

Allakos



Corporate Presentation

November 2023

Developing Therapeutic Antibodies
Targeting Allergic, Inflammatory and
Proliferative Disease

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Allakos Opportunity

Novel Targets

- Lirentelimab (anti-Siglec-8) inhibits mast cells and depletes eosinophils
- AK006 (anti-Siglec-6) selectively and more potently inhibits mast cell activation, including KIT-mediated signaling
- Both lirentelimab and AK006 inhibit mast cell activation via multiple pathways

Significant Need for New Agents

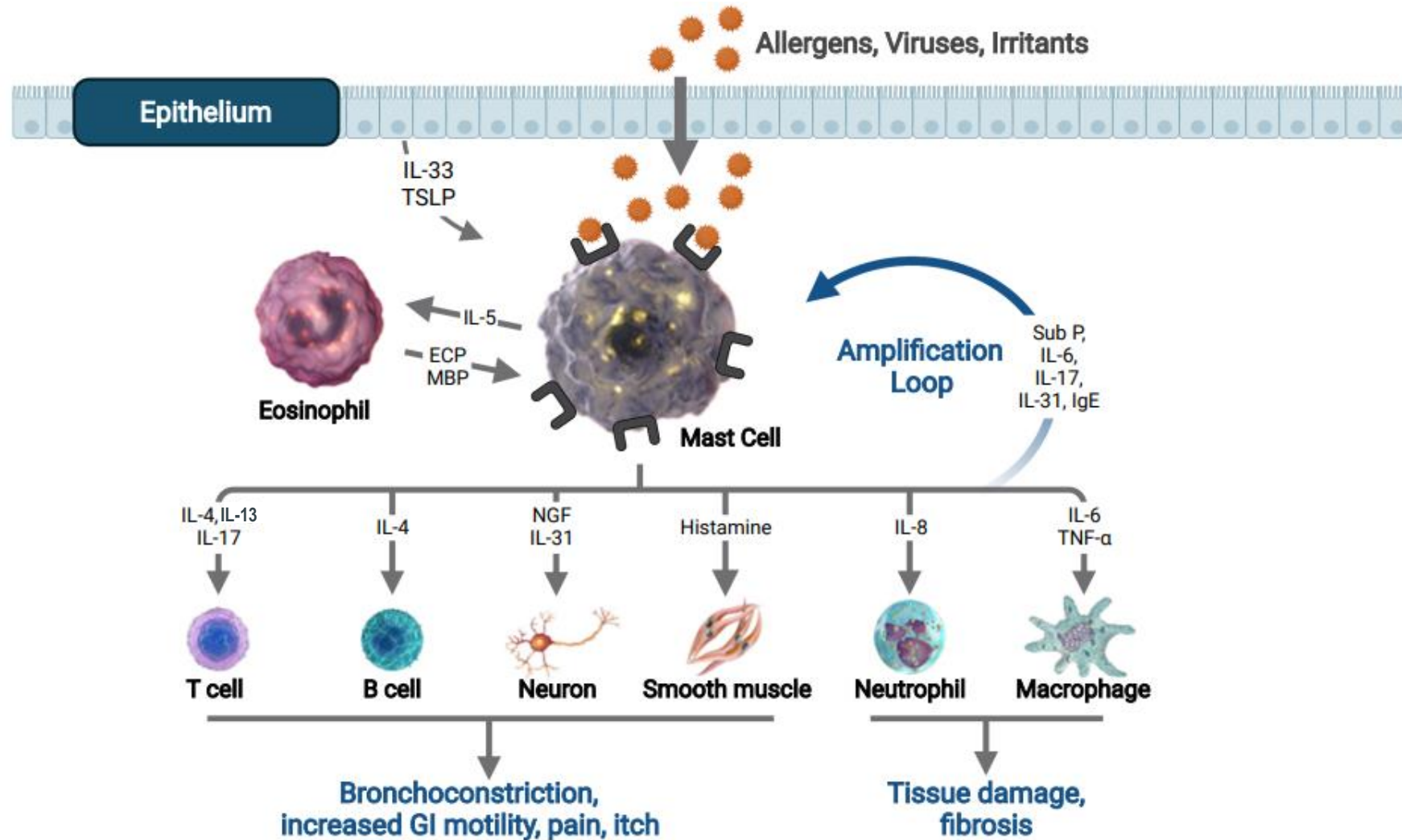
- Lirentelimab targets large indications: Atopic Dermatitis and Chronic Spontaneous Urticaria
- Both lirentelimab and AK006 have potential to treat a broad range of serious, complex inflammatory diseases

Upcoming Data Catalysts and Expected Milestones

Milestones

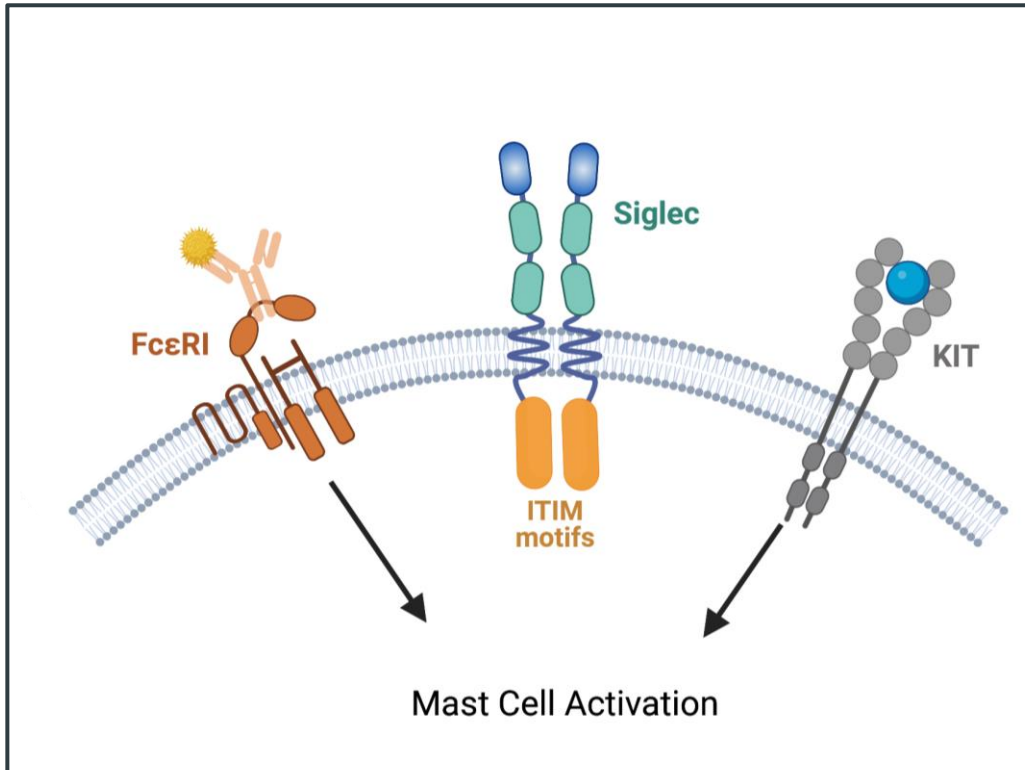
- Late 4Q23 to 1Q24 – Phase 2 Lirentelimab Data in Patients with Atopic Dermatitis
- Late 4Q23 to 1Q24 – Phase 2b Lirentelimab Data in Patients with Chronic Spontaneous Urticaria
- 2Q24 – Initiate a randomized, double-blind, placebo-controlled, CSU cohort in the Phase 1 Study of AK006

Mast Cells and Eosinophils Are Key Drivers of Inflammatory Disease



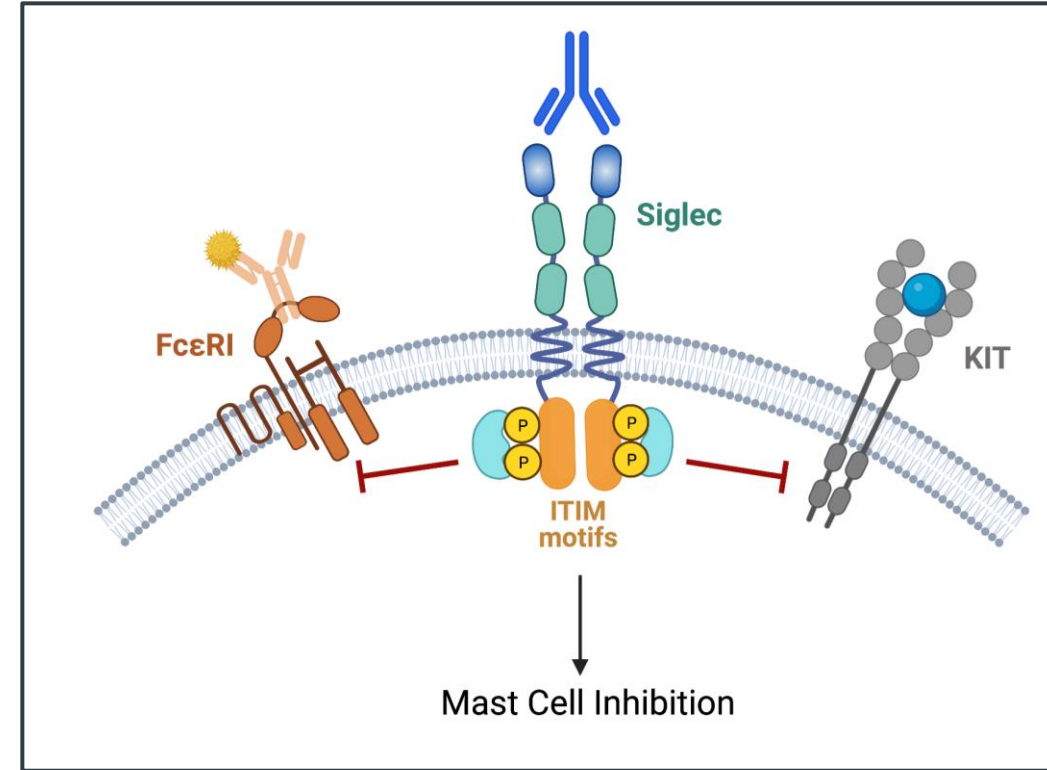
Leveraging the Native Inhibitory Function of Siglecs on Mast Cells

Activated State



Mast cells can be activated by numerous receptors leading to mast cell degranulation and release of histamine, TNFα and other inflammatory mediators

Siglec-Mediated Inhibition

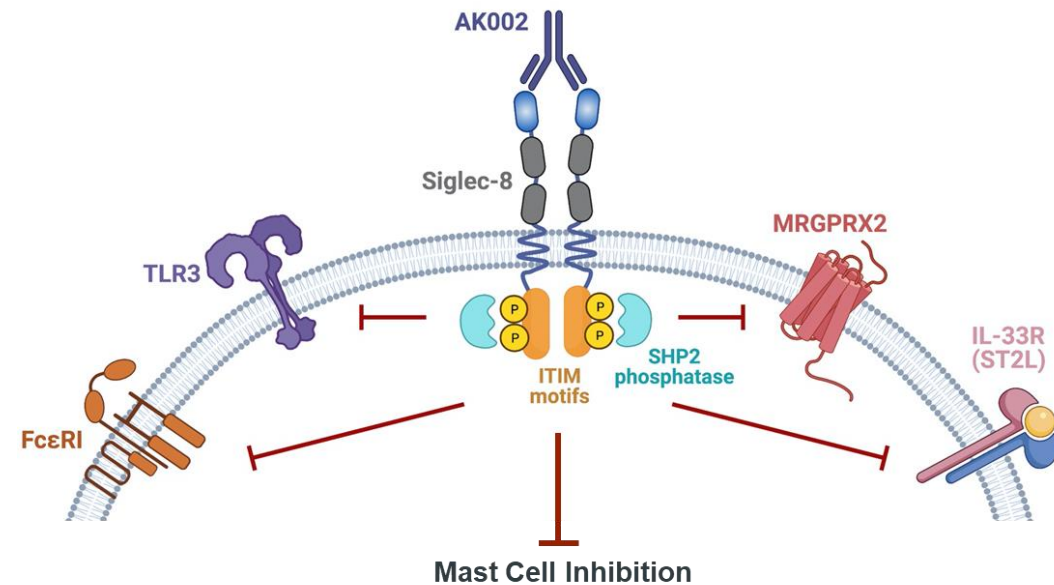


Activation of Siglec-6 or Siglec-8 with an agonistic antibody activates inhibitor machinery inside cell which attenuates activating signals

Lirentelimab Inhibits Mast Cells and Depletes Eosinophils

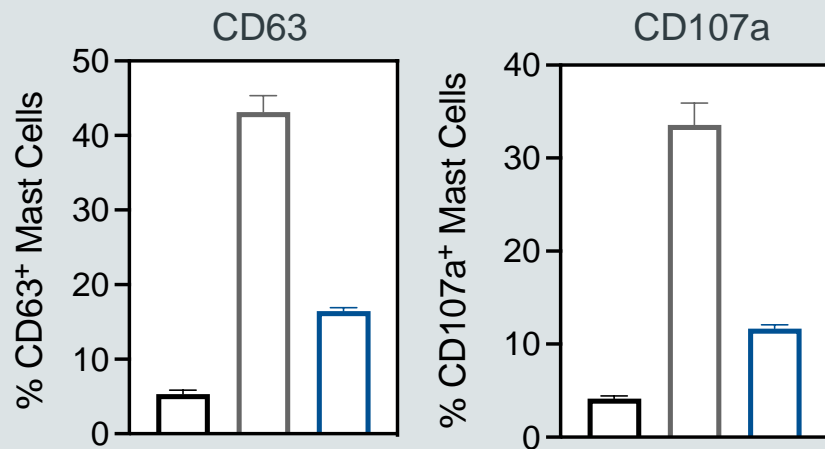
Lirentelimab (Anti-Siglec-8)

- Lirentelimab has been tested in three open-label trials in mast cell driven diseases:
 - Chronic Urticaria
 - Indolent Systemic Mastocytosis (ISM)
 - Severe Allergic Conjunctivitis (SAC)
- Lirentelimab treatment led to clinical activity in these indications
- Lirentelimab's mast cell inhibition is broad and inhibits mast cell activation via multiple pathways including IgE, IL-33, KIT, TLR-3, 7 & 8, TSLP and MRGPRX2
- Lirentelimab is currently being tested in two large, randomized, placebo-controlled trials

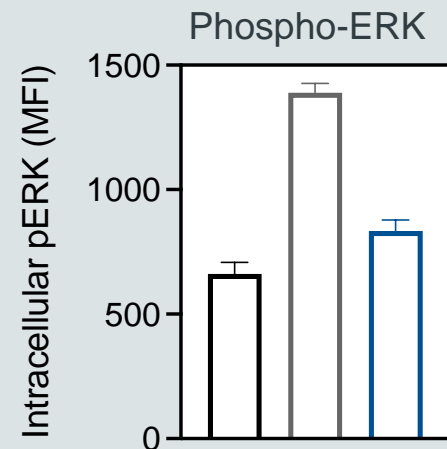


Lirentelimab Inhibits IgE-Mediated Mast Cell Activation

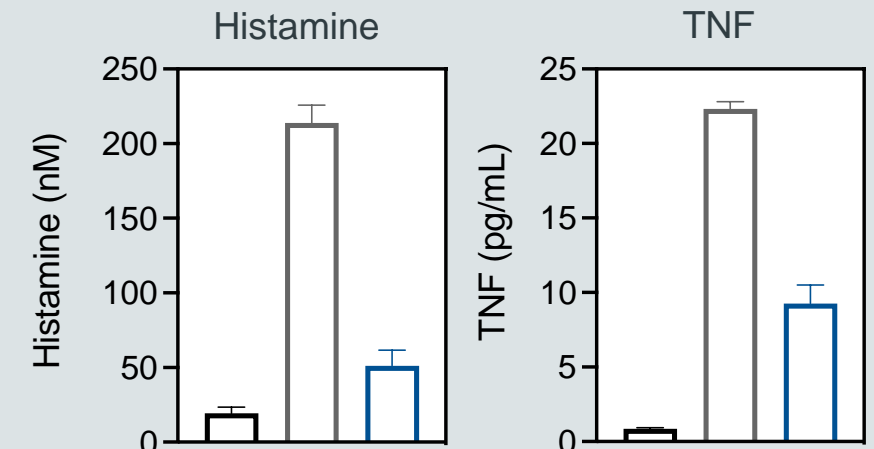
Mast Cell Degranulation



Intracellular Signaling



Mediator Production

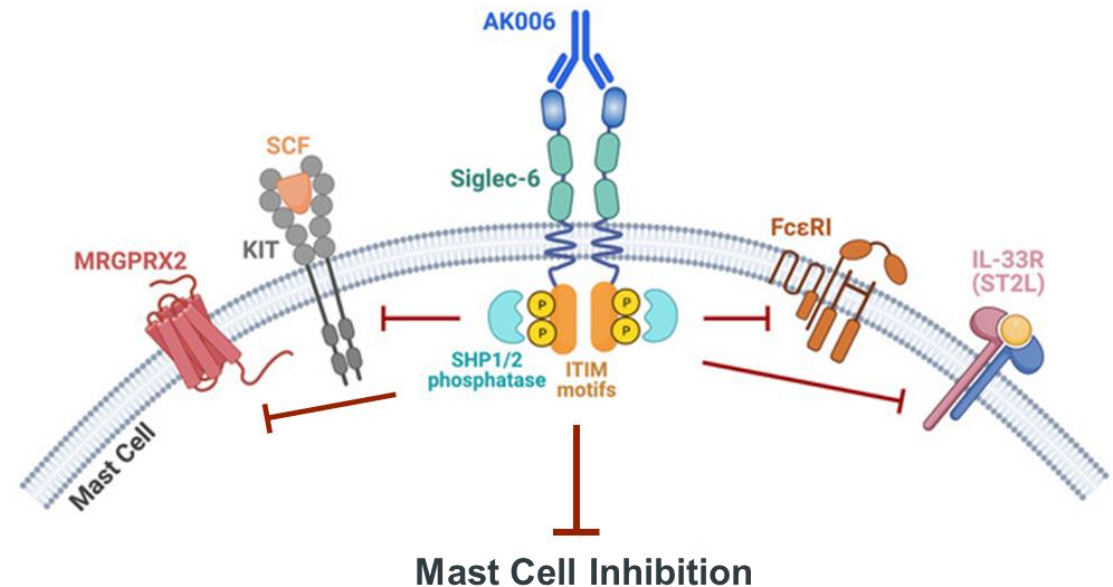


■ NS
 ■ ISO + anti-FcεRI
 ■ AK002 + anti-FcεRI

AK006 is Engineered for Deeper Mast Cell Inhibition

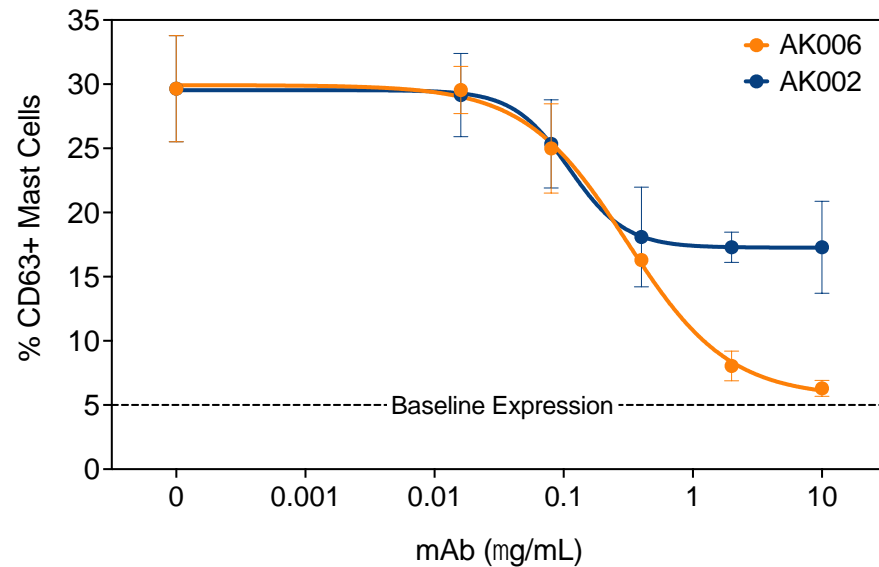
AK006 (Anti-Siglec-6)

- AK006 is a Siglec-6 mAb that selectively inhibits mast cells and reduces their numbers
 - Engineered for optimal mast cell inhibition
 - Reduces mast cells via ADCP in presence of activated macrophages
- AK006 is a more potent mast cell inhibitor
- AK006 mast cell inhibition is broad and inhibits mast cell activation via multiple pathways including IgE, IL-33, KIT, C5a and MRGPRX2
- The Phase 1 study of AK006 consists of single and multiple ascending doses administered in healthy volunteers, followed by a randomized, double-blind, placebo-controlled, CSU cohort



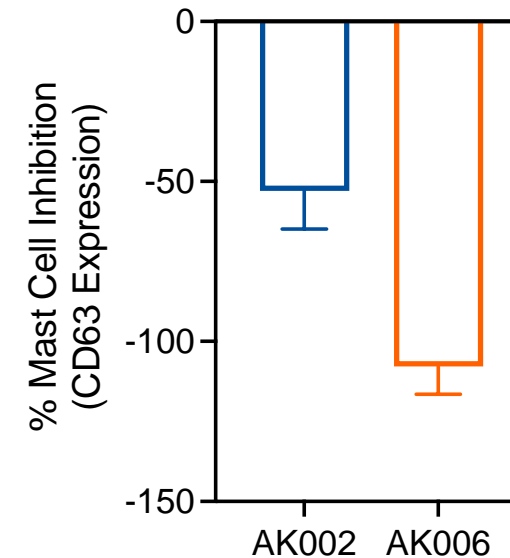
AK006 is a More Potent Mast Cell Inhibitor

IgE-Activated Human Tissue Mast Cells



- Human mast cells were activated with anti-FcεRI and treated with isotype, AK002 or AK006
- Human mast cells treated with AK006 displayed deeper inhibition than AK002 or isotype

KIT-mediated Mast Cell Activation Model in Siglec Transgenic Mice



- Siglec-6 and Siglec-8 transgenic mice were dosed with placebo control, isotype, AK002, or AK006 and then received recombinant stem cell factor (ligand for KIT) via intravenous injection
- Treatment with AK006 inhibited stem cell factor-induced mast cell activation to a greater extent than AK002

Allakos Pipeline

Program	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Milestone
Lirentelimab (Anti-Siglec-8)	Atopic Dermatitis						Topline expected late 4Q23 to 1Q24
	Chronic Spontaneous Urticaria						Topline expected late 4Q23 to 1Q24
AK006 (Anti-Siglec-6)	Healthy Volunteers & CSU						Expected initiation of CSU cohort in 2Q24
AK068 (Siglec-6/Siglec-8 Bispecific)	Inflammatory Diseases						Ongoing
T Cell Immunomodulatory Receptors	Inflammatory Diseases						Ongoing
AK007 (Anti-Siglec-10)	Immuno-Oncology						Ongoing

Significant Opportunity Exists to Treat Inflammation & Immunology

	Rheumatoid Arthritis	Psoriasis	Ulcerative Colitis	Crohn's Disease	Asthma	Atopic Dermatitis	Chronic Spontaneous Urticaria	Eosinophilic Gastrointestinal Disorders
2022 Estimated WW Sales	~\$27 bn	~\$24 bn	~\$7 bn	~\$16 bn	~\$7 bn	~\$7 bn	~\$1.8 bn	~\$0.1 bn
U.S. Prevalence Moderate-to Severe	1 million	1.2 million	350 thousand	700 thousand	≥1 million	5.5 million	2.0 million	500 thousand – 2 million
Market Maturity	← Mature ————— More Mature ————— Less Mature —————					Immature		
FDA Approved Targeted Agents	<u>TNF-α: 6</u> <u>IL-6R: 2</u> <u>JAK: 3</u> <u>IL-1R: 1</u> <u>CD20: 1</u> <u>CD86: 1</u>	<u>TNF-α: 4</u> <u>IL-17: 3</u> <u>IL-23: 3</u> <u>IL12/IL-23: 1</u> <u>TYK2: 1</u> <u>PDE-4: 1</u>	<u>TNF-α: 3</u> <u>JAK: 2</u> <u>α4β7: 1</u> <u>IL12/IL-23: 1</u> <u>S1P: 1</u>	<u>TNF-α: 3</u> <u>α4β7: 2</u> <u>IL12/IL-23: 1</u> <u>IL-23: 1</u>	<u>IgE: 1</u> <u>IL-5: 3</u> <u>IL-4/IL-13: 1</u> <u>TSLP: 1</u>	<u>IL-4/IL-13: 1</u> <u>IL-13: 1</u> <u>JAK: 2</u>	<u>IgE: 1</u>	<u>IL-4/IL-13: 1</u>

Current Lirentelimab Clinical Development

Lirentelimab for Chronic Spontaneous Urticaria

Chronic Spontaneous Urticaria Overview

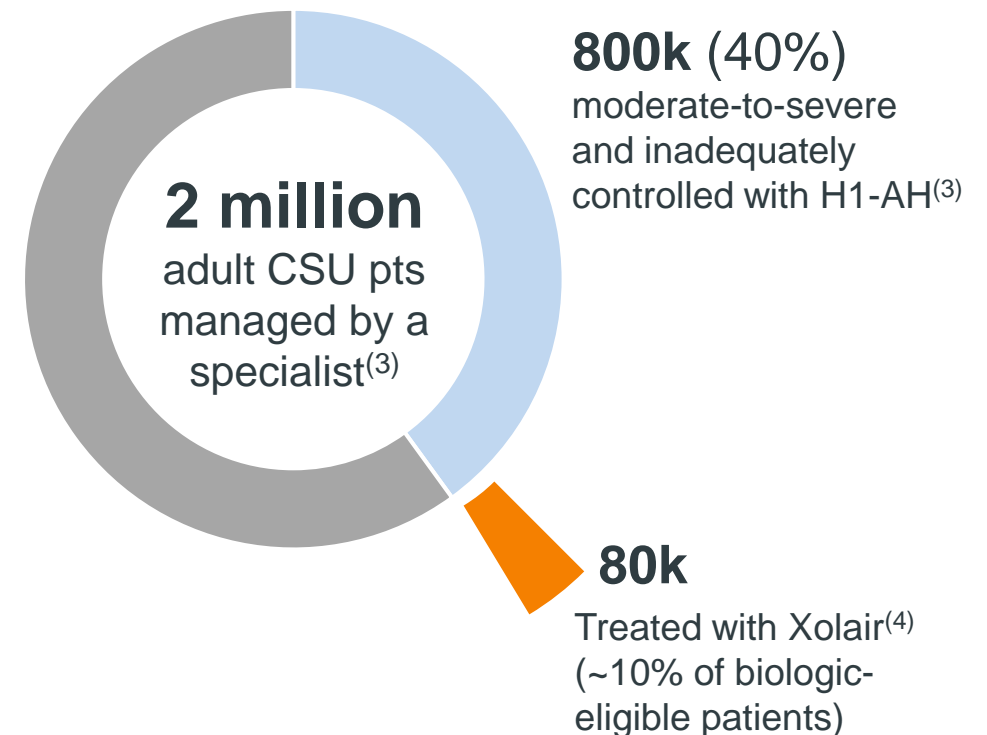
Chronic spontaneous urticaria (CSU) is a chronic inflammatory skin disease believed to be driven primarily by mast cells¹

CSU affects up to 3 million adults in the U.S., and 2 million managed by a specialist (allergist or dermatologist)^{2,3}

An estimated 800k adults with CSU are biologic-eligible, yet only ~10% of eligible patients are currently on a biologic^{3,4}

Xolair® (omalizumab) global CSU sales were estimated to be \$1.6 billion in 2021⁵

Approximately 800k adult CSU patients are eligible for a biologic in the U.S.



Phase 2a Chronic Urticaria Study

Study Design

- Open-label study in patients with Chronic Urticaria (CU)
- Uncontrolled CU (UCT <12) at the time of enrollment
- Diagnosis of CU for at least three months, refractory to antihistamine treatment on 1 to 4x labeled dosage
- 45 patients – 4 cohorts
 - Omalizumab-naïve Chronic Spontaneous Urticaria (CSU)
 - Omalizumab-refractory CSU¹
 - Cholinergic urticaria
 - Symptomatic Dermographism
- 6 monthly doses
- 0.3 mg/kg starting lirentelimab dose; increased to 1.0 mg/kg (dose 2 and 3); if UCT <12, increased to 3.0 mg/kg (dose 4, 5, and 6)

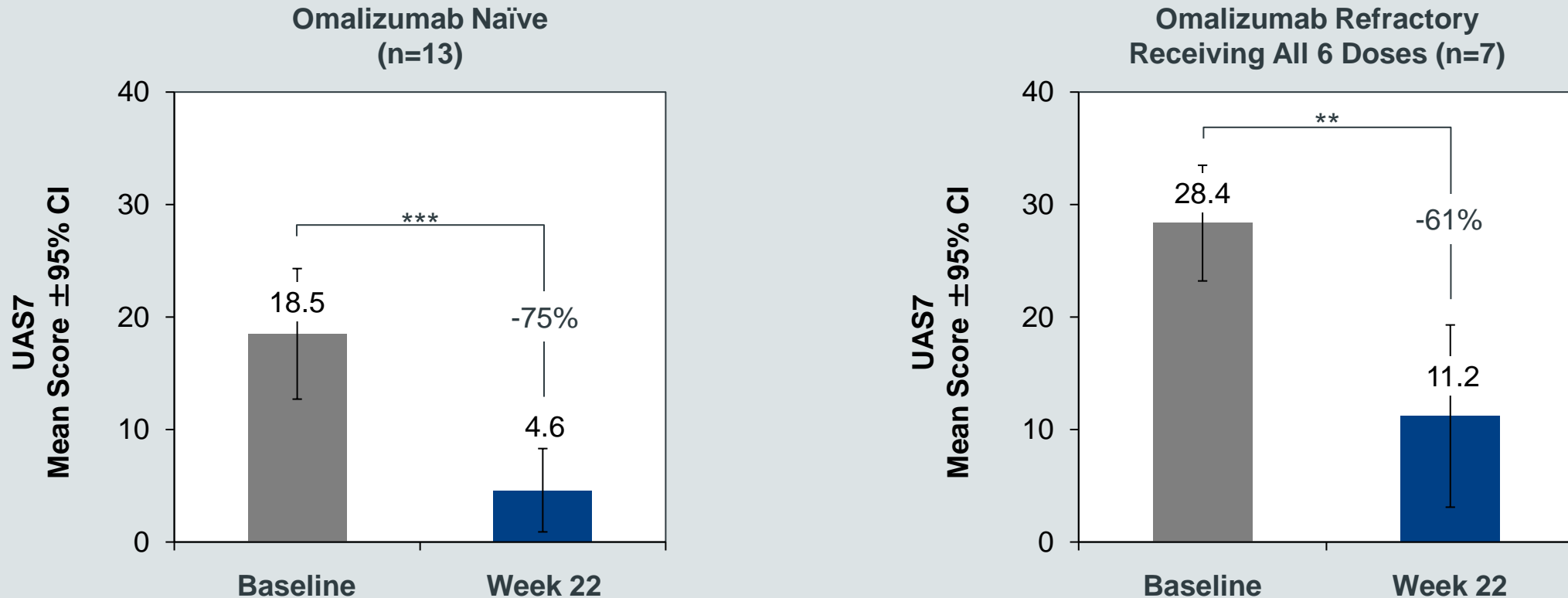
Endpoints

- **Primary Endpoint**
 - Change in Urticaria Control Test (UCT) Week 22 from Baseline
- **Key Secondary Endpoints**
 - Change in UAS7 (for CSU patients)
 - Safety and tolerability

1.) Patients in the omalizumab refractory cohort had urticaria symptoms despite treatment with up to 600 mg (2x highest labeled dose) omalizumab for an average duration of 10 months.

Symptom Improvement by UAS7 with Lirentelimab in CSU

Chronic Spontaneous Urticaria



UAS7 is a validated patient-reported outcome recording the intensity of pruritus (Weekly Itch Severity Score, ISS7) and the number of wheals (Weekly Hives Severity Score, HSS7); each as weekly score range is 0 to 21. UAS7 total scores range from 0 to 42, with lower scores representing fewer symptoms (UAS7 0 = no itch or wheals; UAS7 42 = maximal itch and wheals).

SOURCE: Altrichter S et al. J Allergy Clin Immunol. 2022 May;150(3):736-737

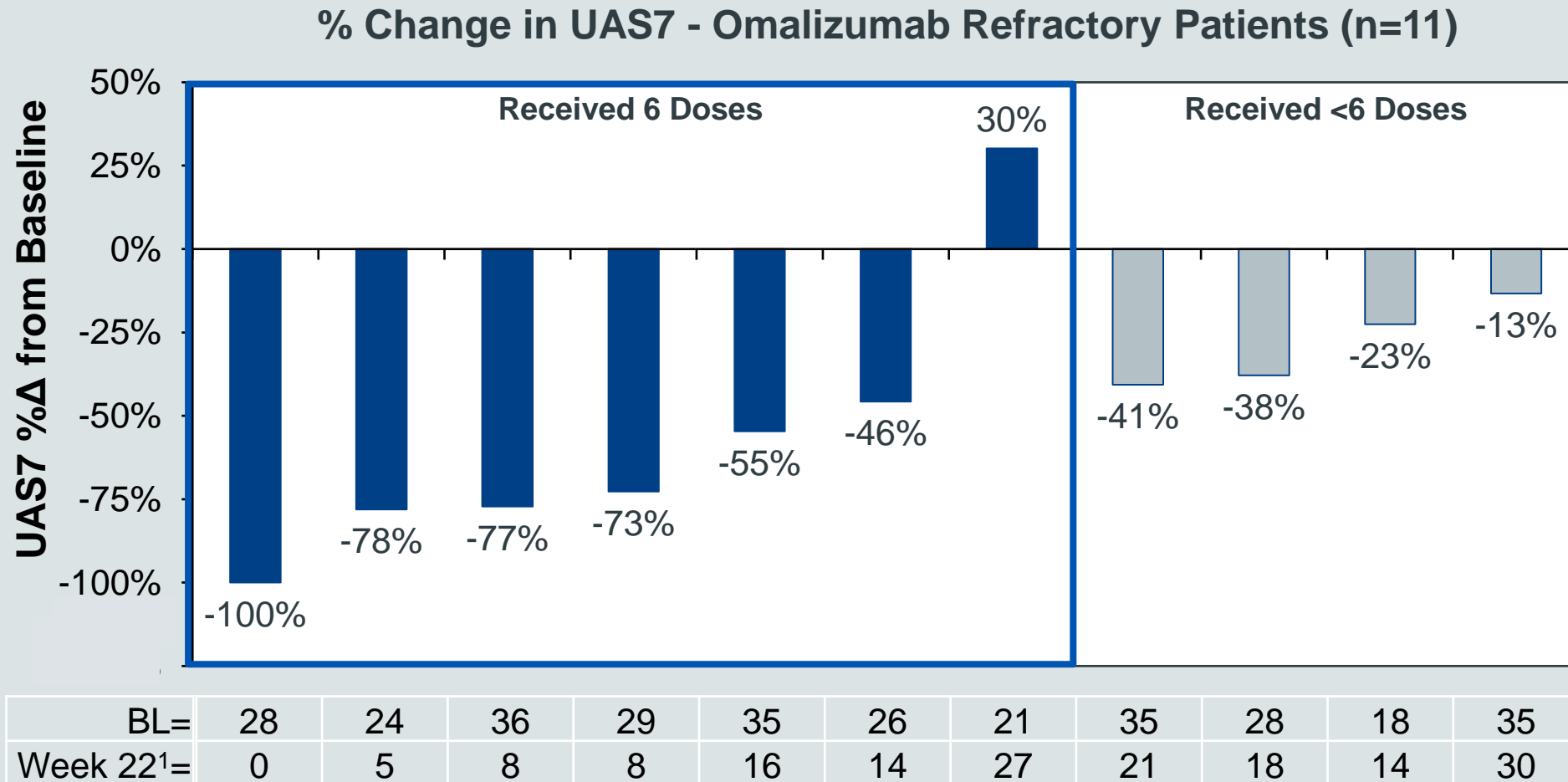
Lirentelimab UAS7 Response in Omalizumab Naïve CSU

Endpoint	Baseline Week 0 (n=13 patients)	Omalizumab Naïve Week 22 (n=13 patients)
Average UAS7 Score	18.5	4.6 (-75%)
Patients with UAS7 \leq 6	0 (0%)	8/13 (62%)
Patients with UAS7 = 0	0 (0%)	7/13 (54%)
Patients with ISS7 = 0	0 (0%)	7/13 (54%)
Patients with HSS7 = 0	0 (0%)	10/13 (77%)

UAS7 is a validated patient-reported outcome recording the intensity of pruritus (Weekly Itch Severity Score, ISS7) and the number of wheals (Weekly Hives Severity Score, HSS7); each as weekly score range is 0 to 21
UAS7 total scores range from 0 to 42, with lower scores representing fewer symptoms (UAS7 0 = no itch or wheals; UAS7 42 = maximal itch and wheals).

SOURCE: Altrichter S et al. J Allergy Clin Immunol. 2022 May;150(3):736-737

61% Improvement in UAS7 in Omalizumab Refractory CSU Patients Who Received 6 Lirentelimab Doses



1.) Last observation carried forward

High UCT Response Rate Observed in Multiple Forms of Urticaria

Indication	UCT Baseline	UCT Week 22	UCT Complete Responders	PCE Response
Chronic Spontaneous Urticaria				
– Naïve (n=13)	3.2	14.2	92%	-
– Xolair Refractory (n=7) ¹	3.1	11.4	57%	-
Cholinergic Urticaria (n=11)	5.4	11.8	82%	100%
Symptomatic Dermographism (n=10)	5.7	9.1	40%	-

Urticaria Control Test (UCT) is a validated 4-item questionnaire that asks patients to retrospectively score four items, on a scale from 0 to 4, the impact of urticaria symptoms on morbidity, quality of life, quality of treatment, and overall disease control over the previous 4 Weeks. UCT ranges 0 to 16 (0=worst possible). UCT complete response: ≥3-point improvement from baseline and score ≥12.

Pulse Controlled Ergometry (PCE) Test utilizes a stationary bike or treadmill for the patient to trigger hives. Positive response = hives appearing ≤10 mins post start of sweating. Negative response (Responder) = no hives ≤10 mins post start of sweating

1.) Xolair refractory patients who received all 6 dose

SOURCE: Altrichter S et al. J Allergy Clin Immunol. 2022 May;150(3):736-737; Altrichter S, et al. EAACI 2019 Presentation.

7/7 (100%) Response Rate by PCE Test in CholU Patients

Cholinergic Patients	Baseline	Week 22
	Response to Provocation ¹	Response to Provocation ¹
CholU-1	+	-
CholU-2	+	-
CholU-3	+	-
CholU-4	+	-
CholU-5 ²	+	-
CholU-6	+	-
CholU-7	+	-

AK002 increased trigger threshold in patients with Cholinergic Urticaria

1. Pulse Controlled Ergometry (PCE) Test utilizes a stationary bike or treadmill for the patient to trigger hives. Positive response = hives appearing ≤10 mins post start of sweating. Negative response (Responder) = no hives ≤10 mins post start of sweating
2. Bad osteoarthritis of knees, patient had warm damp cloth applied that caused wheals and itching. Patient terminated early, not due to any drug related AEs

Phase 2b Chronic Spontaneous Urticaria Study

Study Design

- Multi-center, randomized, DB, placebo-controlled
- Active moderate-to-severe symptoms
- CSU diagnosis with onset ≥ 6 months prior to screening
- Diagnosis of CSU refractory to antihistamines
 - Presence of itch and hives despite current use of antihistamines
 - UAS7 score ≥ 16 and HSS7 score ≥ 8 at baseline
- Includes patients with prior biologics treatment
- 110 adult patients (1:1 randomization)
 - 300 mg Q2W subcutaneous lirentelimab (n=55)
 - Placebo (n=55)

Endpoints

- **Primary Endpoint**
 - Change from baseline in UAS7 at week 12
- **Key Secondary Endpoints**
 - Absolute change in ISS7
 - Absolute change in HSS7
 - Proportion of patients with UAS7=0

Chronic Spontaneous Urticaria Landscape

Drug Name	MOA	UAS7 Response				Opportunity
Xolair® (omalizumab)	Anti-IgE mAb	Dose Group ¹	150 mg	300 mg	Placebo	<ul style="list-style-type: none"> >50% of patients continue to have symptoms Black box for anaphylaxis¹
		UAS7	-14.4 (-48%)	-20.8 (-66%)	-8.0 (-26%)	
		UAS7=0	15%	36%	9%	
Dupixent® (dupilumab)	Anti IL-4/IL-13R mAb	Dose Group ²	300 mg		Placebo	<ul style="list-style-type: none"> Q2W dosing No improvement in Xolair failures³
		UAS7	-20.5 (-65%)		-12.0 (-37%)	
Barzolvolimab	Anti KIT mAb	Dose Group ⁴	75 mg Q4W	150 mg Q4W	300 mg Q8W	<ul style="list-style-type: none"> c-Kit is expressed on hematopoietic stem cells, melanocytes, CNS and germ cells⁵
		UAS7	-17 (-56%)	-23 (-75%)	-24 (-76%)	
		UAS7=0	23%	51%	38%	
Remibrutinib	BTK Inhibitor	Dose Group ⁶	25 mg BID		Placebo	<ul style="list-style-type: none"> BTK is expressed on hematopoietic cells including B cells, myeloid cells, and platelets⁷
		UAS7	-20 & -20 (-65% & -65%)		-12 to -14 (-40% to -46%)	
		UAS7=0	28% to 31%		7% to 11%	

Lirentelimab for Atopic Dermatitis

Atopic Dermatitis Overview

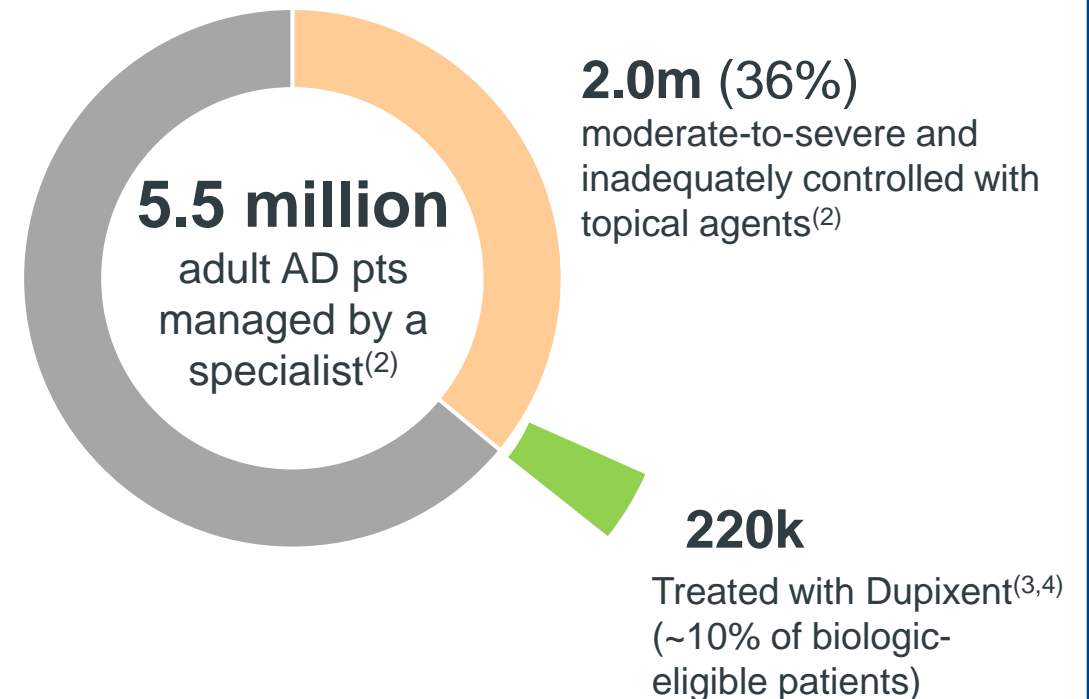
Atopic dermatitis (AD) is a chronic inflammatory skin condition in which mast cells and eosinophils may contribute to pathogenesis¹

AD affects 16 million adults in the U.S., and over 5 million are managed by a specialist (dermatologist or allergist)^{2,3}

An estimated 2 million adults with AD are biologic-eligible, yet only ~10% of eligible patients are currently on a biologic^{3,4}

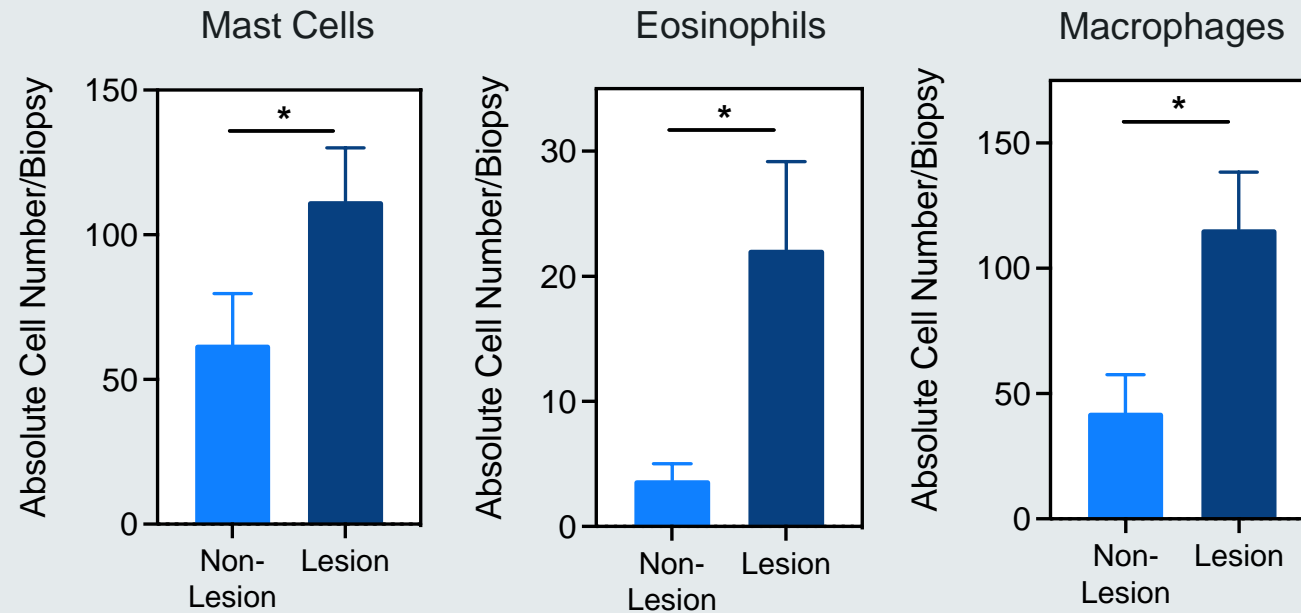
Dupixent® (dupilumab) achieved an estimated \$5 billion in global AD sales in 2021^{4,5}

Approximately 2 million adult AD patients are eligible for a biologic in the U.S.

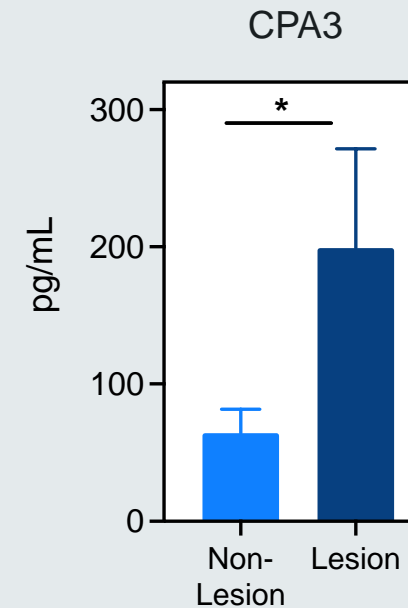


Biopsies of Atopic Dermatitis Lesions Show Evidence of Mast Cell and Eosinophil Activity

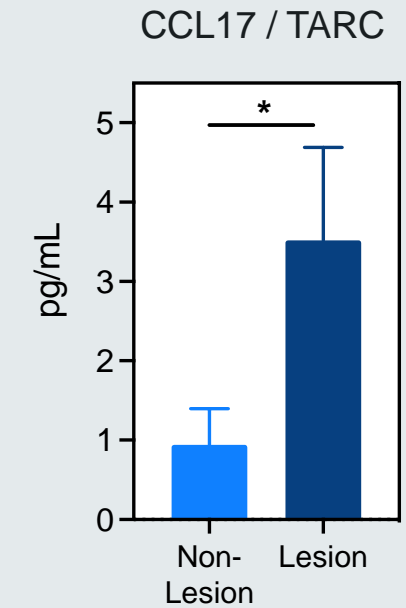
Immune Cell Numbers



Mast Cell Activation



Disease Biomarkers



n=13 biopsy-matched patients

Severe Allergic Conjunctivitis Phase 1b Study

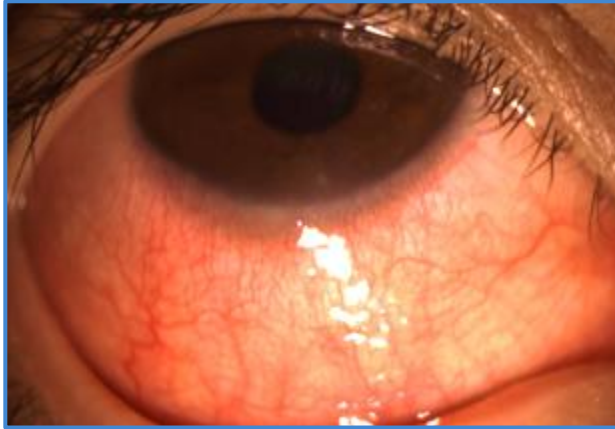
Study Design

- Open-label study in patients with SAC
- Diagnosis of AKC, VKC or PAC
- Average total ACS score of 15 or more from ≥ 14 daily questionnaires during 4-week screening
- 29 patients – 3 cohorts
 - Atopic keratoconjunctivitis
 - Vernal keratoconjunctivitis
 - Perennial allergic conjunctivitis
- 6 monthly doses
- 0.3 mg/kg starting dose, followed by 1.0 mg/kg then either 1.0 mg/kg or 3.0 mg/kg, based on symptoms

Endpoints

- **Primary Endpoint**
 - Safety and tolerability
- **Key Secondary Endpoints**
 - Allergic Conjunctivitis Symptom (ACS) PRO:
 - Itching, photophobia, foreign body sensation, ocular pain, and lacrimation
 - Ocular Symptom Score (OSS) Investigator assessment:
 - Itching, redness, tearing, and chemosis
 - Atopic comorbidities assessment:
 - Atopic dermatitis, asthma, rhinitis

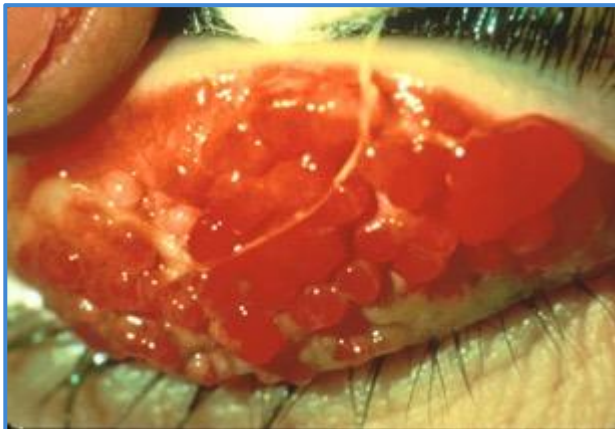
Severe Allergic Conjunctivitis



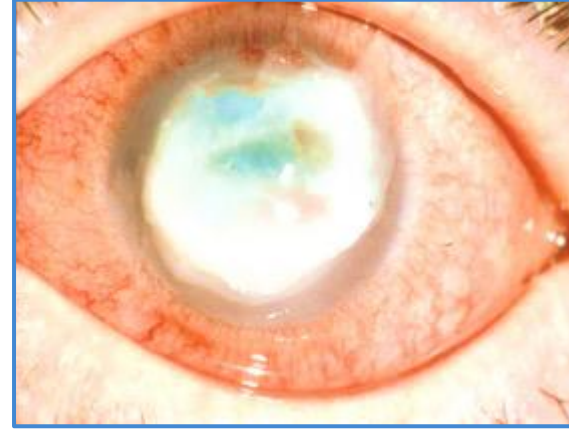
**Redness,
Chemosis**



**Photophobia,
Watering,
Periorbital
Swelling**



**Giant
Papillae**

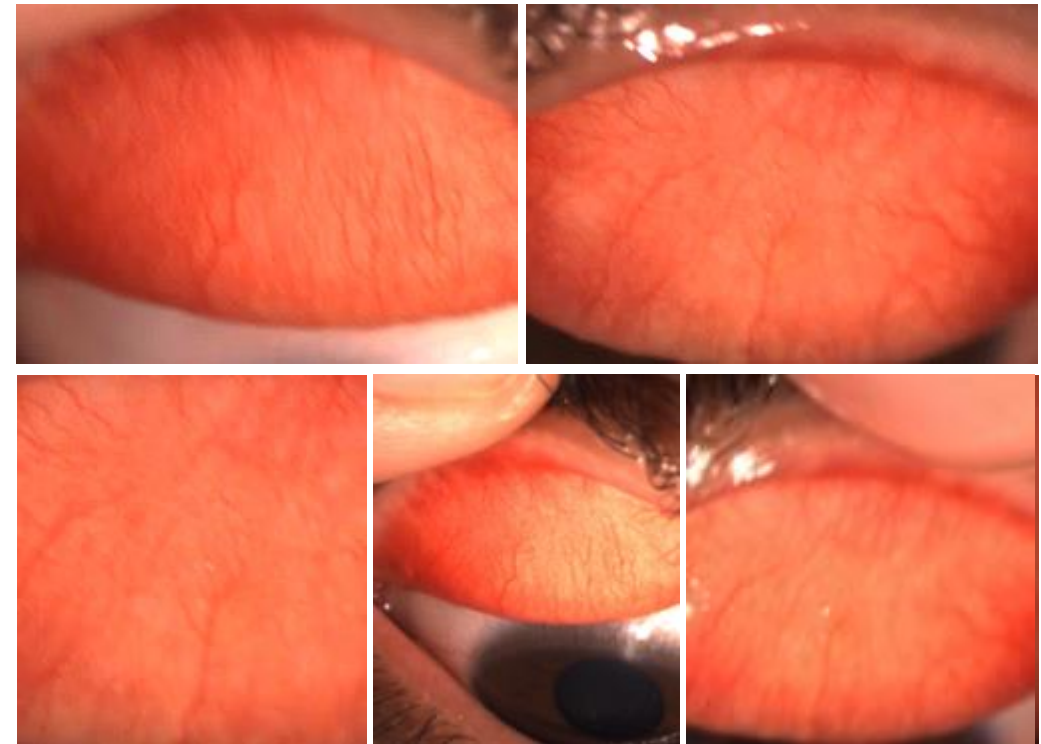
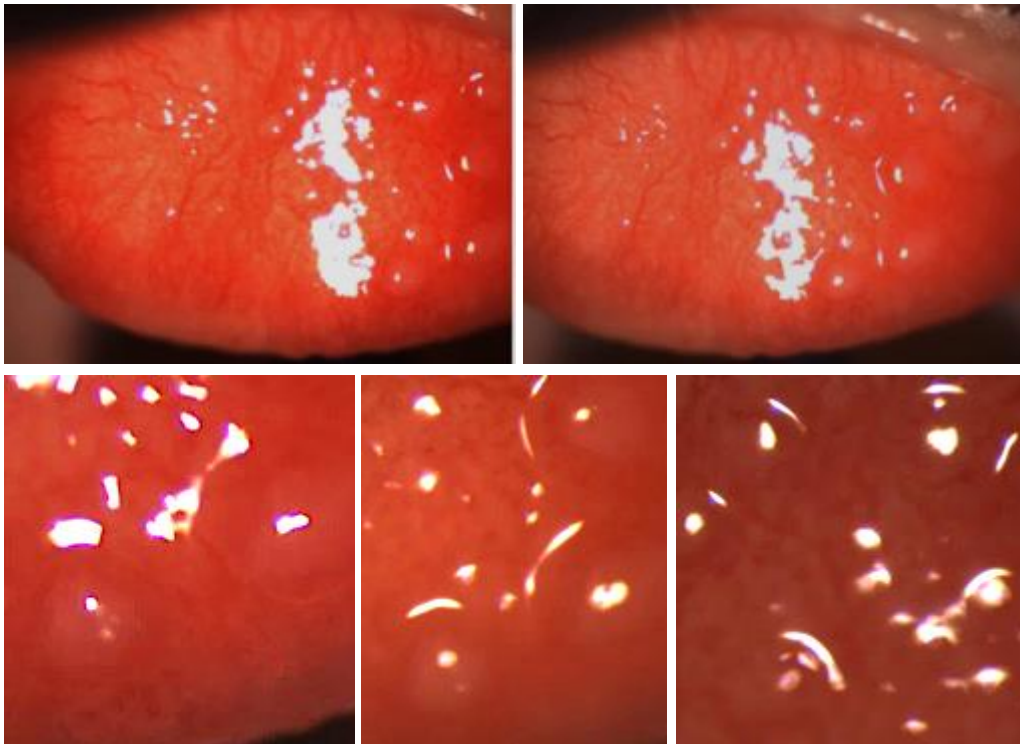


**Corneal
Ulcer
(Vision Loss)**

Case Study: Reversal of Neovascular and Inflammatory Changes

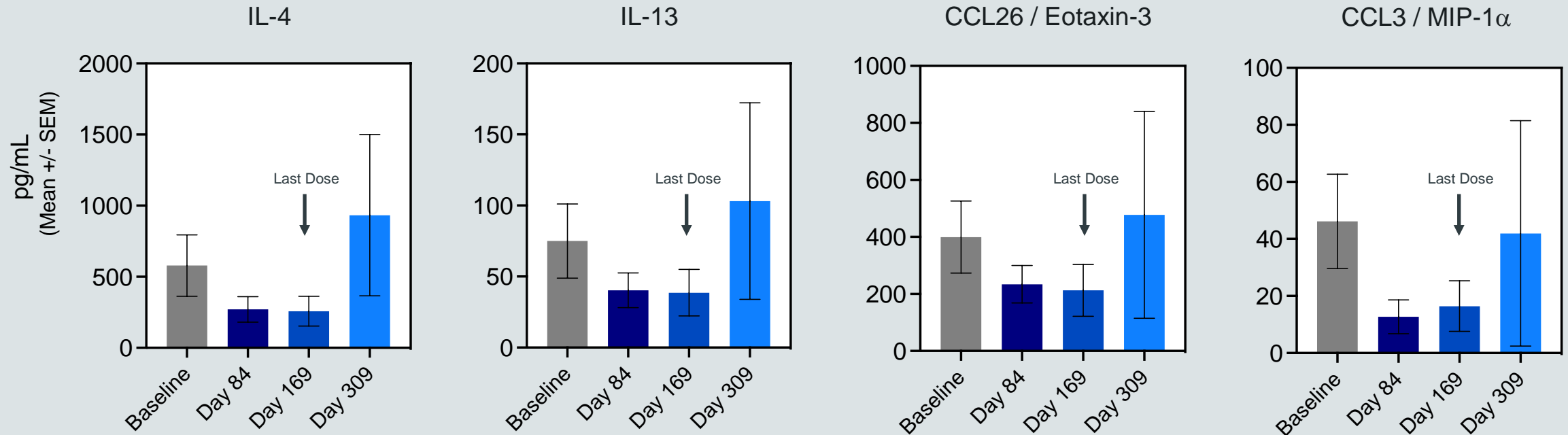
Prior to Lirentelimab

After 3 Doses of Lirentelimab

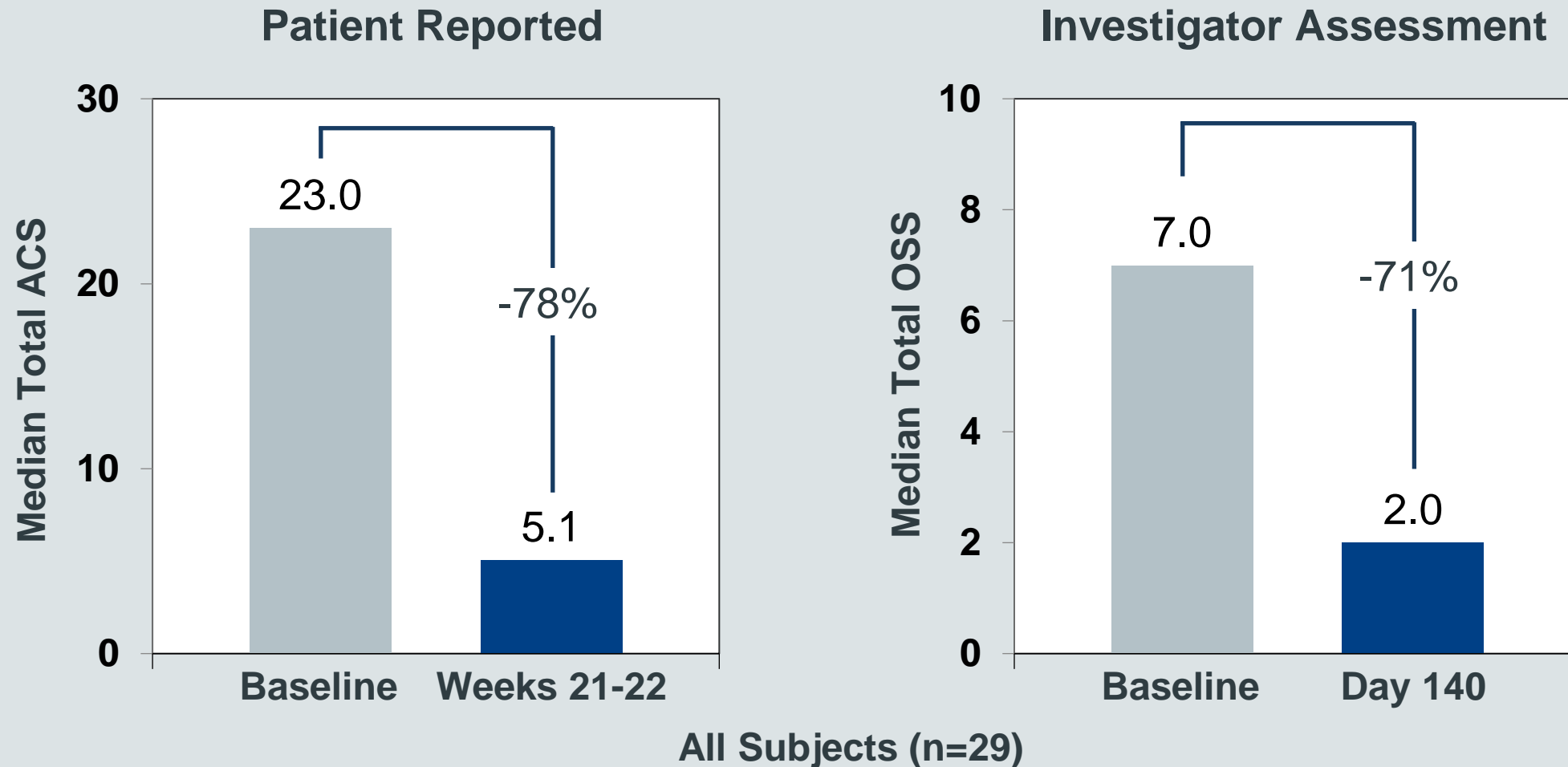


Lirentelimab Reduced Clinically-Relevant Cytokines in Phase 1 Severe Allergic Conjunctivitis Study

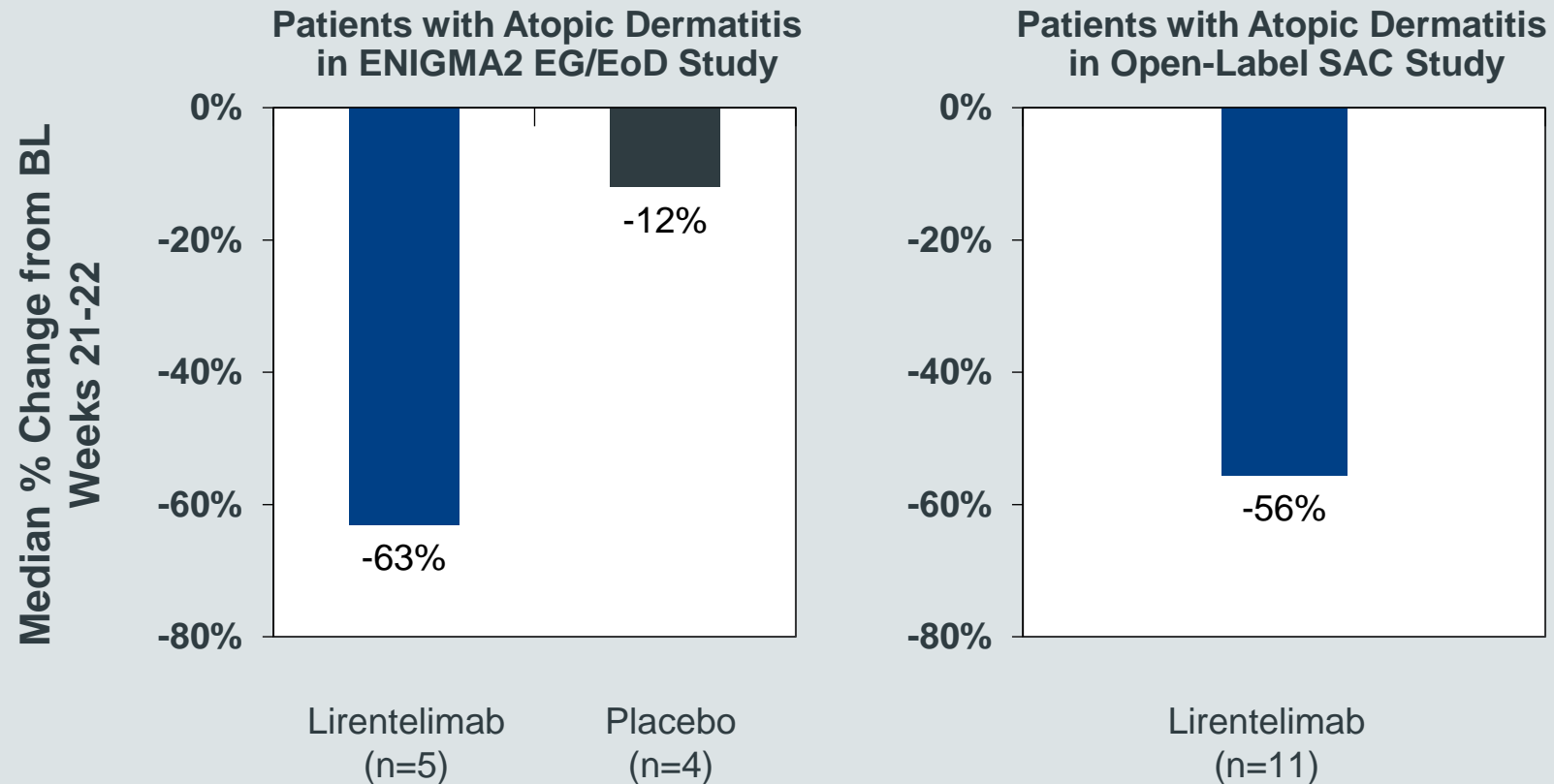
Ocular Inflammation via Tear Cytokines



Improvements in Allergic Conjunctivitis Signs & Symptoms



Lirentelimab Improved Atopic Dermatitis Symptoms in ENIGMA2 and SAC Studies



Patients with comorbid atopic dermatitis filled in a daily global disease severity questionnaire on a ten-point scale (scale of 0 to 10).

SOURCE: ENIGMA2 data on file, Post-hoc exploratory analysis; SAC Study prospective analysis from Anesi, S. et al. Journal of Allergy and Clinical Immunology 2022

Phase 2 Atopic Dermatitis Study Design

Study Design

- Multi-center, randomized, DB, placebo-controlled
- Chronic disease that has been present ≥ 3 years
 - EASI score ≥ 16
 - Involvement of $\geq 10\%$ of body surface area
 - IGA score ≥ 3
 - Inadequate control by topical treatments
- Includes patients with prior biologics treatment
- 130 adult patients (1:1 randomization)
 - 300 mg Q2W subcutaneous lirentelimab (n=65)
 - Placebo (n=65)

Endpoints

- **Primary Endpoint**
 - Proportion of patients who achieve eczema area and severity index (EASI)-75 at week 14
- **Key Secondary Endpoints**
 - Percent change in EASI from baseline to week 14
 - Proportion of patients who achieve an IGA score of 0 or 1 AND a ≥ 2 -point improvement in Investigator Global Assessment (IGA) at week 14

Atopic Dermatitis Landscape

Drug Name	MOA	EASI-75 Response	IGA Response	Opportunity
Dupixent® (dupilumab)	Anti IL-4/IL-13R mAb	44% – 51% vs. 12 – 15% placebo ¹	36 – 38% vs. 9 – 10% placebo ¹	<ul style="list-style-type: none"> >50% of patients continue to have symptoms Conjunctivitis in ~26%² Q2W dosing¹
Adbry™ (tralokinumab)	Anti IL-13 mAb	25% – 33% vs. 10% – 13% placebo ³	16 – 21% vs. 7 – 9% placebo ³	<ul style="list-style-type: none"> >50% of patients continue to have symptoms Conjunctivitis in ~10%³ Q2W dosing³
Lebrikizumab	Anti IL-13 mAb	51% – 59% vs. 16% – 18% placebo ⁴	33% – 43% vs. 11% – 13% placebo ⁴	<ul style="list-style-type: none"> >50% of patients continue to have symptoms Conjunctivitis in ~10%⁴ Q2W dosing⁴
Rinvoq® (upadacitinib)	JAK Inhibitor	60% – 80% vs. 13% – 16% placebo ⁵	39% – 62% vs. 5% – 8% placebo ⁵	<ul style="list-style-type: none"> Black box warnings for: major cardiac events, infections, malignancies⁵
Cibinqo™ (abrocitinib)	JAK Inhibitor	40% – 62% vs. 10% – 12% placebo ⁵	24% – 44% vs. 8% – 9% placebo ⁶	<ul style="list-style-type: none"> Black box warnings for: major cardiac events, infections, malignancies⁶

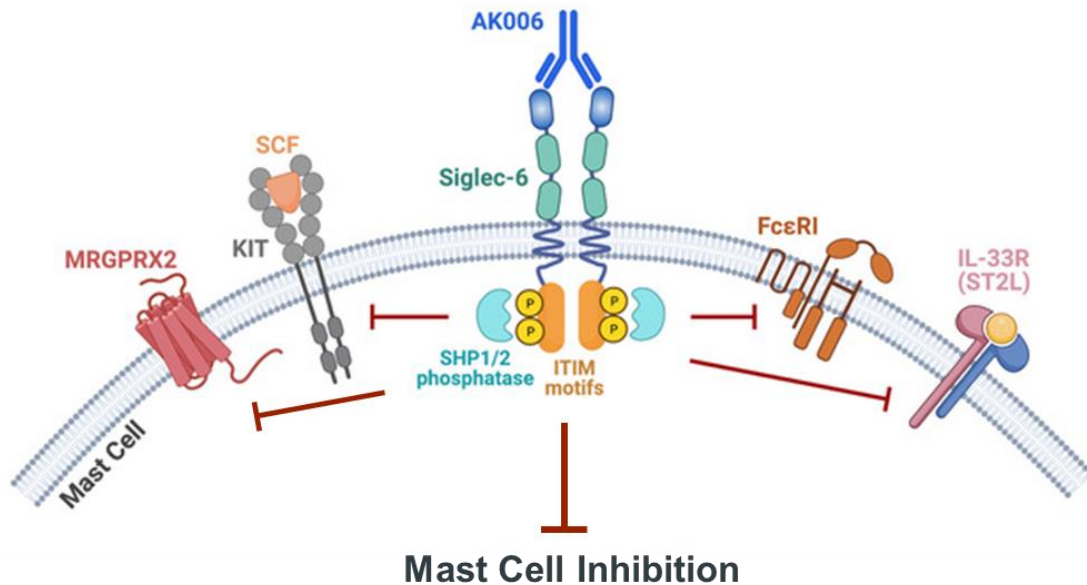
Lirentelimab Safety

Safety Summary

- Intravenous (IV) lirentelimab has been administered in >750 patients, and with >300 patients on treatment for one year or more
 - Most common adverse event has been infusion-related reactions (IRR)
 - IRRs commonly associated with IV administered ADCC antibodies
 - No long-term safety findings to date
- Subcutaneous (SC) lirentelimab is currently being used and will be used in all future studies
 - SC lirentelimab in Phase 1 healthy volunteers was well tolerated (n=36)
 - No injection site reaction or injection reactions
 - No treatment related adverse events
 - No serious adverse events

AK006: Siglec-6 mAb that Selectively and Potently Inhibits Mast Cells

AK006: Siglec-6 mAb That Inhibits and Depletes Mast Cells



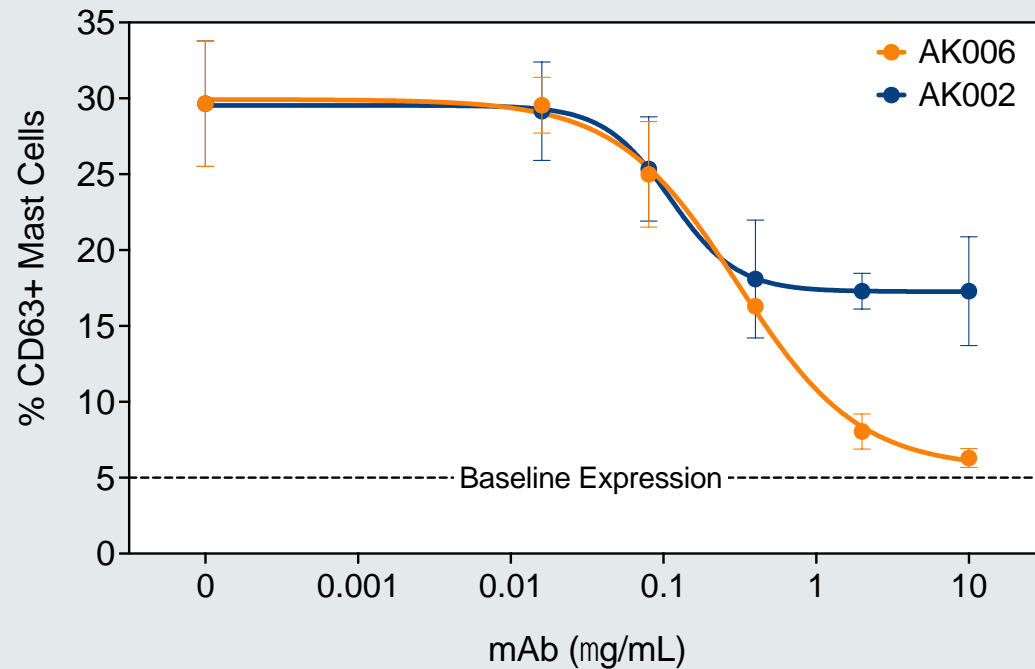
AK006 is a humanized IgG1 agonistic Siglec-6 mAb that selectively inhibits mast cells and reduces their numbers:

- AK006 inhibits mast cell activation via multiple stimuli including IgE, IL-33, SCF, C5a, MRGPRX2 and others
- Reduction of mast cells via antibody dependent cellular phagocytosis (ADCP) in the presence of activated macrophages

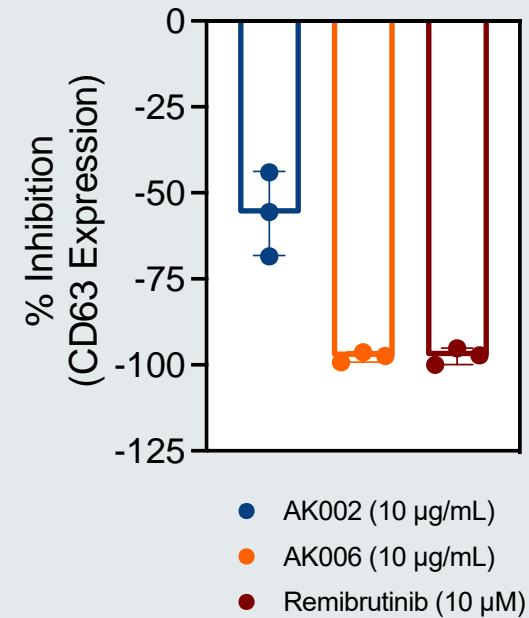
The Phase 1 study of AK006 consists of single and multiple ascending doses administered in healthy volunteers, followed by a randomized, double-blind, placebo-controlled, CSU cohort

AK006 Potently Inhibits IgE-Mediated Mast Cell Activation

AK006 Inhibits IgE-Mediated Mast Cell Activation in Human Tissue



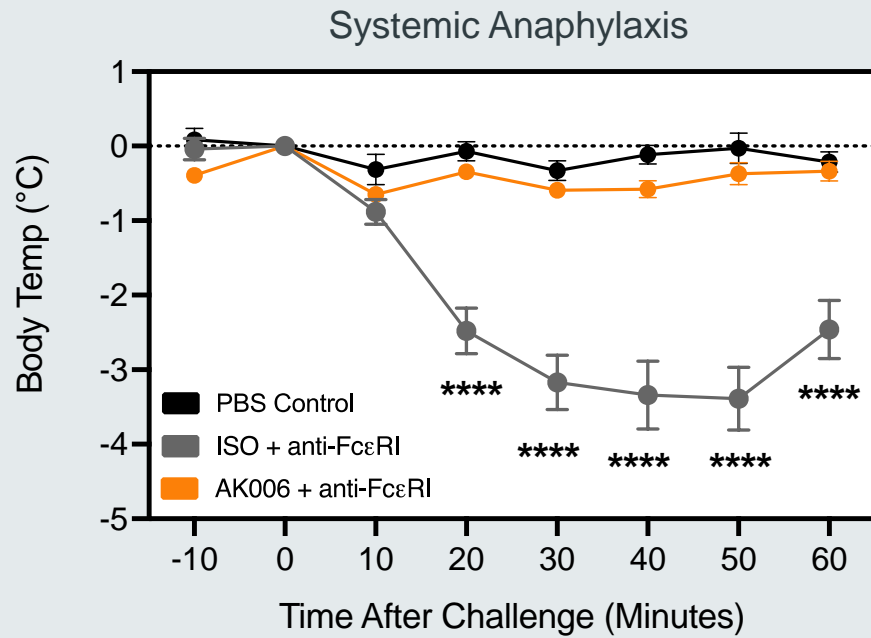
AK006 Demonstrates Comparable IgE-Mediated Mast Cell Inhibition as BTK Inhibitor in Human Tissue



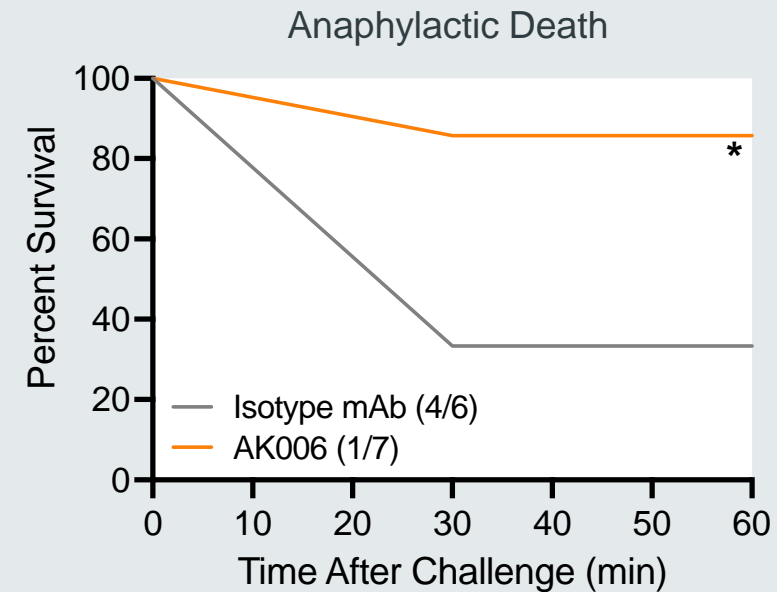
AK006 has potentially clinically meaningful mast cell inhibition

AK006 Protects Against Systemic Anaphylaxis in Humanized Mice

Humanized Mouse Model of Anaphylaxis



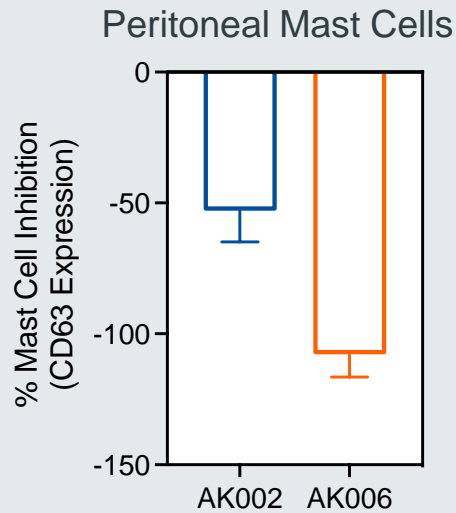
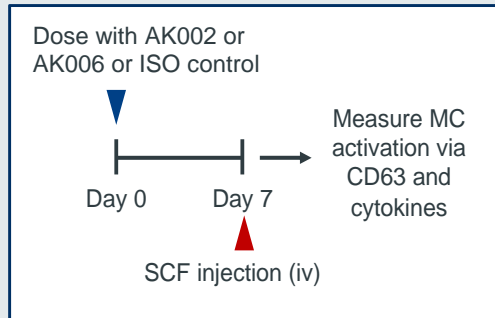
Humanized Model of Anaphylactic Death



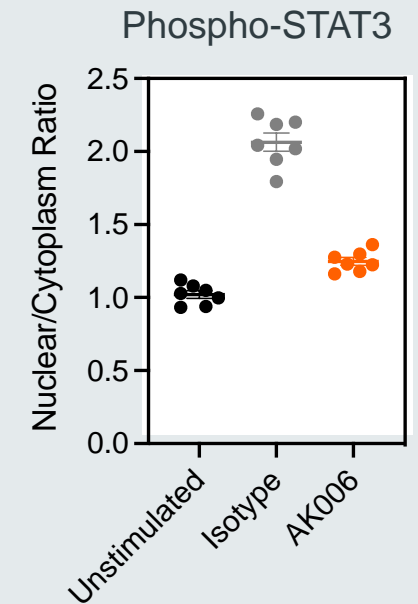
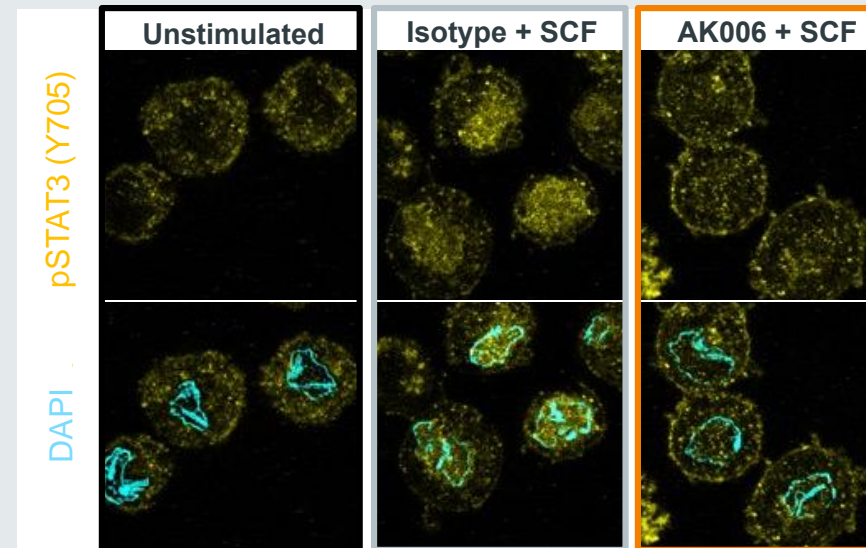
AK006 inhibits IgE-mediated mast cell activation in vivo

AK006 Inhibits KIT-Driven Mast Cell Activation

KIT-Driven Mast Cell Activation Mouse Model



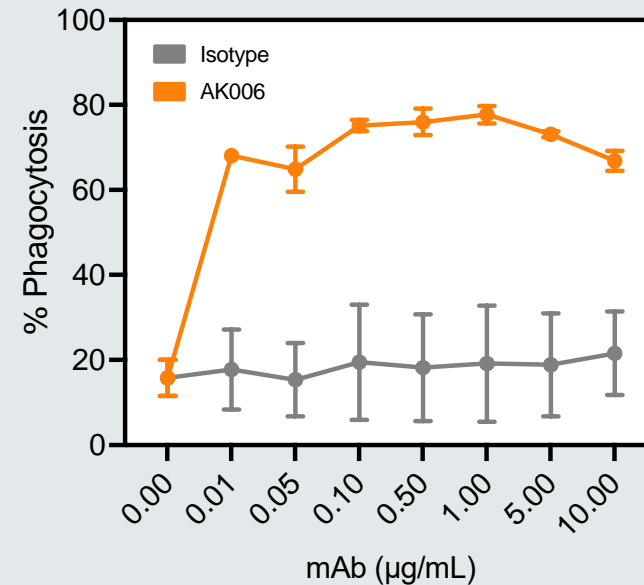
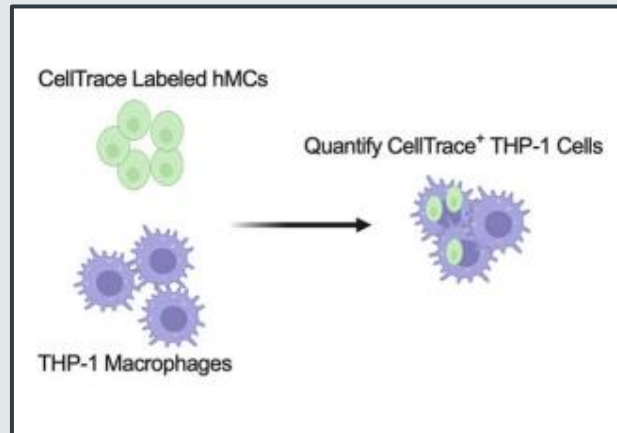
p-STAT3 Imaging in KIT-Activated Human Mast Cells



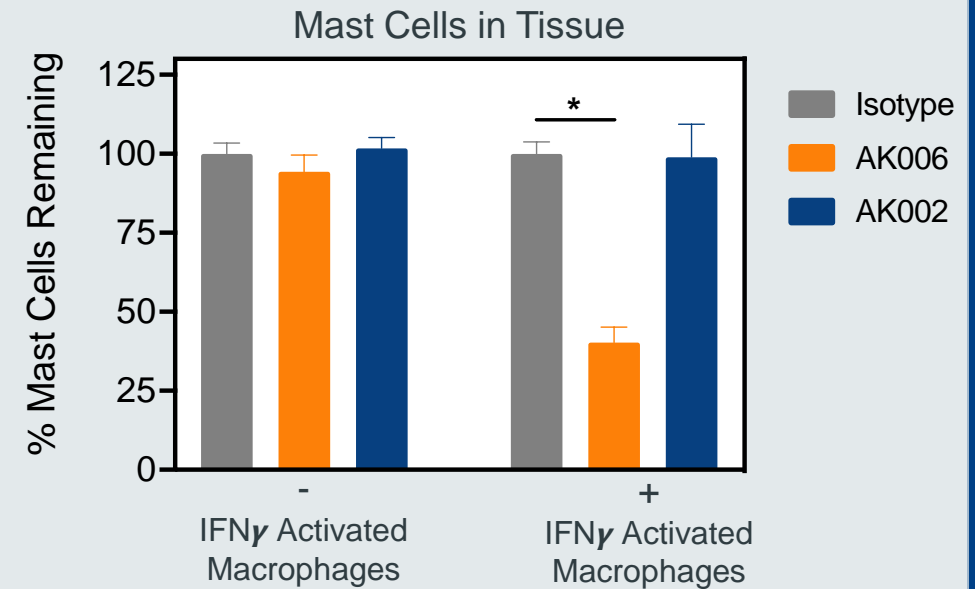
AK006 reduces KIT-mediated MC activation via inhibition of STAT phosphorylation and translocation to the nucleus

AK006 Reduces Human Mast Cells via Antibody-Dependent Cellular Phagocytosis

In Vitro ADCP Assay

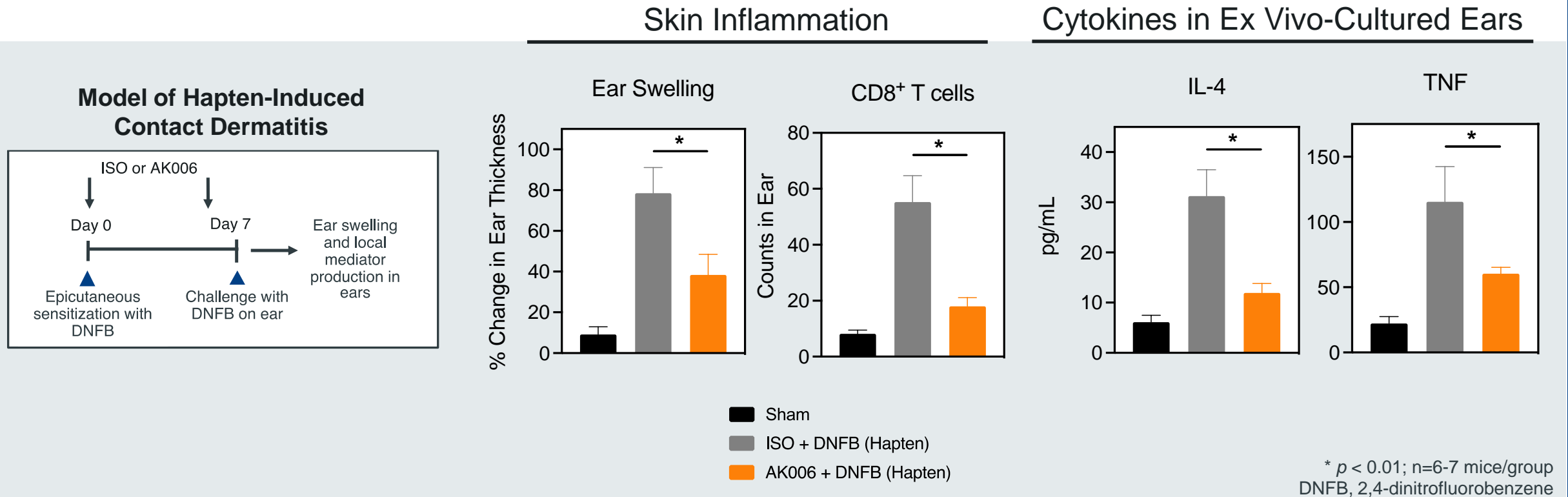


Ex Vivo Human Tissue Mast Cells



AK006 induces dual mechanism of mast cell inhibition and reduction

AK006 Inhibits Allergic Contact Dermatitis in Siglec-6 Transgenic Mice

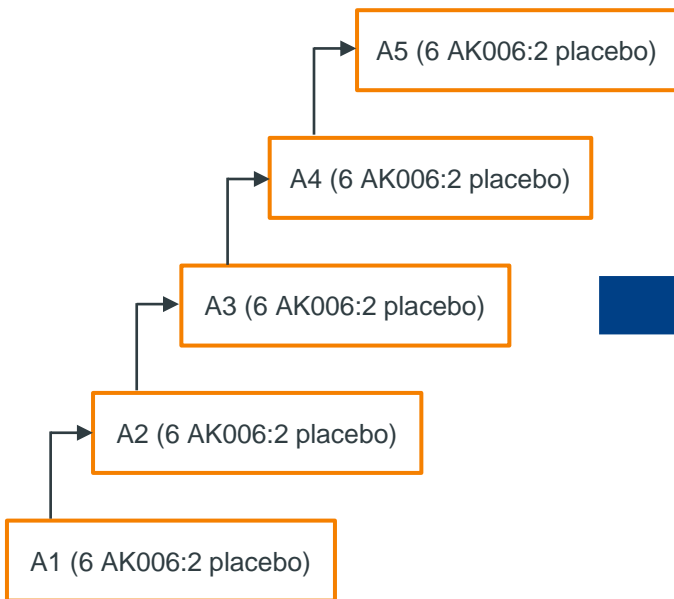


AK006 reduces skin inflammation in mice

AK006 Phase 1 Trial

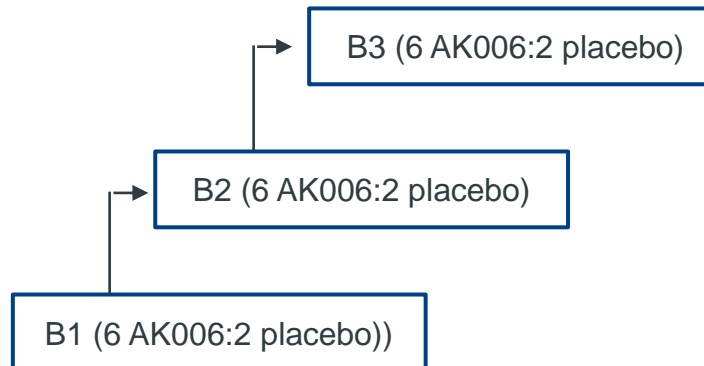
Part A: Single Ascending Doses

- Initiated 3Q23
- Double blind, placebo controlled SAD in 40 Healthy Volunteers



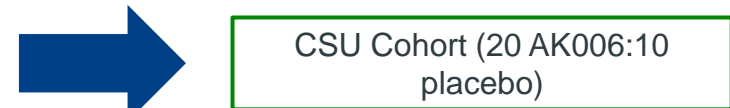
Part B: Multiple Ascending Doses

- Double blind, placebo controlled MAD in 24 Healthy Volunteers



Part C: Chronic Spontaneous Urticaria

- Expected Initiation Q2'24
- Double blind, placebo controlled multidose study in approximately 30 patients with CSU
- Option to enroll additional 30 patients (2:1 randomized) at same or 2nd dose level



Financial Overview & Key Milestones

Balance Sheet and IP Protection

Cash, Cash Equivalents and Investments in Marketable Securities as of September 30, 2023	\$193.9 M
– 3Q23 Net Cash Used	\$27.2 M
Common Shares Outstanding as of September 30, 2023	87.5 M



**First lirentelimab U.S patent
to expire in 2035 without
extensions**

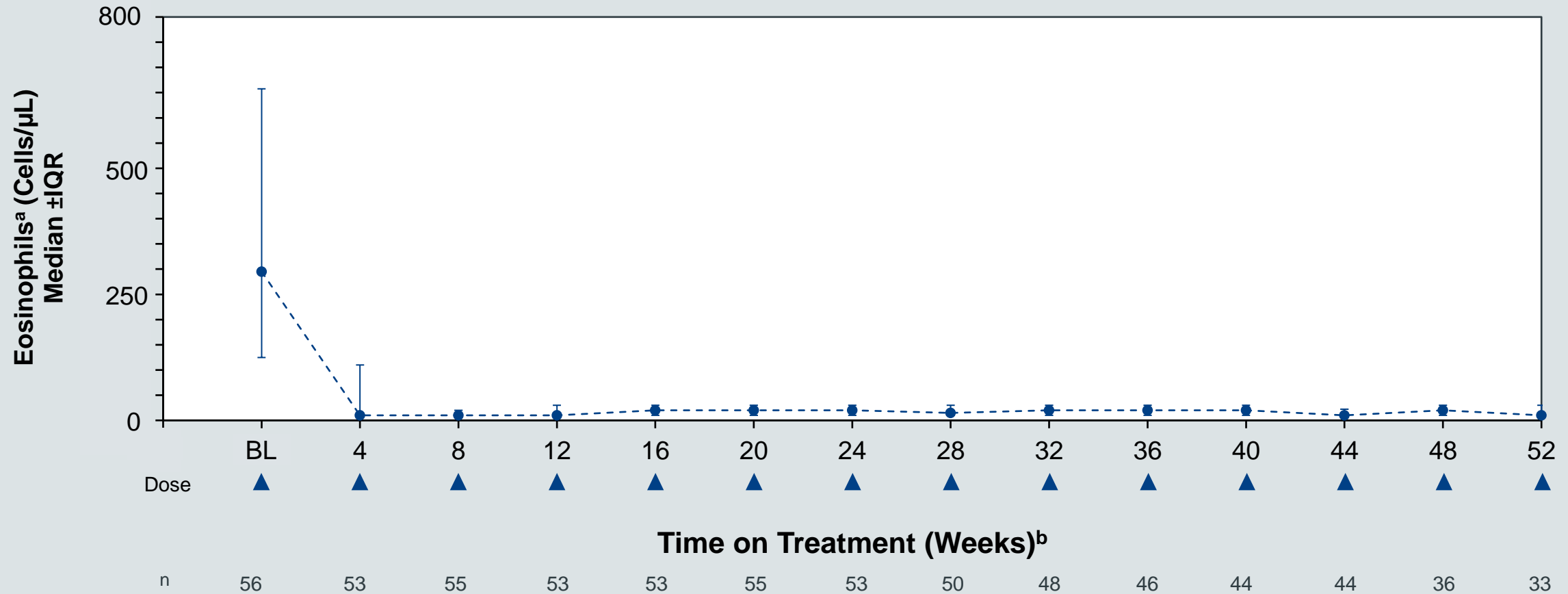


**Manufacturing SC
lirentelimab at 17K liter
scale**

Appendix

Sustained Depletion of Blood Eosinophil Counts

Phase 2 ENIGMA1 Study and Open-Label Extension



SOURCE: Dellon ES, et al. New England Journal of Medicine. 2020;383:1624-1634.

a. Blood eosinophils collected just prior to each infusion

b. Inclusive of Lirentelimab exposure during the open-label portion of the Phase 2 ENIGMA 1 study