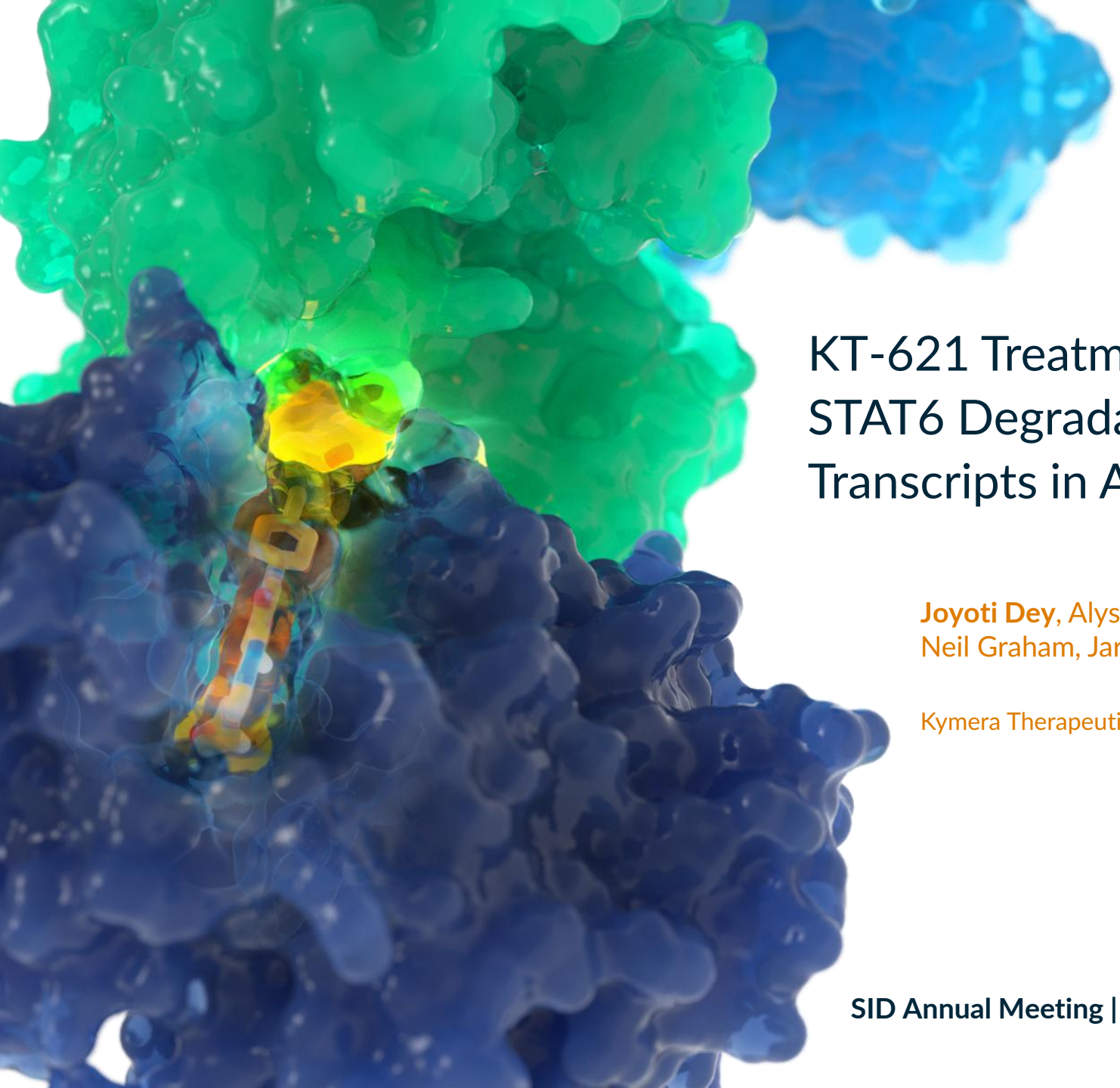

May 16, 2026

KT-621 Treatment Induces Rapid and Deep STAT6 Degradation and Modulation of Th2 Gene Transcripts in Atopic Dermatitis Lesional Skin

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Kymera Therapeutics, Inc., Watertown, MA, USA

SID Annual Meeting | Chicago, IL | May 13-16, 2026

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Conflict of Interest Disclosure

Joyoti Dey, Alyssa Fasciano, Rahul Karnik, Heather Paleczny, Neil Graham, Jared Gollob, Nello Mainolfi, and Sudha Visvanathan are employees with shares and stock options of Kymera Therapeutics, Inc.

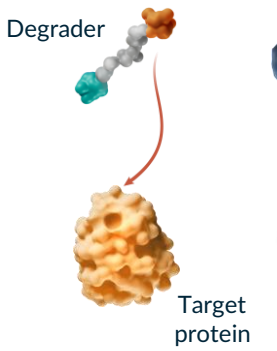
This study was funded by Kymera Therapeutics, Inc.

Targeted Protein Degradation: Achieving Biologics-Like Activity With Oral Medicines

Targeted Protein Degradation (TPD) Mechanism of Action

Harnessing the E3 Ubiquitin Proteasome System

1 Catching the Target Protein



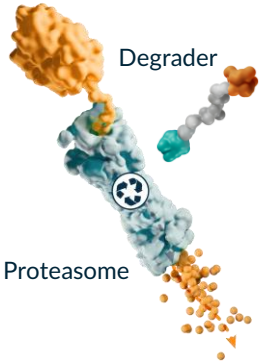
Degrader molecule engages target protein and E3 ubiquitin ligase to bring them in close proximity

2 Presenting the Target Protein

3 Tagging the Target Protein

E3 ligase places a chain of ubiquitin molecules on the target protein

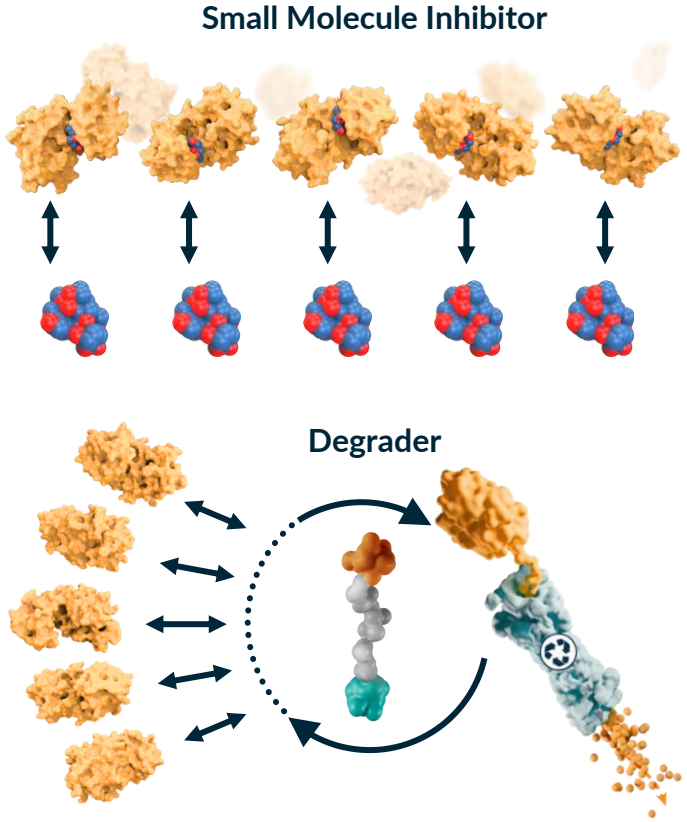
4 Degrading the Target Protein



Ubiquitin is recognized by the proteasome to selectively degrade the target protein

Degraders Enable Continuous, Complete Pathway Blockade

Superior to Traditional Small Molecule Inhibitors



STOICHIOMETRIC INHIBITION

Pharmacodynamic (PD) effect correlated to drug exposure pharmacokinetics (PK) (stoichiometric) requiring continuous high drug exposures to block protein function

CONTINUOUS DEGRADATION

PD not directly correlated to PK (catalytic), allowing fast, complete protein elimination and continuous pathway blockade with low/short drug exposures

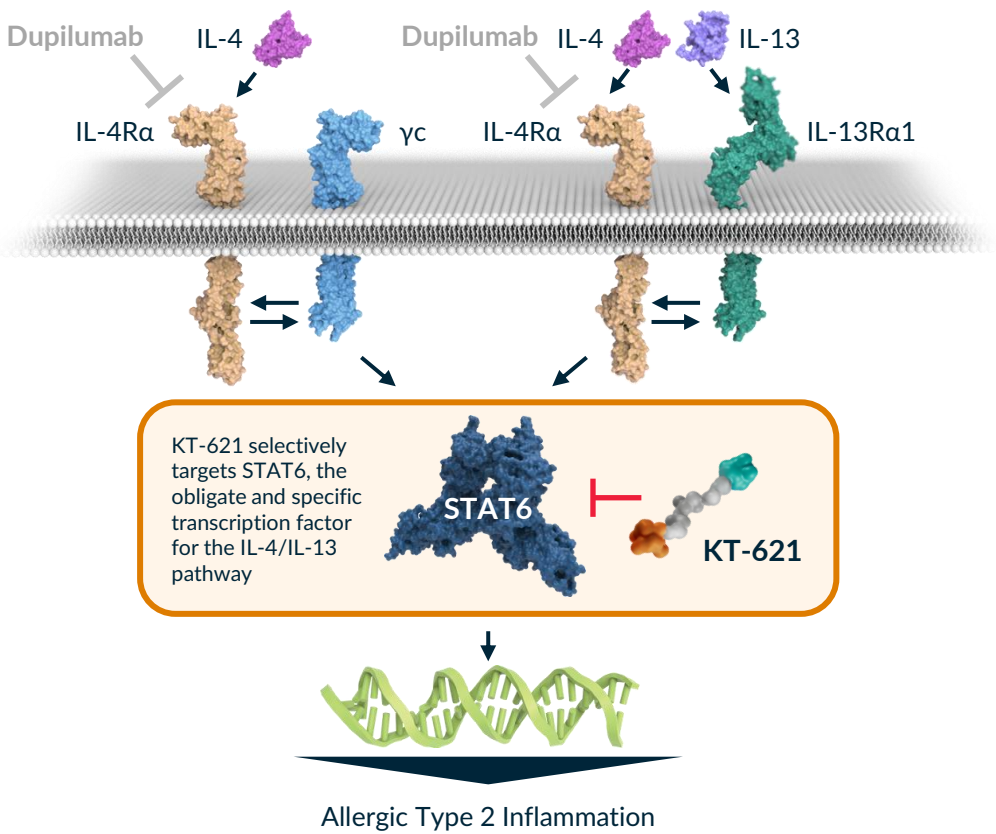
Catalytic activity of degraders enables a single molecule to drive degradation of multiple copies of the target protein, delivering deep and continuous pathway blockade with biologics-like activity in a pill

Mainolfi N, Rasmusson T. *Annual Reports Med Chem*. 2017;50:301-334.
PD, pharmacodynamics; PK, pharmacokinetics; TPD, targeted protein degradation.

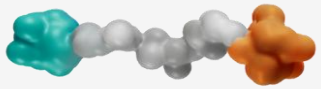
STAT6: Highly Validated, Historically Undrugged Target for Treatment of Type 2 Inflammatory Diseases

STAT6
TRANSCRIPTION FACTOR

- STAT6 is the specific transcription factor in the IL-4/IL-13 pathway[1-3]
- IL-4/IL-13 is clinically validated by dupilumab across multiple Type 2 diseases:
  - AD, asthma, COPD, EoE, CRSwNP, CSU, PN, BP[4]
- STAT6 is genetically validated by human GoF and heterozygous LoF alleles, and mouse knockout phenotype[1,5]
- While several therapies target the upstream IL-4/IL-13 receptors, there are no known drugs that selectively target this pathway with oral delivery[4]



KT-621
FIRST-IN-CLASS, ORAL, ONCE-DAILY, STAT6 DEGRADER[6]



- Provides complete STAT6 degradation selectivity in human PBMC proteome at 100 x DC_{90} and picomolar potency across all disease-relevant cell types
- Fully blocks IL-4/IL-13 pathway in human Type 2 functional assays and in vivo models
- In a first-in-human Phase 1a study in healthy volunteers, KT-621 demonstrated deep STAT6 degradation in blood and skin following low daily oral doses, reductions of multiple disease relevant Type 2 biomarkers, and a safety profile undifferentiated from placebo

1. Kaplan MH, et al. *Immunity*. 1996;4:313-319; 2. Takeda K, et al. *J Immunol*. 1996;157(8):3220-3222; 3. Junttila IS. *Front Immunol*. 2018;9:888; 4. Kolkhir P, et al. *Nat Rev Drug Discov*. 2023;22(9):743-767; 5. Sharma M, et al. *J Exp Med*. 2023;220(5):e20221755; 6. Shabbir A, et al. European Academy of Dermatology and Venereology Congress; Sept 17-20, 2025; Paris, France.
AD, atopic dermatitis; BP, bullous pemphigoid; COPD, chronic obstructive pulmonary disease; CRSwNP, chronic rhinosinusitis with nasal polyps; CSU, chronic spontaneous urticaria; DC_{90}, 90% degradation concentration; EoE, eosinophilic esophagitis; γc, gamma chain; GoF, gain of function; IL, interleukin; LoF, loss of function; PBMC, peripheral blood mononuclear cells; PN, prurigo nodularis; STAT6, signal transducer and activator of transcription 6.

KT-621 BroADen Phase 1b Study Design

BROADEN STUDY

Open-label, multicenter, single-arm study evaluated the safety, tolerability, PK, PD, and clinical activity of oral KT-621 in adults with moderate-to-severe AD

Screening

Baseline entry criteria:

- Adult, patients with moderate-to-severe AD
  - EASI ≥16
  - vIGA-AD™ ≥3
  - Weekly average PP-NRS ≥4
  - ≥10% BSA
  - Documented TCS failure

Each Cohort Dosed for 28 Days

Cohort 1: KT-621 100 mg QD (n=10)

Cohort 2: KT-621 200 mg QD (n=12)

14 Days

Follow-Up

Endpoints

Primary
- Safety

Secondary
- Plasma PK

Exploratory
- STAT6 degradation in blood and skin lesions
- Type 2 biomarkers in blood and skin lesions
- Clinical activity: EASI, vIGA-AD, BSA, SCORAD
- PROs: PP-NRS, POEM

Prior biologics were allowed, after washout, if patient had responded to treatment. Concurrent medications for AD not permitted.
AD, atopic dermatitis; BSA, body surface area; EASI, Eczema Area and Severity Index; PD, pharmacodynamics; PK, pharmacokinetics; POEM, Patient Oriented Eczema Measure; PP-NRS, Peak Pruritus Numerical Rating Scale; PRO, patient-reported outcome; QD, once daily; SCORAD, SCORing Atopic Dermatitis; STAT6, signal transducer and activator of transcription 6; TCS, topical corticosteroid; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis.

KT-621 BroADen Phase 1b Demographics and Baseline Characteristics

Generally Well-Balanced Across Treatment Cohorts

BROADEN STUDY

Patient Demographics

	100 mg (n=10)	200 mg (n=12)	Overall (n=22)
Gender, n (%)			
Female	6 (60.0)	7 (58.3)	13 (59.1)
Male	4 (40.0)	5 (41.7)	9 (40.9)
Age, years, mean (SD)	30.1 (8.5)	33.0 (11.4)	31.7 (10.1)
BMI, kg/m^2, mean (SD)	32.8 (11.5)	30.8 (9.2)	31.7 (10.1)
Ethnicity, n (%)			
Hispanic or Latino	3 (30.0)	2 (16.7)	5 (22.7)
Non-Hispanic or Latino	7 (70.0)	10 (83.3)	17 (77.3)
Race, n (%)			
White	4 (40.0)	3 (25.0)	7 (31.8)
Black or African American	5 (50.0)	7 (58.3)	12 (54.5)
Asian	0	1 (8.3)	1 (4.5)
Mixed/Other	1 (10.0)	1 (8.3)	2 (9.1)

Patient Baseline Characteristics

	100 mg (n=10)	200 mg (n=12)	Overall (n=22)
vIGA-AD™, n (%)			
Moderate (3)	6 (60.0)	6 (50.0)	12 (54.5)
Severe (4)	4 (40.0)	6 (50.0)	10 (45.5)
EASI Score, mean (SD)	23.5 (7.5)	26.1 (9.0)	24.9 (8.3)
Other Disease Characteristics, mean (SD)			
PP-NRS	7.4 (1.2)	7.6 (0.9)	7.5 (1.0)
SCORAD	55.7 (15.6)	63.8 (13.4)	60.1 (14.7)
BSA (%)	29.1 (9.8)	30.0 (15.1)	29.6 (12.7)
POEM	16.1 (6.74)	20.8 (5.15)	18.6 (6.25)
Comorbid Type 2 Diseases, n (%)			
Asthma	1 (10.0)	3 (25.0)*	4 (18.2)
Allergic Rhinitis	2 (20.0)	7 (58.3)	9 (40.9)
Prior Systemic AD Tx, n (%)	1 (10.0)†	4 (33.3)‡	5 (22.7)

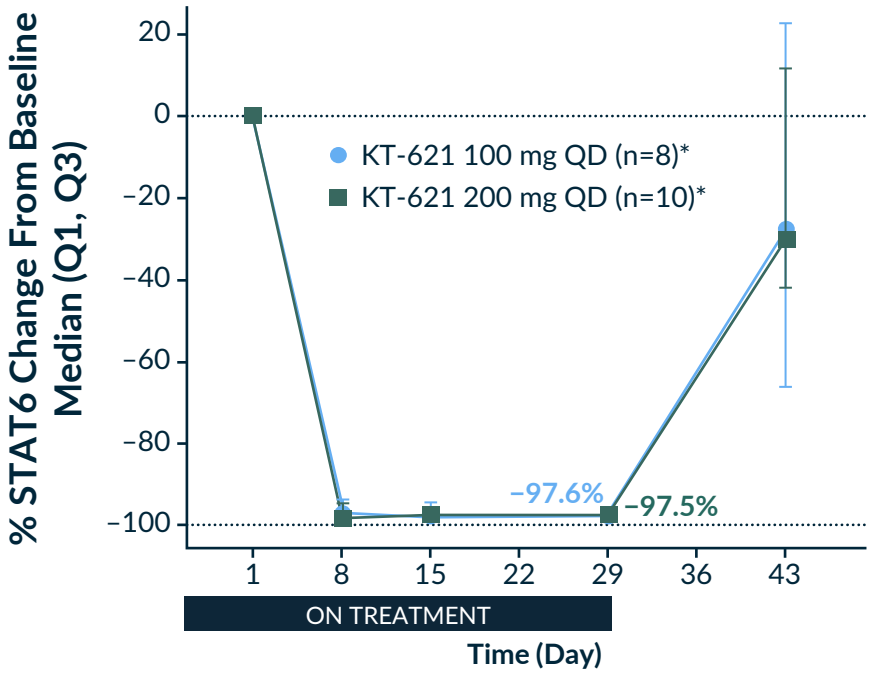
*Three patients also had comorbid allergic rhinitis. †Patient had prior dupilumab treatment. ‡Two patients had prior dupilumab treatment, one had prior tralokinumab treatment, and one had received both agents.
AD, atopic dermatitis; BMI, body mass index; BSA, body surface area; EASI, Eczema Area and Severity Index; POEM, Patient Oriented Eczema Measure; PP-NRS, Peak Pruritus Numerical Rating Scale; SCORAD, SCORing Atopic Dermatitis; SD, standard deviation; Tx, therapy; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis.

KT-621 Achieved Rapid and Deep STAT6 Degradation in Blood and Skin

Degradation Maintained for 28 Days Across Both Dose Cohorts

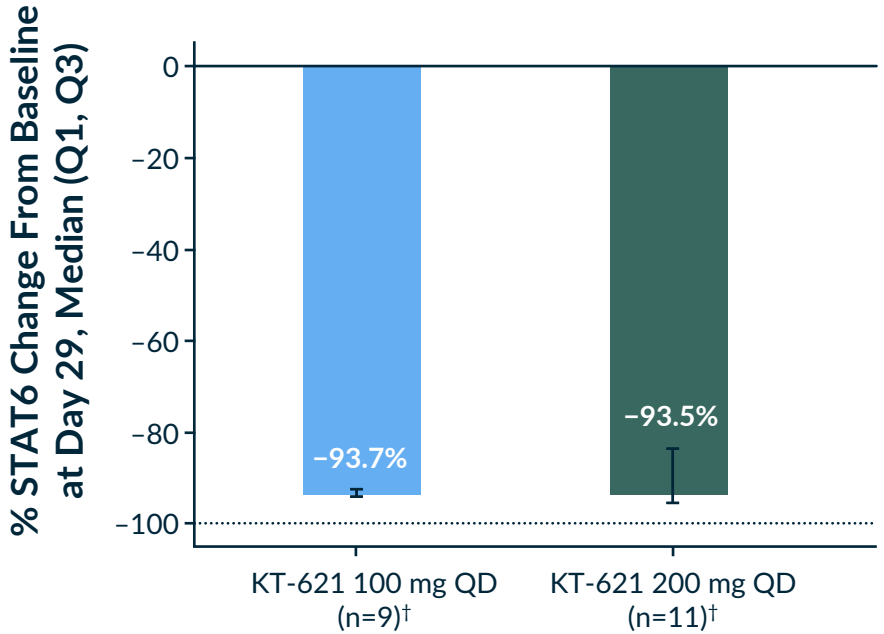
Median STAT6 Degradation in Blood

Method: Flow Cytometry



Median STAT6 Degradation in Skin

Method: Targeted Mass Spectrometry

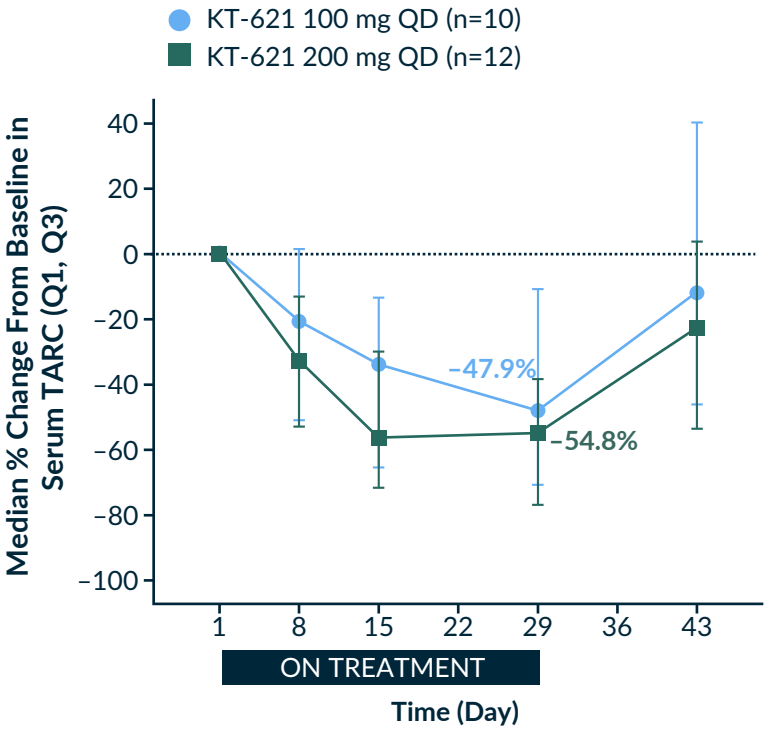


- Median STAT6 degradation of 98% in blood in both dose groups maintained throughout the treatment period
- Deep skin degradation of 94% in both dose groups with multiple patients' STAT6 levels below the lower limit of quantification

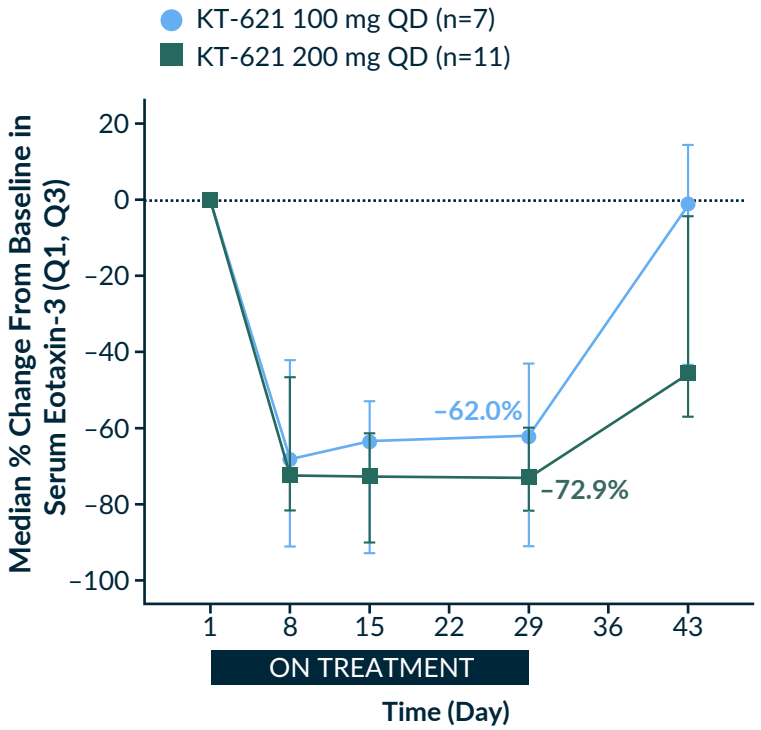
n values reflect the number of participants with available samples at Day 29. *Two patients (one each in 100 mg and 200 mg dose groups) did not have baseline samples collected, and two Day 29 samples (one in each dose group) were unevaluable due to shipping issues that led to loss of stability. †Two patients (one in each dose group) did not consent to Day 29 biopsies.
Q1, lower quartile; Q3, upper quartile; QD, once daily; STAT6, signal transducer and activator of transcription 6.

KT-621 Demonstrated Marked Reductions in Type 2 Inflammation Biomarkers in Blood With Corresponding Improvements in EASI

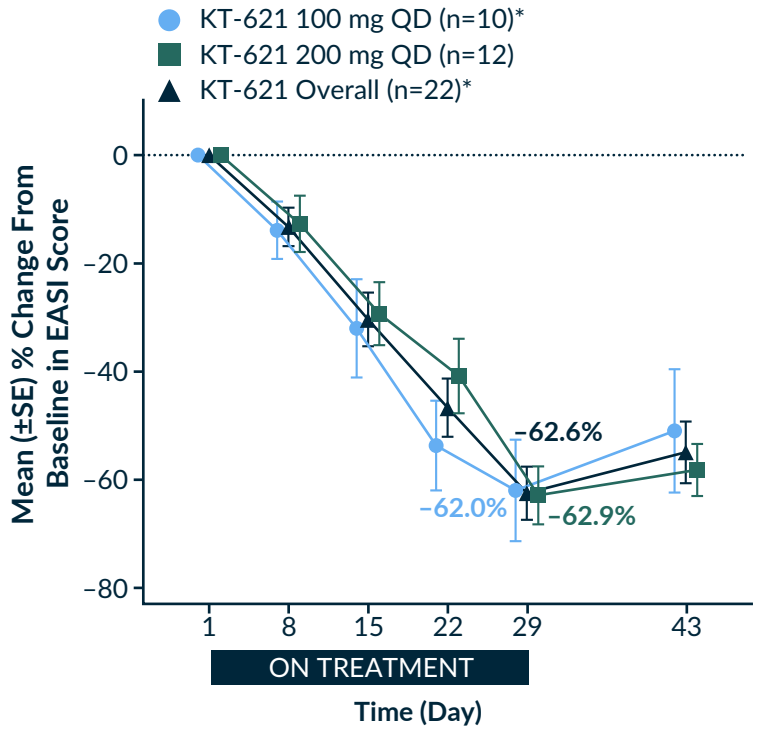
Median % Change From Baseline in TARC



Median % Change From Baseline in Eotaxin-3



Mean % Change From Baseline in EASI



- Rapid and robust reduction of TARC and Eotaxin-3 across both dose cohorts
- Marked and early improvements in mean EASI across both dose cohorts, with responses evident by Day 8 and continuing through Week 4 without apparent plateau

n values reflect the number of participants with available samples at Day 29. *One patient in the 100 mg cohort missed Day 29 visit (n=9 for 100 mg and n=21 for overall at Day 29).
EASI, Eczema Area and Severity Index; Q1, lower quartile; Q3, upper quartile; QD, once daily; SE, standard error; TARC, thymus and activation-regulated chemokine.

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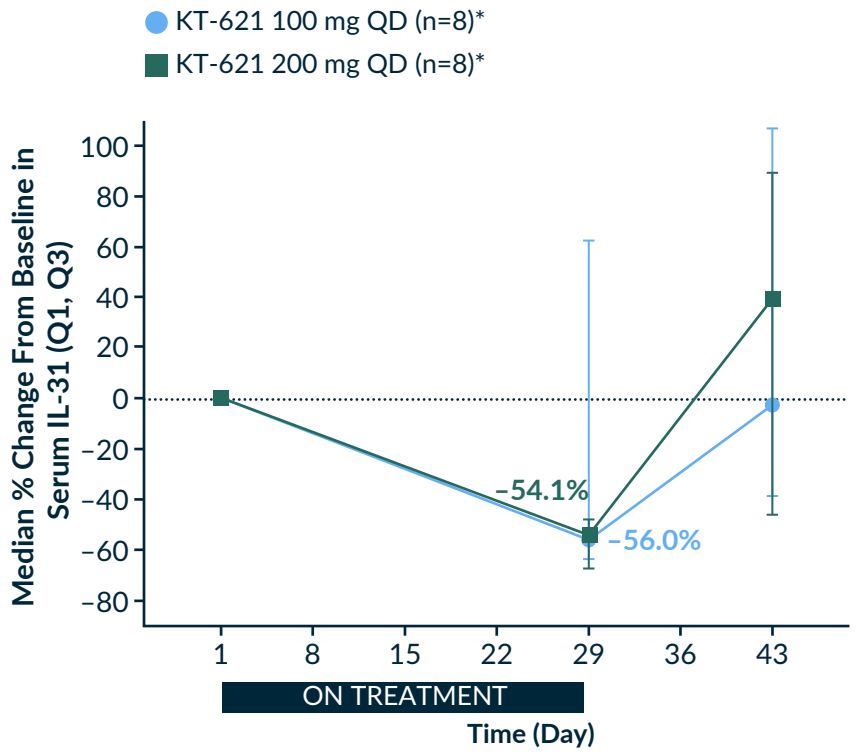
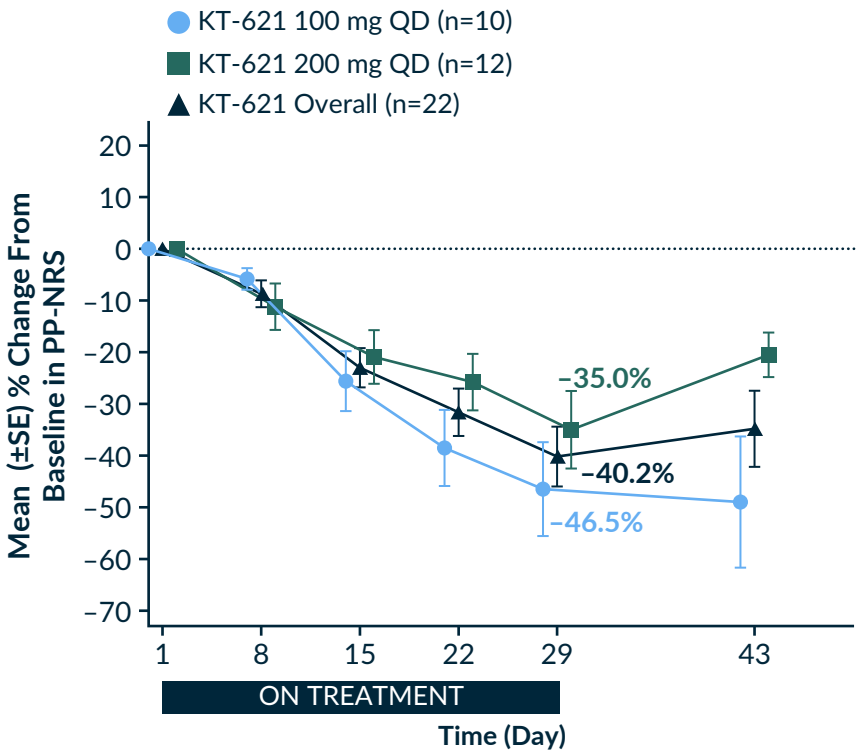
KT-621 Showed Marked Reductions in IL-31 in Blood, Which Corresponded to Improvements in PP-NRS by Week 4

Median % Change From Baseline in IL-31



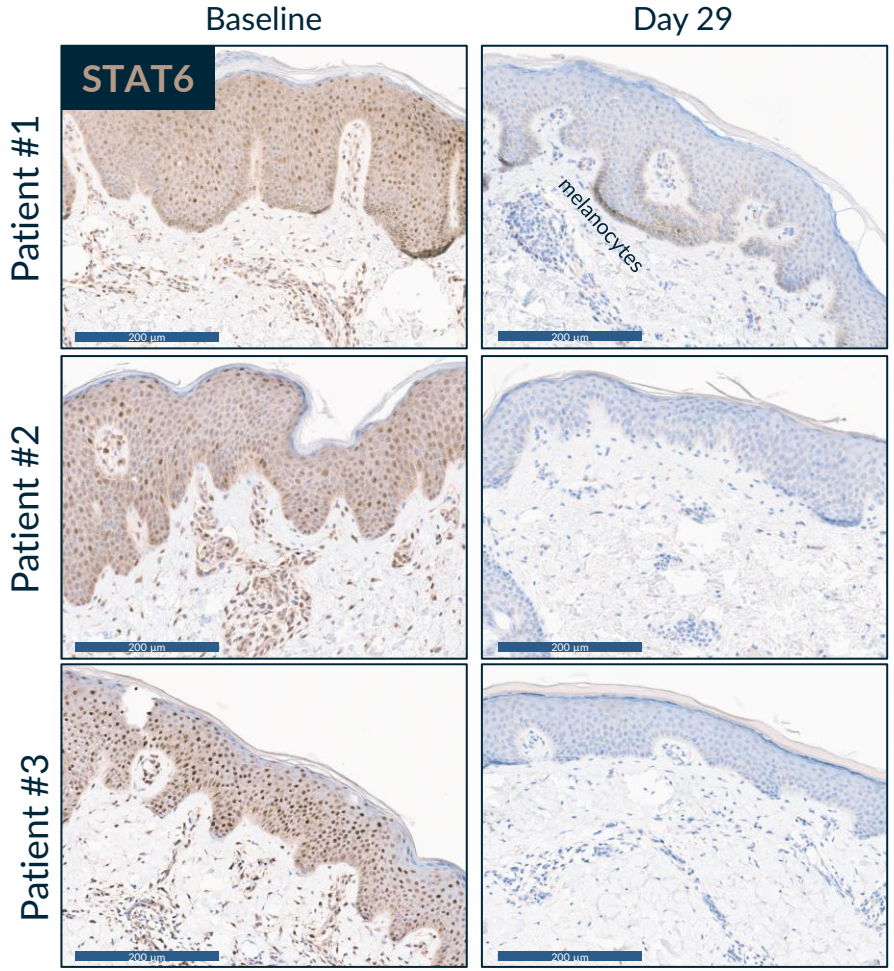
Mean % Change From Baseline in PP-NRS

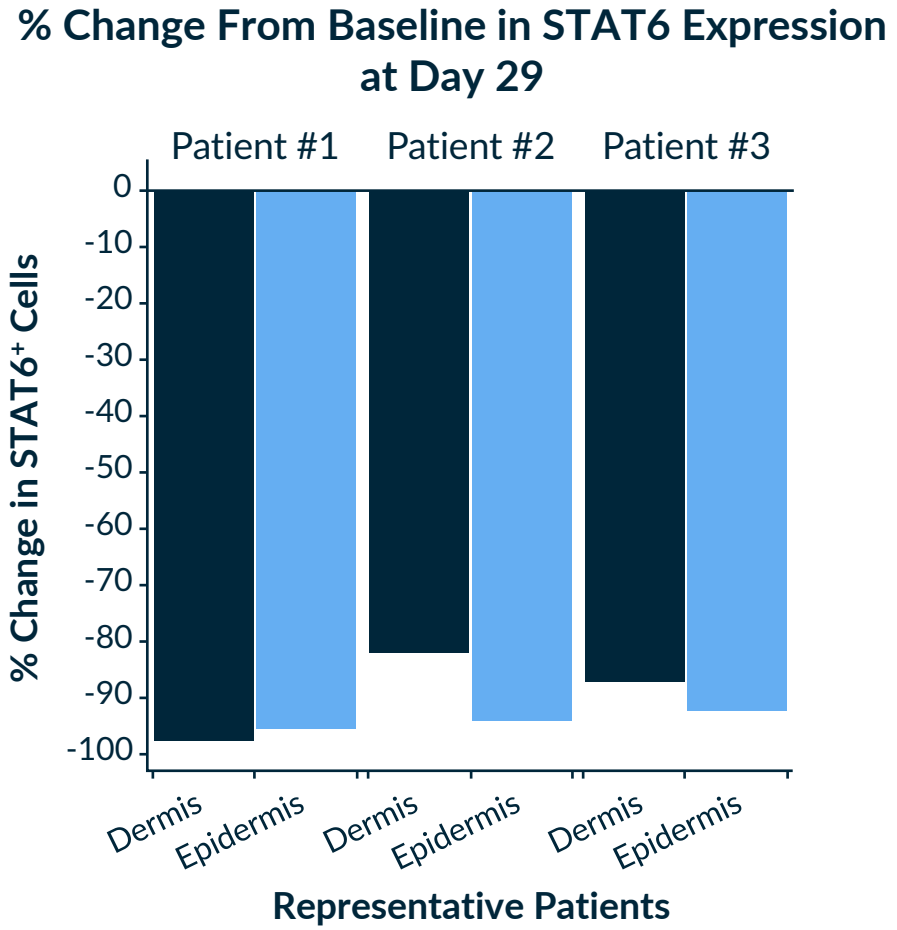


- First known demonstration of serum IL-31 reduction in patients with AD in response to IL-4/IL-13 pathway inhibition, with up to 56% median reduction by Week 4
- Early and progressive reductions in mean PP-NRS, with 40% improvement overall by Week 4 and no evidence of plateau during treatment duration

n values reflect the number of participants with available samples at Day 29. *In the 100 mg group, two patients had baseline levels below the LLOQ and change could not be calculated at Day 29; in the 200 mg group, data for three patients were not available and one had baseline level below LLOQ at Day 29.
AD, atopic dermatitis; IL, interleukin; LLOQ, lower limit of quantification; PP-NRS, Peak Pruritus Numerical Rating Scale; Q1, lower quartile; Q3, upper quartile; QD, once daily; SE, standard error.

KT-621 Leads to Marked Reductions in Epidermal and Dermal STAT6 Expression in Lesional Skin Biopsies





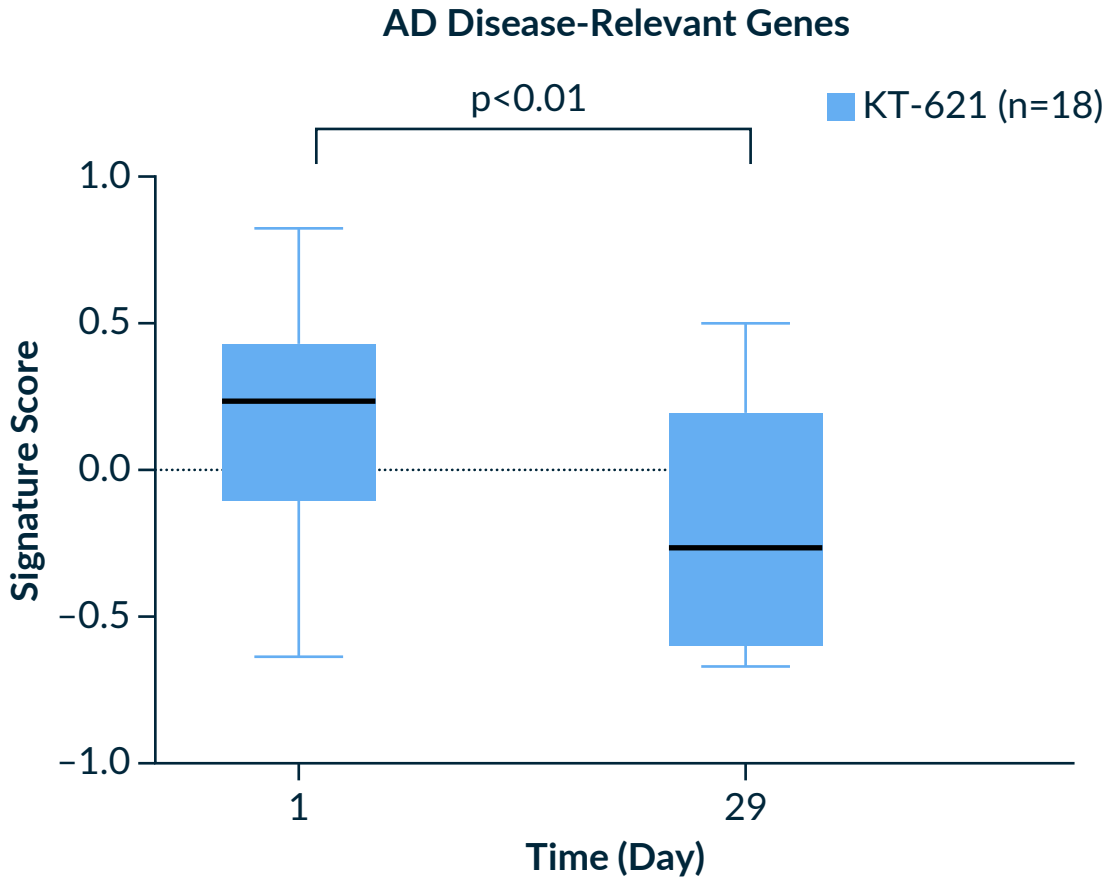
- Robust STAT6 reduction across epidermis and dermis, confirming strong target engagement in lesional skin

Scale bar = 200 µm. STAT6⁺ cells were measured in formalin-fixed, paraffin-embedded baseline and Day 29 biopsies by immunohistochemistry with digital image analysis, segmented by epidermis and dermis.
STAT6, signal transducer and activator of transcription 6.

KT-621 Significantly Downregulated AD Disease-Relevant Gene Set in Lesional Skin Biopsies

Genes in signature*

- CCL26/Eotaxin-3 (Type 2)
- CCL18/PARC (Type 2)
- CCL13/MCP-4 (Type 2)
- CCL17/TARC (Type 2)
- MMP12 (general inflammation)
- CXCL1/GRO-α (Th17)
- KRT16/Keratin 16 (skin hyperplasia)
- POSTN/Periostin (fibrosis)
- TSLP
- OSMR/Oncostatin-M receptor (itch)
- S100A12 (Th17/Th22)
- PI3/Peptidase inhibitor 3 (Th17)



- Broad downregulation of AD disease-relevant genes in lesional skin after 4 weeks of dosing, consistent with robust suppression of Type 2 inflammation by KT-621

1. Hänzelmann S, et al. *BMC Bioinformatics*. 2013;14:7.
n values reflect the number of participants with available samples at Day 29. In the 100 mg group, one patient did not consent to biopsy; in the 200 mg group, one patient did not consent to Day 29 biopsy, one patient's Day 29 biopsy was lost, and one patient had poor quality sequencing. *Signature scores were generated by GSVA.[1]
AD, atopic dermatitis; CCL, C-C motif chemokine ligand; CXCL, C-X-C motif chemokine ligand; GRO, growth-regulated oncogene; GSVA, gene set variation analysis; MCP, monocyte chemoattractant protein; MMP, matrix metalloproteinase; PARC, pulmonary and activation-regulated chemokine; TARC, thymus and activation-regulated chemokine; Th, T helper; TSLP, thymic stromal lymphopoietin.

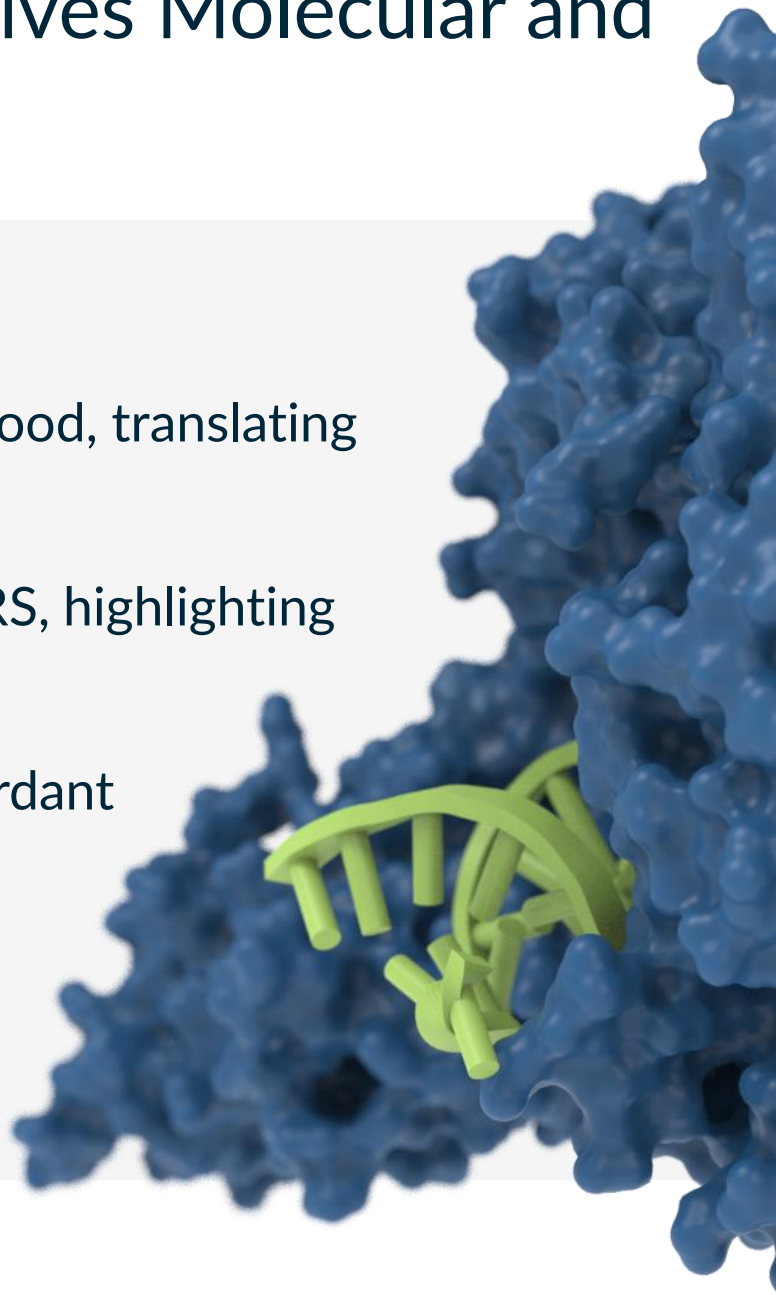
KT-621 Phase 1b Safety Summary

- Well-tolerated with favorable safety at both 100 mg and 200 mg doses
- No SAEs or severe AEs
- No dose-dependent pattern in the TEAEs
- No related TEAEs or TEAEs leading to discontinuation
- No AEs of conjunctivitis (or of any ocular disorder), herpes infections, or arthralgias
- No clinically relevant changes in vital signs, laboratory tests, or ECGs

AE, adverse event; ECG, electrocardiogram; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

KT-621: First Evidence That STAT6 Targeting Drives Molecular and Clinical Responses in Patients With AD

- Deep, rapid STAT6 degradation in both blood and lesional skin
- Broad and robust suppression of Type 2 inflammation biomarkers in blood, translating to rapid improvements in EASI
- Strong decreases in IL-31 in blood and marked improvements in PP-NRS, highlighting the impact on a key clinical manifestation of AD
- Markedly reduced epidermal and dermal STAT6 expression with concordant downregulation of AD-relevant gene expression in lesional skin, demonstrating robust tissue-level activity
- Favorable safety profile and tolerability at both 100 mg and 200 mg doses



AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IL, interleukin; PP-NRS, Peak Pruritus Numerical Rating Scale; STAT6, signal transducer and activator of transcription 6.

KT-621: BROADEN2 Phase 2b Trial

Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Dose-ranging

BROADEN2 TRIAL

Adult & Adolescent Patients With Moderate-to-Severe AD
Ages 12–75 years

Baseline entry criteria:
EASI ≥16
vIGA-AD ≥3
PP-NRS ≥4
BSA ≥10%
Documented TCS failure

Design

- Randomized, double-blind, placebo-controlled
- ~200 patients
- Daily dose for 16 weeks; 52-week open-label extension

Dosing

- Three KT-621 doses + one placebo (1:1:1:1)

Endpoints

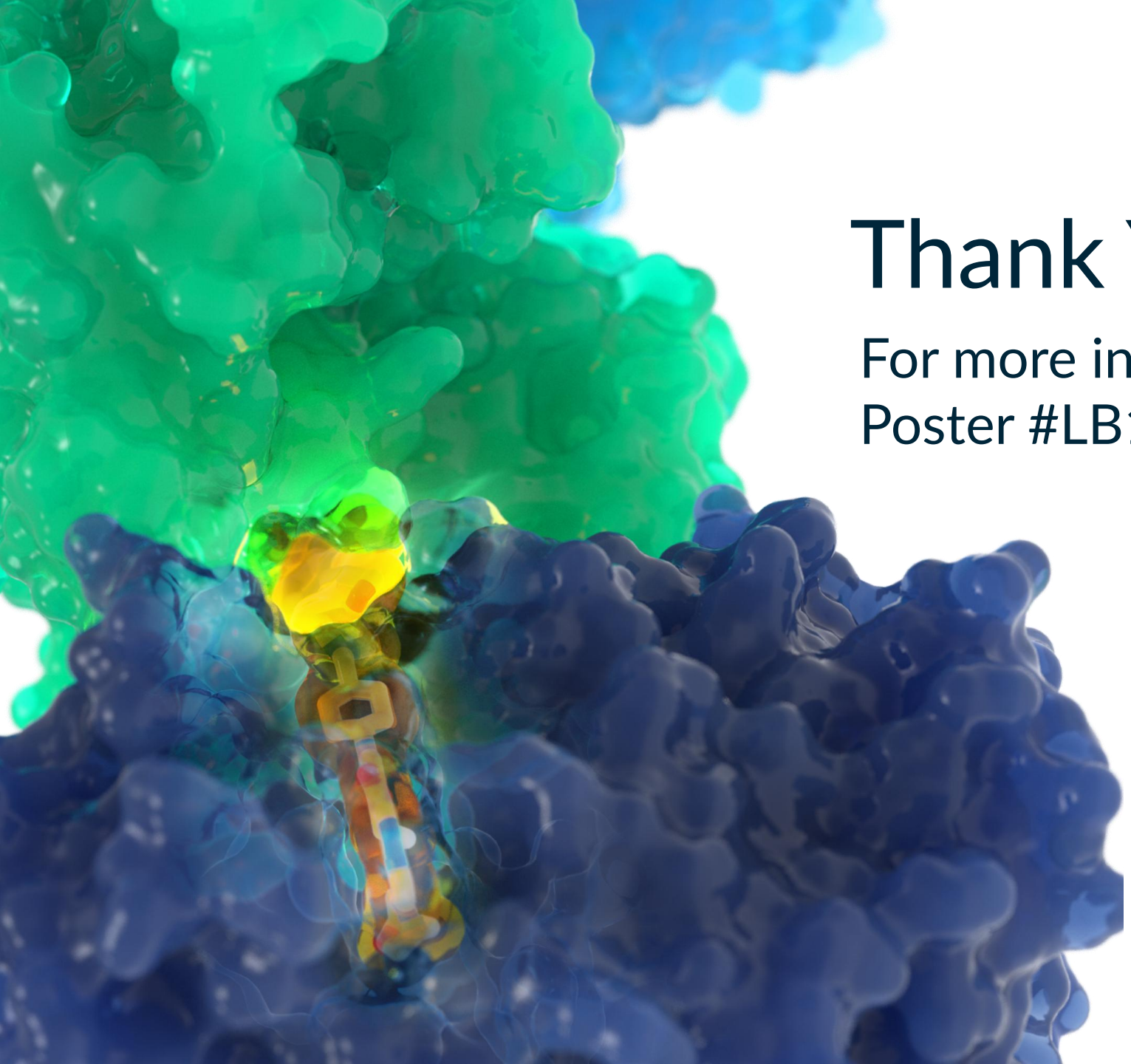
- Primary endpoint: Percent change from baseline in EASI score at week 16
- Secondary endpoints include:
  - EASI-50, EASI-75, vIGA-AD 0 or 1
  - ≥4-point improvement from baseline in PP-NRS

Key Trial Aim

Establish clinical activity and safety in **AD to select dose to support Phase 3 studies** in multiple dermatological and gastrointestinal indications

Status update:
Ongoing;
Data expected by mid-2027

AD, atopic dermatitis; BSA, body surface area; EASI, Eczema Area and Severity Index; PP-NRS, Peak Pruritus Numerical Rating Scale; TCS, topical corticosteroid; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis.



Thank You

For more information, please visit our Poster #LB1157 or www.kymeratx.com

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