Peak Trial: Bezuclastinib + Sunitinib in Gastrointestinal Stromal Tumors (GIST) Top-Line Results

Investor Webcast
November 10, 2025

Real Challenges. Real Solutions.

Precision therapies for genetically defined diseases

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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 on 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; and the fact that interim clinical data may not be indicative of future results, 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.

Agenda and Speakers

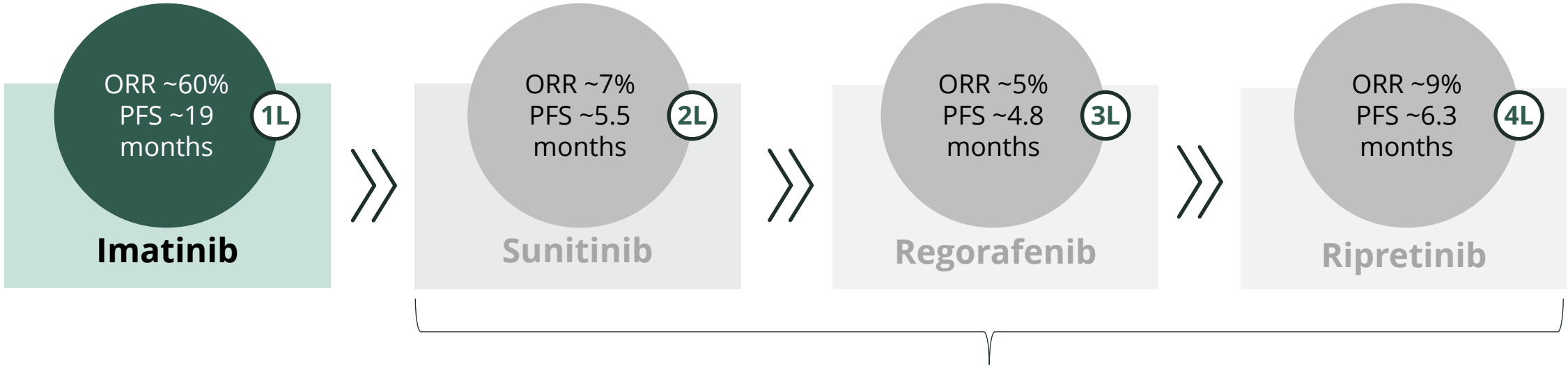
Andrew Robbins
President and Chief Executive Officer

Neeta Somaiah, M.D.
Professor and Department Chair,
Department of Sarcoma Medical Oncology,
Division of Cancer Medicine, The University
of Texas MD Anderson Cancer Center

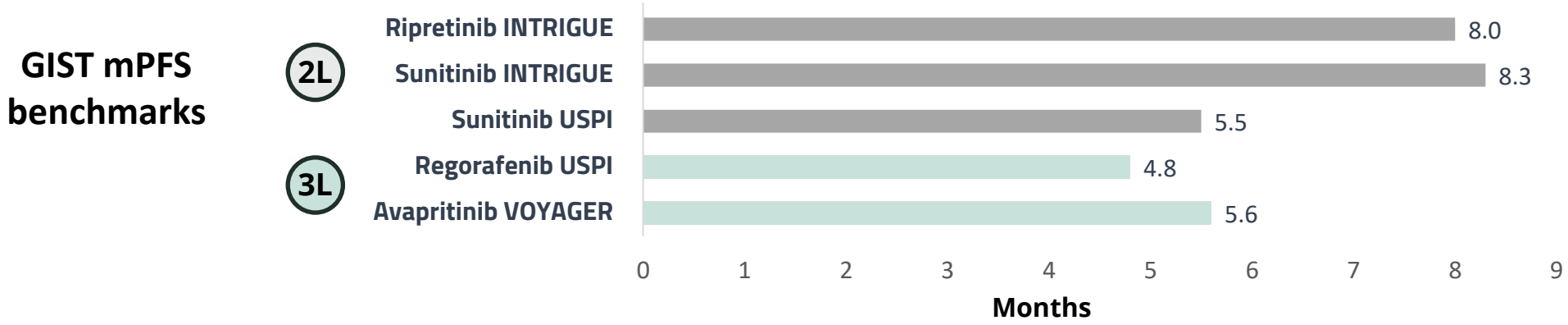
Jessica Sachs, M.D.
Chief Medical Officer

• Introduction	Andrew Robbins
• GIST Disease Overview • Peak Top-Line Results • Patient Cases	Dr. Neeta Somaiah
• Summary	Andrew Robbins
• Q&A	All

Unmet Medical Need Remains for Patients with Imatinib-Resistant or Intolerant GIST



Modest historical performance of novel agents in imatinib-resistant setting emphasizes unmet need



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

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Peak Phase 3 Top-Line Results

Real Challenges. Real Solutions.

Precision therapies for genetically defined diseases

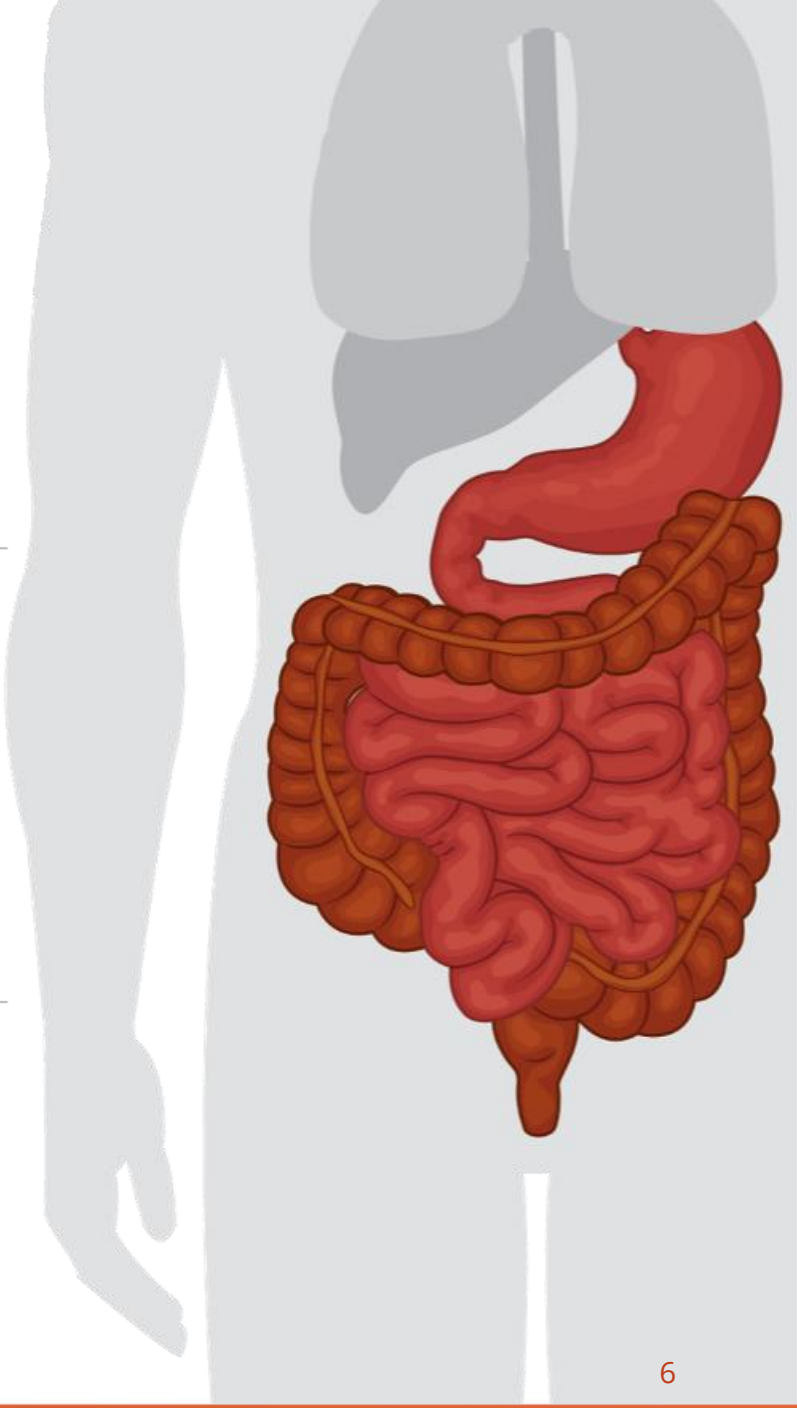
Full Results Expected to be Presented at an Upcoming Medical Meeting

Significant Unmet Need Remains for Patients with Gastrointestinal Stromal Tumors (GIST)

- Up to 6,000 GIST cases diagnosed annually in US, over 80% of which express KIT mutations, typically exons 11 and 9.[1,2]
- Tumors can start anywhere in the GI tract, but they occur most often in the stomach (about 60%) or the small intestine (about 35%).[1]
- While imatinib provides disease control in the majority of patients in the 1L setting, ~60% of patients with GIST develop resistance within 2 years, primarily due to mutations in exon 13/14 and/or exon 17/18.[1,2]
- Additional FDA-approved sequential lines of therapy include sunitinib, regorafenib, and ripretinib; however, each is only effective against a subset of resistance mutations and disease progression results from clonal heterogeneity.

Symptoms[3]

Diarrhea, Nausea, Vomiting, Abdominal pain, Bloating, Gastroesophageal reflux disease, GI bleeding, Loss of appetite, Weight loss



[1] Key statistics for gastrointestinal stromal tumors. American Cancer Society.
[2] Gramza AW, Corless CL, Heinrich MC., 2009.
[3] Signs and symptoms of gastrointestinal stromal tumors. American Cancer Society.
L: Line of Therapy

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

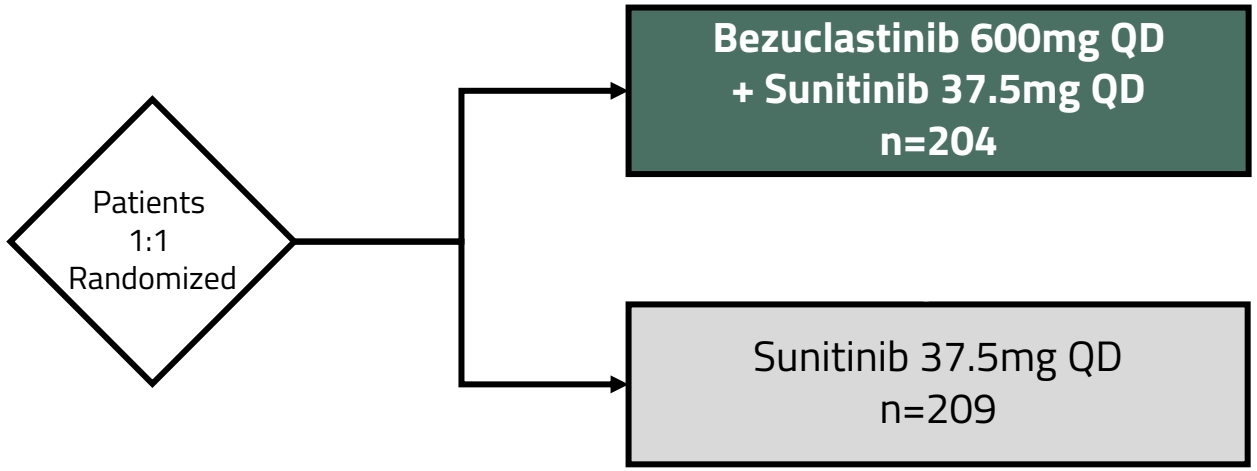
- No single TKI inhibits all KIT mutations. [1-11]
- The combination of bezuclastinib + sunitinib inhibits mutations in KIT exons 9, 11, 13, 14, 17, and 18, targeting the full spectrum of primary and secondary mutations relevant in advanced GIST.

Treatments	Exon 9	Exon 11	Exon 13	Exon 14	Exon 17	D816V	Exon 18
Imatinib	Moderate	Strong	No	No	No	No	No
Regorafenib	Strong	Strong	No	Strong	Moderate	No	Strong
Velzatinib (IDRX-42)	Strong	Strong	Moderate	No	Strong	No	Strong
Ripretinib	Moderate	Strong	Moderate	No	Strong	Strong	Strong
Sunitinib	Strong	Strong	Strong	Strong	No	No	No
Bezuclastinib + Sunitinib	Strong	Strong	Strong	Strong	Strong	Strong	Strong

No Inhibition Moderate Inhibition Strong Inhibition

[1] Plexxikon. Data on file.
[2] Serrano C et al. Br J Cancer, 2019.
[3] Evans EK et al. Sci Transl Med, 2017.
[4] Trent J et al. CTOS [presentation]. 2020.
[5] Smith P et al. AACR [poster]. 2018.
[6] Wagner AJ et al. JAMA Oncol. 2021.
[7] Serrano C and Fletcher O. Oncotarget, 2019.
[8] Muhlenberg T et al. J Clin Oncol, 2024.
[9] Heinrich MC, et al. Nature Medicine, 2024.
[10] Blum SM, et al. JMedChem, 2023.
[11] Wagner AJ et al. CTOS 2022.

Peak: Randomized Clinical Study Evaluating Bezuclastinib in Combination with Sunitinib in Patients with GIST



Crossover allowed following BICR confirmed PD

Patient Eligibility
• Age ≥ 18 years • Histologically confirmed GIST with at least 1 measurable lesion per mRECIST v1.1 • Locally advanced, unresectable or metastatic GIST • Documented disease progression on or intolerance to imatinib

Primary Endpoint	• Progression Free Survival per BICR
Key Secondary Endpoints	• Objective Response Rate per BICR • Overall Survival
Secondary Endpoints	• Progression Free Survival per Investigator • Disease Control Rate • Time to Response • Duration of Response

Data cut-off as of 30Sep2025
QD: Once daily; BICR: blinded independent central review; PD: Progressive Disease

Peak Part 2 Population is Representative of Second-Line Patients with GIST

Patient Demographics	Bezuclastinib + Sunitinib	Sunitinib	Overall
# Patients	204	209	413
Male, n (%)	131 (64.2)	133 (63.6)	264 (63.9)
Median Age in years, (range)	63 (32 - 83)	64 (30 – 88)	63 (30 – 88)
ECOG PS at baseline, n (%)			
0	140 (68.6)	132 (63.2)	272 (65.9)
1	61 (29.9)	74 (35.4)	135 (32.7)
2	3 (1.5)	3 (1.4)	6 (1.5)

Region	Bezuclastinib + Sunitinib	Sunitinib	Overall
North America, n (%)	76 (37.3)	85 (40.7)	161 (39.0)
Europe, n (%)	94 (46.1)	94 (45.0)	188 (45.5)
Latin America, n (%)	20 (9.8)	11 (5.3)	31 (7.5)
Asia-Pacific, n (%)	14 (6.9)	19 (9.1)	33 (8.0)

Baseline Characteristics	Bezuclastinib + Sunitinib	Sunitinib	Overall
KIT Mutations per molecular pathology report, n (%)			
Mutation Detected			
Any Exon 9	31 (15.2)	34 (16.3)	65 (15.7)
Exon 11 only	120 (58.8)	126 (60.3)	246 (59.6)
Neither Exon 9 nor 11	10 (4.9)	11 (5.3)	21 (5.1)
Other	30 (14.7)	34 (16.3)	64 (15.5)
No KIT Mutation Detected	13 (6.4)	4 (1.9)	17 (4.1)
Treatment History			
Imatinib intolerance	6 (2.9)	8 (3.8)	14 (3.4)
Prior Radiotherapy	14 (6.9)	8 (3.8)	22 (5.3)
Prior Anti-Cancer Surgery	156 (76.5)	167 (79.9)	323 (78.2)

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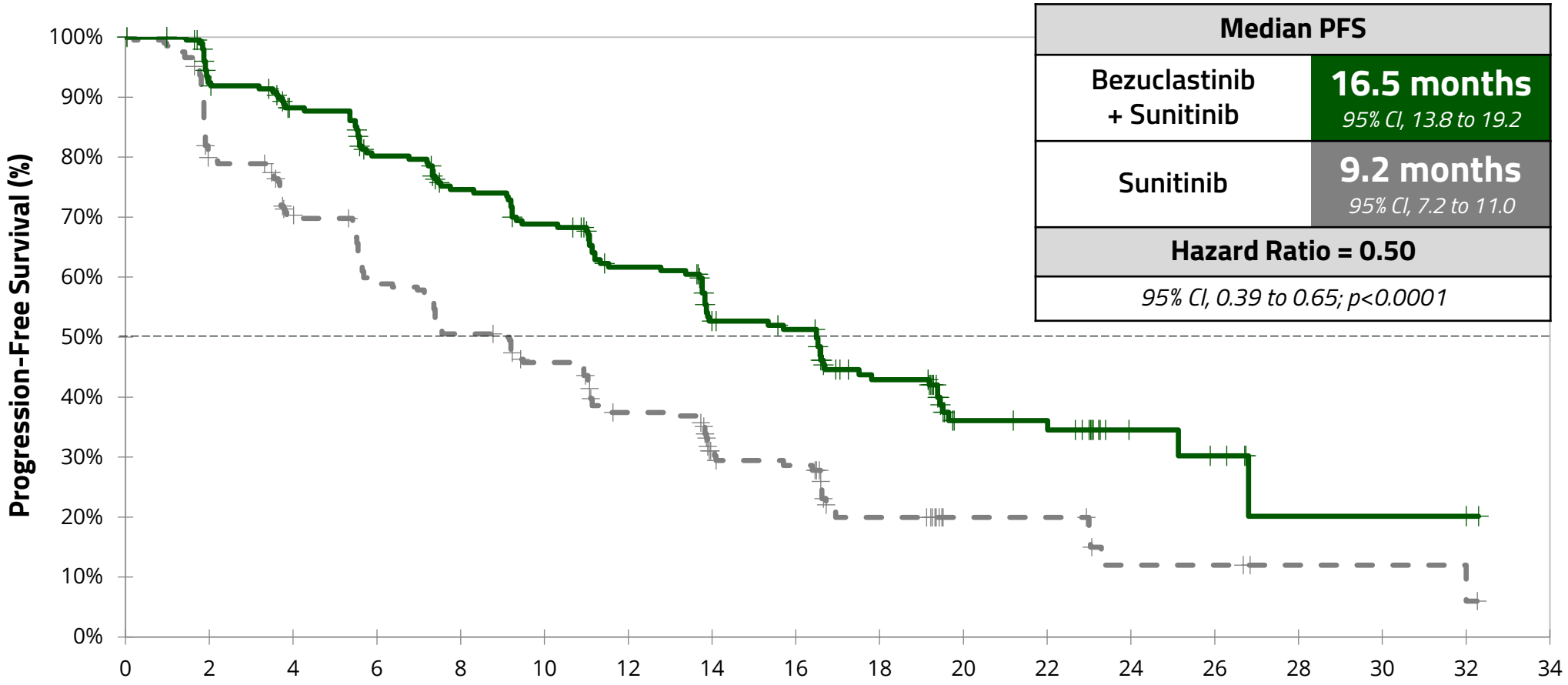
Data cut-off as of 30Sep2025

Bezuclastinib Combination Extends PFS with 50% Reduction in Risk of Progression or Death



Median PFS	
Bezuclastinib + Sunitinib	**16.5 months** *95% CI, 13.8 to 19.2*
Sunitinib	**9.2 months** *95% CI, 7.2 to 11.0*
Hazard Ratio = 0.50	
95% CI, 0.39 to 0.65; p<0.0001	

Patients at Risk

Bezuclastinib + Sunitinib	204	180	166	146	130	119	102	76	72	51	24	23	8	6	2	2	2	0
Sunitinib	209	161	137	113	97	85	64	39	35	19	9	9	4	4	2	2	2	0

PFS: Progression-Free Survival; mRECIST v1.1: modified Response Evaluation Criteria in Solid Tumors version 1.1; BICR: Blinded Independent Central Review

Data cut-off as of 30Sep2025

Bezuclastinib + Sunitinib Demonstrates Unprecedented 46% Objective Response Rate

ORR per BICR , %, n [95% CI]	
Bezuclastinib + Sunitinib (n=204)	**45.6%** *93 [38.6, 52.7]*
Sunitinib (n=209)	**25.8%** *54 [20.0, 32.3]*
Difference in ORR, % [95% CI]; P Value	
19.8 [10.6, 28.6]; **P Value <0.0001**	

BOR per BICR, n (%)	Bezuclastinib + Sunitinib	Sunitinib
Complete Response (CR)	**13 (6.4)**	**4 (1.9)**
Partial Response (PR)	**80 (39.2)**	**50 (23.9)**
Stable Disease (SD)	91 (44.6)	108 (51.7)
Progressive Disease (PD)	15 (7.4)	41 (19.6)
Not Evaluable (NE)	5 (2.5)	6 (2.9)

Data cut-off as of 30Sep2025 ; BICR: blinded independent central review; ORR: Objective Response Rate; BOR: Best Overall Response

Bezuclastinib + Sunitinib is Generally Well Tolerated with a Favorable Safety Profile

	Study Treatment	
	Bezuclastinib + Sunitinib (n=204)	***Sunitinib (n=208)[1]***
TEAEs, n (%)	204 (100)	207 (99.5)
TRAEs, n (%)	202 (99.0)	204 (98.1)
Gr3+ TRAEs, n (%)	146 (71.6)	109 (52.4)
Bezuclastinib related Gr3+	126 (61.8)	N/A
Sunitinib related Gr3+	141 (69.1)	109 (52.4)
SARs, n (%)	34 (16.7)	24 (11.5)
Bezuclastinib related SAEs	25 (12.3)	N/A
Sunitinib related SAEs	31 (15.2)	24 (11.5)
TRAEs leading to death, n (%)	0	1 (0.5)
Reductions of either drug due to TRAEs, n (%)	114 (55.9)	92 (44.2)
DC of study treatment due to TRAEs, n (%)	15 (7.4)	8 (3.8)

Randomized Period Data; 1: One patient randomized to sunitinib but never dosed

- The incidence of TEAEs and TRAEs was similar between treatment arms
- No TRAEs leading to death in patients on bezuclastinib + sunitinib combination
- Only TRAEs leading to discontinuation of either drug in >1 patient on the combination arm were neutropenia (2.9%), ALT/AST increased (1.5%), and diarrhea (1%)

Data cut-off as of 30Sep2025; SAE: serious adverse event; TEAE: treatment-emergent adverse event; TRAE: treatment-related adverse event; SAR: serious adverse reaction; DC: discontinuation

All Grade TEAEs ≥ 20% Demonstrate Balance Between Arms

	Bezuclastinib + Sunitinib (n=204)		Sunitinib (n=208)[1]	
Preferred term, n (%)	***All Grade***	***Grade 3+***	***All Grade***	***Grade 3+***
Diarrhea	159 (77.9)	16 (7.8)	138 (66.3)	15 (7.2)
ALT/AST increased*	115 (56.4)	22 (10.8)	35 (16.8)	3 (1.4)
Hypertension	106 (52.0)	60 (29.4)	108 (51.9)	57 (27.4)
Taste disorder*	97 (47.5)	0	52 (25.0)	0
Nausea	81 (39.7)	1 (0.5)	56 (26.9)	2 (1.0)
Hair color changes	79 (38.7)	0	37 (17.8)	0
Fatigue	72 (35.3)	9 (4.4)	70 (33.7)	5 (2.4)
Neutropenia*	71 (34.8)	31 (15.2)	70 (33.7)	32 (15.4)
PPE	59 (28.9)	6 (2.9)	95 (45.7)	5 (2.4)
Vomiting	56 (27.5)	2 (1.0)	45 (21.6)	4 (1.9)
Decreased appetite	55 (27.0)	6 (2.9)	46 (22.1)	0
Anemia	54 (26.5)	19 (9.3)	42 (20.2)	10 (4.8)
Abdominal pain	51 (25.0)	6 (2.9)	52 (25.0)	4 (1.9)
Stomatitis	46 (22.5)	6 (2.9)	68 (32.7)	10 (4.8)
GERD	45 (22.1)	0	30 (14.4)	0
Dyspepsia	43 (21.1)	5 (2.5)	29 (13.9)	0
Thrombocytopenia*	39 (19.1)	2 (1.0)	55 (26.4)	9 (4.3)

Randomized Period Data; 1: One patient randomized to sunitinib but never dosed

- TEAEs reported at a higher frequency (>15%) in combination arm: ALT/AST increased, taste disorder, and hair color changes
- TEAEs reported less frequently in combination arm: PPE, stomatitis and thrombocytopenia
- The safety profile of bezuclastinib combination is generally consistent with the known safety profile of sunitinib alone and no new risks were identified with the combination

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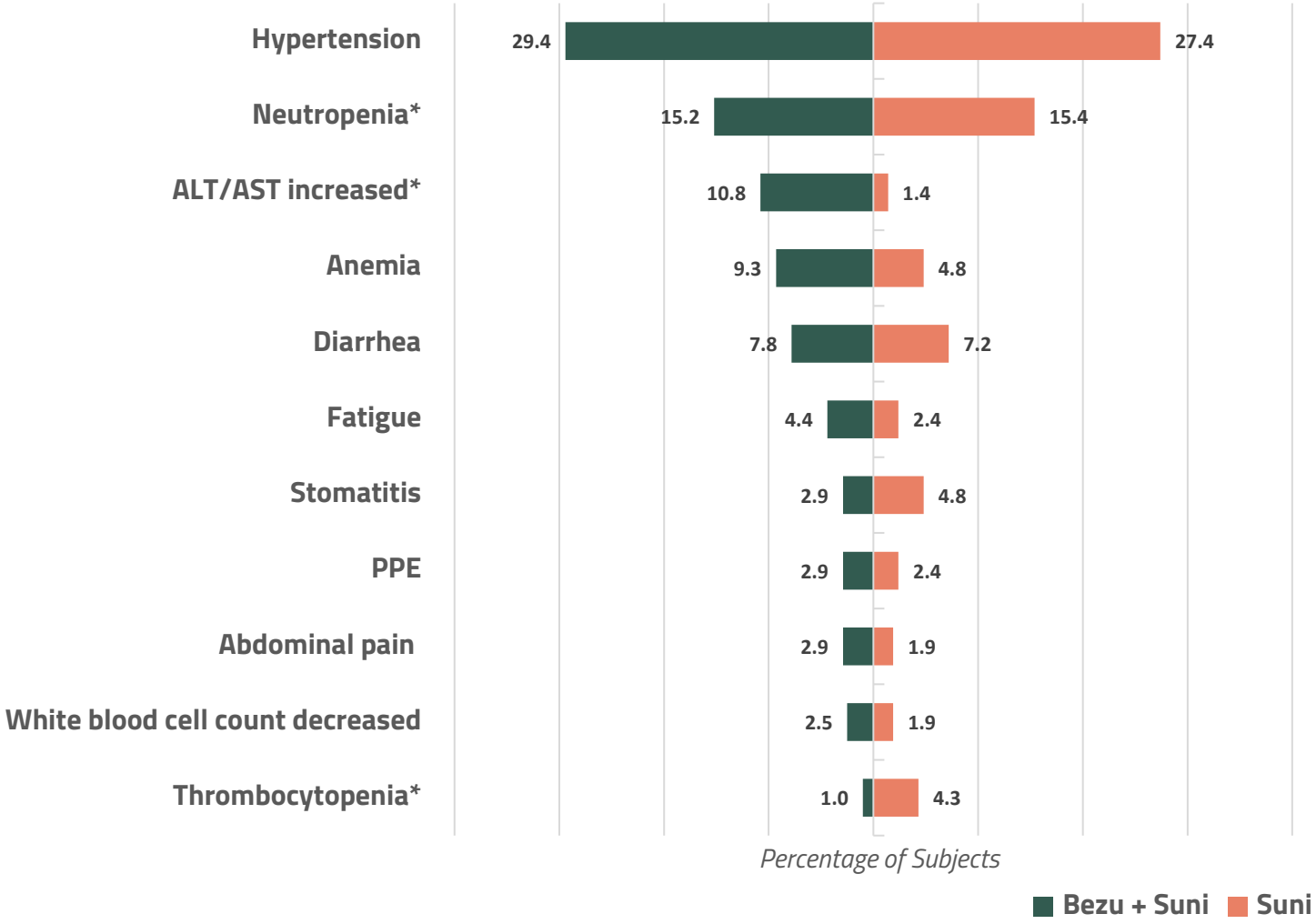
Data cut-off as of 30Sep2025; *Pooled terms; TEAE, treatment-emergent adverse event; PPE, Palmar-Plantar Erythrodysesthesia; GERD Gastroesophageal Reflux Disease

Incidence of Grade 3+ TEAEs (≥2%) Balanced Across Arms



- Majority of the Gr 3+ TEAEs were reported at a similar rate between combination and monotherapy arms; ALT/AST increase and anemia reported at higher incidence in the combination arm
- No increase in frequency of severe events observed in combination arm for some key risks seen with sunitinib (hypertension, neutropenia and diarrhea)
- ALT/AST elevations led to bezuclastinib dose reductions in 12.7% of patients and only 1.5% of patients discontinued. All Grade 3 ALT/AST events resolved, and no Grade 4 elevations were reported across the study

Data cut-off as of 30Sep2025; *Pooled Terms; PPE: Palmar-Plantar Erythrodysesthesia

66 yo Man with Metastatic GIST who Experienced an Early (PR at C3, CR at C9) and Durable Response to bezuclastinib + sunitinib (ongoing at C26)

Relevant Medical History

Site of tumor diagnosis: Jejunum/Ileum

Sites of disease:
- Target lesions: Peritoneum, mesentery, small intestine
- Baseline Sum of Diameters: 84 mm

Relevant comorbidities: Obesity; hypertension; anemia; elevated ALT and creatinine; abdominal distention; leg swelling; back pain; GERD

Peak Treatment and Dose Modifications

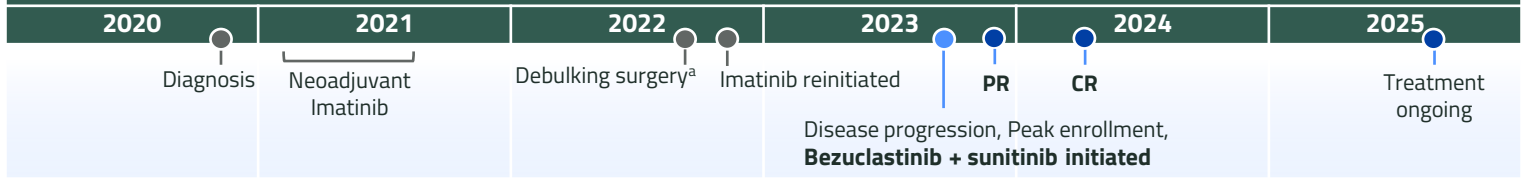
Bezuclastinib 600 mg QD + sunitinib 37.5 mg QD

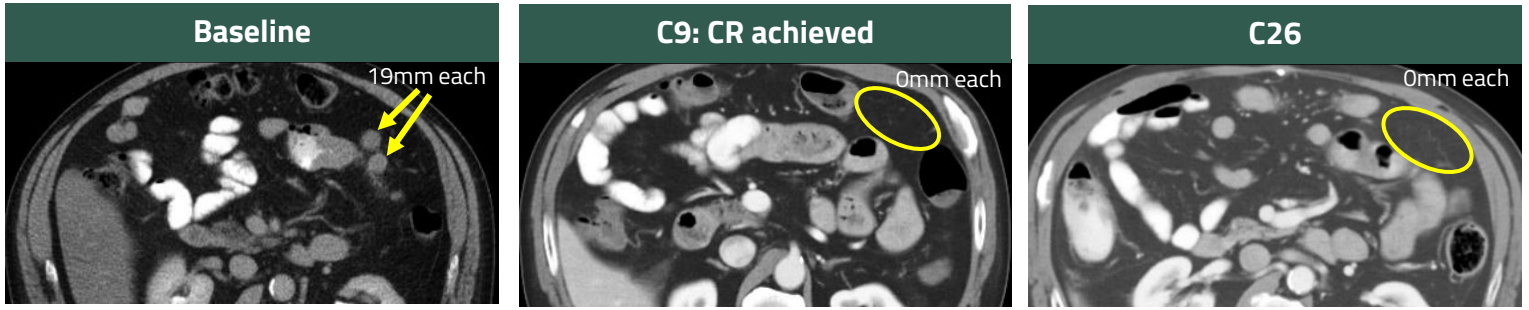
- Sunitinib reduced to 25 mg for diarrhea

TRAEs (maximum Gr reported)

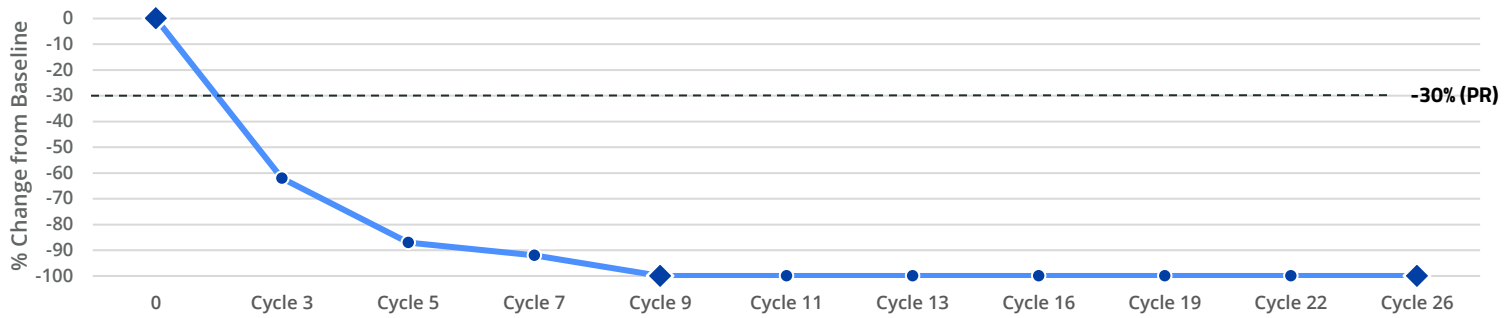
Gr 1	• Acneiform dermatitis • Hair color changes • Nausea
Gr 2	• Localized edema
Gr 3	• Diarrhea (resolved) • Neutropenia (resolved)

Treatment History





Response in Target Lesions over Time



Data cut-off as of 30Sep2025; C: Cycle; 1 cycle = 28 days; [a]Excision of abdominal tumors, intestinal resection; AE: adverse event; ALT: alanine transaminase; Gr: grade; GERD: gastroesophageal reflux disease; TRAE: treatment-related AE

69 yo Man with Metastatic GIST Responded to bezuclastinib + sunitinib Treatment at Cycle 5 (PR) and is Continuing to Benefit at Cycle 38

Relevant Medical History

Site of tumor diagnosis: Small intestine/bowel

Sites of disease:
- Target lesions: Peritoneum
- Baseline Sum of Diameters: 65 mm

Relevant comorbidities: Hemorrhoids; Gr 1 hypertension, Gr 1 anemia, anxiety, sleep apnea, hyperlipidemia, irregular heartbeat

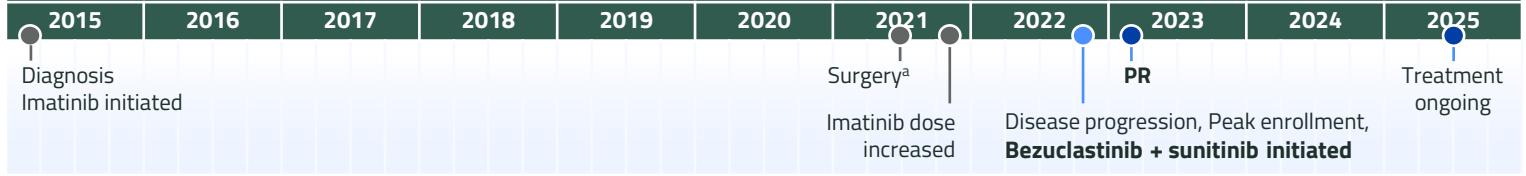
Peak Treatment and Dose Modifications

Bezuclastinib 600 mg QD + sunitinib 37.5 mg
- Following Gr 3 anemia/neutropenia:
  - Bezuclastinib interrupted→resumed at 600mg
  - Sunitinib interrupted→reduced to 25 mg

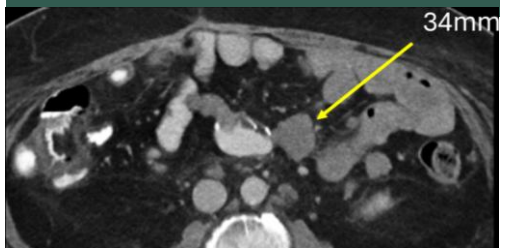
TRAEs (maximum Gr reported)

Gr 1	• Diarrhea • Hair color changes
Gr 2	• Hypertension • Hypothyroidism
Gr 3	• Neutropenia (resolved) • Anemia (related to Sunitinib only, resolved)

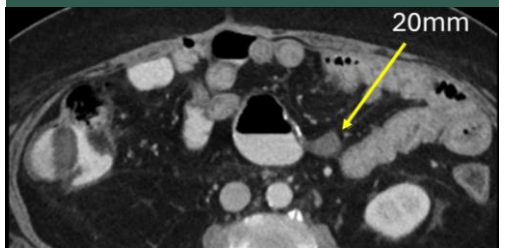
Treatment History



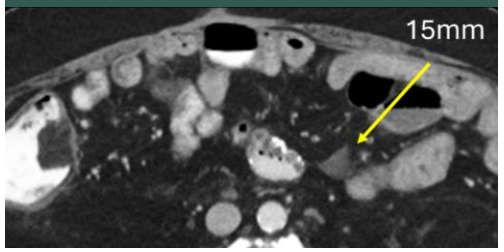
Baseline



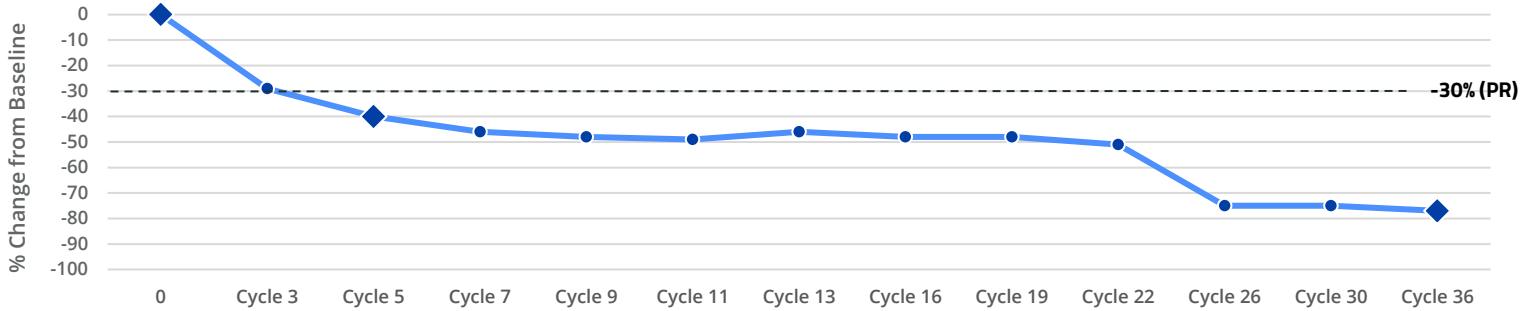
C5: PR achieved



C36



Response in Target Lesions over Time



Data cut-off as of 30Sep2025; 1 cycle = 28 days

[a]Multiple bowel/colon excisions and resections (Jan/Mar/Sep 2021), partial omentectomy (Sep2021).

AE, adverse event; C, cycle; Gr, grade; PR, partial response; QD, once daily; TRAE, treatment-related AE.

We Believe Peak Results are Transformative and Practice Changing

- Bezuclastinib combination establishes first new benchmark for 2L GIST in 20 years
  - **50% reduced risk of progression or death** compared to current standard of care
  - **16.5 months mPFS** compared to 9.2 months for sunitinib alone ($p<0.0001$)
  - **46% ORR** compared to 26% for sunitinib alone ($p<0.0001$)
  - OS immature with event rate of less than 20% at time of PFS analysis

- Generally well tolerated with **no unique risks observed** when compared to the known safety profile of sunitinib

- Estimated **19 months+ mean treatment duration** for bezuclastinib combination patients based on projection for patients remaining on combination therapy

- Active **Expanded Access Program allowing immediate availability** of the bezuclastinib combination for 2L patients with GIST

- **NDA submission** for bezuclastinib in imatinib-resistant or intolerant GIST planned 1H 2026 based on results of the Peak trial

Bezuclastinib GIST Expanded Access Program is Currently Open to Requests for Access from Treating Physicians in the United States (NCT06948955[1])

Aim

Designed to provide bezuclastinib coadministered with sunitinib outside of a clinical trial to real-world patients with GIST 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 600 mg QD plus sunitinib 37.5 mg QD. 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 histologically confirmed locally advanced metastatic and/or unresectable GIST, disease progression on imatinib or intolerance to imatinib	Discontinuation of investigational bezuclastinib due to toxicity or withdrawal of consent
Lack of adequate disease control on current therapies	Pregnant or currently breastfeeding

1. ClinicalTrials.gov. Expanded Access to Bezuclastinib to be Coadministered With Sunitinib for Patients With Gastrointestinal Stromal Tumors Identifier: NCT06948955. Retrieved July 16, 2025 from: https://clinicaltrials.gov/study/NCT06948955. ; *Other protocol-defined criteria apply

Several Additional Near Term Cogent Biosciences Catalysts

Top-line Results: Expected Dec 2025

Apex ADVANCED SM

Single-arm → **Bezuclastinib 150 mg QD**

Primary endpoint: ORR using mIWG-MRT-ECNM

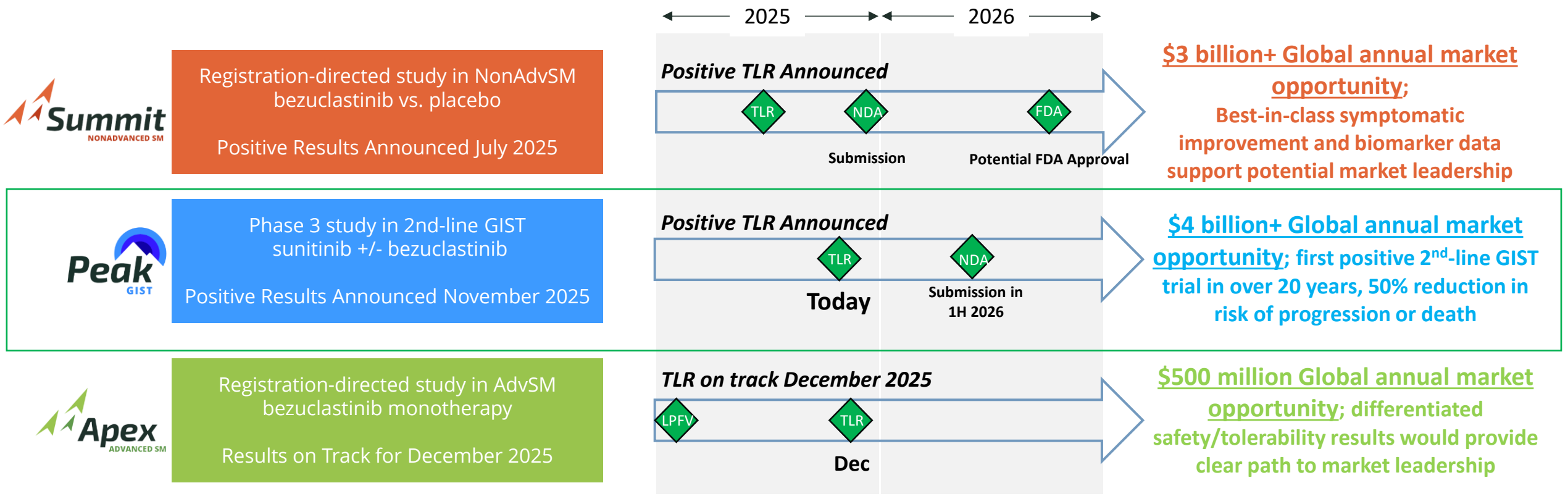
- ***Apex enrollment complete Q1 2025; TLR on track for Dec 2025***
- ***Positive Summit results provide expected read-through to Apex***
- ***Current standard of care associated with significant safety concerns; no other investigational products in clinical development***

Key Entry Criteria

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

- **ASH 2025 Presentations**
  - Two oral presentations from Summit in NonAdvanced Systemic Mastocytosis (NonAdvSM)
  - Novel selective JAK2 V617F inhibitor showcasing best-in-class potential
- **Submit first NDA for bezuclastinib in NonAdvSM expected by the end of 2025**
- **Submit NDA for bezuclastinib in imatinib-resistant or intolerant GIST patients expected in the first half of 2026**

Bezuclastinib Emerging as Potential Best-in-Class KIT Inhibitor Across Indications



Estimated aggregate global annual sales opportunity >$7.5 billion with limited competition; IP protection anticipated through 2043 based on strength of COM, PTE and pending formulation patent application

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TLR: Top-line results including primary endpoint, COM: Composition of Matter; PTE: Patent term extension


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