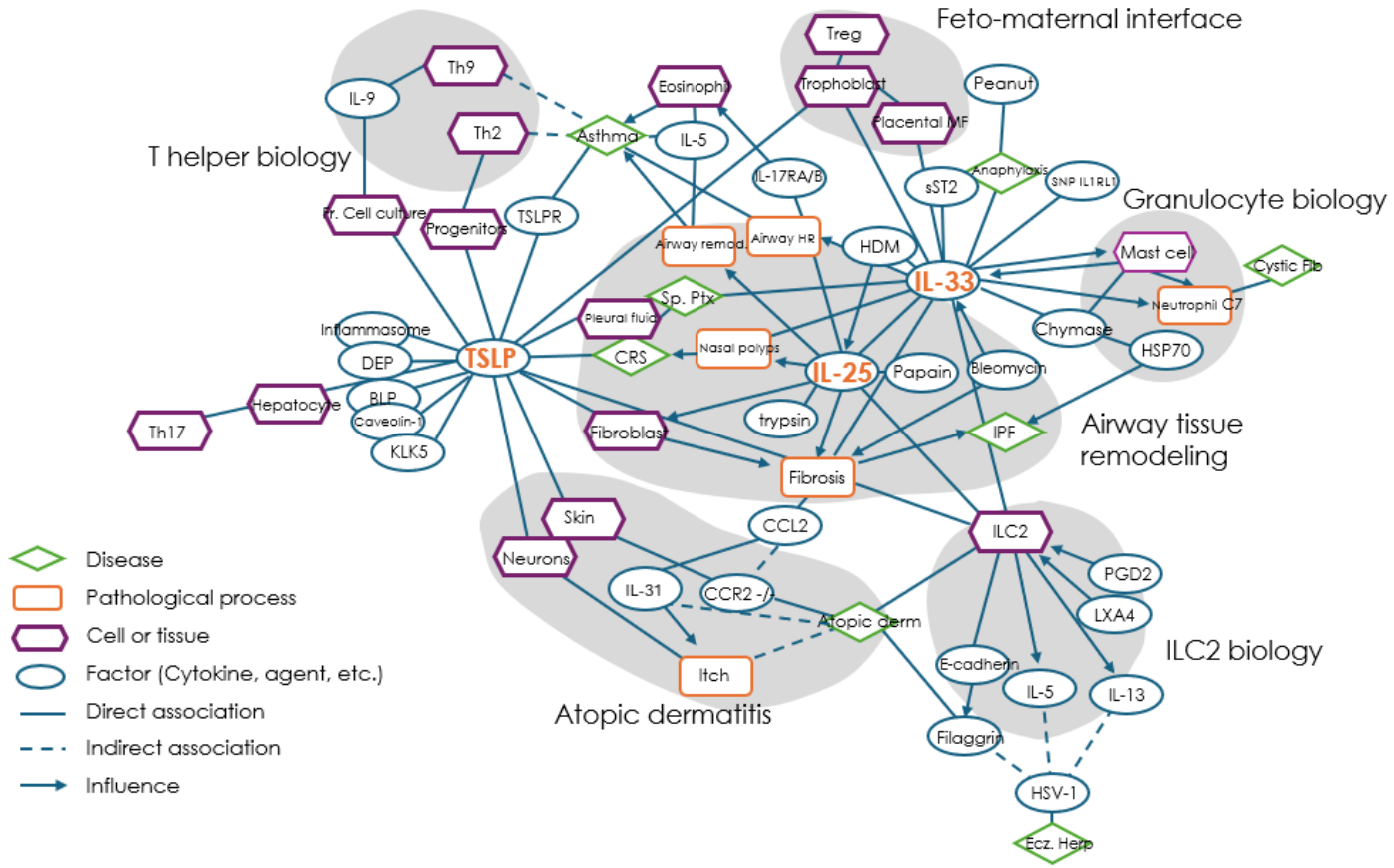
Developing Next-Generation Bispecific Antibodies

Patient *Focused Innovation*

Next Generation Bispecific Antibodies

Designing Optimal Synergies with TSLP for I&I Diseases



Modified from Divekar *et al.*, 2015

Critical role of epithelium-derived cytokines in dermatological and respiratory / airway I&I disorders guides design of potent and selective bispecific antibodies

Opportunities for Aclaris Next Generation BsAbs

Multispecific Antibodies Can Expand Therapeutic Optionality

Pruritis (Itch)	• TSLP combinations with itch mediators may have a positive impact on itch and QoL in AD and other dermatological diseases
Alarmin Combinations	• Could impact initiation of allergic response and associated downstream inflammation and enhance anti-viral immunity during respiratory virus infections
Synergistic Effect with TSLP	• May amplify immune responses, particularly the development of Type 2 inflammation, which is central to allergic diseases like asthma, AD, and others
Eosinophil-Driven Diseases	• Allergic disorders, skin conditions, fungal infections, autoimmune diseases, others • Causes multiple disorders including eosinophilic cystitis, fasciitis, pneumonia, gastrointestinal disorders, granulomatosis with polyangiitis, hypereosinophilic syndrome

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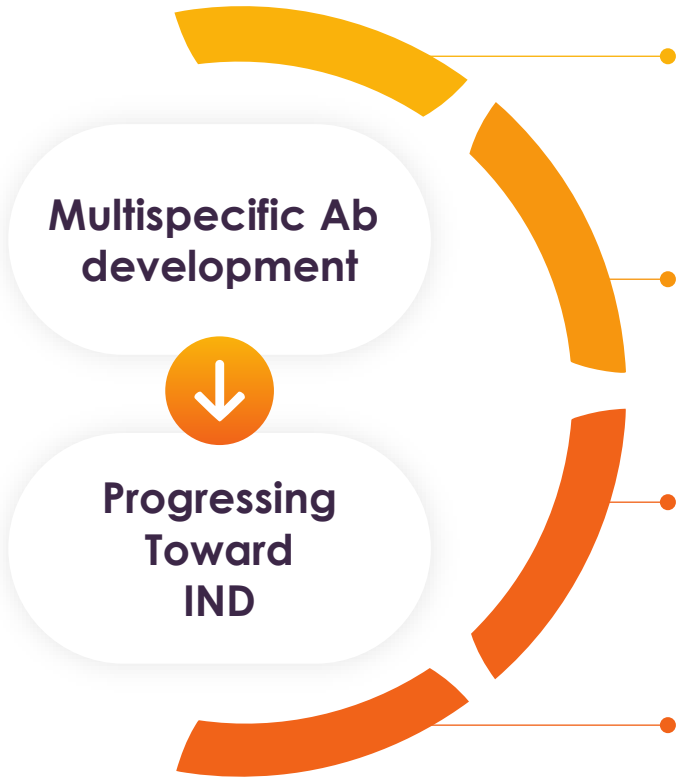
Next Generation Bispecific Antibodies

Progressing Toward IND



- Multispecific approach enables synergistic target binding and addresses shortcomings of multi-drug administration
- Initial assessment of bispecific targets completed (αTSLP + undisclosed)
- Campaigns progressing: Hit optimization toward lead candidate selection ongoing
- Additional bispecific and trispecific modalities under initial consideration

Targeting first IND from bispecific antibody development efforts in 2027

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Broad Clinical and Preclinical I&I Pipeline

Potential Best-in-Class Inhibitors of Immunoinflammatory Cascade

Oral Kinase Inhibitors

ITK Franchise

First Generation

ATI-2138
ITK/JAK3
Phase 2a Complete

Next Generation

ITK Selectives
Preclinical Development
ITK | ITK/TXK

Next Gen IND: 2H 2026

Biologics

Antibody Franchise

Monoclonal Antibodies

Bosakitug (ATI-045)
αTSLP
Phase 2 Ongoing

Multispecific Antibodies

ATI-052
αTSLP/IL-4Rα
Phase 1a/1b Ongoing

Next Gen
Multispecifics
Discovery

αTSLP/X (undisclosed 1)
αTSLP/X (undisclosed 2)
αTSLP/X (undisclosed 3)

Initial IND: 2027

Other multispecific antibodies in discovery

All future development, clinical, and regulatory timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors

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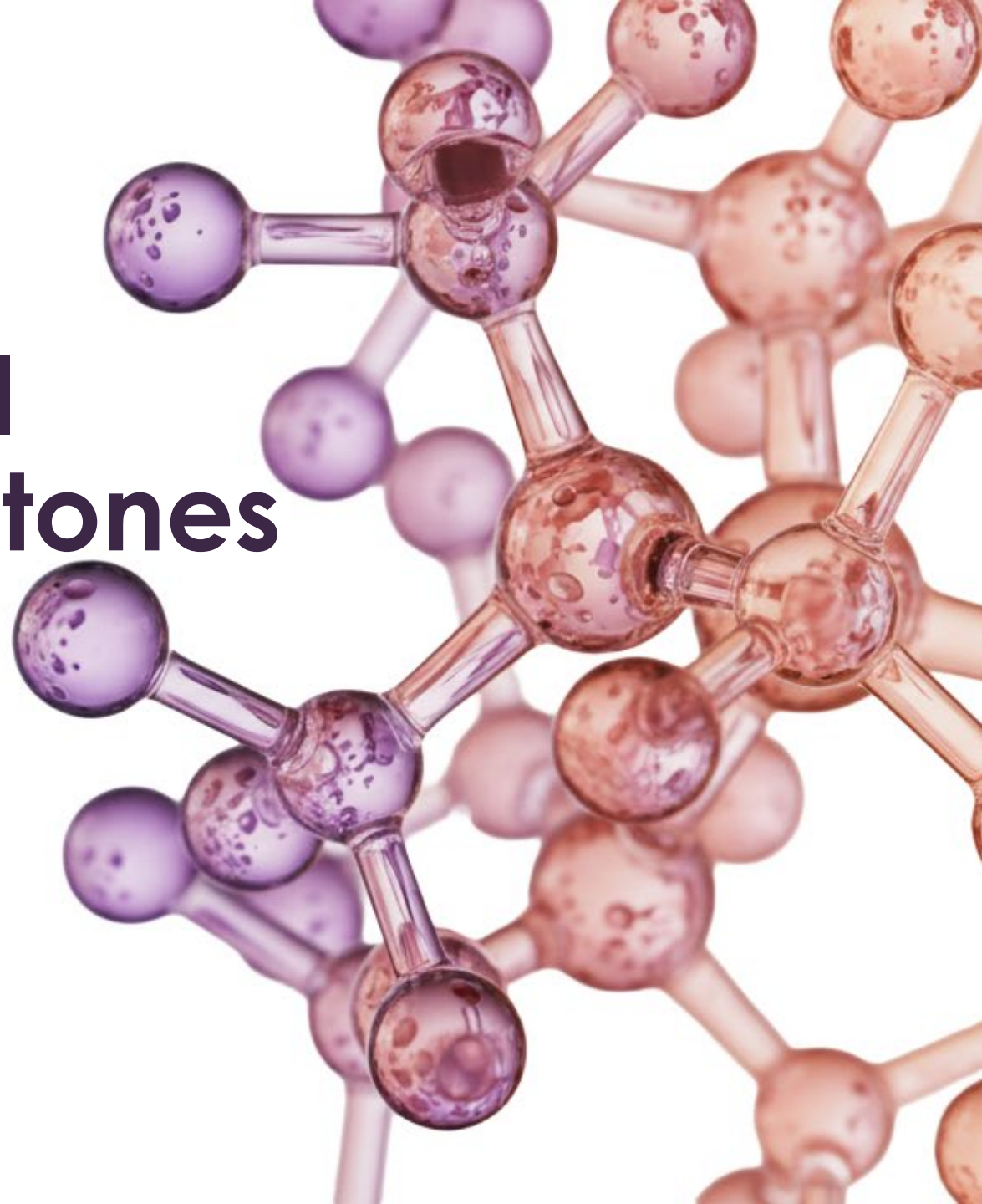
Efficient Clinical Trial Execution and Milestones

Derisking Small and Large Molecule Assets with Time- and Cost-Efficient Clinical Evaluation

Jesse Hall, MD
Chief Medical Officer



Patient *Focused Innovation*

Broad Clinical and Preclinical I&I Pipeline

Potential Best-in-Class Inhibitors of Immunoinflammatory Cascade

Oral Kinase Inhibitors

ITK Franchise

First Generation

ATI-2138
ITK/JAK3
Phase 2a Complete

Next Generation

ITK Selectives
Preclinical Development
ITK | ITK/TXK

Next Gen IND 2H 2026

Biologics

Antibody Franchise

Monoclonal Antibodies

Bosakitug (ATI-045)
αTSLP
Phase 2 Ongoing

ATI-052
αTSLP/IL-4Rα
Phase 1a/1b Ongoing

Multispecific Antibodies

Next Gen
Multispecifics
Discovery

αTSLP/X (undisclosed 1)
αTSLP/X (undisclosed 2)
αTSLP/X (undisclosed 3)

Initial IND: 2027

Other multispecific antibodies in discovery

All future development, clinical, and regulatory timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors

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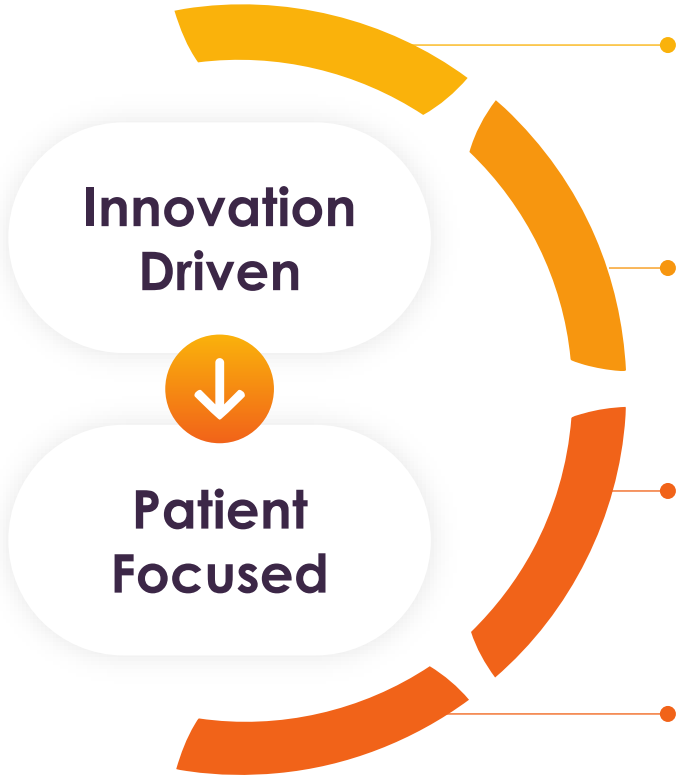
Aclaris Therapeutics

Innovating in Immuno-Inflammatory Disorders



Leadership in I&I/immuno-dermatology
Potential Best-in-Class molecules and "white space"

Multiple shots on goal with a diversified pipeline

Near term catalysts expected in next 6-12 months and beyond

Strong cash runway to execute on Aclaris clinical programs

Advancing potential industry-leading inhibitor franchises designed to address validated, therapeutically-relevant immune targets

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Broad Immunology Development Pipeline

*This trial is sponsored and conducted by Chia Tia Tianqing Pharmaceuticals Group, Co., Ltd. ("CTTQ") or its affiliates; Aclaris will not develop bosakitug in this indication on its own.

All future development, clinical, and regulatory timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors

Clinical Focus in 2025

2025 provides foundation for multiple ongoing clinical programs and data readouts in 2026

2025 clinical goals:

- Program execution, financial discipline
- Establishment of foundation for continued execution in 2026 and beyond

Fully integrated Biosion molecules and team members and have continued to build out our clinical capabilities

Derisking of clinical programs:

- Clinical validation of ITK pathway
- Focused on enrolling patients that meet the strict enrollment criteria
- Advancing the ATI-052 program in HV
- Preparing for new INDs in 2026 and beyond

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Portfolio Execution

Strong Execution in 2025 Creates Packed 2026

	2025	2026
ATI-052	IND filed and cleared Phase 1a FPI in NA 6-month tox dosing started 3Q25 Phase 1a LPI: complete dosing Preliminary PK results in house	Phase 1a SAD/MAD (PK Profile, ADA, etc.) top line results Target Engagement (ex-vivo assay in HV) Initiation of Phase 1b POC Phase 1b top line results
Bosakitug	IND filed and cleared Phase 2 FPI in NA	Top line results from AD Phase 2
ATI-2138	AD Positive Phase 2a top line results Completion of chronic tox studies	Initiation of Phase 2 in 2nd Indication
ITK selective		IND and prep for clinical start

All future development, clinical, and regulatory timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors

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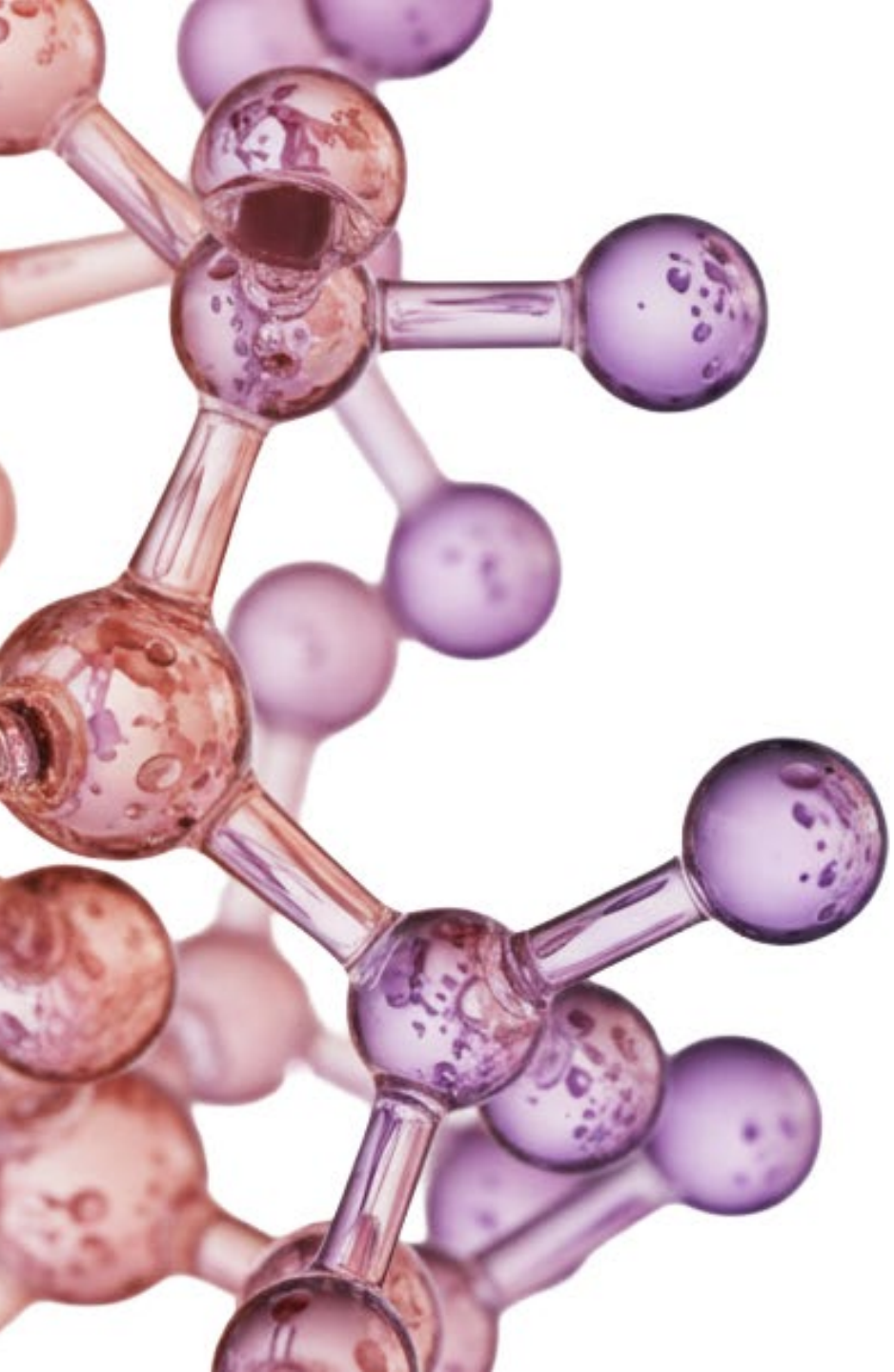

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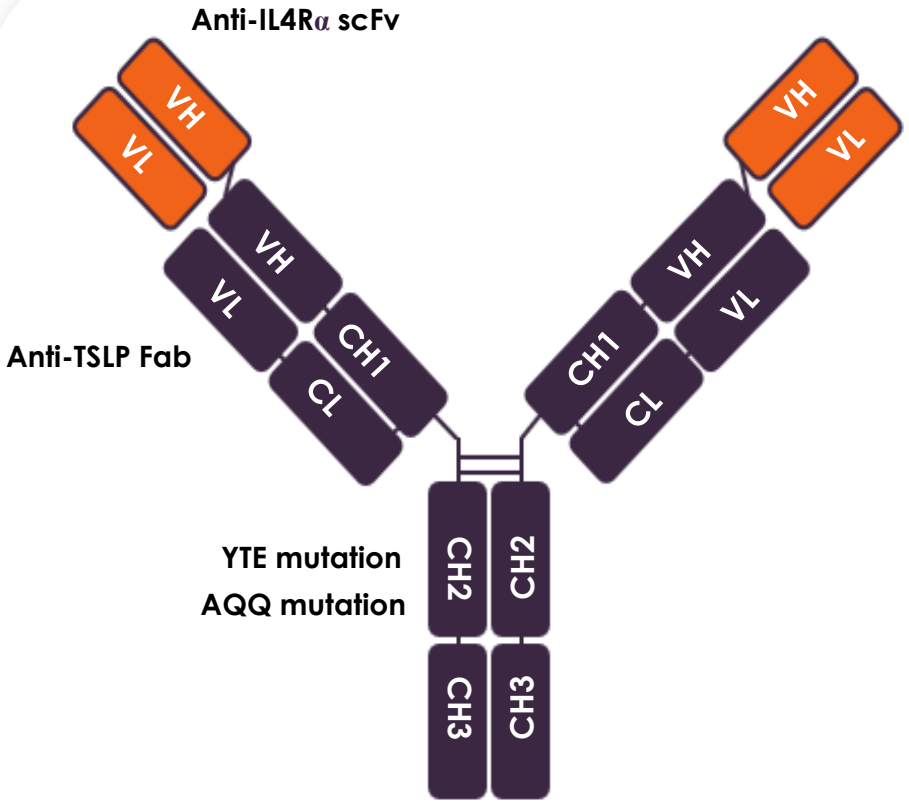
ATI-052: Anti-TSLP x IL-4Rα Bispecific Antibody Program

Highly Potent and Bioactive Investigational Product Candidate

ATI-052: Key Asset Highlights

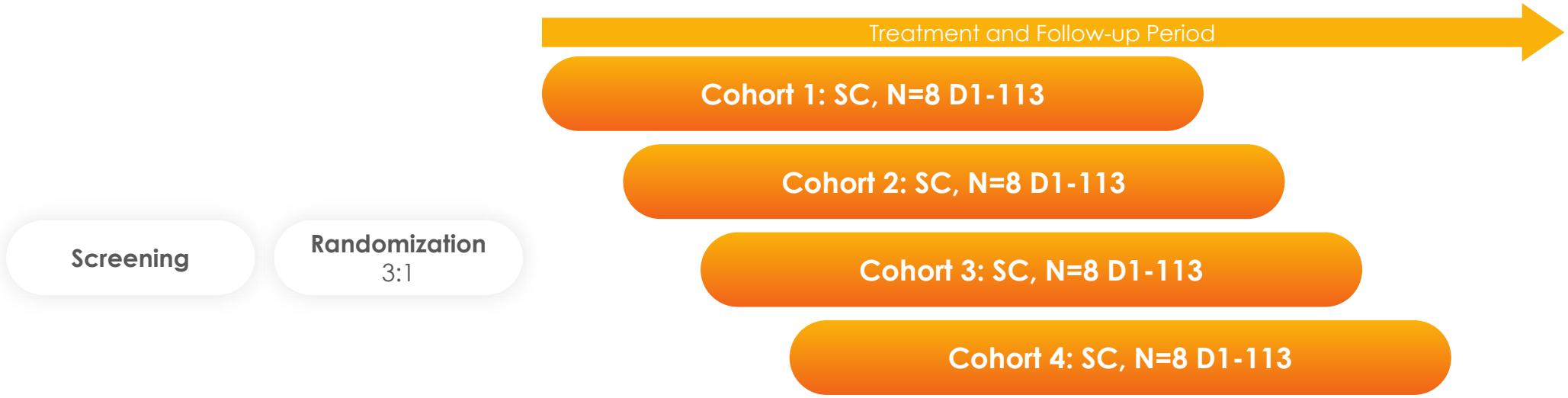
Potential Best-in-Class Bispecific Anti-TSLP/IL-4R mAb

- **Same antibody binding regions of ATI-045** + IL-4Rα
  - Retains dissociation kinetics, residence time, and potency advantages
- **Half-life enhanced:** Engineered to bind more tightly to FcRn
- **Reduced off-target binding:** Engineered to silence effector functionality
- **Significantly more potent** than the combination of dupilumab and tezepelumab
- **Potential to show superior activity** in certain dermatological and respiratory I&I disorders

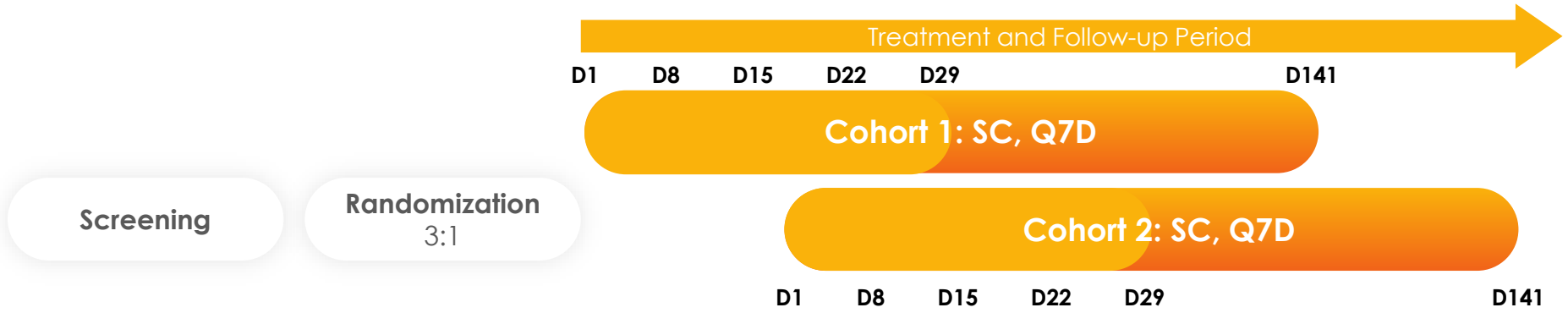


Placebo Controlled Phase 1a/1b Program Ongoing

Part A Single Ascending Dose (SAD) in Healthy Volunteers



Part B Multiple Ascending Dose (MAD) in Healthy Volunteers



Phase 1a/1b ATI-052 Program

Anticipated Key Learnings and Milestones

Key Learnings Expected in 2025

- Initial PK
- Safety and Tolerability
- TMDD role
- Indications of prolonged exposure

Expected Milestones

- Complete SAD/MAD assessment YE 2025
- SAD/MAD results 1Q 2026
- Initiate Phase 1b POC trial in asthma 1H 2026
- Initiate Phase 1b POC trial in AD 1H 2026
- Phase 1b top line POC results 4Q 2026
- Full PK profile (half-life, ADA, etc.)
- Pathway engagement ex-vivo from HV study
- Pathway engagement in diseased population

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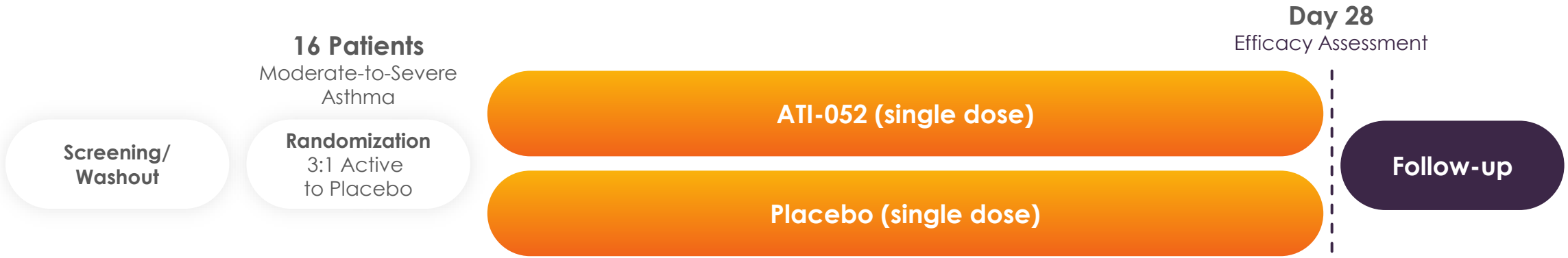
Next Steps with ATI-052

Expected Asthma Phase 1b POC Study Design



Patient Selection	Moderate-to-severe defined as (GINA 3-5) adult asthmatics, excluding prior biologics	Type 2 asthma with active inflammation: FeNO baseline ≥ 25 ppb, Blood Eos ≥ 150
Primary Endpoint	To evaluate the safety and tolerability of ATI-052 compared to placebo in patients with moderate-to-severe asthma	
Other endpoints Day 28	Key Clinical Efficacy Assessment	Emphasis on PD assessments: FeNO, FEV1, Blood Eos, TARC (CCL17), Periostin, IGE, Cytokines (IL-4,IL-5,IL-13)

Asthma Trial Expected to Initiate 1H 2026

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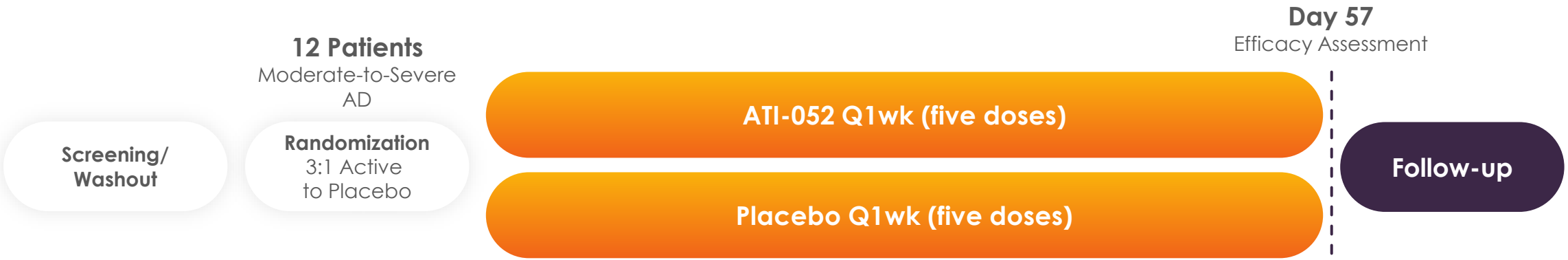
Next Steps with ATI-052

Expected Atopic Dermatitis (AD) Phase 1b POC Study Design



Patient Screening	Central photography to confirm diagnosis and extent of disease
Primary Endpoint	To evaluate the safety and tolerability of ATI-052 compared to placebo in patients with moderate-to-severe atopic dermatitis
Other Endpoints	AD clinical efficacy assessments (EASI, BSA, IGA) PD endpoints measured by assays including lesional and non-lesional skin tape strips

Atopic Dermatitis Trial Expected to Initiate 1H 2026

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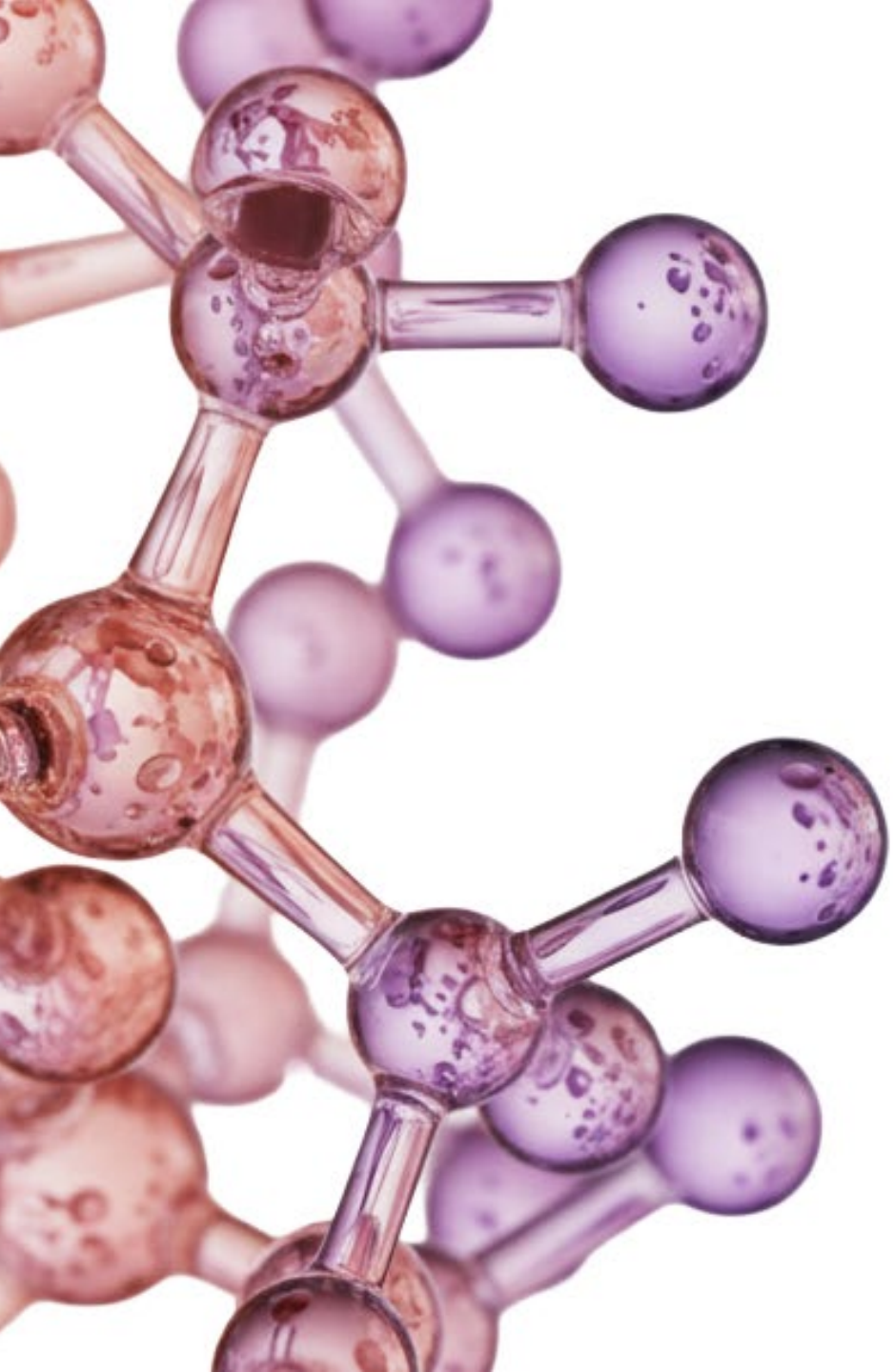

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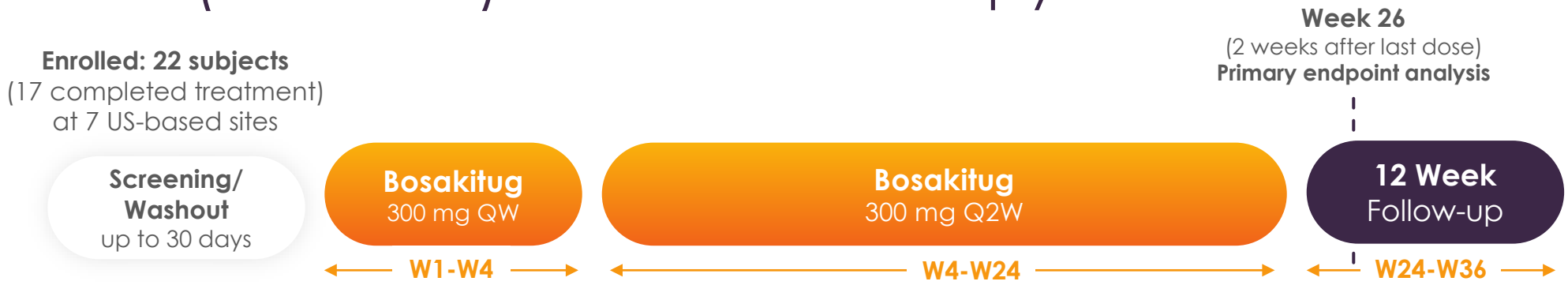
Bosakitug (ATI-045) Anti-TSLP Monoclonal Antibody Program

Differentiated Investigational Product Candidate with Best-in-Class Potential

Clinical Translation

Phase 2a (US-Based) POC Monotherapy Trial



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
Primary Objective (Week 24)	To evaluate the efficacy, safety and tolerability of bosakitug as monotherapy in subjects with moderate to severe AD
Secondary Objectives (Week 24)	To evaluate the pharmacokinetics, immunogenicity and pharmacodynamic biomarkers of ATI-045 in subjects with moderate to severe AD

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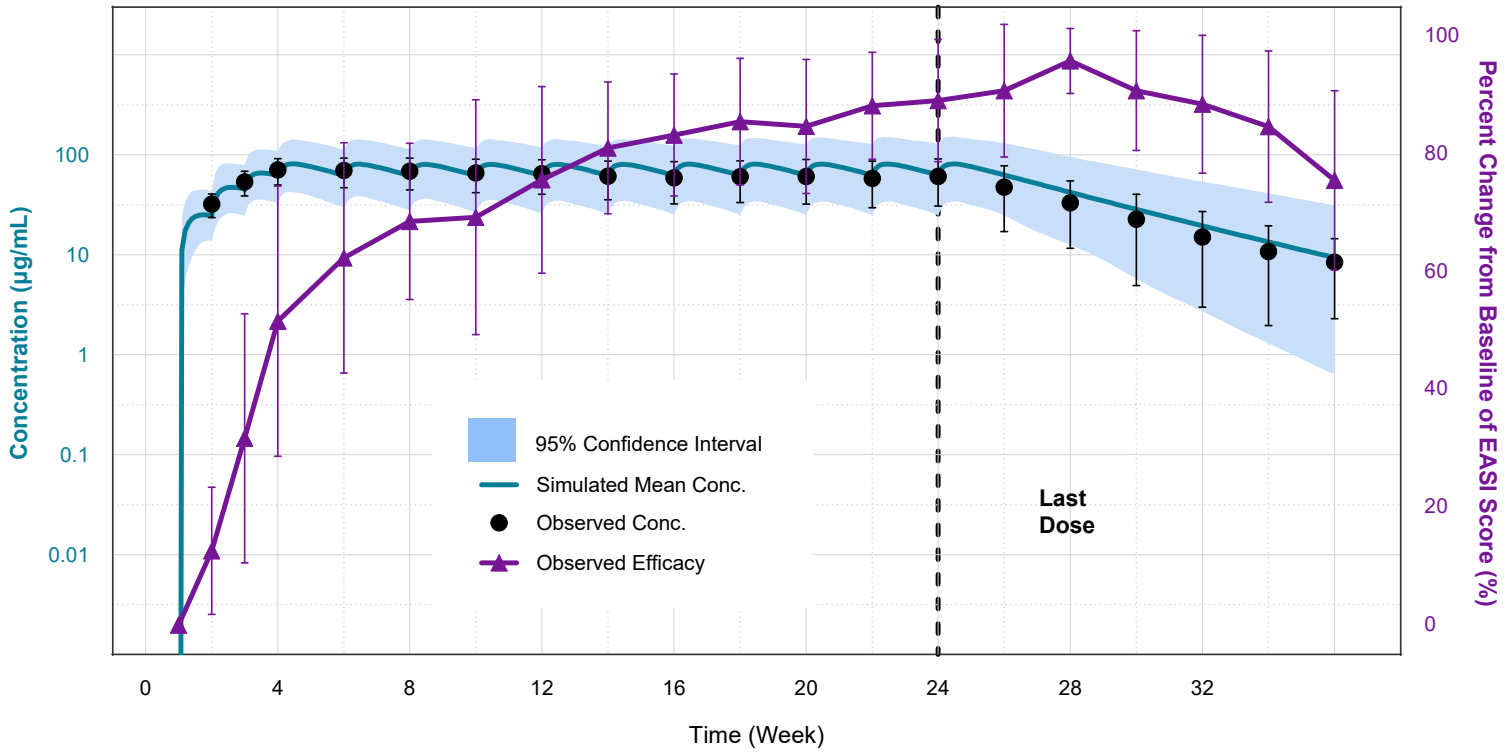
Bosakitug Exposure and Efficacy Time Profile

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

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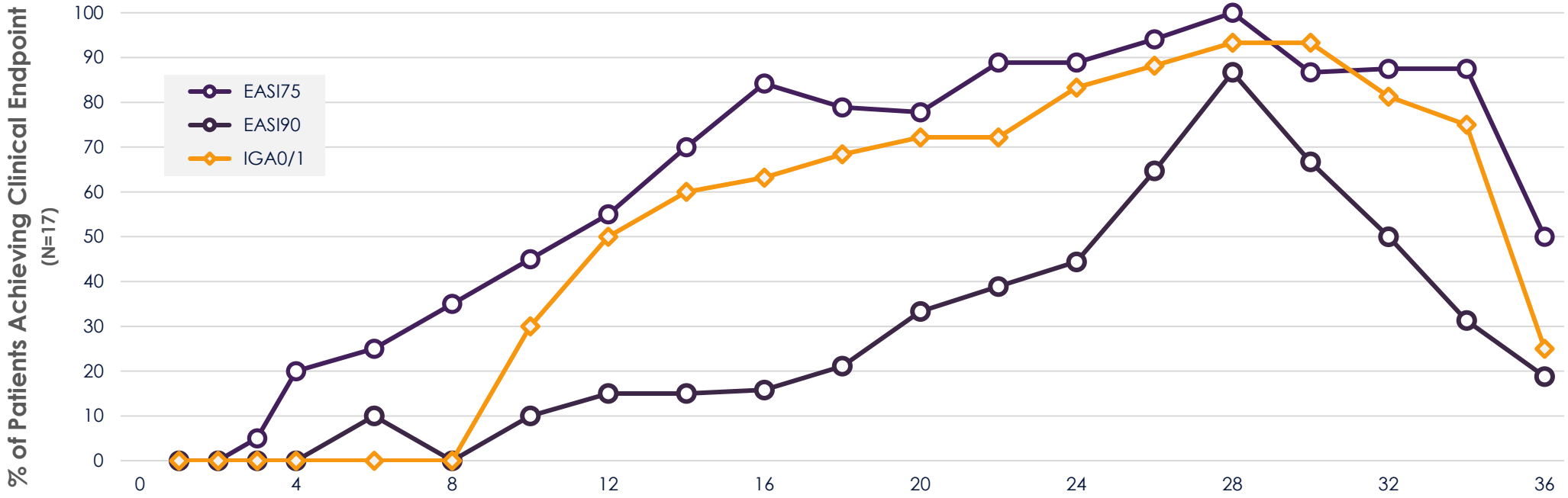
Phase 2a (US-Based) POC Monotherapy Trial

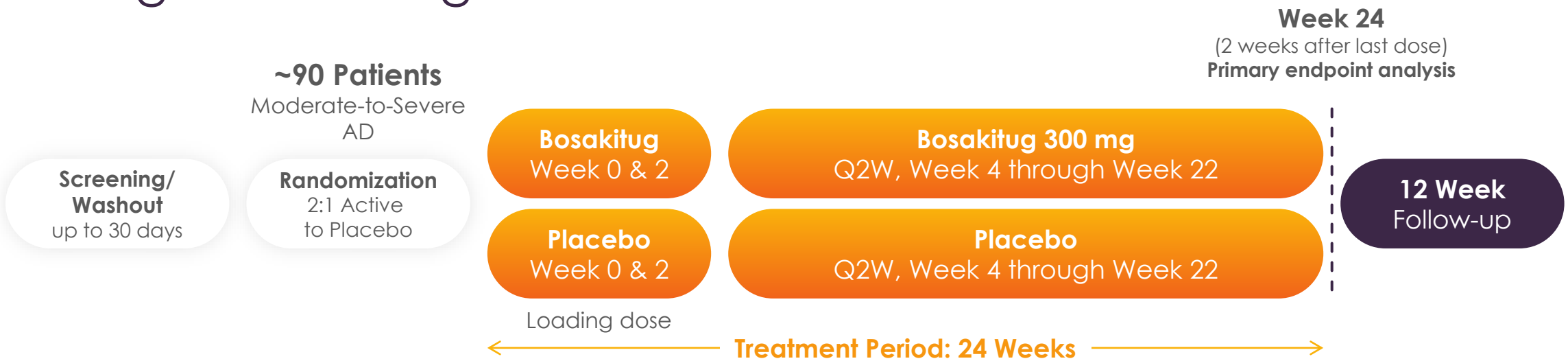
Bosakitug Demonstrated Improvement in Efficacy Measures

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



Phase 2 Monotherapy Trial Ongoing

Dosing Proceeding to Plan



Primary Objective (Week 24)	To evaluate the efficacy of Bosakitug compared to placebo, as measured by the change in Eczema Area and Severity Index (EASI) score in patients with moderate-to-severe AD	
Secondary Objectives (Week 24)	To evaluate the safety, tolerability & treatment effect of Bosakitug compared to placebo, on additional clinical outcome measures	• EASI response (EASI-50, EASI-75, EASI-90) • Validated Investigator Global Assessment (IGA) response • Body Surface Area (BSA) response • Peak Pruritus Numerical Rating Scale (PP-NRS) score

Derisking High Placebo Rates in Atopic Dermatitis

Defining a New Industry Standard in Eligibility Review

Enrolling Patients That Meet Strict Eligibility Criteria

Three step process provides robust patient screening prior to randomization

- Central vendor provides standardized photographic equipment and trains each site to support consistent inter-site photographic proof of disease
- All patients screened serially by multiple readers for lesion severity and affected body surface area (extent of disease) consistent with moderate-to-severe AD

Process designed to enable trials to (1) only enroll patients with AD (2) with moderate-to-severe disease based on disease extent and severity

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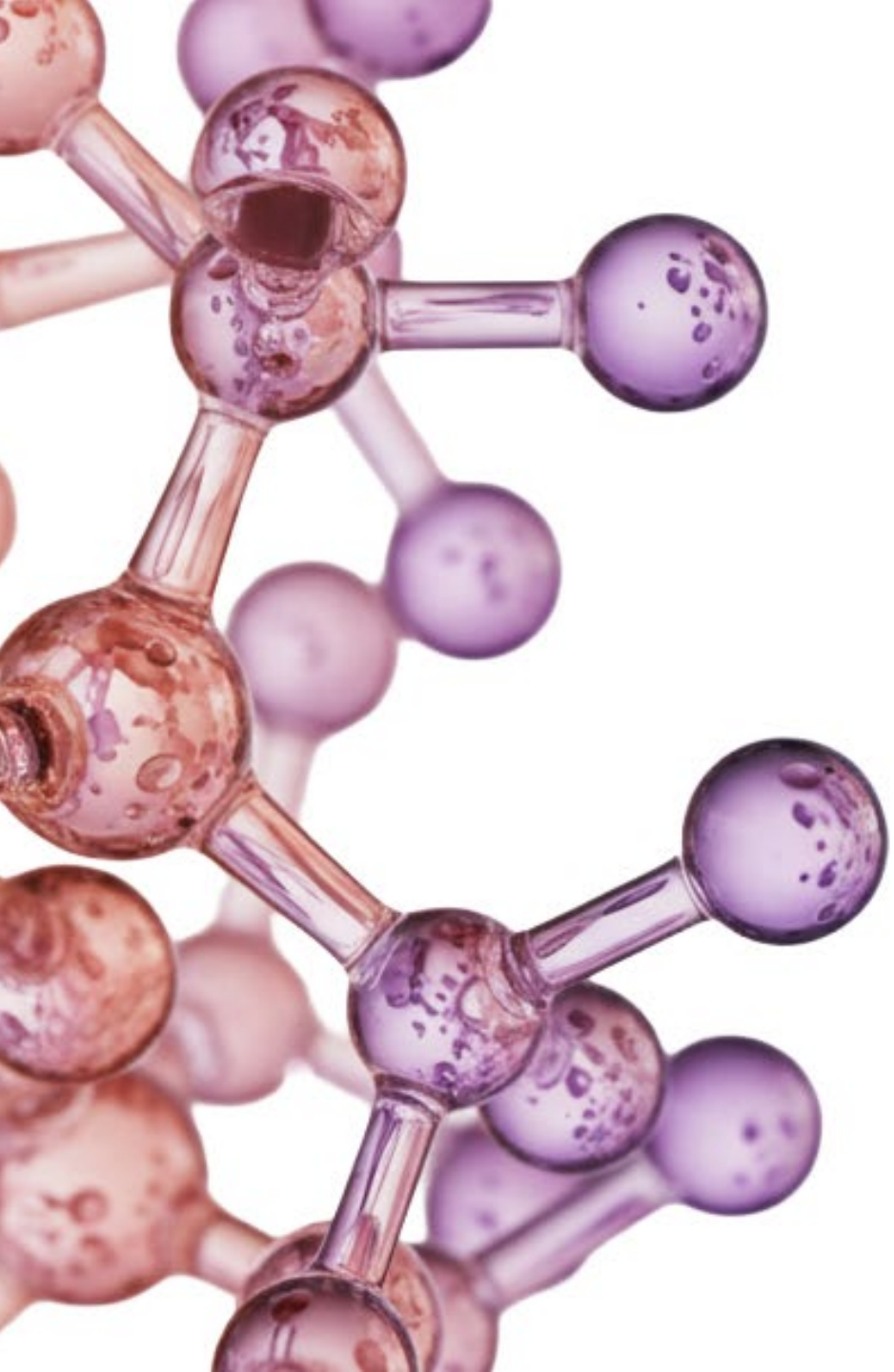
Next Steps with Bosakitug

Competitively Positioned as Potential Best-in-Class TSLP mAb

- Preclinical and clinical data generated to date reinforce the enhanced potency of bosakitug and support further development in dermatological conditions
  - Two-arm placebo-controlled Phase 2 trial of bosakitug in moderate-to-severe AD ongoing (initiated 2Q 2025); dosing underway
    - Results expected in 2H 2026
- Aclaris is seeking partners to develop bosakitug in respiratory indications; further global (excluding China) development in these indications is dependent on entering into potential partnerships



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

Potent and Selective Investigational Drug Candidate with Strong Tolerability Profile

ATI-2138

Positive Phase 2a Results Inform Trials in Additional Indications

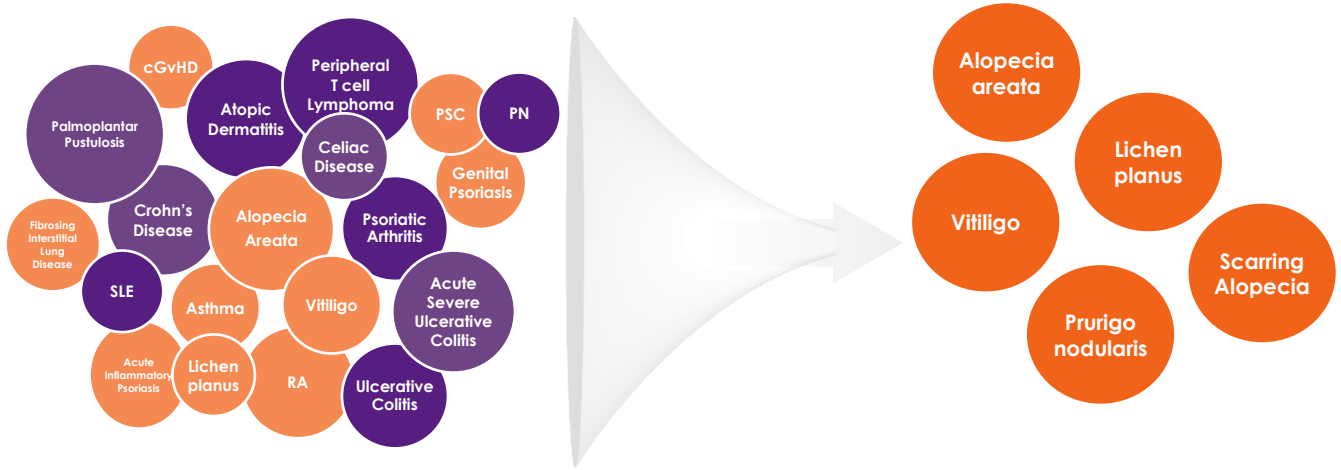
- Positive results from single arm OL Phase 2a trial in AD provide proof of concept:
  - PD results that validate ITK as a therapeutic target
  - Favorable tolerability profile of ATI-2138
  - Clinically meaningful improvements from baseline in assessments of disease severity including:
    - Extent and severity of AD (Eczema Area and Severity Index (EASI))
    - Percent of patients experiencing a greater than or equal to four-point improvement in worst itch in the last 24 hours (Peak Pruritus Numerical Rating Scale (PP-NRS))
    - Body Surface area (BSA)
- Aclaris is exploring further development of ATI-2138 in indications relevant to the mechanism of action with ample available white space

ATI-2138

Oral Small Molecule Covalent ITK & JAK3 Inhibitor for I&I Disease

- Unique dual pharmacology; best-in-class potential
- Potent compound that interrupts TCR signaling by inhibiting ITK and JAK3 signaling of common γ chain cytokines in lymphocytes
- Highly selective for both ITK and JAK3
- Isoform specificity spares JAK1 and JAK2 signaling
- Potential applicability in a variety of I&I indications based on its mechanism of action; targets evolve with competitive dynamics

Wide array of potential targets for 2138



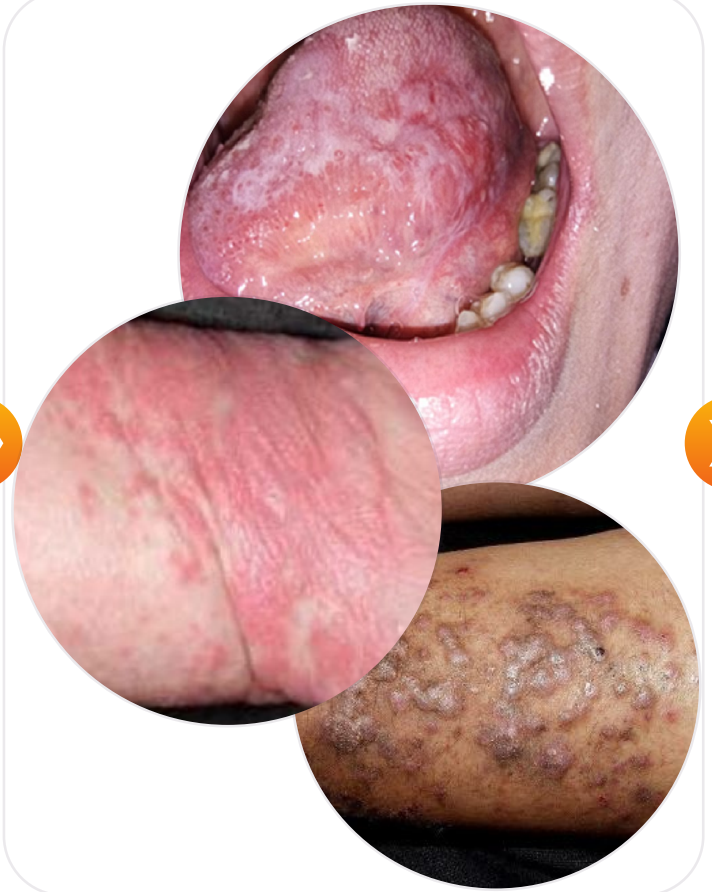
Prioritized potential areas of focus

Next Clinical Steps with ATI-2138

The Lichen Planus Opportunity

An unaddressed chronic, inflammatory, immune-mediated disorder

- Affects skin, mucous membrane, hair and nails; multiple clinical subtypes
- Most common symptoms: severe itch, Wickham's striae, sores, scales/plaques, hair loss, fatigue
- Oral lichen planus (OLP) (50%+ of cases) is of particular clinical significance due to malignant potential
- Prevalence = 0.2-1% worldwide; associated with hepatitis C, autoimmune conditions, certain medications



Large unsatisfied market; ample "white space"

- Market opportunity
  - U.S. addressable patients: ~200K systemic-eligible
  - Global addressable: ~2–3M
  - Peak U.S. revenue potential: $500M–1B
  - Global peak revenue: $1.2–1.4B
  - No approved oral LP therapy → white space opportunity
- Unsatisfied market; management focuses on immunosuppression and symptom control

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ATI-2138 in Lichen Planus

Dual Pharmacology Creates Ideal Mechanistic Fit

Lichen planus

- Chronic inflammatory skin disease
- Aberrant activation of TH1/2/17 and cytotoxic CD8 T-cells
- IFN mediated pathology in affected skin
- Severe itch associated with IL31 up-regulation
- Fibrosis common

ATI-2138

- Activity demonstrated in open-label AD study suggests strong fit for LP
  - Downregulation of Th1/2/17 activation markers
  - Inhibition of biomarkers down-stream of IFNy (CXCL11, CXCL9)
  - Significant reductions in itch
  - Strong downregulation of fibrosis markers
- Efficacy of calcineurin inhibitors in LP support T-cell mediated pathology

Potential Lichen Planus Clinical Program

Dose ranging three indication basket study (mucosal and cutaneous LP, Lichen planopilaris)

Proposed efficacy endpoints

- Primary: Investigator's Global Assessment (IGA); 0 (clear) to 4 (severe)
- Secondary: Numeric Rating Scale (NRS) for itch; 0 (none) to 10 (worst imaginable)

Next Steps

- Complete trial design, market analysis, and TPP of Lichen planus
- Finalize assessment of additional potential future targets
  - Other immunological disorder opportunities based on mechanism may include Hidradenitis suppurativa, Prurigo nodularis, scarring alopecia, vitiligo, etc.
- Initiate Phase 2 in 1H 2026

Target indication for ATI-2138 based on current development strategy

Opportunity in Alopecia

Market is Rapidly Evolving but Opportunities Remain

- Market and competitive landscape dynamics shape indication selection process
- Strong mechanistic rationale: JAK3 inhibition shown to be effective in alopecia areata
- Multiple types of alopecia exist, some of which are under evaluation
  - Scarring (cicatricial) alopecia
  - Alopecia areata
  - Others

Continued Clinical Momentum in 2026

Four Expected Clinical Programs

Innovation Driven

Patient Focused

ATI-052

Top line SAD/MAD results in 1Q 2026

Top line Proof-of-Concept results in asthma and AD in 2H 2026

Next generation ITK inhibitors

First IND from ITK selective program in 2H 2026

ATI-2138

Phase 2b initiation in second indication, likely Lichen planus, in 1H 2026

Top line results in 2027

Bosakitug (ATI-045)

Phase 2 in atopic dermatitis ongoing

Top line results in 2H 2026

Advancing potentially industry-leading inhibitor franchises designed to address validated, therapeutically-relevant immune targets

All future development, clinical, and regulatory timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors

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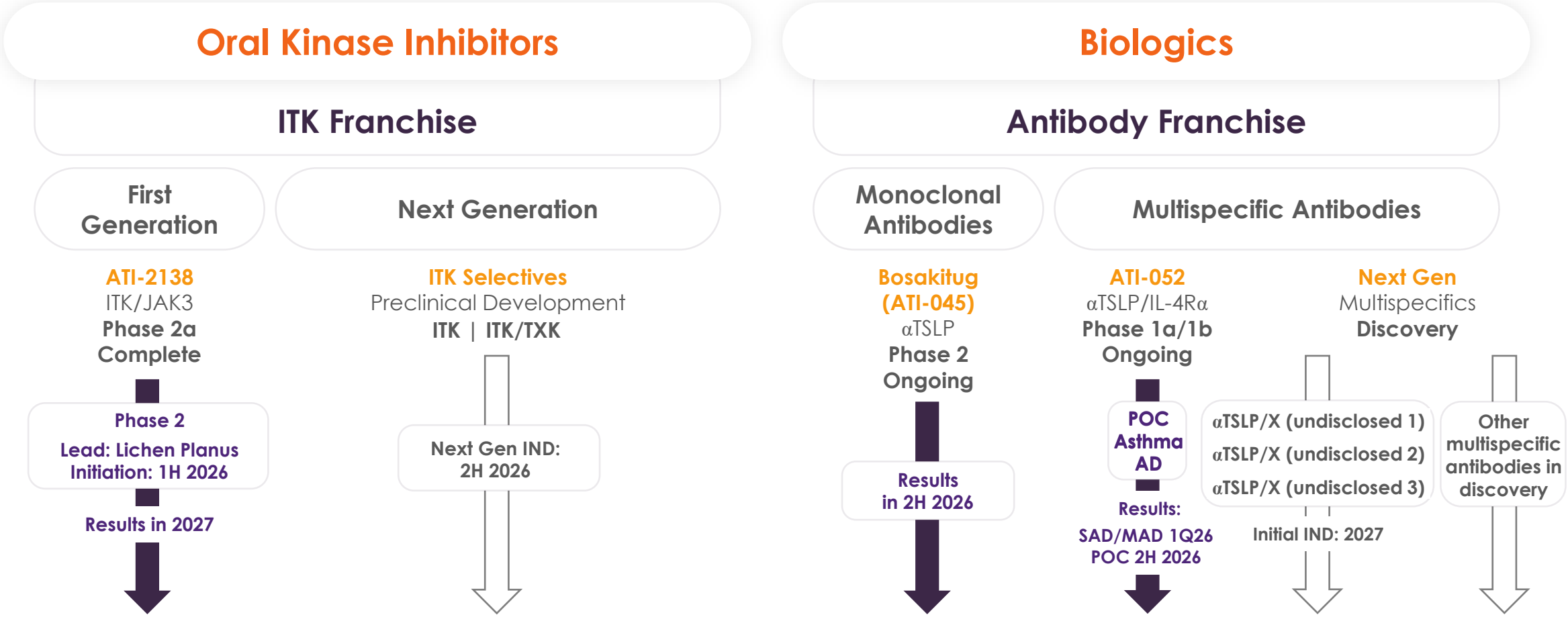
Broad Clinical and Preclinical I&I Pipeline

Potential Best-in-Class Inhibitors of Immunoinflammatory Cascade



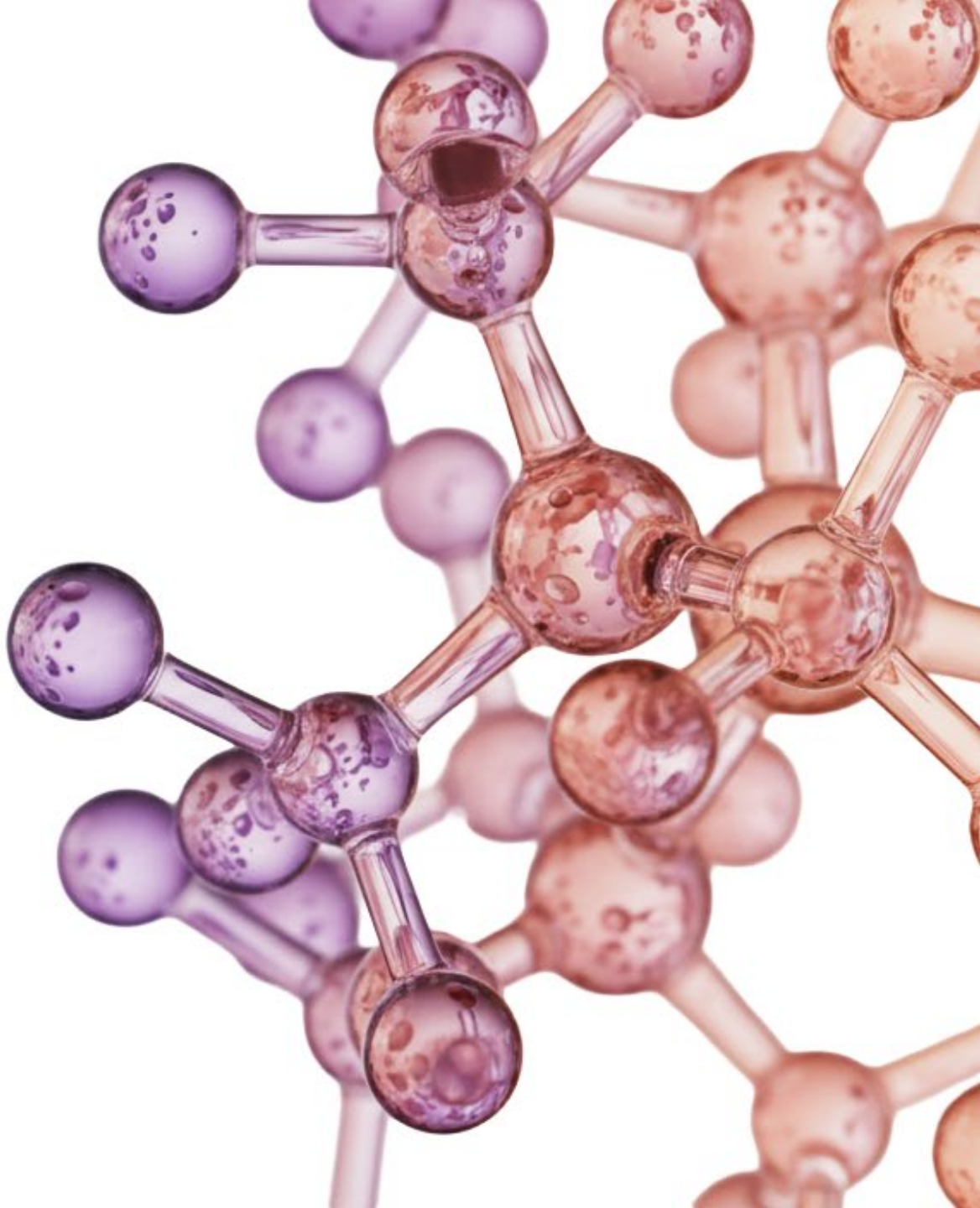
All future development, clinical, and regulatory timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors

Aclaris Therapeutics

Developing Therapeutic Franchises to Address Gaps in Important I&I Diseases

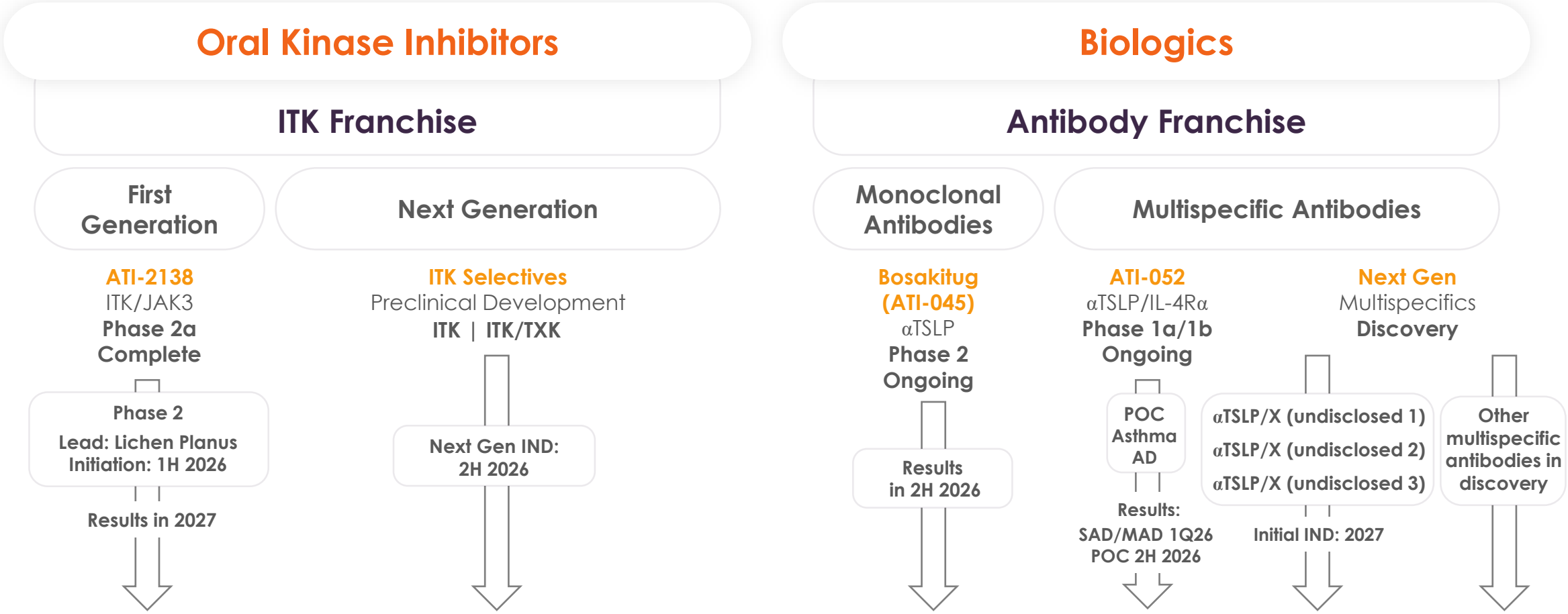
Dr. Neal Walker
Chief Executive Officer

Patient *Focused Innovation*



Broad Clinical and Preclinical I&I Pipeline

Potential Best-in-Class Inhibitors of Immunoinflammatory Cascade



All future development, clinical, and regulatory timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors

2025/2026: Executing on Rich Clinical Catalyst Calendar

2025

- ✓ **ATI-052**
  IND Clearance by FDA
- ✓ **Bosakitug (ATI-045)**
  Initiation of Phase 2 Trial in Atopic Dermatitis
- ✓ **ATI-052**
  Initiation of Phase 1a/1b Program
- ✓ **ATI-2138**
  Atopic Dermatitis Phase 2a Top Line Data
  July 2025
- ☐ **ATI-052**
  Completion of dosing in Phase 1a SAD/MAD HV Portion
  Year-end 2025

2026

- ☐ **ATI-052**
  Phase 1a/1b Top Line Data
  Phase 1a SAD/MAD: Early 2026
  Phase 1b POC: 2H 2026
- ☐ **Bosakitug (ATI-045)**
  Atopic Dermatitis Phase 2 Top Line Data
  2H 2026
- ☐ **ATI-2138**
  Initiation of Phase 2 in Second Indication (e.g., Lichen Planus)
  1H 2026
- ☐ **ITK Next Generation Program**
  IND Submission and Start of Phase 1 Program
  2026

All timelines are expectations, are based on current beliefs and assumptions, and are subject to change based on a variety of factors.

Aclaris Today

- Unique **State-of-the-Art R&D capabilities and World Class Scientists**
- **Four potential Best-in-Class clinical stage assets** in 2026 targeting validated and therapeutically-relevant immune targets highlighted by a **potential Best-in-Class bispecific and oral ITK inhibitor**
- **Rich calendar of data events** expected throughout 2026 and 2027
- A cash runway expected to provide **approximately three years of capital**, with opportunities to expand it further *without* dilution

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Patient *Focused Innovation*

Developing Therapeutic Franchises to Address Gaps in Important I&I Diseases

2025 R&D Day

October 14, 2025