



**Jasper Therapeutics**

**Corporate Presentation**

*December 2024*

# Safe Harbor Statements

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# Briquilimab: Franchise Potential in Mast Cell Diseases

## c-Kit inhibition a clinically validated MOA

- 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











## Clinical Profile supports optimal biologic dosing

- Briquilimab directly blocks ligand binding with high potency
- SPOTLIGHT results show rapid onset of effect and >80% complete response rate
- SPOTLIGHT data demonstrate favorable safety profile
- Multiple doses/regimens being evaluated to balance depth of response, safety and durability

## Franchise Potential in mast cell driven diseases

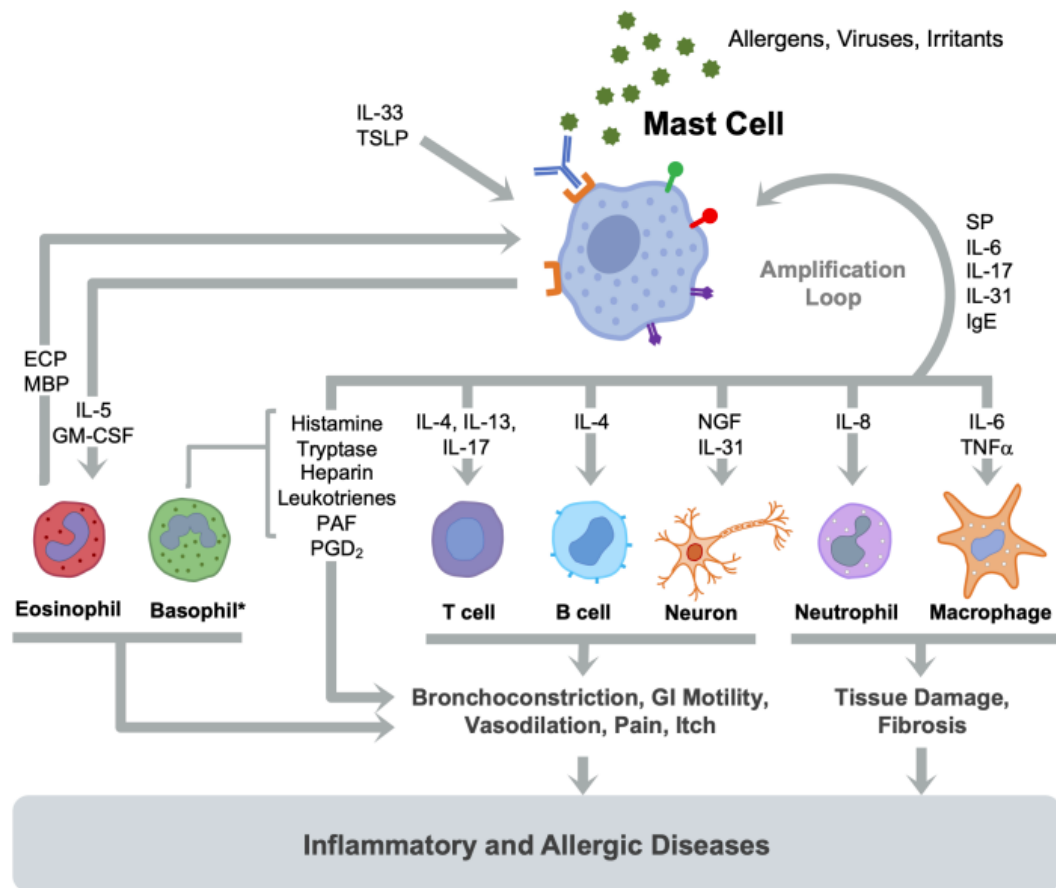
- CSU: BEACON study 12-week data for all cohorts through 240mg in early Jan 2025
- ClndU: Enrolling patients in SPOTLIGHT study 180mg cohort
- Asthma: Enrolling patients in Phase 1b/2a ETESIAN study, initial data expected in 2H 2025
- Additional mast cell mediated indications under evaluation

# Expanded mast cell portfolio presents exciting new opportunities in mast cell diseases

| 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>360mg cohort enrolling, other cohorts fully enrolled</li> <li>12-week clinical data expected in early Jan 2025</li> </ul> |
| Chronic Inducible Urticaria              |    |    |         |         |         | <ul style="list-style-type: none"> <li>83% Complete Response with 120mg</li> <li>Favorable safety profile</li> <li>Commencing enrollment in 180mg cohort</li> </ul>  |
| Asthma                                   |    |    |         |         |         | <ul style="list-style-type: none"> <li>CTA Authorized</li> <li>Enrolling in Phase 1b/2a study</li> <li>Initial clinical data expected 2H 2025</li> </ul>   |
| New Mast Cell Indication                 |    |    |         |         |         | <ul style="list-style-type: none"> <li>Multiple indications under assessment</li> </ul>  |
| <b>Stem Cell Diseases (Intravenous)</b>  |   |  |         |         |         |  |
| SCID                                     |  |  |         |         |         | <ul style="list-style-type: none"> <li>Enrolling patients</li> <li>Discussing potential BLA filing with the FDA</li> </ul>   |

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

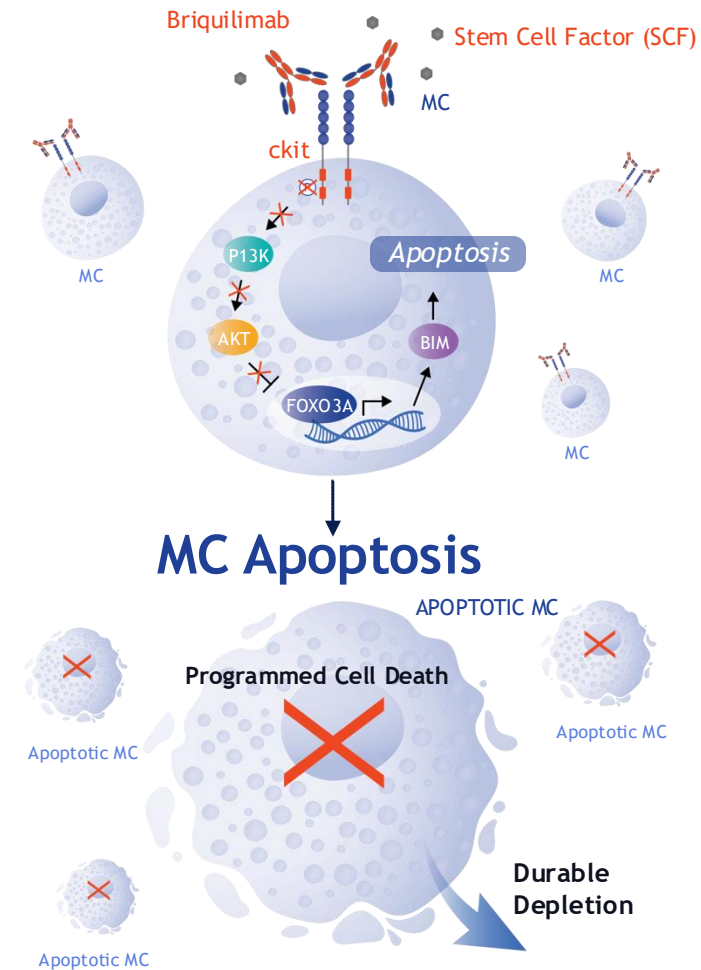


Metz et al. Allergy (2023)

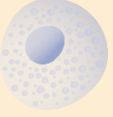




- Mast cells are primitive immune cells involved in protection against venom and parasitic infection
- Mast cells triggered by allergens, viruses and other irritants degranulate and release pro-inflammatory compounds implicated in large number of immunologic diseases
  - Allergy
  - Asthma
  - Atopic Dermatitis
  - COPD
  - Eosinophilic Esophagitis
  - Prurigo Nodularis
  - Chronic Inducible Urticaria
  - Chronic Spontaneous Urticaria
- Currently approved therapies targeting mast cell driven diseases rely on mast cell 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

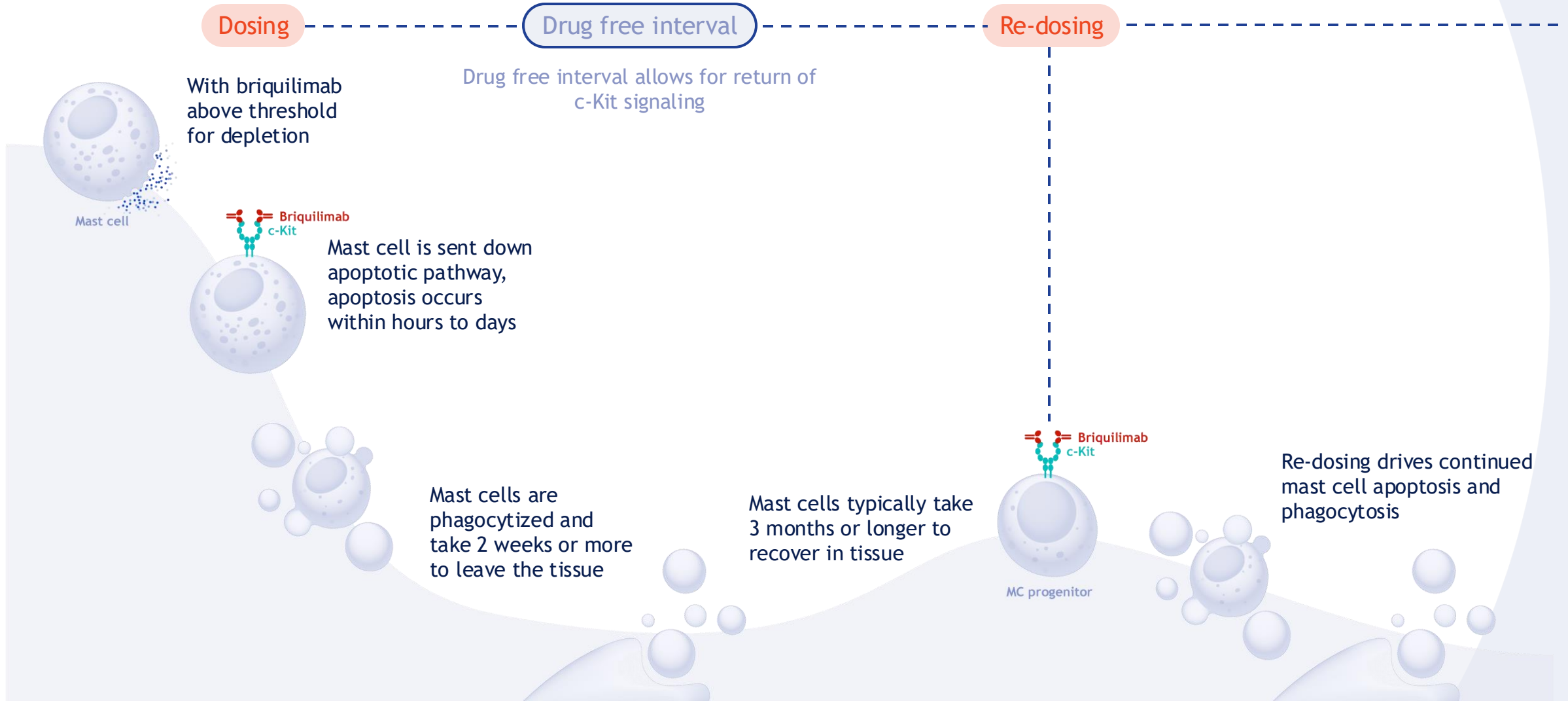
- Briquilimab is an aglycosylated IgG1 anti c-Kit antibody with high affinity to c-Kit
  - Aglycosylated c-Kit antibodies avoid indiscriminate ADCC driven killing of other c-Kit expressing cells<sup>1</sup>
  - Kd < 5pM affinity to human c-Kit with IC50 ~ 70pM
  - Human mast cell survival bioassay IC50 ~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



# 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 Optimal Biologic Dosing   |
|--|--------------------------------------|--|--|
|  <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</b> with rapid recovery expected after c-Kit signaling restored |
|  <b>Melanocyte</b>                 | Proliferation and melanin production | Blocks melanocyte proliferation and melanogenesis <sup>3</sup>       | Hair and skin hypopigmentation mitigated by exposure-free intervals, enabling melanogenesis  |
|  <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 after c-Kit signaling restored                              |

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







Briquilimab in CIndU

# CIndU can be a severe & debilitating disease resulting in a major negative impact on quality of life

- Chronic inducible urticaria (CIndU) is a debilitating inflammatory condition of the skin with a specific trigger such as heat, cold, sunlight, rubbing or scratching the skin or tight clothing
- Mast cell degranulation, leading to the release of histamine and other inflammatory mediators, is the key driver of severe itching, hives and angioedema in CIndU patients
- CIndU patients **suffer both physically and psychologically**. Severe disease has a similar **negative impact on QoL** as other dermatologic diseases like plaque psoriasis
- Targeting the c-Kit receptor with briquilimab disrupts a critical survival on mast cells leading to mast cell apoptosis and disease resolution



# Phase 1b/2a SPOTLIGHT study of subcutaneous briquilimab in CIndU

Open-label, cold urticaria & symptomatic dermographism, single ascending dose study

## Screening/Eligibility

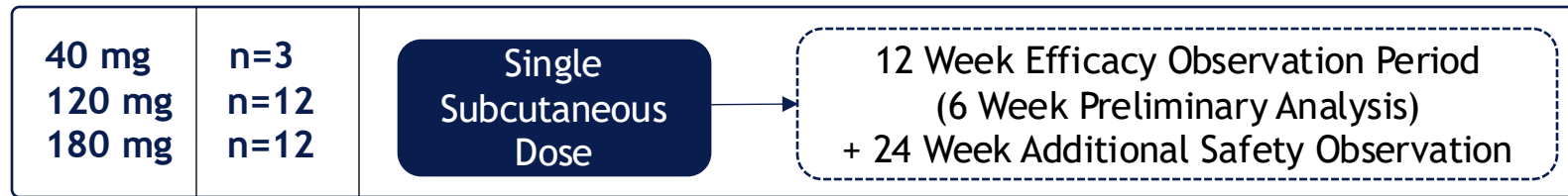
- Diagnosis of Cold Urticaria (ColdU) or Symptomatic Dermographism (SD) for  $\geq 3$  mos.
- H1-antihistamine-failed
- 18+ years

## Study Operations

- **EU Lead: Martin Metz, MD**
- 6 sites in the EU
- N = ~27
- 180mg enrollment upcoming

## Key Assessments

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



## Provocation Tests Used for Clinical Evaluation

*FricTest™ - Symptomatic Dermographism*

*CR - No response at Fric Level 4*

*PR -  $\geq 2$  pin improvement*



*TempTest™ - Cold Induced Urticaria*

*CR - Negative test at  $\leq 4^\circ\text{C}$*

*PR - Improvement by  $\geq 4^\circ\text{C}$*



# SPOTLIGHT Baseline Demographics

|   | Briquilimab 40mg<br>(n=3) | Briquilimab 120mg<br>(n=12) |
|---|---------------------------|-----------------------------|
| Age (years), mean $\pm$ SD                        | 35.3 $\pm$ 8.0            | 46.4 $\pm$ 13.8             |
| Female, n (%)                                     | 1 (33%)                   | 8 (67%)                     |
| Weight (kg), median (range)                       | 86.0 (69-94)              | 99.0 (57-115)               |
| Cold Urticaria, n                                 | 1                         | 4                           |
| Symptomatic Dermographism, n                      | 2                         | 8                           |
| Baseline Provocation Threshold                    |                           |                             |
| TempTest™ (°C), mean (range)                      | 16.0 (16-16)              | 20.8 (15-27)                |
| FricTest™ (Pin Count), mean (range)               | 3.5 (3-4)                 | 3.9 (3-4)                   |
| Urticaria Control Test (UCT) score, mean $\pm$ SD | 3.7 $\pm$ 2.5             | 6.3 $\pm$ 3.3               |
| Tryptase (ng/ml), mean (range)                    | 4.7 (4.1-5.3)             | 7.6 (3.6-25.7)              |

# SPOTLIGHT 6 Week Efficacy Evaluation

Briquilimab 120mg single dose achieved 83% (10 of 12) complete response

|   | Briquilimab<br>40mg<br>(n=3) | Briquilimab<br>120mg<br>(n=12) | Briquilimab<br>All doses<br>(n=15) |
|---|------------------------------|--------------------------------|------------------------------------|
| Complete Response, n (%)                        | 1 (33%)                      | 10 (83%)                       | 11 (73%)                           |
| ColdU, n  | 0                            | 3                              | 3                                  |
| Symptomatic Dermographism, n                    | 1                            | 7                              | 8                                  |
| Partial Response, n (%)                         | 2 (66%)                      | 1 (8%)                         | 3 (20%)                            |
| ColdU, n  | 1                            | 0                              | 1                                  |
| Symptomatic Dermographism, n                    | 1                            | 1                              | 2                                  |
| Complete or Partial Response at any time, n (%) | 3 (100%)                     | 11 (92%)                       | 14 (93%)                           |

# SPOTLIGHT 6 Week Efficacy Evaluation

## Rapid Onset of Effect

- >70% of 120mg patients with a CR or PR at 1 week assessment

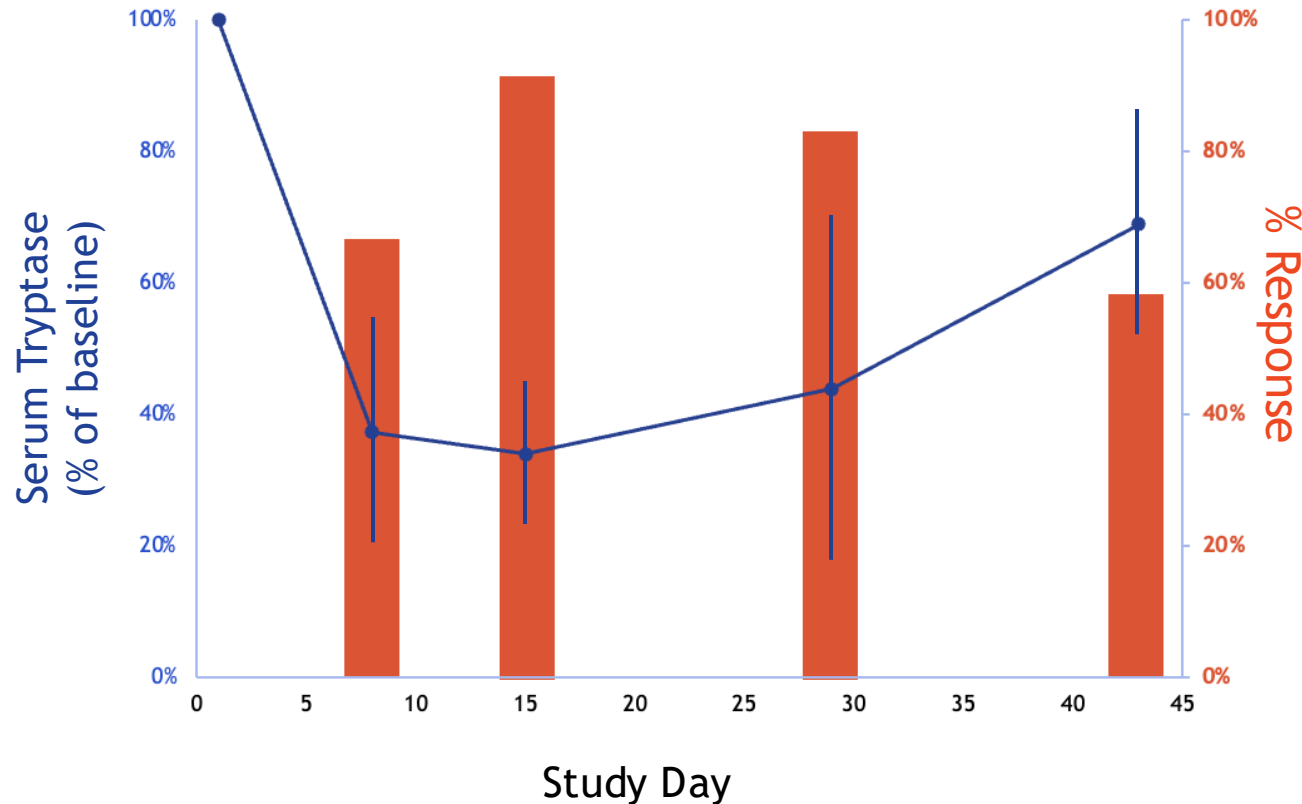
## Depth of Response

- 93% (14 of 15) of patients reporting a clinical response
- 92% (11 of 12) patients at the 120mg dose achieving a CR or PR by week 2
- 83% (10 of 12) patients at the 120 mg dose reported as well controlled or complete disease control by UCT score at week 4

## Durability of Effect

- 6 CRs and 1 PR continue at six weeks, durability assessment ongoing

# SPOTLIGHT: Complete or partial response and serum tryptase through 6 weeks with briquilimab 120mg (n=12)



- Significant clinical response occurs within one week following dosing
- Serum tryptase reductions occur within the first week following dosing
  - Magnitude of tryptase reductions do not appear to be predictive of clinical response
  - i.e. Tryptase reductions as low as 50% associated with Complete Response in preliminary SPOTLIGHT data
- Serum tryptase recovery does not predict the timing of return of symptoms
  - Patients maintained CR even with tryptase recovering to 70%+ of baseline in preliminary SPOTLIGHT data

# SPOTLIGHT safety and tolerability

|  | Briquilimab 40mg<br>(n=3) | Briquilimab 120mg<br>(n=12) |
|--|---------------------------|-----------------------------|
| Any adverse event*                           | 2**                       | 10***                       |
| Any serious adverse event                    | 0                         | 0                           |
| Hypersensitivity reaction                    | 0                         | 0                           |
| Any adverse event leading to discontinuation | 0                         | 0                           |
| Adverse event leading to death               | 0                         | 0                           |
| Adverse event $\geq$ grade 3                 | 0                         | 0                           |

\*AEs occurring in  $\geq 2$  participants: fatigue, dizziness, headache, nasopharyngitis, blood CK increased, diarrhea, muscle tightness, nausea

\*\*AE report of Grade 1 neutropenia at Day 94, ANC 1825, resolved by Day 164

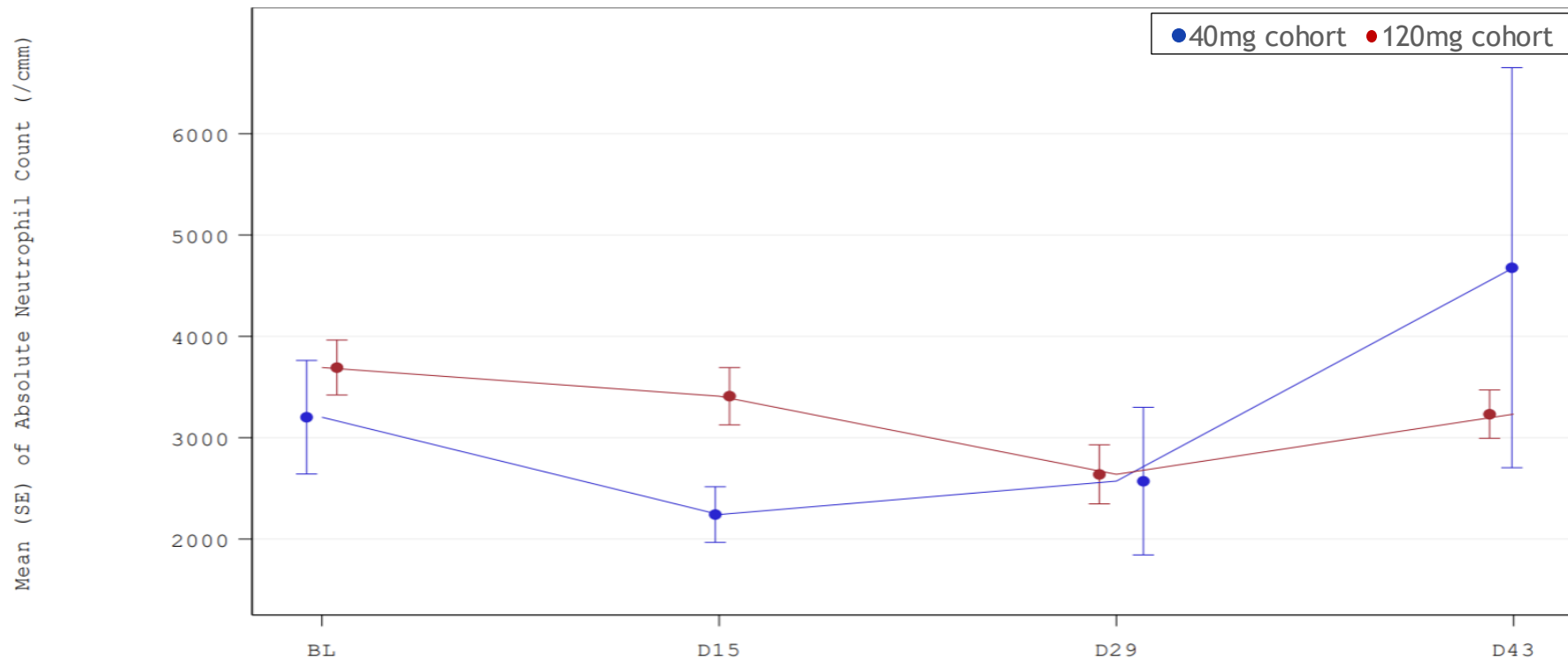
\*\*\*AE report of Grade 1 neutrophil decreased at Day 29, ANC 1570, resolved by next measurement, Day 39




# SPOTLIGHT Absolute Neutrophil Count

No ANC values observed below 1500 and no association with infection

Figure AD\_F0007. Mean (SE) of Absolute Neutrophil Count (/cmm) over Visit by Cohort (up to Week 6 (Day 43))  
Safety Analysis Set





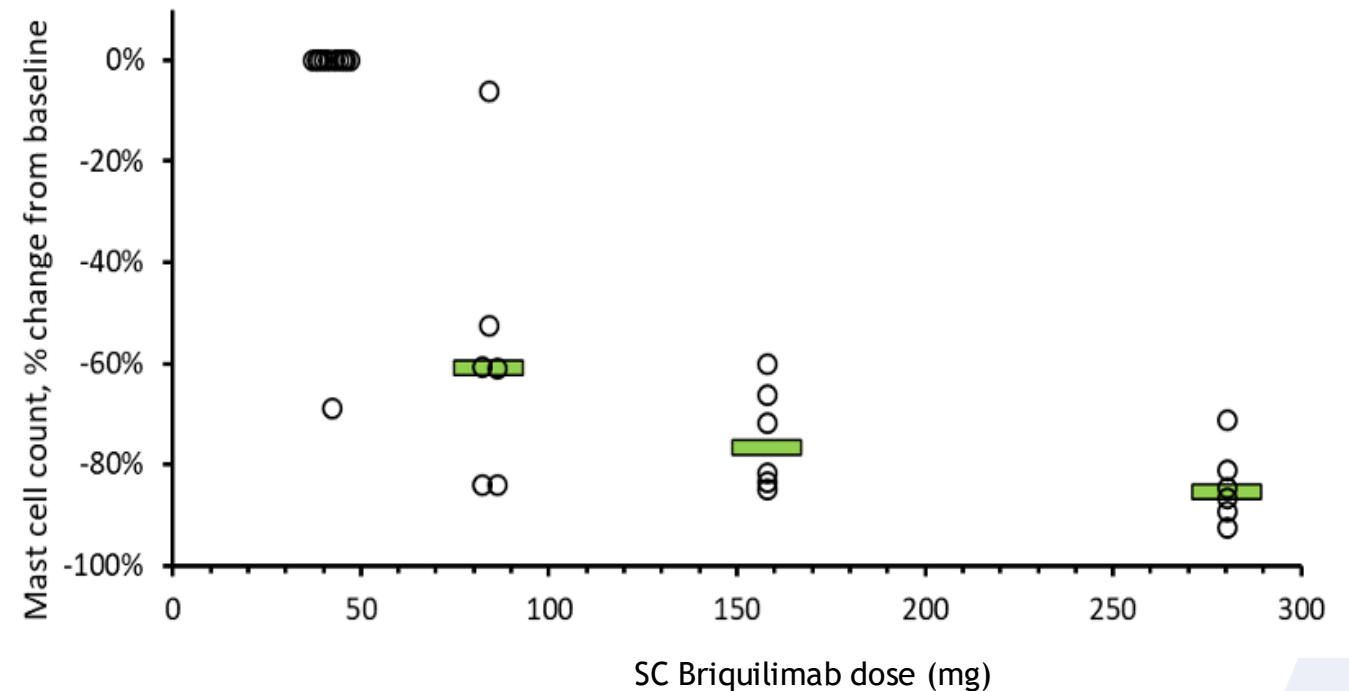
# Briquilimab in Chronic Spontaneous Urticaria

# 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 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: Martin Metz, MD
- ~30 sites in the US & EU
- N = ~50

## Key Assessments

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

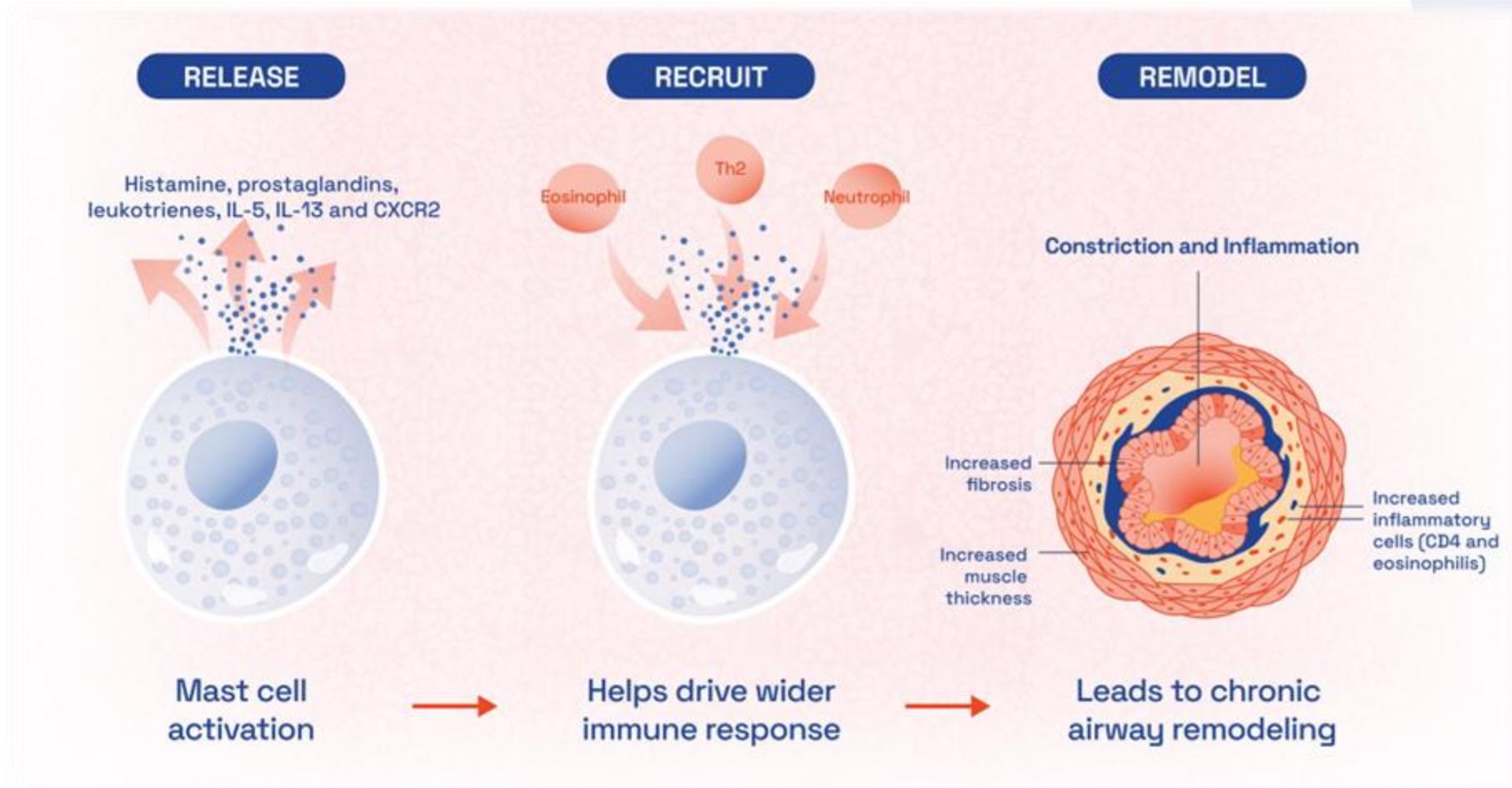
|  | Patients (Randomization)                                      | Dose (Frequency)  | Cohorts  | Key Assessments & Follow Up  |
|--|---|---|--|--|
| Part 1<br>Open Label<br>(n=6)                              | 3+3<br>3+3  | 10 mg<br>40 mg  | Dose W0, 4, 12, 20<br>Dose W0, 4, 12, 20   | Day 8 - Safety Assessment<br>Week 12 - UAS7 Efficacy Assessment<br>24 week - Follow Up |
| Part 2<br>Double-Blind<br>Placebo-<br>Controlled<br>(n=36) | n=8 (3:1)<br>n=6 (2:1)<br>n=6 (2:1)<br>n=8 (3:1)<br>n=8 (3:1) | 80 mg (Q8W)<br>120 mg (Q8W)<br>120 mg (Q12W)<br>180 mg (Q12W)<br>180 mg (Q8W) | Dose W0, 8, 16, 24<br>Dose W0, 8, 16, 24<br>Dose W0, 12, 24<br>Dose W0, 12, 24<br>Dose W0, 8, 16, 24 | Day 8 - Safety Assessment<br>Week 12 - UAS7 Efficacy Assessment<br>24 week - Follow Up |
| Part 3<br>Double-Blind<br>Placebo-Controlled<br>(n=8)      | n=4 (3:1)<br>n=4 (3:1)  | 240 mg<br>360 mg  | Single Dose<br>Single Dose   | Day 8 - Safety Assessment<br>Week 12 - UAS7 Efficacy Assessment<br>36 week - Follow Up |



# Briquilimab in Asthma

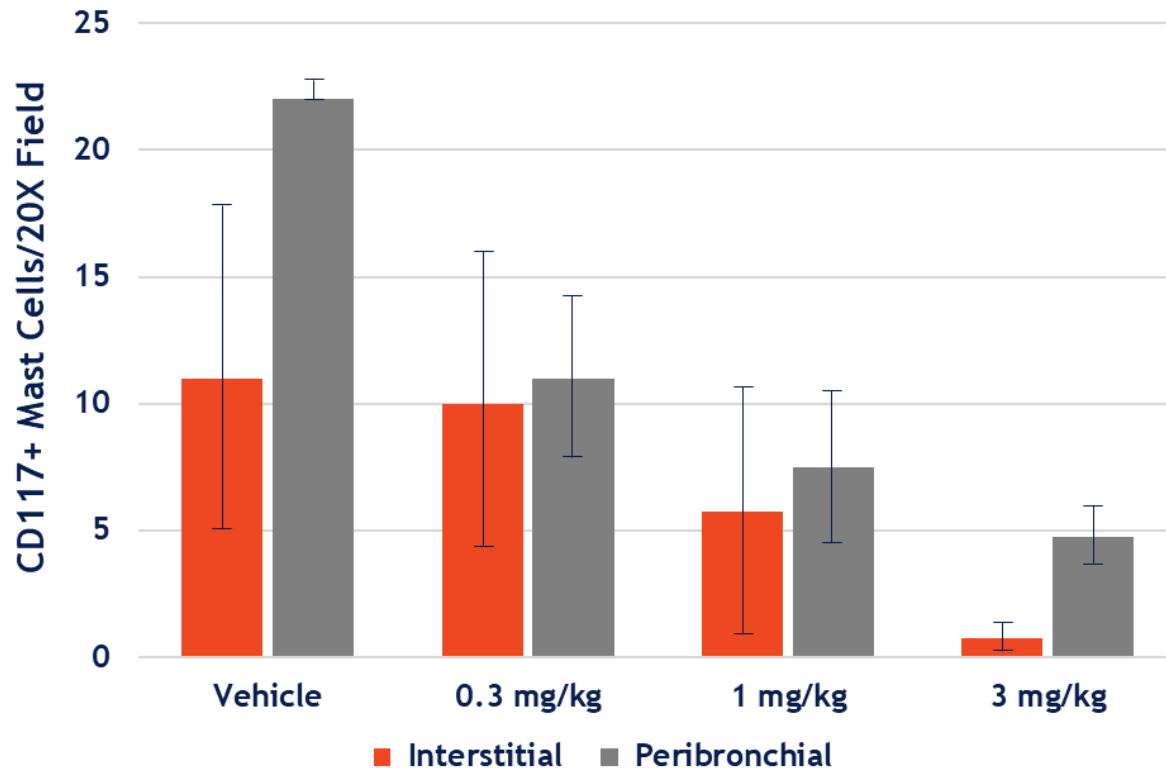
# Mast cells play a critical role in allergic inflammation and tissue remodeling in asthma

- 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>

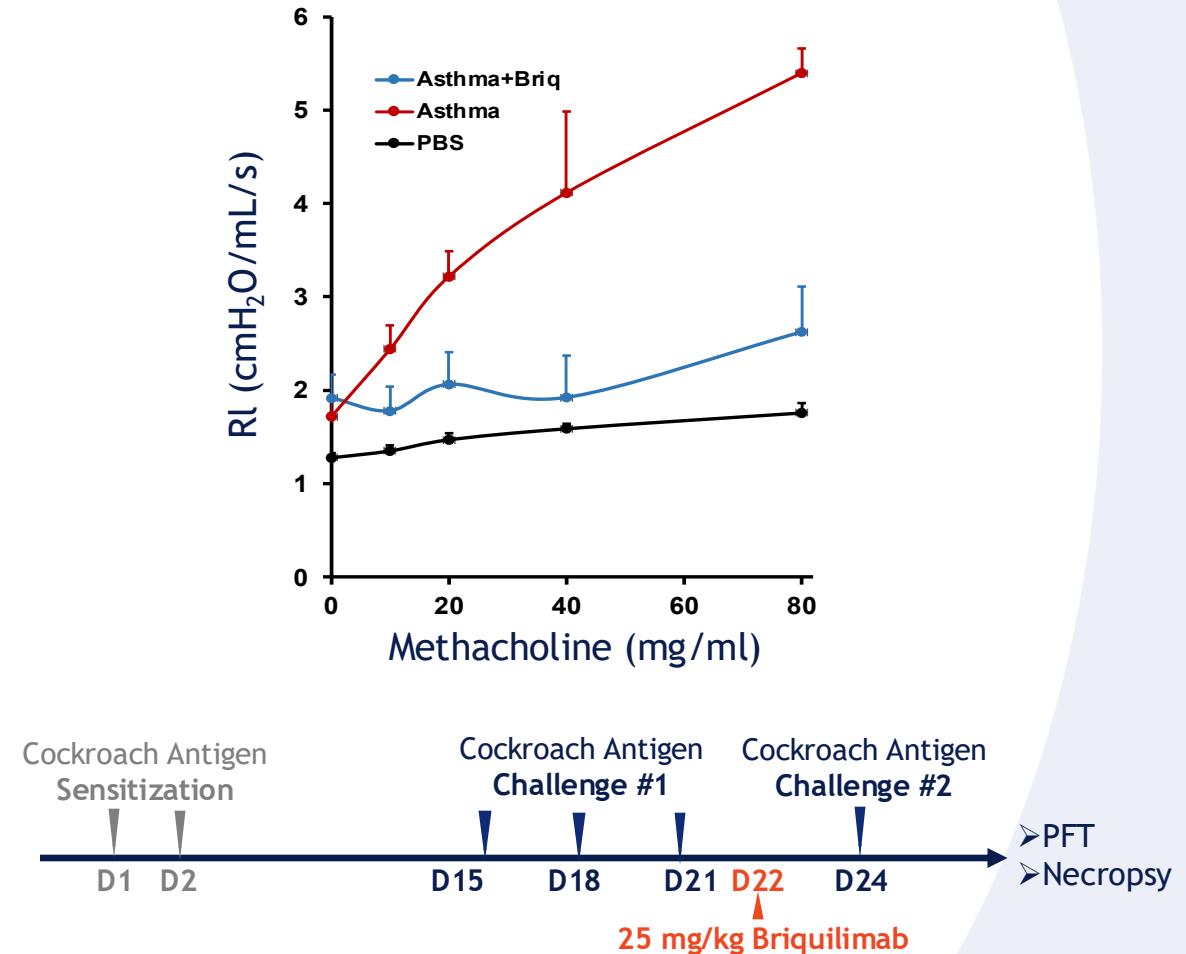


# Single dose of briquilimab depleted lung mast cells in NHP and reduced asthmatic response to allergen in Jasper c-Kit Mouse™

## Lung Mast Cell Counts in African Green Monkeys



## Jasper c-Kit Mouse™ - Pulmonary Resistance





# c-Kit inhibition in severe asthma is demonstrated 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

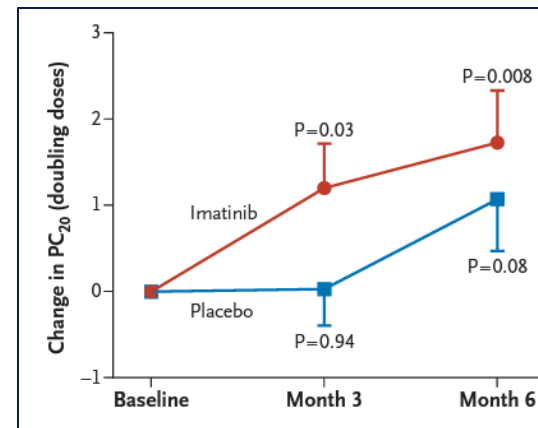


Figure 2. Change in Airway Methacholine Reactivity.

## Serum Tryptase

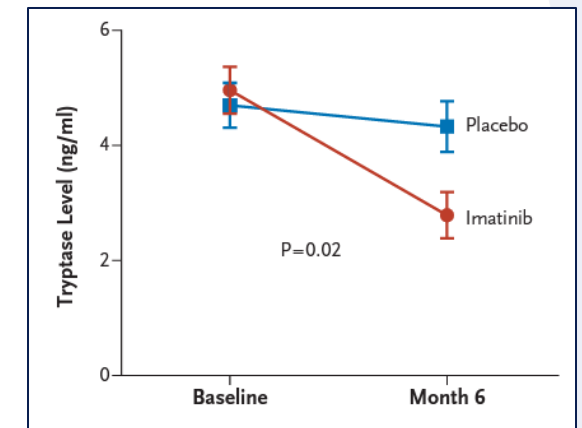


Figure 3. Total Tryptase Levels in Serum.

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 ETESIAN challenge study in allergic asthma

Double-blind, placebo-controlled, single dose study

## Screening/Eligibility

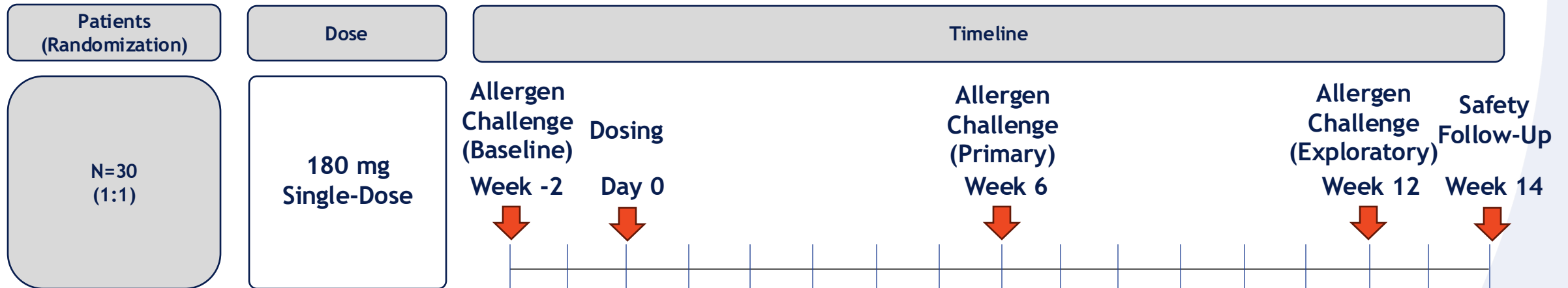
- Diagnosis of stable allergic asthma
- Baseline FEV<sub>1</sub> 70% of predicted value
- Positive methacholine challenge at baseline
- 18-65 years of age

## Study Operations

- Lead Investigator: Paul O'Byrne, MD
- Up to 7 centers in Canada
- N = 30 patients

## Key Assessments

- **Early & Late Asthmatic Response:** % decrease in FEV<sub>1</sub> from baseline
- **Changes in Airway Hyperresponsiveness:** Methacholine PD20 24 hours after allergen challenge
- **Mast Cell Depletion & Recovery:** Serum Tryptase
- **Safety:** TEAEs, SAEs



**Endpoints: Allergen Challenge & Methacholine PD20 measured at 6 weeks (Primary) and 12 weeks (Exploratory)**

# 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

The background of the slide features a light blue gradient with a white curved line across the middle. A vertical line passes through the center, with a red circle at its intersection. Faint, blue-tinted microscopic images of cells are scattered across the background.

# Market Opportunity in Mast Cell Diseases

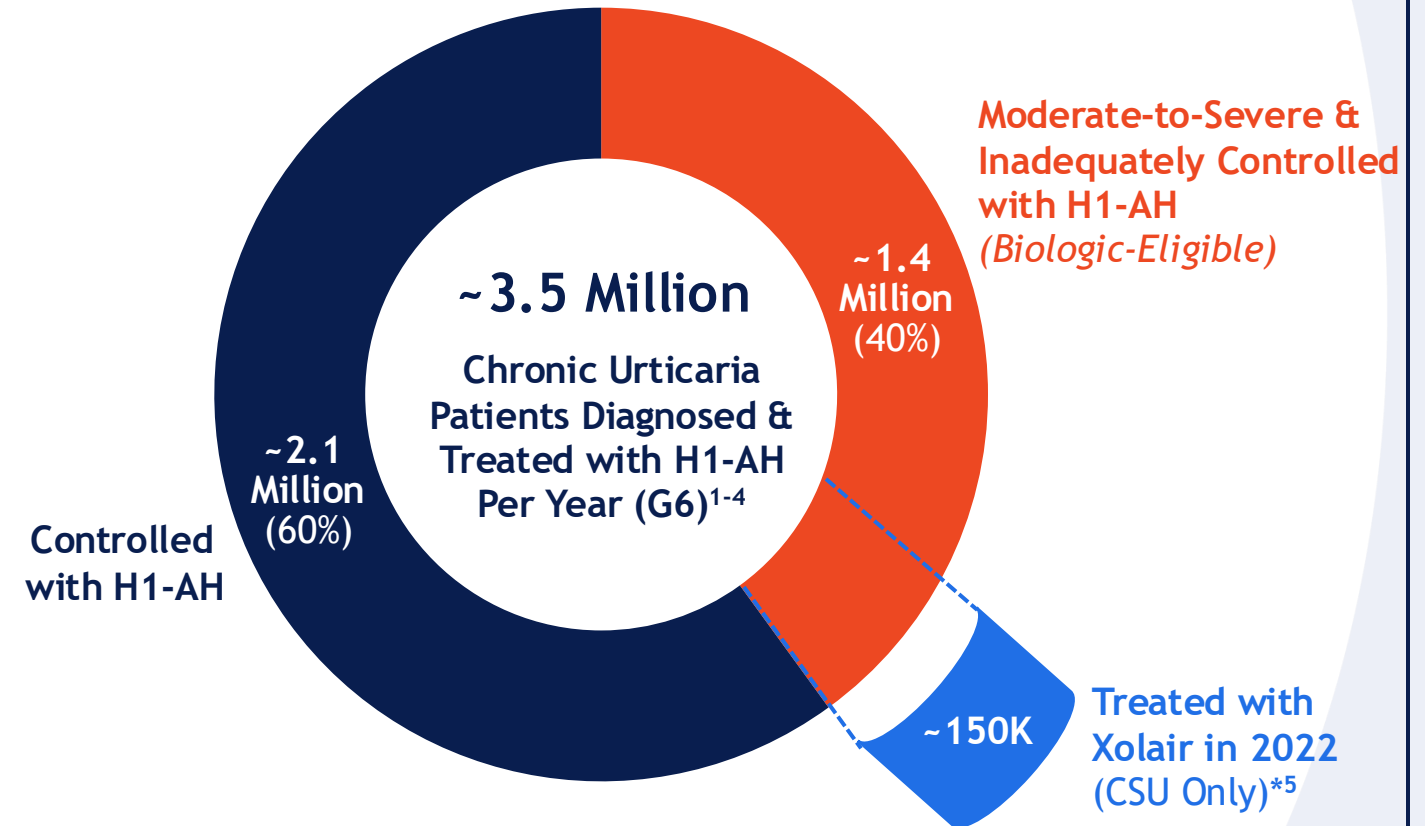
# Chronic urticaria is one of the most prevalent immunological conditions with ~1.4 million biologic eligible patients in the G6

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)

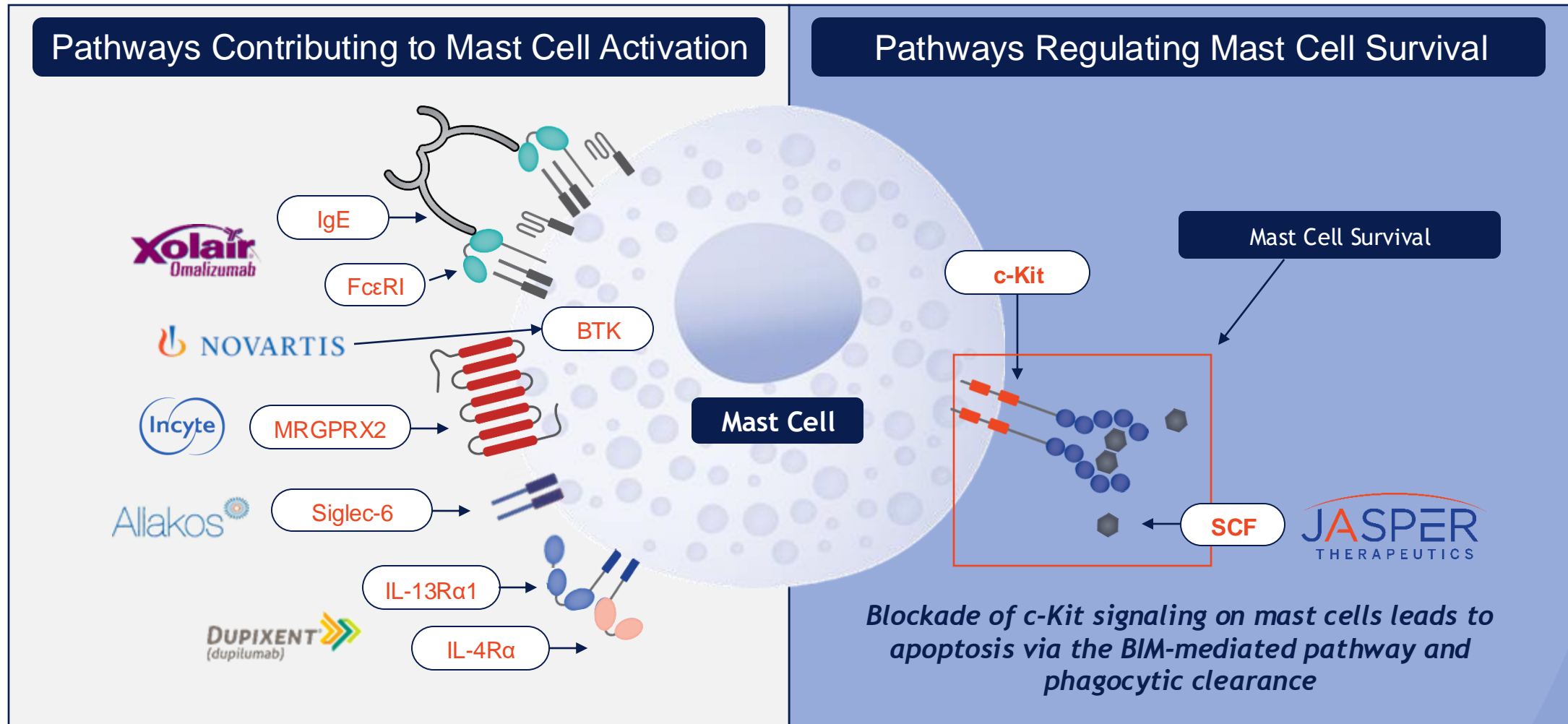
~1.4 million patients have moderate-to-severe disease, in which the disease commonly persists for 5+ years<sup>6</sup>

## Chronic Urticaria Market Opportunity

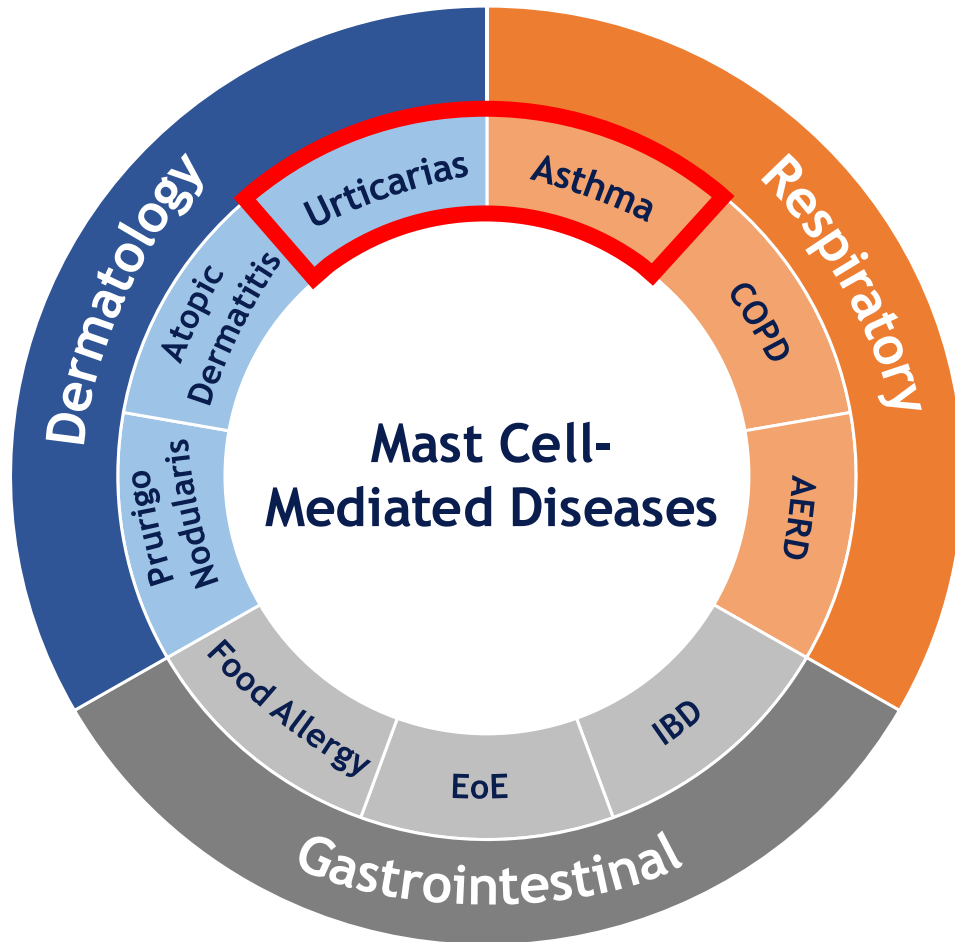


~2/3 chronic urticaria cases are CSU; ~1/3 are CIndU (~15% of patients have both)<sup>1</sup>

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



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

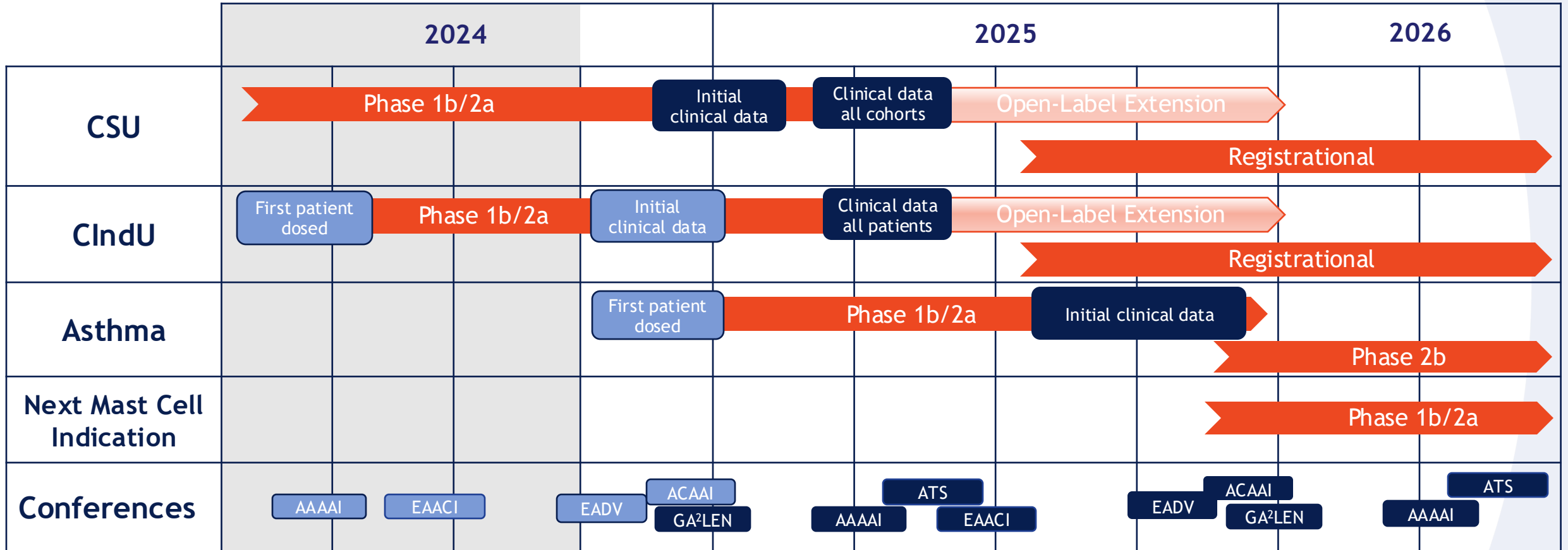


**Currently targeted indications**

| 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)      |

# Key milestones & financials

■ = Completed  
■ = Future events/milestones



## Financial Overview

\$92.5M cash & investments at 9/30/24 \*

Cash runway through 3Q25



# Jasper: Advancing briquilimab in multiple large indications

*Significant data readout expected in January 2025*

## c-Kit inhibition - a novel mechanism driving depletion of mast cells

- Has potential to address diseases impacting millions of patients

## Briquilimab - a clinically validated, potent and differentiated c-Kit inhibitor

- Drives rapid and robust clinical responses while minimizing unwanted adverse effects
- Evaluating additional doses/dose regimens to identify optimal biologic dosing

## Briquilimab - franchise potential in mast cell diseases

- CSU: Phase 1b/2a BEACON study data, including 180 mg and 240 mg cohorts, in January 2025
- ClndU: Phase 1b/2a SPOTLIGHT study commencing 180 mg cohort
- Asthma: Enrolling in Phase 1b/2a ETESIAN study, initial data expected in 2H 2025
- Additional mast cell indication expected to start clinical development in 2025

December 2024



# Jasper Therapeutics

NASDAQ: JSPR