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43rd Annual J.P. Morgan Conference

January 14, 2025 – 7:30 a.m. PT

Real Challenges. Real Solutions.

Precision therapies for genetically defined diseases

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.

Building a Fully Integrated Precision Therapy Company with an Expanding Pipeline of Genetically Validated Targets

- **Bezuclastinib, a potent KIT mutant inhibitor**
  - Exciting clinical data in systemic mastocytosis (SM), driven by potency for KIT D816V, selectivity against other TKI targets and favorable emerging safety profile
  - Promising clinical activity and safety data in combination with sunitinib in imatinib-resistant gastrointestinal stromal tumor (GIST) patients

- **Early clinical and research pipeline of novel, small-molecule targeted therapies for cancer and rare diseases including a highly selective FGFR2 inhibitor, CNS-penetrant ErbB2, H1047R mutant selective PI3Kα inhibitor and KRAS(ON) inhibitor**

- **Experienced leadership and world class research team**

- **Cash runway expected to fund operations into late 2026**

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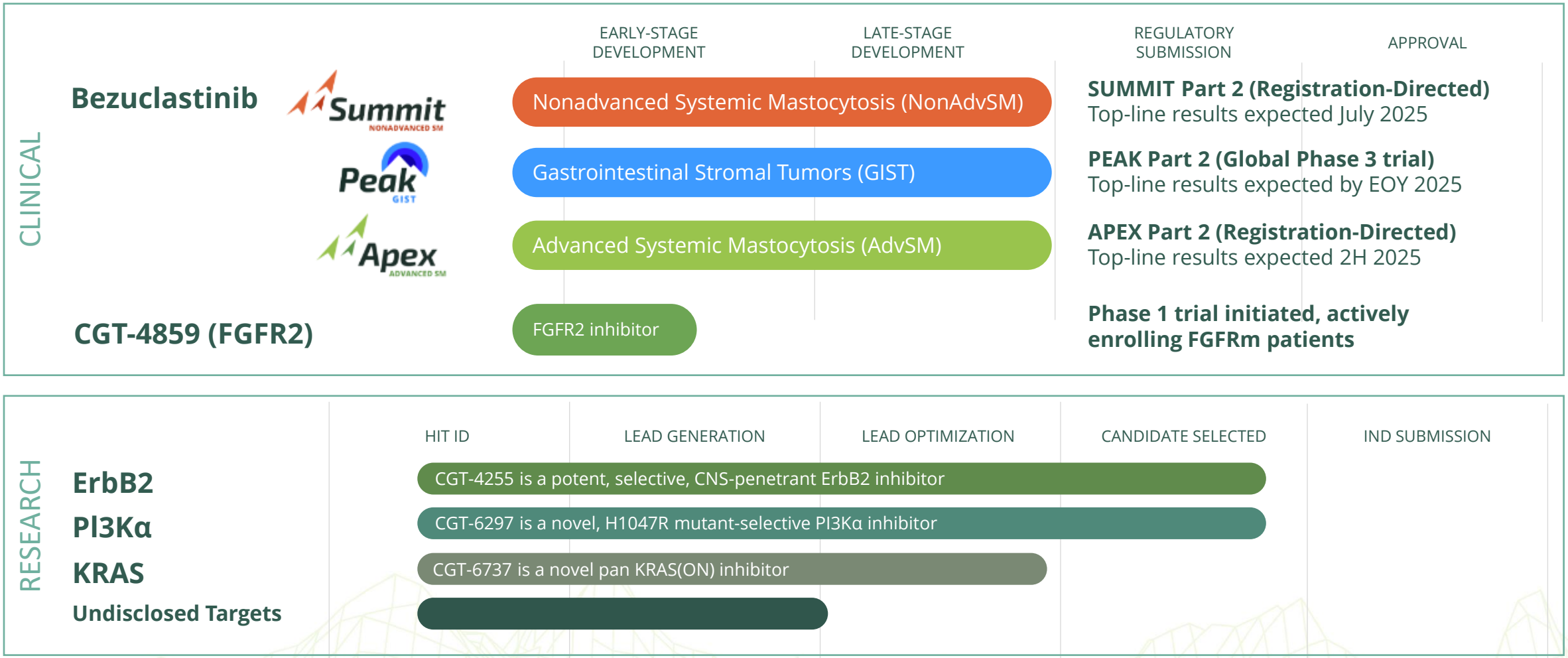
Multiple Clinical and Preclinical Programs with Upcoming Catalysts



$345.5M as of September 30, 2024; expected to fund operations into late 2026

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

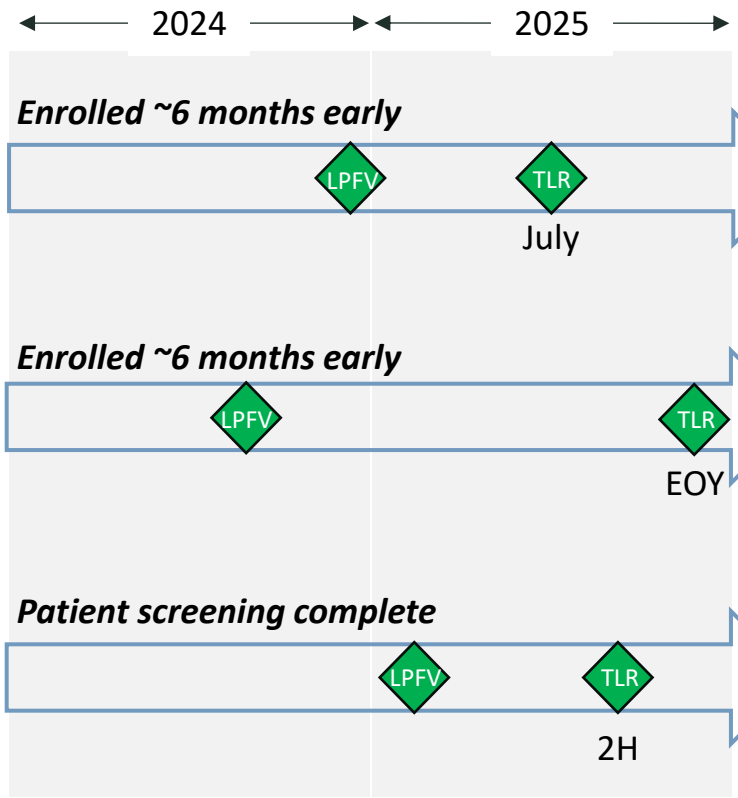
Phase 3 study in 2nd-line GIST sunitinib +/- bezuclastinib

n=413, mPFS primary endpoint

Apex ADVANCED SM

Registration-directed study in AdvSM bezuclastinib monotherapy

n=50-60, 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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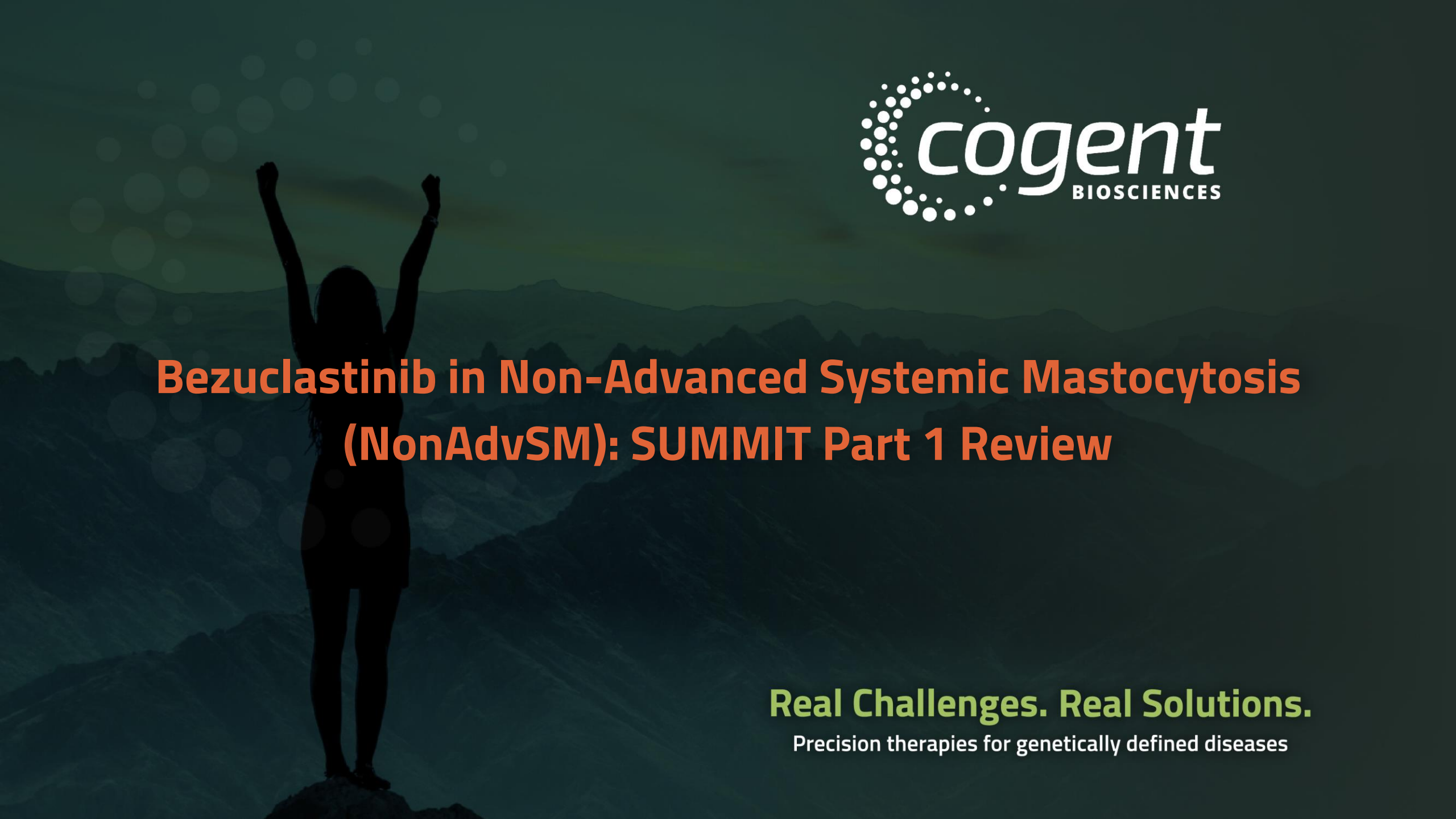
LPFV: Last patient, first visit
TLR: Top-line results including primary endpoint



Bezuclastinib in Non-Advanced Systemic Mastocytosis (NonAdvSM): SUMMIT Part 1 Review

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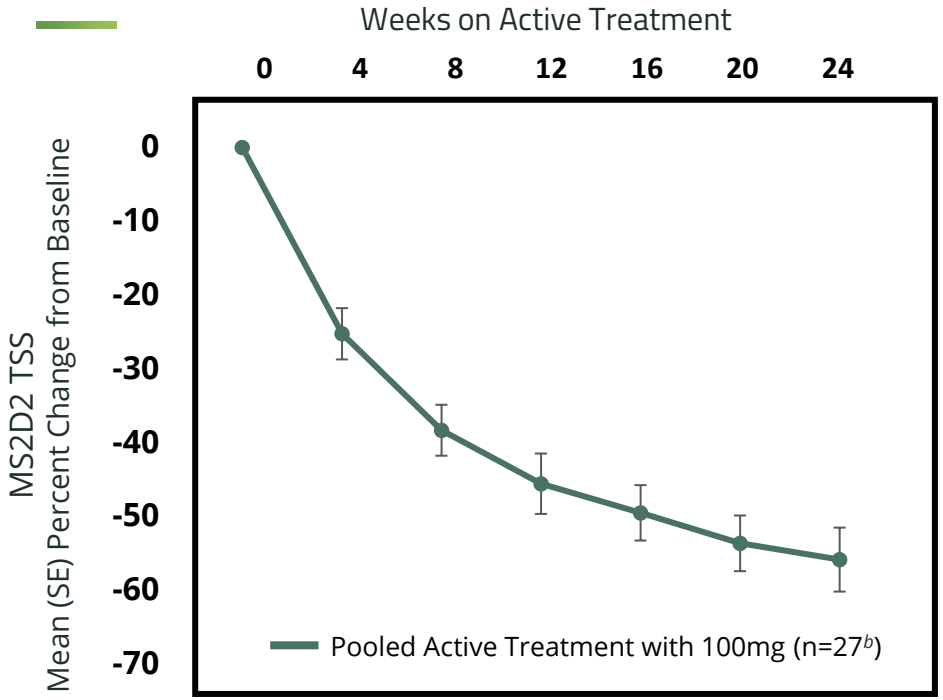
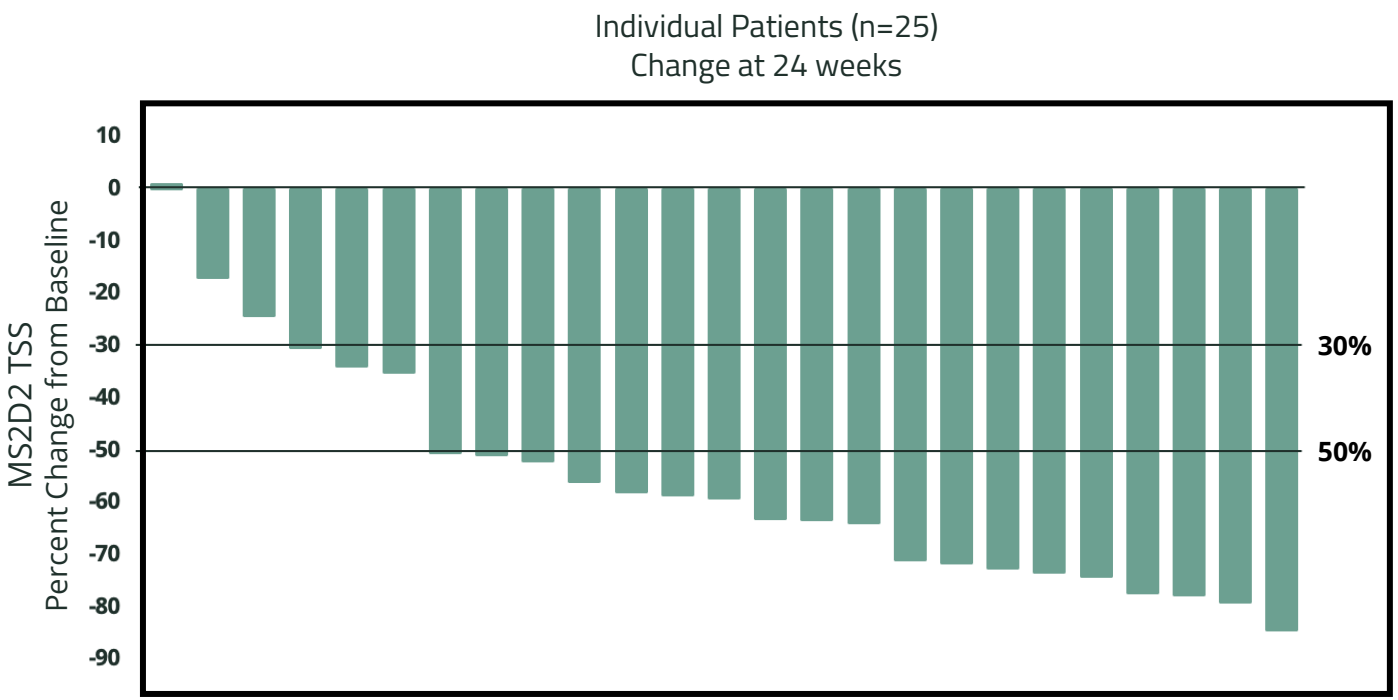
Deep and Sustained Symptomatic Improvement Shown in NonAdvSM Patients From SUMMIT Part 1



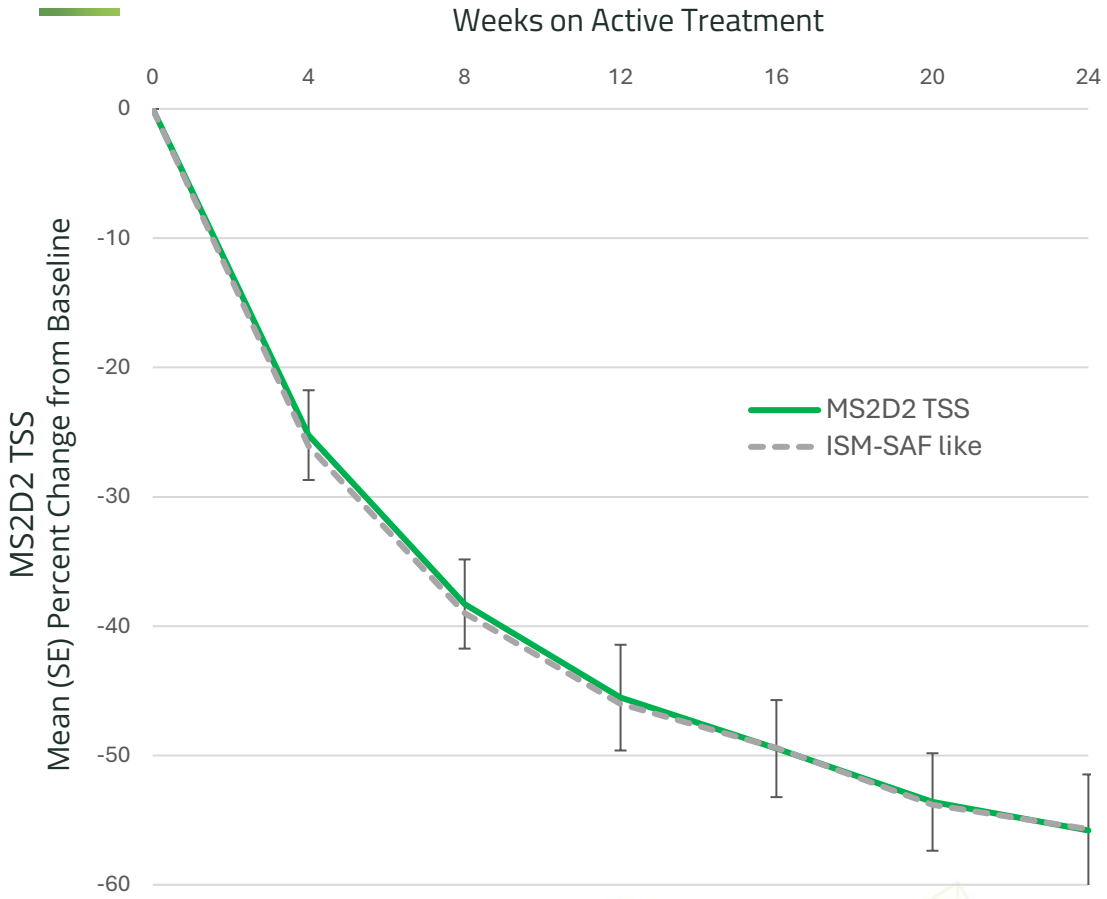


Among patients receiving 100 mg active treatment with bezuclastinib for 24 weeks[a]:

- TSS reduced by a **mean of 27.6 points**
- TSS reduced from baseline by a **mean of 55.8%**
- 30% TSS reduction achieved by **88% of patients**
- 50% TSS reduction achieved by **76% of patients**

[a] Includes all patients who received bezuclastinib 100mg QD through 24 weeks of active treatment.
[b] n=25 or 26 at some timepoints

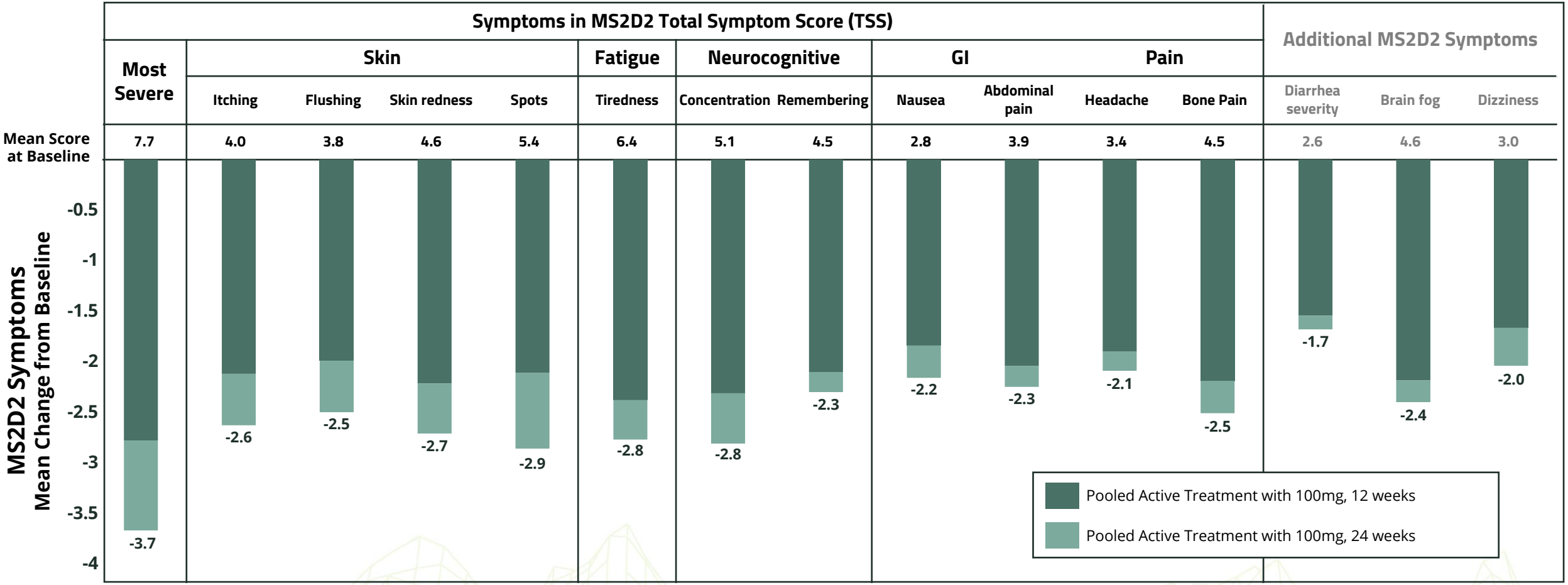
Bezuclastinib Performance Highly Consistent Using Composite Items From Either Available NonAdvSM Scoring Tool (MS2D2 or ISM-SAF)



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

SUMMIT Part 1 Patients Reported Rapid and Continued Deepening of Symptomatic Improvement Across Domains and Items



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. n=27 at baseline, n=26 at 12 weeks, and n=25 at 24 weeks.

Bezuclastinib Well Tolerated Safety Profile in SUMMIT Part 1

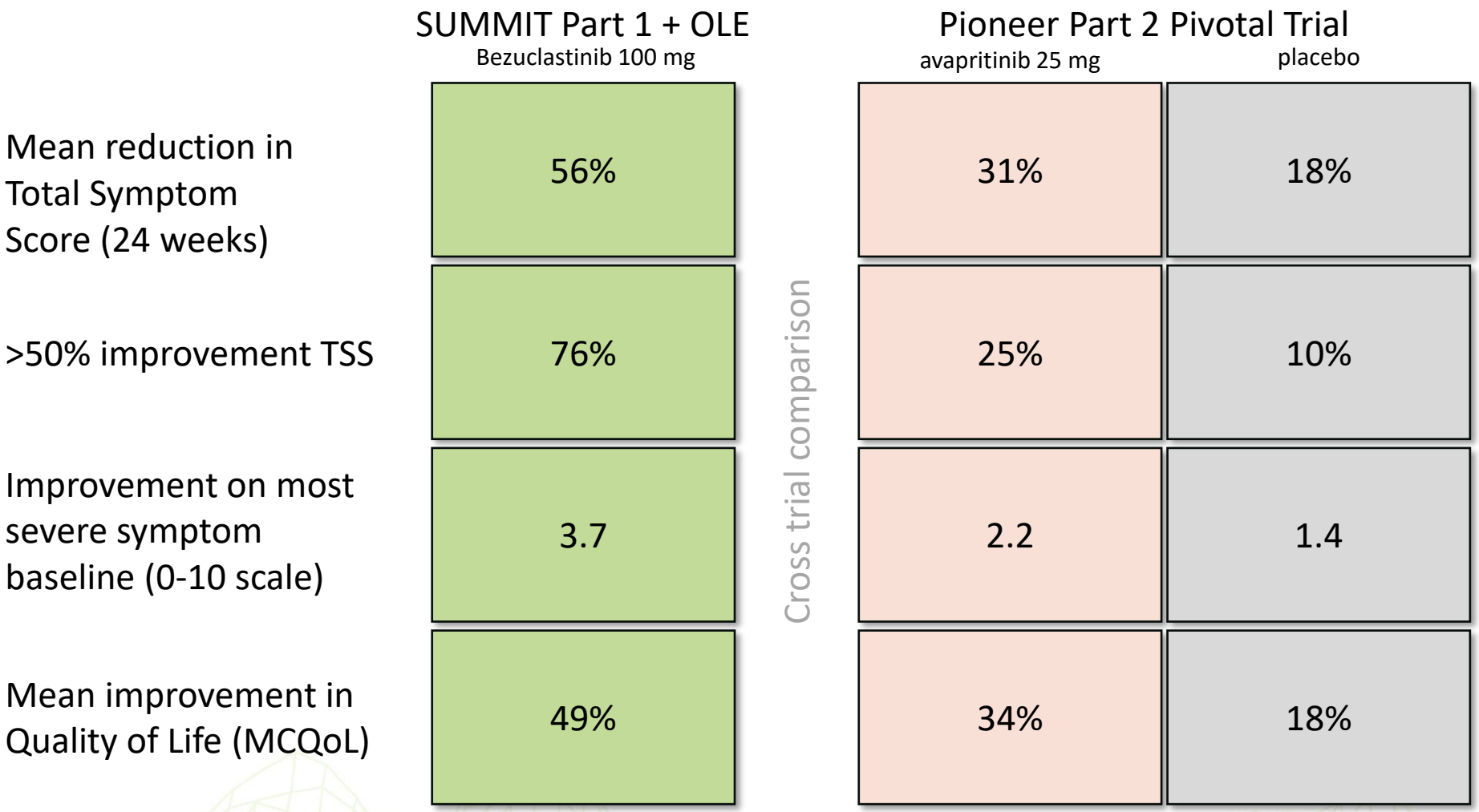
All Cause Treatment-Emergent Adverse Events (TEAE) ≥ 15 %

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

Contextualizing Bezuclastinib Performance in SUMMIT Part 1



In 16 patients with >48 weeks treatment:

- **65% mean TSS improvement**
- **88% achieving at least 50% reduction in TSS**

Bezuclastinib in Gastrointestinal Stromal Tumors (GIST): PEAK Part 1 Review

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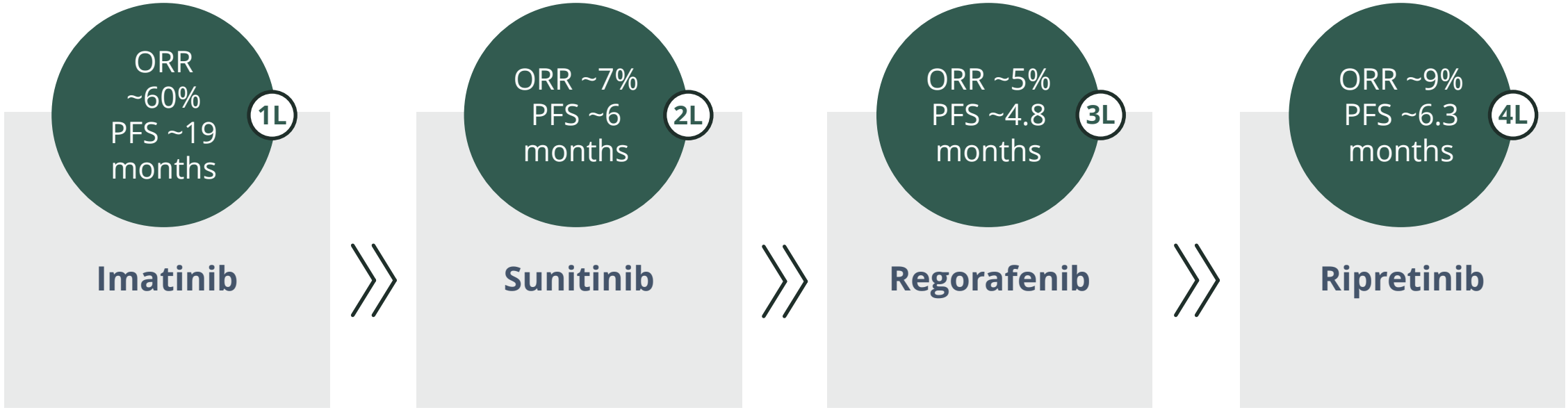
Significant Unmet Need Remains With Currently Approved GIST Therapy



60% of GIST patients develop resistance to Imatinib within two years.[1]

Resistance mutations driven by KIT exon 13 and KIT exon 17

2,000-3,500 imatinib-resistant, annual treatable GIST patients.[1]

ORR/PFS for all approved agents was obtained from labeled information from those agents

[1] Gramza AW, Corless CL, Heinrich MC., 2009.

Bezuclastinib + Sunitinib Combination Treatment Rationale in GIST

- Secondary resistance mutations in the KIT ATP-binding domain (exons 13, 14), activation loop (exons 17, 18), or both can develop and result in resistance to front-line imatinib

- Combination of bezuclastinib (exons 9, 11, **17**, and **18**) and sunitinib (exons 9, 11, **13**, and **14**) targets the full spectrum of primary and **secondary resistance mutations**

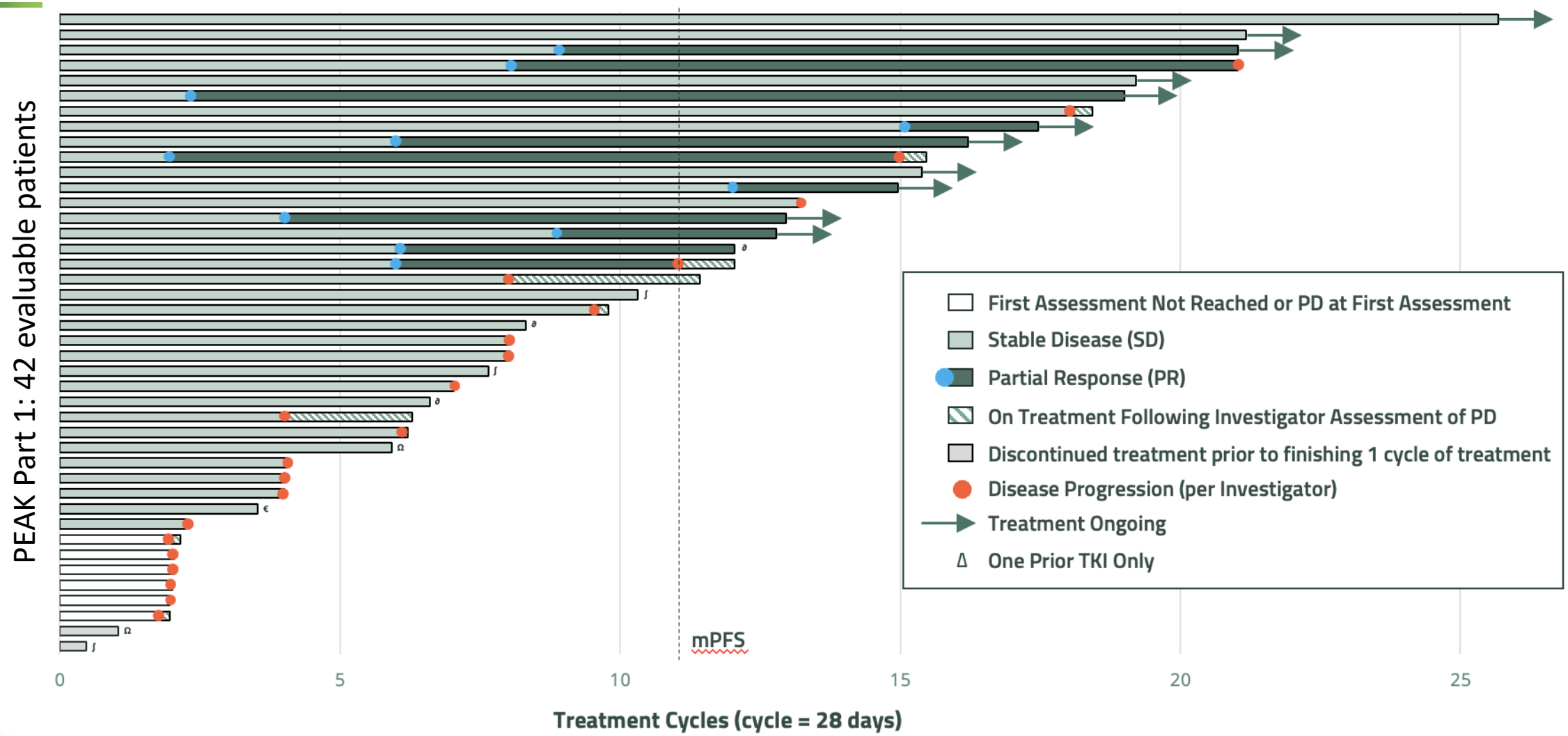
Bezuclastinib + Sunitinib Combination Targets the Full Spectrum of Primary and Secondary Mutations

	Primary		Secondary				Broad Coverage of Spectrum of Mutations
	9	11	13	14	17	18	
Imatinib	√	√	-	-	-	-	-
Ripretinib	~	√	~	√	√	√	~
Sunitinib	√	√	√	√	-	-	-
Bezuclastinib	√	√	~	-	√	√	-
Bezuclastinib + Sunitinib	√	√	√	√	√	√	√

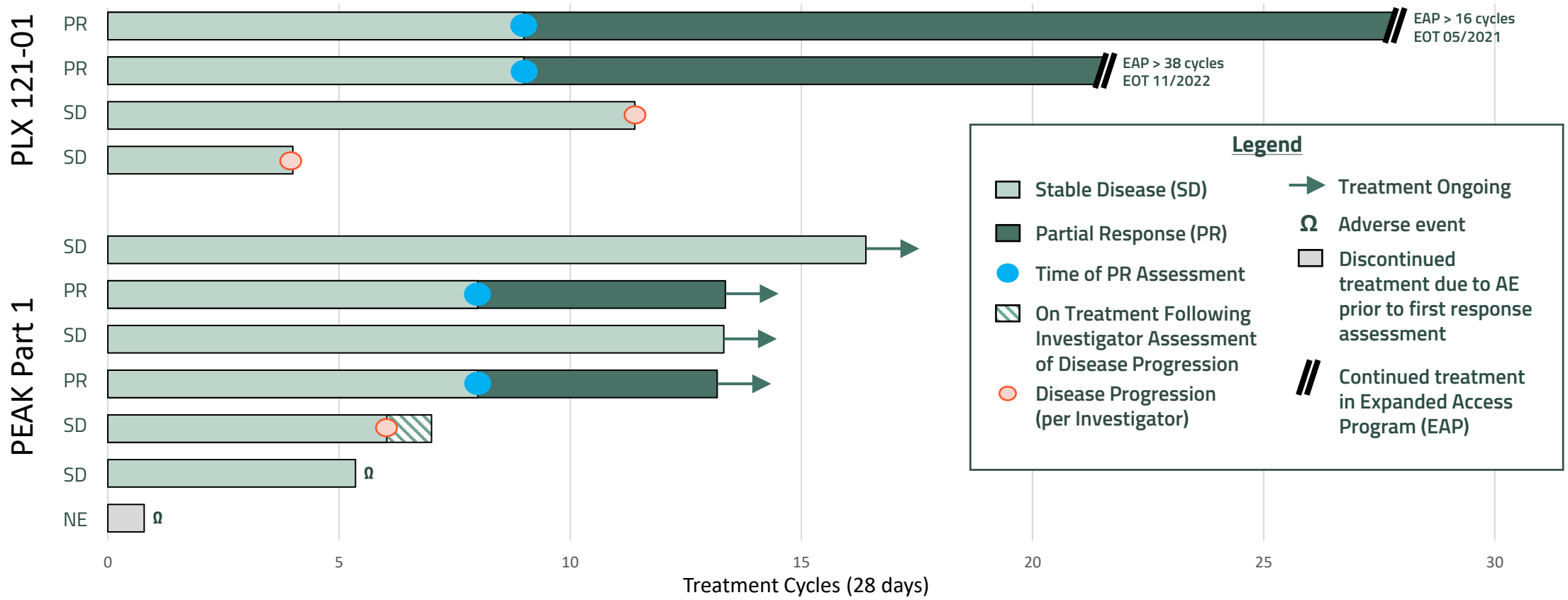
√ = strong inhibition ~ = moderate inhibition - = no inhibition

Gramza AW, et al. Clin Cancer Res, 2009;15(24):7510-7518. [2]Arshad J et al. JCO Precis Oncol, 2020;4:66-73. [3]Casali PG, et al. JCO, 2017;35(15):1713-1720. [4]Serrano C and George S. CCR, 2020;26(19):5078-5085. 5. Wagner et al. [abstract 1251848] 2022. In: CTOS 2022: 1251848.

Robust Clinical Activity for Bezuclastinib + Sunitinib Combination In Heavily Pre-Treated GIST Patients



Bezuclastinib + Sunitinib in 2nd-line GIST: 40% ORR With Durability



GIST mPFS benchmarks

- 8.3 months: sunitinib in INTRIGUE trial (2nd-line)
- 8.0 months: ripretinib in INTRIGUE trial (2nd-line)
- 5.5 months: sunitinib USPI (2nd-line)
- 5.6 months: avapritinib in VOYAGER trial (3rd-line)
- 4.2 months: regorafenib in VOYAGER trial (3rd-line)

PLX 121-01 was an 18-patient study in heavily pretreated GIST population
Peak Part 1 was a 42-patient study studying bezuclastinib+sunitinib combination

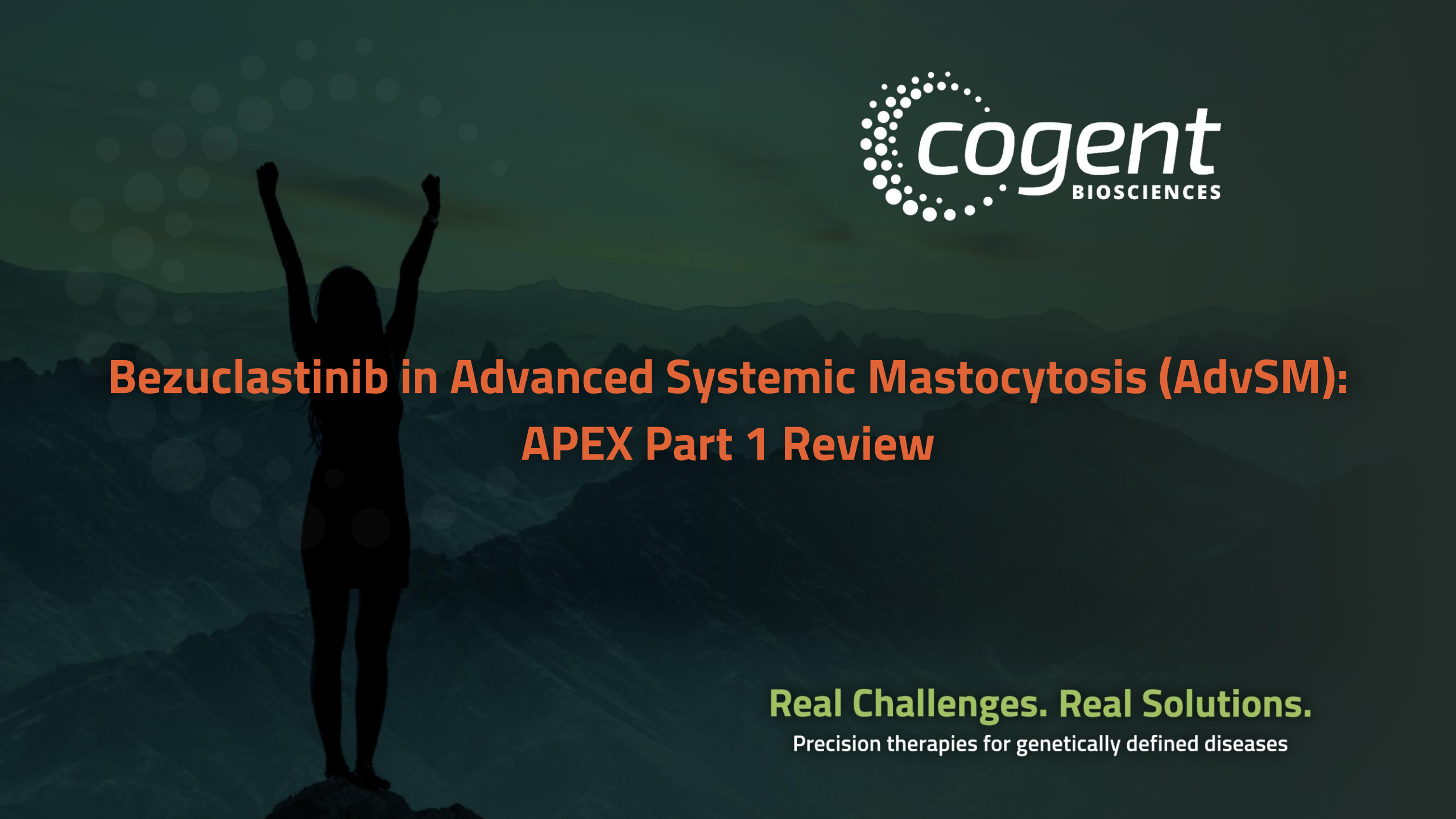
Bezuclastinib + Sunitinib Combination Well Tolerated in Peak Part 1

TEAEs≥15% of Patients All Causality

	Part 1a n=19 (%)		Part 1b *n=23 (%)*		Total *n=42 (%)*	
Preferred Term	**All Grade**	**Grade ≥3**	**All Grade**	**Grade ≥3**	**All Grade**	**Grade ≥3**
Diarrhea	12 (63)	2 (11)	17 (74)	-	**29 (69)**	**2 (5)**
Fatigue	10 (53)	-	13 (57)	-	**23 (55)**	**-**
Hypertension	10 (53)	4 (21)	9 (39)	3 (13)	**19 (45)**	**7 (17)**
Nausea	8 (42)	-	9 (39)	-	**17 (40)**	**-**
Hair color changes	9 (47)	-	6 (26)	-	**15 (36)**	**-**
GERD	4 (21)	-	9 (39)	-	**13 (31)**	**-**
Taste disorder	3 (16)	-	10 (43)	-	**13 (31)**	**-**
Decreased appetite	6 (32)	-	6 (26)	-	**12 (29)**	**-**
Rash	5 (26)	-	6 (26)	-	**11 (26)**	**-**
Neutropenia	5 (26)	-	5 (22)	3 (13)	**9 (21)**	**3 (7)**
ALT/AST increased	4 (21)	1 (5)	5 (22)	1 (4)	**9 (21)**	**2 (5)**
Anemia	3 (16)	-	6 (26)	3 (13)	**9 (21)**	**3 (7)**
Headache	4 (21)	-	5 (22)	-	**9 (21)**	**-**
Abdominal pain	6 (32)	-	2 (9)	-	**8 (19)**	**-**
PPE	5 (26)	-	3 (13)	-	**8 (19)**	**-**
Hypokalemia	5 (26)	1 (5)	2 (9)	-	**7 (17)**	**1 (2)**
Vomiting	3 (16)	-	4 (17)	-	**7 (17)**	**-**

- Majority of TEAEs were low grade and reversible
- Low rate of Grade 3+ events
- Only three patients experienced serious adverse events possibly associated with study medications:
  - Gr 2 neutrophil count decrease and pyrexia and Gr 3 platelet count decrease
  - Gr 2 bacterial peritonitis and Gr 3 febrile neutropenia
  - Gr 3 anemia, asthenia, and edema peripheral
- Limited (29%) dose reductions of any study medications due to TEAEs
- Infrequent (n=2) discontinuations due to TEAEs

The safety and tolerability profile appears generally consistent with published sunitinib monotherapy experience



Bezuclastinib in Advanced Systemic Mastocytosis (AdvSM): APEX Part 1 Review

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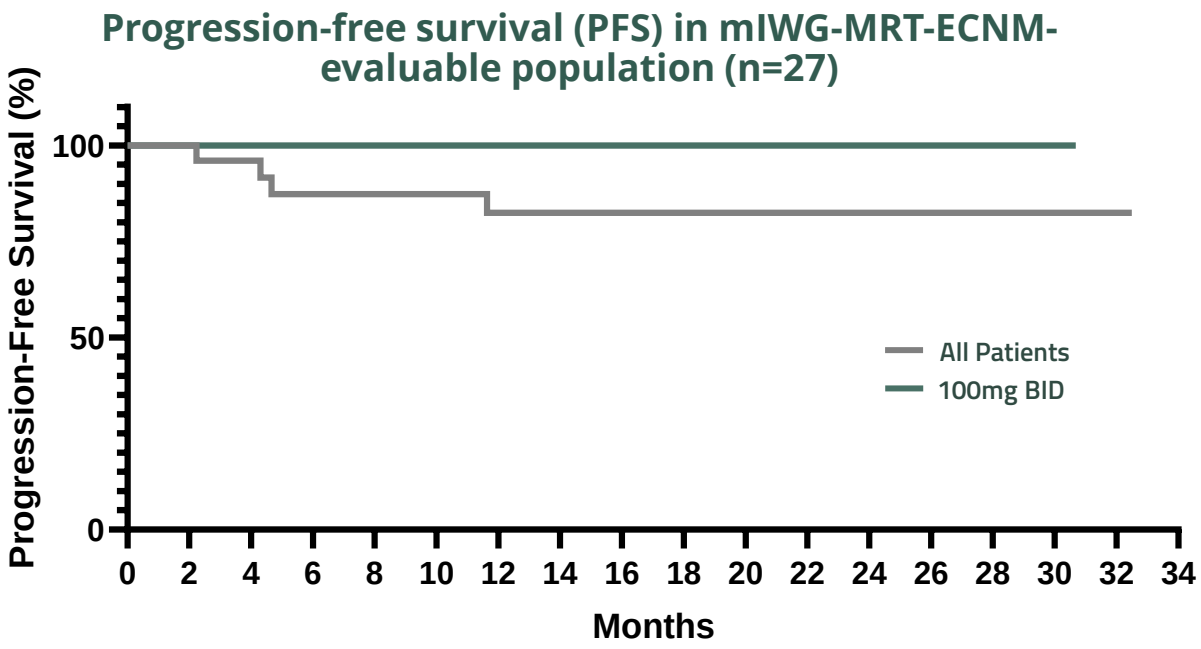
Bezuclastinib Shows Impressive Clinical Activity in ASM Patients

Best Response, criteria	mIWG-MRT-ECNM		PPR
Patient Group (n)	**All**	**KIT-naive**	**All**
	n=27	**n=18**	**n=32**
Overall response rate			
CR + CRh + PR + CI	**14 (52)**	**11 (61)**	
CR + CRh + PR	**13 (48)**	**10 (56)**	**28 (88)**
Complete Response (CR + CRh)	**7 (26)**	**7 (39)**	**14 (44)**
Partial Response (PR)	**6 (22)**	**3 (17)**	**14 (44)**
Clinical Improvement (CI)	**1 (4)**	**1 (6)**	
Stable Disease (SD)	**10 (37)**	**6 (33)**	**1 (3)**
Not evaluable	**3 (11)**	**1 (6)**	**3 (9)**

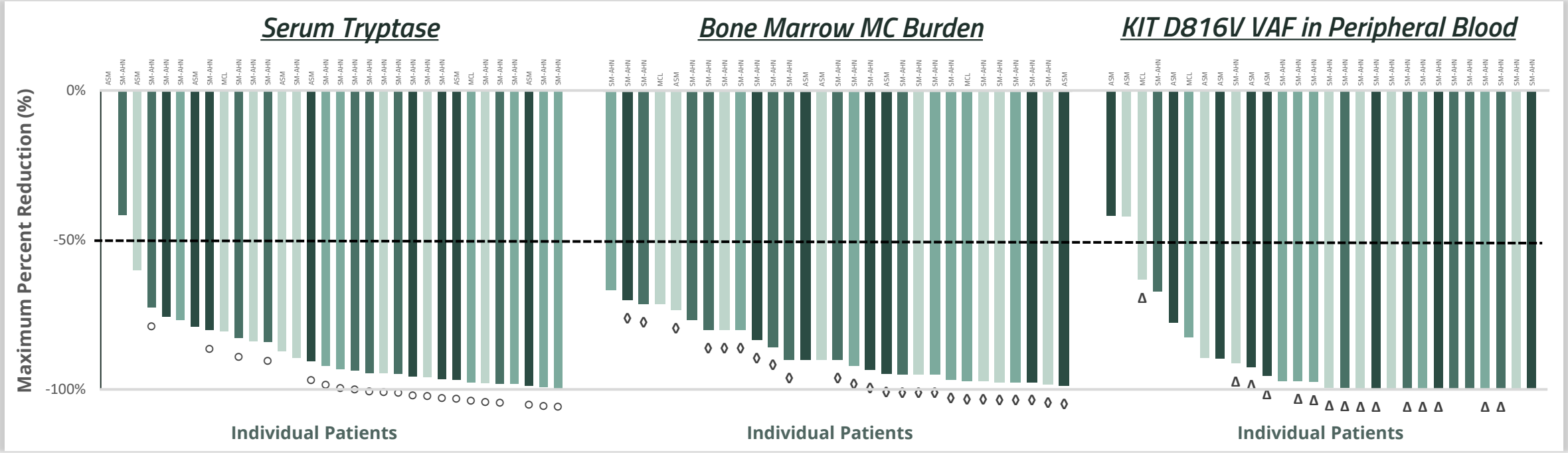


- mPFS **not yet reached** at follow-up of 20 months
- PFS rate was **82% at 24 months**

PPR is derived based on local hematology and central pathology assessments. PFS progression includes death or CRRC assessment of progressive disease

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]).

Bezuclastinib Shows 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

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

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.

PK matched to RP2D
150 mg QD

- 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.

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

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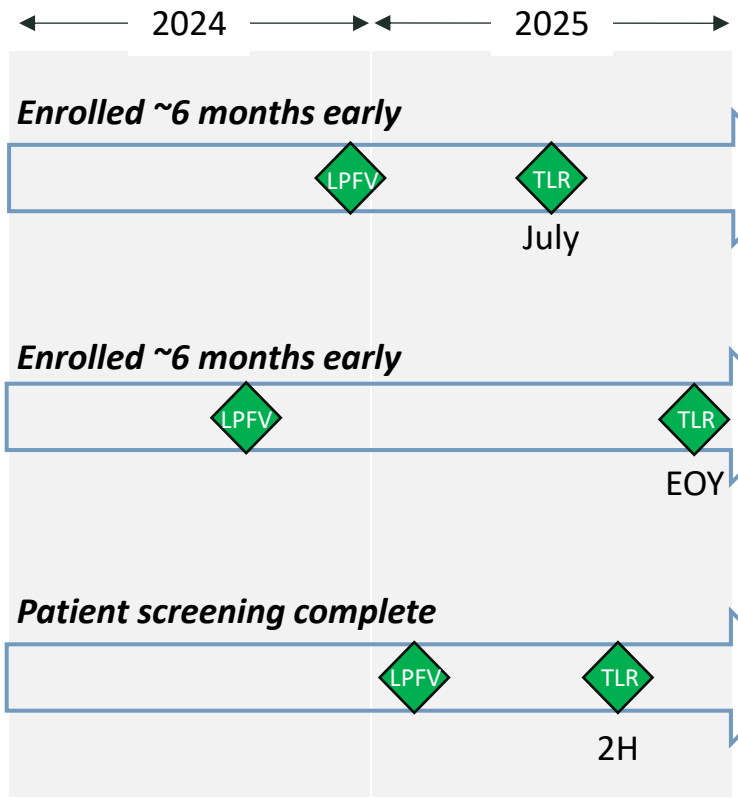

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Thank you
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