PRECISION THAT MOVES™

Staying one step ahead of disease

APRIL 1, 2020

R.S., living with
systemic mastocytosis

Forward-looking statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. The words "aim," "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 the plans, strategies, timelines and expectations of Blueprint Medicines Corporation (the "Company") for the preclinical and clinical development and commercialization of AYVAKIT™ (avapritinib), pralsetinib, fisogatinib, and BLU-263; the plans, timing, design, initiation, enrollment, expectations and announcement of results for the Company's ongoing and planned clinical trials; 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 any of the Company's current or future approved drugs or 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 impact of the COVID-19 pandemic to the Company's business, operations, strategy, goals and anticipated milestones, including the Company's ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved drugs, and launching, marketing and selling current or future approved drugs; the delay of any current or planned clinical trials or the development of the Company's drug candidates, including avapritinib for additional indications, pralsetinib, fisogatinib and BLU-263, or the licensed drug candidate; 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 or marketing applications; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing or AYVAKIT; the Company' ability and plans for maintaining a commercial infrastructure, and successfully launching, marketing and selling its current or future approved drugs; the Company's ability to successfully expand the approved indications for AYVAKIT or obtain marketing approval for AYVAKIT in additional geographies; the Company's ability to develop and commercialize companion diagnostic tests for any of the Company's current or future approved drugs or drug candidates; and the success of the Company's current and future collaborations, partnerships and licenses.

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 its most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q and any other filings it 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 its 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.

Leadership in a time of challenge and uncertainty

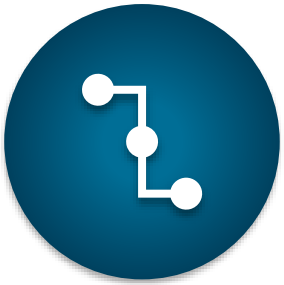
OUR APPROACH TO NAVIGATING THE COVID-19 PANDEMIC

PATIENT CENTERED

Stay focused on the patients who need access to our innovation, perhaps now more than ever

VIGILANT

Constantly assess and customize approaches to potential business impacts



NIMBLE

Leverage global infrastructure including external collaborators and adapt to new ways of working

RESILIENT

Provide support and flexibility to our employees to enable resiliency

3 clinical datasets reported in 2020 to date, with additional disclosures planned

Q1 2020

- ✓ Top-line ARROW data for pralsetinib in RET+ NSCLC
- ✓ Updated PIONEER data for avapritinib in ISM

Q2 2020

- ✓ Top-line ARROW data for pralsetinib in RET+ MTC
- Top-line VOYAGER data for avapritinib in 3L GIST

Q3 2020

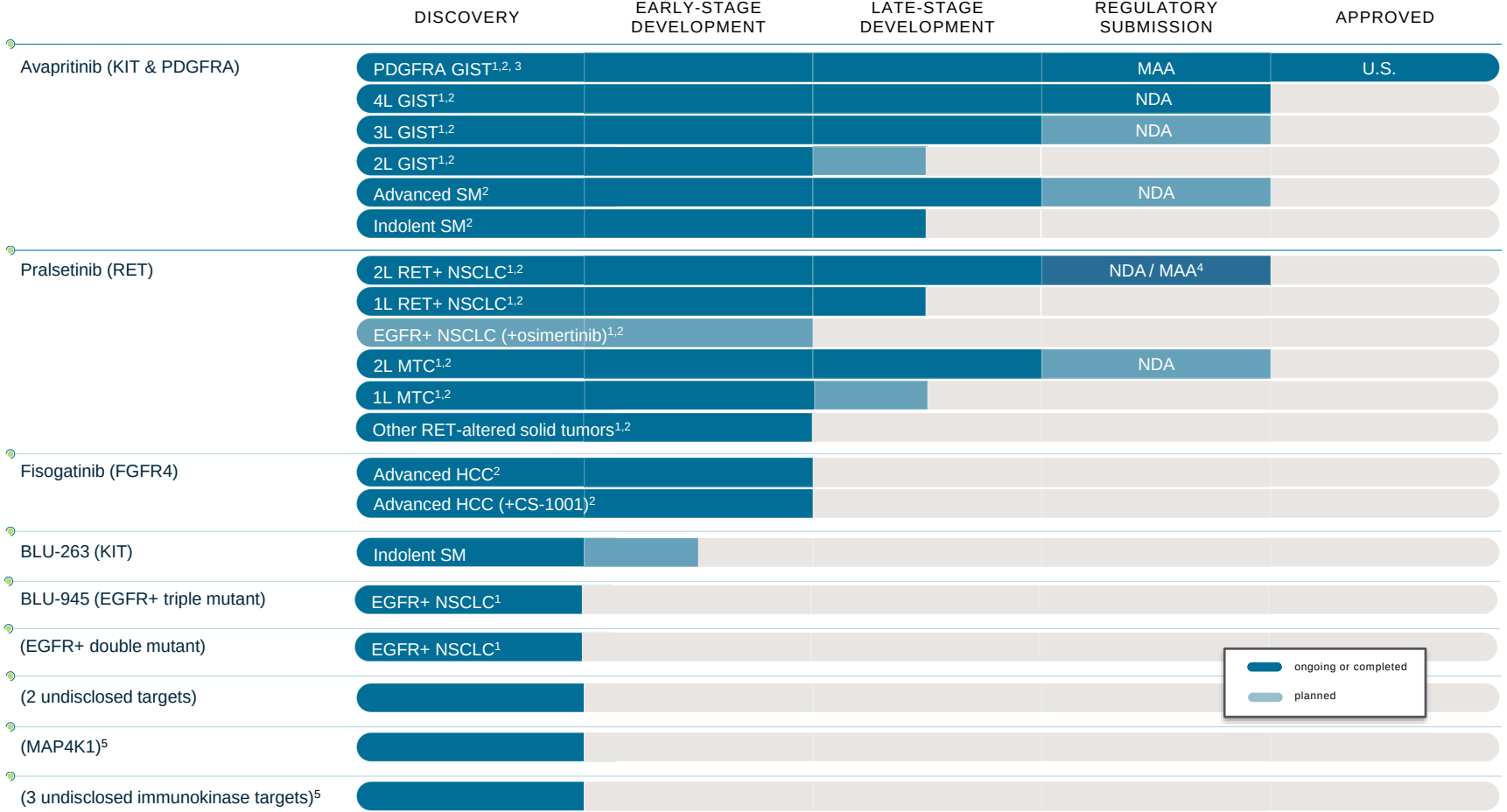
- Top-line EXPLORER and PATHFINDER data for avapritinib in advanced SM

On track to lock VOYAGER trial database in April 2020 and provide top-line data to FDA to enable action on avapritinib NDA for 4L GIST by May 14 PDUFA date

FDA, U.S. Food and Drug Administration; ISM, indolent systemic mastocytosis; GIST, gastrointestinal stromal tumors. MTC, medullary thyroid cancer; NDA, new drug application; NSCLC, non-small cell lung cancer; PDUFA, the Prescription Drug User Fee Act; SM, systemic mastocytosis; 3L, third-line; 4L, fourth-line.

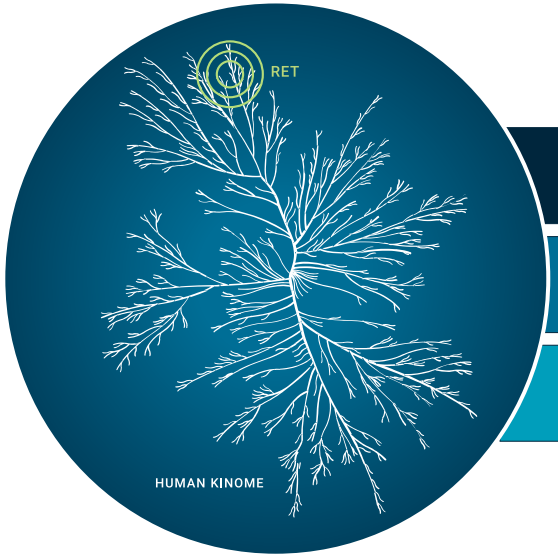
Anticipate multiple commercial launches through 2021

1. Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutant, including PDGFRA D842V mutations. 2. Proposed MAA indication is unresectable or metastatic GIST harboring a PDGFRA D842V mutation. 3. Planned NDA or MAA submissions. MAA, marketing authorization application; 2L, second-line. *All planned commercial launches are subject to regulatory review and approval of marketing applications currently under review or planned.



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. NDA submitted to FDA in March 2020; plan to submit MAA to EMA in Q2 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

Pralsetinib: an investigational precision therapy for RET-altered cancers



LATE CLINICAL DEVELOPMENT	U.S. REGULATORY SUBMISSION STATUS
RET fusion-positive NSCLC	Submitted
Previously treated MTC	Q2 2020*
Other RET-altered tumors	

Pralsetinib

Potent and highly selective RET inhibitor

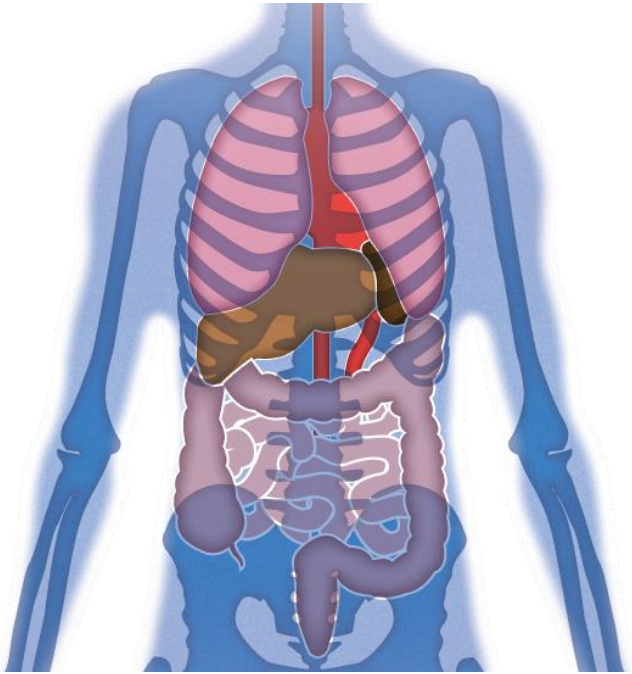
* Planned NDA submission. Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com) (CSTI). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.

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]

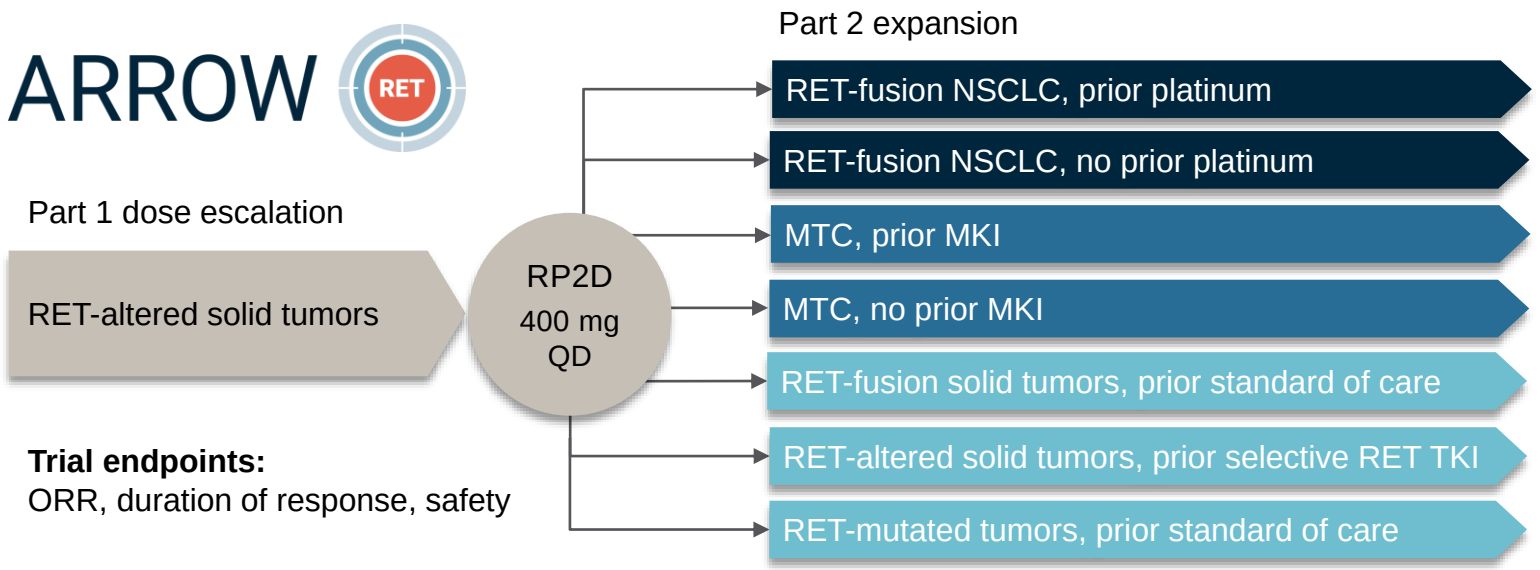


Multiple other tumor types <1% RET-altered, including:[5,6]

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.

Top-line ARROW trial data support registration plans for NSCLC and MTC



Top-line safety[1]
(n=438; 400 mg QD)

- Top-line safety results consistent with prior data
- Pralsetinib was well-tolerated and most AEs were Grade 1 or 2
- Across all patients, 4% discontinued due to treatment-related AEs

1. Phase 1/2 ARROW trial data in patients treated with pralsetinib 400 mg QD reported on April 1, 2020. Data cutoff: February 13, 2020. AE, adverse event; MKI, multi-kinase inhibitor; ORR, overall response rate; QD, once daily; RP2D, recommended phase 2 dose; 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.

Top-line ARROW trial data: RET fusion-positive NSCLC

61%
ORR[1]

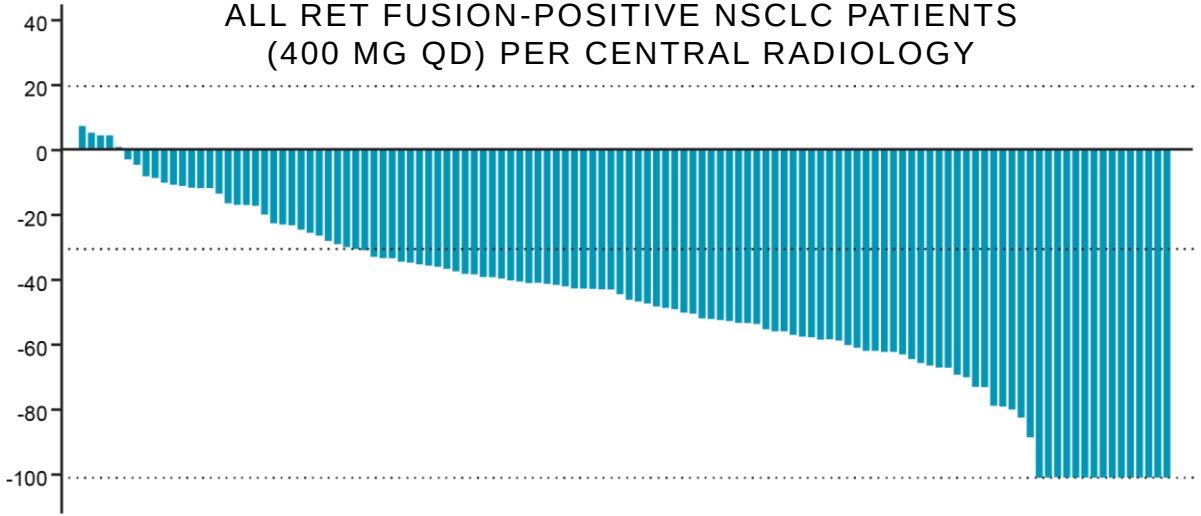
RET-fusion NSCLC with prior platinum chemotherapy

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

Phase 1/2 ARROW trial data in patients with RET fusion-positive NSCLC reported on January 8, 2020. Data cutoff: November 18, 2019.
1. Two responses pending confirmation. 2. All responses confirmed. DOR, duration of response; NE, not estimable.

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.

Top-line ARROW trial data: RET mutant medullary thyroid cancer

60%
ORR[1]

RET-mutated MTC with prior cabozantinib and/or vandetinib treatment

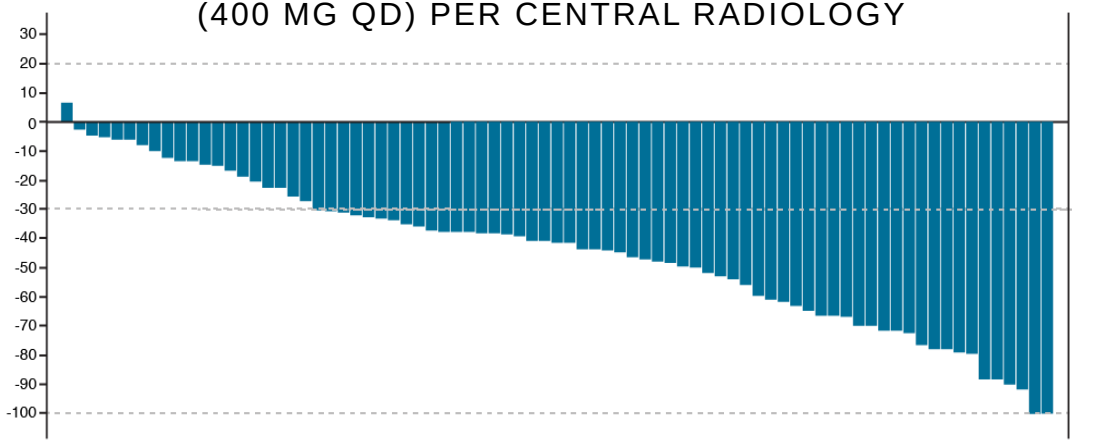
400 mg QD, N=53

74%
ORR[2]

RET-mutated MTC with no prior systemic therapy

400 mg QD, N=19

ALL RET MUTANT MTC PATIENTS
(400 MG QD) PER CENTRAL RADIOLOGY

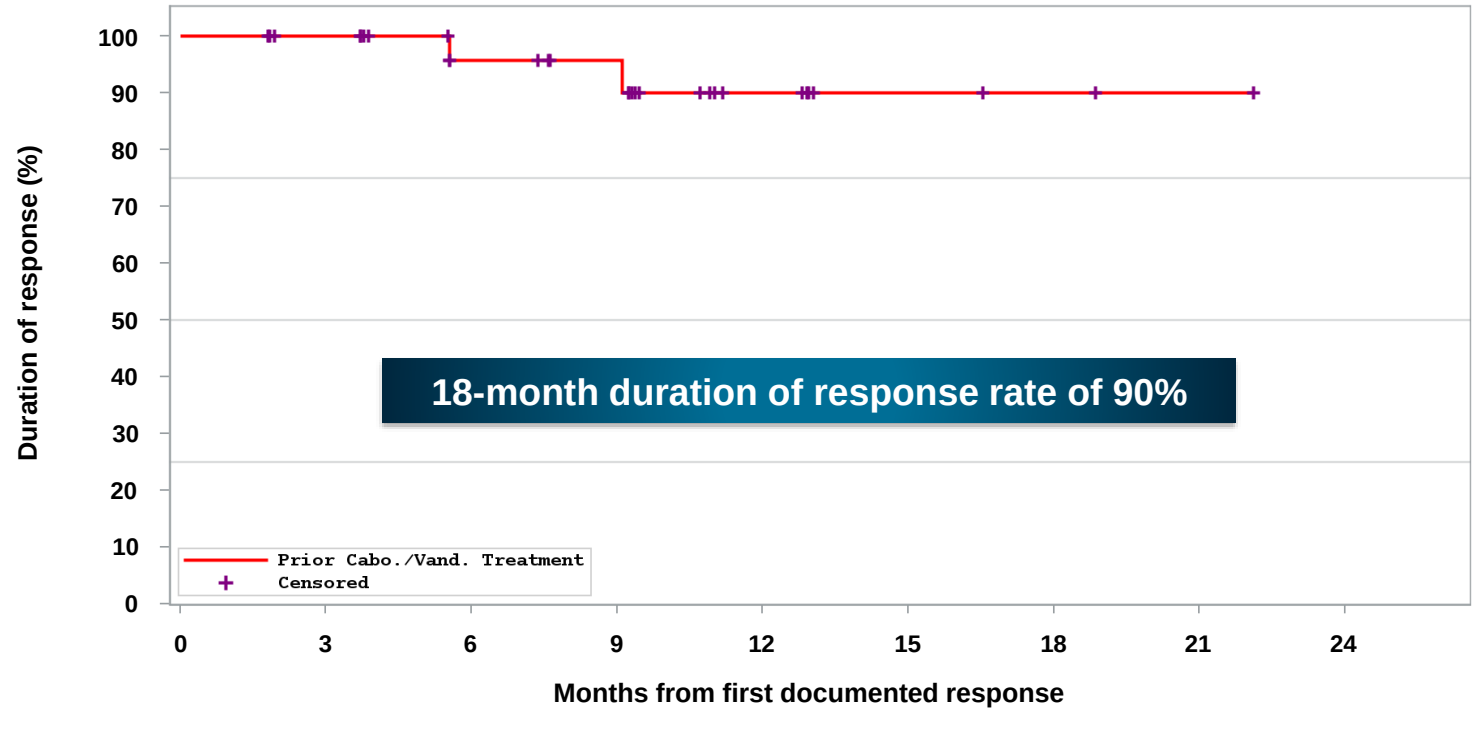


99% OF EVALUABLE PATIENTS HAD TUMOR REDUCTIONS

Median DOR not reached (95% CI: NE, NE) in patients treated with 400 mg QD

Phase 1/2 ARROW trial data in patients with RET mutated MTC reported on April 1, 2020. Data cutoff: February 13, 2020. 1. One response pending confirmation. 2. All responses confirmed.

Prolonged duration of response in patients with previously treated MTC



No. at risk:	31	28	20	17	7	3	2	1	0

Phase 1/2 ARROW trial data in patients with RET mutated MTC reported on April 1, 2020. Data cutoff: February 13, 2020.

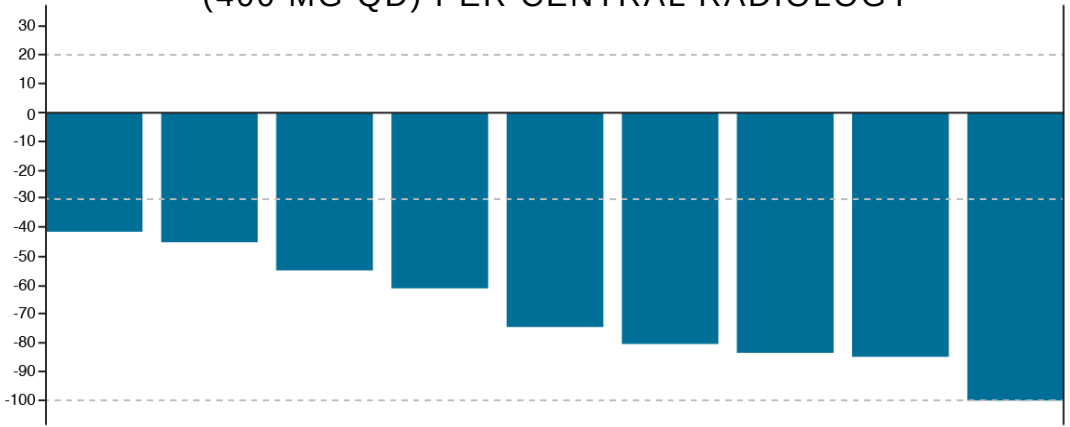
Top-line ARROW trial data: RET fusion-positive thyroid cancer

89%
ORR[1]

RET fusion-positive thyroid cancer with prior systemic therapy

400 mg QD, N=9

RET FUSION-POSITIVE THYROID CANCER PATIENTS (400 MG QD) PER CENTRAL RADIOLOGY



100% OF EVALUABLE PATIENTS HAD TUMOR REDUCTIONS

Median DOR not reached (95% CI: 8.2, NE) in patients treated with 400 mg QD

Phase 1/2 ARROW trial data in patients with RET fusion-positive thyroid cancer reported on April 1, 2020. Data cutoff: February 13, 2020. 1. All responses confirmed.

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[3]

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

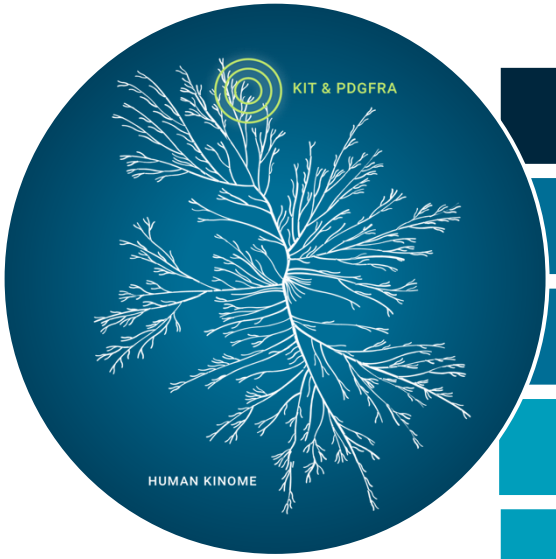
FDA BREAKTHROUGH THERAPY DESIGNATIONS
for RET+ NSCLC and MTC[4]

STRONG ACTIVITY AGAINST BRAIN METASTASES
in patients with RET+ NSCLC[3]

WELL-TOLERATED WITH LOW DISCONTINUATION RATES in advanced cancer populations[1,2,3]

1. Top-line NSCLC data reported on January 8, 2020. Data cutoff: November 18, 2020. 2. Top-line MTC data reported on April 1, 2020. Data cutoff: February 13, 2020. 3. Data reported at ASCO 2019 Annual Meeting. Data cutoff: April 28, 2019. 4. 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.

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. * Planned NDA submission. 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]

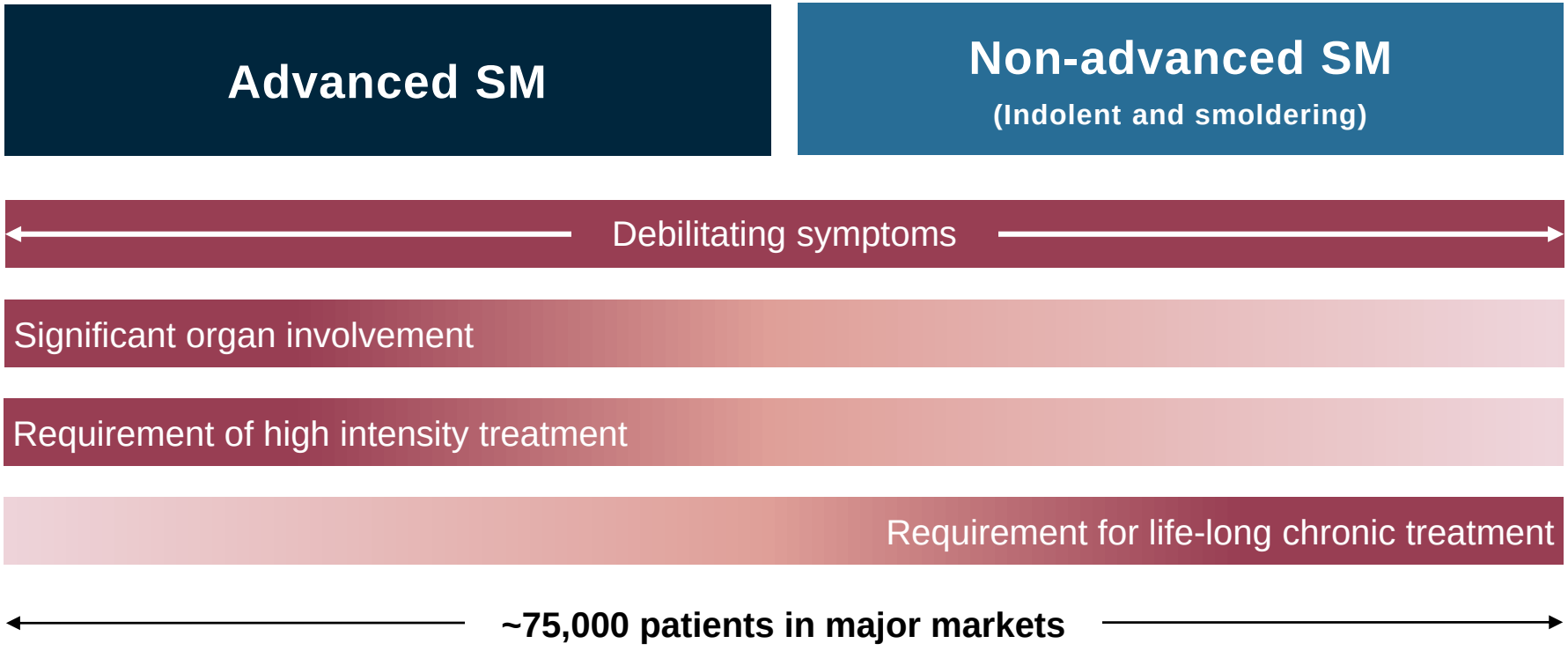
- Edema, nausea, fatigue/asthenia, cognitive impairment, vomiting, decreased appetite, diarrhea, hair color changes, increased lacrimation, abdominal pain, constipation, rash, and dizziness

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

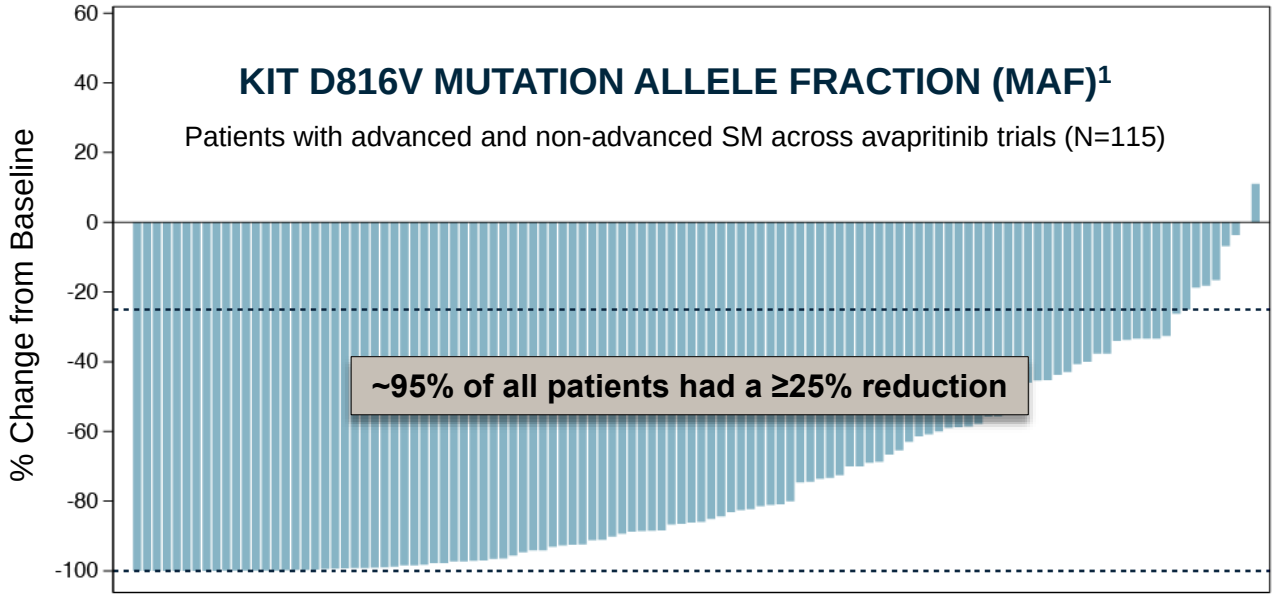
Important safety information and full prescribing information are available at www.AYVAKIT.com. 1. Adverse reactions in 204 patients with unresectable or metastatic GIST who received 300-400 mg once daily of AYVAKIT. CNS, central nervous system.

Systemic mastocytosis is one disease driven by KIT D816V



Patient numbers in major markets based on estimated prevalence for advanced, indolent and smoldering systemic mastocytosis in the US, EU5 and Japan.

Avapritinib is the only highly potent inhibitor of KIT D816V, the common disease driver across systemic mastocytosis



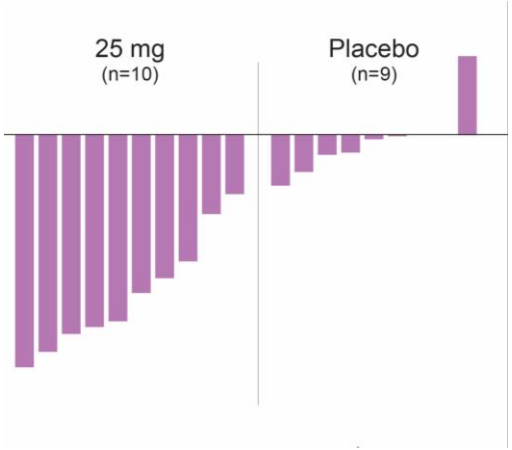
≥25% reduction in KIT D816V MAF is correlated with improved overall survival in advanced SM[2]

1. Analysis of trial data from EXPLORER and PATHFINDER (data cutoff: August 30, 2019) and PIONEER (data cutoff: December 27, 2019).
2. Jawhar, et al. Response and progression on midostaurin in advanced systemic mastocytosis: KIT D816V and other molecular markers. Blood, 2017.

PIONEER trial results: unparalleled clinical profile in patients with indolent SM

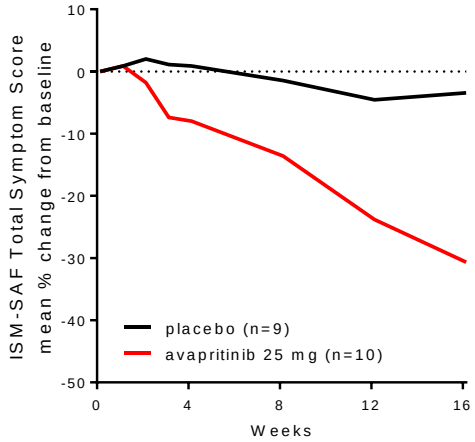
Reduces mast cell burden

KIT D816V mutant allele fraction



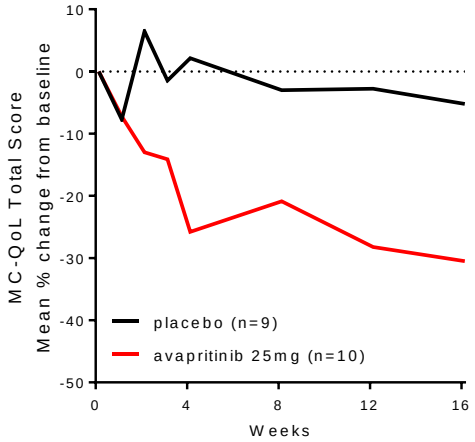
Improves disease symptoms

ISM-SAF total symptom score



Improves quality of life

MC-QoL total score

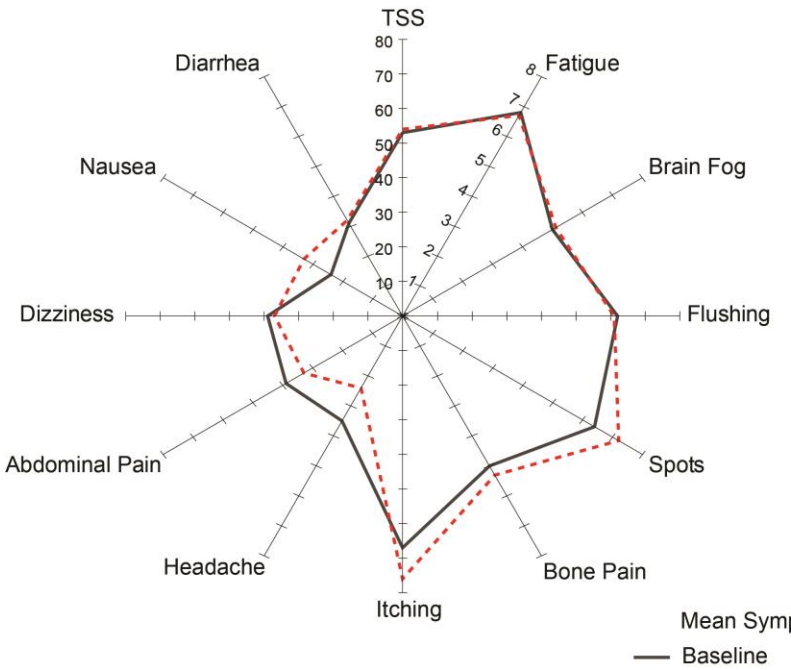


Favorable safety profile supports the selection of avapritinib 25 mg QD as recommended Part 2 dose

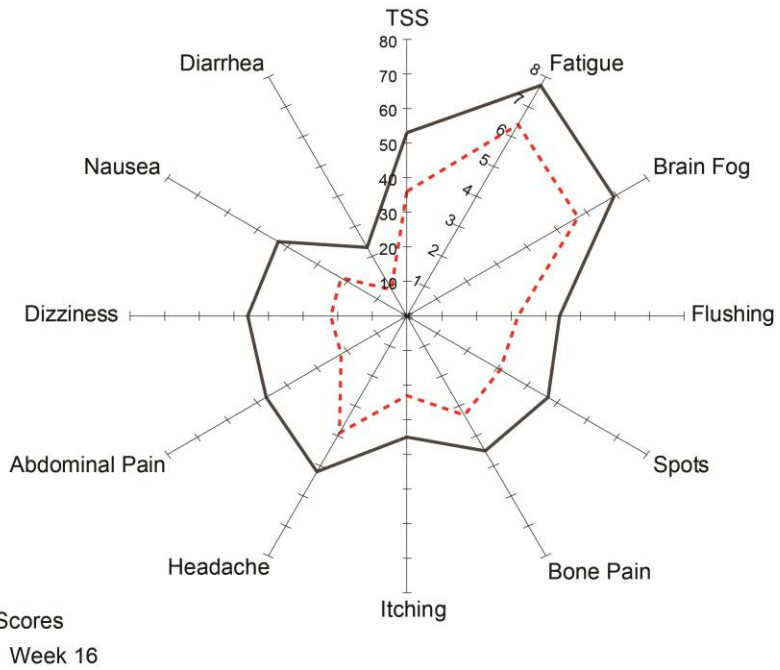
Data reported at AAAAI Annual Meeting in March 2020. Data cutoff: December 27, 2019.

Avapritinib improves all symptoms assessed by the ISM-SAF

placebo



avapritinib 25 mg QD

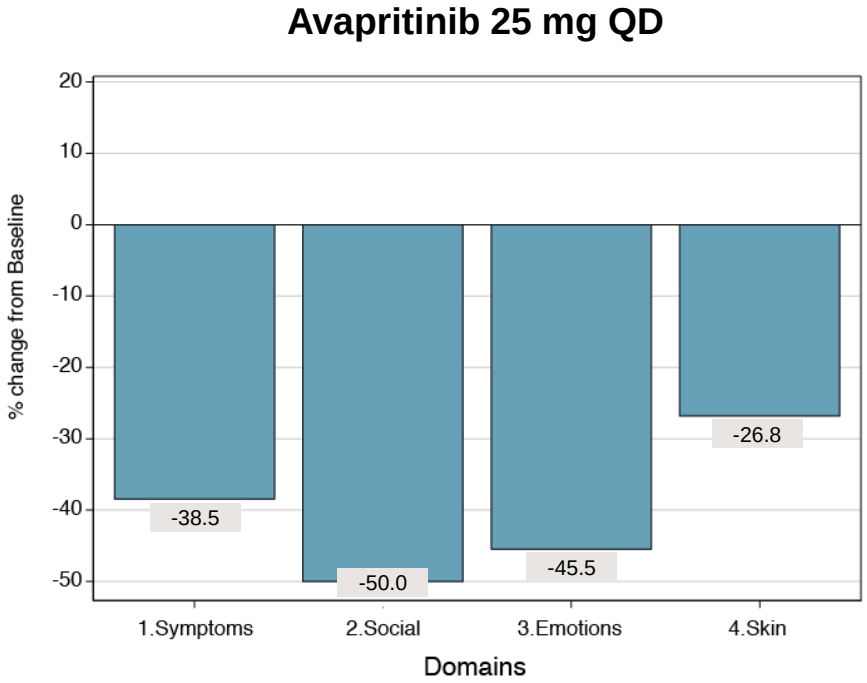


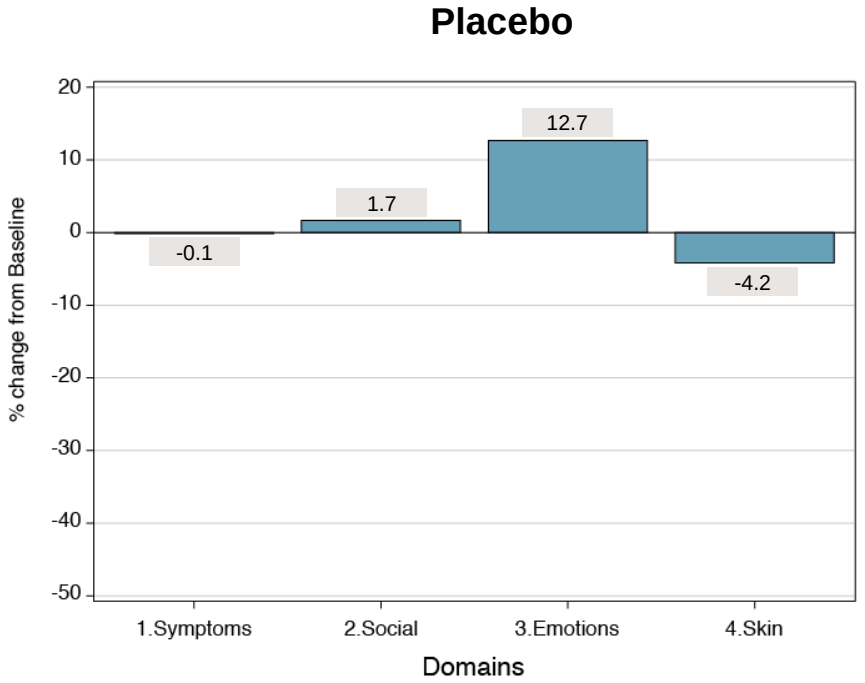
Mean Symptom Scores

Baseline Week 16

Data reported at AAAAI Annual Meeting in March 2020. Data cutoff: December 27, 2019. ISM-SAF, indolent systemic mastocytosis – symptom assessment form.

Avapritinib improves all quality of life domains measured by the MC-QoL



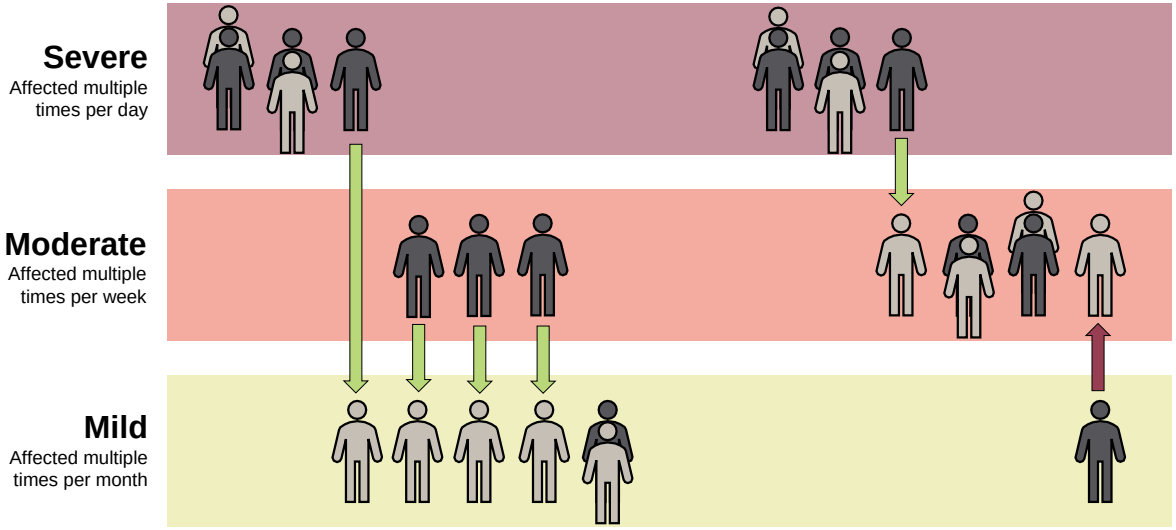


Data cutoff: December 27, 2019. MC-QoL, Mastocytosis Quality of Life Questionnaire.

Avapritinib demonstrates clinically meaningful changes in disease severity, as measured by the MC-QoL

MC-QoL DISEASE SEVERITY[1,2]

(Baseline to Week 16)



Avapritinib 25 mg QD

- 71% with mild disease at 16 weeks
- 86% improved

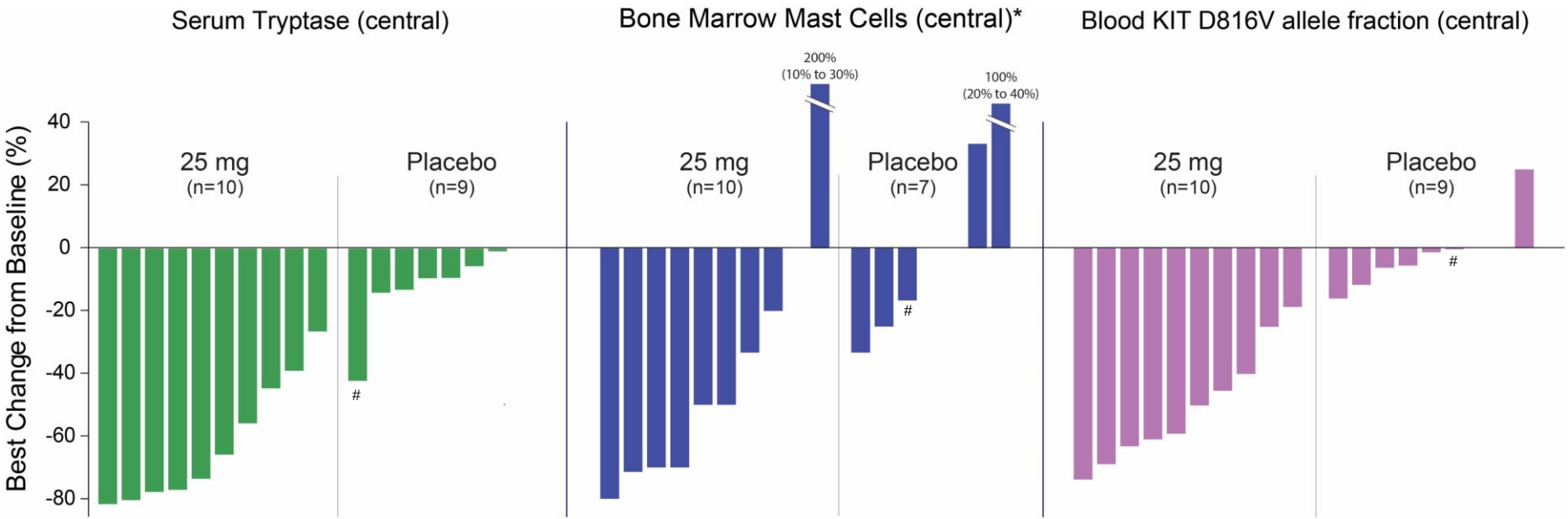
Placebo

- 0% with mild disease at 16 weeks
- 50% worsened

= Baseline = Week 16

[1] PIONEER trial analysis of patients with MC-QoL responses at baseline and 16 weeks. Data cutoff: December 27, 2019. [2] Siebenhaar, et al. Development and Validation of the Mastocytosis Quality of Life Questionnaire: MC-QoL. Allergy, 2016.

Avapritinib improves objective measures of mast cell burden assessed



Data reported at AAAAI Annual Meeting in March 2020. Data cutoff: December 27, 2019. *Bone marrow MC assessment in SM may have variability in sampling due to patchy nature of disease. No patient on study has progressed to advanced disease. #patient received high dose IV steroids.

Safety results for avapritinib 25mg QD are similar to placebo at 16 weeks

AE in >15% of placebo or avapritinib arms	Placebo n=9		avapritinib 25 mg n=10	
Preferred term				
% of subjects with ≥1 AE	any grade	grade 3	any grade	grade 3
	89	**22**	**100**	**0**
Nausea	22	0	10	0
Dizziness	22	0	30	0
Headache	11	0	30	0
Diarrhea	11	0	0	0
Fatigue	11	0	40	0
Face edema	0	0	10	0
Peripheral edema	0	0	10	0
Periorbital edema	0	0	0	0
Bone Pain	22	0	0	0

AVAPRITINIB 25 MG QD

- **No patients had serious AEs**
  - 2 patients treated with placebo had serious AEs, 1 with psychogenic seizure and 1 with diffuse cutaneous mastocytosis
- **No patients had dose modifications**
- **No patients discontinued due to AEs**

Data presented in March 2020 at AAAAI annual meeting. Data cutoff: December 27, 2019.

Next steps for PIONEER trial of avapritinib in indolent SM

PIONEER REGISTRATION-ENABLING PART 2

Design: Randomized, double-blind, placebo-controlled treatment period, followed by open-label expansion

Key endpoints: ISM-SAF total symptom score (primary), measures of mast cell burden, quality of life, concomitant medications

Sample size: ~200 patients

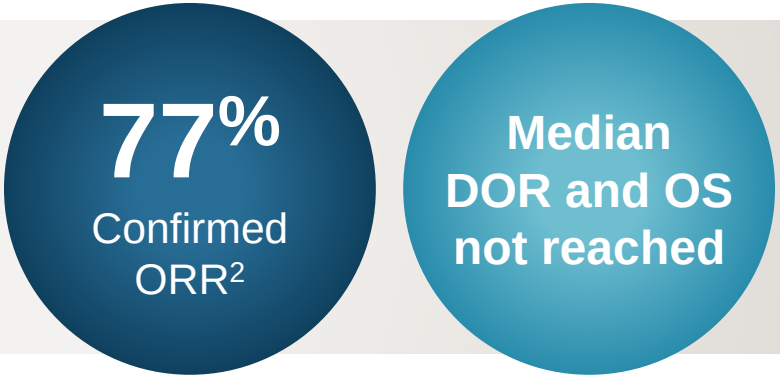
Duration: ~6 months

Timeline: Plan to initiate patient screening in June 2020

EXPLORER trial results: Remarkable response rate and prolonged duration of response in patients with advanced SM

- 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. DOR, duration of response; OS, overall survival.

Fourth quarter & full year 2019 financial results

Balance Sheet (unaudited)	FY ‘19	FY ‘18
Cash, Cash Equivalents and Investments	$548.0M	$494.0M

Statement of Operations (unaudited)	Q4 ‘19	Q4 ‘18	FY ‘19	FY ‘18
Collaboration Revenue	$51.5M	$1.0M	$66.5M	$44.5M
Research & Development Expenses	$88.6M	$70.5M	$331.5M	$243.6M
General & Administrative Expenses	$32.3M	$13.6M	$96.4M	$47.9M
Net Loss	$(66.3)M	$(80.3)M	$(347.7)M	$(236.6)M

Estimated net proceeds of $308.2M from January 2020 follow-on public offering

Based on current operating plans, expect existing cash balance will fund operations into 2H of 2022*

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* Includes January 2020 follow-on public offering and anticipated product revenues. Excludes any potential option fees, milestone payments or other payments under collaboration or license agreements.