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Precision therapies for genetically defined diseases

Corporate Presentation

October 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.

Building a Rational Precision Therapy Company

Focused on Addressing the True Underlying Drivers of Disease and Providing Real Hope for Patients

PLX9486, a potential best-in-class KIT D816V inhibitor, is a foundational program with promising clinical efficacy and safety in gastrointestinal stromal tumors (GIST)

Accelerated timeline to proof-of-concept serum tryptase data in advanced systemic mastocytosis (ASM) and indolent systemic mastocytosis (ISM)

Attractive **systemic mastocytosis** commercial opportunity potentially adds another, larger indication for PLX9486 to pursue beyond GIST

Building a **fully integrated company** with an expanding product pipeline focused on genetically validated targets

Lead Program PLX9486 is a Highly Selective and Potent KIT Mutant Inhibitor with a Potentially Best-in-Class Clinical Profile

PLX9486

- Specifically targets KIT Exon 17 D816V
- Selective versus other targets including wild-type KIT, PDGFRα, VEGFR2, FLT3, FMS
- Worldwide rights to compound exclusively licensed from Plexxikon[1]
- Patent protection through at least 2033[2]

Efficacy Data[3]

11 months PFS shown in 18 heavily treatment-experienced GIST patients treated with PLX9486 in combination with sunitinib

Safety Experience

Single agent & combination activity and safety data in 50+ patients supports further clinical development

Potential Best-in-Class Profile

KIT D816V inhibition supports future studies in mastocytosis; safety 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.
[3] Based on a Phase 1/2 clinical trial including GIST patients conducted by Plexxikon

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By Design, PLX9486 has Potency and Selectivity to KIT D816V

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

Cogent's Lead Program PLX9486 Has Phase 2 Data and Can Rapidly Move Into 3 Mid-to-Late Stage Clinical Trials

Current

PLX9486 with single-agent and combination Phase 1/2 data in 2L+ GIST

Upcoming trial plans pending FDA regulatory feedback

Phase 3 start in **GIST** in combination with sunitinib (2H'2021)

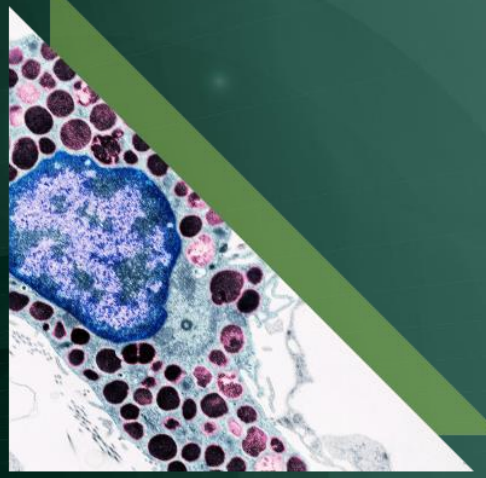
Phase 2 start as single agent in **Advanced Systemic Mastocytosis** (1H'2021)

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

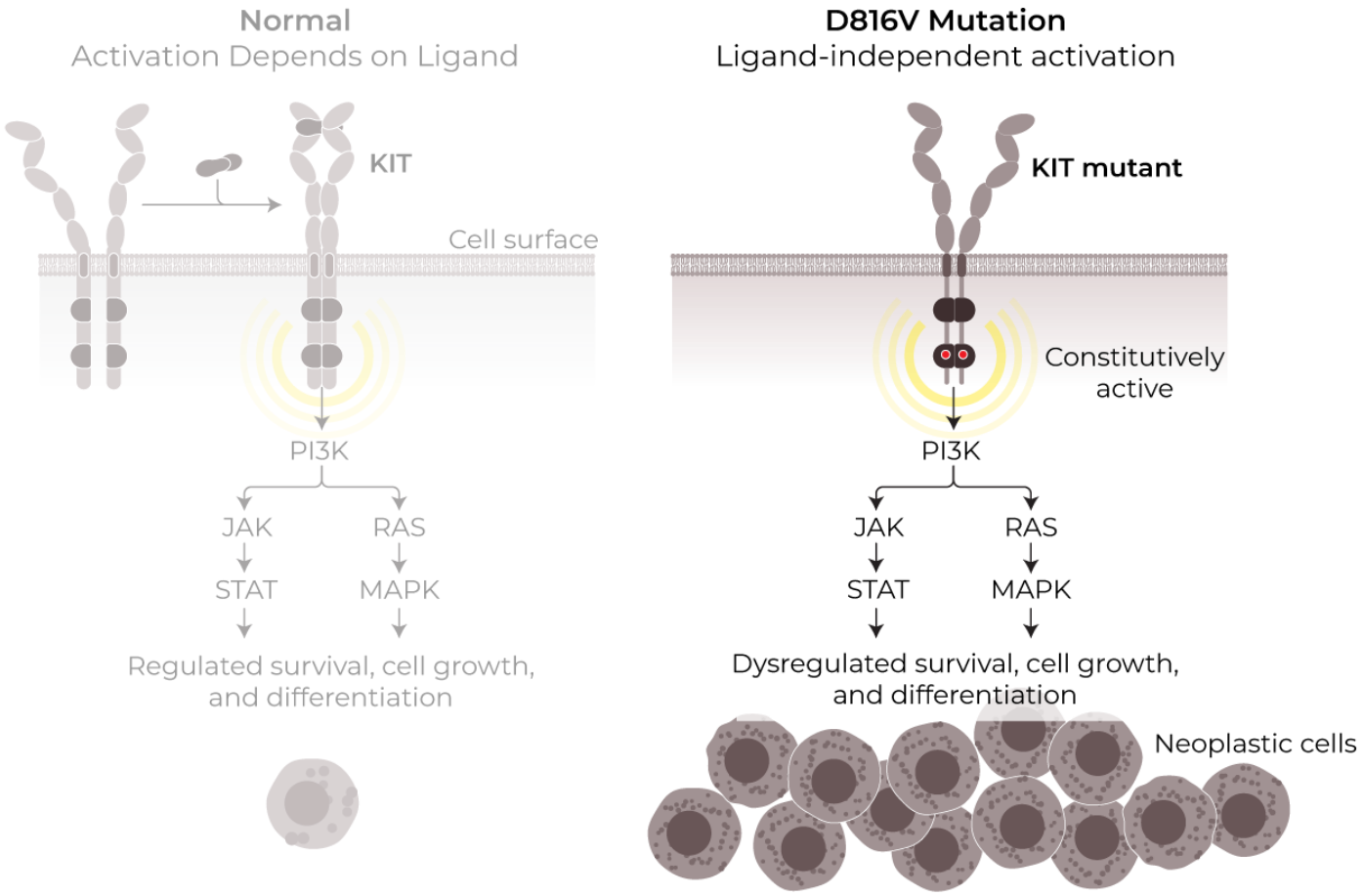
Serum tryptase data will provide rapid proof of concept for ASM & ISM programs

PLX9486 FUTURE CLINICAL PROGRAMS

Advanced Systemic Mastocytosis (ASM)
Indolent Systemic Mastocytosis (ISM)



Both Advanced SM and Indolent SM Are Primarily Driven by D816V Mutations



- The most common KIT mutation in patients with systemic mastocytosis, aspartate to valine at residue 816 (D816V), lies 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

Unmet Need in ASM and ISM

Advanced Systemic Mastocytosis

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

Indolent and Smoldering Mastocytosis

- Poor 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

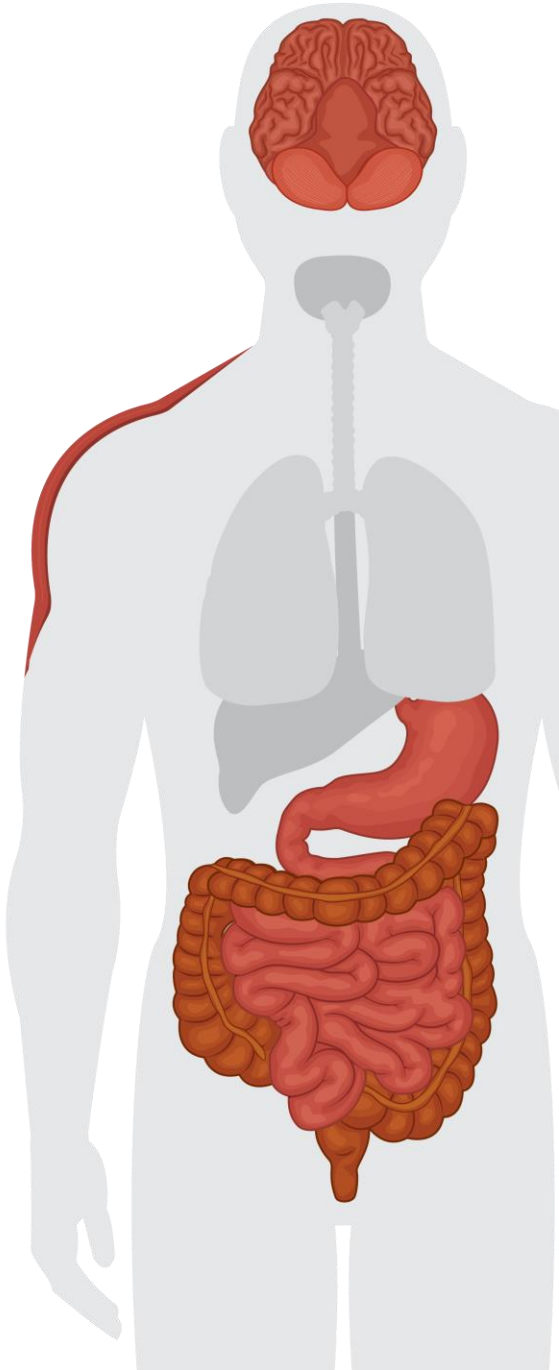
Bone/muscle pain, osteopenia, osteoporosis

Gynecological

Uterine cramps, bleeding

Urinary

Bladder irritability, frequent voiding



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Encouraging Tolerability Profile as Single Agent and Supports Clinical Trials in Mastocytosis

Single agent PLX9486 human safety data in advanced cancer and GIST patients shows a compelling profile for a chronic indication like systemic mastocytosis

Plan to explore a range of doses for the treatment of systemic mastocytosis

Single Agent PLX9486 (All Doses) in Advanced Cancer and GIST Patients

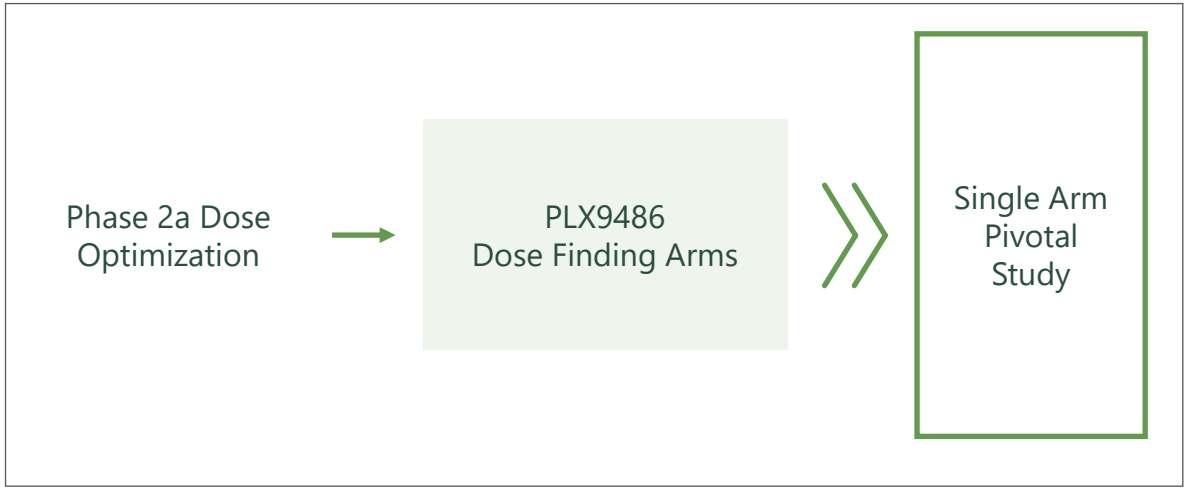
Preferred Term	Total (n=24)	
	Any Grade	CTCAE ≥3
Subjects reporting ≥1 AE	24 (100)	14 (58.3)
Fatigue	12 (50.0)	2 (8.3)
AST Increased	11 (45.8)	0
Diarrhea	10 (41.7)	0
Nausea	10 (41.7)	2 (8.3)
ALT increased	8 (33.3)	0
Vomiting	8 (33.3)	3 (12.5)
Anemia	7 (29.2)	3 (12.5)
Blood ALP increased	7 (29.2)	0
Blood CPK increased	7 (29.2)	2 (8.3)
Edema peripheral	6 (25.0)	0
Abdominal pain	5 (20.8)	1 (4.2)
Decreased appetite	5 (20.8)	1 (4.2)
Dyspnea	5 (20.8)	0
Hyperuricemia	5 (20.8)	3 (12.5)
Abdominal distention	4 (16.7)	0
Hair color changes	4 (16.7)	0
Hypophosphatemia	4 (16.7)	1 (4.2)
Pain	4 (16.7)	0

PLX121-01: All AEs reported in Part 1 >15% (IB Ed 3 - Table 22)

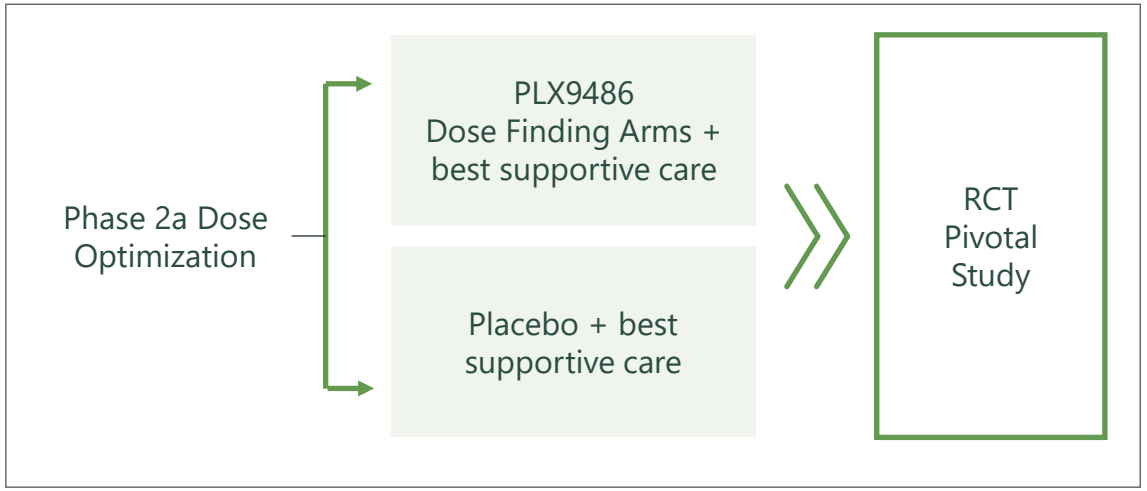
Preliminary Plans: ASM and ISM Registration Clinical Program Design

ASM dose finding study will allow for early signal of activity based on serum tryptase data

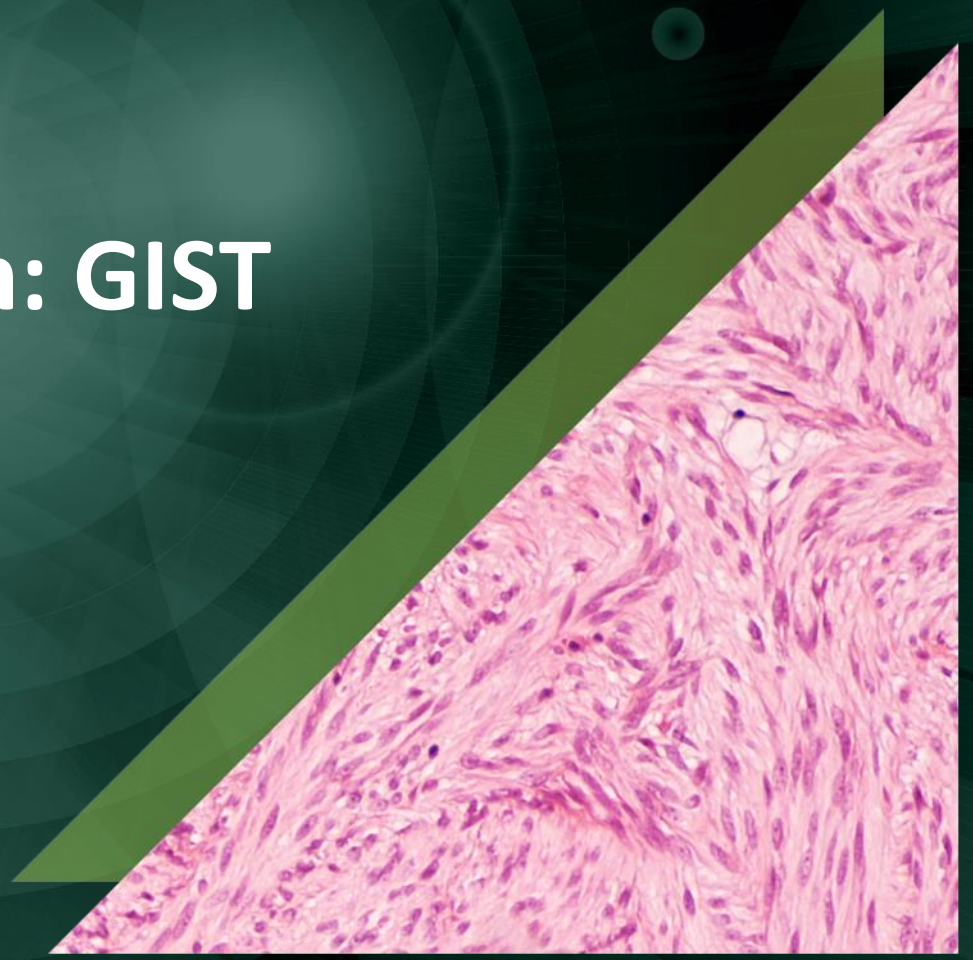
Global Advanced Systemic Mastocytosis (ASM) Program
[Subject to Regulatory Feedback]

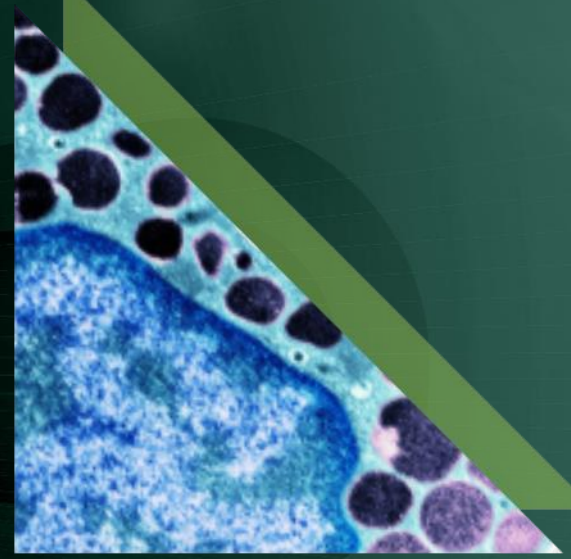


Global Indolent Systemic Mastocytosis (ISM) Program
[Subject to Regulatory Feedback]

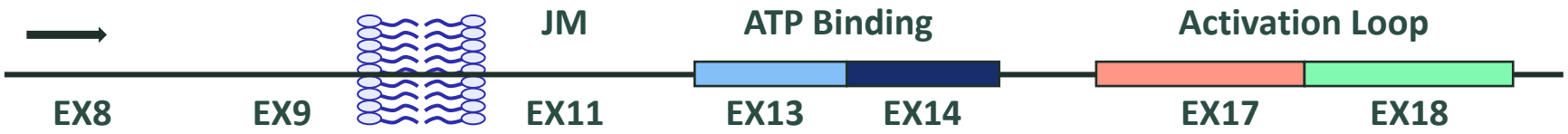


PLX9486 Program: GIST





PLX9486 and Sunitinib Combination Tackle GIST Heterogeneity by Targeting Exon 13 and Exon 17 Simultaneously

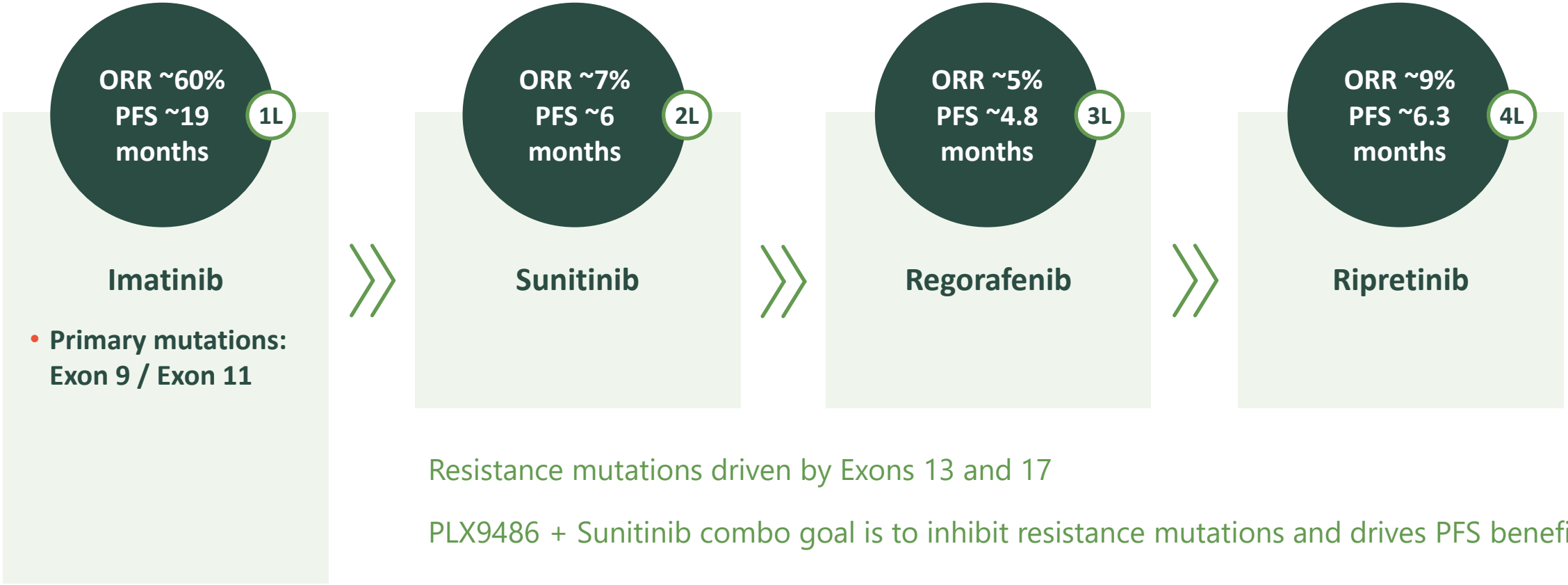


	KIT Primary Mutations			KIT Secondary Mutations			
	Exon 8	Exon 9	Exon 11	Exon 13	Exon 14	Exon 17	Exon 18
Imatinib 1st Line							
Sunitinib 2nd Line							
Regorafenib 3rd Line							
PLX9486							
PLX9486 + Sunitinib							

Sensitive ⟷ Resistant

Ref: June 2018, ASCO: A phase I pharmacokinetic and pharmacodynamic study of PLX9486 alone and in combination with the KIT inhibitors pexidartinib (pexi) or sunitinib in patients with advanced solid tumors and gastrointestinal stromal tumor (GIST)

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



Resistance mutations driven by Exons 13 and 17

PLX9486 + Sunitinib combo goal is to inhibit resistance mutations and drives PFS benefit

Avapritinib approved for PDGFRα Exon 18 mutations (~ 6% of newly diagnosed patients); single-agent avapritinib failed to show benefit in 3L GIST vs. regorafenib

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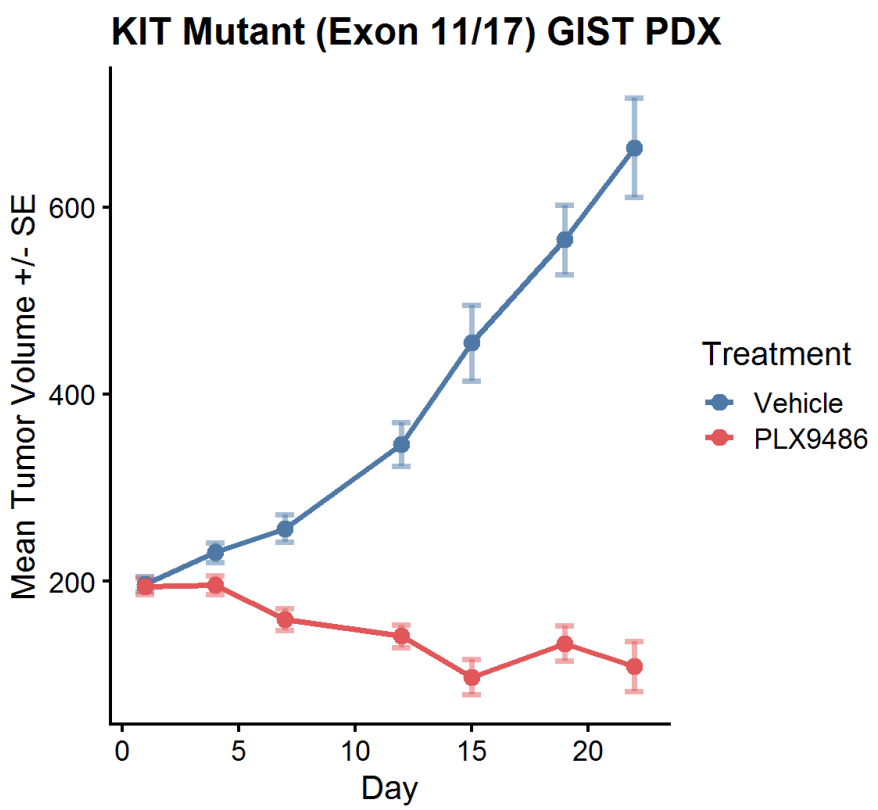
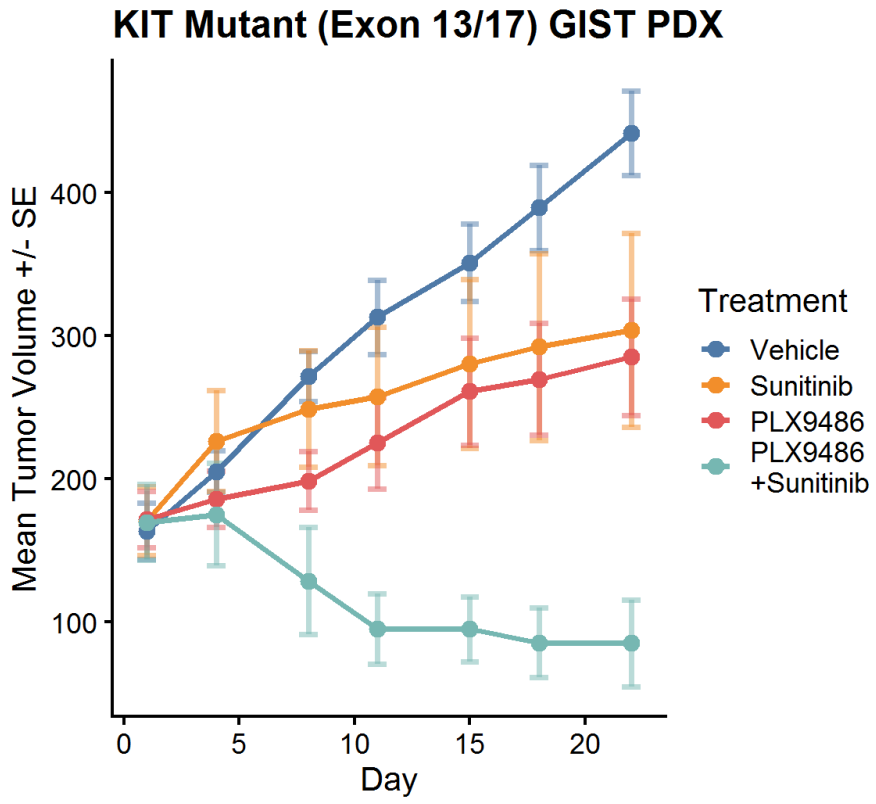
Dual-conformation KIT Inhibition Drives Tumor Regression in Heterogeneous GIST mouse models

Ex11 (W557_K558del), Ex17 (N822K)



Ex13 (K642E), Ex17 (D823Y)



PLX9486 Has Completed a Phase 1b/2a Trial in GIST with Encouraging Results

Phase 1b: Advanced Solid Tumors, Including GIST

PLX9486 Single Agent Dose Escalation (n=24)

Study Objectives

- Safety and PK
- Single agent MTD/RP2D
- Efficacy including ORR (RECIST 1.1), DOR and PFS

Phase 2a: Treatment Refractory GIST

PLX9486 + pexidartinib Dose Finding (n = 12)

PLX9486 + sunitinib Dose Finding (n = 18)

Study Objectives

- Safety and PK of combination regimens
- Combination MTD/RP2D
- Efficacy including ORR (RECIST 1.1), DOR and PFS

PLX9486 Has Completed a P1b/2a Trial in GIST with Encouraging Results

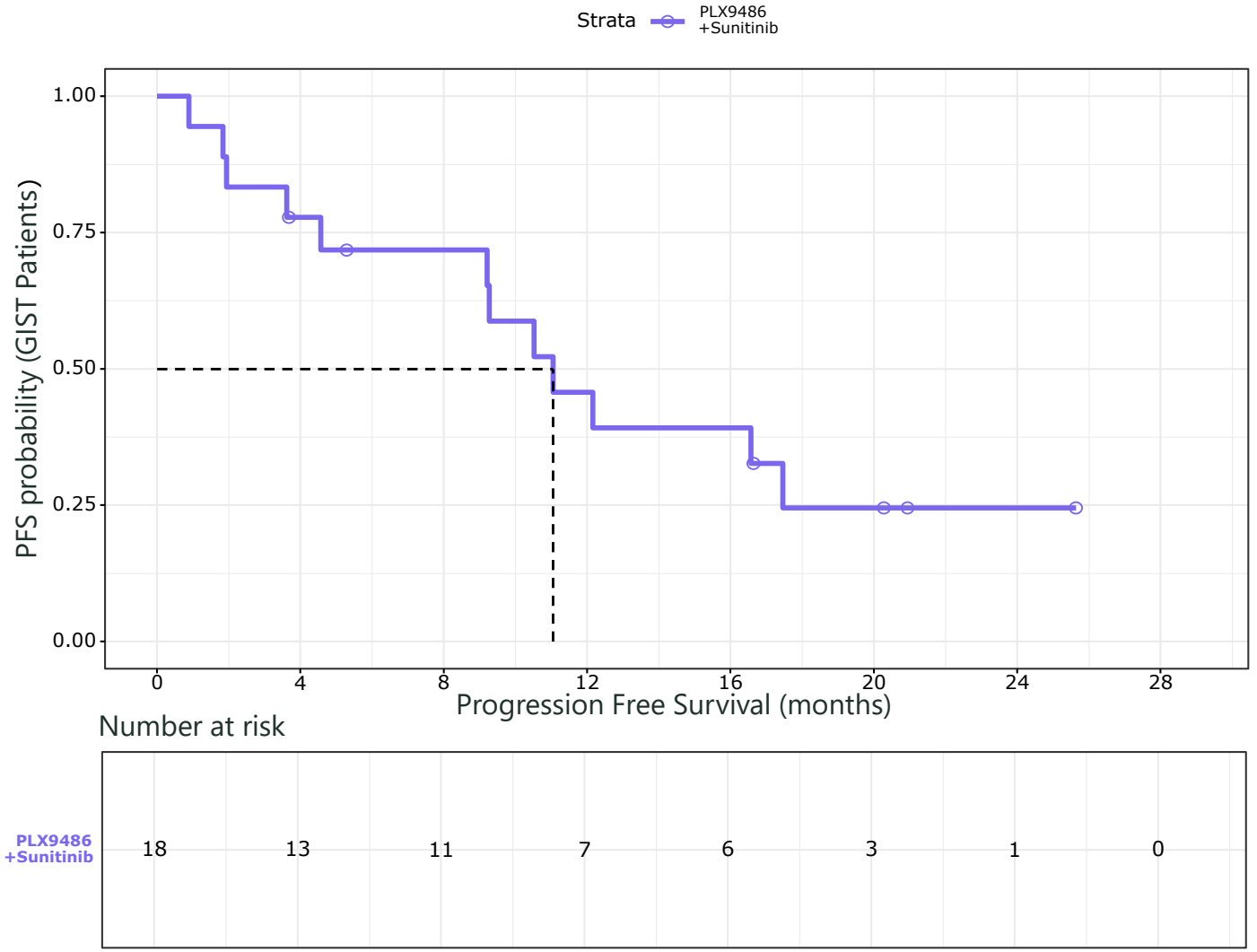
PLX9486 + Sunitinib Has Shown Median PFS of **11 Months** in 18 heavily treatment-experienced GIST patients

16.66% ORR rate (1 CR, 2 PR)

4 patients remain on treatment

Single agent median PFS of 5.8 months was shown in 13 GIST patients treated with 1000 mg total daily dose

PLX9486 + Sunitinib	% Prior Treatment
Prior sunitinib	**72.2%**
≥3 prior TKIs	66.7%
≥4 prior TKIs	50.0%



Data cutoff Q2 2020

Encouraging Tolerability of PLX9486 in Combination With Sunitinib Gives Us Confidence to Move Forward Into a Pivotal Study

Select sunitinib single agent AEs (GIST)

Diarrhea — **40%**

Anorexia — **33%**

Skin discoloration — **30%**

Mucositis/stomatitis — **29%**

Preferred Term	Total (n=17)	
	Any Grade	CTCAE ≥ 3
Subjects reporting ≥ 1 AE	15 (88.2)	11 (64.7)
Diarrhea	10 (58.8)	1 (5.9)
Nausea	9 (52.9)	1 (5.9)
Anemia	8 (47.1)	4 (23.5)
AST increased	8 (47.1)	0
Dysgeusia	7 (41.2)	0
Vomiting	7 (41.2)	0
ALT increased	6 (35.3)	0
Blood ALP increased	6 (35.3)	0
Decreased appetite	6 (35.3)	1 (5.9)
Fatigue	6 (35.3)	2 (11.8)
Hypomagnesemia	6 (35.3)	0
Hypophosphatemia	6 (35.3)	3 (17.6)
Hypertension	5 (29.4)	1 (5.9)
Thrombocytopenia	5 (29.4)	0
Abdominal distension	4 (23.5)	0
Abdominal pain upper	4 (23.5)	0
Dyspepsia	4 (23.5)	0
Hair color changes	4 (23.5)	0
Headache	4 (23.5)	0
Hypoalbuminemia	4 (23.5)	0
Leukopenia	4 (23.5)	1 (5.9)
Neutropenia	4 (23.5)	0
Palmar-plantar erythrodysesthesia	4 (23.5)	0
Rash	4 (23.5)	0

All AEs in Part 2e > 20% (Investigator Brochure)

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** Subject to regulatory approval*

Preliminary Plans: Sunitinib +/- PLX9486 Registrational Programs

Phase 1b/2a data accepted for oral presentation at CTOS 2020

Phase III 2nd Line GIST
(under consideration – seeking FDA feedback)

PLX9486 + sunitinib

sunitinib

Patient Population:
2nd line GIST post-imatinib failure

Primary Endpoint:
PFS

Secondary Endpoints:
ORR, DOR, OS

Phase III Refractory GIST
(under consideration – seeking FDA feedback)

PLX9486 + sunitinib

pending regulatory feedback

Patient Population:
Late line GIST

Primary Endpoint:
PFS

Secondary Endpoints:
ORR, DOR, OS

Anticipated Near-term Milestones

Serum tryptase data will provide rapid proof of concept for ASM & ISM programs

Financial Overview

Cogent's current cash balance includes gross proceeds of a $104.4 million private placement in July 2020 and $8.1 million from the sale of the BOXR technology in August 2020. Based on current projections, current cash will fund Cogent's operations into 2023.

Company Capitalization Structure As of September 10, 2020	Common Shares	Series A Preferred Stock	As Converted Common Shares[1]
Common stock outstanding	42,469,409		42,469,409
Series A Preferred Stock		163,325	163,325,000
	42,469,409	**163,325**	**205,794,409**

[1]*This includes 100% conversion of all outstanding Series A Preferred Stock*

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, M.D.
Chief Medical Officer

JOHN GREEN
Chief Financial Officer

ERIN SCHELLHAMMER
Chief People Officer

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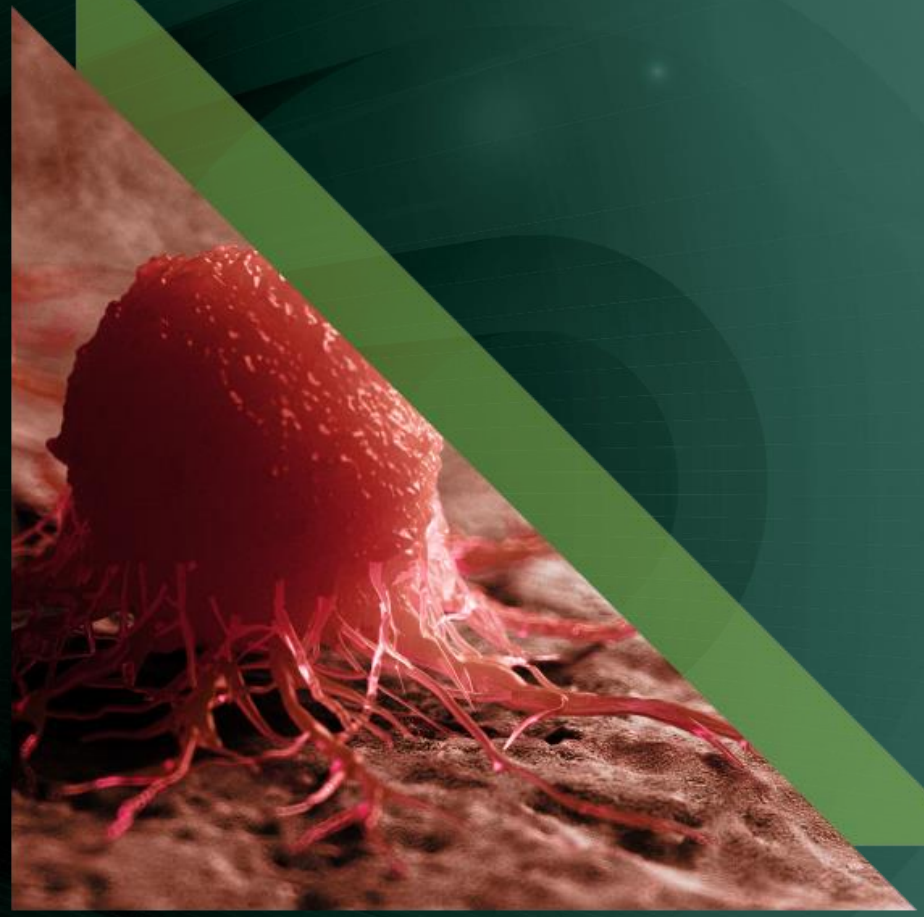
Thank You



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