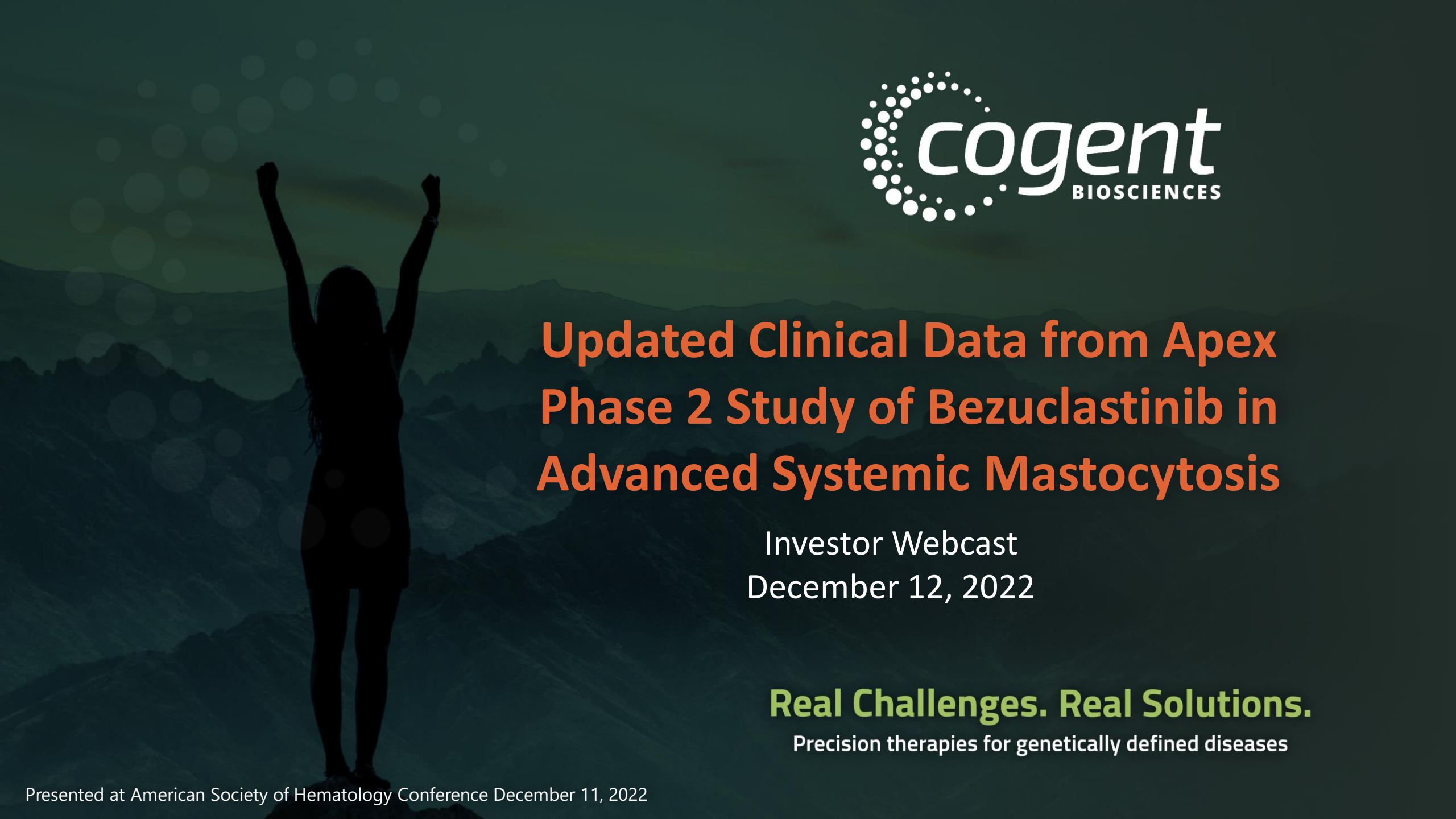

Updated Clinical Data from Apex Phase 2 Study of Bezuclastinib in Advanced Systemic Mastocytosis

Investor Webcast
December 12, 2022

Real Challenges. Real Solutions.

Precision therapies for genetically defined diseases

Presented at American Society of Hematology Conference December 11, 2022

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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.

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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 & Corporate Overview	**Andrew Robbins**
Review of Updated APEX Data with Bezuclastinib in Advanced Systemic Mastocytosis (ASM) patients	**Dr. Daniel DeAngelo**
Presentation Summary	**Andrew Robbins**
Q&A	**Andrew Robbins** **Dr. Jessica Sachs** **Dr. Daniel DeAngelo**

Multiple Clinical and Preclinical Programs with Upcoming Catalysts

Program	Indication	Early Stage Development	Late Stage Development	Regulatory Submission	Approval
Clinical Programs					
Bezuclastinib (KIT inhibitor)	Advanced Systemic Mastocytosis	Apex			
	Nonadvanced Systemic Mastocytosis	Summit			
	Gastrointestinal Stromal Tumors	Peak			

Demonstrating differentiated profile as potential best-in-class selective KIT mutant inhibitor

Research Programs

Indication	Hit ID	Lead Generation	Lead Optimization	GLP	IND Submission
FGFR2					
ErbB2 mut					
Target 3					
Target 4					
Target 5					
Target 6					

Building exciting portfolio of next-generation potent, selective kinase inhibitors

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Cash runway into 2025; $289.1 million as of September 30, 2022

Unmet Need Remains for Advanced Systemic Mastocytosis Patients

Disease Overview: Aggressive and life-threatening form of systemic mastocytosis (SM) that is primarily driven by KIT D816V mutation and leads to uncontrolled proliferation of mast cells (MC)[1,2]

- Subtypes: aggressive SM (ASM); SM with associated hematologic neoplasm (SM-AHN); mast cell leukemia (MCL)[1]
- Based on subtype, the median overall survival ranges from <6 months to 3-4 years[3,4]

Unmet Need Remains: Approved therapies with associated dose-limiting toxicities

- Reported toxicities for marketed therapies: nausea, vomiting, diarrhea, edema, intracranial bleeding, cognitive effects[5-7]

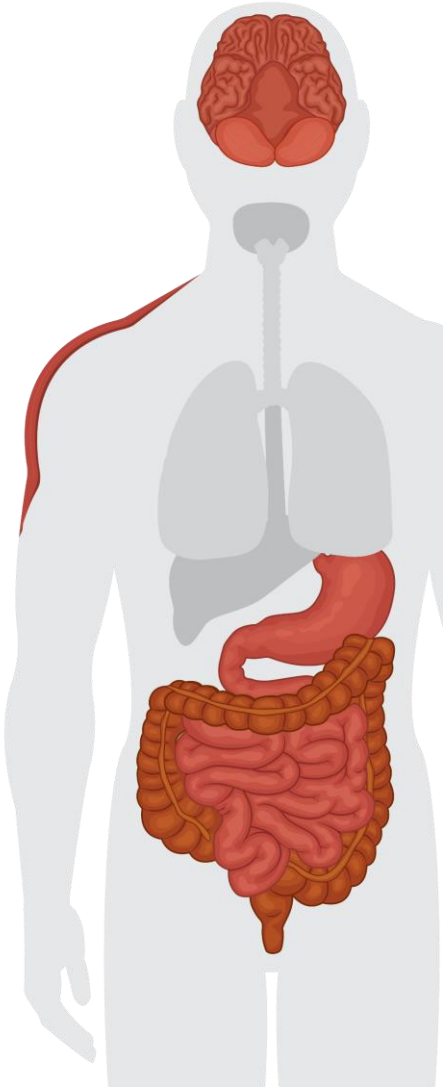
Neurological
Headache, brain fog, cognitive dysfunction, anxiety, depression

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)

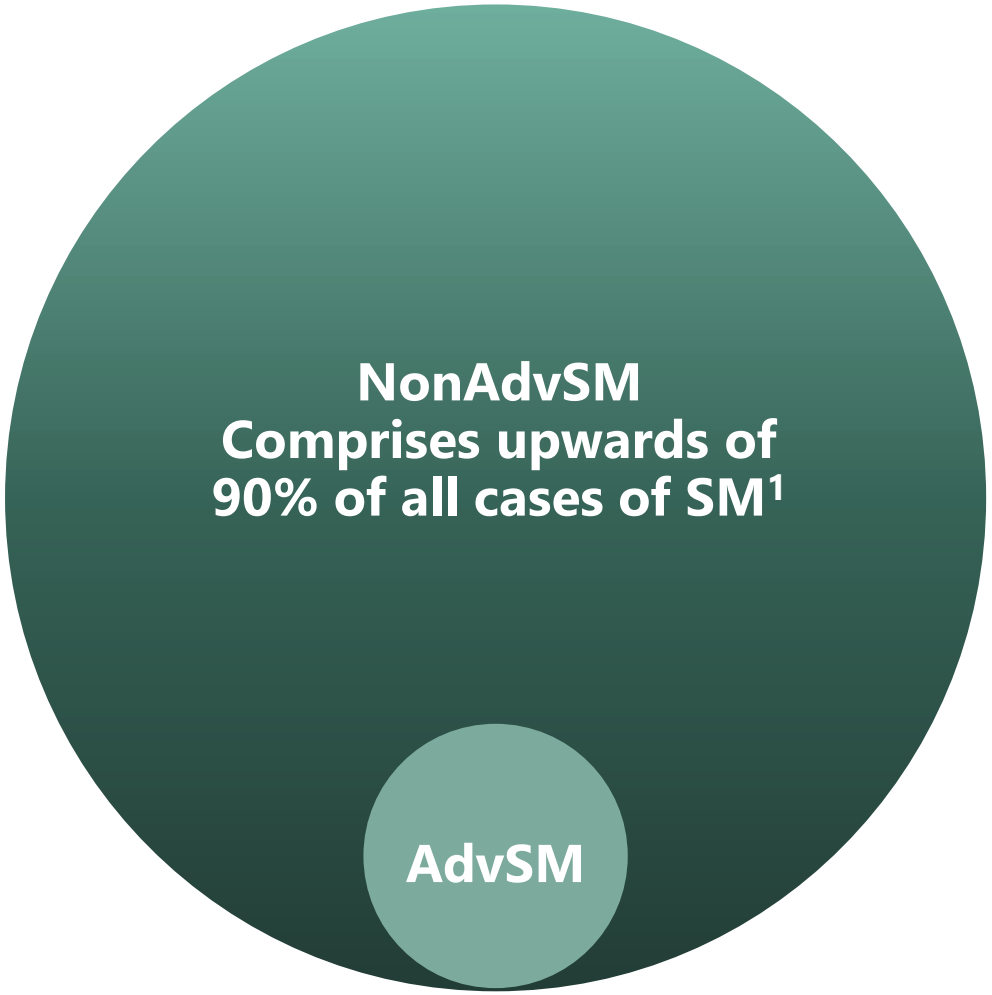
Other
Cardiovascular
Ear/Nose/Throat/Respiratory
Skeletal
Gynecological
Urinary



References: 1Pardanani A. Am J Hematol. 2021;96(4):508-525. 2DeAngelo DJ et al. Nat Med. 2021;27(12):2183-2191. 3Ustun C et al. Haematologica. 2016;101(10):1133-1143. 4Lim K-H et al. Blood. 2009;113(23):5727-5736. 5AYVAKIT (avapritinib) [package insert]. Blueprint Medicines Corporation; 2021. 6Magliacane D et al., Transl Med UniSa. 2014;8:65-74. 7RYDAPT (midostaurin) [package insert]. Novartis Pharmaceuticals; 2021.

Large, Yet Not Well Understood Population of SM Patients

Systemic Mastocytosis: Estimated prevalence in the U.S. is **20,000–30,000**[1] patients



Significant unmet medical need for clinically active, well-tolerated treatment options for this patient population

[1]Coltoff A, Mascarenhas J., 2019.

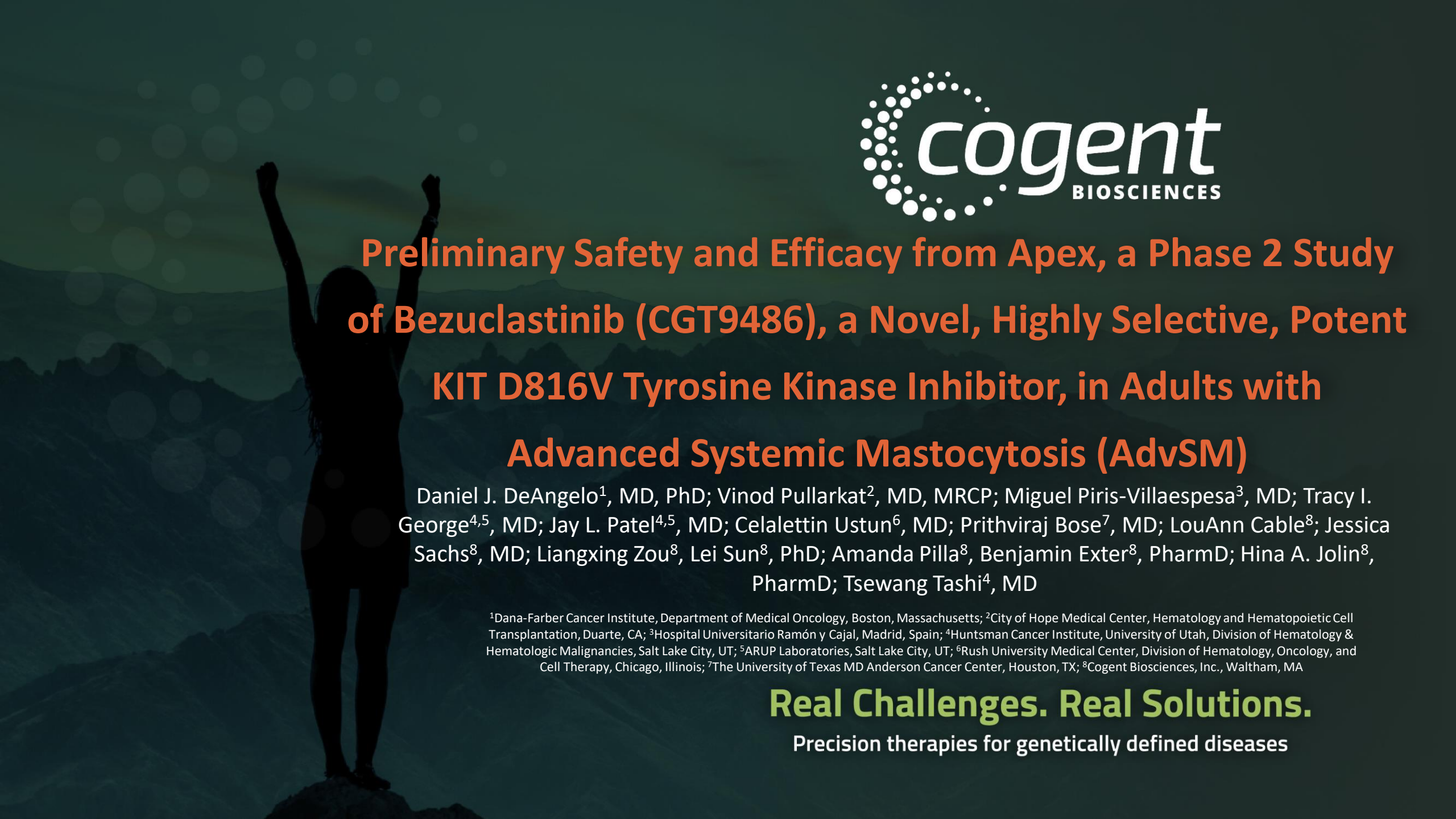
Bezuclastinib: Highly Selective and Potent KIT D816V Inhibitor

- Oral, selective, and type I tyrosine kinase inhibitor (TKI) with potent activity against KIT D816V, an activation loop mutation
- Preclinically, highly active with specificity for mutations in KIT exons 9, 11, 17, and 18
- Spares closely related kinases, has minimal brain penetration, and favorable PK properties[1]
  - Inhibition of closely related kinases have been linked to off-target toxicities, such as bleeding, edema, and pleural effusions[2, 3]

Kinase Inhibition Profile of Clinical Stage and Approved KIT D816V Agents; Cell IC_{50} (nM)

Compound	KIT V560G/D816V (HMC 1.2)	WT KIT	PDGFRα	PDGFRβ	CSF1R	FLT3	KDR
Bezuclastinib	14	121	> 10,000	> 10,000	> 10,000	> 1000	> 1000
Avapritinib	13	114	53	10	249	305	> 1000
BLU-263	6	355	21	6	161	345	> 1000

References: 1Guarnieri A. et al. Abstract P257 Molecular Cancer Therapeutics, 2021. 20(12_Supplement), P257-P257. 2Giles FJ et al, Leukemia. 2009;23(10):1698-1707.
3Liu S, Kurzrock R. Seminars in Oncology. 2015;42(6):863-875



Preliminary Safety and Efficacy from Apex, a Phase 2 Study of Bezuclastinib (CGT9486), a Novel, Highly Selective, Potent KIT D816V Tyrosine Kinase Inhibitor, in Adults with Advanced Systemic Mastocytosis (AdvSM)

Daniel J. DeAngelo[1], MD, PhD; Vinod Pullarkat[2], MD, MRCP; Miguel Piris-Villaespesa[3], MD; Tracy I. George[4,5], MD; Jay L. Patel[4,5], MD; Celalettin Ustun[6], MD; Prithviraj Bose[7], MD; LouAnn Cable[8]; Jessica Sachs[8], MD; Liangxing Zou[8], Lei Sun[8], PhD; Amanda Pilla[8], Benjamin Exter[8], PharmD; Hina A. Jolin[8], PharmD; Tsewang Tashi[4], MD

[1]Dana-Farber Cancer Institute, Department of Medical Oncology, Boston, Massachusetts; [2]City of Hope Medical Center, Hematology and Hematopoietic Cell Transplantation, Duarte, CA; [3]Hospital Universitario Ramón y Cajal, Madrid, Spain; [4]Huntsman Cancer Institute, University of Utah, Division of Hematology & Hematologic Malignancies, Salt Lake City, UT; [5]ARUP Laboratories, Salt Lake City, UT; [6]Rush University Medical Center, Division of Hematology, Oncology, and Cell Therapy, Chicago, Illinois; [7]The University of Texas MD Anderson Cancer Center, Houston, TX; [8]Cogent Biosciences, Inc., Waltham, MA

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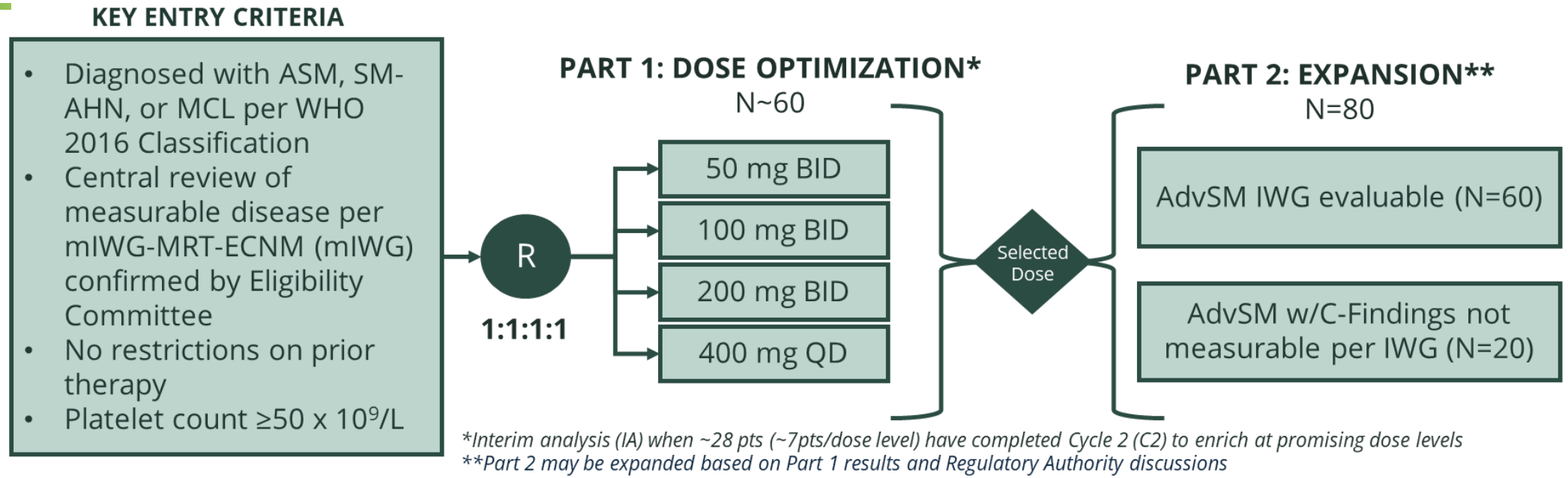
APEX: A Phase 2 Open-Label, Multicenter Clinical Study of Bezuclastinib in Patients with Advanced Systemic Mastocytosis



*Interim analysis (IA) when ~28 pts (~7pts/dose level) have completed Cycle 2 (C2) to enrich at promising dose levels
**Part 2 may be expanded based on Part 1 results and Regulatory Authority discussions

Primary Endpoint

- **Dose Optimization**: Incidence of AEs/SAEs, laboratory changes, PK, biomarkers, ORR
- **Expansion**: ORR (confirmed CR, CRh, PR and CI) per mIWG-MRT-ECNM and assessed by Central Response Review Committee

Other Endpoints

- Safety/Tolerability: Incidence of AEs leading to dose modification, changes in Patient Reported Outcomes (PROs)
- Efficacy: DOR, TTR, PFS, OS, pure pathologic response
- PK/PD: plasma concentration of bezuclastinib, serum tryptase, KIT D816V burden

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Patient Demographics and Characteristics

- 16 patients enrolled; median age: 69 years; Range: 33-87

	Total (N=16)	50mg BID (N=4)	100mg BID (N=3)	200mg BID (N=4)	400mg QD (N=5)
Male, n (%)	**13 (81)**	3 (75)	3 (100)	3 (75)	4 (80)
ECOG PS 0-1, n (%)	**14 (88)**	4 (100)	3 (100)	4 (100)	3 (60)
AdvSM Subtype per Central Eligibility Review, n (%)					
ASM	**3 (19)**	1 (25)	0 (0)	0 (0)	2 (40)
SM-AHN	**12 (75)**	3 (75)	2 (67)	4 (100)	3 (60)
MCL	**1 (6)**	0 (0)	1 (33)	0 (0)	0 (0)
Prior therapy for AdvSM, n (%)[∫]					
Treatment Naïve*	**11 (69)**	3 (75)	2 (67)	3 (75)	3 (60)
Avapritinib	**3 (19)**	0 (0)	1 (33)	1 (25)	1 (20)
Midostaurin	**3 (19)**	0 (0)	1 (33)	1 (25)	1 (20)
***KIT* D816V in Whole Blood, Positive, n (%)**	**14 (88)**	4 (100)	3 (100)	3 (75)	4 (80)
Median KIT D816V VAF, % (range)[‡]	**10.6 (0.02-47.18)**	14.3 (0.02 – 37.4)	7.98 (7.04 – 32.28)	27.85 (8.7 – 47.18)	7.18 (0.93 – 13.48)
Median Bone Marrow MC Burden, % (range)	**30 (7-80)**	45 (20-70)	70 (30-80)	20 (7-30)	30 (10-80)
Median Serum Tryptase, ng/mL (range)	**178 (50-1578)**	334 (169-605)	253 (144-1578)	97 (67.9-121)	232 (50-370)

**Patients who have received no prior SM directed therapies*

[∫] Additional therapies included PEG interferon-α, cladribine, hydroxyurea, azacytidine, decitabine, brentuximab vedotin, and other

[‡] Includes patients with positive KIT D816V

Data as of: 26Oct2022

DeAngelo D,. et al. American Society of Hematology (ASH) 2022 Annual Meeting; New Orleans, LA, 11 Oct 2022: Publication Number: 626

Safety and Tolerability of Bezuclastinib

Treatment Related Adverse Events in > 10% Patients and all Related SAEs

	Total (n=16)		TKI‡ Therapy Naïve (n=13)	Prior TKI‡ Exposure (n=3)	50 mg BID (n=4)	100 mg BID (n=3)	200 mg BID (n=4)	400 mg QD (n=5)
Preferred Term	All grade	Grade ≥3	All grade	All grade	All grade	All grade	All grade	All grade
Hair color changes	**4 (25)**	**0**	2	2	0	2	1	1
Taste disorder^	**4 (25)**	**0**	3	1	1	0	1	2
Neutropenia∫	**4 (25)**	**2 (13)**	4	0	1	1	1	1
Edema peripheral	**3 (19)**	**0**	1	2	0	0	1	2
Thrombocytopenia	**3 (19)**	**1 (6)**	3	0	0	1	0	2
Nausea	**2 (13)**	**0**	1	1	0	1	0	1
Fatigue	**2 (13)**	**0**	1	1	1	0	1	0
Vomiting	**2 (13)**	**0**	1	1	0	1	0	1
Anemia	**2 (13)**	**1(6)**	0	2	0	1	1	0
Hypersensitivity (mediator flare)#	**1 (6)**	**1(6)**	1	0	0	0	0	1

‡SM-directed therapy with midostaurin and avapritinib
^ Includes pooled preferred terms of terms of Taste disorder and Dysgeusia
∫Includes pooled preferred terms of Neutropenia, Neutrophil count decreased, and WBC decreased
#Serious adverse event

- The majority of TEAEs were of low grade with one related SAE and no related Grade 4 events
- No related cognitive effects or bleeding events reported
- The majority of hematological TEAEs were of low grade, reversible and did not require dose modification
- No discontinuations with 3 patients dose reduced due to TEAEs; one re-escalated to randomized dose

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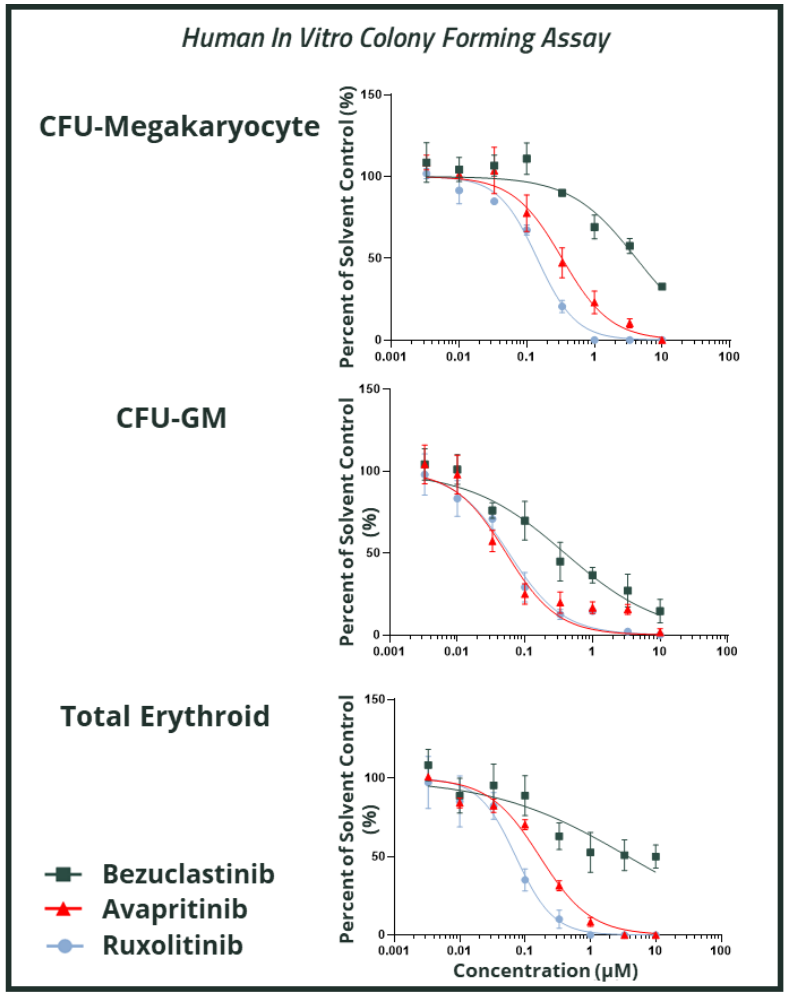
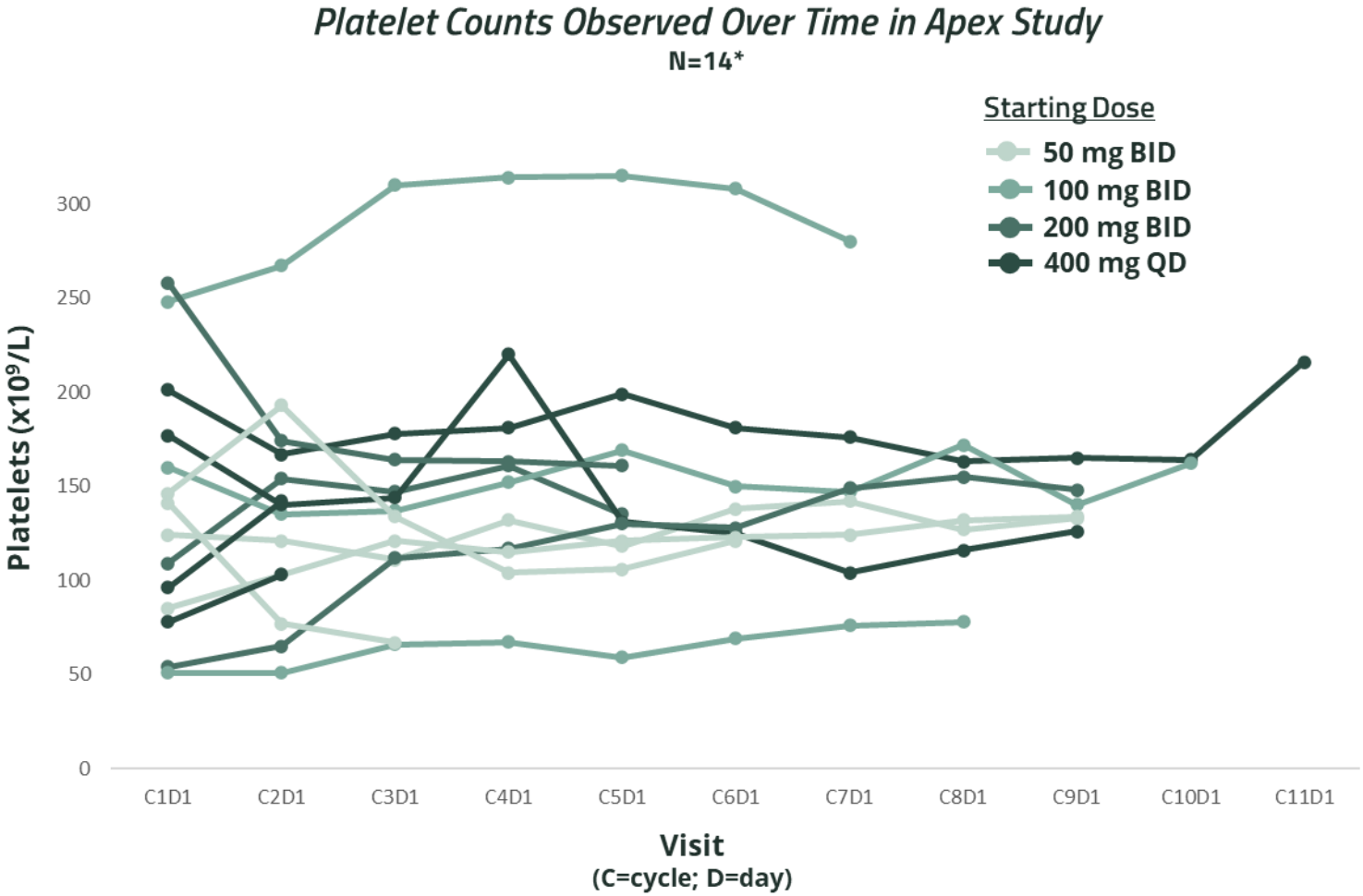
Limited Effect of Bezuclastinib on Platelet Counts in Apex Study, Supported by Preclinical Data





All patients in Apex were required to have platelet count ≥50 x 10^9/L for 2 weeks prior to the first dose of study drug
**Two patients excluded: (1) due to presence of essential thrombocythemia at baseline; (1) no post-baseline assessment*

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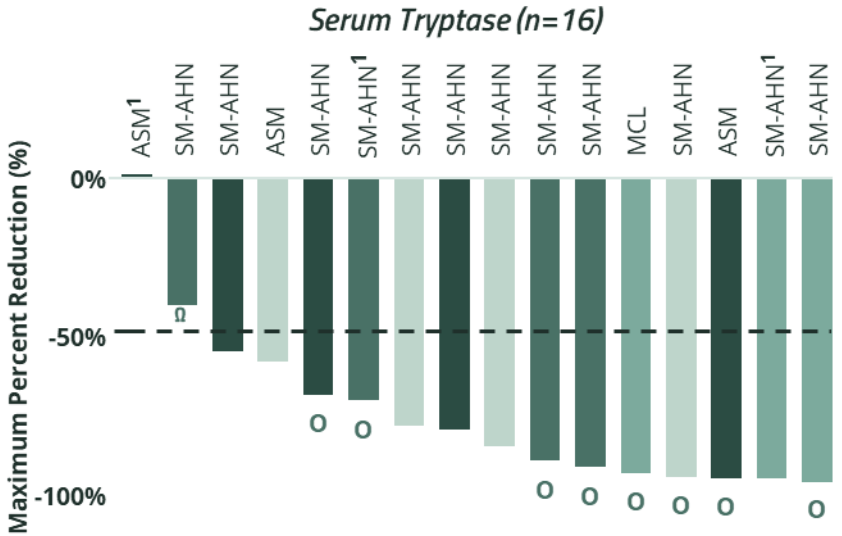
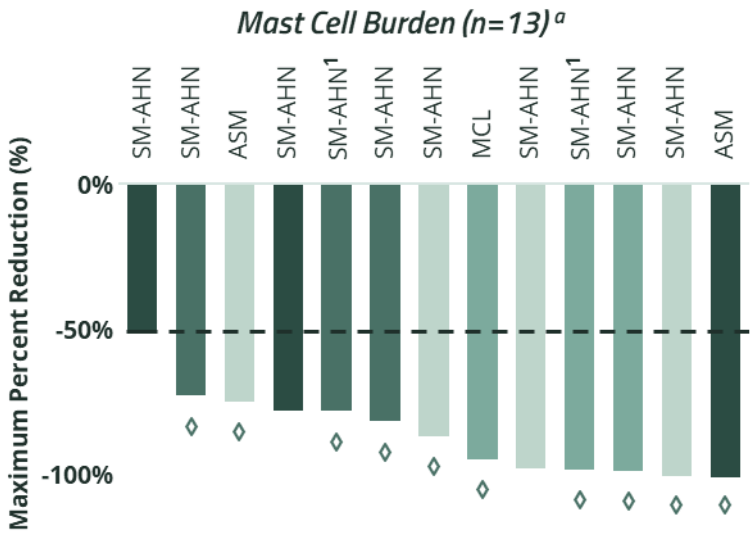
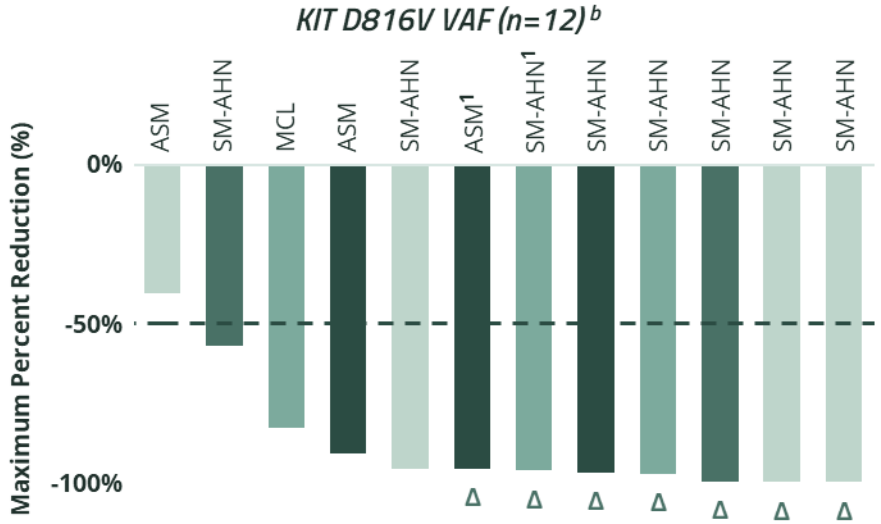
Bezuclastinib Demonstrates Reductions in Markers of Mast Cell Burden

- Serum Tryptase
  - 88% of patients achieved a ≥ 50% reduction
  - 85% median reduction
  - 50% achieved levels <20 ng/mL
- Bone Marrow MC Burden
  - 100% of patients with at least 2 cycles of treatment achieved a ≥ 50% reduction
  - 77% achieved complete clearance of mast cell aggregates by central review
- *KIT* D816V VAF
  - 92% of patients with at least 2 cycles of treatment achieved a ≥ 50% reduction





[a] *Three patients excluded: no post-baseline assessment available*



[b] *Four patients excluded: (2) KIT D816V negative at baseline; (2) no post-baseline assessment available*

Starting Dose
- 50 mg BID
- 100 mg BID
- 200 mg BID
- 400 mg QD

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

[1] *Prior avapritinib and midostaurin*

Ω *Discontinued after 2 doses of study treatment due to investigator decision (femur fracture)*

Data as of: 26Oct2022

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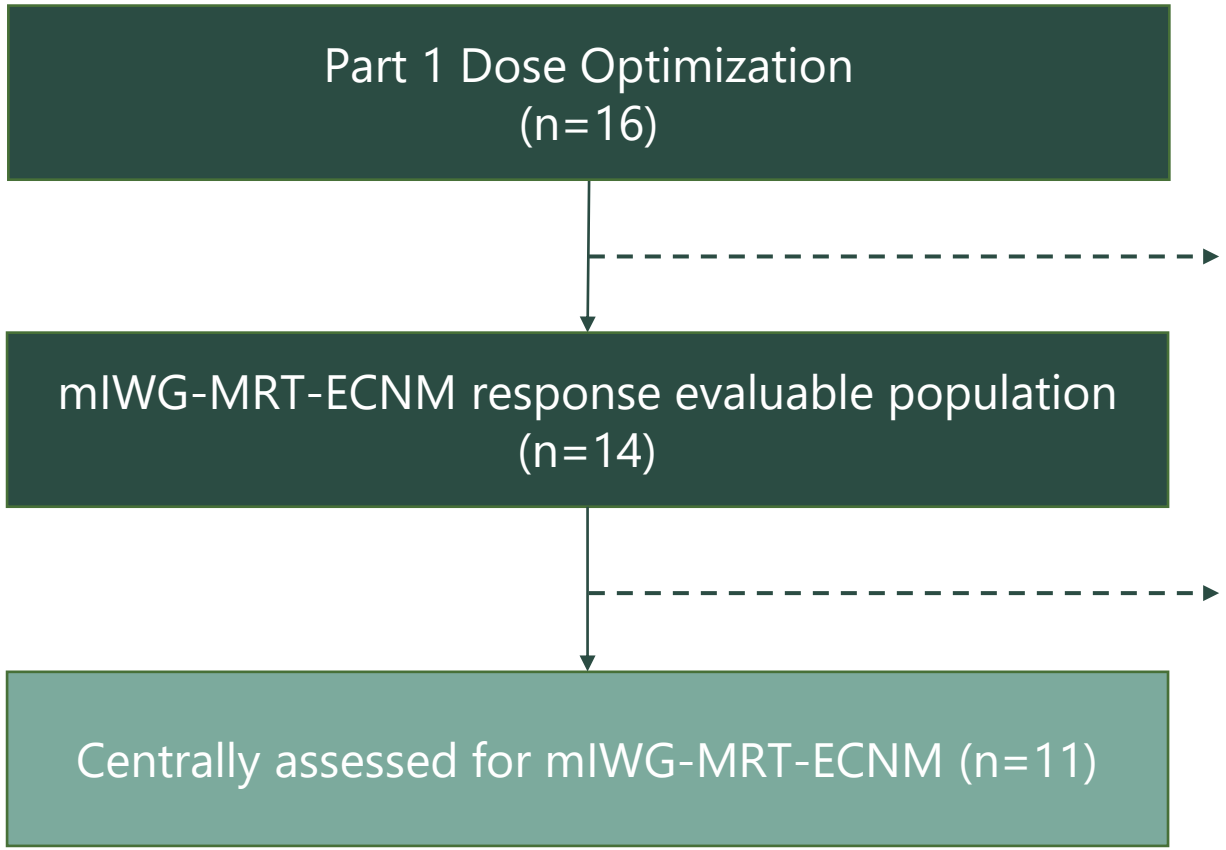
Patients included in mIWG-MRT-ECNM Response Evaluable Population



- **Patients inevaluable (n=2)**
  - n=1 no measurable C-finding at baseline
  - n=1 received confounding concomitant medication
- **Patients excluded (n=3)**
  - n=2 off study prior to first response timepoint
  - n=1 ongoing; has not reached first response timepoint

Response Assessment per mIWG-MRT-ECNM and PPR Criteria

Response Assessment	mIWG-MRT-ECNM Response Criteria*	Pure Pathological Response Criteria
Complete Remission (CR)	✓ Absence of neoplastic MC aggregates in bone marrow ✓ Serum tryptase ≤ 20 ng/mL ✓ Remission of peripheral blood counts ✓ Complete resolution of all mIWG C-findings	✓ Absence of neoplastic MC aggregates in bone marrow ✓ Serum tryptase < 20 ng/mL ✓ Remission of peripheral blood counts
Partial Remission (PR)	✓ Reduction of neoplastic MC in bone marrow by ≥ 50% ✓ Reduction of serum tryptase by ≥ 50% ✓ Resolution of ≥ 1 mIWG C-finding	✓ Reduction of neoplastic MC in bone marrow by ≥ 50% ✓ Reduction of serum tryptase by ≥ 50%
Clinical Improvement (CI)	✓ Resolution of ≥1 mIWG C-finding in the absence of CR, CRh, PR, or PD	Not a part of PPR Criteria

*confirmed response duration must be ≥ 12 weeks

Early Responses Observed by mIWG-MRT-ECNM and PPR Criteria

Best Response, n (%) * β (confirmed and unconfirmed)	Total (n=11)	mIWG-MRT-ECNM per CRRC Assessment (TKI‡ Therapy Naïve) (n=9)	mIWG-MRT-ECNM per CRRC Assessment (Prior TKI‡ Exposure) (n=2)
Overall response rate			
CR + CRh + PR + CI†	**8 (73)**	8 (89)	0 (0)
CR + CRh + PR	**6 (55)**	6 (67)	0 (0)
Complete Response (CR + CRh)	**2 (18)**	2 (22)	0 (0)
Partial Response (PR)	**4 (36)**	4 (44)	0 (0)
Clinical Improvement (CI)	**2 (18)**	2 (22)	0 (0)
Stable Disease (SD)	**3 (27)**	1 (11)	2 (100)

**3 patients pending confirmation of response are included: (2) PR; (1) CR in patients diagnosed with SM-AHN*
β mIWG-evaluable patients who have at least one post-baseline assessment are included
‡ SM-directed therapy with midostaurin and avapritinib
† Primary endpoint of Apex study

Best Response, n (%) α	Total (n=12)	PPR per Investigator Assessment (TKI‡ Therapy Naïve) (n=10)	PPR per Investigator Assessment (Prior TKI‡ Therapy) (n=2)
Overall response rate (CR + PR)	**9 (75)**	7 (70)	2 (100)
Complete Response (CR)	**3 (25)**	3 (30)	0 (0)
Partial Response (PR)	**6 (50)**	4 (40)	2 (100)
Stable Disease (SD)	**3 (25)**	3 (30)	0 (0)

α PPR-evaluable patients who have at least one post-baseline assessment are included.
‡ SM-directed therapy with midostaurin and avapritinib

- Median duration on treatment = 27 weeks (range: 0.3-40)
- First confirmed CRh by mIWG documented as early as 8 weeks and first confirmed CR as early as 20 weeks

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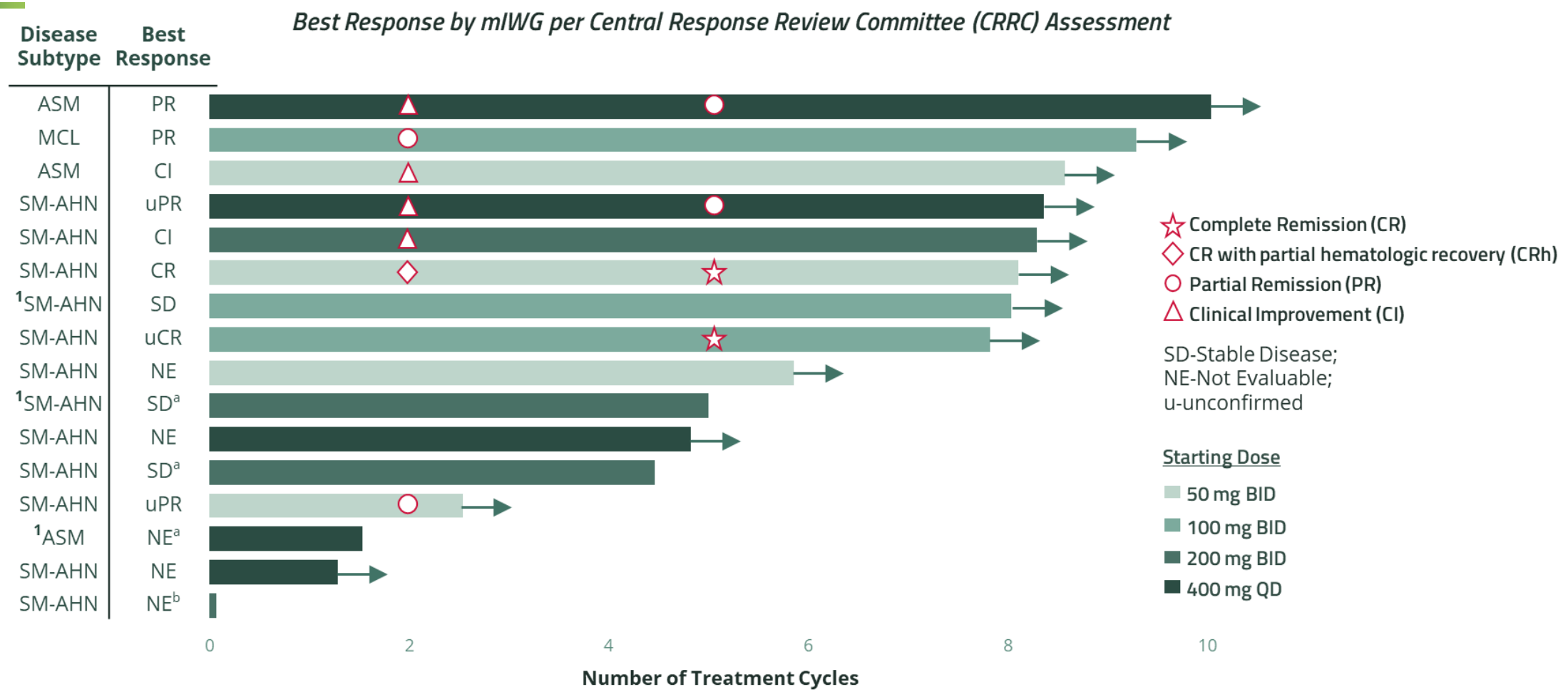
Early Responses Observed by mIWG-MRT-ECNM Criteria



[1] *Prior avapritinib and midostaurin.*

[a] *Discontinued due to disease progression*

[b] *Discontinued after 2 doses of study treatment due to investigator decision (femur fracture)*

Includes confirmed and unconfirmed responses

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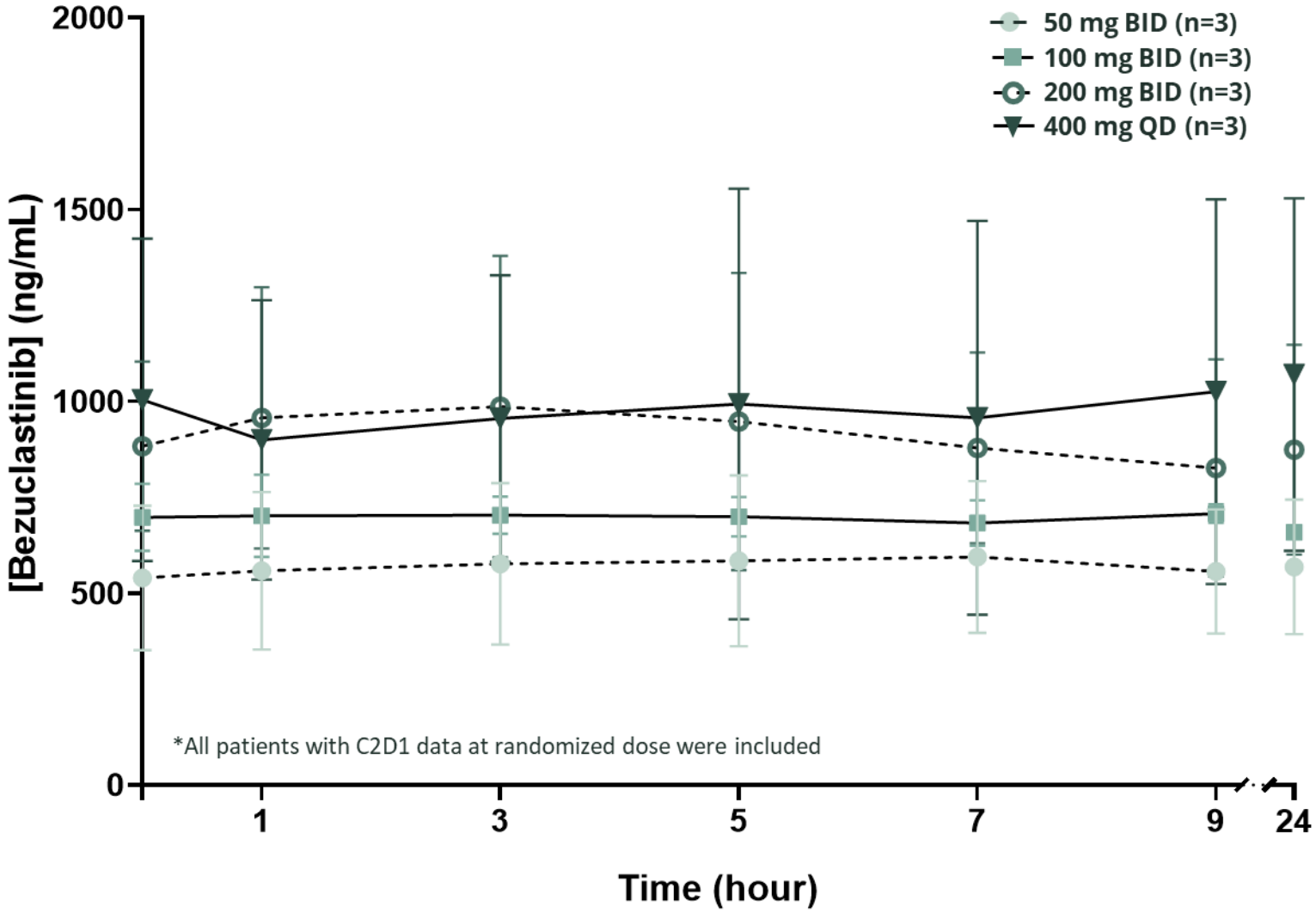
Dose Dependent Increase in Steady State (Cycle 2 Day 1) Bezuclastinib Exposure Regardless of BID or QD Dosing



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Bezuclastinib Clinical Data Summary

- **The highly potent and selective TKI bezuclastinib was generally well-tolerated across all dose levels and continues to demonstrate a differentiated safety profile**
  - No related cognitive effects or bleeding events reported
  - Limited effect of bezuclastinib on platelet counts in patients, supported by preclinical data
- **Treatment with bezuclastinib resulted in encouraging early signs of clinical activity demonstrated across all dose levels**
  - mIWG-MRT-ECNM: 89% overall response rate (CR + CRh + PR + CI) in TKI therapy-naïve patients and 73% in all patients at median follow up of 27 weeks
    - First confirmed CRh by mIWG as early as 8 weeks and first confirmed CR as early as 20 weeks
  - 88%, 92%, and 100% of patients with available data achieved a 50% reduction in serum tryptase, *KIT* D816V VAF, and bone marrow MC burden, respectively
- **Enrollment to Part 1 is ongoing**

Multiple Clinical and Preclinical Programs with Upcoming Catalysts

Program	Indication	Early Stage Development	Late Stage Development	Regulatory Submission	Approval
Clinical Programs					
Bezuclastinib (KIT inhibitor)	Advanced Systemic Mastocytosis	Apex			
	Nonadvanced Systemic Mastocytosis	Summit			
	Gastrointestinal Stromal Tumors	Peak			

Demonstrating differentiated profile as potential best-in-class selective KIT mutant inhibitor

Research Programs

Indication	Hit ID	Lead Generation	Lead Optimization	GLP	IND Submission
FGFR2					
ErbB2 mut					
Target 3					
Target 4					
Target 5					
Target 6					

Building exciting portfolio of next-generation potent, selective kinase inhibitors

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Cash runway into 2025; $289.1 million as of September 30, 2022

Q&A

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THANK YOU
Real Challenges. Real Solutions.
Precision therapies for genetically defined diseases