



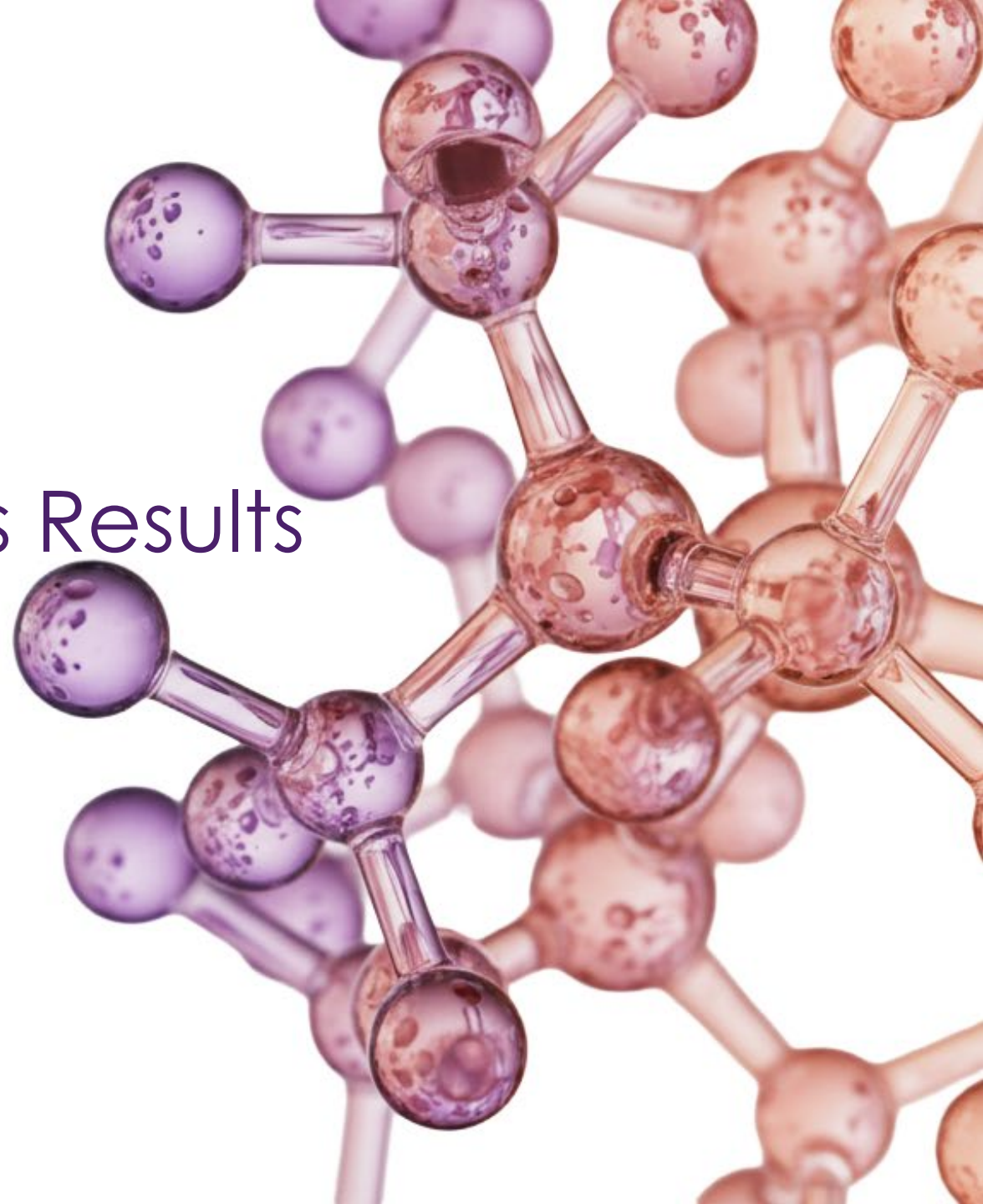
ATI-052

Phase 1b Primary Analysis Results Atopic Dermatitis and Asthma

October 27, 2026

EMPOWERING PATIENTS THROUGH

**THERAPEUTIC
INNOVATION**



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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 ATI-052, an investigational bispecific antibody, including the potential for ATI-052 to be best-in-class and have best-in-class attributes, the potential to increase the efficacy ceiling and show superior activity compared to other therapies, the potential for ATI-052 to have up to quarterly dosing, the potential for synergy of TSLP and IL-4R α , the market opportunity for ATI-052, and the development of ATI-052 and Aclaris’ other 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. 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, potential changes to interim, topline and preliminary data as more subject data become available, 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, 2025, 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.

ATI-052: Potential Best-in-Class Bispecific mAb

Phase 1b POC Results Validate Preclinical Potency Differentiation

400+ hours

Up to 116x longer residence time on TSLP than comparator antibodies

\$19B+¹

In annual sales across the mechanisms it targets

Proof-of-Concept Achieved in Atopic Dermatitis (AD) & Asthma

Combines **two significant mechanisms** in one molecule:
anti-TSLP, anti-IL-4R α

Potential to **raise efficacy ceiling** +
provide **rapid response**

Demonstrated potential for
additivity/synergy of targets

Modulated all three TH cell
endotypes: **Th1, Th2, Th17**

Favorable tolerability profile observed

4x

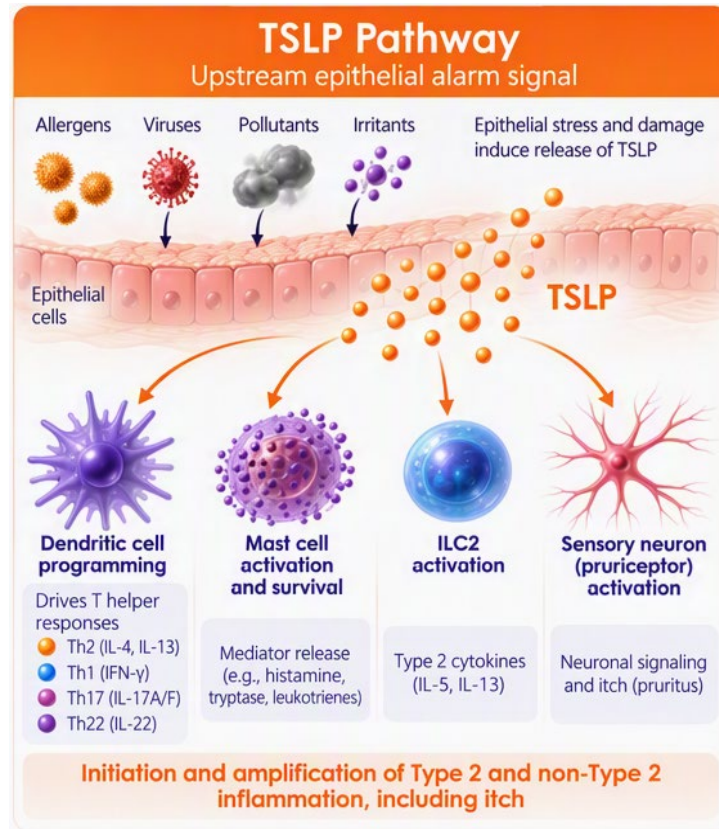
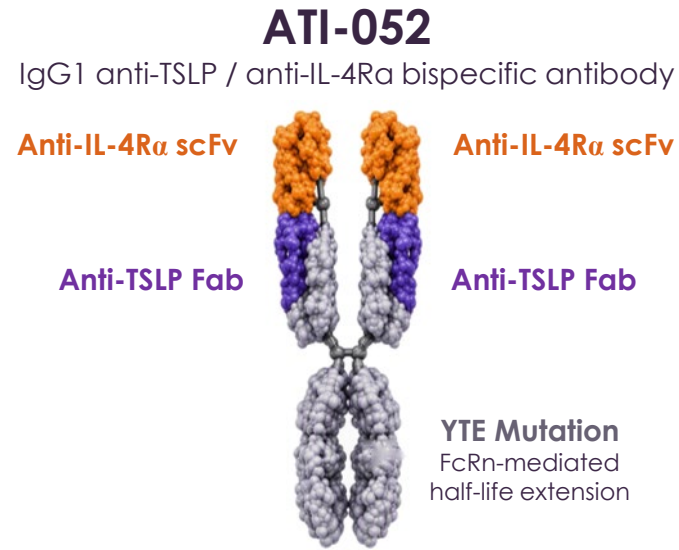
More potent than dupilumab +
tezepelumab combined

**Up to
Quarterly**

Dosing potential

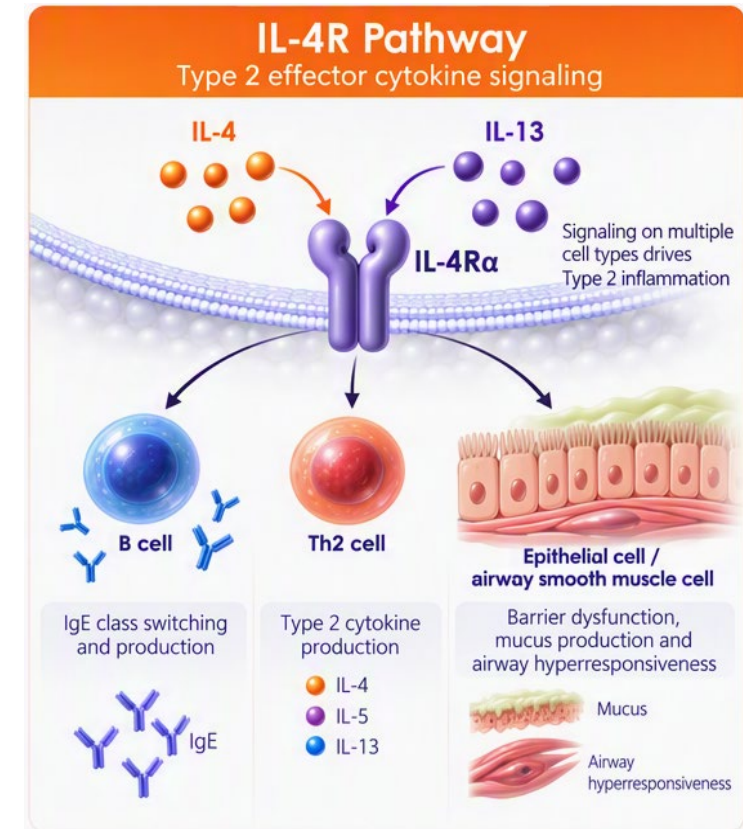
Two Validated Mechanisms

A More Complete Approach to Inflammatory Disease



Molecular architecture

- Bivalent for both TSLP and IL-4Ra (four total binding sites)
- Unique multi-paratopic TSLP binding
- Potential best-in-class potency for TSLP with long retention time
- YTE Fc mutation engineered for $T_{1/2}$ extension



ATI-052 Pathways

Simultaneous control of upstream disease initiation and downstream Type 2 effector pathways

Individual Components of ATI-052 are Both Important

ATI-052 Targets The Two Most Broadly Validated Nodes In Type 2 Disease:
TSLP and IL-4R α

Approval Status by Indication/Mechanism			
	TSLP	IL-4R α	IL-13
EoE	<div><div>✓</div><div>NDA Filing Expected</div></div>	<div><div>✓</div></div>	<div><div>✗</div></div>
Asthma	<div><div>✓</div></div>	<div><div>✓</div></div>	<div><div>✗</div></div>
COPD	<div><div>✗</div></div>	<div><div>✓</div></div>	<div><div>✗</div></div>
CRSwNP	<div><div>✓</div></div>	<div><div>✓</div></div>	<div><div>✗</div></div>
AD	<div><div>✗</div></div>	<div><div>✓</div></div>	<div><div>✓</div></div>
Validated	3/5	5/5	1/5
	<div><div>✓</div> Approved</div>	<div><div>✗</div> Not approved</div>	

Blocking IL-4R α blocks both IL-4 and IL-13

IL-4 biology is directly implicated in asthma and other Th2 diseases

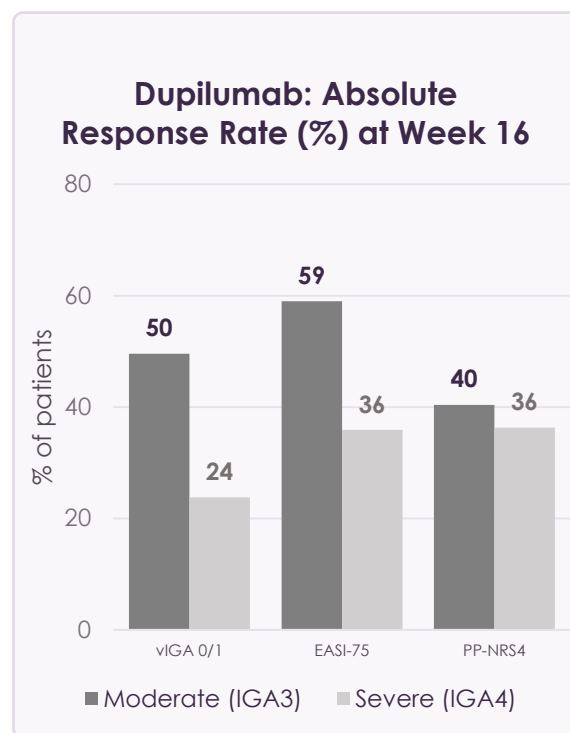
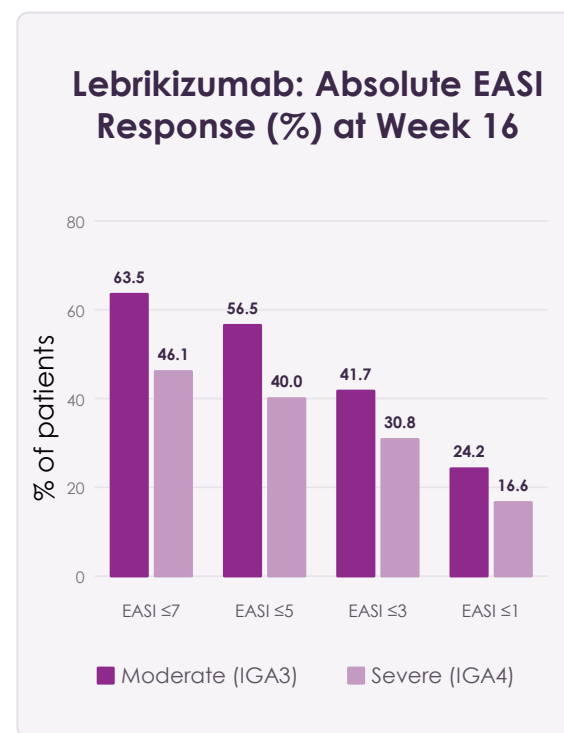
IL-13–selective antibodies have failed to show competitive efficacy to dupilumab in late-stage trials in asthma and EoE

0
of 8

IL-13–selective
programs
approved in
asthma or EoE

ASTHMA 6 programs, none approved		
<div><div>✗</div> Lebrikizumab Roche</div>	<div><div>✗</div> Tralokinumab AstraZeneca</div>	<div><div>✗</div> GSK679586 GSK</div>
<div><div>✗</div> Anrukinzumab Pfizer</div>	<div><div>✗</div> IMA-026 Pfizer</div>	<div><div>✗</div> Dectrekumab Novartis</div>
EoE 2 programs, none approved		
<div><div>✗</div> Dectrekumab Novartis</div>	<div><div>✗</div> Cendakimab BMS</div>	

Baseline Severity Impacts Response Rates



Difficulty in Treating Severe AD

Understanding Severity:

- Two ways to determine severity: EASI and vIGA; both must be assessed
- EASI incorporates both extent and severity; vIGA provides a direct measure of disease severity

Absolute vs. Relative Reduction:

- Patients with severe disease need a larger improvement in score than those with milder disease to reach the same target score.

Severe AD represents a higher bar for success

ATI-052 Positive Phase 1b Primary Analysis Results: AD

Strong POC in Severe AD (78% vIGA4); Efficacy Signals Support Advancement to Phase 2

Measure (D57)	ATI-052 Load-in Doses (480 mg)	Placebo	PBO-Adj. Change	Objective
% Reduction from Baseline in EASI	58%	13%	45%	Sustained skin improvement
EASI-50	78%	0%	78%	Encouraging Early Endpoints
% PP-NRS Reduction	38%	-5%	43%	Itch Improvement
PD Biomarker Analysis	Deep reduction of established AD biomarkers & suppression of Th1, Th2, Th17 and myeloid inflammatory pathways observed			Evidence of Additivity / Synergy
Safety and Tolerability	Favorable safety profile with no conjunctivitis observed			Strong tolerability profile

ATI-052 has the potential to set a new efficacy ceiling in AD
and other Th2 driven diseases

ATI-052 Positive Phase 1b Primary Analysis Results: Asthma

Strong POC in Mild-to-Moderate Asthma; Rapid Response Supports Advancement to Phase 2

Measure (D15)	ATI-052 Single Dose (480mg)	Placebo	PBO-Adj. Change	Objective
% Reduction in FeNO	59%	15%	44%	Target Engagement
Increase in FEV1 (ITT)	200 mL	0 mL	200 mL	Large Airway Improvement
Increase in FEV1 (FEV1 <80% at BL)	350 mL	-140 mL	490 mL	
Safety and Tolerability	Favorable safety profile with no conjunctivitis observed			Strong Tolerability profile

ATI-052 has the potential to set a new efficacy ceiling in asthma and other Th2 driven diseases

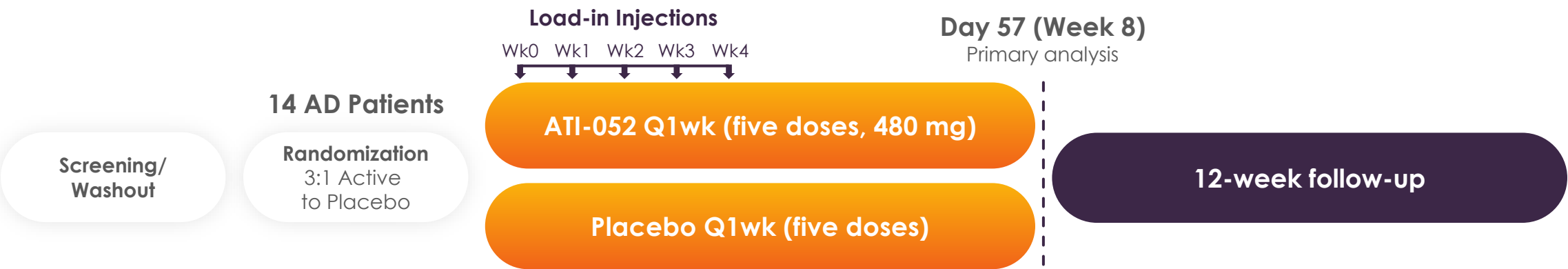
8 NOTE: FEV1 <80% at BL = pre-BD FEV1 value of < 80% at baseline + post-BD reversibility of FEV1 ≥ 12% and ≥ 200 mL or documented history of post-BD FEV1 reversibility during last 12 months at screening. BD = bronchodilator; FEV1 = Forced expiratory volume in 1 second; PBO = placebo; BL = baseline; ITT = intent-to-treat; FeNO = fractional exhaled nitric oxide.



ATI-052 POC in Atopic Dermatitis (AD)

Data cutoff date: August 20, 2026

Phase 1b POC Trial in Severe Atopic Dermatitis



Strategy	First signal-finding clinical trial to assess the efficacy of load-in doses only (no doses after week 4) in severe AD patient population
Location	United States: Multi-site
Primary Endpoint	Safety and tolerability
Other Endpoints	AD clinical efficacy assessments (EASI, PP-NRS, etc.) PD endpoints measured by assays including lesional and non-lesional skin tape strips

Baseline Demographics and Disease Severity

Characteristic	ATI-052 (N=11)	Placebo (N=3)
Age, mean (SD), y	27.8 (6.0)	38.3 (13.1)
Female, n (%)	6 (54.5)	1 (33.3)
Weight, mean (SD), kg	82.4 (18.5)	102.0 (4.8)
Duration of AD from diagnosis, mean (SD), y	21.8 (8.2)	23.1 (4.8)
Race, n (%)		
White	4 (36.4)	2 (66.7)
Black or African American	5 (45.5)	1 (33.3)
Asian	2 (18.2)	0
Baseline EASI, mean (SD)	28.3 (7.5)	23.2 (0.8)
Baseline vIGA=4, n (%)	9 (81.8)	1 (33.3)
Baseline weekly PP-NRS, mean (SD)	6.7 (1.7)	7.1 (1.5)
BSA affected, mean (SD)	41.4 (13.7)	35.0 (14.4)

Per Protocol Analysis Population

Defined prior to unblinding

Reasons for Exclusion	ATI-052	Placebo
Received rescue medication	0	2
Took only 2 doses	1	0
Eligibility criteria not met	1	0

Increased Percentage of African American and vIGA 4 Provides a More Severe / Difficult-to-Treat Patient Population¹

NOTE: vIGA = Validated Investigator Global Assessment for Atopic Dermatitis; EASI = Eczema Area and Severity Index; PP-NRS = Peak Pruritus Numerical Rating Scale; BSA = Body Surface Area; NC = not calculable
SOURCE: 1. Sanyal RD, Guttman-Yassky E, et al. *Ann Allergy Asthma Immunol*. 2019.

ATI-052 Was Well Tolerated, With a Favorable Safety Profile

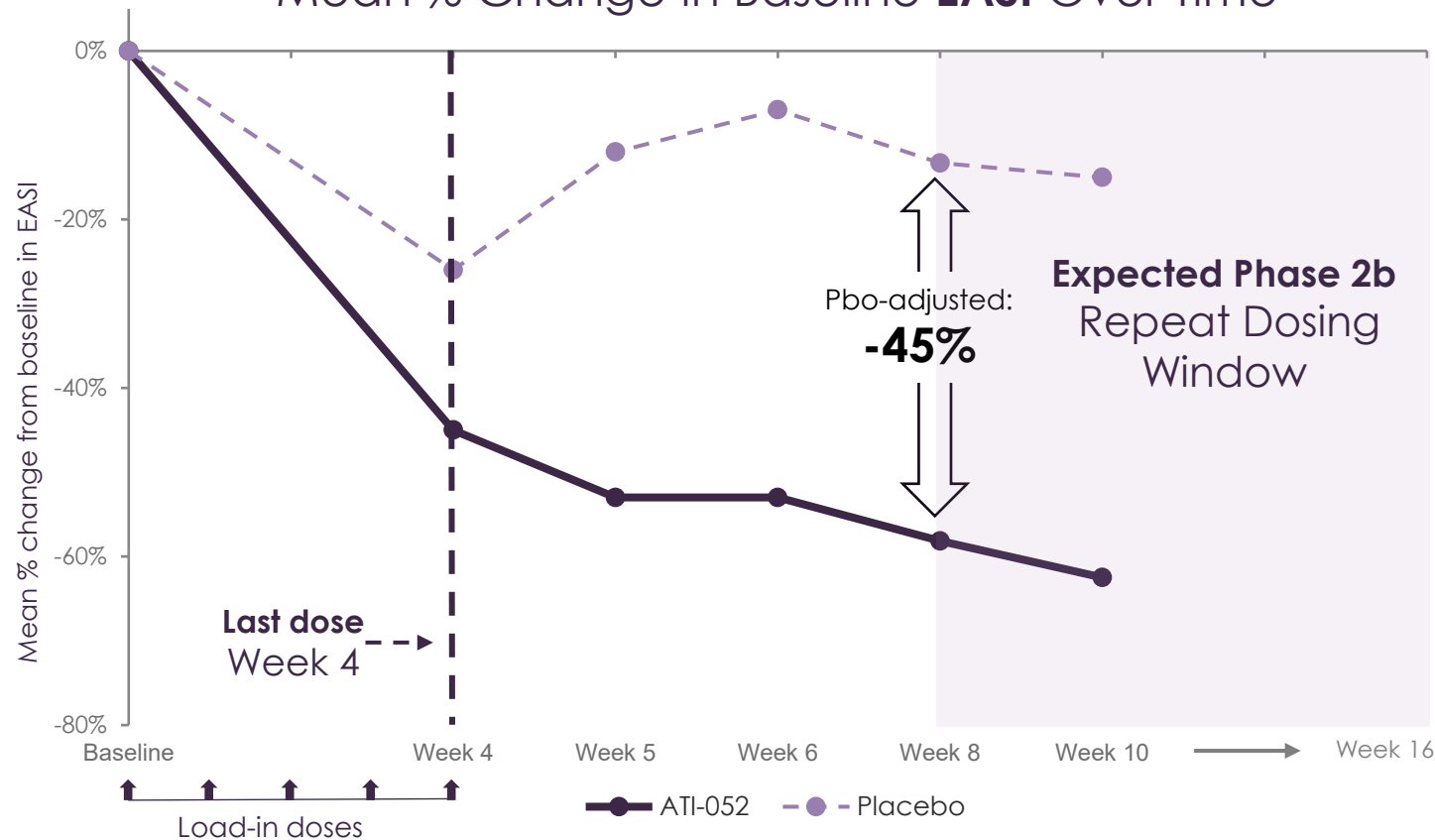
Safety Summary	ATI-052 N=11 (%)	Placebo N=3 (%)
Patients reporting ≥1 TEAE	6 (54.5)	2 (66.7)
Patients reporting ≥1 serious TEAE	0	0
Patients reporting ≥1 Grade 3 or 4 TEAE	0	0
Patients who discontinued due to TEAE	0	0
Patients reporting ≥1 TRAE (only ISRs)	2 (18.2)	1 (33.3)

- Tolerability similar between active and placebo arms
- Injection site reactions (ISR) were transient, almost exclusively Grade 1, and observed only at two timepoints
- Preliminary safety observed after Day 57 consistent with that observed through Day 57
- **No conjunctivitis** observed in the Phase 1a/1b ATI-052 program

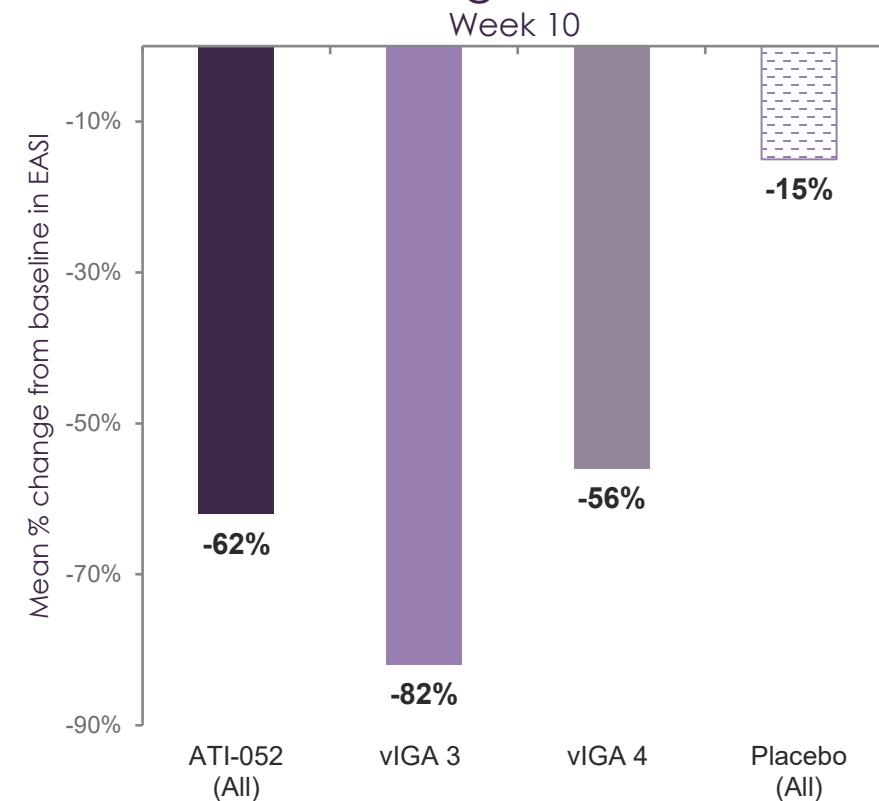
ATI-052 Demonstrated Robust EASI Improvement

Enrolled a Challenging Population to Treat: 78% Baseline vIGA4

Mean % Change in Baseline **EASI** Over Time



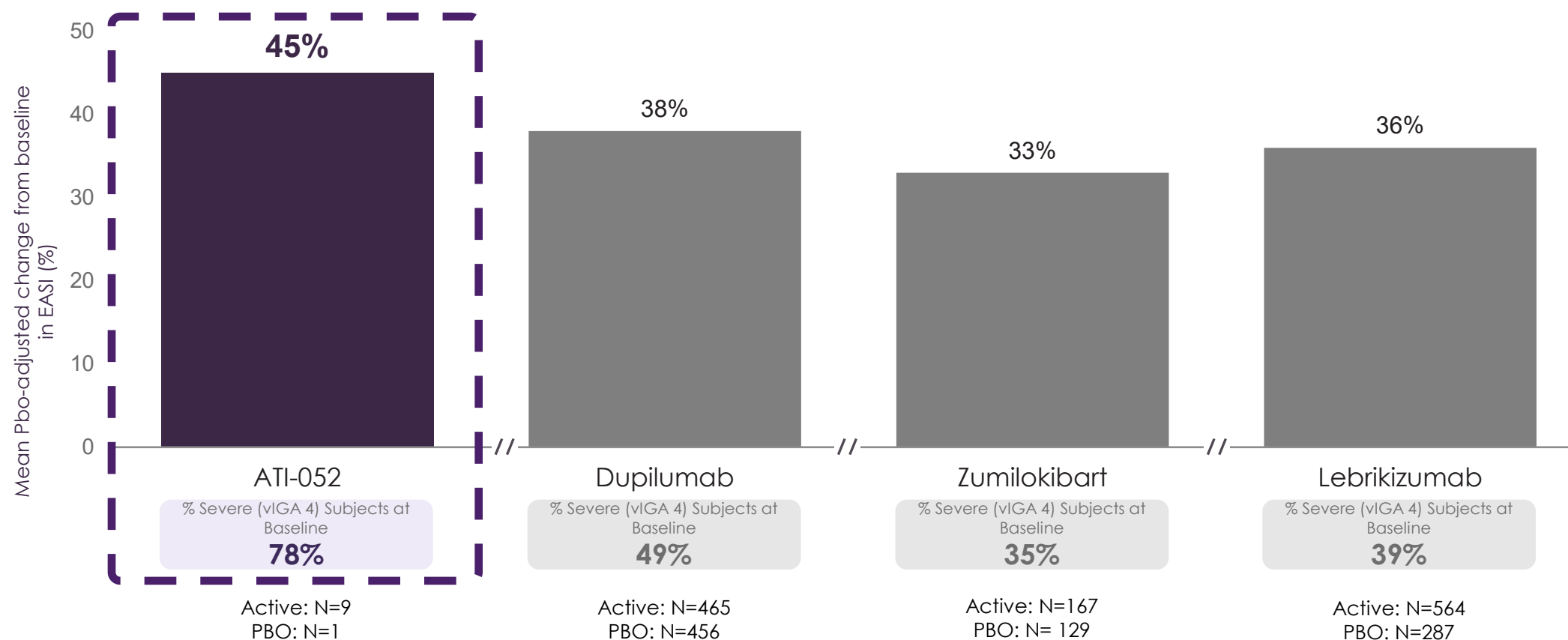
Mean % Change in Baseline **EASI**



EASI Improvement Maintained in Severe Patient Population Through Week 16 after Load-In Doses Only

Early Efficacy Signal In Severe Disease Supports Advancement to Phase 2b

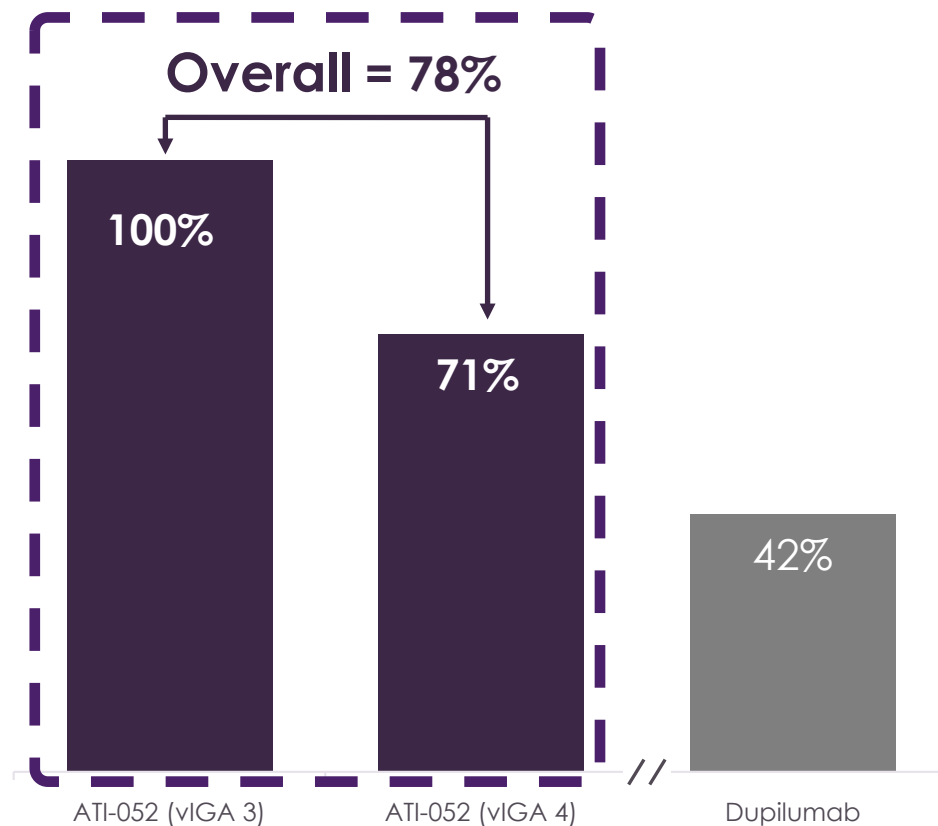
Mean Placebo-adj. Change from Baseline in **EASI** (%), Week 8



NOTE: ATI-052 results presented for per protocol population. Missing data were not imputed. Sample sizes vary by endpoint and visit. Data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted. PBO = placebo.

ATI-052 Demonstrated Robust EASI-50 Response

Pbo-adj. **EASI-50** Response (%), Week 8



89%
of ATI-052 Subjects Achieved
EASI-50 During the Study¹

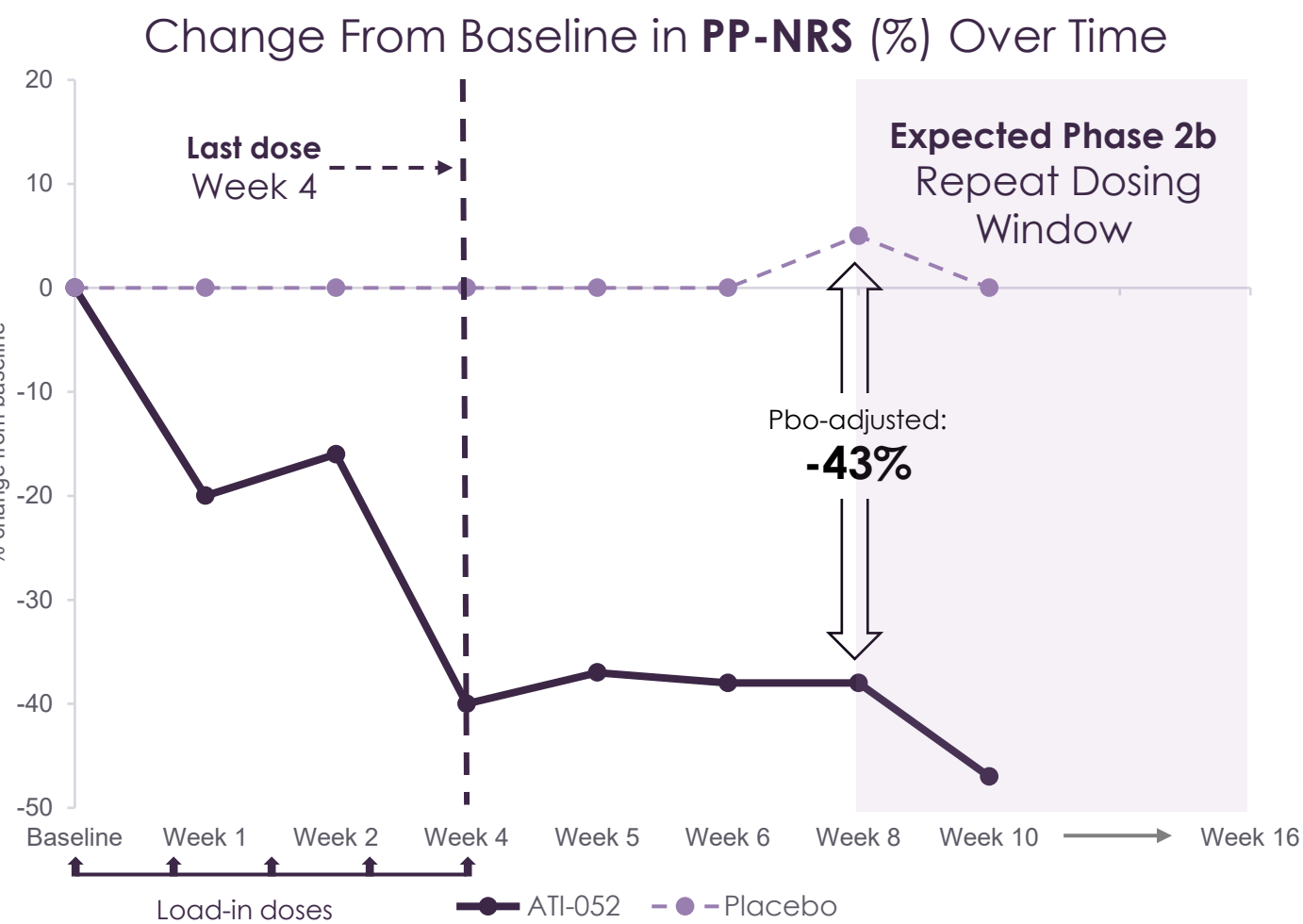
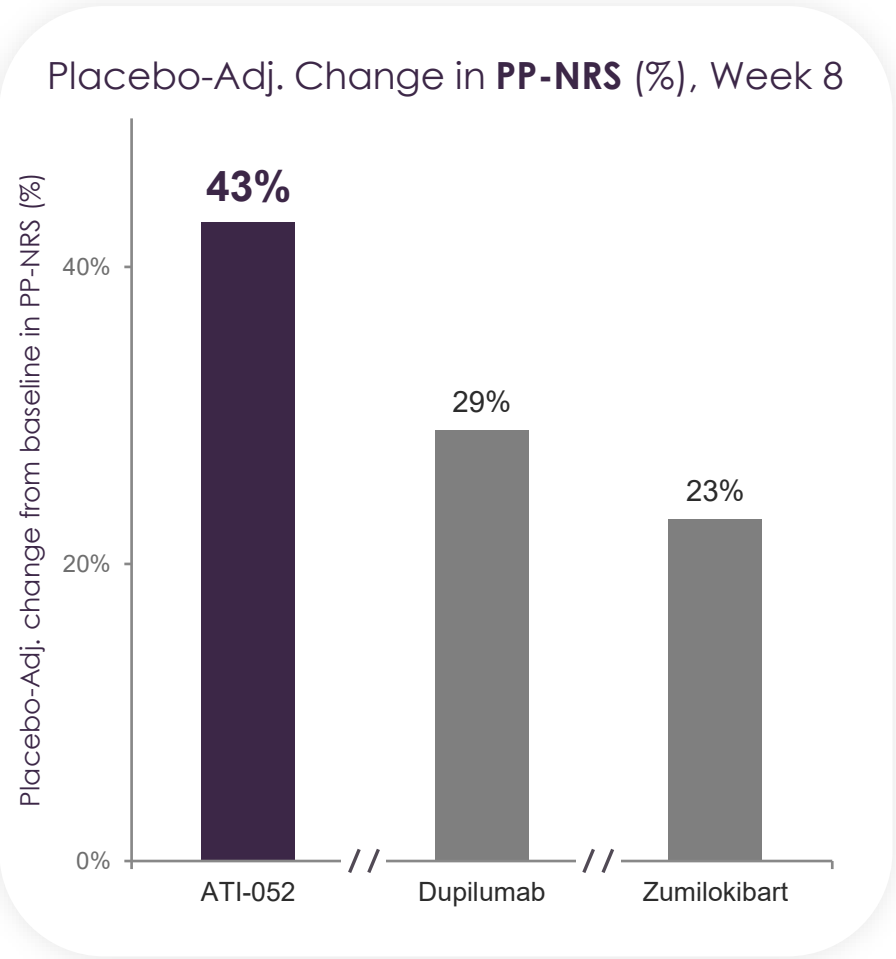
NOTE: ATI-052 results presented for per-protocol population. Missing data were not imputed. Sample sizes vary by endpoint and visit. ATI-052 placebo-adjusted results use the overall placebo group as the comparator. All subgroup analyses were conducted post hoc. Data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted. PBO = placebo.

1. Post hoc analysis including unscheduled visits. Each subject counted once if the criterion was met at any visit.

SOURCE: Dupilumab: SOLO 1/2, 300 mg q2w pooled, approx. (Thaçi D, Simpson EL, et al. J Dermatol Sci. 2019;94(2):266–275).

Rapid, Deep and Durable Reductions in Itch Observed

Itch Relief Emerged Week One and Continued to Deepen Through Week 10

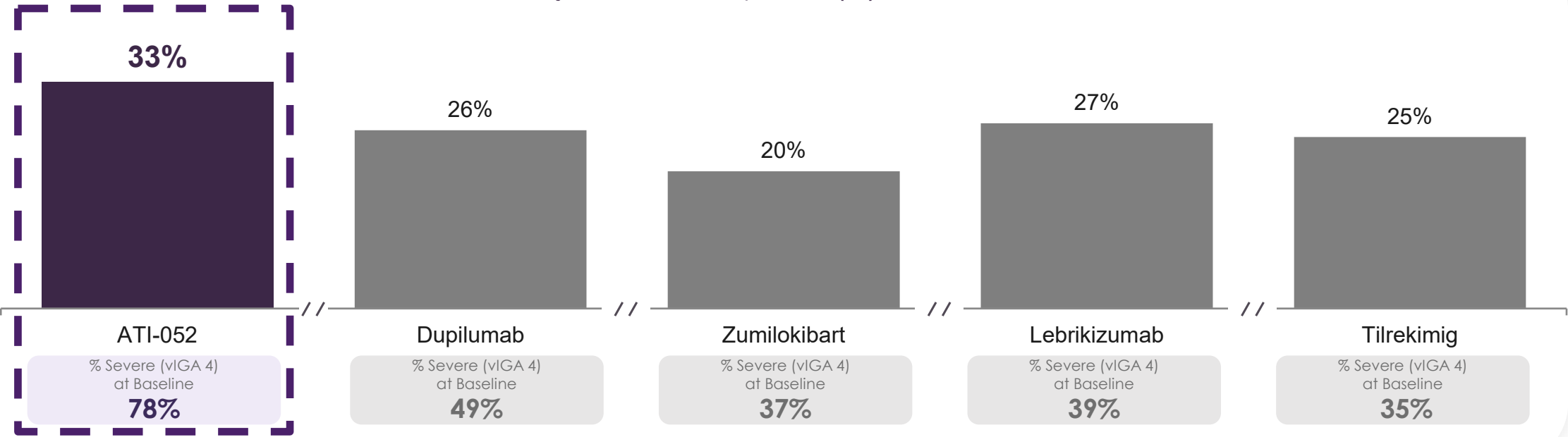


NOTE: ATI-052 results presented for per protocol population. Missing data were not imputed. Sample sizes vary by endpoint and visit. Data after Day 57 are preliminary and based on partial dataset. Data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.
SOURCE: Dupilumab: SOLO 1/2, 300 mg q2w pooled, approx. (Thaçi D, Simpson EL, et al. J Dermatol Sci. 2019;94(2):266–275.). Zumilokibart: APEX Part A mid dose (Apogee, APEX Part A 16-week data presentation July 7, 2025).

ATI-052 Showed Clinically Meaningful Improvements in Itch

Improved Placebo-Adjusted PP-NRS Response Observed

Pbo-adj. **PP-NRS4** Response (%), Week 8



NOTE: ATI-052 results presented for per protocol population. Missing data were not imputed. Sample sizes vary by endpoint and visit. Data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted. PBO = placebo; PP-NRS4 = ≥4 points of reduction from baseline in weekly averages of Peak Pruritus Numerical Rating Scale (PP-NRS).

17 SOURCE: Dupilumab: PP-NRS4 - SOLO 1/2, 300 mg q2w pooled, approx. (Thaçi D, Simpson EL, et al. J Dermatol Sci. 2019;94(2):266–275.). Zupilokibart: APEX Part B mid dose (Apogee, APEX Part B 16-week data presentation, May 27, 2026). Lebrikizumab: ADvocate 1/2, 250 mg q2w averaged, approx. (Silverberg, NEJM 2023;388:1080). Tilrekimig: 400mg + 200 mg q4w averaged (Active: N=70, PBO: N=20) (EADV 2026, Vienna, Sept 30 to Oct 3, 2026).

Photographic Examples of Clinical Activity

Baseline

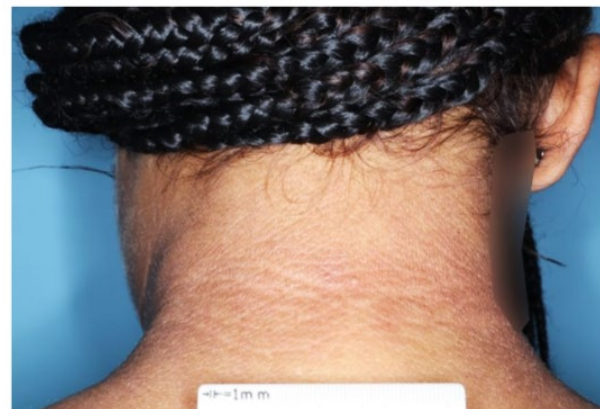
Subject #1
vIGA 3 at
Baseline



Subject #2
vIGA 4 at
Baseline



Week 8



Potential Best-in-Class Pharmacodynamic Profile

DR. EMMA GUTTMAN LAB · MT SINAI

Skin Tape Strip Analysis

O-link proteomics (300+ analytes)

INTERNAL ANALYSIS

Endogenous Serum Biomarkers (MSD-Select)

CCL17/TARC, IL-5

TSLP + IL-4R α | Evidence of Potential Additivity/Synergy Between Targets

Broad Pathway Modulation

Marked downregulation of inflammatory mediators pertinent to AD observed

Pathways modulated

Th1

Th2

Th17/Th22

Fibrosis

Itch

Normalization of Skin Proteome

Immune protein expression in lesional skin closely resembled non-lesional skin

Proteome shift

Lesional → Non-lesional

Pronounced Biomarker Reduction

Pronounced reduction of established dupilumab biomarkers observed

Additional suppression

Th1

Th17

Myeloid

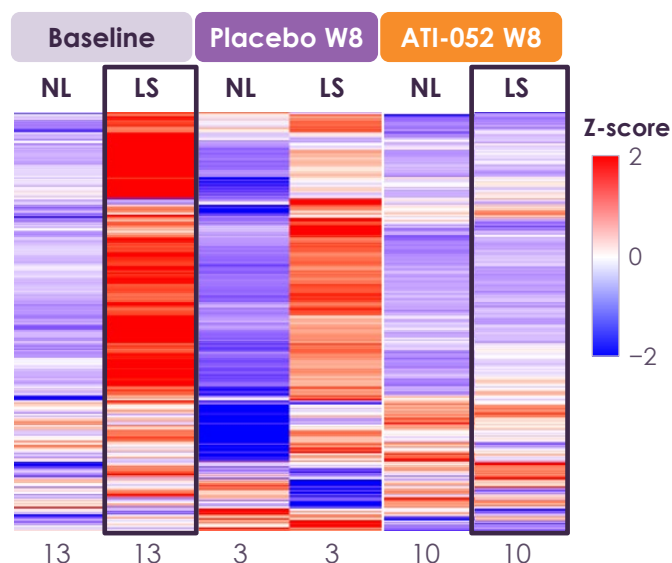
Innate

ATI-052 Normalized Skin Proteome

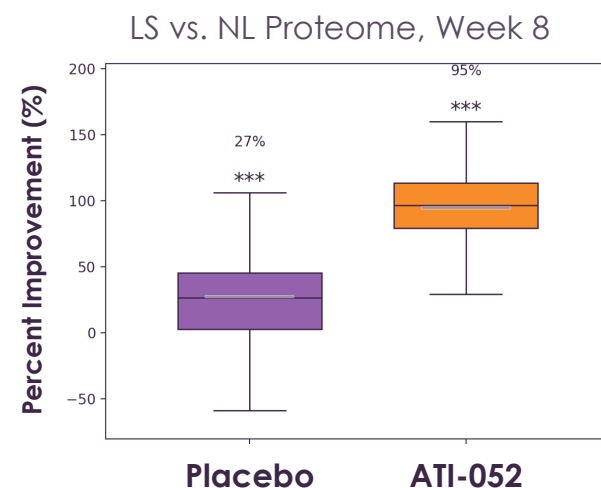
ATI-052 Activity in Lesional Skin | Potential for Disease Modification

PROTEOME HEATMAP

LS: Lesional Skin
NL: Non-Lesional Skin



% IMPROVEMENT



KEY RESULTS

95%

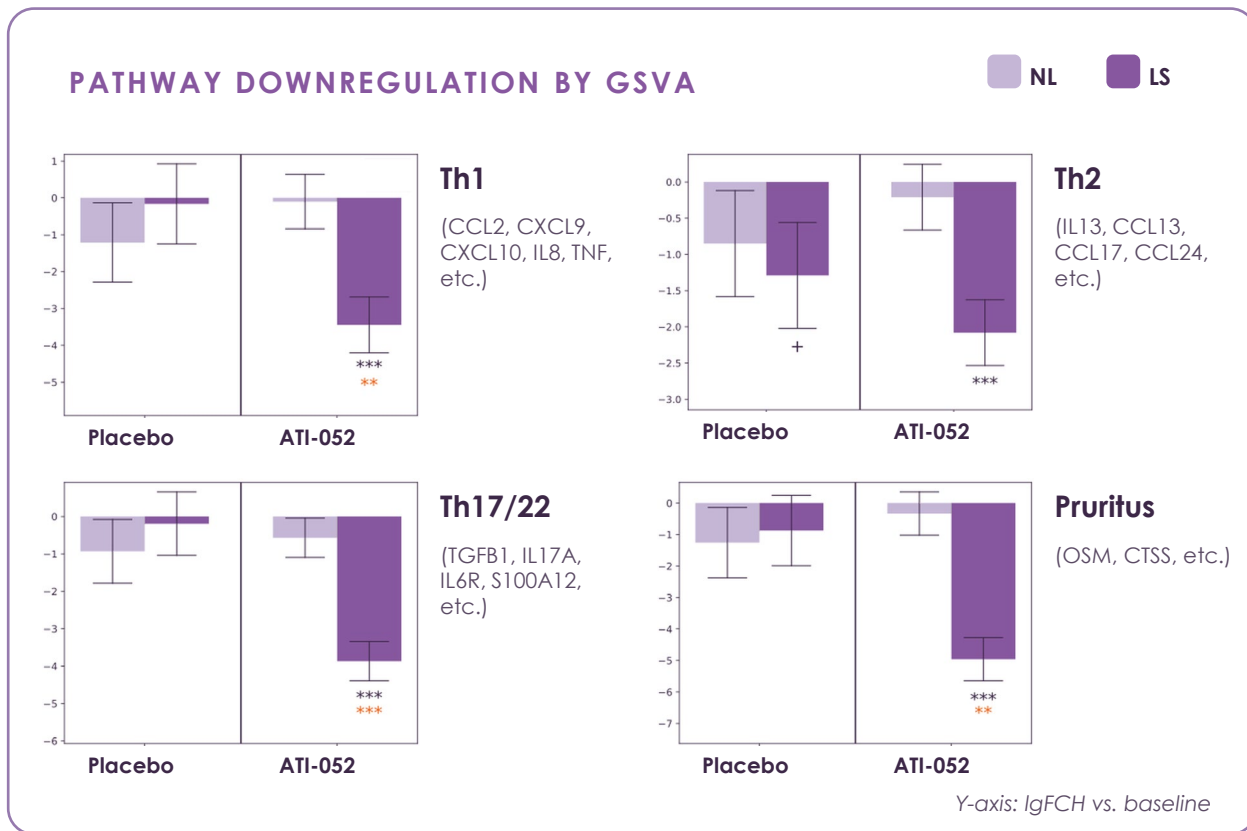
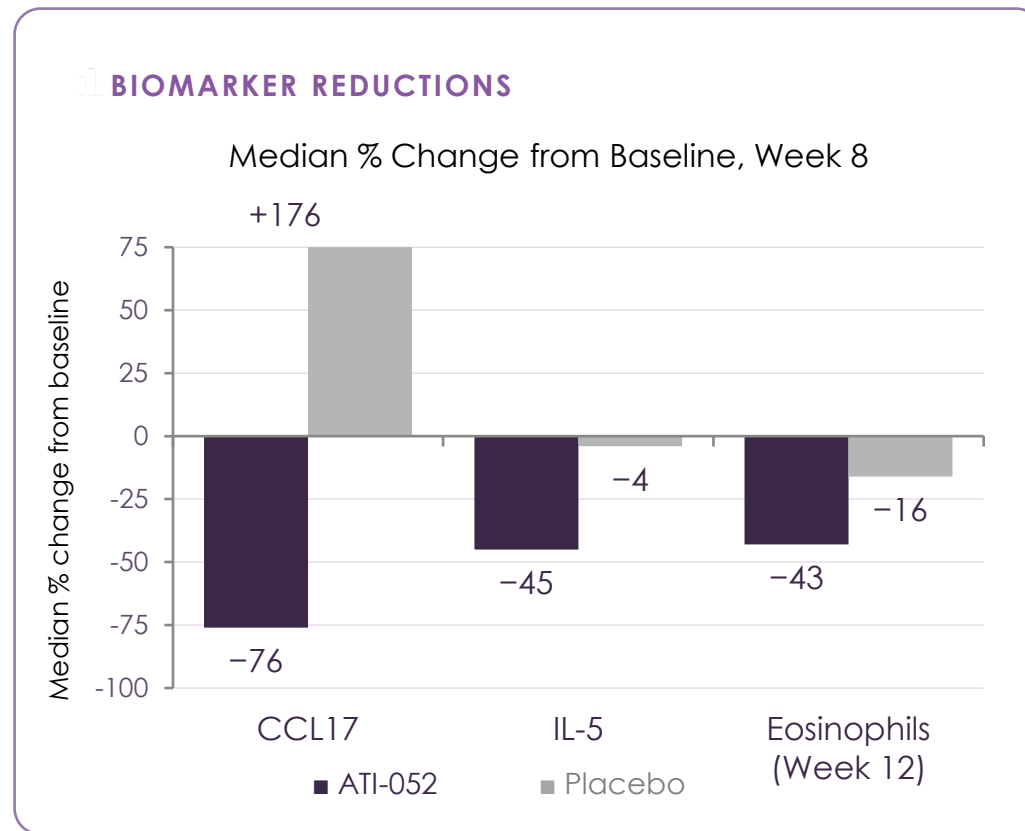
overall improvement in LS vs. NL proteome observed by Week 8

66%

overall improvement in LS vs. NL skin with dupilumab by Week 16

Results provided validation of additive/synergistic activity of dual IL-4R α + TSLP inhibition by ATI-052

ATI-052 Demonstrated Broad and Deep Biomarker Reductions



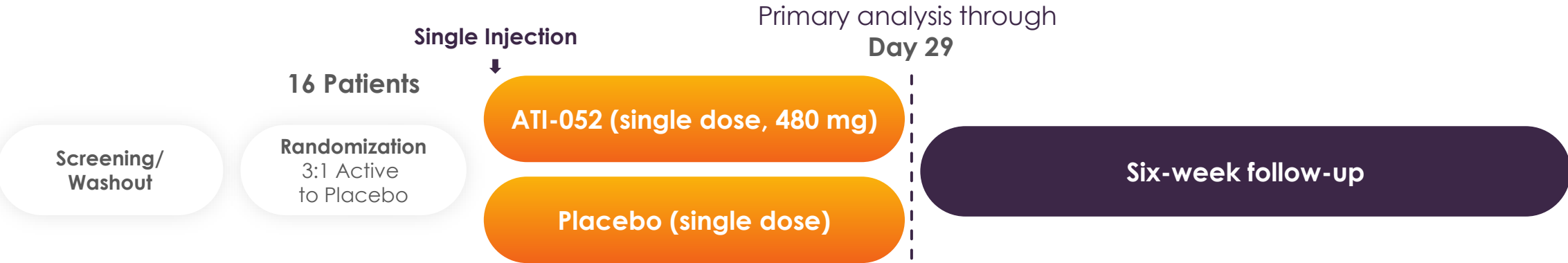
Downregulation of Th1, Th2, Th17/22 and Pruritus Signatures Observed



ATI-052 POC in Asthma

Data cutoff date: September 24, 2026

Phase 1b POC Trial in Asthma



Strategy	Clinical trial to assess a single dose of ATI-052 in a mild-to-moderate asthma population	
Location	United States and Europe: Multi-site	
Primary Endpoint	Safety and tolerability	
Other endpoints	Key Clinical Efficacy Assessment: FEV1, AX	PD assessments: FeNO, Blood Eos, TARC (CCL17), Periostin, Cytokines

Baseline Demographics and Asthma Severity

Characteristic	ATI-052 (N=12)	Placebo (N=4)
Age, mean (SD), y	44.4 (12.6)	39.8 (17.6)
Female, n (%)	3 (25.0)	3 (75.0)
Weight, mean (SD), kg	86.0 (12.8)	75.8 (23.2)
Duration of asthma from diagnosis, mean (SD), y	23.6 (12.0)	22 (20.8)
FeNO, mean (SD), ppb	72.3 (33.3)	97.3 (62.5)
Blood eosinophil count, mean (SD), cells/ μ L	378.3 (227.6)	395.0 (183.6)
<300 n (%)	5 (41.7)	2 (50.0)
$\geq$ 300 n (%)	7 (58.3)	2 (50.0)
FEV1, mean L, (SD)	2.85 (0.98)	3.16 (0.71)
FEV1, mean % predicted, (SD)	75.6 (22.1)	98.7 (22.8)
<80% n (%)	6 (50.0)	1 (25.0)
$\geq$80% n (%)	6 (50.0)	3 (75.0)

Strong Tolerability Profile Observed with ATI-052

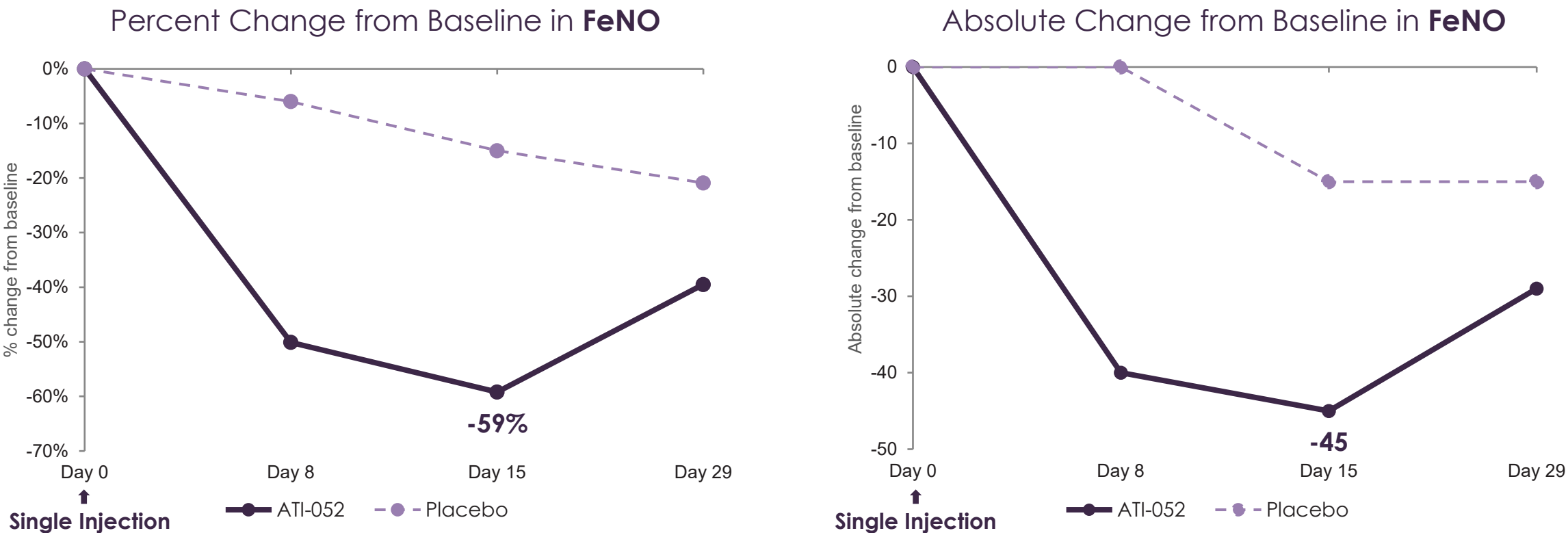
Favorable Safety Profile

Safety Summary	ATI-052 (N=12)	Placebo (N=4)
Patients reporting ≥1 TEAE, n (%)	6 (50)	1 (25)
Patients reporting ≥1 serious TEAE, n (%)	0	0
Patients reporting ≥1 Grade 3 or 4 TEAE, n (%)	0	0
Patients who discontinued due to TEAE, n (%)	0	0
Patients reporting ≥1 TRAE, n (%) (ISR)	1 (8.3)	0

- ATI-052 was well tolerated with Grade 1 ISRs as the most frequent AE
- **No conjunctivitis** observed in the Phase 1a/1b ATI-052 program

Rapid FeNO Suppression Observed from Single Dose of ATI-052

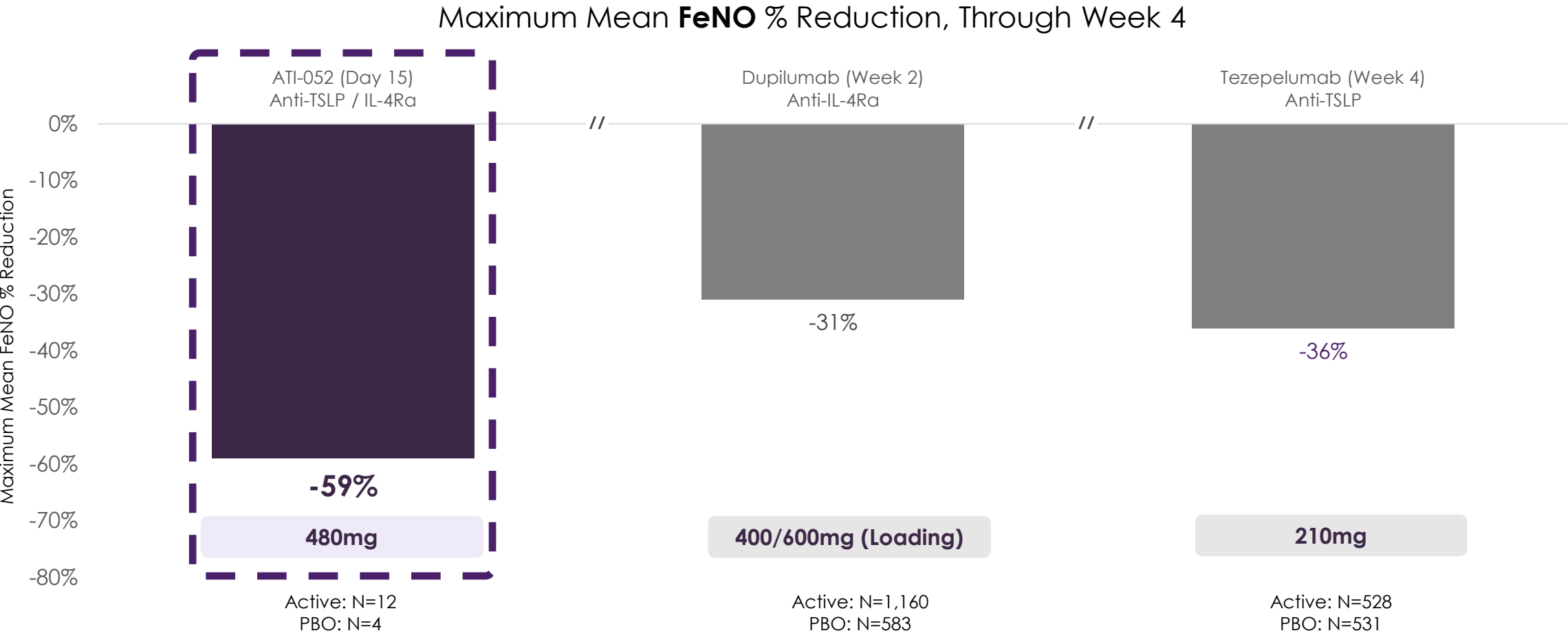
Maximum FeNO Reduction of 59% and 45ppb Validate Potency of ATI-052



Rapidity and Depth of FeNO Suppression Observed After a Single Dose of ATI-052; Provides Strong Signal and Proof-of-Concept



Single Dose of ATI-052 Demonstrated Deep Reduction in FeNO



NOTE: Data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

SOURCE: Tezepelumab: approx. (Menzies-Gow et al., *N Engl J Med.* 2021;384:1800-1809). Dupilumab: approx. (Pavord ID, et al. *J Allergy Clin Immunol Pract.* 2024;12(7):1763-177).

Similar Results Observed in Both T2-Low and T2-High Sub-Populations

60%

FeNO Reduction in Eos ≥ 300
Subgroup (T2-High) at Day 15

58%

FeNO Reduction in Eos < 300
Subgroup (T2-Low) at Day 15

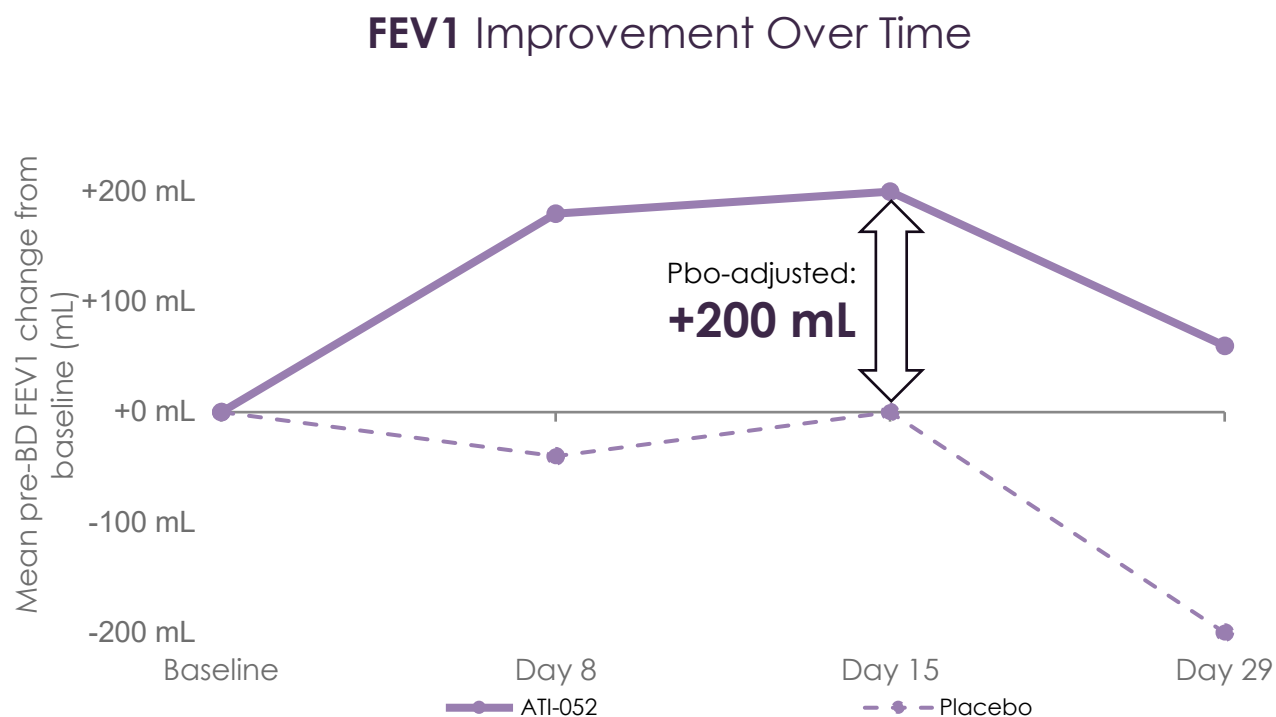
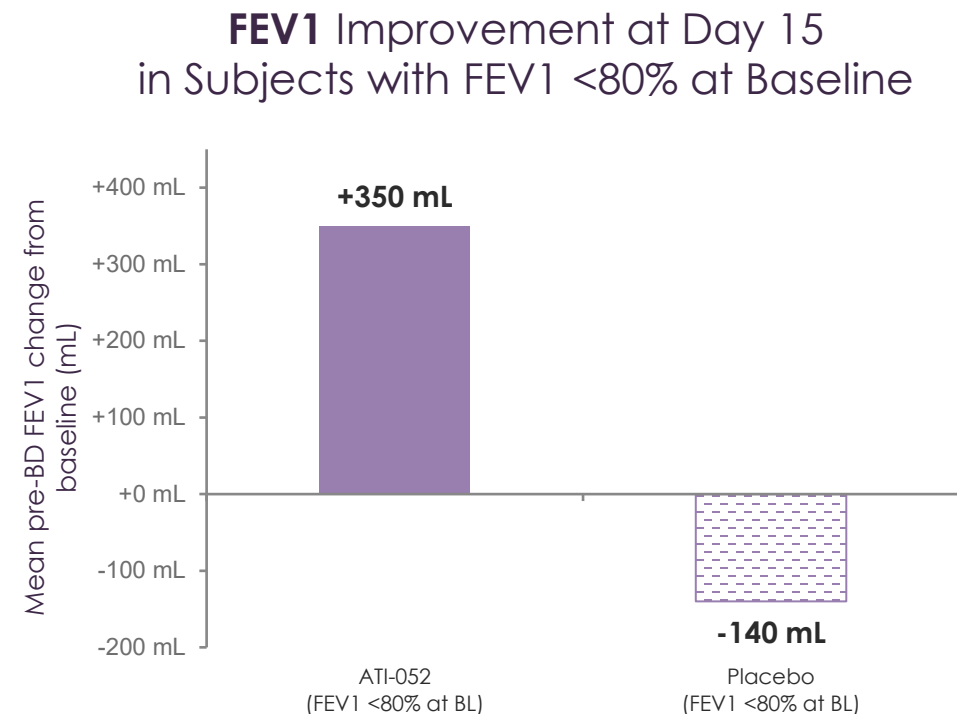
58%

of ATI-052 Subjects Achieved
FeNO Normalization (≤ 25 ppb)
at Day 15

FEV1 Improvement Was Also Observed in T2-High and T2-Low Sub-Populations

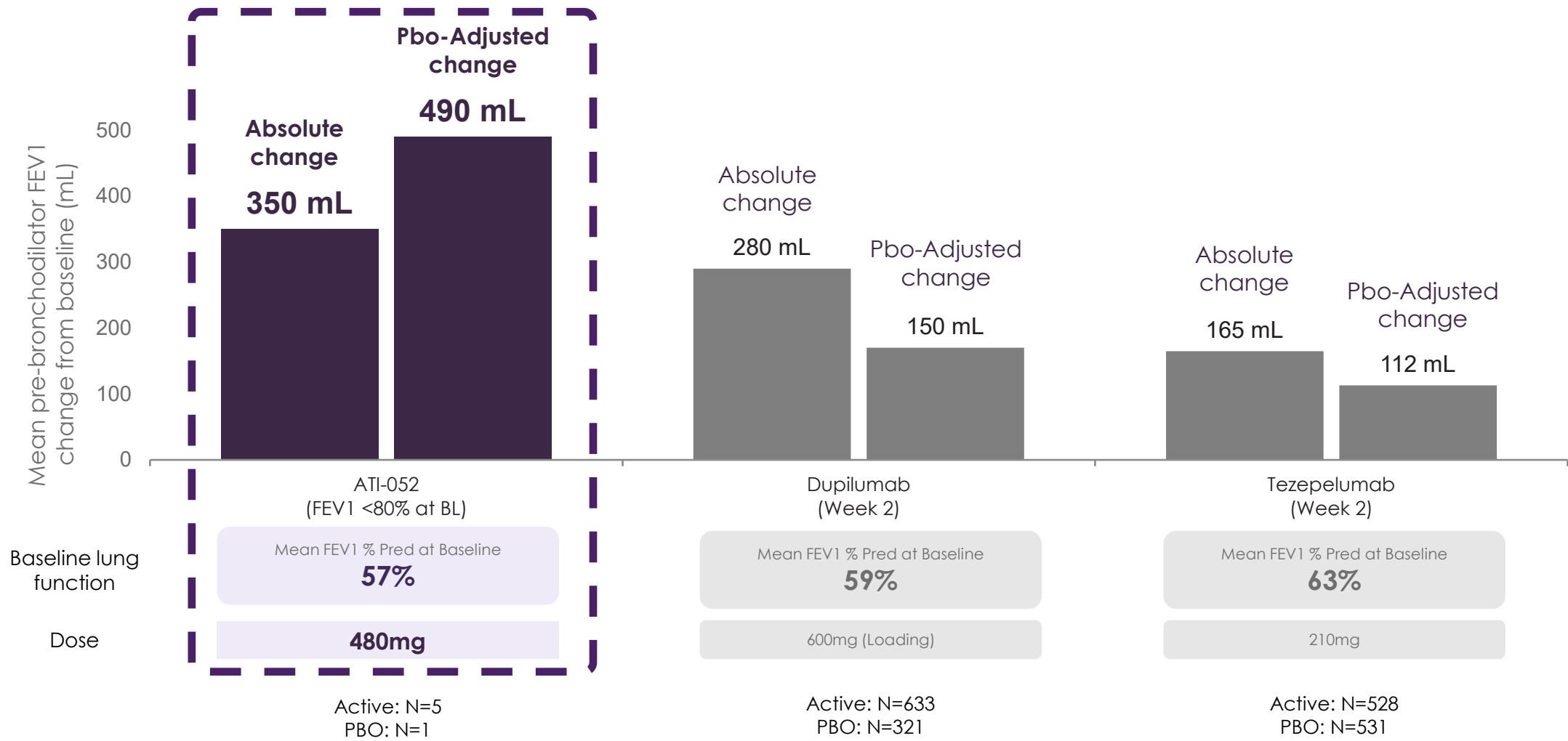
Rapid FEV1 Improvement Observed

Single Dose of ATI-052 Increased Absolute and Pbo-Adjusted FEV1



FEV1 Improvement Aligned with FeNO Suppression; Strong Signal and Proof-of-Concept

ATI-052 Improved FEV1 at Day 15

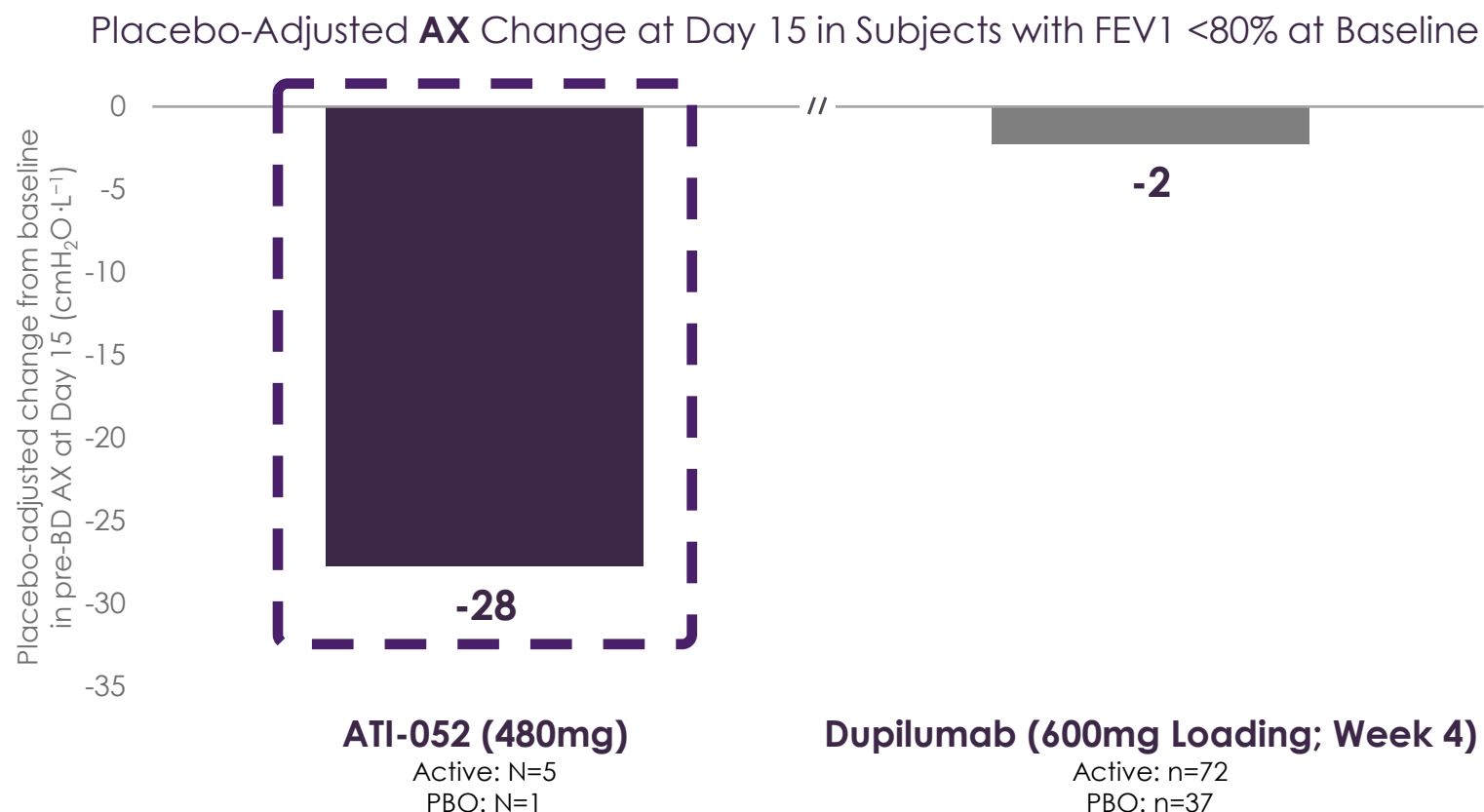


NOTE: All subgroup analyses were conducted post hoc. FEV1 <80% at BL = pre-BD FEV1 value of < 80% at baseline + post-BD reversibility of FEV1 ≥ 12% and ≥ 200 mL or documented history of post-BD FEV1 reversibility during last 12 months at screening. BD = bronchodilator; FEV1 = Forced expiratory volume in 1 second; PBO = placebo; BL = baseline. Data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

SOURCE: Tezepelumab: approx. (Menzies-Gow et al., *N Engl J Med.* 2021;384:1800-1809). Dupilumab: approx.(Castro et al. *N Engl J Med.* 2018;378:2486-2496).

ATI-052 Demonstrated Rapid Small Airway Disease (SAD) Improvement

AX (Area Under Reactance Curve) as a Marker of SAD Improvement



Small Airway Disease

- **Highly prevalent** in asthma across GINA Steps
- More than **doubles** exacerbation risk
- Nearly **3X the risk** when small airway disease is severe
- **1 in 3** 'well-controlled' patients has hidden SAD

NOTE: All subgroup analyses were conducted post hoc. FEV1 <80% at BL = pre-BD FEV1 value of < 80% at baseline + post-BD reversibility of FEV1 ≥ 12% and ≥ 200 mL or documented history of post-BD FEV1 reversibility during last 12 months at screening. BD = bronchodilator; FEV1 = Forced expiratory volume in 1 second; PBO = placebo; BL = baseline. Unit conversion: 1 kPa/L = 10.1972 cmH₂O·L⁻¹. Data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

SOURCE: Dupilumab: (Washko GR, et al. *J Allergy Clin Immunol*. 2025). Galant S, et al. *Lancet Respir Med*. 2025;13:990-1000.

ATI-052: Key Learnings and Next Steps

Key Learnings

Additivity/synergy potential demonstrated across preclinical, clinical, and PD measures

Breadth and depth of response:

- Clinical and PD evidence of activity against all 3 inflammatory endotypes in severe AD
- Both FENO & FEV1 improvements in T2 high & T2 low asthma patients

Strong evidence of TSLP involvement in AD

- Complete normalization of skin proteome
- Reduction in IL-5 and eosinophils

Encouraging early durability in severe AD patients

- Maintenance of response to at least week 16 (12 weeks after load in doses)
- Maintenance dosing expected to be the same in asthma and AD

Strong and potentially differentiated tolerability profile throughout the Phase 1 program including no conjunctivitis

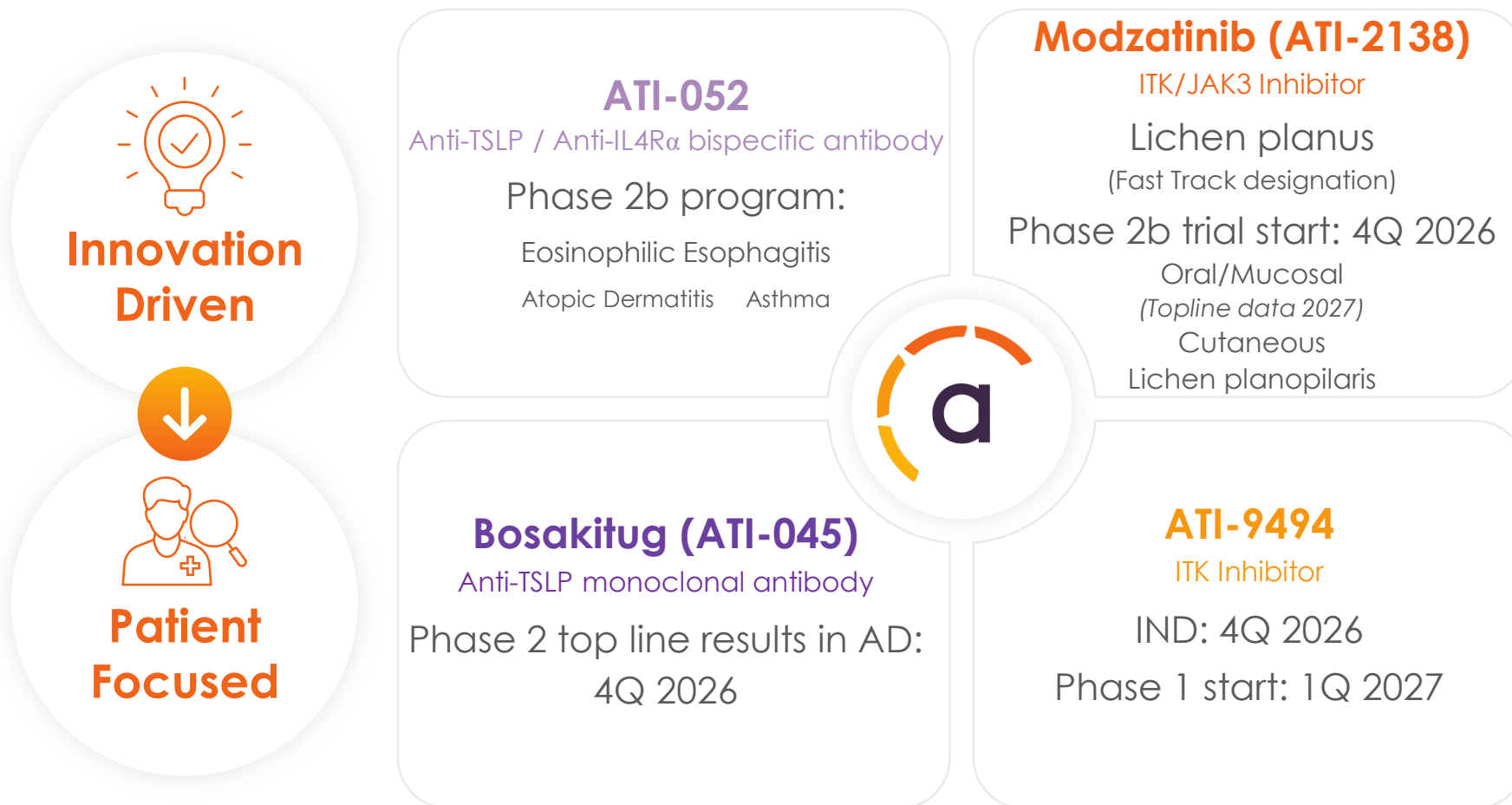
Go Forward Plan

ATI-052 is a potent, broadly acting compound with potential best-in-class activity

Moving into staged Phase 2b program

Opportunity to raise the efficacy ceiling with ATI-052 for patients

Continued Clinical Momentum Through 2027





ATI-052

Phase 1b Primary Analysis Results Atopic Dermatitis and Asthma

October 27, 2026

EMPOWERING PATIENTS THROUGH

**THERAPEUTIC
INNOVATION**

