## **Jasper Therapeutics**

**Corporate Presentation** 

March 2024

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### Briquilimab: Franchise Potential in Mast Cell Diseases

<u>c-Kit inhibition</u> a promising new MOA in mast cell diseases	<ul> <li>Mast cells are key drivers in immunological and dermatological diseases with high unmet need</li> <li>Mast cell depletion has distinct potential to deliver safe and durable disease control</li> <li>c-Kit inhibition is the only therapeutic mechanism shown to significantly deplete mast cells</li> <li>c-Kit inhibition has demonstrated clinical proof of concept in multiple mast mediated diseases</li> </ul>
<u>Briquilimab</u> a potent c-Kit inhibitor	<ul> <li>Briquilimab is a potent c-Kit inhibitor proven to drive mast cell depletion</li> <li>Briquilimab could allow for less frequent dosing</li> <li>Dosing and PK profile could minimize unwanted adverse effects</li> <li>Therapeutic potential extends beyond mast cell diseases into stem cell diseases</li> </ul>
Robust pipeline multiple company- led clinical programs	a coor inst patient dosed in mase is za beneon stady (initiat data expected so zoz i)



# Expanded portfolio presents exciting new opportunities in mast cell diseases

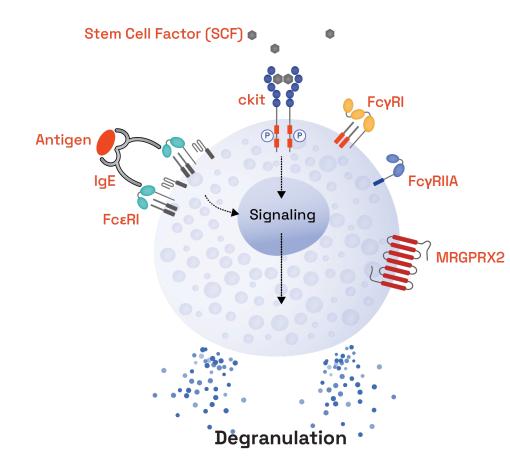
Indication	Sponsor	Research	Preclinical	Clinical	Program Milestones	
Briquilimab						
Mast Cell Diseases (Subcutaneou	is)					
Chronic Spontaneous Urticaria	JASPER				<ul> <li>IND cleared; EU CTA authorized</li> <li>Enrolling patients</li> <li>Initial clinical data expected in 3Q 2024</li> </ul>	
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Stem Cell Diseases (Intravenous)						
Low-to-Intermediate Risk MDS	JASPER				<ul> <li>Enrolling patients</li> <li>Initial clinical data expected by mid-year 2024</li> </ul>	
SCID	JASPER				Enrolling patients     Potential BLA filing	
Fanconi Anemia	Stanford University				<ul> <li>First 4 patients achieved full chimerism &amp; count recovery</li> <li>Expansion to Phase 2a (enrolling)</li> </ul>	
Sickle Cell Disease					• First 3 patients with full chimerism & Hb increase (enrolling)	
Chronic Granulomatous Disease	NIH				Enrolling patients	
GATA2 MDS	National Institutes of Health				Study start up	

Investigator Sponsored Studies

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



# Mast cells are key drivers of the inflammatory response in a number of allergic and dermatologic diseases

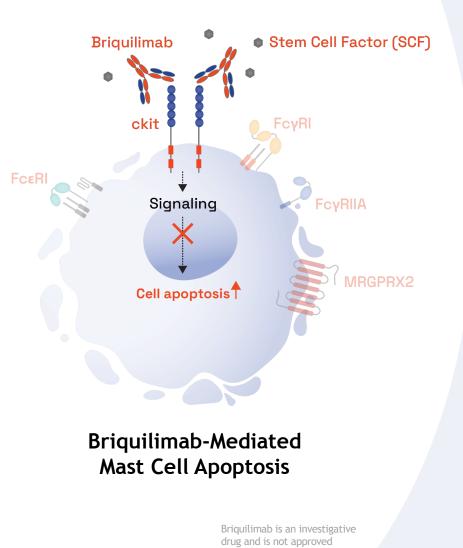


- Mast cells are the most potent drivers of inflammatory response in skin, lungs and gut
- Activated mast cells release pro-inflammatory compounds that drive diseases such as Chronic Spontaneous Urticaria, Chronic Inducible Urticaria, Asthma and many others
- Current approved therapies targeting mast cell driven diseases have limited efficacy and limited durability of response



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

- SCF signaling through c-Kit prevents mast cells apoptosis via the Bim-mediated pathway<sup>1</sup>
- Blockade of c-Kit signaling on mast cells leads to organized cell death and phagocytic clearance<sup>2</sup>
  - Partial c-Kit inhibition blunts mast cell activation
- Aglycosylated c-Kit antibodies avoid indiscriminate ADCC driven killing of other c-Kit expressing cells<sup>3</sup>
- Unwanted effects on other c-Kit expressing cells can be minimized by the recovery of c-Kit signaling once the mast cells are depleted



for any indication

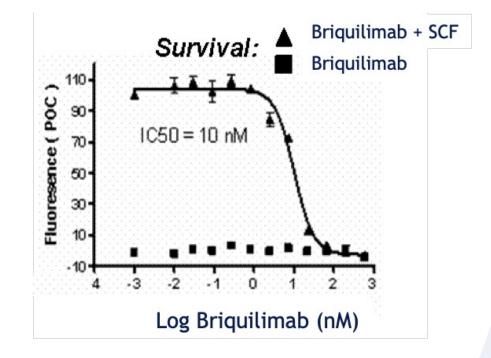


Moller C et al. Blood (2005)
 Hundley TR et al. Blood (2004)
 Arnold JN et al. Annu Rev Immunol (2007)

# Briquilimab potently blocks c-Kit signaling leading to durable mast cell depletion

- Briquilimab is an aglycosylated IgG1 anti c-Kit antibody with high affinity to c-Kit (Kd <5pm)
- Briquilimab potently blocks c-Kit signaling by blocking the SCF ligand binding site on the receptor and triggering apoptosis
- Mast cell depletion occurs within hours to days

1 Jasper internal data



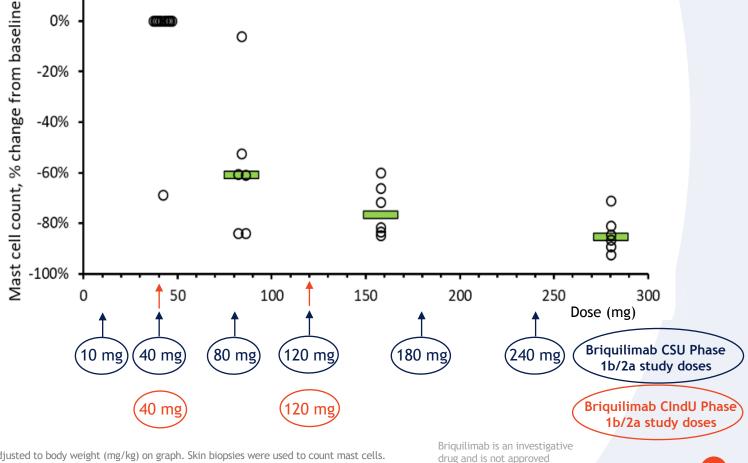
Mast cell survival assay<sup>1</sup>



# Briquilimab delivered with a single subcutaneous injection significantly depletes skin mast cells in humans

- A single subcutaneous dose at / above ~80mg potently depletes mast cells in the skin of healthy volunteers
- Skin mast cell depletion highly correlated to serum briquilimab exposure after subcutaneous administration
- Significant depletion by day 7, with durable response lasting at least 29 days
- Once depleted with an anti-c-Kit antibody, skin mast cells take at least 3 months to recover, potentially leading to durable disease control<sup>2</sup>

Skin mast cell depletion 4 weeks after single dose (≥42 mg)<sup>1</sup> Briquilimab Healthy Volunteer Phase 1 Subcutaneous Study



for any indication

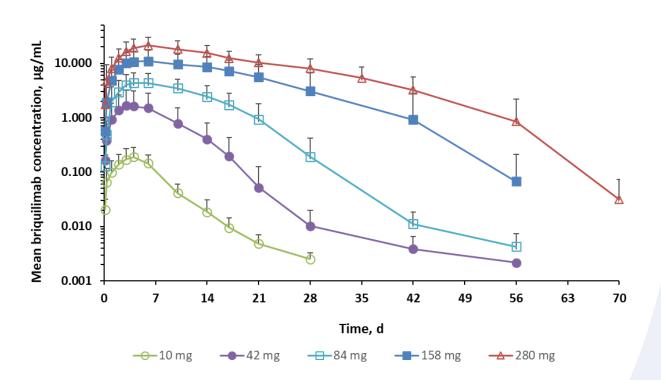


1 Jasper internal data (Phase 1a, healthy volunteer study); Dose is adjusted to body weight (mg/kg) on graph. Skin biopsies were used to count mast cells. 2 Maurer et al, GA<sup>2</sup>LEN Global Urticaria Forum - Berlin, December 6, 2022

# Briquilimab's favorable pharmacokinetic properties may enable optimal biologic dosing

- Briquilimab is designed to minimize unwanted c-Kit-related effects
- Subcutaneous dosing leads to predictable PK profile
- Low frequency of ADAs and do not appear to affect PK
- Drug elimination profile is favorable for minimizing off target effects
  - Clearance to allow for return of c-Kit signaling once the mast cells are depleted
  - No modifications to extend FcRn recycling

#### Pharmacokinetics (≥10 mg)<sup>1</sup> Briquilimab Healthy Volunteer Phase 1 Subcutaneous Study





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

- c-Kit is expressed on mast cells, hemopoietic stem cells, melanocytes, taste buds, spermatogonia and Cajal (GI) cells, which all may be impacted by anti-c-Kit agents
- Briquilimab's favorable elimination kinetics may allow for an improved safety profile on these other cell types

#### **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



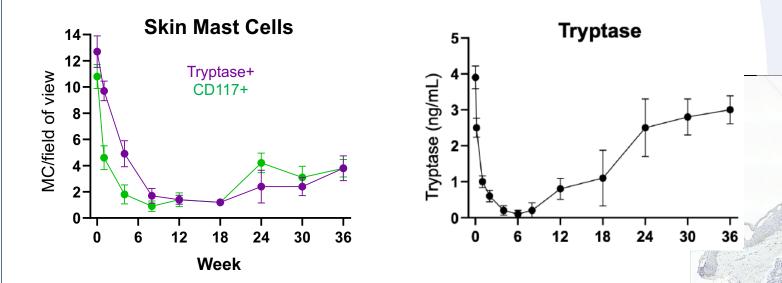
### Briquilimab in Chronic Urticaria



Phase 1b/2a dose<sup>2</sup>frequ<sup>2</sup>encles<sup>3</sup>selected to align with<sup>6</sup> mast celt<sup>4</sup> <sup>30</sup> recovery in the skin, which typically takes 3 months or longer

- Single administration of antic-Kit leads to deep depletion of skin mast cells
- Following depletion, mast cell recovery in the skin takes at least three months<sup>1</sup>
- Serum tryptase recovery precedes return of urticarial symptoms and skin mast cells
  - Likely due to earlier recovery of lung and gut mast cells

#### 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 is an investigative drug and is not approved for any indication



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

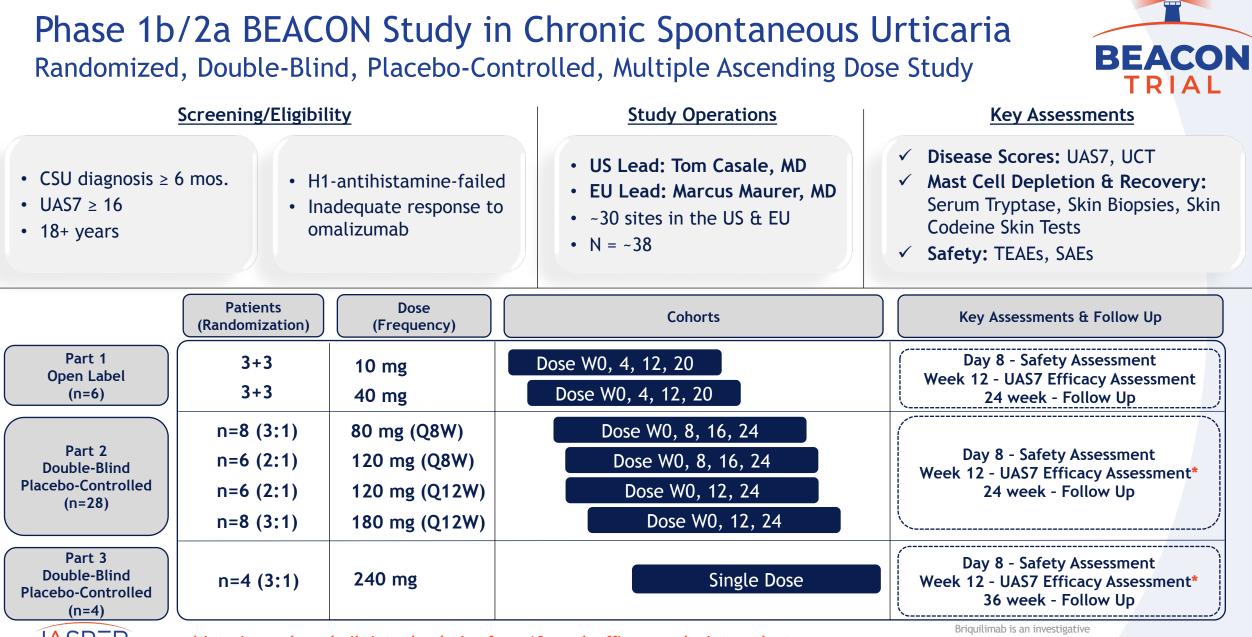


**Study Goal:** identify the optimal therapeutic doses & dosing frequency of subcutaneous briquilimab to inform future registrational trials

#### **Key Objectives:**

- Study multiple briquilimab dose levels, and intervals ranging from 4 to 12+ weeks to study the effects of:
  - Mast cell depletion and disease symptom/disease modifications
  - Briquilimab drug clearance
  - Time to return of disease symptoms
  - Briquilimab on other c-Kit expressing cell lineages
- Part 1 intended to identify the minimally effective dose
- Treat the highest unmet need population for clearest efficacy signal Status: IND cleared (US), CTA authorized (EU), patient enrollment ongoing





JASPER

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

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



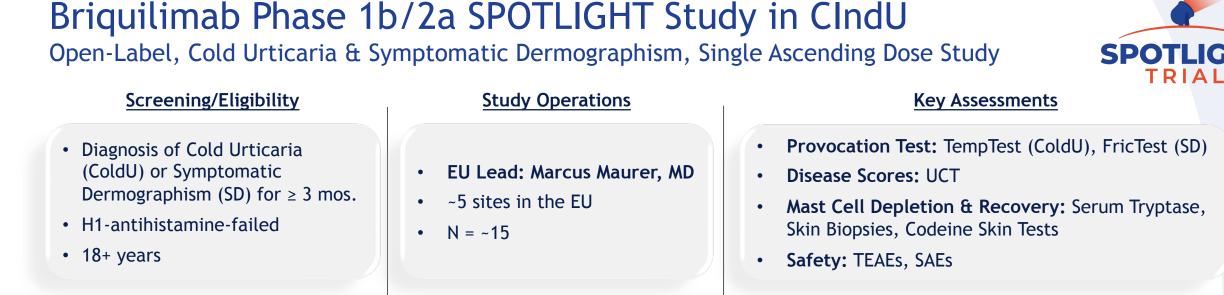
**Study Goal:** identify therapeutic doses of subcutaneous briquilimab to inform future registrational trials

#### **Key Objectives:**

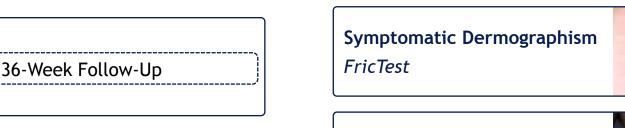
- Demonstration of efficacy and safety in a second dermatological indication
- Study design intended to identify minimally effective dose
- Provocation study enables a clear demonstration of potential drug effect
- Assess the effects of single dose briquilimab on mast cell depletion and disease symptoms/disease modification

Status: CTA authorized (EU), FPI targeted Q1 2024





#### **Provocation Tests Used for Clinical Evaluation**



#### Provocation test measured at 12 weeks (Primary Endpoint)

#### \* CCCC

TempTest

**Cold Urticaria** 



Pin 1

Pin 2

Pin 4

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



N=15

40 mg

120 mg

Single

Dose

### Market Opportunity in Mast Cell Diseases

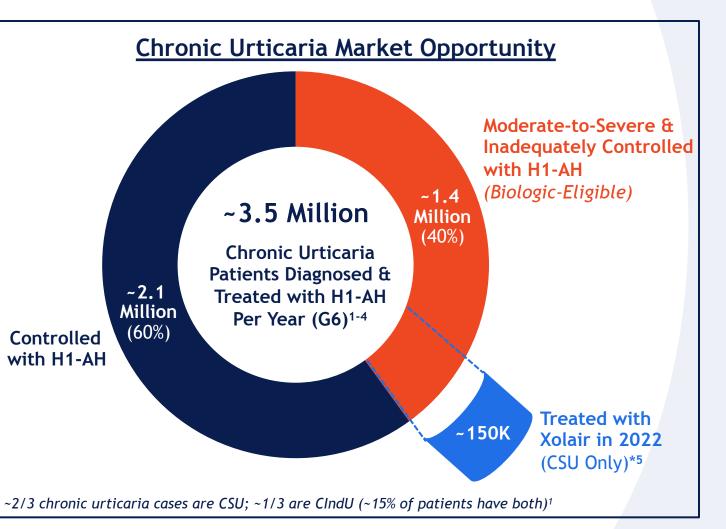


# Chronic urticaria is one of the most prevalent dermatologic conditions with ~1.4 million biologic eligible patients in the G6

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-tosevere disease, in which the disease commonly persists for 5+ years<sup>6</sup>





\*Approximately 50% of patients receiving Xolair have an inadequate response (Xolair prescribing information); H1-AH = H1-antihistamines
1 Kolkhir P, et al. Nature Reviews. 2022; 2 Balp MM, et al., EADV 2023; 3 Novartis R&D Day, Dec. 2021; 4 Decision Resources Group, Chronic Urticaria, Dec. 2023; 5 IQVIA sales data; 6 Saini S, Kaplan A. JACI Practice. 2018.

### 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)	++	++
lgE*	Signal inhibition	4 weeks (SQ)	+	×
IL-4/IL-13	Cytokine inhibition	2 weeks (SQ)	+	×
ВТК	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

 $\circ$  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

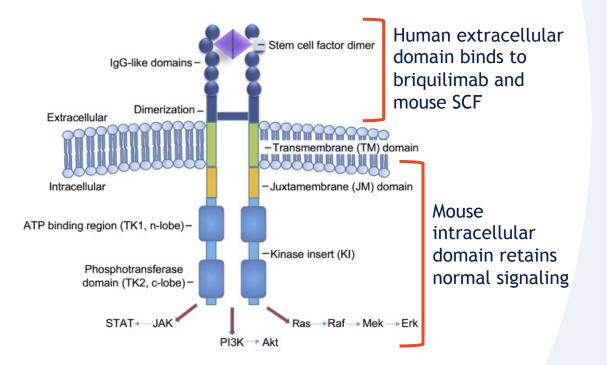


## Jasper's c-Kit Mouse<sup>TM</sup> enables direct in-vivo disease model testing to support briquilimab's significant mast cell franchise opportunity

- 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
- Multiple diseases models that can now be directly tested to develop broad franchise strategy
  - Allergy
  - Anaphylaxis
  - Asthma
  - Atopic Dermatitis
  - COPD

- Conjunctivitis
- Eosinophilic Esophagitis (EoE)
- Inflammatory Bowel Disease
- Prurigo Nodularis
- Rhinitis



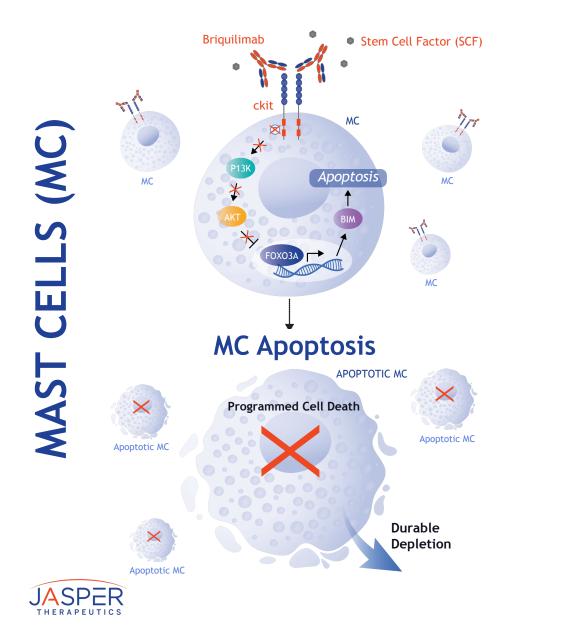


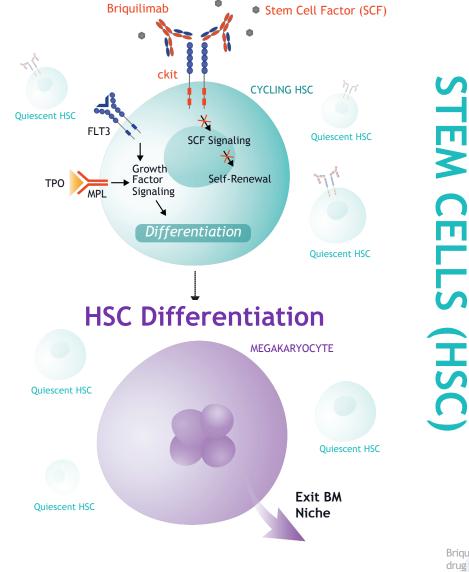


### Briquilimab in Low-to-Intermediate Risk MDS & Bone Marrow Transplant



### SCF blockade drives differential impact on mast cells and stem cells

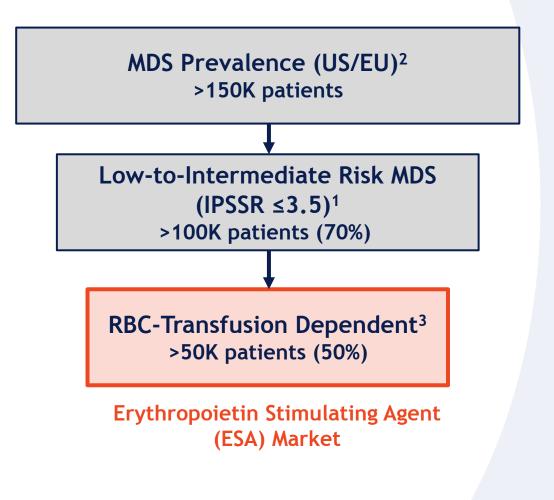




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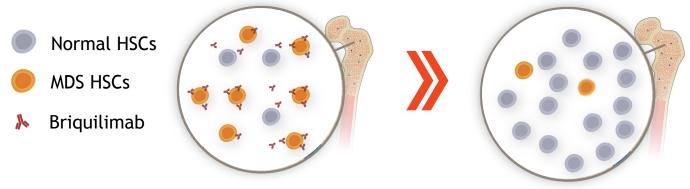
Briquilimab's ability to directly deplete cancerous stem cells may be leveraged as a disease-modifying therapeutic in low-to-intermediate risk MDS patients

- 70% of myelodysplastic syndrome (MDS) patients have low to intermediate risk (LR-MDS) disease and are typically treated with ESA, other growth factors and/ or transfusions<sup>1</sup>
- Current treatments only treat symptoms and do not delay disease progression to AML or High Risk MDS
- By directly targeting c-Kit-reliant MDS stem cells, briquilimab may be the first disease modifying therapeutic for LR-MDS patients
- Jasper's ongoing study is designed to examine the impact of briquilimab to shift towards healthier bone marrow and restoration of normal hemopoiesis





### Briquilimab Phase 1 trial in patients with LR-MDS



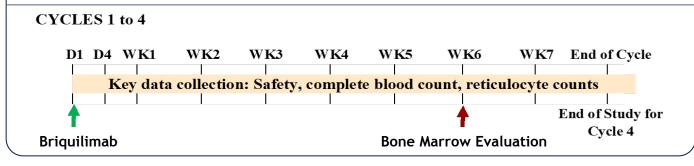
Restoration of healthy bone marrow following briquilimab treatment

#### **Screening/Eligibility**

- IPSS-R very low, low or intermediate risk MDS patients
- RBC transfusion dependence, thrombocytopenia or neutropenia

#### Single Arm, MAD, Open Label Design (Enrolling)

- Dosing: Up to 4 cohorts 0.3, 0.6, 0.9 and 1.2 mg/kg; Every 8 weeks
- Size: 3-6 per cohort



#### **Screening/Eligibility**

- Primary: Safety, tolerability
- Secondary: PK, Efficacy by HI-E/HI-P/HI-N, duration of response, reduction in RBC transfusions, ORR, progression free survival
- Exploratory: Depletion of leukemic MDS and normal stem & progenitor cells, molecular characteristics of LSCs/HSCs/HPCs, cytokine profile, immunogenicity

### Briquilimab is also being tested as a novel conditioning agent for bone marrow transplant

- Briquilimab c-Kit inhibition temporarily creates space in specialized bone marrow niches
  - May drive non-quiescent HSCs to differentiate
  - Combination with radiation required for full depletion
- Briquilimab based bone marrow transplant conditioning regimens has been tested in SCID, Sickle Cell Disease, Fanconi Anemia, CGD, AML and MDS
  - Large unmet need for reduced toxicity bone marrow conditioning regimens
  - No briquilimab-related SAEs. Patients range in age from 3 months to 79 years
  - NIH sponsorship of studies in Sickle Cell, Beta Thalassemia, CGD, GATA-2 MDS; Stanford sponsorship in Fanconi
- Potential approval in SCID provides strategic opportunity for early product launch and Priority Review Voucher



# Expanded portfolio presents exciting new opportunities in mast cell diseases

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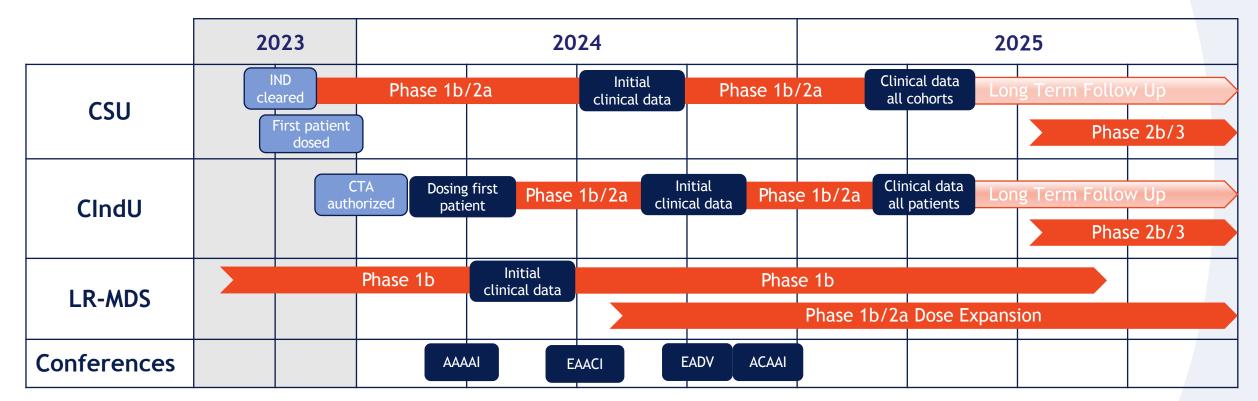
Investigator Sponsored Studies

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### Key milestones & financials





Г	Financia	Financial Overview				
	\$86.9M cash & investments at 12/31/23*	Cash runway	y through 3Q25*			
JASPER	*Completed \$50m equity financing in February 2024, cash runway inclusive of financing		Briquilimab is an investigative drug and is not approved for any indication			

### Jasper: Advancing briquilimab in multiple large indications Several significant data readouts expected in 2024

#### c-Kit inhibition - a 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 in skin

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

- CSU: Phase 1b/2a BEACON study enrolling (initial data expected 3Q 2024)
- CIndU: Phase 1b/2a SPOTLIGHT study initiating (initial data expected 2H 2024)
- LR-MDS: Phase 1 study ongoing (initial data expected by mid-year 2024)
- Additional mast cell mediated indications under evaluation



March 2024

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## **Jasper Therapeutics**

NASDAQ: JSPR

