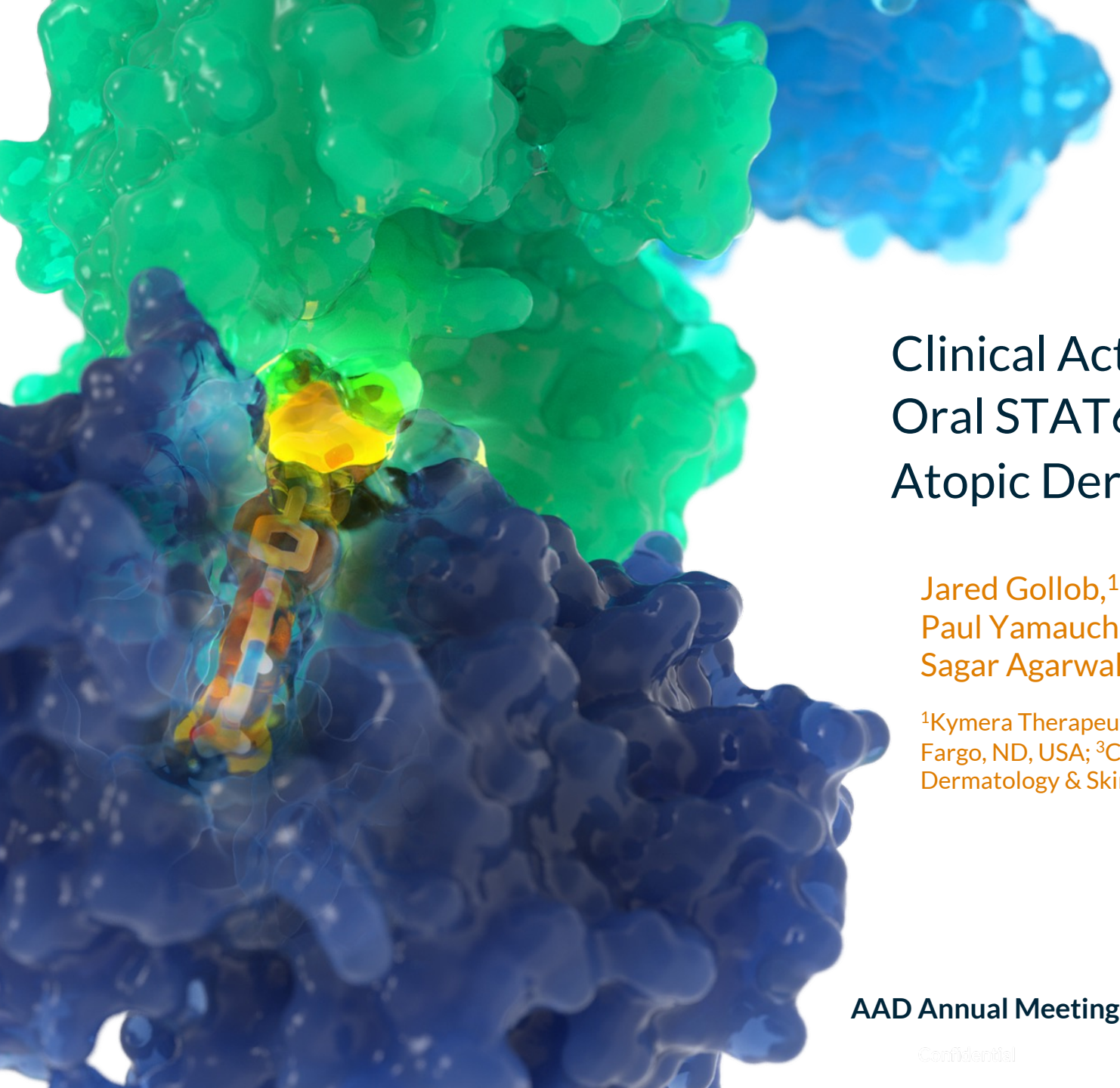

March 28, 2026

Clinical Activity and Safety of KT-621, an Oral STAT6 Degrader, in Moderate-to-Severe Atopic Dermatitis: Phase 1b Trial Results

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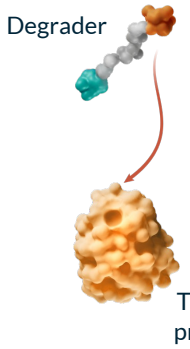
Targeted Protein Degradation: Achieving Biologics-like Activity with Oral Medicines

Targeted Protein Degradation (TPD) Mechanism of Action

Harnessing the E3 Ubiquitin Proteasome System

1

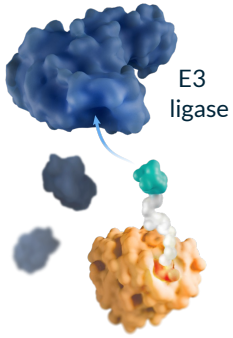
Catching the Target Protein



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

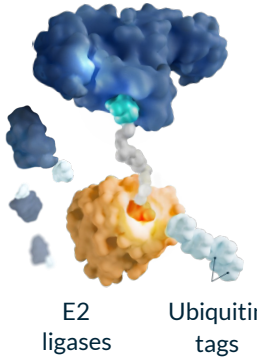
2

Presenting the Target Protein



3

Tagging the Target Protein



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

4

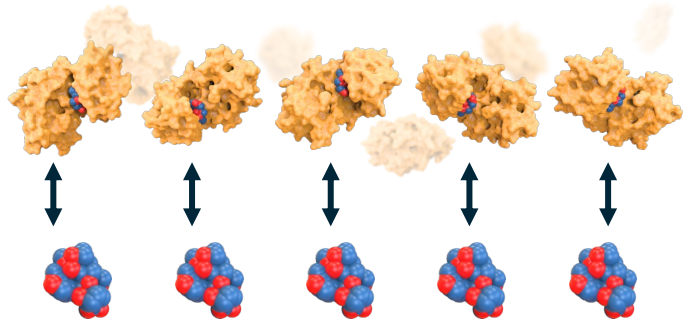
Degrading the Target Protein

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

Degraders Enable Continuous, Complete Pathway Blockade

Superior to Traditional Small Molecule Inhibitors

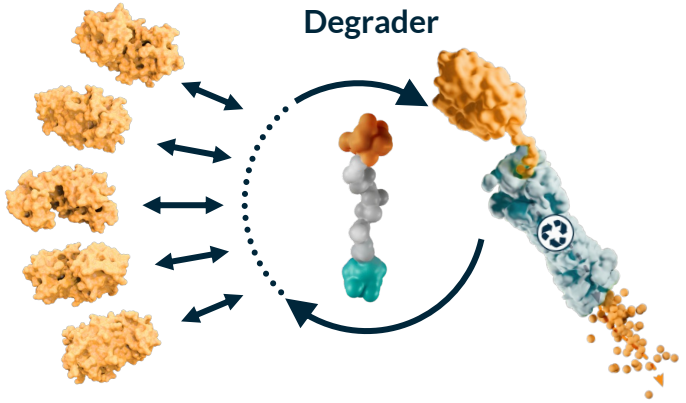
Small Molecule Inhibitor



STOICHIOMETRIC INHIBITION

Pharmacodynamic effect (PD) correlated to drug exposure pharmacokinetics (PK) (stoichiometric) requiring continuous high drug exposures to block protein function[1]

Degrader



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.

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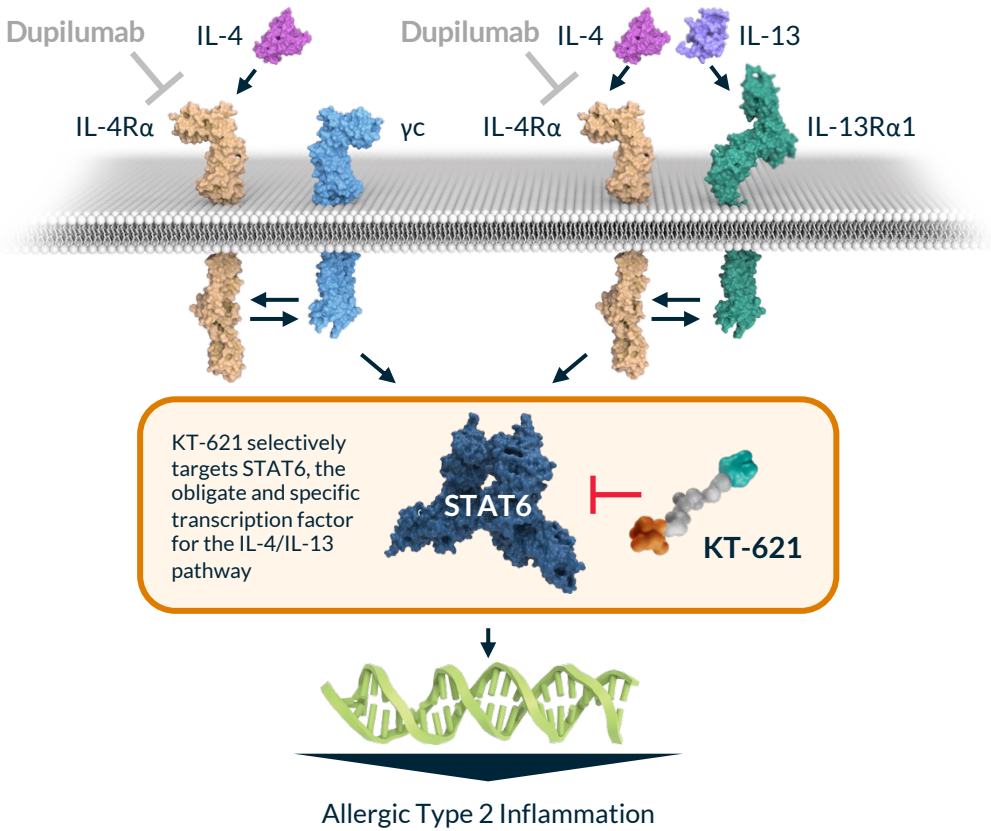
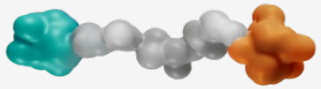
STAT6: Highly Validated, Historically Undrugged Target for Treatment of Type 2 Inflammatory Diseases

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 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 the Phase 1 healthy volunteer trial, 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; 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.

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KT-621 BroADen Phase 1b Study Design

BROADEN STUDY

Open-label, multicenter, single-arm study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and clinical activity of oral KT-621 in adults with moderate to severe atopic dermatitis

Screening

Baseline entry criteria:

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

Each Cohort Dosed for 28 Days

Cohort 1	Cohort 2
KT-621 100 mg QD (n=10)	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; 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.

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KT-621 BroADDen 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)	7 (58.3)	13 (59.1)
Male	4 (40)	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)	2 (16.7)	5 (22.7)
Non-Hispanic or Latino	7 (70)	10 (83.3)	17 (77.3)
Race, n (%)			
White	4 (40)	3 (25)	7 (31.8)
Black or African American	5 (50)	7 (58.3)	12 (54.5)
Asian	0	1 (8.3)	1 (4.5)
Mixed/Other	1 (10)	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)	6 (50)	12 (54.5)
Severe (4)	4 (40)	6 (50)	10 (45.5)
EASI Score, mean (SD)	23.5 (7.5)	26.1 (9)	24.9 (8.3)
Other Disease Characteristics, Mean (SD)			
Peak Pruritus NRS	7.4 (1.2)	7.6 (0.9)	7.5 (1)
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)	3 (25)*	4 (18.2)
Allergic Rhinitis	2 (20)	7 (58.3)	9 (40.9)
Prior Systemic AD Tx, n (%)	1 (10)†	4 (33.3)‡	5 (22.7)

*The 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; NRS, numerical rating scale; POEM, Patient Oriented Eczema Measure; SCORAD, SCORing Atopic Dermatitis; SD, standard deviation; Tx, therapy; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis.

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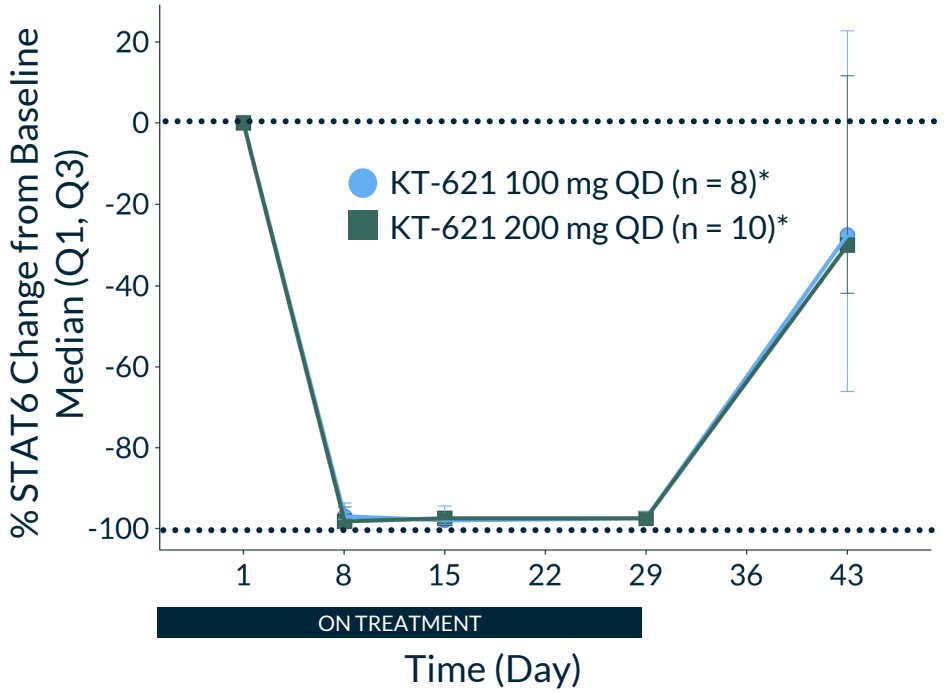
KT-621 Achieved Deep STAT6 Degradation in Blood and Skin

Degradation Maintained for 28 Days Across Both Dose Cohorts

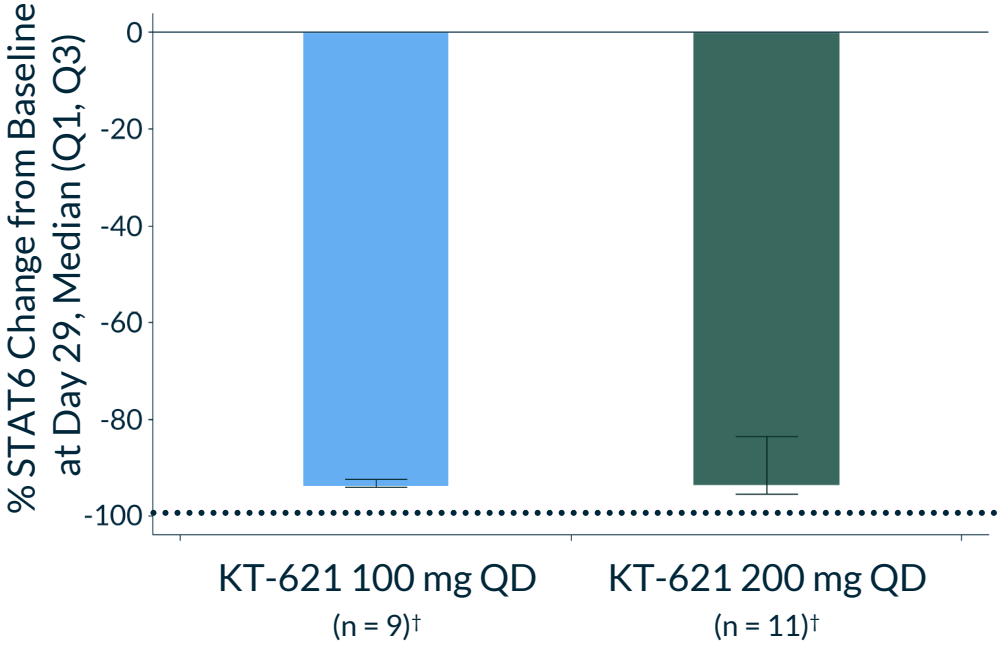
Median STAT6 Degradation in Blood

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 LLOQ (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 D29 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 D29 biopsies.
LLOQ, lower limit of quantification; QD, once daily; PK, pharmacokinetics; STAT6, signal transducer and activator of transcription 6.

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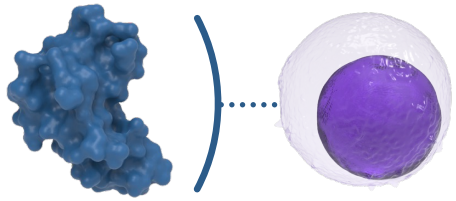
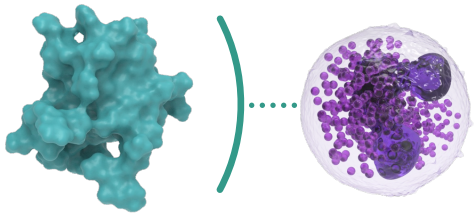
Disease-Relevant Biomarkers of Type 2 Inflammation

TARC (CCL17)



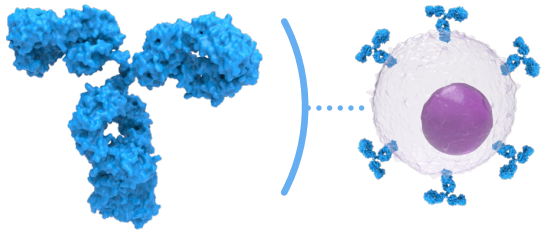
- TARC drives chemotaxis of CCR4-expressed T cells to inflammatory sites
- Validated biomarker of Type 2 inflammation in patients[1]

Eotaxin-3 (CCL26)



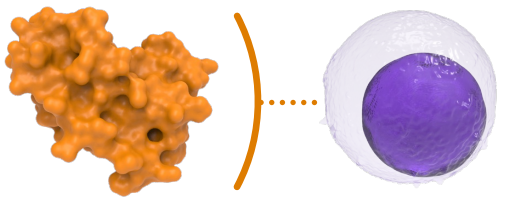
- Eotaxin-3 drives chemotaxis of CCR3-expressed inflammatory cells (e.g., eosinophils) to inflamed sites
- Highly specific downstream cytokine of the IL-4/IL-13 pathway[1]

IgE



- IgE activates mast cells and basophils to release Type 2 cytokines (e.g., IL-4, IL-13)
- IL-4 promotes B-cell class switching, amplifying IgE production
- IgE half-life ~3 days, but IgE-producing cells persist longer[1]

IL-31



- IL-31 is a key pruritogenic cytokine produced by activated Type 2 cells[2]
- Signals through the IL-31RA/OSMR complex on neurons, keratinocytes, and immune cells, linking immune activation to itch

1. Hamilton JD, et al. *Clin Exp Allergy*. 2021;51(7):915-931; 2. Raap U, et al. *J Allergy Clin Immunol*. 2008;122:421-423.
AD, atopic dermatitis; CCL, C-C motif chemokine ligand; CCR, C-C chemokine receptor; IgE, immunoglobulin E; IL, interleukin; OSMR, oncostatin M receptor; TARC, thymus and activation-regulated chemokine.

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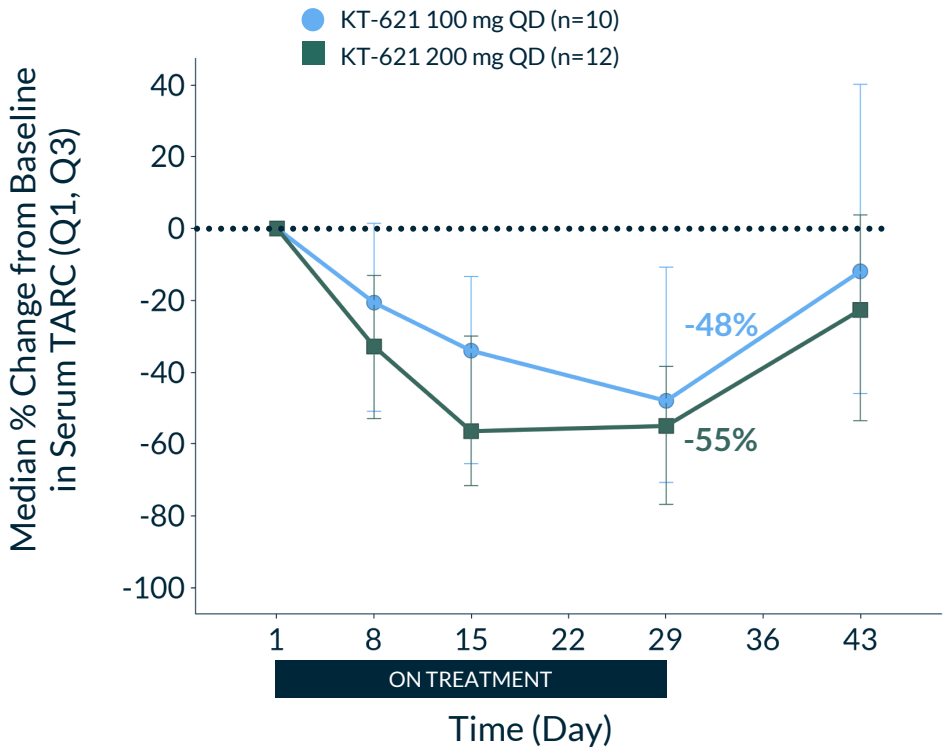
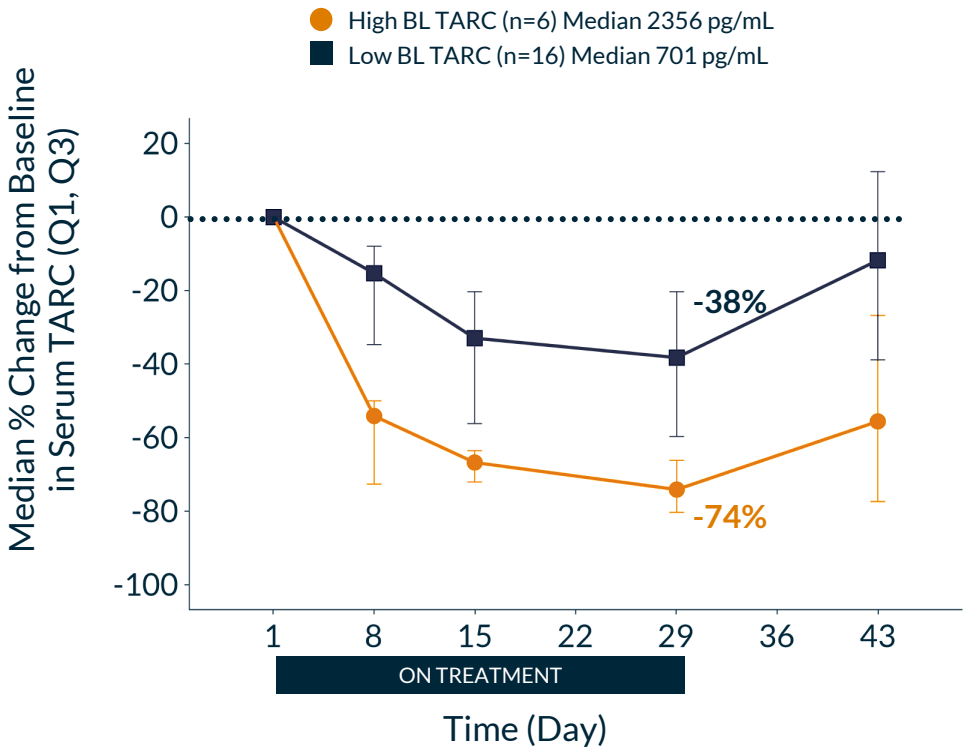
KT-621 Achieved Median TARC Reduction of up to 74%

Stratified by Dose



Stratified by Baseline TARC (1600 pg/mL)



- Rapid and robust reduction of TARC across both dose cohorts
- Magnitude of TARC reduction was a function of baseline TARC level, consistent with findings in dupilumab trials of AD and other Type 2 diseases[1]

1. Hamilton JD, et al. *Clin Exp Allergy*. 2021;51(7):915-931.
N values reflect the number of participants with available samples at Day 29. Stratification by TARC based on lower bound of 95% confidence interval for median baseline TARC levels from the dupilumab SOLO 1 and 2 AD studies.[1]
AD, atopic dermatitis; BL, baseline; Q1, lower quartile; Q3, upper quartile; QD, once daily; TARC, thymus and activation-regulated chemokine.

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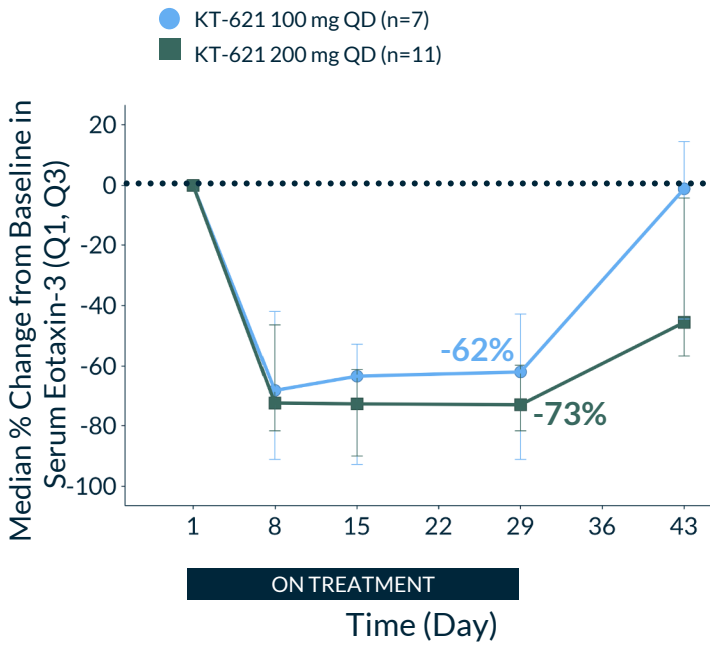
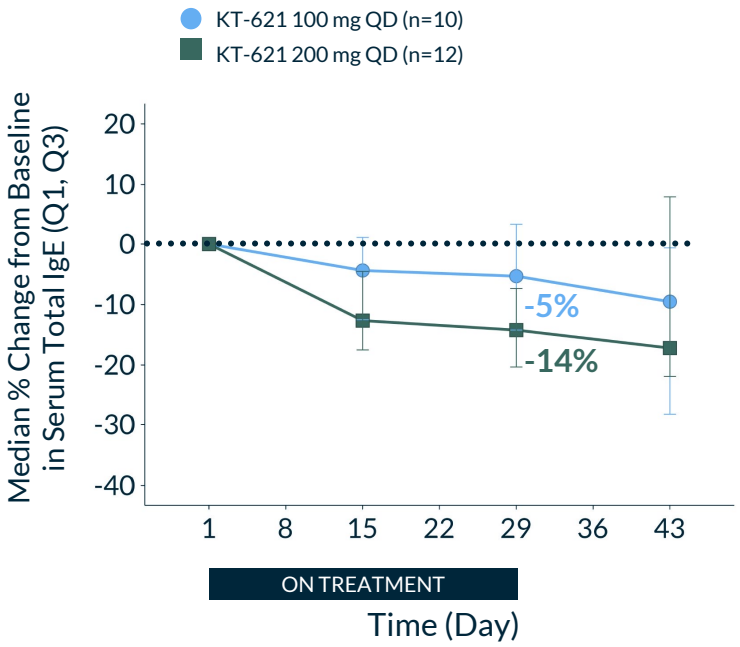
KT-621 Impacted Multiple Additional Type 2 Biomarkers

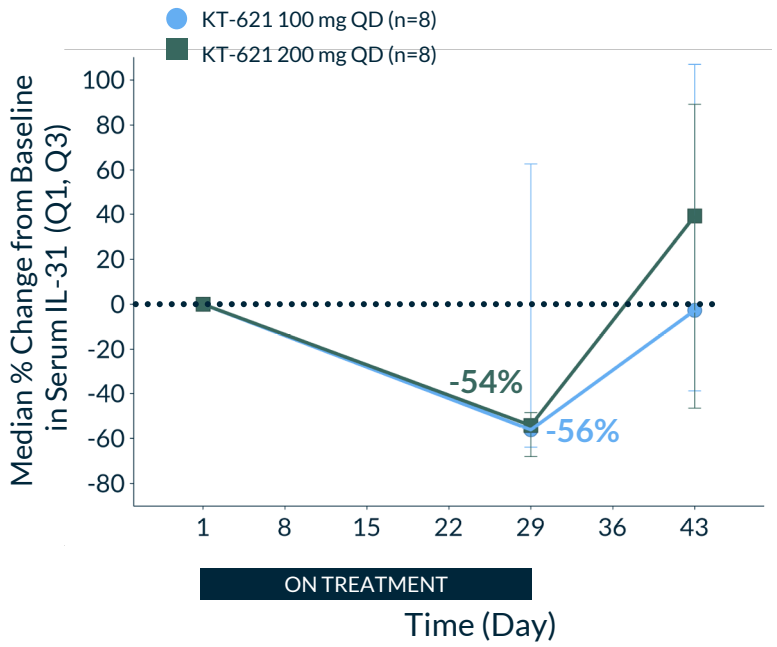
Median % Change from Baseline in Eotaxin-3



Median % Change from Baseline in IgE



Median % Change from Baseline in IL-31



- Similar reductions across both dose groups
- Strong impact on Eotaxin-3
- Modest IgE reduction consistent with need for months of pathway suppression to affect IgE-switched B cells and plasma cells
- First known demonstration of IL-31 reduction in blood of AD patients in response to IL-4/IL-13 pathway inhibition

N values reflect the number of participants with available samples at Day 29. Four patients had baseline levels below the lower limit of quantification (LLOQ) of assay; hence, change could not be calculated at D29.
AD, atopic dermatitis; IgE, immunoglobulin E; IL, interleukin; Q1, lower quartile; Q3, upper quartile; QD, once daily.

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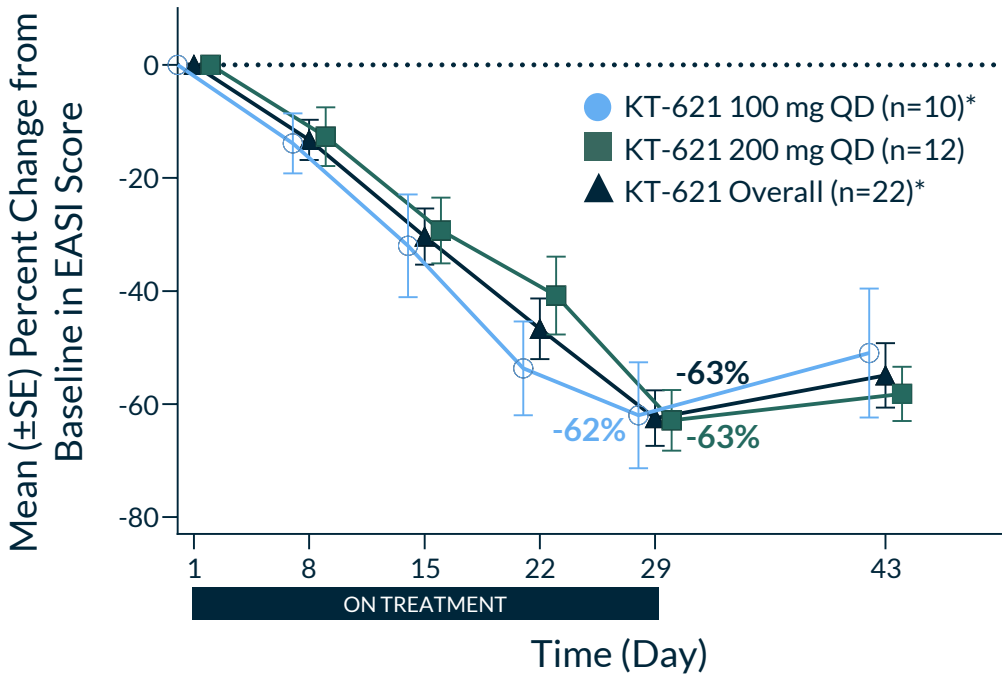
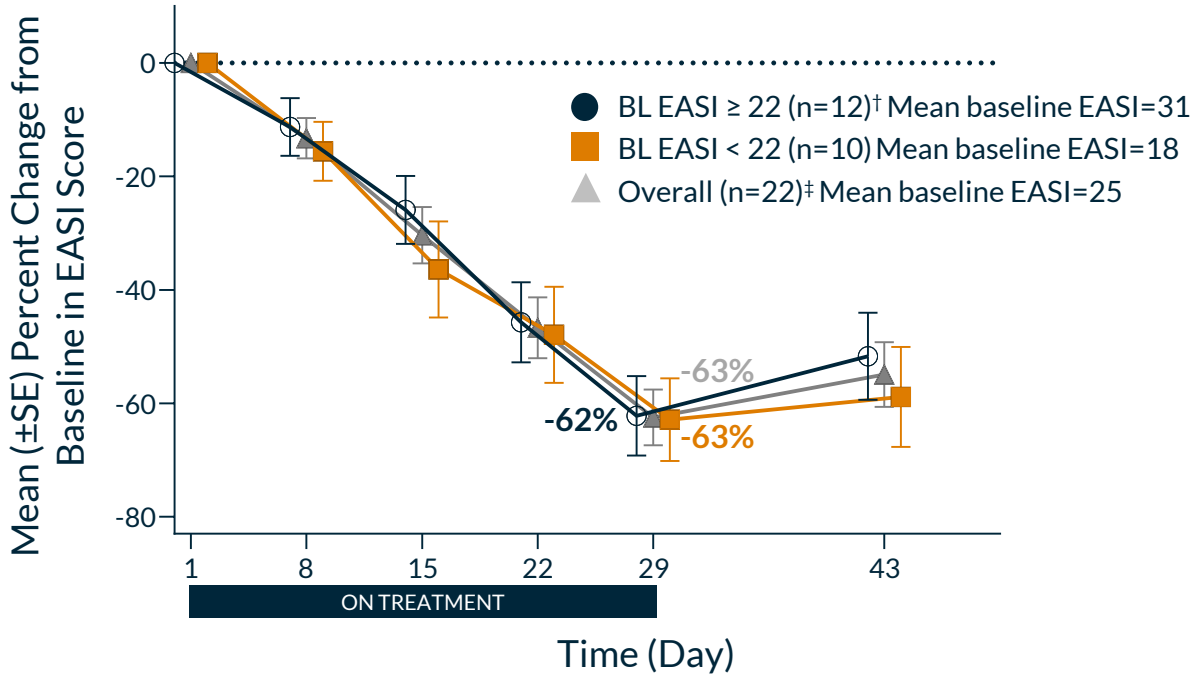
KT-621 Achieved Mean EASI Reduction of up to 63% by Week 4

Mean % Change from Baseline in EASI



Mean % Change in EASI: Stratified by Baseline EASI



- KT-621 demonstrated rapid and robust mean EASI reduction in both dose cohorts
- Reductions seen as early as Day 8 without apparent plateau after 4 weeks of dosing
- Magnitude of EASI reduction similar across the full range of baseline EASI scores

Analysis based on observed cases at each visit; *One patient in the 100 mg cohort missed the D29 visit (n=9 for 100 mg and n=21 for Overall at D29); †n=11 at D29; ‡n=21 at D29.
BL, baseline; EASI, Eczema Area and Severity Index; QD, once daily; SE, standard error.

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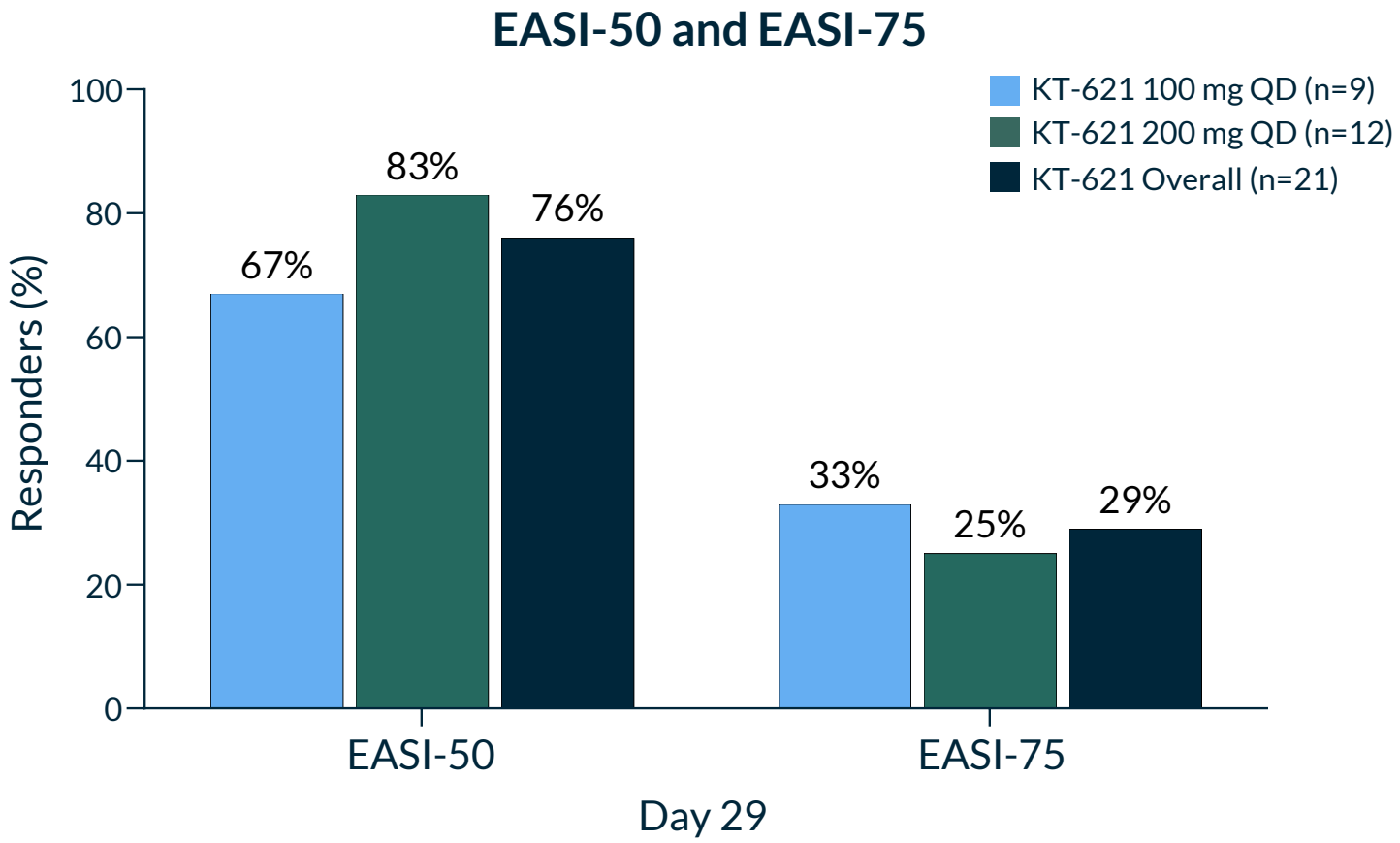
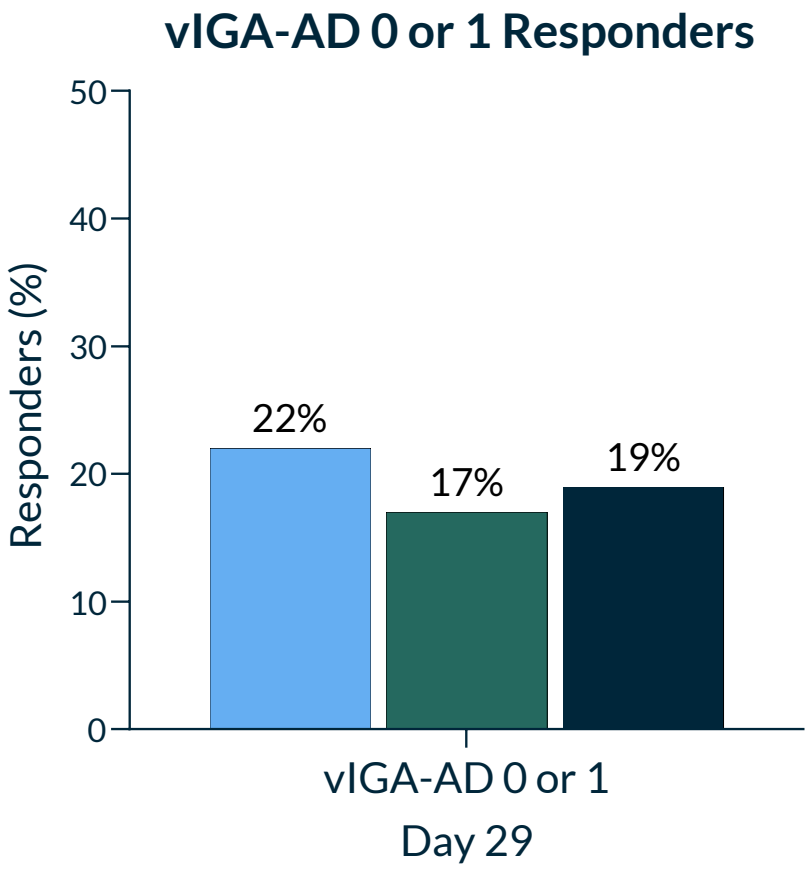
KT-621 Substantially Improved Disease Burden as Measured by EASI-50, EASI-75, and vIGA-AD™ 0 or 1 at Week 4





Analysis based on observed cases at D29.
EASI, Eczema Area and Severity Index; QD, once daily; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis.

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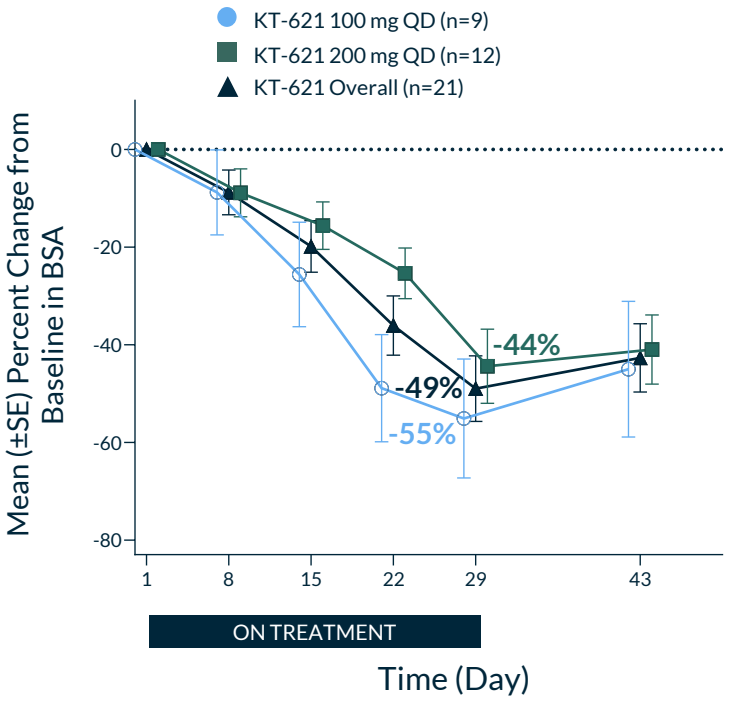
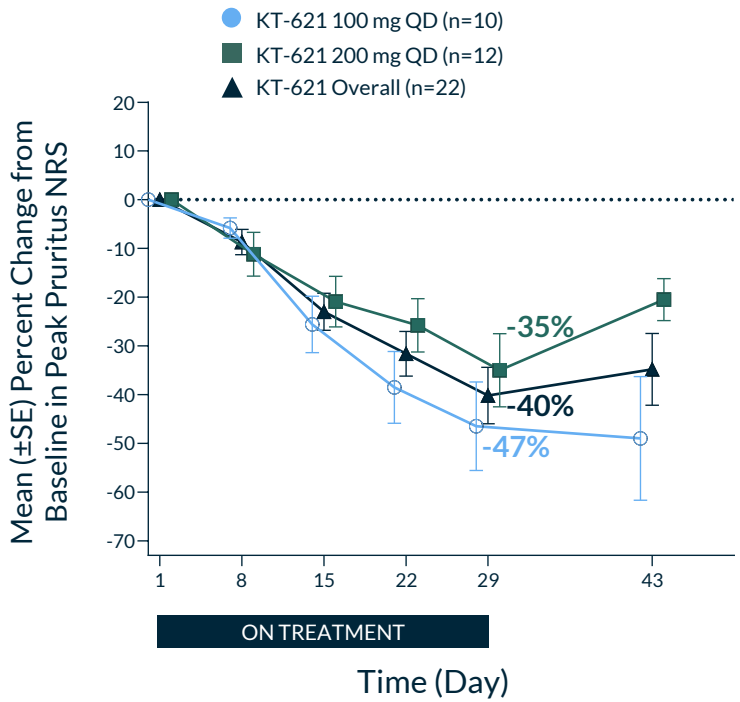
KT-621 Achieved Robust and Consistent Improvements in BSA, Peak Pruritus, and Patient Reported Severity of Disease (POEM)

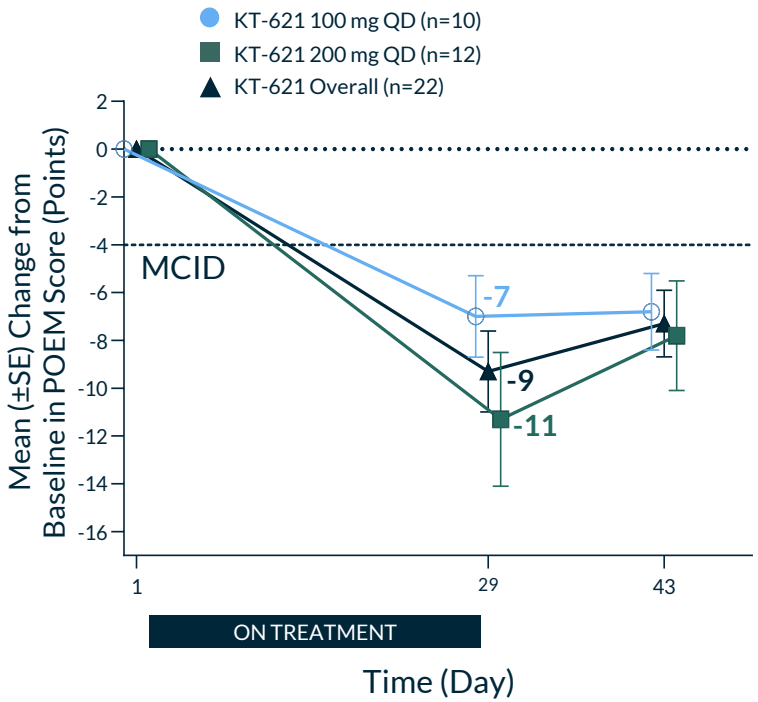
Mean % Change in Total BSA



Mean % Change in Peak Pruritus NRS



Mean Change in POEM



- Reductions in BSA seen as early as Day 8 without apparent plateau during treatment duration
- Patients reported rapid reduction in mean Peak Pruritus NRS without apparent plateau during treatment duration
- Improvement in POEM surpassed the minimum clinically important difference (MCID) of > 4-point change

Analysis based on observed cases at each visit.
BSA, body surface area; MCID, minimum clinically important difference; QD, once daily; POEM, Patient Oriented Eczema Measure; PPNRS, Peak Pruritus Numerical Rating Scale; SE, standard error.

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KT-621 Phase 1b Safety Summary

- Well-tolerated with favorable safety at both 100 mg and 200 mg
- 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.

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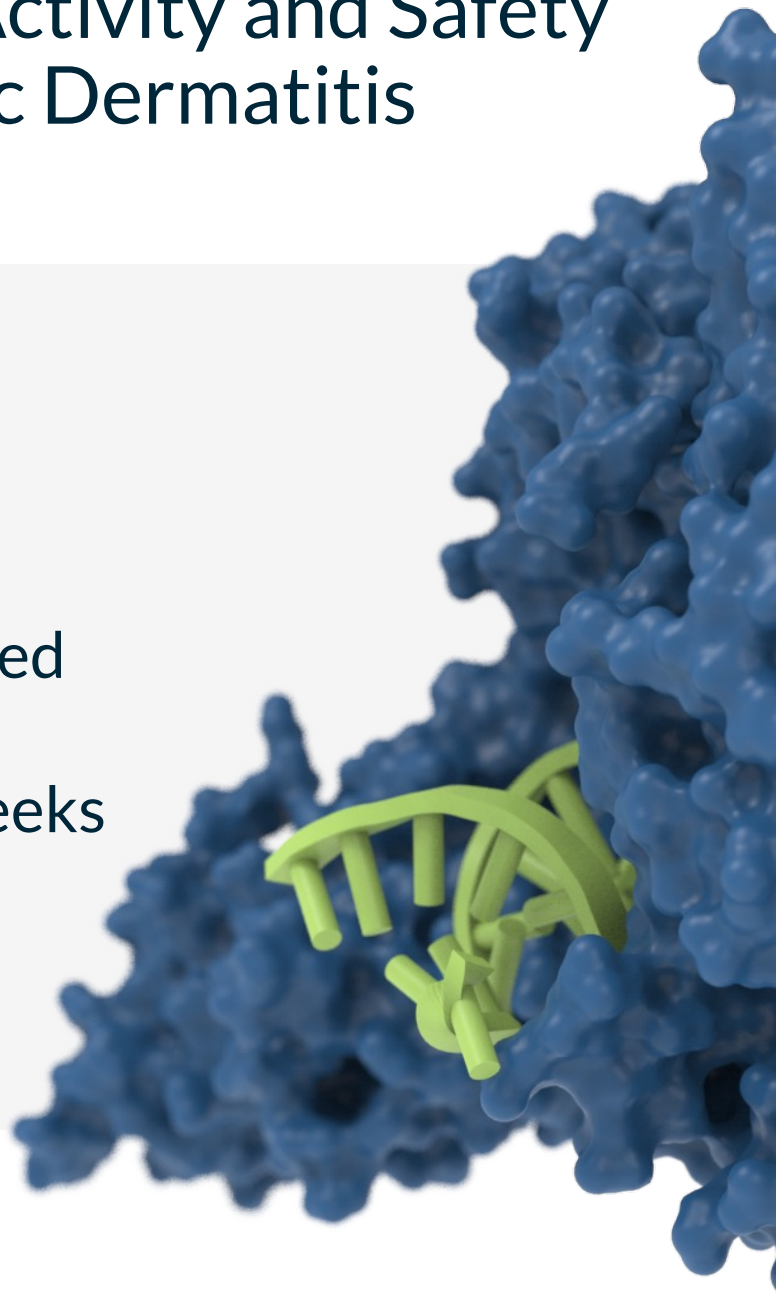
KT-621: First Evidence Demonstrating Clinical Activity and Safety of a STAT6-targeted Drug in Patients with Atopic Dermatitis

- Deep STAT6 degradation in blood and lesional skin
- Robust suppression of Type 2 inflammation
- Meaningful improvements across both clinician assessed and patient reported outcomes in moderate to severe atopic dermatitis in line with pathway biologics at 4 weeks
- Favorable safety profile and tolerability at both 100 mg and 200 mg doses



STAT6, signal transducer and activator of transcription 6.

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KT-621: BROADEN2 Phase 2b Trial

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

BROADEN2 TRIAL

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

Baseline entry criteria:
EASI ≥ 16
vIGA-AD ≥ 3
Peak Pruritus 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 Peak Pruritus 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; NRS, Numerical Rating Scale; TCS, topical corticosteroid; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis.

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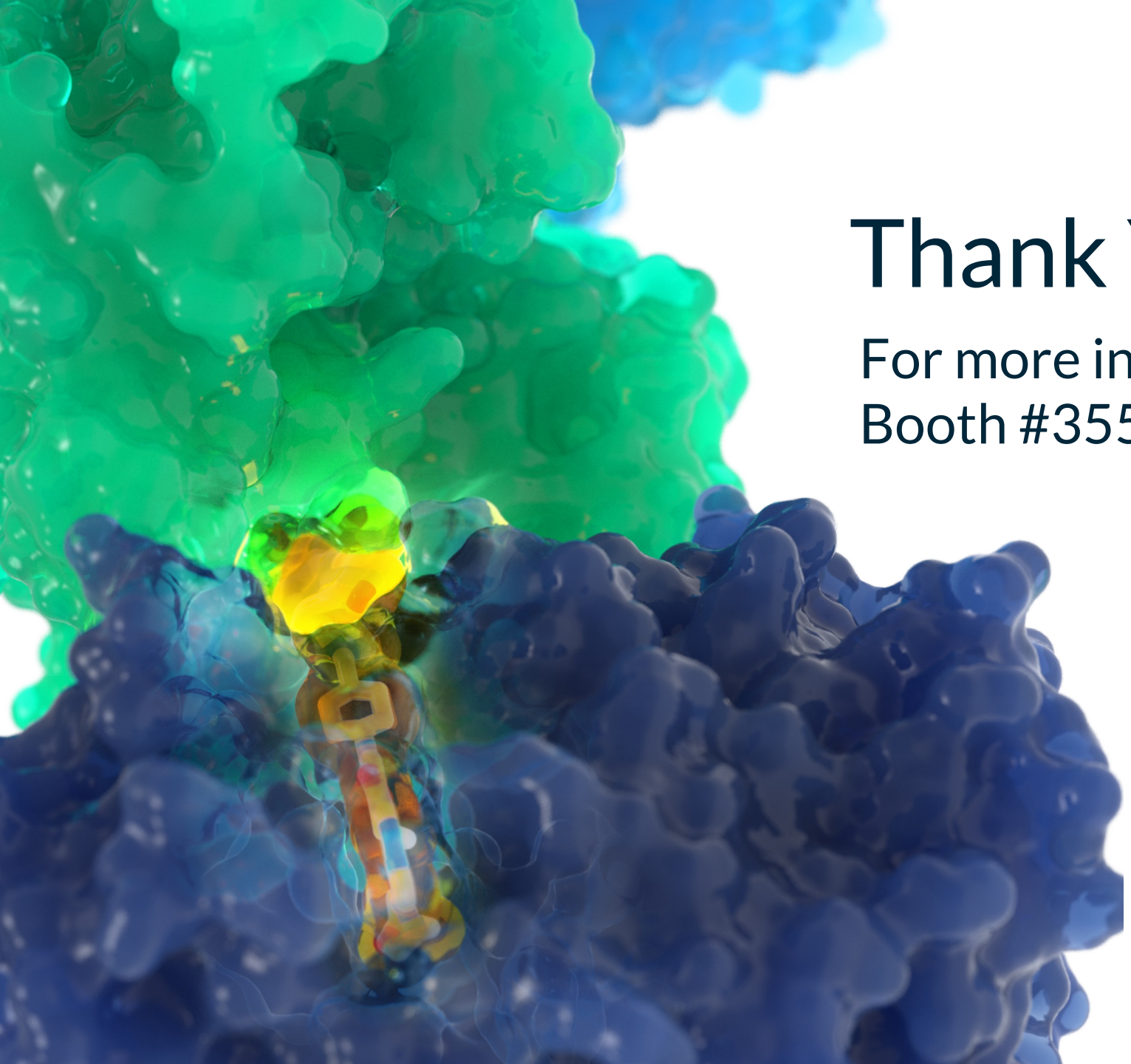

Thank You

For more information, please visit our Booth #3551 or www.kymeratx.com

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