May 20, 2024

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Jasper Therapeutics: Briquilimab in Asthma

NASDAQ: JSPR



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Today's agenda and presenters

Торіс	Presenter	Title (Affiliation)	
Jasper Introduction	Ronald Martell	Chief Executive Officer (Jasper)	
The Biology of Mast Cells in Asthma & Briquilimab Preclinical Data	Wendy Pang, MD, PhD	Senior Vice President, Research & Translational Medicine (Jasper)	
Current Treatments & Unmet Need in Asthma	Joshua Boyce, MD	Professor (Harvard Medical School); Chief, Division of Allergy & Clinical Immunology (Brigham and Women's)	
Briquilimab Clinical Development	Edwin Tucker, MD, MRCP	Chief Medical Officer (Jasper)	
Closing Remarks	Ronald Martell	Chief Executive Officer (Jasper)	



Mast cells are potent drivers of inflammatory response in the 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 are triggered by allergens, viruses and other irritants that degranulate and release pro-inflammatory compounds implicated in large number of immunologic diseases
- Limited function or need for mast cells in modern settings



Depletion of mast cells with briquilimab, an anti c-Kit monoclonal antibody, 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
- Briquilimab blocks c-Kit signaling at the SCF ligand binding site on the receptor and triggers apoptosis
- Mast cell recovery in the skin takes 3 months or longer¹, potentially leading to durable disease control





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		
Respiratory	Fibromyalgia		
Asthma	Hereditary Alpha Tryptasemia (HaT)		
Allergic Rhinitis	Idiopathic Anaphylaxis		
Allergic Rhinitis Aspirin Exacerbated Respiratory Disease (AERD)	Idiopathic Anaphylaxis Insulin-Dependent Diabetes Mellitus		
Allergic Rhinitis Aspirin Exacerbated Respiratory Disease (AERD) Chronic Obstructive Pulmonary Disease (COPD)	Idiopathic Anaphylaxis Insulin-Dependent Diabetes Mellitus Mast Cell Activation Syndrome (MCAS)		
Allergic Rhinitis Aspirin Exacerbated Respiratory Disease (AERD) Chronic Obstructive Pulmonary Disease (COPD) Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)	Idiopathic Anaphylaxis Insulin-Dependent Diabetes Mellitus Mast Cell Activation Syndrome (MCAS) Mast Cell Leukemia		
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Wendy Pang, MD, PhD

The Biology of Mast Cells in Asthma & Briquilimab Preclinical Data



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

- Mast cells are distributed throughout multiple compartments in the lung¹
- Mast cells release mediators and recruit other cell types into the airway that drive inflammation throughout all phases of the asthmatic response²





Méndez-Enríquez E, Hallgren J. Mast cells and their progenitors in allergic asthma. Front Immunol. 2019;10:442022.
 Galli SJ, Tsai M, Piliponsky AM. The development of allergic inflammation. Nature. 2008;454(7203):445-454.

Tryptase is elevated in the lungs of severe asthma patients independent of type 2 inflammation

Tryptase in bronchoalveolar lavage (BAL) and plasma are significantly elevated in severe asthma¹



*p < 0.05, **p < 0.01, ***p < 0.001

Elevated tryptase in severe asthma is independent of type 2 inflammation¹





Note: BAL was performed in human asthma patients and tryptase levels were measured (anti-tryptase antibody developed by Genentech).
 Maun HR, Jackman JK, Choy DF, et al. An allosteric anti-tryptase antibody for the treatment of mast cell-mediated severe asthma. Cell. 2019;179(2):417-431.e19.

Briquilimab is a monoclonal antibody optimally designed to directly block c-Kit signaling and trigger mast cell apoptosis

Briquilimab

Blocks SCF binding to c-KIT (CD117) to potently inhibit receptor signaling



- Full length, humanized IgG1
- Targets receptor binding pocket
- Aglycosylated via N297Q mutation
- No FcRn engineering
- Kd < 5pM affinity to human c-Kit
- Briquilimab completely blocks SCF binding (Biacore Ki ~70pM)
- Human mast cell survival bioassay IC50 ~12.5nM
- No c-Kit agonist activity
- Does not bind to Fc gamma I, II or III receptors (no ADCC)
- PK clearance allows for restoration of c-Kit signaling on other c-Kit expressing cells after mast cells are depleted
- Well tolerated as demonstrated across 10 ongoing and completed trials



Jasper's c-Kit MouseTM 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[™] allows briquilimab to be tested across numerous immunology and inflammation disease models

Jasper c-Kit Mouse™





Single dose of briquilimab studied in a therapeutic model of allergen induced asthma in Jasper's c-Kit MouseTM

The cockroach antigen-induced model is a prevalent preclinical tool for asthma as it exhibits several major features of disease, including airway hyperresponsiveness to methacholine, airway inflammation and remodeling

Study Design¹:





* 25 mg/kg briquilimab dose in h/mCD117 mice corresponds to ~2 mg/kg in human, as determined through allometric scaling.
1 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.

Single dose of briquilimab depleted lung mast cells and reduced asthmatic response to methacholine in h/mCD117 mice

Lung Mast Cells¹



Pulmonary Resistance¹





PBS: Phosphate buffered saline

1 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.

Briquilimab drives dose-dependent depletion of lung mast cells in primates



- Mast cells visualized by CD117 immunohistochemistry in lung samples at Day 28 after weekly dosing of briquilimab^{1*}
- Briquilimab significantly depleted both interstitial and peribronchial lung mast cells versus control



*Vehicle control (n=2), 0.3 mg/kg (n=4), 1.0 mg/kg (n=3), 3.0 mg/kg (n=2) 1 Jasper internal data.

Joshua Boyce, MD



- Chief, Division of Allergy and Clinical Immunology, Brigham and Women's Hospital
- Albert L. Sheffer Professor of Medicine in the Field of Allergic Disease at Harvard Medical School
- Effect of KIT Inhibition by Imatinib on Airway Mast Cells in Patients with Severe Refractory Asthma (KIA) trial investigator



Joshua Boyce, MD

Current Treatments & Unmet Need in Asthma



Biologic therapies have revolutionized the treatment of severe asthmatics with inadequate response to ICS/LABA/LAMAs



- Severe asthma is a potentially life-threatening inflammatory disorder characterized by persistent asthma symptoms, despite use of high doses of ICS and LABA/LAMA¹
- Asthma severity increases with age and the median age of severe asthma is 45-60 years^{2,3}
- ~300,000 patients currently receive biologic therapies in the US & EU⁴

- 1 2022 GINA Main Report, Global Initiative for Asthma GINA.
- 2 Rönnebjerg L, Axelsson M, Kankaanranta H, et al. Severe asthma in a general population study: prevalence and clinical characteristics. J Asthma Allergy. 2021;14:1105-1115.
- 3 Zein JG, Dweik RA, Comhair SA, et al. Asthma is more severe in older adults. PLoS One. 2015;10(7):e0133490.
- 4 TD Cowen Analyst Research 2023 (Sanofi).
- 5 GlobalData.

Selection of biologic therapy in severe asthma is based on disease biomarkers





*Demonstrated skin test or in vitro reactivity to a perennial aeroallergen

1 Theofani E, Tsitsopoulou A, Morianos I, Semitekolou M. Severe asthmatic responses: the impact of tslp. International Journal of Molecular Sciences. 2023;24(8):7581.

Patients with allergic or type 2 low asthma have limited treatment choices compared to patients with eosinophilic disease

	Severe Asthma				
	Type 2 High			Type 2 Low	
Asthma Endotype ¹	Eosinophilic Only	Eosinophilic & Allergic	Allergic Only	Type 2 Low	
% of Total Moderate-to- Severe Asthma Patients ^{2,3}	~30% of patients	~15% of patients	~25% of patients	~30% of patients	
FDA Approved Therapies⁴	 ✓ Nucala (IL-5) - 2015 ✓ Cinqair (IL-5) - 2016 ✓ Fasenra (IL-5) - 2017 ✓ Dupixent (IL-4/IL-13) - 2018 ✓ Tezspire (TSLP) - 2021 	 ✓ Xolair (IgE) - 2003 ✓ Nucala (IL-5) - 2015 ✓ Cinqair (IL-5) - 2016 ✓ Fasenra (IL-5) - 2017 ✓ Dupixent (IL-4/IL-13) - 2018 ✓ Tezspire (TSLP) - 2021 	 ✓ Xolair (IgE) - 2003 ✓ Tezspire (TSLP) - 2021 	✓ Tezspire (TSLP) - 2021	

>50% of patients have limited treatment options



1 2022 GINA Main Report, Global Initiative for Asthma - GINA.

2 TD Cowen Respiratory Outlook 2024 (Sanofi/Regeneron/AstraZeneca).

3 Jasper Primary Research 2024.

4 Drug product prescribing information.

Most asthma biologics have endotype-based label restrictions*

	Xolair (IgE)	Nucala (IL-5)	Fasenra (IL-5)	Dupixent (IL-4/13)	Tezspire (TSLP)
Labeled Indication ¹	Moderate-to-severe asthma with a positive skin test or in vitro reactivity	Severe asthma with an eosinophilic phenotype (>150 cells/ml)	Severe asthma with an eosinophilic phenotype (>150 cells/ml)	Moderate-to-severe asthma with an eosinophilic phenotype (>150 cells/ml) or OCS dependent	Severe asthma
Dosing Regimen ¹	SC (Q2W or Q4W)	SC (Q4W)	SC (Q4W, Q8W)	SC (Q2W)	SC (Q4W)
Annualized Exacerbation Risk Reduction (AERR) ¹	41%-44% @W52	52% @W52	28%-51% @W52	46%-47% @W52	56%-71% @W52



*Cinqair (reslizumab) is an anti-IL-5 mAb FDA approved for severe eosinophilic asthma. Not included in the table due to its intravenous route of administration and very little physician uptake.

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

1 Drug product prescribing information.

<u>Imatinib Phase 2:</u> c-Kit inhibition with a TKI improved airway response in patients with severe asthma challenged with methacholine

KIT Inhibition by Imatinib in Patients with Severe Refractory Asthma (KIA)¹

- Phase 2 randomized, double-blind, placebo-controlled trial in patients with poorly controlled severe asthma
- Conducted at seven academic centers in the US from Nov. 2010 to July 2015
- Imatinib significantly improved airway response to methacholine challenge and reduced serum tryptase when compared to placebo
- In patients with severe asthma, imatinib also decreased mast-cell counts and BAL tryptase levels in the lungs



"These results suggest that *KIT-dependent processes and mast cells contribute to the pathobiology* of severe asthma"



<u>Masitinib Phase 3:</u> c-Kit inhibition with a TKI led to reduction of severe asthma exacerbations vs. placebo but was limited by off-target GI toxicity¹

	Exposure	SAER	Rate Ratio [95% CI]	Reduction ^a	P-value
Primary population (primary analysis)					
Masitinib (240)	13.7 months	0.34	0.65 [0.47, 0.90]	35%	0.010
Placebo (115)	13.8 months	0.48			
Eosinophil (≥150 cell/µL) subgroup (primary analysis)					
Masitinib (181)	13.2 months	0.34	0.62 [0.42, 0.91]	38%	0.016
Placebo (87)	13.4 months	0.51			
Intention-to-treat (sensitivity analysis)					
Masitinib (279)	13.1 months	0.34	0.67 [0.49, 0.93]	33%	0.016
Placebo (140)	12.8 months	0.44			
Full analysis set (sensitivity analysis)					
Masitinib (269)	13.2 months	0.34	0.67 [0.49, 0.92]	33%	0.015
Placebo (133)	13.1 months	0.45			

Notes: n: number of patients in analysis. ^aReduction in the severe asthma exacerbation rate relative to placebo.

Abbreviations: SAER, severe asthma exacerbation rate (annualized rate adjusted for the overall time on treatment); CI, confidence interval.



<u>NIH PreCISE Phase 2:</u> c-Kit inhibition with a TKI in severe asthma is an active area of ongoing clinical interest

Study Details1:

- PreCISE is an NIH-funded research study to evaluate several novel interventions (shown below) in 600 patients with severe asthma
- Three study phases: (1) screening/treatment assignment based on biomarkers, (2) double-blind placebo-controlled cross-over, and (3) multiperiod cross-over with different treatments
- Study is fully enrolled with data anticipated Q1 2025

Study Arms*:

Compound	Drug target	Targeted subgroup
Imatinib	C-Kit	Eos < 300/µL
Clazakizumab	IL-6	IL-6 > 3.1 ng/mL
MCTs	Metabolic pathways	FENO > 15 ppb
Broncho-Vaxom	Microbiome	$Eos > 300/\mu L$
Itacitinib	JAK1/3	Eos > $300/\mu$ L or Feno > 25 ppb

TABLE I. Compounds and targeted subgroups



*Based on KIA study, "In the imatinib group, decreases in airway hyperresponsiveness were inversely correlated with baseline peripheral-blood eosinophil counts (r²=0.218, P=0.03)."

1 Georas SN, Wright RJ, Ivanova A, et al. The precision interventions for severe and/or exacerbation-prone (Precise) asthma network: an overview of network organization, procedures, and interventions. J Allergy Clin Immunol. 2022;149(2):488-516.e9.

Severe asthma patients have significant unmet needs that may be broadly addressed by c-Kit inhibition

- New treatments are needed for patients with severe asthma
- Preclinical evidence that targeting the mast cell reduces asthmatic response
- Imatinib and masitinib clinical evidence that c-Kit inhibition improves airway response and reduces exacerbations across severe asthma endotypes
- Mast cell depletion may lead to broad therapeutic benefit in asthma patients across endotypes
- Asthma challenge study design is an appropriate proof-of-concept to evaluate the clinical potential of briquilimab



Edwin Tucker, MD, MRCP

Briquilimab Clinical Development





IASPER

drug and is not approved for any indication

Briquilimab significantly depletes mast cells

- A single subcutaneous dose of briquilimab potently depletes mast cells in the skin of healthy volunteers
- Depletion is demonstrated in as early as 7 days
- Depletion is consistently observed across rodents, NHPs, and humans

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





Briquilimab studies in CSU & CIndU will provide initial data in mast cell indications





Chronic Spontaneous Urticaria (Phase 1b/2a)

Key Design Features

- Patients with inadequate response to omalizumab
- Multiple dose, testing 8/12-week dosing intervals
- UAS7 @ W12

<u>Timing</u>

- FPI: November 2023
- Enrollment: Ongoing
- Data expected: 3Q 2024

Chronic Inducible Urticaria (Phase 1b/2a)

Key Design Features

- Cold Urticaria & Symptomatic Dermographism
- Single dose
- Provocation test @ W12

Timing

- FPI: March 2024
- Enrollment: Ongoing
- Data expected: 2H 2024



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



Ronald Martell

Closing Remarks



Mast cell depletion offers a novel therapeutic approach for asthma



<u>Mast cell depletion</u>: 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



<u>Airway remodeling</u>: reduction of inflammation by mast cell depletion may reduce excess inflammation and epithelial remodeling



<u>Durability and convenience</u>: 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



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)
- CIndU: 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

