Efficacy and Safety Data of AK002, an Anti-Siglec-8 Monoclonal Antibody, in Patients with Multiple Forms of Uncontrolled Chronic Urticaria (CU): Results from an Open-label Phase 2a Study

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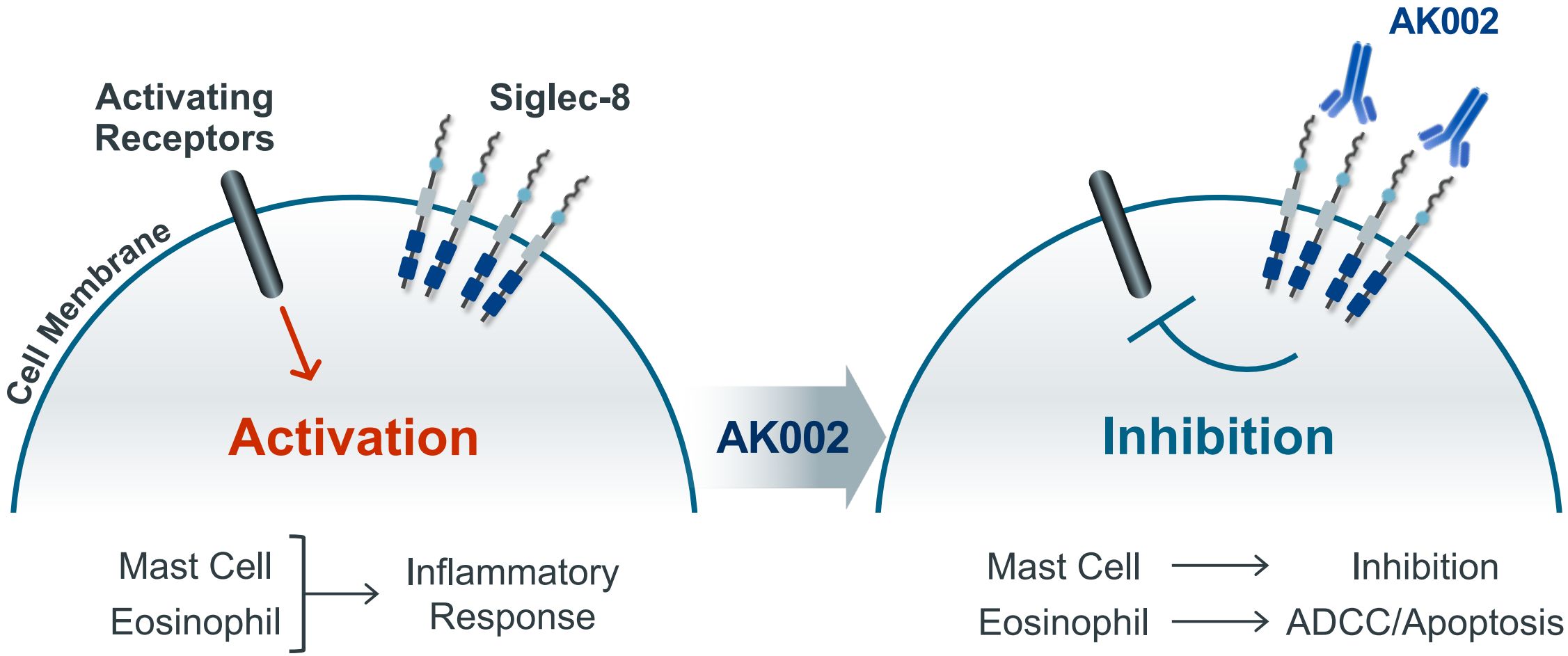
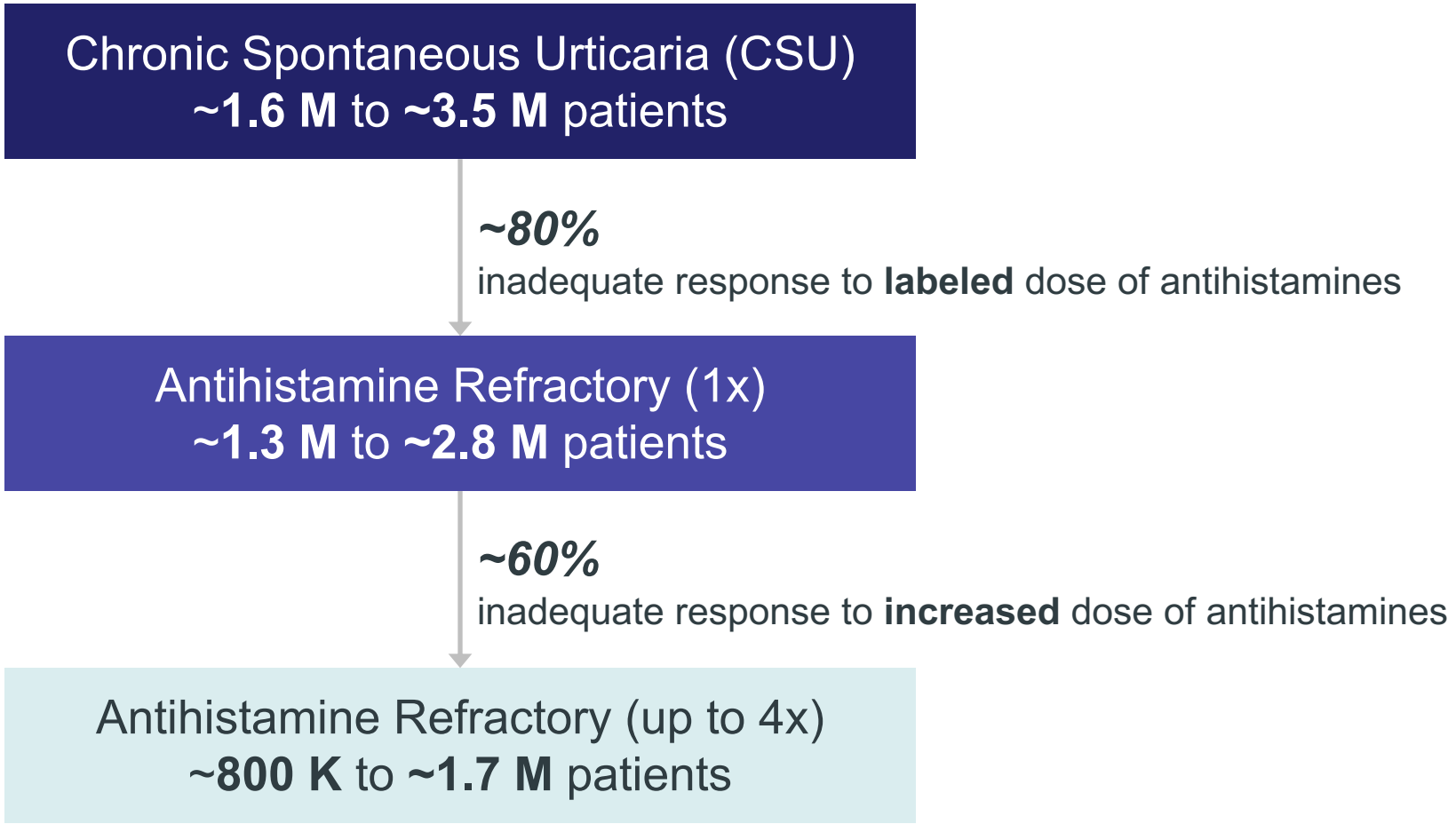
Disclosures

- Marcus Maurer is the principal investigator of this study
- Marcus Maurer is or recently was a speaker and/or advisor for and/or has received research funding from Allakos, Aralez, AstraZeneca, FAES, Genentech, Menarini, Novartis, Moxie, MSD, Pfizer, Roche, Sanofi, UCB, and Uriach.

AK002 Targets Siglec-8 on Mast Cells and Eosinophils

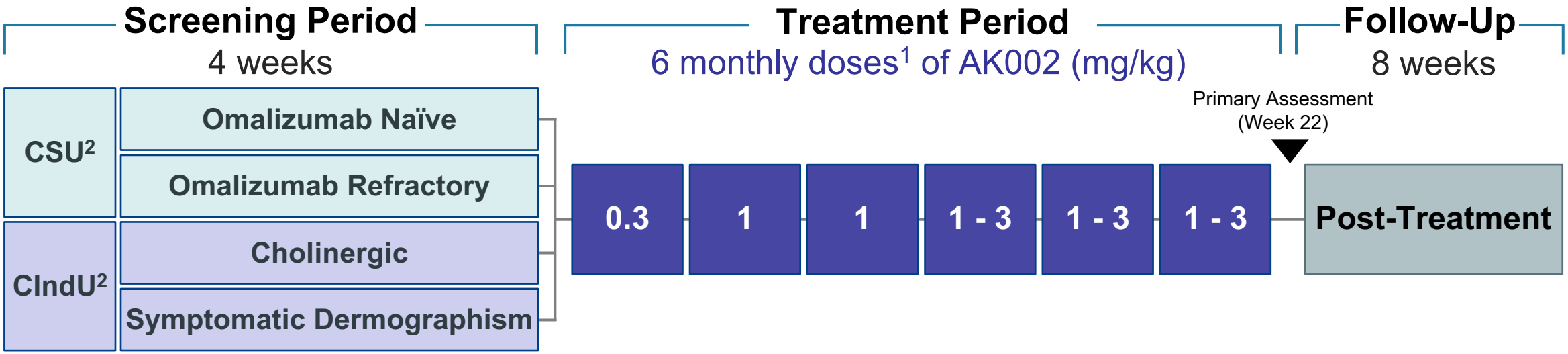


Prevalence of Antihistamine-Refractory CSU in US



Source: Maurer et al. *Allergy*. 2011 Mar;66(3):317-30; Staevska et al. *J Allergy Clin Immunol*. 2010 Mar;125(3):676-82; Van den Elzen et al. *Clin Transl Allergy* (2017) 7:4

Study Design



- Enrolled pts with CU
  - Refractory to antihistamine treatment up to 4-fold dosage
  - Uncontrolled CU (UCT <12)
- CSU pts refractory to omalizumab
  - OMA treatment duration ~10 months, up to 600 mg
- No use of OMA within 2 months of enrollment

Primary Objective:

- Efficacy: Change in Urticaria Control Test (UCT) Week 22 to Baseline

Secondary Objectives:

- Safety and tolerability
- Patient reported outcome (CSU only):
  - Urticaria Activity Score weekly average (UAS7)
- Provocation test:
  - Cholinergic: Pulse Controlled Ergometry Test (PCE)

- 3 visits
- Safety, tolerability, PD, and efficacy measures are assessed

1 Increase to 3 mg/kg if UCT score <12 for doses 3-6
2 CSU, Chronic spontaneous urticaria; CIndU, chronic inducible urticarias

Baseline Patient Characteristics

	Chronic Spontaneous Urticaria		Chronic Inducible Urticaria	
	Omalizumab Naïve (N=14)	Omalizumab Refractory (N=12)	Cholinergic Urticaria (N=11)	Symptomatic Dermographism (N=10)
Age	66 (30-75)	29 (22-60)	33 (18-62)	27 (19-56)
Female	93%	83%	55%	60%
BMI	32 (20-44)	27 (20-42)	27 (23-39)	30 (22-36)
UCT	3.2	3.7	5.4	5.7
UAS7	18.5	28.7	-	-

Chronic Spontaneous Urticaria (CSU)

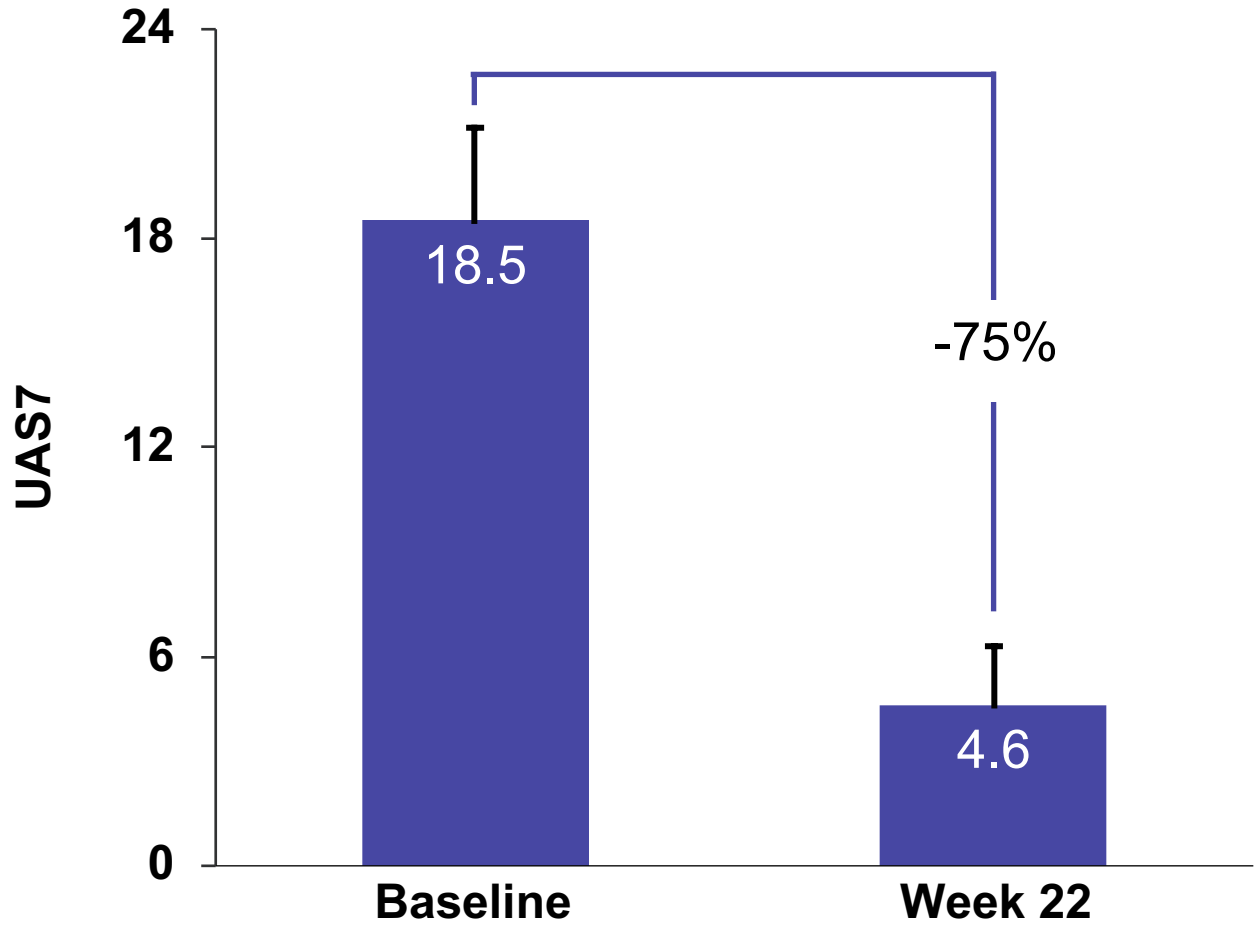
Omalizumab Naïve Cohort

Patients with inadequate response to antihistamines (up to 4x labelled dose)

High Levels of Response by UCT in CSU Omalizumab-Naïve Pts

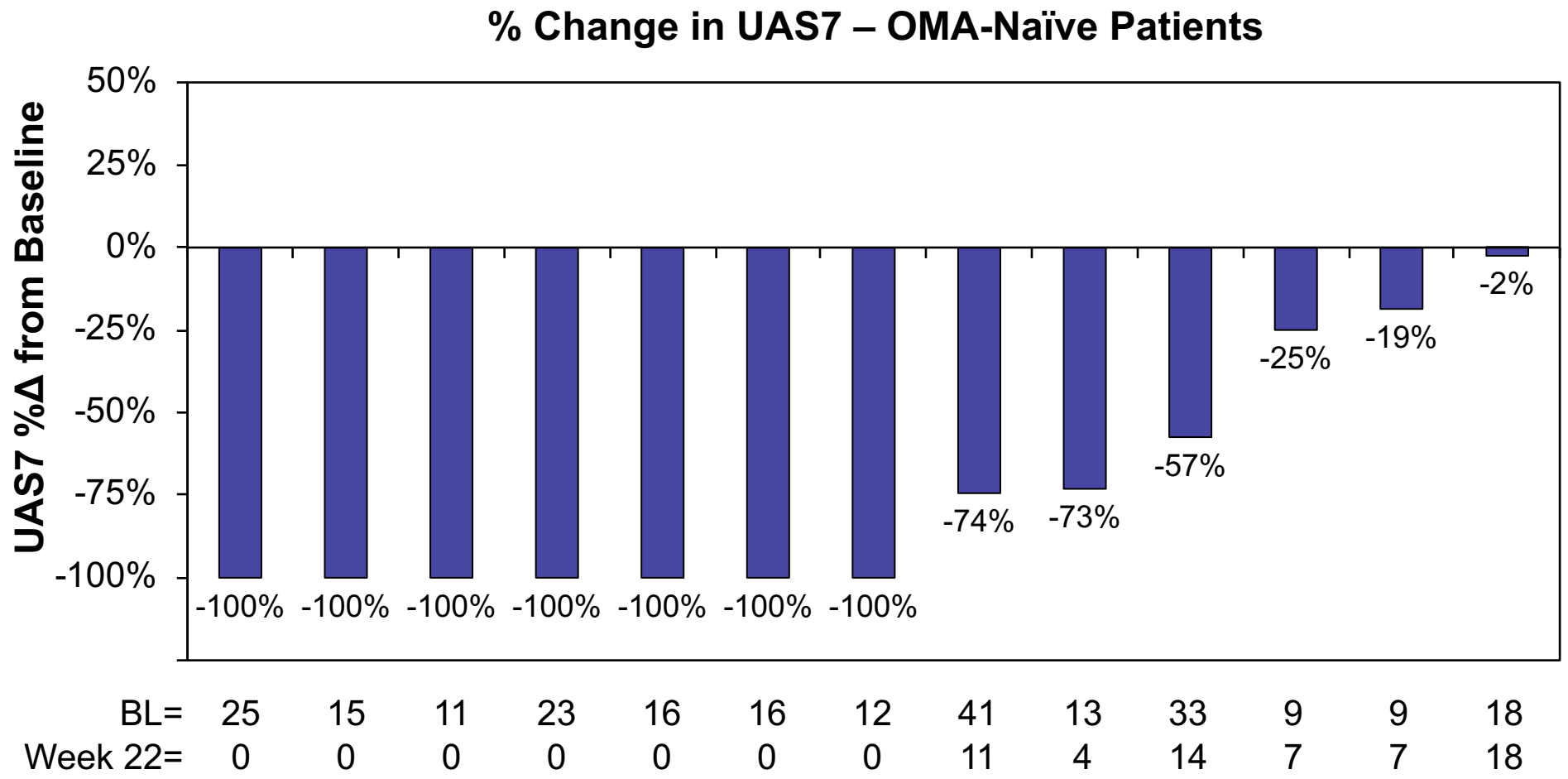
Endpoint	Week 22
UCT Complete Response	12/13 (92%)
UCT Partial Response	0/13 (0%)
UCT No Response	1/13 (8%)

75% Improvement in Mean UAS7 in Omalizumab-Naïve Pts



(n=13)

Reduction in UAS7 in Omalizumab-Naïve Patients



Chronic Spontaneous Urticaria (CSU)

Omalizumab Refractory Cohort

Patients with inadequate response to omalizumab and antihistamines (up to 4x labelled dose)

Omalizumab Refractory Cohort – Medical History

Inadequate disease control despite extensive use of omalizumab (OMA)

Prior OMA Treatment Experience

- **Average treatment duration:** ~10 months
- **Treatment regimen:**
  - Omalizumab: up to 600 mg
  - Antihistamine: up to 4x labeled dose
- **Average UCT score on Omalizumab:** 4.1

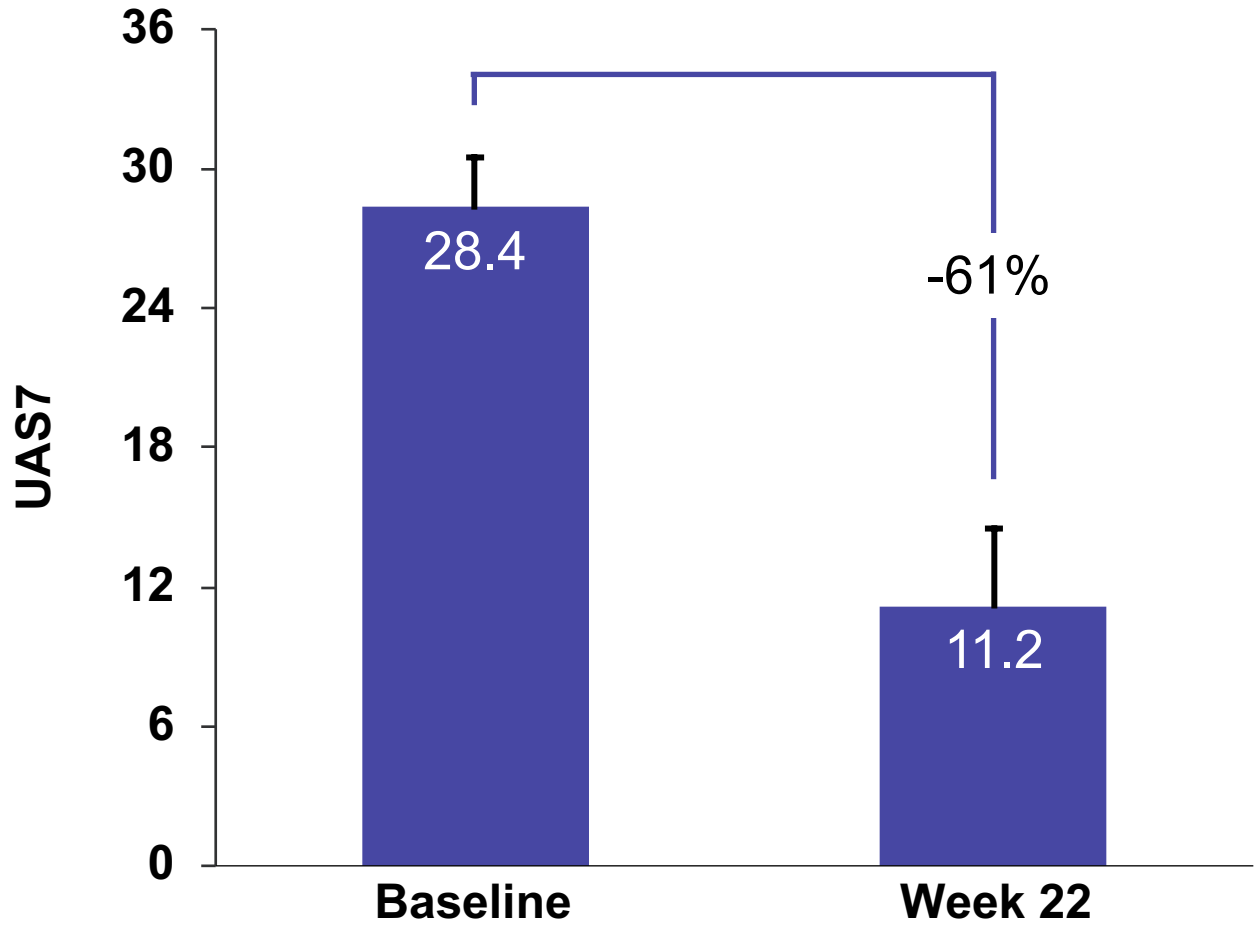
At Baseline for AK002 Study

- **Time since last OMA dose:** >2 months
- **Treatment regimen:**
  - Antihistamine: up to 4x labeled dose
- **Average UCT score at baseline:** 3.7

Substantial Disease Control in OMA-Refractory Patients

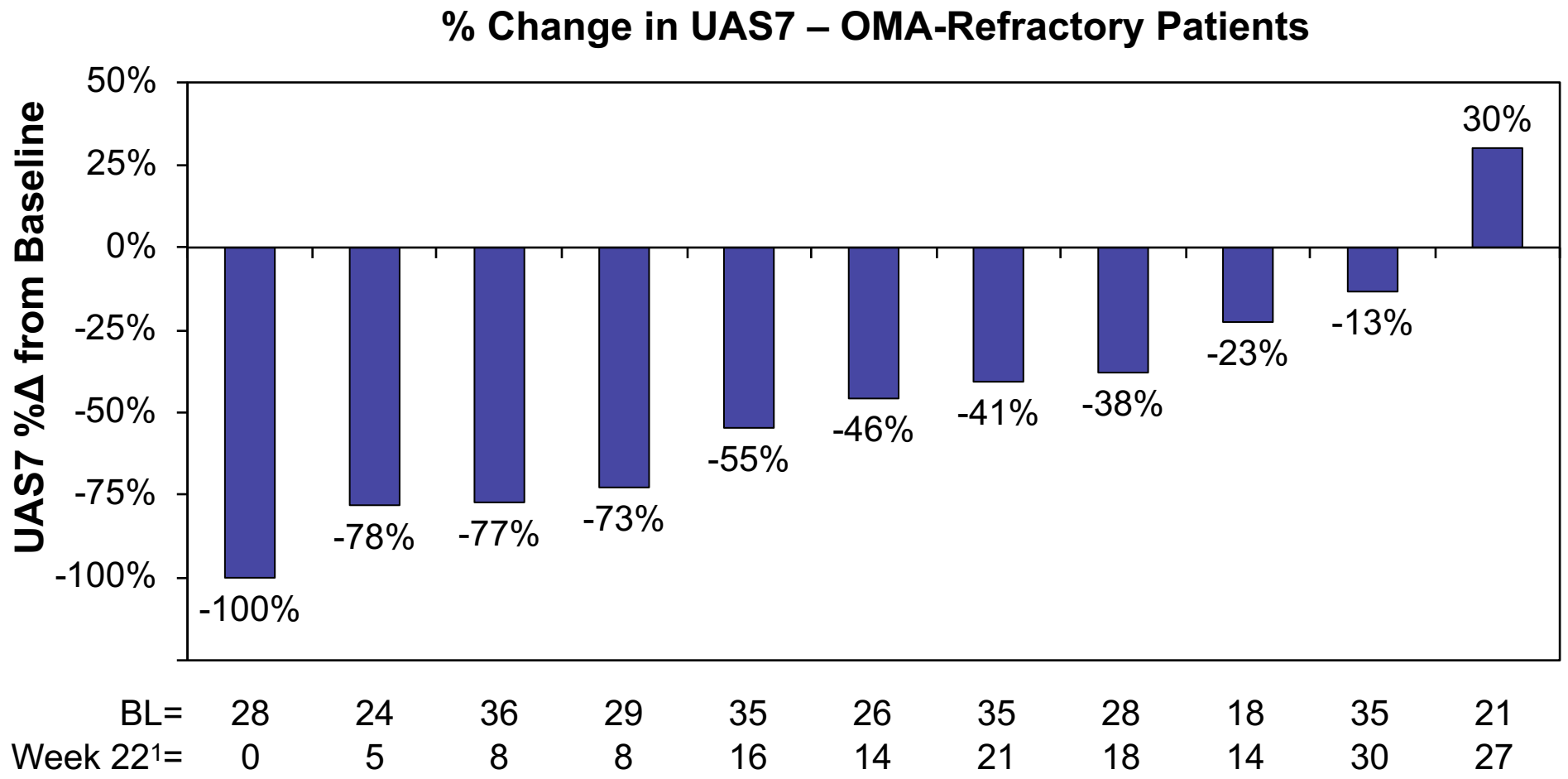
Endpoint	Week 22
UCT Complete Response	4/11 (36%)
UCT Partial Response	2/11 (18%)
UCT No Response	5/11 (45%)

61% Improvement in Mean UAS7 in OMA-Refractory Pts



Patients receiving 6 doses (n=7)

8/11 (73%) OMA-Refractory Patients Achieved ΔUAS7≥10 (MID)



1 Last observation carried forward

Chronic Inducible Urticaria (CIndU)

Symptomatic Dermographism and Cholinergic Urticaria Cohorts

Patients with inadequate response to antihistamines (up to 4x dose)

7/10 (70%) Response Rate in Symptomatic Dermographism

Endpoint	Week 22
UCT Complete Response	4/10 (40%)
UCT Partial Response	3/10 (30%)
UCT No Response	3/10 (30%)

7/10 (70%) Response Rate in Symptomatic Dermographism

Endpoint	Week 22
UCT Complete Response	4/10 (40%)
UCT Partial Response	3/10 (30%)
UCT No Response	3/10 (30%)
FricTest® No Itch	5/10 (50%)
FricTest® No Wheals	4/10 (40%)

9/11 (82%) Complete Response Rate in Cholinergic Patients

Endpoint	Week 22
UCT Complete Response	9/11 (82%)
UCT Partial Response	0/11 (0%)
UCT No Response	2/11 (18%)

9/11 (82%) Complete Response Rate in Cholinergic Patients

Endpoint	Week 22
UCT Complete Response	9/11 (82%)
UCT Partial Response	0/11 (0%)
UCT No Response	2/11 (18%)
PCE Test Response	7/7 (100%)

100% Response Rate by PCE Test in Cholinergic Urticaria Pts

	Baseline		End of Study	
	Provocation[1]	Number of Wheals	Provocation	Number of Wheals after 30 mins
CholU-1	+	21 - 50	-	0
CholU-2	+	1 - 20	-	0
CholU-3	+	1 - 20	-	0
CholU-4	+	>50	-	0
CholU-5[2]	+	Positive	-	0
CholU-6	+	>50	-	0
CholU-7	+	>50	-	<50

1 Provocation - exercise on stationary bike elevates body temperature to trigger symptoms, positive response if occurring in ≤10 minutes from 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

Summary of Primary Assessment: High Response Rate by UCT with AK002 in Chronic Urticarias

	Chronic Spontaneous Urticaria		Chronic Inducible Urticaria	
Urticaria Control Test Response	CSU OMA-Naïve (n=13)	CSU OMA-Refractory (n=7)[1]	Cholinergic (n=11)	SDerm[2] (n=10)
Complete Response[3]	92%	57%	82%	40%
Partial Response	0%	29%	0%	30%
No Response	8%	14%	18%	30%

1 Patients who received 6 doses
2 Symptomatic Dermographism, an inducible physical urticaria
3 UCT complete response: ≥3-point improvement from baseline and score ≥12; partial response ≥3-point improvement from baseline; no response <3-point improvement from baseline

Safety

- Generally well-tolerated
- No drug-related Serious Adverse Events
- Most common adverse event was mild to moderate infusion-related reactions (IRRs; flushing, feeling of warmth, headache, nausea, or dizziness)
  - 34% IRRs rate on first infusion
  - 5.5% IRRs rate on subsequent infusions

AK002 in Chronic Urticaria

Demonstrated activity in all forms of antihistamine-refractory Chronic Urticaria tested

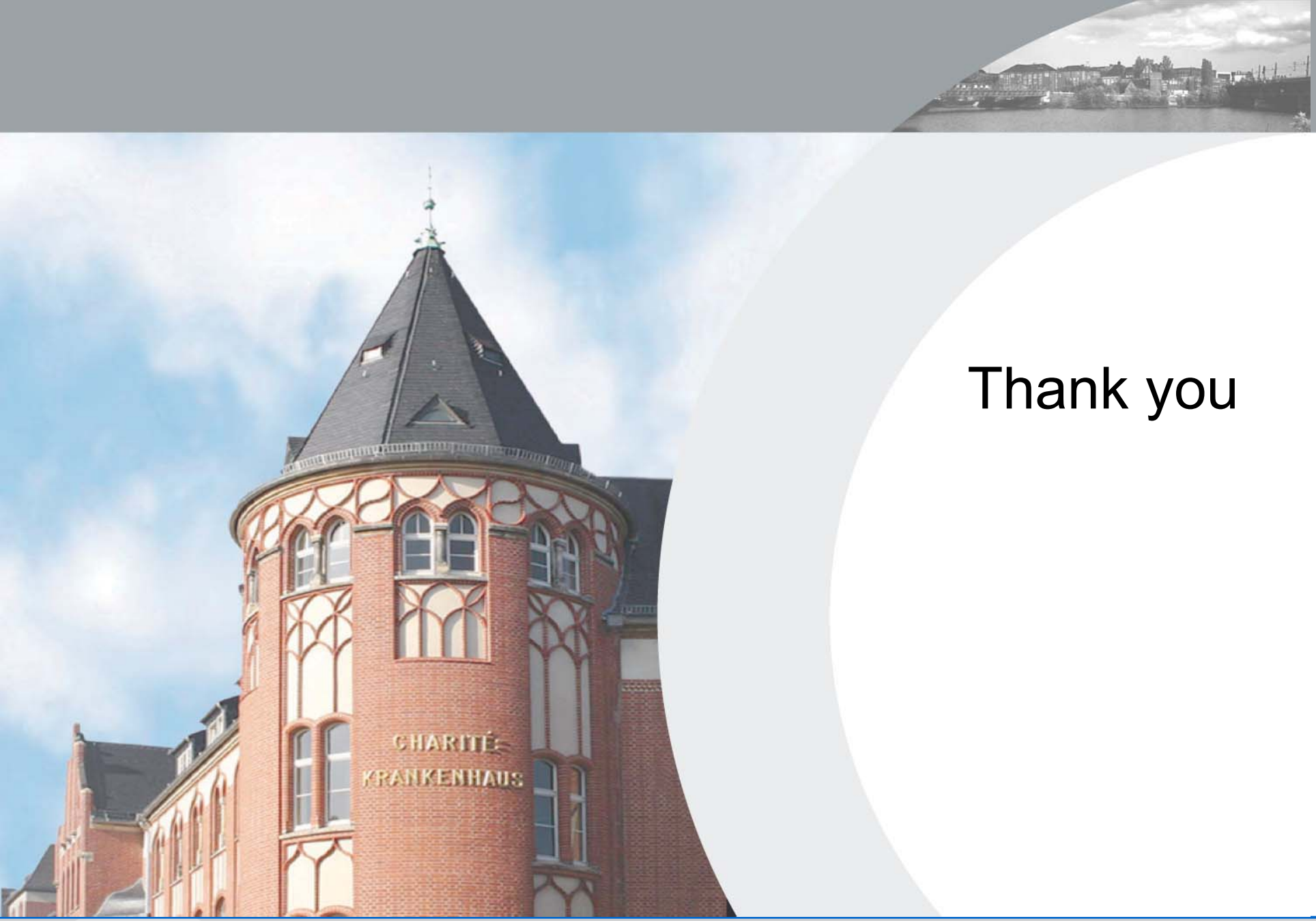
Substantial activity in patients refractory to omalizumab

Continued activity observed in 12-month open-label extension

AK002 is potentially a front-line biologic treatment for Chronic Urticaria

AK002 Has the Potential to Treat Multiple Allergic & Inflammatory Diseases

Gastrointestinal	Eye	Skin	Systemic
Eosinophilic Esophagitis	Atopic Keratoconjunctivitis	Chronic Urticaria	Indolent Systemic Mastocytosis
Eosinophilic Gastritis	Perennial Allergic Conjunctivitis	Atopic Dermatitis	Idiopathic MCAS
Eosinophilic Gastroenteritis	Vernal Keratoconjunctivitis		Asthma
Eosinophilic Colitis			IPF
IBD			
IBS			



Thank you