

Allakos



Corporate Presentation

October 2024

Developing Therapeutic Antibodies
Targeting Allergic, Inflammatory and
Proliferative Disease

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Allakos Opportunity

Novel Target

- AK006 (anti-Siglec-6 mAb) selectively inhibits multiple modes of mast cell activation
 - Inhibits IgE-dependent and IgE-independent mast cell activation pathways, including IgE, KIT and MRGPRX2
 - Depletes mast cells by ADCP in the presence of activated macrophages

Significant Need for New Agents

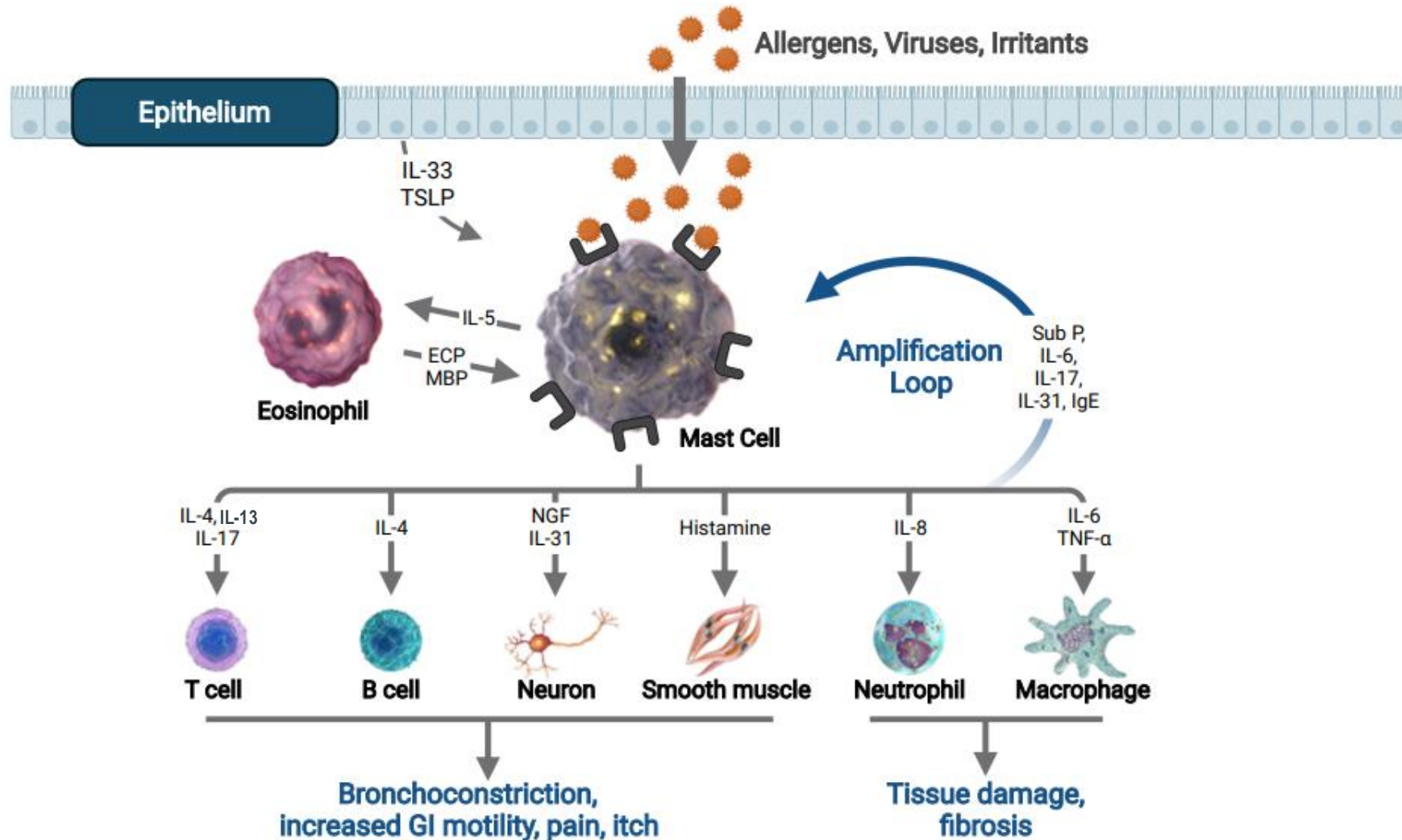
- AK006 has the potential to treat a broad range of mast cell driven diseases
- IV and SC formulations of AK006 achieved high Siglec-6 occupancy on skin mast cells
- SC Formulation of AK006 has high bioavailability and was well-tolerated
- AK006 is being tested in Chronic Spontaneous Urticaria (CSU)

Upcoming Data Catalysts and Expected Milestones

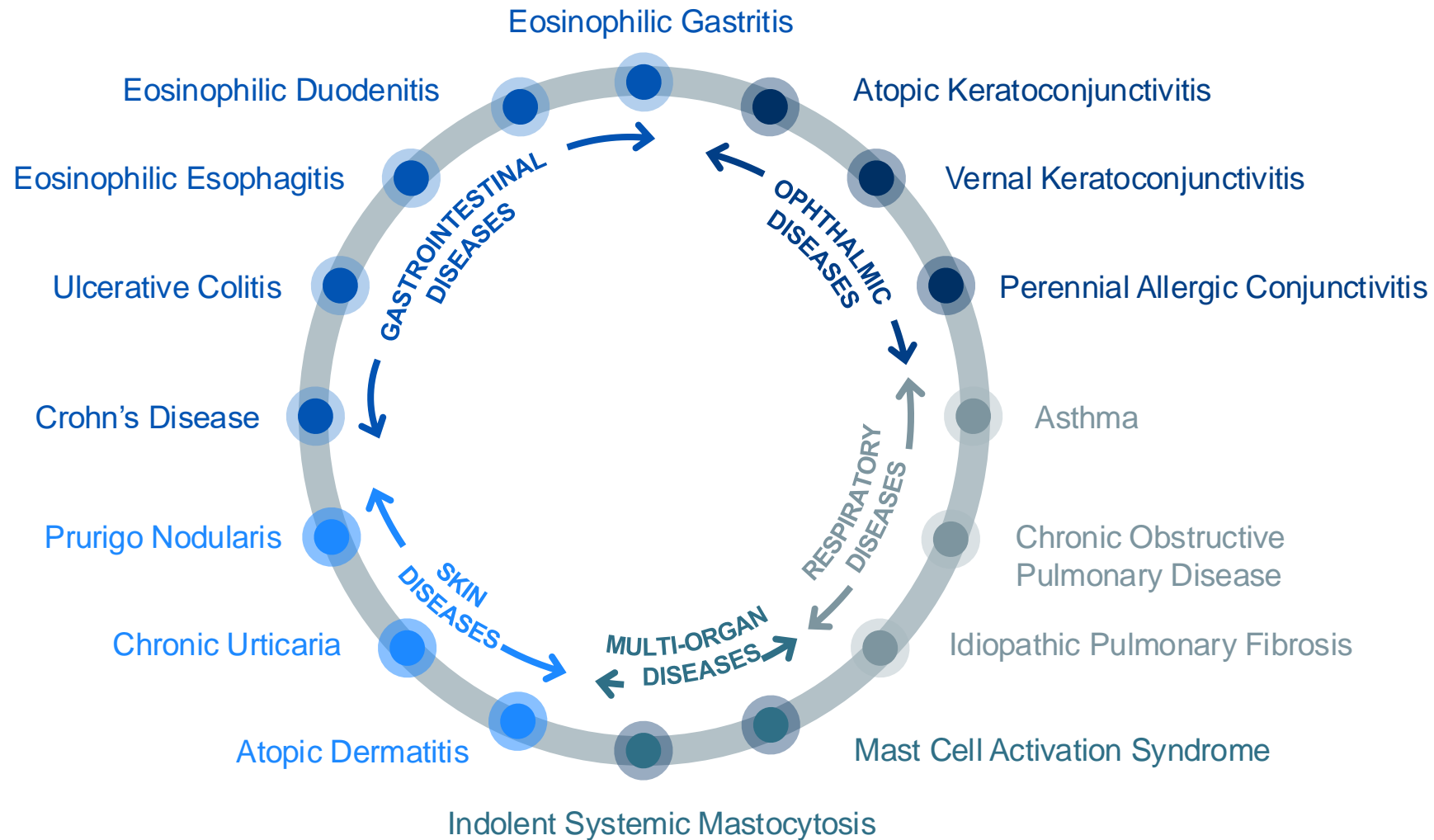
Milestones

- Early Q1'25 – Report topline Phase 1 data of AK006 in patients with CSU

Mast Cells Are Key Drivers of Inflammatory Disease

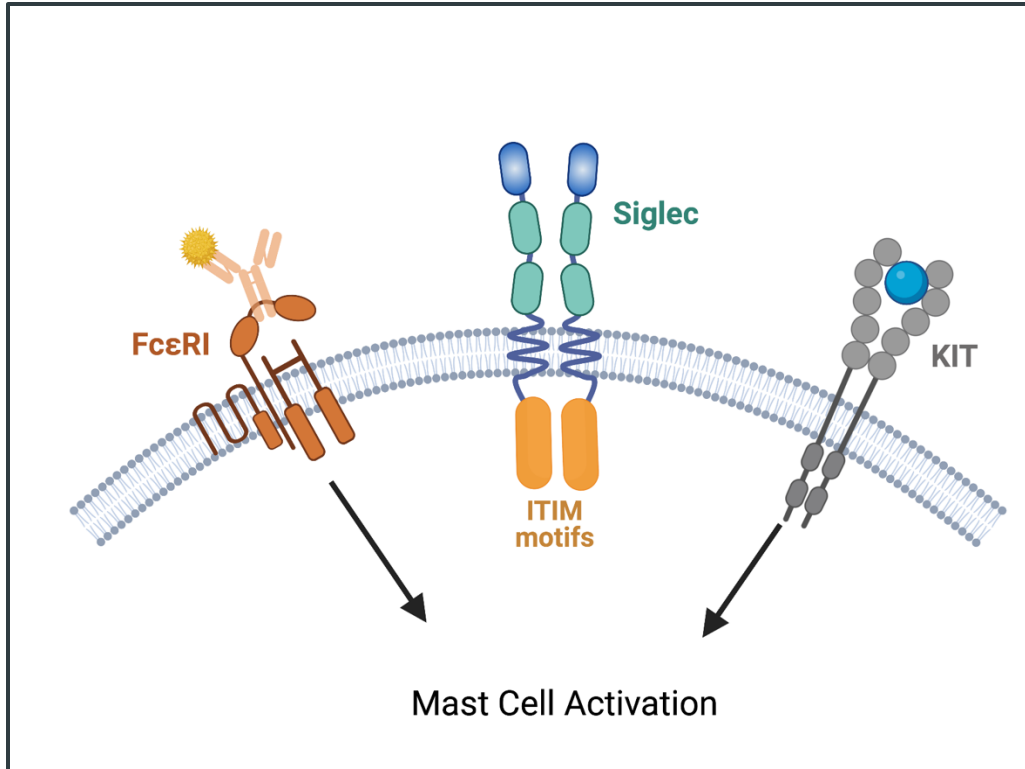


Mast Cells Play a Significant Role in Many Diseases



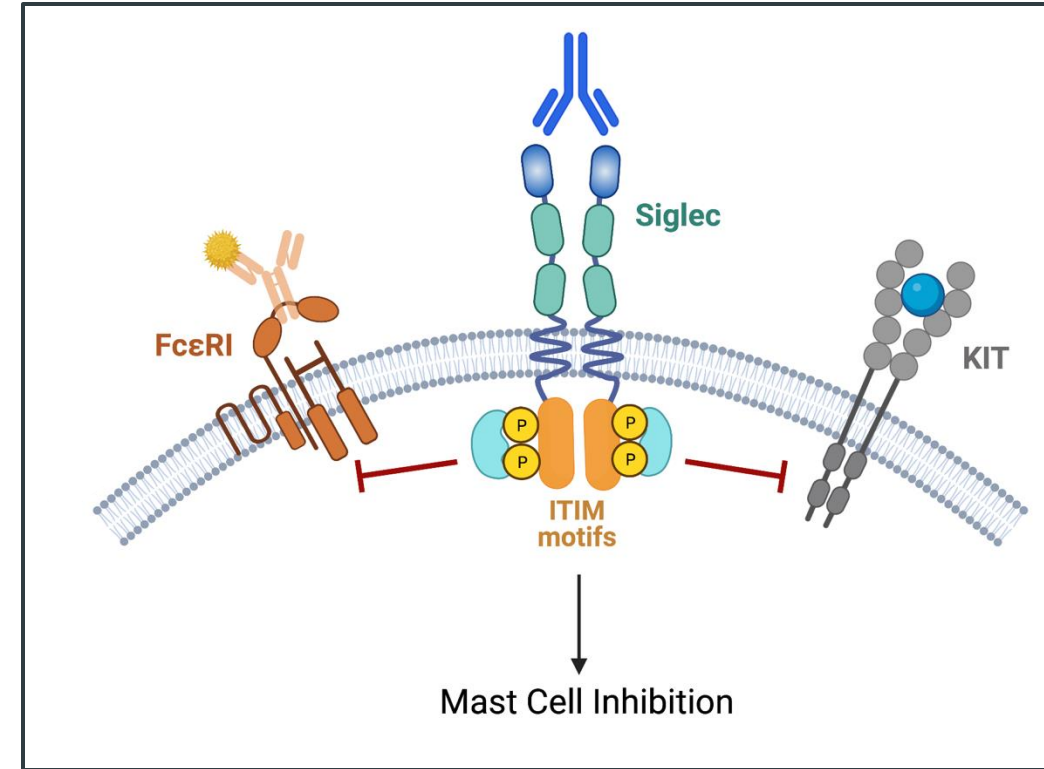
Leveraging the Native Inhibitory Function of Siglecs on Mast Cells

Activated State



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

Siglec-Mediated Inhibition



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

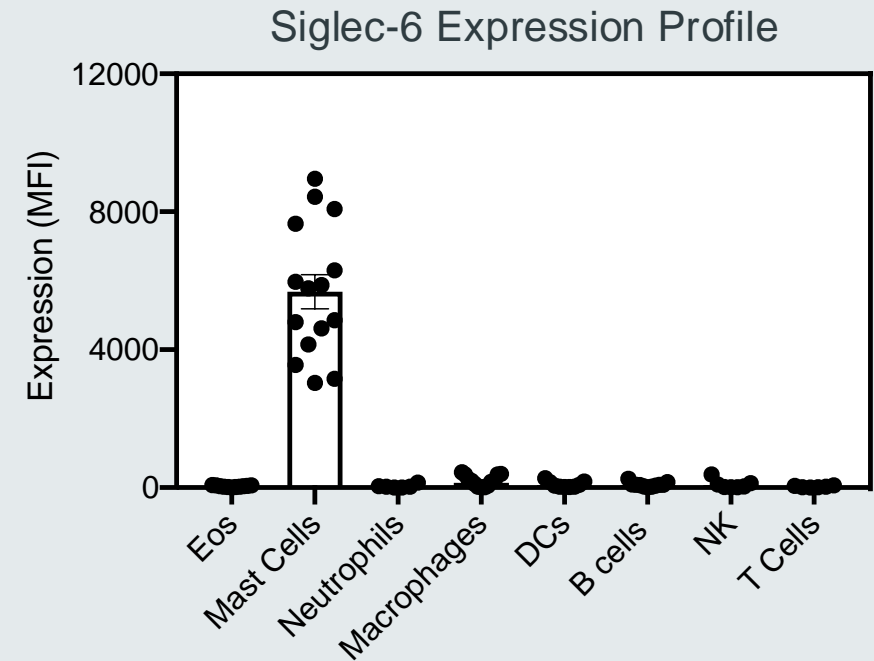
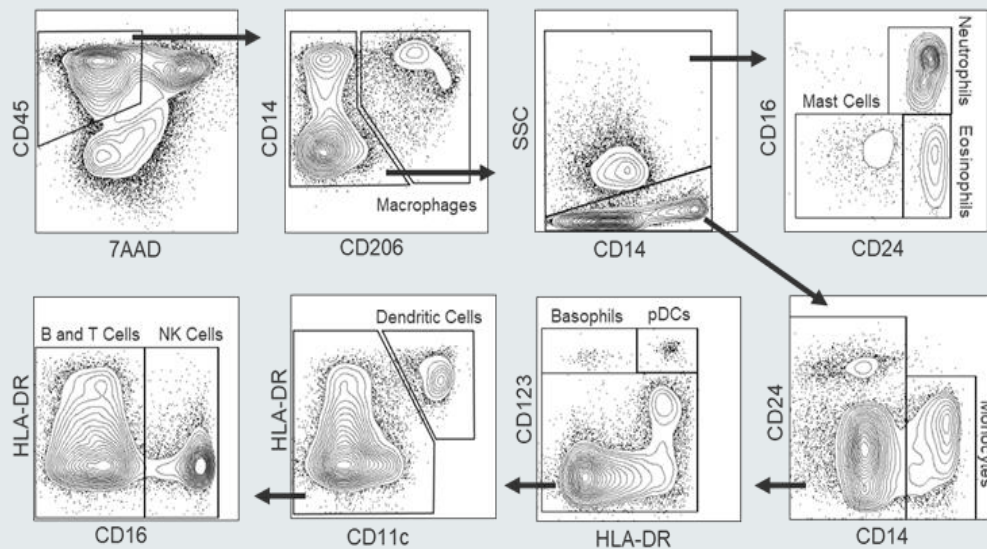
Allakos Pipeline

Program	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Milestone
AK006 (Anti-Siglec-6)	Healthy Volunteers & CSU	[Progress bar spanning Discovery, Preclinical, and Phase 1]					CSU results expected early Q1'25
AK068 (Siglec-6/Siglec-8 Bispecific)	Inflammatory Diseases	[Progress bar spanning Discovery and Preclinical]					Ongoing
Undisclosed	Inflammatory Diseases	[Progress bar in Discovery]					Ongoing

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

Siglec-6 Is Selectively Expressed on Human Tissue Mast Cells

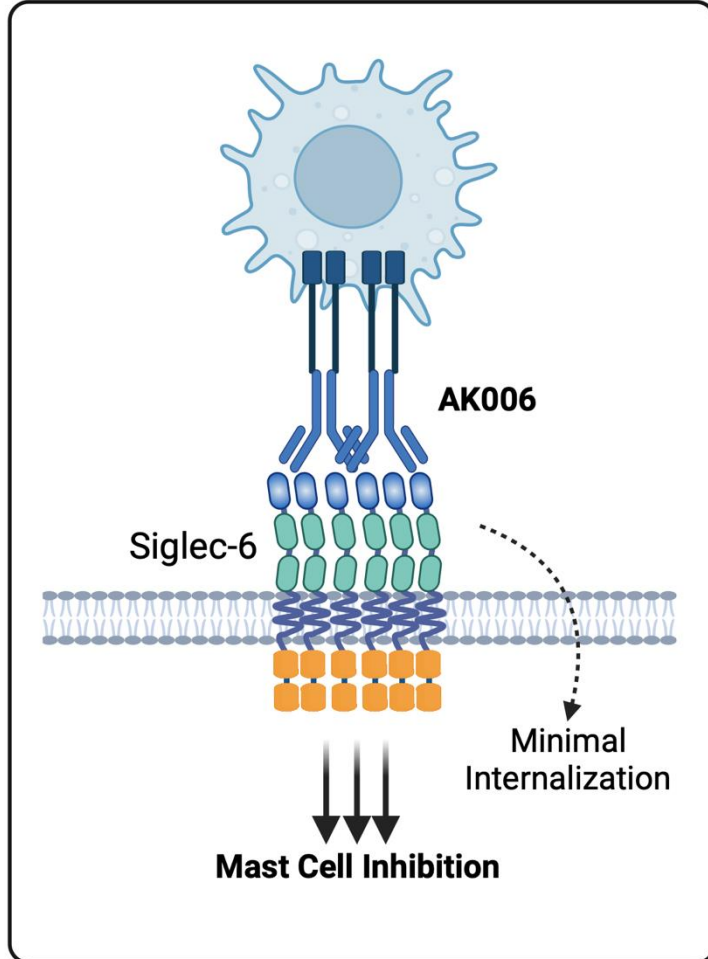
Gating Strategy for Immune Cells in Human Tissue



Siglec-6 represents a selective mast cell inhibitory receptor

AK006 was Designed to Activate the Native Function of Siglec-6

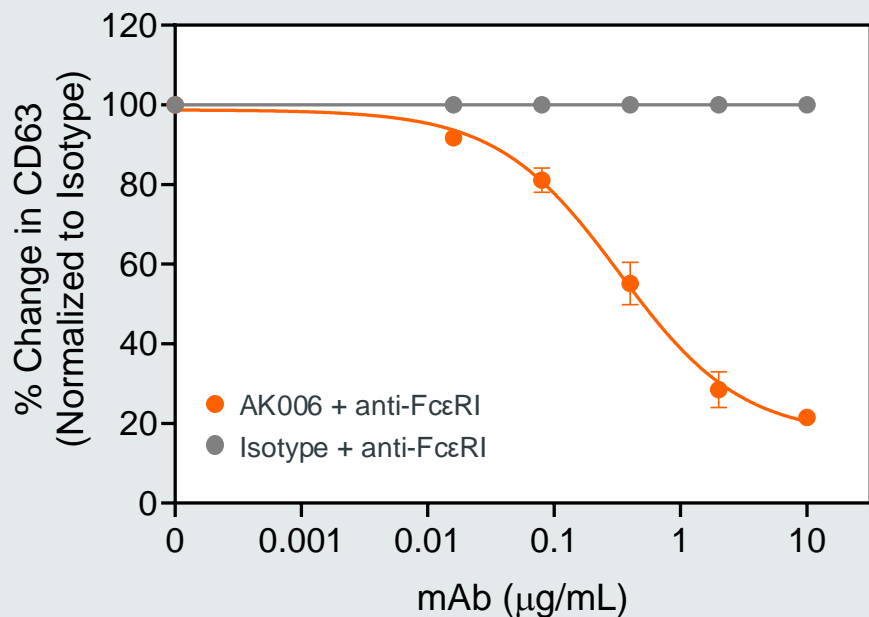
AK006 Mechanism of Action



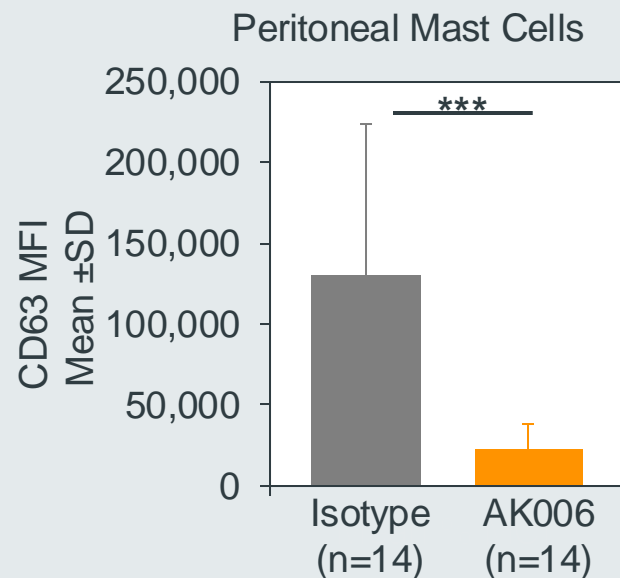
- The inhibitory mechanism has the potential to inhibit multiple modes of mast cell activation
- Mast cell inhibition by AK006 requires Fc-Fc γ receptor interaction
- AK006 has high residence time due to minimal receptor internalization, potentially leading to higher levels of inhibition
- AK006 induces antibody dependent cellular phagocytosis in the presence of activated macrophages

AK006 Displays High levels of Mast Cell Inhibition in Preclinical Studies

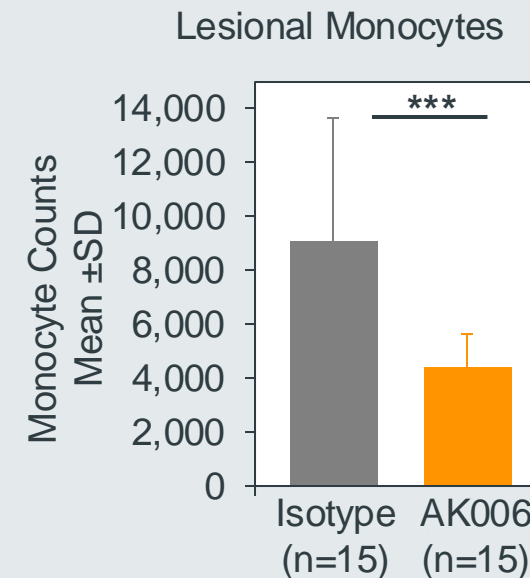
IgE Activation



KIT Activation



MRGPRX2 Activation



n=3 human donors

AK006 inhibits IgE-dependent and IgE-independent modes of mast cell activation

*** p < 0.001

SOURCE: Korver, W. et al *Allergy* 2024; Allakos data on file

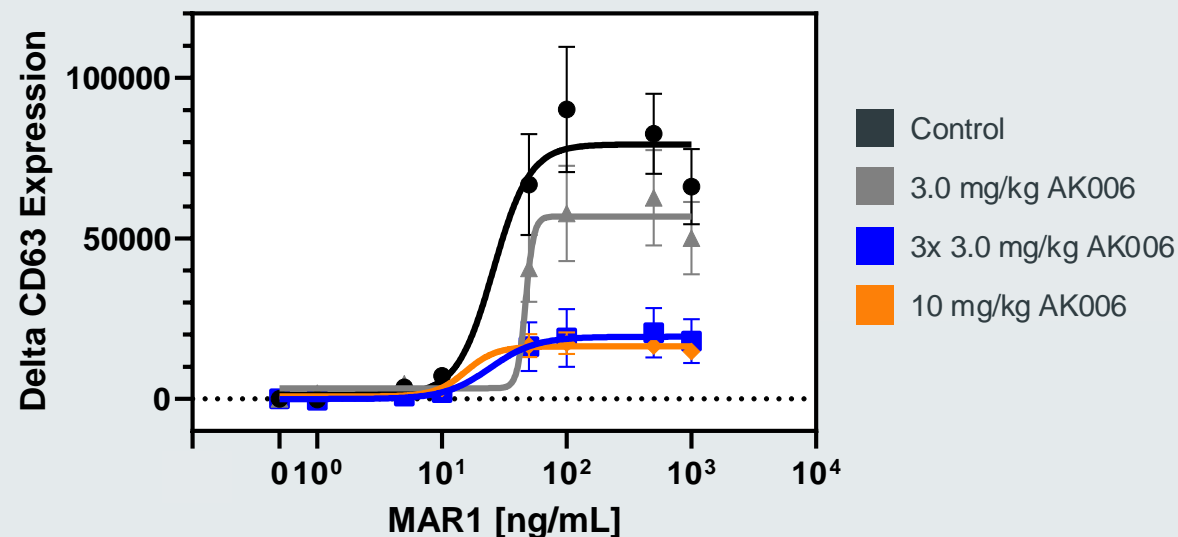
Systemic Administration of AK006 Prevents Ex-Vivo IgE Activation of Mast Cells

i.v. AK006 3 mg/kg or
i.v. AK006 10 mg/kg or
i.v. AK006 3 mg/kg Q4D



Peritoneal Mast Cells are isolated and challenged with anti-FcεRI antibody for 20 minutes.

Mast Cell Activation



Multiple dosing of AK006 provides more potent Mast Cell inhibition

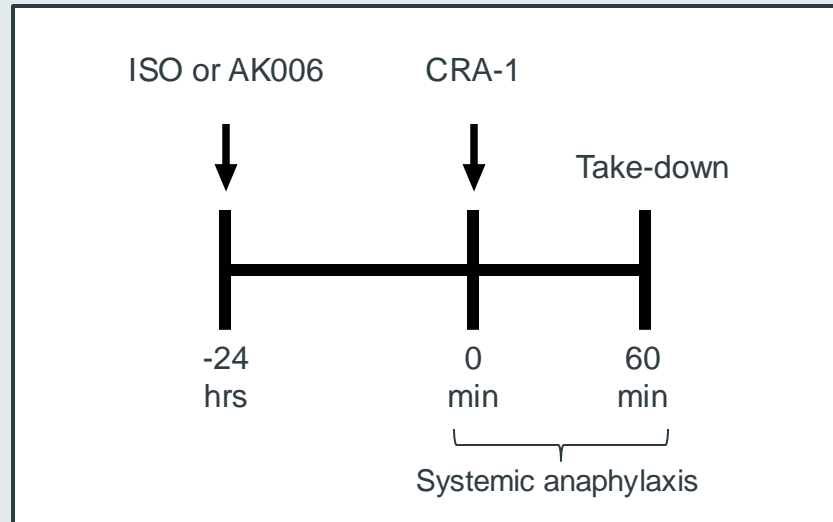
N = 4-6 mice per group

SOURCE: Allakos data on file

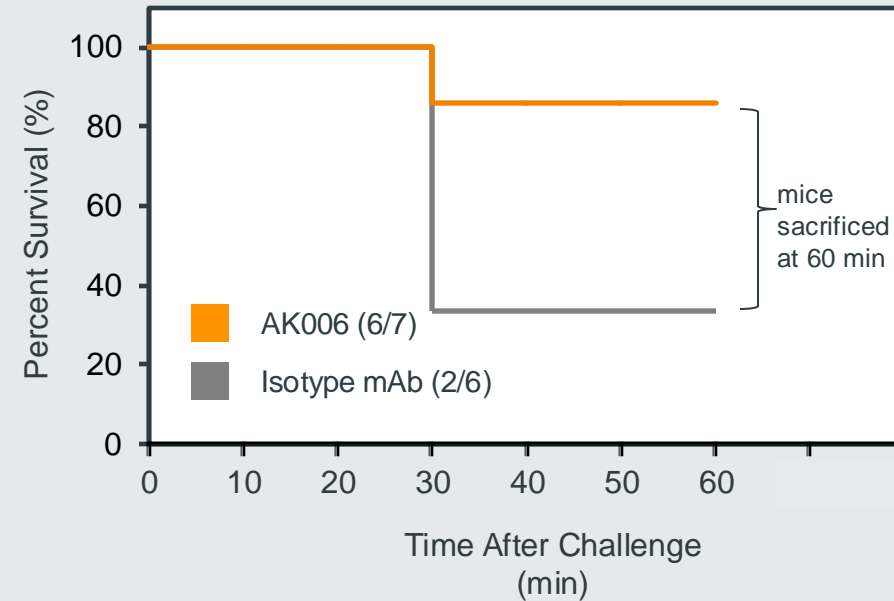
AK006 Protects Against Systemic Anaphylaxis in Humanized Mice

Humanized Model of Anaphylactic Death

Experimental Design



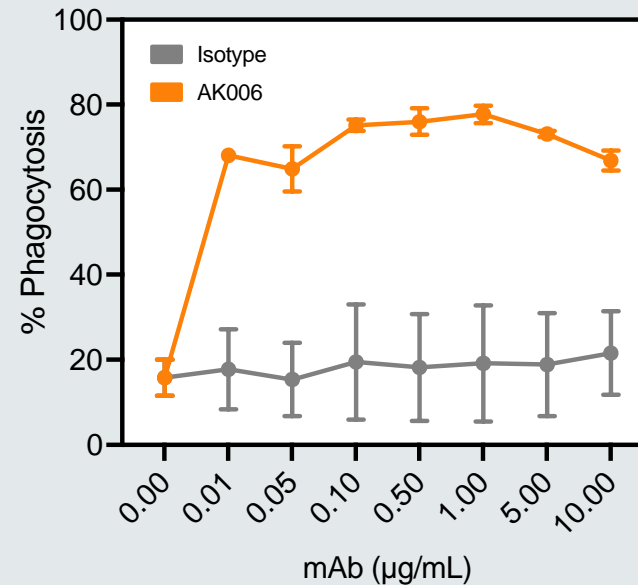
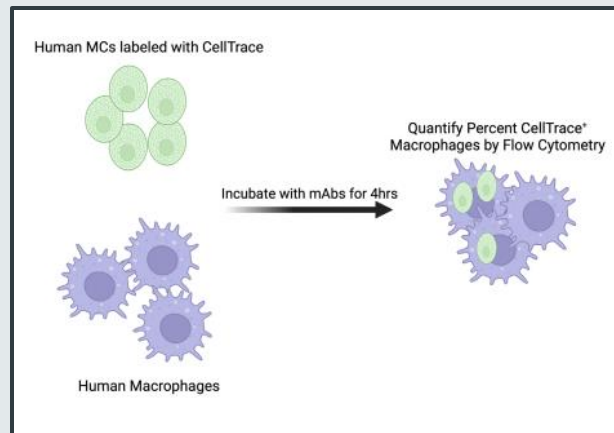
Kaplan-Meier



AK006 protects mice from IgE-induced anaphylactic death

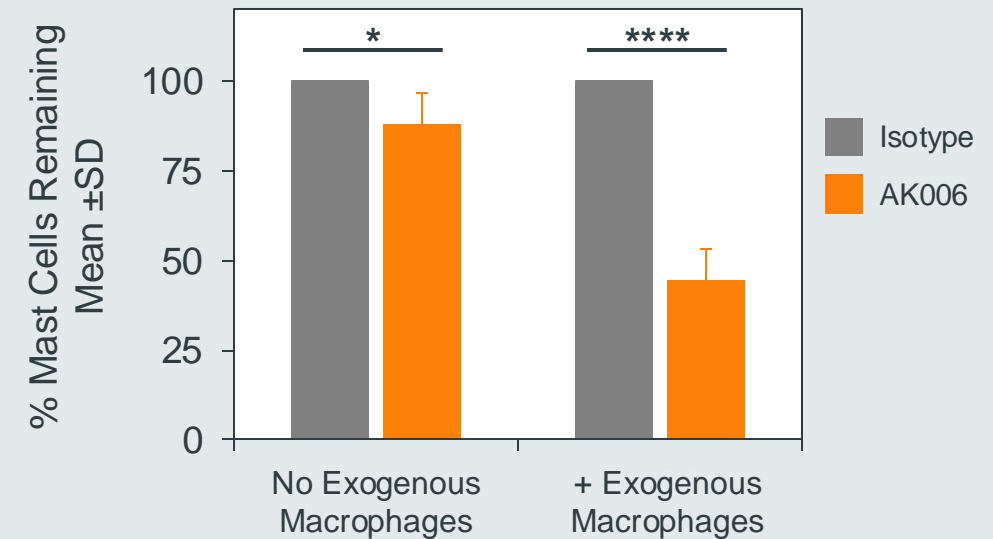
AK006 Reduces Human Mast Cells via Antibody-Dependent Cellular Phagocytosis in Preclinical Studies

In Vitro ADCP Assay



Ex Vivo Human Tissue Mast Cells

Mast Cells in Tissue

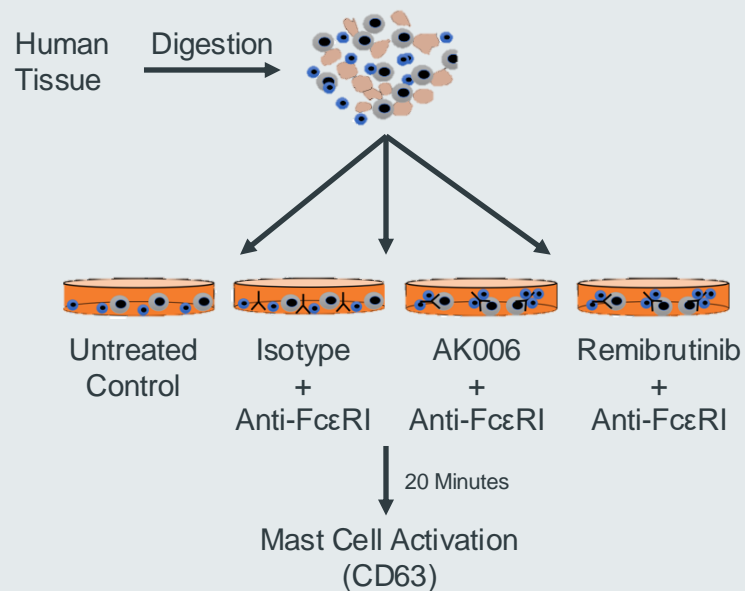


In addition to mediating broad inhibition, AK006 can reduce mast cell numbers

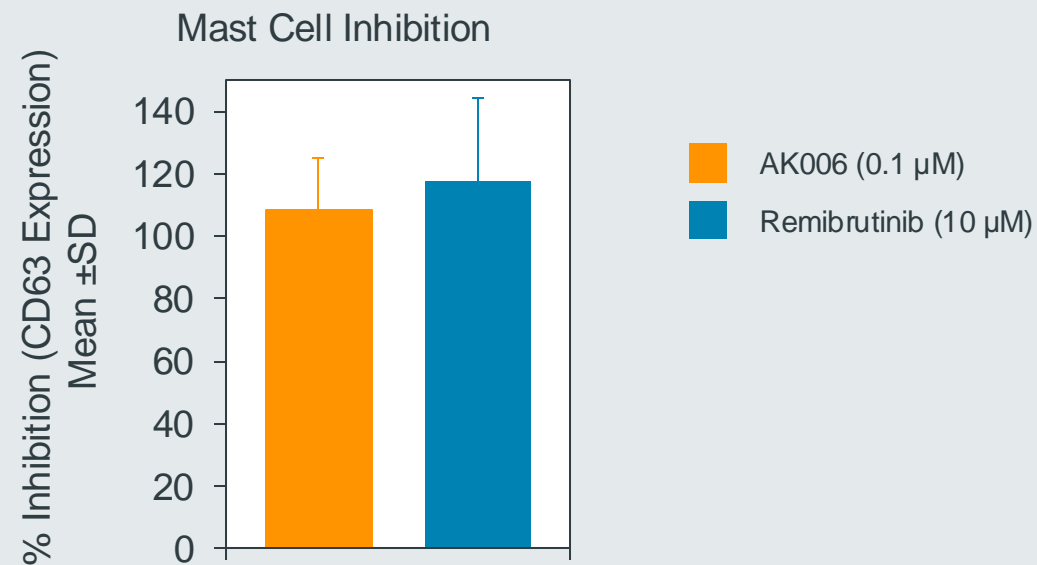
* p < 0.05; **** p < 0.0001; n=2 human donors

AK006 Inhibits IgE-Mediated Mast Cell Activation Similar to Remibrutinib

Human Mast Cell Activation Assay



IgE-Activated Human Tissue Mast Cells



n=5 human donors

SOURCE: Allakos data on file

AK006 in Phase 1 Clinical Study in Healthy Volunteers and Chronic Spontaneous Urticaria

AK006 Phase 1 Study Design

Trial Cohorts

Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) Cohorts in Healthy Volunteers

- Randomized, double-blind, placebo-controlled
- Intravenous AK006
 - SAD: 5, 20, 80, 240, 720 mg
 - MAD: 80, 240, 720 mg monthly
- Subcutaneous AK006
 - 150 and 720 mg

Planned CSU Cohort

- Randomized, double-blind, placebo-controlled
- Moderate-to-severe antihistamine refractory CSU
 - UAS7 score ≥ 16 and HSS7 score ≥ 8 at baseline
- Four doses of AK006 IV given monthly

Endpoints

SAD and MAD Cohort

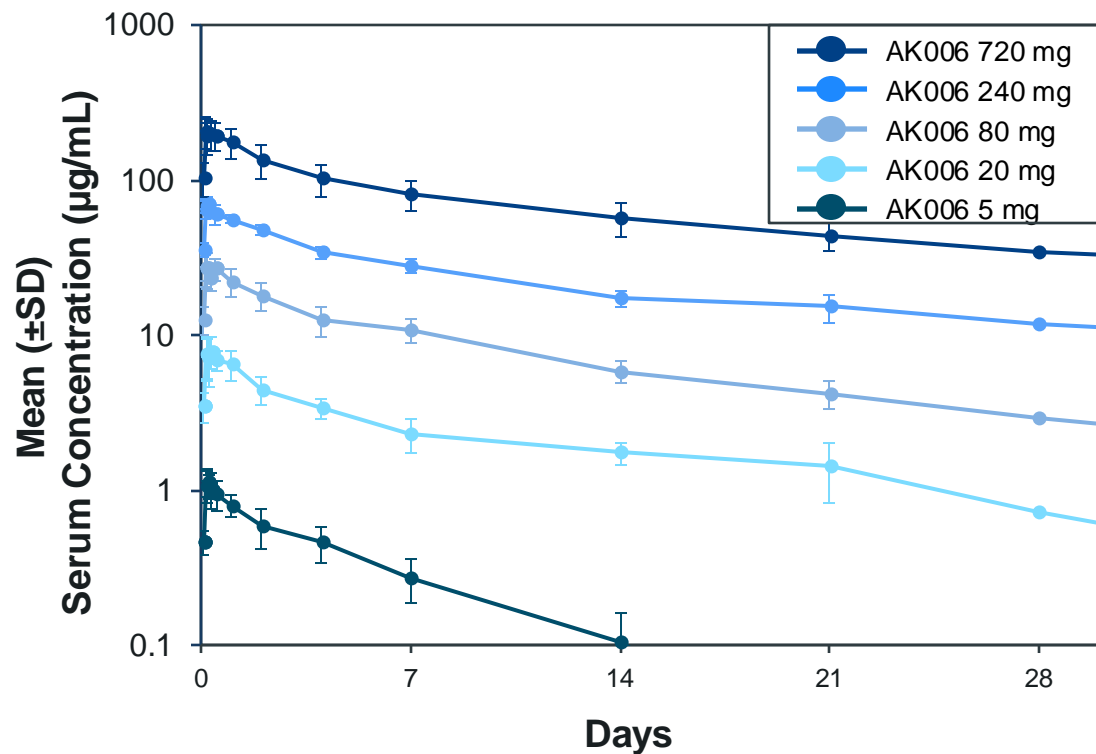
- Safety and tolerability
- Pharmacokinetics
- Pharmacodynamics
- Target receptor engagement in skin biopsies
- SC Bioavailability

CSU Cohort

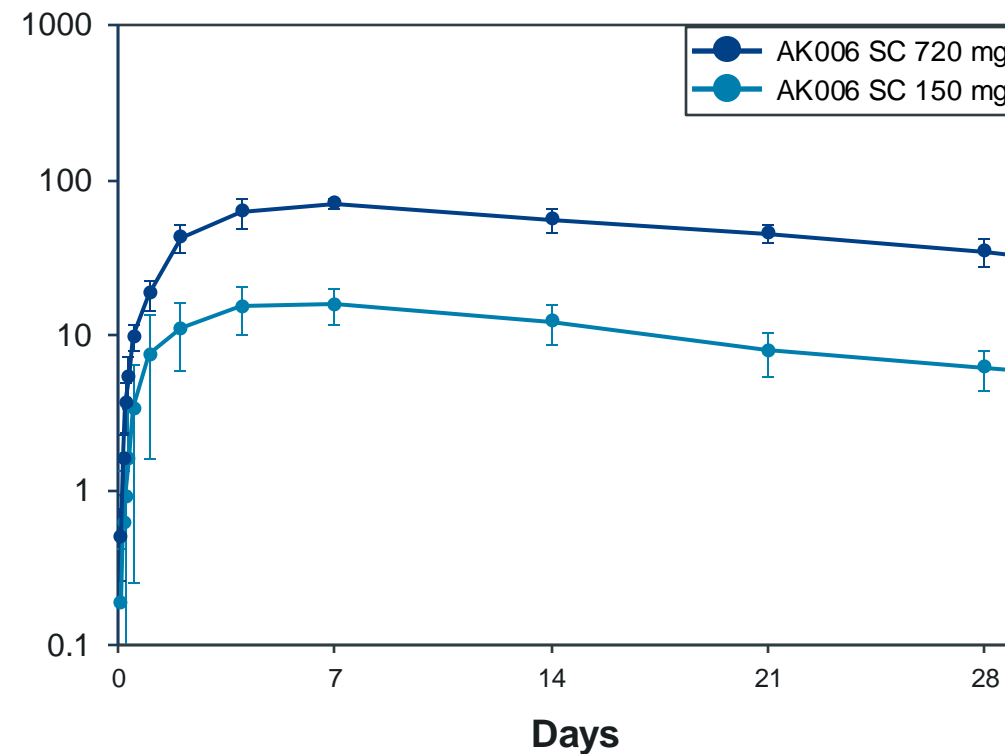
- Therapeutic activity assessed by changes in UAS7 at week 14
- Safety and tolerability

Subcutaneous AK006 has 77% Bioavailability

Single-dose IV



Single-dose SC



SC and IV AK006 have good pharmacokinetic properties
with a half life of 12-22 days

High Siglec-6 Occupancy is Observed at Low Doses

The high occupancy levels on skin mast cells from healthy volunteer biopsies confirm that systemically administered AK006 has good distribution into the skin

SC and IV AK006 provided mean Siglec-6 receptor occupancy >90% with low receptor internalization

High doses of AK006 provided high occupancy at Day 113 suggesting the potential for infrequent dosing

Siglec-6 Receptor Occupancy

(mean, %)

Route	Dose Cohort (mg)	n	S6 % Receptor Occupancy			% Surface Siglec-6 Day 29 [†]
			Baseline	Day 29	Day 113 [*]	
IV & SC	PBO	19	0	2	2	103
	5	7	0	45	-	82
SAD IV	20	6	0	92	-	68
	80	6	0	96	-	133
	240	6	0	94	93	162
	720	6	0	101	94	139
SC	150	6	0	78	54	88
	720	6	0	94	98	102

Each patient (n) received a biopsy at (1) baseline and (2) either Day 8 or Day 29;

* Day 113 samples were not collected for 5mg, 20mg, 80mg dose groups

† % Total Siglec-6 on cell surface at Day 29 relative to baseline

AK006 was Well-Tolerated with a Favorable Safety Profile

- Single and multiple doses of IV AK006 and single doses of SC up to 720 mg were well-tolerated with a favorable safety profile. In the safety profile to date:
 - No treatment emergent SAEs in subjects on AK006
 - There were no treatment emergent adverse events leading to discontinuation of AK006
 - There were no dose limiting toxicities
 - The most common adverse events ($\geq 10\%$) occurring more frequently in subjects on AK006 were headache and dysmenorrhea, all of which were mild-to-moderate in severity

AK006 for Chronic Spontaneous Urticaria

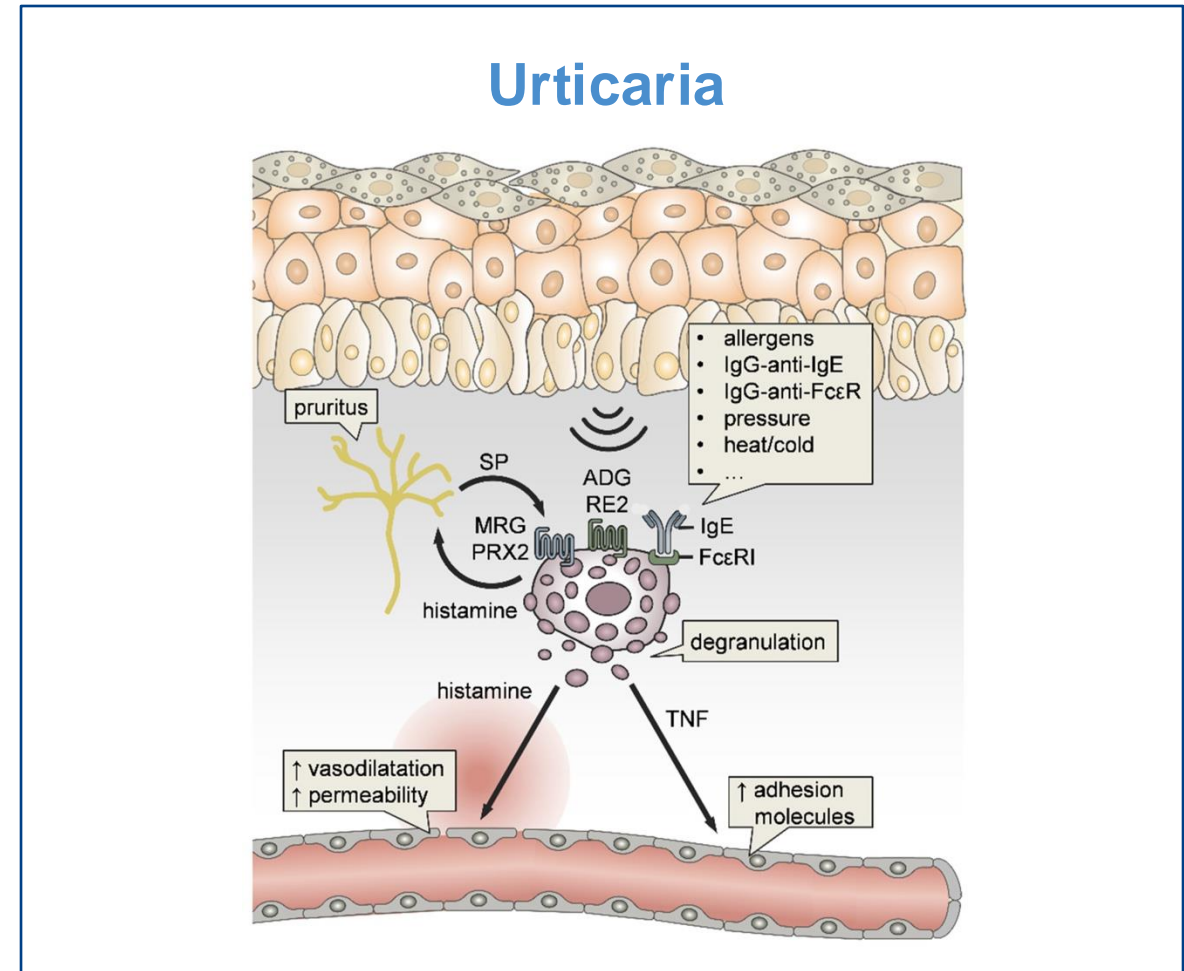
AK006 May Inhibit Disease Driving Pathways in Urticaria

Activated mast cells drive the pathogenesis of urticaria via release of inflammatory mediators resulting in pruritus, vasodilation, and increased vascular permeability

IgE activation of mast cells, from autoantibodies or allergens, has been identified as driving pathogenesis in a proportion of patients with chronic urticaria

IgE-independent mast cell activation, via MRGPRX2 and other mast cell receptors, is also believed to contribute to symptoms

Blocking both IgE activation and IgE-independent mast cell activation could result in improved patient outcomes in CSU



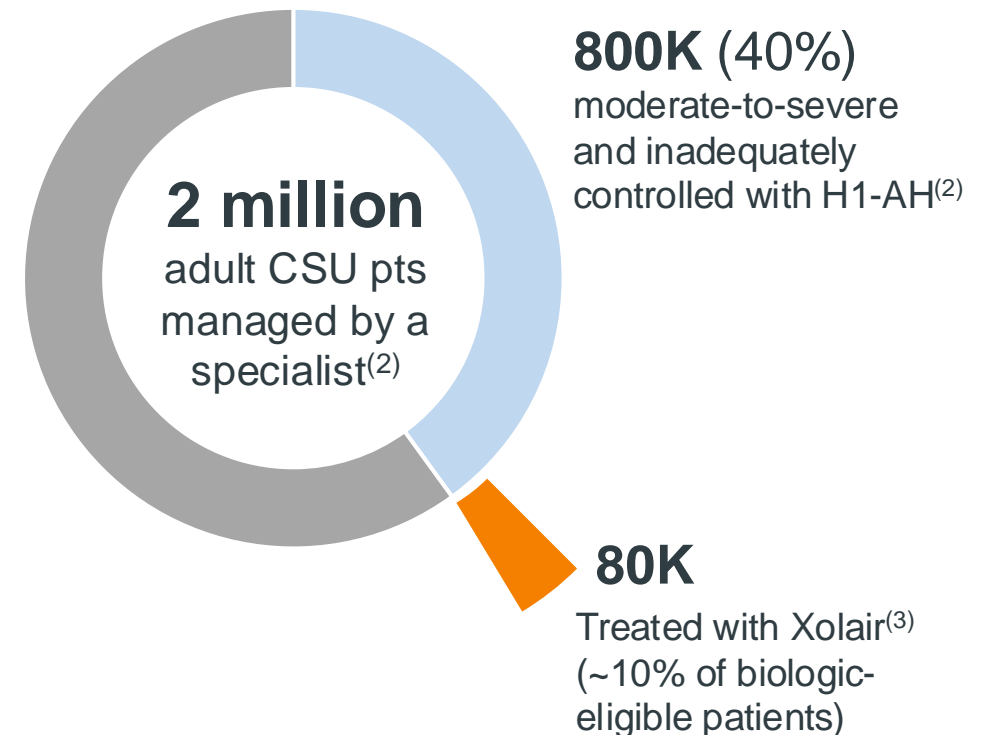
Chronic Spontaneous Urticaria Opportunity

CSU affects up to 3 million adults in the U.S., with 2 million managed by a specialist (allergist or dermatologist)^{1,2}

An estimated 800K adults with CSU are biologic-eligible, yet only approximately 10% of eligible patients are currently on a biologic^{2,3}

Currently only Xolair is approved for the treatment of antihistamine CSU. Xolair® (omalizumab) global CSU sales were estimated to be \$1.6 billion in 2021⁴

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



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 Slow onset of action 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	Placebo	<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%)	-10 (-35%)	
		UAS7=0	23%	51%	38%	6%	
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%		

Financial Overview & Key Milestones

Data Catalysts and Expected Milestones

- ✓ **Q2 2024:** Report SAD and MAD safety, pharmacokinetics (PK), and pharmacodynamic (PD) results from the Phase 1 IV AK006 trial in healthy volunteers, including data to confirm Siglec-6 receptor occupancy in skin biopsy samples.
- ✓ **Q2 2024:** Initiate the randomized, double-blind, placebo-controlled Phase 1 trial of IV AK006 in patients with chronic spontaneous urticaria (CSU).
- ✓ **Q3 2024:** Report subcutaneous (SC) AK006 safety, PK, and PD results from the Phase 1 trial in healthy volunteers, including data to confirm Siglec-6 receptor occupancy in skin biopsy samples.
- **Early Q1 2025:** Report topline data from the Phase 1 trial of IV AK006 in patients with CSU.



Balance Sheet and IP Protection

Cash, Cash Equivalents and Investments in Marketable Securities as of December 31, 2023	\$170.8 M
– Estimated 2024 cash used in restructuring (lirentelimab closeout, severance and other costs)	\$30 M
– Estimated 2024 cash used in ongoing business operations	\$55 to \$60 M
Estimated, Cash, Cash Equivalents and Investments in Marketable Securities at year end 2024	\$81 to \$86 M
Common Shares Outstanding as of December 31, 2023	87.8 M

Allakos expects that the restructuring activities will extend the cash runway into mid-2026



**AK006 composition of matter
to expire in 2042 without extensions**



**Planning subcutaneous AK006
for Phase 2 studies**