



# KYMERA



## Revolutionizing Immunology with Oral Medicines

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January 2026

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# Well Positioned to Redefine Immunology with Novel Oral Medicines

**Unrivaled science and expertise:** Innovative, experienced team and capabilities to develop revolutionary oral therapies to transform the treatment of immunological diseases

**Patient-first mentality, with urgency:** Rapidly advancing first-in-industry oral degraders with biologics-like activity

**Defining and surpassing clinical benchmarks:** Demonstrated compelling clinical translation of degraders' impact on clinical endpoints

**Scaling for the future:** Building a fully integrated global company to deliver a new class of immunology medicines

# Kymera: Industry Leader in Developing Oral Degrader Medicines

## UNIQUE STRATEGIES

**Target Selection:**  
Pursuing historically undrugged targets in highly validated pathways

**Immunology Focus:**  
Building an industry leading pipeline of oral medicines with biologics-like activity to transform treatments for patients

## LEADING CAPABILITIES

**Unique Chemistry Capabilities:**  
Finding ligands to historically undrugged targets; designing degraders with absolute selectivity and atomic level understanding of MOA

**Redefining Drug Development:**  
Developed new principles to match biologics activity with oral drugs

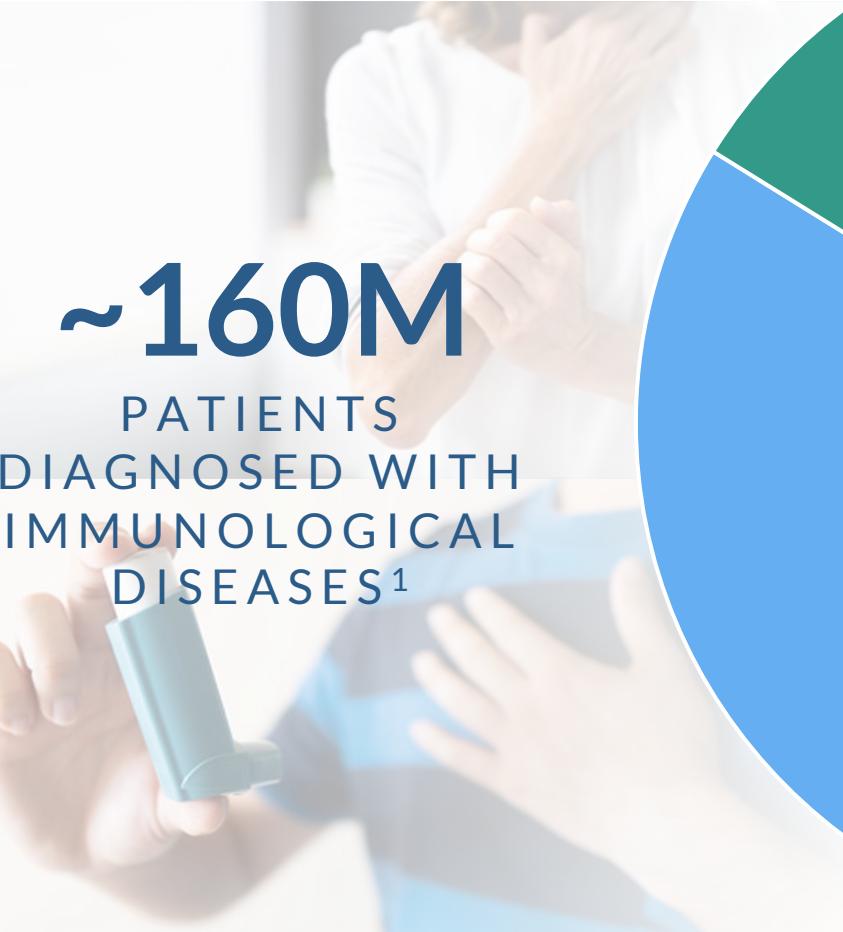
## NOVEL INSIGHTS

**Translation:**  
Deep expertise in target-drug interplay to optimize drug disposition and degradation across tissues and cell types

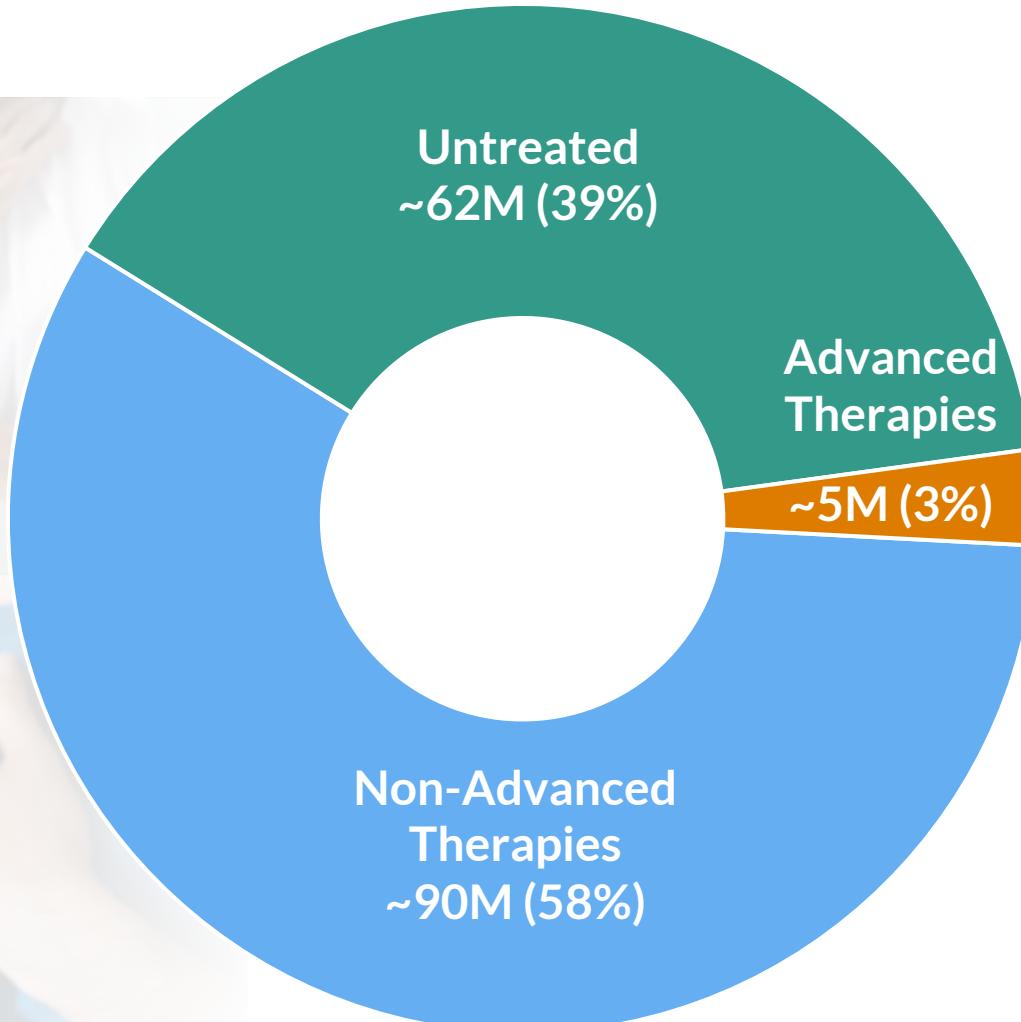
**Accelerated Development:**  
Leverage learnings and innovation (e.g., new biomarkers, endpoints) from early studies to inform and derisk mid/late-stage development; addressing multiple large indications with high unmet need

# Immunology Remains a Large Underserved Market

Millions of Patients Do Not Have Access to Advanced Systemic Therapies



**~160M**  
PATIENTS  
DIAGNOSED WITH  
IMMUNOLOGICAL  
DISEASES<sup>1</sup>



**>\$100B**  
IN ANNUAL SALES  
FOR ADVANCED  
THERAPIES<sup>2</sup>

<sup>1</sup>Diagnosed prevalent patient population for US/EU5/JP (GlobalData; 2023); key immunologic diseases includes AD, Asthma, CD, COPD, HS, MS, PsA, PsO, RA, SLE, UC;

<sup>2</sup>Market Forecasts for US/EU5/JP (GlobalData; 2023).

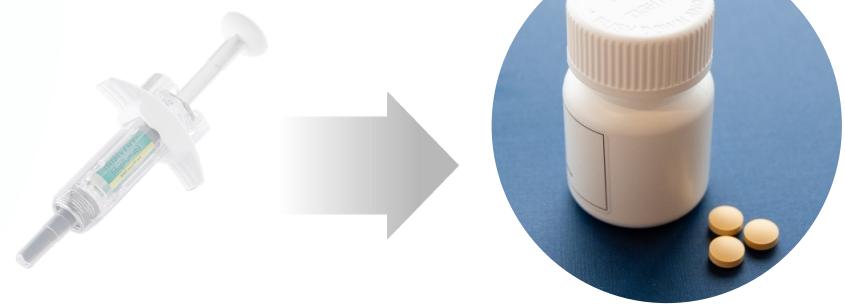
# Advanced Systemic Therapies Are Mostly Injectable Biologics

Biologics Have Numerous Limitations, Making Orals Preferred by Most Patients

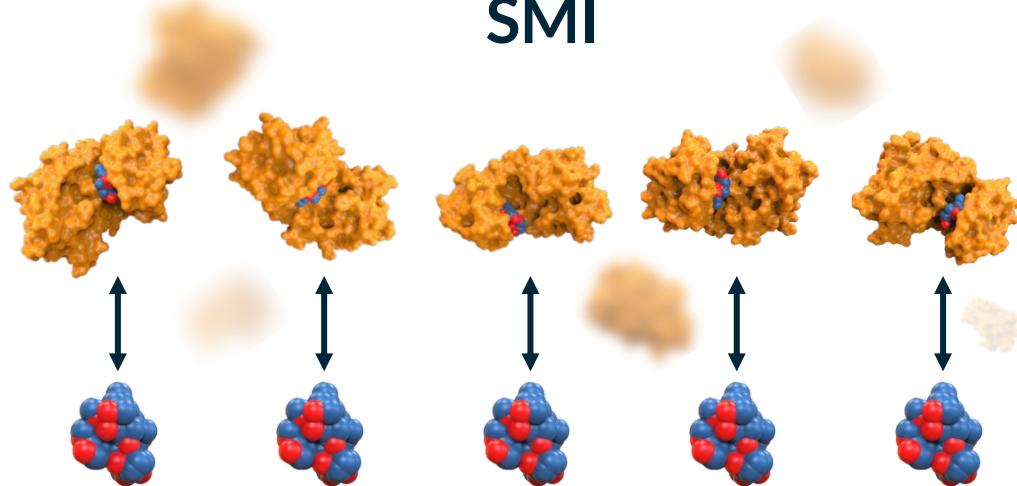


- Inconvenient, burdensome, and often painful for patients
- Immunogenicity risks
- In-office injection training costs HCPs valuable time and resources
- Expensive to manufacture; cold chain delivery/storage

**>90%**  
WOULD SWITCH  
TO AN ORAL  
OPTION<sup>1</sup>



# Degraders Allow for Continuous, Biologics-like, Complete Pathway Blockade Unlike Traditional Small Molecule Inhibitors (SMI)

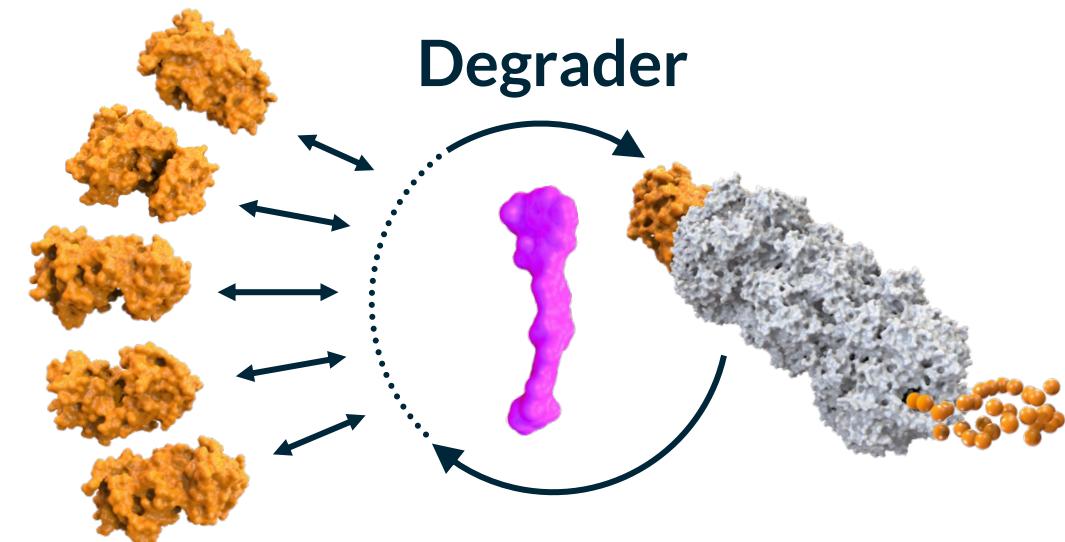


SMI

## STOICHIOMETRIC INHIBITION

Pharmacodynamic effect (PD) correlated to drug exposure (PK), (stoichiometric) requiring continuous high drug exposures to block protein function<sup>1</sup>

- Oral drugs with biologics-like activity, unlocking target classes unreachable by other modalities
- High selectivity, strong potency, and catalytic mechanism enable full and constant target suppression with low doses
- Achieves full pathway blockade, matching biologics-like depth of immune modulation



Degrader

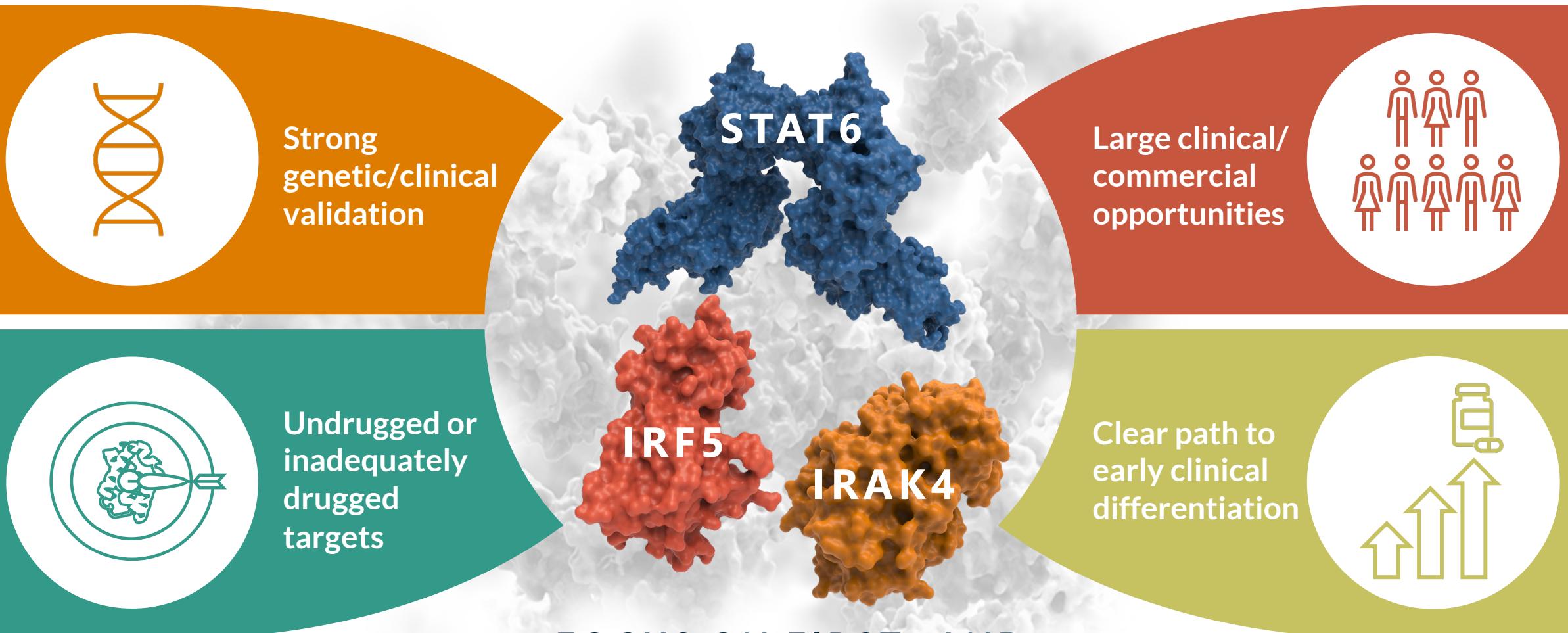
## CATALYTIC DEGRADATION

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

Oral degraders that combine the activity of injectable biologics with the convenience of oral drugs have the potential to transform current treatment paradigms

<sup>1</sup>Mainolfi et al, Annual Reports in Medchem, 2017; PD: Pharmacodynamics; PK: Pharmacokinetics; SMI: Small Molecule Inhibitors.

# Unique Target Selection Strategy Drives Best-In-Class Pipeline



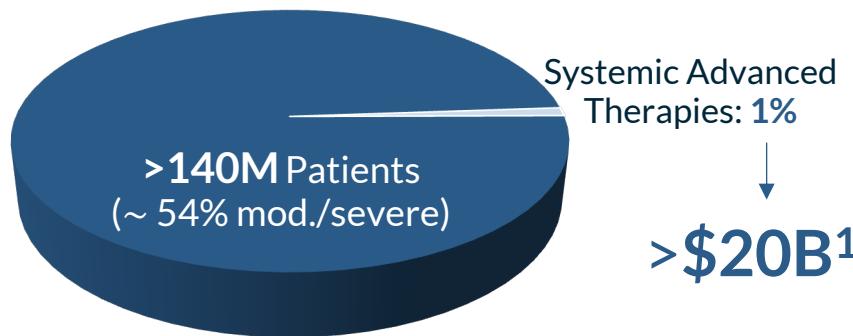
**FOCUS ON FIRST- AND  
BEST-IN-CLASS OPPORTUNITIES**

# Oral Degraders with Biologics-like Efficacy Can Transform Immunology

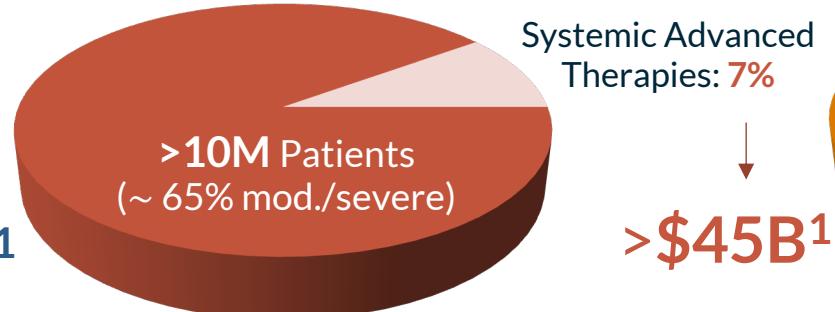
## Existing Therapies Address 10% or Less of Diagnosed Patients<sup>1</sup>



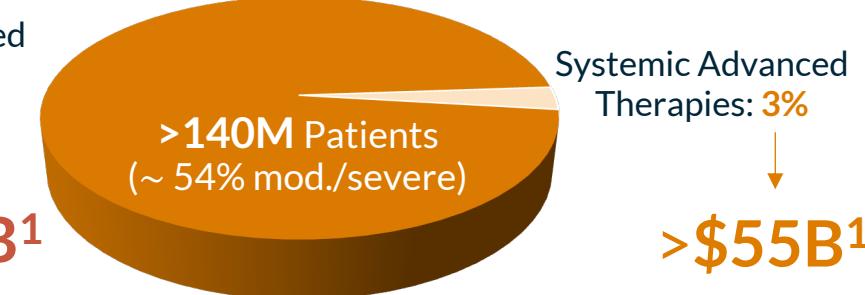
**Key Indications:** AD, Asthma, COPD, EoE, CRSwNP, CSU, PN, BP



**Key Indications:** SLE, RA, UC, CD, Sjögren's, SSc, DM



**Key Indications<sup>2</sup>:** HS, AD, Asthma, COPD, RA, SLE, UC, CD

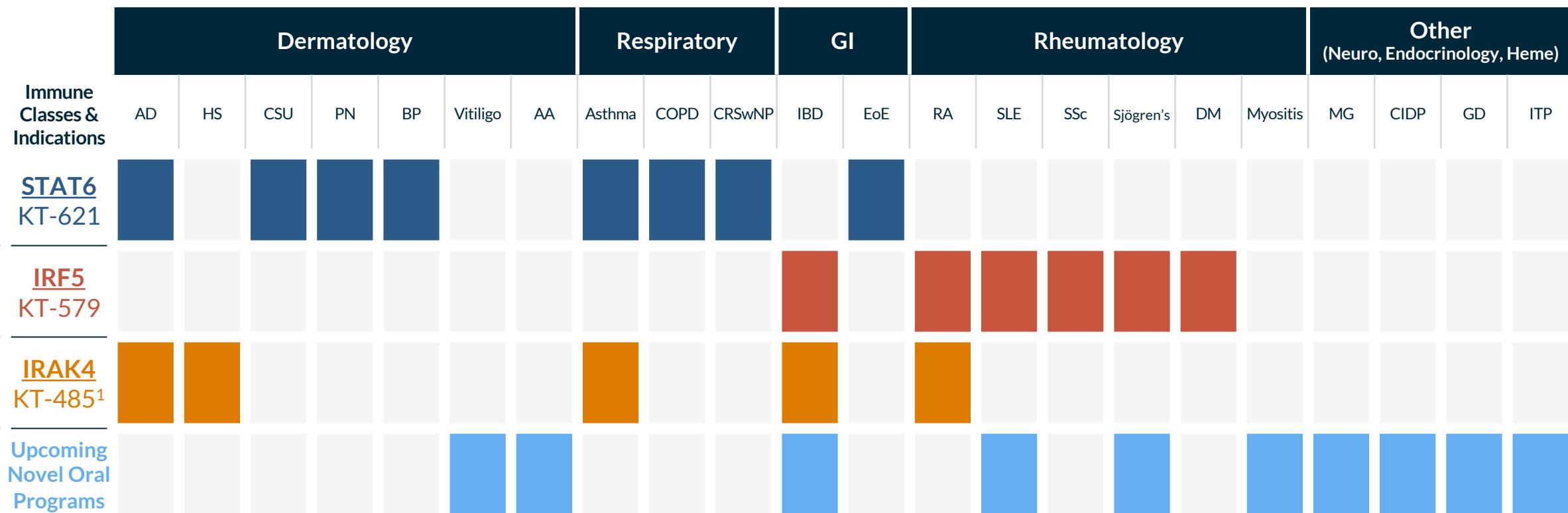


<sup>1</sup>GlobalData (2023) diagnosed prevalent patient population and forecasted sales for approved systemic advanced therapies in US/EU5/JP  
STAT6 estimates include only AD, Asthma, COPD; IRF5 estimates include only SLE, RA, UC, CD; IRAK4 estimates include all noted indications).

<sup>2</sup>Diseases where IL-1R/TLR pathway has been implicated in pathogenesis.

# Opportunity to Address a Wide Range of Immunology Indications

## Orals with Biologics-Like Activity to Transform Immunology



**Synergies and know-how across key immunological pathways creates multiple development and combination opportunities and positions Kymera to expand access to systemic advanced therapies for broad patient populations**

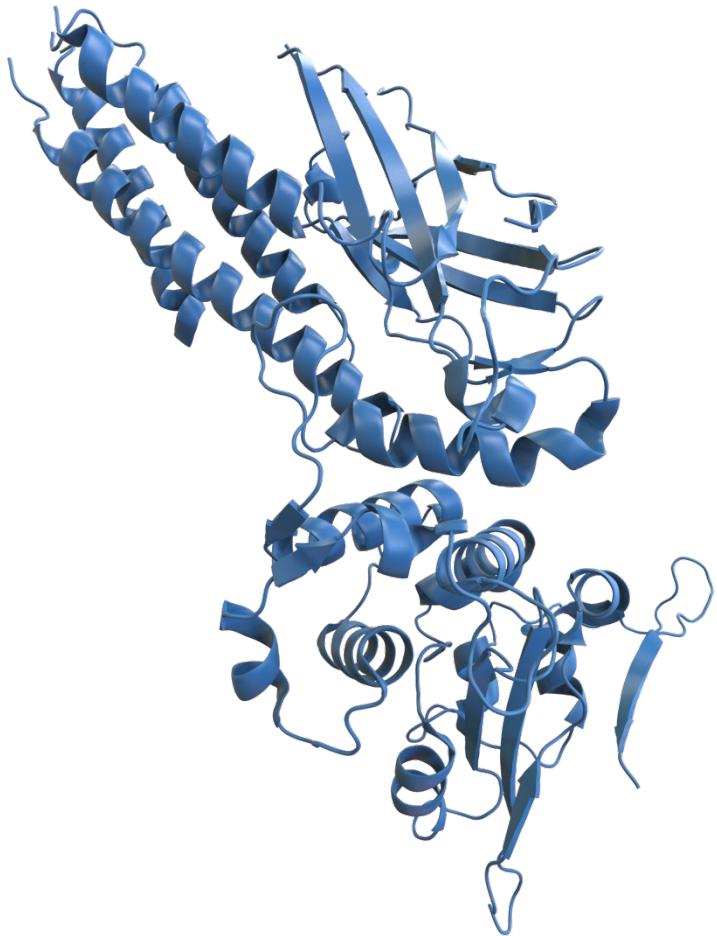
AD: atopic dermatitis; HS: hidradenitis suppurativa; CSU: chronic spontaneous urticaria; PN: prurigo nodularis; BP: bullous pemphigoid; AA: alopecia areata; COPD: chronic obstructive pulmonary disease; CRSwNP: chronic rhinosinusitis with nasal polyps; IBD: inflammatory bowel disease; EoE: eosinophilic esophagitis; RA: rheumatoid arthritis; SLE: systemic lupus erythematosus; SSc: systemic sclerosis; DM: dermatomyositis; MG: myasthenia gravis; CIDP: chronic inflammatory demyelinating polyneuropathy; GD: Graves' disease; ITP: immune thrombocytopenic purpura; <sup>1</sup>Diseases where IL-1R/TLR pathway has been implicated in pathogenesis.

# Building a Best-In-Industry Oral Immunology Pipeline

	Potential Indications	IND-Enabling	Phase 1	Phase 2	Phase 3	Upcoming Milestones
<b>Immunology - Wholly-Owned Oral Small Molecule Degraders</b>						
STAT6	AD, Asthma, COPD, EoE, CRSwNP, CSU, PN, BP, others		KT-621 - AD			Ph2b AD Data: By mid-2027 Ph2b Asthma Data: Late-2027
			KT-621 - Asthma			
IRF5	Lupus, Sjögren's, RA, IBD, SSc, DM, others	KT-579				Ph1 HV Start: 1Q26 Ph1 HV Data: 2H26
<b>Partnered Programs</b>						
IRAK4	HS, AD, RA, Asthma, IBD, others <sup>2</sup>	KT-485 <sup>1</sup>				 Ph1 Start: 2026
CDK2 <sup>3</sup>	Breast cancer and other solid tumors	Molecular Glue				

Combining the convenience of oral drugs and the activity of biologics to expand access to systemic advanced therapies for millions of patients around the world

<sup>1</sup>KT-485 (SAR447971) 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; <sup>2</sup>Diseases where IL-1R/TLR pathway has been implicated in pathogenesis. <sup>3</sup>Partnered with Gilead, exclusive option and license agreement to accelerate the development and commercialization of a novel molecular glue degrader program.

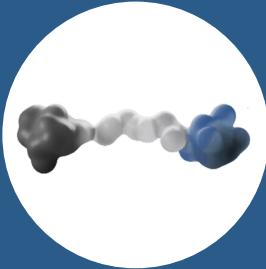


# First-in-Class Oral STAT6 Degrader Program

Dupilumab-like activity in a pill

# KT-621 Summary

## Dupilumab-like Activity in a Pill



KT-621 is the **first highly selective, potent, oral STAT6 degrader** in the clinic

- In preclinical *in vitro* and *in vivo* studies, it is equal or superior to dupilumab
- Phase 1b AD data showed deep STAT6 degradation in blood and skin, robust reductions in disease-relevant Type 2 biomarkers, meaningful improvements on clinical endpoints and PROs in AD and comorbid asthma and allergic rhinitis, and a favorable safety profile

## OPPORTUNITY

- Over 140M<sup>1</sup> potential patient impact; only ~1% has access to advanced systemic therapies
  - Market (with single digit % penetration) projected to reach **>\$27B** by 2030<sup>1</sup>
  - An **oral pill with dupi-like efficacy** can transform the treatment paradigm of Type 2 diseases
- .....▶ **Potential to access patients beyond biologics-eligible, across all disease severities and ages**

## STATUS & UPCOMING MILESTONES

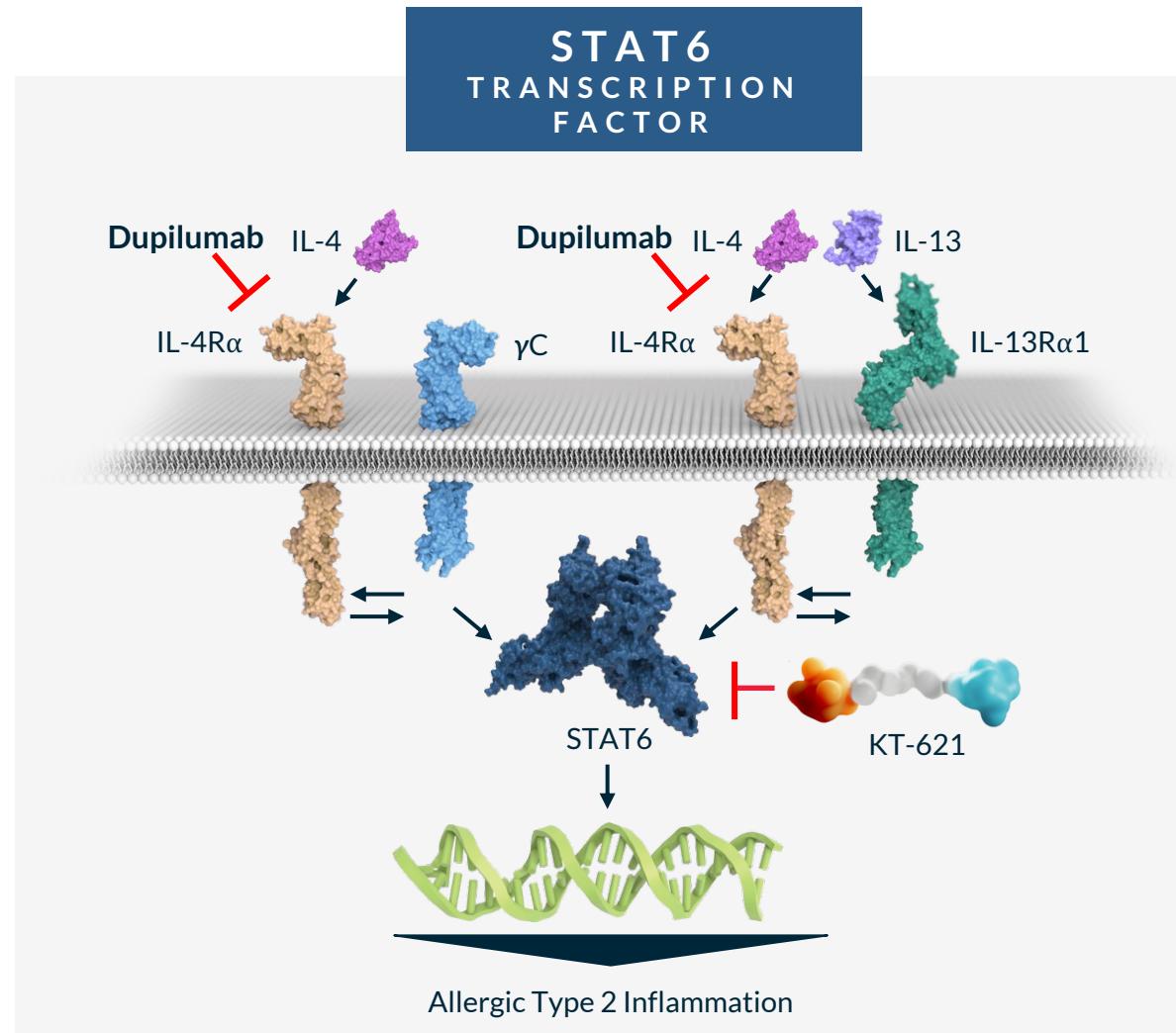
- BROADEN2 Phase 2b AD study ongoing, with data by mid-2027
- BREADTH Phase 2b asthma trial initiated, with data in late-2027

<sup>1</sup>GlobalData (2023 diagnosed prevalent patient population and forecasted sales of systemic advanced therapies for AD, Asthma, and COPD only in US/EU5/JP).

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# STAT6 Transcription Factor: Highly Validated but Undrugged Target

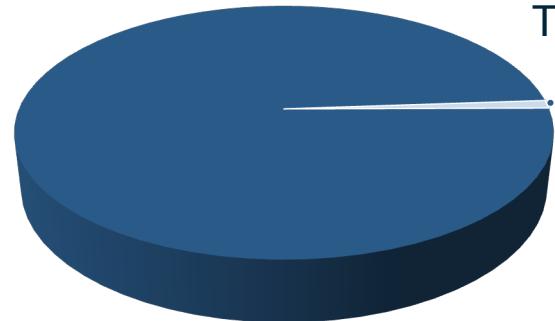
- STAT6 is the specific transcription factor in the IL-4/IL-13 pathway
- IL-4/IL-13 is clinically validated by dupilumab across multiple Type 2 diseases:
  - AD, asthma, COPD, EoE, CRSwNP, CSU, PN, BP
- STAT6 is genetically validated by human GoF and heterozygous LoF alleles
- While several therapies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



Sharma et al, 2023; Takeda et al, 1996; Kaplan et al, 1996; Juntila, 2018; Kolkhir et al, 2023; AD: Atopic Dermatitis; COPD: Chronic Obstructive Pulmonary Disease; EoE: Eosinophilic Esophagitis; CRSwNP: Chronic Rhinosinusitis with Nasal Polyps; CSU: Chronic Spontaneous Urticaria; PN: Prurigo Nodularis; BP: Bullous Pemphigoid; GoF: Gain of Function; LoF: Loss of function.

# STAT6 Opportunity to Serve Millions of Patients with Type 2 Inflammation

>140M

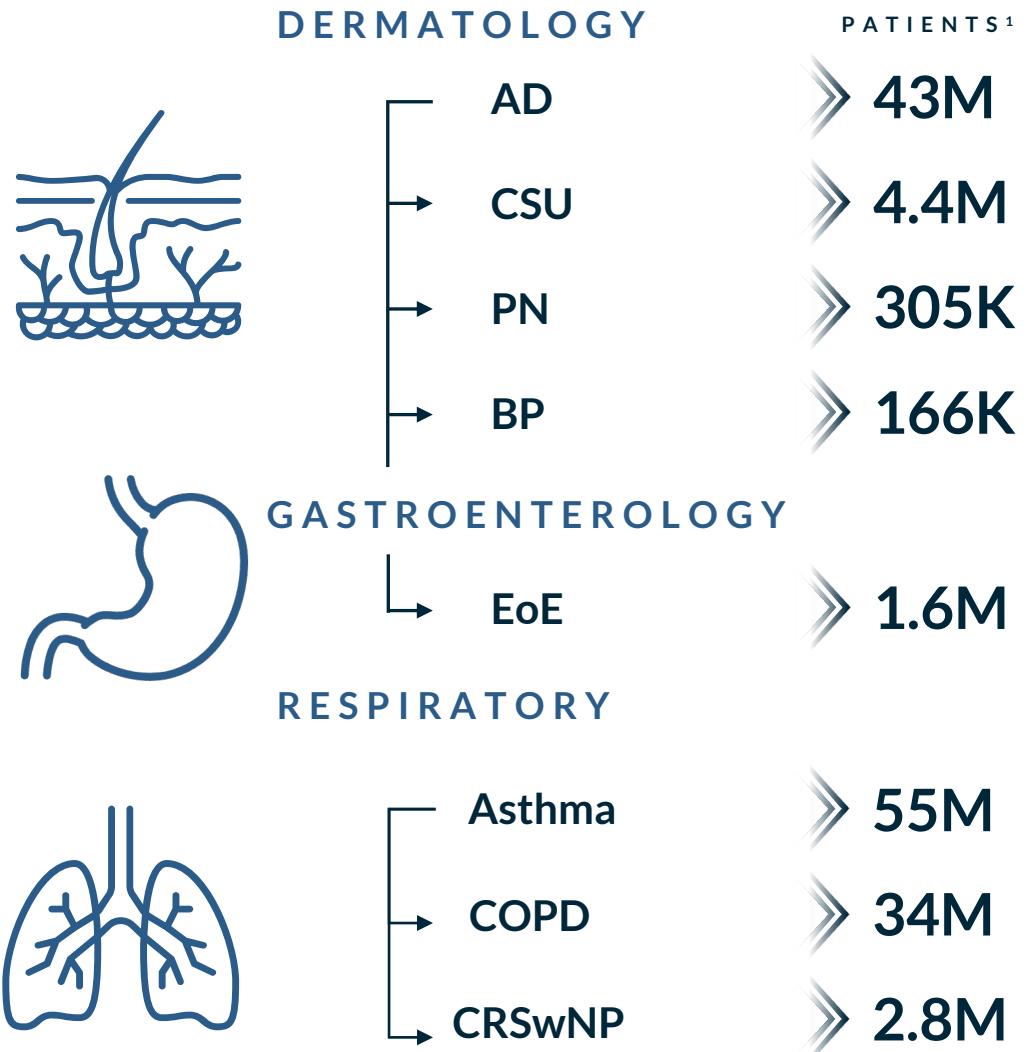


TOTAL POTENTIAL  
PATIENT IMPACT<sup>1</sup>

An oral STAT6 degrader has the potential to transform the treatment paradigm for Type 2 diseases and tap into large underserved markets

Systemic Advanced Therapies: 1%

>\$20B Market



<sup>1</sup>Diagnosed prevalent patient population for US/EU5/JP (GlobalData; 2023); <sup>2</sup>Estimate based on GlobalData 2023 market forecasts for AD, Asthma, and COPD in US/EU5/JP then extrapolated to remaining Type 2 indications; AD: Atopic Dermatitis; COPD: Chronic Obstructive Pulmonary Disease; EoE: Eosinophilic Esophagitis; CRSwNP: Chronic Rhinosinusitis with Nasal Polyps; CSU: Chronic Spontaneous Urticaria; PN: Prurigo Nodularis; BP: Bullous Pemphigoid.

# Current Treatments Do Not Address Patients' Needs

>55% of Adults with Moderate/Severe AD and 60% of Adult Asthma Patients Report Inadequate Disease Control<sup>1,2</sup>

## INADEQUATE SYSTEM OF CARE

- **Topical treatments (AD) and inhalers (asthma)** are limited to the mildest cases
- **Biologics** associated with high treatment burden and cost/access concerns
- **Current oral therapies (JAKs and oral steroids)** come with serious efficacy and/or safety limitations

## CURRENT TREATMENT LIMITATIONS

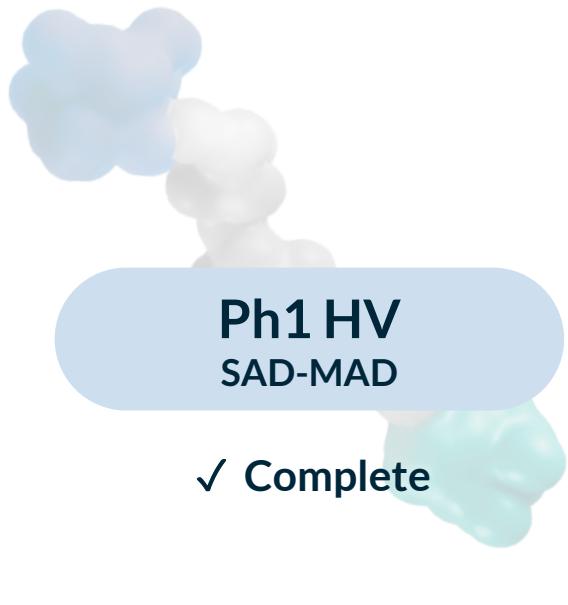
- Needle fear/fatigue
- Burdensome dosing (up to 4 injections in 1<sup>st</sup> month)
- Complex treatment initiation (blood testing)
- Inconsistent adherence
- Side effect and safety issues

## PATIENTS WANT

- Rapid onset of relief and durable efficacy
- **Convenience of a daily pill;** >90% of patients on biologics would switch to an oral option<sup>3</sup>
- No treatment initiation requirements
- No side effects or safety issues
- HCP confidence in prescribing

**KT-621 has the potential to offer “what patients want”, transforming the treatment of AD, asthma, and other Type 2 diseases**

# KT-621 Development Plan Enables Efficient Path to Registration Across All Type 2 Diseases



## BROADEN STUDY

Ph1 HV  
SAD-MAD

✓ Complete

Ph1b AD  
Single Arm, Open Label

✓ Complete

## BROADEN2 TRIAL

Ph2b AD  
Dose Ranging

Ongoing  
Data expected by mid-2027

Ph3  
Dose

Ph3: AD (Initial),  
EoE, CSU, PN, BP

## BREADTH TRIAL

Ph2b Asthma  
Dose Ranging

Initiated  
Data expected late-2027

Ph3  
Dose

Ph3: Asthma (Initial),  
COPD, CRSwNP

Initial parallel Phase 2b trials in moderate to severe AD and asthma have the potential to support subsequent Phase 3 trials across multiple dermatology, GI, and respiratory indications

# KT-621 Data Provide Validation and Derisk Future Clinical Trials

## Preclinical

### POTENCY

- < 100 pM DC90 in all relevant human cell types

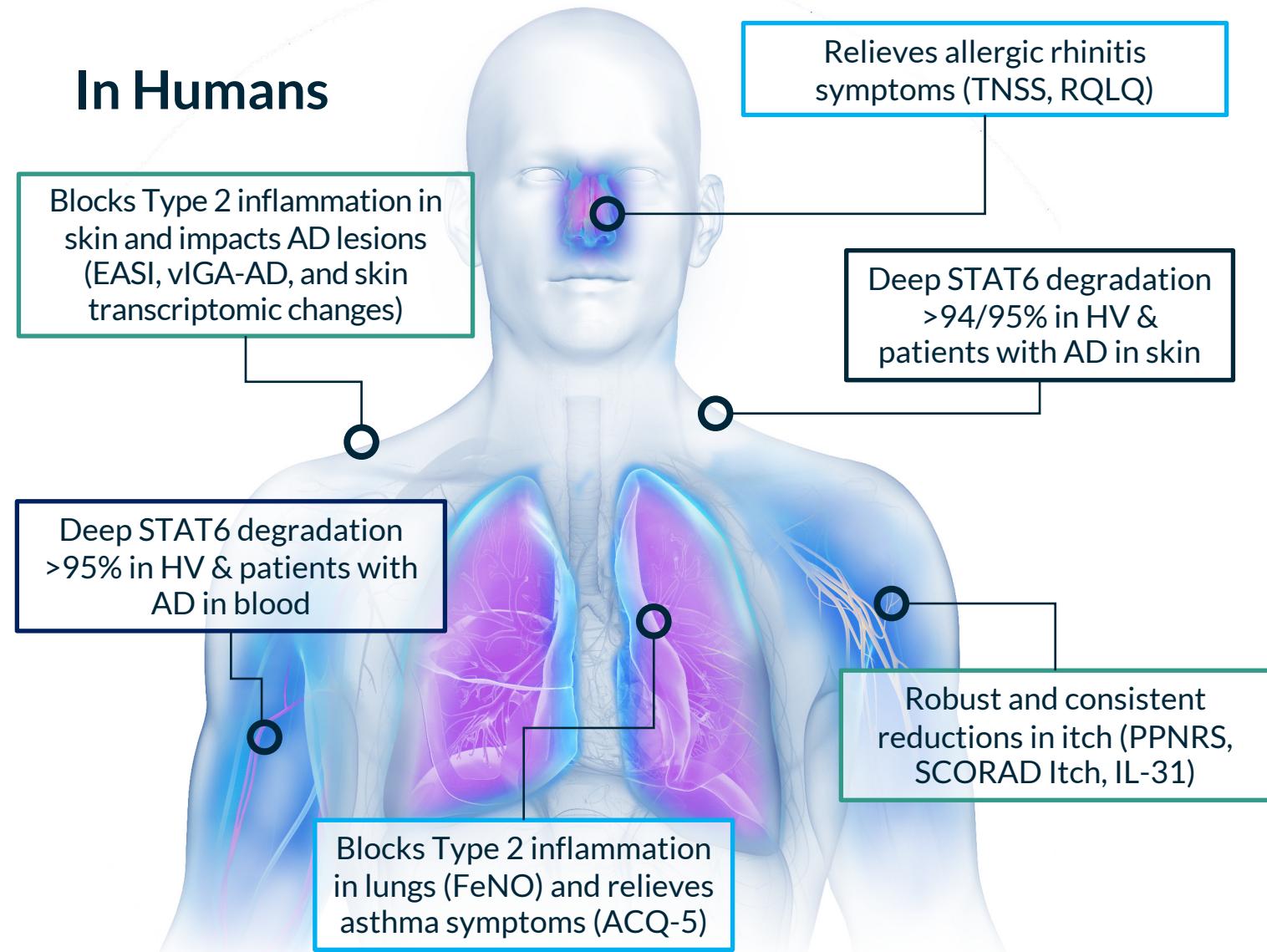
### EFFICACY

- Blocked IL-4 and IL-13 signaling in human cells and *in vivo* systems equally or more potently than dupilumab
- Robust activity in asthma and AD in mouse models

### SAFETY

- No AEs at any doses in:
  - 4 weeks rat and NHP GLP tox
  - 4 months rat and NHP GLP tox
  - Embryofetal development tox in rat, rabbit and NHP

## In Humans



# KT-621: BROADEN2 Phase 2b Trial

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



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

**Baseline entry criteria:**  
EASI  $\geq$  16;  
vIGA-AD  $\geq$  3;  
Peak Pruritus NRS  $\geq$  4;  
BSA  $\geq$  10%;  
Documented TCS  
failure for AD

## 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 0/1
  - At least a 4-point improvement from baseline in Peak Pruritus NRS

## Key Trial Aim

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

Status update:  
**Ongoing, also including  
adolescents;**  
**Data expected by mid-2027**

# KT-621: BREADTH Phase 2b Trial

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



**Adult, Moderate to Severe Eosinophilic Asthma Patients**

**Baseline entry criteria:**

Blood eosinophils  $\geq$  300 cell/uL

FeNO  $\geq$  25 ppb

Pre-bronchodilator FEV1 40-80% of predicted normal

## Design

- Randomized, double-blind, placebo-controlled
- ~264 patients
- Daily dose for 12-weeks

## Dosing

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

## Endpoints

- Primary endpoint: Percent change from baseline in pre-bronchodilator FEV1 at week 12
- Secondary endpoints include:
  - Change from baseline in ACQ-5, AQLQ

## Key Trial Aim

Establish clinical activity and safety in asthma to select Phase 3 dose to support registrational studies in multiple respiratory indications

Status update:  
**Initiated January 2026;**  
**Data expected late-2027**

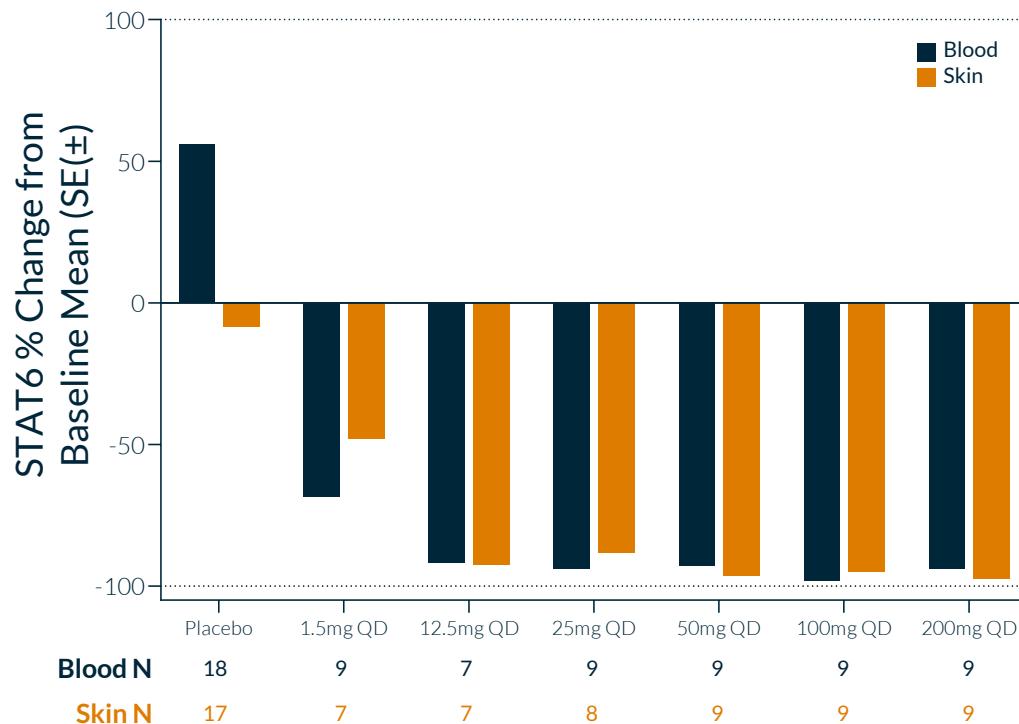
# KT-621 Phase 1a Healthy Volunteer and Phase 1b BroADen AD Clinical Trial Data



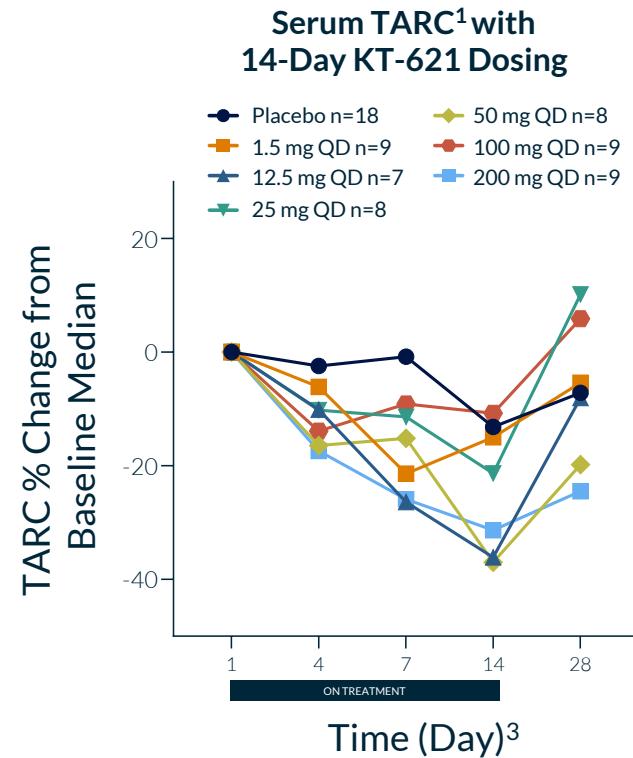
# KT-621: Compelling Clinical Profile

KT-621 Phase 1 Healthy Volunteer Data Suggests Potential for Dupilumab-like Activity in a Pill

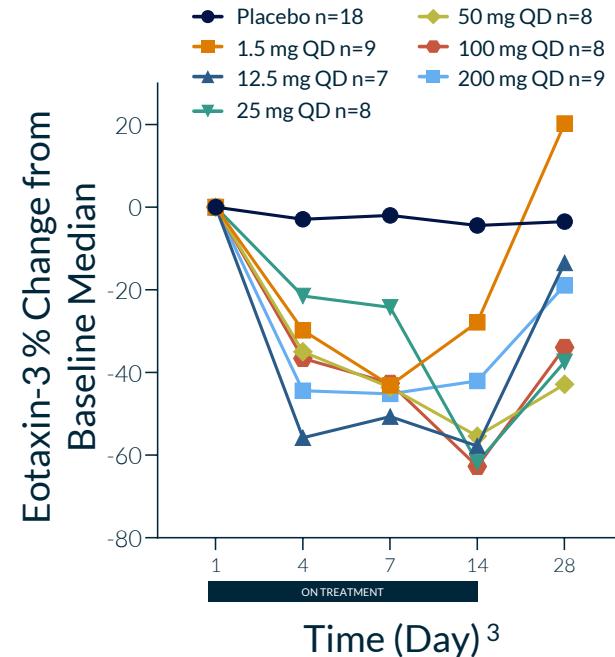
## Robust STAT6 Degradation in Blood and Skin Following Low Daily Oral Doses



## Reductions in Multiple Disease-Relevant Type 2 Biomarkers



## Serum Eotaxin-3<sup>2</sup> with 14-Day KT-621 Dosing



Favorable safety profile: well-tolerated across all dose levels with safety profile undifferentiated from placebo

<sup>1</sup>TARC levels measured in serum using MSD VPLEX; <sup>2</sup>Eotaxin-3 levels measured in serum using MSD VPLEX; <sup>3</sup>Compound dosed on Day 1; For more information on KT-621's Phase 1 healthy volunteer clinical trial, visit [Kymera's website](#).

# BroADen KT-621 Phase 1b AD Study Surpassed Objectives

Effects on All Type 2 Biomarkers and Clinical Endpoints Were in Line with or in Some Cases Numerically Exceeded Published Data for Dupilumab at Week 4

## Endpoints

### BroADen Phase 1b Results Highlights

#### STAT6 Degradation

- ✓ Strong fidelity of translation from Phase 1a healthy volunteer study to AD patients with deep STAT6 degradation in blood and skin

#### Type 2 Biomarkers

- ✓ Robust reductions in Type 2 biomarkers in blood, skin lesions and lung (FeNO)

#### Clinical Endpoints

- ✓ Meaningful improvements of clinical endpoints and patient-reported outcomes in AD, comorbid asthma and allergic rhinitis

#### Safety

- ✓ Well-tolerated and favorable safety profile similar to Phase 1a healthy volunteer study

Clinical data continue to support a potential dupilumab-like profile in AD and other Type 2 diseases with a once daily, oral drug

No head-to-head trials have been conducted comparing KT-621 to dupilumab. Phase 1 clinical data for KT-621 may not be directly comparable to dupilumab's clinical data due to differences in molecule composition, trial protocols, dosing regimens, and patient populations and characteristics. Accordingly, cross-trial comparisons may not be reliable.

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# BROADEN STUDY

## Phase 1b in Moderate to Severe Atopic Dermatitis Patients

### Baseline entry criteria:

- Adult, moderate to severe AD patients

EASI            **≥16**

vIGA-AD      **≥3**

PPNRS         **≥4**

BSA            **≥10%**

- Documented TCS (Topical Corticosteroid) failure for AD
- Prior biologics allowed, after washout, if patient has responded to treatment
- Concurrent medications for AD not permitted

EASI: Eczema Area and Severity Index; vIGA-AD: Validated Investigator Global Assessment for Atopic Dermatitis; PPNRS: Peak Pruritus Numerical Rating Scale; BSA: Body Surface Area; TCS: Topical Corticosteroid.



### Design

- Single arm, open label
- 22 patients
- Oral, once daily dose for 28 days
- 14-day follow-up after dosing completed



### Dosing

- Two sequential dose cohorts
  - 100 mg (10 patients)
  - 200 mg (12 patients)



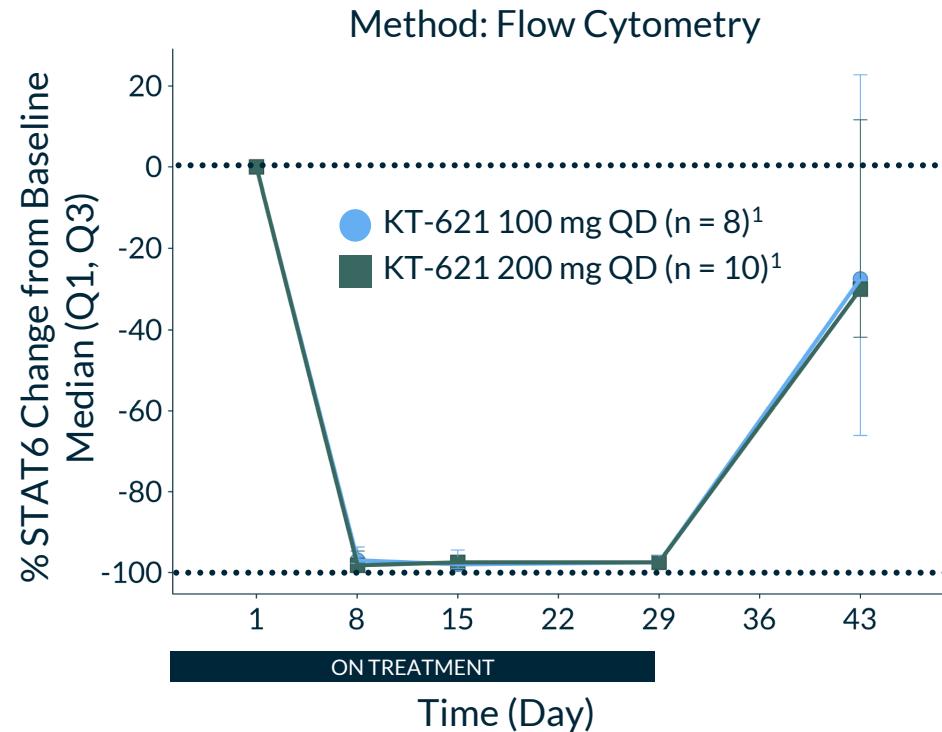
### Endpoints

- Safety
- Pharmacokinetics
- STAT6 degradation
- Type 2 biomarkers in blood, skin lesions and lung
- Clinical activity (EASI, PPNRS, vIGA-AD, patient-reported outcomes)

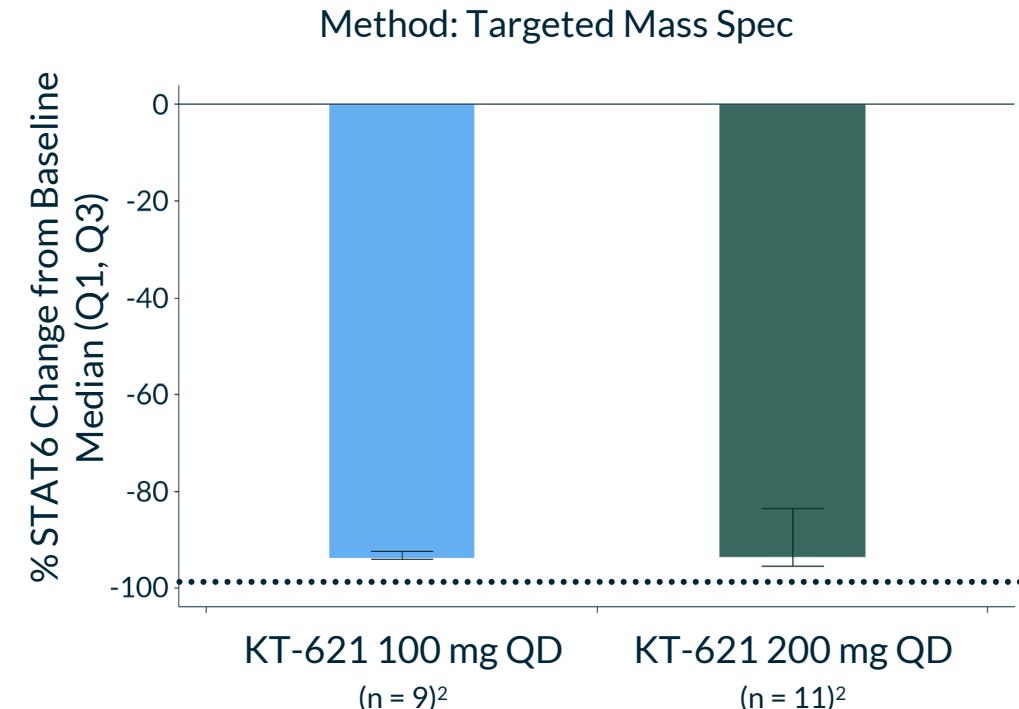
# KT-621 Achieved Deep STAT6 Degradation in Blood and Skin

## Degradation Maintained for 28 Days Across Both Dose Cohorts

### Median STAT6 Degradation in Blood



### Median STAT6 Degradation in Skin

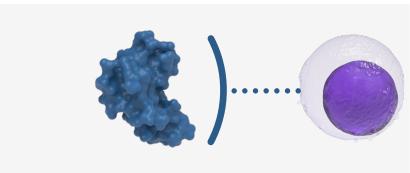
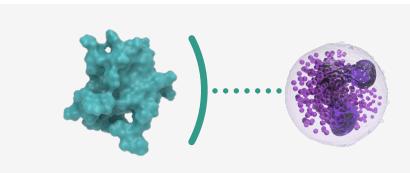
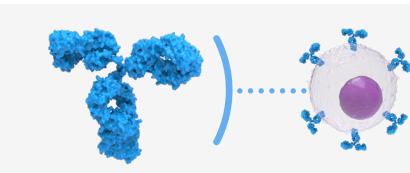
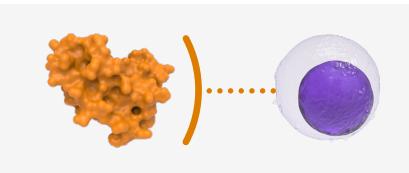
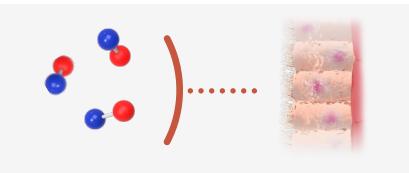


- Median STAT6 degradation of 98% in blood in both dose groups maintained throughout the treatment period
- Deep skin degradation of 94% in both dose groups with multiple patients' STAT6 levels below the LLOQ (lower limit of quantification)

Note: N values reflect the number of participants with available samples at Day 29; <sup>1</sup>Two patients (one each in 100 mg and 200 mg dose groups) did not have baseline samples collected, and two D29 samples were unevaluable due to shipping issues that led to loss of stability; <sup>2</sup>Two patients did not consent to D29 biopsies; PK: Pharmacokinetics.

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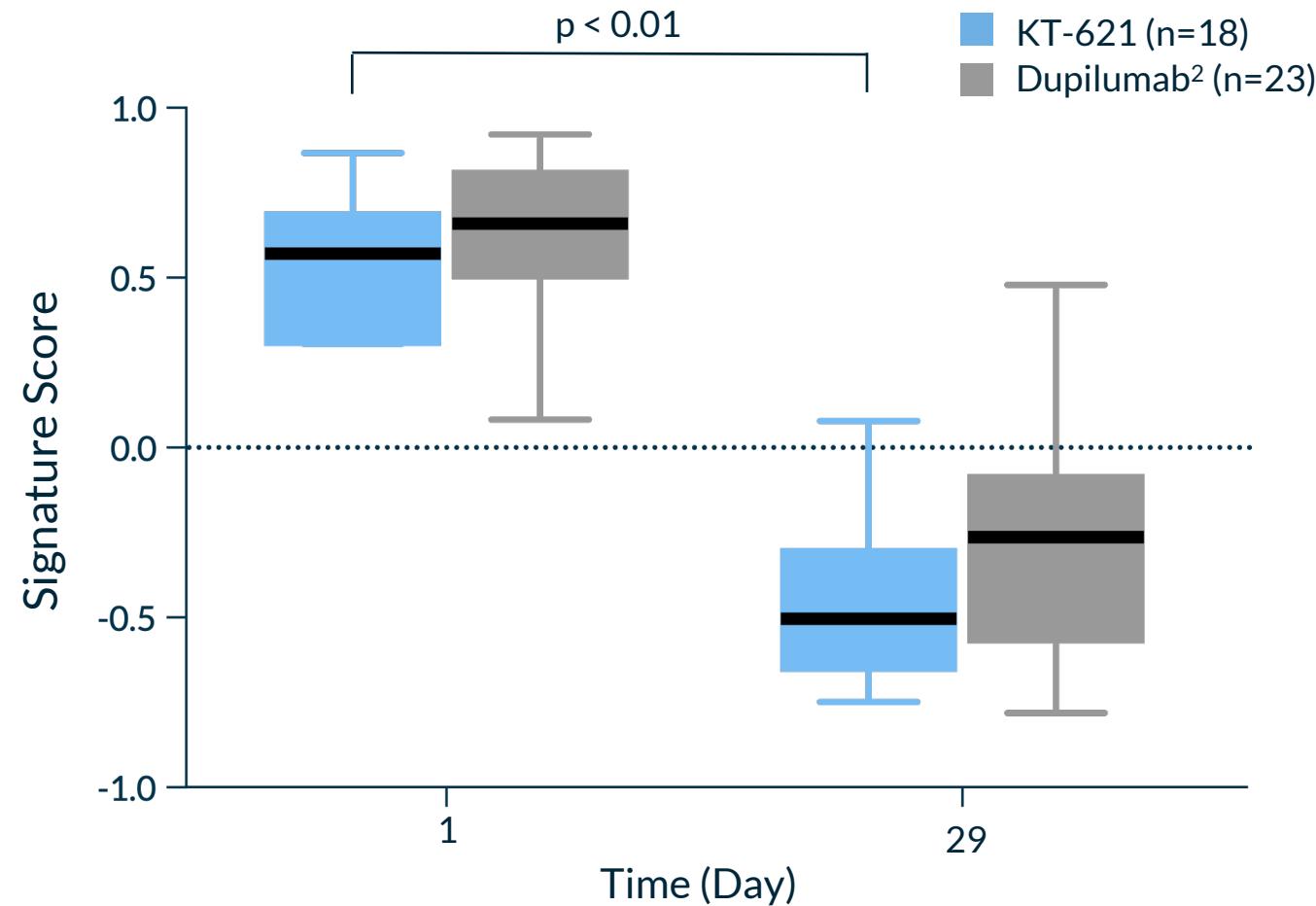
# Robust Impact on All Disease-Relevant Biomarkers of Type 2 Inflammation in BroADen Phase 1b AD Trial

TARC (CCL17)	Eotaxin-3 (CCL26)	IgE	IL-31	FeNO
				
Validated biomarker of Type 2 inflammation suppression in patients  Drives chemotaxis of CCR4-expressed T cells to inflammatory sites	Highly specific downstream cytokine of the IL-4/13 pathway  Drives chemotaxis of CCR3-expressed inflammatory cells to inflamed sites	IL-4 promotes B-cell class switching, amplifying IgE production  IgE activates mast cells and basophils to release Type 2 cytokines	Key pruritogenic cytokine produced by activated Type 2 cells <sup>1</sup>  Signals through the IL-31RA/OSMR complex on neurons, keratinocytes, and immune cells, linking immune activation to itch	Marker of Type 2 airway inflammation in asthma <sup>2</sup>  FeNO reflects airway epithelial iNOS activity driven by IL-4/13 signaling  Historically not measured in AD patients
Median % Inhibition at Day 29				
<b>KT-621</b>	<b>74%<sup>3</sup></b>	<b>73%</b>	<b>14%</b>	<b>54%</b>
Dupilumab <sup>4</sup>	74%	51% (in Asthma)	~15%	Not measured
				Not measured

<sup>1</sup>Raab et al, *Journal of Allergy and Clinical Immunology*, 2008; <sup>2</sup>Chung et al, *Lancet*, 2021; <sup>3</sup>Represents TARC reduction in patients with elevated baseline TARC levels, defined as the lower bound of the 95% confidence interval for median baseline TARC levels from the dupilumab SOLO1-2 AD studies; <sup>4</sup>Hamilton et al, *Clinical & Experimental Allergy*, 2021.

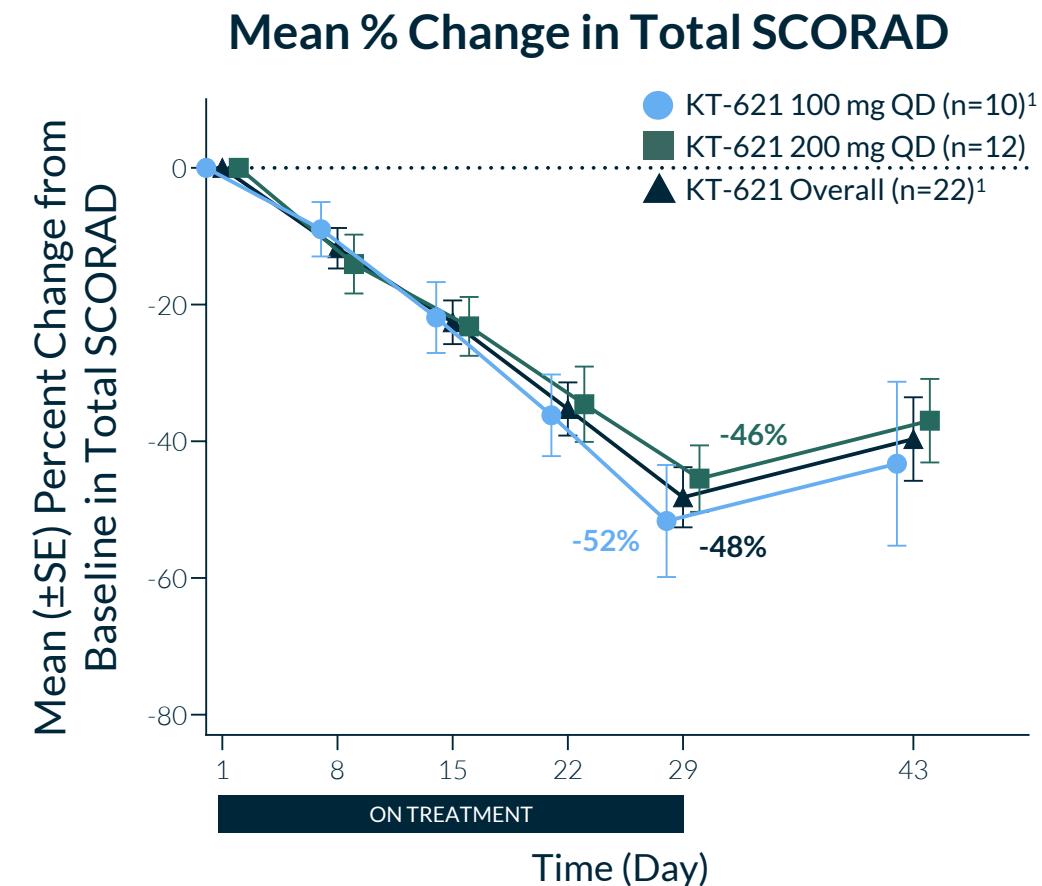
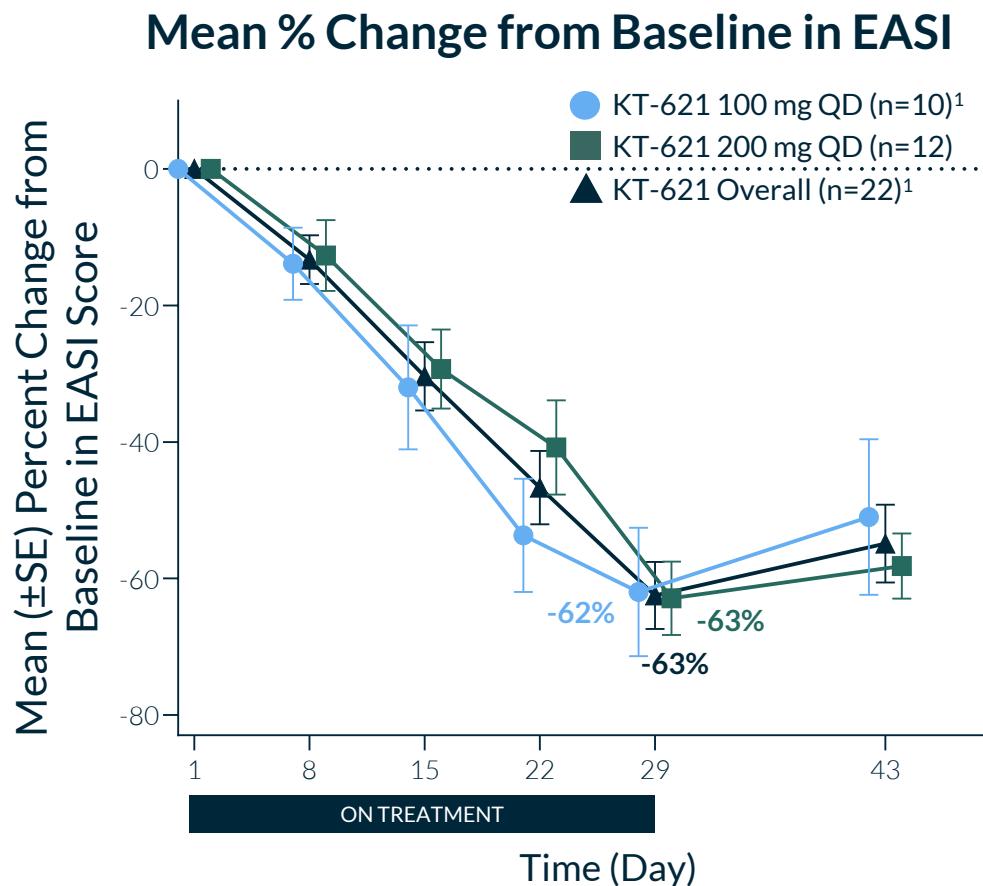
# KT-621 Significantly Downregulated Core Type 2 Inflammation Gene Set in Skin Lesions of AD Patients

- Genes in signature<sup>1</sup>:
  - CCL26/Eotaxin-3
  - CCL17/TARC
  - CCL18/PARC
  - CCL13/MCP-4
- Changes in transcriptome comparable to published data for dupilumab at week 4<sup>2</sup>



Note: 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 D29 biopsy, one patient D29 biopsy was lost, and one patient had poor quality sequencing; <sup>1</sup>Signature scores generated by GSVA (Hänelmann et al, BMC Bioinformatics, 2013); <sup>2</sup>Dupilumab data from Guttman-Yassky et al, JACI, 2019; P-value < 0.01 for paired t-test between D1 and D29 for both treatments.

# KT-621 Achieved Rapid and Robust Reductions in EASI and SCORAD Across All Patients

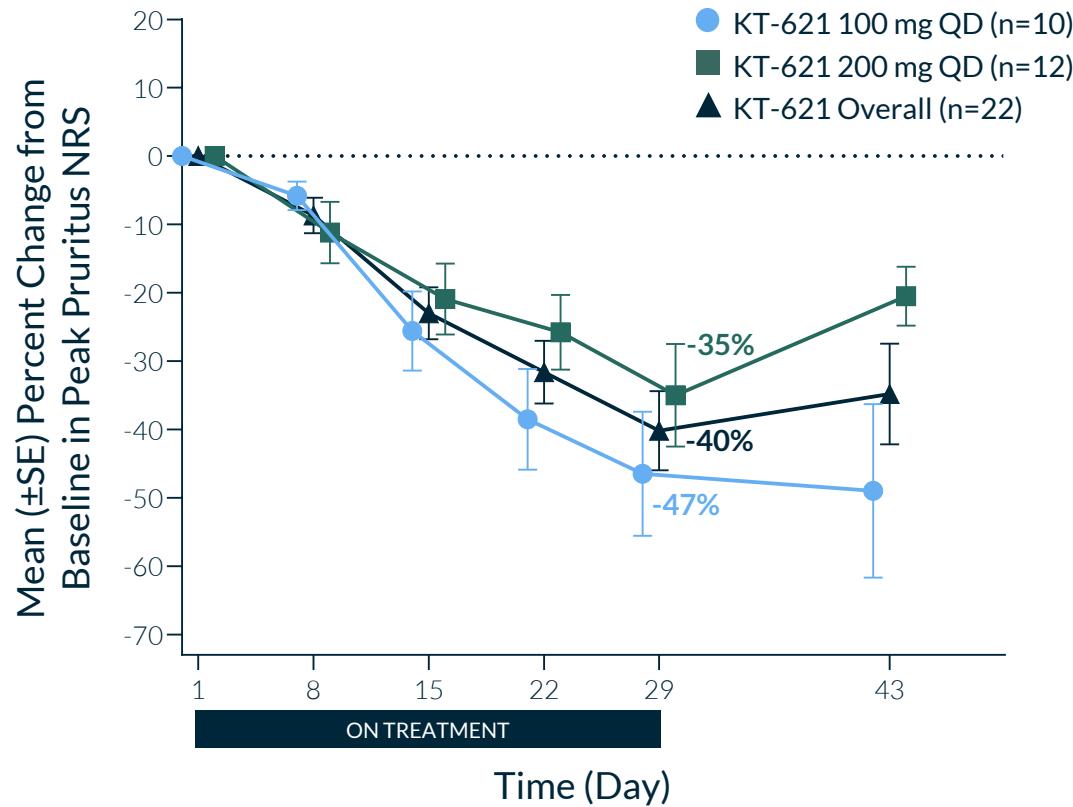


- Reductions seen as early as Day 8 without apparent plateau during treatment duration
- Achieved robust clinical improvement across EASI-50 (76% overall), EASI-75 (29% overall) and vIGA-AD (19% overall)

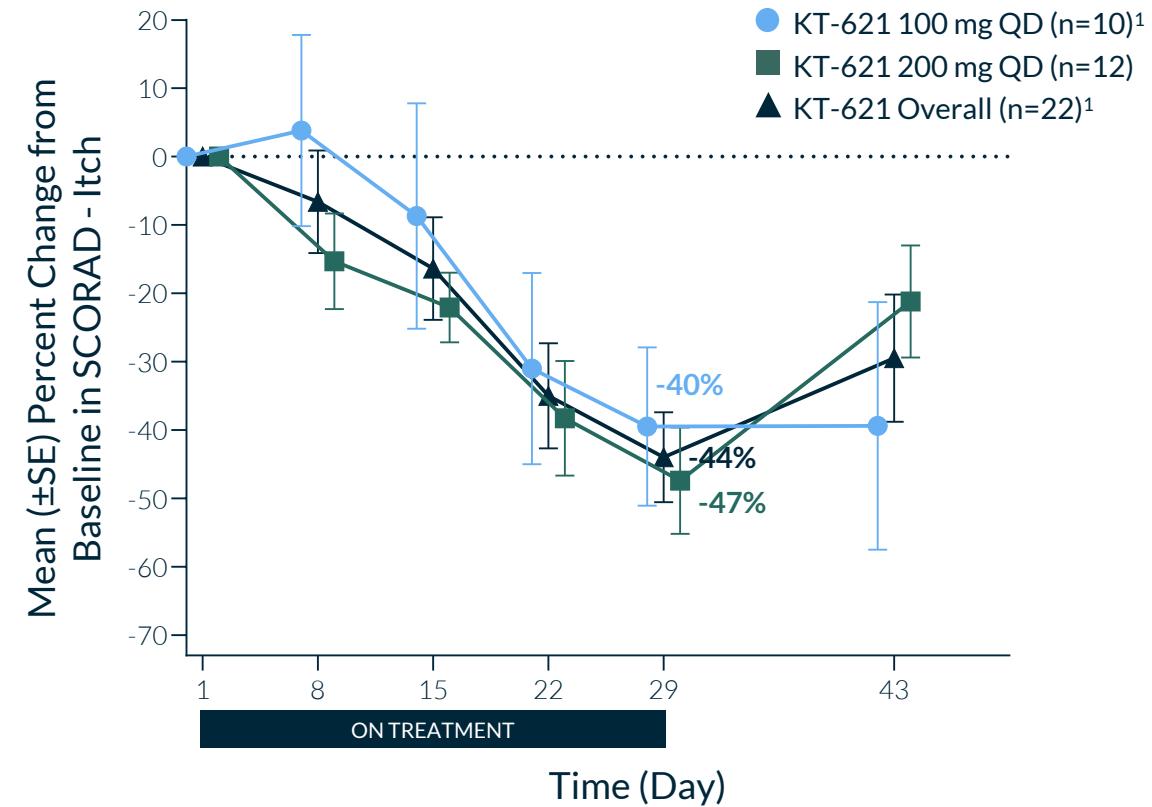
Note: Analysis based on observed cases at each visit; <sup>1</sup>One patient in the 100 mg cohort missed the D29 visit (n=9 for 100 mg and n=21 for Overall at D29); EASI: Eczema Area and Severity Index; SCORAD: SCORing Atopic Dermatitis.

# KT-621 Achieved Robust and Consistent Reductions in Itch Across Independent Clinical Measures

Mean % Change in Peak Pruritus NRS



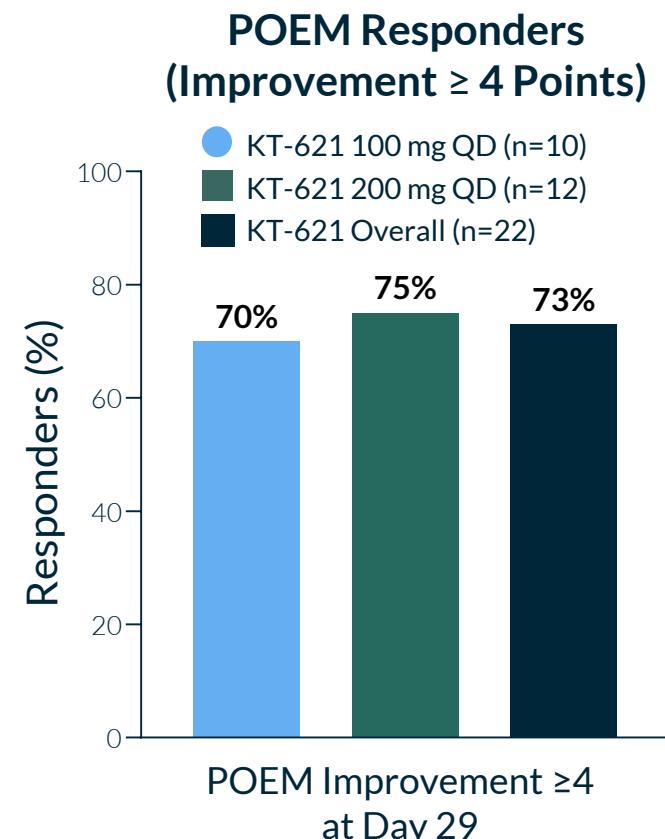
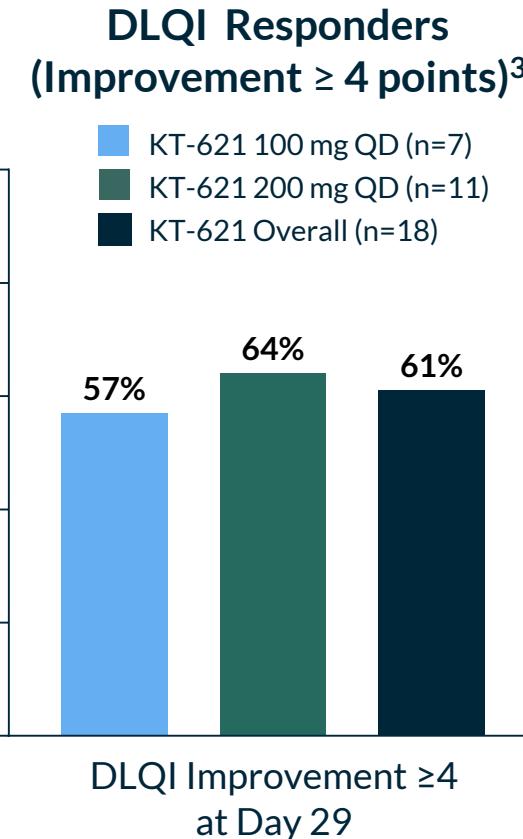
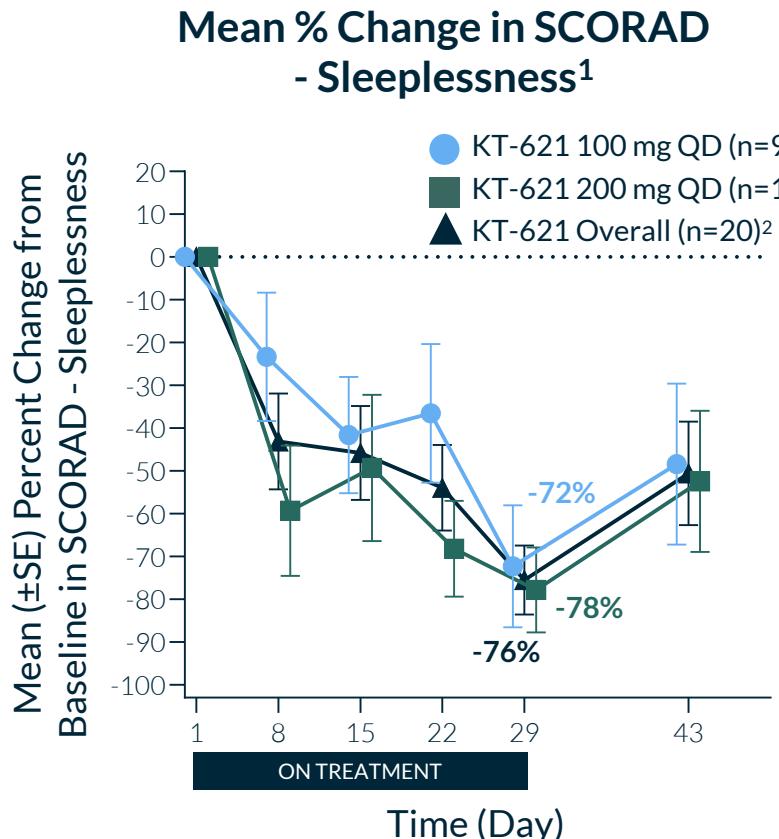
Mean % Change in SCORAD Itch



- KT-621 achieved rapid and robust mean Peak Pruritus NRS and SCORAD-Itch reduction without apparent plateau during treatment duration

Note: Analysis based on observed cases at each visit; <sup>1</sup>One patient in the 100 mg cohort missed the D29 visit (n=9 for 100 mg and n=21 for Overall at D29); PPNRS: Peak Pruritus Numerical Rating Scale; SCORAD: SCORing Atopic Dermatitis.

# KT-621 Achieved Robust Improvement in Patient Reported Outcomes and Quality of Life Measures

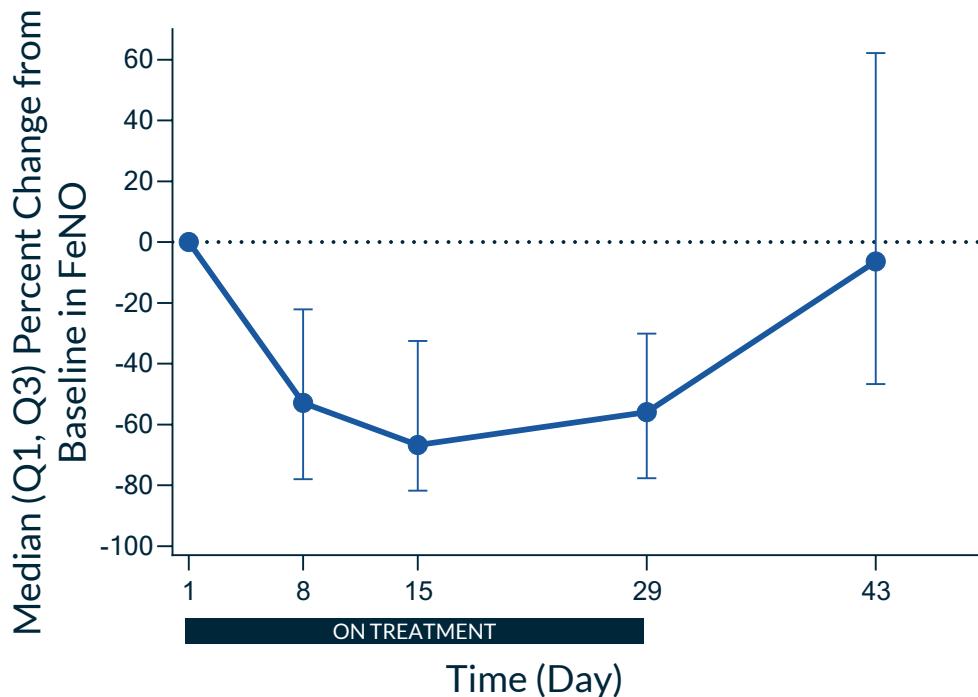


- KT-621 achieved rapid and robust mean SCORAD-Sleeplessness reduction in both dose cohorts
- POEM and DLQI are patient-reported measures evaluating severity, experience, and quality of life; demonstrated improvements are greater than the minimum clinically important difference (MCID)

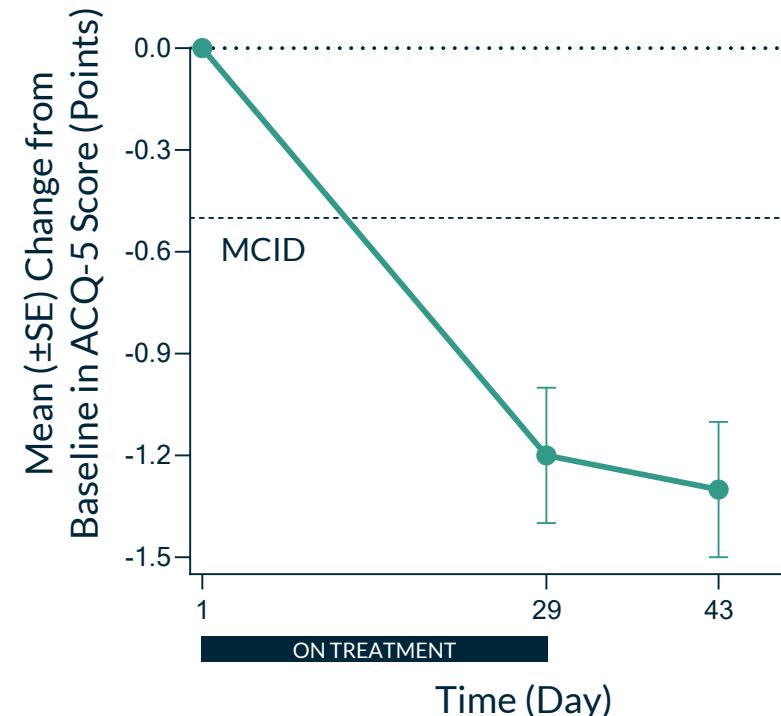
Note: Analysis based on observed cases at each visit. <sup>1</sup>Only patients with non-zero baseline sleeplessness are included; <sup>2</sup>One patient in the 100 mg cohort missed the D29 visit (n=8 for 100 mg and n=19 for Overall at D29); <sup>3</sup>Only patients with baseline DLQI score  $\geq 4$  included; SCORAD: SCORing Atopic Dermatitis. DLQI: Dermatology Life Quality Index; POEM: Patient-Oriented Eczema Measure.

# KT-621 Achieved Robust Impact on FeNO and ACQ-5 in AD Patients with Comorbid Asthma

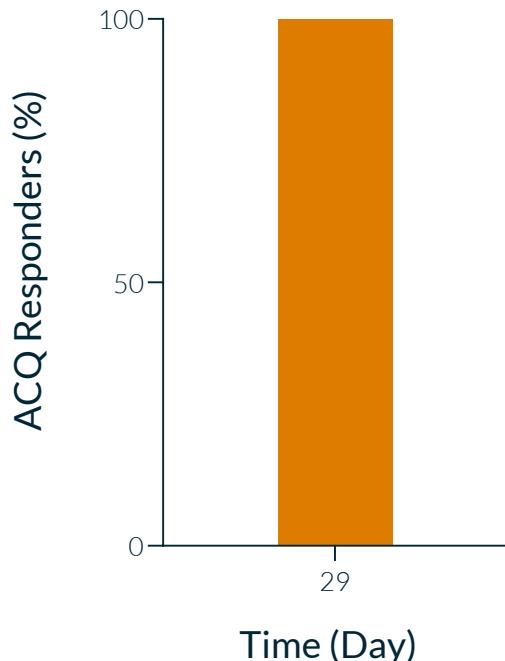
Median % Change from Baseline in FeNO (n=4)



Mean Point Change in ACQ-5 (n=4)



ACQ-5 Responders (Improvement  $\geq 0.5$ , n=4)



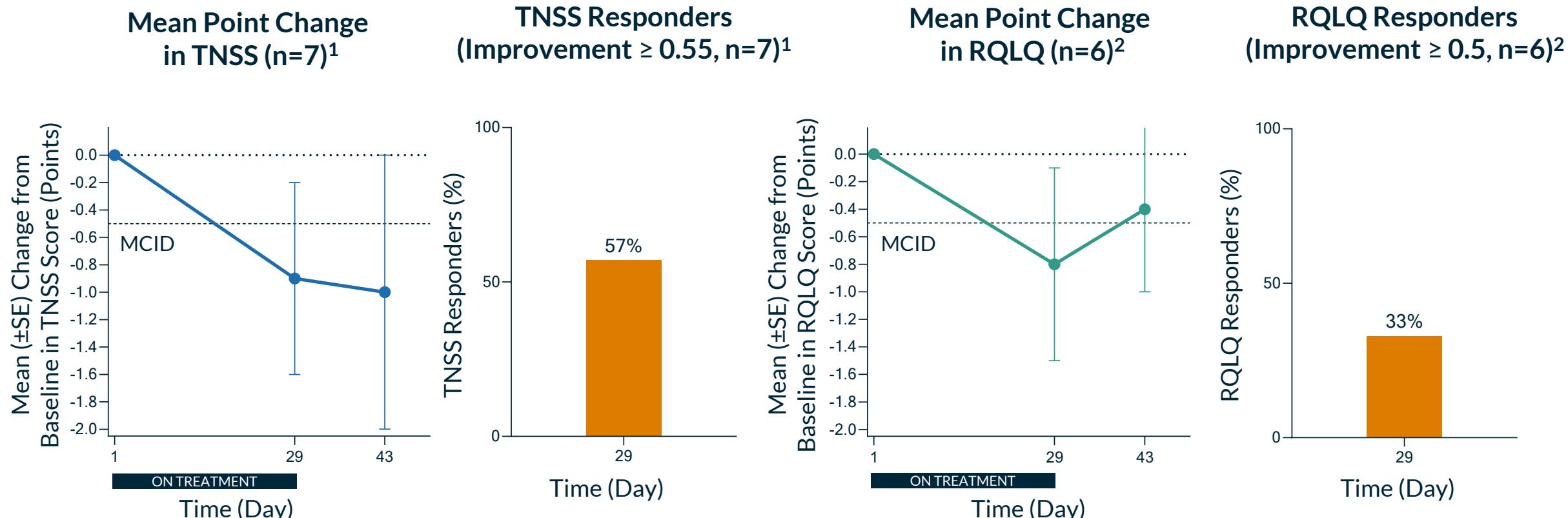
- KT-621 achieved 56% median FeNO reduction at Day 29, exceeding dupilumab (31%) in asthma studies at week 4<sup>1</sup>
- All 4 patients had clinically meaningful reduction in ACQ-5 (mean change of -1.2 points) and a 100% responder rate

Note: Analysis based on observed cases at each visit; Mean baseline FeNO of 49 ppb and ACQ-5 of 2.5; <sup>1</sup>Pavord et al. JACI. 2024; FeNO: Fractional Exhaled Nitric Oxide; ACQ-5: Asthma Control Questionnaire-5; MCID: Minimum Clinically Important Difference.

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KYME RA 31

# KT-621 Achieved Robust Impact on TNSS and RQLQ in AD Patients with Comorbid Allergic Rhinitis



- At Day 29, KT-621 achieved mean changes of -0.9 and -0.8 points in TNSS and RQLQ, respectively
- TNSS and RQLQ responder rates were 57% and 33%, respectively

Note: Analysis based on observed cases at each visit; <sup>1</sup>Only patients with baseline TNSS score  $\geq 0.55$  are included; <sup>2</sup>Only patients with baseline RQLQ score  $\geq 0.5$  are included; Mean baseline TNSS and RQLQ of 4.4 and 2.4, respectively; MCID: Minimum Clinically Important Difference; TNSS: Total Nasal Symptom Score; RQLQ: Rhinoconjunctivitis Quality of Life Questionnaire.

# KT-621 Demonstrated Robust Improvements Across All Key Clinical Efficacy Endpoints

Results in Line With or in Some Cases Numerically Exceeded Published Data for Dupilumab at Week 4

	KT-621 100 mg QD Day 29 (n=10)	KT-621 200 mg QD Day 29 (n=12)	KT-621 Overall Day 29 (n=22)	Dupilumab 300 mg Q2W D28 Ph3 (n=457) <sup>1</sup>
Mean % Change in EASI	-62%	-63%	-63%	-52%
EASI-50	67%	83%	76%	57%
EASI-75	33%	25%	29%	28%
Mean % Change in PPNRS	-47%	-35%	-40%	-33%
Mean % Change in SCORAD	-52%	-46%	-48%	-41% <sup>2</sup>
vIGA-AD 0 and 1	22%	17%	19%	12%
Mean % Change in % Body Surface Area	-55%	-44%	-49%	-36% <sup>2</sup>
Mean % Change in SCORAD - Sleeplessness	-72%	-78%	-76%	NR
Mean % Change in SCORAD - Itch	-40%	-47%	-44%	NR
POEM Responders	70%	75%	73%	69% at Week 16
DLQI Responders	57%	64%	61%	69% at Week 16

<sup>1</sup>Dupilumab Phase 3 data derived or digitized from the pooled data of SOLO1 and SOLO2 studies (Thaci et al, Dermatological Science, 2019; Cather et al, Dermatol Ther, 2022);

<sup>2</sup>Data from 64 patients in dupilumab Phase 2b study (Thaci et al, Lancet, 2016); EASI: Eczema Area and Severity Index; vIGA-AD: Validated Investigator Global Assessment for Atopic Dermatitis; PPNRS: Peak Pruritus Numerical Rating Scale; SCORAD: SCORing Atopic Dermatitis; NR: Not Reported.

# KT-621 BroADen Phase 1b Safety Summary

- Well-tolerated with favorable safety at both 100 mg and 200 mg with a profile similar to what was observed in the Phase 1a healthy volunteer trial
- 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

# Kymera Completes the Clinical Translation of STAT6 Degradation

Study	Data	Potential for "Dupilumab-in-a-pill" Profile
Human Genetics	STAT6 is a key driver of Type 2 inflammation	✓
Preclinical	KT-621 degraded STAT6 and blocked IL-4/13 Type 2-driven inflammation <i>in vitro/in vivo</i> as effectively as dupilumab	✓
Phase 1a Healthy Volunteers	KT-621 safely and deeply degraded STAT6, blocking IL-4/13 biomarkers equally or numerically better than dupilumab	✓
BroADen Phase 1b AD Patients	KT-621 safely and deeply degraded STAT6 and demonstrated meaningful improvements on: <ul style="list-style-type: none"><li>- Type 2 biomarkers in blood and skin</li><li>- FeNO in AD and comorbid asthma patients</li><li>- Clinical endpoints in patients with AD, comorbid asthma and allergic rhinitis</li></ul> Results in line with or in some cases numerically exceeded published data for dupilumab at week 4	✓

KT-621 clinical data continues to support STAT6 degradation as a potentially transformative approach for Type 2-driven inflammatory diseases, with a once-a-day, oral drug



# First-in-Class Oral IRF5 Degrader Program

## Drugging a Genetically Validated Transcription Factor with an Oral Degrader

# KT-579 Overview

## Potential First-in-Class Opportunity with Oral Small Molecule Profile



KT-579 is a first-in-class, potent, selective, **oral IRF5 degrader**

- IRF5 has the potential to be the first broad anti-inflammatory to affect immune dysregulation while sparing normal cell function

- Human and mouse genetics de-risk safety and clinical indications

- IRF5 degradation *in vivo* leads to robust cytokine inhibition and *in vivo* efficacy in models of lupus and RA superior to approved drugs in the space

- KT-579 fully degrades IRF5 across multiple preclinical species with a favorable safety profile

### OPPORTUNITY

- Over 10M potential patient impact<sup>1</sup>

- WW market for SLE, LN, RA, IBD alone was >\$45B in 2023 and **projected to grow to >\$55B by 2029<sup>1</sup>**

- Large potential for **oral degrader with biologics-like activity** to block established pro-inflammatory pathways, IFN response, & key pathogenic cell types



**Potential to expand access to oral systemic advanced therapies in many diseases with no or suboptimal oral options**

### STATUS

- IND-enabling studies completed

### UPCOMING MILESTONES

- Phase 1 HV start: Q1 2026
- Phase 1 HV data: 2H 2026

<sup>1</sup>GlobalData (2023) diagnosed prevalent patient population and forecasted sales for approved systemic advanced therapies in US/EU5/JP

# IRF5: Targeting a Genetically Validated Undrugged Transcription Factor

## Target Biology and Rationale

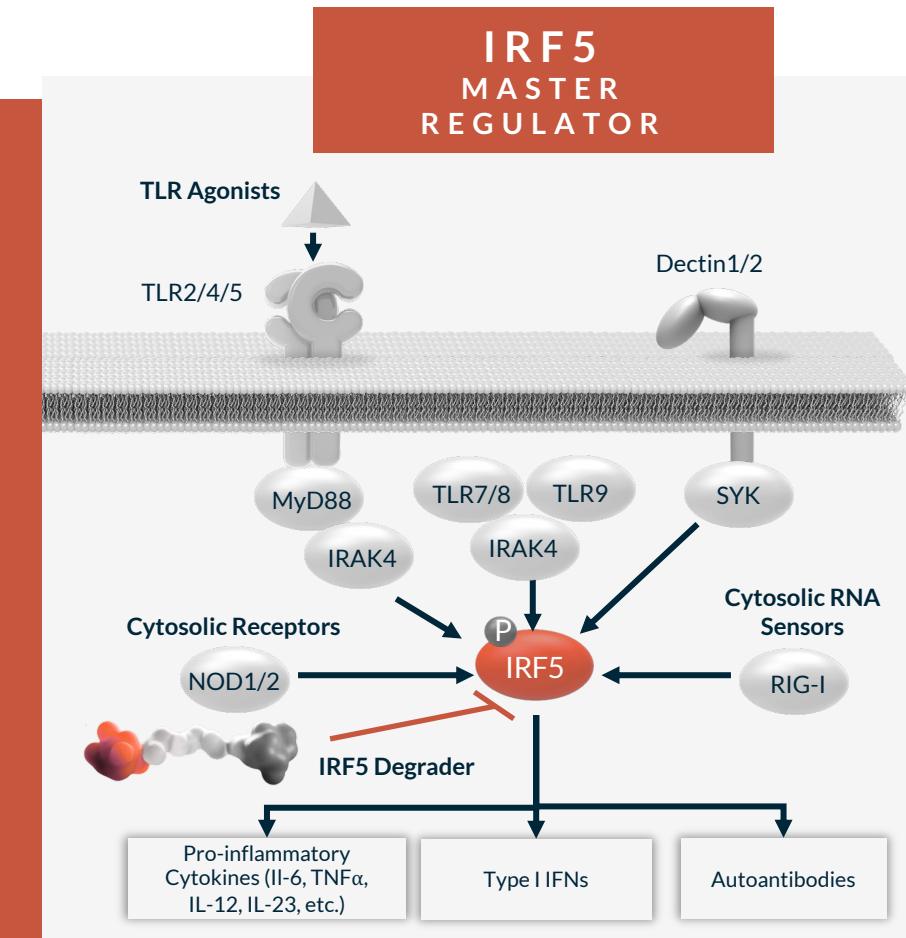
- IRF5 regulates pro-inflammatory cytokines, Type I IFN production and autoantibody production in a cell and activation-specific manner
- Targeting IRF5 has the potential to block cell-specific immune dysregulation while sparing normal cell function

## Genetically and Clinically Validated

- IRF5 functional risk variants associate with increased susceptibility to SLE, Sjögren's, RA, IBD, and SSc<sup>1,2</sup>
- IRF5 regulated pathways have been clinically validated by multiple drugs (i.e., anti-IFN, -TNF, IL-6, IL-12, IL-23 Ab, B cell targeting agents)

## IRF5 Degrader Advantage

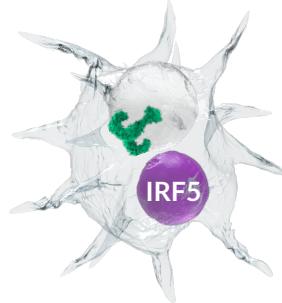
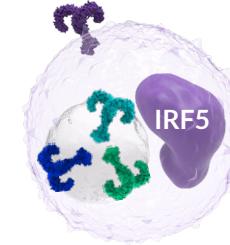
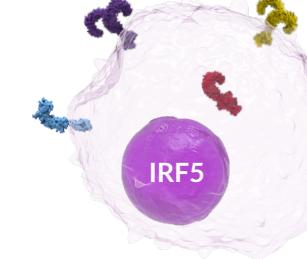
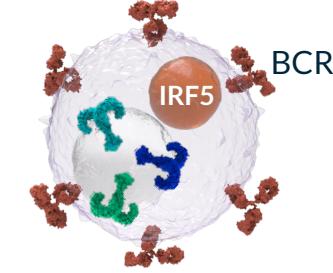
- Conventional approaches have failed to effectively and selectively block IRF5 due to multiple activation steps and IRF family member homology
- TPD allows for a single and specific binding event to drive depletion of the protein and disrupt all IRF5 signaling



**IRF5** is a genetically validated transcription factor and a master regulator of immunity

# Stimuli and Cell Specific IRF5 Activation in Clinically Validated Pathways

IRF5 degradation has the potential to selectively block inflammation and restore immune regulation by inhibiting pro-inflammatory cytokines, Type I IFN and autoantibody production

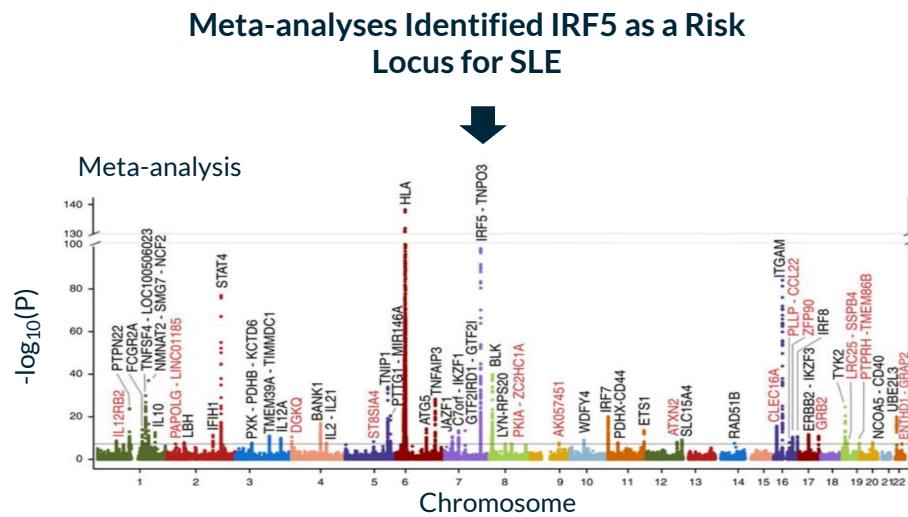
Activation by TLR2, -4, -5, -7, -8, -9, Dectin 1, -2				Activation by TLR7, -8, -9
<b>Cell-Specific IRF5 Activation By Pattern Recognition Receptors</b>				
<b>Dendritic Cells</b>		<b>Monocytes</b>	<b>M1 Macrophages</b>	<b>B cells</b>
<b>Pathogenic Immune Response</b>	Pro-inflammatory Cytokines <b>TNF<math>\alpha</math>, IL-1b, IL-6, IL-12p40, IL-23</b>		Type I IFNs	Autoantibodies
<b>Clinical Pathway Validation</b>				 

Blocking IRF5 activity has the potential for more effective, tolerated and durable responses in autoimmune diseases such as SLE, Sjögren's, RA, and IBD

# IRF5 Genetically Validated in Multiple Autoimmune Diseases

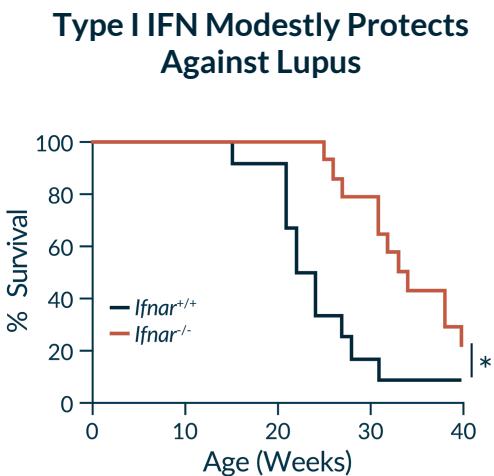
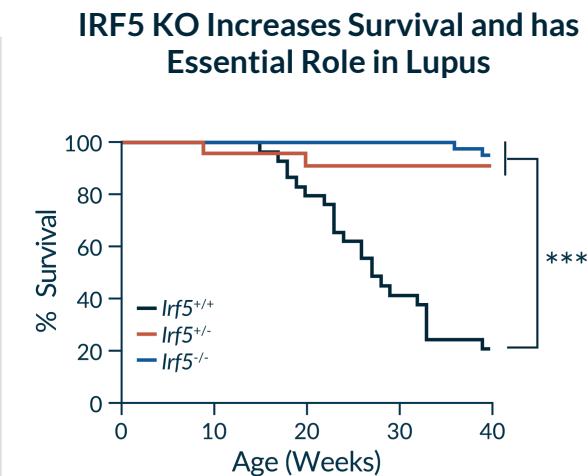
## Human Genetics

- Multiple GWAS studies identify IRF5 as an autoimmune susceptibility gene<sup>1</sup>
- IRF5 risk haplotypes and hyperactivated IRF5 levels in SLE patients associated with high serum IFN $\alpha$  levels, anti-dsDNA or anti-RNA binding protein antibodies
- Genetic associations and functional variants also identified in RA, IBD, SSc, and MS



## Mouse IRF5 KO Studies

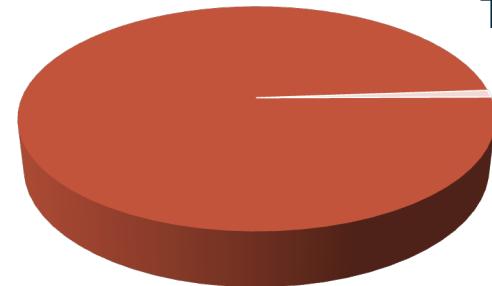
- KO mice are viable and fertile; with normal B cell development
- IRF5 KO mouse can protect or attenuate disease in models of SLE, SSc, RA and IBD
- In a mouse model of lupus (FcγIIB<sup>-/-</sup>, Yaa) IRF5 plays an essential role in lupus pathogenesis, that is independent of Type I IFN pathways<sup>2</sup>



<sup>1</sup>Santana-de Anda et al. Autoimmunity Reviews. 2011; <sup>2</sup>Richez et al. J Immunol. 2010; \*\*\*p < 0.0001, \*\*p = 0.0043.

# IRF5: A Novel Mechanism in High Unmet Need Indications in I&I

>10M



>\$45B Market

TOTAL POTENTIAL  
PATIENT IMPACT<sup>1</sup>

IRF5 functional risk variants associate with increased susceptibility to multiple diseases, and IRF5 regulated pathways have been clinically validated by multiple drugs



## RHEUMATOLOGY

	PATIENTS <sup>1</sup>
RA	4.7M
Lupus <sup>2</sup>	1.2M
Sjögren's	765K
SSc	200K
DM	>100K



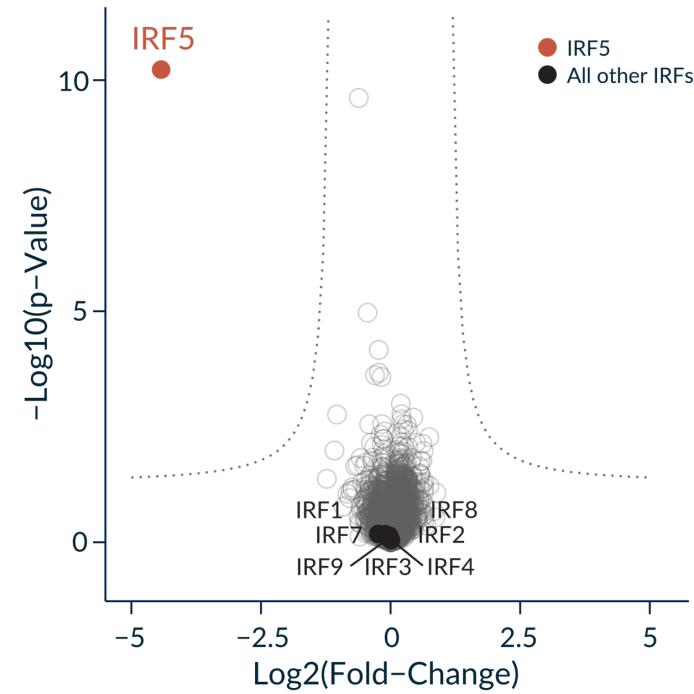
## GASTROENTEROLOGY

UC	1.9M
CD	1.5M

<sup>1</sup>GlobalData (2023 diagnosed prevalent patient population US/EU5/JP); <sup>2</sup>Lupus includes SLE, CLE, LN.

# KT-579: An Exquisitely Selective and Picomolar Oral IRF5 Degrader

KT-579: 10xDC<sub>90</sub> in hPBMCs @ 24 hrs



## Selectivity Binding and Cellular Assays

IRF3, 4, 6, 7, 8 SPR binding, Kd (nM)

KT-579

>10,000

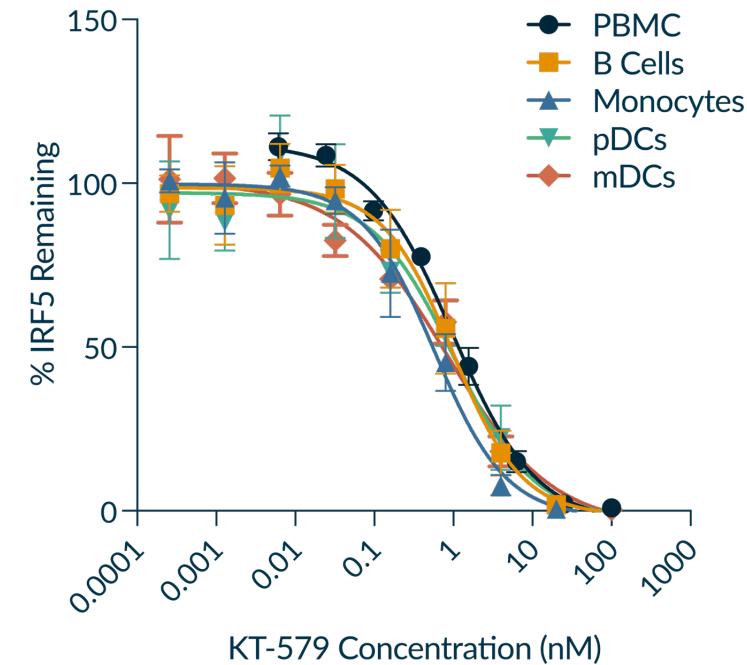
IRF3 Degradation DC<sub>50</sub> (nM)

>10,000

IRF7 Degradation DC<sub>50</sub> (nM)

>10,000

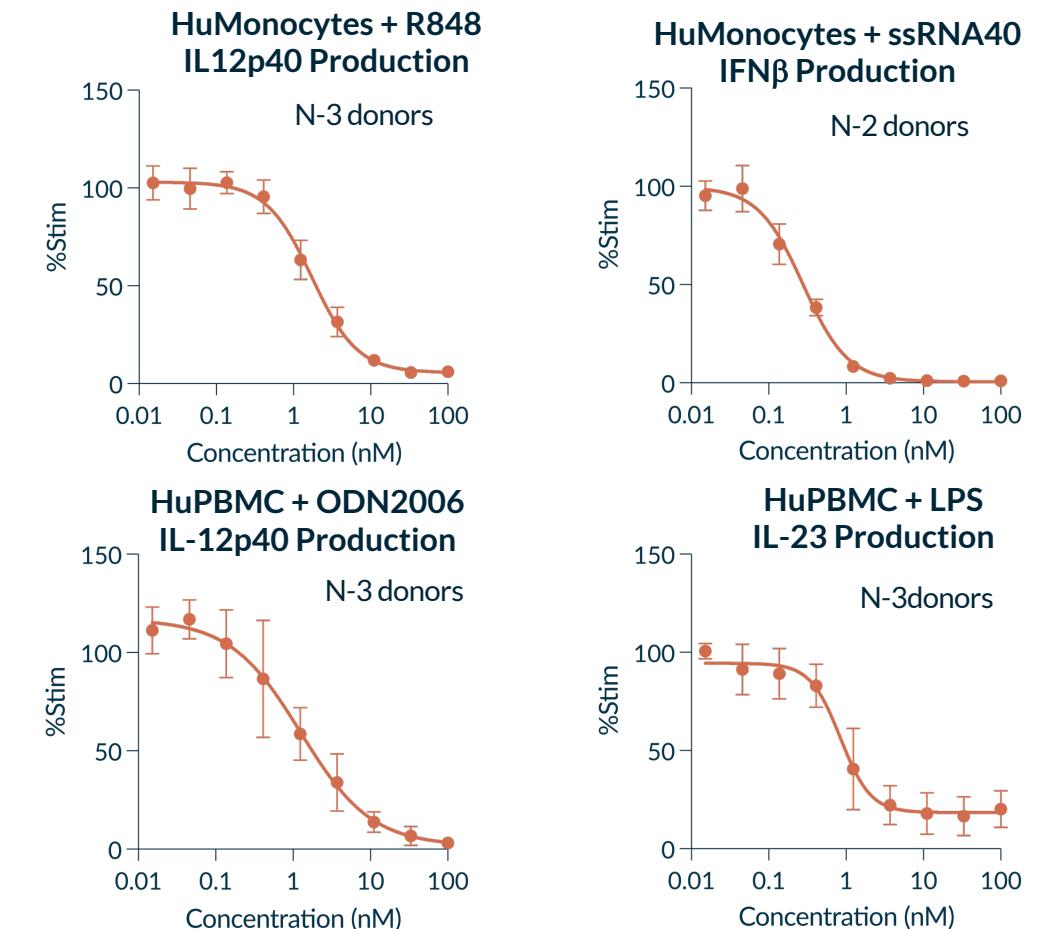
Equipotent Degradation in Relevant hPBMC Subsets @ 24hrs



Cell Subsets	KT-579 DC <sub>50</sub> (nM)
PBMC	0.8
CD19+ B cells	1.0
CD14+ Monocytes	0.6
HLA-DR+CD123+ pDCs	0.9
HLA-DR+CD11c mDCs	0.9

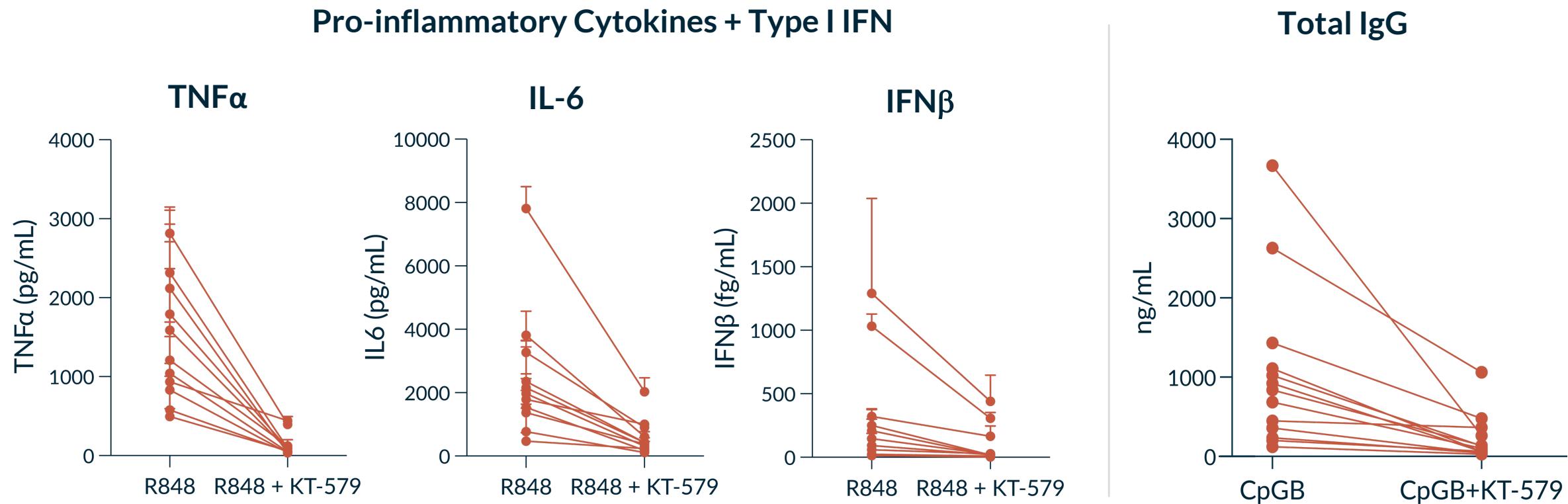
# KT-579 Potently Inhibits Production of Key Pro-Inflammatory Cytokines and Type I IFN in Human Primary Cellular Assays

Biology	Receptor	Stim	Cell	Cytokine Readout	KT-579 DC <sub>50</sub> (nM)
<b>Type I IFN Production</b>					
	TLR8	ssRNA40	Monocytes	IFN $\beta$	0.3
	TRL7/8	R848	Monocytes	IFN $\beta$	0.4
	TLR9	ODN2006	PBMC	IFN $\beta$	0.8
<b>Pro-inflammatory Cytokine Production</b>					
	TLR7/8	R848	B cells	TNF $\alpha$	0.4
	TLR8	ssRNA40	Monocytes	TNF $\alpha$	1.3
	TL7/8	R848	Monocytes	IL-12p40	0.5
	TLR9	ODN2006	PBMC	IL-12p40	1.8
	TLR7/8	R848	Monocytes	IL-1 $\beta$	0.15
	TLR4	LPS	PBMC	IL-23	1.1



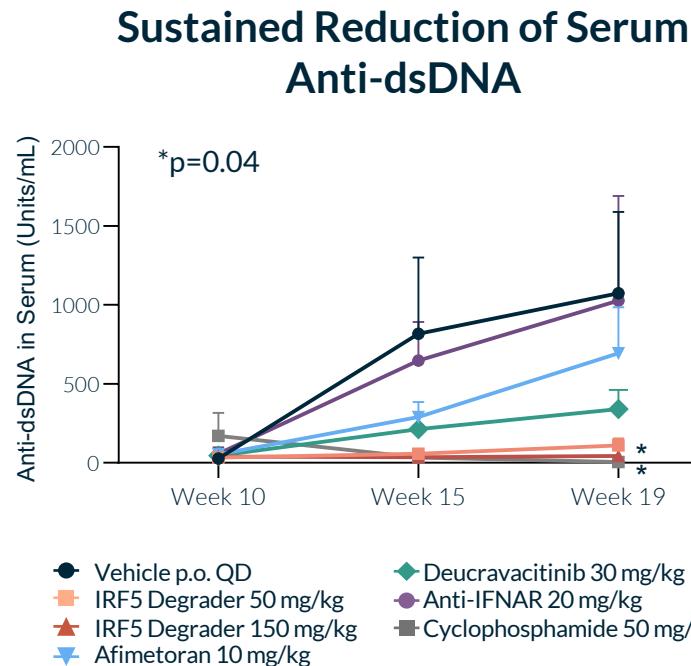
IRF5 degradation inhibits proinflammatory cytokines (TNF $\alpha$ , IL-12, IL-23, IL-1) and Type I IFN (IFN $\beta$ ) downstream of TLR4, TLR7, TLR8, and TLR9 activation

# KT-579 Effectively Blocks TLR Induced Pro-inflammatory Cytokines and Type I IFN Induction and Reduces Total IgG levels in SLE PBMC Samples



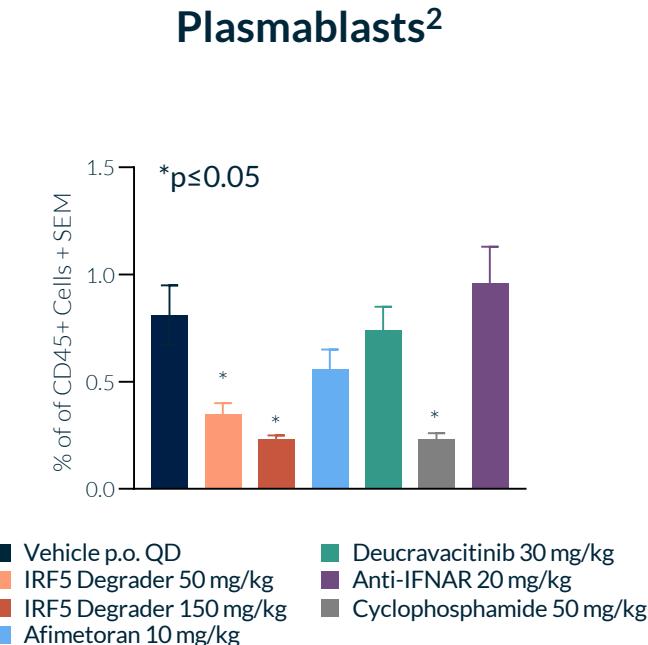
- KT-579 inhibits TLR7/8 pro-inflammatory cytokines and Type I IFN that are commonly elevated in autoimmune diseases
- KT-579 reduces TLR9 (CpG-B) induced plasmablast differentiation and inhibits IgG production in SLE derived B cells

# KT-579 Superior Activity in the MRL/Ipr<sup>1</sup> Model of Lupus



## All KT-579 Treated Mice Survived Length of Study

Treatment	#Total survival
Vehicle	10/15
KT-579 50 mg/kg, p.o.	15/15
KT-579 200 mg/kg, p.o.	15/15
Afimetorin, 10 mg/kg, p.o.	13/15
Deucravacitinib, 30 mg/kg, p.o.	13/15
Cyclophosphamide, 50 mg/kg, i.p.	14/15
Anti-IFNAR mAb, 20 mg/kg, s.c.	9/15

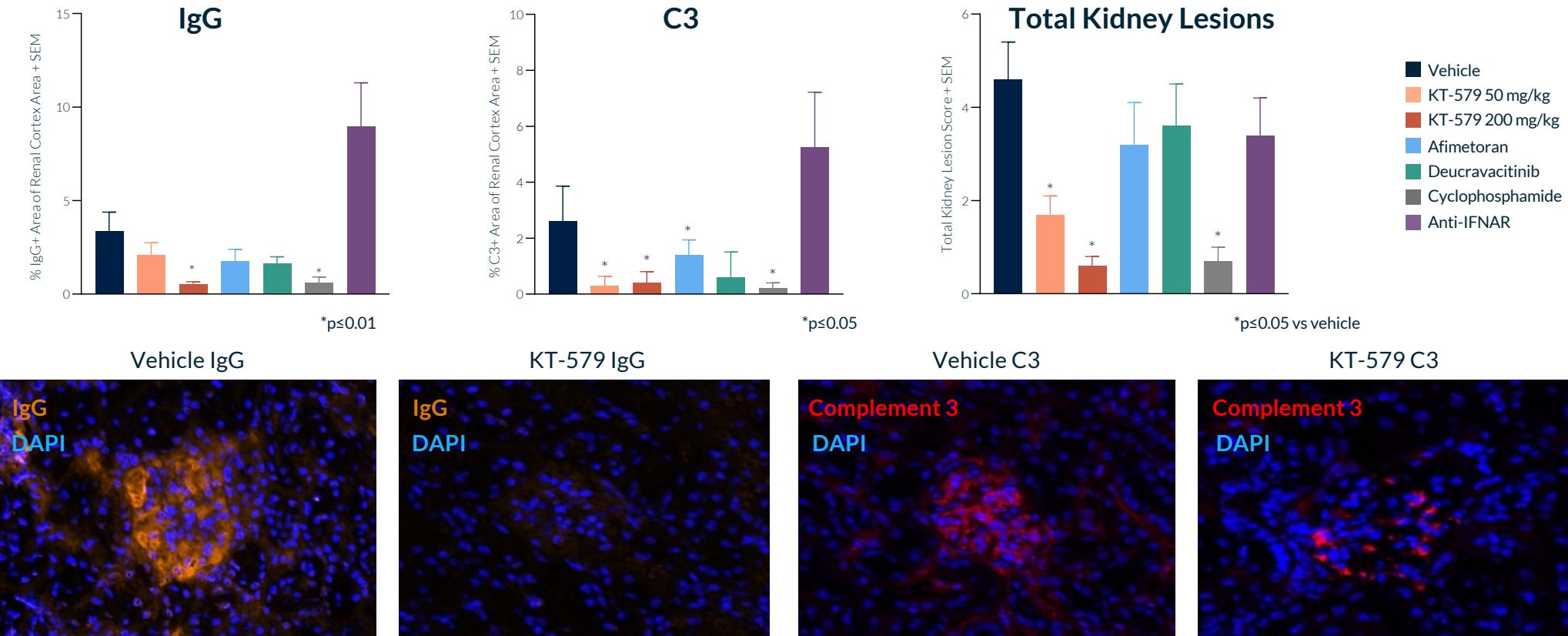


- KT-579 administered once daily for 63 days was well tolerated and prevented mortality more effectively than all other approved or clinically active comparator agents tested
- KT-579 led to sustained reduction of serum anti-dsDNA levels and reduction in splenic plasmablasts, differentiated B cells, and plasma cells, achieving effects comparable to, or better than, standard of care

<sup>1</sup>MRL/Ipr mice have a susceptible genetic background and single inactivating mutation in FAS gene, quickly developing lupus-like symptoms and manifestations; <sup>2</sup>Plasmablast phenotype: B220low-CD138hi-CD44+

# KT-579 Significantly Decreases IgG, Complement 3 (C3) and Renal Disease Progression

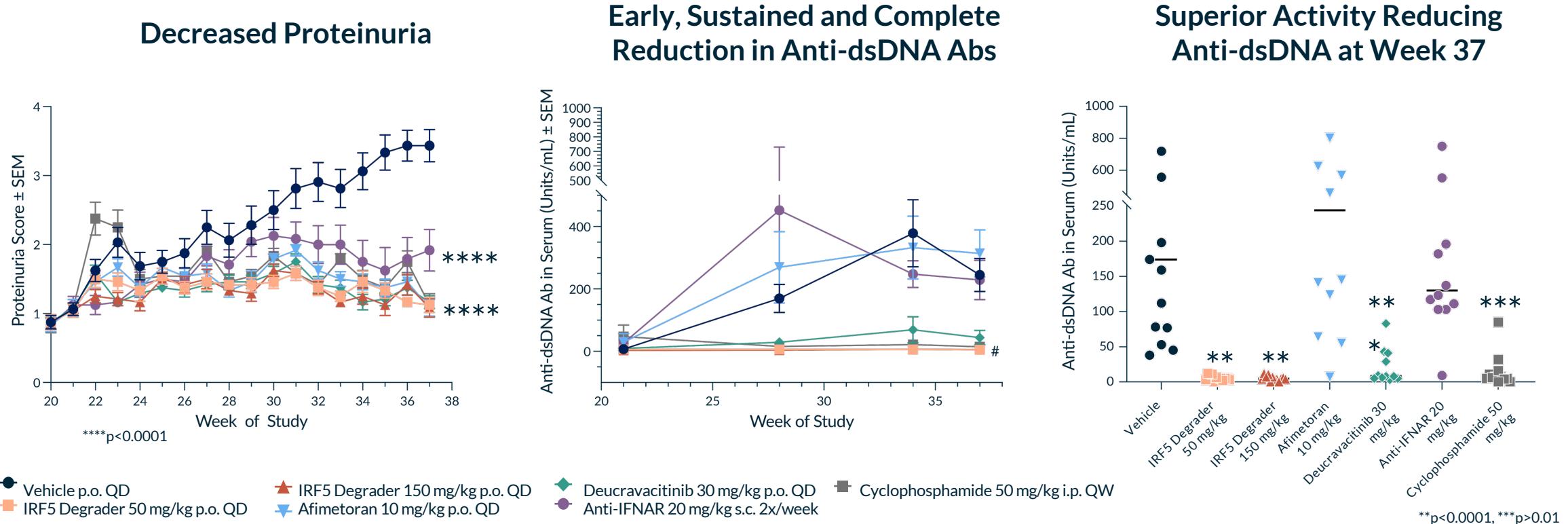
## Assessment of Terminal Kidney Collected from Surviving MRL/lpr Mice at Week 19



Representative images (10x) of IgG and C3 staining in vehicle vs KT-579 treated MRL/lpr kidney glomerular structures

Clear reduction in IgG/complement glomeruli staining indicating reduced kidney disease involvement in SLE MRL/lpr mouse model with IRF5 degrader as compared to standard of care

# IRF5 Degradation Demonstrated Generally Better Outcomes than Approved or Clinically Active Drugs in NZBW1 Spontaneous<sup>1</sup> Mouse Lupus Model

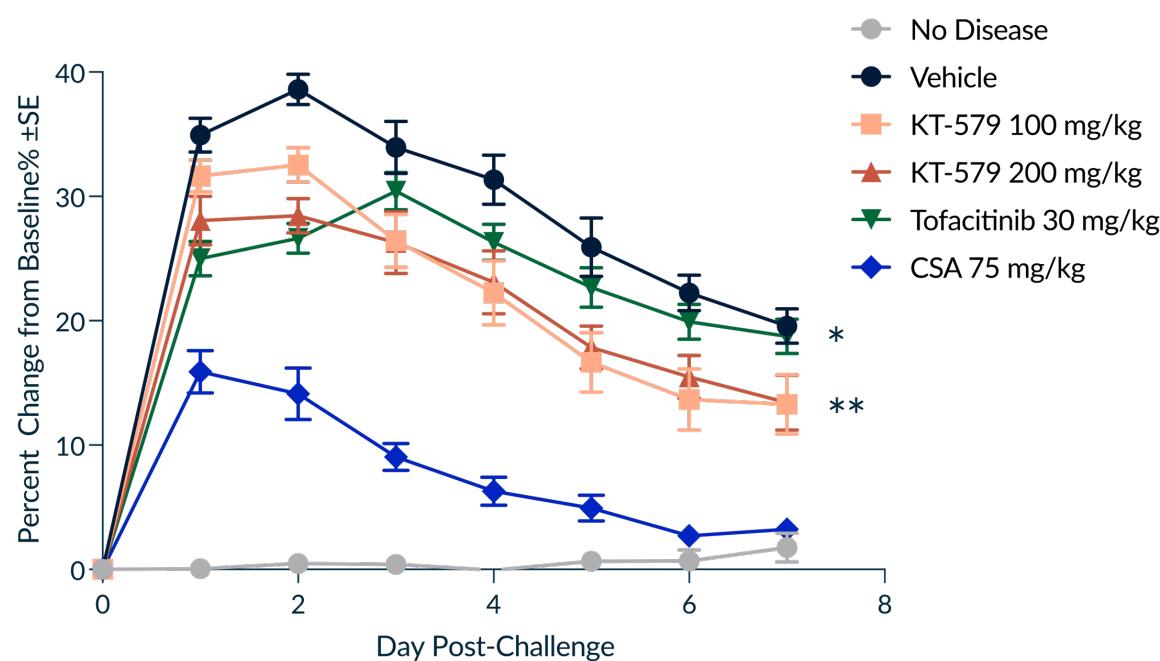


- IRF5 degrader, dosed once a day for 107 days, leading to 80% and >90% IRF5 degradation, led to decreased proteinuria and near complete reduction of serum anti-dsDNA Abs superior to standard of care, approved and clinically active agents tested
- Significantly reduces key interferon genes (OAS1, IFIT1, IF44) at 150mg/kg in the blood from NZB.W1 mice comparable to other test agents

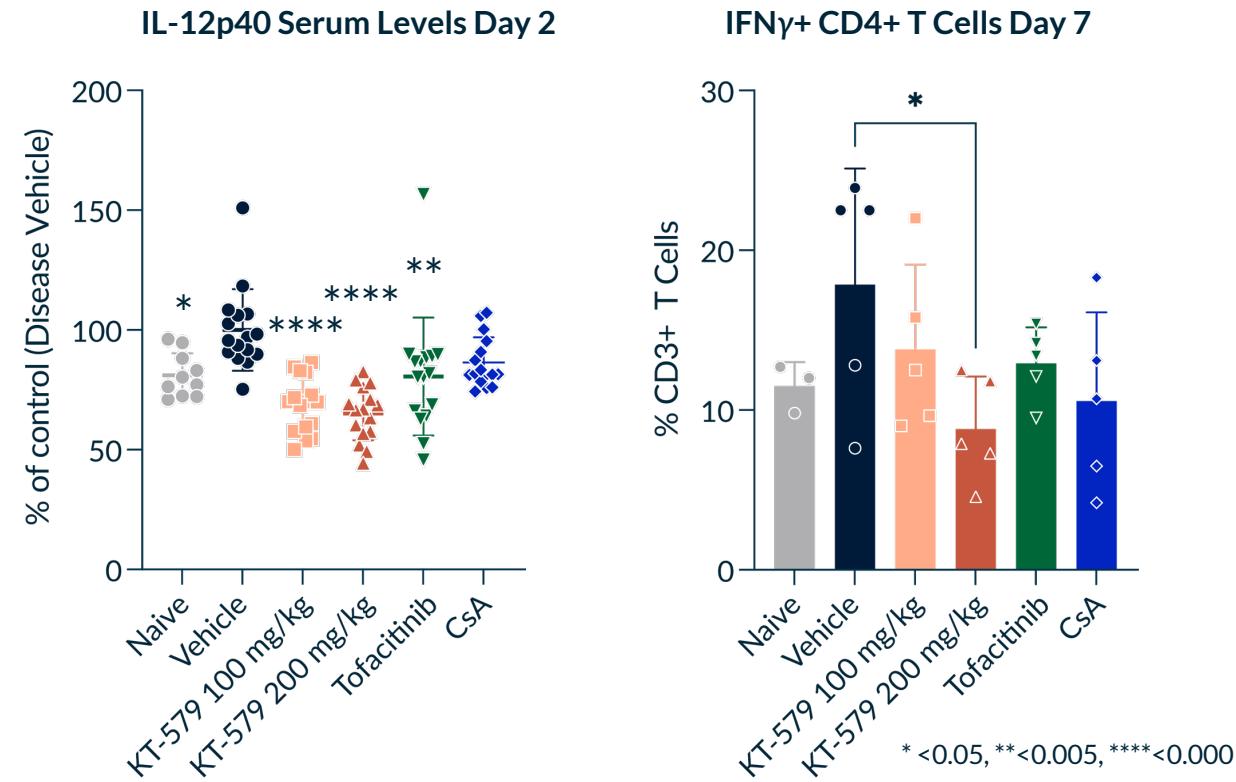
<sup>1</sup>NZBW1 mice develop a similar disease to human SLE, characterized by anti-dsDNA ANA production, and immune complex mediated nephritis due to defects in multiple genes; #IRF5 Degrader 50 mg/kg p.o. and 150 mg/kg p.o. lines are overlapping.

# KT-579 Reduces Joint Swelling in a Mouse Model of RA

Treatment with KT-579 Leads to Significant Reduction in Joint Swelling Comparable to Tofacitinib in the AIA<sup>1</sup> Mouse Model of RA



Reduction in Circulating IL-12 Levels and Infiltrating Synovial IFNγ+ Th1 Cells



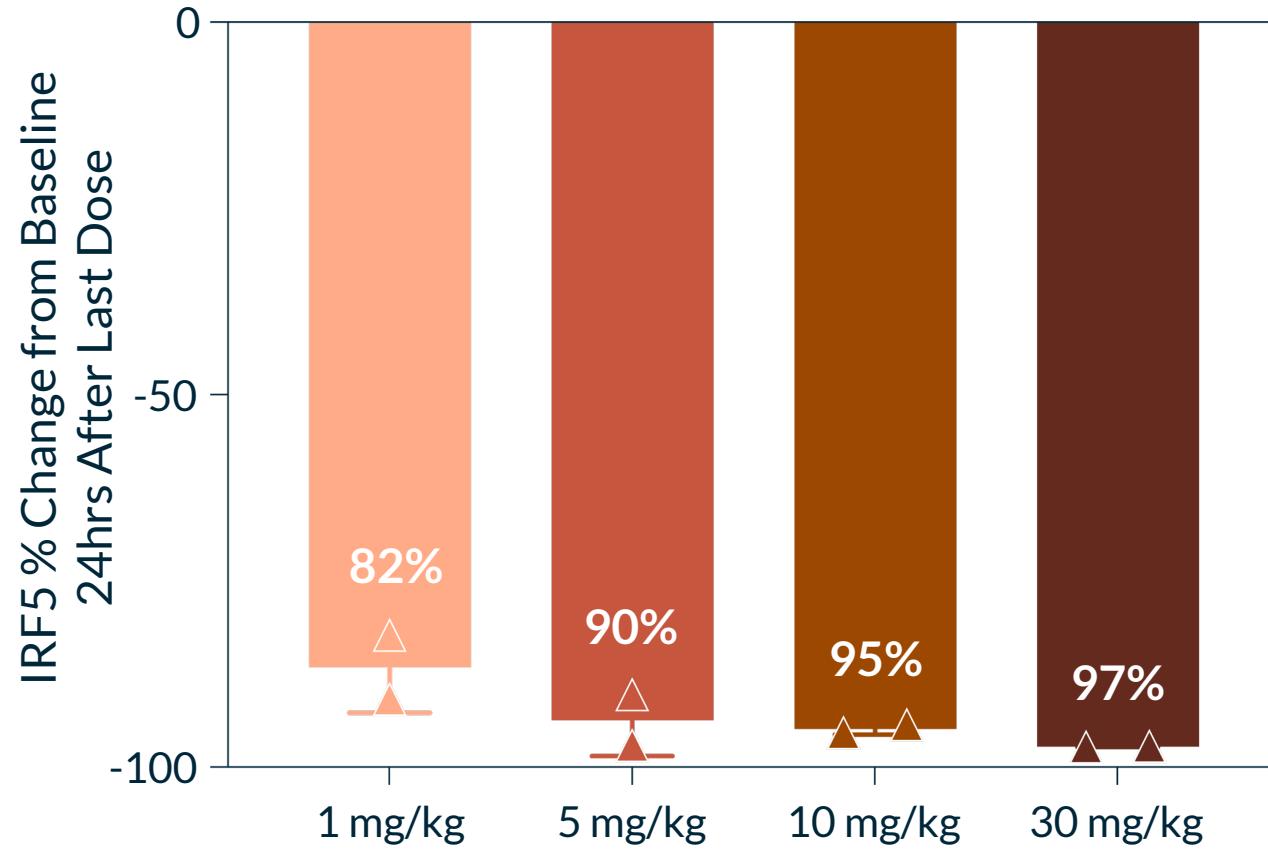
Daily oral dosing of KT-579, leading to ~90% IFR5 degradation, results in significant reduction of circulating pro-inflammatory cytokines, joint swelling and pathogenic infiltrating T cells

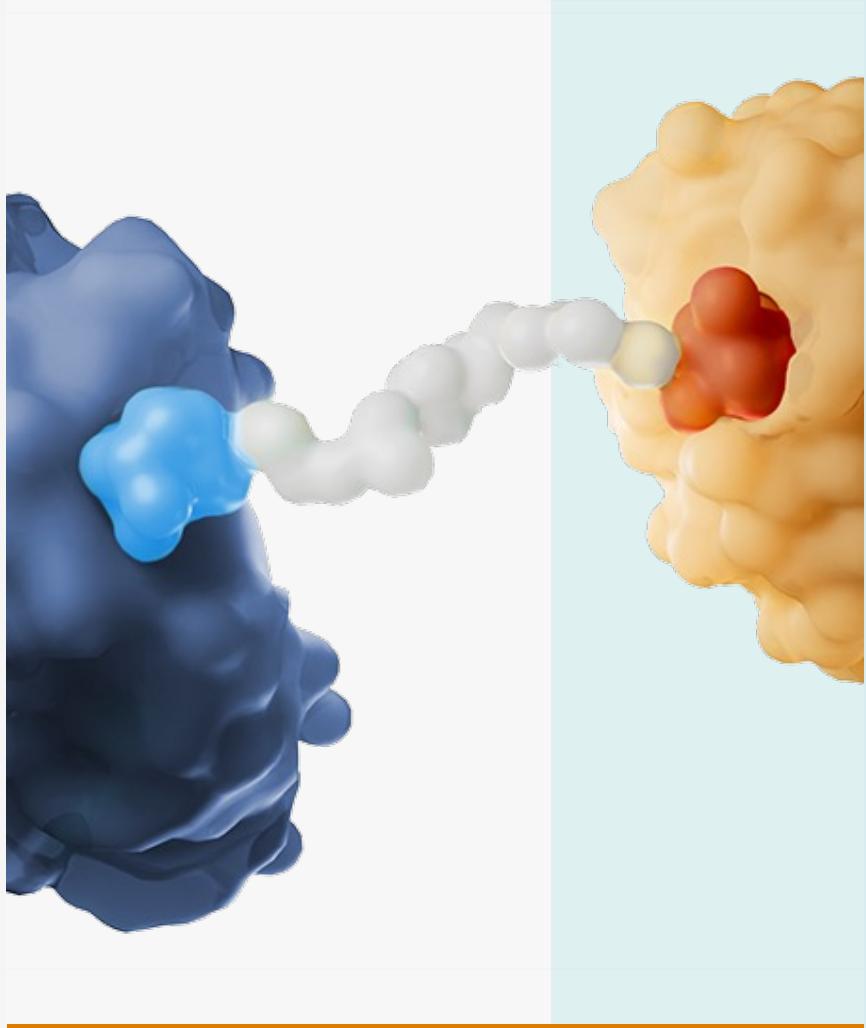
<sup>1</sup>Antigen induced arthritis (AIA) model was established by sensitization with methylated bovine serum albumin (mBSA). 14 days later mice were challenged with mBSA (Day 0) that induced rapid inflammation and swelling at site of injection. Samples for analysis collected on Day 2 and Day 7.

# KT-579 Potently Degrades at Low Oral Doses in NHP with an Excellent Safety Profile

- KT-579 potently degrades IRF5 across multiple preclinical species with low oral doses
- KT-579 completed non-GLP toxicity studies in NHP and rodents with no adverse effects at up to 200-fold predicted human efficacious exposure

IRF5 Degradation in NHP Blood Post 7 Days of KT-579 QD Oral Dosing





# Partnered Oral Degrader Programs

# IRAK4 Overview

## Combined Activity of Upstream Biologics (anti-IL-1/18/33/36) in a Pill



KT-485, a second generation IRAK4 degrader, is a highly selective, potent, oral IRAK4 degrader

- KT-485 has increased selectivity and potency over KT-474 including absence of any QTc signal and has been prioritized for clinical development by Sanofi

- Learnings from the clinical studies of KT-474 will be applied to accelerate development of KT-485

- Phase 1 studies of KT-485 are expected to initiate in 2026

### OPPORTUNITY

- Over 140M potential patient impact<sup>1</sup>
- >\$55B in combined global drug sales<sup>2</sup> opportunity
- Large potential for **oral degraders with best-in-pathway efficacy** across Th1-Th17 and Th2 Diseases



Potential to deliver the combined activity of upstream biologics in an oral drug for multiple diseases

### STATUS

- Partnered with Sanofi
- KT-485 completed IND-enabling studies

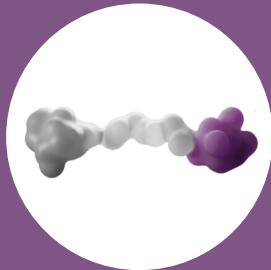
### UPCOMING MILESTONES

- Phase 1 start: 2026

<sup>1</sup>GlobalData (2023 diagnosed prevalent patient population for US/EU5/JP); <sup>2</sup>GlobalData (2023 sales for AD, HS, Asthma, COPD, UC, CD, RA, SLE).

# CDK2 Overview

## Novel Molecular Glue (MG) Degrader



**Potential best-in-class profile**, with exquisite selectivity for CDK2

- CDK2 is a master regulator of the cell cycle with strong genetic and clinical validation and broad oncology treatment potential including breast cancer and other solid tumors
- Unlike inhibitors, CDK2 molecular glue degraders selectively degrade CDK2 while sparing closely related kinases like CDK1, offering a potentially broader therapeutic index

### OPPORTUNITY

- ~500k potential patient impact in multiple tumor types<sup>1</sup>

- CDK4/6 inhibitor class ~\$13B in WW revenue in 2024; projected to grow to \$18B by 2030<sup>2</sup>



**CDK2 MGs offer an oral therapeutic option with the potential to selectively target cancer cells with minimal impact on healthy tissue**

### STATUS

- Partnered with Gilead to accelerate development and commercialization, with up to \$750 million in total payments, including \$85 million in upfront and potential option exercise payments
- Kymera will lead all research activities for the CDK2 MG program

<sup>1</sup>GlobalData (2025 diagnosed incident patient population for US/EU5/JP); <sup>2</sup>CDK4/6 inhibitor class includes palbociclib, abemaciclib, and ribociclib; Future revenue projection reflects GlobalData's consensus forecast.

# 2026: Catalysts for Growth



Unlocking high value targets to revolutionize immunology with oral degrader medicines

## KT-621 First-in-Class Oral STAT6 Degrader

- Complete enrollment in BROADEN2 Phase 2b AD study in 2026; report data by mid-2027
- Advance BREADTH Phase 2b asthma study; report data in late-2027

## KT-579 First-in-Class Oral IRF5 Degrader

- Initiate Phase 1 HV trial in Q1 2026
- Report Phase 1 HV data in 2H 2026

## Research

- Advance at least one new development candidate towards IND for a first-in-class, oral immunology program in 2026

## Partnered Programs

- Collaborate with Sanofi to advance KT-485, oral IRAK4 degrader, into a Phase 1 clinical trial in 2026
- Collaborate with Gilead to advance oral CDK2 molecular glue degrader program in preclinical studies

# Thank You

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NASDAQ: KYMR

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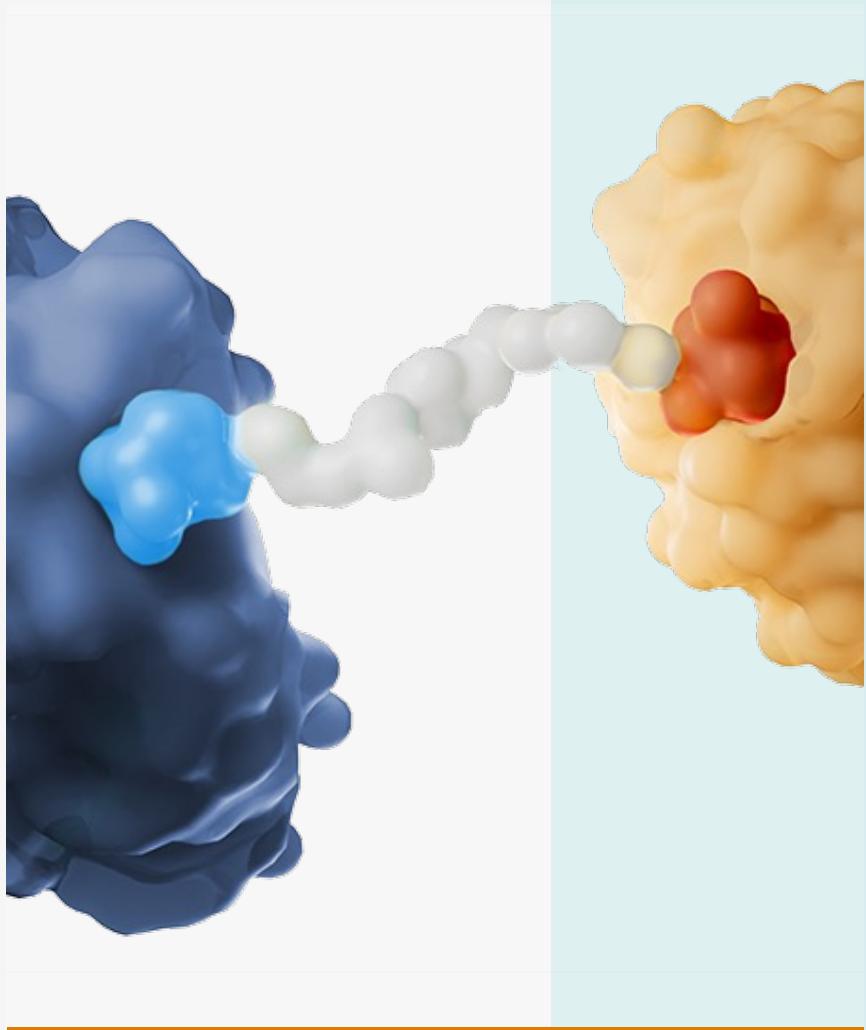
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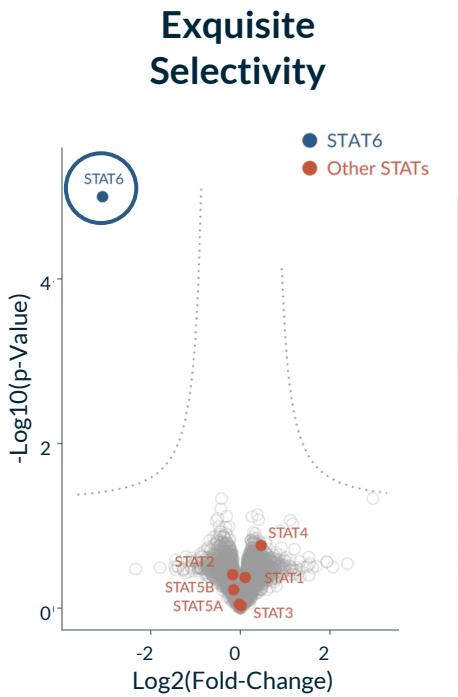




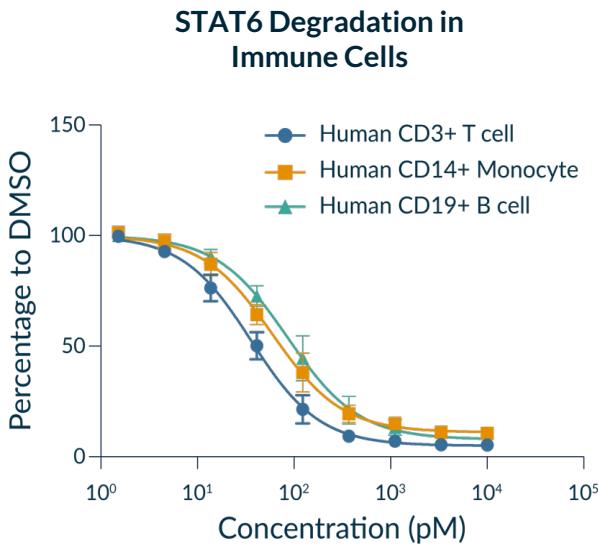
## Appendix: First-in-Class Oral STAT6 Degrader Program

# KT-621: Compelling Preclinical Profile

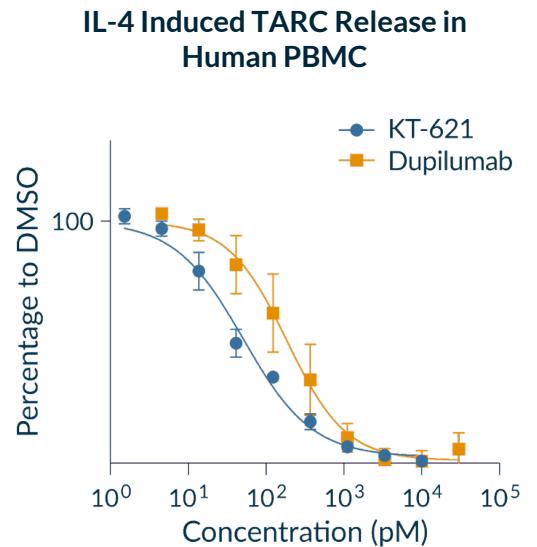
Preclinical Package Suggests Potential for Dupilumab-like Activity in a Pill



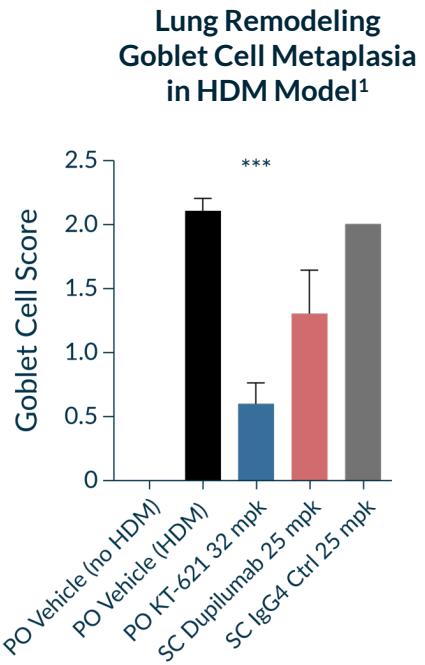
**Robust Degradation in Relevant Cell Types**



**Full Inhibition of IL-4/IL-13 Pathways, More Potent than Dupilumab**



**Excellent Preclinical Activity Comparable or Superior to Dupilumab**



**Favorable safety profile: well-tolerated in multiple preclinical species and safety studies at concentrations 40-fold above efficacious dose with up to 4 months of dosing**

<sup>1</sup>A lung inflammation model induced by intranasal house dust mite (HDM) administration with dominant Type 2 inflammation in the IL4/IL4RA humanized mice, Le Floc'h et al, Allergy, 2020; \*Significance to PO vehicle (HDM); #Significance to SC IgG4 Ctrl 25 mpk; \*\*\*p ≤ 0.001. For more information on KT-621's preclinical profile, visit [Kymera's website](#).

# KT-621 Phase 1a Healthy Volunteer Trial: Safety Summary

Well Tolerated Across All Doses Evaluated and Safety Profile Undifferentiated from Placebo

- No Serious Adverse Events
- No Severe Adverse Events
- No dose dependent pattern in Treatment Emergent Adverse Events (TEAEs)
- No Treatment Related AE (TRAE) reported in >1 participant
- No related TEAEs leading to discontinuation
- No clinically relevant changes in vital signs, laboratory tests, and ECGs

TRAEs by Preferred Term: SAD Cohorts			
AE Term (severity)	SAD Placebo (n=12)	SAD KT-621 (n=36)	
Headache (mild)	1 (8.3%)	0	
TRAEs by Preferred Term: MAD Cohorts			
AE Term (severity)	MAD Placebo (n=18)	MAD KT-621 (n=52)	
Nausea (mild)	1 (5.6%)	0	
Asthenia (mild)	0	1 (1.9%)	

# KT-621 BroADen Phase 1b Demographics

Generally Well-Balanced Across Treatment Cohorts

	100 mg (n=10)	200 mg (n=12)	Overall (n=22)
<b>Gender, n (%)</b>			
Female	6 (60)	7 (58.3)	13 (59.1)
Male	4 (40)	5 (41.7)	9 (40.9)
<b>Age, years, mean (SD)</b>	30.1 (8.5)	33.0 (11.4)	31.7 (10.1)
<b>BMI, kg/m<sup>2</sup>, mean (SD)</b>	32.8 (11.5)	30.8 (9.2)	31.7 (10.1)
<b>Ethnicity, n (%)</b>			
Hispanic or Latino	3 (30)	2 (16.7)	5 (22.7)
Non Hispanic or Latino	7 (70)	10 (83.3)	17 (77.3)
<b>Race, n (%)</b>			
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)

For more information on KT-621's BroADen Phase 1b atopic dermatitis trial, visit [clinicaltrials.gov \(NCT06945458\)](https://clinicaltrials.gov/ct2/show/NCT06945458); BMI: Body Mass Index; SD: Standard Deviation.

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KYME RA 58

# KT-621 BroADen Phase 1b Baseline Disease Characteristics

Generally Well-Balanced Across Treatment Cohorts

	100 mg (n=10)	200 mg (n=12)	Overall (n=22)
<b>vIGA-AD, n (%)</b>			
Moderate (3)	6 (60)	6 (50)	12 (54.5)
Severe (4)	4 (40)	6 (50)	10 (45.5)
<b>EASI Score, mean (SD)</b>	23.5 (7.5)	26.1 (9)	24.9 (8.3)
<b>Other Disease Characteristics, Mean (SD)</b>			
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)
<b>Comorbid Type 2 Diseases, n (%)</b>			
Asthma	1 (10)	3 (25) <sup>3</sup>	4 (18.2)
Allergic Rhinitis	2 (20)	7 (58.3)	9 (40.9)
<b>Prior Systemic Therapy for AD, n (%)</b>	1 (10) <sup>1</sup>	4 (33.3) <sup>2</sup>	5 (22.7)

<sup>1</sup>Patient had prior dupilumab treatment; <sup>2</sup>Two patients had prior dupilumab treatment, one had prior tralokinumab treatment, and one had received both agents; <sup>3</sup>The three patients also have comorbid Allergic Rhinitis; For more information on KT-621's BroADen Phase 1b atopic dermatitis trial, visit clinicaltrials.gov (NCT06945458); EASI: Eczema Area and Severity Index; vIGA-AD: Validated Investigator Global Assessment for Atopic Dermatitis; PPNRS: Peak Pruritus Numerical Rating Scale; BSA: Body Surface Area; SCORAD: SCORing Atopic Dermatitis; SD: Standard Deviation.

# Example of Clinical and Biomarker Response to KT-621 in BroADen Patient with Severe AD and Prior Dupilumab Treatment

Pre and Day 29 Photos for EASI-75 Responder

Baseline

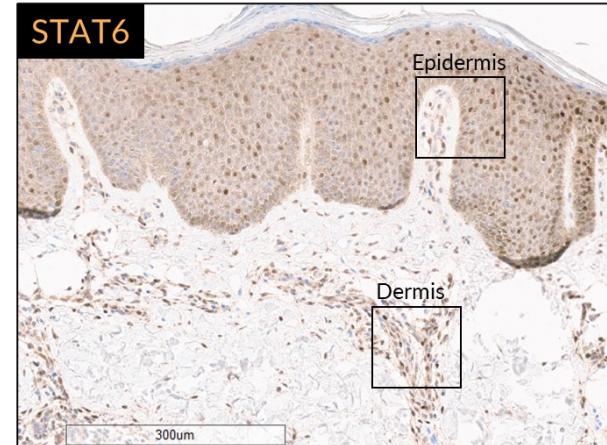


Day 29

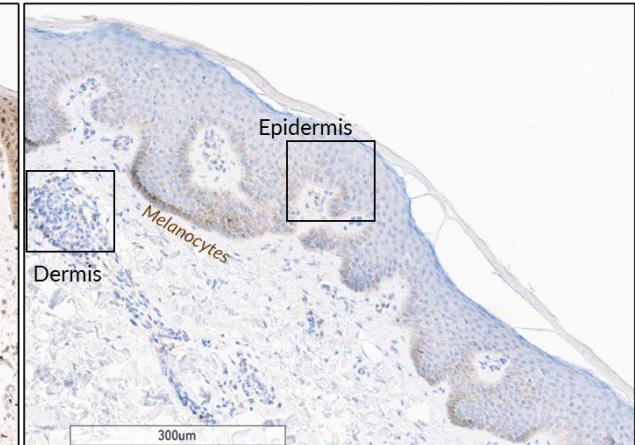


STAT6 Staining IHC

Baseline

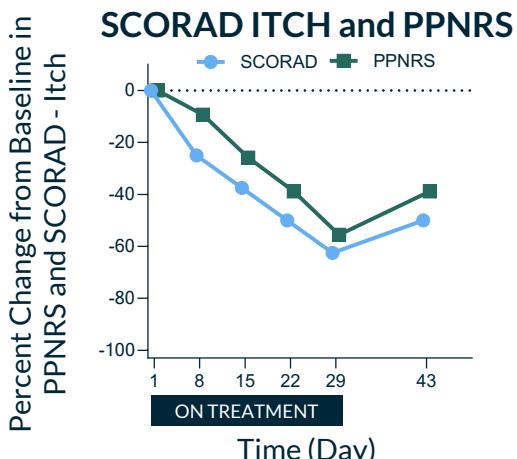
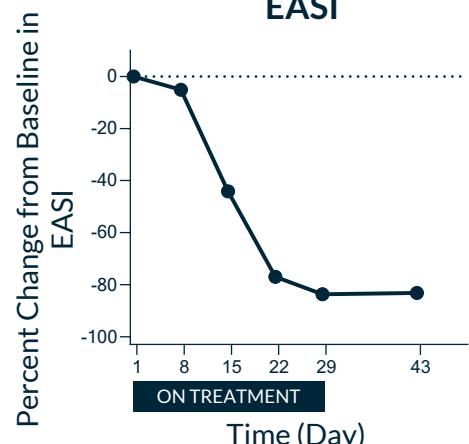


Day 29



% Change in EASI and Itch<sup>1</sup>

EASI



Biomarker Changes at D29

	Blood STAT6	Skin STAT6	Serum TARC	Serum Eotaxin-3	Serum IgE	Skin Eotaxin-3	Skin KRT16
Change from Baseline	-95%	-94%	-78%	-96%	-19%	-92%	-93%

<sup>1</sup>Baseline EASI = 37.4, Baseline Pruritus NRS = 7.7; For more information on KT-621's BroADen Phase 1b atopic dermatitis trial, visit clinicaltrials.gov (NCT06945458); EASI: Eczema Area and Severity Index; SCORAD: SCORing Atopic Dermatitis; PPNRS: Peak Pruritus Numerical Rating Scale; IHC: Immunohistochemistry.

# Atopic Dermatitis: Intensely Pruritic, Chronic and Underserved Disease

## Opportunity Exists to Transform the Treatment Paradigm

- Chronic inflammatory disease that causes **inflamed and irritated skin**, making it itchy and painful
- Majority of patients have **disease onset as children** and carry the disease burden into **adulthood**
- Can significantly impact a **patient's quality of life**, disrupting daily activities
- Common comorbidities include **asthma** and **allergic rhinitis**
- Many options only address symptoms, **not underlying Type 2 inflammation**
- Estimated **43 million** adults in US/EU5/JP<sup>1</sup>
- **Less than 1 million** patients currently on dupilumab<sup>2</sup>



**“There remains a clear need for new oral therapies that can address the underlying biology of the disease while potentially offering patients greater convenience.”**

**– Eric Simpson, MD, MCR,**  
Frances J. Storrs Medical Dermatology  
Professor and Director of CLEAR Eczema  
Center, Oregon Health & Science University

<sup>1</sup>GlobalData (2023 diagnosed prevalent patient population for AD in US/EU5/JP); <sup>2</sup>GlobalData.

# Asthma: Chronic, Inflammatory Lung Disease

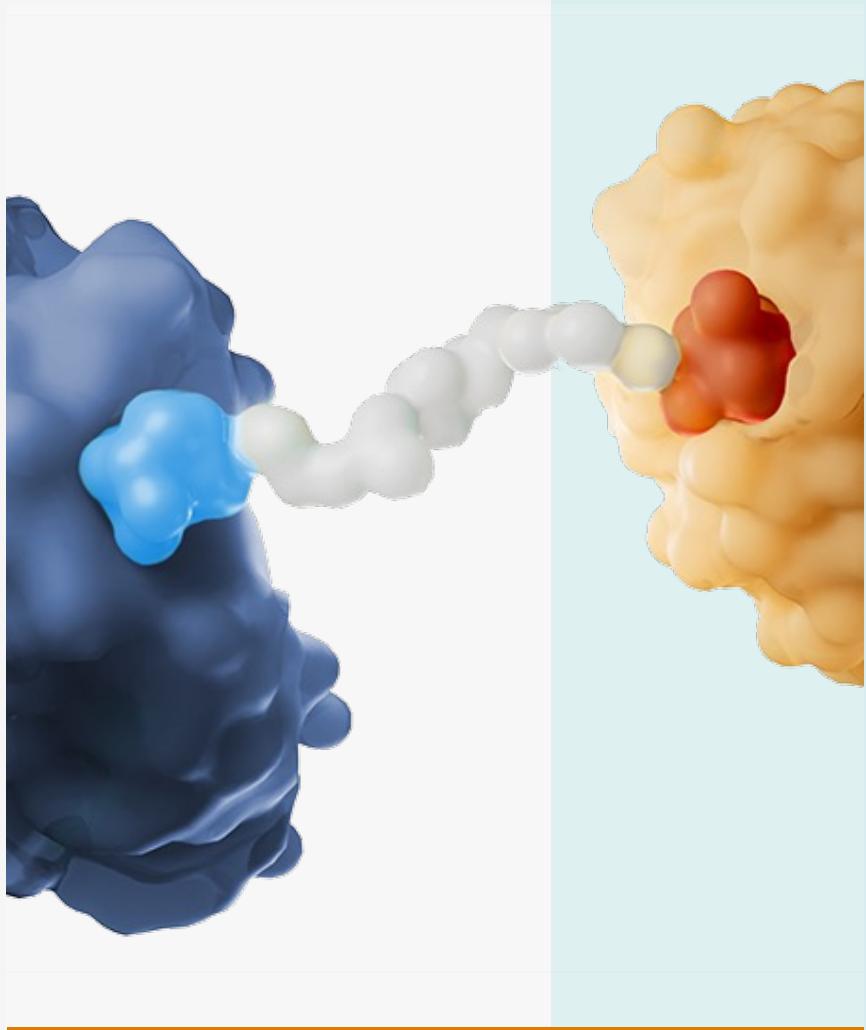
## Opportunity Exists to Transform the Treatment Paradigm

- The airways in lungs to become swollen and inflamed, causing coughing, shortness of breath, chest tightness or pain, and **making it harder to breathe**
- **Symptoms may resemble other lung conditions**, called asthma mimics, and can be misdiagnosed as a result
- Can significantly impact a **patient's quality of life** and lead to permanent lung damage
- Many options only address symptoms, **not underlying Type 2 inflammation**
- Estimated **55 million** adults in US/EU5/JP<sup>1</sup>
- **Less than 1 million** patients currently on dupilumab<sup>2</sup>



**Participant expressed hope “for future treatments that are easier to use...and better routes of administration than inhalers or injections due to fear of needles.”**

**- Little Airways, Big Voices<sup>3</sup>**  
Patient Focused Drug Development: Asthma



## Appendix: Partnered Programs

# IRAK4 Biology and Target Rationale

## Target Rationale

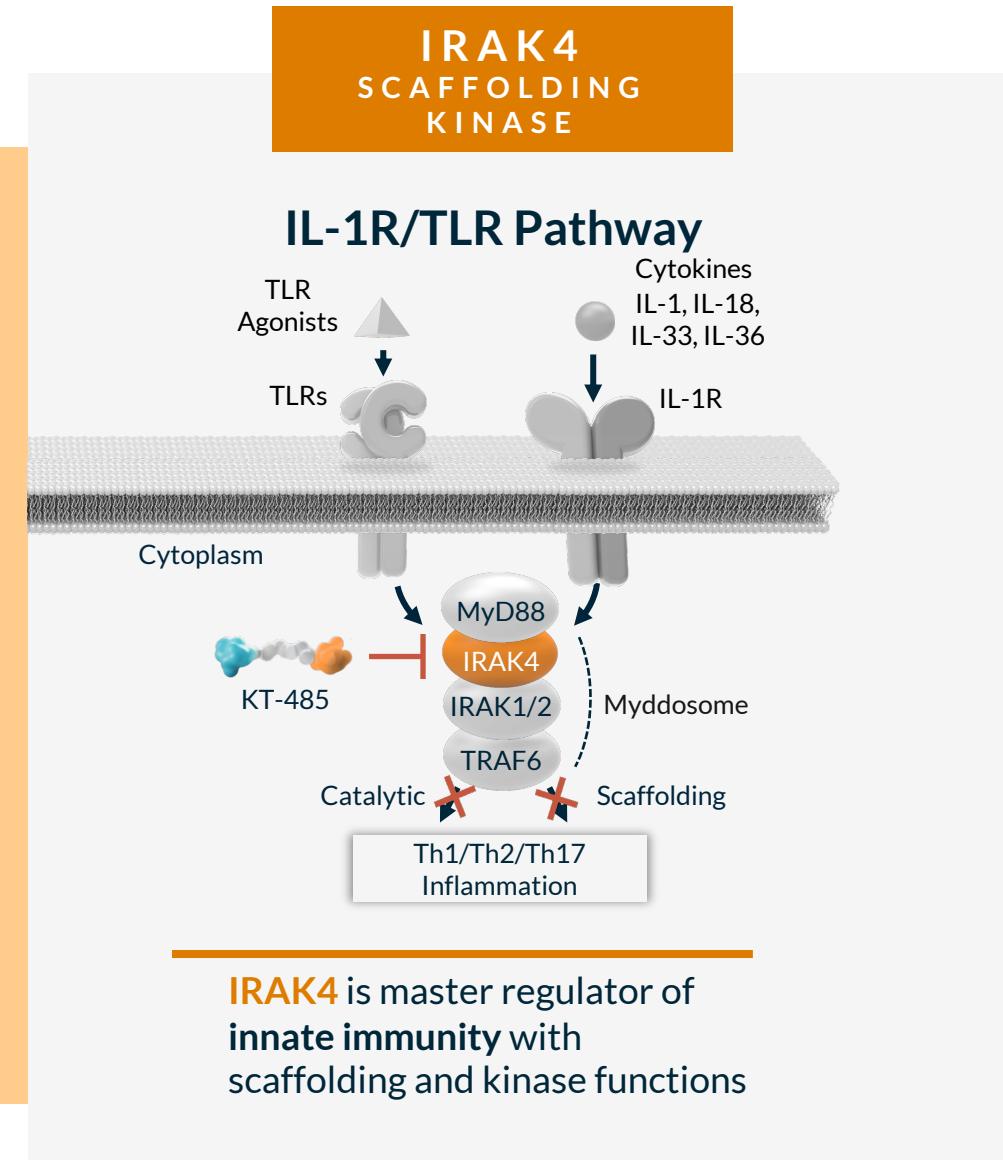
- IRAK4 is an obligate node in IL-1R/TLR signaling, and its degradation is the only approach to fully block the pathway

## Human Genetics

- Adult humans with IRAK4 null mutation are healthy

## Clinical Pathway Validation

- IRAK4 degradation has the potential to achieve a broad, well-tolerated anti-inflammatory effect
- Multiple development opportunities in immune-inflammatory diseases which signal through MyD88/IRAK4 have been clinically validated<sup>1</sup>:
  - IL-1 $\alpha$ /IL-1 $\beta$ : RA, CAPS, HS, AD, RP, Gout
  - IL-18: AD, Macrophage Activation Syndrome
  - IL-36: Generalized Pustular Psoriasis
  - IL-33: Asthma, COPD
  - IRAK4 SMI: RA



<sup>1</sup>Diseases where IL-1R/TLR pathway has been implicated in pathogenesis; Figure adapted from West NT. *Front Immunol* 2019.

# CDK2 Molecular Glue Degrader Advantage

## Target Biology and Rationale

- Regulates the G1-S transition, with its partner CCNE
- CCNE is often overexpressed or amplified in HGSOC and CDK4/6i resistant breast cancers, driving uncontrolled cell proliferation

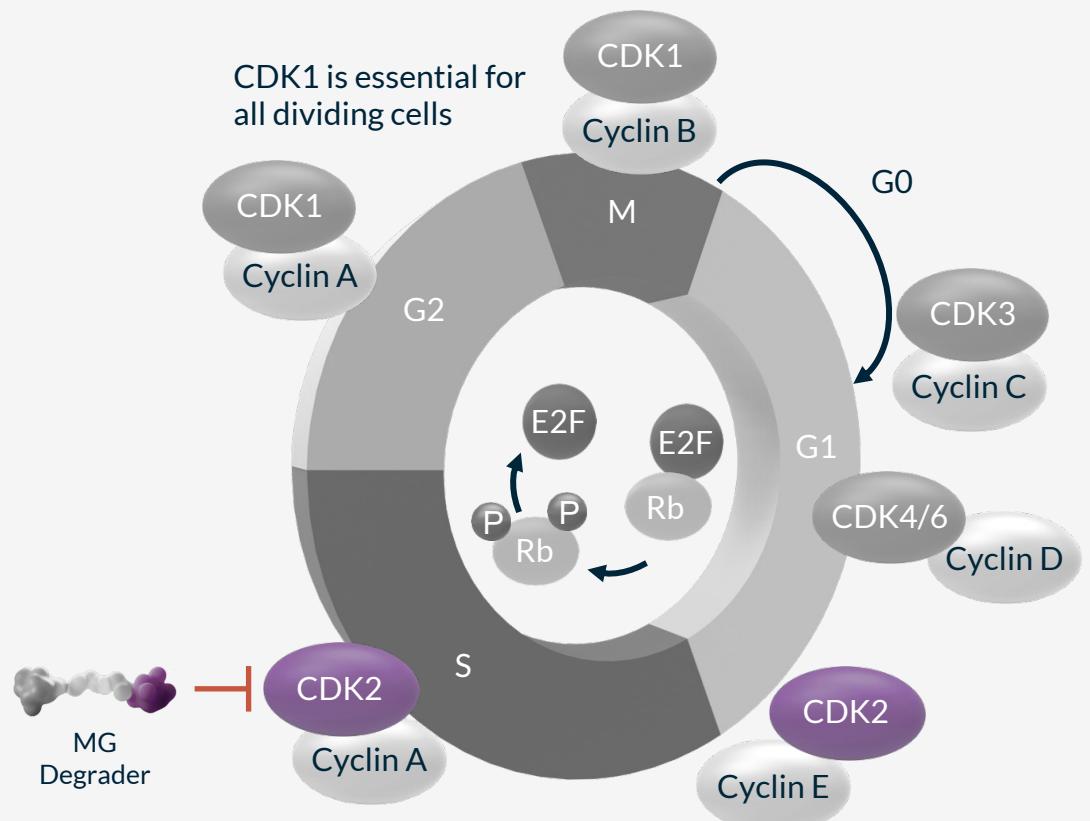
## Genetically Validated

- DEPMAP identifies CCNE1 amplification as a biomarker of dependency for CDK2 across cancer cell types
- High CCNE activity is associated to resistance of CDK4/6 therapies

## Advantages of MG Degraders

- CDK2 inhibitors face challenges due to similarity with other CDKs, including CDK1, causing toxicities before effective CDK2-pRB pathway inhibition can be achieved
- MG degraders offer greater selectivity, and potentially broader therapeutic index with more complete CDK2 pathway inhibition

CDK2  
MASTER CELL CYCLE  
REGULATOR



# Abbreviations

<b>Ab</b>	Antibody	<b>EoE</b>	Eosinophilic Esophagitis	<b>IgE</b>	Immunoglobulin E
<b>AD</b>	Atopic Dermatitis	<b>EU</b>	European Union	<b>IHS4</b>	International Hidradenitis Suppurativa Severity Score
<b>AIA</b>	Antigen-Induced Arthritis	<b>FDA</b>	Food and Drug Administration	<b>IL</b>	Interleukin
<b>ASMS</b>	Affinity Selection Mass Spectrometry	<b>FeNO</b>	Fractional Exhaled Nitric Oxide	<b>IND</b>	Investigational New Drug Application
<b>AN Count</b>	Abscess and Inflammatory Nodule Count	<b>FIH</b>	First-in-Human	<b>IRAK4</b>	Interleukin 1 Receptor Associated Kinase 4
<b>BID</b>	Twice a day	<b>GI</b>	Gastrointestinal	<b>IRF5</b>	Interferon Regulatory Factor 5
<b>BP</b>	Bullous Pemphigoid	<b>GLP</b>	Good Laboratory Practice	<b>JP</b>	Japan
<b>BSA</b>	Body Surface Area	<b>GOF</b>	Gain of Function	<b>KO</b>	Knockout
<b>CAPS</b>	Cryopyrin-Associated Periodic Syndrome	<b>GWAS</b>	Genome-Wide Association Study	<b>LABA</b>	Long-Acting Beta Agonist
<b>CD</b>	Crohn's Disease	<b>HD</b>	High Dose	<b>LAMA</b>	Long-Acting Muscarinic Antagonist
<b>CDK2</b>	Cyclin-Dependent Kinase 2	<b>HDM</b>	House Dust Mite	<b>LD</b>	Low Dose
<b>COPD</b>	Chronic Obstructive Pulmonary Disease	<b>HiSCR</b>	Hidradenitis Suppurativa Clinical Response	<b>LLOQ</b>	Lower Limit of Quantification
<b>CRSwNP</b>	Chronic Rhinosinusitis with Nasal Polyps	<b>hPBMC</b>	Human Peripheral Blood Mononuclear Cells	<b>LOF</b>	Loss of Function
<b>Cryo-EM</b>	Cryo-Electron Microscopy	<b>HS</b>	Hidradenitis Suppurativa	<b>LPS</b>	Lipopolysaccharide Solution
<b>Ctrl</b>	Control	<b>HTS</b>	High Throughput Screening	<b>LTRA</b>	Leukotriene Receptor Antagonist
<b>CSU</b>	Chronic Spontaneous Urticaria	<b>HV</b>	Healthy Volunteers	<b>MAD</b>	Multiple Ascending Dose Study
<b>DC<sub>#</sub></b>	Degradation Concentration	<b>I&amp;I</b>	Immunology and Inflammation	<b>MOA</b>	Mechanism of Action
<b>DCs</b>	Dendritic Cells	<b>IA</b>	Interim Analysis	<b>NF-κB</b>	Nuclear Factor Kappa B
<b>DEL</b>	DNA-Encoded Library	<b>IBD</b>	Inflammatory Bowel Disease	<b>NHP</b>	Nonhuman Primate
<b>DLQI</b>	Dermatology Life Quality Index	<b>IC<sub>#</sub></b>	Inhibitory Concentration	<b>nM</b>	Nanomolar
<b>DM</b>	Dermatomyositis	<b>ICS</b>	Inhaled Corticosteroid	<b>NRS</b>	Numerical Rating Scale
<b>DMSO</b>	Dimethyl Sulfoxide	<b>IFN</b>	Interferon	<b>PBMC</b>	Peripheral Blood Mononuclear Cells
<b>dsDNA</b>	Double-Stranded DNA	<b>ISG</b>	Interferon-Stimulated Gene	<b>Pbo</b>	Placebo
<b>EASI</b>	Eczema Area and Severity Index	<b>IGA</b>	Investigator Global Assessment	<b>PGA</b>	Physician Global Assessment

# Abbreviations

<b>Ph</b>	Phase	<b>SMI</b>	Small Molecule Inhibitor
<b>PK/PD</b>	Pharmacokinetics/Pharmacodynamics	<b>SOC</b>	Standard of Care
<b>pM</b>	Picomolar	<b>SSc</b>	Systemic Sclerosis
<b>PN</b>	Prurigo Nodularis	<b>STAT</b>	Signal Transducer and Activator of Transcription
<b>POC</b>	Proof-of-Concept	<b>STAT6</b>	Signal Transducer and Activator of Transcription 6
<b>POEM</b>	Patient-Oriented Eczema Measure	<b>TARC</b>	Thymus and Activation-Regulated Chemokine
<b>PPNRS</b>	Peak Pruritus Numerical Rating Scale	<b>TEAE</b>	Treatment Emergent Adverse Event
<b>PRRs</b>	Pattern Recognition Receptors	<b>Th1</b>	T Helper 1
<b>PsO</b>	Psoriasis	<b>Th2</b>	T Helper 2
<b>pSTAT</b>	Signal Transducer and Activator of Transcription	<b>Th17</b>	T Helper 17
<b>QD</b>	Once a day	<b>TLR</b>	Toll-like Receptors
<b>QoL</b>	Quality of Life	<b>TNSS</b>	Total Nasal Symptom Score
<b>R&amp;D</b>	Research and Development	<b>TPD</b>	Targeted Protein Degradation
<b>RA</b>	Rheumatoid Arthritis	<b>TPP</b>	Target Product Profile
<b>RNA</b>	Ribonucleic Acid	<b>TRAE</b>	Treatment Related Adverse Event
<b>ROW</b>	Rest of World	<b>TYK2</b>	Tyrosine Kinase 2
<b>RP</b>	Recurrent Pericarditis	<b>UC</b>	Ulcerative Colitis
<b>RQLQ</b>	Rhinoconjunctivitis Quality of Life Questionnaire	<b>US</b>	United States
<b>SAD</b>	Single Ascending Dose study	<b>vIGA-AD</b>	Validated Investigator Global Assessment for AD
<b>SAE</b>	Serious Adverse Event	<b>WW</b>	Worldwide
<b>SCORAD</b>	SCORing Atopic Dermatitis		
<b>SD</b>	Single Dose		
<b>SLE</b>	Systemic Lupus Erythematosus		