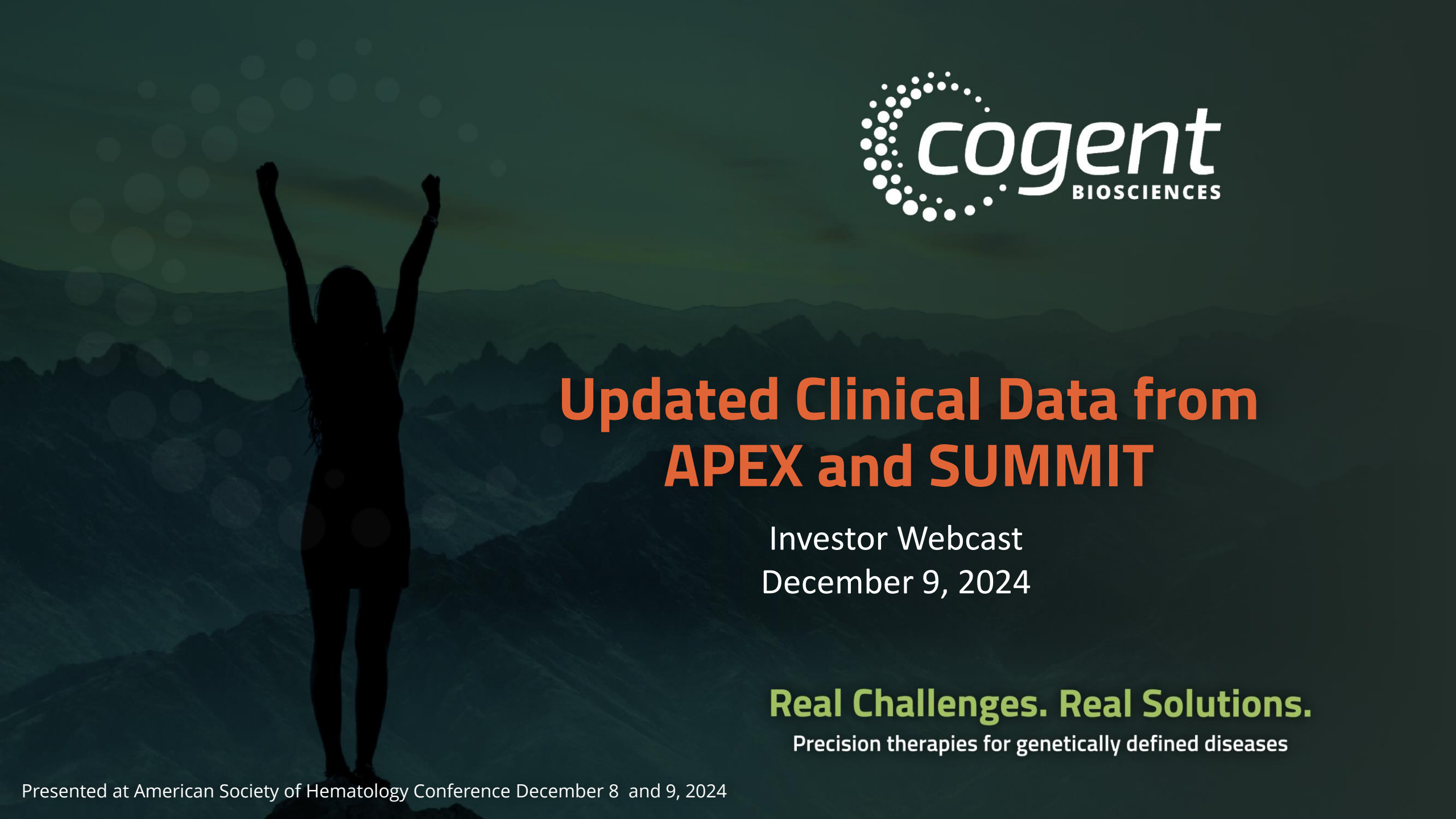


Updated Clinical Data from APEX and SUMMIT

Investor Webcast
December 9, 2024

Real Challenges. Real Solutions.

Precision therapies for genetically defined diseases

Presented at American Society of Hematology Conference December 8 and 9, 2024

Forward Looking Statements and Risk Factors

This presentation and the accompanying oral commentary contain forward-looking statements that involve risks, uncertainties and assumptions. If the risks or uncertainties ever materialize or the assumptions prove incorrect, our results may differ materially from those expressed or implied by such forward looking statements. All statements other than statements of historical fact could be deemed forward-looking, including, but not limited to, any statements of the plans, strategies, and objectives of management for future operations, including our clinical development and commercialization plans and timelines; any projections of financial information; any statement about historical results that may suggest trends for our business; any statement of expectation or belief regarding future events; potential markets or market size, technology developments, our clinical and research pipelines, clinical and pre-clinical data or the implications thereof, enforceability of our intellectual property rights, competitive strengths or our position within the industry; any statements regarding the anticipated benefits of our collaborations or other strategic transactions; and any statements of assumptions underlying any of the items mentioned.

These statements are based on estimates and information available to us at the time of this presentation and are not guarantees of future performance. Actual results could differ materially from our current expectations as a result of many risks and uncertainties, including but not limited to, risks associated with: the potential impacts of raising additional capital, including dilution to our existing stockholders, restrictions our operations or requirements that we relinquish rights to our technologies or product candidates; business interruptions resulting from the coronavirus disease outbreak or similar public health crises, which could cause a disruption of the development of our product candidates and adversely impact our business; the success, cost, and timing of our product development activities and clinical trials; the timing of our planned regulatory submissions to the FDA for our product candidate bezuclastinib and feedback from the FDA as to our plans; our ability to obtain and maintain regulatory approval for our bezuclastinib product candidate and any other product candidates we may develop, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate; the potential for our identified research priorities to advance our bezuclastinib product candidate; the ability to license additional intellectual property relating to our product candidates from third-parties and to comply with our existing license agreements and collaboration agreements; the ability and willingness of our third-party research institution collaborators to continue research and development activities relating to our product candidates; our ability to commercialize our products in light of the intellectual property rights of others; our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates; the scalability and commercial viability of our manufacturing methods and processes; the commercialization of our product candidates, if approved; our plans to research, develop, and commercialize our product candidates; our ability to attract collaborators with development, regulatory, and commercialization expertise; our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates; among others. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to our business in general, see our periodic filings filed from time to time with the Securities and Exchange Commission. Unless as required by law, we assume no obligation and do not intend to update these forward-looking statements or to conform these statements to actual results or to changes in our expectations.

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.

Any data pertaining to Cogent product candidates is interim data and may include investigator-reported interim data for which Cogent has not yet independently reviewed the source data. The interim data may not be representative of the final results that may be obtained in the corresponding trials and results from earlier trials may not be representative of results obtained in later trial or pivotal trials.

Agenda and Speakers

Andrew Robbins
President and
Chief Executive Officer

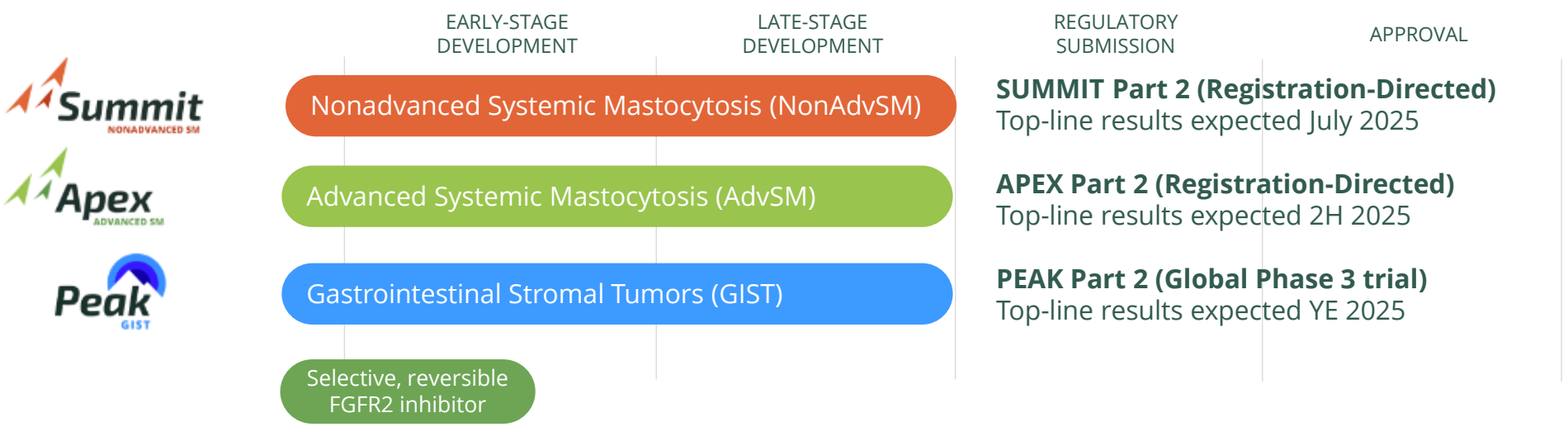
Daniel J. DeAngelo, M.D., Ph.D.
Chief of the Division of Leukemia
Dana-Farber Cancer Institute

Jessica Sachs, M.D.
Chief Medical Officer

• Introduction and Corporate Overview	Andrew Robbins
• Review of APEX and SUMMIT Data	Dr. Daniel DeAngelo
• Presentation Summary	Andrew Robbins
• Q&A	All

Cogent Building Robust Pipeline; Focus Today on SM Clinical Trials

CLINICAL PROGRAMS



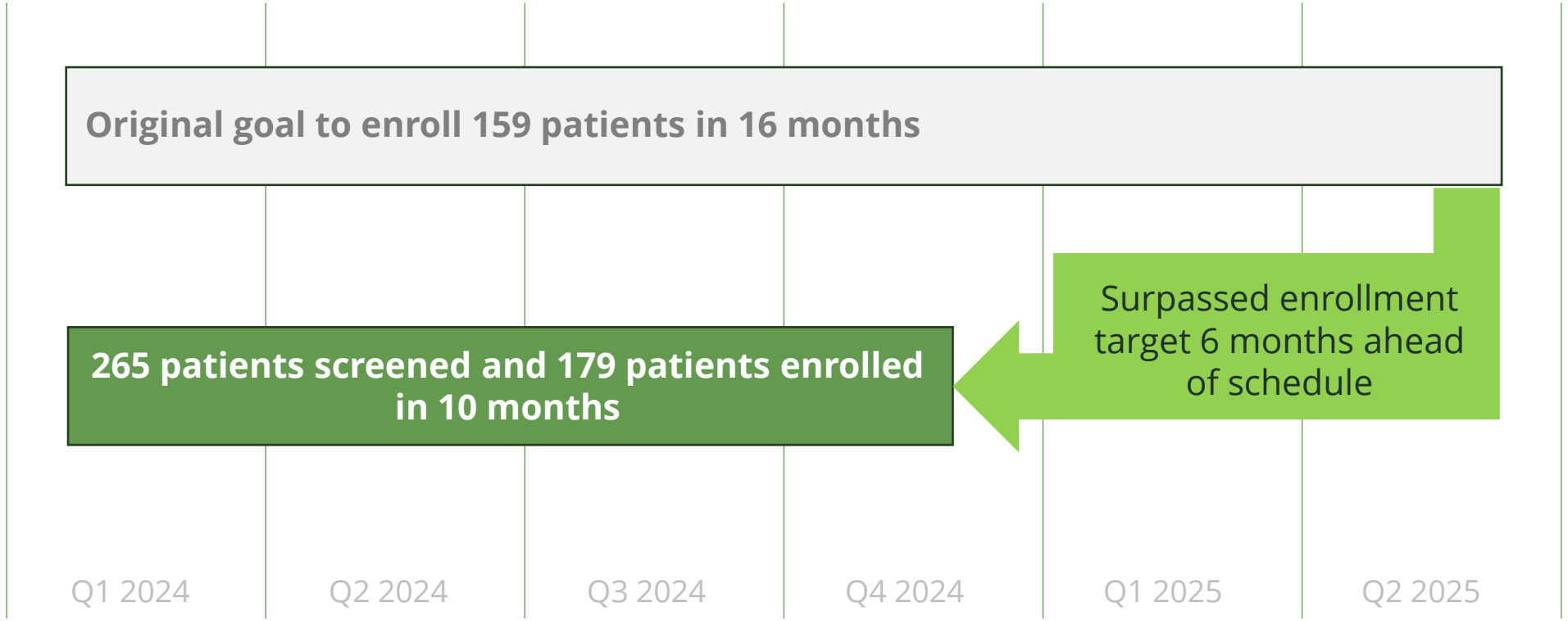
RESEARCH PROGRAMS

$345.5M as of September 30th; cash runway into late 2026, significantly past TLRs

SUMMIT Part 2 Enrollment Complete!

Based on timeline from prior NonAdvSM trial

Based on actual investigator interest and patient demand



Top-Line Results now expected July 2025

Bezuclastinib: A Highly Selective and Potent KIT Mutant Inhibitor with Potential to Demonstrate Best-in-Class Clinical Profile

Bezuclastinib

- Specifically targets KIT mutations including exon 17 D816V
- Selective versus other targets including PDGFRα, PDGFRβ, VEGFR2, FLT3, CSF1R and KDR
- Molecularly designed to avoid CNS penetration
- Worldwide rights to compound exclusively licensed from Plexxikon[1]
- Potential patent protection through at least 2043[2]

Encouraging Clinical Activity

Promising initial data across all three ongoing studies: APEX in AdvSM patients, SUMMIT in NonAdvSM patients, and PEAK in GIST patients

Attractive Emerging Safety Profile

Well-tolerated with encouraging safety profile across 600+ patients in single agent & combination dosing including data from our ongoing APEX, SUMMIT and PEAK studies

Potential Best-in-Class KIT mutant inhibitor

KIT D816V inhibition supports studies in systemic mastocytosis and GIST; safety results support potential for broad use

cogent BIOSCIENCES

[1] Plexxikon is eligible for mid- to high- single-digit royalties and additional development milestones.

[2] Existing patent protection through at least 2033, not including available patent term extension. Additional protection anticipated from patent application relating to optimized formulation of bezuclastinib.

Bezuclastinib Offers 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

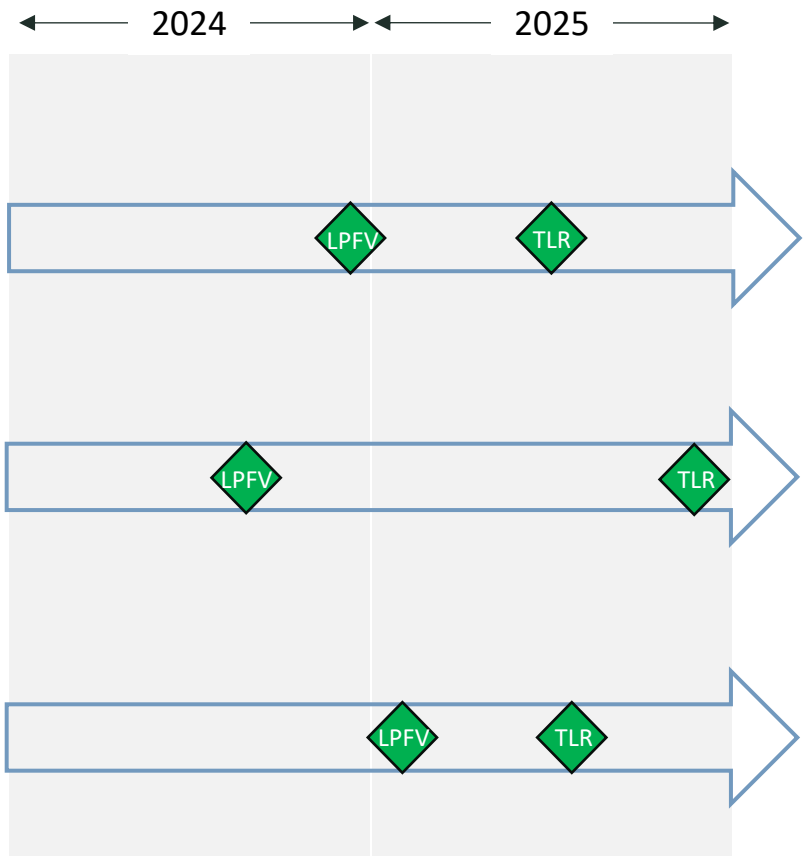
Phase 3 study in 2nd-line GIST bezuclastinib +/- sunitinib

n=413, mPFS primary endpoint

Apex ADVANCED SM

Registration-directed study in AdvSM bezuclastinib monotherapy

n=65, 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

Unmet Need Remains for Systemic Mastocytosis Patients

Disease Overview: Systemic mastocytosis (SM) is primarily driven by KIT D816V mutation and leads to uncontrolled proliferation of mast cells (MC)[1]

- ~90% of patients present with indolent, or non-advanced systemic mastocytosis (NonAdvSM)
- ~10% of patients present with advanced systemic mastocytosis (AdvSM)
  - Aggressive SM (ASM); SM with associated hematologic neoplasm (SM-AHN); mast cell leukemia (MCL)[1]
  - Prior to KIT inhibitors development, based on subtype, the median overall survival ranges from <6 months to 3-4 years[2,3]

Unmet need remains for new therapies, effective at targeting overactive mast cells, while delivering a well-tolerated patient experience

- Reported toxicities for marketed therapies in AdvSM include, but are not limited to,: nausea, vomiting, diarrhea, edema, intracranial bleeding, cognitive effects[4,5]
- Tolerability-limited dosing of marketed therapy for NonAdvSM may preclude optimal efficacy

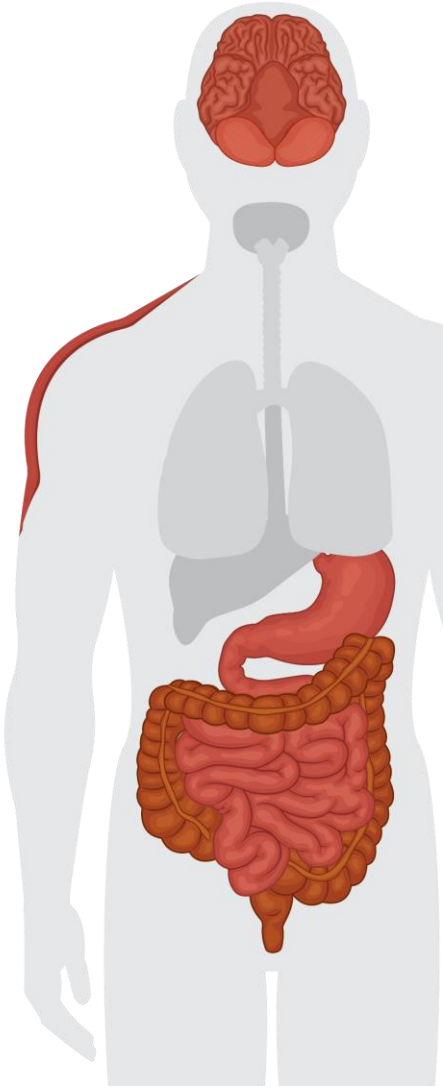
Neurological
Headache, brain fog, cognitive dysfunction, anxiety, depression

Systemic
Anaphylaxis

Cutaneous (skin)
Flushing of the face/neck/chest, hives, skin rashes, itching with or without rash

Gastrointestinal
Diarrhea, nausea, vomiting, abdominal pain, bloating, gastroesophageal reflux disease (GERD)

Other
Cardiovascular
Ear/Nose/Throat/Respiratory
Skeletal
Gynecological
Urinary



References: [1]Pardanani A. Am J Hematol. 2021;96(4):508-525. [2]Ustun C et al. Haematologica. 2016;101(10):1133-1143. [3]Lim K-H et al. Blood. 2009;113(23):5727-5736. [4]AYVAKIT (avapritinib) [package insert]. Blueprint Medicines Corporation; 2023. [5]RYDAPT (midostaurin) [package insert]. Novartis Pharmaceuticals; 2021.

Reviewing Pioneer Part 2 24-Week Results

At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Mean change in TSS (95% CI)	–15.58 (–18.61, –12.55)	–9.15 (–13.12, –5.18)	0.003

Mean reduction in TSS at 24 weeks[1]

At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Proportion of patients with **≥50% reduction in TSS** (95% CI)	24.8% (17.9–32.8)	9.9% (4.1–19.3)	0.005

Patients achieving >50% improvement TSS

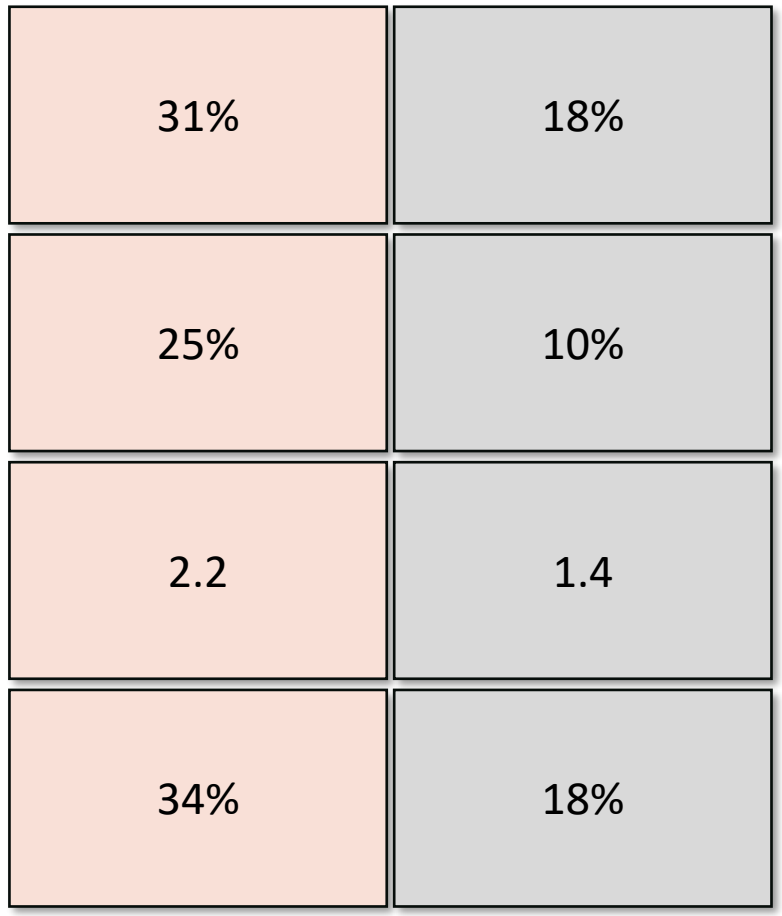
At Week 24	Avapritinib 25 mg QD (n=131)	Placebo (n=66)	P-value
Mean change in most severe symptom score (SD)	–2.22 (2.30)	–1.42 (1.88)	0.015

Improvement on most severe symptom baseline (0-10 scale)

At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Mean % change MC-QoL (95% CI)	–34.3% (–39.9, –28.7)	–17.9% (–25.1, –10.8)	0.001

Mean improvement in Quality of Life (MCQoL)

Pioneer Part 2 Pivotal Trial



1- Reductions calculated using baseline TSS mean severity of 50.2 and 52.4 for avapritinib and placebo cohort, respectively

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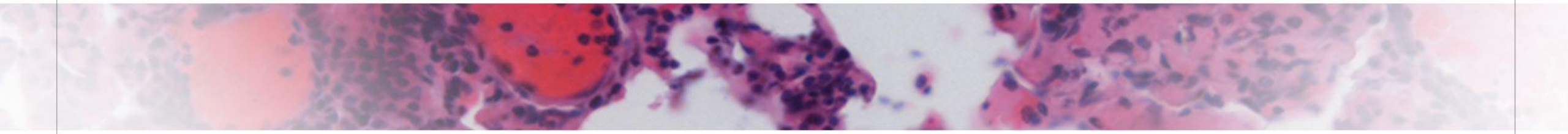


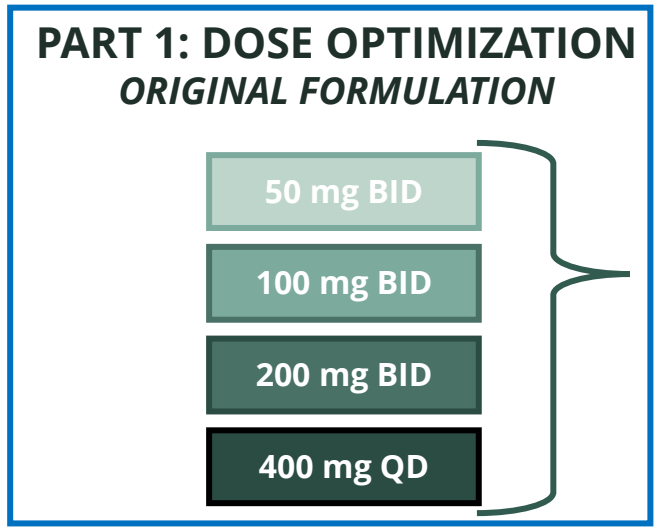
Apex Part 1: Updated Assessment of Bezuclastinib (CGT9486), a Selective KIT D816V Tyrosine Kinase Inhibitor, in Patients with Advanced Systemic Mastocytosis (AdvSM)

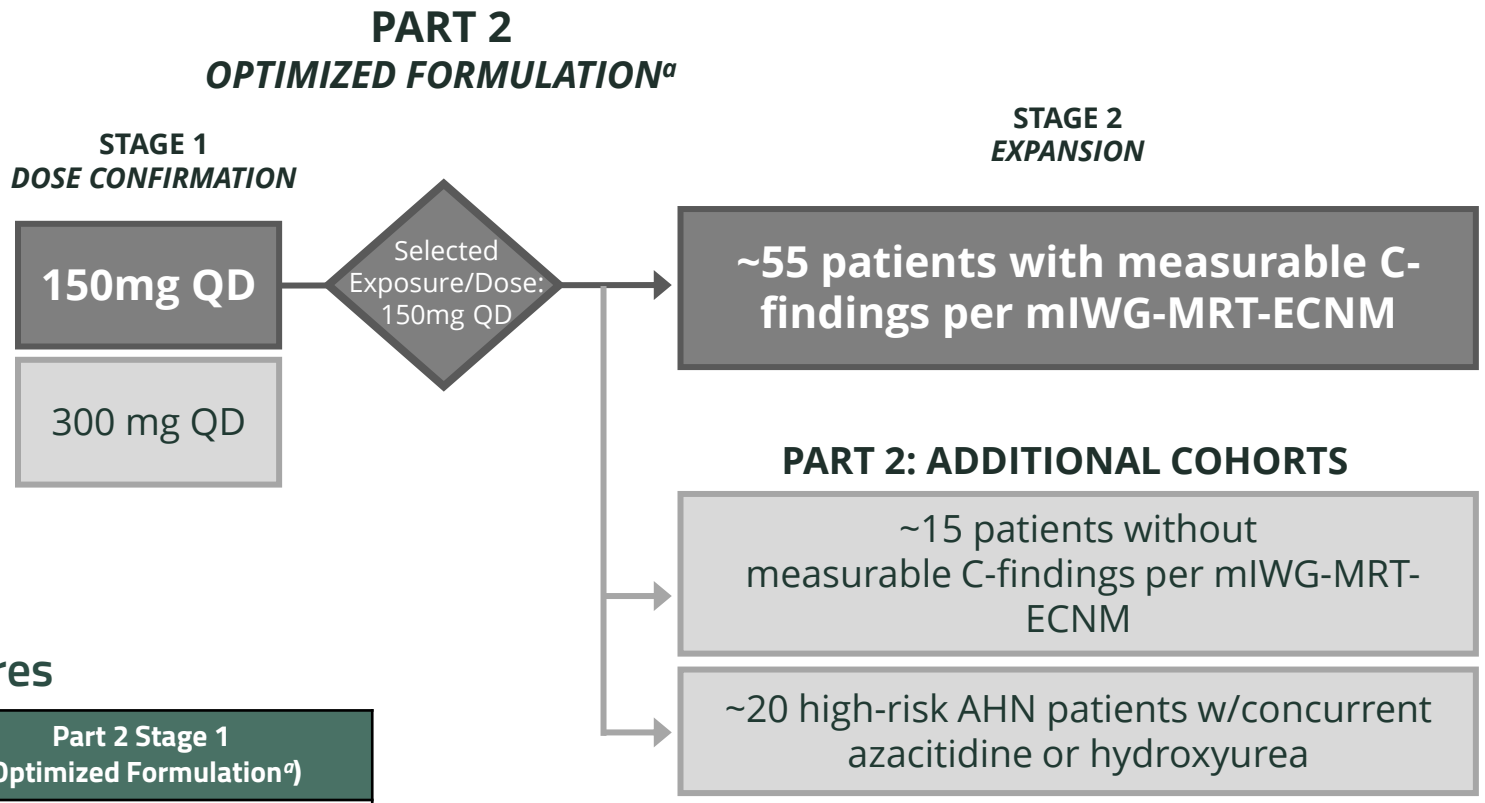
Daniel J. DeAngelo[1], Jason Gotlib[2], Vinod Pullarkat[3], Pankit Vachhani[4], Tsewang Tashi[5], Stephanie Lee[6], Gary Schiller[7], Anthony M. Hunter[8], Miguel Piris-Villaespesa[9], Helena Pomares-Marin[10], Cristina Bulai Livideanu[11], Khalid Shoumariyeh[12], Jonathan Lambert[13], Tracy I. George[14], Jay Patel[14], Cristina Papayannidis[15], Tania Jain[16], Michael Deininger[17], Andreas Reiter[18], Gabriela Hobbs[19], Lei Sun[20], Deepak Nagendra[20], Jenna Zhang[20], Amanda Pilla[20], Kim Dishman[20], Marcus A. Carden[20], Deepti H. Radia[21]

1. Dana-Farber Cancer Institute, Boston, MA, USA;2. Stanford Cancer Institute, Stanford, CA; 3. City of Hope, Duarte, CA; 4. University of Alabama at Birmingham, Birmingham, Alabama; 5. Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; 6. St. Michael's Hospital, Toronto, Canada; 7. David Geffen School of Medicine at UCLA, Los Angeles; 8. Emory University School of Medicine, Atlanta, GA, USA; 9. Hospital Universitario Ramón y Cajal, Madrid; 10. Institut Catala d'Oncologia Hospitalet – Hospital Duran I Reynals, Barcelona, Spain; 11. CEREMAST Toulouse, Dermatology Department, Toulouse University Hospital, Toulouse, France; 12. University Hospital Freiburg, Freiburg, Germany; 13. University College London Hospitals NHS Foundation Trust, London; 14. University of Utah, ARUP Laboratories, Salt Lake City, UT, USA; 15. IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli",Bologna, ITA; 16. Johns Hopkins University, Baltimore, MD, USA; 17. Versiti Blood Research Institute, Milwaukee, WI, USA; 18. University Medical Centre, Mannheim, Germany;19. Massachusetts General Hospital, Boston, MA, USA; 20. Cogent Biosciences, Inc., Waltham, MA, USA; 21. Guy's and St. Thomas' NHS Foundation Trust, London

Apex (NCT04996875): A Phase 2 Open-Label, Multicenter Clinical Study of Bezuclastinib in Patients with Advanced Systemic Mastocytosis

FOCUS OF PRESENTATION





Mean (CV%) Steady-State (Cycle 2 Day 1) Exposures

Study Part (Formulation)	Part 1 (Original Formulation)	Part 2 Stage 1 (Optimized Formulation[a])
Bezuclastinib Dose	100 mg BID (N=7)	150 mg QD (N=10)
$C_{max, ss}$ (ng/mL)	861 (26.8)	850 (29.9)
$AUC_{0-24hr,ss}$ (ng*hr/mL	18,900 (30.8)	17,600 (31.3)

150 mg QD of the optimized formulation delivers similar exposures to 100 mg BID of original formulation

[a]The original formulation was modified to improve bioavailability.

DeAngelo DJ, et al. American Society of Hematology (ASH) 2024; San Diego, CA, 8 Dec 2024: Publication Number: 659

Patient Demographics and Characteristics

33 patients enrolled[a]; median age: 68 years; range: 33-87

	Total (N=32)	50mg BID (N=8)	100mg BID (N=7)	200mg BID (N=8)	400mg QD (N=9)
Male, n (%)	**21 (65.6)**	6 (75.0)	4 (57.1)	5 (62.5)	6 (66.7)
ECOG PS, n (%)					
0-1	**27 (84.4)**	8 (100)	5 (71.4)	7 (87.5)	7 (77.8)
2-3	**5 (15.6)**	0	2 (28.6)	1 (12.5)	2 (22.2)
AdvSM Subtype per Central Eligibility Review, n (%)					
ASM	**7 (21.9)**	2 (25)	0	0	5 (55.6)
SM-AHN[b]	**23 (71.9)**	5 (62.5)	6 (85.7)	8 (100)	4 (44.4)
MCL	**2 (6.3)**	1 (12.5)	1 (14.3)	0	0
Prior TKI therapy for AdvSM, n (%)[c]					
TKI Naïve[d]	**22 (69)**	7 (88)	4 (57)	6 (75)	5 (56)
Avapritinib	**5 (16)**	0	2 (29)	2 (25)	1 (11)
Midostaurin	**10 (31)**	1 (13)	3 (43)	2 (25)	4 (44)
SRSF2/ASXL1/RUNX1 Mutation in Peripheral Blood	**19 (59.4)**	5 (62.5)	5 (71.4)	5 (62.5)	4 (44.4)
***KIT* D816V in Whole Blood, Positive, n (%)**	**29 (90.6)**	8 (100)	6 (85.7)	7 (87.5)	8 (88.9)
Median *KIT* D816V VAF, % (range)	**6.1 (0-47.2)**	3.4 (0-39.0)	29.2 (0-38.9)	2.9 (0-47.2)	1.9 (0-42.2)
Median Bone Marrow MC Burden, % (range)	**30 (5-90)**	50 (20-70)	70 (5-90)	10 (5-30)	40 (10-80)
Median Serum Tryptase, ng/mL (range)	**153.5 (35-1578)**	178 (130-605)	233 (54-1578)	97 (35-131)	182 (50-370)
Patients evaluable with mIWG-MRT-ECNM C-findings	**27 (84.4)**	7 (87.5)	6 (85.7)	7 (87.5)	7 (77.8)
Median (range) time on treatment, months	**16.2 (0.1-32.2)**	18.0 (4.7-30.9)	23.0 (10.2-31.3)	7.0 (0.1-16.6)	17.4 (1.2-32.2)

Data as of: 11Oct2024
DeAngelo DJ, et al. American Society of Hematology (ASH) 2024; San Diego, CA, 8 Dec 2024: Publication Number: 659

[a]One patient never dosed was excluded
[b]CMML [n=18]; MDS and/or MPN [n=5]
[c]Additional therapies included cytoreductives and biologics
[d]Patients who have received no prior SM-directed therapy with midostaurin and/or avapritinib

Apex Part 1: Responses by mIWG-MRT-ECNM Criteria Were Observed In Both TKI Exposed and Naïve Patients

	Confirmed mIWG-MRT-ECNM Responses per CRRC		
Best Response, n (%) [Ω]	All	TKI[‡] Therapy Naïve	Prior TKI[‡] Exposure
	N=27	N=18	N=9
Overall response rate			
CR + CRh + PR + CI[†]	**14 (52)**	**11 (61)**	**3 (33)**
CR + CRh + PR	**13 (48)**	**10 (56)**	**3 (33)**
Complete Response (CR + CRh)	**7 (26)**	**7 (39)**	**0**
Partial Response (PR)	**6 (22)**	**3 (17)**	**3 (33)**
Clinical Improvement (CI)	**1 (4)**	**1 (6)**	**0**
Stable Disease (SD)	**10 (37)**	**6 (33)**	**4 (44)**
Not evaluable	**3 (11)**	**1 (6)**	**2 (22)**

[Ω]5 patients without measurable C-finding at baseline were excluded for being non-evaluable per mIWG-MRT-ECNM criteria; one additional patient was excluded due to discontinuation prior to first dose (not dosed [ND]).
[‡] SM-directed therapy with midostaurin only (n=4) or midostaurin and avapritinib (n=5)
[†] Primary endpoint of Apex study
Data as of: 11Oct2024
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Bezuclastinib Treatment Results in a High Response Rate Based on PPR Criteria

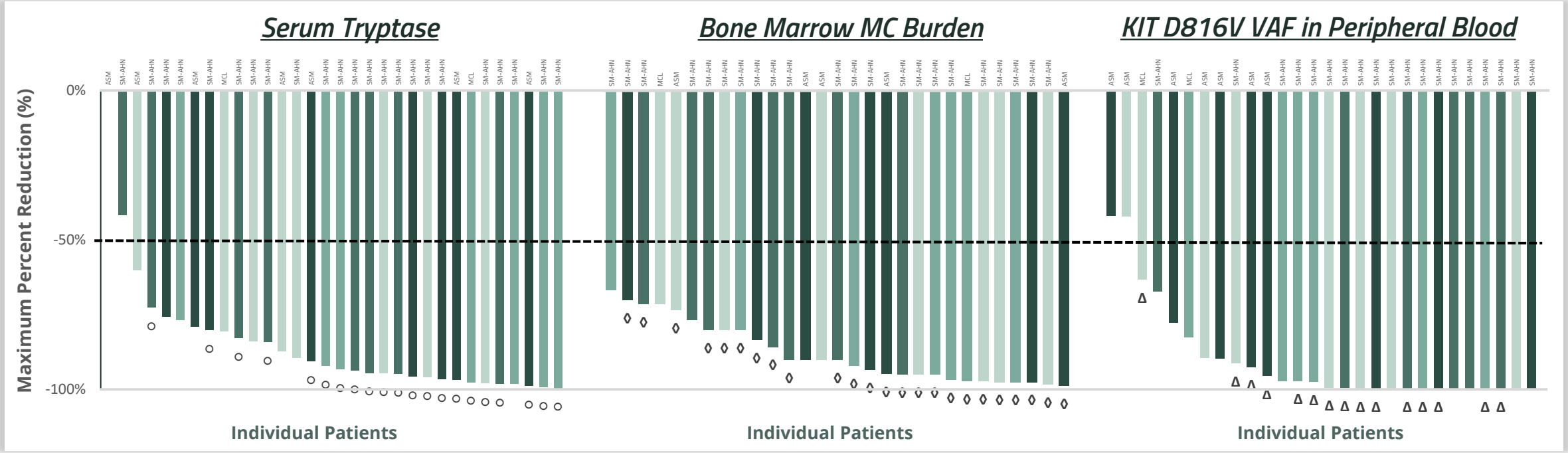
Pure Pathologic Response (PPR)[1]: Objective measure evaluating mast cell burden, serum tryptase level, and CBC results without challenges of C-finding (organ damage) assessments

Best PPR[a] Response, n (%)	All
	N=32
Overall response rate (CR + PR)	28 (88)
Complete Response (CR/CRh)	14 (44)
Partial Response (PR)	14 (44)
Stable Disease (SD)	1 (3)
Not Evaluable	3 (9)

- Median (range) time to achieve PPR response of PR or better (CR, CRh, or PR) was 2.1 (1.8-10.2) months

[a]PPR is derived based on local hematology and central pathology assessments.
1. Shomali and Gotlib. Int J Mol Sci. 2021; 22(6):2983.
Data as of: 11Oct2024
DeAngelo DJ, et al. American Society of Hematology (ASH) 2024; San Diego, CA, 8 Dec 2024: Publication Number: 659

Bezuclastinib Demonstrates Deep Reductions in Markers of Mast Cell Burden



- 94% (30/32) achieved ≥50% reduction
- 100% (29/29) with at least 2 cycles of treatment achieved ≥50% reduction
- 66% (21/32) achieved <20 ng/mL

- 100% (29/29) with baseline and ≥1 post-baseline assessment achieved ≥50% reduction
- 83% (24/29) achieved complete clearance of mast cell aggregates by central review

- 93% (26/28) achieved a ≥50% reduction
- 71% (15/21) achieved VAF <1%

50 mg BID
100 mg BID
200 mg BID
400 mg QD

Milestone Achieved
○ <20 ng/mL serum tryptase
◊ Complete clearance of mast cell aggregates
Δ < 1% *KIT* D816V VAF

Data as of: 11Oct2024
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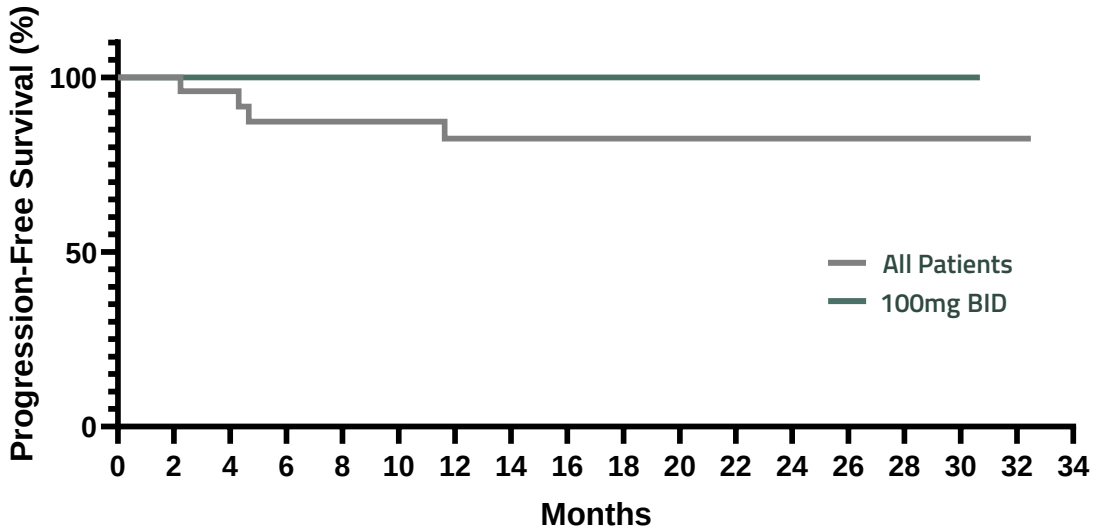
Median PFS and Duration of Response Were Not Reached

Progression-free survival (PFS[a]) in mIWG-MRT-ECNM-evaluable population (n=27)



Pts at Risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34
All Pts	27	25	22	19	19	19	17	15	12	9	9	7	6	6	2	2	1	0
100 BID	7	7	7	7	7	7	7	7	6	5	4	4	3	3	3	2	0	0

- Median PFS not yet reached at median study follow-up of 20 months
- PFS rate was 82% at 24 months

Duration of response (DOR) (N=27)

- Median duration of response not yet reached
- Median (range) time to achieve mIWG-MRT-ECNM confirmed response of PR or better (CR, CRh, PR) was 2.2 (1.9-7.5) months

Disease Progression in Overall Population (N=32)

- No patients had SM progression
- 7 patients developed progression of AHN
  - AML transformation (3), progression of MDS (2), worsening of CMML (2)
  - 3 patients remained on bezuclastinib and began treatment with azacitidine in the rollover cohort

[a]PFS progression includes death or CRRC assessment of progressive disease
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Bezuclastinib Continues to Demonstrate an Encouraging Safety Profile

Treatment Related Adverse Events in > 10% Patients

	Total (n=32) n (%)		50 mg BID (n=8) n (%)	100 mg BID (n=7) n (%)	200 mg BID (n=8) n (%)	400 mg QD (n=9) n (%)
Preferred Term	**All grade**	**Grade ≥3**	**All grade**	**All grade**	**All grade**	**All grade**
Hair color changes	**11 (34)**	**-**	-	4 (57)	3 (38)	4 (44)
ALT/AST increased*	**10 (31)**	**2 (6)**	4 (50)	2 (29)	2 (25)	2 (22)
Thrombocytopenia*	**9 (28)**	**3 (9)**	1 (13)	4 (57)	2 (25)	2 (22)
Neutropenia*	**9 (28)**	**5 (16)**	1 (13)	3 (43)	2 (25)	3 (33)
Taste disorder*	**6 (19)**	**-**	1 (13)	1 (14)	1 (13)	3 (33)
Fatigue	**5 (16)**	**-**	3 (38)	-	2 (25)	-
Peripheral edema	**4 (13)**	**-**	-	1 (14)	1 (13)	2 (22)
Periorbital edema	**4 (13)**	**1 (3)**	-	-	3 (38)	1 (11)
Anemia	**4 (13)**	**1 (3)**	-	1 (14)	2 (25)	1 (11)
Blood ALP increased	**4 (13)**	**-**	1 (13)	-	1 (13)	2 (22)

*Includes pooled terms.

- Median duration of treatment 16.2 months (range: 0.1-32.2)
- The majority of hematological adverse events were low grade, reversible, and did not require dose reduction
- No intracranial bleeding events were reported
- Treatment related SAEs reported in 4 patients including Gr4 Thrombocytopenia, Gr4 GGT increased (confounded by cholelithiasis and underlying ampullary lesion), Gr3 Hypersensitivity (mediator flare), and Gr3 Leishmaniasis
- 12 patients required dose reduction due to AEs, 8 of which were at 400 mg total daily dose
- 2 patients discontinued due to treatment related adverse events of transaminase increased
- 100mg BID tolerability: 2 patients required dose reductions for thrombocytopenia and no discontinuations due to AEs.

Data as of: 11Oct2024
DeAngelo DJ, et al. American Society of Hematology (ASH) 2024; San Diego, CA, 8 Dec 2024: Publication Number: 659

100mg BID of Bezuclastinib Original Formulation Resulted in Optimal Efficacy

Confirmed mIWG-MRT-ECNM Responses in All Patients (n=27) and By Dose

Best Response, n (%) Ω	All (N=27)	50 BID (n=7)	100 BID (n=6)	200 BID/400 QD (n=14)
Overall response rate				
CR + CRh + PR + CI†	**14 (52)**	**4 (57)**	**5 (83)**	**5 (36)**
CR + CRh + PR	**13 (48)**	**3 (43)**	**5 (83)**	**5 (36)**
Complete Response (CR + CRh)	**7 (26)**	**2 (29)**	**3 (50)**	**2 (14)**
Partial Response (PR)	**6 (22)**	**1 (14)**	**2 (33)**	**3 (21)**
Clinical Improvement (CI)	**1 (4)**	**1 (14)**	**0**	**0**
Stable Disease (SD)	**10 (37)**	**3 (43)**	**1 (17)**	**6 (43)**
Not evaluable	**3 (11)**	**0**	**0**	**3 (21)**

Ω5 patients without measurable C-findings per mIWG-MRT-ECNM at baseline were excluded; one additional patient was excluded due to discontinuation prior to first dose (not dosed [ND]).
† Primary endpoint of Apex study
Data as of: 11Oct2024
DeAngelo DJ, et al. American Society of Hematology (ASH) 2024; San Diego, CA, 8 Dec 2024: Publication Number: 659

Bezuclastinib Has an Encouraging Safety Profile With Deep, Durable Responses in Patients with AdvSM

- **Bezuclastinib continues to demonstrate an encouraging safety and tolerability profile while providing durable responses**
  - 52% ORR per mIWG-MRT-ECNM and 88% ORR per PPR criteria
  - Deep reductions demonstrated across commonly used biomarkers of mast cell activity
  - Median DOR and median PFS were not reached and PFS rate was 82% at 24 months
  - The majority of hematological adverse events were low grade, reversible, and did not require dose reduction
- **100mg BID dose resulted in optimal efficacy and safety outcomes**
  - 83% overall response rate per mIWG-MRT-ECNM
  - All patients receiving 100mg BID achieved PR or better based on PPR criteria
  - No discontinuations due to AEs with 100mg BID dose
  - Exposures at 100mg BID dose are similar to selected dose for Part 2
- **Enrollment to Part 2 is ongoing**
  - A cohort evaluating bezuclastinib with concurrent AHN therapy is enrolling

Data as of: 11Oct2024
DeAngelo DJ, et al. American Society of Hematology (ASH) 2024; San Diego, CA, 8 Dec 2024: Publication Number: 659

Presented at 66th American Society of Hematology (ASH) Annual Meeting and Exposition
Dec 9, 2024 ▪ San Diego
Poster 4556

Updated Efficacy and Safety Results of Patients Receiving Selected 100mg Bezuclastinib Dose and Participating in the Open-Label Extension of Summit: A Randomized, Double-Blind, Placebo Controlled Phase 2 Clinical Trial of Bezuclastinib in Adult Patients with NonAdvanced Systemic Mastocytosis

Lindsay A. M. Rein[1], Daniel J. DeAngelo[2], Brian D. Modena[3], Stephen T. Oh[4], Cristina Bulai Livideanu[5], Celalettin Ustun[6], Nathan Boggs[7], Michael Manning[8], Anthony M. Hunter[9], Cem Akin[10], Arnold Kirshenbaum[11], Ingunn Dybedal[12], Cecilia Arana Yi[13], Richard Herrscher[14], Mariana Castells[15], Frederick Lansigan[16], Tracy I. George[17], Jay Patel[17], Lei Sun[18], Nisha Shah[18], Jenna Zhang[18], Amanda Pilla[18], Priya Singh[18], Marcus A. Carden[18], Frank Siebenhaar[19,20], Prithviraj Bose[21]

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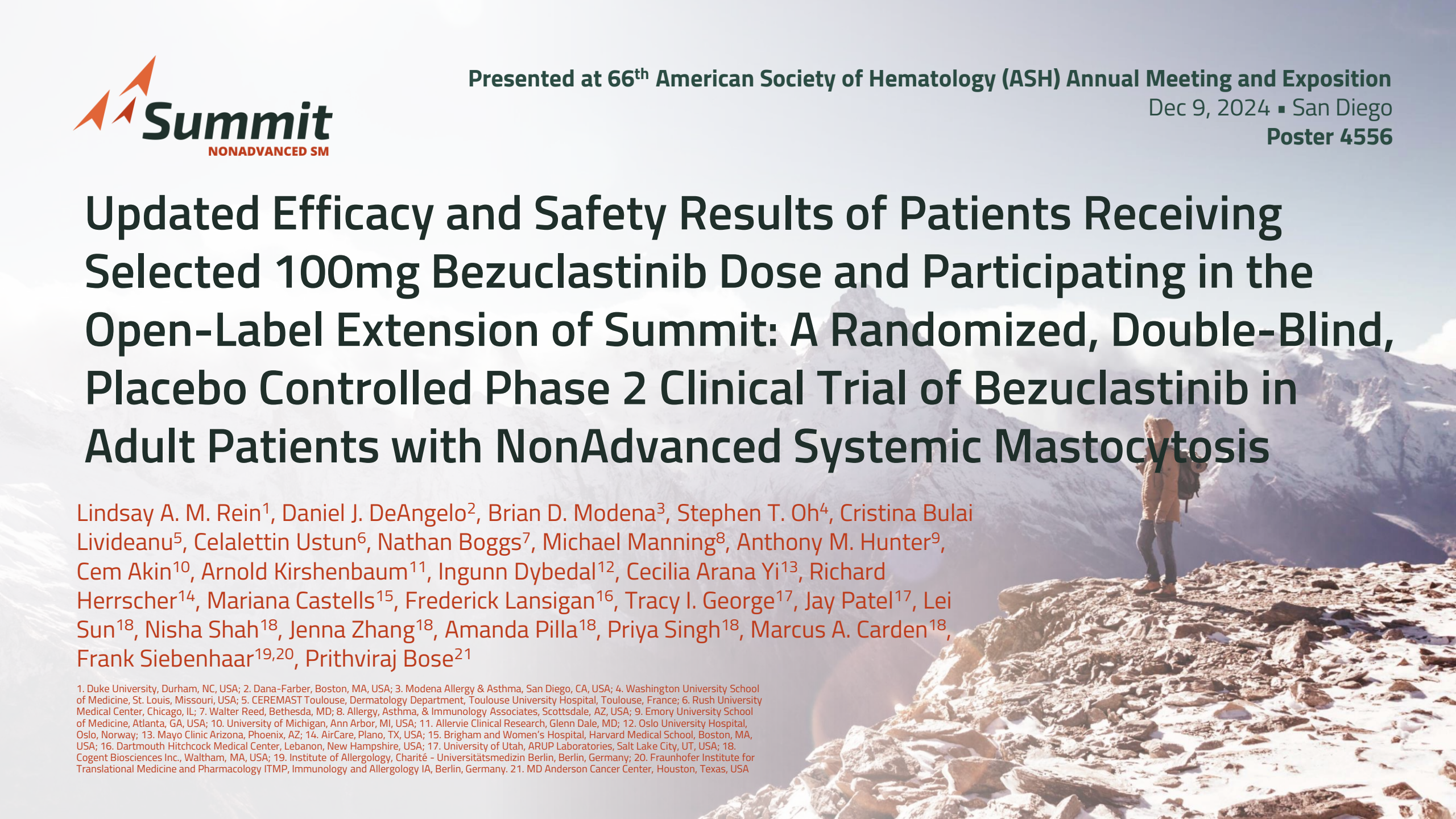
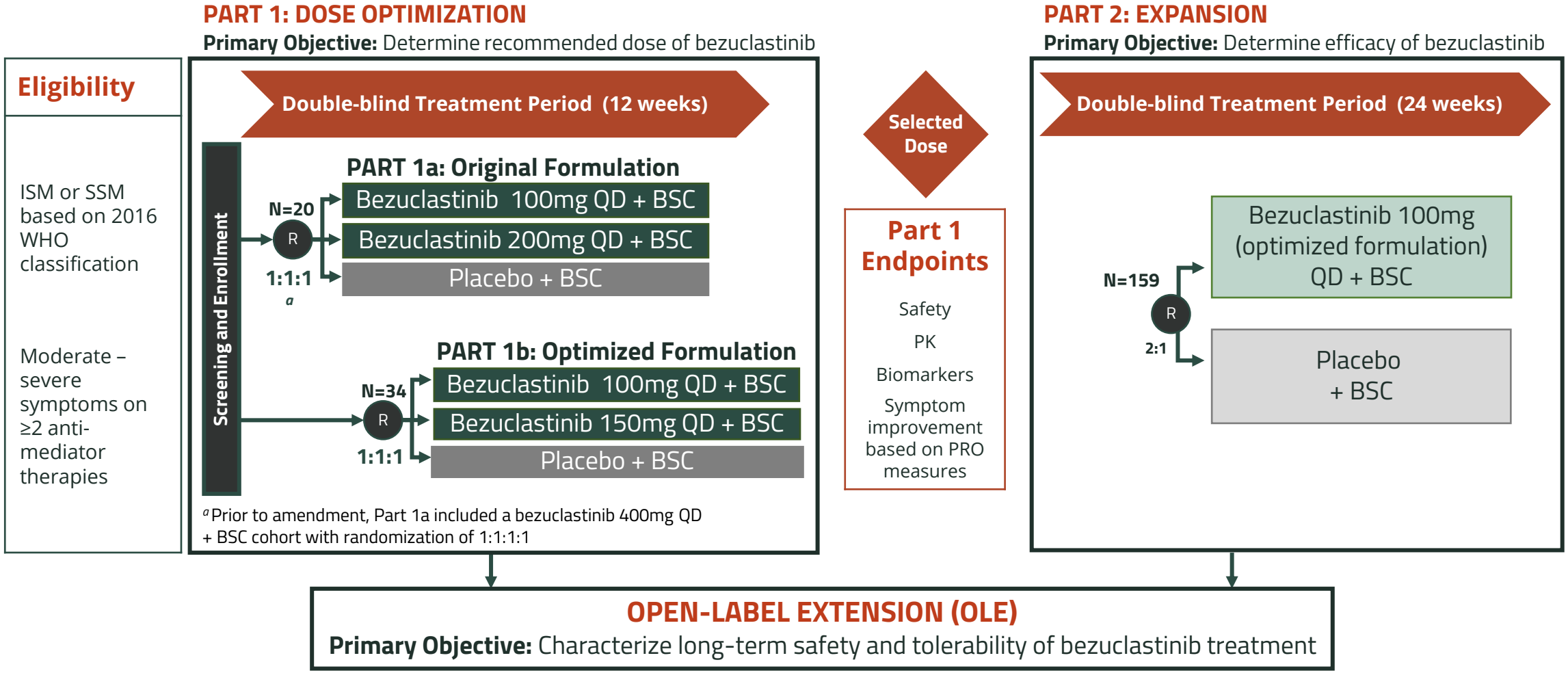


Summit (NCT05186753): Phase 2 Double-Blind, Placebo-Controlled Randomized Clinical Study Evaluating Bezuclastinib in NonAdvSM

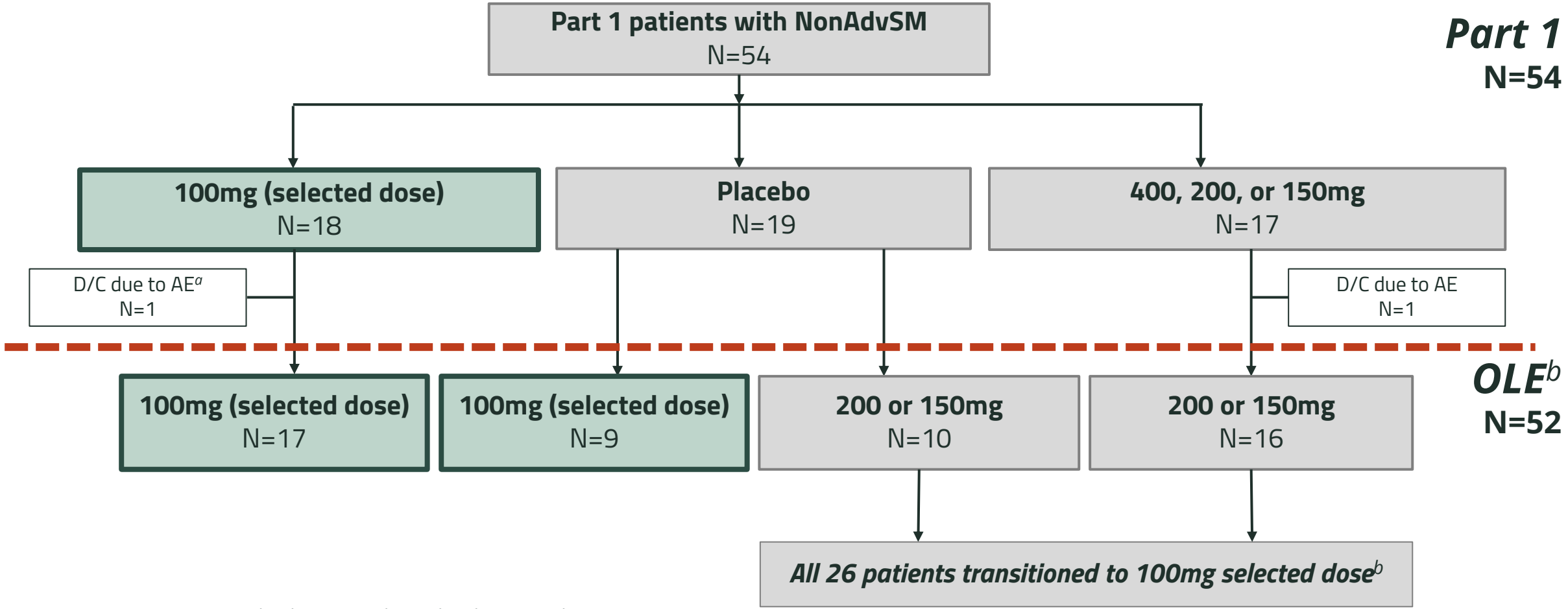
Figure 2. Summit Phase 2 Study Design



All data herein are as of data cut-off date of 29-Aug-2024.
BSC: Best supportive care

Disposition for Part 1 Patients Receiving the Selected Dose of 100mg QD Bezuclastinib

Figure 3. Summit Part 1 Patient Disposition



[a]Patient who discontinued completed Part 1 and is included in analyses where applicable.
[b]Timing of transition varied for each patient depending on time of enrollment.

Data cut 29-Aug-2024

Part 1 – All NonAdvSM Patients with Moderate to Severe Disease and Only Treated with 100mg or Placebo

Table 2. Patient Baseline Demographics, Characteristics, Mast Cell Burden, and Quality of Life (QoL)

Double-blind + Open-Label Extension 100mg	
	Total Active (N=27)
Patient Demographics	
Female, n (%)	**18 (66.7)**
Median Age in years, (range)	**52 (36-76)**
ECOG PS at screening, n (%)	
0	**12 (44.4)**
1	**14 (51.9)**
2	**1 (3.7)**
Clinical Characteristics	
Number of Baseline Supportive Care Meds, n (%)	
2	**12 (44.4)**
3	**8 (29.6)**
4+	**7 (25.9)**
Prior avapritinib, n (%)	**1 (3.7)**

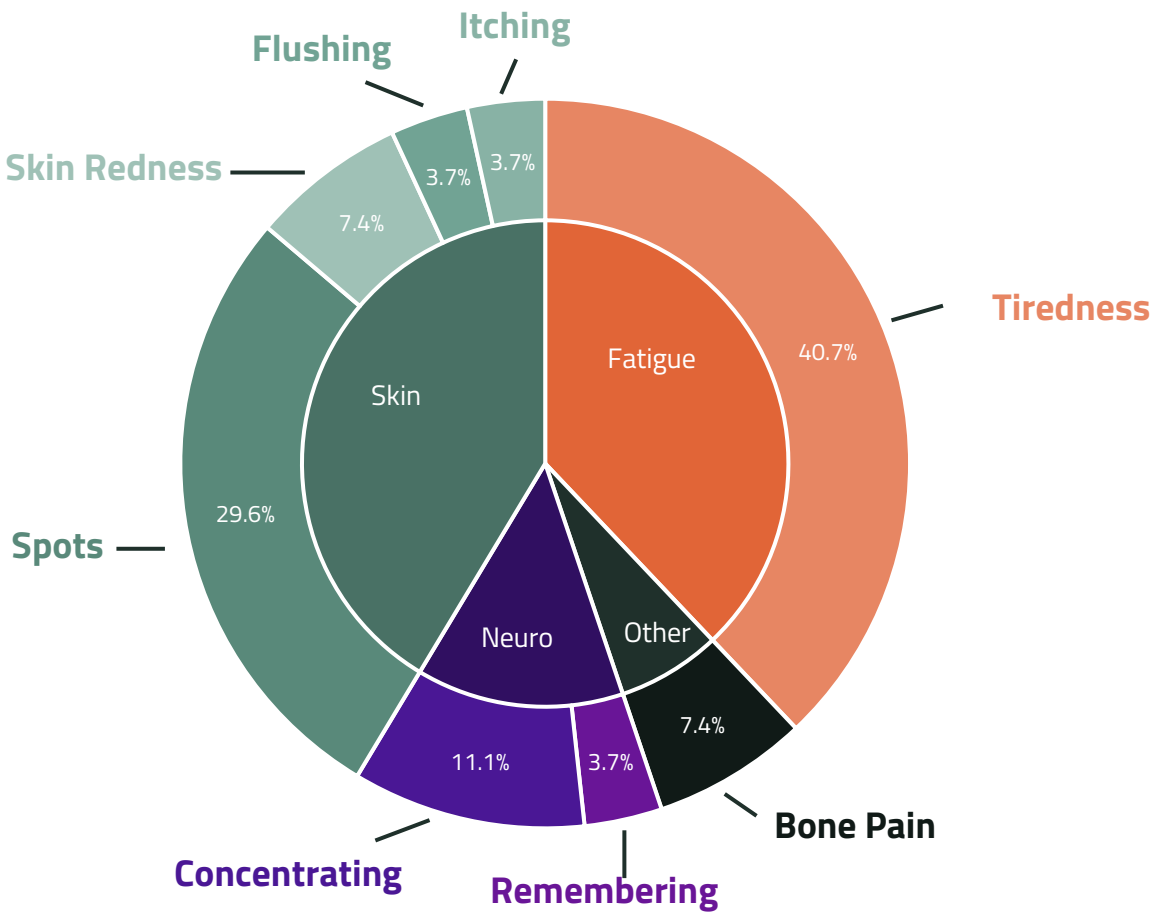
Data cut 29-Aug-2024

Part 1 – All NonAdvSM Patients with Moderate to Severe Disease and Only Treated with 100mg or Placebo

Table 2. Patient Baseline Demographics, Characteristics, Mast Cell Burden, and Quality of Life (QoL)

Double-blind + Open-Label Extension 100mg	
	Total active N=27
Baseline Mast Cell Burden	
KIT D816V in Whole Blood, Positive, n (%)	21 (77.7)
Median Bone Marrow MC Burden, % (range)	10 (1-30)
Median Serum Tryptase at baseline, ng/mL (range)	37 (9.8-275)
< 20 ng/mL, n (%)	6 (22.2)
≥ 20 ng/mL, n (%)	21 (77.7)
Baseline QoL Measures	
Mean (SD) MS2D2 TSS at Baseline	48.3 (19.3)
Mean (SD) MCQoL at Baseline	52.7 (16.1)
Mean (SD) MAS at Baseline	42.3 (14.3)

Figure 4. Most Severe MS2D2 TSS Symptom Identified by Patients (n=27[a])



[a]Patients with more than one severe symptom of the same rating is included more than once.

Data cut 29-Aug-2024

Safety and Tolerability in Patients Randomized to 100mg in Part 1 + OLE

Table 3. All Cause Treatment-Emergent Adverse Events (TEAE) ≥ 15 %

Double-blind + Open-Label Extension 100mg		
Preferred Term	**Total Active[a] *(n=27)***	
	Gr1/2	***Gr3***
Hair color changes	21	-
ALT/AST increased	6	3
Nausea	7	-
URTI	7	-
Diarrhea	6	-
Headache	6	-
Pruritus	5	-
Arthralgia	5	-
GERD	5	-
Peripheral edema	4	-
Alopecia	4	-

[a]Among the nine patients randomized to placebo, only TEAEs that occurred after crossover to bezuclastinib treatment are included.

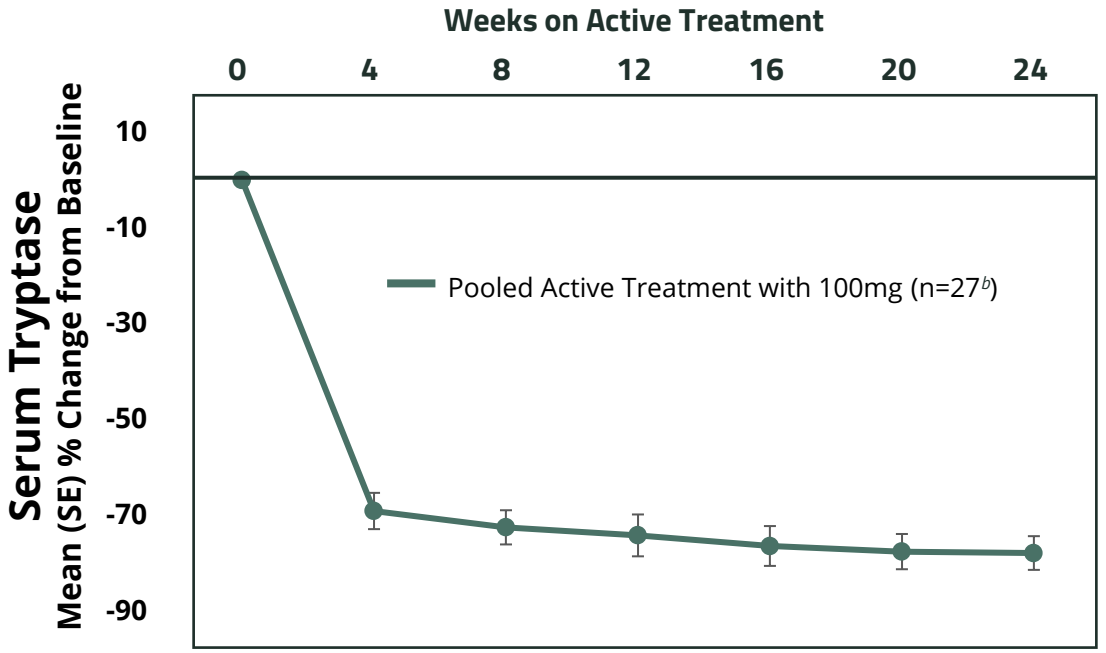
- Median (range) duration on bezuclastinib:
  - Active (N=18): 56 weeks (9.3-80.9)
  - Placebo → Active (N=9): 40 weeks (30.3-72.1)
- The majority of TEAEs were low grade and reversible
- No treatment-related bleeding or cognitive impairment events reported
- Among patients experiencing LFT elevations:
  - 5 patients resolved without dose modification and remain on study
  - 2 patients resolved with dose reduction, including one patient with a possibly related Gr 3 SAE who subsequently re-escalated to original dose, and remains on study (72 weeks)
  - 2 patients with Gr 3 events resolved following discontinuation

Data cut 29-Aug-2024

Bezuclastinib 100mg Led to Rapid, Deep, and Sustained Reductions in Serum Tryptase Over the Course of 24 Weeks of Treatment

- 89% of patients had a ≥50% decrease in serum tryptase levels by 4 weeks of treatment with bezuclastinib 100mg QD
- Of patients with baseline serum tryptase ≥20ng/mL, 95% (20/21) of patients treated with 100mg bezuclastinib achieved <20ng/mL
- Of patients with baseline serum tryptase ≥11.4ng/mL, 84% (21/25) of patients treated with 100mg bezuclastinib achieved <11.4ng/mL

Figure 5. Mean Percent Change from Baseline in Serum Tryptase in Pooled[a] Patients Receiving 100mg Bezuclastinib

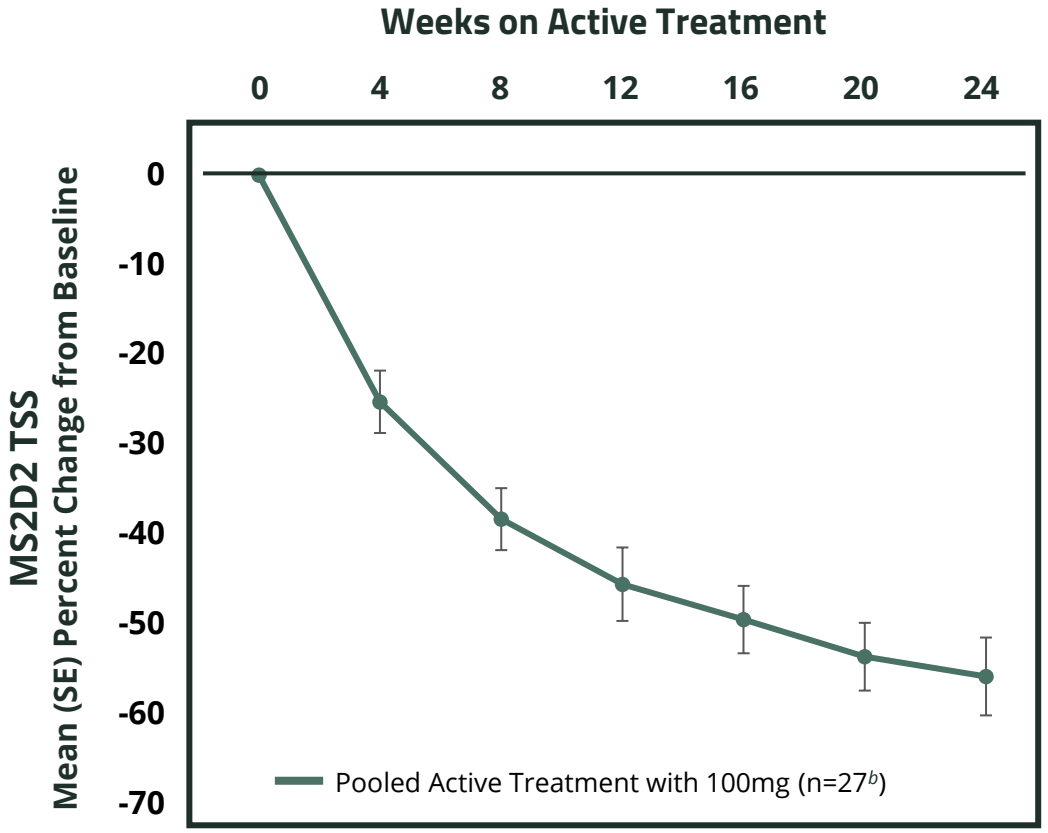


[a]Includes all patients who received bezuclastinib 100mg QD during Part 1 or OLE. Change from baseline is taken during 24 weeks of active therapy.
[b]n=24, 25, or 26 at some timepoints

Data cut 29-Aug-2024

Patients Receiving Bezuclastinib 100mg in Part 1 + OLE Reported Sustained Improvements in Symptom Severity

Figure 6. Mean Percent Change from Baseline in MS2D2 Total Symptom Score Over Time in Pooled[a] Patients Receiving 100mg Bezuclastinib



Among patients receiving 100mg active treatment with bezuclastinib for 24 weeks:

- MS2D2 Total Symptom Score reduced by a mean of 27.6 points
- MS2D2 Total Symptom Score reduced from baseline by a mean of 55.8%

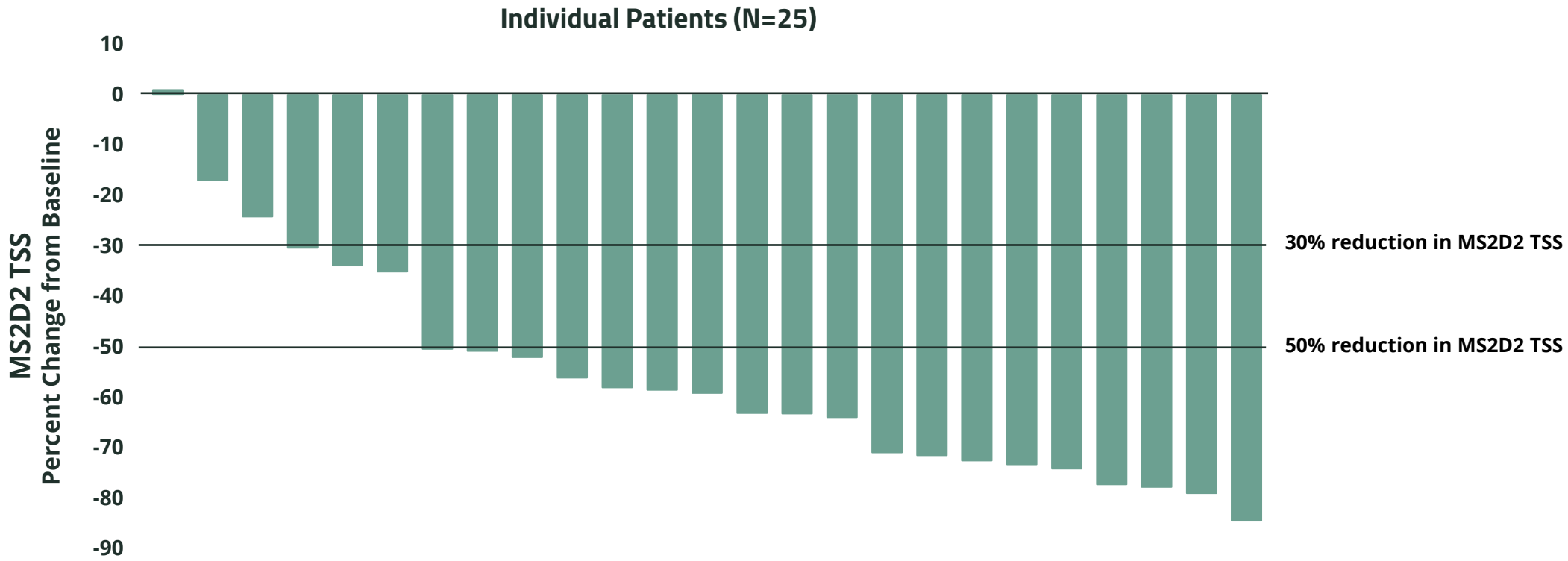
By 24 weeks of active treatment, 31% of patients had reductions or discontinuations in BSC medications[c]

[a]Includes all patients who received bezuclastinib 100mg QD through 24 weeks of active treatment.
[b]n=25 or 26 at some timepoints
[c]Per protocol, best supportive care (BSC) modification was only allowed in the OLE.

Data cut 29-Aug-2024

Bezuclastinib 100mg in Part 1 + OLE Showed Significant Clinical Improvements in Symptoms of Non-Advanced SM

Figure 7. Percent Change from Baseline in MS2D2 Total Symptom Score after 24 Weeks Active Treatment in Individual Patients Receiving 100mg Bezuclastinib



Among patients receiving 100mg active treatment with bezuclastinib for 24 weeks:

- 88% of patients reached at least 30% reduction in MS2D2 TSS
- 76% of patients reached at least 50% reduction in MS2D2 TSS

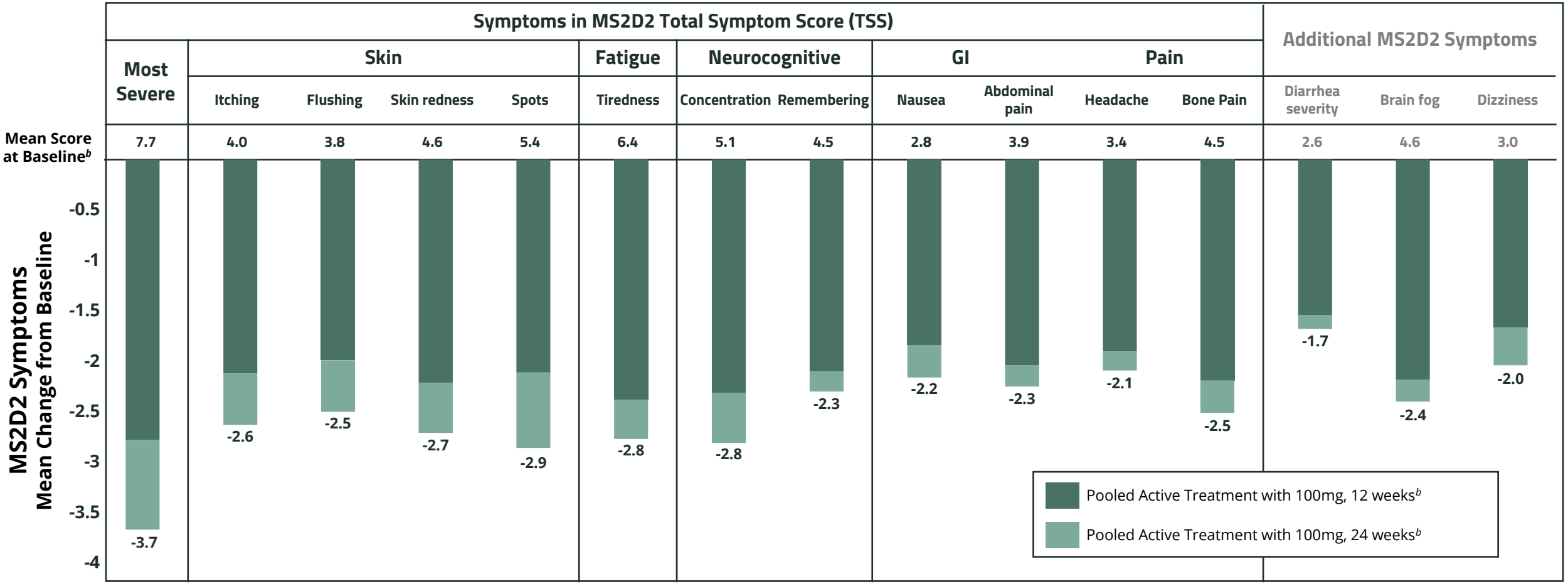
Summit NONADVANCED SM

[a]Includes all patients who received bezuclastinib 100mg QD during Part 1 or OLE. The reported change is at 24 weeks of active therapy.

Data cut 29-Aug-2024

Patients Receiving Bezuclastinib 100mg Demonstrated Clinically Meaningful Changes in Symptoms that Deepened with 24 Weeks of Treatment

Figure 8. Mean Change from Baseline in MS2D2 Symptom Score in Pooled[a] Patients Receiving 100mg Bezuclastinib



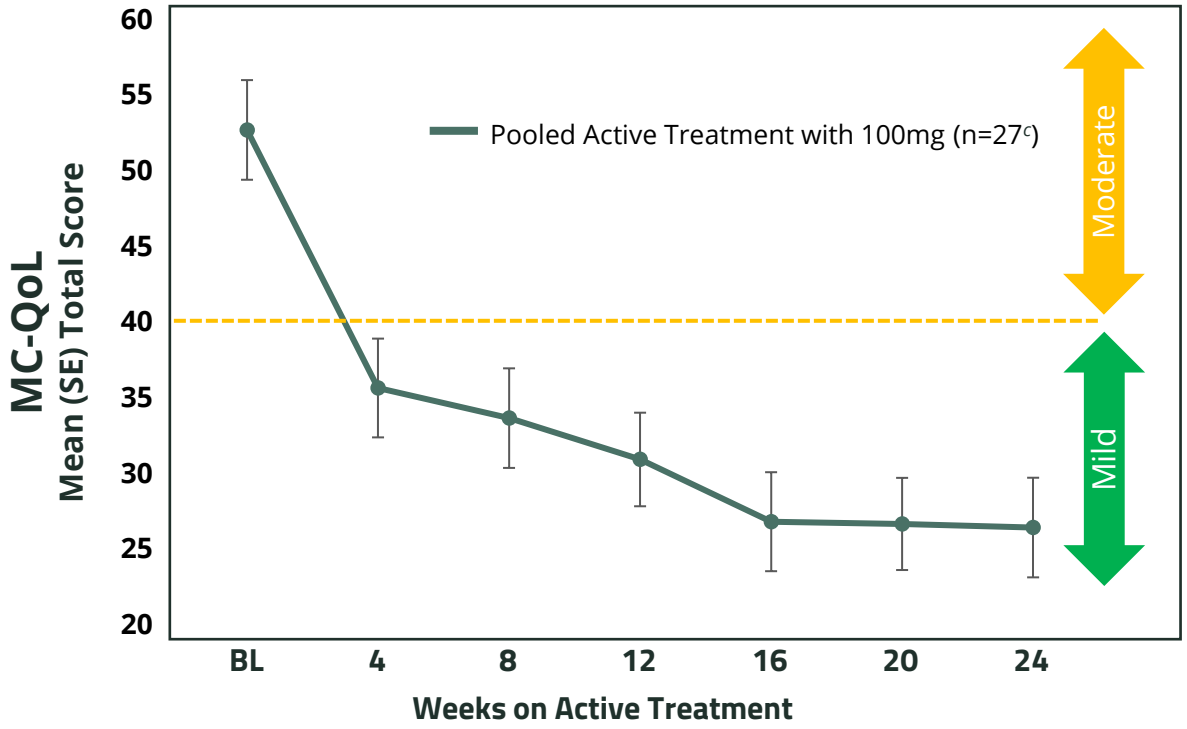
[a]Includes all patients who received bezuclastinib 100mg QD during Part 1 or OLE. Change from baseline is taken after 12 and 24 weeks of active therapy.
[b]N=27 at baseline, N=26 at 12 weeks, and N=25 at 24 weeks.

Data cut 29-Aug-2024

Deepening of Health-related QoL Improvements Were Observed in MC-QoL Total Score and Across All MC-QoL Domains During 24 Weeks of Treatment With 100mg Bezuclastinib

- Patients receiving 100mg bezuclastinib had significant improvement in quality of life with a reduction from 'moderate' to 'mild' disease
- Among patients receiving 100mg active treatment with bezuclastinib for 24 weeks, MC-QoL Total Score reduced by an average of 25.4 points
- Among patients receiving 100mg active treatment with bezuclastinib for 24 weeks, MC-QoL Total Score reduced from baseline by an average of 48.9%

Figure 9. Mean Total Score in MC-QoL, a Quality-of-Life Measure[a], in Pooled[b] Patients Receiving 100mg Bezuclastinib



[a]MC-QoL is a disease-specific HRQoL questionnaire with 27 items in 4 domains. Total score is linearly transformed to a 0 to 100 scale.[11]
[b]Includes patients who received bezuclastinib 100mg QD through 24 weeks of active treatment.
[c]N=23-25 depending on timepoint.
11. Siebenhaar F, Sander B, Tram H, Ellrich A, Maurer M, Weller K. Development and validation of the mastocytosis activity score. Allergy. 2018;00:1–8.

Summit NONADVANCED SM

Data cut 29-Aug-2024

Data From Part 1+OLE of Summit Demonstrated that 100mg Bezuclastinib is Safe and Led to Robust Improvements in Symptoms and Biomarkers of Mast Cell Burden in Patients with NonAdvSM

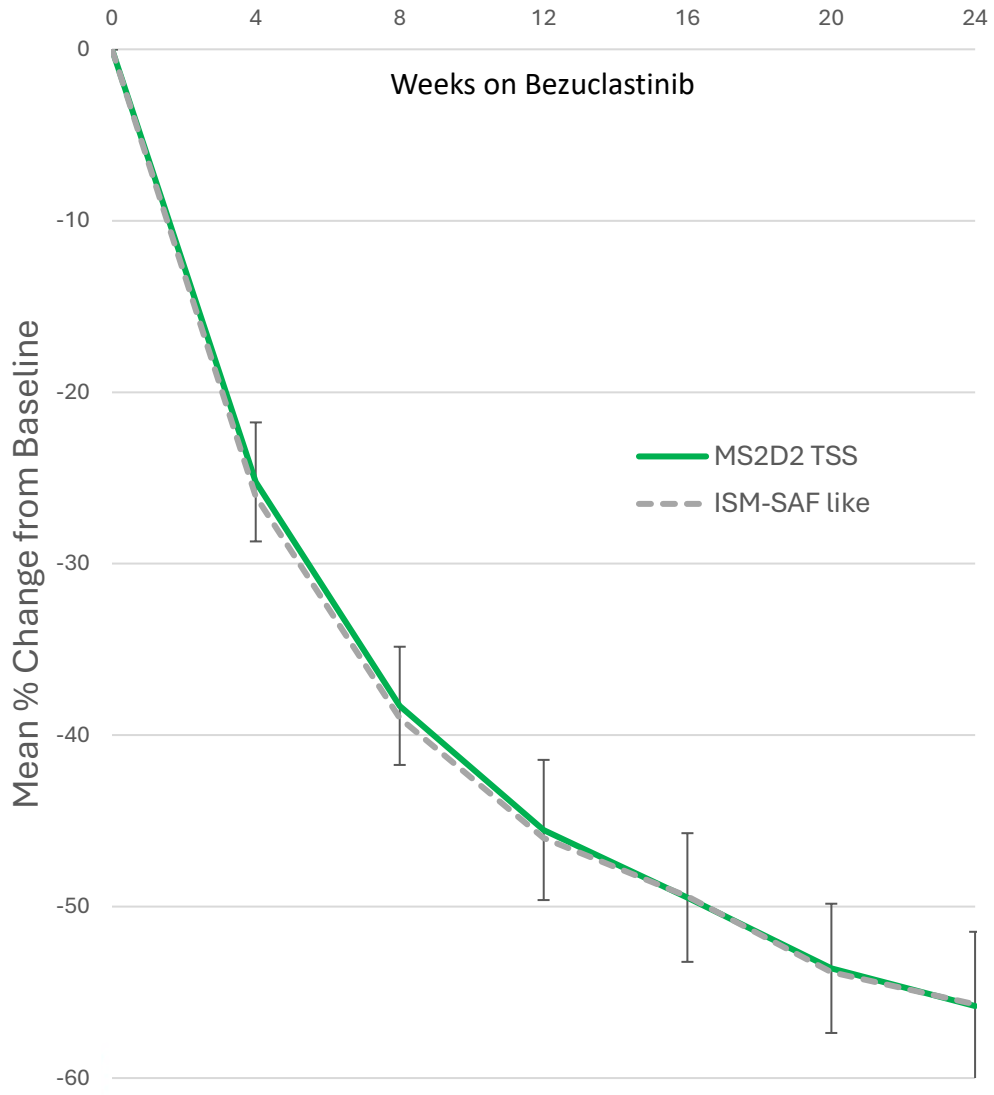
- Favorable safety and tolerability profile with continued treatment to 24 weeks:
  - The majority of TEAEs were low grade and reversible
  - No treatment-related bleeding or cognitive impairment AEs reported
- Rapid and sustained reductions in symptom severity based on MS2D2 and MC-QoL measures and objective biomarkers of NonAdvSM:
  - 76% and 88% of patients treated with 100mg achieved at least a 50% and 30% reduction in total symptom severity at Week 24, respectively
  - Substantial reduction in the patients' most severe symptoms at 12 weeks with continued improvement at 24 weeks
  - Clinically significant, deep reductions across all symptoms within MS2D2 that are sustained for 24 weeks
  - 89% of patients had a ≥50% decrease in serum tryptase levels by 4 weeks which was sustained through 24 weeks
  - After 24 weeks, 31% of patients had reductions or discontinuations of BSC medications

Summit Part 2 has completed enrollment ahead of schedule.

Additional Data

cogent BIOSCIENCES

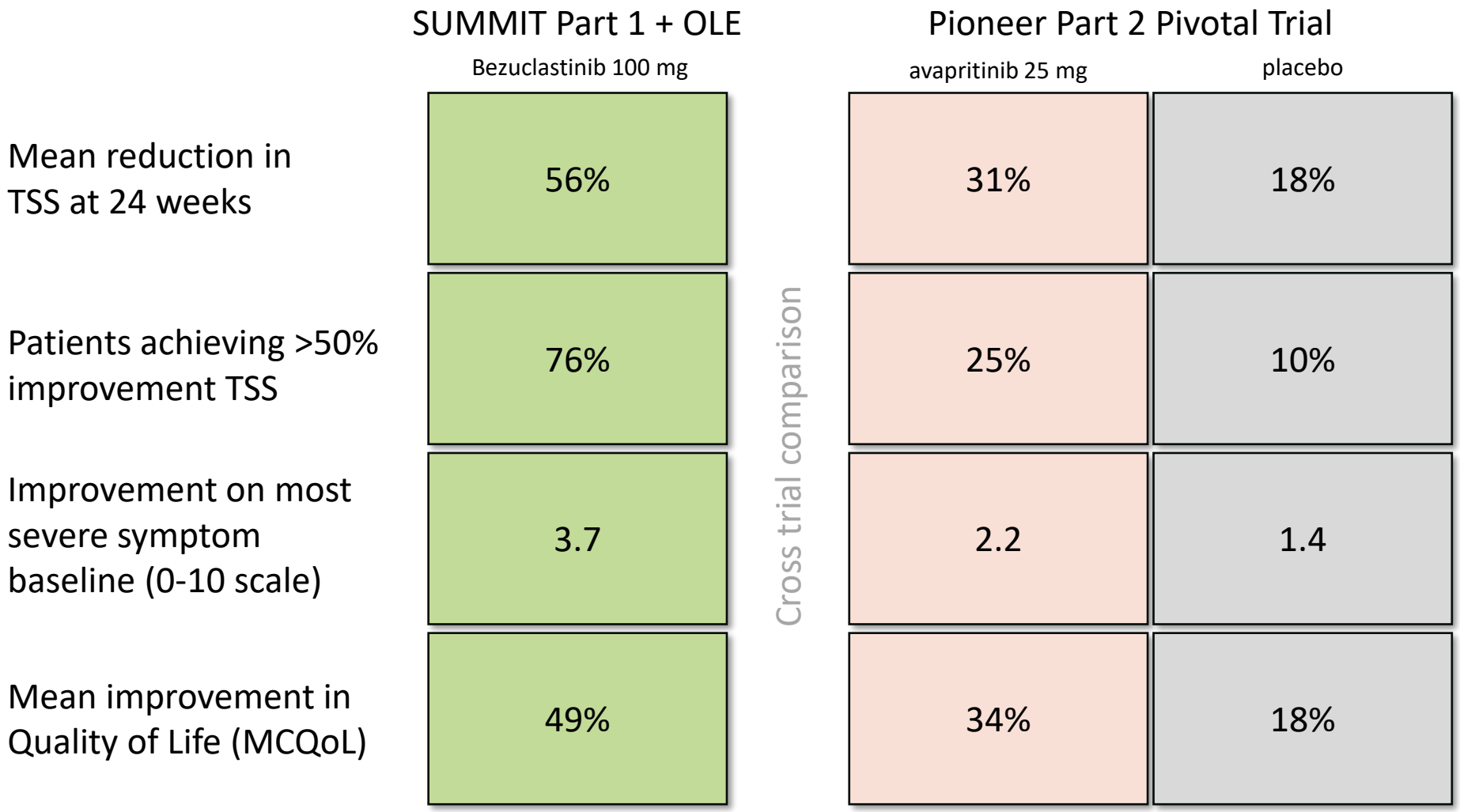
SUMMIT ASH 2024 Symptomatic Improvement Results Nearly Identical Using Composite Items From Either MS2D2 or ISM-SAF



MS2D2 Items 0-110 Scale	ISM-SAF Items 0-110 Scale
Itching	Itching
Flushing	Flushing
Spots	Spots
Headache	Headache
Bone Pain	Bone Pain
Feeling Tiredness	Feeling Tiredness
Nausea	Nausea
Abdominal Pain	Abdominal Pain
Skin redness	Diarrhea
Difficulty Concentrating	Dizziness
Difficulty Remembering	Brain Fog

June 2024 – Cogent announced alignment with FDA on use of MS2D2 for use in SUMMIT Part 2

Contextualizing SUMMIT ASH 2024 Bezuclastinib 24-Week Results



Bezuclastinib Shows Early Signals of Deepening Symptomatic Improvement

- Within the patient group presented today, 16 patients have reached 48 weeks of active treatment:
    - 65% mean reduction in MS2D2 Total Symptom Score
    - 88% of patients achieved at least 50% reduction in MS2D2 TSS

Bezuclastinib Offers 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

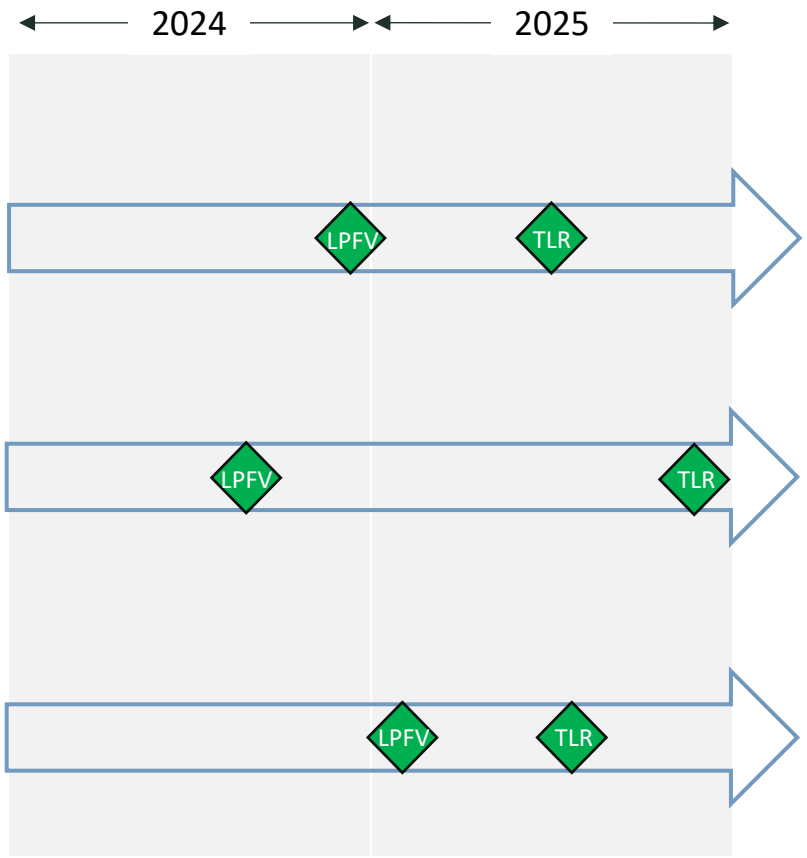
Phase 3 study in 2nd-line GIST bezuclastinib +/- sunitinib

n=413, mPFS primary endpoint

Apex ADVANCED SM

Registration-directed study in AdvSM bezuclastinib monotherapy

n=65, 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


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BIOSCIENCES
Q&A
Real Challenges. Real Solutions.
Precision therapies for genetically defined diseases