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Developing Precision Therapies for Genetically Defined Diseases

Corporate Presentation

August 2021

Forward-Looking Statements and Risk Factors

This presentation and the accompanying oral commentary contain forward-looking statements that involve risks, uncertainties and assumptions. If the risks or uncertainties ever materialize or the assumptions prove incorrect, our results may differ materially from those expressed or implied by such forward looking statements. All statements other than statements of historical fact could be deemed forward-looking, including, but not limited to, any statements of the plans, strategies, and objectives of management for future operations, including our clinical development and commercialization plans; any projections of financial information; any statement about historical results that may suggest trends for our business; any statement of expectation or belief regarding future events; potential markets or market size, technology developments, our clinical product pipeline, clinical data or the implications thereof, enforceability of our intellectual property rights, competitive strengths or our position within the industry; any statements regarding the anticipated benefits of our collaborations or other strategic transactions; and any statements of assumptions underlying any of the items mentioned.

These statements are based on estimates and information available to us at the time of this presentation and are not guarantees of future performance. Actual results could differ materially from our current expectations as a result of many risks and uncertainties, including but not limited to, risks associated with: the potential impacts of raising additional capital, including dilution to our existing stockholders, restrictions our operations or requirements that we relinquish rights to our technologies or product candidates; business interruptions resulting from the coronavirus disease outbreak or similar public health crises, which could cause a disruption of the development of our product candidates and adversely impact our business; the success, cost, and timing of our product development activities and clinical trials; the timing of our planned regulatory submissions to the FDA for our product candidate bezuclastinib and feedback from the FDA as to our plans; our ability to obtain and maintain regulatory approval for our bezuclastinib product candidate and any other product candidates we may develop, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate; the potential for our identified research priorities to advance our bezuclastinib product candidate; the ability to license additional intellectual property relating to our product candidates from third-parties and to comply with our existing license agreements and collaboration agreements; the ability and willingness of our third-party research institution collaborators to continue research and development activities relating to our product candidates; our ability to commercialize our products in light of the intellectual property rights of others; our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates; the scalability and commercial viability of our manufacturing methods and processes; the commercialization of our product candidates, if approved; our plans to research, develop, and commercialize our product candidates; our ability to attract collaborators with development, regulatory, and commercialization expertise; our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates; among others. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to our business in general, see our periodic filings filed from time to time with the Securities and Exchange Commission. Unless as required by law, we assume no obligation and do not intend to update these forward-looking statements or to conform these statements to actual results or to changes in our expectations.

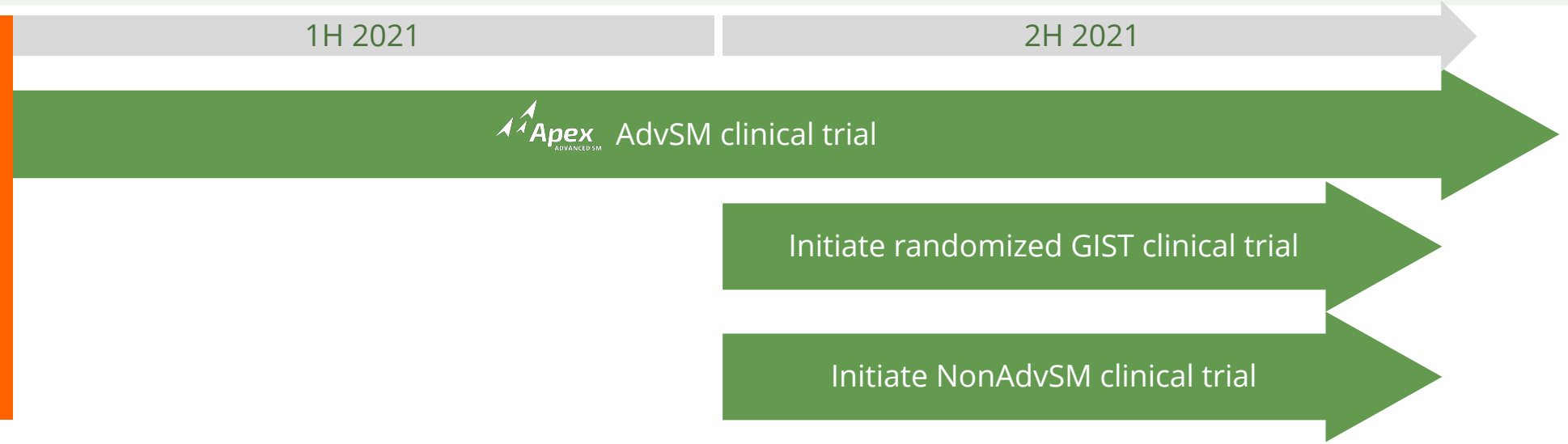
All of Cogent Biosciences, Inc. (“Cogent”) product candidates are investigational product candidates and their safety and efficacy have not yet been established. Cogent has not obtained marketing approval for any product, and there is no certainty that any marketing approvals will be obtained or as to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

Any data pertaining to Cogent product candidates is interim data and may include investigator-reported interim data for which Cogent has not yet independently reviewed the source data. The interim data may not be representative of the final results that may be obtained in the corresponding trials and results from earlier trials may not be representative of results obtained in later trial or pivotal trials.

Cogent Biosciences: Emerging Leader in Precision Medicines for Genetically Defined Diseases

Bezuclastinib (CGT9486), a potential **best-in-class KIT mutant inhibitor**, has demonstrated promising clinical activity and safety results in a Phase 1/2 clinical trial in patients with gastrointestinal stromal tumors (GIST), supporting accelerated timelines to proof-of-concept in systemic mastocytosis (SM)

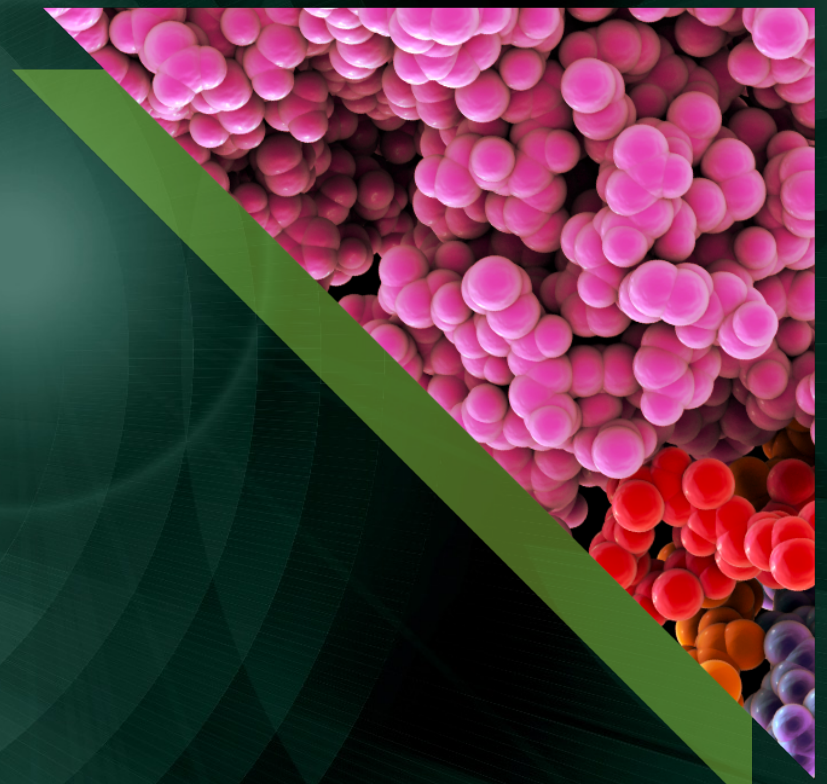
Broad clinical development plan designed to move bezuclastinib rapidly to high unmet need patient populations

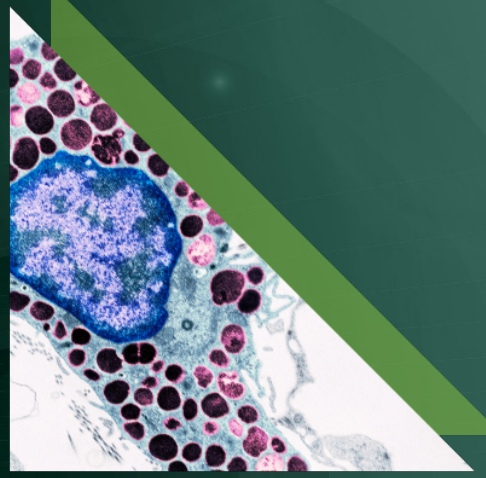


April 2021: Formed Cogent Research Team, an internal effort to create a pipeline of novel, small-molecule targeted therapies for patients fighting rare, genetically-driven diseases

As of June 30, 2021, our cash balance is $218.1 million.

Bezuclastinib: Next-Generation KIT Mutant Inhibitor





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Bezuclastinib is 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 wild-type KIT, PDGFRα, VEGFR2, FLT3 and CSF1R
- Worldwide rights to compound exclusively licensed from Plexxikon[1]
- Patent protection through at least 2033[2]

Encouraging Clinical Activity

12 months mPFS demonstrated with combination of bezuclastinib + sunitinib in heavily pre-treated GIST patients

Attractive Emerging Safety Profile

Well tolerated with no significant safety signals across 50+ patients in single agent & combination dosing

Potential Best-in-Class KIT mutant inhibitor

KIT D816V inhibition supports future studies in systemic mastocytosis and GIST; safety results support potential for broad use

[1] Plexxikon is eligible for mid- to high- single-digit royalties and additional development milestones. License includes rights to CGT0206, an additional selective KIT inhibitor in preclinical development
[2] Does not include available patent term extension

Bezuclastinib Designed as Potent and Selective KIT Mutant Inhibitor

Bezuclastinib is a Type I Inhibitor designed to selectively bind the active conformation of mutant KIT

- Comparable potency observed relative to avapritinib with potential selectivity advantages
- Limited blood-brain-barrier penetration and no CNS toxicities identified in preclinical studies

Potency

Assay	IC50 (nM)	
	Bezuclastinib	Avapritinib
KIT D814Y autophosphorylation (murine P815 cells)[a]	12	22
BA/F3 KIT D816V growth[b]	12	13.5
KIT D816V kinase activity (Reaction Bio)[b]	1.125	0.4143

[a] Comparison of bezuclastinib data with previously published avapritinib data
[b] Direct comparison within experiments using non-GMP syntheses
Note: No head-to-head clinical trials have been conducted between bezuclastinib and avapritinib.

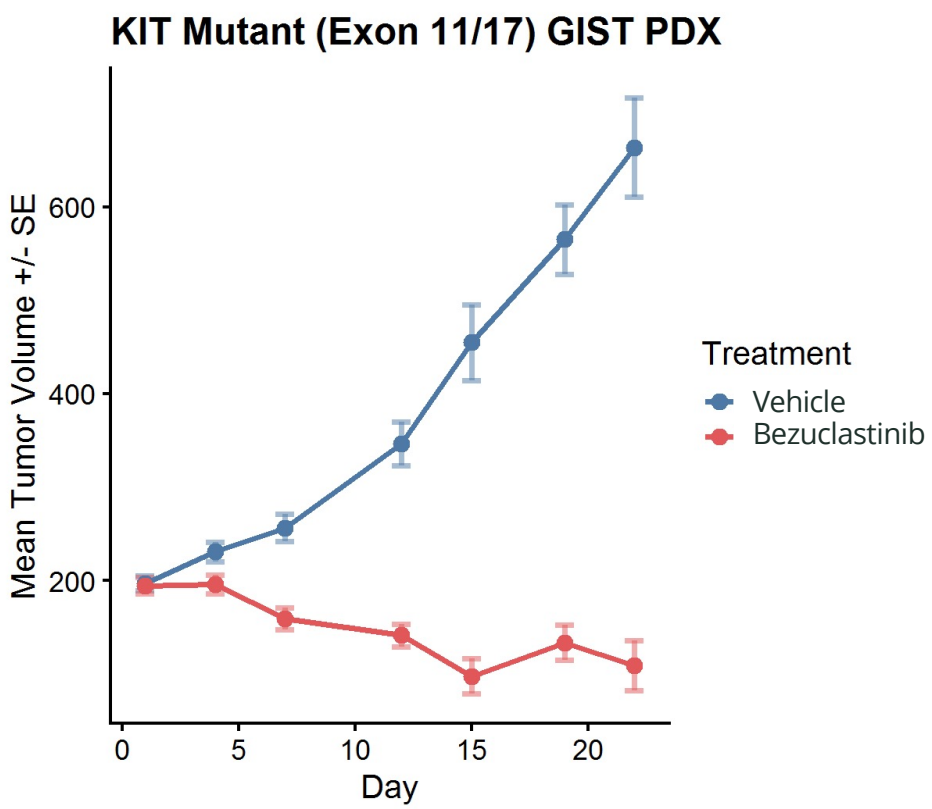
Selectivity

Enzyme	IC50 (nM) Bezuclastinib
c-Kit (wt)	>5000*
c-Kit (D816V)	1.125
FMS	602.4
KDR/VEGFR2	>5000*
PDGFRα	>5000*
PDGFRα (D842V)	104.3

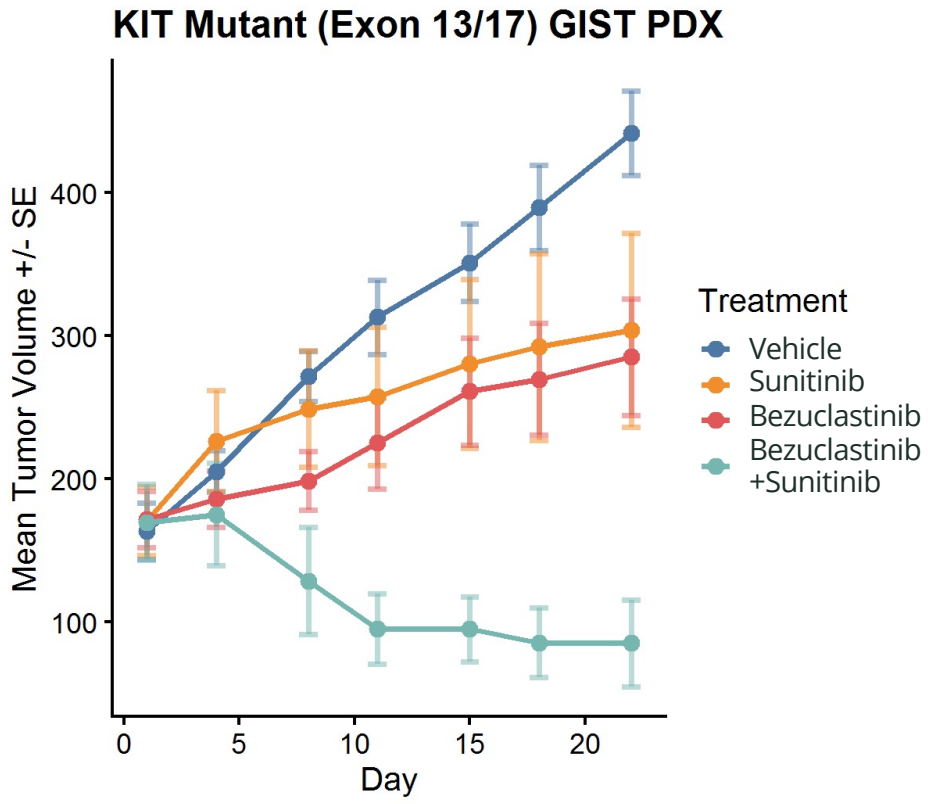
*Highest concentration tested in biochemical assay

KIT Inhibition Drives Tumor Regression in Heterogeneous GIST Patient-Derived Xenograft Models

Ex11 (W557_K558del), Ex17 (Y823D)

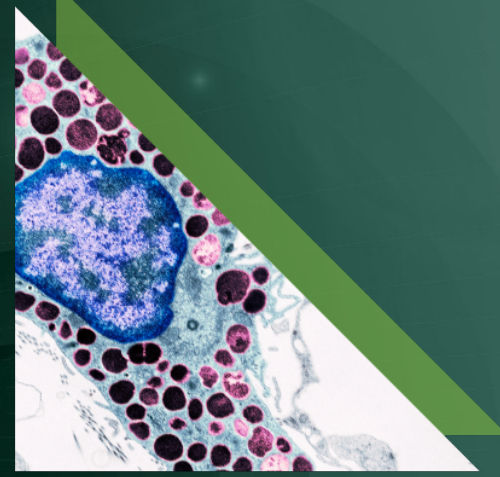


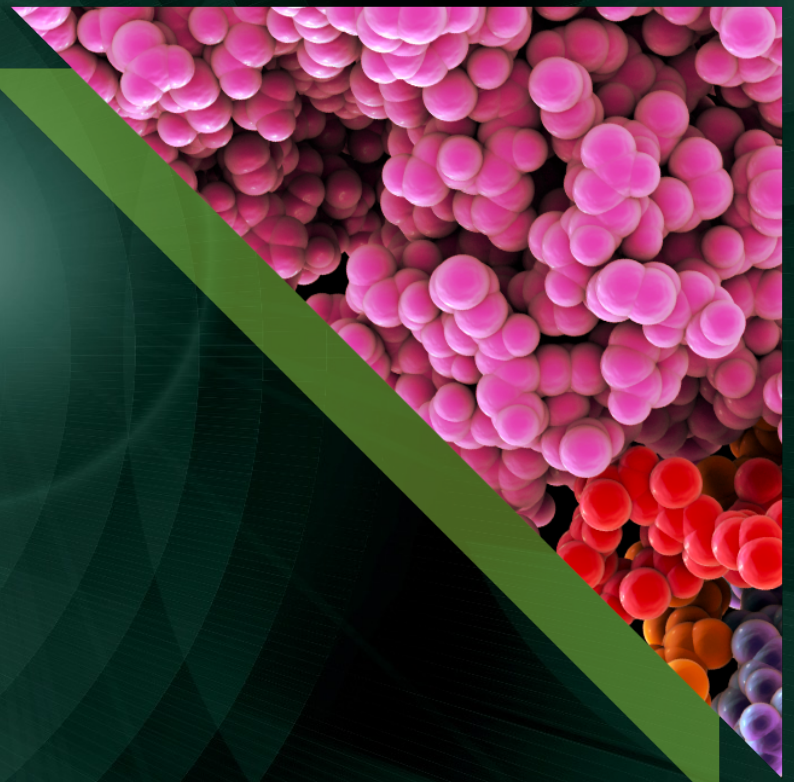
Ex13 (K642E), Ex17 (N822K)



Source: Internal Plexxikon studies

Systemic Mastocytosis & KIT Exon 17 D816V Mutations





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Significant Unmet Need Remains for Systemic Mastocytosis Patients

Systemic Mastocytosis

- Disease driven by over-accumulation of mast cells across various internal organs in the body[1]

Advanced Systemic Mastocytosis (AdvSM)

- Median survival of < 3.5 years[2]
- FDA approved drug, Rydapt (Midostaurin), broad spectrum TKI, challenging tolerability

Non-Advanced Systemic Mastocytosis (NonAdvSM)

- Significantly impacts quality of life including potentially life-threatening anaphylaxis[3]
- No approved therapies: current treatments include H1 and H2 anti-histamines, mast cell stabilizers, leukotriene inhibitors

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

Light-headedness, syncope (fainting), rapid heart rate, chest pain, low blood pressure, high blood pressure at reaction start, blood pressure instability

Ear/Nose/Throat/Respiratory

Nasal itching and congestion, throat itching and swelling, wheezing, shortness of breath

Skeletal

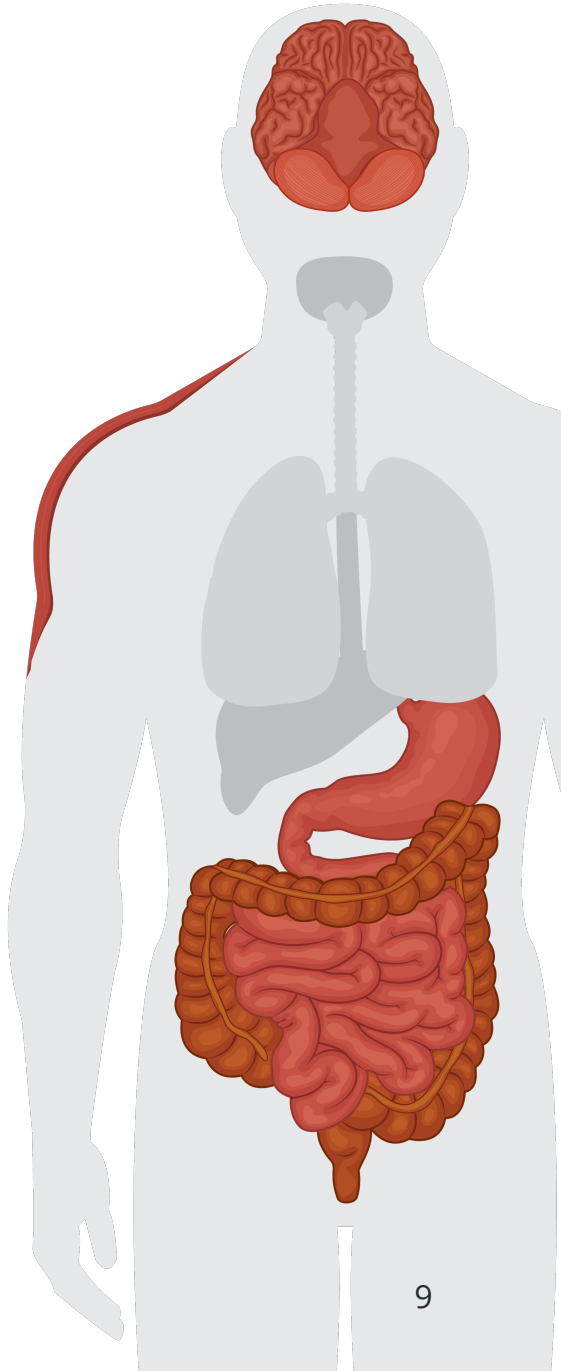
Bone/muscle pain, osteopenia, osteoporosis

Gynecological

Uterine cramps, bleeding

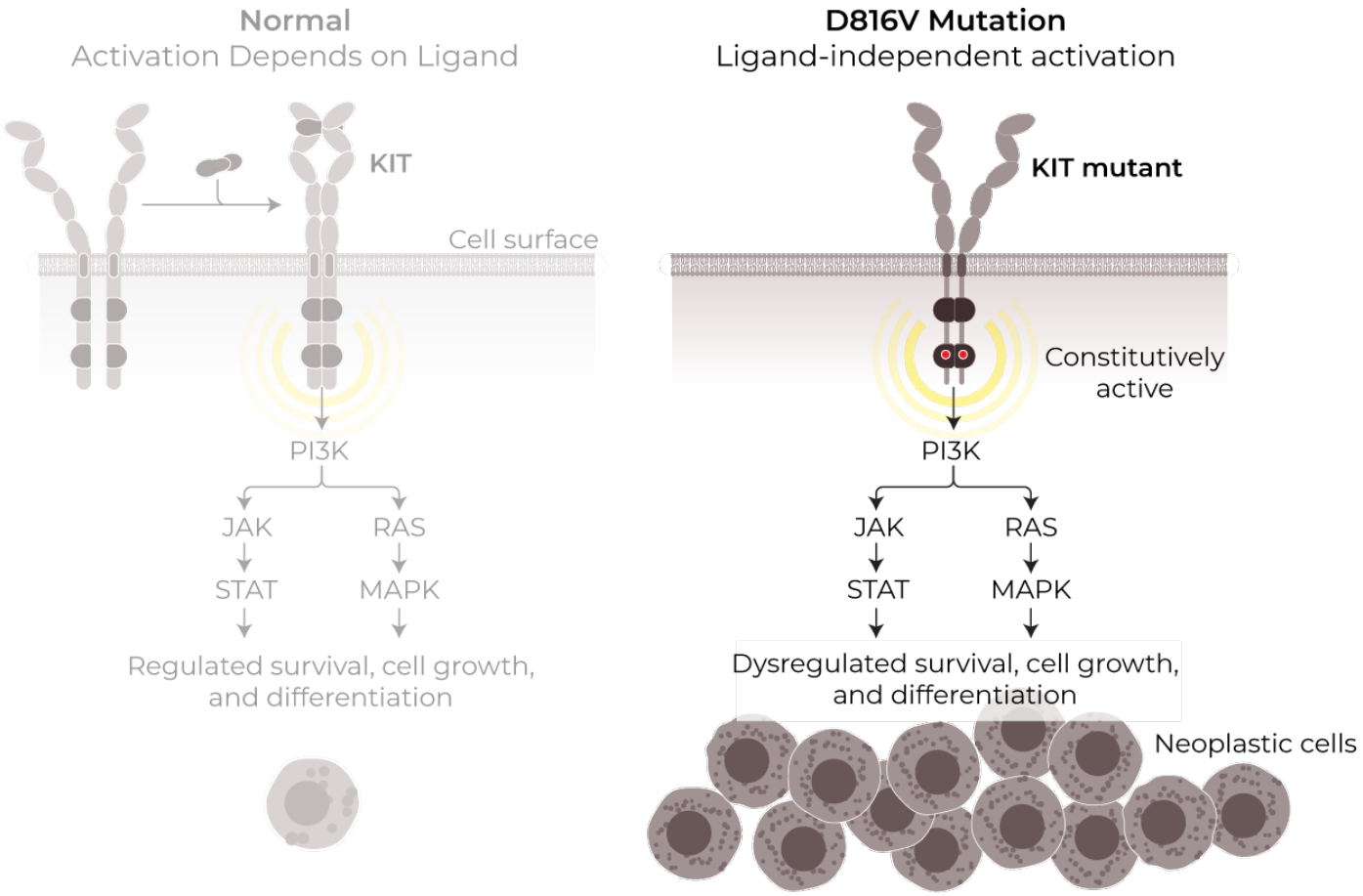
Urinary

Bladder irritability, frequent voiding



[1] https://rarediseases.info.nih.gov/diseases/8616/systemic-mastocytosis
[2] https://ashpublications.org/blood/article/113/23/5727/25879/Systemic-mastocytosis-in-342-consecutive-adults
[3] https://ashpublications.org/blood/article/121/16/3085/31589/How-I-treat-patients-with-indolent-and-smoldering

Systemic Mastocytosis (SM): Primarily Driven by KIT Exon 17 D816V Mutations



KIT exon 17 D816V mutation is detected in >95% of SM patients[1]

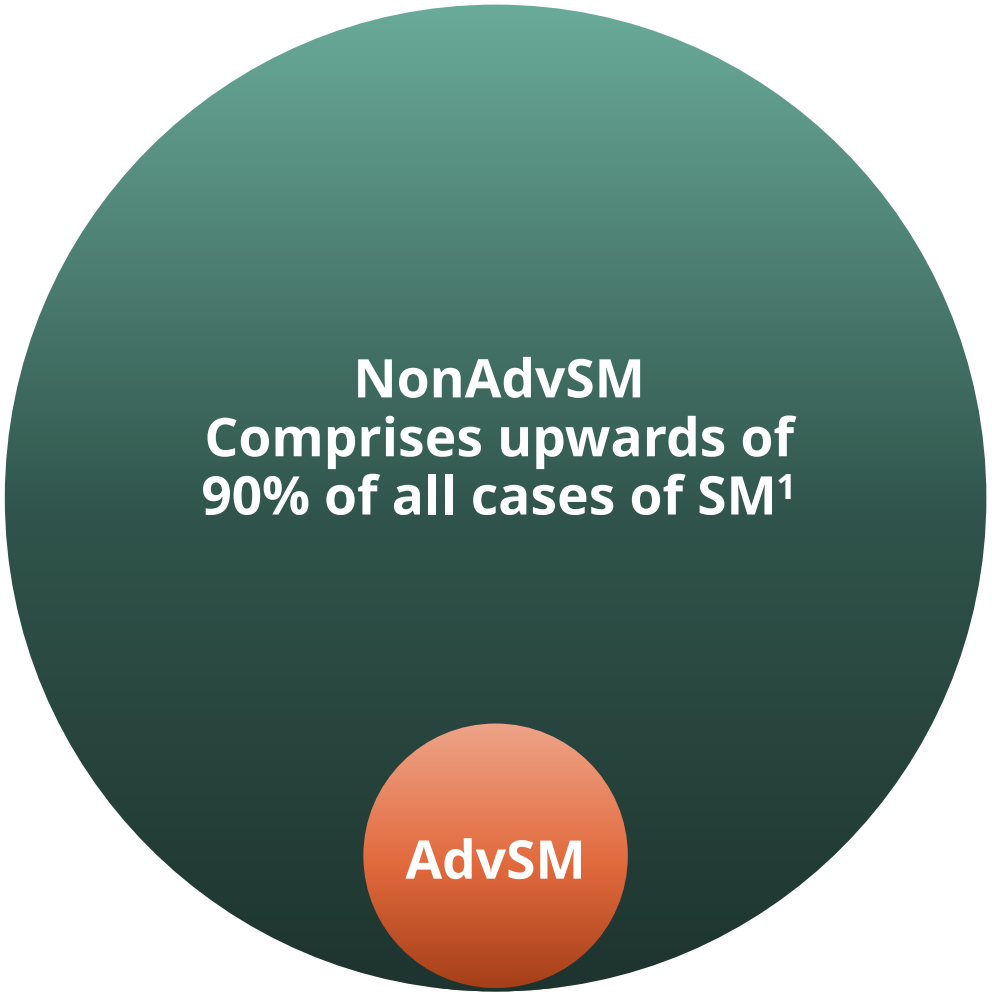
- Occurs within the activation loop domain and causes a conformational change in the enzymatic pocket of the receptor
- This conformational change results in ligand independent constitutive activation of KIT and leads to increased proliferation

Inhibition of KIT exon 17 mutations has shown clinical activity in both AdvSM and NonAdvSM

[1] Garcia-Montero et al, 2006; Jara-Acevedo et al, 2015; Vaes et al, 2017

Large, Yet Not Well Understood Population of SM Patients

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



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

[1]https://www.sciencedirect.com/science/article/abs/pii/S0145212619300566

Bezuclastinib Positioned to Move Rapidly Into AdvSM and NonAdvSM Clinical Studies

Pre-clinical KIT selectivity and potency along with clinical experience, safety, and target engagement

Apex ADVANCED SM

Phase 2 start as single agent in **Advanced Systemic Mastocytosis** (1H'2021)

Phase 2 start as single agent in **Non-Advanced Systemic Mastocytosis** (2H'2021)

Certain markers, such as serum tryptase, are considered to reflect the burden of mast cells for SM patients…

…these markers are expected to provide early information on clinical activity in the planned SM clinical trials

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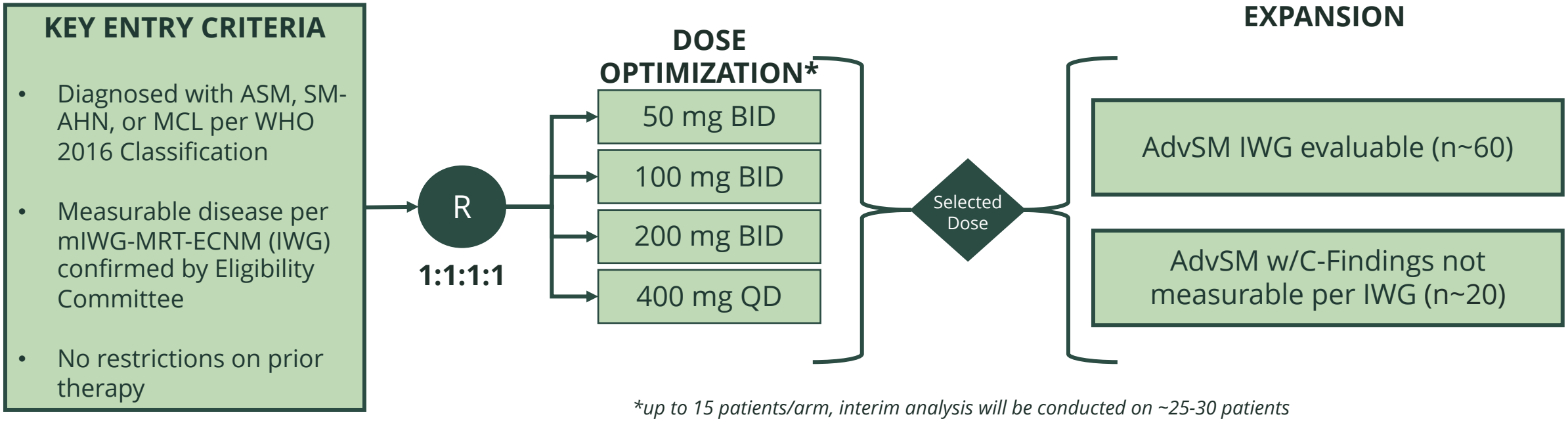
Apex: A Phase 2 Study of the Safety & Efficacy of Bezuclastinib in Patients with Advanced Systemic Mastocytosis (AdvSM)



**up to 15 patients/arm, interim analysis will be conducted on ~25-30 patients*

Primary Endpoint:

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

Other Endpoints:

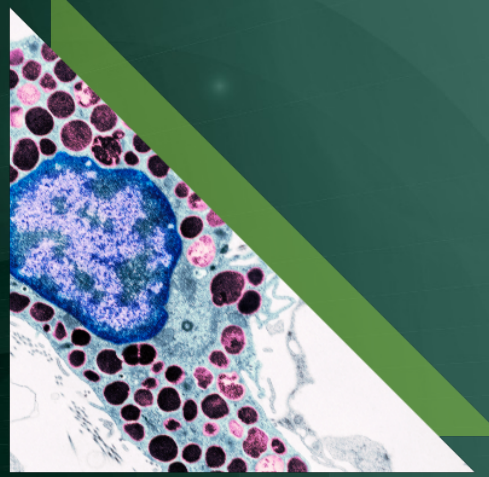
- Safety/Tolerability: Incidence of AEs leading to dose modification, changes in PROs
- Efficacy: DOR, TTR, PFS, OS, pure pathologic response
- PK/PD: plasma concentration of bezuclastinib, serum tryptase, KIT D816V burden

CR = Complete Response
ASM = Aggressive Systemic Mastocytosis
SM-AHN = Systemic Mastocytosis with Associated Hematologic Neoplasm
MCL = Mast Cell Leukemia

DOR = Duration of Response
CRh = CR with incomplete hematologic recovery
PR = Partial Response
CI = Clinical Improvement

PRO = Patient reported outcome
TTR = Time to Response
PFS = Progression Free Survival
OS = Overall Survival

GIST &
KIT Exon 13/17 Mutations



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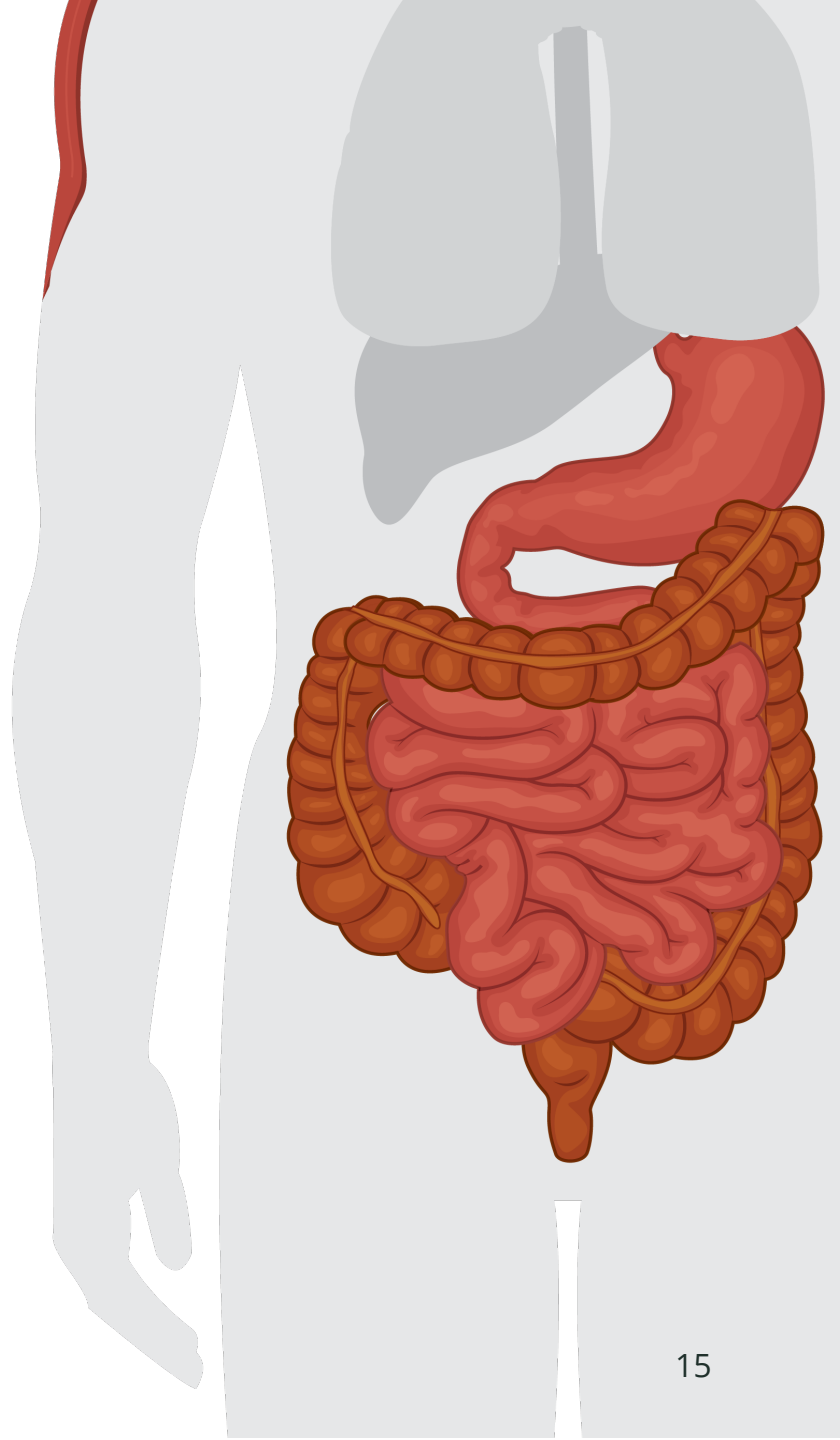
Significant Unmet Need Remains for GIST Patients

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]
- 83% 5-year survival rate[3]
- Current FDA approved therapies include imatinib, sunitinib, regorafenib, and ripretinib
- 60% of GIST patients develop resistance to imatinib (10% primary, 50% secondary resistance)[1]

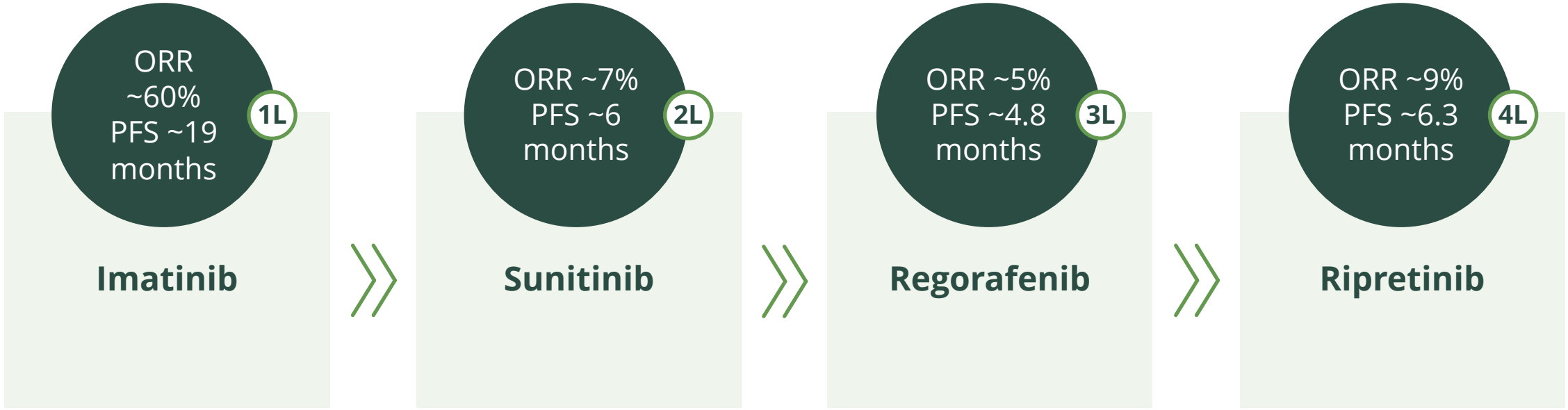
Symptoms[4]

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



[1] https://clincancerres.aacrjournals.org/content/15/24/7510
[2] https://www.cancer.org/cancer/gastrointestinal-stromal-tumor/about/key-statistics.html
[3] https://www.cancer.org/cancer/gastrointestinal-stromal-tumor/detection-diagnosis-staging/survival-rates.html
[4] https://www.cancer.org/cancer/gastrointestinal-stromal-tumor/detection-diagnosis-staging/signs-symptoms.html

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



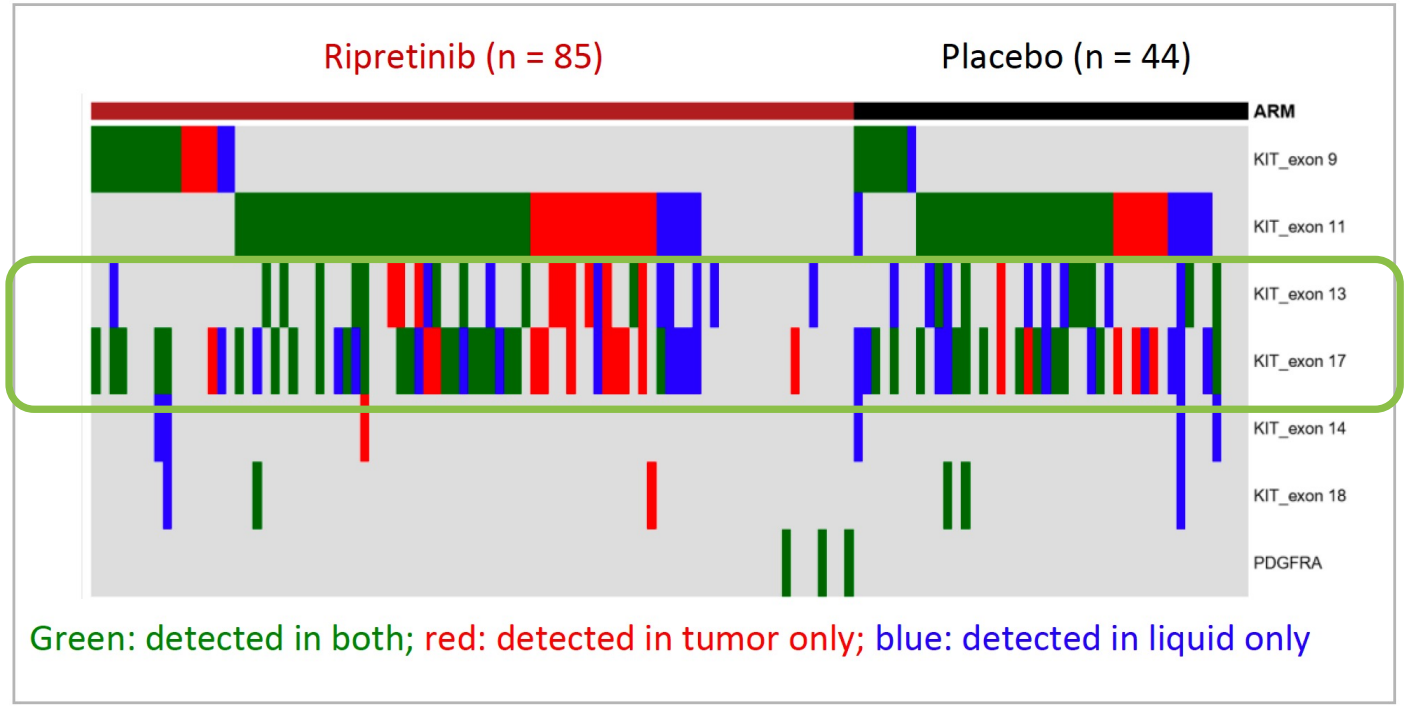
60% of GIST patients develop resistance to Imatinib.[1]

Resistance mutations driven by KIT exon 13 and KIT exon 17

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

[1] https://clincancerres.aacrjournals.org/content/15/24/7510
ORR/PFS for all approved agents was obtained from labeled information from those agents

Gastrointestinal Stromal Tumor (GIST): Imatinib-resistance Linked to KIT Exon 13 and KIT Exon 17 Mutations



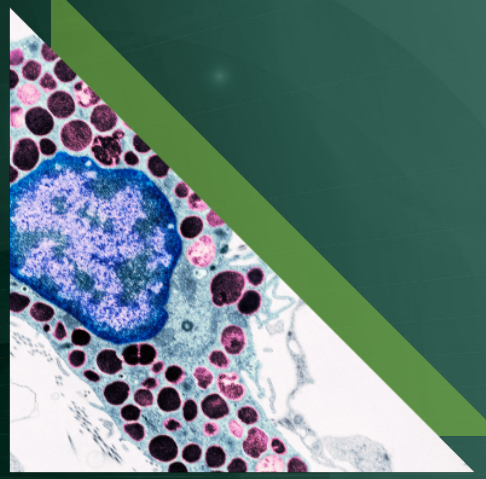
Imatinib-resistant patients most commonly exhibited secondary KIT exon 13 and/or KIT exon 17 mutations[1]

- 15-26 different mutations were found in KIT exons 17/18 in both tumor and liquid biopsies
- 5-12 different mutations were found in KIT exons 13/14 in both tumor and liquid biopsies

These study results support that there is a strong biologic rationale to treat imatinib-resistant GIST patients with combination of bezuclastinib **(KIT exon 17 inhibitor) + sunitinib (KIT exon 13 inhibitor)**

[1] Extracted from 2020 Connective Tissue Oncology Society Meeting Slides (Deciphera)

Phase 1/2 Study of Bezuclastinib + Sunitinib in Heavily Pre-Treated GIST Patients



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Study PLX121-01: Phase 1/2 Study of Bezuclastinib + Sunitinib

Eligibility

- Relapsed/Refractory GIST
- Previous imatinib treatment

Design for Part 2e

- 3+3 dose escalation
- 3 combination dose levels based on bezuclastinib single agent experience

NCT#02401815

Part 2e: Bezuclastinib **+ sunitinib**

Dose Level 1 (N=3)	→	Dose Level 2 (N=5)	→	Dose Level 3 (N=10)
bezuclastinib: 500mg sunitinib: 25 mg		bezuclastinib: 1000mg sunitinib: 25 mg		bezuclastinib: 1000mg sunitinib: 37.5 mg

All doses PO once daily

Primary Objective

Characterize the safety and tolerability of combination in patients with GIST

Secondary Objectives

Overall response rate per RECIST v1.1

Clinical benefit rate (CBR): CR + PR + SD ≥ 16 weeks

Exploratory Objective

Changes in circulating tumor DNA (ctDNA) and correlation with response and survival

Criteria for Dose Limiting Toxicities

Assessed during Cycle 1 (28 days)

Nonhematologic

- Gr ≥ 3 AE of laboratory toxicity despite adequate supportive care

Hematologic

- Gr 4 anemia, neutropenia, or thrombocytopenia
- Gr 3 neutropenia/thrombocytopenia lasting > 7 days

Demographics and Prior Therapy: Heavily Pretreated GIST Patients

	Total (N=18)	Dose Level 1 (n=3)	Dose Level 2 (n=5)	Dose Level 3 (n=10)
Age, Median (range)	62 (44 – 78)	57 (46 – 68)	55 (44 – 78)	62 (53 – 65)
Sex, male, n (%)	9 (50)	0	3 (60)	6 (60)
Prior Regimens, Median (range)	3 (1 – 6)	2 (1 – 2)	3 (1 – 6)	4 (1 – 5)
Imatinib, n (%)	18 (100)	3 (100)	5 (100)	10 (100)
Sunitinib, n (%)	13 (72)	1 (33)	4 (80)	8 (80)
Regorafenib, n (%)	12 (67)	0	4 (80)	8 (80)
Ripretinib, n (%)	5 (28)	1 (33)	1 (20)	3 (30)
≥ 3 prior lines, n (%)	12 (67)	0	4 (80)	8 (80)
Prior treatment with bezuclastinib (previously enrolled on another arm)	**3 (17)**	0	0	**3 (30)**

DL 1 = bezuclastinib 500 mg + sunitinib 25 mg; DL 2 = bezuclastinib 1000 mg + sunitinib 25 mg; DL3 = bezuclastinib 1000 mg + sunitinib 37.5 mg

All doses PO once daily

Bezuclastinib Combination has Tolerable Preliminary Safety Profile in GIST Patients

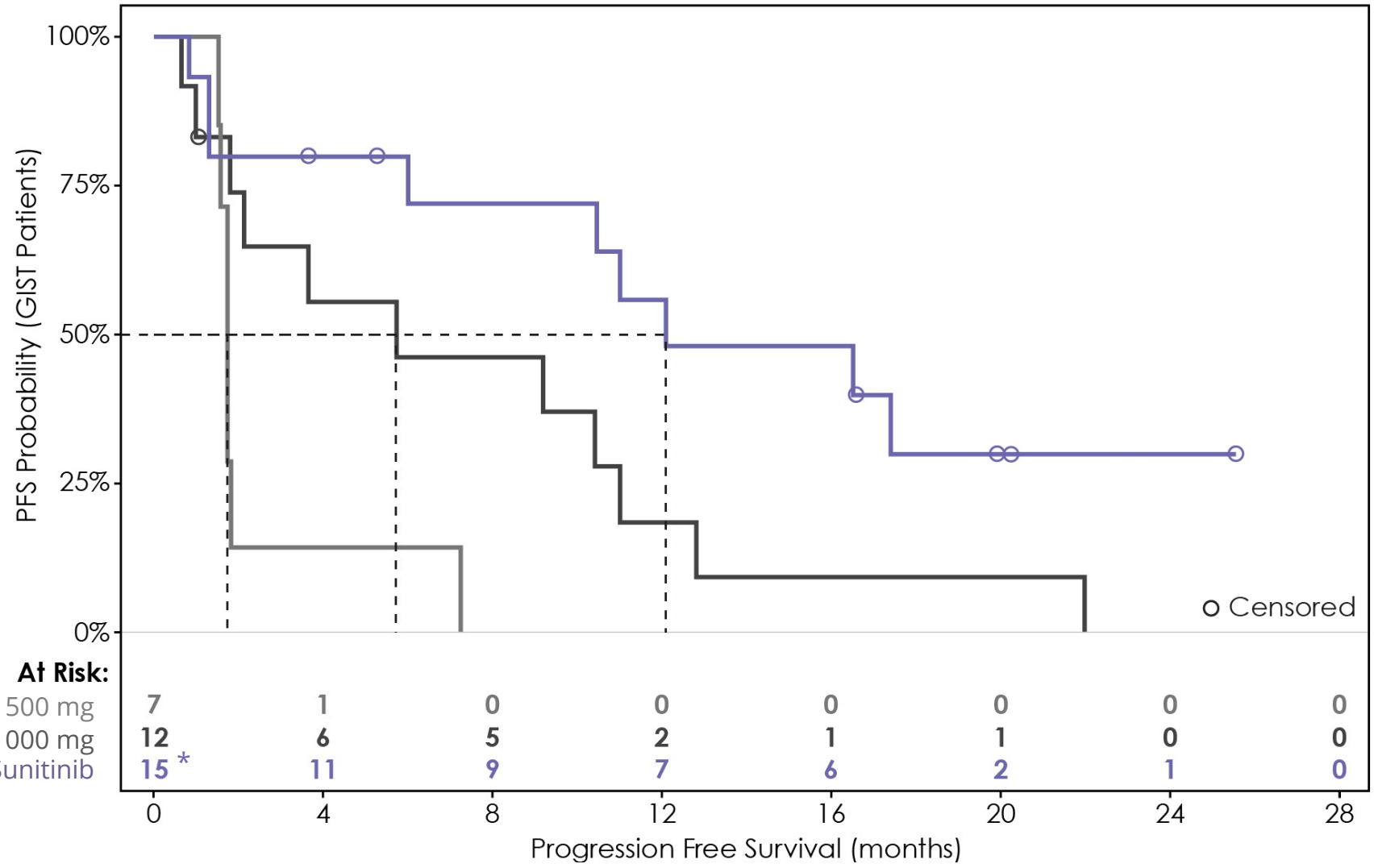
Preferred term, n	Total (n=18)		Dose Level 1 (n=3)		Dose Level 2 (n=5)		Dose Level 3 (n=10)	
	Any Gr	Gr ≥ 3	Any Gr	Gr ≥ 3	Any Gr	Gr ≥ 3	Any Gr	Gr ≥ 3
Any AE	18	16	3	2	5	5	10	9
Diarrhea	13	2	3	0	2	1	8	1
Anemia	9	5	3	1	2	1	4	3
Hypophosphatemia	7	3	1	1	3	1	3	1
Fatigue	7	2	1	0	2	0	4	2
Hypertension	7	2	0	0	3	2	4	0
Lymphopenia	3	2	1	0	0	0	2	2

DL 1 = bezuclastinib 500 mg + sunitinib 25 mg; DL 2 = bezuclastinib 1000 mg + sunitinib 25 mg; DL3 = bezuclastinib 1000 mg + sunitinib 37.5 mg

- Combination safety results generally similar to that of single-agent sunitinib observed in a separate, third-party clinical study (Demetri et al, Lancet 2006)
- Severe events did not appear to be dose-dependent
- Dose modification guidelines for treatment-related AEs allowed majority of patients to remain on treatment
  - One patient had a treatment-related AE leading to withdrawal of study treatment (gr 3 anemia)
  - Three patients required dose reduction
- One AE (sepsis) led to death (not related to study treatment; post-operative complication)

Bezuclastinib + Sunitinib: 12-Month mPFS in Heavily Pretreated GIST Patients

- **Estimated 12-month mPFS in bezuclastinib-naïve patients receiving combination**
- **Improvement in mPFS in patients receiving higher dose of single-agent bezuclastinib**
- **In subset of patients with ≥ 2 prior therapies (n=11), estimated PFS remains 12 months**

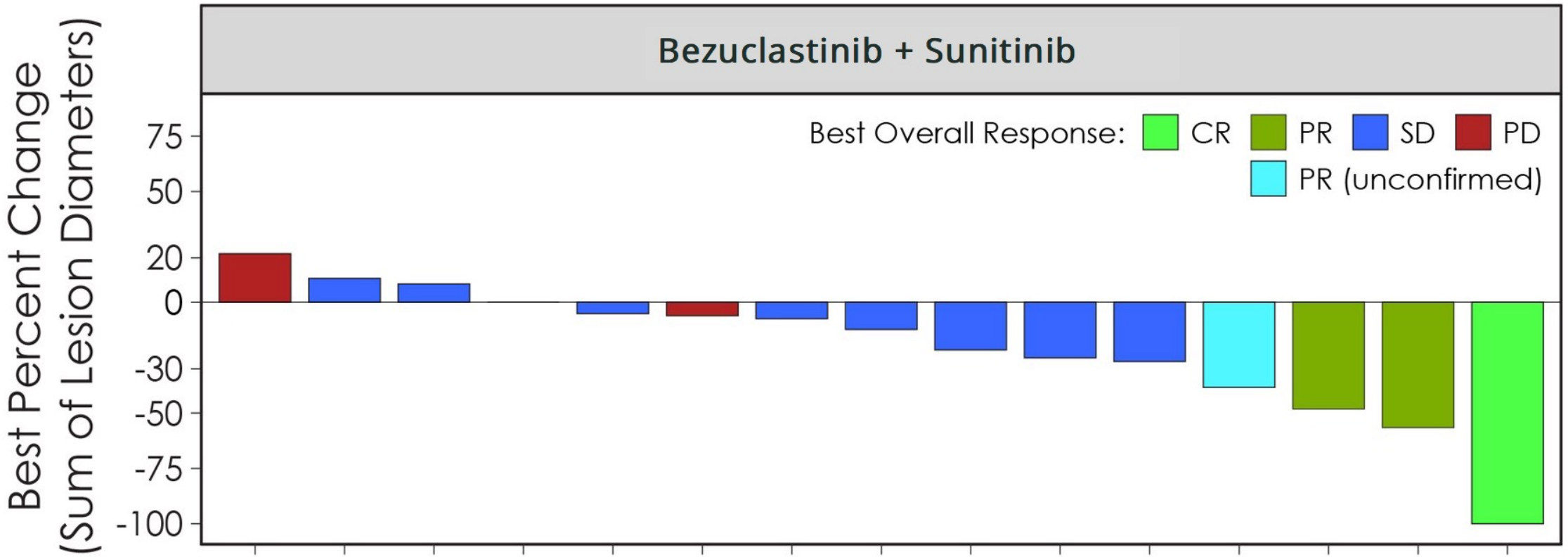


* Excludes combination therapy patients who had previously received bezuclastinib.

db snapshot: 10July2020

Bezuclastinib + Sunitinib: Reductions in Tumor Size Observed in Majority of Patients

Best Overall Response: **ORR = 20%** (1 CR, 2PR)
CBR = 80%



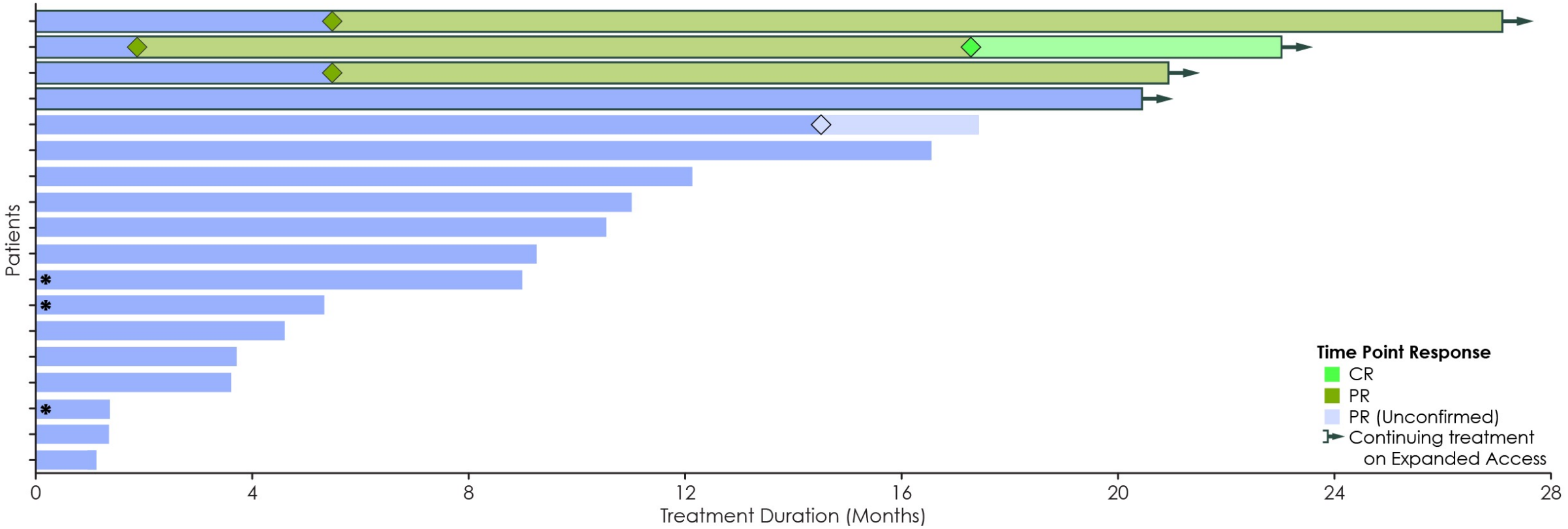
- Excludes combination therapy patients who had previously received bezuclastinib in an earlier treatment arm

ORR: Overall Response Rate (CR+PR)
CBR: Clinical benefit rate (CR+PR+SD at 16 weeks)

db snapshot: 10July2020

Durable Responses in Patients Treated with Bezuclastinib + Sunitinib

- The median duration of bezuclastinib + sunitinib treatment was 10 months (range: 1 to 27 months)
- Four patients remain on therapy, including 1 CR, 2 PR, and 1 SD
- Durable response >18 months in patients achieving confirmed response



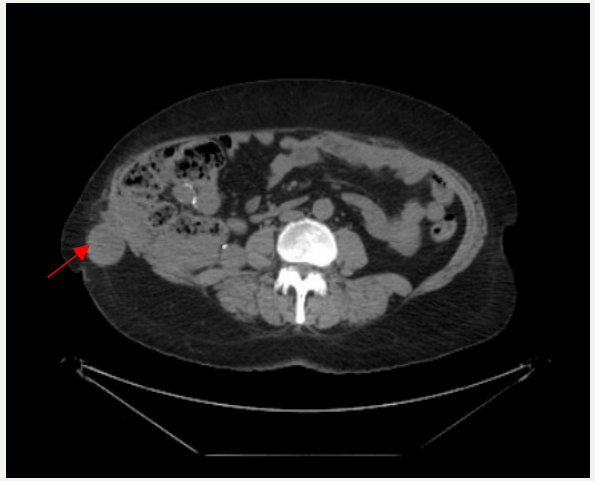
* Patient previously received bezuclastinib.

db snapshot: 10July2020

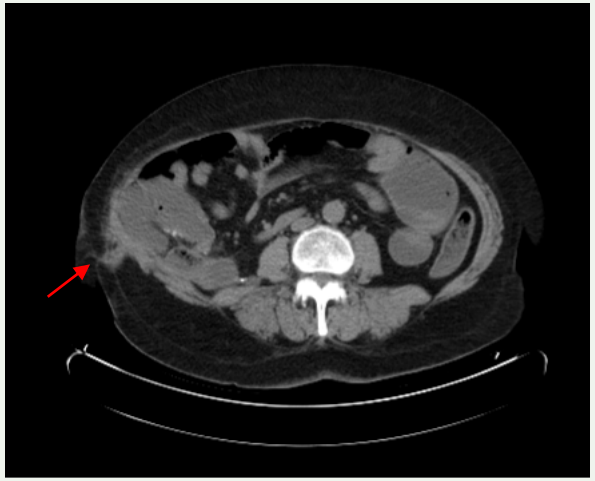
Patient Achieved Complete Response Following Three Prior Therapies when Treated at RP2D of Bezuclastinib + Sunitinib

- 65 yr old female previously refractory to imatinib (PD) and sunitinib (PD); intolerant to regorafenib
- Metabolically active right abdominal and subcutaneous masses
- Mutation status (ctDNA): KIT exon 11 & 17
- Continues on treatment > 27 months

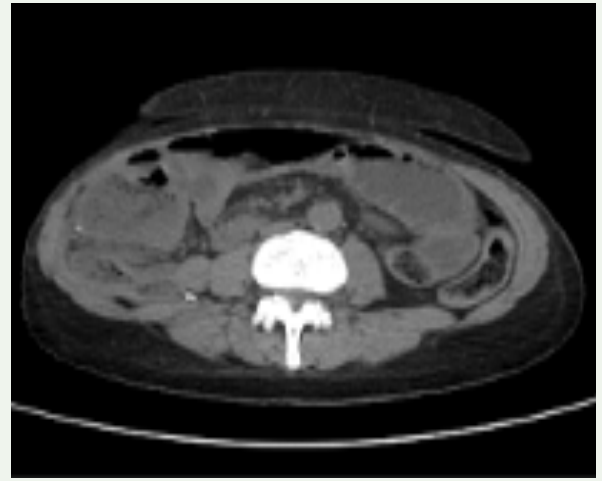
Study Entry



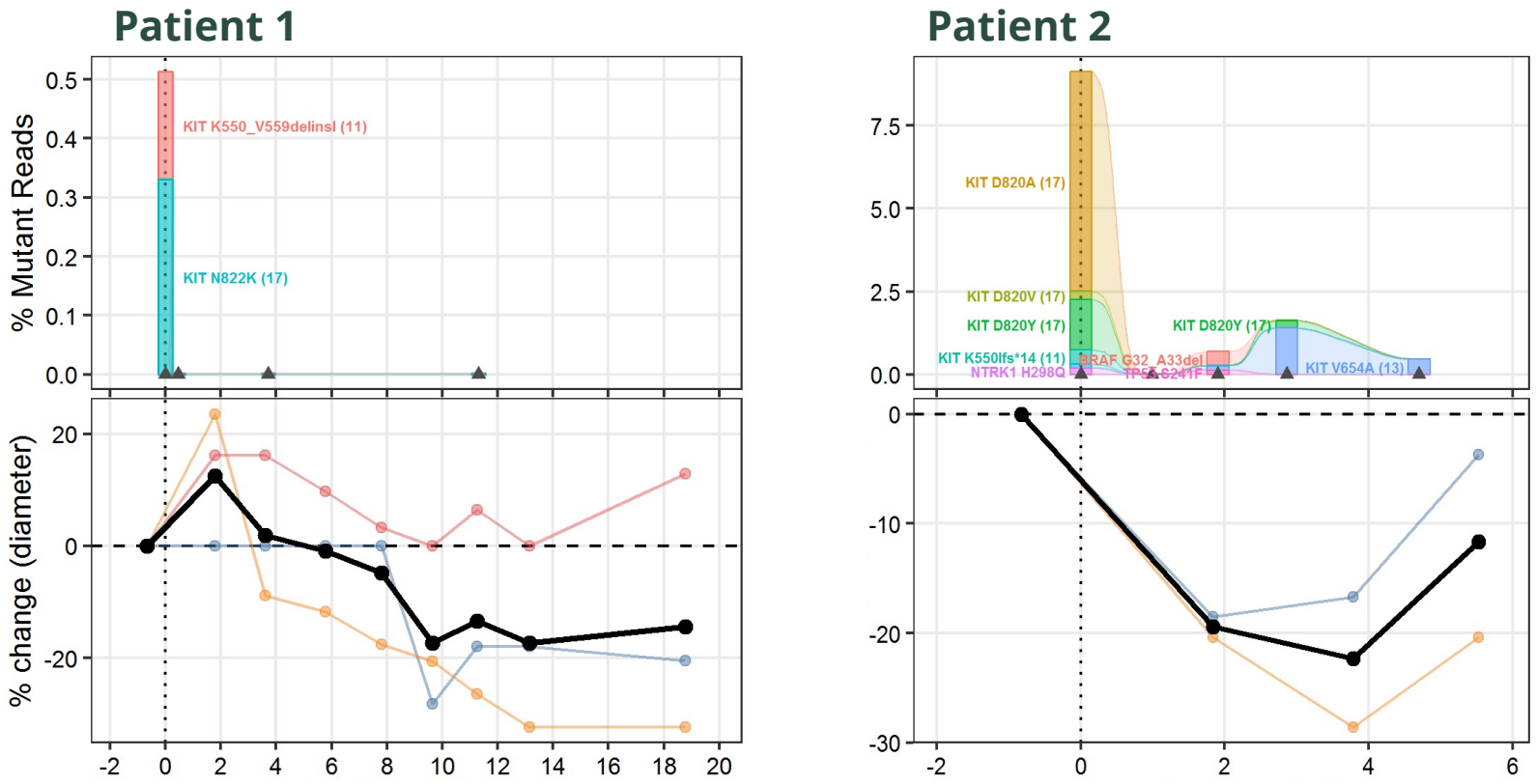
PR – Cycle 3



CR – Cycle 18



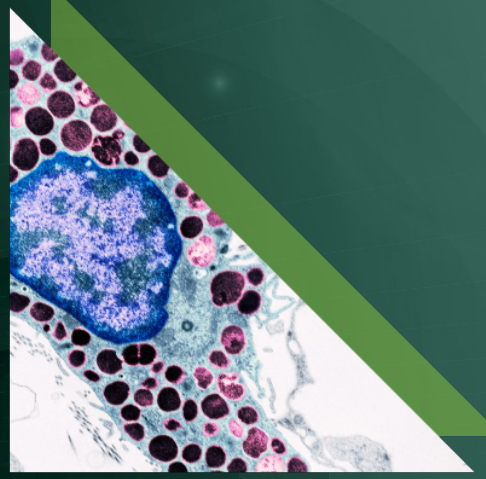
Bezuclastinib Monotherapy Exploratory Analysis: Changes in ctDNA Support Specificity of Kinase Inhibition



db snapshot: 10July2020

Black line: represents average of Sum of Product Diameters
Individual lesions represented in color

Cogent Biosciences: Emerging Leader in Field of Precision Medicines for Genetically Defined Diseases



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Experienced Leadership Team

Cogent's leadership possesses biotech and large pharma drug development experience and deep scientific expertise in developing precision medicines for genetically defined diseases.

ANDREW ROBBINS
Chief Executive Officer & President

JESSICA SACHS, MD
Chief Medical Officer

JOHN ROBINSON, PhD
Chief Scientific Officer

BRAD BARNETT
Chief Technology Officer

ERIN SCHELLHAMMER
Chief People Officer

EVAN KEARNS, JD
Chief Legal Officer

JOHN GREEN
Chief Financial Officer

SARA SALTZMAN
SVP, Regulatory Affairs

World-Class Research Team

Based in Boulder, CO, the Cogent Research Team is a world-class discovery organization focused on creating the next generation of small molecule medicines designed to bring hope to patients fighting genetically-driven diseases.

JOHN ROBINSON, PhD
Chief Scientific Officer

FRANCIS SULLIVAN, PhD
VP, Enzymology and Structural Biology

BRAD FELL
VP, Head of Medicinal Chemistry

SHANNON WINSKI, PhD
VP, Pharmacology and Toxicology

Scientific Advisory Board

Comprised of world-class experts involved in the discovery and development of novel therapeutics for patients with genetically-driven diseases, to provide external perspective for the Cogent Research Team as it develops a robust portfolio of novel, small molecule discovery programs designed to address significant patient unmet needs.

RYAN CORCORAN, MD, PhD

MICHAEL VASCONCELLES, MD

SRDAN VERSTOVSEK, MD, PhD

KWOK-KIN WONG, MD, PhD

Financial Overview

As of June 30, 2021, Cogent Biosciences had cash and cash equivalents of $218.1 million. We believe our cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements into 2024.

Company Capitalization Structure As of June 30, 2021	Converted Common Shares
Common stock outstanding	39,830,767
Series A Preferred Stock (1)	25,822,250
Adjusted fully diluted Common stock outstanding	**65,653,017**

[1] *This includes 100% conversion of all outstanding Series A Preferred Stock, post 1-for-4 reverse split.*

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Thank You

CogentBio.com

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