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Corporate Presentation

November 2024

Real Challenges. Real Solutions.

Precision therapies for genetically defined diseases

Forward-Looking Statements and Risk Factors

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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; 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; business interruptions resulting from public health crises, which could cause a disruption of the development of our product candidates and adversely impact our business; 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's 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.

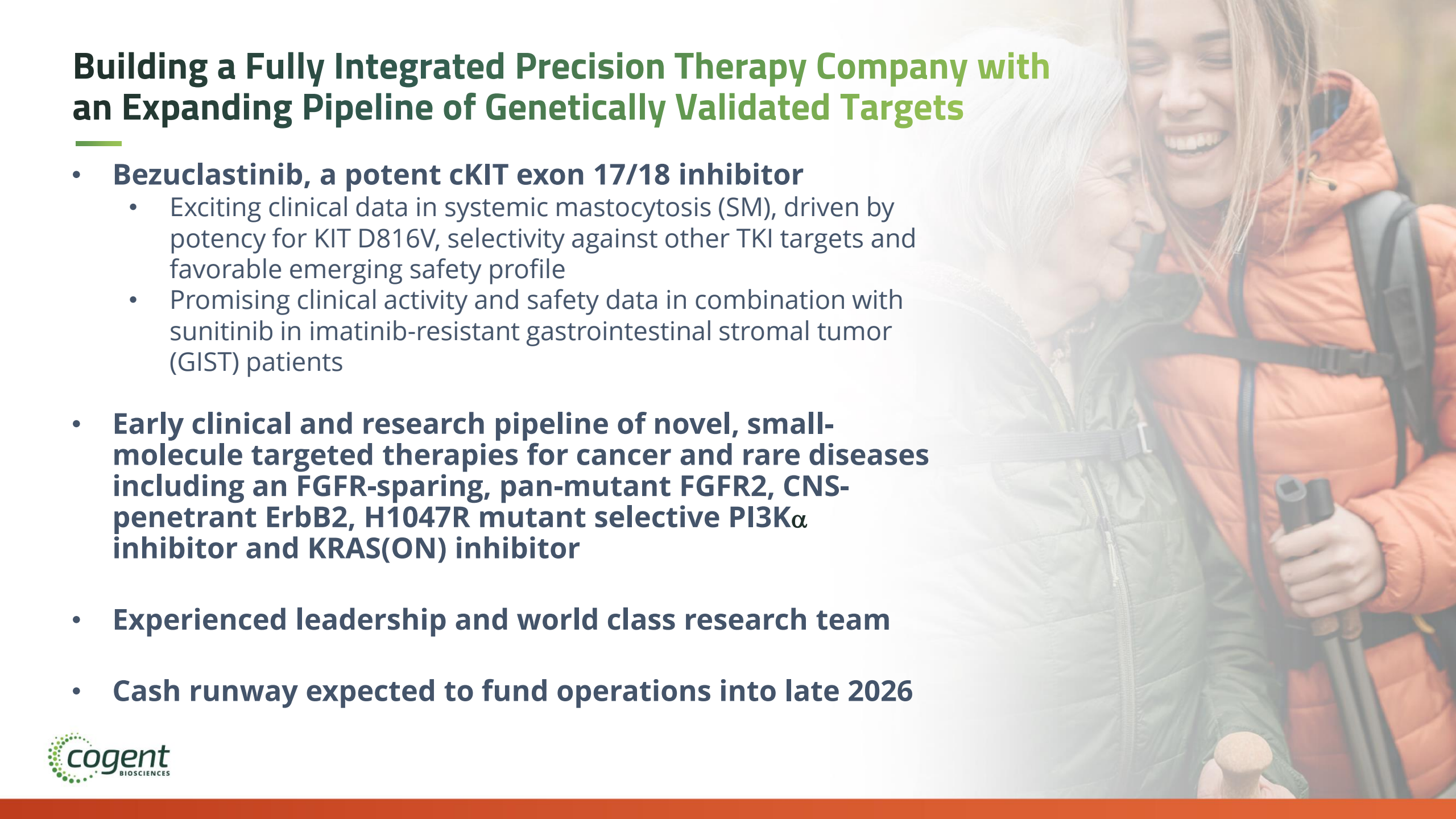
Building a Fully Integrated Precision Therapy Company with an Expanding Pipeline of Genetically Validated Targets

- **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

- **Early clinical and research pipeline of novel, small-molecule targeted therapies for cancer and rare diseases including an FGFR-sparing, pan-mutant FGFR2, 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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Leadership with Deep Scientific Expertise in Precision Medicine

Andrew Robbins
President &
Chief Executive Officer

Jessica Sachs, MD
Chief Medical Officer

Cole Pinnow
Chief Commercial Officer

John Robinson, PhD
Chief Scientific Officer

Evan Kearns, JD
Chief Legal Officer

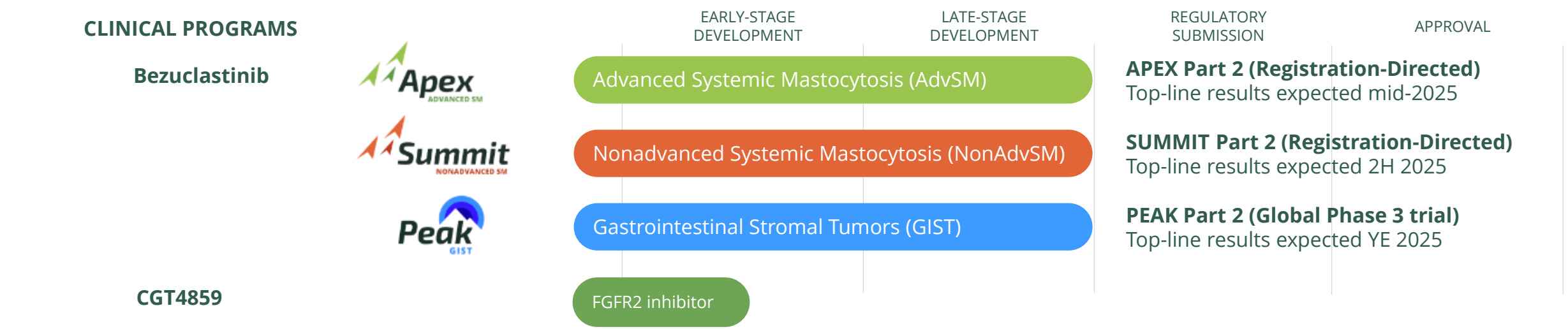
John Green
Chief Financial Officer

Erin Schellhammer
Chief People Officer

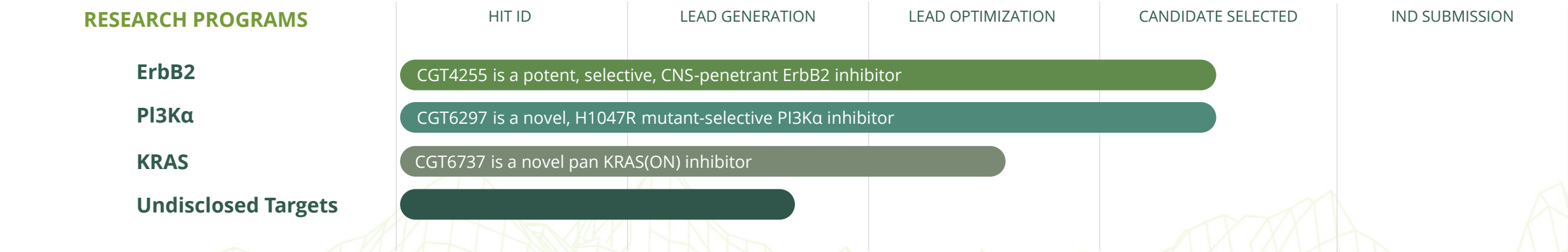
Brad Barnett
Chief Technology Officer

Multiple Clinical and Preclinical Programs with Upcoming Catalysts

CLINICAL PROGRAMS



RESEARCH PROGRAMS



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

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

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[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.

KIT MUTANT COMPETITIVE LANDSCAPE
Minimal Late-Stage Competitive Activity with Clear Path to Best-in-Class Position

Gastrointestinal Stromal Tumors (GIST)

	sunitinib	ripretinib	bezuclastinib + sunitinib
Exon 13/14 potent:	✓	✗	✓
Exon 17/18 potent:	✗	✓	✓
2nd-line status:	Approved	Negative Phase 3	Phase 3 ongoing

Active trials

Late-stage:	None	Exon 11+ 17/18 only
Early-stage:	IDRX-42 in first-in-human clinical studies	

Systemic Mastocytosis

	avapritinib	elenestinib	bezuclastinib
D816V potent:	✓	✓	✓
CNS selective:	✗	✓	✓
PDGFR sparing:	✗	✗	✓
FLT3/CSF1R sparing:	✗	✗	✓
ASM:	Approved	Phase 1/2	Phase 2
NonAdvSM:	Approved	Phase 2/3	Phase 2

Active trials

Early-Stage Trials: None

Bezuclastinib Offers Best-in-Class KIT Inhibitor Opportunity

Summit NONADVANCED SM

Registration-directed study in NonAdvSM
bezuclastinib vs. placebo
n=159, 24-week MS2D2 primary endpoint[1]

Peak GIST

Phase 3 study in 2nd-line GIST
bezuclastinib +/- sunitinib
n=388, mPFS primary endpoint

Apex ADVANCED SM

Registration-directed study in AdvSM
bezuclastinib monotherapy
n=65, ORR primary endpoint

$1.5 billion US annual market opportunity; SUMMIT Part 1b results provide path to market leadership

$700 million US annual market opportunity, no competition for broad 2nd-line GIST population

$300 million US annual market opportunity; avapritinib safety/tolerability concerns provides path to market leadership

Aggregate US annual sales opportunity $2.5 billion with limited competition

As of September 30, 2024, $345.5M cash on hand expected to fund all top-line readouts and into late 2026

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LPFV: Projected last patient, first visit signifies end of enrollment period
TLR: Projected top-line results from primary endpoint of trial
[1]PROM to measure endpoints subject to final FDA validation

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

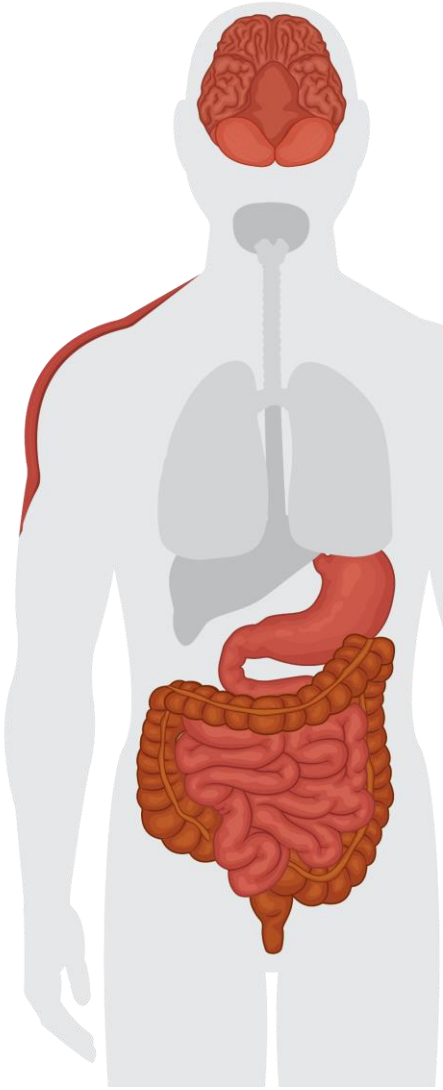
Neurological
Headache, brain fog, cognitive dysfunction, anxiety, depression

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



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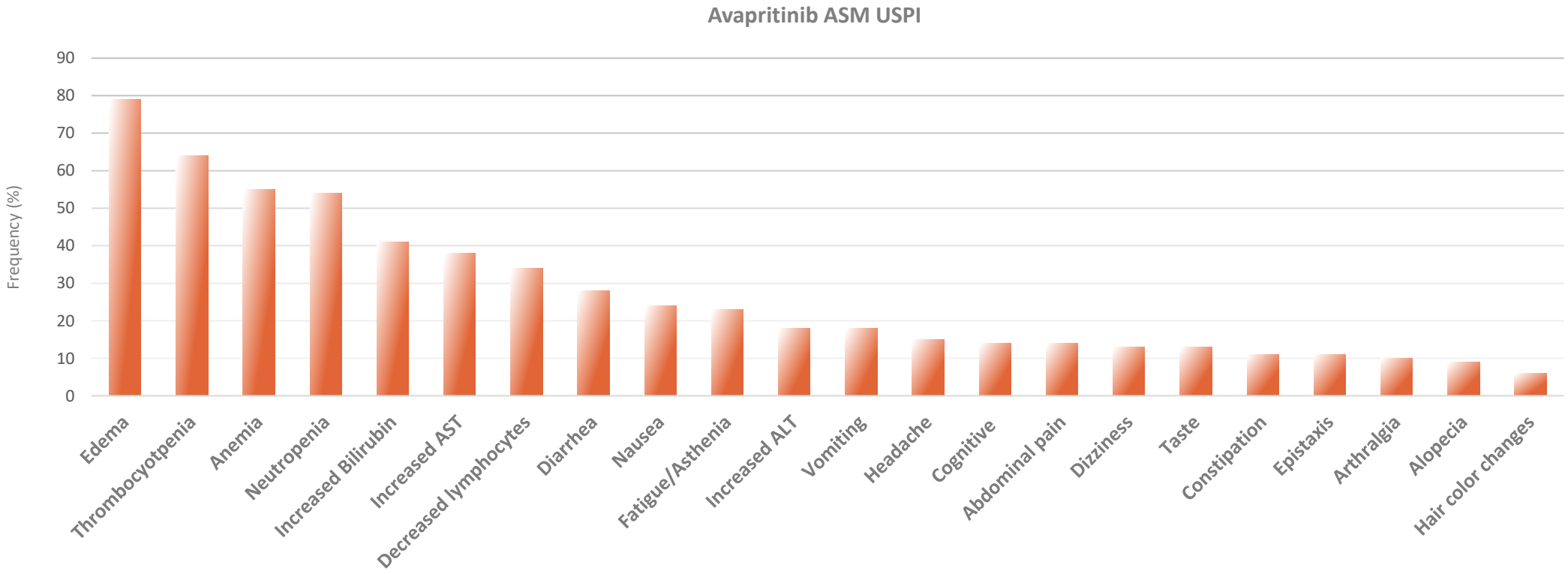
References: [1]Pardanani A. Am J Hematol. 2021;96(4):508-525. [2]Ustun C et al. Haematologica. 2016;101(10):1133-1143. [3]Lim K-H et al. Blood. 2009;113(23):5727-5736. [4]AYVAKIT (avapritinib) [package insert]. Blueprint Medicines Corporation; 2023. [5]RYDAPT (midostaurin) [package insert]. Novartis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

AdvSM Avapritinib Safety & Tolerability

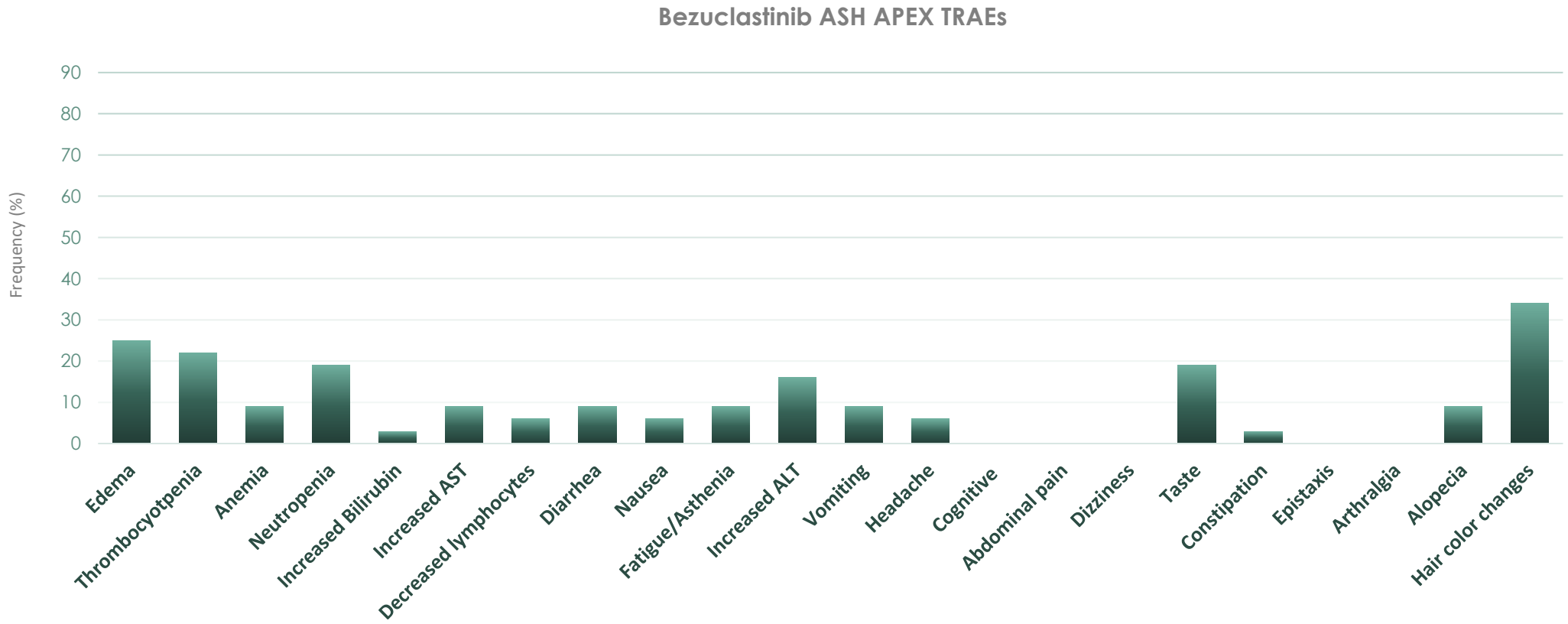
	Median duration of exposure	Gr3+ AE	SAE	Reductions due to AEs	Discontinuations due to AE	Intracranial Bleeding	AEs leading to Death
Avapritinib (n=80) *(Recommended dose 200mg)*	7.5 months	72%	34%	68%	10%	3 patients	3 patients
Avapritinib (n=148) *(All doses)*	10.3 months	81%	49%	70%	15%	11 patients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



• AYVAKIT® (avapritinib) [US package insert]; AYVAKIT® FDA Medical Review
• Lab abnormalities terms in AVA USPI are based on lab worsening from baseline

AdvSM Bezuclastinib APEX ASH Safety & Tolerability

	Median duration of exposure[1]	Gr3+ AE	SAE	Reductions due to AEs	Discontinuations due to AE	Intracranial Bleeding	AEs leading to Death
Bezuclastinib (n=32) *(All doses)*	7.2 months	63%	28%	28%	9%	0 patients	0 patients



[1]Data from ongoing APEX trial
APEX data as of 25Sep2023

BEZUCLASTINIB IN ADVANCED SYSTEMIC MASTOCYTOSIS

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Safety and Efficacy of Bezuclastinib (CGT9486), a Novel, Highly Selective, Potent KIT D816V Tyrosine Kinase Inhibitor, in Patients with Advanced Systemic Mastocytosis (AdvSM): Results From Part 1 of the Phase 2 Apex Trial

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[1]University of Alabama Birmingham, [2]Huntsman Cancer Institute, University of Utah, Division of Hematology & Hematologic Malignancies, Salt Lake City, UT; [3]David Geffen School of Medicine at UCLA, Los Angeles, [4]St. Michael's Hospital, Toronto, [5]Hospital Universitario Ramón y Cajal, Madrid; [6]Institut Catala d'Oncologia, Barcelona; [7]CEREMAST Toulouse, CHU Toulouse; [8]University College London Hospitals NHS Foundation Trust, London; [9]Emory University School of Medicine, Atlanta; [10]ARUP Laboratories, University of Utah School of Medicine, Salt Lake City; [11]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli",Bologna, ITA; [12]University of Freiburg, Freiburg; [13]Cogent Biosciences, Inc., Waltham, MA; [14]City of Hope Medical Center, Duarte, CA

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Precision therapies for genetically defined diseases

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

2023

KEY ENTRY CRITERIA

- ASM, SM-AHN, or MCL per WHO 2022 Classification
- Confirmed measurable disease per mIWG-MRT-ECNM (mIWG)
- No restrictions on prior therapy
- Platelet count ≥50 x 10^9/L

PART 1: DOSE OPTIMIZATION FORMULATION A

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

→ Selected Exposure/Dose

PART 2: EXPANSION OPTIMIZED FORMULATION B∫

- ~65 patients @ 150mg QD
- ~10 patients @ 300 mg QD*

PART 2: ADDITIONAL COHORTS

- ~15 patients w/o measurable C-findings @ 150mg QD
- ~20 high-risk AHN patients @ 150mg QD w/concomitant AHN therapies
- Other patient sub-groups under consideration

Primary Endpoint

- **Part 1:** Incidence of AEs/SAEs, laboratory changes, PK, biomarkers, ORR
- **Part 2:** 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, BM mast cells

∫Formulation B is an optimized formulation with improved bioavailability
*Designed to explore the effect of exceeding IC90 KIT D816V engagement in AdvSM patients.

Bezuclastinib Continues to Demonstrate a Differentiated Safety Profile

2023

- The majority of adverse events were of low grade and reversible.
- No related cognitive impairment or bleeding events reported.
- The majority of hematological adverse events were of low grade, reversible and did not require dose reduction.
- Related SAEs reported in 4 patients including Gr4 Thrombocytopenia, Gr3 Hypersensitivity (mediator flare), Gr3 Leishmaniasis, and Gr3 DILI (presented with late onset [day 488] and mixed cholestatic pattern of injury and subject was subsequently found to have biliary outflow tract obstruction).
- 9/32 patients required dose reduction due to adverse events, 6 of whom were at 400 mg; 3/32 patients discontinued due to adverse events.

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)**	**0**	0	4 (57)	3 (38)	4 (44)
Thrombocytopenia*	**7 (22)**	**2 (6)**	0	4 (57)	1 (13)	2 (22)
Transaminase increased*	**7 (22)**	**1 (3)**	3 (38)	2 (29)	1 (13)	1 (11)
Neutropenia*	**6 (19)**	**3 (9)**	1 (13)	2 (29)	1 (13)	2 (22)
Taste disorder*	**6 (19)**	**0**	1 (13)	1 (14)	1 (13)	3 (33)
Peripheral edema	**4 (13)**	**0**	0	1 (14)	1 (13)	2 (22)
Periorbital edema	**4 (13)**	**1 (3)**	0	0	3 (38)	1 (11)

Includes pooled preferred terms

DILI – Drug Induced Liver Injury
Data as of: 25Sep2023
Vachhani P,. et al. American Society of Hematology (ASH) 2023; San Diego, CA, 11 Dec 2023: Publication Number: 4567

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

2023

- 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 (%)[a]	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)

[a]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

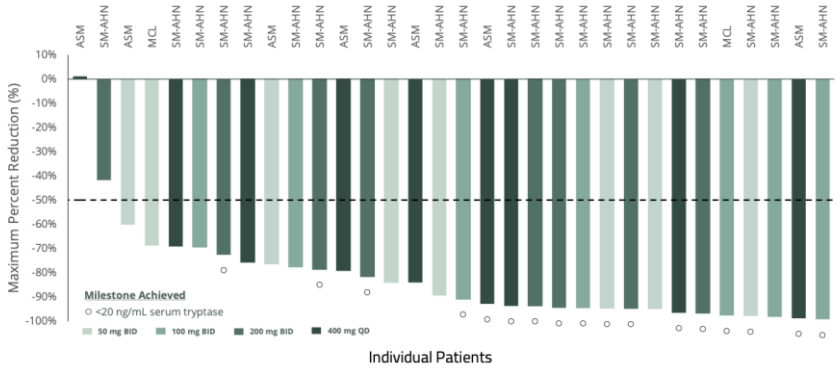
Table 4. Apex Part 1: Responses Observed by PPR Criteria

Best Response, n (%) [a]	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)

[a] 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§)*

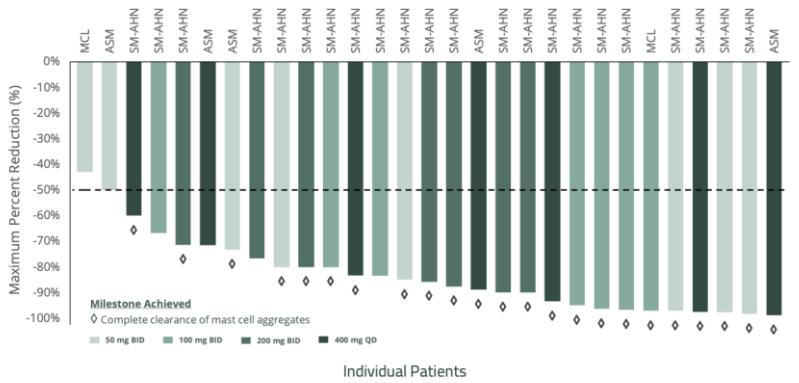


§One patient without post-baseline data was excluded

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)

Data as of 25Sep2023

Vachhani P, et al. American Society of Hematology (ASH) 2023; San Diego, CA, 11 Dec 2023: Publication Number: 4567

BEZUCLASTINIB IN NONADVANCED SYSTEMIC MASTOCYTOSIS

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Development of MS2D2 Total Symptom Score

- Rigorous process, in accordance with FDA guidelines, was followed for the development of a novel patient reported outcomes measure (PROM)
- Literature review, patient and physician interviews, and data from SUMMIT Part 1 were used to design a reliable, valid and fit-for-purpose PROM
- In June 2024, Cogent reached alignment with the FDA on use of MS2D2 in SUMMIT Part 2

MS2D2 TSS

MS2D2 TSS Additions based on:
- Literature review
- Patient interviews
- SUMMIT Part 1 psychometric analysis

Itching
Flushing
Spots
Skin redness
Difficulty Concentrating
Difficulty Remembering
Nausea
Abdominal Pain
Headache
Bone Pain
Feeling Tiredness

MS2D2 TSS comprised of 11 items scored on 0-110 scale

MS2D2 TSS Exclusions based on:
- FDA feedback
- KOL advice
- SUMMIT Part 1 psychometric analysis

Brain Fog
Dizziness
Diarrhea Severity

Each of these items are being collected as part of MS2D2 secondary analyses in SUMMIT Part 2

Initial Results from Summit: An Ongoing, 3-Part, Multi-Center, Randomized, Double-Blind, Placebo-Controlled Phase 2 Clinical Study of Bezuclastinib in Adult Patients with NonAdvanced Systemic Mastocytosis (NonAdvSM)

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American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting
Washington D.C.
25 Feb 2024
Poster #694.

Nonclinical Data Suggests Optimal Activity Against Mastocytosis May Require Higher Exposures Than Clinically Tolerable With Available Therapy

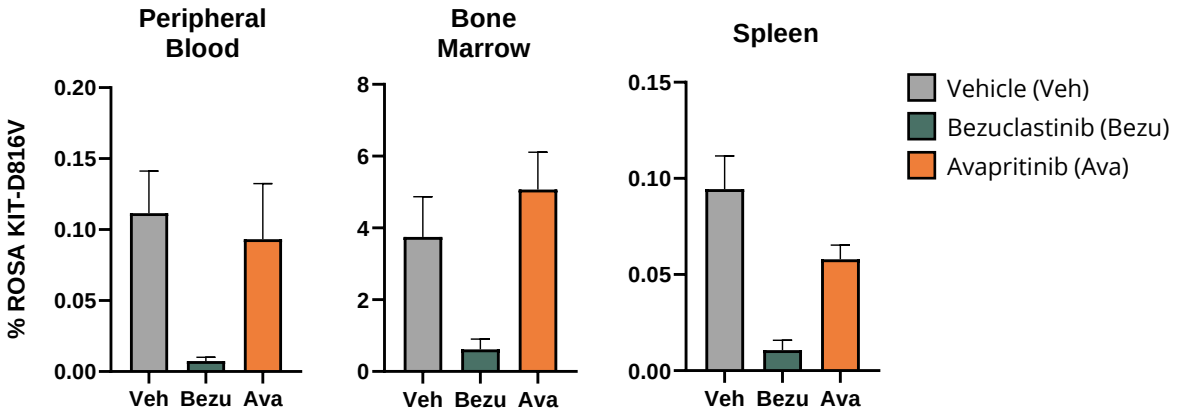
American Academy of Allergy Asthma & Immunology
ANNUAL MEETING
WASHINGTON, DC · FEBRUARY 23-26, 2024

- Mice engrafted with SCF-independent human ROSA$^{KIT\ D816V}$ cells[8] were treated daily for 8 weeks with a KIT inhibitor at doses matching clinical exposures observed in NonAdvSM patients
- Only bezuclastinib led to statistically significant decreases ($p<0.05$) in mutant MC burden compared to vehicle
- At exposures comparable to those achieved in NonAdvSM patients, bezuclastinib led to statistically significant decreases ($P<0.05$) in bone marrow and spleen compared to avapritinib

Total Drug Exposure Ratio Measured in SM Mouse Model

	Mouse Plasma AUC_{0-24} (ng·hr/mL)[a]	NonAdvSM Clinical Plasma AUC_{0-24} (ng·hr/mL)[b]	Total Drug Exposure Ratio (mouse/clinic)
Bezuclastinib	11775	16900	**0.7X**
Avapritinib	2118	1548	**1.4X**

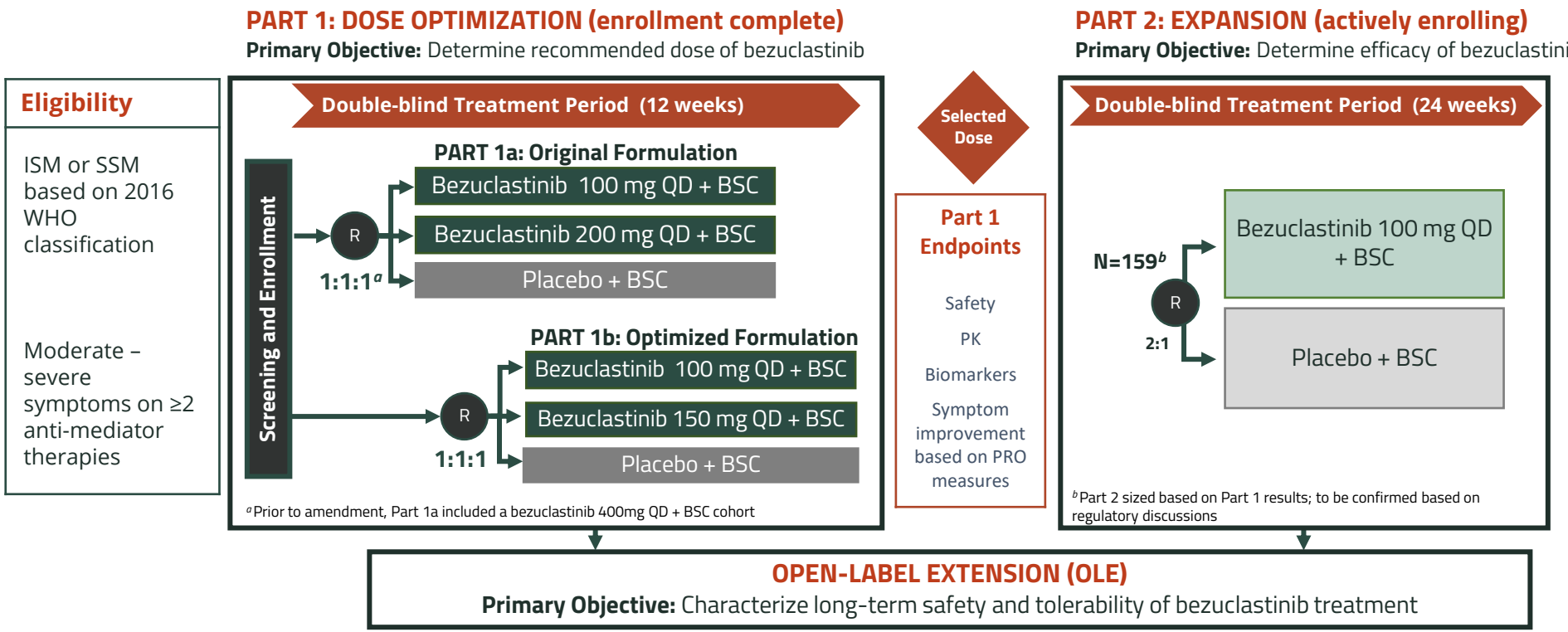
MC Burden in SM Mouse Model



8. Saleh et al. Blood, 2014, 124(1):111-120.
[a]Plasma exposures were measured at study end and corrected for difference in plasma protein binding
[b]Arithmetic mean steady state AUC for bezuclastinib 100mg (Summit) or avapritinib 25mg (EPAR, table 9)

Modena B., et al. AAAAI Annual Meeting; Washington D.C. 25 Feb 2024: Poster #694.
As of data cut-off date of 18-Dec-2023.

SUMMIT: Phase 2 Clinical Study Evaluating Bezuclastinib in NonAdvSM



BSC: Best supportive care

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As of data cut-off date of 18-Dec-2023.

SUMMIT Part 1 Enrolled NonAdvSM Patients with Moderate to Severe Disease

Patient Demographics, Characteristics, and Disposition

Patient Demographics	Part 1a (N=20)	Part 1b (N=34)
Female, n (%)	15 (75)	21 (61.8)
Median Age in years, n (range)	50.5 (38 – 75)	52.0 (27-76)
ECOG PS, n (%)		
0	3 (15)	16 (47.1)
1	15 (75)	17 (50.0)
2	2 (10)	1 (2.9)
Clinical Characteristics	**Part 1a (N=20)**	**Part 1b (N=34)**
NonAdv Subtype per PI, n (%)		
Indolent SM (ISM)	18 (90)	33 (97)
Smoldering SM (SSM)	2 (10)	1 (3)
Median (range) MAS Total Score at Eligibility	45.56 (26.3 – 71.6)	43.44 (28.6 – 65.4)
Mast Cell Burden	**Part 1a (N=20)**	**Part 1b (N=34)**
***KIT* D816V in Whole Blood, Positive, n (%)**	15 (75)	28 (82.4)
Median KIT D816V VAF, % (range)	0.49 (BLD – 32.48)	0.085 (BLD - 19.58)
Median Bone Marrow MC Burden, % (range)	22.5 (1 – 80)	15 (2 – 50)
Median Serum Tryptase, ng/mL (range)	74.35 (10.2- 592.0)	37.15 (9.2 - 206.0)
<20 ng/mL, n (%)	3 (15)	7 (20.6)
≥20 ng/mL, n (%)	17 (85)	27 (79.4)

SM Therapy	Part 1a (N=20)	Part 1b (N=34)
Prior avapritinib, n (%)	1 (5.0)	1 (2.9)
Baseline Supportive Care Medications, Median (range)	3 (2-7)	2.5 (2 – 9)
H1 blockers, n (%)	19 (95)	30 (88.2)
H2 blockers, n (%)	18 (90)	27 (79.4)
Leukotriene receptor antagonists, n (%)	8 (40)	14 (41.2)
Proton pump inhibitors, n (%)	7 (35)	9 (26.5)
Cromolyn sodium, n (%)	4 (20)	3 (8.8)
Omalizumab, n (%)	3 (15)	1 (2.9)
Corticosteroids, n (%)	1 (5)	1 (2.9)
Patient Disposition	**Part 1a (n=20)**	**Part 1b (N=34)**
Months on Study (Part 1 + OLE), median (range)	7.03 (2.8 – 16.0)	4.09 (2.7-6.6)
Completed Part 1 (a or b), n (%)	20 (100)	34 (100)
On Study as of Data Cut-off, n (%)	18 (90)	33 (97.1)
Discontinued study, n (%)	2 (10)	1 (2.9)
AE, n (%)	1 (5)	1 (2.9)
Patient Decision, n (%)	1 (5)	0

BLD, below the limit of detection

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Bezuclastinib 100 mg QD Optimized Formulation Selected as Summit Part 2 Dose Based on Part 1 Safety, PK, Biomarker and Efficacy Results

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Encouraging Safety and Tolerability Profile for Bezuclastinib 100 mg Dose in Part 1b

- The majority of TEAEs were low grade and reversible without dose modification
- No bleeding or cognitive impairment events reported across bezuclastinib cohorts
- No dose reductions at 100mg cohort; two dose reductions at 150mg: Gr1 ALT, Gr2 abdominal pain
- Only one SAE reported in bezuclastinib cohorts (150mg patient experienced ALT/AST increase that led to discontinuation)

All TEAEs Occurring >1 Patient in Any Cohort in Part 1b

	Placebo *(n=12)*		Bezuclastinib			
			100mg QD *(n=11)*		150mg QD *(n=11)*	
Preferred Term	Gr 1/2	Gr 3+	Gr 1/2	Gr 3+	Gr 1/2	Gr 3+
Hair color changes	-	-	3	-	7	-
Diarrhea	2	-	2	-	2	-
Nausea	3	-	3	-	1	-
Taste disorder#	-	-	1	-	2	-
Dizziness	2	-	-	-	2	-
Fatigue	1	-	-	-	2	-
Noncardiac chest pain	1	-	-	-	2	-
ALT/AST increased#	1	-	-	-	1	1*
Neutropenia#	-	-	-	-	1	1*
COVID-19	3	-	1	-	-	-
Insomnia	2	-	-	-	-	-
Decreased appetite	2	-	-	-	-	-
Vomiting	2	-	-	-	-	-
Urticaria	2	-	-	-	-	-
Palpitations	2	-	-	-	-	-

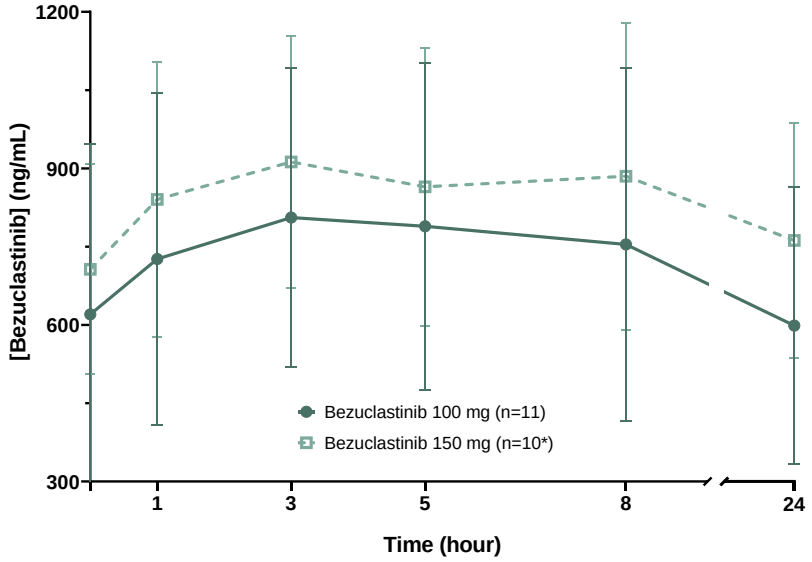
*Events occurred in a single patient

Pooled PTs

Modena B., et al. AAAAI Annual Meeting; Washington D.C. 25 Feb 2024: Poster #694.
As of data cut-off date of 18-Dec-2023.

Bezuclastinib Demonstrated Dose Dependent Increase in Mean Steady State Exposure

Summit Part 1b: Mean (± SD) Concentration on C2D1 (Steady State)



Comparable Exposures for Low and High Dose Across Part 1a and 1b

	Dose (mg), Study Part	N	Mean S.S. $AUC_{0\text{-}24h}$ (ng.h/mL)
Low Dose	**100, 1a**	7	16900
	100, 1b	11	16900
High Dose	**200, 1a**	5	19200
	150, 1b	10*	19700

*Excludes one patient with undetectable trough and anomalous low C2D1 exposure

Modena B., et al. AAAAI Annual Meeting; Washington D.C. 25 Feb 2024: Poster #694.
As of data cut-off date of 18-Dec-2023.

Bezuclastinib Elicited Deep Reductions Across Markers of Mast Cell Burden Within 12 Weeks

Serum Tryptase

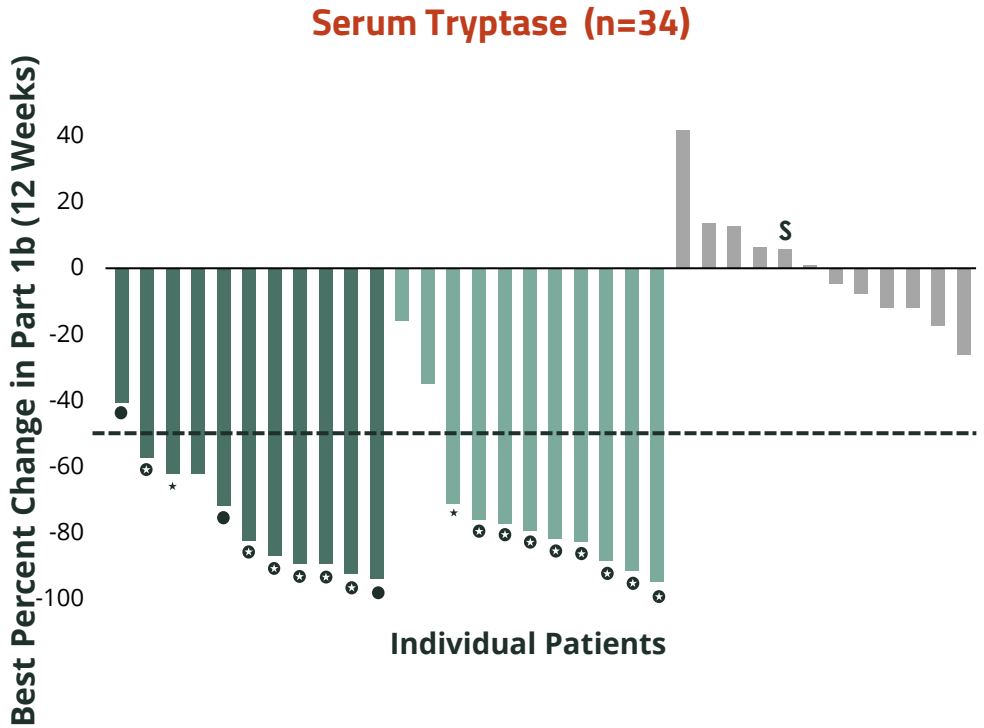
- Of patients with baseline tryptase ≥20ng/mL, nearly all patients treated with bezuclastinib achieved <20ng/mL (100% on 100 mg, 89% on 150 mg, 0% on placebo)
  - Overall, mean time to tryptase <20ng/mL was 4.5 weeks for patients treated with bezuclastinib
- Of patients with baseline tryptase ≥11.4ng/mL: 70% on 100mg, 90% on 150mg and 0% on placebo achieved <11.4ng/mL

KIT D816V VAF

- Among patients with detectable KIT D816V at baseline: 100% on 100mg, 89% on 150mg and 0% on placebo achieved at least 50% reduction or undetectable KIT D816V at Week 12

Bone Marrow Mast Cells (BM MC)

- Among patients with evaluable BM: 86% on 100mg, 78% on 150mg and 40% on placebo achieved ≥50% reduction in BM MC at Week 12
  - Mean % change from baseline in BM MC at Week 12 for patients treated with bezuclastinib 100mg was -70% vs -30% on placebo



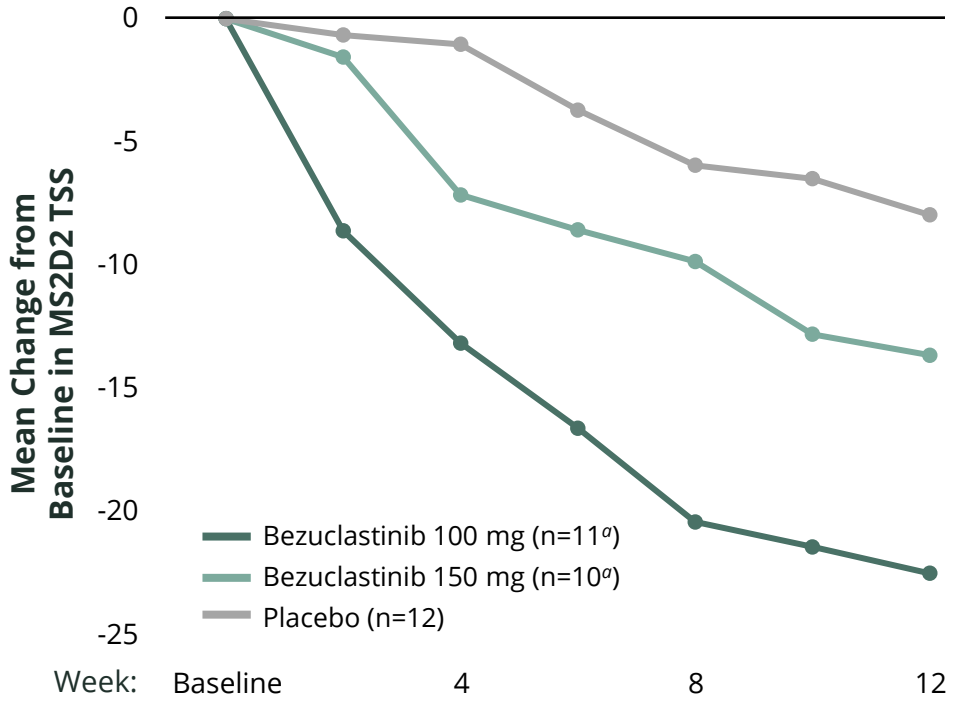
[μ]In order to achieve, serum tryptase must have been above the threshold at baseline

Modena B., et al. AAAAI Annual Meeting; Washington D.C. 25 Feb 2024: Poster #694. As of data cut-off date of 18-Dec-2023.

Patients Treated With Bezuclastinib 100 mg Reported Rapid and Significant Improvement in Symptom Severity

- 51% mean improvement in overall symptom severity (MS2D2 TSS) from baseline at Week 12 for patients receiving 100 mg bezuclastinib vs. 18% improvement for placebo patients
- Patients treated with 100 mg bezuclastinib reported a significant reduction in total symptom severity vs. placebo at Week 12 (-23.78 vs. -9.03; p=0.0003)
- 70% of patients treated with 100 mg bezuclastinib achieved ≥50% reduction in MS2D2 TSS at Week 12 vs. 8% placebo patients

Symptom Severity Measured by MS2D2



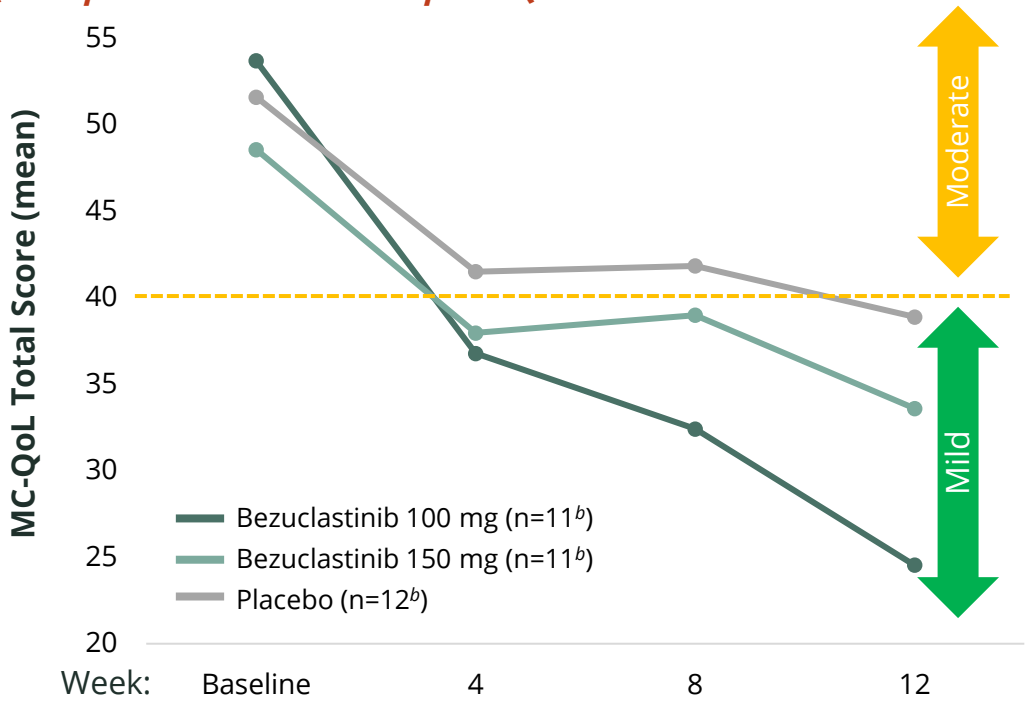
[a]Data are unavailable for 1 patient at selected timepoints

Modena B., et al. AAAAI Annual Meeting; Washington D.C. 25 Feb 2024: Poster #694.
As of data cut-off date of 18-Dec-2023.

Patients Treated With Bezuclastinib 100 mg Reported Rapid and Significant Improvement in Quality of Life

- 49% mean improvement in quality of life (MC-QoL) from baseline at Week 12 in patients treated with 100 mg bezuclastinib vs 24% for placebo
- Patients reported a significant improvement in quality of life after 12 weeks of bezuclastinib 100mg QD compared to placebo (–24.86 vs. -12.39, p=0.046)

Quality-of-Life Measured by MC-QoL[a]



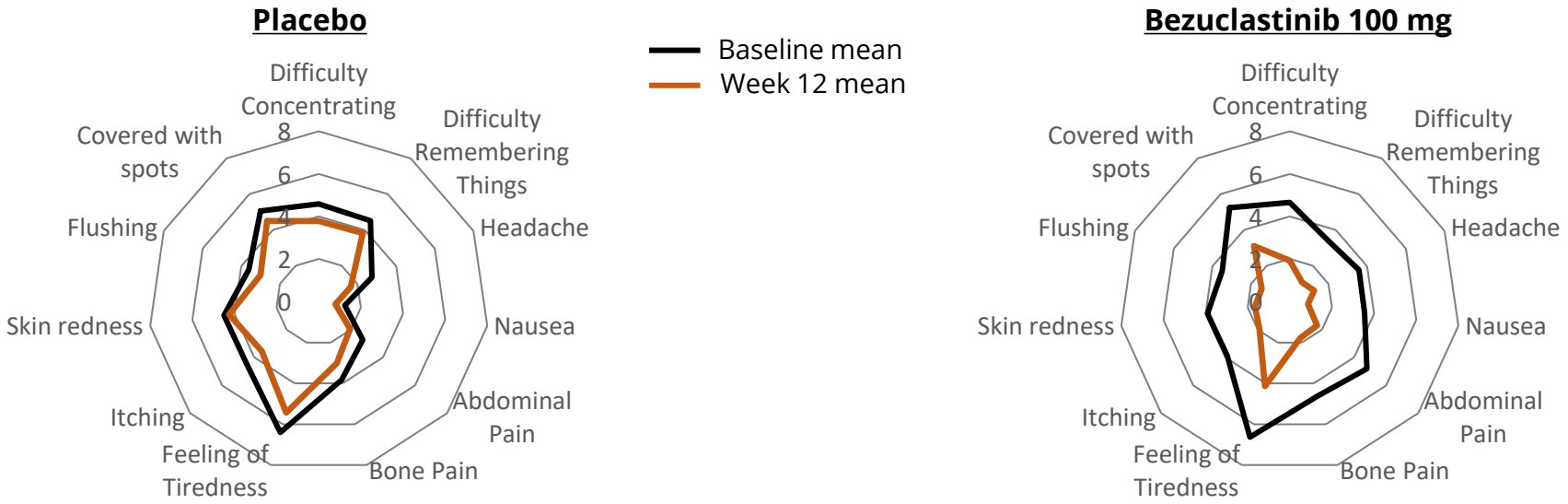
[a]MC-QoL is a disease-specific HRQoL questionnaire with 27 items in 4 domains. Total score is linearly transformed to a 0 to 100 scale.[10]
[b]Data are unavailable for 2 patients at selected timepoints

10. 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.

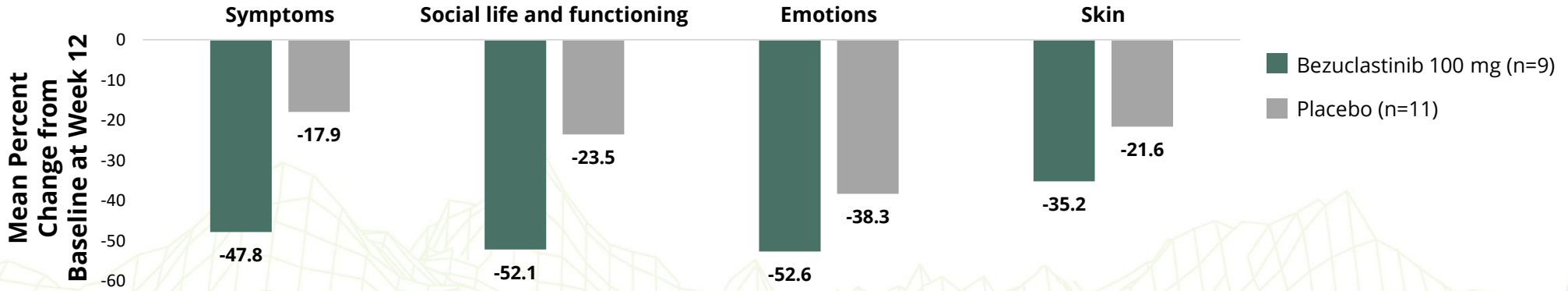
Modena B., et al. AAAAI Annual Meeting; Washington D.C. 25 Feb 2024: Poster #694.
As of data cut-off date of 18-Dec-2023.

Bezuclastinib 100mg Demonstrated Improvement Compared to Placebo Across Symptoms of SM

Greater Improvement Observed in the MS2D2 TSS With 12 Weeks of Bezuclastinib 100 mg vs Placebo



Health-Related QoL Across All MC-QoL[a] Domains Improved With 12 Weeks of Bezuclastinib 100mg vs Placebo



[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.[9]

9. Siebenhaar et al. Allergy 2016 71(6):869-77.

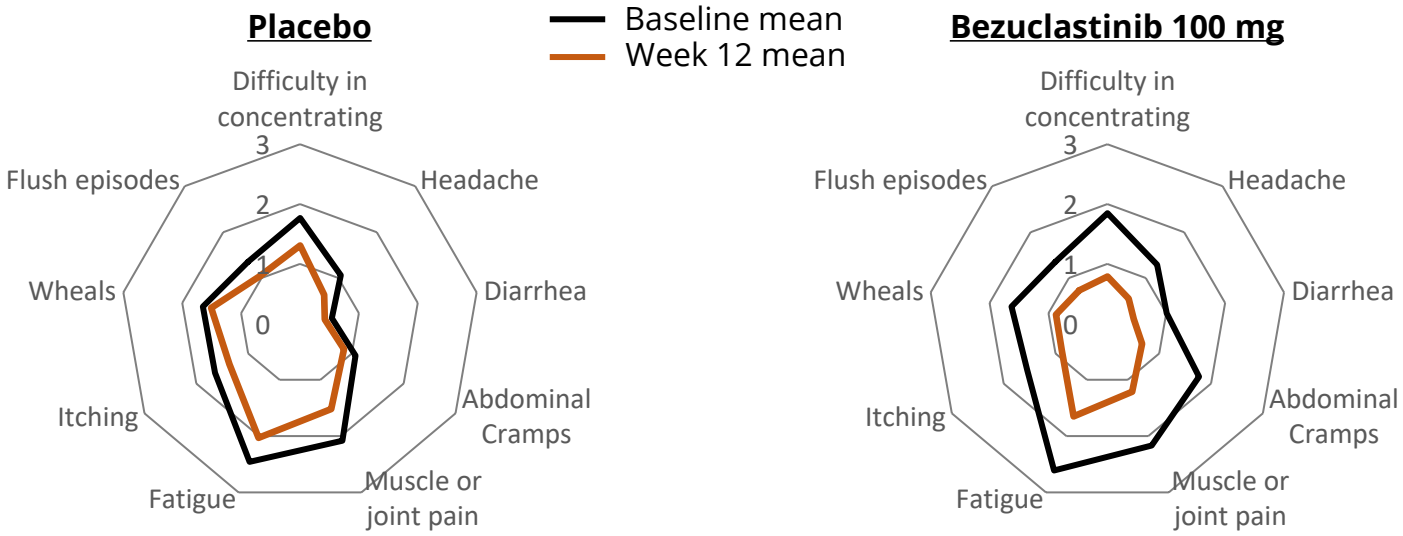
Modena B., et al. AAAAI Annual Meeting; Washington D.C. 25 Feb 2024: Poster #694.

As of data cut-off date of 18-Dec-2023.

Bezuclastinib 100 mg Demonstrated Improvement Compared to Placebo Across Symptoms of SM

Bezuclastinib 100 mg Improved Symptom Severity, As Measured by the Mastocytosis Activity Score[a] (MAS), Compared to Placebo

- 41% mean improvement from baseline in MAS at Week 12 for patients receiving 100 mg bezuclastinib vs. 21% improvement for placebo
- 50% of patients treated with 100 mg bezuclastinib achieved ≥50% improvement in MAS at week 12 vs. 0% placebo patients



[a]MAS is a disease-specific PROM used to assess symptom severity and consists of 9 items.[10] Severity of each item is rated from not at all (0) to very severe (4). For the Week 12 assessment, items are scored daily for 14 consecutive days prior to the end of the 12-week treatment period. The scores shown here are a mean for subjects in the 100mg cohort (N=10) versus the placebo cohort (N=12)

10. 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.

Modena B., et al. AAAAI Annual Meeting; Washington D.C. 25 Feb 2024: Poster #694.
As of data cut-off date of 18-Dec-2023.

Conclusions: Totality of Results from Summit Part 1 Support 100 mg QD as the Optimal Dose of Bezuclastinib for Patients With NonAdvSM

In Part 1b, bezuclastinib 100mg QD resulted in:

- Safety and tolerability profile generally consistent with placebo results
  - No bleeding, cognitive impairment, or edema AEs reported
  - No dose reductions or discontinuations due to AEs

- Rapid reductions across markers of mast cell burden, supported by KIT D816V mechanism and exposure evidence from nonclinical studies

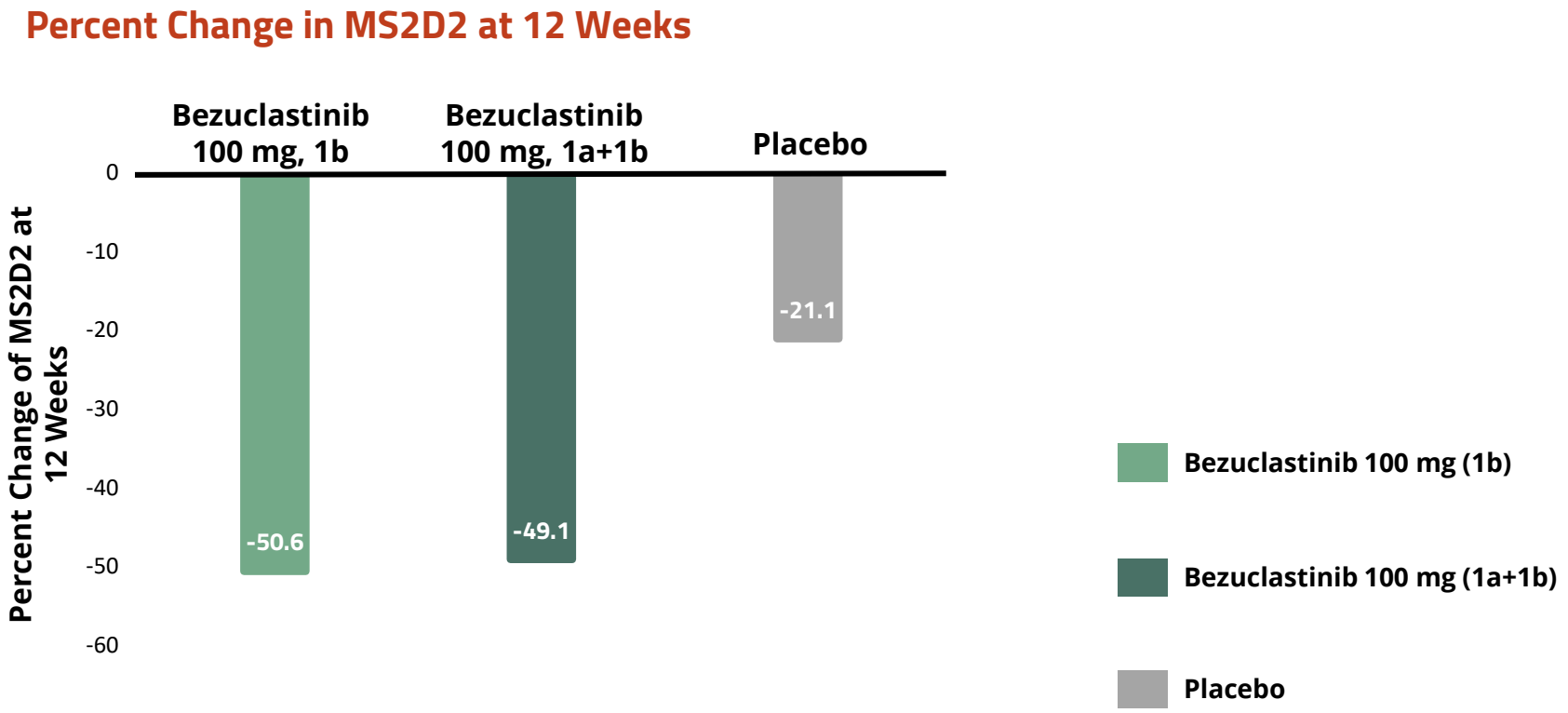
- Significant improvement versus placebo at 12 weeks in both symptom severity and quality of life, based on mean change from baseline in MS2D2 and MC-QoL total scores which corresponds to:
  - 51% reduction in symptom severity (measured by MS2D2)
  - 49% improvement in health-related quality-of-life (measured by MC-QoL)

- 70% of patients achieving ≥50% improvement in symptom severity versus 8% on placebo, as measured by MS2D2

Summit Part 2 is expected to include 159 patients

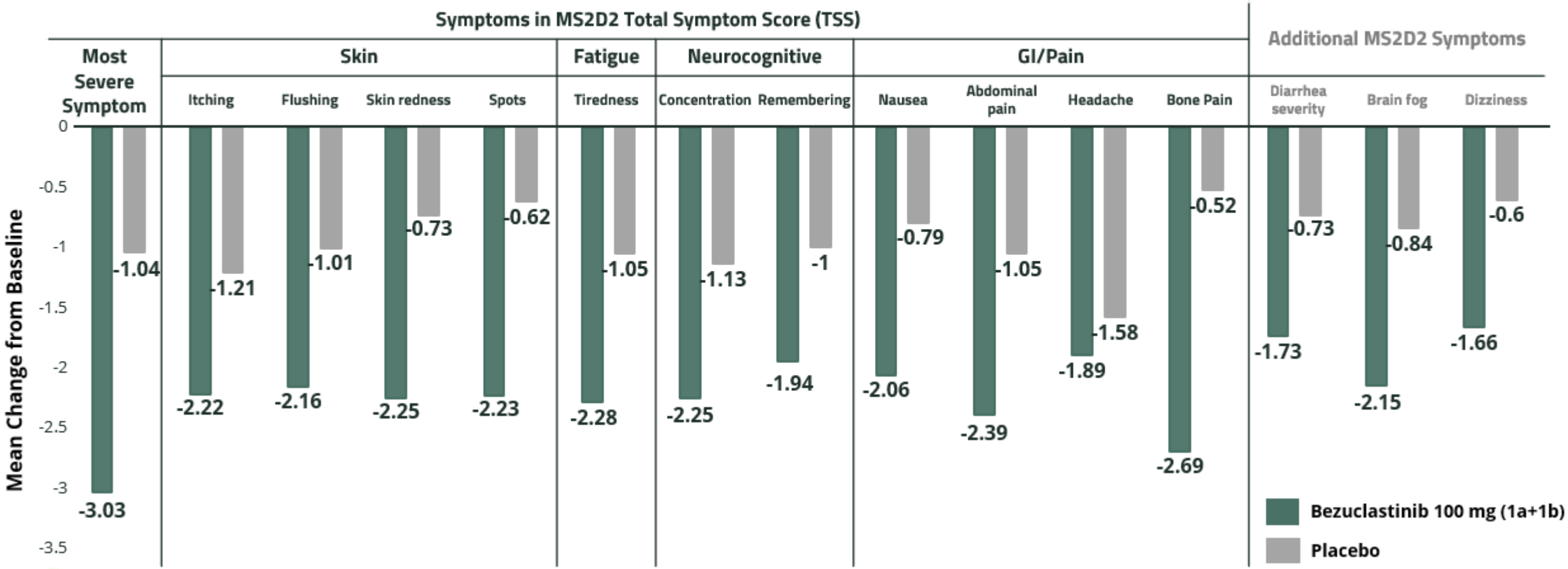
Modena B., et al. AAAAI Annual Meeting; Washington D.C. 25 Feb 2024: Poster #694.
As of data cut-off date of 18-Dec-2023.

Symptomatic Improvement on 12 Week MS2D2 TSS Consistent Across All Part 1 Patients Treated With 100 mg



Bezuclastinib 100 mg (1a+1b) Treatment Resulted in Improvement Across All Symptoms of NonAdvSM Within 12 Weeks as Measured by MS2D2

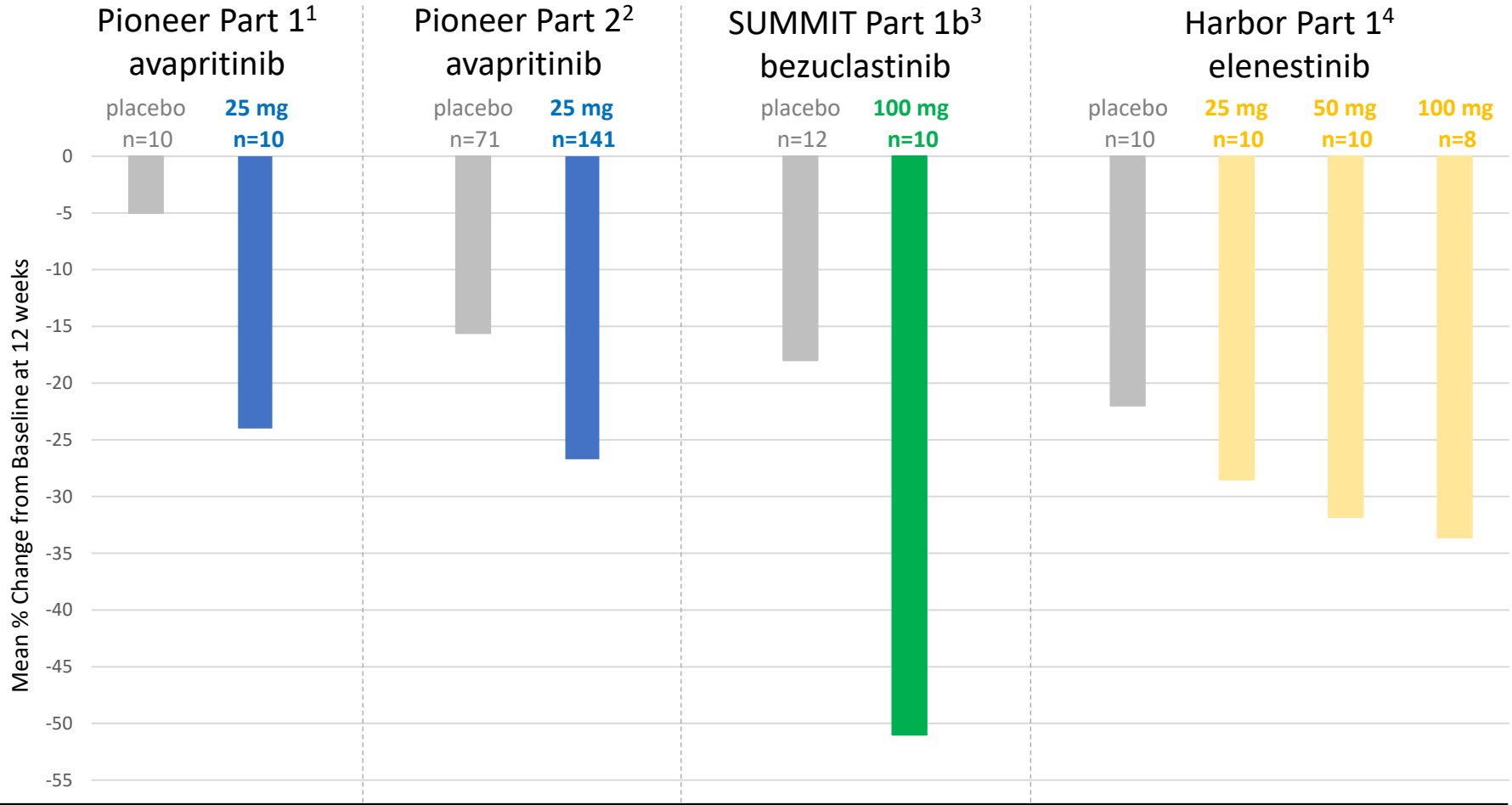
Mean Change from Baseline in MS2D2 Symptoms and Most Severe Symptom



Rein, LAM,. et al. European Hematology Association (EHA) Hybrid Congress; June 14, 2024: Madrid, Spain; Poster P1055

Cross-trial Efficacy Comparison of KIT D816V Inhibitors in NonAdvSM

- Results shown from RP2D for avapritinib and bezuclastinib; elenestinib RP2D yet to be announced
- Symptomatic severity assessed using ISM-SAF (avapritinib & elenestinib) and MS2D2 (bezuclastinib), each fit-for-purpose PROMs designed to measure NonAdvSM symptoms
- Pioneer 2, SUMMIT and Harbor Part 1 conducted with patients blinded to laboratory values (eg. serum tryptase) – placebo effect reported appears consistent across studies

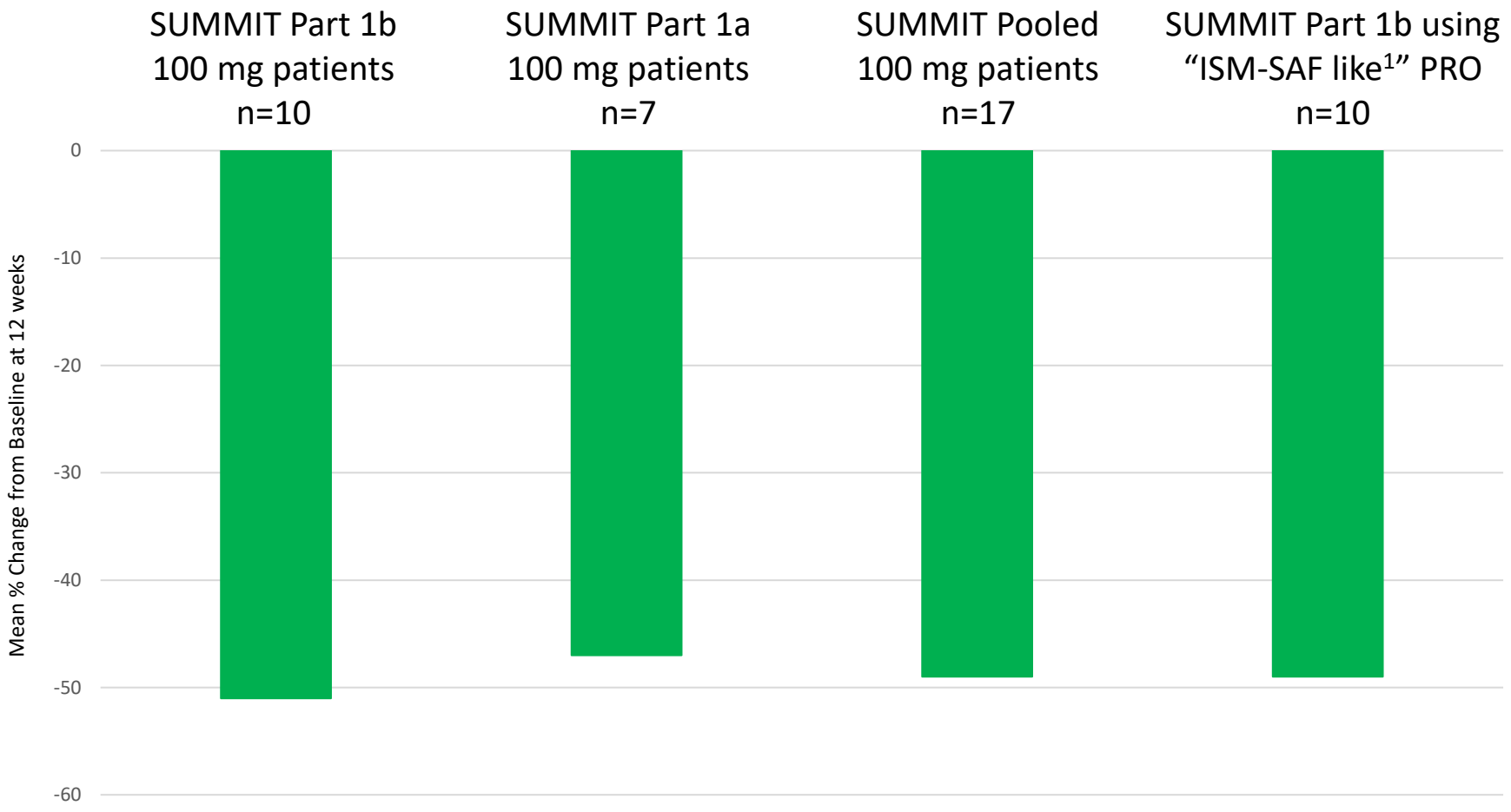


Patients achieving >50% reduction TSS :	n/a		10%	**18%**	8%	**70%**	n/a	

1 – ASH 2020 presentation, Blueprint Medicines: estimated from line graph presented; 2 – AAAAI 2023 presentation, Blueprint Medicines, estimated from line graphs presented and imputed from mean absolute change from baseline using baseline severity; 3 – AAAAI 2024 Presentation, Cogent Biosciences; 4 – ASH 2023 presentation, Blueprint Medicines

Consistent Magnitude of Symptomatic Improvement for Patients Receiving 100 mg Bezuclastinib

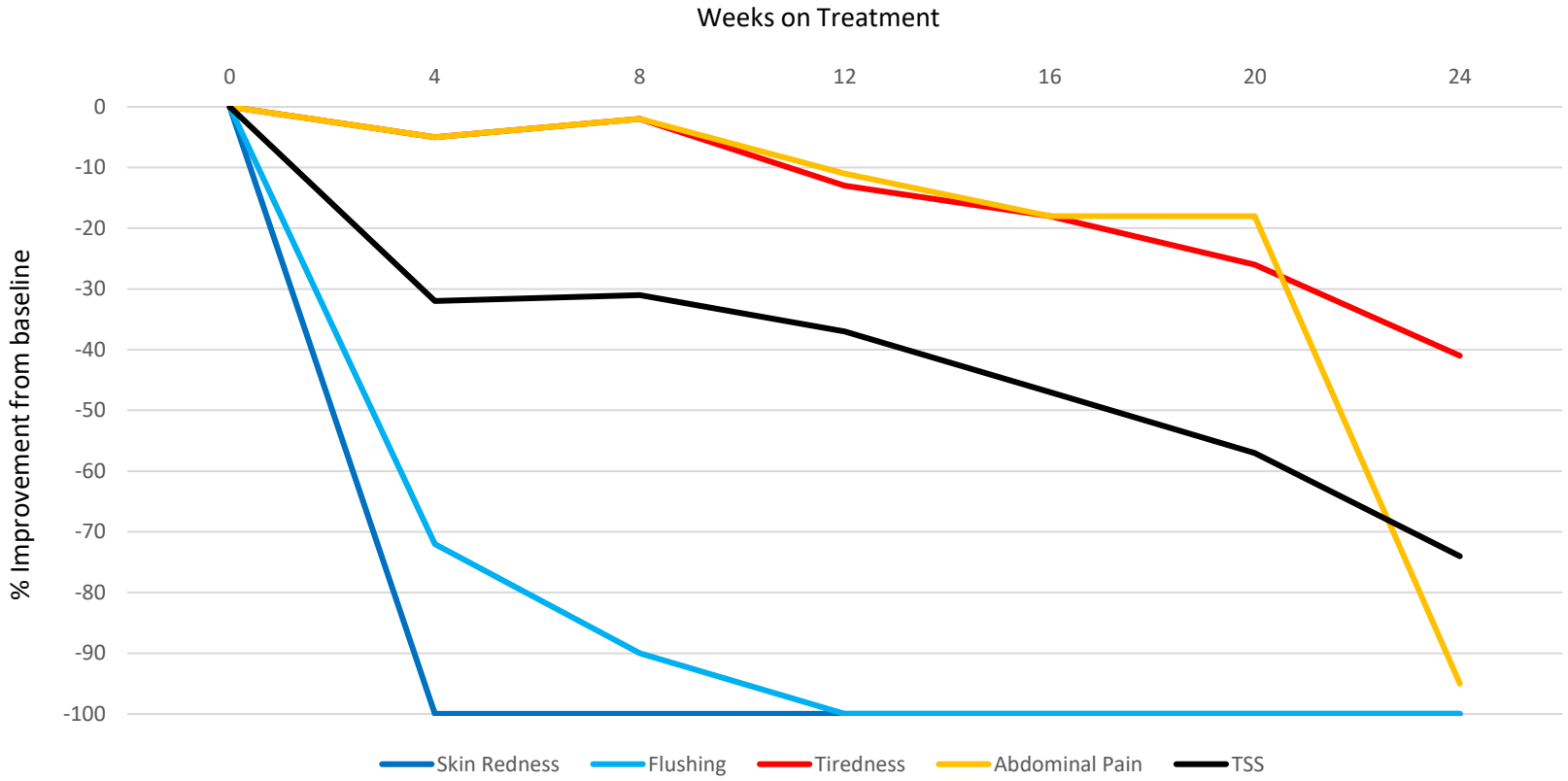
- 100 mg bezuclastinib patients reported very similar symptomatic improvement (week 12 mean change TSS) across SUMMIT 1a and 1b
- Constructing a scoring system using the same symptoms as ISM-SAF results in consistent week 12 mean change in TSS vs. MS2D2
- Improvements across domains in SUMMIT Part 1 support finding that magnitude of effect is not sensitive to item selection in TSS



[1]ISM-SAF is Blueprint Medicine's proprietary PRO tool used for assessing symptomatic improvement in NonAdvSM patients, and is not available for use by Cogent; data shown in this column were constructed using the same symptom items as the ones used in Blueprint's PRO

Optimizing Dose in NonAdvSM is Critical as Adverse Events May Confound TSS

- 52yr old patient receiving 150 mg bezuclastinib in Part 1b
- Serum tryptase reduced from 74.1 ng/ml baseline to 8.6 ng/ml at week 12
- Skin symptoms resolved quickly, but TSS at week 12 only -37% due to persistent tiredness and Gr 2 abdominal pain
- Dose reduced to 100 mg at week 20. Following dose reduction, rapid elimination of abdominal pain, improvement in tiredness and resulting TSS of -73% by week 24



BEZUCLASTINIB IN GASTROINTESTINAL STROMAL TUMORS

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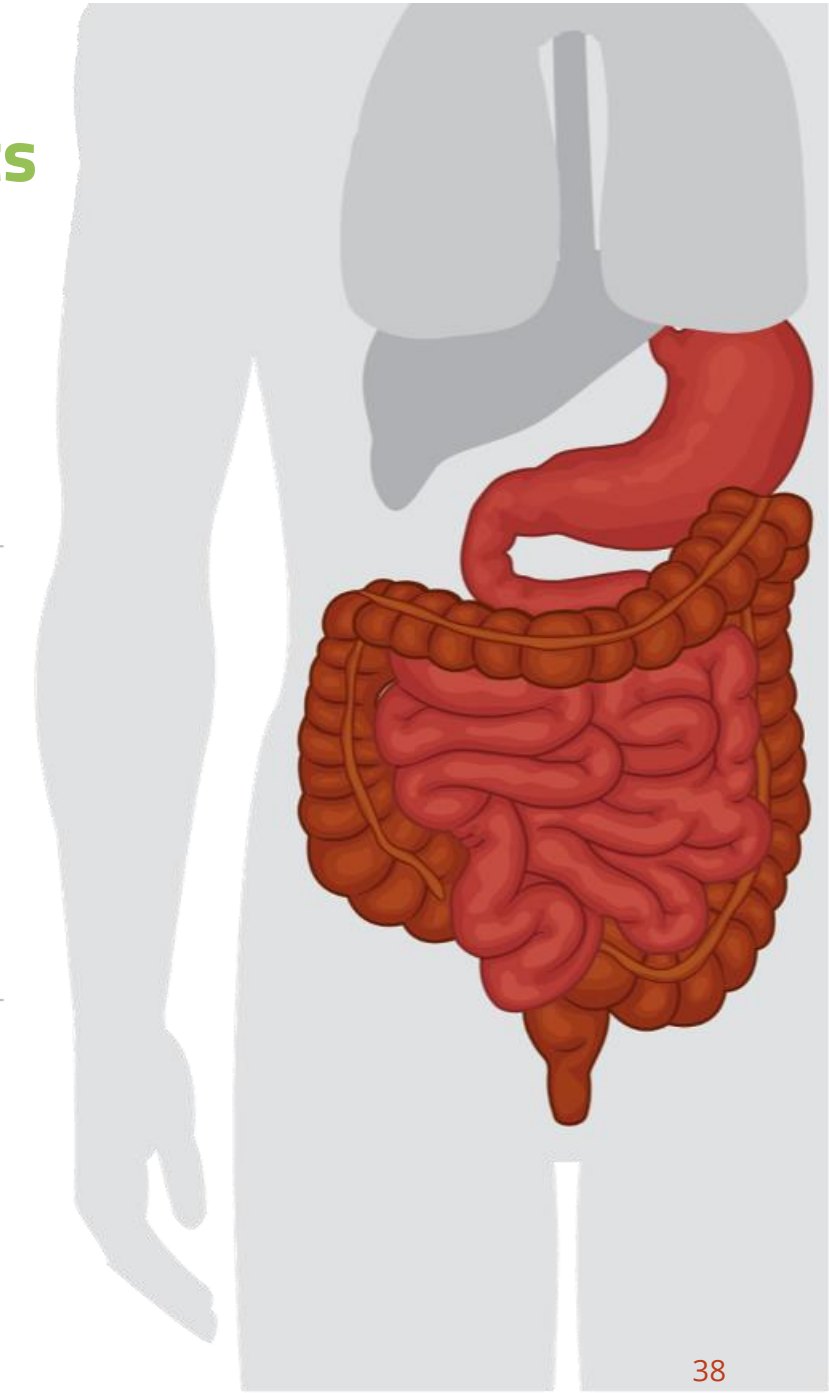
Significant Unmet Need Remains for GIST Patients

Gastrointestinal Stromal Tumor (GIST)

- Between 4,000 to 6,000 GIST cases diagnosed each year in the United States[1]
- Tumors can start anywhere in the GI tract, but they occur most often in the stomach (about 60%) or the small intestine (about 35%)[2]
- Current FDA approved therapies include imatinib, sunitinib, regorafenib, and ripretinib
- 60% of GIST patients develop resistance to imatinib within 2 years (10% primary, 50% secondary resistance)[1]

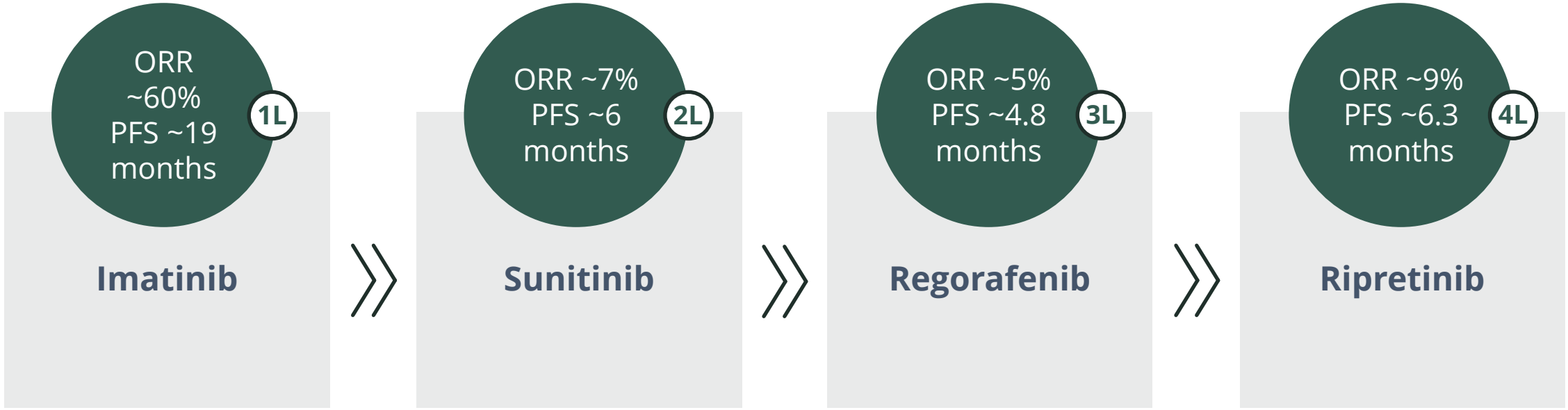
Symptoms[3]

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.

Mutations in KIT Exon 13 and KIT Exon 17 are Key Drivers of Resistance



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.

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]
- Phase 1/2 Bezuclastinib + Sunitinib: 12-month mPFS in heavily pre-treated GIST patients

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.

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

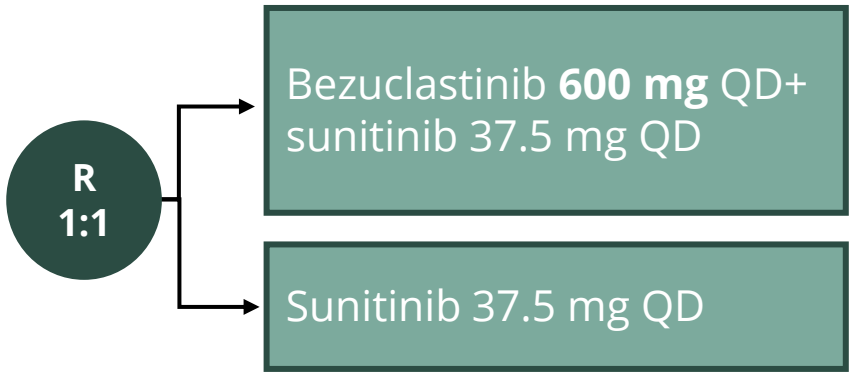
PART 1A LEAD-IN
N=19

Cohort 1 (n=5)
Bezuclastinib **300 mg** QD + Sunitinib 37.5 mg QD

Cohort 2 (n=5)
Bezuclastinib **600 mg** QD + Sunitinib 37.5 mg QD

Expansion (n=9)
Bezuclastinib **600 mg** QD + Sunitinib 37.5 mg QD

PART 2 RANDOMIZED STUDY
N=413



Primary endpoint: mPFS (median Progression Free Survival)

Top-line Results Expected YE 2025

Demographic and Baseline Characteristics in Peak Lead-In

- 39 patients enrolled in Part 1; median age 58 years (range: 33-77)

Baseline Characteristics	Part 1a N=19 (%)	Part 1b N=20 (%)	Total N=39 (%)
Male, n (%)	13 (68.4)	18 (90.0)	**31 (79.5)**
ECOG Performance Status (baseline)			
0	12 (63.2)	10 (50.0)	**22 (56.4)**
1	6 (31.6)	10 (50.0)	**16 (41.0)**
2	1 (5.3)	0 (0)	**1 (2.6)**
Total number of prior TKI therapies			
0	0 (0)	0 (0)	**0 (0)**
1	7 (36.8)	0 (0)	**7 (17.9)**
2	7 (36.8)	4 (20.0)	**11 (28.2)**
≥3	5 (26.3)	16 (80.0)	**21 (53.8)**

As of 29-Mar-2023 Data-cut
Safety Analysis Set: All treated pts

Baseline Characteristics	Part 1a N=19 (%)	Part 1b N=20 (%)	Total N=39 (%)
Primary Tumor Location at Diagnosis			
Stomach	4 (21.1)	4 (20.0)	**8 (20.5)**
Small Intestine	8 (42.1)	14 (70.0)	**22 (56.4)**
Other abdominal locations	7 (36.8)	2 (10.0)	**9 (23.1)**
Primary Mutation‡			
Exon 9^	2 (10.5)	7 (35.0)	**9 (23.1)**
Exon 11^	13 (68.4)	14 (70.0)	**27 (69.2)**
Other/unknown	4 (21.1)	0	**4 (10.3)**
Prior Radiotherapy	4 (21.1)	5 (25.0)	**9 (23.1)**
Prior anti-cancer surgery	15 (78.9)	19 (95.0)	**34 (87.2)**

‡Per archival samples taken any time from primary diagnosis to screening
^One patient in Part 1b with both exon 9 and exon 11 appears twice in the Part 1b and Total column

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

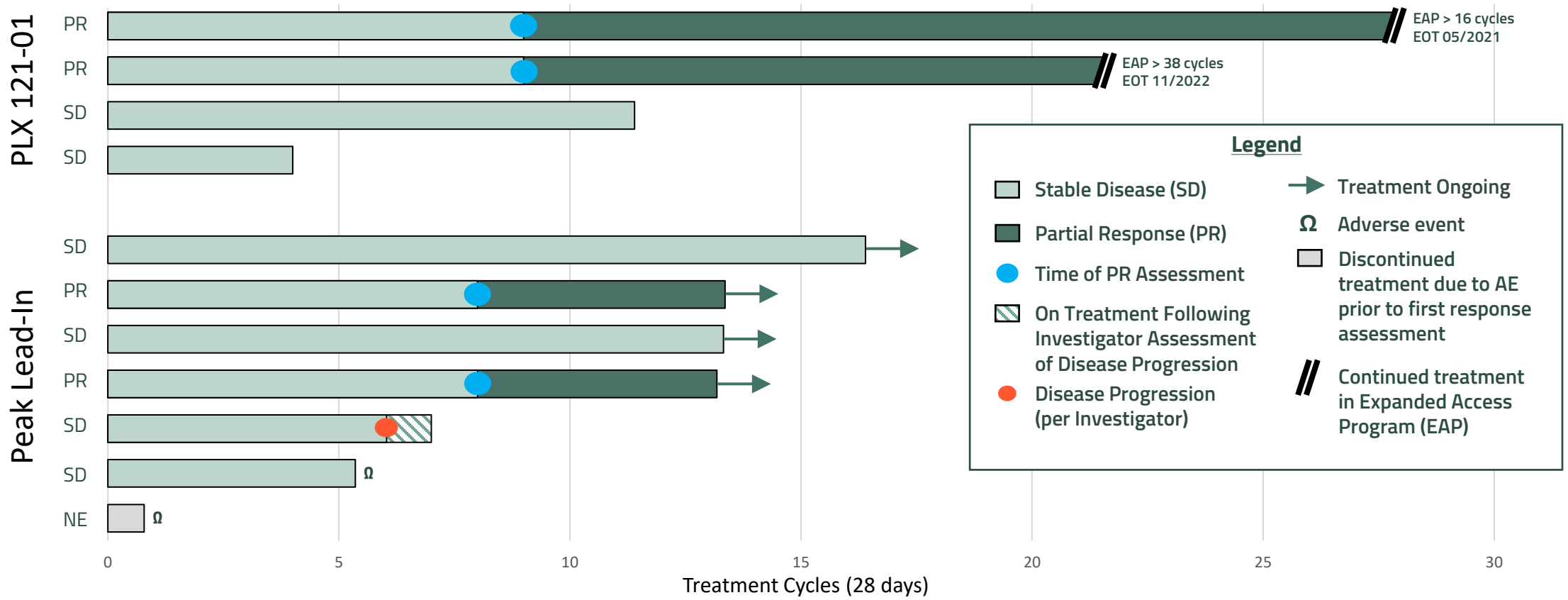
- Majority of TEAEs were of low CTCAE grade and reversible
- Low rate of Grade 3+ events
- Only three patients experienced serious adverse events possibly associated with study medications:
  - Gr 2 neutrophil count decrease and pyrexia and Gr 3 platelet count decrease
  - Gr 2 bacterial peritonitis 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

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

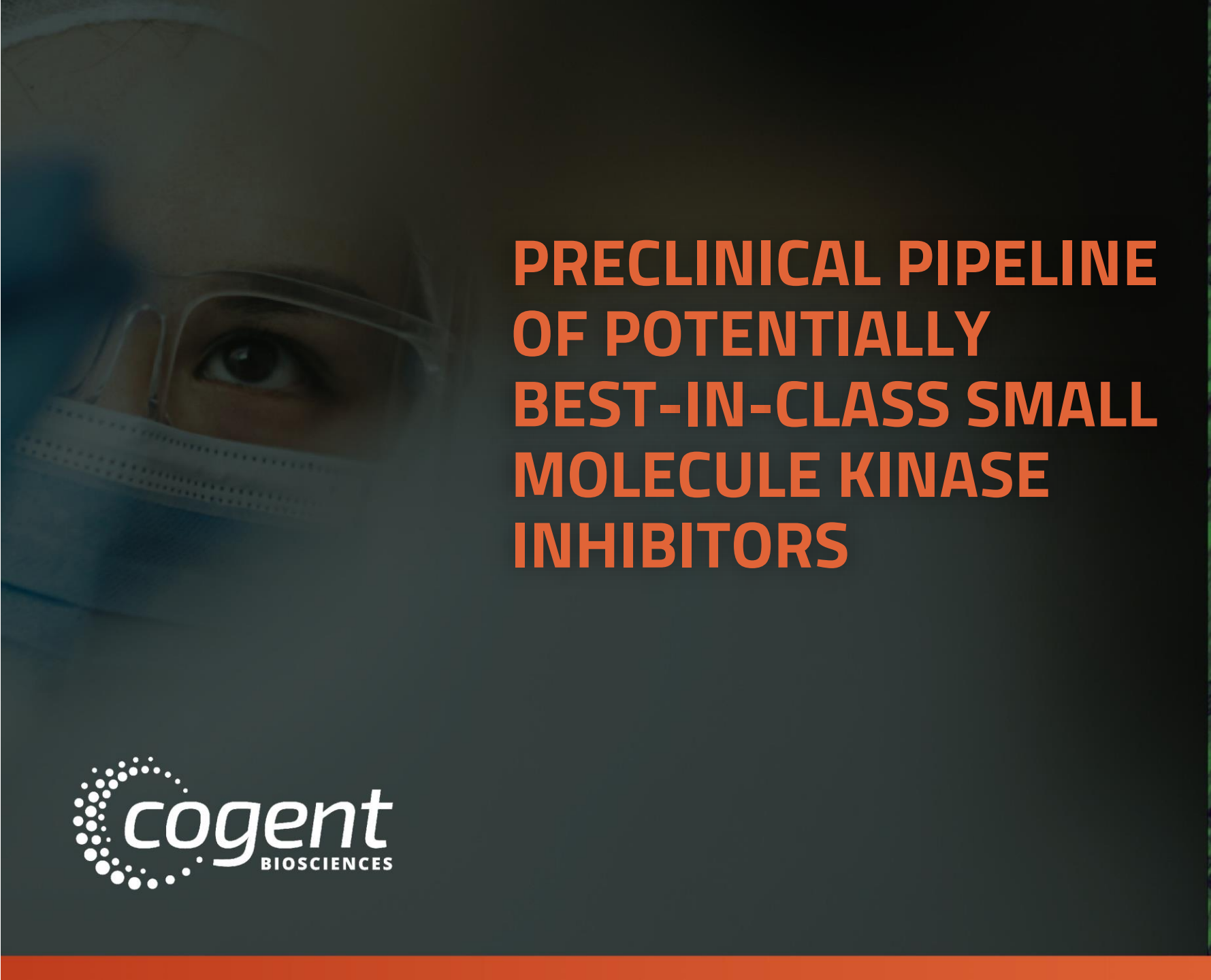
Bezuclastinib + Sunitinib in 2nd-line GIST: Encouraging ORR & Durability



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: 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 Lead-In was a 42-patient study in the combination of Sutent and Bezuclastinib



PRECLINICAL PIPELINE OF POTENTIALLY BEST-IN-CLASS SMALL MOLECULE KINASE INHIBITORS

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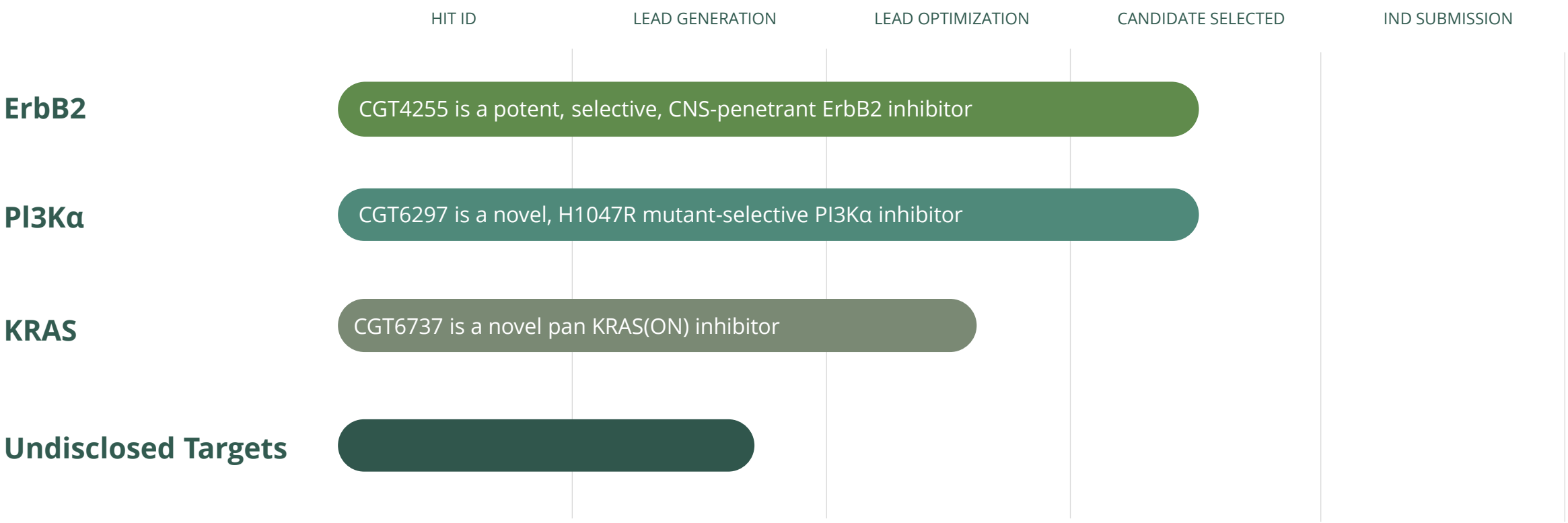
Building a Portfolio of Discovery Stage Programs

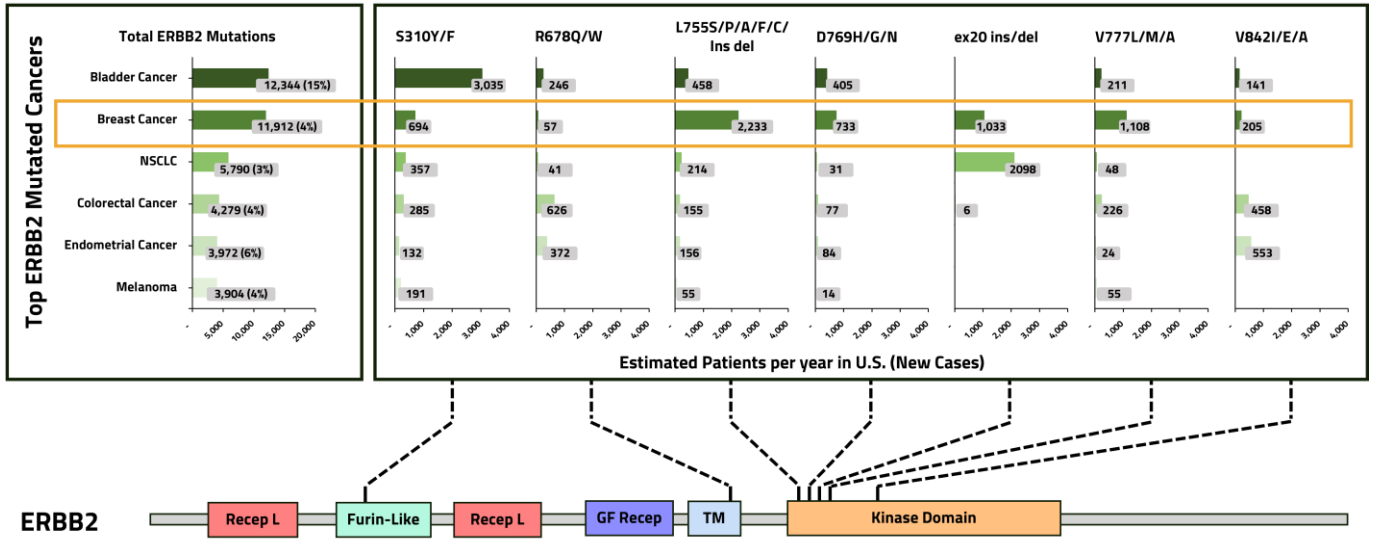


Creating potential best-in-class small molecule kinase inhibitors for genetically defined oncology and rare disease

Creating a Best-in-Class EGFR-sparing, pan-mutant ErbB2 Inhibitor

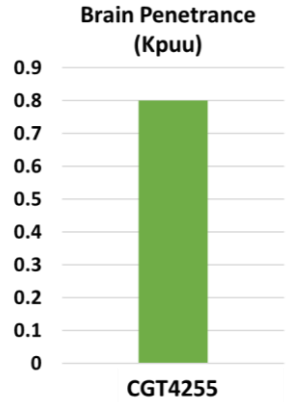
CGT4255 is a highly potent and selective ErbB2 inhibitor targeting resistance (YVMA), kinase, and extracellular domain mutations, with best-in-class potential performance in multiple underserved patient populations

Prevalence of Oncogenic Mutations of ErbB2[4,5]



	ErbB2 Cellular IC_{50} Inhibition of pErbB2				
	ErbB2 WT	L755S	YVMA	S310F	V842I
CGT4255	8 nM	9 nM	3 nM	7 nM	15 nM

Adjusted for FBS-binding



Observed Kpuu when dosed at 100 mg/kg; 1h time point in mice

Outperform:

- Minimal shift across all relevant mutations, YVMA and ErbB2 wt isoforms
- Best in class potential CNS exposure
- Superior whole blood stability across ErbB2-covalent MOA/drug class
- Superior *in vitro and in vivo* performance vs. SOC- ex.~Tucatinib
- Ability to combine therapeutically with ADC, other TKIs and mAbs

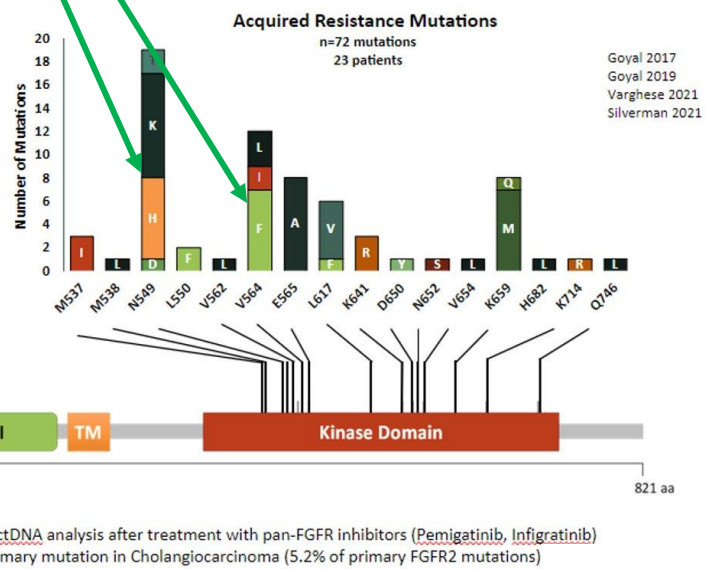
Optimizing Best-in-Class FGFR1-sparing, pan-mutant FGFR2 Inhibitor

CGT4859 demonstrates potent cellular inhibition of key gatekeeper and molecular brake mutations (V564I, N549K) that have been shown as main mechanisms of resistance to existing FGFR-directed therapies

Target	Pemigatinib	Erdafitinib	Futibatinib	RLY-4008	CGT4859
			Cellular pFGFR Inhibition IC_{50}		
FGFR2-WT	2nM	2nM	2nM	4nM	2nM
			Fold Shift vs FGFR2 Cellular IC_{50}		
FGFR1-WT	7x	4x	2x	250x	140x
FGFR2-V564F	>500x	>500x	64x	<1x	3x
FGFR2-V564I	38x	1x	1x	11x	4x
FGFR2-N549K	165x	40x	3x	7x	3x
FGFR3-V555M	>500x	75x	112x	48x	4x
chemotype	reversible	reversible	covalent	covalent	reversible

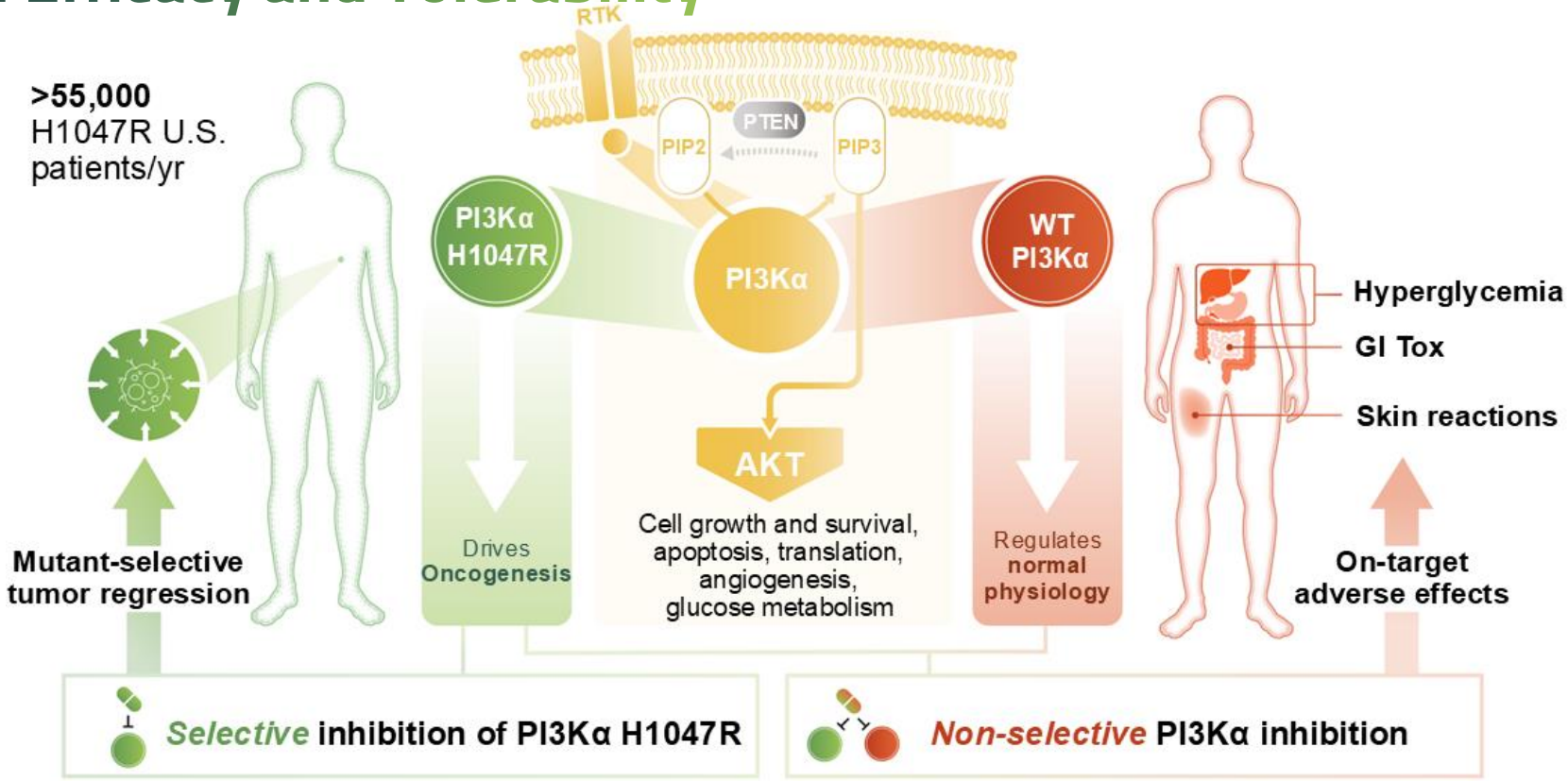
This series of analogs are the first publicly disclosed FGFR1 sparing, reversible FGFR2 inhibitors that address all the major activating and resistance mutations

Fig. 1b FGFR2 Resistance Mutations in Cholangiocarcinoma occur in the kinase domain in response to pan-FGFR inhibition



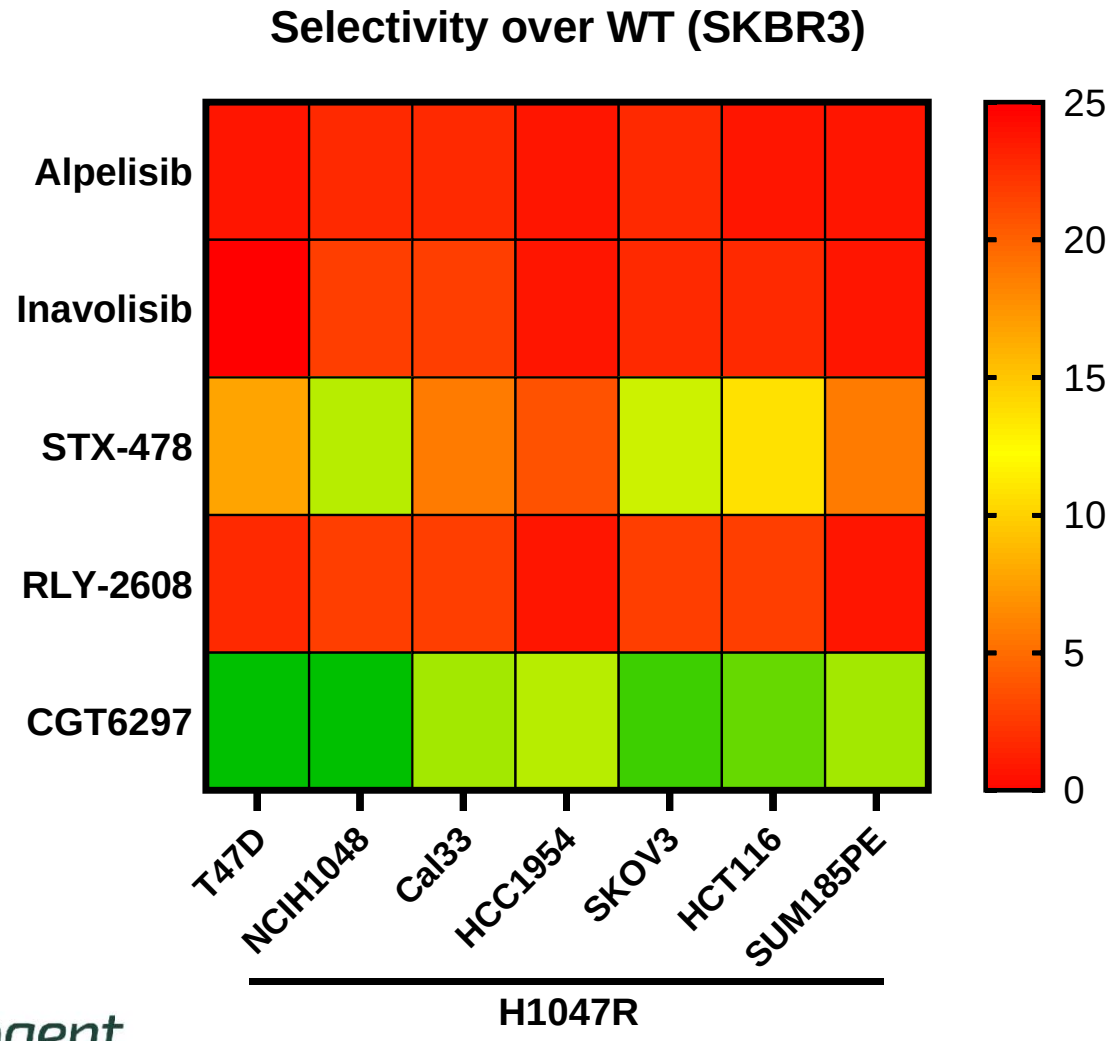
- Resistance mutations detected in patients through ctDNA analysis after treatment with pan-FGFR inhibitors (Pemigatinib, Infigratinib)
- **FGFR2-N549K/D/H/S/T** also occur as a common primary mutation in Cholangiocarcinoma (5.2% of primary FGFR2 mutations)

Selective PI3Kα H1047R Inhibition Avoids PI3Kα Wild Type Toxicity for Improved Efficacy and Tolerability



- On-target inhibition of wild type PI3Kα by approved inhibitors leads to tolerability issues including hyperglycemia, hyperinsulinemia, gastrointestinal issues, and skin reactions[1]
- Increases in insulin result in activation of PI3Kα in tumor cells and diminished efficacy[1]
- A mutant selective inhibitor will avoid these toxicities resulting in better tolerability, greater target coverage, and improved efficacy compared to approved agents

CGT6297 is a PI3Kα H1047R Kinase Domain Mutant Selective Allosteric Inhibitor



- CGT6297 was tested in a panel of PI3Kα H1047R mutant and PI3Kα WT mechanistic cell assays measuring inhibition of pAKT
- Low nM potency was observed for CGT6297 across PI3Kα H1047R mutant lines
- CGT6297 is selective for PI3Kα H1047R over PI3Kα WT with a selectivity window of 25x comparing mutant T47D to WT SKBR3
- Alpelisib, Inavolisib, and RLY-2608[4] have no selectivity over WT; STX-478[5] shows 10x T47D to WT SKBR3 selectivity in this assay

CGT6737 Shows nM Binding to KRAS(ON) with Selectivity Over H/NRAS

RAS(ON) SPR Binding Assay K_D								
	KRAS						HRAS	NRAS
	WT	G12V	G12D	G12C	G13D	Q61H	WT	WT
CGT6737	1.3 nM	1.6 nM	0.6 nM	0.3 nM	1.1 nM	1.9 nM	>5000 nM	>5000nM

- Kinetic SPR binding assay of CGT6737 to WT and mutant KRAS(ON) loaded with the GTP stable analog GMPPCP
- Confirms CGT6737 binds to active forms of KRAS(ON) consistent with crystallographic data
- **Similar SPR experiment with HRAS and NRAS shows >1000x selectivity for KRAS(ON) over H/NRAS isoforms**
- **Selectivity for KRAS over other RAS isoforms may provide tolerability advantages vs. Pan-RAS inhibition**
  - Barbicid et. al. reported that the genetic deletion of H-, N-, and K-RAS in mice stopped proliferation, and induced senescence in keratinocytes, leading to severe hypoproliferation in vivo

CGT6737 is a pM KRAS Inhibitor with Selectivity over H/NRAS

Cell Line	Tumor Type	Mutation	CGT6737 Cellular IC_{50}	RMC-6236 Cellular IC_{50}
PC-9	Non-small cell lung cancer	($KRAS^{WT}$)	14 nM	2.7 nM
NCI-H2009	Non-small cell lung cancer	$KRAS^{G12A}$	0.12 nM	0.75 nM
NCI-H358	Non-small cell lung cancer	$KRAS^{G12C}$	0.25 nM	0.27 nM
AsPC-1	Pancreatic cancer	$KRAS^{G12D}$	0.64 nM	1.4 nM
A549	Non-small cell lung cancer	$KRAS^{G12S}$	0.13 nM	0.59 nM
SW480	Colorectal cancer	$KRAS^{G12V}$	0.57 nM	0.28 nM
HCT116	Colorectal cancer	$KRAS^{G13D}$	0.66 nM	0.79 nM
NCI-H460	Non-small cell lung cancer	$KRAS^{Q61H}$	0.15 nM	0.50 nM

- Mechanistic cellular IC_{50}s measuring inhibition of pERK were determined for CGT6737 and RMC-6236 across a variety of cell lines and tumor types to capture inhibition of a range of KRAS mutations
- Both compounds are potent inhibitors of KRAS mutations with IC_{50}s in the pM range for most mutations

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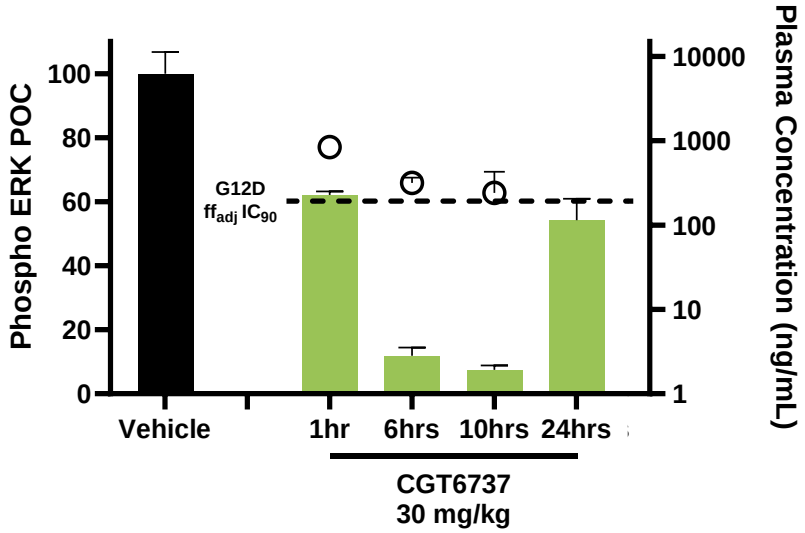
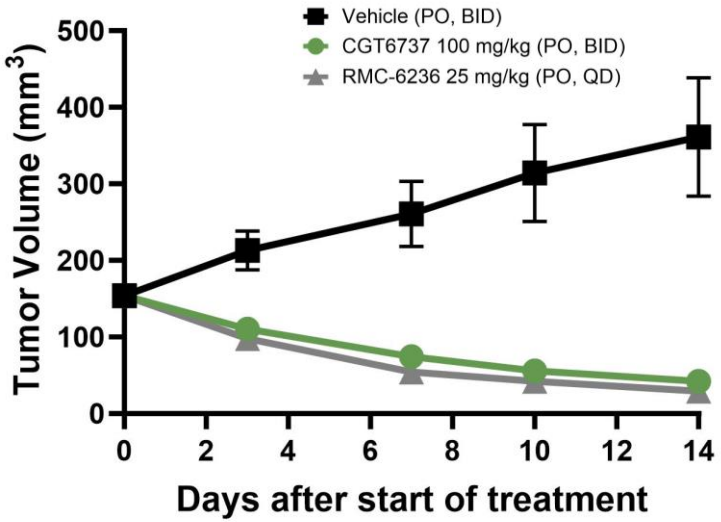
CGT6737 is Efficacious in PK/PD as well as KRASG12D & KRASG12C TGI Models

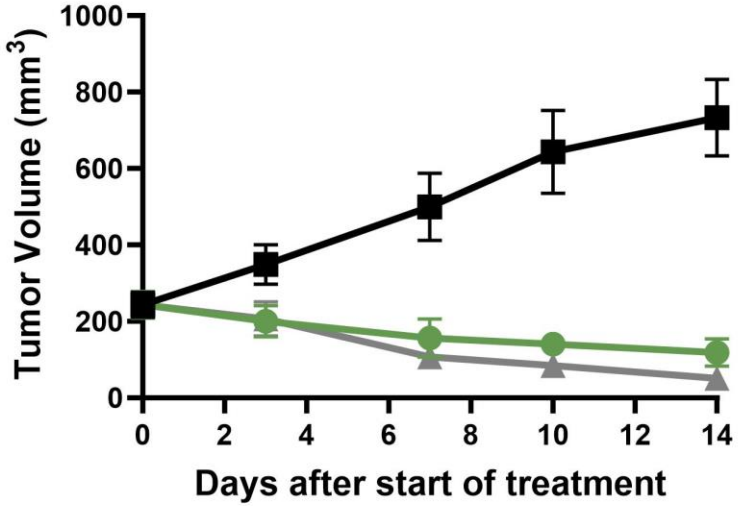
AsPC1 KRAS^{G12D} PK/PD Mouse Model



MIA PaCa-2 KRAS^{G12C} TGI



AsPC1 KRAS^{G12D} TGI



- PK/PD: 90% Inhibition of pERK was observed at 10 hr for the 30 mg/kg dose group
- CGT6737 was dosed PO BID at 100 mg/kg in both MIA PaCa-2 KRAS^{G12C} and AsPC-1 KRAS^{G12D} TGI models
  - RMC-6236 was dosed at 25 mg/kg PO to match clinically relevant exposures
- Similar efficacy was observed for CGT6737 and RMC-6236 in both TGI models
- Lead optimization of CGT6737 is ongoing

Cogent Biosciences: Anticipated Upcoming Catalysts

Clinical Milestones

- ✓ Present results from SUMMIT Part 1 at AAAAI in Q1 2024
- ✓ Initiate global, registration-directed SUMMIT Part 2 trial in 1H 2024
- ✓ Initiate Phase 1 trial of CGT4859, a potential best-in-class FGFR2 inhibitor, in 2H 2024
- Complete enrollment in SUMMIT Part 2 (NonAdvSM) in 1Q25; topline results 2H 2025
- APEX Part 2 (AdvSM) topline results mid-2025
- Phase 3 PEAK (2L GIST) topline results YE 2025

Research Milestones

- ✓ Initiate IND-enabling studies for CNS-penetrant, potent ErbB2 inhibitor
- ✓ Select clinical candidate and initiate IND-enabling studies for a novel H1047R PI3Kα inhibitor

$345.5M as of September 30, 2024; expected to fund operations into late 2026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Precision therapies for genetically defined diseases