SUMMIT Trial: Bezuclastinib in NonAdvSM Patients Top-Line Results

Investor Webcast
July 7, 2025

Real Challenges. Real Solutions.

Precision therapies for genetically defined diseases

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All of Cogent Biosciences, Inc. (“Cogent”) product candidates are investigational product candidates and their safety and efficacy have not yet been established. Cogent has not obtained marketing approval for any product, and there is no certainty that any marketing approvals will be obtained or as to the timelines on which they will be obtained.

Agenda and Speakers

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• Introduction	Andrew Robbins
• NonAdvSM Disease Overview • SUMMIT Top-Line Results • Patient Case Studies	Dr. Nathan Boggs and Dr. Lindsay Rein
• Summary	Andrew Robbins
• Q&A	All

Bezuclastinib Offers Potential Best-in-Class KIT Inhibitor Opportunity

Summit NONADVANCED SM

Registration-directed study in NonAdvSM bezuclastinib vs. placebo

n=179, 24-week MS2D2 primary endpoint

Peak GIST

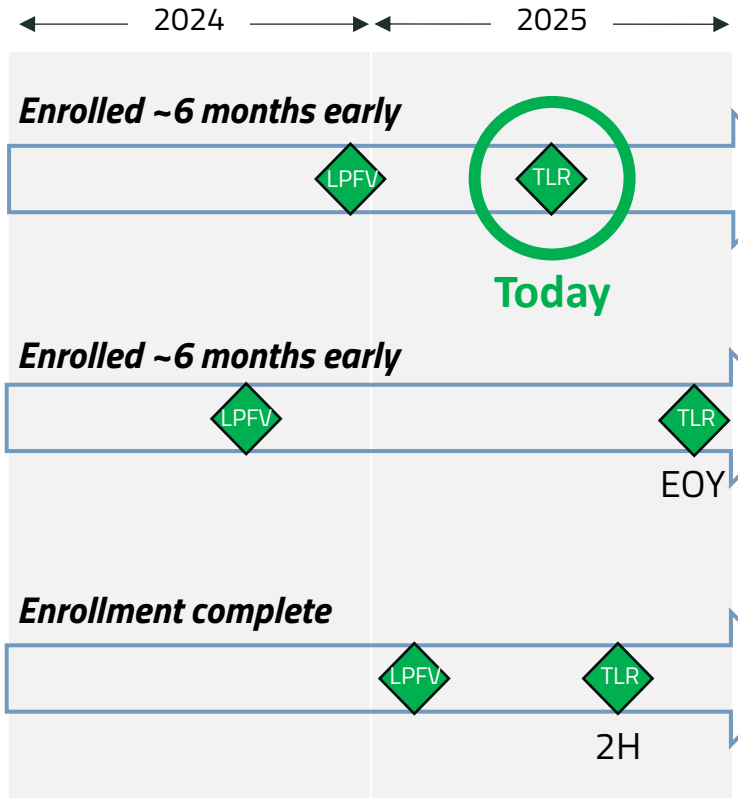
Phase 3 study in 2nd-line GIST sunitinib +/- bezuclastinib

n=413, mPFS primary endpoint

Apex ADVANCED SM

Registration-directed study in AdvSM bezuclastinib monotherapy

n=58, ORR primary endpoint



$2 billion+ US annual market opportunity; differentiated symptom improvement provides path to market leadership

$1 billion+ US annual market opportunity, limited competition for 2nd-line GIST population

$300 million US annual market opportunity; differentiated safety/tolerability results provides path to market leadership

Aggregate US annual sales opportunity >$3 billion with limited competition

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LPFV: Last patient, first visit

TLR: Top-line results including primary endpoint

SUMMIT Part 2
Top-line Results

Real Challenges. Real Solutions.

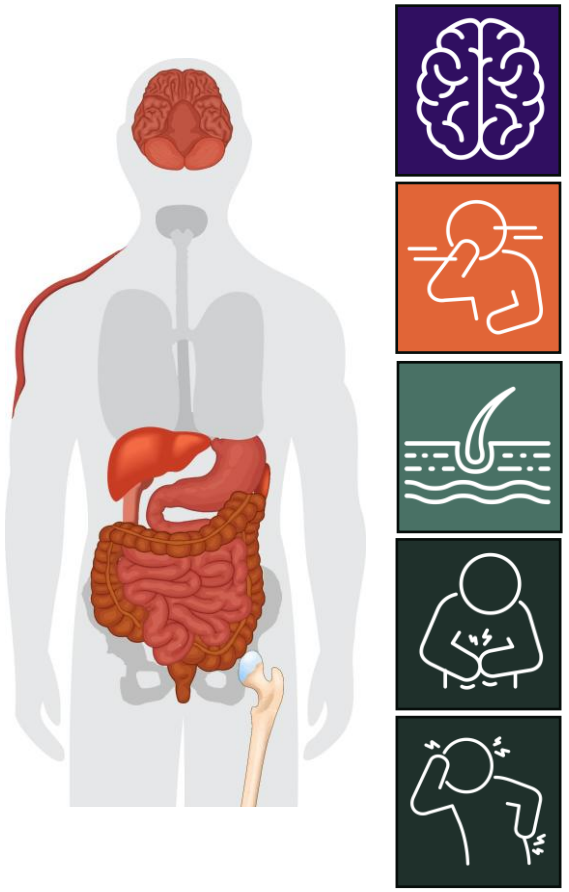
Precision therapies for genetically defined diseases

Full Results Expected to be Presented at an Upcoming Medical Meeting

Systemic Mastocytosis (SM) is a Rare and Debilitating Disease Characterized by Neoplastic Mast Cell Infiltration of Extracutaneous Tissues and Symptoms of Mast Cell Activation[1]

- Nonadvanced SM (NonAdvSM)[2] includes indolent SM (ISM), bone marrow mastocytosis (BMM), as well as smoldering SM (SSM).[3]
- Patients with NonAdvSM experience a variety of disabling, potentially serious and severe symptoms which may significantly reduce health-related quality of life. Symptoms are caused by mast cell reactions and can include life-threatening anaphylaxis.[4]
- Agents targeting *KIT* D816V are used to treat Advanced SM (AdvSM) and NonAdvSM, but unmet need remains.[5-7]
  - AEs like cognitive impairment, bleeding, and edema can limit dosing of other agents[6]
  - Available medications do not adequately control symptoms for patients[1,8]
  - SSM has no disease modifying therapies approved

Figure 1. Symptoms of Nonadvanced Systemic Mastocytosis[1]



Neurocognitive
Difficulty Concentrating, Difficulty Remembering, Brain Fog, Cognitive Dysfunction, Anxiety, Depression

Fatigue
Tiredness

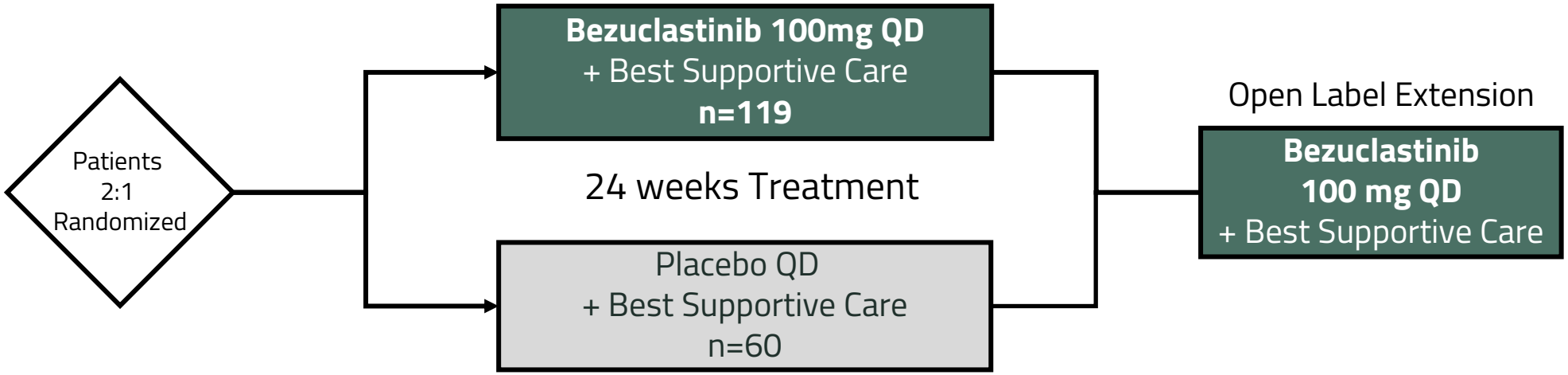
Skin
Itching, Flushing, Skin Redness, Spots

Gastrointestinal
Nausea, Abdominal Pain, Diarrhea, Vomiting, Bloating, Gastroesophageal Reflux Disease (GERD)

Pain
Headache, Bone Pain, Joint Pain

1. Pardanani A. AmJ Hematol 2021; 96(4):508-525. 2. NORD 2021. Mastocytosis; available at: https://rarediseases.org/rare-diseases/mastocytosis/. 3. Trizuljak J, et al. Allergy 2020 Aug;75(8):1927-1938. 4. Pyatilova P and Siebenhaar F. Immunol Allergy Clin North Am 2023; 43(4):751-762. 5. DeAngelo D, et al. Nat Med, 2021, 27(12):2183-2191. 6. Ayvakit (avapritinib) [product information]. Cambridge, MA: Blueprint Medicines Corporation; May 2023. 7. DeAngelo et al. [abstract] In: Blood (ASH) 2022; 140 (Supplement 1): 1512-13. 8. Akin C, et al. J Allergy Clin Immunol, 2022, 149(6):1912-1918.

SUMMIT Part 2: Double-Blind, Placebo-Controlled Randomized Clinical Study Evaluating Bezuclastinib in Non-Advanced Systemic Mastocytosis Patients



Patient Eligibility
• Age ≥ 18 years • NonAdvSM confirmed by central pathology review • Receiving BSC, defined as ≥ 2 anti-mediator therapies • Moderate-to-severe symptoms of NonAdvSM • Prior therapy with approved treatments allowed

Primary Endpoint	• Mean change in TSS at Week 24
Key Secondary Endpoints*	• ≥ 50% Reduction in Serum Tryptase • ≥ 50% Reduction in KIT D816V VAF • ≥ 50% Reduction in TSS • ≥ 50% Reduction in Bone Marrow MC • ≥ 30% Reduction in TSS

Data cut-off as of 22May25
QD: Once daily, BSC: Best supportive care, TSS: Total Symptom Score, OLE: Open-label Extension
* For key secondary endpoints, reductions in TSS and objective measures of mast cell burden represent proportion of patients with ≥30% and ≥50% reductions in each parameter at Week 24.

SUMMIT Part 2 Population Had Significant Disease Burden Representative of Moderate-to-Severe NonAdvSM Patients

Patient Demographics	Bezuclastinib	Placebo	Overall
# Patients	119	60	179
Female, n (%)	74 (62.2)	44 (73.3)	118 (65.9)
Median Age in years, (range)	51 (24-73)	52 (23-78)	51 (23-78)
ECOG PS at baseline, n (%)			
0	58 (48.7)	30 (50.0)	88 (49.2)
1	50 (42.0)	26 (43.3)	76 (42.5)
2	11 (9.2)	4 (6.7)	15 (8.4)

Clinical Characteristics	Bezuclastinib	Placebo	Overall
NonAdv Subtype, n (%)			
Indolent SM (ISM)	97 (81.5)	50 (83.3)	147 (82.1)
Smoldering SM (SSM)	8 (6.7)	4 (6.7)	12 (6.7)
Bone Marrow Mastocytosis (BMM)	14 (11.8)	6 (10.0)	20 (11.2)

Region	Bezuclastinib	Placebo	Overall
North America, n (%)	53 (44.5)	28 (46.7)	81 (45.3)
Europe, n (%)	64 (53.8)	30 (50.0)	94 (52.5)
Asia-Pacific, n (%)	2 (1.7)	2 (3.3)	4 (2.2)

Systemic Mastocytosis Therapy	Bezuclastinib	Placebo	Overall
Prior KIT Inhibitor[1]	17 (14.3)	5 (8.3)	22 (12.3)
Prior Avapritinib, n (%)	11 (9.2)	3 (5.0)	14 (7.8)
Prior Midostaurin, n (%)	6 (5.0)	0	6 (3.4)
# of BSC Meds, median (range)	3 (0-6)	3 (1-7)	3 (0-7)

Baseline Mast Cell Burden	Bezuclastinib	Placebo	Overall
Median KIT D816V in Whole Blood, % (range) Below limit of detection (BLD), n (%)	0.22 (0-32) 28 (23.5)	0.30 (0-34) 12 (20.0)	0.25 (0-34) 40 (22.3)
Median BM MC Burden, % (range)	10 (1-75)	10 (1-75)	10 (1-75)
Median Serum Tryptase at baseline, ng/mL (range) Serum Tryptase < 20 ng/mL, n(%)	40 (6-448) 22 (18.5)	41 (7-692) 10 (16.7)	40 (6-692) 32 (17.9)

Baseline QoL Measures	Bezuclastinib	Placebo	Overall
Mean MS2D2 TSS, (range)	57.1 (18-105)	52.6 (13-91)	55.6 (13-105)
Mean MCQoL, (range)[2]	59.5 (23-96)	55.5 (18-89)	58.2 (18-96)
Mean MAS, (range)	50.4 (26-94)	47.0 (27-86)	49.3 (26-94)

1. KIT Inhibitors included: avapritinib, imatinib, midostaurin, dasatinib, masitinib
2. MC-QOL baseline collection n= Bezuclastinib: 111, Placebo: 52 Overall: 163

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Data cut-off as of 22May25

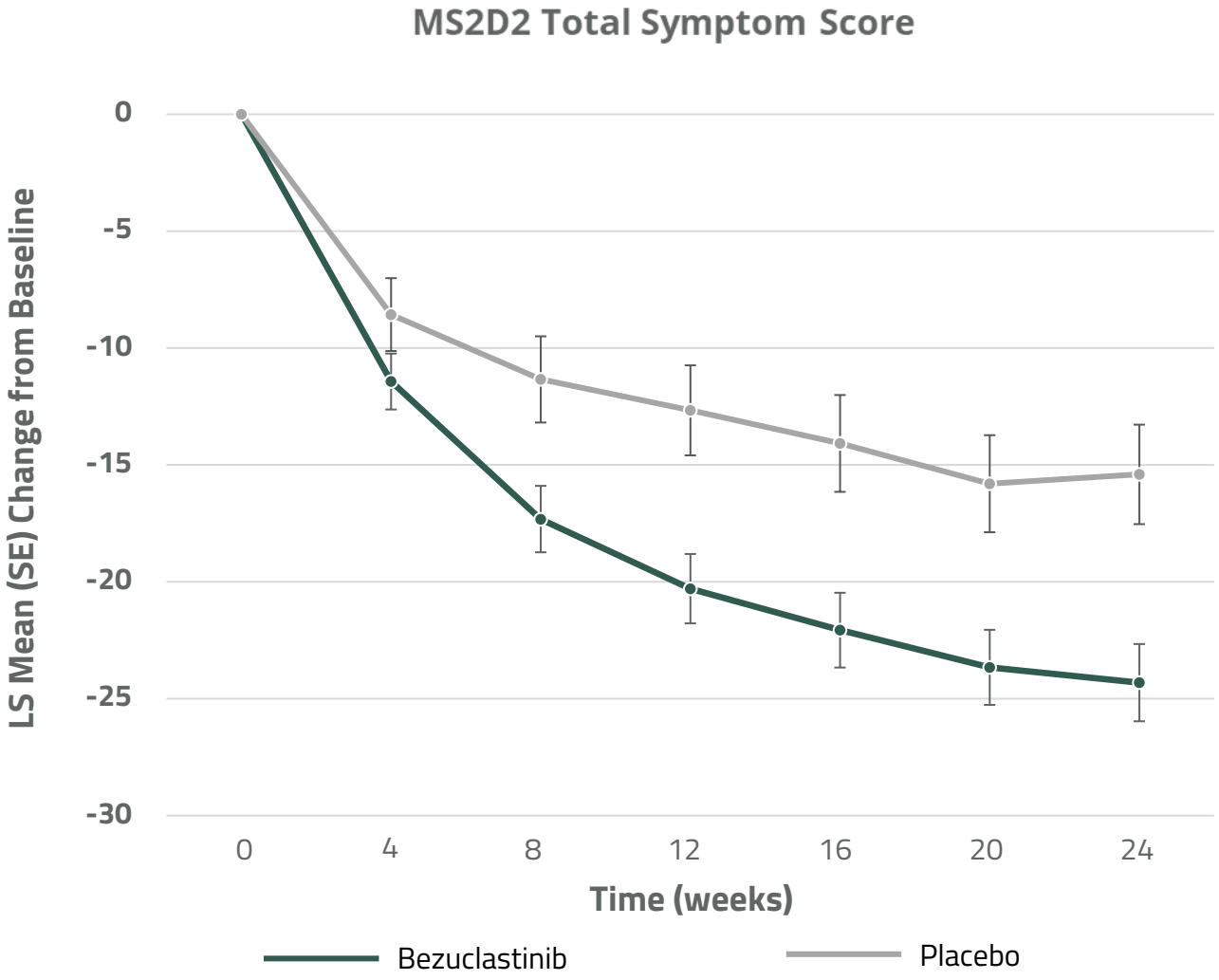
SUMMIT Results Demonstrate Clinically Meaningful and Statistically Significant Effects Across All Primary and Secondary Endpoints

Clinical Outcome Measures		P-Value[1]
Primary Endpoint	Mean Change in TSS at Week 24	**0.0002**
Secondary Endpoints[2]	≥ 50% Reduction in Serum Tryptase	**<0.0001**
	≥ 50% Reduction in KIT D816V VAF	**<0.0001**
	≥ 50% Reduction in TSS	**0.0142**
	≥ 50% Reduction in Bone Marrow MC	**< 0.0001**
	≥ 30% Reduction in TSS	**0.0004**
	Mean Change in Most Severe Symptom Score	**0.0001**

Data cut-off as of 22May25 TSS: total symptom score, VAF: variant allele fraction, MC: mast cell

1. Two-sided p-values < 0.05 indicated statistical significance. 2. For secondary endpoints, reductions in TSS and objective measures of mast cell burden represent proportion of patients with ≥30% and ≥50% reductions in each parameter at Week 24. All endpoints are key secondary endpoints, except "Mean Change in Most Severe Symptom Score" which is an additional secondary endpoint.

Treatment with Bezuclastinib Results in Clinically Meaningful Decreases in Patient-Reported Symptoms and Objective Measures of Disease Burden



Mean Change in TSS at Week 24 [95 % CI]		
Bezuclastinib	**Placebo**	**P-Value**
-24.32 *(-27.56, -21.08)*	-15.41 *(-19.58, -11.24)*	0.0002
-8.91 *(-13.56, -4.26)*		

≥50% Reduction in Serum Tryptase at Week 24		
Bezuclastinib	**Placebo**	**P-Value**
87.4%	0%	<0.0001

Data cut-off as of 22May25 TSS: Total Symptom Score

Bezuclastinib Demonstrated a Favorable and Manageable Safety Profile

	Bezuclastinib 100mg QD (N=118)	Placebo (N=60)
TEAEs, n (%)	116 (98.3)	53 (88.3)
SAEs, n (%)	5 (4.2)	3 (5.0)
Reductions due to TRAEs, n (%)	13 (11.0)	0
DCs due to TRAEs, n (%)	7 (5.9)	0
TEAEs ≥ 10% that occurred in greater frequency in bezuclastinib arm , n (%)		
Hair color changes	82 (69.5)	3 (5.0)
Altered taste*	28 (23.7)	0
Nausea	26 (22.0)	8 (13.3)
ALT/AST increased*	26 (22.0)	4 (6.6)
Headache	21 (17.8)	7 (11.7)
Alopecia	14 (11.9)	2 (3.3)
ALP increased	12 (10.2)	2 (3.3)

*Pooled terms

- Majority of TEAEs were of low grade (70% Gr1) and reversible
- Variety of AEs occurred more often in placebo group: Dizziness (10% vs. 12%), Fatigue (7% vs. 12%), Arthralgia (6% vs. 15%), Diarrhea (13% vs. 18%)
- The only hepatic AEs reported were transient and manageable lab abnormalities
- Only 5.9% of patients experienced ≥Gr 3 ALT/AST elevations, and no patients with transaminase AEs required hospitalization or treatment intervention
- All DCs due to treatment-related AEs were due to transaminase elevations and all subjects fully resolved

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Data cut-off as of 22May25
TEAE: Treatment Emergent Adverse Event

Case Study 1: 44 yo Woman with ISM Randomized to 100 mg Bezuclastinib

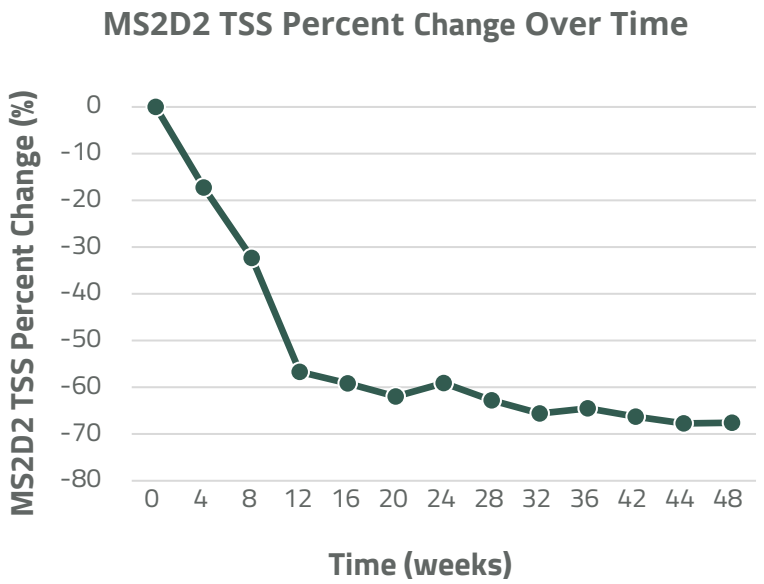
- **Discontinued <u>all</u> BSC Medications in OLE**
- **Patient remains on study more than 1 year with continued benefit**

SM-Related Medical History
Monomorphic Maculopapular Cutaneous Mastocytosis / Grade 3
Splenomegaly / Grade 1

Other Relevant Medical History
Obesity / Grade 3
Asthma / Grade 2

Best Supportive Care (BSC) Medications
Famotidine
Loratadine
Cromolyn

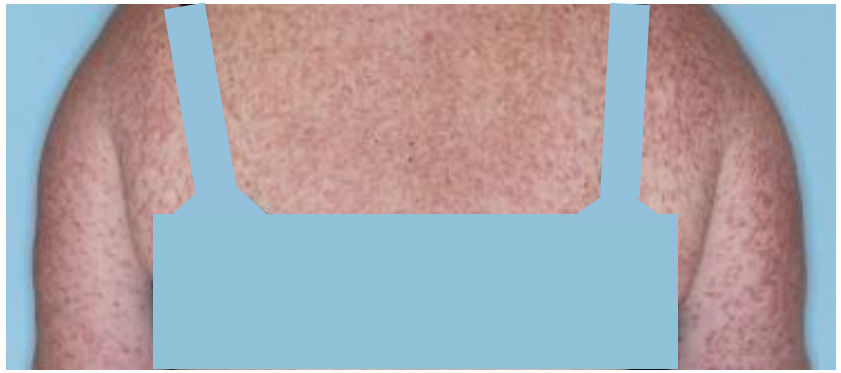
Treatment-Related AEs
Dysgeusia / Grade 1
Hoarseness / Grade 1
Hair Color Changes / Grade 1



	BL	Wk 12	Wk 24	Wk 48	% Decrease BL → Wk48
Tryptase (ng/mL)	39.4	3.5	2.7	3.4	**91%**
KIT D816V VAF (%)	0.19	0.03	Not Detected	0.03	**84%**
BM MC Burden (%)	10		1		**90%[1]**
CD25 Expression (%)	100		0		**100%[1]**
MS2D2 TSS (0 – 110)	67.9	29.4	27.8	22	**68%**
Most Severe Domain: Neurocognitive (0-10)	7.8	3.4	2.7	2.8	**65%**

1. BM not collected at week 48 for this patient, so % reduction is based on week 24.

BL



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Data cut-off as of 22May25

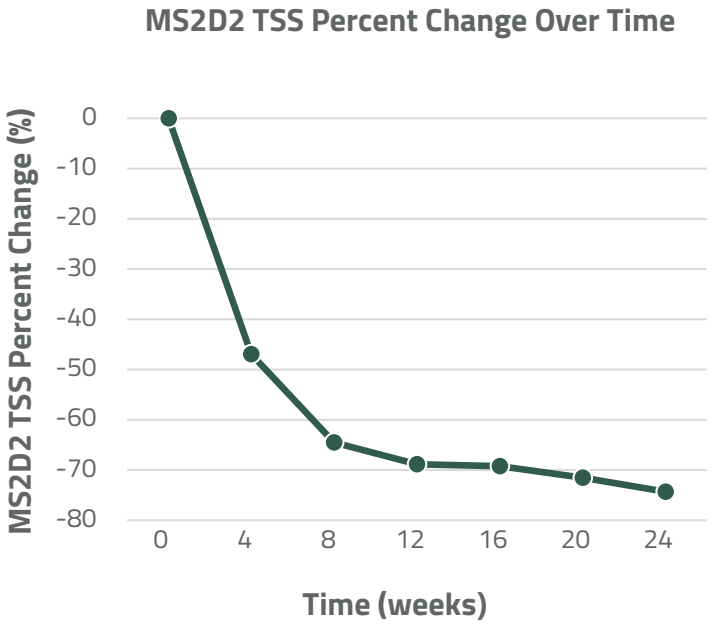
Case Study 2: 63 yo Man with Long History of SM and High-Risk Features Randomized to 100 mg Bezuclastinib

- **Discontinued 3 BSC medications in OLE:** cetirizine, cromolyn and montelukast and cromolyn nasal
- **Patient remains on study for 32 weeks with continued benefit**

SM-Related Medical History
Osteoporosis / Grade Unknown
GERD / Grade 1
Maculo-papular rash / Grade 1
Flushing / Grade 1
Urticaria Pigmentosa / Grade 1

Best Supportive Care (BSC) Medications
Montelukast
Famotidine
Cromolyn
Cetirizine

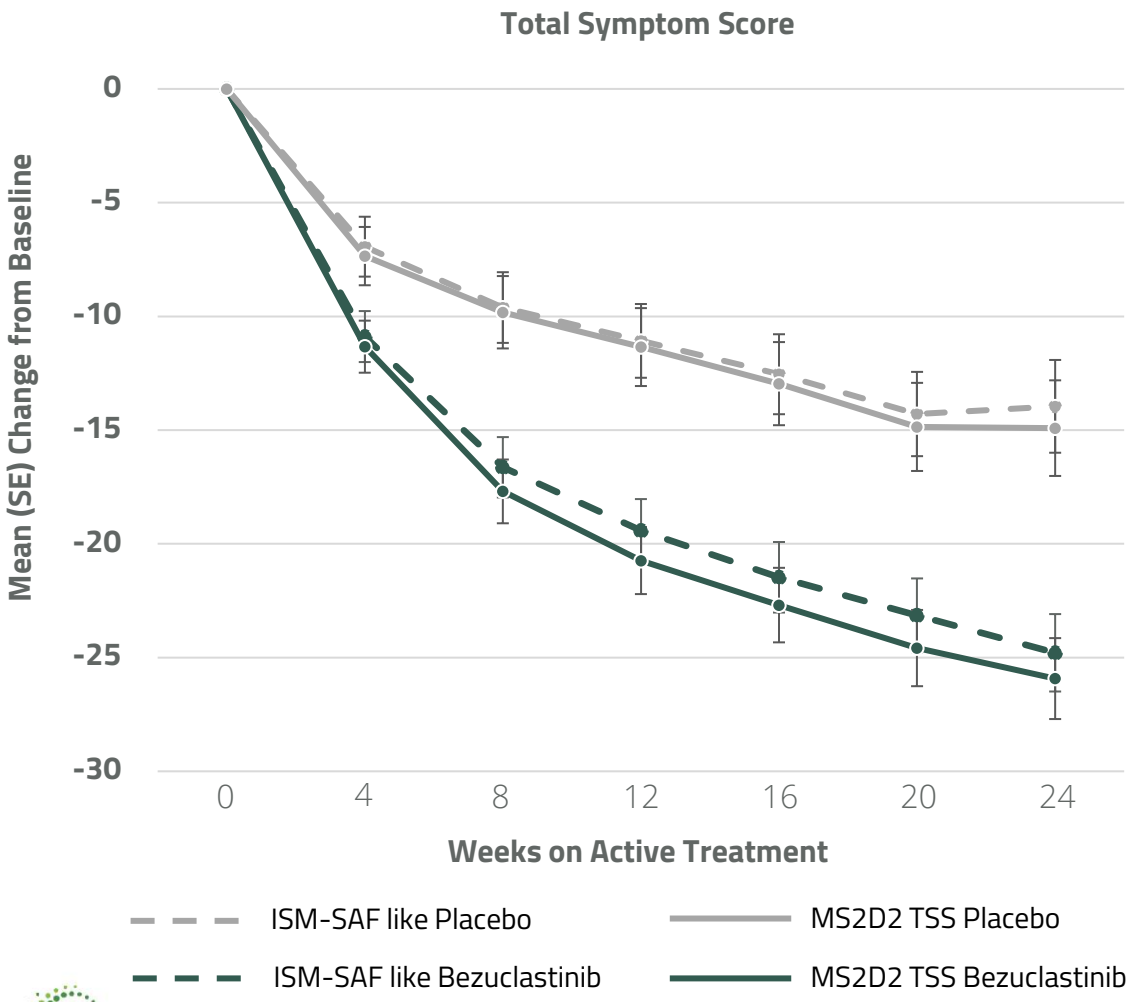
Treatment-Related AEs
Hair Color Changes / Grade 1



	BL	Week 12	Week 24	% Decrease BL → Wk24
Tryptase (ng/mL)	95.5	8.7	7.9	**92%**
KIT D816V VAF (%)	5.04		2.07	**59%**
BM MC Burden (%)	10		3	**70%**
CD25 Expression (%)	100		0	**100%**
MS2D2 TSS (0 – 110)	75.9	23.6	19.5	**74%**
Most Severe Domain: Skin (0-10)	8.1	3.9	3.3	**60%**

Data cut-off as of 22May25

Highly Consistent Results Using Composite Items Included in Either MS2D2 or ISM-SAF TSS



	MS2D2: 11 Items **0-110 Scale, Each Item 10 Points**	ISM-SAF: 11 Items 0-110 Scale, Each Item 10 Points
Skin	**Itching** **Flushing** **Spots** **Skin Redness**	Itching Flushing Spots
GI	**Abdominal Pain** **Nausea**	Abdominal Pain Nausea Diarrhea
CNS	**Headache** **Difficulty Remembering** **Difficulty Concentrating**	Headache Brain Fog Dizziness
Systemic	**Bone Pain** **Feeling of Tiredness**	Bone Pain Fatigue

MS2D2 is highly analogous to ISM-SAF, inclusion of specific items within composite TSS endpoint derived from NonAdvSM patient baseline data and FDA interaction

Data cut-off as of 22May25

Bezuclastinib Systemic Mastocytosis Expanded Access Program (NCT06915766[1]) Provides No-Cost Access to Patients in Need

AIM

Designed to provide bezuclastinib outside of a clinical trial to real-world patients with AdvSM or NonAdvSM who meet specific criteria including, but not limited to, having no comparable or satisfactory alternative therapy to treat the disease.

METHODS

Patients will receive oral bezuclastinib 100mg QD (NonAdvSM) or 150mg QD (AdvSM).

Treating physician to assess patients, report any SAEs, and determine treatment duration.

Key inclusion criteria*	Key exclusion criteria*
Age ≥ 18 years	Eligibility for and/or enrolled in an ongoing bezuclastinib clinical trial
Diagnosis of any NonAdvSM or AdvSM subtypes according to WHO classification for SM	Discontinuation of investigational bezuclastinib due to toxicity or withdrawal of consent
Lack of adequate disease control on current therapies	Pregnant or currently breastfeeding

*Other protocol-defined criteria apply.

SM EAP is currently open to requests for access from treating physicians in the United States.

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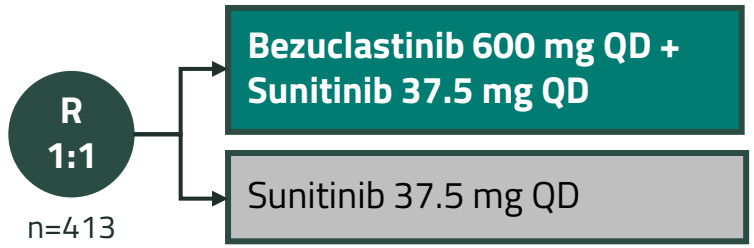
1. ClinicalTrials.gov. Expanded Access to Bezuclastinib for Patients With NonAdvanced Systemic Mastocytosis or Advanced Systemic Mastocytosis. Identifier: NCT06915766. Retrieved July 6, 2025 from: https://clinicaltrials.gov/study/NCT06915766.

Topline Results from PEAK and APEX Pivotal Trials On Track 2H 2025

Peak GIST



Primary endpoint: Progression Free Survival

- ***PEAK enrollment Q4 2022 – Q3 2024; Blinded events on track to deliver TLR by EOY 2025***
- ***2nd-line GIST: No new drugs approved since 2006***
- ***No other investigational products have initiated pivotal trials***
- ***>$1 billion US TAM opportunity***

KEY ENTRY CRITERIA

- Locally advanced, unresectable or metastatic GIST
- Disease progression on or intolerance to imatinib
- No other prior treatment (other than imatinib)

Apex ADVANCED SM

Primary endpoint: ORR using mIWG-MRT-ECNM

- ***APEX enrollment complete Q1 2025; TLR on track for 2H 2025***
- ***Positive SUMMIT results provide expected read-through to APEX***
- ***SOC associated with significant safety concerns; no other investigational products in clinical development***
- ***~$300 million US TAM opportunity***

KEY ENTRY CRITERIA

- Centrally Confirmed ASM, SM-AHN or MCL
- Measurable disease per mIWG-MRT-ECNM
- ECOG PS 0 to 3

SUMMIT Results are Transformative

- **Bezuclastinib establishes new benchmarks for NonAdvSM symptomatic reduction**
  - 24.3 point reduction from baseline at 24 weeks
  - 8.91 point placebo-adjusted effect size, representing 57% improvement over approved KIT therapy
- **Bezuclastinib associated with powerful improvement in objective measures of mast cell burden**
  - 87.4% of patients demonstrating a ≥50% reduction in serum tryptase
- **Favorable tolerability profile, positioning bezuclastinib for long-term use in chronic disease population**
  - Significant majority of TEAEs reported as Gr 1
  - Only 5.9% patients discontinued, all due to higher grade ALT/AST; all resolved rapidly after D/C
  - Other than lab abnormalities, no hepatic events reported
- **SUMMIT TSS results with either MS2D2 or ISM-SAF composite items led to highly consistent results**
- **On track for NDA submission by end of 2025**
- **Two additional near-term pivotal trial TLR: PEAK in 2nd-line GIST, APEX in AdvSM**
- **Strong existing balance sheet with access to significant capital via recently announced debt facility**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Q&A
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