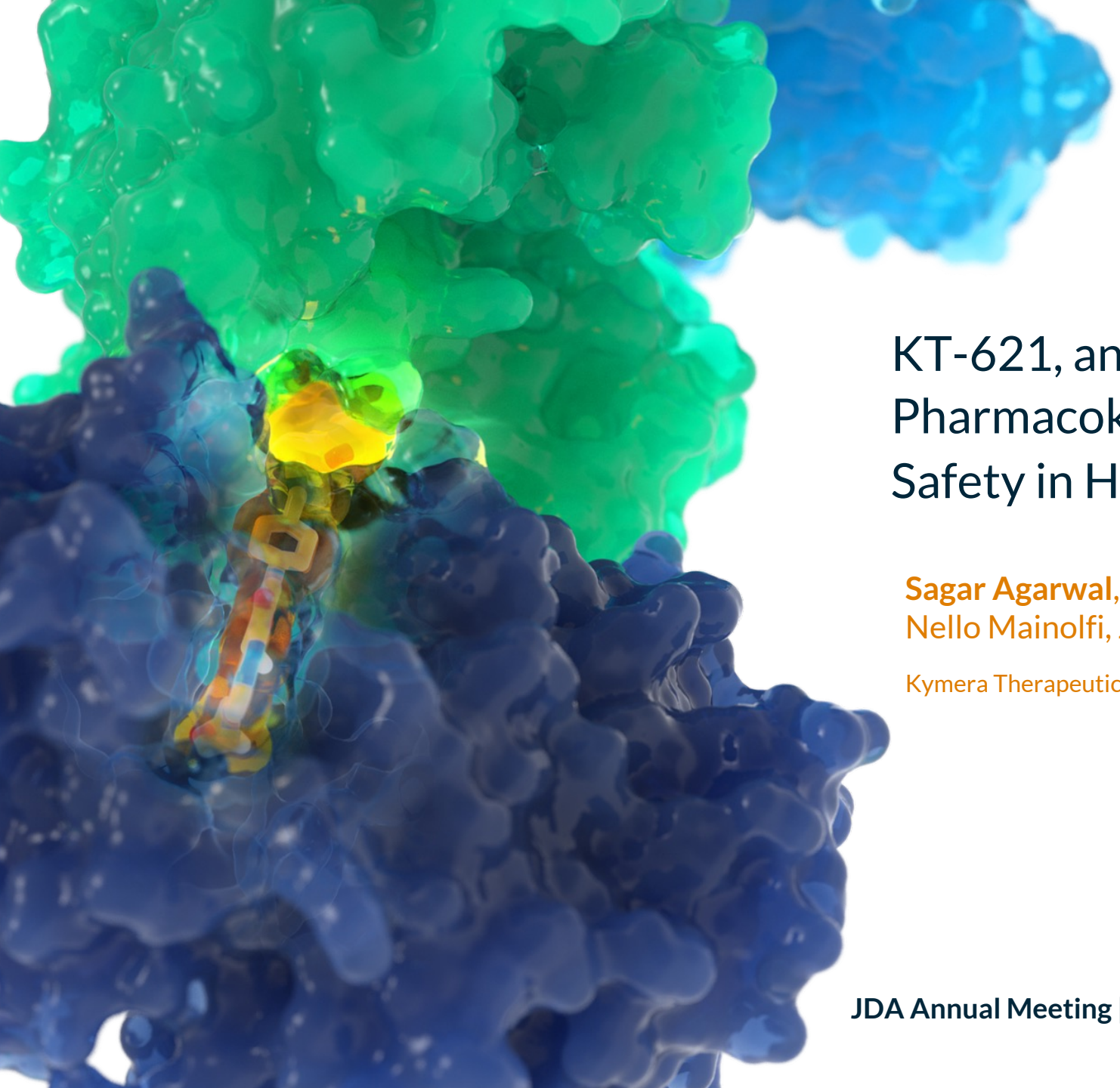


June 12, 2026

KT-621, an Oral, Once Daily STAT6 Degrader: Pharmacokinetics, Pharmacodynamics, and Safety in Healthy Japanese Adults

Sagar Agarwal, Alice A. McDonald, Evelyn Wang, Heather Paleczny, Nello Mainolfi, Jared Gollob, and Michael B. Feldman

Kymera Therapeutics, Inc., Watertown, MA, USA

JDA Annual Meeting | Kyoto | June 11-14, 2026

KYMERA

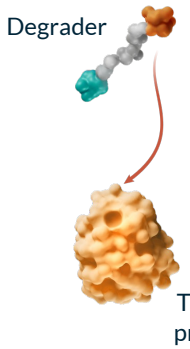
Targeted Protein Degradation: Achieving Biologics-like Activity With Oral Medicines

Targeted Protein Degradation (TPD) Mechanism of Action

Harnessing the E3 Ubiquitin Proteasome System

1

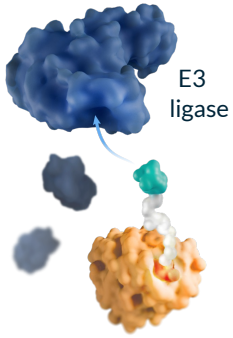
Catching the Target Protein



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

2

Presenting the Target Protein



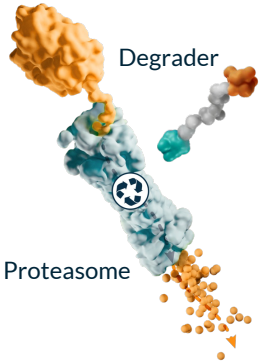
3

Tagging the Target Protein

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

4

Degrading the Target Protein

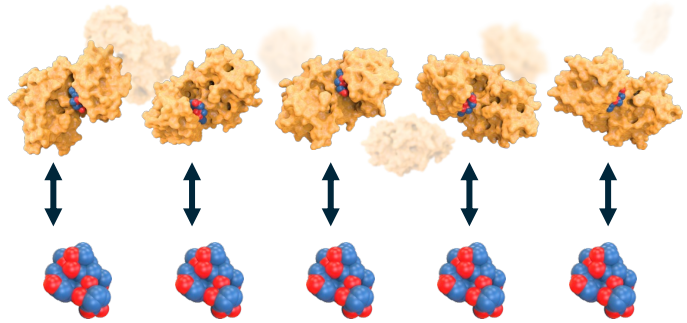


Ubiquitin is recognized by the proteasome to selectively degrade the target protein

Degraders Enable Continuous, Complete Pathway Blockade

Superior to Traditional Small Molecule Inhibitors

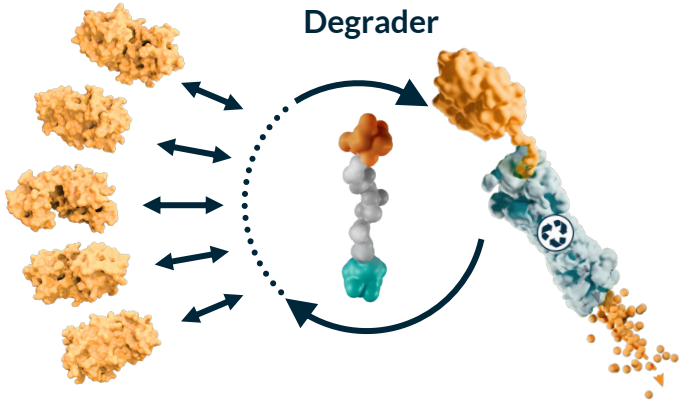
Small Molecule Inhibitor



STOICHIOMETRIC INHIBITION

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

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

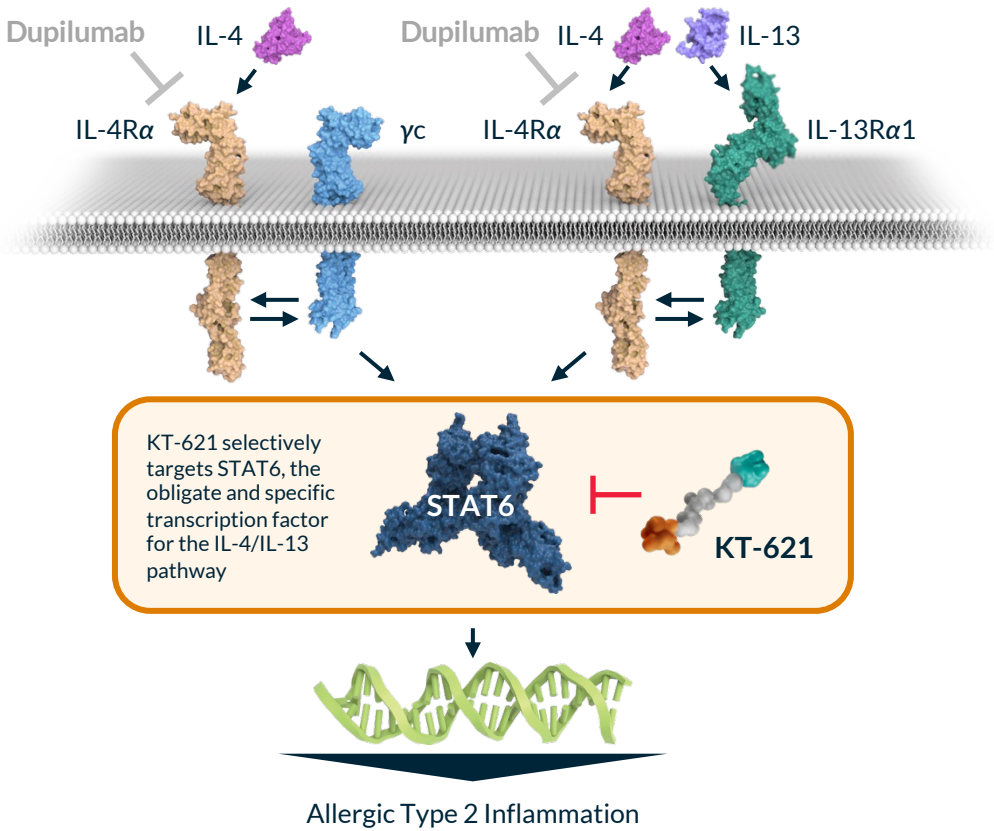
Mainolfi N, Rasmusson T. *Annual Reports Med Chem.* 2017;50:301-334.
PD, pharmacodynamics; PK, pharmacokinetics; TPD, targeted protein degradation.

KYMERA

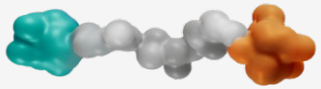
STAT6: Highly Validated, Historically Undrugged Target for Treatment of Type 2 Inflammatory Diseases

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 via 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 adults, 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 Phase 1 Study in Healthy Japanese Adults

A Phase 1, Randomized, Placebo-Controlled, Multiple-Dose Study of Orally Administered KT-621 in Healthy Japanese Adults

Screening

Baseline entry criteria:
First-generation Japanese adults

- Aged 18–55 years
- Body weight of ≥50 kg (male) or ≥40 kg (female)
- BMI of 18.0–30.0 kg/m²

Each Cohort Dosed for 7 Days

Cohort 1 (n=12) Randomized 3:1	Cohort 2 (n=12) Randomized 3:1
KT-621 25 mg QD (n=9)	KT-621 100 mg QD (n=9)
Placebo QD (n=3)	Placebo QD (n=3)

Objectives & Endpoints

Primary

- Safety

Secondary

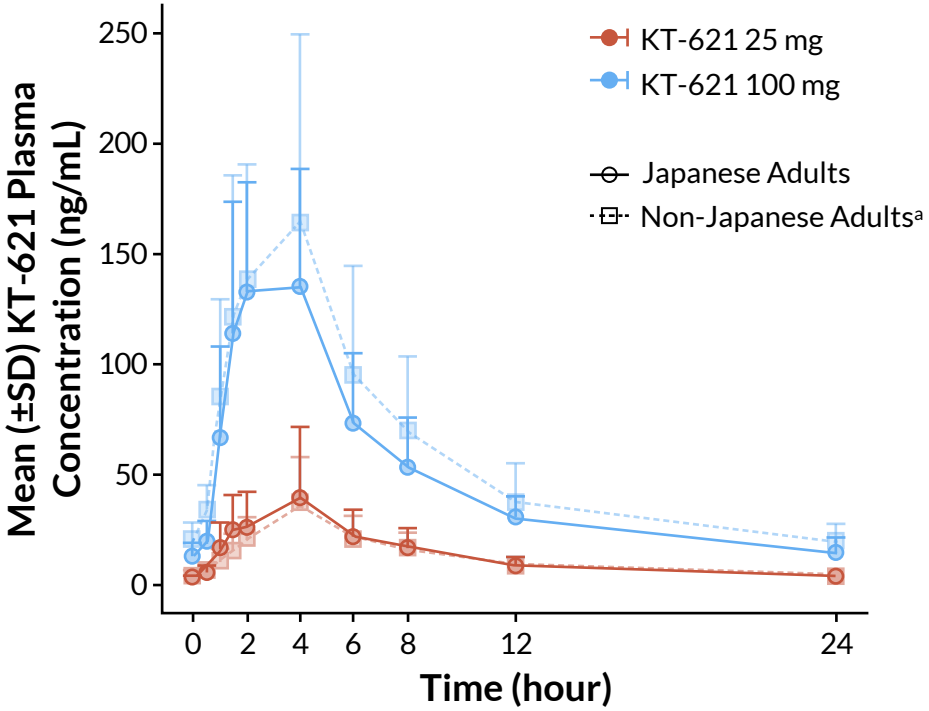
- Plasma and urine PK

Exploratory

- STAT6 degradation in whole blood

BMI, body mass index; PK, pharmacokinetics; QD, once daily; STAT6, signal transducer and activator of transcription 6.

KT-621 Demonstrated Linear and Predictable PK in Healthy Japanese Adults



Mean (%CV) Steady-State (Day 7) KT-621 PK Parameters in Japanese and Non-Japanese Adults

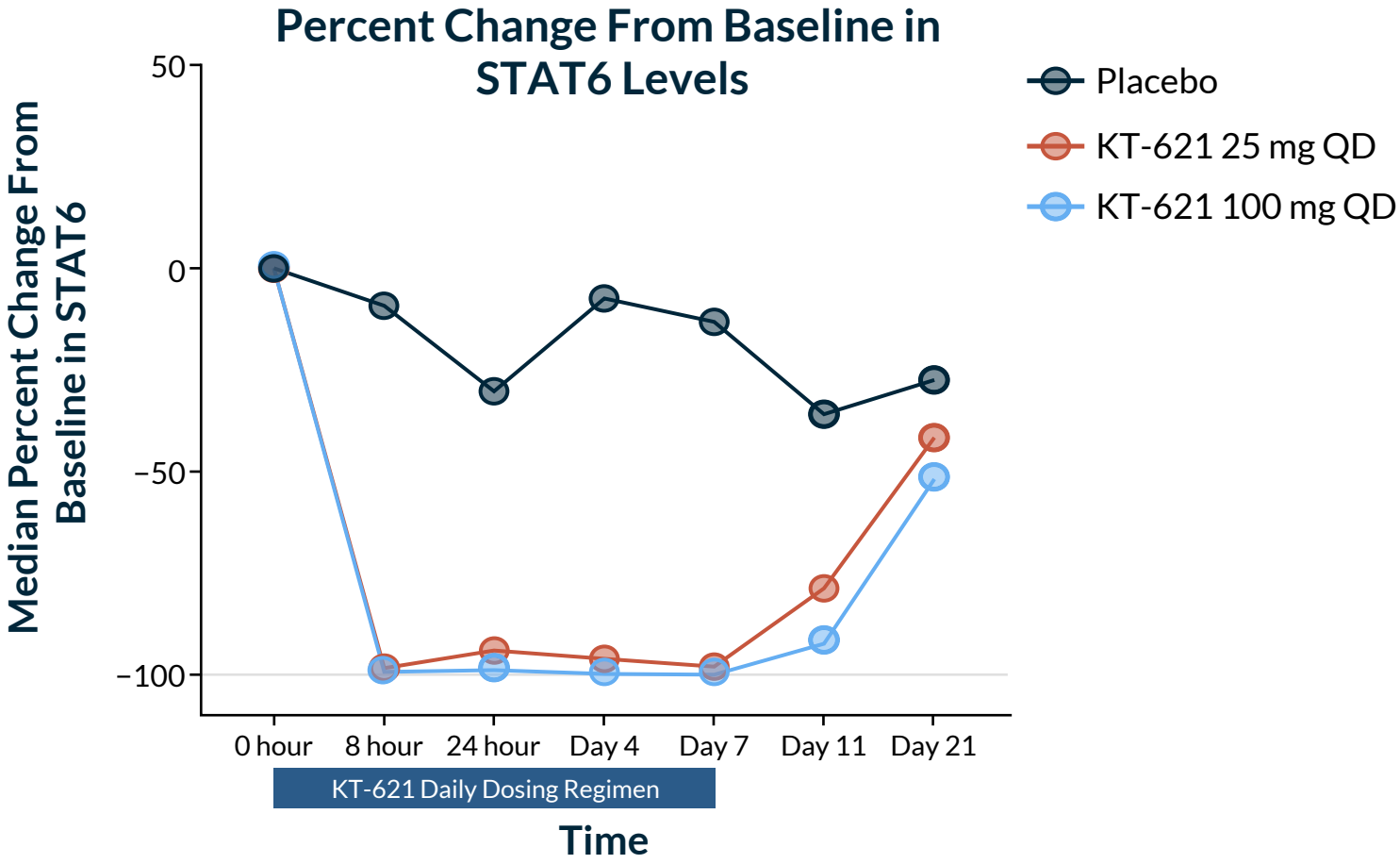
	KT-621 25 mg QD		KT-621 100 mg QD	
	Japanese (n=9)	Non-Japanese[a] (n=9)	Japanese (n=9)	Non-Japanese[a] (n=9)
C_{max}, ng/mL	45.9 (64.5%)	36.3 (59.0%)	165 (28.8%)	180 (43.5%)
T_{max}, hour	4.0 (1.5, 6.0)	3.0 (2.0, 4.0)	4.0 (1.5, 4.0)	4.0 (2.0, 4.0)
AUC_{0-24}, ng·hour/mL	320 (47.2%)	305 (34.3%)	1170 (33.8%)	1450 (41.2%)
C_{trough}, ng/mL	3.55 (39.3%)	3.99 (35.1%)	14.2 (47.9%)	19.6 (36.8%)
$t_{1/2}$, hour	12.6 (57.6%)	16.8 (33.5%)	16.9 (25.5%)	19.9 (18.3%)
Accum Ratio AUC	1.09 (19.4%)	1.34 (35.5%)	1.13 (23.3%)	1.33 (28.0%)

Median (min, max) is presented for T_{max}

- KT-621 was rapidly absorbed after oral dosing with a median T_{max} of 4 hours, followed by elimination with a mean half-life ($t_{1/2}$) of 12–17 hours
- Plasma exposure increased approximately dose-proportionally between 25 and 100 mg doses
- Renal elimination of KT-621 was negligible, <0.1% of the administered dose excreted unchanged in urine
- KT-621 PK was comparable between healthy Japanese and non-Japanese adults

[a]Non-Japanese adult data were obtained from the first-in-human Phase 1a study of KT-621 in healthy adults.
Accum, accumulation; AUC_{0-24}, area under the concentration-time curve from time 0 to 24 hours; C_{max}, maximum plasma concentration; C_{trough}, observed concentration at the end of the dosing interval; CV, coefficient of variation; max, maximum; min, minimum; PK, pharmacokinetics; QD, once daily; SD, standard deviation; $t_{1/2}$, terminal elimination half-life; T_{max}, time of maximum observed concentration.

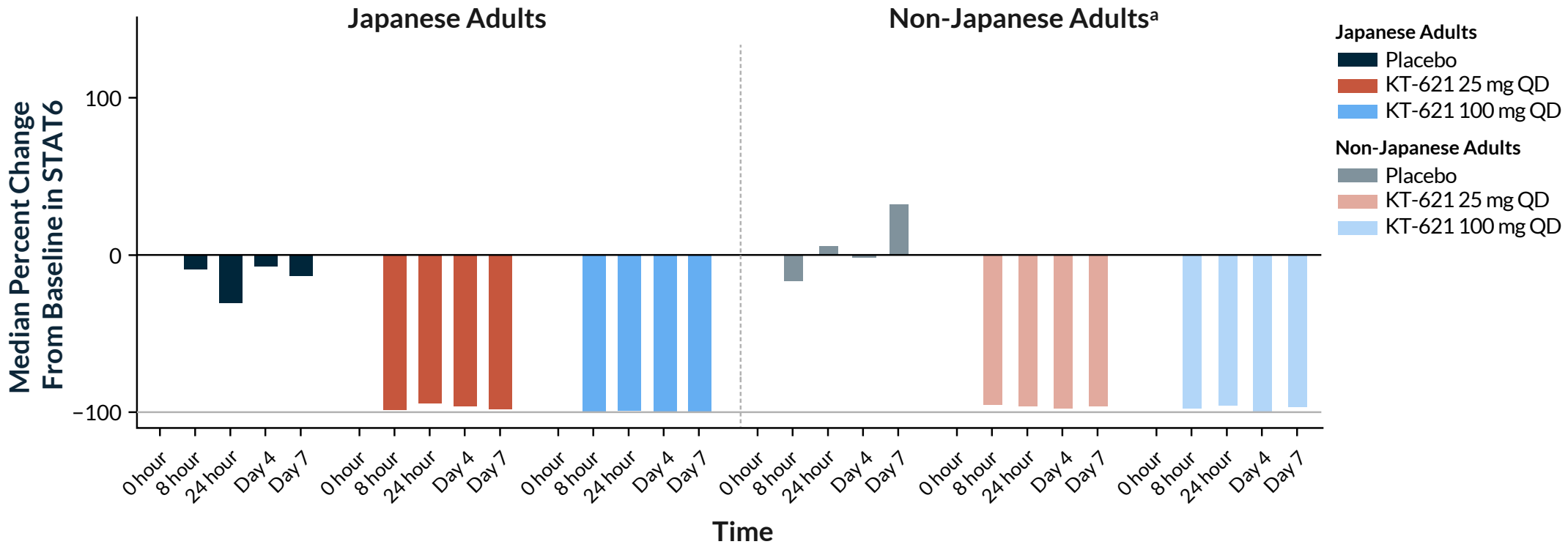
KT-621 Achieved Rapid, Deep, and Prolonged STAT6 Degradation in Whole Blood of Healthy Japanese Adults



- KT-621 achieved >95% STAT6 degradation by 8 hours which was maintained at both doses through Day 7 dosing
- STAT6 levels in whole blood began to return toward baseline as measured 4 days after the last dose

QD, once daily; STAT6, signal transducer and activator of transcription 6.

KT-621: STAT6 Degradation Was Comparable in Healthy Japanese and Non-Japanese Adults



- KT-621 demonstrated >95% STAT6 degradation in whole blood in Japanese and non-Japanese adults throughout the dosing regimen

Median Percent Change From Baseline in STAT6 (Day 7)

Study	Japanese		Non-Japanese[a]	
Dose	Median (n)	Q1, Q3	Median (n)	Q1, Q3
Placebo	-13% (6)	-62%, 110%	32% (17)	-24%, 81%
25 mg QD	-98% (9)	-99%, -95%	-96% (8)	-97%, -94%
100 mg QD	-100% (9)	-100%, -100%	-97% (8)	-100%, -92%

p<0.0001 for all comparisons between KT-621 and placebo.
[a]Non-Japanese adult data were obtained from the first-in-human Phase 1a study of KT-621 in healthy adults.
Q, quartile; QD, once daily; STAT6, signal transducer and activator of transcription 6.

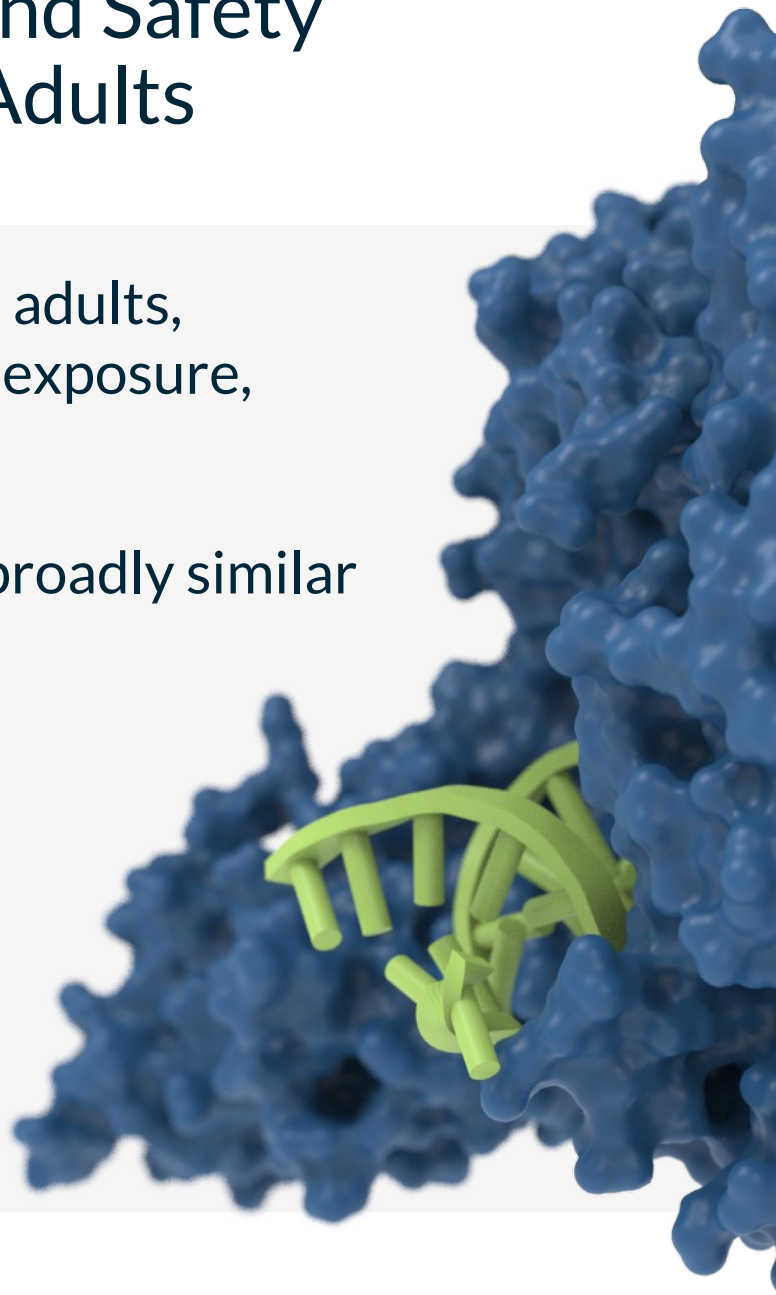
KT-621 Was Safe and Well Tolerated in Healthy Japanese Adults

- No serious or severe AEs occurred
- No dose-dependent pattern was observed in treatment-emergent AEs (TEAEs)
- No TEAEs led to discontinuation
- No clinically significant changes in vital signs, laboratory tests, or ECGs were observed following oral administration of KT-621
- Safety findings were consistent with those observed in healthy non-Japanese adults

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

KT-621: First Evidence Demonstrating PK, PD, and Safety of a STAT6-Targeted Drug in Healthy Japanese Adults

- KT-621 demonstrated a favorable PK profile in healthy Japanese adults, with rapid absorption and dose-proportional increases in plasma exposure, comparable to non-Japanese adults
- Deep STAT6 degradation in Japanese adults was achieved, with broadly similar kinetics and magnitude to non-Japanese adults
- KT-621 was safe and well tolerated across both doses
- Safety, tolerability, PK, and PD in healthy adults of Japanese descent are comparable to those of non-Japanese adults, supporting including Japanese adults in Phase 2b studies without dose modification



PD, pharmacodynamics; PK, pharmacokinetics; 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
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.

Thank You

For more information, please visit
our Poster #EP6-4 (Abstract #10061)
or www.kymeratx.com

JDA Annual Meeting | Kyoto | June 11-14, 2026