



**Jasper Therapeutics**

**Corporate Presentation**

*June 2024*

# Safe Harbor Statements

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# Briquilimab: Franchise Potential in Mast Cell Diseases

## c-Kit inhibition clinically validated MOA in mast cell diseases

- c-Kit inhibition is the only therapeutic mechanism shown to significantly deplete mast cells
- Mast cell depletion has unique potential to deliver safe and durable disease control
- c-Kit inhibition has demonstrated clinical proof of concept in multiple mast cell mediated diseases

## Briquilimab a potent c-Kit inhibitor















- Briquilimab is a potent c-Kit inhibitor proven to drive mast cell depletion
- Briquilimab could allow for less frequent dosing
- Optimal biologic dosing and PK profile could minimize unwanted adverse effects

## Robust pipeline multiple company- led clinical programs

- CSU: Enrolling patients in Phase 1b/2a BEACON study (initial data expected 3Q 2024)
- ClndU: Enrolling patients in Phase 1b/2a SPOTLIGHT study (initial data expected 2H 2024)
- Asthma: Enrollment in Phase 1b/2a study expected to commence Q4 2024
- Additional mast cell mediated indications under evaluation

# Expanded portfolio presents exciting new opportunities in mast cell diseases

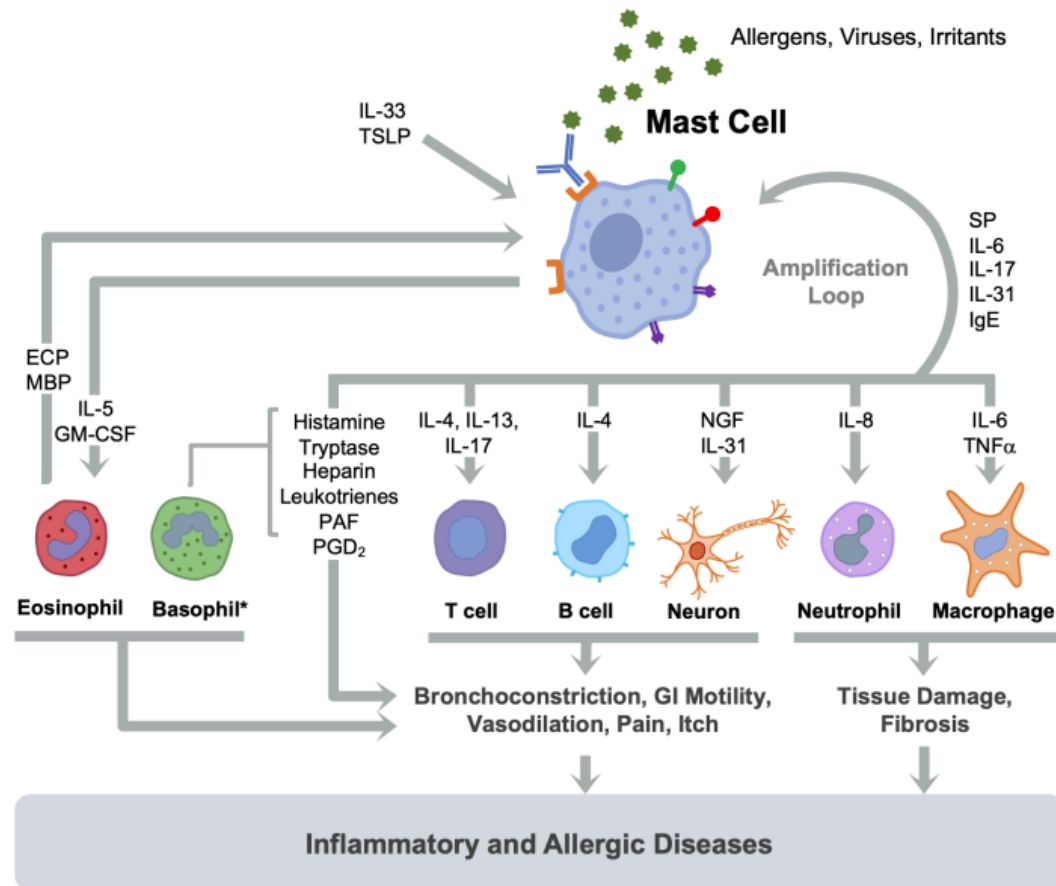
Investigator Sponsored Studies

Indication	Sponsor	Preclinical	Phase 1	Phase 2	Phase 3	Program Milestones
<b>Briquilimab</b>						
<b>Mast Cell Diseases (Subcutaneous)</b>						
Chronic Spontaneous Urticaria						<ul style="list-style-type: none"> <li>Phase 1b/2a being conducted in the US and EU</li> <li>Actively enrolling patients</li> <li>Initial clinical data expected in 3Q 2024</li> </ul>
Chronic Inducible Urticaria						<ul style="list-style-type: none"> <li>Phase 1b/2a study being conducted in the EU</li> <li>Actively enrolling patients</li> <li>Initial clinical data expected in 2H 2024</li> </ul>
Asthma						<ul style="list-style-type: none"> <li>Enrollment in Phase 1b/2a expected Q4 2024</li> <li>Initial clinical data expected 2H 2025</li> </ul>
<b>Stem Cell Diseases (Intravenous)</b>						
Low-to-Intermediate Risk MDS						<ul style="list-style-type: none"> <li>Enrolling patients</li> <li>Initial clinical data expected 2H 2024</li> </ul>
SCID						<ul style="list-style-type: none"> <li>Enrolling patients</li> <li>Discussing potential BLA filing with the FDA</li> </ul>
Fanconi Anemia						<ul style="list-style-type: none"> <li>First 6 patients achieved full chimerism &amp; count recovery; expansion to Phase 2a (enrolling)</li> </ul>
SCD / CGD / GATA2 MDS						<ul style="list-style-type: none"> <li>First 3 patients with full chimerism &amp; Hb increase (SCD)</li> <li>Enrolling patients (CGD)</li> <li>Study start up (GATA2 MDS)</li> </ul>

SCD, sickle cell disease; CGD, chronic granulomatous disease; MDS, myelodysplastic syndrome.

**Jasper maintains full worldwide rights to develop and commercialize briquilimab in all indications**

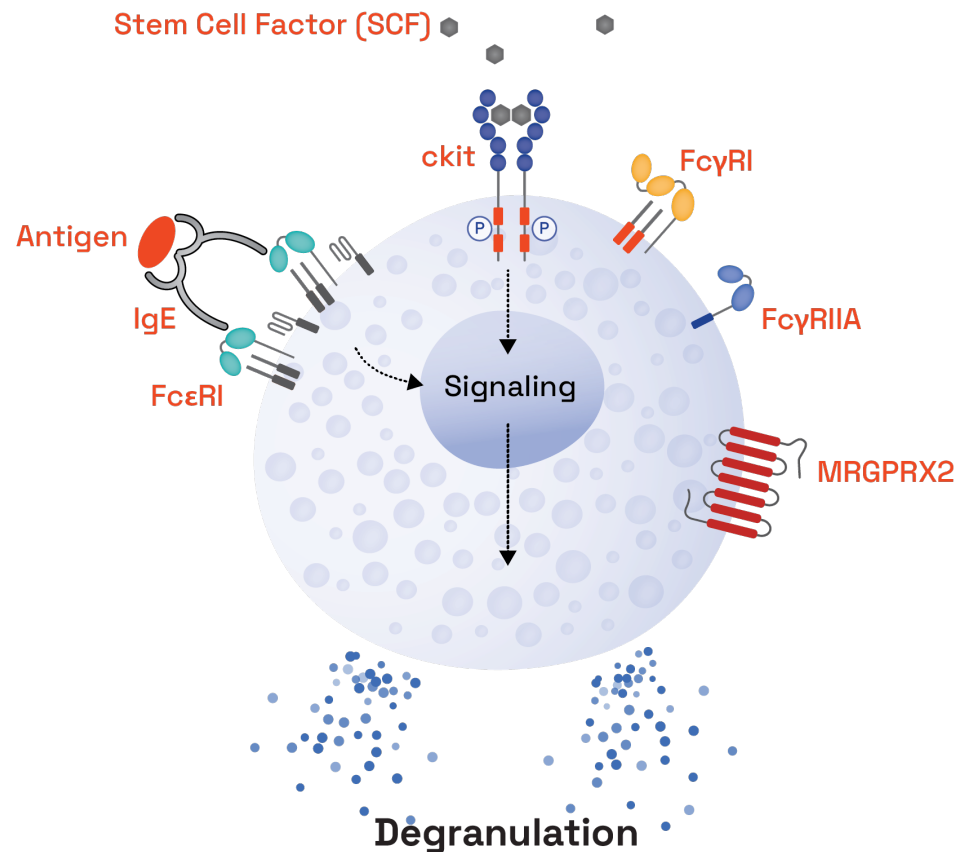
# Mast cells are the most potent drivers of inflammatory response in skin, lungs and gut



Metz et al. Allergy (2023)

- Mast cells are primitive immune cells involved in protection against venom and parasitic infection
- Mast cells triggered by allergens, viruses and other irritants degranulate and release pro-inflammatory compounds implicated in large number of immunologic diseases
- Limited function or need for skin mast cells in modern settings

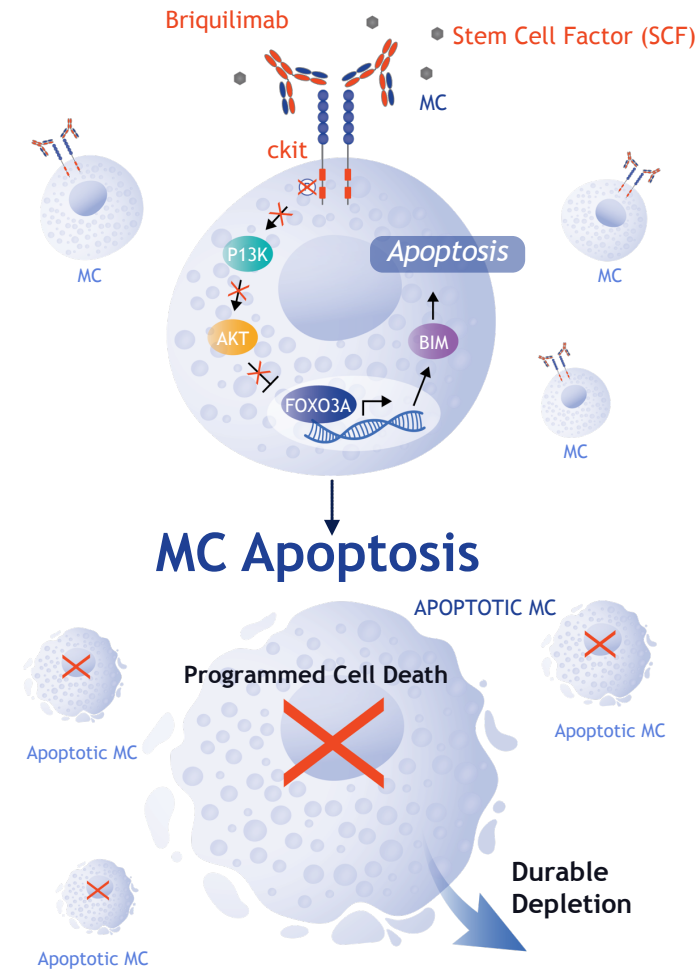
# Mast cells are key drivers of the inflammatory response in a number of immunologic diseases with high unmet need



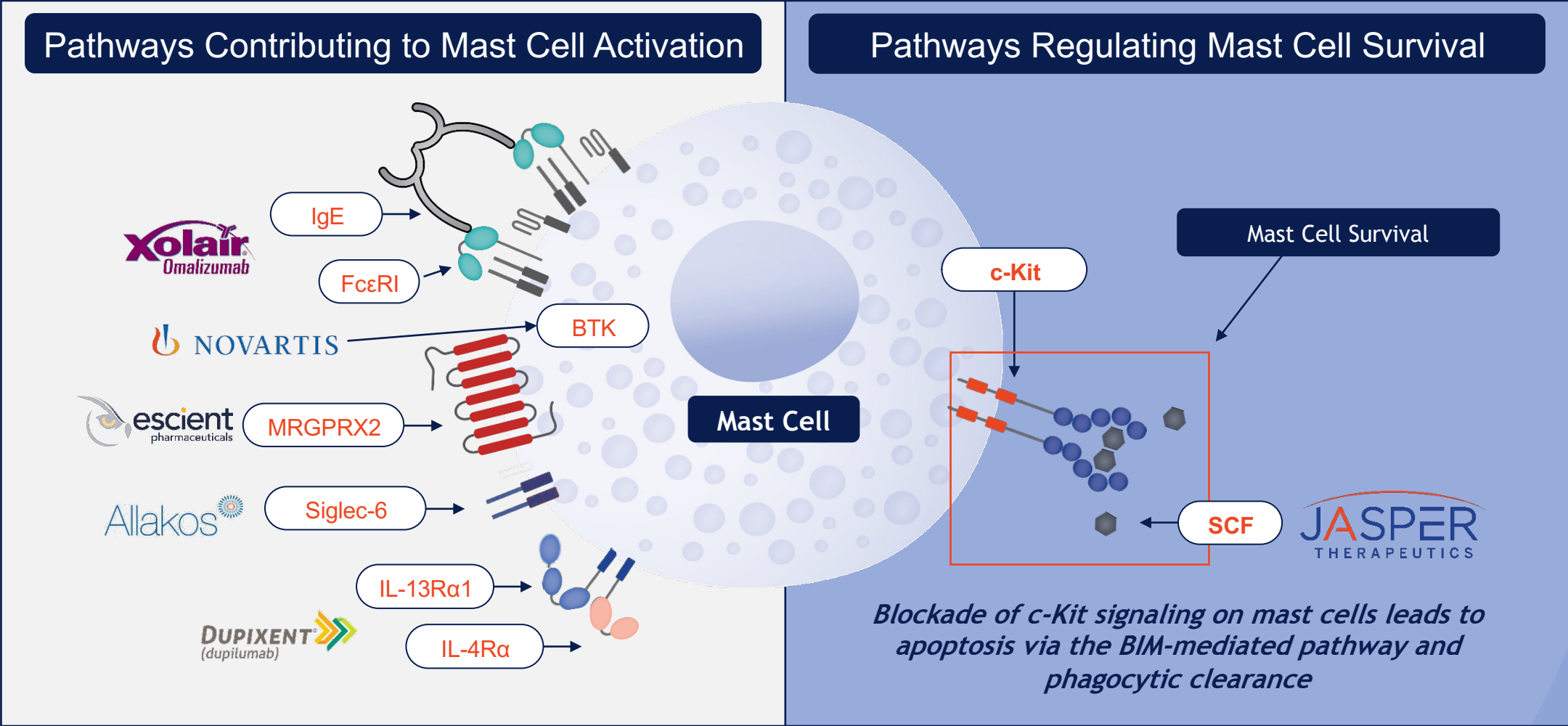
- Activated mast cells are the perpetrating cell driving diseases such as:
  - Asthma
  - Atopic Dermatitis
  - Chronic Rhinosinusitis
  - COPD
  - Eosinophilic Esophagitis (EoE)
  - Prurigo Nodularis
  - Urticaria
- Currently approved therapies targeting mast cell driven diseases rely on indirect mast inhibition and have limited efficacy and durability of response

# Depletion of mast cells by anti-c-Kit monoclonal antibody blockade is a novel approach with potential to deliver safe and durable disease control

- Briquilimab is an aglycosylated IgG1 anti c-Kit antibody with high affinity to c-Kit
  - Aglycosylated c-Kit antibodies avoid indiscriminate ADCC driven killing of other c-Kit expressing cells<sup>1</sup>
  - Kd < 5pM affinity to human c-Kit with IC50 ~ 70pM
  - Human mast cell survival bioassay IC50 ~12.5nM
  - Half life of 9 days
- Briquilimab blocks c-Kit signaling at the SCF ligand binding site on the receptor triggering apoptosis
  - Mast cell depletion occurs within hours to days
- Mast cell recovery in the skin takes 3 months or longer<sup>2</sup>, potentially leading to durable disease control



# Mast cell depletion may lead to deeper and more durable efficacy compared to inhibition and silencing approaches

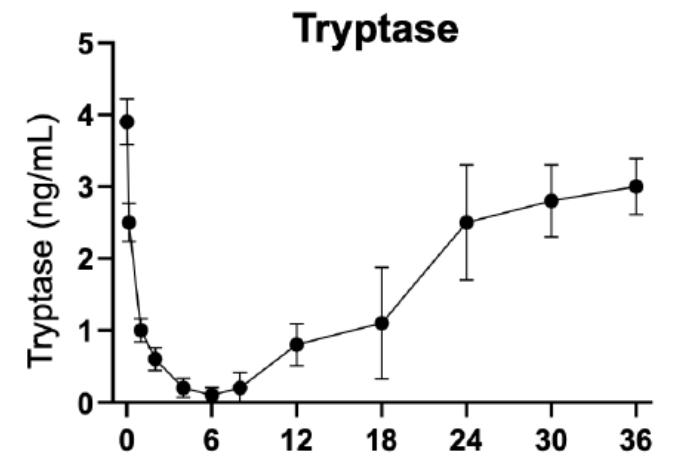
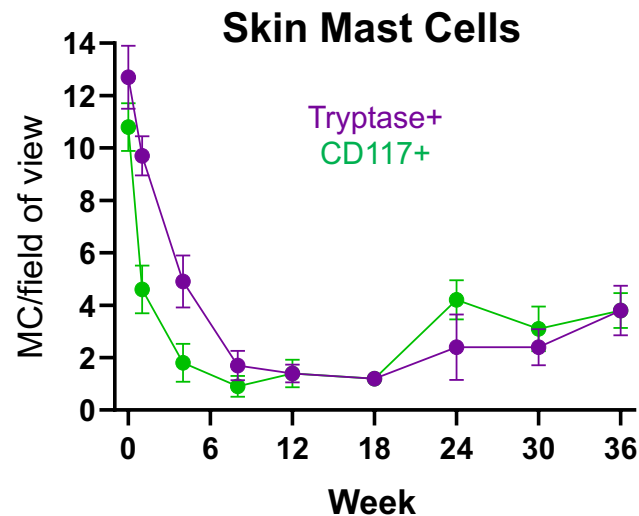




# Single administration of anti-c-Kit antibody leads to rapid and durable depletion of skin mast cells

- Significant depletion of mast cells occurs within one week following dosing
- Serum tryptase reduction correlates to mast cell depletion
- Serum tryptase recovery precedes return of urticarial symptoms and skin mast cells
- Following depletion, mast cell recovery in the skin takes at least three months<sup>1</sup>

## Single Dose of Barzolvolimab in CIndU (3 mg/kg IV)



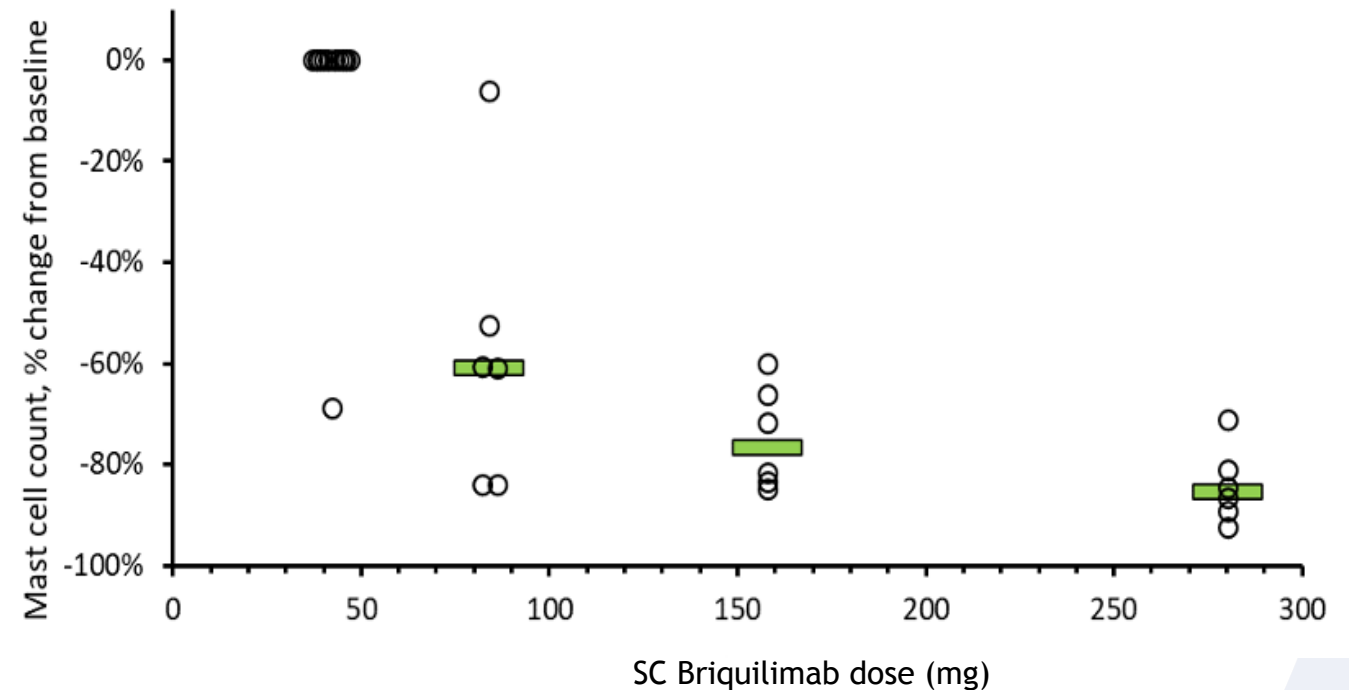
Minimal recovery of skin mast cells by week 36 following single administration of barzolvolimab IV in CIndU patients<sup>1</sup>

# Briquilimab significantly depletes skin mast cells in humans at subcutaneous (SC) doses above ~80 mg

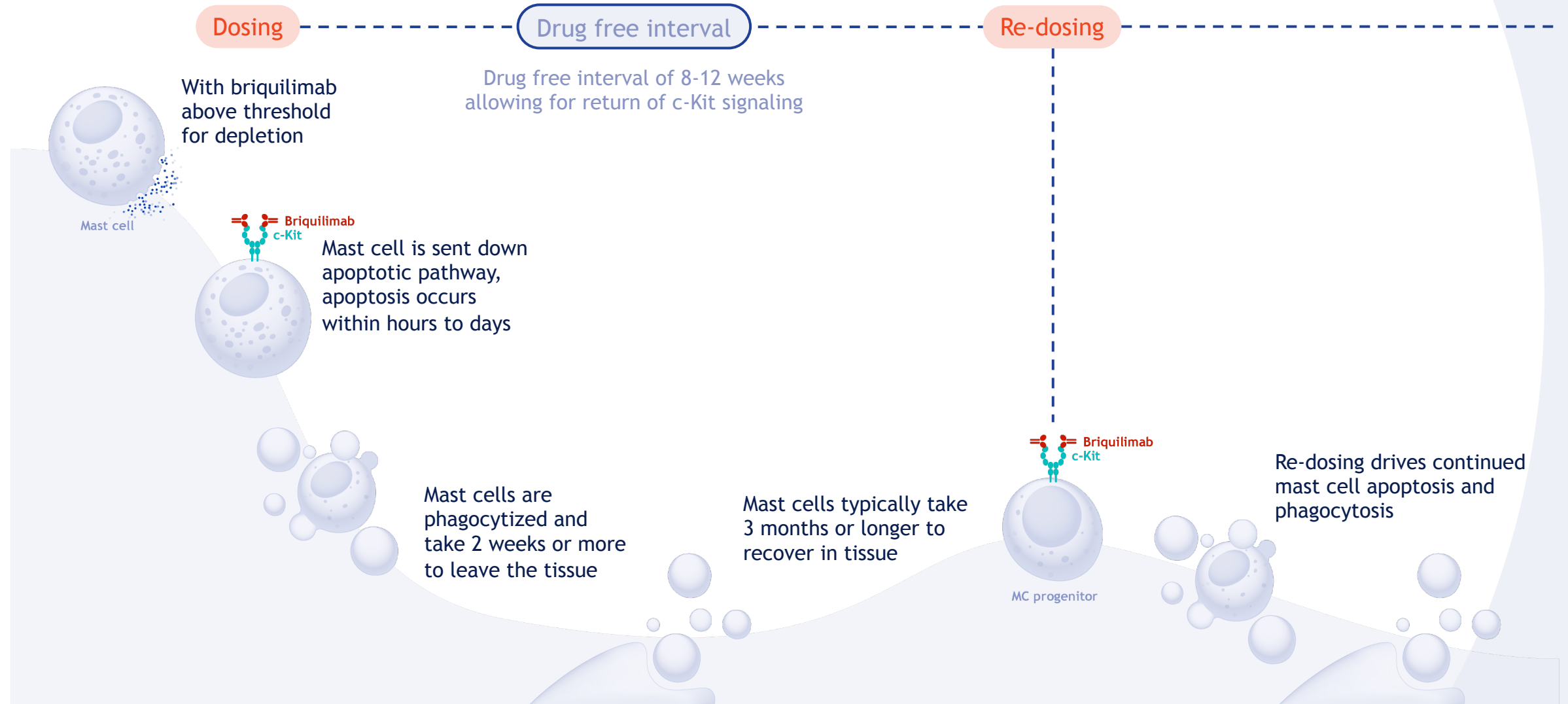
- Single SC dose at or above ~80 mg potently depletes mast cells in the skin of healthy volunteers
- Cmax reached at ~day 5
- Depletion begins occurring as early 7 days following SC dosing
- Robust depletion at day 29
- Briquilimab's favorable pharmacokinetic properties may enable optimal biologic dosing

## Briquilimab Healthy Volunteer Phase 1 Subcutaneous Study

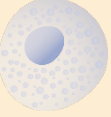




Skin mast cell depletion 4 weeks after single dose (42 mg, 84mg, 158mg, 280mg)<sup>1</sup>



# Briquilimab design and characteristics enable optimal biologic dosing and could minimize unwanted effects of c-Kit inhibition



# Transient blockade of c-Kit leads to temporary and reversible effects on other cells expressing c-Kit

Cell type	Role of c-Kit	Impact of c-Kit Blockade	Benefit of Short Half-Life Exposure
 <b>Mast cell</b>	Survival signal	Mast cell apoptosis via the Bim-mediated pathway <sup>1</sup>	<b>Mast cells are depleted and take months to repopulate</b>
 <b>Stem Cell (HSC)</b>	Cellular maintenance	Differentiation and exit out of the bone marrow niche <sup>2</sup>	<b>Mild, transient drop in a subset of cycling neutrophils and reticulocytes with rapid recovery expected after c-Kit signaling restored</b>
 <b>Melanocyte</b>	Proliferation and melanin production	Blocks melanocyte proliferation and melanogenesis <sup>3</sup>	<b>Potential graying</b> with prolonged c-Kit inhibition and pigmentation expected to return after c-Kit signaling restored
 <b>Spermatogonial Progenitor</b>	Downstream survival signal	Downstream (non-stem cell) progenitor cell apoptosis <sup>4</sup>	<b>Transient drop in sperm count</b> , and effects on fully reversible given lack of effect on spermatogonial stem cells (SSCs)
 <b>Taste Cell</b>	Cellular maintenance	Disruption of specific mature taste cell subpopulations <sup>5</sup>	<b>Potential impairment of salt and umami taste</b> with rapid recovery expected to return after c-Kit signaling restored

# Briquilimab safety profile to-date supports development in a wide variety of mast cell diseases

- Briquilimab's dosing schedule and favorable elimination kinetics may allow for an improved safety profile
- Low frequency of ADAs (14%) and do not appear to affect PK

## Relevant Preclinical & Clinical Experience

- NHP Chronic Toxicology Study
  - Paleness in skin & fur, depletion of colonic mast cells, decrease in reticulocytes and RBC mass, impact on spermatogenesis
  - All effects, except for paleness in skin/fur, reversible at highest dose of 300mg/kg weekly for 26 weeks
- Healthy Volunteer Subcutaneous Studies (n=77 briquilimab-treated)
  - TEAEs in the HV studies, in the highest frequency of reporting, were Headache, Nausea, Upper Respiratory Tract Infection, Back Pain and Dizziness
    - All were mild or moderate in severity and all resolved with no medical intervention
  - One Grade 3 allergic reaction reported

# Depletion of mast cells by anti-c-Kit monoclonal antibody blockade is a novel approach to treat mast cell driven diseases



**Rapid onset of effect:** Mast cell depletion occurs within days<sup>1</sup>



**Clinical validation:** Mast cells are critical effector cells in several diseases



**Duration of response:** Once depleted, mast cells take at least 3 months to recover, potentially leading to convenient dosing at Q12W<sup>3</sup>



**Specificity of response:** Mast cell depletion leaves other healthy adaptive and innate immune responses intact<sup>4</sup>



**Response across populations:** c-Kit inhibition has been shown to benefit in several mast cell driven diseases, including chronic urticarias, PN and asthma, among others<sup>2,3,5</sup>



# Briquilimab in Chronic Urticaria

# Briquilimab Phase 1b/2a BEACON study in patients with Chronic Spontaneous Urticaria (CSU) ongoing



**Study Goal:** identify the optimal therapeutic doses & dosing frequency of subcutaneous briquilimab to inform future registrational trials

## Key Objectives:

- Study multiple briquilimab dose levels, and intervals up to every 12 weeks to determine optimal biologic dosing via assessment of:
  - Mast cell depletion and disease symptom/disease modifications
  - Briquilimab drug clearance
  - Time to return of disease symptoms
  - Briquilimab effect on other c-Kit expressing cell lineages
- Identify dose and dosing schedule for registrational trial

**Status: Patient enrollment ongoing at sites in US and EU**



# Phase 1b/2a BEACON Study in Chronic Spontaneous Urticaria

## Randomized, Double-Blind, Placebo-Controlled, Multiple Ascending Dose Study



### Screening/Eligibility

- CSU diagnosis  $\geq$  6 mos.
- UAS7  $\geq$  16
- 18+ years
- H1-antihistamine-failed
- Inadequate response to omalizumab

### Study Operations

- US Lead: Tom Casale, MD
- EU Lead: Marcus Maurer, MD
- ~30 sites in the US & EU
- N = ~38

### Key Assessments

- ✓ Disease Scores: UAS7, UCT
- ✓ Mast Cell Depletion & Recovery: Serum Tryptase, Skin Biopsies
- ✓ Safety: TEAEs, SAEs

	Patients (Randomization)	Dose (Frequency)	Cohorts	Key Assessments & Follow Up
Part 1 Open Label (n=6)	3+3 3+3	10 mg 40 mg	Dose W0, 4, 12, 20 Dose W0, 4, 12, 20	Day 8 - Safety Assessment Week 12 - UAS7 Efficacy Assessment 24 week - Follow Up
Part 2 Double-Blind Placebo-Controlled (n=28)	n=8 (3:1) n=6 (2:1) n=6 (2:1) n=8 (3:1)	80 mg (Q8W) 120 mg (Q8W) 120 mg (Q12W) 180 mg (Q12W)	Dose W0, 8, 16, 24 Dose W0, 8, 16, 24 Dose W0, 12, 24 Dose W0, 12, 24	Day 8 - Safety Assessment Week 12 - UAS7 Efficacy Assessment* 24 week - Follow Up
Part 3 Double-Blind Placebo-Controlled (n=4)	n=4 (3:1)	240 mg	Single Dose	Day 8 - Safety Assessment Week 12 - UAS7 Efficacy Assessment* 36 week - Follow Up

\* Interim analyses built into the design for a 12-week efficacy endpoint readout

Briquilimab is an investigational drug and is not approved for any indication

# Briquilimab Phase 1b/2a SPOTLIGHT study in patients with Chronic Inducible Urticaria (CIndU)



**Study Goal:** identify therapeutic doses of subcutaneous briquilimab to inform future registrational trials

## Key Objectives:

- Assess the effects of single dose briquilimab on mast cell depletion and disease symptoms/disease modification to inform optimal biologic dosing in future studies
- Demonstration of efficacy and safety in a second indication
- Provocation study enables a clear demonstration of potential drug effect

**Status: Patient enrollment ongoing at sites in EU**

# Briquilimab Phase 1b/2a SPOTLIGHT Study in CIndU

Open-Label, Cold Urticaria & Symptomatic Dermographism, Single Ascending Dose Study



## Screening/Eligibility

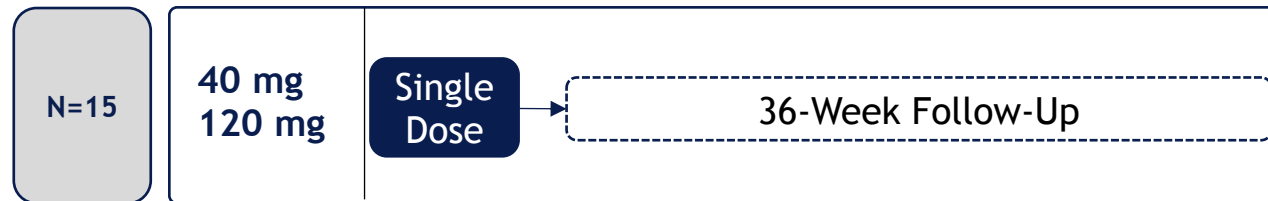
- Diagnosis of Cold Urticaria (ColdU) or Symptomatic Dermographism (SD) for  $\geq 3$  mos.
- H1-antihistamine-failed
- 18+ years

## Study Operations

- EU Lead: Marcus Maurer, MD
- ~5 sites in the EU
- N = ~15

## Key Assessments

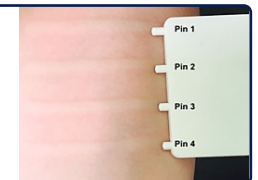
- **Provocation Test:** TempTest (ColdU), FricTest (SD)
- **Disease Scores:** UCT
- **Mast Cell Depletion & Recovery:** Serum Tryptase, Skin Biopsies
- **Safety:** TEAEs, SAEs



Provocation test measured at 12 weeks (Primary Endpoint)

## Provocation Tests Used for Clinical Evaluation

Symptomatic Dermographism  
*FricTest*



Cold Urticaria  
*TempTest*

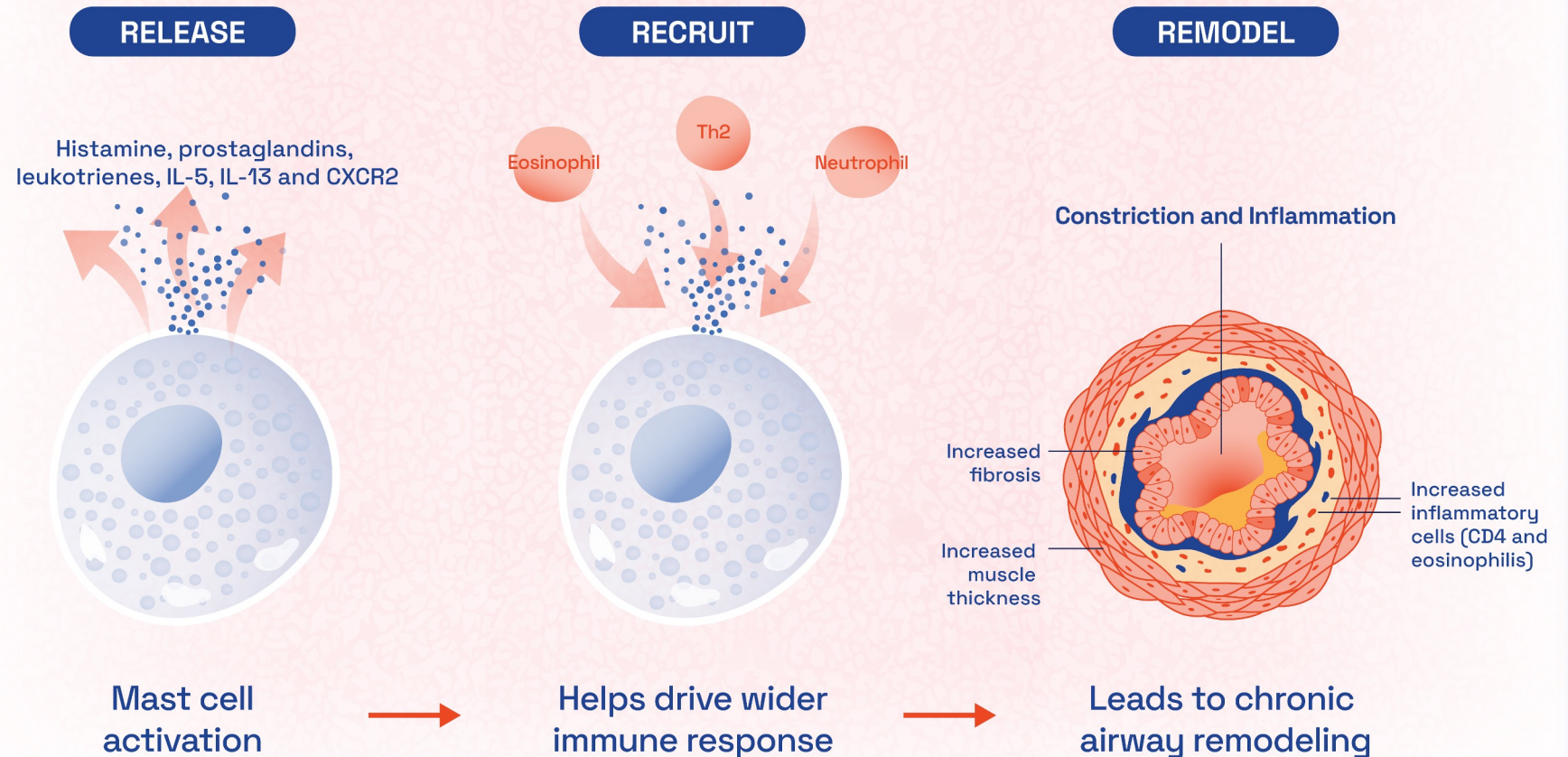




# Briquilimab in Asthma

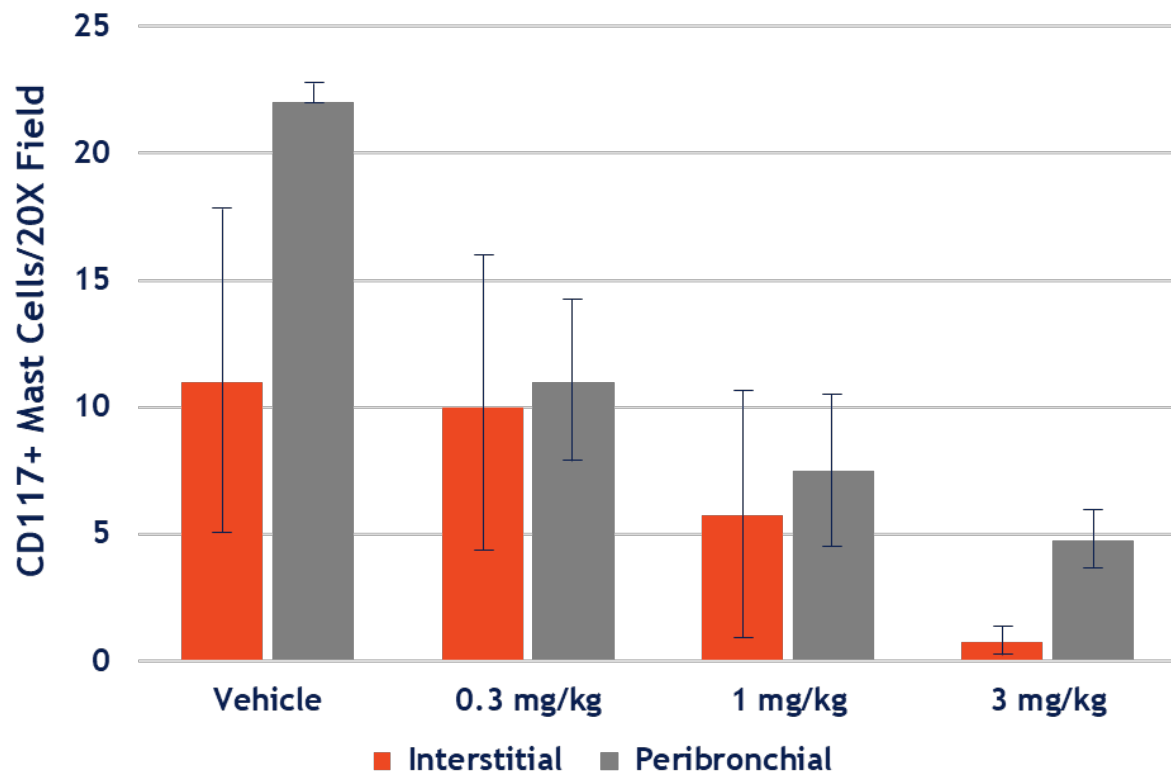
# Mast cells play a critical role in allergic inflammation and tissue remodeling in asthma

- Mast cells are distributed throughout multiple compartments in the lung<sup>1</sup>
- Mast cells release mediators and recruit other cell types into the airway that drive inflammation throughout all phases of the asthmatic response<sup>2</sup>

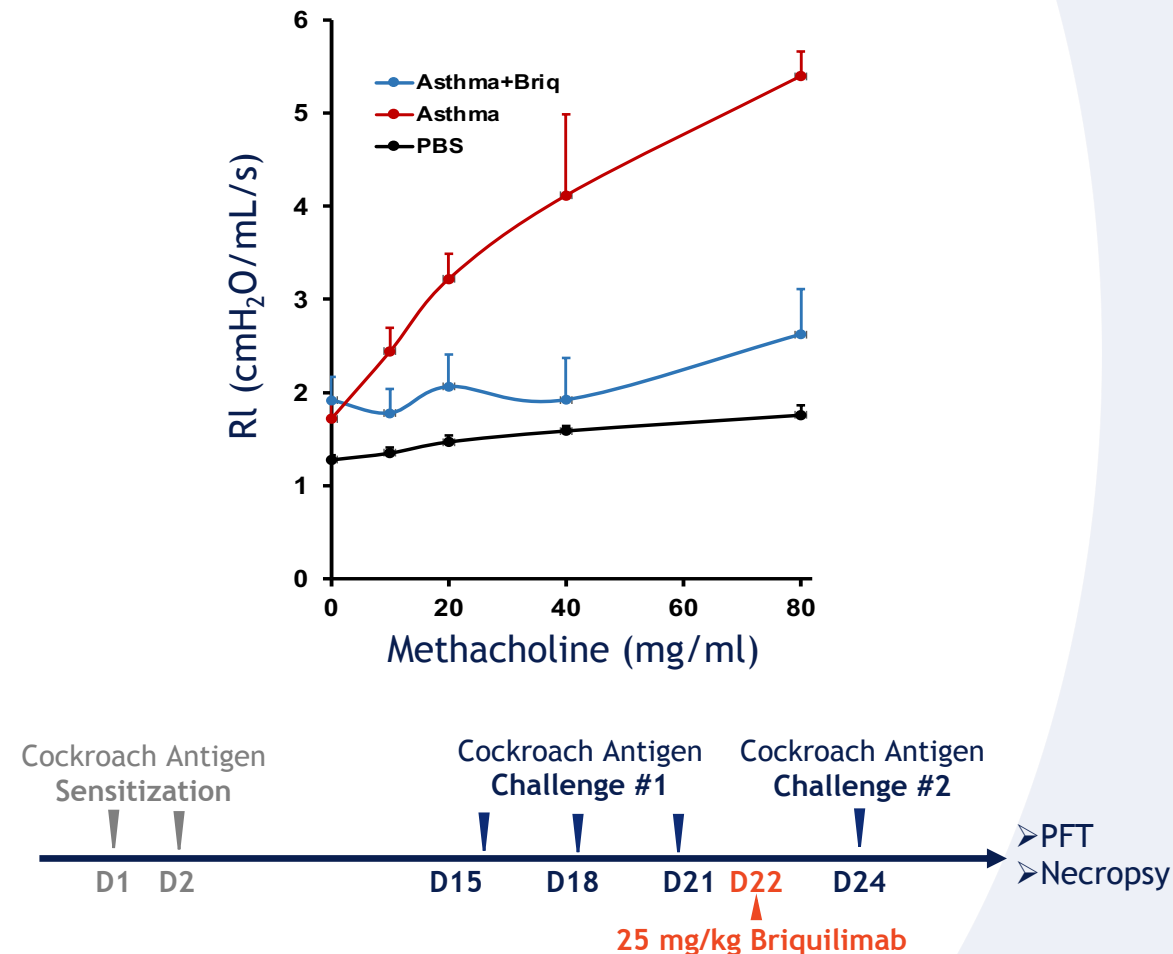


# Single dose of briquilimab depleted lung mast cells in NHP and reduced asthmatic response to allergen in Jasper c-Kit Mouse™

## Lung Mast Cell Counts in African Green Monkeys



## Jasper c-Kit Mouse™ - Pulmonary Resistance



# c-Kit inhibition in severe asthma is well supported across preclinical and clinical Phase 2 and Phase 3 data sets

- ✓ Mast cells are central to asthma pathophysiology<sup>1</sup>
- ✓ Preclinical evidence shows that briquilimab depletes lung mast cells and reduces asthmatic response to allergen<sup>2</sup>
- ✓ Clinical evidence that c-Kit inhibition improves airway response and reduces exacerbations across severe asthma endotypes<sup>3,4</sup>
  - ✓ Imatinib Phase 2 data - challenge model
  - ✓ Masitinib Phase 3 data - reduction in exacerbations

## Airway Hyperresponsiveness

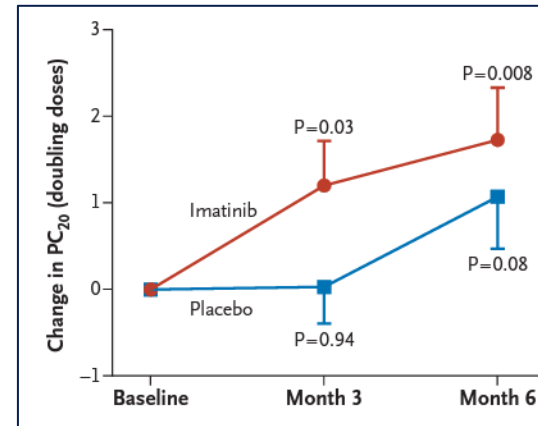


Figure 2. Change in Airway Methacholine Reactivity.

## Serum Tryptase

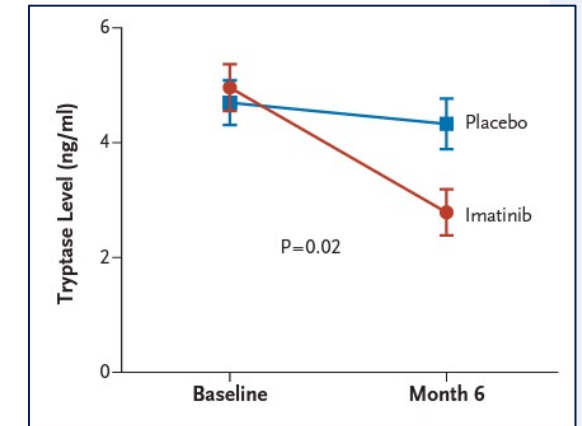


Figure 3. Total Tryptase Levels in Serum.

In patients with severe asthma, imatinib decreased airway hyperresponsiveness, MC counts, and tryptase release<sup>3</sup>

1 Galli SJ, Tsai M, Piliponsky AM. The development of allergic inflammation. *Nature*. 2008;454(7203):445-454.

2 Yu, M, et al. "Briquilimab, an Anti-CD117 (c-Kit) Antibody, Prevents Cockroach Allergen-Induced Allergic Asthma in Mice Expressing Chimeric Human and Mouse CD117." *AAAAI* February 23-26, 2024.

3 Cahill KN, Katz HR, Cui J, et al. Kit inhibition by imatinib in patients with severe refractory asthma. *N Engl J Med*. 2017;376(20):1911-1920.

4 Davidescu L, Ursol G, Korzh O, et al. Efficacy and safety of masitinib in corticosteroid-dependent severe asthma: a randomized placebo-controlled trial. *J Asthma Allergy*. 2022;15:737-747.

# Briquilimab Phase 1b/2a asthma challenge study

**Study Goal:** demonstrate proof-of-concept in asthma with a therapeutic dose of subcutaneous briquilimab to inform future trials

## Key Objectives:

- Demonstration of safety and efficacy in a new immunology and inflammation indication
- Challenge study has a high predictive value for success of future trials
- Assess the early and late asthmatic response and airway hyperresponsiveness following briquilimab administration
- Study design intended to be efficient, enabling rapid advancement of clinical program

Status: FPI targeted in Q4 2024



# Mast cell depletion offers a novel therapeutic approach for asthma



**Mast cell depletion:** briquilimab has demonstrated the ability to deplete mast cells throughout multiple tissue types



**Early and late phase response:** early phase in asthma is driven by mast cell degranulation, which may also drive the late phase recruitment of other cell types to the lung



**Airway remodeling:** reduction of inflammation by mast cell depletion may reduce excess inflammation and epithelial remodeling



**Durability and convenience:** mast cell depletion may lead to durable effect based on long periods of mast cell recovery lasting weeks to months



**Broad response:** c-Kit targeting may have an impact across multiple asthma endotypes



Market Opportunity in Mast Cell Diseases

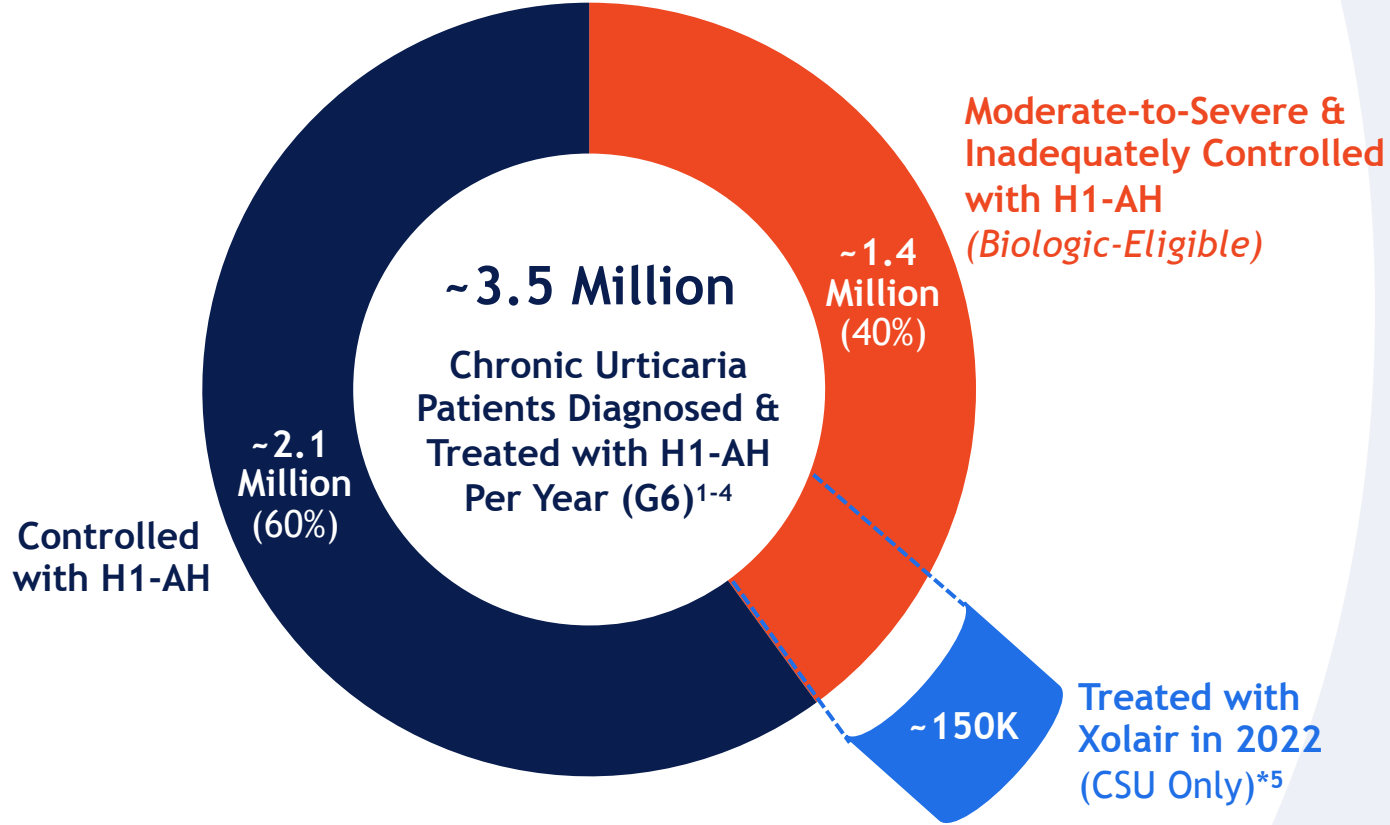
# Chronic urticaria is one of the most prevalent immunological conditions with ~1.4 million biologic eligible patients in the G6

Chronic urticaria is a devastating disease characterized by severe itching, hives/wheals, inflammation, and/or angioedema occurring for >6 weeks

Chronic urticaria symptoms can arise spontaneously (CSU) or after known triggers (CIndU)

~1.4 million patients have moderate-to-severe disease, in which the disease commonly persists for 5+ years<sup>6</sup>

## Chronic Urticaria Market Opportunity



~2/3 chronic urticaria cases are CSU; ~1/3 are CIndU (~15% of patients have both)<sup>1</sup>

# c-Kit blockade has achieved deeper and more consistent responses in chronic urticaria than other approaches

Target <sup>1</sup>	Mechanisms	Dosing Frequency	CSU Efficacy <sup>2</sup>	CIndU Efficacy <sup>2</sup>
c-Kit	Mast cell depletion	4 to 12+ weeks (SQ)	++	++
IgE*	Signal inhibition	4 weeks (SQ)	+	×
IL-4/IL-13	Cytokine inhibition	2 weeks (SQ)	+	×
BTK	Signal inhibition	Twice daily (Oral)	+	?
MRGPRX2	Signal inhibition	Daily (Oral)	?	?
JAK	Signal inhibition	Unknown (Oral)	?	?
Siglec-6	Signal inhibition	Unknown (SQ)	?	?

\*Xolair (omalizumab) FDA Approved for use in chronic spontaneous urticaria

# Briquilimab is a Differentiated c-Kit Inhibiting mAb

## c-Kit Abs in Development

### **c-Kit (CD117) monoclonal antibody**

- c-Kit antibodies in development are humanized, aglycosylated IgG1 inhibitors of c-Kit signaling

### **On-target depletion of mast cells**

- Early clinical data suggests dose-dependent inhibition of c-Kit on mast cells in the skin

### **Predictable SQ PK/PD profile**

- Established in multiple early stage trials

## Key Differentiators for Briquilimab

### **Briquilimab directly blocks SCF binding**

- Direct and potent blockage of natural ligand binding to the c-Kit receptor, limiting signal leakage

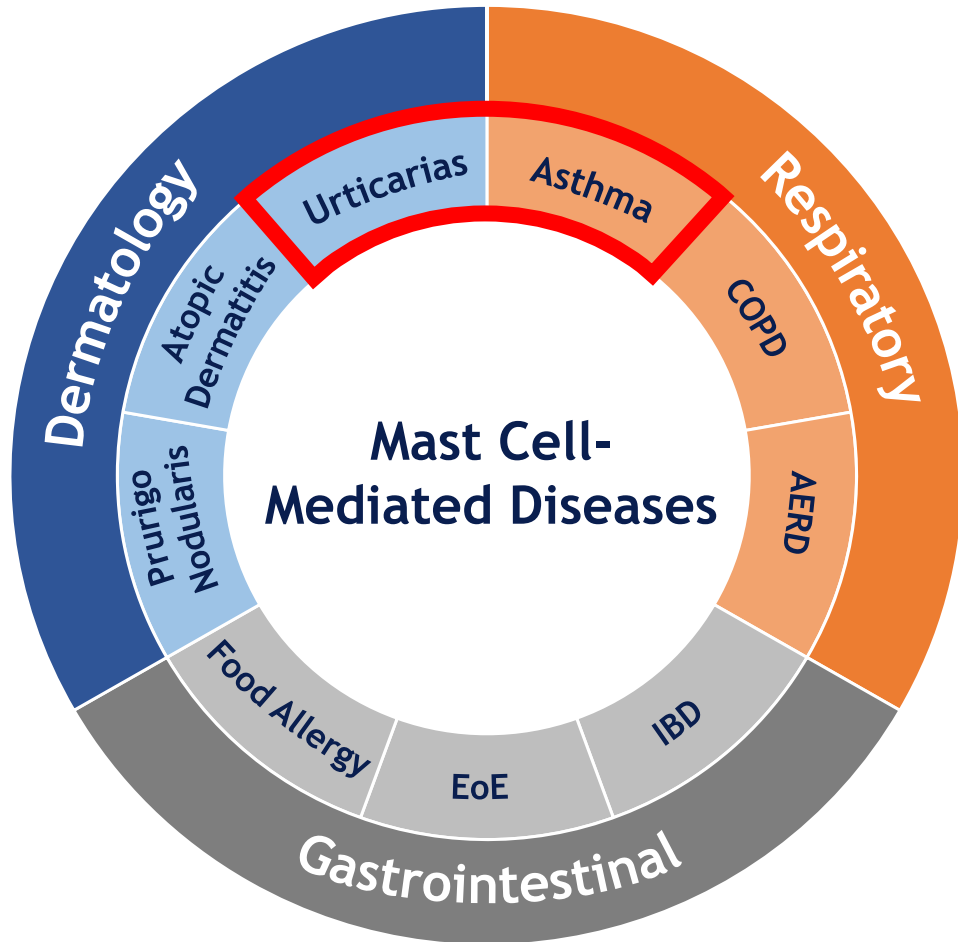
### **Shorter half-life / safety**

- Sufficient to deplete mast cells while minimizing unwanted effects on other c-Kit expressing cells

### **Optimized dosing**

- Less frequent dosing potentially leading to fewer side effects and greater compliance

# Mast cells play a central role in many diseases, presenting numerous potential opportunities for briquilimab in immunology and inflammation

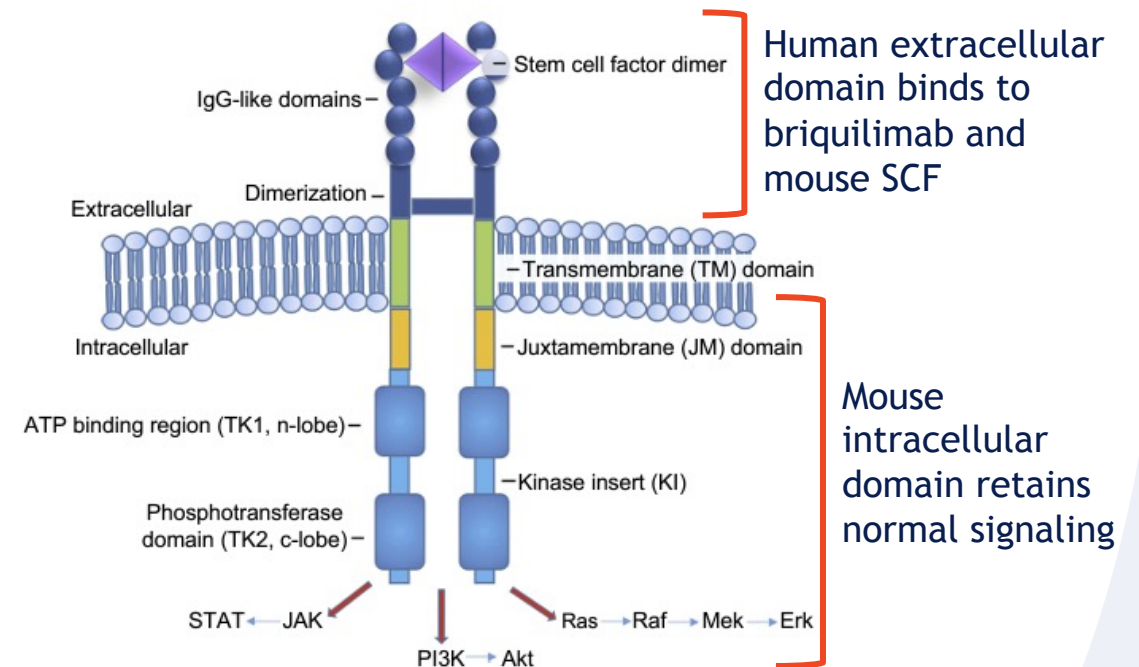


Dermatology	Other
Chronic Spontaneous Urticaria	Allergic Conjunctivitis
Chronic Inducible Urticaria	Age-Related Macular Degeneration (AMD)
Allergic Contact Dermatitis	Alpha-1 Antitrypsin Deficiency
Alopecia Areata	Alzheimer's Disease
Atopic Dermatitis	Angioedema
Bullous Pemphigoid	Celiac Disease, Dermatitis Herpetiformis
Prurigo Nodularis	Chronic GvHD
Psoriasis	Cystitis
Rosacea	Endometriosis
<b>Respiratory</b>	Fibromyalgia
<b>Asthma</b>	Hereditary Alpha Trypsinemia (HaT)
Allergic Rhinitis	Idiopathic Anaphylaxis
Aspirin Exacerbated Respiratory Disease (AERD)	Insulin-Dependent Diabetes Mellitus
Chronic Obstructive Pulmonary Disease (COPD)	Mast Cell Activation Syndrome (MCAS)
Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)	Mast Cell Leukemia
Idiopathic Pulmonary Fibrosis	Mastocytosis (KIT negative)
<b>Gastrointestinal</b>	Migraine
Eosinophilic Esophagitis (EoE)	Multiple Sclerosis
Food Allergy & Oral Immunotherapy	Pancreatitis (acute/chronic)
IBD (Crohn's, Ulcerative Colitis)	Rheumatoid Arthritis
Irritable Bowel Syndrome (IBS)	Sickle Cell Disease (Sickle Crisis)

# Jasper's c-Kit Mouse™ enables direct in-vivo disease model testing to support briquilimab's significant mast cell franchise opportunity















- c-Kit antibodies designed against human receptor do not bind to wild type mouse c-Kit, thereby limiting disease model testing
- Jasper's proprietary transgenic mouse allows for direct in-vivo testing of briquilimab
  - Transgenic mouse with human c-Kit ectodomain and mouse c-Kit intracellular domain allows for briquilimab binding leading to mast cell apoptosis

## Jasper c-Kit Mouse™



# Expanded portfolio presents exciting new opportunities in mast cell diseases

Investigator Sponsored Studies

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Fanconi Anemia						<ul style="list-style-type: none"> <li>First 6 patients achieved full chimerism &amp; count recovery; expansion to Phase 2a (enrolling)</li> </ul>
SCD / CGD / GATA2 MDS						<ul style="list-style-type: none"> <li>First 3 patients with full chimerism &amp; Hb increase (SCD)</li> <li>Enrolling patients (CGD)</li> <li>Study start up (GATA2 MDS)</li> </ul>

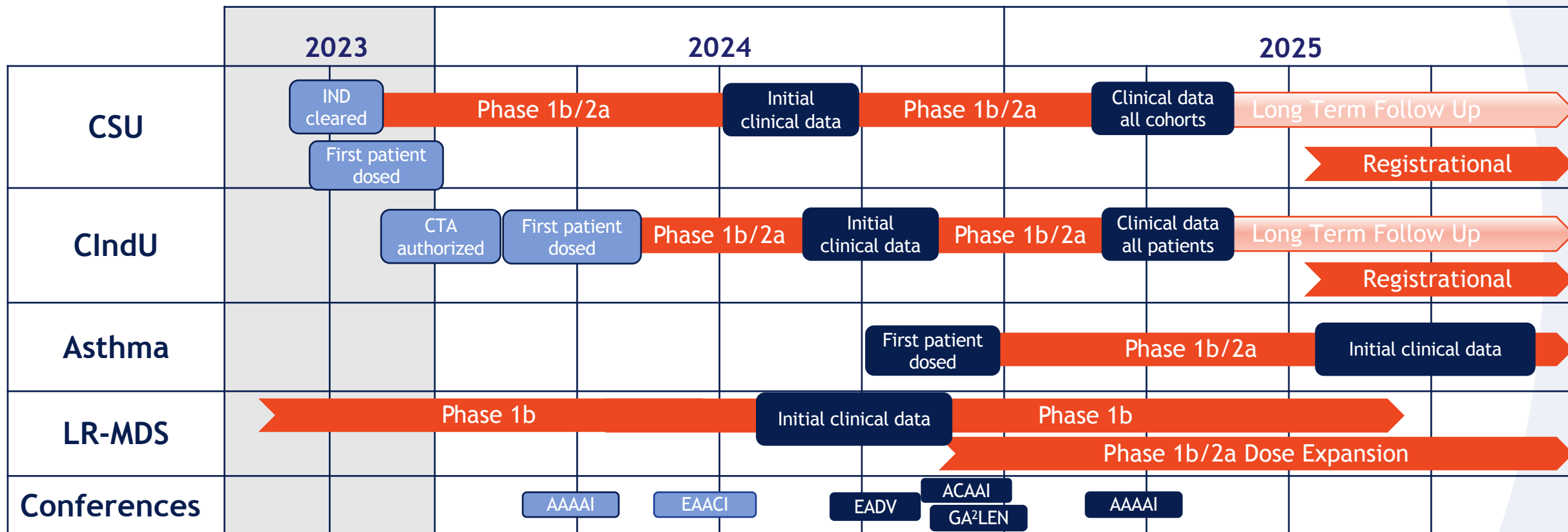
SCD, sickle cell disease; CGD, chronic granulomatous disease; MDS, myelodysplastic syndrome.

**Jasper maintains full worldwide rights to develop and commercialize briquilimab in all indications**



# Key milestones & financials

■ = Completed  
■ = Future events/milestones



## Financial Overview

\$118.5M cash & investments at 3/31/24 \*

Cash runway through 3Q25

# Jasper: Advancing briquilimab in multiple large indications

*Several significant data readouts expected in 2024*

## **c-Kit inhibition - a clinically validated mechanism driving depletion of mast cells**

- Has potential to address diseases impacting millions of patients

## **Briquilimab - a potent and differentiated c-Kit inhibitor**

- Drives mast cell depletion while potentially minimizing unwanted adverse effects
- Evaluating less-frequent dosing aligned with duration of mast cell depletion

## **Briquilimab - franchise potential in mast cell diseases**

- CSU: Phase 1b/2a BEACON study enrolling (initial data expected 3Q 2024)
- ClndU: Phase 1b/2a SPOTLIGHT study enrolling (initial data expected 2H 2024)
- Asthma: Enrollment in Phase 1b/2a study expected to commence 4Q 2024
- Additional mast cell indications under evaluation

June 2024



# Jasper Therapeutics

NASDAQ: JSPR