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42nd Annual J.P. Morgan Conference

January 9, 2024 – 4:30 p.m. PT

Real Challenges. Real Solutions.

Precision therapies for genetically defined diseases

Forward-Looking Statements and Risk Factors

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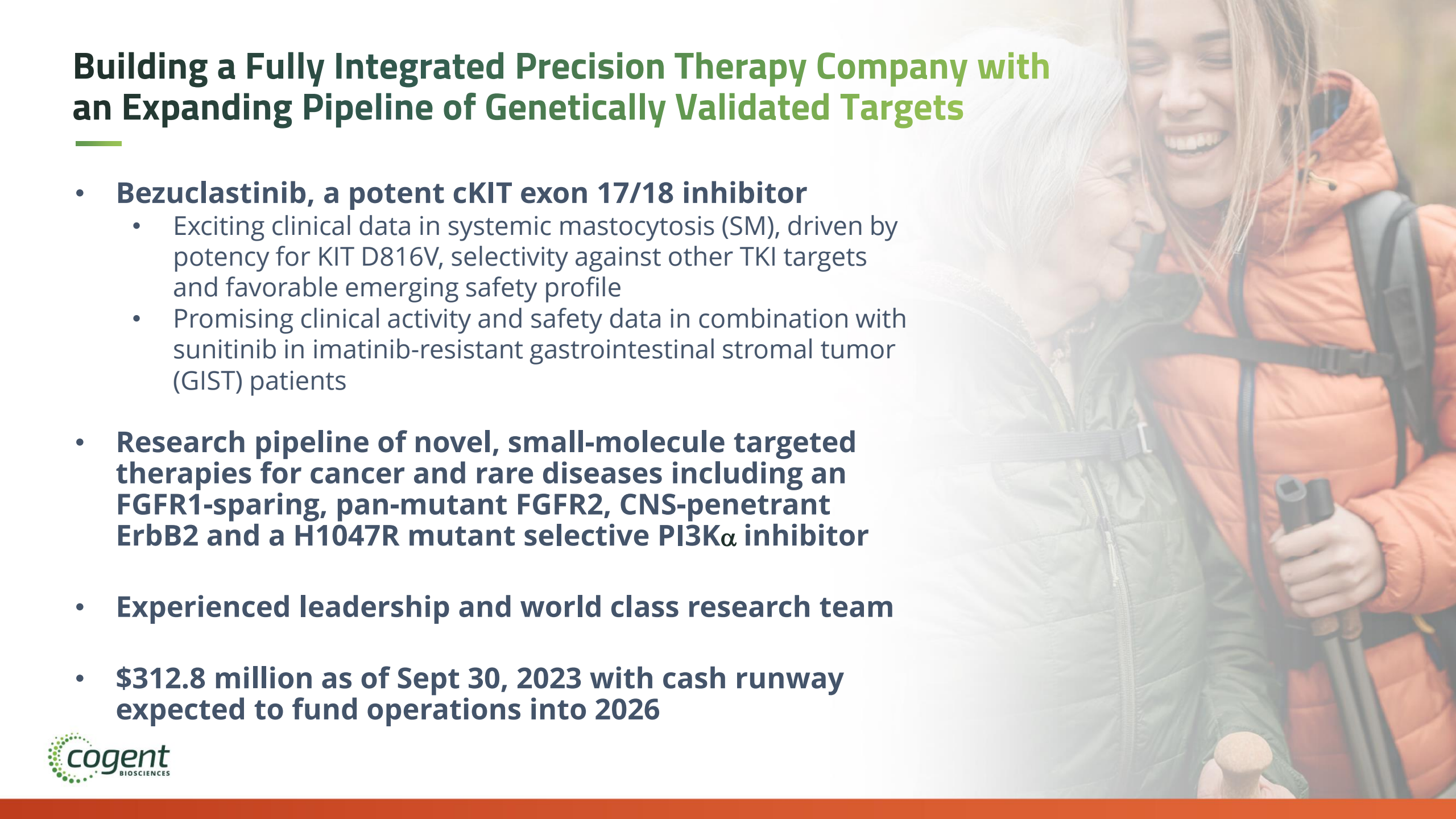
All of Cogent Biosciences, Inc. (“Cogent”) product candidates are investigational product candidates and their safety and efficacy have not yet been established. Cogent has not obtained marketing approval for any product, and there is no certainty that any marketing approvals will be obtained or as to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

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 cKIT exon 17/18 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
- **Research pipeline of novel, small-molecule targeted therapies for cancer and rare diseases including an FGFR1-sparing, pan-mutant FGFR2, CNS-penetrant ErbB2 and a H1047R mutant selective PI3Kα inhibitor**
- **Experienced leadership and world class research team**
- **$312.8 million as of Sept 30, 2023 with cash runway expected to fund operations into 2026**



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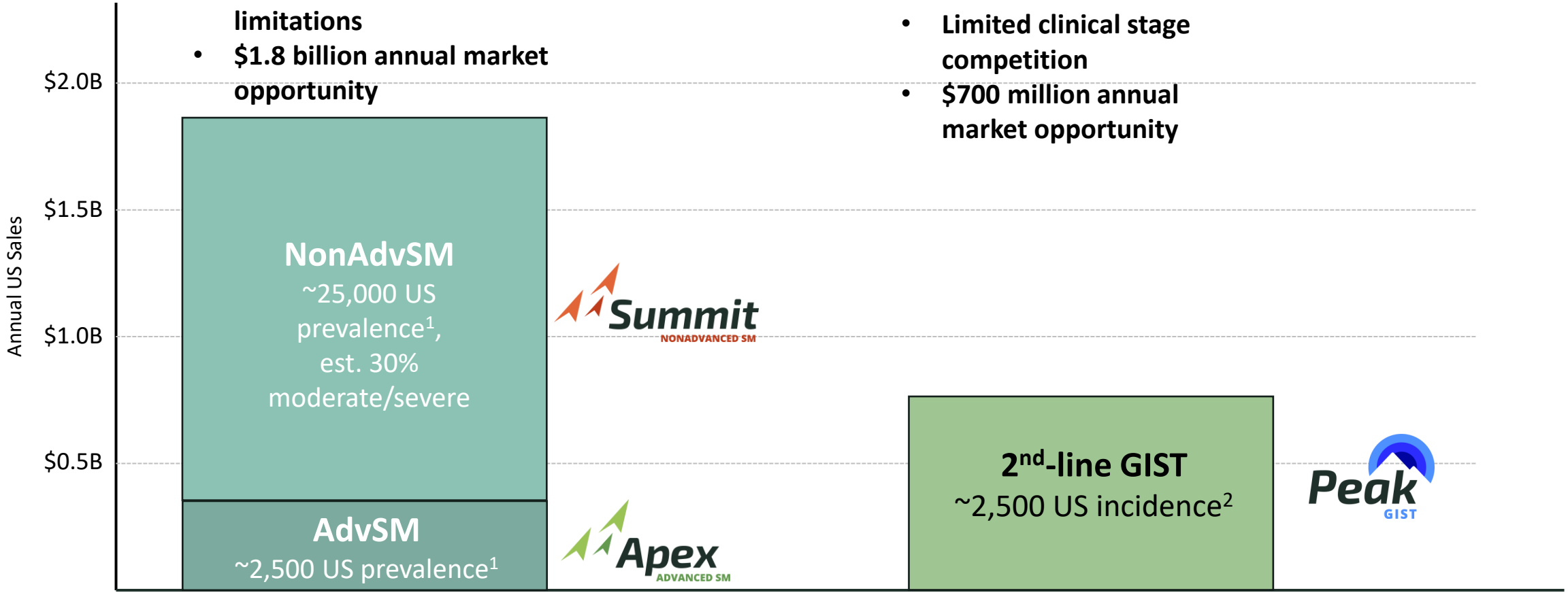
Bezuclastinib Commercial Market: Two Distinct, Attractive Franchises

Systemic Mastocytosis

- One approved drug with limitations
- $1.8 billion annual market opportunity

Gastrointestinal Stromal Tumors (GIST)

- Add-on to current SOC
- Limited clinical stage competition
- $700 million annual market opportunity



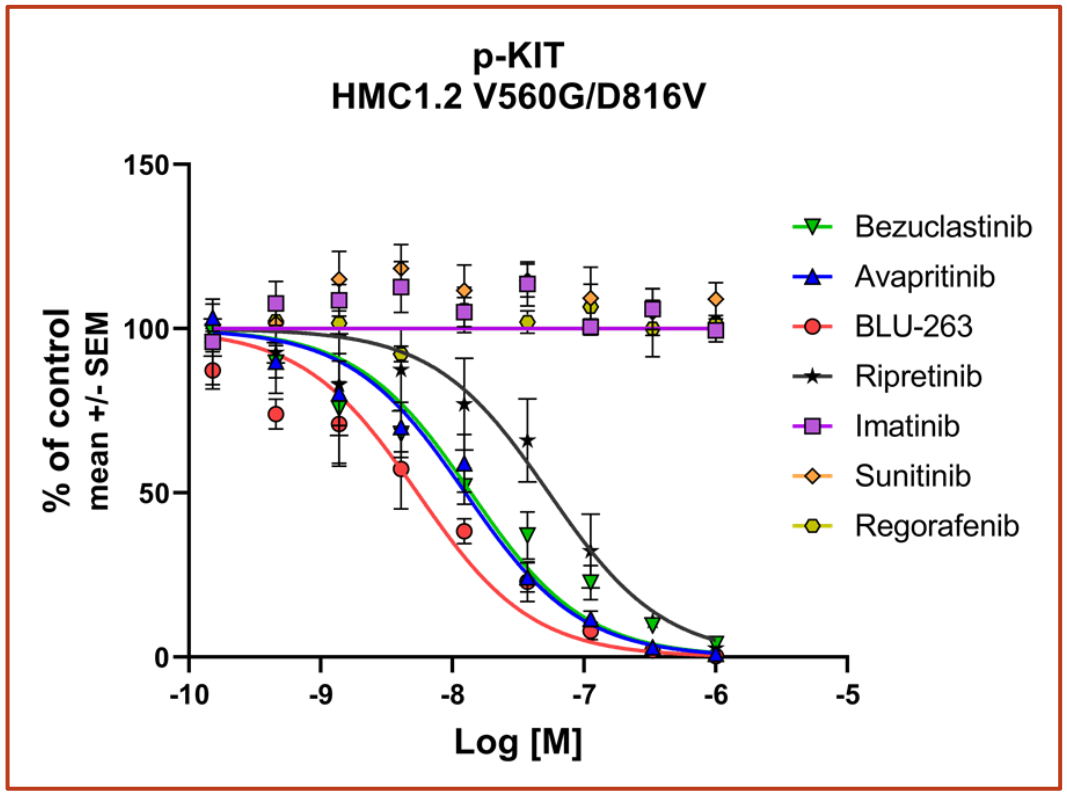
$1.8 billion **US Market Potential** **$700 million**

References: [1] Coltoff A, Mascarenhas J., 2019. [2] Gramza AW, Corless CL, Heinrich MC., 2009, https://www.cancer.net/cancer-types/gastrointestinal-stromal-tumor-gist/statistics, Internal Cogent models.

Differentiating Characteristics of Bezuclastinib

- Potent inhibitor of KIT exon 17/18
- Selective against key anti-targets
- Limited CNS distribution

Bezuclastinib Demonstrates Effective Potency Against KIT exon 17 D816V



HMC1.2 human mast cells (V560G/D816V) were treated with inhibitors for 1 hour followed by analysis for phosphorylated c-KIT ELISA (R&D Systems)

Compound	Cell IC_{50} (nM)
	KIT V560G/D816V (HMC 1.2)
Bezuclastinib	**14**
Avapritinib	13
BLU-263	6
Ripretinib	54
Imatinib	>1000
Sunitinib	>1000
Regorafenib	>1000

IC_{50} values from ELISA in (A) in nM are represented for bezuclastinib and other KIT inhibitors

Guarnieri et al, AACR Annual Meeting 2022.

Bezuclastinib Demonstrates Advantageous Selectivity Within Class

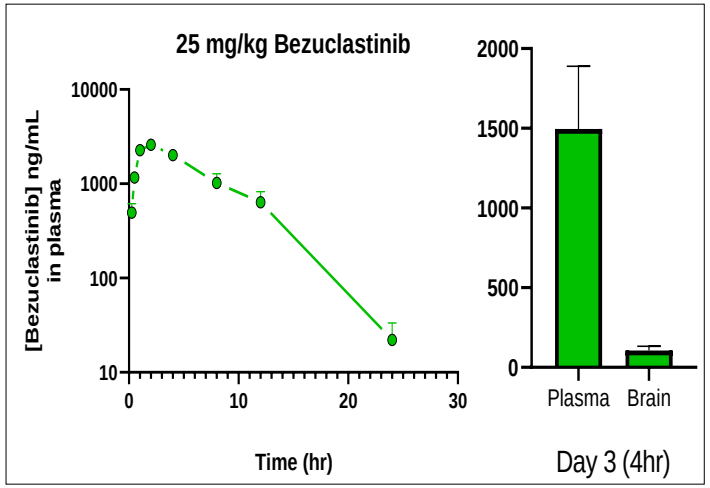
- Bezuclastinib is highly active with specificity for mutations in KIT exons 9, 11, 17, and 18
- Importantly, bezuclastinib spares closely related kinases including PDGFR, CSF1R and FLT3[1] Inhibition of closely related kinases have been linked to off-target toxicities, such as intracranial bleeding, periorbital and peripheral edema, and pleural effusions[2, 3]

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

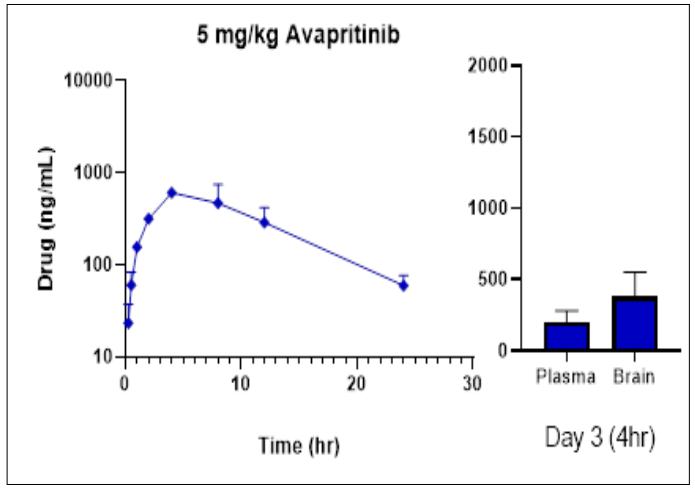
Compound	KIT D816V (HMC 1.2)	WT KIT	PDGFRα	PDGFRβ	CSF1R	FLT3	KDR
Bezuclastinib	14	121	> 10,000	> 10,000	> 10,000	> 1000	> 1000
Avapritinib	13	114	53	10	249	305	> 1000
BLU-263	6	355	21	6	161	345	> 1000

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

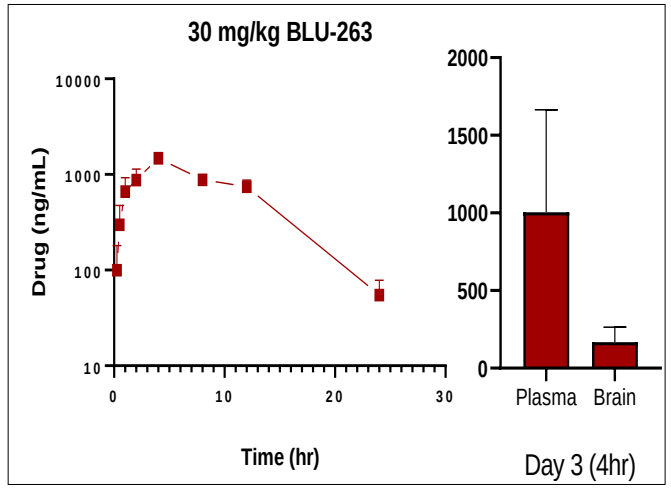
Bezuclastinib Demonstrates Minimal Brain Penetration



$t_{1/2}$ (h)	C_{max} (ng/mL)	AUC_{last} (ng·hr/mL)	Brain:Plasma ratio
7	2592 ± 364	21509 ± 2558	0.07



$t_{1/2}$ (h)	C_{max} (ng/mL)	AUC_{last} (ng·hr/mL)	Brain:Plasma ratio
13	672 ± 102	6980 ± 1156	2.0



$t_{1/2}$ (h)	C_{max} (ng/mL)	AUC_{last} (ng·hr/mL)	Brain:Plasma ratio
4	1470 ± 222	16200 ± 414	0.18

- Bezuclastinib shows minimal brain penetration with brain to plasma ratio of 0.07 compared to 2.0 for avapritinib
- The absence of brain penetration is a preferred feature for a KIT A-Loop inhibitor given the CNS-related adverse events that have been observed in this targeted class[1,2]

[1]RyDAPT [package insert]. East Hanover, New Jersey: Novartis Pharmaceuticals; 2021;
[2]AYVAKIT [package insert]. Cambridge, MA: BluePrint Medicines; 2021
As presented at AACR Annual Meeting 2022 on April 10, 2022

Bezuclastinib Emerging with Best-in-Class Clinical Profile for Systemic Mastocytosis Patients

APEX in ASM: Rapid & Deep Reductions in Biomarkers Leading to Impressive ORR

- 56% ORR by mIWG and 86% ORR by PPR in 1st-line patients
  - 100% ORR by mIWG for patients receiving 200mg daily dose
- 94% of patients achieved >50% reduction in serum tryptase
- 97% of patients achieved >50% reduction in mast cell burden

Table 3. Apex Part 1: Responses Observed by mIWG-MRT-ECNM

Best Response, n (%)[§]	Total* Confirmed and unconfirmed mIWG-MRT-ECNM Responses per CRRC Assessment (n=27)	Confirmed mIWG-MRT-ECNM Responses per CRRC Assessment (n=27)	mIWG-MRT-ECNM per CRRC Assessment* (TKI‡ Therapy Naïve) (n=18)	mIWG-MRT-ECNM per CRRC Assessment* (Prior TKI‡ Exposure) (n=9)
Overall response rate				
CR + CRh + PR + CI†	**15 (56)**	12 (44)	11 (61)	4 (44)
CR + CRh + PR	**14 (52)**	10 (37)	10 (56)	4 (44)
Complete Response (CR + CRh)	**6 (22)**	6 (22)	6 (33)	0 (0)
Partial Response (PR)	**8 (30)**	4 (15)	4 (22)	4 (44)
Clinical Improvement (CI)	**1 (4)**	2 (7)	1 (6)	0 (0)
Stable Disease (SD)	**9 (33)**	12 (44)	6 (33)	3 (33)
Not evaluable	**3 (11)**	3 (11)	1 (6)	2 (22)

§5 patients without measurable C-finding at baseline were Not mIWG-MRT-ECNM Evaluable (NE) and therefore are excluded; one additional patient was excluded due to discontinuation prior to first dose (Not Dosed [ND]).
*4 patients who remain on therapy but have not yet reached the 12-week confirmation duration for partial response (PR) are included
‡ SM-directed therapy with midostaurin and/or avapritinib
† Primary endpoint of Apex study

Data as of: 25Sep2023

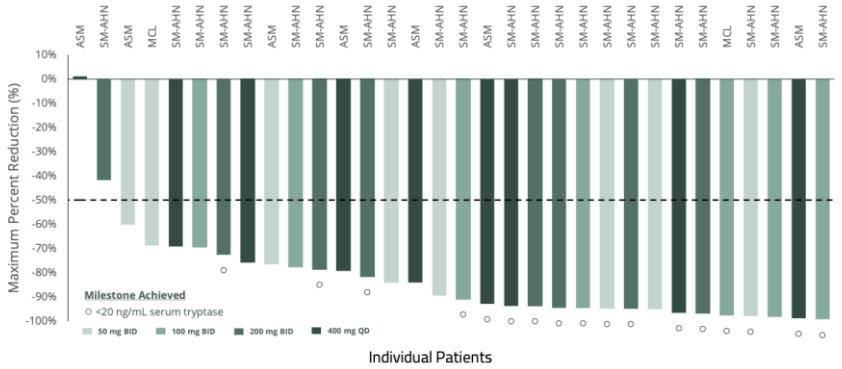
Table 4. Apex Part 1: Responses Observed by PPR Criteria

Best Response, n (%) [¤]	Total (n=32)	PPR per Investigator Assessment (TKI‡ Therapy Naïve) (n=22)	PPR per Investigator Assessment (Prior TKI‡ Therapy) (n=10)
Overall response rate (CR + PR)	**24 (75)**	19 (86)	5 (50)
Complete Response (CR)	**13 (41)**	12 (55)	2 (20)
Partial Response (PR)	**11 (34)**	7 (32)	3 (33)
Stable Disease (SD)	**5 (16)**	2 (9)	3 (33)
Not Evaluable	**3 (9)**	1 (5)	2 (20)

¤ One patient was excluded due to discontinuation prior to first dose (Not Dosed [ND]).
‡ SM-directed therapy with midostaurin and/or avapritinib

Data as of: 25Sep2023

Figure 4. Deep Reductions in Serum Tryptase, *(n=32§)*

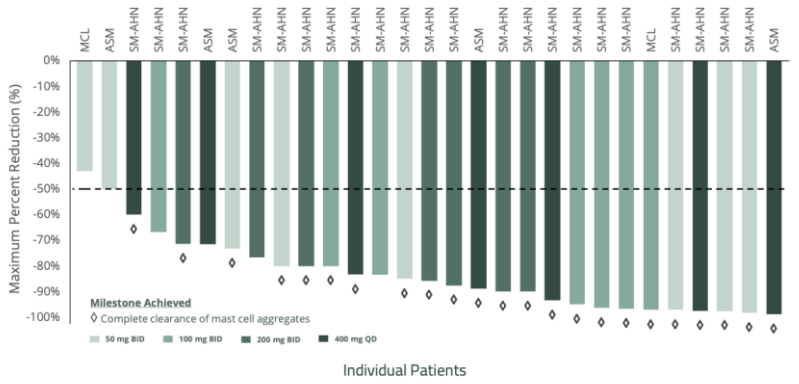


§One patient without post-baseline data was excluded

Data as of: 25Sep2023

- 94% (30/32) of patients achieved a ≥ 50% reduction
- 100% (29/29) of patients with at least 2 cycles of treatment achieved a ≥ 50% reduction
- 53% (17/32) achieved below 20 ng/mL
- Median time to first serum tryptase <20 ng/mL was 4.0 weeks (range: 1.1-66.9)

Figure 6. Deep Reductions in Mast Cell Burden, *(n=29§)*



§Four patients without post-baseline data were excluded

Data as of: 25Sep2023

- 97% (28/29) of patients with baseline and at least 1 post-baseline assessment achieved a ≥ 50% reduction
- 79% (23/29) achieved complete clearance of mast cell aggregates by central review
- Median time to first clearance of mast cell aggregates was 9.0 weeks (range: 7.3-34.3)

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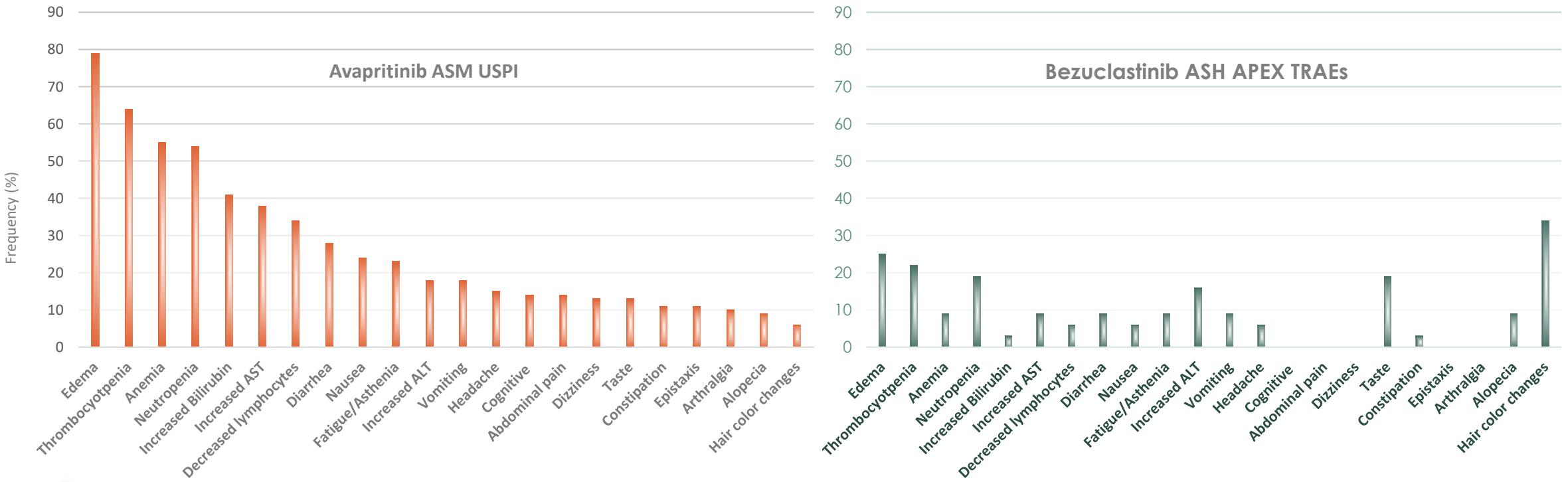
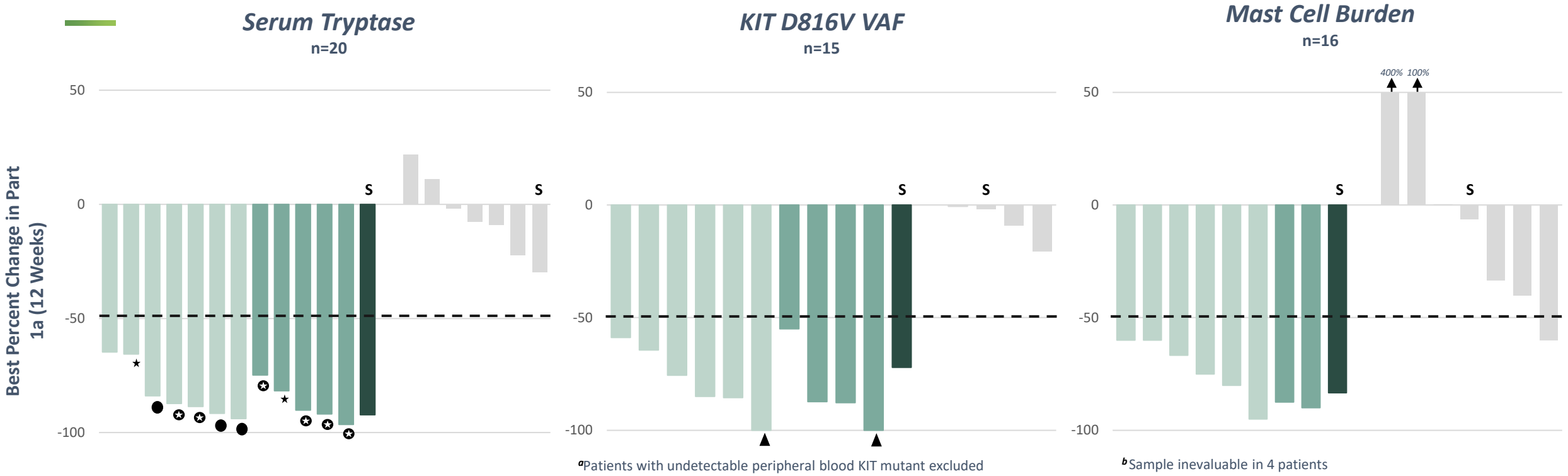
ASM Clinical Trials: Safety & Tolerability Summary of KIT Inhibitors

	Median duration of exposure	Gr3+ AE	SAE	Reductions due to AEs	Discontinuations due to AE	Intracranial Bleeding	AEs leading to Death
Avapritinib (n=80) *(Recommended dose 200mg)*	7.5 months	72%	34%	68%	10%	3 patients	3 patients
Avapritinib (n=148) *(All doses)*	10.3 months	81%	49%	70%	15%	11 patients	9 patients
Bezuclastinib (n=32) *(All doses)*	7.2 months	63%	28%	28%	9%	0 patients	0 patients



- AYVAKIT® (avapritinib) [US package insert]; AYVAKIT® FDA Medical Review
- Lab abnormalities terms in AVA USPI are based on lab worsening from baseline; Bezu includes lab abnormalities reported as AEs
- APEX data as of 25Sep2023

SUMMIT: Preserving Dose Intensity Resulted in Striking Biomarker Reductions



[a]Patients with undetectable peripheral blood KIT mutant excluded

[b]Sample inevaluable in 4 patients

- 90% (9/10) of patients with baseline serum tryptase ≥20ng/mL achieved <20ng/mL after 12 weeks of bezuclastinib
- 67% (8/12) of patients with baseline serum tryptase ≥11.4ng/mL achieved <11.4ng/mL after 12 weeks of bezuclastinib

Dose
- 100 mg QD bezuclastinib
- 200 mg QD bezuclastinib
- 400 mg QD bezuclastinib
- Placebo

Serum Tryptase Outcomes
- ● Achieved <20ng/mL[μ]
- ★ Achieved <11.4ng/mL[μ]
- ✪ Achieved both[μ]

KIT D816V VAF Outcomes
- ▲ Achieved <0.03% (LLD)

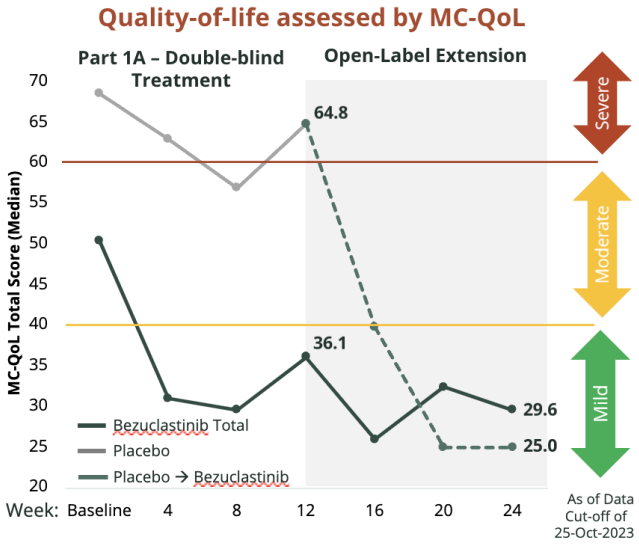
S SSM

[μ]In order to achieve, serum tryptase must have been above the threshold at baseline
LLD, lower limit of detection

As of Data Cut-off of 25-Oct-2023

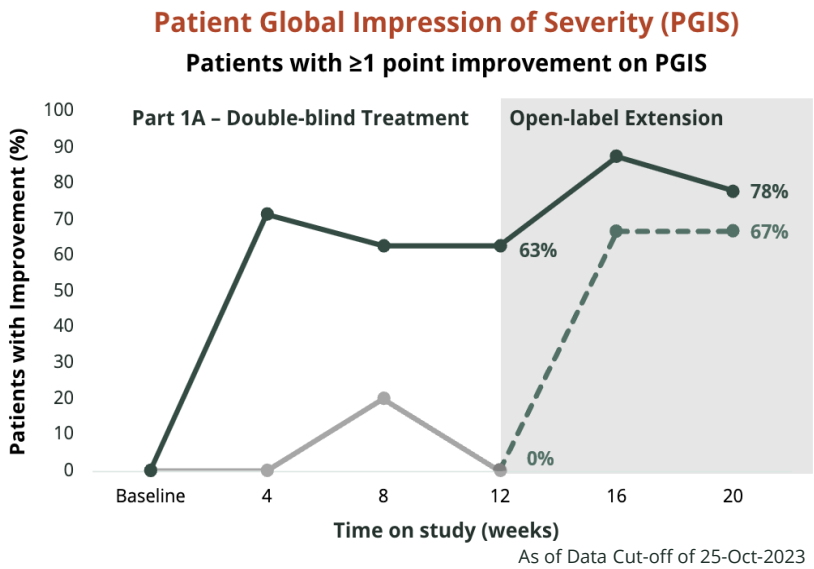
SUMMIT: Preliminary Patient Reported Outcomes Data Suggests Rapid Symptomatic Improvement

MC-QoL



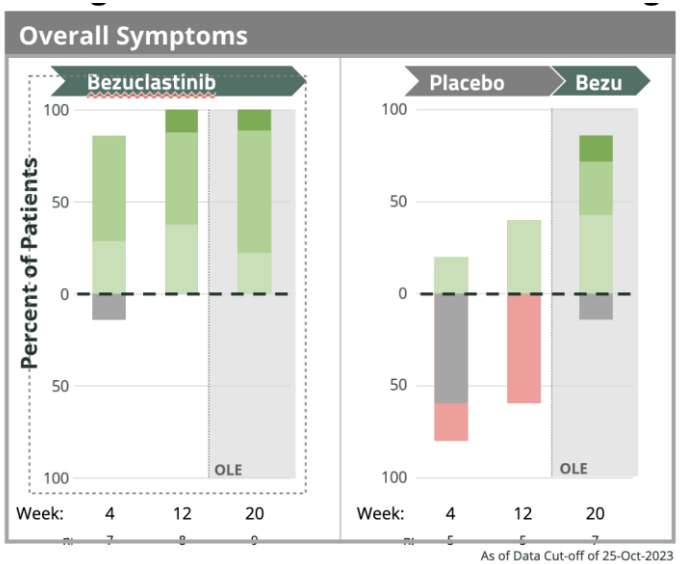
- 37% median best improvement within 12 weeks
- 57% median best improvement within 20 weeks
- 75% median best improvement for placebo cross within 8 weeks

PGIS



- 71% of patients had meaningful improvement by week 4
- 78% of patients had meaningful improvement by week 20
- 67% of placebo cross patients had meaningful improvement by week 4

PGIC



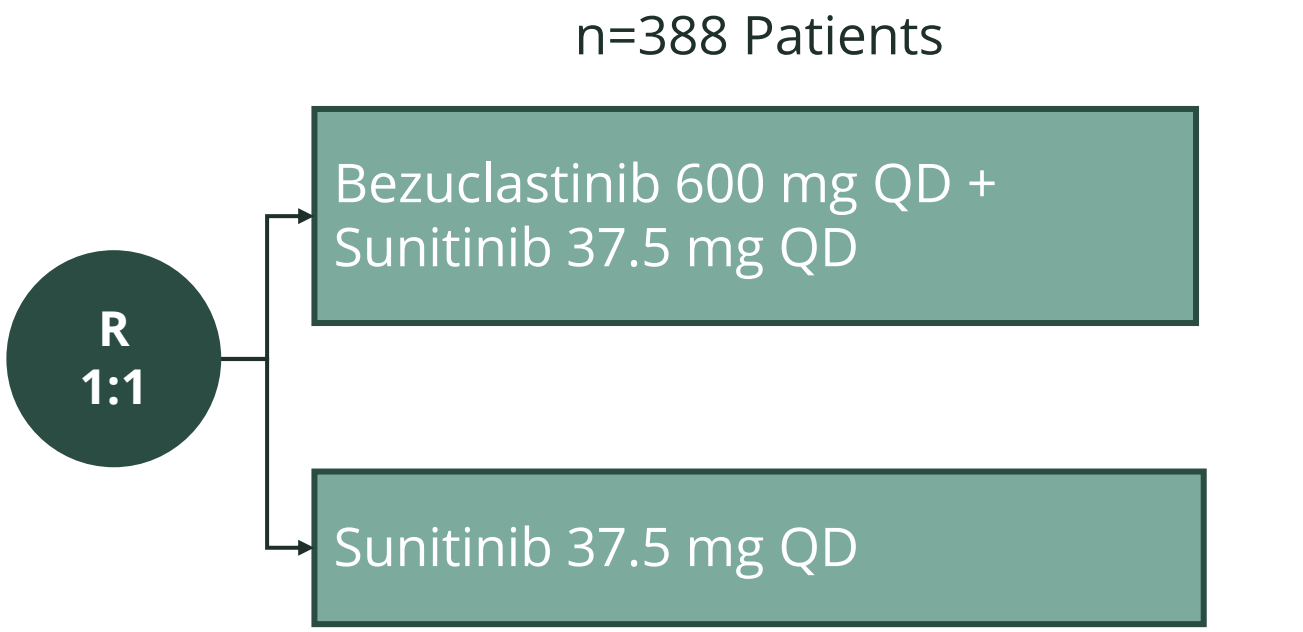
- 63% of patients had meaningful improvement by week 12
- 78% of patients had meaningful improvement by week 20
- 43% of placebo cross patients had meaningful improvement by week 8

Phase 3 PEAK study for 2nd-line GIST patients on track to complete enrollment in 2024

PEAK: Global Phase 3 Pivotal Trial in 2nd-line GIST Patients

KEY ENTRY CRITERIA

- Histologically confirmed Gastrointestinal Stromal Tumors (GIST) w/at least 1 measurable lesion per mRECIST v1.1
- Locally advanced, unresectable or metastatic
- Documented disease progression on or intolerance to imatinib
- ECOG Performance Status 0-2
- No other prior treatment (other than imatinib)



Primary endpoint: median Progression Free Survival

Rationale for Treatment of GIST with Bezuclastinib in Combination with Sunitinib

- Global standard for 1st-line therapy of advanced KIT-mutant GIST is treatment with imatinib, which targets primary KIT mutations in exons 9 and 11.
- Secondary resistance mutations in the KIT ATP-binding domain (exons 13, 14), activation loop (exons 17, 18), or both can develop and result in loss of imatinib-sensitivity[1-4]
- While no single tyrosine kinase inhibitor (TKI) inhibits all mutations, the combination of bezuclastinib (targeting exons 9, 11, **17**, and **18**) and sunitinib (targeting exons 9, 11, **13**, and **14**) targets the full spectrum of primary and **secondary resistance mutations**.[5]

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

[1]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.

Bezuclastinib + Sunitinib Combination Well Tolerated in Peak Lead-In Trial

- Majority of TEAEs were of low CTCAE 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 (24%) dose reductions of any study medications due to TEAEs
- Infrequent (n=2) discontinuations due to TEAEs
  - Gr 2 Rash; Gr 1 abdominal pain and Gr 3 diarrhea

TEAEs >15%	Total (n=42)	
	All Grade (%)	Grade 3/4 (%)
Diarrhea	52	5
Fatigue	43	-
Nausea	33	-
Hair Color Changes	31	-
Hypertension	31	14
Taste disorder	29	-
GERD	19	-
ALT/AST increased	19	5
Neutropenia	17	5
Rash	17	-

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

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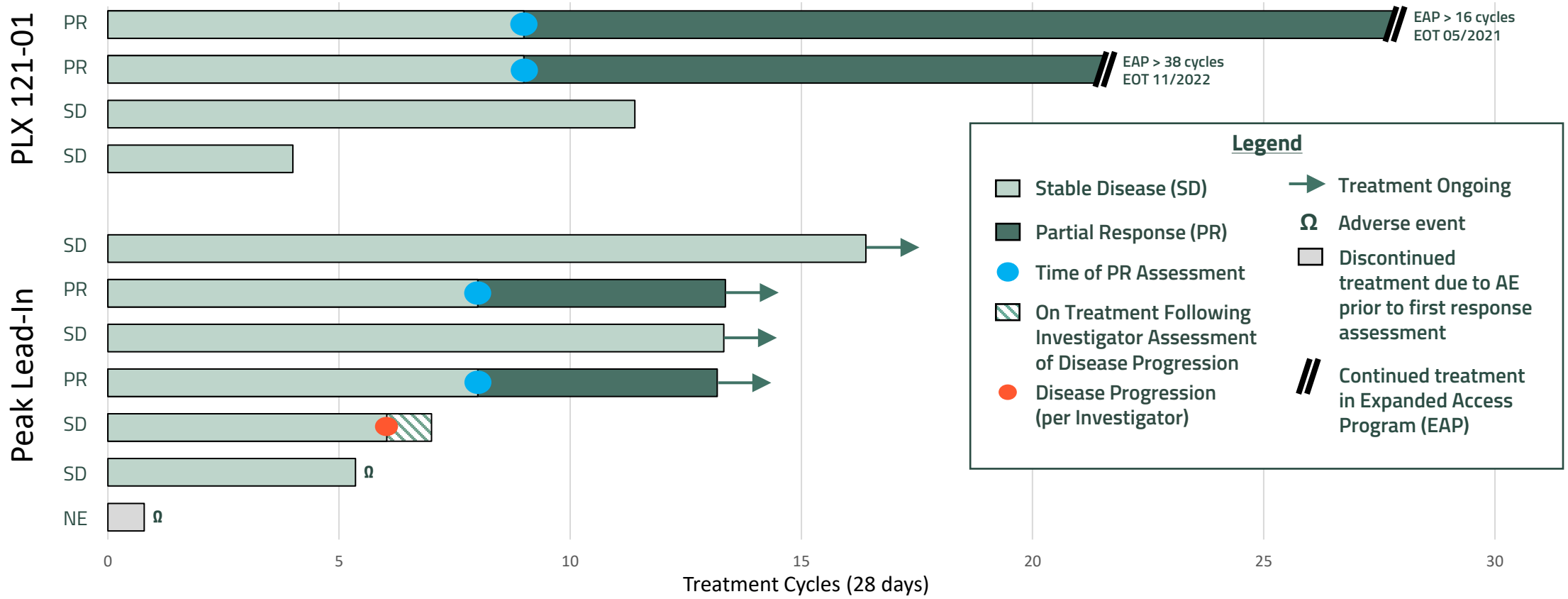
Somaiah N., et al. CTOS Annual Meeting; Dublin, Ireland, 1-4 November 2023

Bezuclastinib + Sunitinib in 2nd-line GIST: Encouraging ORR & 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: avapritnib in VOYAGER trial (3rd-line)
- 4.2 months: regorafenib in VOYAGER trial (3rd-line)

Cogent Biosciences: Anticipated 2024 Milestones & Catalysts

Cogent Biosciences: Upcoming Catalysts

Clinical Milestones

- Present results from complete SUMMIT Part 1 at AAAAI in Q1 2024
- Initiate global, registration-directed SUMMIT Part 2 trial in 1H 2024
- Complete enrollment in global, pivotal Phase 3 PEAK trial by YE 2024
- Complete enrollment in registration-directed APEX Part 2 by YE 2024

Research Milestones

- Initiate Phase 1 trial of CGT4859, a potential best-in-class, FGFR2 inhibitor in 2H 2024
- Initiate IND-enabling studies for CNS-penetrant, potent ErbB2 inhibitor
- Select clinical candidate and initiate IND-enabling studies for a novel H1047R PI3Kα inhibitor

Expected cash runway into 2026; $312.8 million as of September 30, 2023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Real Challenges. Real Solutions.
Precision therapies for genetically defined diseases