cogent BIOSCIENCES

Precision therapies for genetically defined diseases

Jefferies Virtual London Healthcare Conference

November 18, 2020

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.

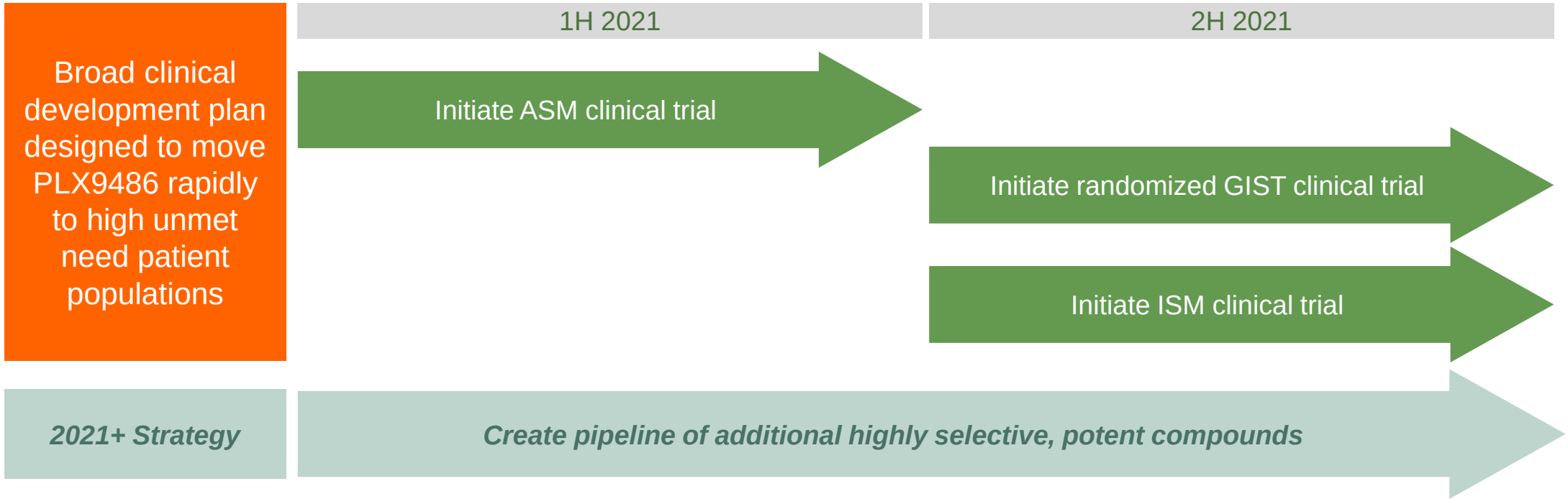
These statement are based on estimates and information available to us at the time of this presentation and are not guarantees of future performance. Actual results could differ materially from our current expectations as a result of many risks and uncertainties, including but not limited to, risks associated with: the success, cost and timing of our product development activities and clinical trials; our ability to obtain regulatory approval for and to commercialize our product candidates; our ability to establish a commercially-viable manufacturing process and manufacturing infrastructure; regulatory requirements and regulatory developments; the effects of competition and technological advances; our dependence on third-party collaborators and other contractors in our research and development activities, including for the conduct of clinical trials and the manufacture of our product candidates; our ability to obtain, maintain, or protect intellectual property rights related to 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 (“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.

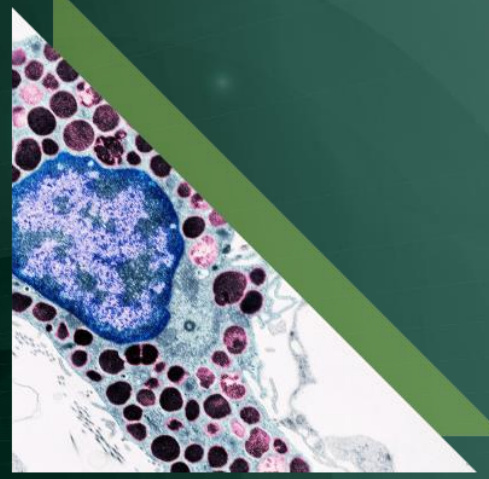
Cogent Biosciences: Emerging Leader in Precision Medicines for Genetically Defined Diseases

PLX9486, a potential **best-in-class KIT exon 17 inhibitor**, has demonstrated promising clinical efficacy and safety in gastrointestinal stromal tumors (GIST), along with accelerated timelines to proof-of-concept in systemic mastocytosis



Cogent is well capitalized with **$129.4 million** as of September 30, 2020

PLX9486: Next-Generation KIT exon 17 Inhibitor



cogent BIOSCIENCES

PLX9486 is a Highly Selective and Potent KIT Mutant Inhibitor with Potential to Demonstrate Best-in-Class Clinical Profile

PLX9486

- Specifically targets KIT exon 17 D816V mutations
- Selective versus other targets including wild-type KIT, PDGFRα, VEGFR2, FLT3 and FMS
- 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 PLX9486 + 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 exon 17 inhibitor

KIT D816V inhibition supports future studies in systemic mastocytosis and GIST; safety profile supports broad use

[1] Plexxikon is eligible for mid- to high- single-digit royalties and additional development milestones. License includes rights to PLX0206, an additional selective KIT inhibitor in preclinical development
[2] Does not include available patent term extension

PLX9486 Designed as Potent and Selective KIT exon 17 D816V Inhibitor

PLX9486 is a Type I Inhibitor designed to selectively bind the active conformation of mutant KIT

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

Potency

Assay	IC50 (nM)	
	PLX9486	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 PLX9486 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 PLX9486 and avapritinib.

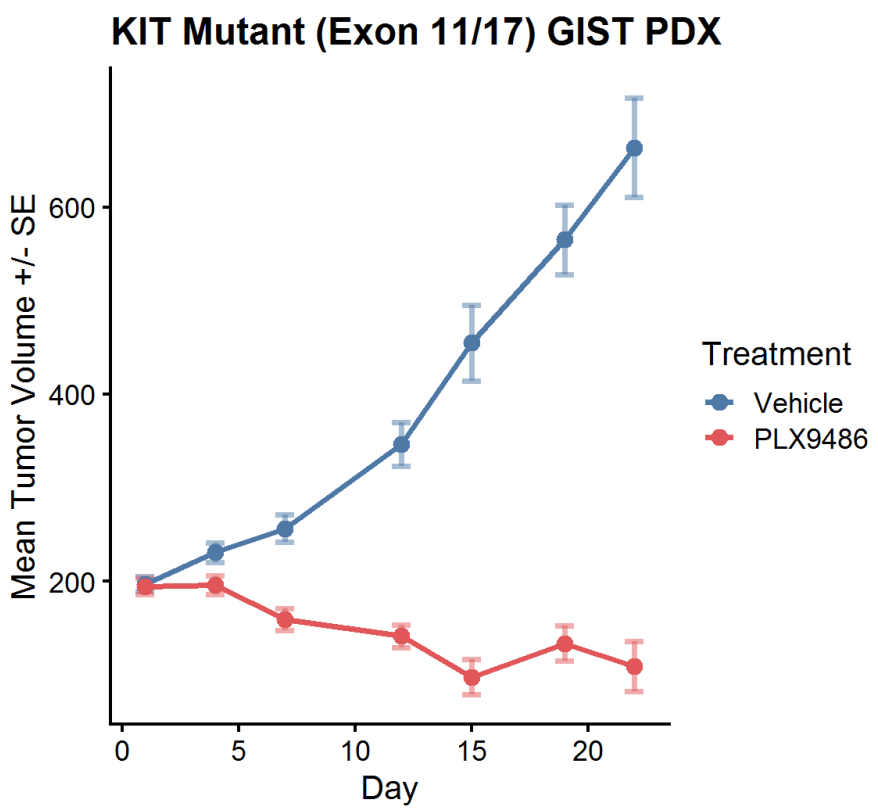
Selectivity

Enzyme	IC50 (nM) **PLX9486**
c-Kit (wt)	>5000*
c-Kit (D816V)	1.125
FMS	602.4
KDR/VEGFR2	>5000*
PDGFRα	>5000*
PDGFRα (D842V)	104.3

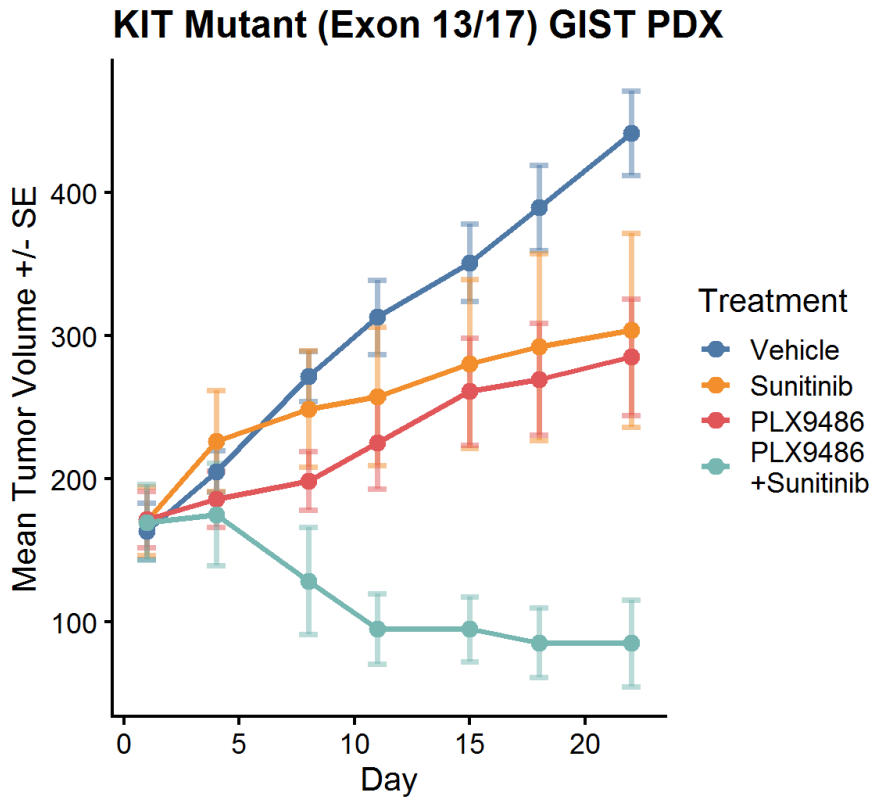
*Highest concentration tested in biochemical assay

Dual-conformation KIT Inhibition Drives Tumor Regression in Heterogeneous GIST mouse models

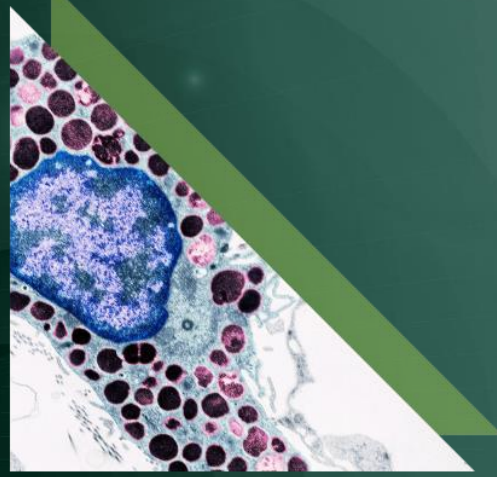
Ex11 (W557_K558del), Ex17 (N822K)



Ex13 (K642E), Ex17 (D823Y)



Systemic Mastocytosis & KIT exon 17 D816V mutations



cogent BIOSCIENCES

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

Advanced Systemic Mastocytosis (ASM)

- Median survival of approximately ≤ 3.5 years
- FDA approved drug, Rydapt (Midostaurin), broad spectrum TKI, challenging tolerability

Indolent and Smoldering Mastocytosis (ISM)

- Significantly impacts quality of life
- 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

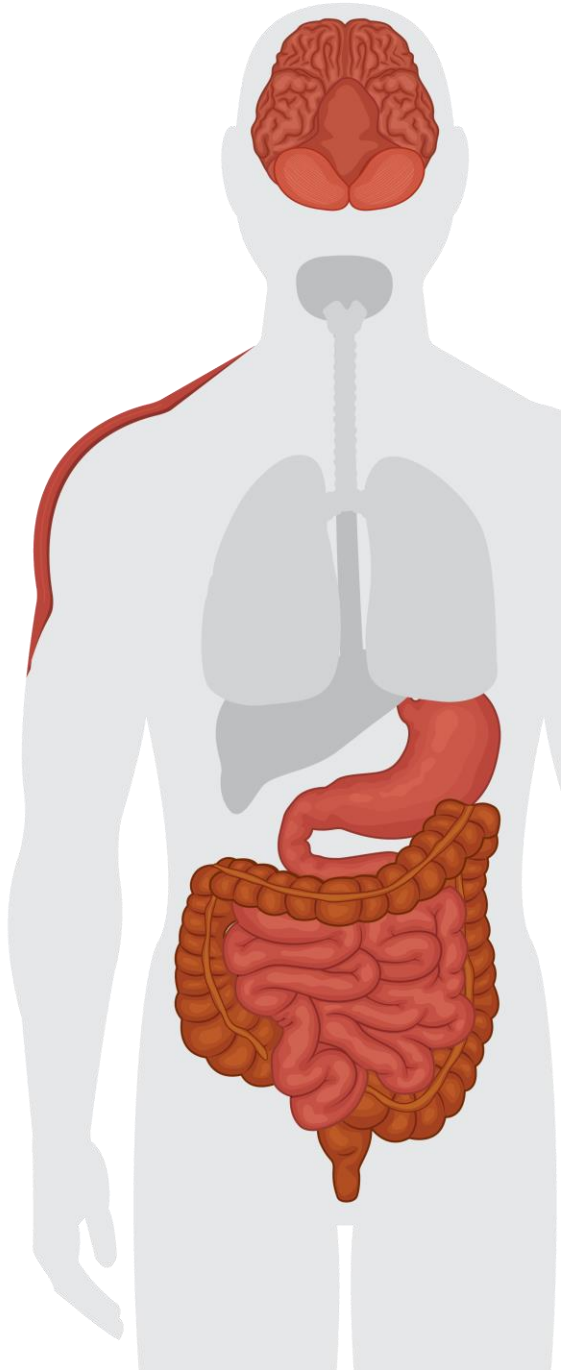
Bone/muscle pain, osteopenia, osteoporosis

Gynecological

Uterine cramps, bleeding

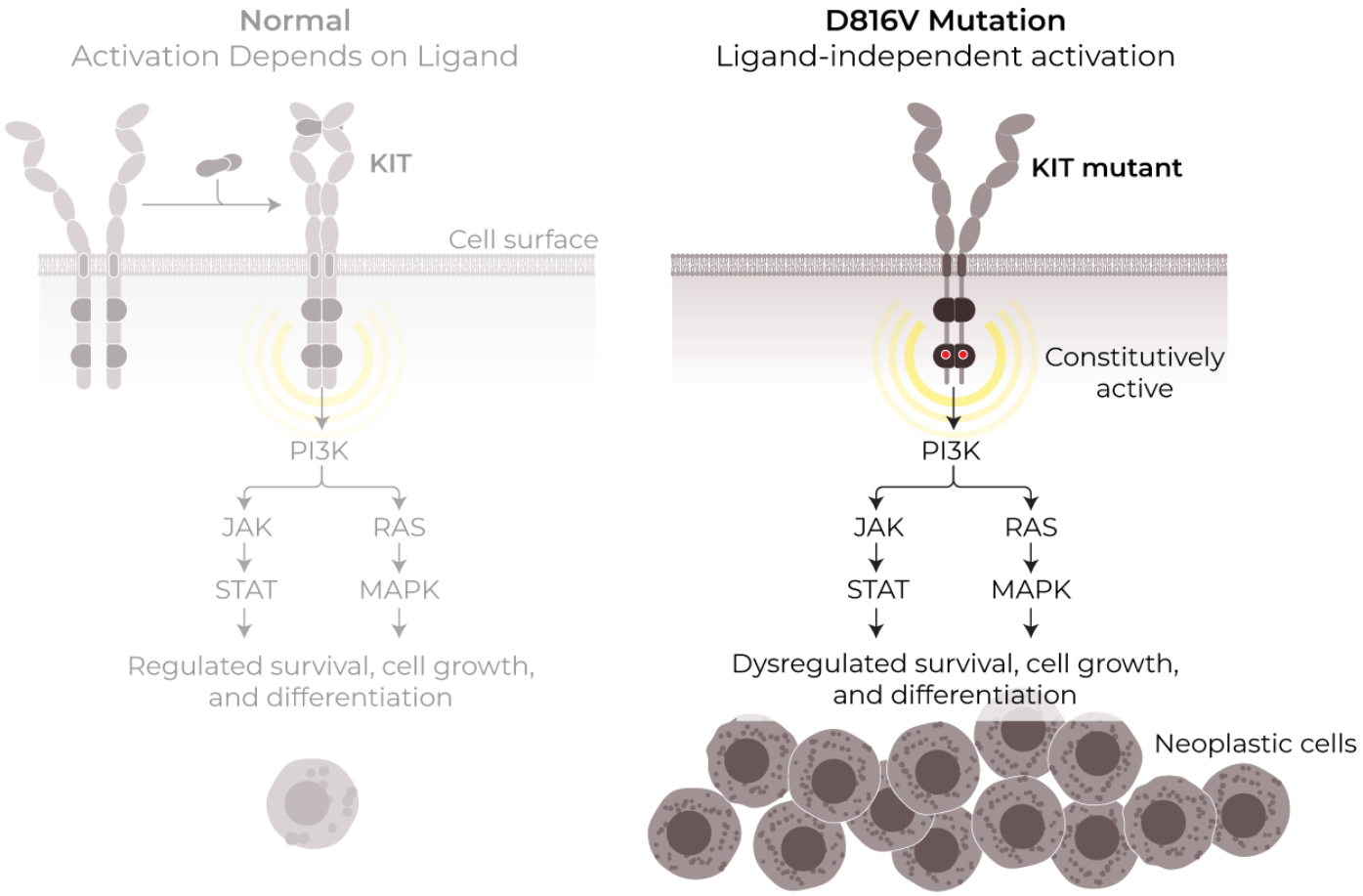
Urinary

Bladder irritability, frequent voiding



cogent BIOSCIENCES

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



KIT exon 17 D816V mutation is detected in >90% 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 ASM and ISM

[1]https://www.nejm.org/doi/full/10.1056/NEJMoa1513098

Large, Yet Not Well Understood Population of SM Patients

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

PLX9486 Positioned to Move Rapidly Into ASM and ISM Clinical Studies

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

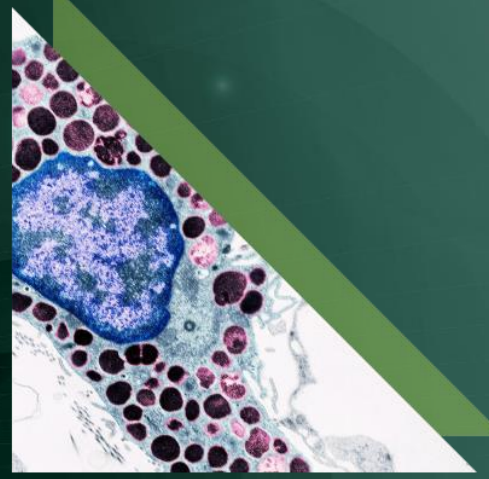
Phase 2 start as single agent in **Advanced Systemic Mastocytosis** (1H'2021)

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

Serum tryptase level is used as diagnostic marker for SM patients and considered to reflect the burden of mast cells…

…will provide a well understood and accepted rapid clinical proof of concept for ASM & ISM clinical trials

GIST &
KIT exon 13/17 mutations



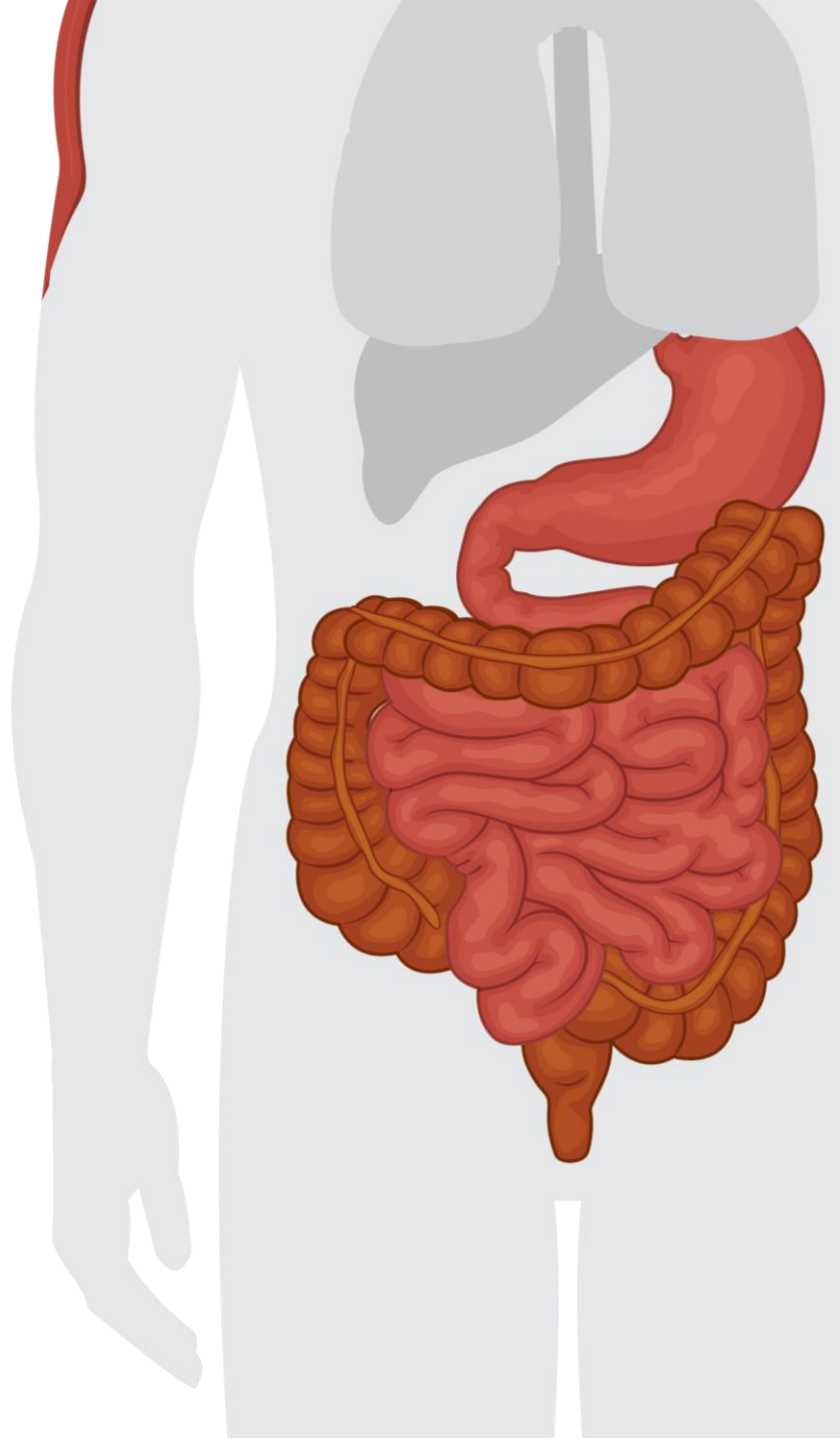
Significant Unmet Need Remains for GIST Patients

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]

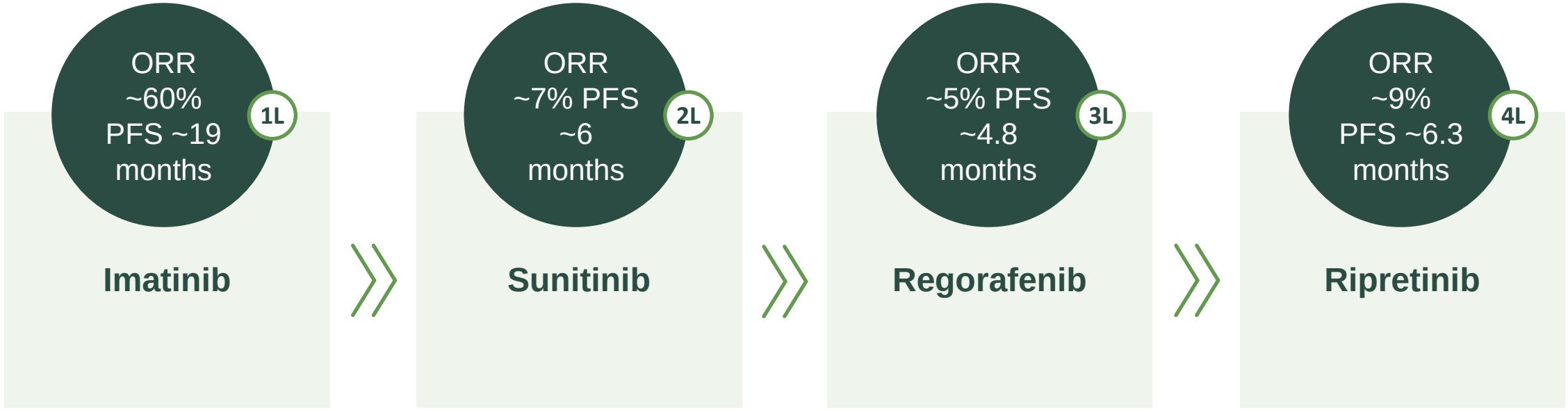
Symptoms[4]

Diarrhea, Nausea, Vomiting, Abdominal Pain, Bloating, Gastroesophageal reflux disease GERD, 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



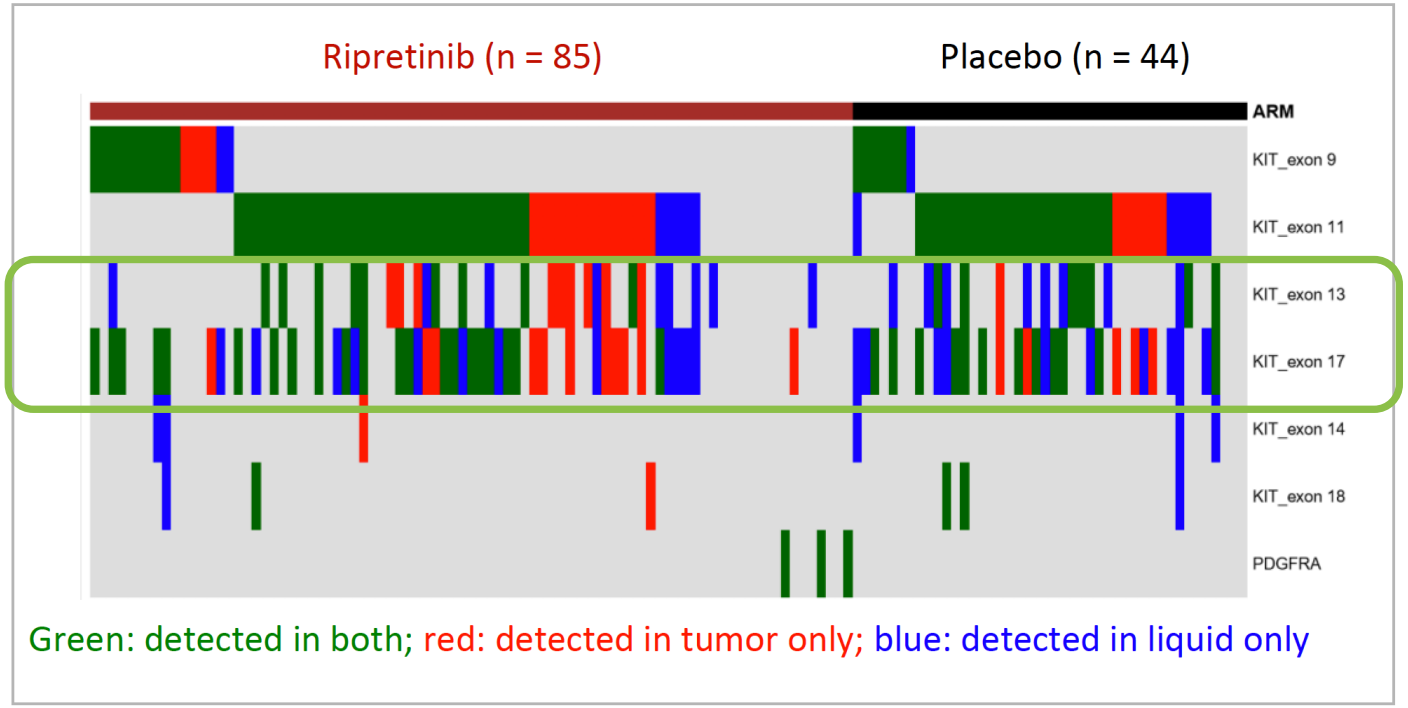
60% of GIST patients develop resistance to Imatinib.[1]

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

Gastrointestinal Stromal Tumor (GIST): Imatinib-resistance linked to KIT exon 13 and KIT exon 17 mutations



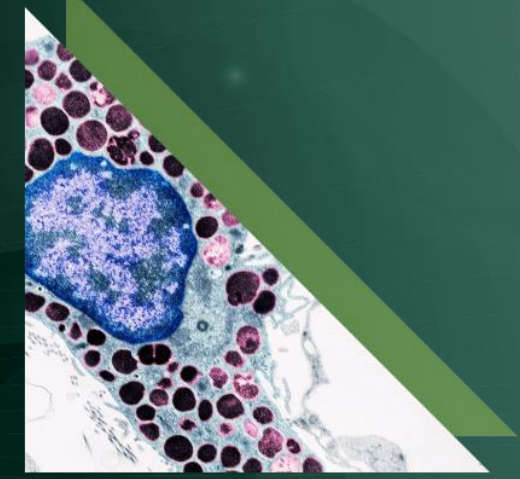
Imatinib-resistant patients most commonly exhibit secondary KIT exon 13 and/or KIT exon 17 mutations[1]

- 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

Strong biologic rationale to treat imatinib-resistant GIST patients with combination of PLX9486 (KIT exon 17 inhibitor) + sunitinib (KIT exon 13 inhibitor)

[1] Deciphera CTOS Annual Meeting 2020, November 17, 2020

Phase 1/2 Study of PLX9486 + sunitinib in Heavily Pre-Treated GIST Patients



cogent BIOSCIENCES

Study PLX121-01: Phase 1/2 Study of PLX9486 + Sunitinib

Eligibility

- Relapsed/Refractory GIST
- Previous imatinib treatment

Design for Part 2e

- 3+3 dose escalation
- 3 combination dose levels based on PLX9486 single agent experience

NCT#02401815

Part 2e: PLX9486 + Sunitinib

Dose Level 1 (N=3)
PLX9486: 500mg
Sunitinib: 25 mg

→

Dose Level 2 (N=5)
PLX9486: 1000mg
Sunitinib: 25 mg

→

Dose Level 3 (N=10)
PLX9486: 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

cogent BIOSCIENCES

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 PLX9486 (previously enrolled on another arm)	**3 (17)**	0	0	**3 (30)**

DL 1 = PLX9486 500 mg + Sunitinib 25 mg; DL 2 = PLX9486 1000 mg + Sunitinib 25 mg; DL3 = PLX9486 1000 mg + Sunitinib 37.5 mg

All doses PO once daily

cogent BIOSCIENCES

db snapshot: 10July2020

Combination Safety Profile Generally Similar to Single-Agent sunitinib

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

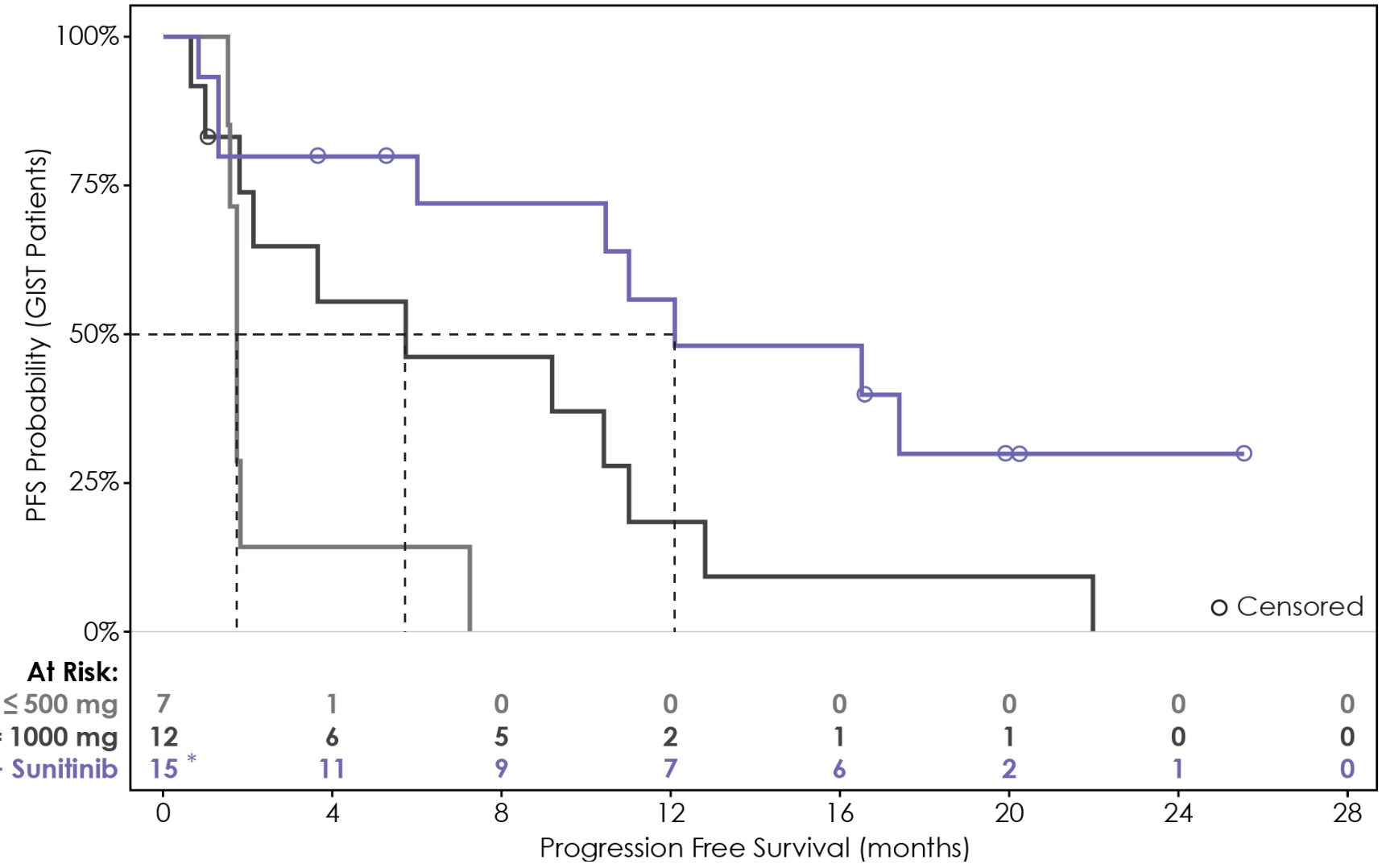
DL 1 = PLX9486 500 mg + Sunitinib 25 mg; DL 2 = PLX9486 1000 mg + Sunitinib 25 mg; DL3 = PLX9486 1000 mg + Sunitinib 37.5 mg

- Combination safety profile generally similar to that of single-agent sunitinib (Demetri et al, Lancet 2006)
- Severe events do 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) leading to death (not related to study treatment; post-operative complication)

db snapshot: 10July2020

PLX9486 + Sunitinib: 12-Month mPFS in Heavily Pretreated GIST Patients

- **Estimated 12-month mPFS in PLX9486-naïve patients receiving combination**
- **mPFS improvement for patients receiving higher dose of single-agent PLX9486**
- **In subset of patients with ≥ 2 prior therapies (n=11), estimated PFS remains 12 months**

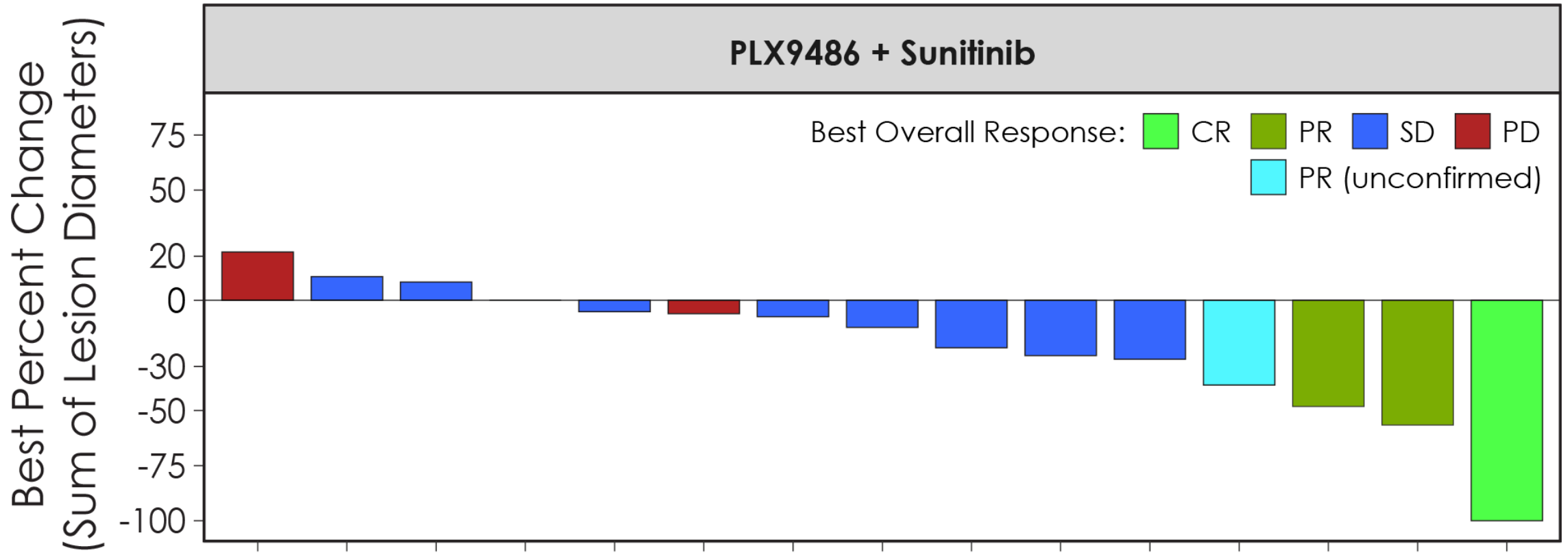


* Excludes combination therapy patients who had previously received PLX9486.

db snapshot: 10July2020

PLX9486 + Sunitinib: Clinical Benefit Observed in Majority of Patients

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



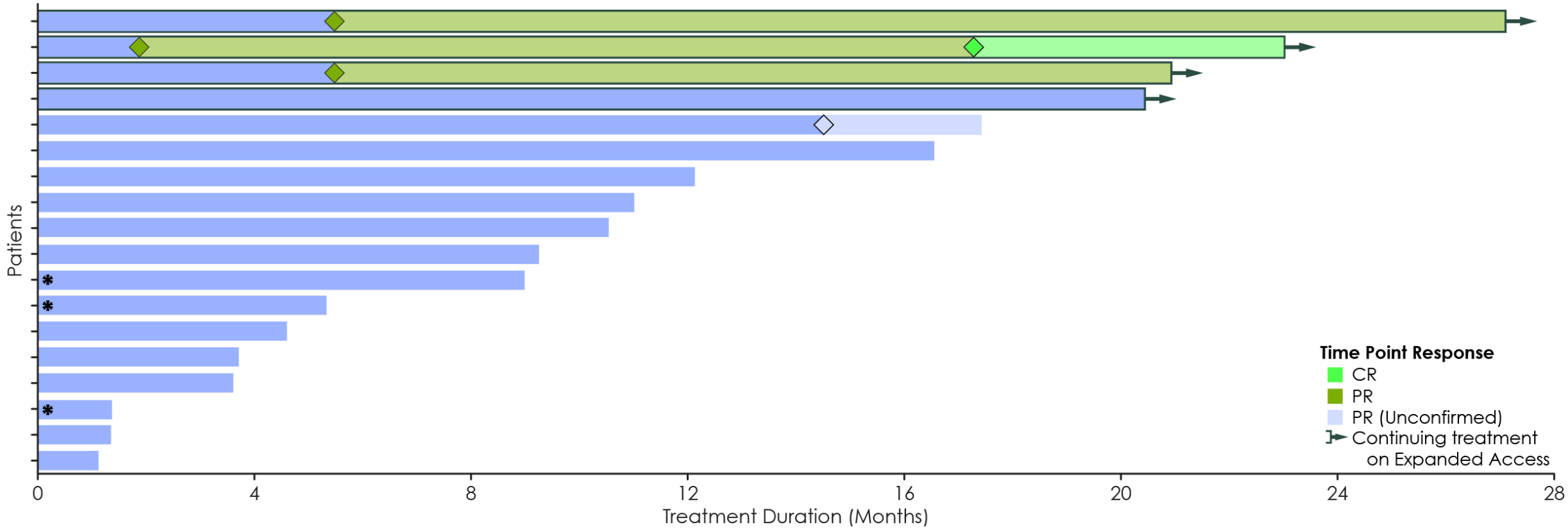
- Excludes combination therapy patients who had previously received PLX9486

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 PLX9486 + Sunitinib

- The median duration of PLX9486 + sunitinib treatment was 10 months (range: 1 to 27 months)
- Four patients remain on therapy, including 1 CR and 2 PR
- Durable response >18 months in patients achieving confirmed response



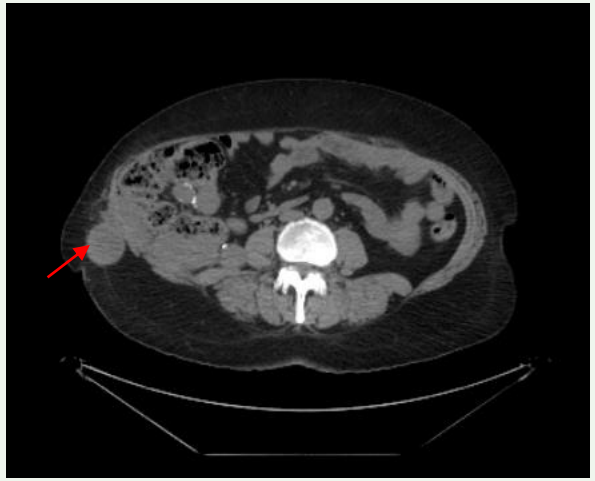
* Patient previously received PLX9486.

db snapshot: 10July2020

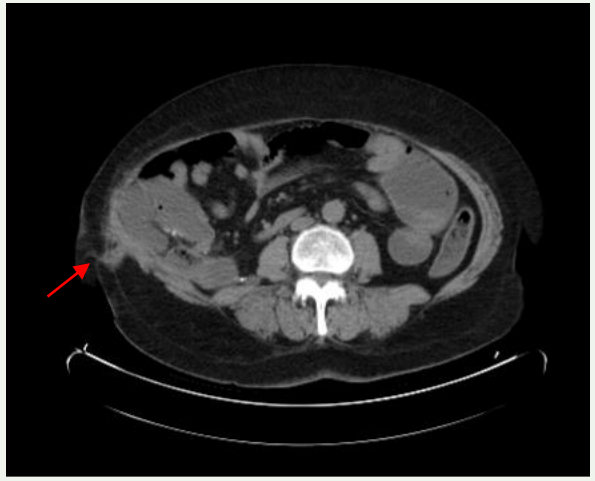
Patient Achieved Complete Response Following Three Prior Therapies When Treated at RP2D of PLX9486 + Sunitinib

- 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

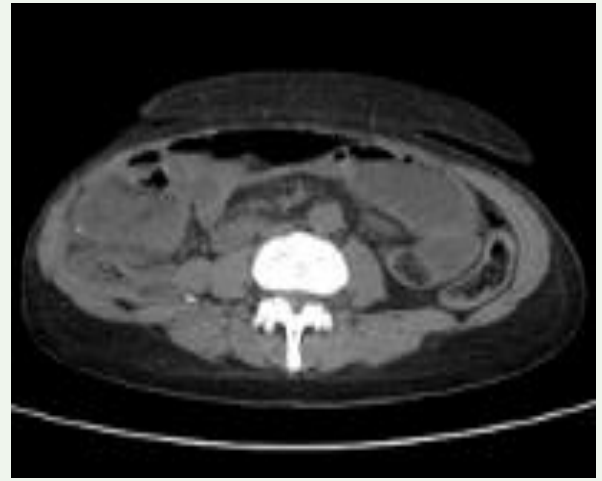
Study Entry



PR – Cycle 3

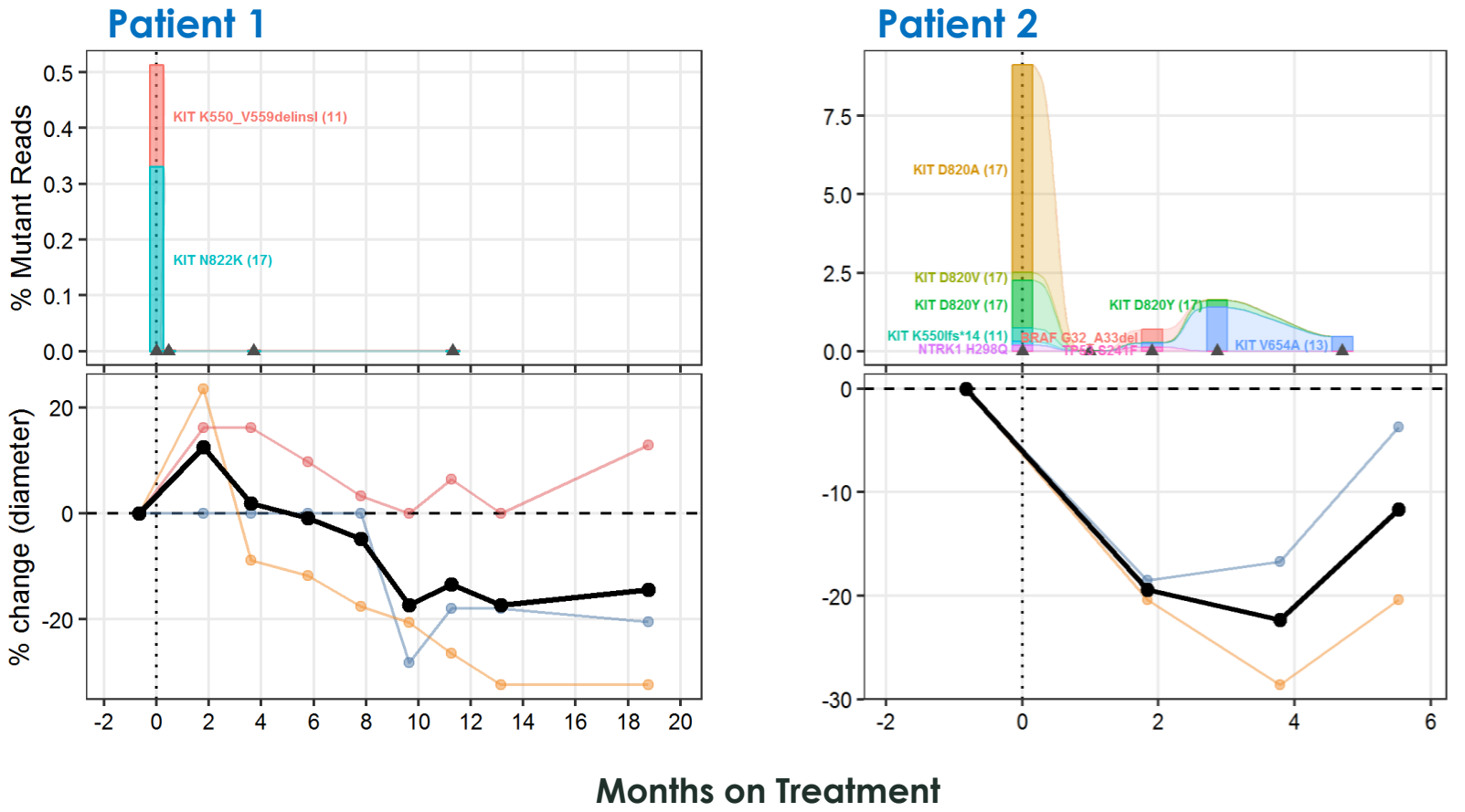


CR – Cycle 18



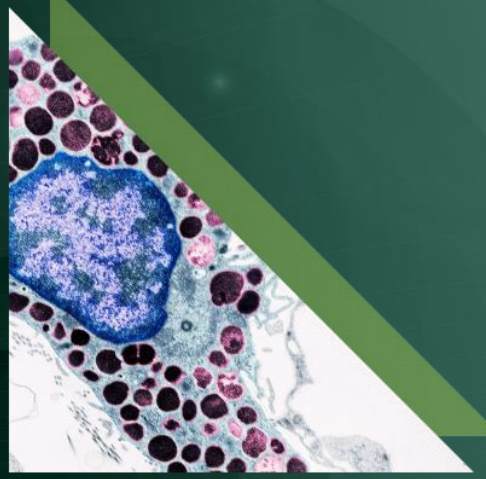
cogent BIOSCIENCES

PLX9486 Monotherapy Exploratory Analysis: Changes in ctDNA Support Specificity of Kinase Inhibition



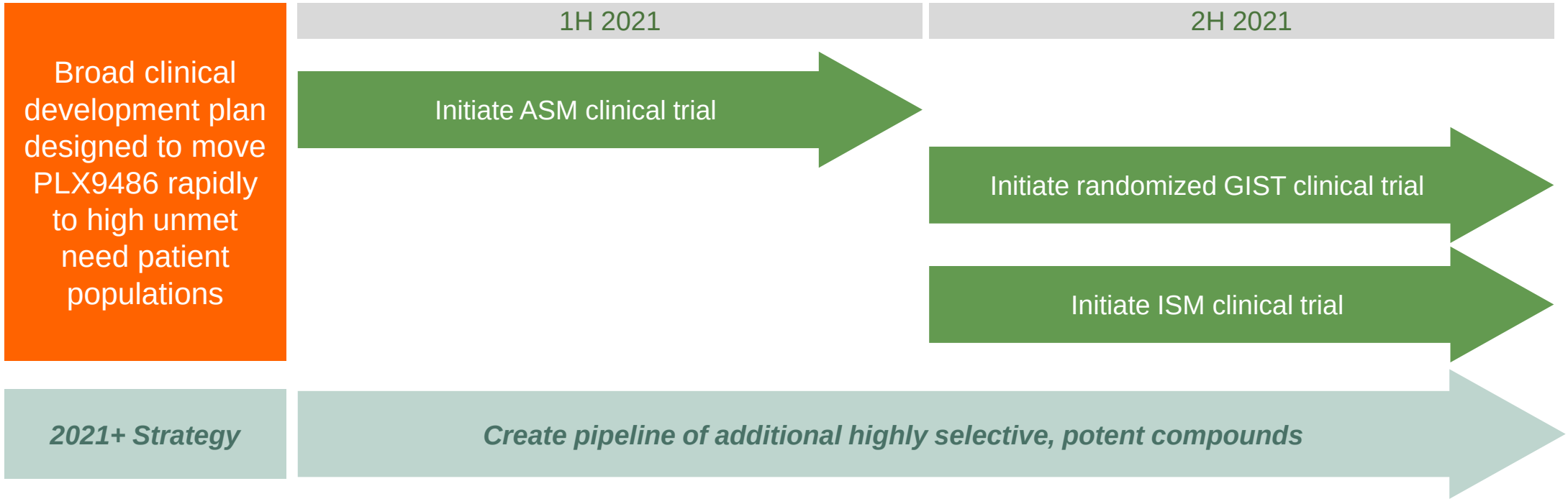
Black line: represents average of Sum of Product Diameters
Individual lesions represented in color

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



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

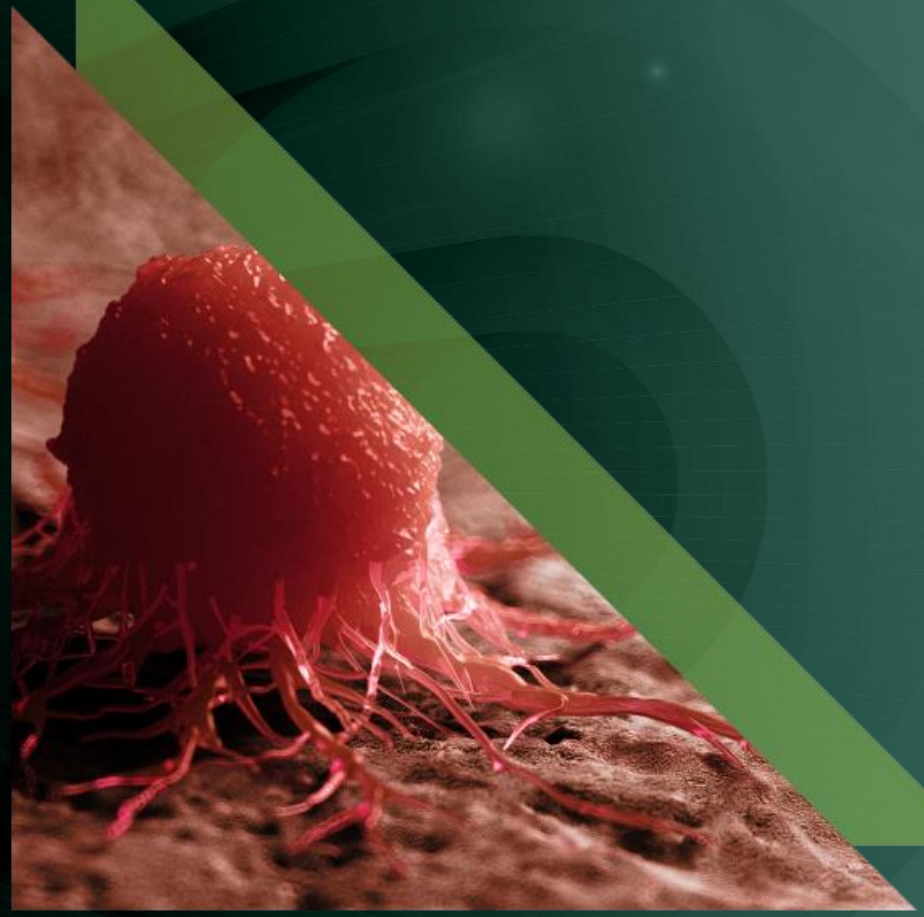
PLX9486, a potential **best-in-class KIT exon 17 inhibitor**, has demonstrated promising clinical efficacy and safety in gastrointestinal stromal tumors (GIST), along with accelerated timelines to proof-of-concept in systemic mastocytosis



Cogent is well capitalized with **$129.4 million** as of September 30, 2020

cogent BIOSCIENCES

Thank You



CogentBio.com

Cogent Biosciences, Inc. | 200 Cambridge Park Drive
Suite 2500 | Cambridge, MA 02140 USA