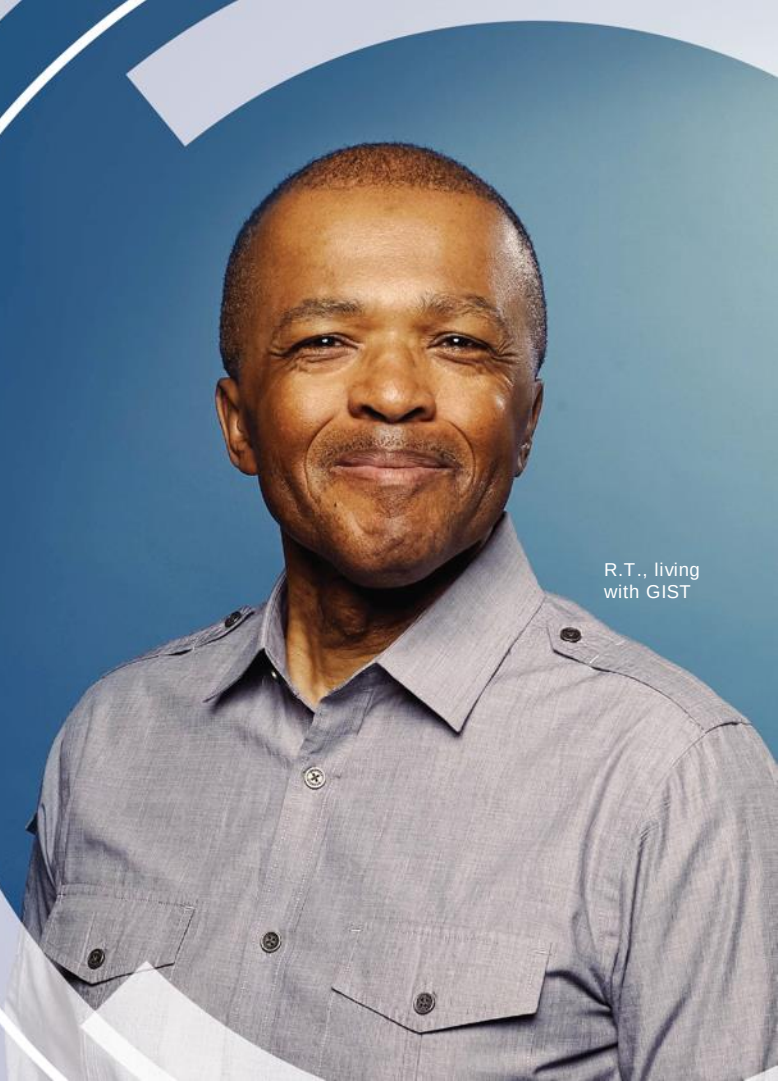
PRECISION THAT MOVES™

Staying one step ahead of disease

J.P. Morgan Healthcare Conference

JANUARY 13-16, 2020



R.T., living with GIST

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 Blueprint Medicines’ 2020 key milestones; Blueprint Medicines’ plans, strategies, timelines and expectations for the preclinical and clinical development and commercialization of AYVAKIT™ (avapritinib), pralsetinib, fisogatinib, and BLU-263; plans and timelines for submitting marketing applications for avapritinib and pralsetinib and, if approved, commercializing avapritinib for additional indications or pralsetinib; the potential benefits of Blueprint Medicines’ current and future drug candidates in treating patients; expectations regarding Blueprint Medicines’ existing cash, cash equivalents and investments; and Blueprint Medicines’ strategy, goals and anticipated milestones, business plans and focus. Blueprint Medicines has based these forward-looking statements on management’s current expectations, assumptions, estimates and projections. While Blueprint Medicines 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 Blueprint Medicines’ 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 Blueprint Medicines’ drug candidates, including avapritinib, pralsetinib, fisogatinib and BLU-263, or the licensed products, including BLU-782; Blueprint Medicines’ advancement of multiple early-stage efforts; Blueprint Medicines’ 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 Blueprint Medicines’ 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 or marketing applications; Blueprint Medicines’ ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing; Blueprint Medicines’ ability and plans for establishing a commercial infrastructure, and successfully launching, marketing and selling its current or future approved products; Blueprint Medicines’ ability to successfully expand the indications for AYVAKIT in the future; Blueprint Medicines’ ability to develop and commercialize companion diagnostic tests for its current and future drug candidates; and the success of Blueprint Medicines’ 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”).

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This presentation also contains estimates, projections and other statistical data made by independent parties and by Blueprint Medicines relating to market size and growth and other data about Blueprint Medicines’ 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 Blueprint Medicines’ future performance and the future performance of the markets in which Blueprint Medicines operates are necessarily subject to a high degree of uncertainty and risk.

2020 Blueprint: three key themes

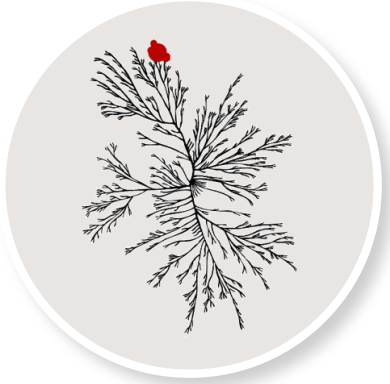
AYVAKIT™
avapritinib | tablets

Now approved in the U.S.

Fully integrated commercial-stage company, with multiple planned global regulatory submissions for avapritinib and pralsetinib

R.S., living with SM

Expanded strategic focus on systemic mastocytosis and related mast cell disorders



Continuous strengthening of pipeline, with plans to nominate up to 3 development candidates this year

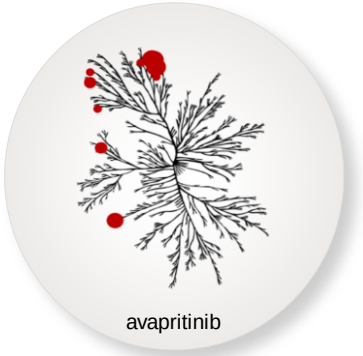
blueprint™ MEDICINES

SM, systemic mastocytosis. 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.

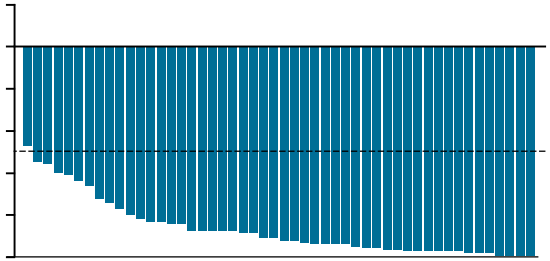
The rapid evolution of Blueprint Medicines

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

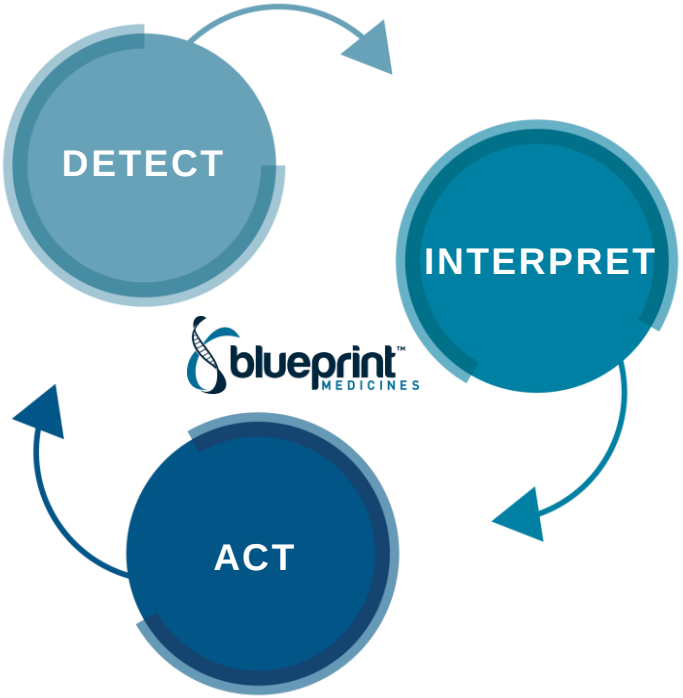


Avapritinib in advanced systemic mastocytosis: change in serum tryptase[1]

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

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

A powerful vision for delivering durable benefit with targeted therapy



HIGHLY SELECTIVE INHIBITORS

Potent inhibition of genetic drivers leads to rapid, deep and durable responses

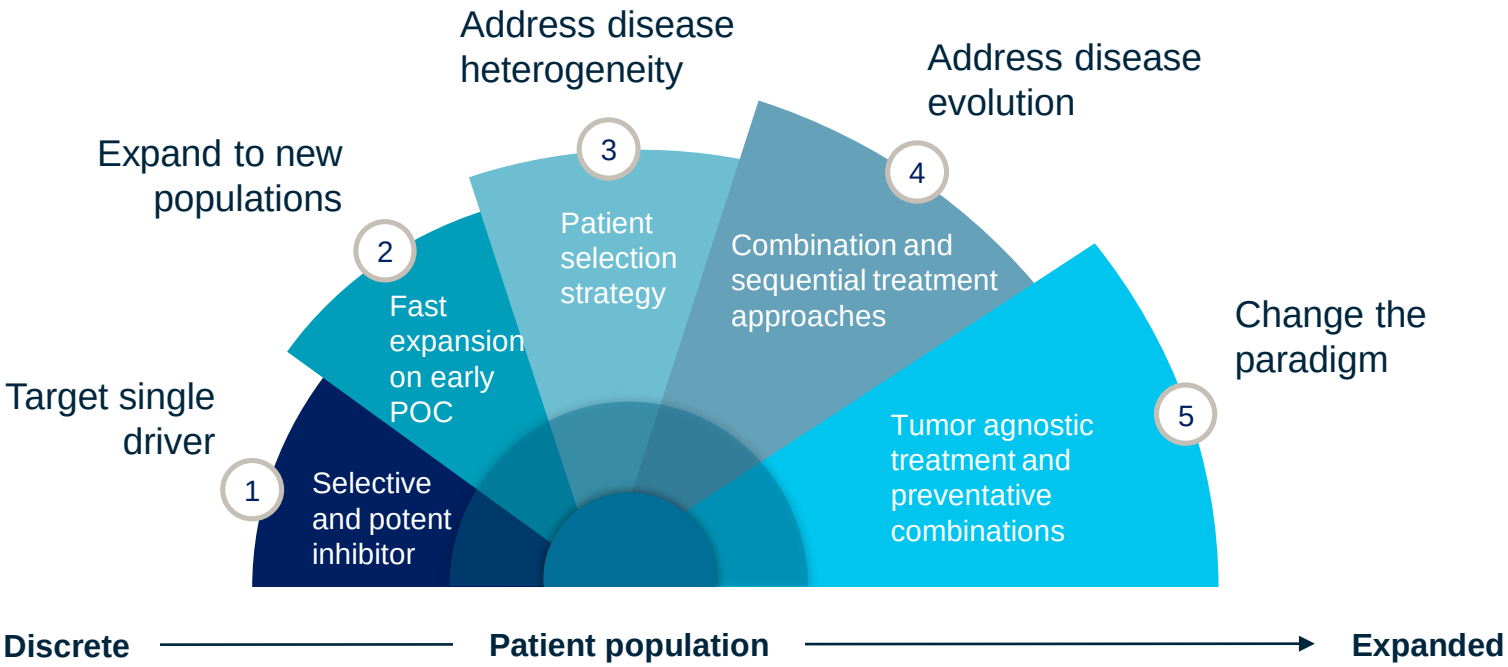
PATIENT SELECTION

Understanding of disease heterogeneity enables responder hypotheses

ADAPTIVE ABILITY

Research engine rapidly empowers solutions for acquired resistance

Expand applications to reach broader patient populations

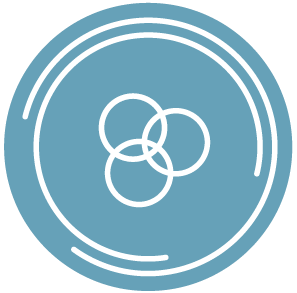


POC, proof of concept

Build therapeutic leadership by leveraging insights and efficiencies

Next-generation inhibitors

Combination strategies



Enhanced patient selection

CLINICAL AND COMMERCIAL SCALE

TRANSLATIONAL INSIGHTS

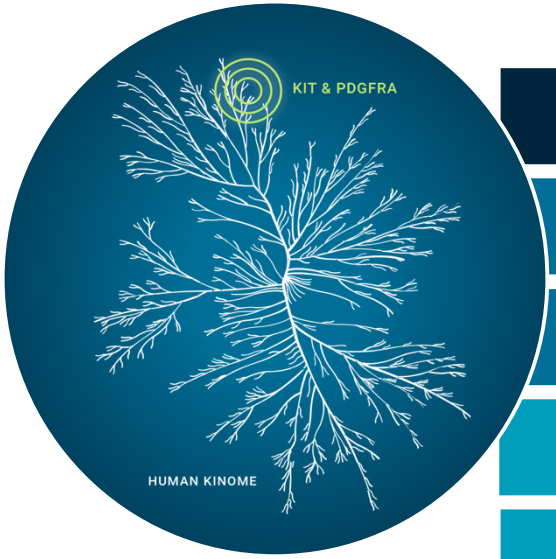
blueprint MEDICINES

Seek to deliver a portfolio of new medicines to patients globally

MULTIPLE ANTICIPATED COMMERCIAL LAUNCHES THROUGH 2021

1. Approved in the U.S. for unresectable or metastatic GIST harboring a PDGFRA exon 18 mutant, including PDGFRA D842V mutations. 2. The proposed MAA indication is unresectable or metastatic GIST harboring a PDGFRA D842V mutation. 3. Represents planned NDA/MAA submissions. GIST, gastrointestinal stromal tumor; MAA, marketing authorization application; MTC, medullary thyroid cancer; NDA, new drug application; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis; 2L, second-line; 3L, third-line; 4L, fourth-line

Avapritinib: a precision therapy with broad potential



Avapritinib

Potent and highly selective KIT and PDGFRA inhibitor

LATE CLINICAL DEVELOPMENT	U.S. REGULATORY SUBMISSION STATUS
PDGFRA exon 18 mutant GIST	APPROVED[1]
4L GIST	SUBMITTED
3L GIST	2H 2020
Advanced SM	2H 2020
Indolent and smoldering SM	

1. Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. 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.

AYVAKIT™ (avapritinib) is now approved in the United States

AYVAKIT™
avapritinib | tablets

INDICATION

AYVAKIT is indicated for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations

AVAILABLE DOSE STRENGTHS

100, 200 and 300 mg tablets

First precision therapy for GIST • Approved regardless of line of therapy
Only highly effective treatment for PDGFRA exon 18 mutant GIST

Full approval of AYVAKIT based on Phase 1 NAVIGATOR trial

EFFICACY PARAMETER	PDGFRA EXON 18 (N=43)	PDGFRA D842V (N=38)
Overall response rate (95% CI)	84% (69%, 93%)	89% (75%, 97%)
Complete response, n (%)	3 (7%)	3 (8%)
Partial response, n (%)	33 (77%)	31 (82%)
Duration of response	n=36	N=34
Median in months (range)	Not reached (1.9+, 20.3+)	Not reached (1.9+, 20.3+)

Full prescribing information is available at www.AYVAKIT.com. CI, confidence interval.

Not for promotional use.

Safety highlights from AYVAKIT prescribing information

MOST COMMON ADVERSE REACTIONS (≥20%; ANY GRADE):[1]

- Edema, nausea, fatigue/asthenia, cognitive impairment, vomiting, decreased appetite, diarrhea, hair color changes, increased lacrimation, abdominal pain, constipation, rash, and dizziness

WARNINGS AND PRECAUTIONS:

- Intracranial hemorrhage
  - Occurred in 1% of 267 patients with GIST who received AYVAKIT
- CNS adverse reactions
  - Occurred in 58% of 335 patients who received AYVAKIT
    - Cognitive impairment: 41% (3.6% Grade 3 or 4)
  - Overall, 3.9% of patients required treatment discontinuation due to a CNS adverse reaction
- Embryo-fetal toxicity

Important safety information and full prescribing information are available at www.AYVAKIT.com. 1. Adverse reactions in 204 patients with unresectable or metastatic GIST who received 300-400 mg once daily of AYVAKIT. CNS, central nervous system.

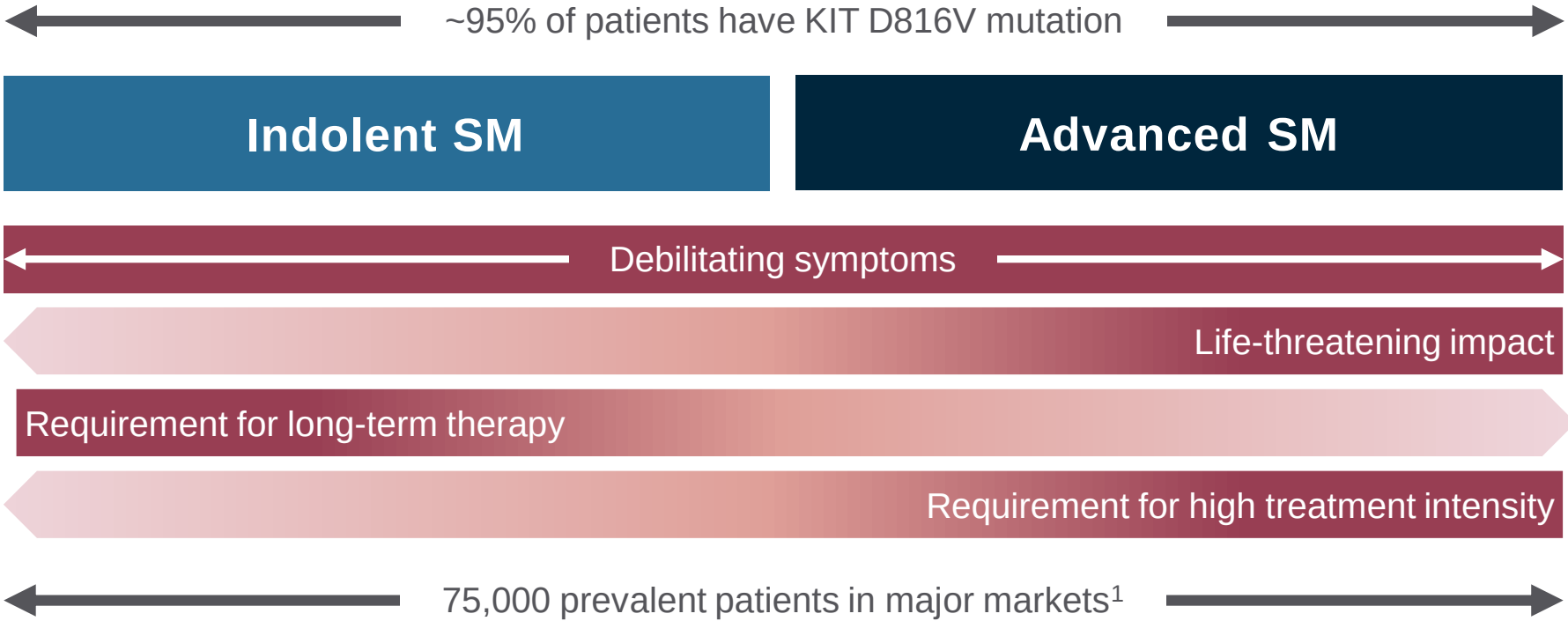
Strategic imperatives for the AYVAKIT launch

J.D., living with GIST

- Be recognized as the leader in precision medicine by hematology/oncology centers of excellence
- Drive positive first experiences with AYVAKIT among GIST prescribers
- Provide best-in-class patient support to optimize patient access and adherence
- Catalyze patient identification in GIST and across portfolio therapeutic areas

Focused portfolio field footprint with ~40 area business managers

Systemic mastocytosis is one disease with a common genetic driver



Major markets include US, EU5 and Japan. 1. Cohen S et al Br J Haematol (2014) 166(4):521-8 and World Bank Population estimates.

Comprehensive systemic mastocytosis clinical trial program

EXPLORER

Advanced SM

Phase 1 dose-escalation trial with open-label expansion

PATHFINDER

Advanced SM

Phase 2 single-arm trial

PIONEER

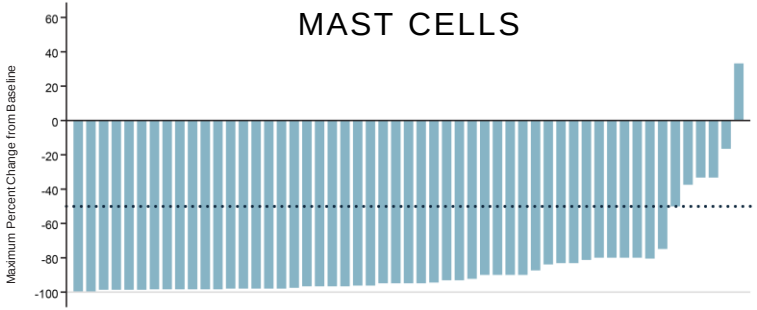
Indolent SM

Phase 2 randomized, double-blind, placebo-controlled trial

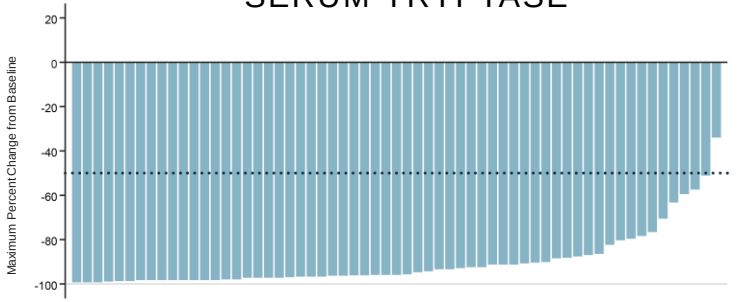
EXPLORER trial data for patients with advanced SM:

Profound activity on all measures of mast burden in nearly all patients

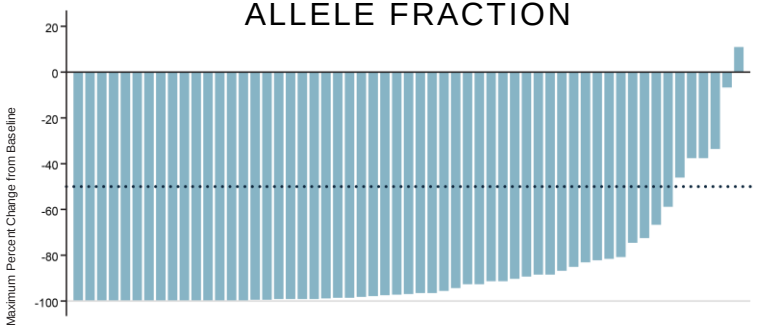
BONE MARROW MAST CELLS



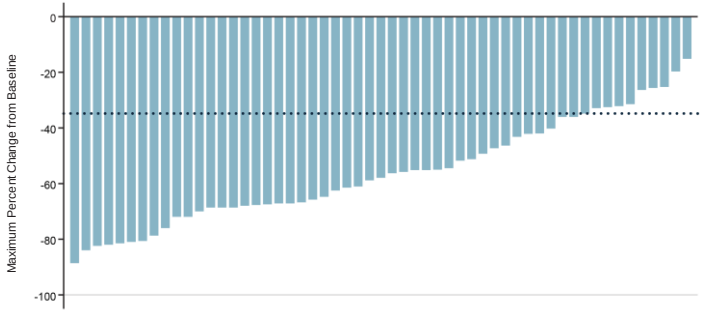
SERUM TRYPTASE



KIT D816V MUTANT ALLELE FRACTION



SPLEEN VOLUME

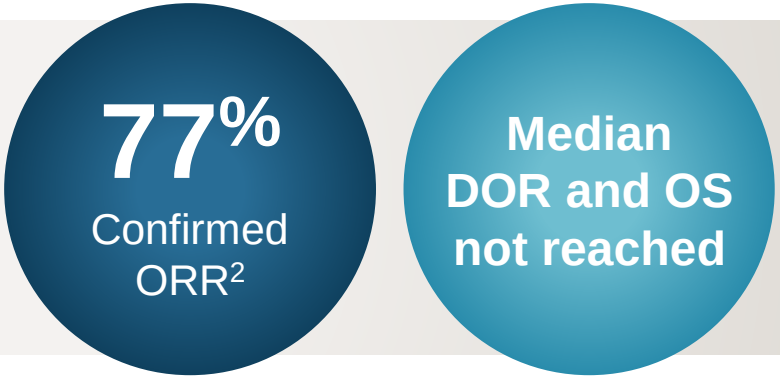


EXPLORER trial data reported on December 8, 2019. Data cutoff: August 30, 2019.

EXPLORER trial data for patients with advanced SM:
Remarkable response rate and prolonged duration of response

- FDA breakthrough therapy designation[3]
- Robust activity across all disease subtypes
- Median follow up of 21 months with ongoing treatment up to ~3.5 years[1]

BEST RESPONSE PER IWG-MRT-ECNM CRITERIA
ALL DOSES (N=48)[1]



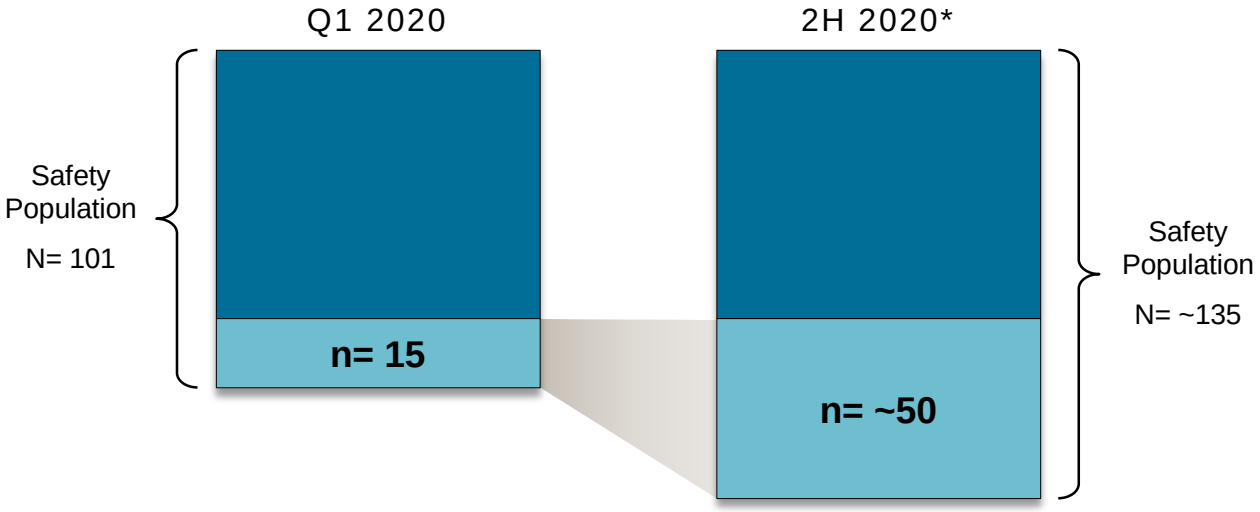
SAFETY
ALL DOSES (N=80)[1]

- Avapritinib was generally well-tolerated, and most AEs were grade 1 or 2[4]
- Most common treatment-emergent AEs were periorbital edema, anemia, diarrhea, fatigue, peripheral edema, nausea, thrombocytopenia, vomiting and cognitive effects
- Across all doses, 6 patients discontinued treatment due to treatment-related AEs

1. EXPLORER trial data reported on December 8, 2019. Data cutoff: August 30, 2019. 2. ORR defined as complete remission with full or partial recovery of peripheral blood counts, partial remission or clinical improvement. 3. 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. 4. After the data cutoff date, one patient with SM and an associated hematologic neoplasm (SM-AHN) of myelodysplastic syndrome had a Grade 5 intracranial bleed. At the time of the bleeding event, the patient had severe thrombocytopenia and experienced a serious injury involving head trauma. AE, adverse events. DOR, duration of response; ORR, overall response rate; OS, overall survival.

Adjustment of NDA submission timing for avapritinib for advanced SM enhances dataset at 200 mg QD dose and increases probability of success

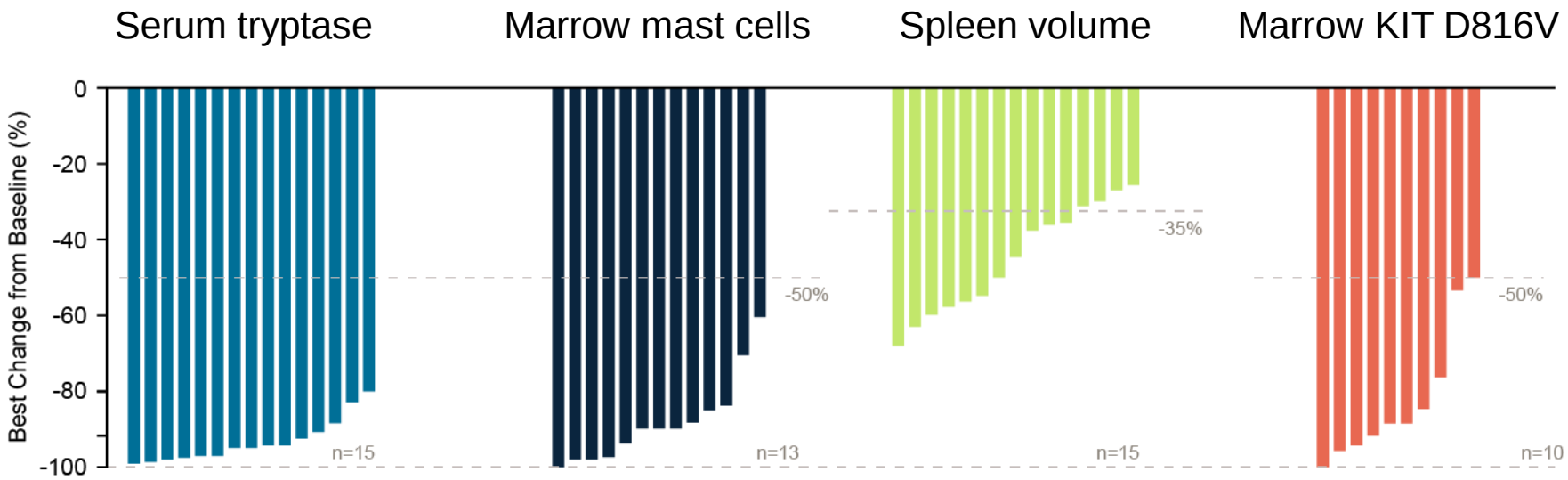
COMBINED EXPLORER AND PATHFINDER TRIAL DATASET



- Based on ongoing discussions with FDA, now plan to submit supplemental NDA for avapritinib for advanced SM in 2H 2020
- Plan to include additional patients treated with a starting dose of 200 mg QD, the proposed indicated dose
- Target enrollment for efficacy in PATHFINDER trial is complete and follow-up is ongoing

* Estimated based on Blueprint Medicines' clinical trial plan. QD, once daily.

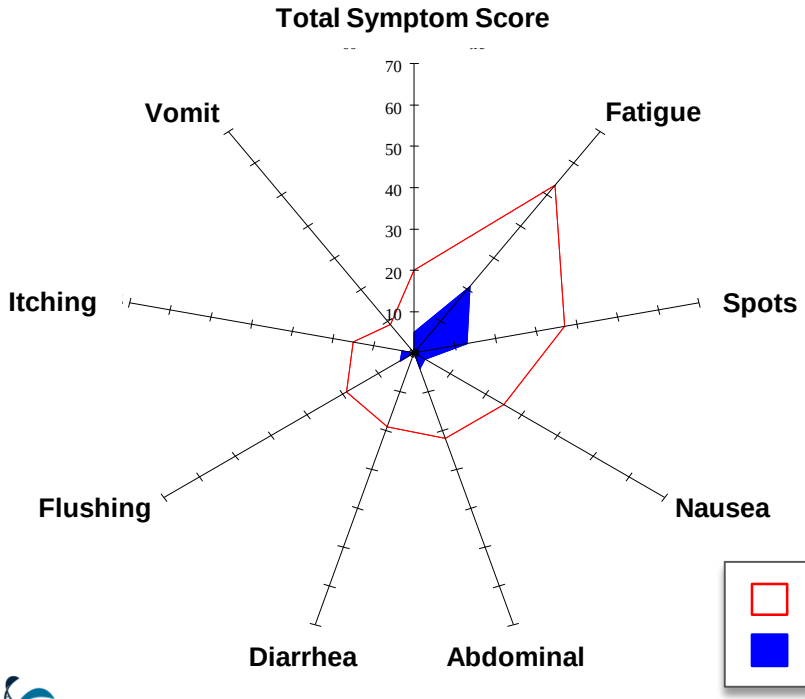
EXPLORER trial data for patients with indolent SM:
Robust reductions on measures of mast cell burden



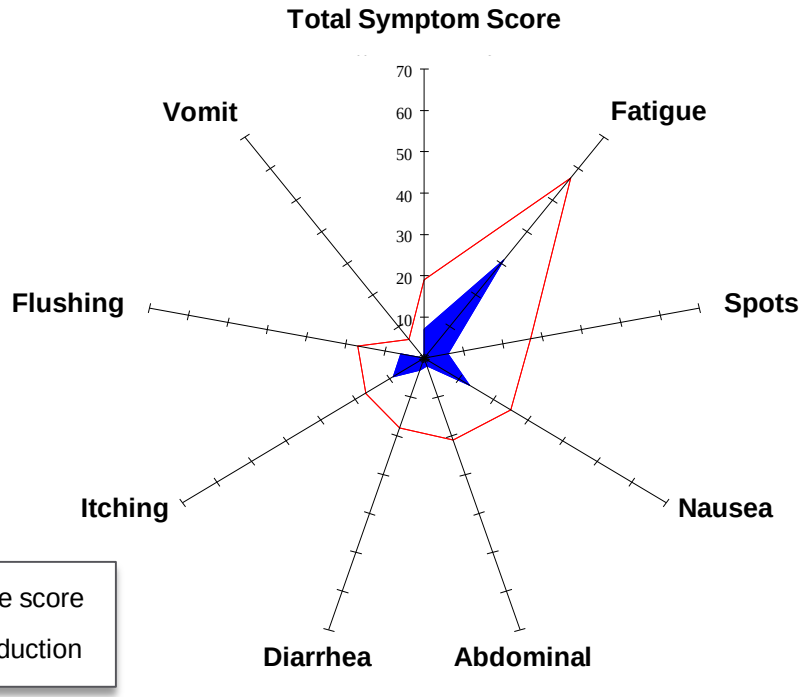
Data presented at the European Hematology Association Annual Meeting in June 2019. Data cutoff date: January 2, 2019.

EXPLORER trial data for patients with indolent SM:
Improvement in disease symptoms and PRO survey total symptom score

INDOLENT SM PATIENTS (N=5)



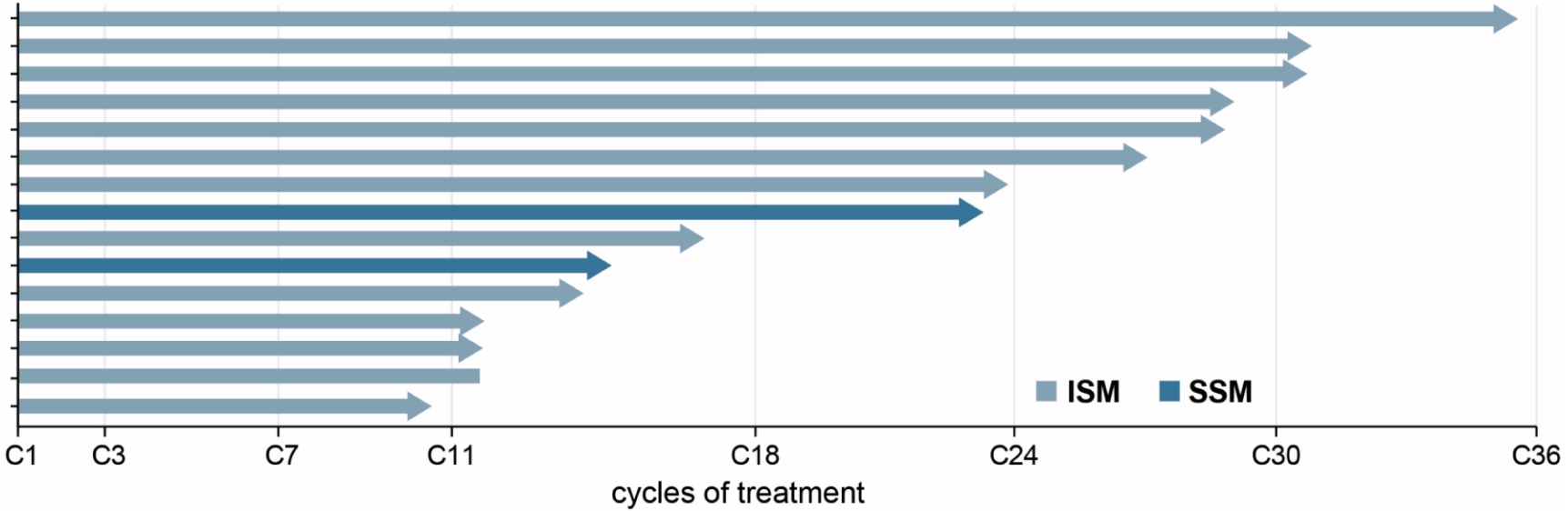
ALL PATIENTS (N=39)



EXPLORER trial data analysis. Data cutoff date: August 30, 2019. PRO, patient reported outcomes.

EXPLORER trial data for patients with indolent SM:
Prolonged durations of therapy at low doses

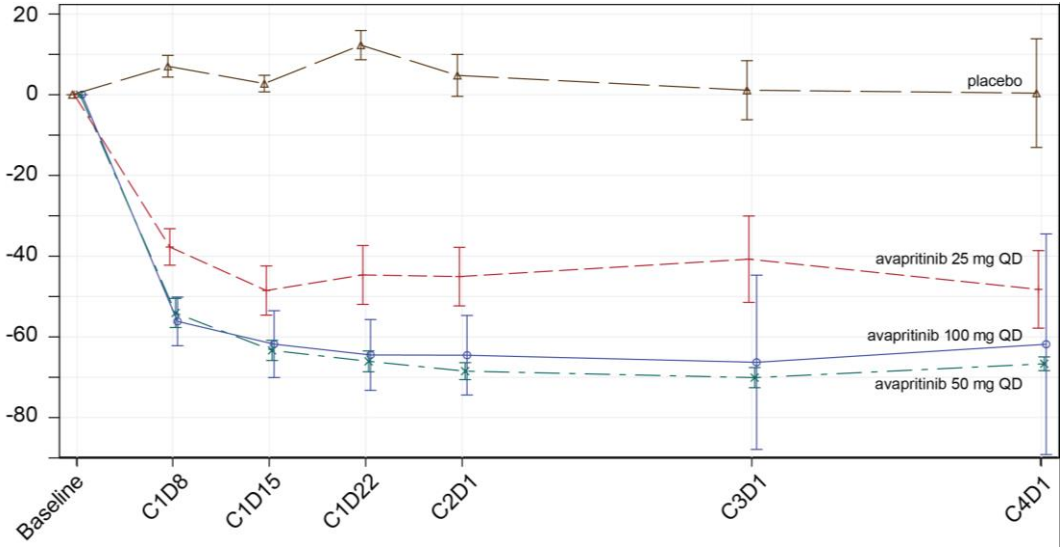
- 14 of 15 (93%) remained on treatment up to nearly 3 years (cycle 36)
- Average dose was 126 mg with 73% treated at 100 mg QD



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

PIONEER trial data for patients with indolent SM:
All avapritinib doses showed rapid and robust reductions in serum tryptase

MEAN PERCENT CHANGE IN SERUM TRYPTASE



BASELINE CHARACTERISTICS

- Significant symptom burden in every patient enrolled
- 84% of screened patients met minimum symptom burden eligibility requirement
- Baseline median Total Symptom Score was 52 (range: 19–100)

SAFETY (N=30) ALL DOSES

- Most reported AEs were grade 1 or 2
- No intracranial bleeding, thrombocytopenia or anemia reported
- No patients discontinued treatment due to an AE

PIONEER data presented at ASH 2019 Annual Meeting. Data cutoff: November 12, 2019.

Next steps for the PIONEER trial of avapritinib in indolent SM

- ✓ Complete enrollment of dose-finding Part 1
- ✓ Report initial safety and serum tryptase data at ASH 2019 Annual Meeting
- ○ Plan to report additional Part 1 data in late-breaking oral abstract at AAAAI 2020 on March 14, 2020
- ○ Complete enrollment of the registration-enabling Part 2 by the end of 2020

AAAAI, American Academy of Allergy, Asthma & Immunology; RP2D, recommended part 2 dose.

BLU-263 was advanced based on insights from avapritinib

POTENT

Sub-nanomolar potency against KIT D816V

SELECTIVE

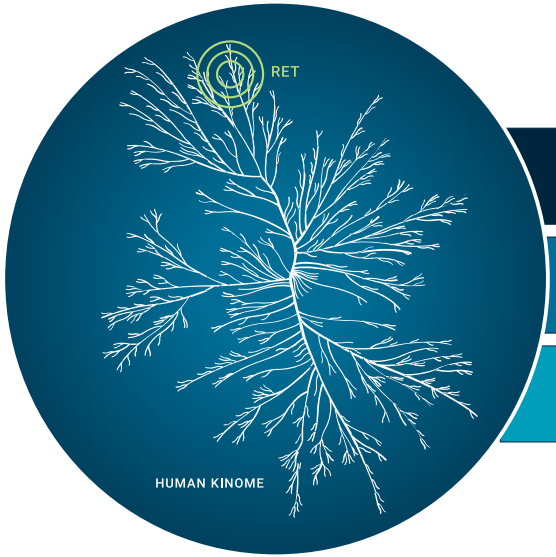
Highly selective for KIT, with low off-target activity

CNS PROFILE

Designed to not cross blood-brain barrier

PLAN TO INITIATE PHASE 1 TRIAL IN HEALTHY VOLUNTEERS IN 1H 2020

Pralsetinib: an investigational precision therapy for RET-altered cancers



LATE CLINICAL DEVELOPMENT	U.S. REGULATORY SUBMISSION STATUS
RET fusion NSCLC	Q1 2020
2L MTC	Q2 2020
RET-altered tumors	

Pralsetinib

Potent and highly selective RET inhibitor

INITIATED ROLLING NDA SUBMISSION TO FDA FOR RET FUSION NSCLC IN JANUARY 2020

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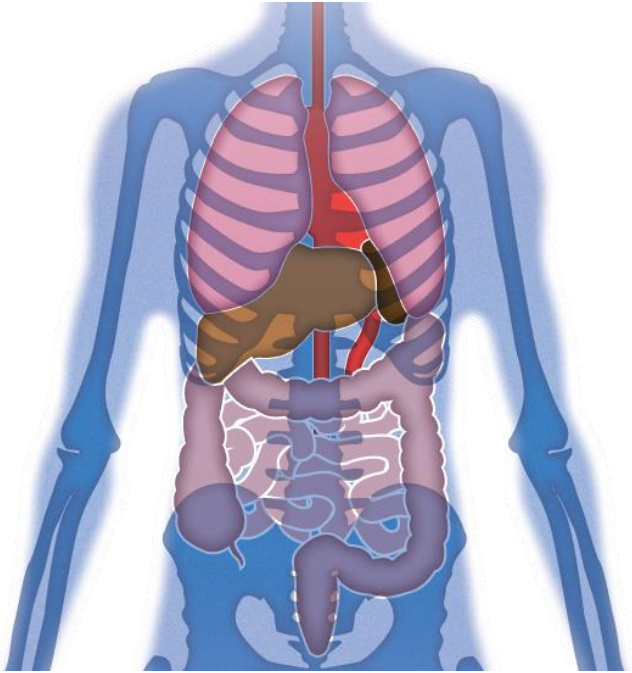
RET alterations: oncogenic drivers lacking a targeted therapeutic approach

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.

Pralsetinib is a potential best-in-class selective RET inhibitor and the cornerstone of our lung cancer portfolio

EQUIPOTENT INHIBITION
of RET fusions and mutations, including predicted gatekeeper resistance mutations

CLINICAL RESPONSES
in 2 of 4 patients previously treated with selpercatinib[2]

HIGH RESPONSE RATES AND DURABLE ACTIVITY
in RET+ NSCLC[1] and MTC[2] patients

FDA BREAKTHROUGH THERAPY DESIGNATIONS
for RET+ NSCLC and MTC[3]

STRONG ACTIVITY AGAINST BRAIN METASTASES
in patients with RET+ NSCLC[2]

WELL-TOLERATED WITH LOW DISCONTINUATION RATES in advanced cancer populations[1,2]

1. Top-line NSCLC data reported on January 8, 2020. Data cutoff date: November 18, 2020. 2. Data presented at ASCO Annual Meeting in June 2019. Data cutoff date: April 28, 2019. 3. FDA has granted breakthrough therapy designations to pralsetinib for the treatment of RET fusion-positive NSCLC that has progressed following platinum-based chemotherapy and RET-mutant MTC that requires systemic treatment and for which there are no acceptable alternative treatments.

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.

Centrally reviewed top-line ARROW trial data showed robust and durable clinical activity for pralsetinib in RET fusion NSCLC

61%
ORR[1]

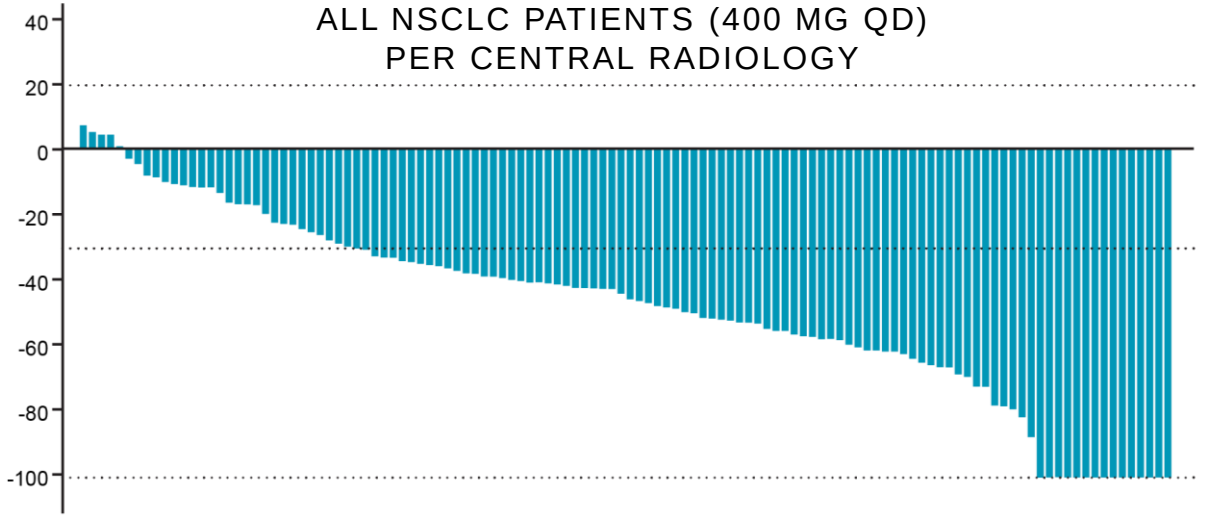
RET-fusion NSCLC with prior platinum chemotherapy

400 mg QD, N=80

73%
ORR[2]

RET-fusion NSCLC with no prior systemic therapy

400 mg QD, N=26



- Median DOR not reached (95% CI: 11.3 months, NE) in patients treated with 400 mg QD
- Safety results (N=354; 400 mg QD) were consistent with prior data; most reported AEs were grade 1 or 2
- Overall, 4% of patients discontinued treatment due a treatment-related AE

Top-line data from the Phase 1/2 ARROW trial in patients with RET fusion NSCLC. Data cutoff date: November 18, 2019. 1. Two responses pending confirmation. 2. All responses confirmed. CR, complete response; NE, not estimable; PD, progressive disease; PR, partial response; SD, stable disease.

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

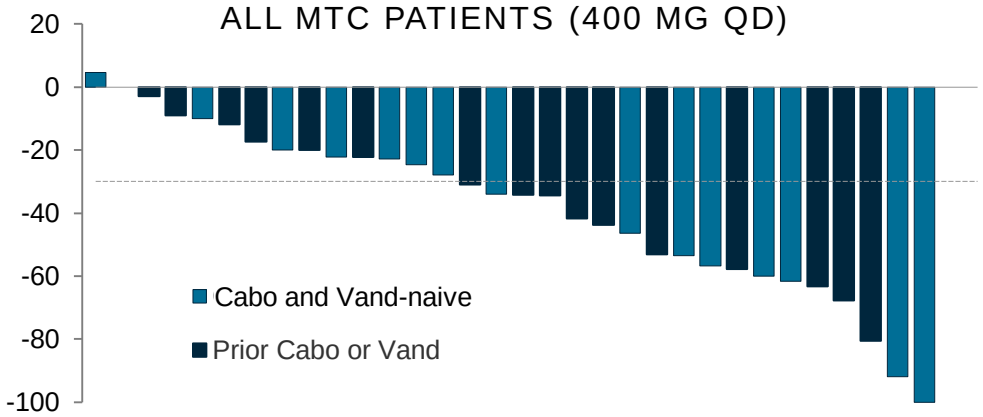
[1] Drillon, et al. Nature Reviews Clinical Oncology, 2017.

ARROW trial data presented at ASCO 2019 showed robust and durable clinical activity for pralsetinib in MTC and other RET-altered cancers

63%
ORR[1]

RET-mutant MTC previously treated with an MKI

400 mg QD, n=16



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. All responses were investigator assessed. [1] Two responses pending confirmation. [3] Six patients were evaluable for response assessment (3 confirmed PRs, 2 PRs pending confirmation). Cabo, cabozantinib; Vand, vandetinib.

A powerful scientific platform with a focused research strategy

Difficult-to-drug

Kinase targets that are difficult to drug with existing technologies

Treatment-resistant

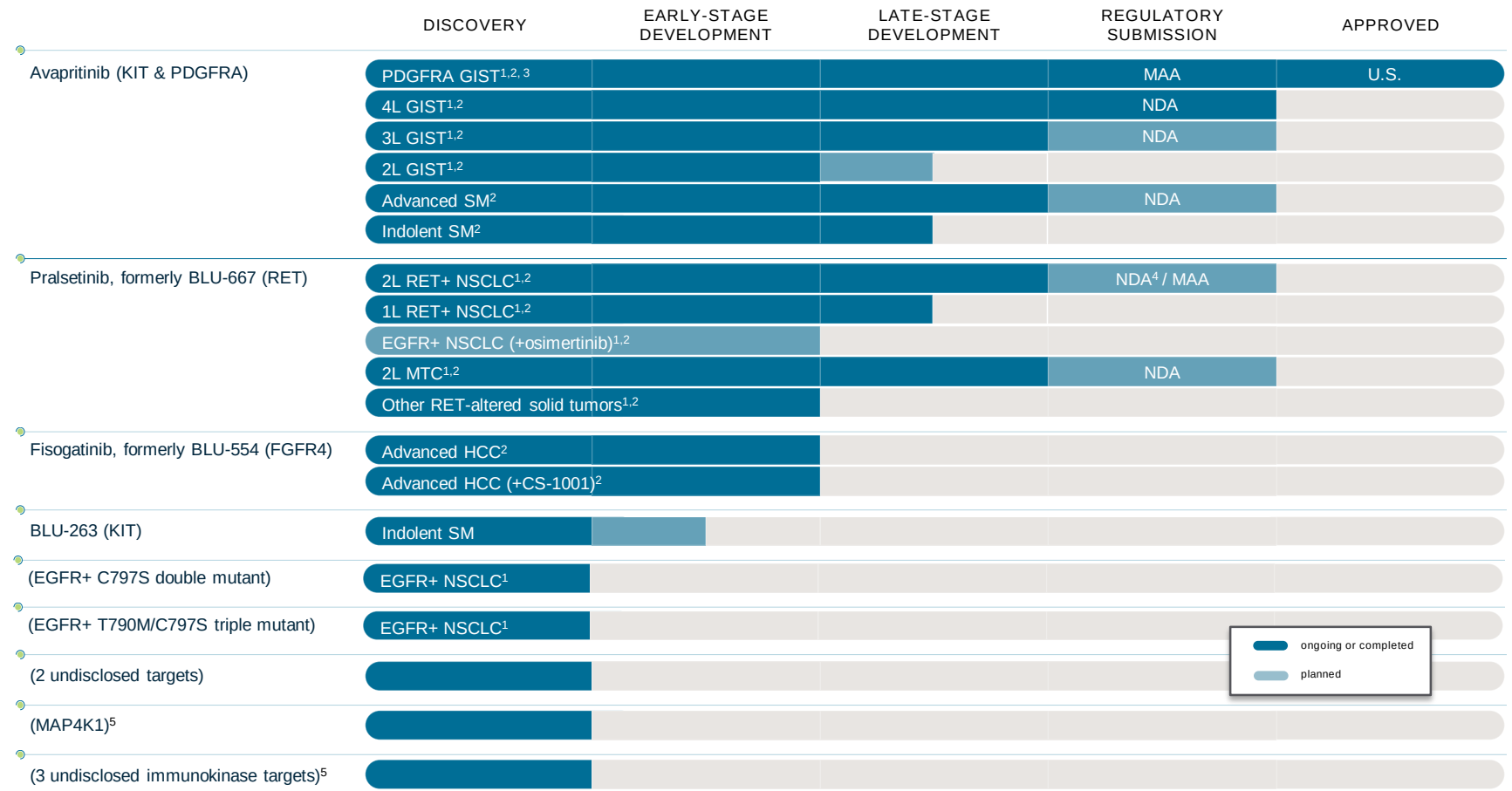
Kinase targets characterized by alterations promoting resistance to existing therapies

Novel biology

New kinase targets identified via computational and cell biology

Nominated potential first-in-class development candidate for resistant EGFR+ triple mutant NSCLC

Plan to nominate up to 2 additional development candidates in 2020



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. Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. The proposed MAA indication is unresectable or metastatic GIST harboring a PDGFRA D842V mutation. 4. Expect to complete rolling NDA in Q1 2020. 5. 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; HCC, hepatocellular carcinoma.

Strong financial position entering 2020

Balance Sheet	September 30, 2019*	December 31, 2018
Cash, Cash Equivalents and Investments	$594.5M	$494.0M

Statement of Operations	Three Months Ended September 30,	
	2019*	2018*
Collaboration Revenue	$9.1M	$1.1M
Research & Development Expenses	$81.5M	$64.6M
General & Administrative Expenses	$25.6M	$12.0M
Net Loss	$(94.3)M	$(72.7)M

Based on current operating plans, expect existing cash balance will fund operations into 2H 2021**

blueprint MEDICINES

* Unaudited

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

Anticipated 2020 milestones

REGULATORY APPROVALS

- Avapritinib in fourth-line GIST in the U.S. in Q2 2020
- Avapritinib in PDGFRA D842V GIST in the EU in Q3 2020
- Pralsetinib in RET+ NSCLC in the U.S. by the end of 2020

REGULATORY SUBMISSIONS

- Pralsetinib NDA to FDA for RET+ NSCLC in Q1 2020
- Pralsetinib NDA to FDA for 2L RET+ MTC in Q2 2020
- Avapritinib sNDA to FDA for advSM in 2H 2020
- Avapritinib sNDA to FDA for 3L GIST in 2H 2020
- Pralsetinib MAA to EMA for RET+ NSCLC in Q2 2020

TOP-LINE REGISTRATION DATA

- Avapritinib VOYAGER trial in 3L GIST in Q2 2020

MEDICAL MEETING PRESENTATIONS

- Avapritinib PIONEER trial Part 1 in ISM in Q1 2020
- Pralsetinib ARROW trial in RET+ NSCLC in 2020
- Pralsetinib ARROW trial in RET+ MTC in 2020
- Avapritinib VOYAGER trial in 3L GIST in 2020
- Avapritinib EXPLORER and PATHFINDER trials in advSM in 2H 2020

COMPLETE TRIAL ENROLLMENT

- Avapritinib PIONEER trial Part 2 in ISM by the end of 2020

TRIAL INITIATIONS

- BLU-263 Phase 1 trial in healthy volunteers in 1H 2020
- Pralsetinib Phase 3 trial in 1L MTC in 2H 2020

RESEARCH PIPELINE

- Nominate up to 3 development candidates in 2020

advSM, advanced systemic mastocytosis; sNDA, supplemental new drug application.