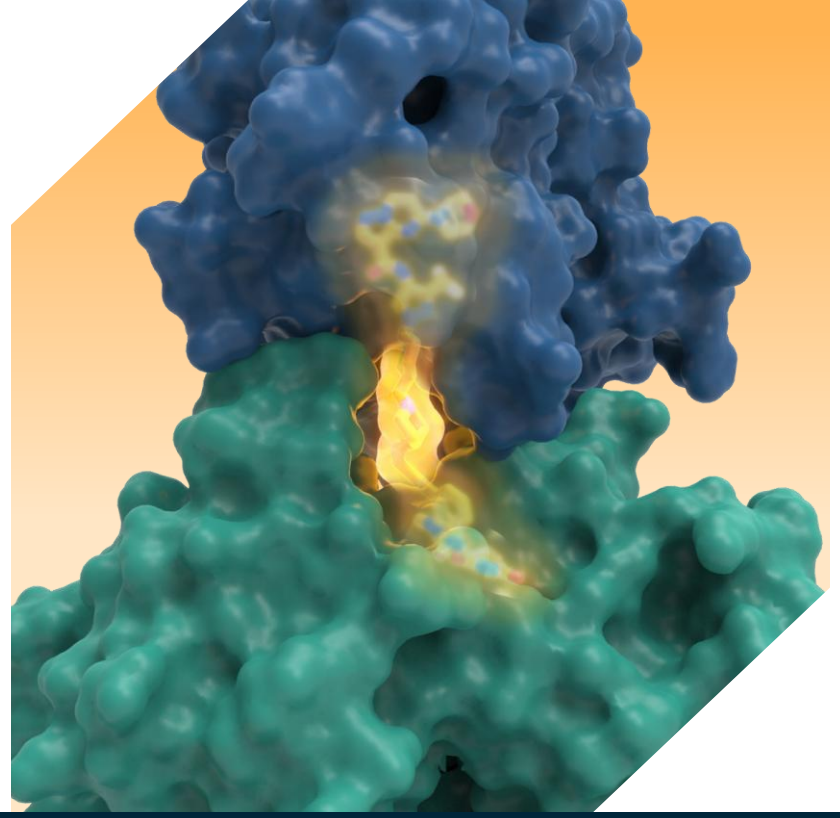

KYMERA

May 2025

Revolutionizing Immunology: Oral Medicines with Biologics-like Activity

Jared Gollob, MD, Chief Medical Officer, Kymera Therapeutics

American Thoracic Society – Respiratory Innovation Summit

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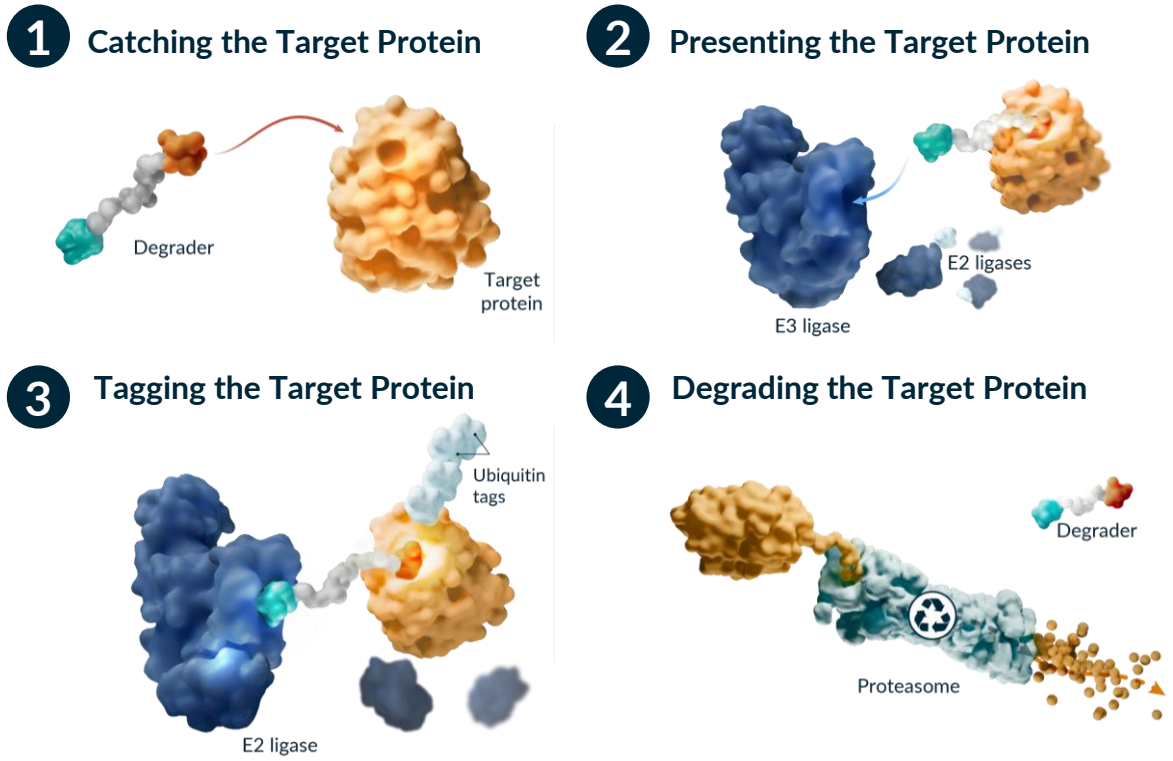
Kymera is a Leader in Targeted Protein Degradation (TPD): Oral Drugs with Biologics-Like Efficacy

Science-driven Clinical Stage Organization with Industry-leading Oral Immunology Pipeline

- **Novel technology:** Leverages natural protein recycling machinery to target disease-causing proteins
- **Best-in-industry capabilities:** Hit finding and optimization of oral protein degraders
- **Unique target selection strategy:** Pursuing traditionally undrugged targets in highly validated pathways
- **Exceptional preclinical to clinical translation:** >90% target degradation in all programs with desired tolerability and efficacy profiles



By combining the **"right target" with the disruptive potential of TPD, Kymera is delivering oral therapies with biologics-like profiles** for the first time in industry with the potential to expand access to millions of patients around the world

Small Molecule Oral Degraders Can Transform Immunology

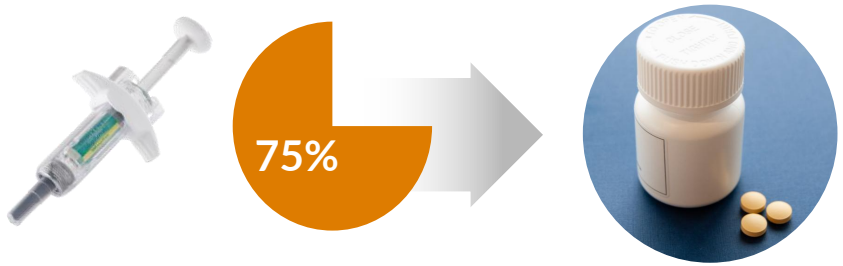
Potentially Superior Profile to Injectable Biologics and Traditional Small Molecule Inhibitors

Biologics can have several limitations, making orals preferred by most patients

DUPIXENT® (dupilumab) Injection

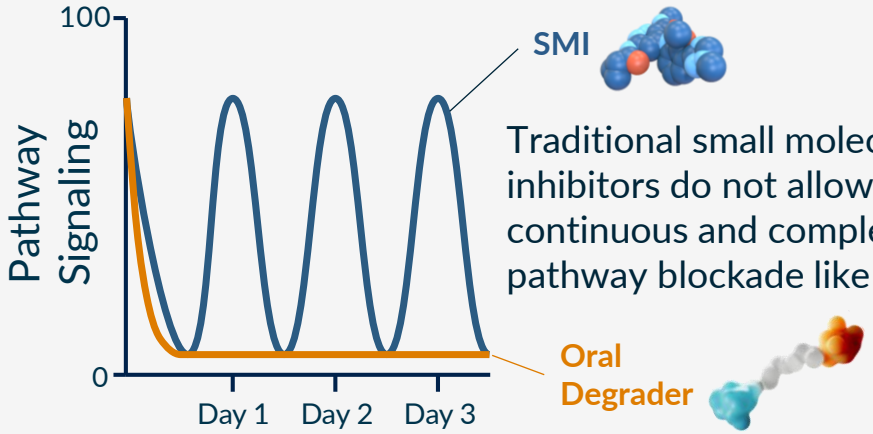
Skyrizi® risankizumab-rzaa

- Expensive, challenging to prescribe/reimburse
- Immunogenicity
- Cold storage
- Inconvenient and/or painful route of administration for patients

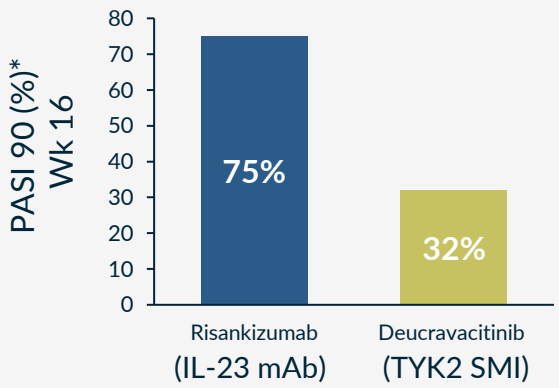


In industry surveys[1], **75%** of patients would switch from injectable biologics to oral with similar profile

Traditional SMI's insufficiently block pathways, which can limit efficacy



Traditional small molecule inhibitors do not allow continuous and complete pathway blockade like degraders



Anti IL-23 biologic dramatically more effective than TYK2 SMI in PsO[2]

[1]J&J Business Review Dec '23 (survey of N=395 patients with moderate-to-severe psoriasis); [2]Skyrizi (IL-23 mAb) and Sotyktu (TYK2 SMI) package inserts

Building the Best-in-Industry Oral Immunology Pipeline

Unique Target Selection Strategy

- Undrugged or inadequately drugged targets
- Strong genetic/clinical pathway validation
- Clear path to early clinical differentiation
- Multiple indications with significant unmet medical need

	Potential Indications	2025	1H 2026	Upcoming Milestones
Immunology – Oral Small Molecule Degraders				
STAT6 **KT-621**	AD, Asthma, COPD, PN, CRSwNP, EoE, BP, CSU, others	Phase 1 HV Results; Ph1 HV; Ph1b AD; Biomarkers in blood & skin lesions, 28-day efficacy	Ph2b AD; Ph2b Asthma	Ph1 HV Data: June Ph1b AD Data: 4Q25 Ph2b AD Start: 4Q25 Ph2b Asthma Start: 1Q26
IRF5 **KT-579**	Lupus, Sjögren's, RA, IBD, SSc, DM, others	IND Enabling; Program & data disclosure	IND; Ph1; Safety, degradation	Ph1 Start: Early 2026
Partnered with Sanofi/Kymera Opt-In Potential				
IRAK4 **KT-474**[1]	HS, AD, RA, Asthma, IBD, others[2]	Ph2b HS; Ph2b AD		Ph2b Completion: HS: 1H26 AD: Mid-2026

[1]KT-474 (SAR444656) partnered with Sanofi, with Kymera option to participate in the development and commercialization, and 50/50 profit split, in the United States. Double digit tiered royalties in ROW. [2]Current indications: HS and AD. Other diseases shown, where IL-1R/TLR pathway has been implicated in pathogenesis, are additional potential opportunities.

STAT6 Degrader: Opportunity for Dupilumab-Like Activity in a Pill

Highly Validated but Undrugged Target

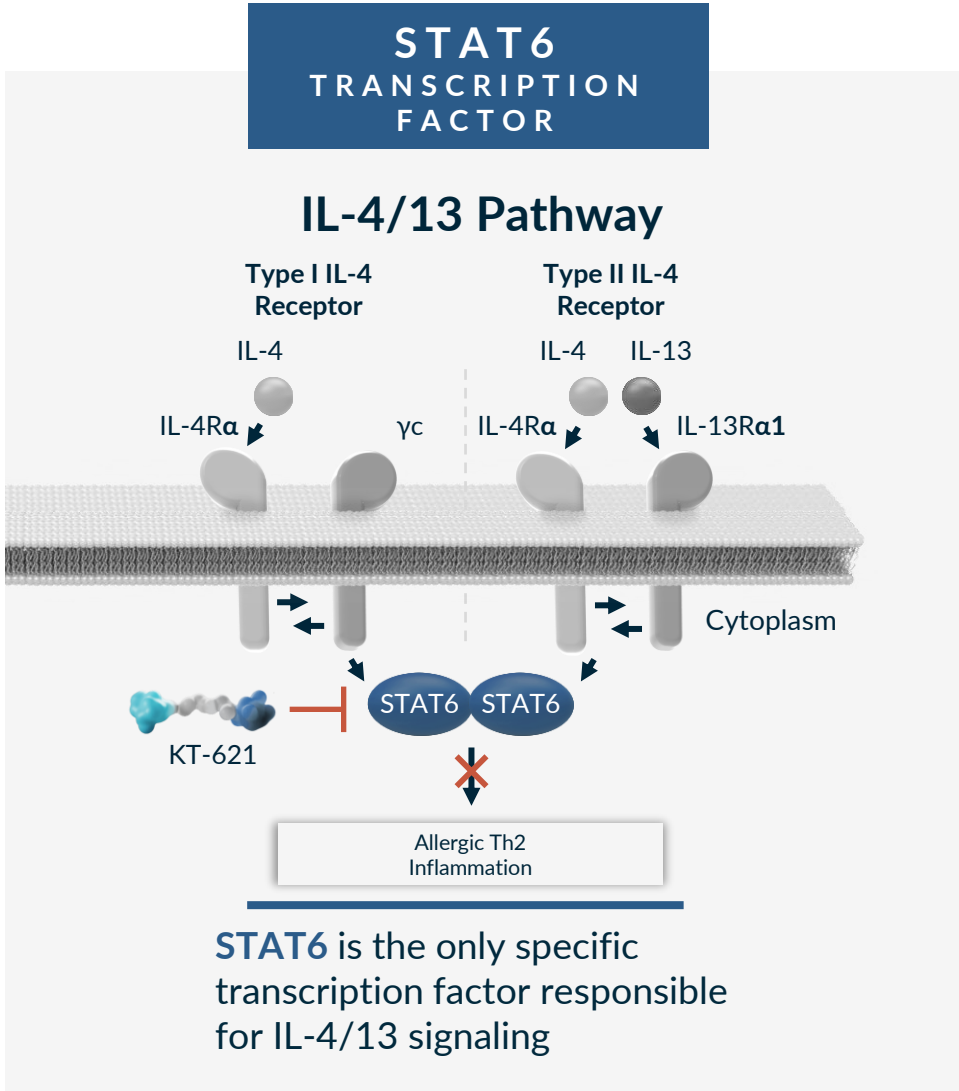
- IL-4/IL-13 pathway highly validated by **dupilumab (IL-4Rα mAb): approved in 7 indications**
- STAT6 is the **specific transcription factor for IL-4/IL-13 signaling**
- STAT6 targeting **has potential to phenocopy IL-4/IL-13 targeting**
- Human **gain-of-function of STAT6 causes severe allergic disease**[1]
- Human heterozygous **LOF are healthy** and protected against Th2 inflammation[2]

Clear Degrader Advantage

- **Only STAT6 degradation** has the potential to fully block IL-4/IL-13 signaling with an oral daily drug

Addresses Unmet Patient Need

- Dupilumab indications include AD, Asthma, COPD, CRSwNP, EoE, PN and CSU
- **Potential for oral drug with dupilumab-like activity and safety**

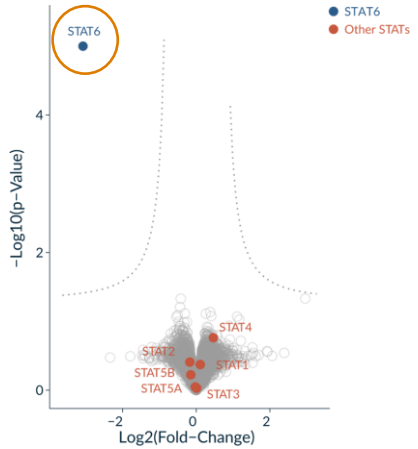


STAT6 is the only specific transcription factor responsible for IL-4/13 signaling

[1]Sharma et al. J Exp Med. 2023; Suratannon et al. J Allergy Clin. Immunol. 2022; Takeuchi et al. J Allergy Clin Immunol. 2022
[2]Kristjansdottir et al, Journal of Allergy and Clinical Immunology. 2024

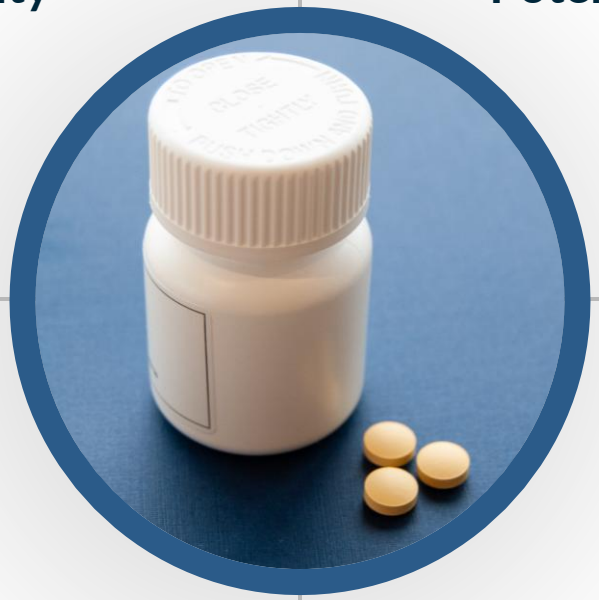
KT-621 Preclinical Profile: First Investigational Oral STAT6 Degrader to Advance into the Clinic

Highly Selective STAT6 Degrader with No Impact on Other STAT Family Members

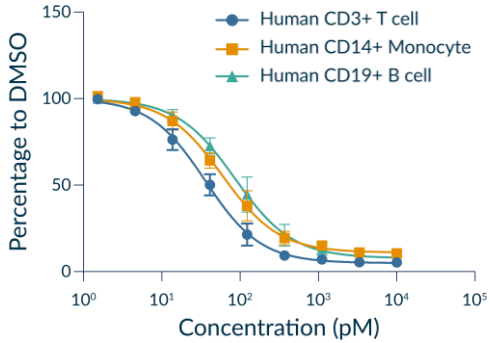


Exquisite Selectivity

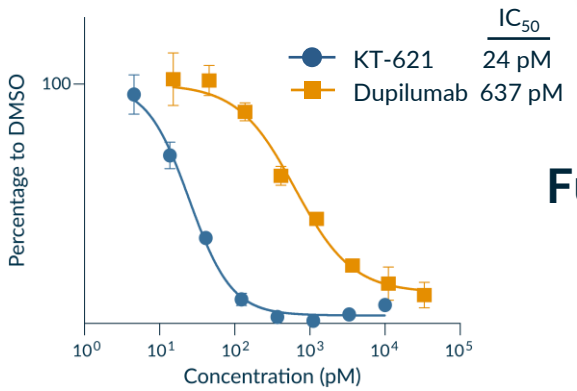
Picomolar Potency



STAT6 Degradation in Immune Cells



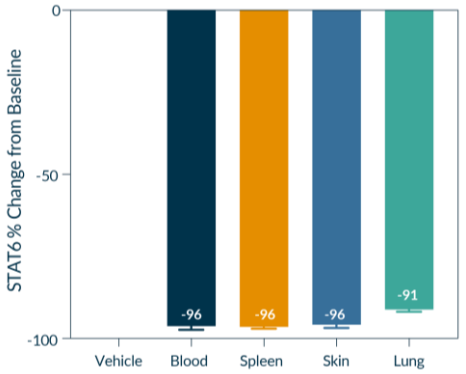
IL-13 Induced Periostin Release in Human Bronchial Smooth Muscle Cells



Full Inhibition of IL-4/IL-13 Pathways

Near-Complete STAT6 Degradation Across Tissues at Low Oral Doses *In Vivo* and Clean Preclinical Safety Profile

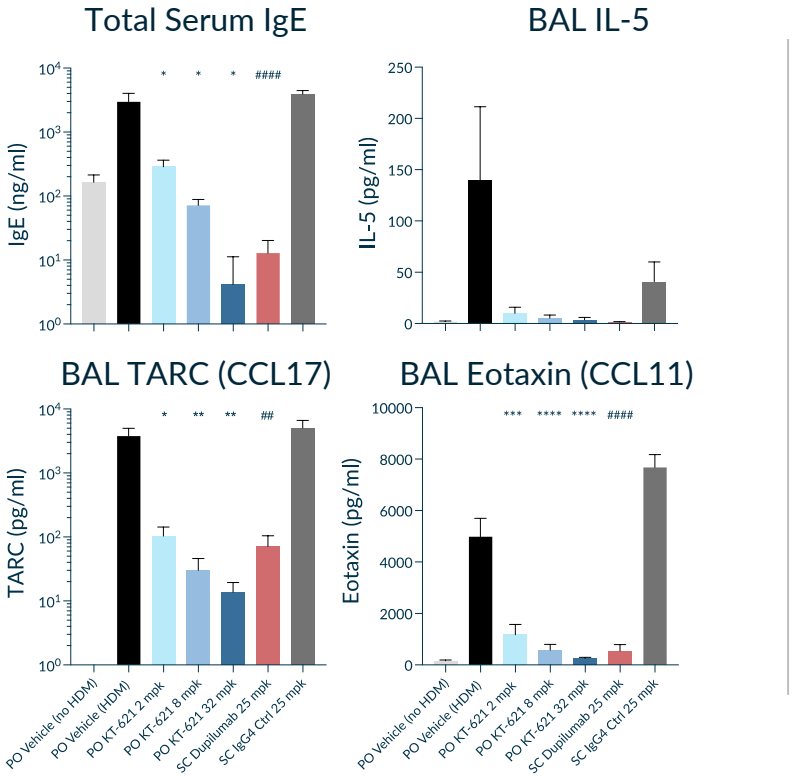
STAT6 Degradation in NHP Tissues Post 14 Days of KT-621 10 mpk QD Oral Dosing



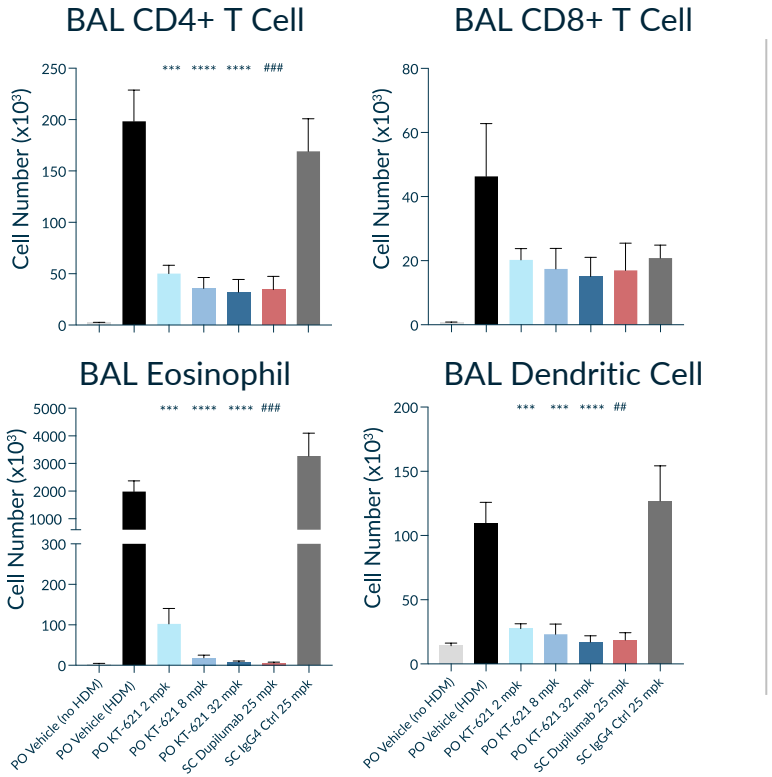
Wang et al. American Thoracic Society (2024)

KT-621 Blocks Th2 Inflammation *In Vivo* Equal to or Better than an IL-4Rα Saturating Dose of Dupilumab in the Intranasal HDM Asthma Model

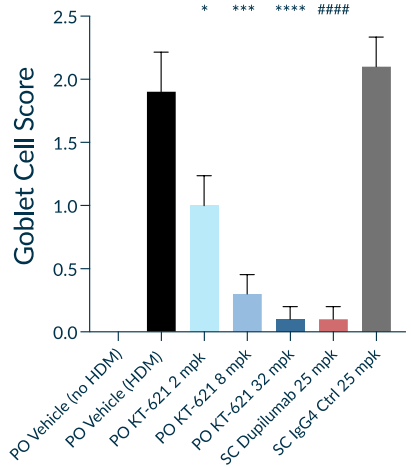
Serum IgE and Lung Cytokines



Inflammatory Lung Infiltrate



Lung Goblet Cell Metaplasia



New! **Additional HDM asthma model data to be shared at ATS on May 19 Poster #P1564**

- **KT-621 dosed QD orally for 31 days. 2/8/32 mpk doses showed 72/85/91% STAT6 degradation respectively in mouse spleen**
- **Dupilumab dosed 9 times subcutaneously, 25 mpk BIW (IL-4Rα saturating dose), effect equivalent to 300 mg every other week in human**
- **KT-621 reduced disease severity in the lung with amelioration of lung remodeling seen after low daily oral doses of KT-621 comparable to dupilumab**

A lung inflammation model induced by intranasal house dust mite administration with dominant Th2 inflammation in the IL4/IL4RA humanized mice (Le Floc'h et al. *Allergy*. 2020); BAL – bronchoalveolar lavage; *Significance to PO vehicle (HDM); # Significance to SC IgG4 Ctrl 25 mpk.

KT-621 Development Path to Key Proof-of-Concept Inflection Points

	Trial Objectives
Phase 1 Healthy Volunteers *(Completed – Data in June 2025)*	Safety and tolerability of robust STAT6 degradation in blood and skin measured over 14 days / Impact on Th2 biomarkers
Phase 1b Atopic Dermatitis Patients *(Ongoing – Data in Q4 2025)*	Impact on Th2 biomarkers with dupilumab-like signature measured over 28 days / Clinical endpoints
Parallel Phase 2b Trials in Atopic Dermatitis (*Start in Q4 2025*) & Asthma Patients (*Start in Q1 2026*)	Clinical activity in two initial Th2 diseases to support subsequent registrational studies across multiple indications

Initial development in atopic dermatitis and asthma expected to accelerate development and enable dose selection for subsequent parallel Phase 3 registration studies across multiple dermatology, respiratory, and GI indications