Precision that Moves™

Staying one step ahead of disease

NOVEMBER 21, 2019

Forward-looking statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “target” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. In this presentation, forward-looking statements include, without limitation, statements regarding plans and timelines for the development of avapritinib, pralsetinib, fisogatinib and BLU-263, including the timing, design, implementation, enrollment, plans and announcement of results regarding ongoing and planned clinical trials for the drug candidates of Blueprint Medicines Corporation (the “Company”); plans and timelines for current and future marketing applications for avapritinib and pralsetinib; plans, timelines and expectations for the review and administrative split by the Food and Drug Administration (the “FDA”) of the new drug application (“NDA”) for avapritinib for the treatment of adult patients with PDGFRA Exon 18 mutant GIST, regardless of prior therapy, and fourth-line GIST, including any extension of the regulatory action date for the fourth-line GIST population; plans, timelines and expectations for top-line data from the VOYAGER trial; plans and timelines for nominating additional development candidates and expectations for those development candidates to be first-in-class; the potential benefits of the Company’s current and future drug candidates in treating patients; expectations regarding the Company’s existing cash, cash equivalents and investments; and the Company’s strategy, goals and anticipated milestones, business plans and focus. The Company has based these forward-looking statements on management’s current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks, uncertainties and other important factors, many of which are beyond the Company’s control and may cause actual results, performance or achievements to differ materially from those expressed or implied by any forward-looking statements. These risks and uncertainties include, without limitation, risks and uncertainties related to the delay of any current or planned clinical trials or the development of the Company's drug candidates, including avapritinib, pralsetinib, fisogatinib and BLU-263, or the licensed products, including BLU-782; the Company's advancement of multiple early-stage efforts; the Company's ability to successfully demonstrate the efficacy and safety of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; the preclinical and clinical results for the Company's drug candidates, which may not support further development of such drug candidates; actions or decisions of regulatory agencies or authorities, which may affect the initiation, timing and progress of clinical trials; the FDA's intent to administratively split the proposed indications for avapritinib into two separate NDAs, which may not mean that either indication is approved; a delay in the review of the proposed indications as a result of the administrative split of the current NDA; FDA concerns regarding whether the response rate in the fourth-line GIST population was reasonably likely to predict clinical benefit in that population; there can be no assurance that the VOYAGER top-line data will be sufficient for the FDA's review of the proposed fourth-line indication or that there will not be a delay in the availability of VOYAGER top-line data; the Company’s ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing; the Company's ability to develop and commercialize companion diagnostic tests for its current and future drug candidates; and the success of the Company’s current and future collaborations, partnerships, and license, including its collaborations with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, “Roche”) and CStone Pharmaceuticals (“CStone”) and its license agreement with Clementia Pharmaceuticals Inc. (“Clementia”).

These and other risks and uncertainties are described in greater detail under “Risk Factors” in the Company’s filings with the Securities and Exchange Commission (“SEC”), including the Company’s most recent Quarterly Report on Form 10-Q and any other filings the Company has made or may make with the SEC in the future. The Company cannot guarantee future results, outcomes, levels of activity, performance, developments, or achievements, and there can be no assurance that the Company’s expectations, intentions, anticipations, beliefs, or projections will result or be achieved or accomplished. The forward-looking statements in this presentation are made only as of the date hereof, and except as required by law, the Company undertakes no obligation to update any forward-looking statements contained in this presentation as a result of new information, future events or otherwise.

This presentation also contains estimates, projections and other statistical data made by independent parties and by the Company relating to market size and growth and other data about the Company’s industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of the Company’s future performance and the future performance of the markets in which the Company operates are necessarily subject to a high degree of uncertainty and risk.

Our core mission and foundational principles

Blueprint Medicines aims to deliver
on the promise of precision medicine to improve and extend
the lives of patients with cancer and rare diseases.

HIGHLY SELECTIVE INHIBITORS

PATIENT SELECTION

ADAPTIVE ABILITY

Our core mission and foundational principles

Blueprint Medicines aims to deliver
on the promise of precision medicine to improve and extend
the lives of patients with cancer and rare diseases.

TRANSFORMATIVE BENEFIT

Life-changing outcomes for patients

URGENCY

Expedited development and regulatory pathways

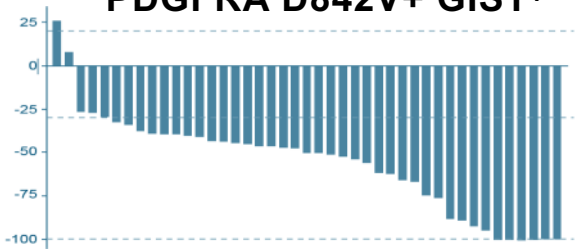
EFFICIENCY

Increased probability of success

Principles in action: expedited development of avapritinib and pralsetinib

AVAPRITINIB

PDGFRA D842V+ GIST[1]



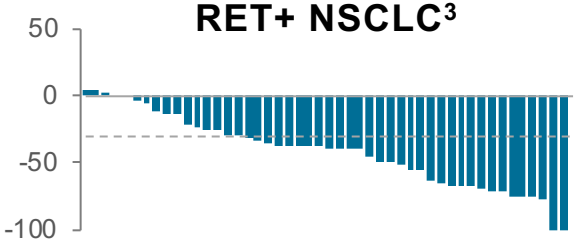
Breakthrough therapy designation[2]

~4 years

from IND to initial NDA submission

PRALSETINIB

RET+ NSCLC[3]



Breakthrough therapy designation[4]

~3 years

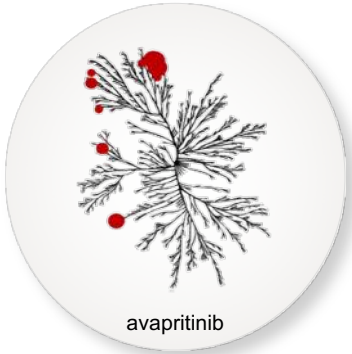
from IND to planned initial NDA submission

1. Data presented at ASCO 2019 Annual Meeting on June 1, 2019. Data cutoff date: November 16, 2018. 2. Avapritinib granted Breakthrough Therapy Designation for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRA D842V mutation. 3. Data presented at ASCO Annual Meeting in June 2019. Includes NSCLC patients treated at the recommended Phase 2 dose of 400 mg QD and enrolled as of November 14, 2018 with follow-up through a data cutoff date of April 28, 2019. 4. Pralsetinib granted Breakthrough Therapy Designation for the treatment of patients with RET-fusion positive NSCLC that has progressed following platinum-based chemotherapy and for the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments.

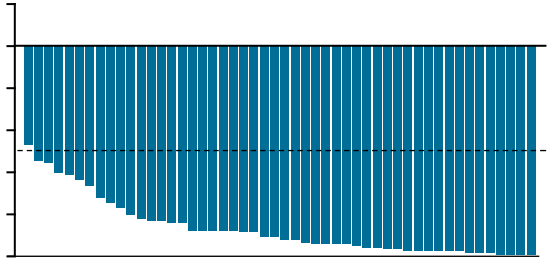
The rapid evolution of Blueprint Medicines

IMAGINING A NEW PLATFORM	BUILDING THE PIPELINE	REALIZING THE VISION
2011 – 2014	2015 – 2019	2020 – FUTURE

HIGHLY SELECTIVE KINASE MEDICINE DISCOVERY PLATFORM



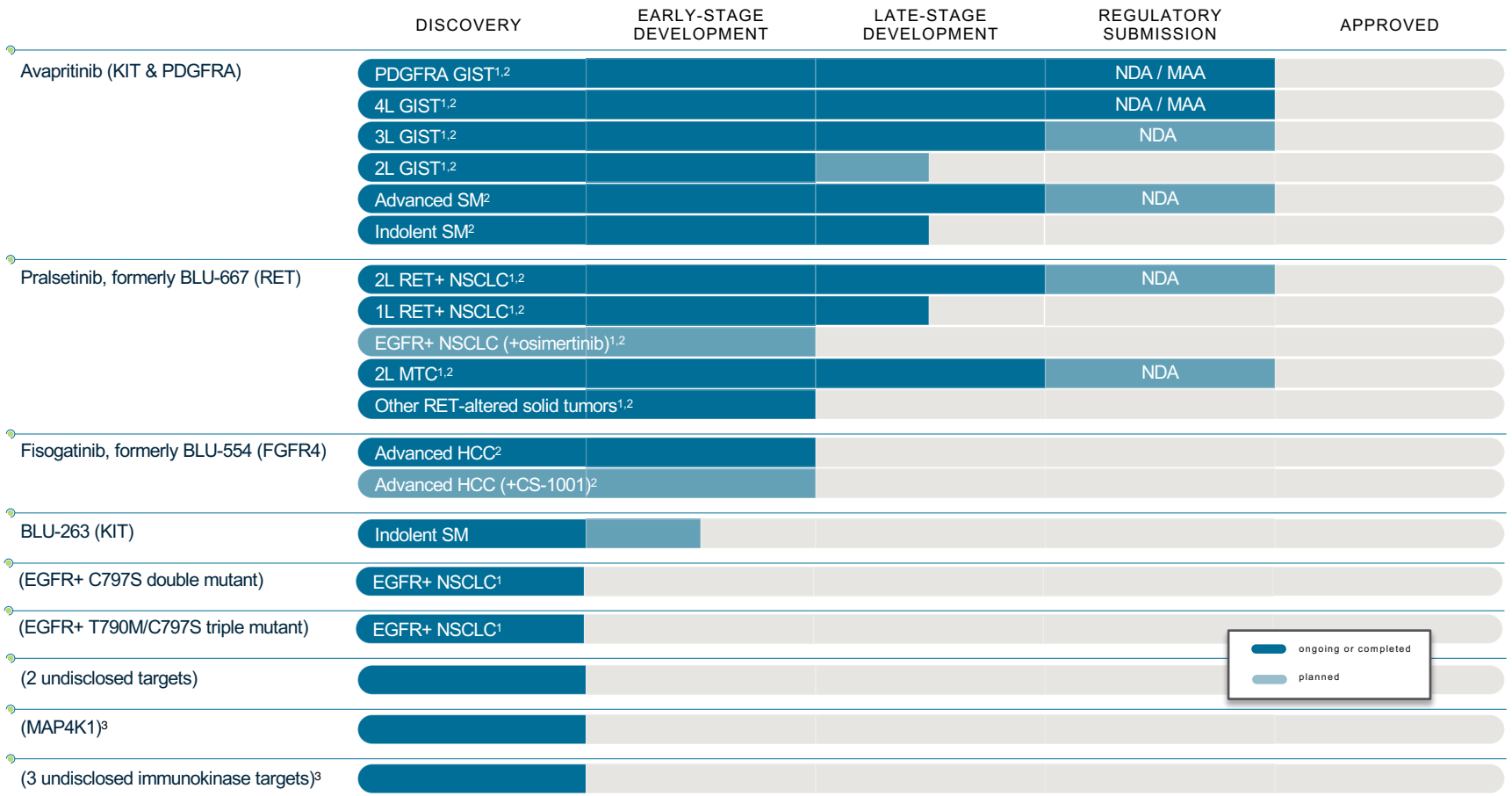
RAPID CLINICAL PROOF-OF-CONCEPT ACROSS MULTIPLE PROGRAMS



Avapritinib in advanced systemic mastocytosis: change in serum tryptase[1]

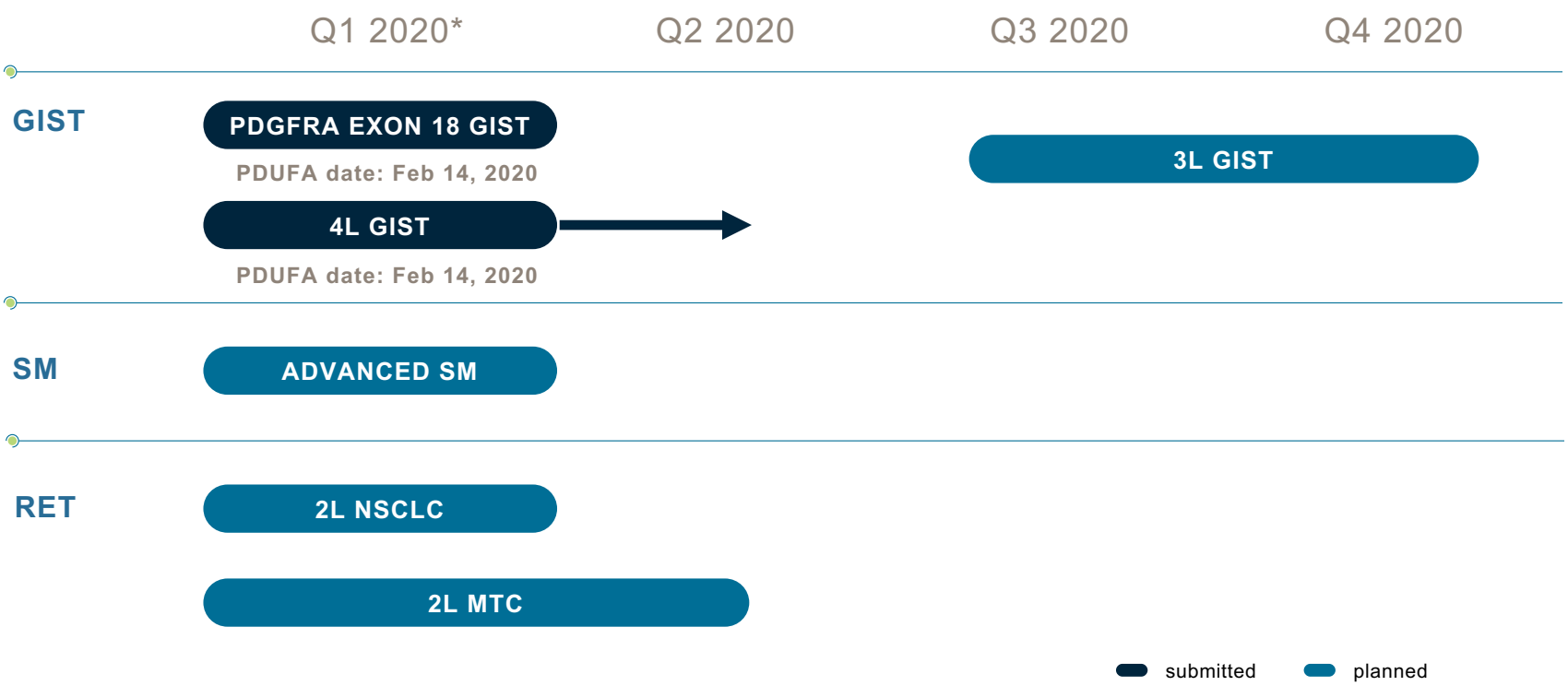
- Integrated commercialization
- Indication expansion
- Therapeutic area leadership
- Innovative kinase biology

Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com) (CSTI). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content. 1 Data presented at the European Hematology Association Annual Meeting in June 2019. Data cutoff date: January 2, 2019.



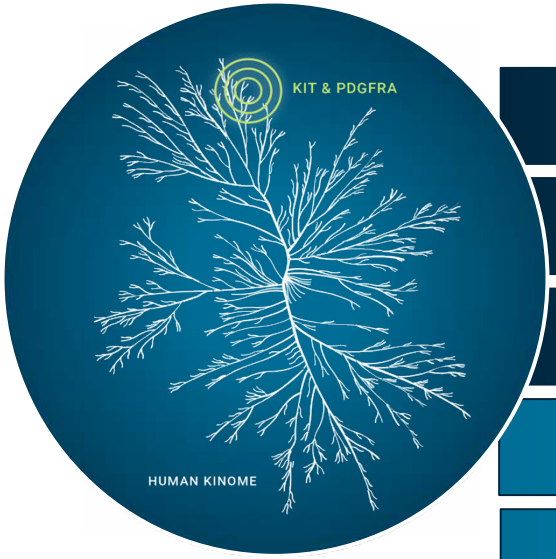
1. Unresectable or metastatic disease. 2. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains all rights in the rest of the world. 3. In collaboration with Roche. Blueprint Medicines has U.S. commercial rights for up to two programs. Roche has worldwide commercialization rights for up to two programs and ex-U.S. commercialization rights for up to two programs. 1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line; GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; MAA, marketing authorization application; MTC, medullary thyroid cancer; NDA, new drug applicaton; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

Submitted and planned New Drug Applications in 2020



* Assumes administrative split by FDA into two separate NDAs for proposed indications under initial NDA submitted for avapritinib in GIST and extension of up to 3 months for the PDUFA date for the 4L indication. PDUFA, Prescription Drug User Fee Act

Avapritinib: an investigational precision therapy with broad potential



Avapritinib

Potent and highly selective KIT and PDGFRA inhibitor

LATE CLINICAL DEVELOPMENT	U.S. REGULATORY SUBMISSION PLANS
PDGFRA Exon 18 mutant GIST	**Submitted***
4L GIST	**Submitted***
3L GIST	2020
Advanced SM	Q1 2020
Indolent and smoldering SM	

* FDA intends to administratively split initial NDA into two separate NDAs for proposed indications. An extension of up to three months for the PDUFA action date for the fourth-line indication will likely be required to provide top-line VOYAGER data to inform FDA review of the proposed fourth-line indication.
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Beyond imatinib, there are no highly effective therapies for advanced GIST

ALL GIST

1L	2L	3L	4L
ORR ~51%	ORR ~7%	ORR ~5%	ORR ~0%
PFS ~19 months	PFS ~6 months	PFS ~4.8 months	PFS 1.8 months*

PDGFRα D842V GIST

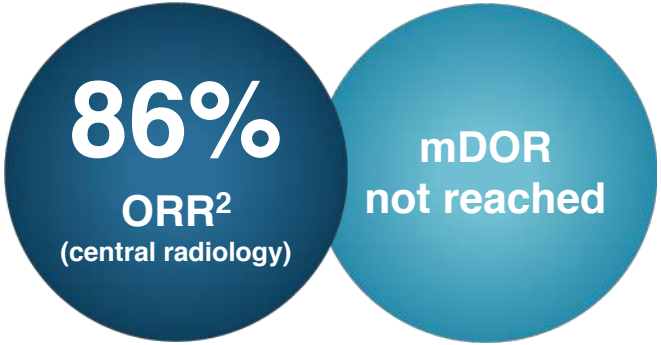
ORR ~0%

PFS ~3 months

* Re-challenged with Gleevec.

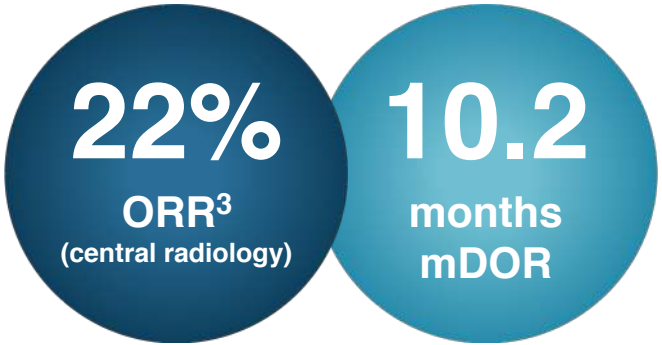
Pivotal avapritinib data in GIST reported at ASCO in June 2019

PDGFRA Exon 18 Mutant GIST (n=43)[1]



Breakthrough Therapy Designation[4]

4L GIST (n=111)[1]



Safety Results (N=204):

- Avapritinib was generally well-tolerated and most AEs reported by investigators were Grade 1 or 2
- Grade ≥3 treatment-related AEs included anemia, fatigue, blood bilirubin increased, cognitive effects and diarrhea
- Across all doses, 8.3% of patients discontinued avapritinib due to treatment-related AEs

[1] Response evaluable patients treated with a starting dose of 300 or 400 mg QD. [2] One response pending confirmation for ORR in PDGFRA Exon 18 mutant GIST. [3] One response pending conformation for ORR in 4L GIST. There were 8 patients with PDGFRA D842V mutations, and when these patients were removed from the analysis, the ORR is 17% and DOR remains unchanged. [4] Avapritinib granted Breakthrough Therapy Designation for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation. Data reported at ASCO 2019 Annual Meeting on June 1, 2019.Data cutoff date: November 16, 2018. AE, adverse events; mDOR, median duration of response; ORR, objective response rate; QD, once daily.

Systemic mastocytosis is one disease with a common genetic driver

ADVANCED SYSTEMIC MASTOCYTOSIS

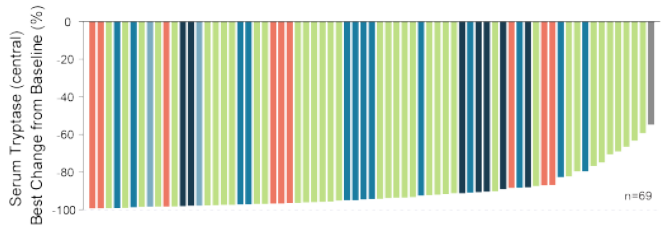
INDOLENT SYSTEMIC MASTOCYTOSIS

KIT D816V
mutation
frequency

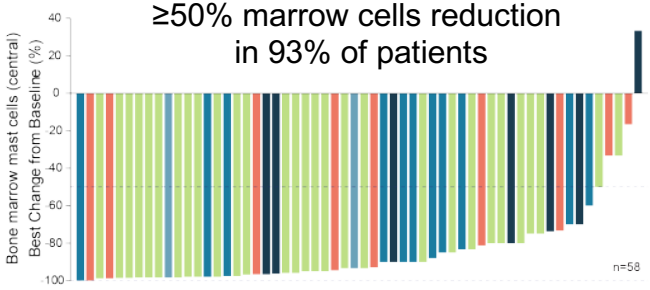
~95% of
patients

EXPLORER trial data showed decline in mast cell burden in evaluable patients across all patient subtypes

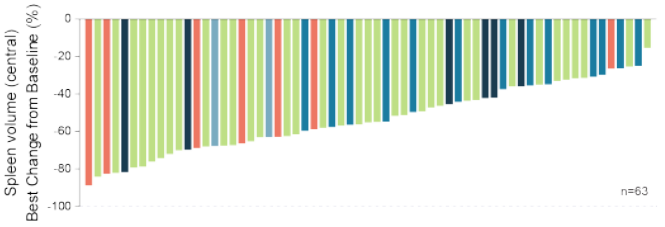
≥50% tryptase reduction in 100% of patients



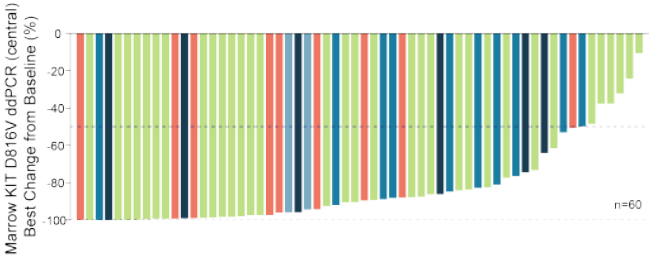
≥50% marrow cells reduction in 93% of patients



≥35% reduction in spleen volume in 81% of patients



Marrow KIT D816V becomes undetectable in 33% of patients



central adjudicated diagnosis

ISM SSM ASM SM-AHN MCL CMML

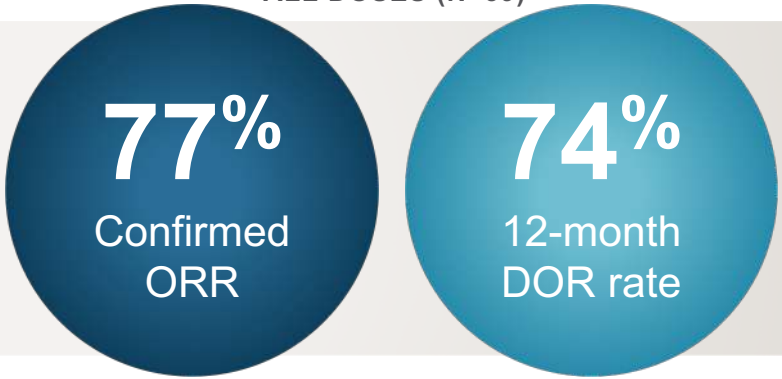
advanced SM

Data presented at the European Hematology Association Annual Meeting in June 2019. Data cutoff date: January 2, 2019.

EXPLORER data showed profound clinical activity in patients with advanced SM

BEST RESPONSE PER IWG-MRT-ECNM CRITERIA[1]

ALL DOSES (N=39)



BREAKTHROUGH THERAPY DESIGNATION[2]

Plan to submit NDA for avapritinib for advanced SM in Q1 2020, based on combined data from EXPLORER and PATHFINDER trials

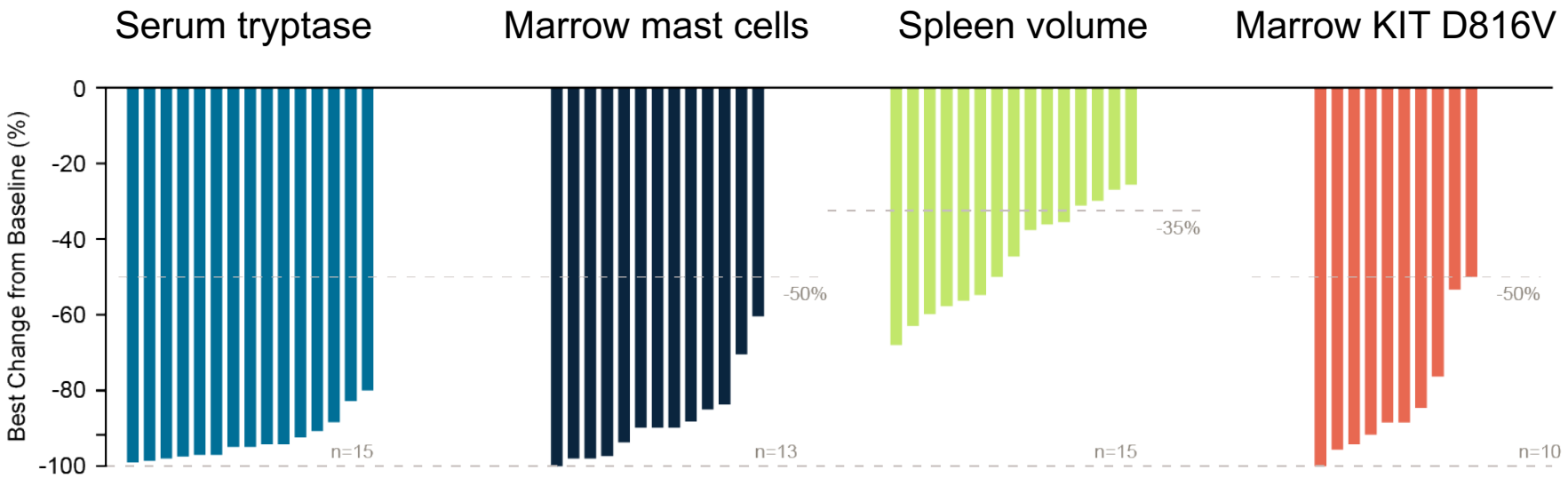
SAFETY (n=69)

- Avapritinib was generally well-tolerated
- Most adverse events reported by investigators were Grade 1 or 2
- 66% of patients had Grade 3 and 4 treatment-related AEs
- Cytopenias were the most common Grade 3 and 4 treatment-related AE
- Across all doses, 4% of patients discontinued treatment due to treatment-related AEs

blueprint™ MEDICINES

1 Data presented at the European Hematology Association Annual Meeting in June 2019. Data cutoff date: January 2, 2019.
2 Avapritinib granted Breakthrough Therapy Designation for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia. ORR, overall response rate; DOR, duration of response; AE, adverse event.

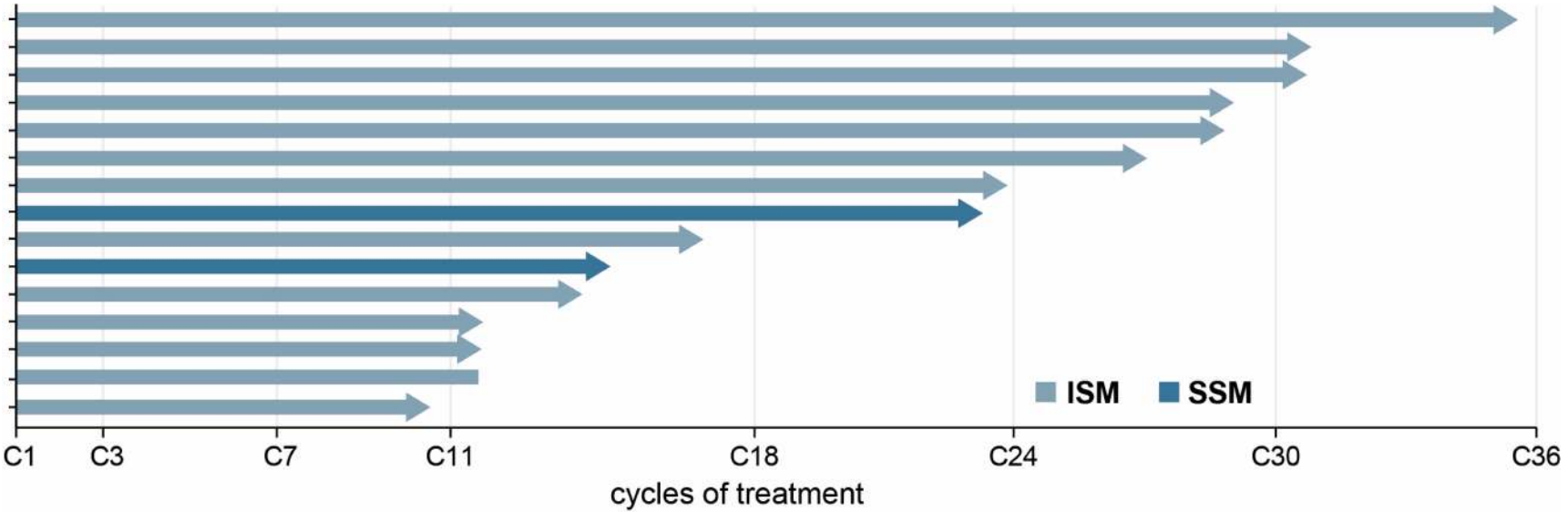
Indolent SM patients enrolled in EXPLORER trial had deep reductions on objective measures of mast cell burden



Data presented at the European Hematology Association Annual Meeting in June 2019. Data cutoff date: January 2, 2019.

EXPLORER data showed ISM and SSM patients with long durations of therapy at low doses

- 14 of 15 (93%) remain on treatment up to nearly 3 years (cycle 36)
- Current average dose is 126 mg with 73% now treated at 100 mg QD



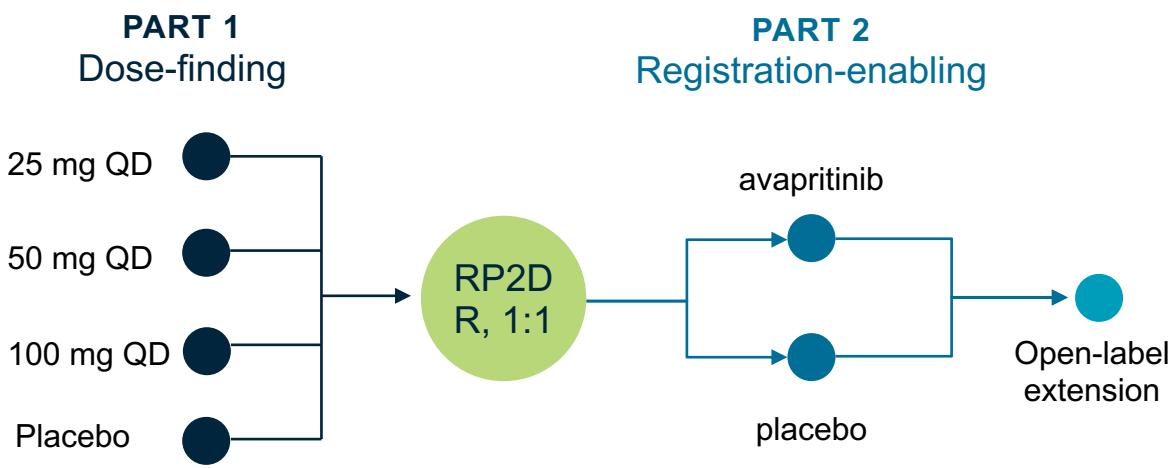
EXPLORER trial data analysis. Data cutoff date: January 2, 2019.
ISM, indolent SM; QD, once daily; SSM, smoldering SM.

PIONEER trial designed to evaluate avapritinib in indolent SM

PIONEER

Indolent SM

Phase 2 registration-enabling randomized, placebo-controlled trial inpatients with indolent SM



- **Eligibility:** Moderate-to-severe indolent or smoldering SM
- **Key endpoints:** ISM-SAF total symptom score (primary), quantitative measures of mast cell burden, safety
- Enrollment of Part 1 is complete with 39 patients on study; no patients have discontinued due to an adverse event to date[1]
- Plan to disclose initial data from Part 1 at ASH meeting in December 2019
  - Investor event and webcast planned for Sunday, December 8

[1] As of November 1, 2019.
R, randomized; RP2D, recommended part 2 dose; ASH meeting, American Society of Hematology Annual Meeting & Exposition

BLU-263 rapidly progressed based on insights from avapritinib

POTENT
Sub-nanomolar potency against KIT D816V

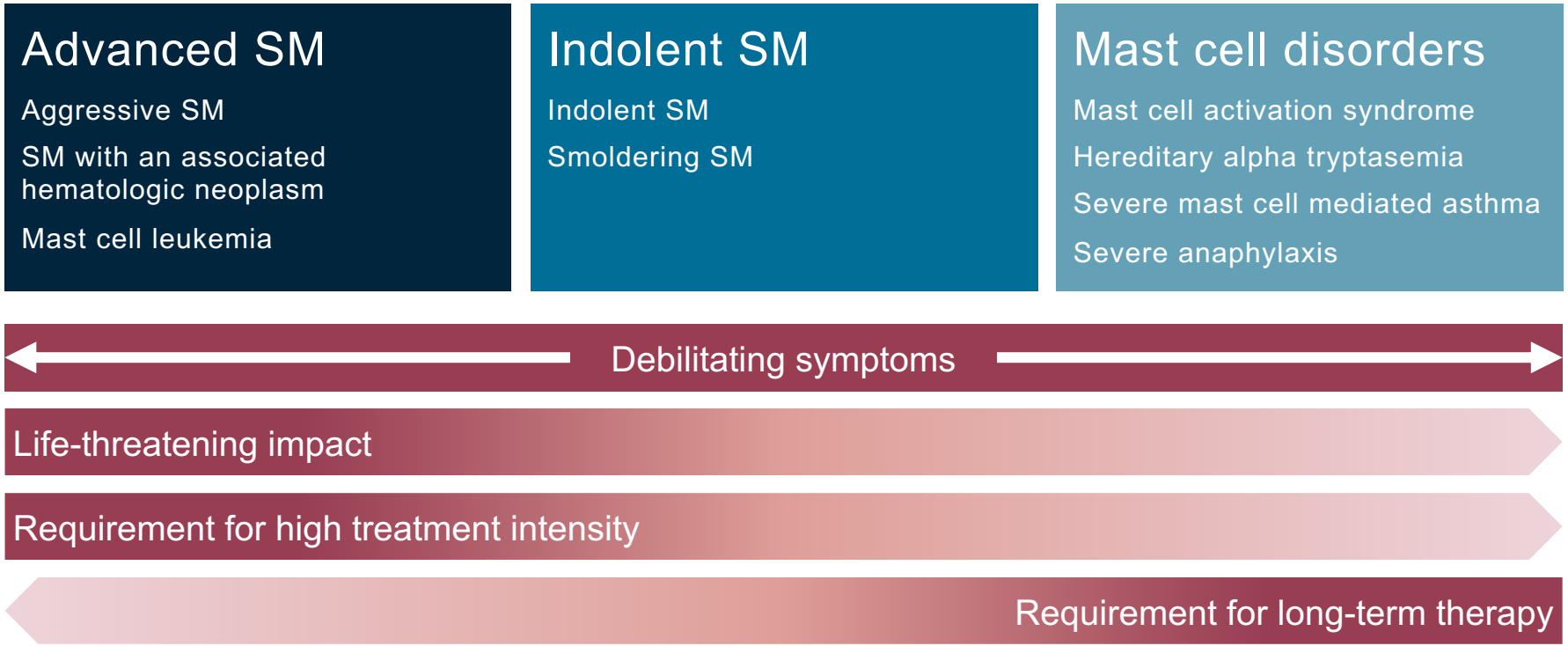
SELECTIVE
Highly selective for KIT, with low off-target activity

CNS PROFILE
Designed to not cross blood-brain barrier

Plan to submit IND application for BLU-263 for indolent SM to FDA in 1H 2020

CNS, central nervous system; IND application, investigational new drug application.

Disease spectrum across systemic mastocytosis and other mast cell disorders

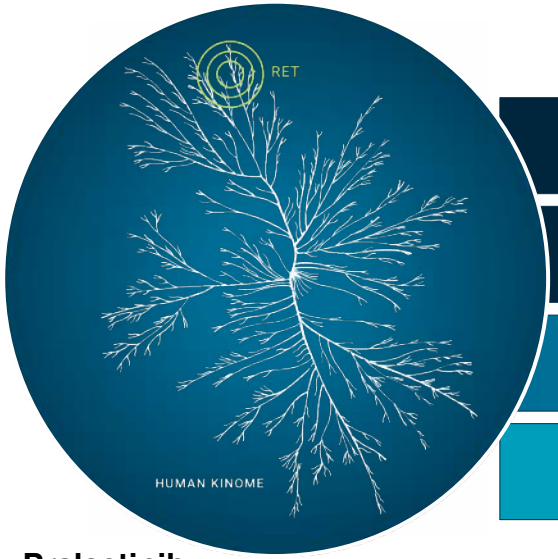


Planned BLU-263 clinical trial and future potential exploration

Advanced SM	Indolent SM	Mast cell disorders
Aggressive SM SM with an associated hematologic neoplasm Mast cell leukemia	Indolent SM Smoldering SM	Mast cell activation syndrome Hereditary alpha tryptasemia Severe mast cell mediated asthma Severe anaphylaxis
AVAPRITINIB EXPLORER	AVAPRITINIB PIONEER	BLU-263 (under evaluation)
AVAPRITINIB PATHFINDER	BLU-263 (trial planned)*	

* Plan to submit IND application in 1H 2020.

Pralsetinib: an investigational precision therapy for RET-altered cancers



	LATE CLINICAL DEVELOPMENT	U.S. REGULATORY SUBMISSION PLANS
2L RET-fusion NSCLC		Q1 2020
1L RET-fusion NSCLC		
2L MTC		1H 2020
Other RET-altered solid tumors		

Pralsetinib

Potent and highly selective RET inhibitor

Target NSCLC and MTC populations have unresectable or metastatic disease.

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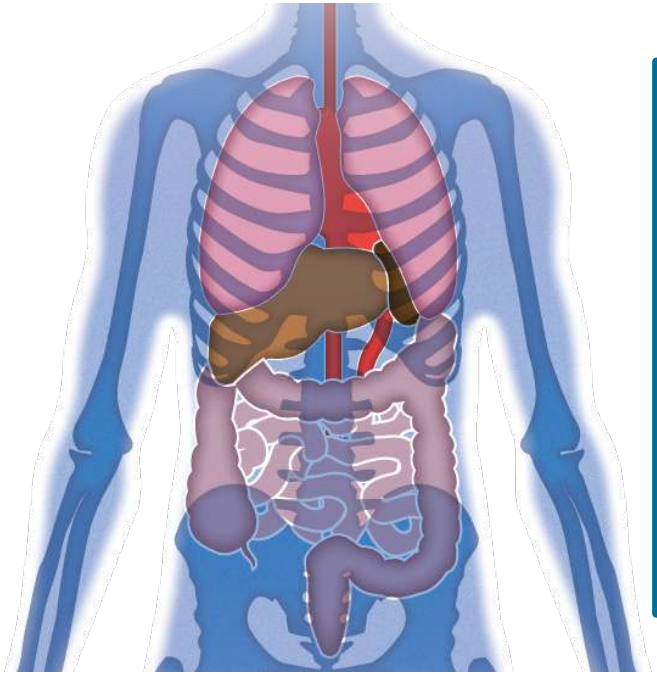
RET alterations: oncogenic drivers lacking a targeted therapeutic approach

Non-small cell lung cancer:
~1-2% RET fusions[1,2]

Advanced medullary thyroid cancer:
~90% RET mutations[3]

Papillary thyroid cancer:
~20% RET fusions[4]

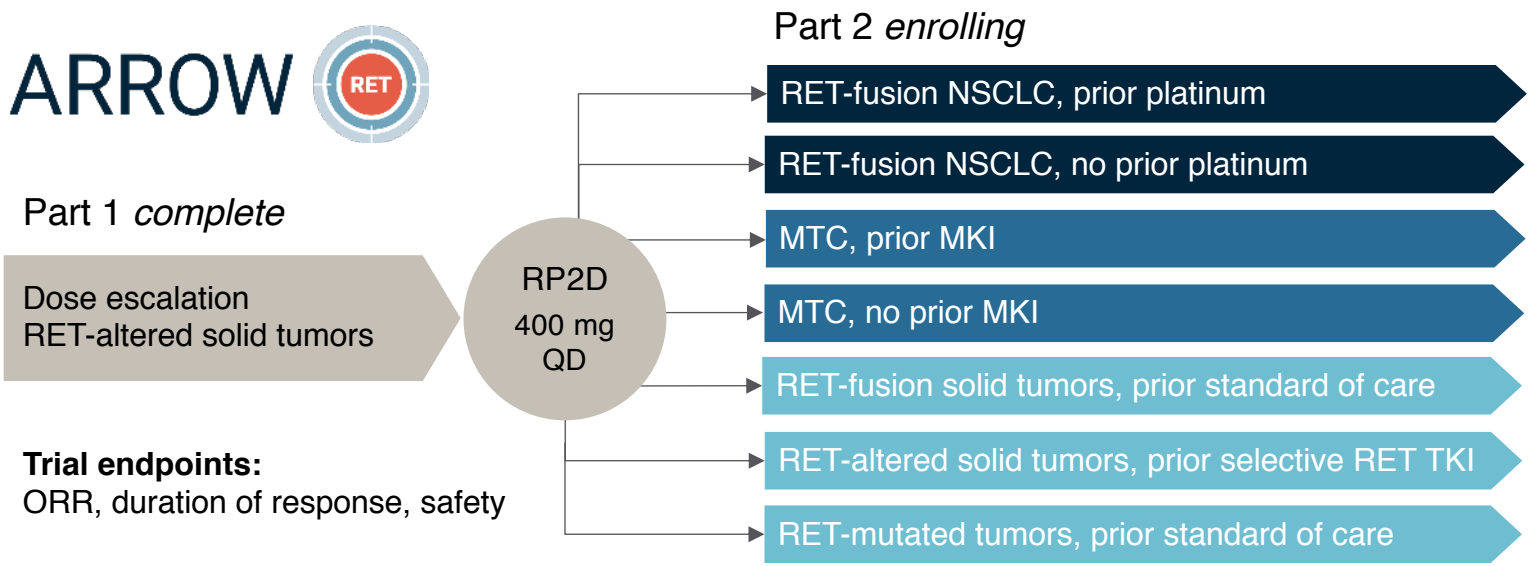


Multiple other tumor types <1% RET-altered, including:[5,6]

esophageal
pancreatic
breast
melanoma
colorectal
leukemia

[1] Lipson, et al. Nat Med 2012. [2] Takeuchi, et al. Nat Med 2012. [3] Romei, et al. Oncotarget 2018. [4] Santoro, et al. J Clin Invest 1992. [5] Kato, et al. Clin Cancer Res 2017. [6] Ballerini, et al. Leukemia 2012.

Updated ARROW trial data presented at ASCO 2019



Safety[1] (n=226)

- Pralsetinib was well-tolerated and most AEs were Grade 1 or 2 and reversible
- Across all patients, 4% discontinued due to treatment-related AEs

[1] Data presented at ASCO Annual Meeting in June 2019. Includes NSCLC and MTC patients treated at the recommended Phase 2 dose of 400 mg QD and enrolled as of November 14, 2018 with follow-up through a data cutoff date of April 28, 2019. MKI, multi-kinase inhibitor; TKI, tyrosine kinase inhibitor.

NSCLC patients with RET fusions have no highly effective treatment options

- **Chemotherapy:** nonspecific, low response rates, significant toxicity
- **Checkpoint inhibition:** Preliminary evidence for lack of benefit in RET-altered NSCLC[1]
- **Multi-kinase inhibitors:** ↓ activity, ↑ off-target toxicity[2,3]
- Growing understanding of RET-driven resistance
- No selective RET inhibitors are approved

[1] Mazieres, et al. JCO 2018. [2] Drillon, et al. Lancet 2017. [3] Yoh, et al. Lancet Respir Med 2017.

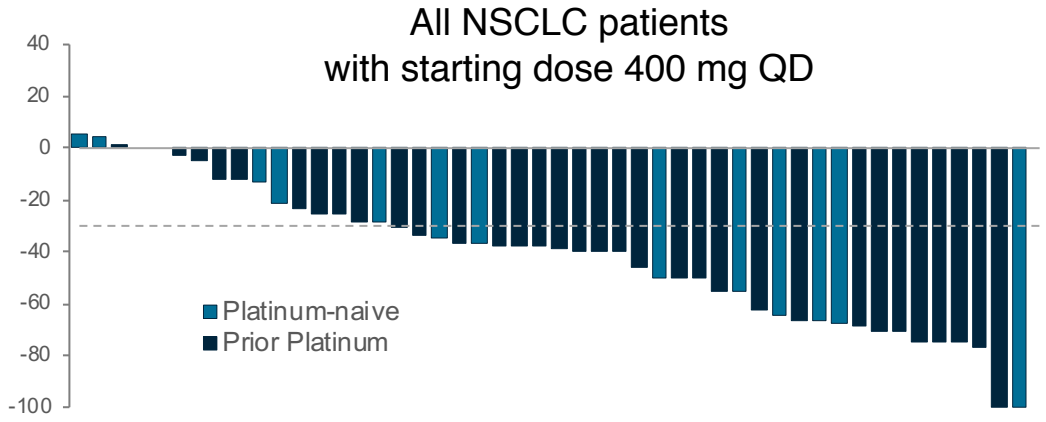
Pralsetinib showed robust and durable clinical activity in RET fusion NSCLC

60%
Confirmed ORR

RET-fusion NSCLC with prior platinum chemotherapy

400 mg QD, n=35

Breakthrough Therapy Designation[1]

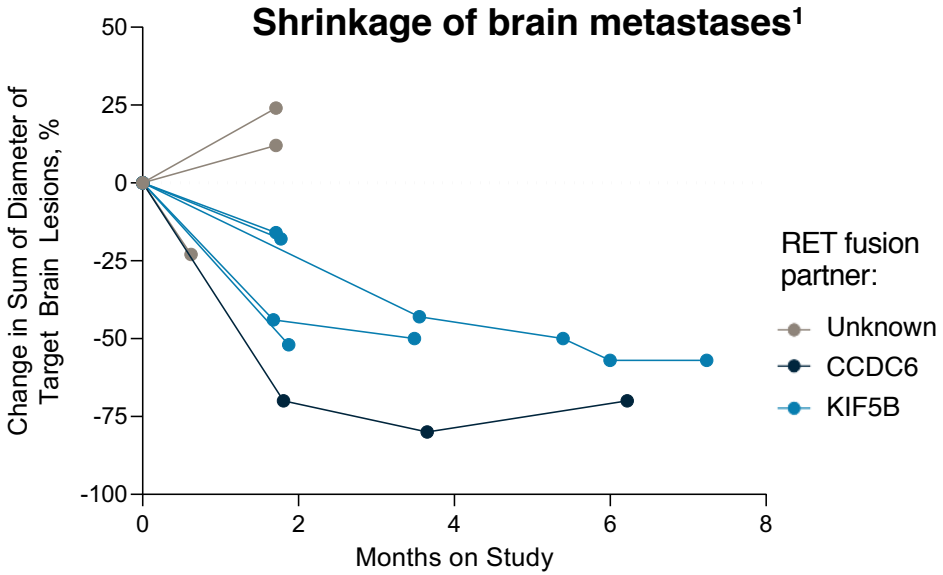


ADDITIONAL RESULTS

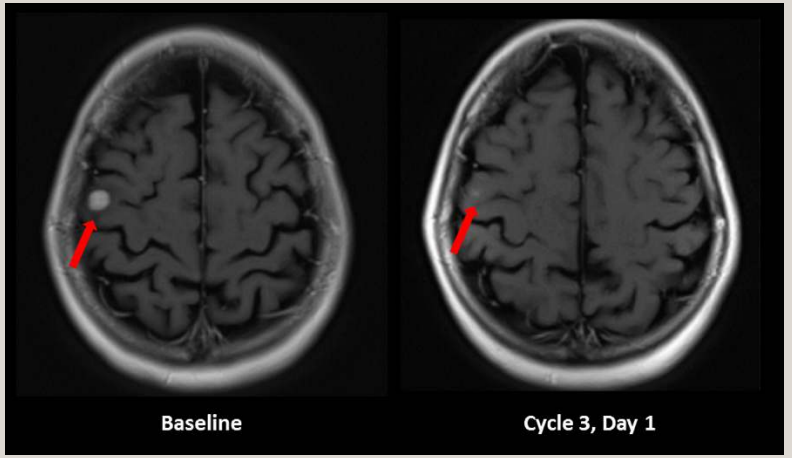
- Across all NSCLC patients, 96% disease control rate
- 71% ORR in patients naïve to prior systemic therapy
- Median duration of response not reached; 82% of responders remain on treatment with durations up to 15.6 months

Data presented at ASCO Annual Meeting in June 2019. Includes NSCLC patients treated at the recommended Phase 2 dose of 400 mg QD and enrolled as of November 14, 2018 with follow-up through a data cutoff date of April 28, 2019. [1] Pralsetinib granted Breakthrough Therapy Designation for RET fusion-positive NSCLC that has progressed following platinum-based chemotherapy.

Pralsetinib showed strong activity against NSCLC brain metastases



- 78% had shrinkage of measurable brain metastases
- No patients had progression due to new CNS involvement



- 52-year-old woman, RET fusion+ NSCLC, prior platinum and checkpoint inhibitor
- Near-complete resolution of previously untreated target brain metastasis after two months of pralsetinib 400 mg QD
- Continues to receive treatment with ongoing confirmed PR (70% shrinkage) at 10+ months (data cut-off 16 Aug 19)

[1] Data presented at ASCO Annual Meeting in June 2019 for 9 patients with brain lesion(s) identified as RECIST 1.1 target lesions at baseline. All patients treated at 400 mg QD. Data cut-off: April 28, 2019. Case courtesy of Dr. Stephen Liu, Georgetown University, Washington, D.C.

RET-altered thyroid cancer patients may benefit from highly targeted therapy

- **Multi-kinase inhibitors** are approved for MTC, but have important limitations:[1]
  - 25-44% ORR
  - Off-target toxicity often requiring dose modification or discontinuation
  - Emergence of resistance
- No selective RET inhibitors are approved

[1] Drillon, et al. Nature Reviews Clinical Oncology, 2017.

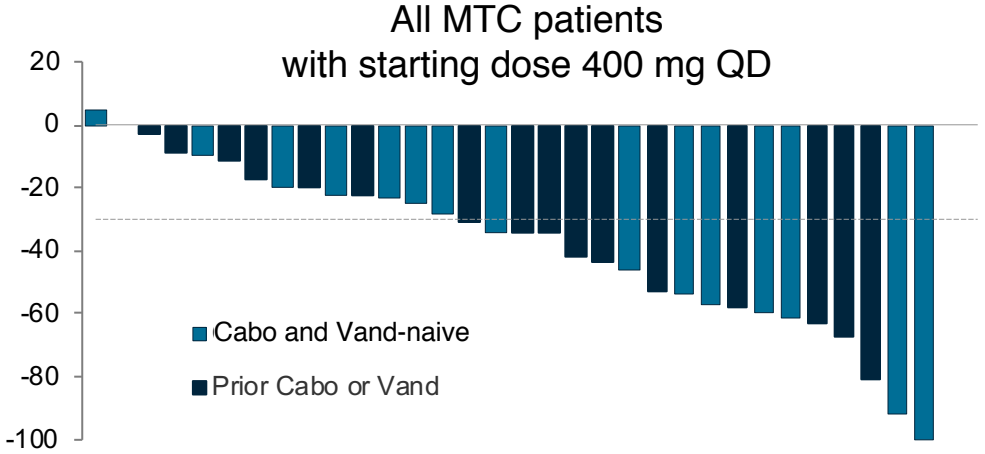
Pralsetinib shows robust and durable clinical activity in patients with MTC and other RET-altered cancers

63%
ORR[1]

RET-mutant MTC previously treated with an MKI

400 mg QD, n=16

Breakthrough Therapy Designation[2]

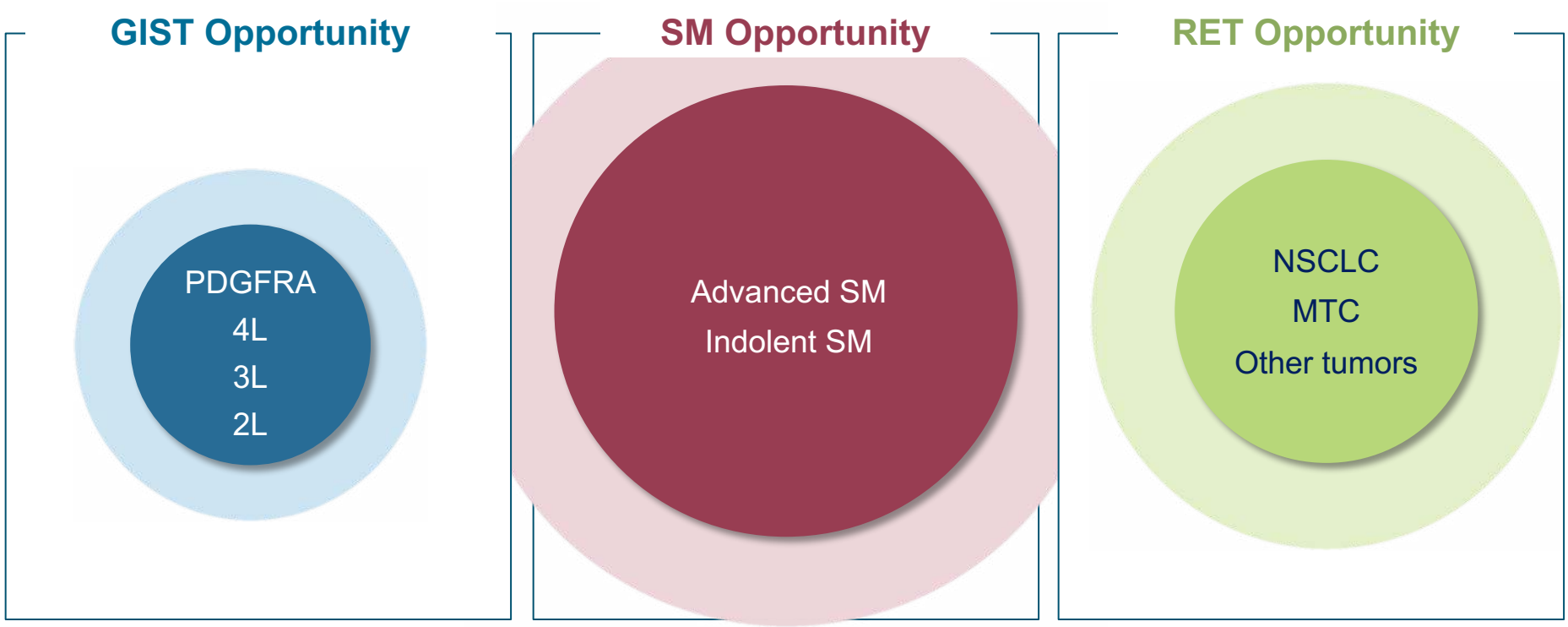


ADDITIONAL RESULTS

- Across all MTC patients, 97% disease control rate
- Median duration of response not reached; all responders remain on treatment with durations up to 15.6 months
- 83% ORR in papillary thyroid cancer[3]
- Additional clinical responses observed in pancreatic cancer and intrahepatic bile duct carcinoma

Data presented at ASCO Annual Meeting in June 2019. Includes MTC patients treated at the recommended Phase 2 dose of 400 mg QD and enrolled as of November 14, 2018 with follow-up through a data cutoff date of April 28, 2019. [1] Two responses pending confirmation. [2] Pralsetinib granted Breakthrough Therapy Designation for RET-mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments.
[3] Six patients were evaluable for response assessment (3 confirmed PRs, 2 PRs pending confirmation). Cabo, cabozantinib; Vand, vandetininb.

We are pursuing a highly attractive set of opportunities across our portfolio



Figures are illustrative.

A powerful scientific platform with a focused research strategy

Difficult-to-drug

Kinase targets that are difficult to drug with existing technologies

Treatment-resistant

Kinase targets characterized by alterations promoting resistance to existing therapies

Novel biology

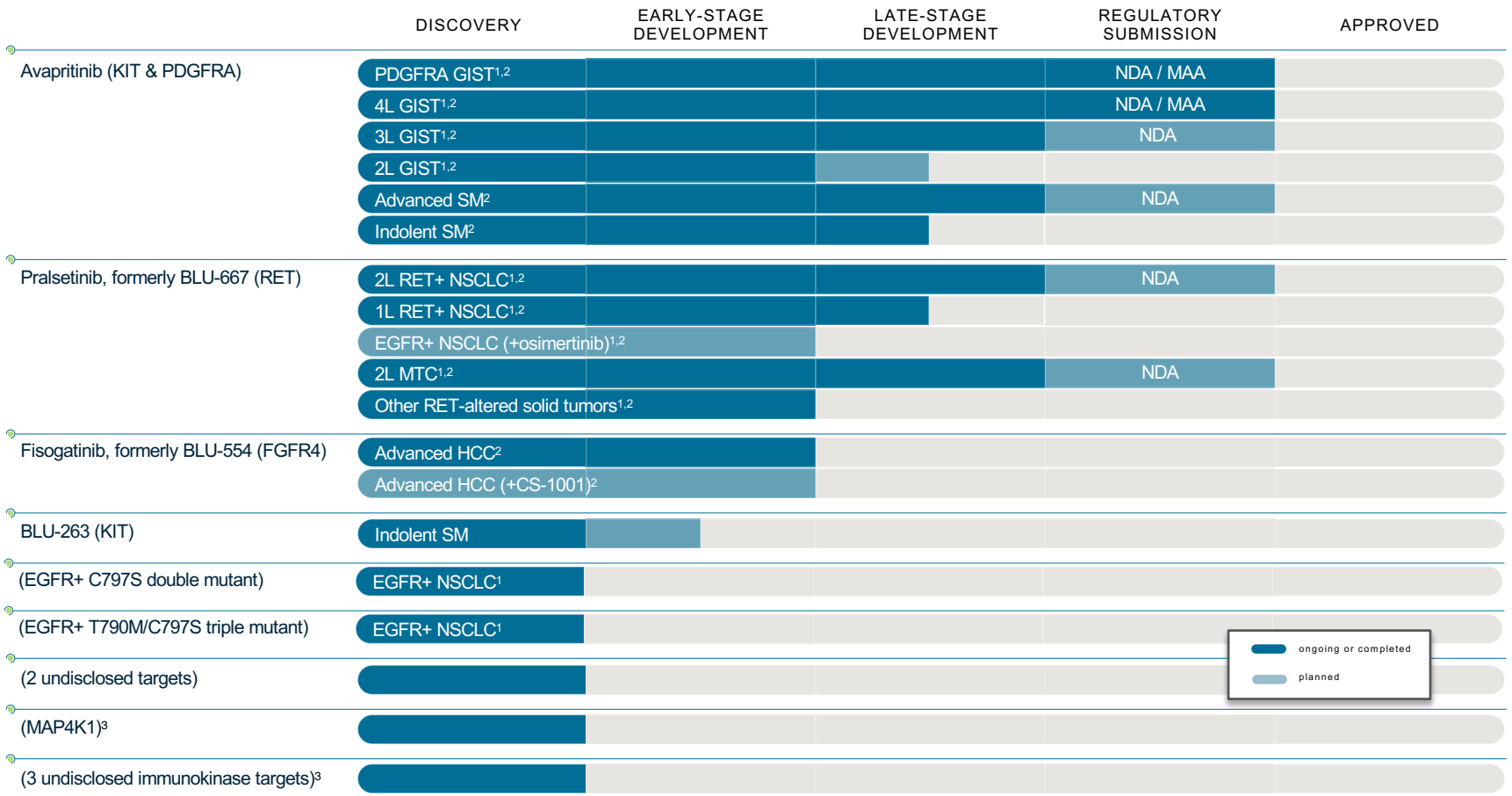
New kinase targets identified via computational and cell biology

Four research programs announced at R&D Day on November 5, 2019 including potential first-in-class EGFR and MAP4K1 inhibitors

Based on current operating plans, expect existing cash balance will fund operations into the second half of 2021*

SHARES OUTSTANDING** *as of 9/30/19*	CASH, CASH EQUIVALENTS AND INVESTMENTS** *as of 9/30/19*
49.2 million (basic) ***55.2 million (fully diluted)***	***$594.5 million***

*Includes $25.0 million upfront cash payment from Clementia and $8.0 million research milestone achieved in the third quarter of 2019 under the Roche collaboration but excludes any additional potential option fees, milestone payments or other payments from Roche, CStone or Clementia.
**Unaudited.



1. Unresectable or metastatic disease. 2. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains all rights in the rest of the world. 3. In collaboration with Roche. Blueprint Medicines has U.S. commercial rights for up to two programs. Roche has worldwide commercialization rights for up to two programs and ex-U.S. commercialization rights for up to two programs. 1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line; GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; MAA, marketing authorization application; MTC, medullary thyroid cancer; NDA, new drug applicaton; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

Precision that Moves

Staying one step ahead of disease