PRECISION THAT MOVES™

Staying one step ahead of disease

July 20, 2020

blueprint™ MEDICINES

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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 and other current or future drug candidates; 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 in additional geographies or 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; the collaboration agreement among the Company, Roche and Genentech, including anticipated upfront, milestone and other payments, equity investment and other financial terms of the collaboration agreement; plans to develop a next-generation RET inhibitor; plans and timelines for submitting additional marketing applications for pralsetinib and, if approved, commercializing pralsetinib; plans to expand investment in systemic mastocytosis and pipeline programs; expectations regarding the Company's existing, cash, cash equivalents and investments, including expectations for achieving a self-sustainable financial profile and a reduced reliance on capital markets; 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 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 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.

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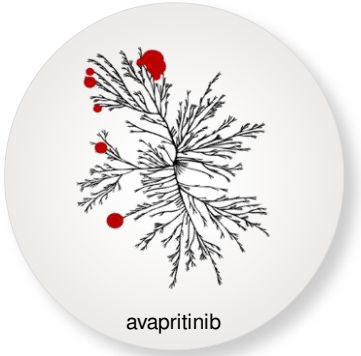
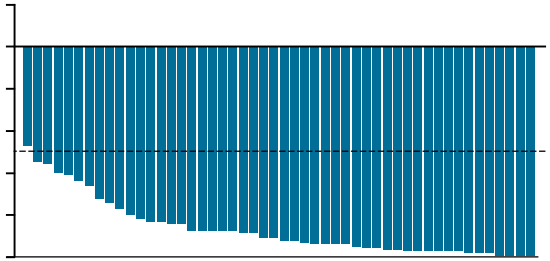
The rapid evolution of Blueprint Medicines

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.

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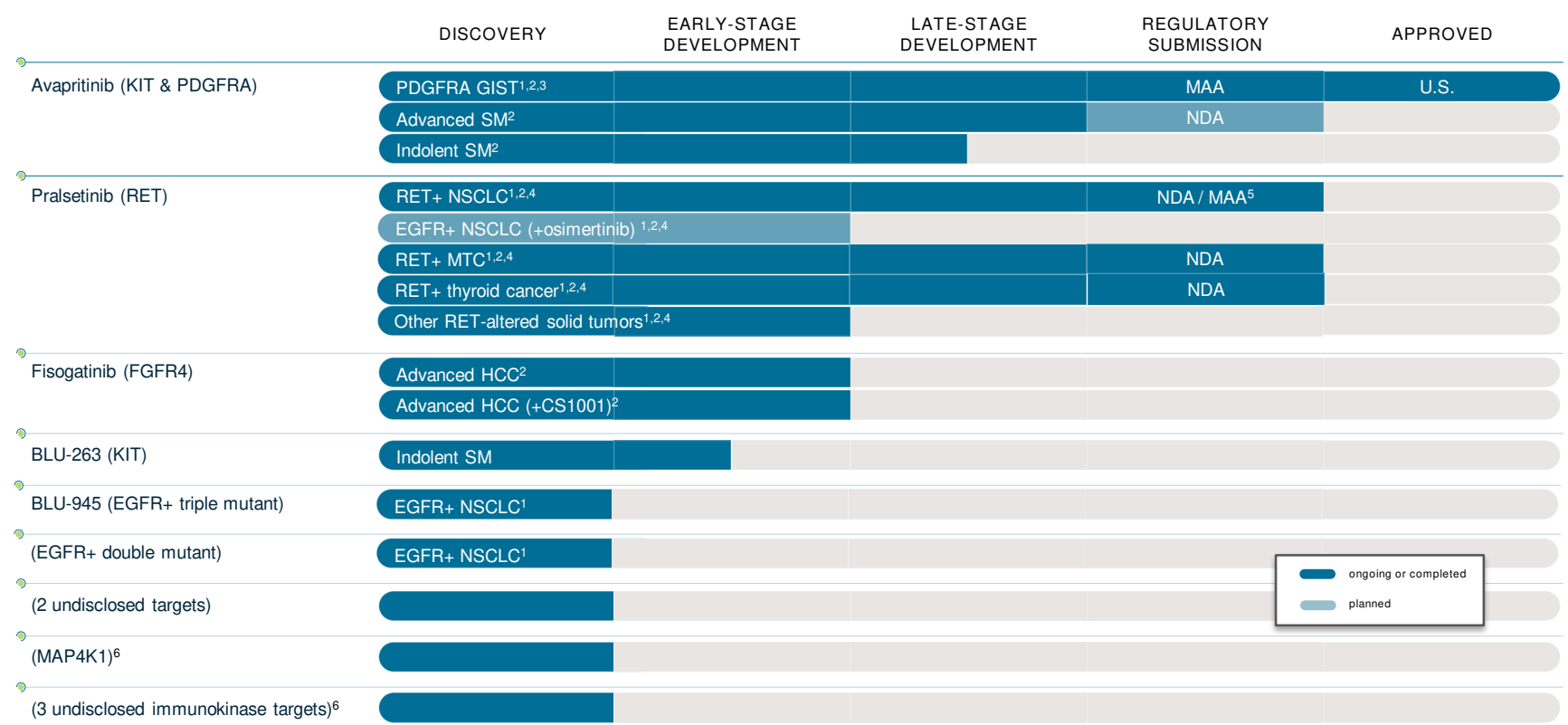

1. Unresectable or metastatic disease. 2. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan. 3. Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. The proposed indication for the MAA is unresectable or metastatic GIST harboring a PDGFRA D842V mutation. 4. In collaboration with Roche. Blueprint Medicines and Roche have co-exclusive rights to develop and commercialize pralsetinib in the U.S., and Roche has exclusive rights to develop and commercialize pralsetinib outside the U.S., excluding the CStone territory. 5. The proposed indication for the MAA is locally advanced or metastatic RET fusion-positive NSCLC previously treated with platinum-based chemotherapy. 6. 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. GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; MAA, marketing authorization application; MTC, medullary thyroid cancer; NDA, new drug application; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

Updated as of July 14, 2020.

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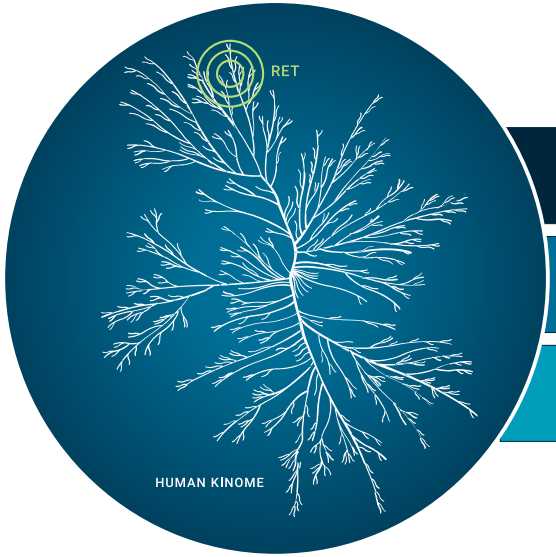
Pralsetinib: an investigational precision therapy for RET-altered cancers



LATE CLINICAL DEVELOPMENT	U.S. REGULATORY SUBMISSION STATUS
RET+ NSCLC	Submitted
RET+ thyroid cancer	Submitted
Other RET+ solid tumors	

PRALSETINIB

POTENT AND HIGHLY SELECTIVE RET INHIBITOR

NDA for RET+ NSCLC granted priority review with November 23, 2020 PDUFA action date

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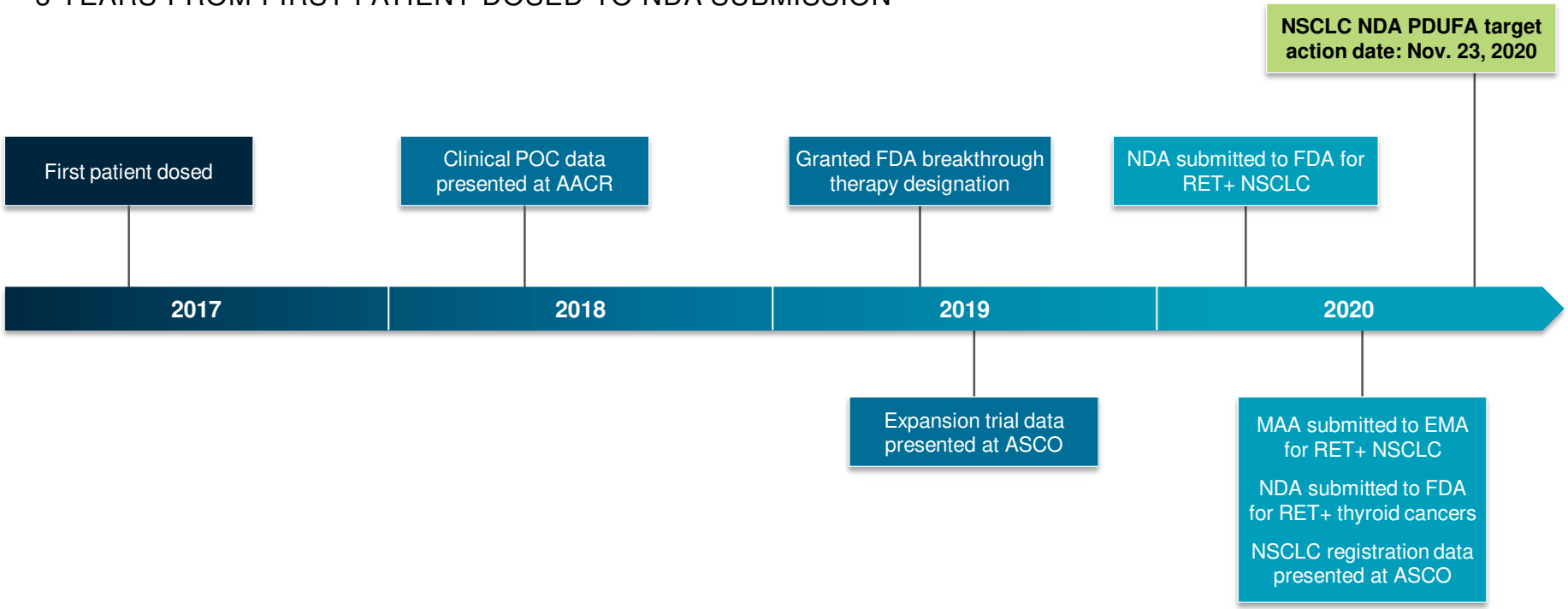
Pralsetinib's rapid development path reflects our precision therapy expertise and culture of urgency and efficiency

~3 YEARS FROM FIRST PATIENT DOSED TO NDA SUBMISSION



AACR, American Academy of Cancer Research Annual Meeting; ASCO, American Society of Clinical Oncology Annual Meeting; EMA, European Medicines Agency; FDA, U.S. Food and Drug Administration; PDUFA, Prescription Drug User Fee Act; POC, proof of concept.

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Blueprint Medicines and Roche: a transformative partnership for pralsetinib

STRATEGIC IMPERATIVES	COLLABORATION STRUCTURE & IMPACT
1 Bring pralsetinib faster to more patients globally	• Co-commercialize pralsetinib in the U.S., equally sharing responsibilities, profits and losses • Grant Roche license to commercialize pralsetinib outside of the U.S., excluding Greater China[1] • Co-develop pralsetinib globally, expanding into new treatment settings • Explore co-development of a next-generation selective RET inhibitor
2 Continue to build best-in-class precision medicine capabilities	
3 Transform the company with path to financial independence	• Reduce reliance on capital markets to finance company • Expand investment in systemic mastocytosis and pipeline programs

1. Greater China comprises Mainland China, Hong Kong, Macau and Taiwan.

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Summary of financial terms

2ND LARGEST BIOPHARMACEUTICAL COLLABORATION IN 2020 TO DATE[1]

UPFRONT	$775M, with $675M in cash and $100M equity investment at $96.57 per share[2]
MILESTONES	Up to $927M in contingent payments, with approximately $90M in potential near-term milestones
ROYALTIES	Tiered high-teens to mid-twenties on aggregate net sales outside U.S.
U.S. P&L	Companies to equally share profits and losses
DEVELOPMENT	Costs shared 45% Blueprint / 55% Roche up to pre-specified limit, then % reduction for Blueprint

1. Based on upfront payment. Source: company information, third party press releases and SEC filings. 2. Closing for a minority portion of the equity investment is subject to the expiration or termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions.

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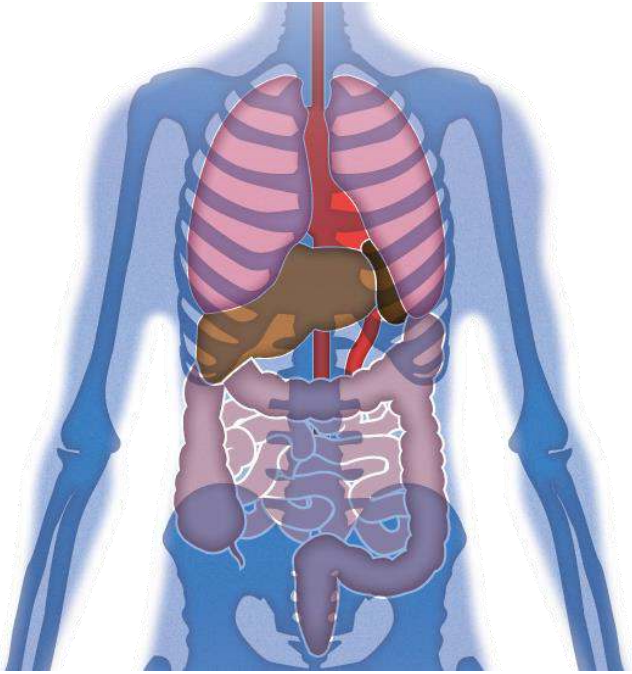
RET alterations: oncogenic drivers lacking a targeted therapeutic approach

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

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

Papillary thyroid cancer:
~10~20% 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.

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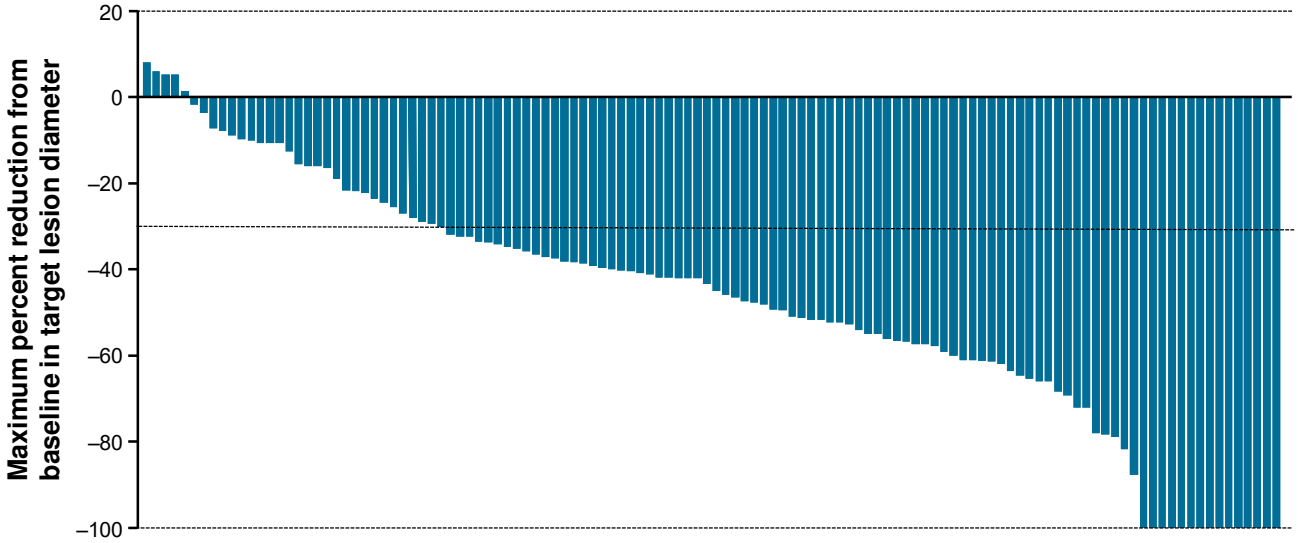
Robust clinical activity in NSCLC patients regardless of prior therapy

TUMOR SHRINKAGE PER CENTRAL RADIOLOGY



OVERALL RESPONSE RATE

61% (95% CI: 50-72%)	**Prior platinum chemo (n=80)[1]**
73% (95% CI: 52-88%)	**No prior systemic therapy (n=26)**

12% complete response rate in patients with no prior systemic therapy

Data presented at ASCO 2020 virtual annual meeting. Data cutoff: November 18, 2019. 1. Two responses pending confirmation at the time of data cutoff were subsequently confirmed. CI, confidence interval.

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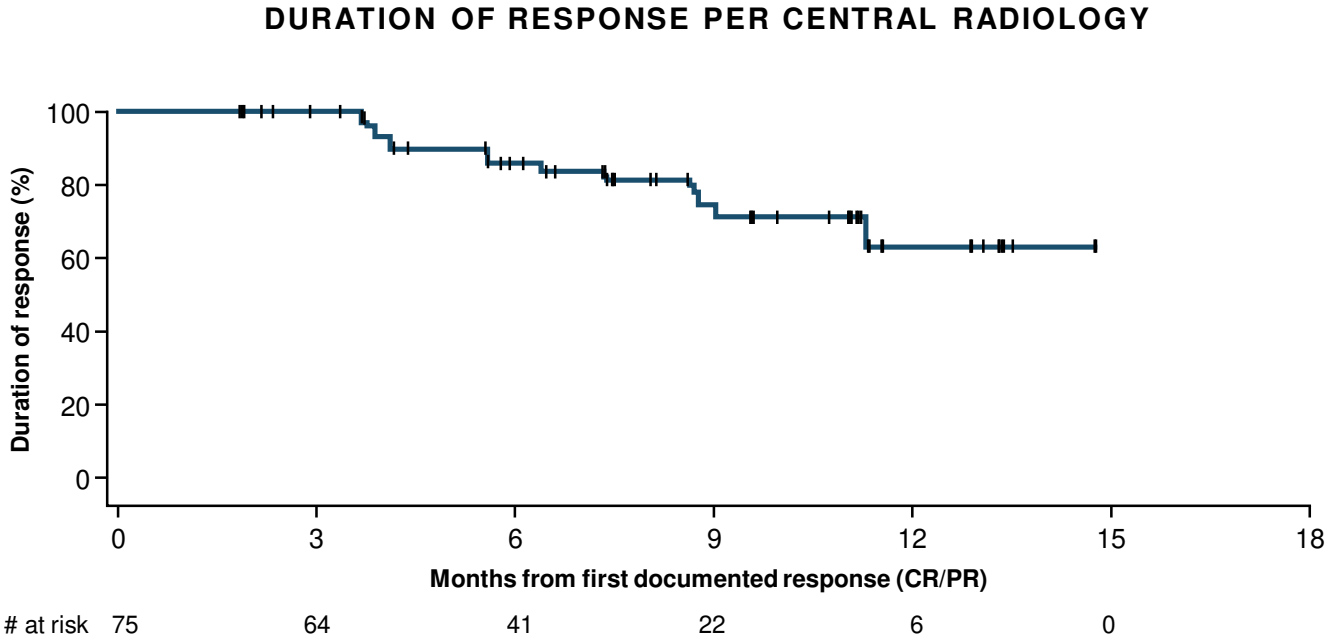
Prolonged duration of response in NSCLC patients regardless of prior therapy



NR
(95% CI: 11.3 m - NR)
Median DOR

86%
6-month DOR

74%
Responders on treatment

Data presented at ASCO 2020 virtual annual meeting. Data cutoff: November 18, 2019. CR, complete response; PR, partial response. NR, not reached.

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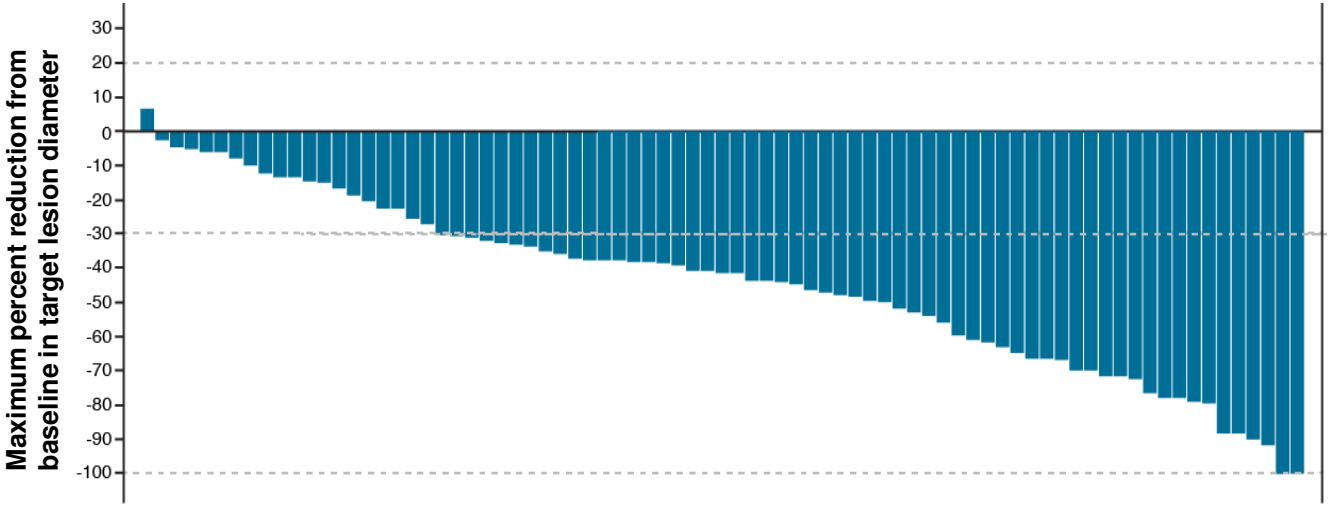
Robust clinical activity in MTC patients regardless of prior therapy

TUMOR SHRINKAGE PER CENTRAL RADIOLOGY



OVERALL RESPONSE RATE

60% (95% CI: 46-74%)	**Prior MKI treatment (n=53)[1]**
74% (95% CI: 49-91%)	**No prior systemic therapy (n=19)**

Tumor shrinkage in 99% of patients regardless of prior therapy

Top-line ARROW trial data in patients with RET+ MTC reported on April 1, 2020. Data cutoff: February 13, 2020. 1. One response pending confirmation. MKI, multi-kinase inhibitor.

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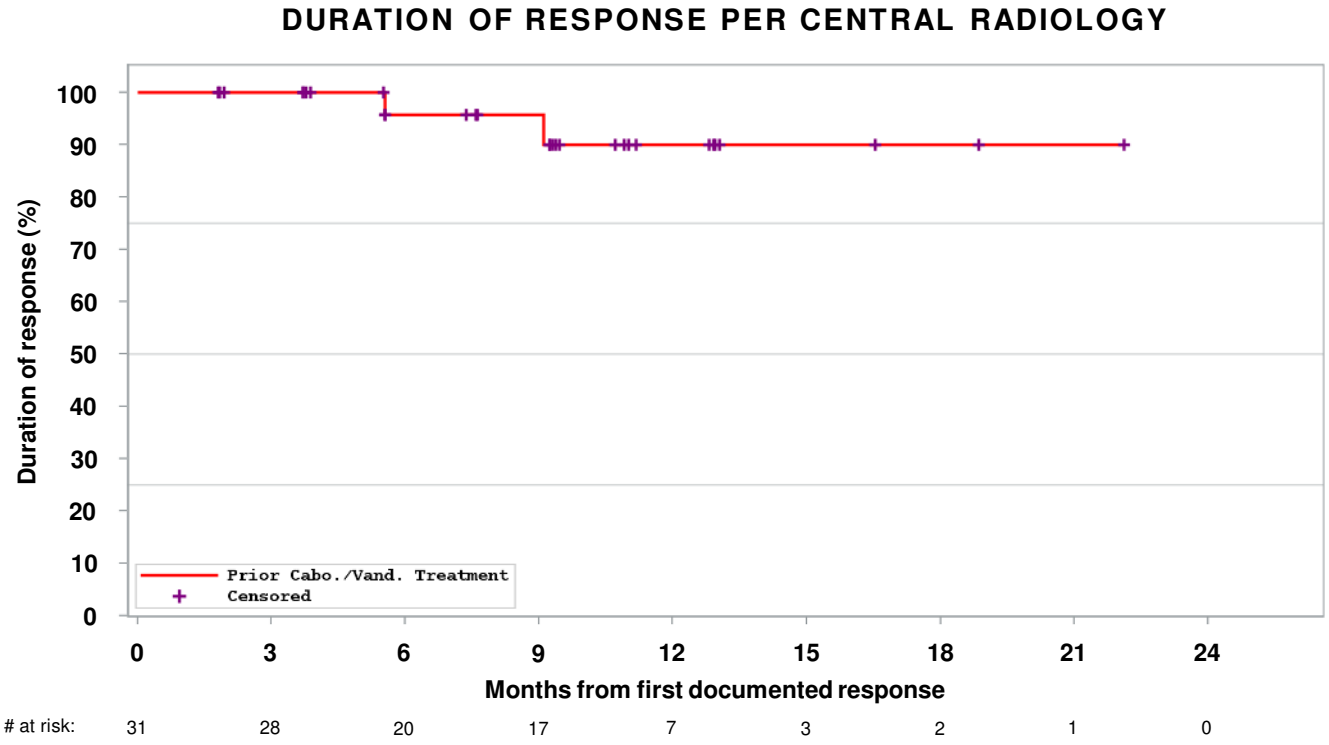
Prolonged duration of response in patients with previously treated MTC



NR
(95% CI: NE-NE)
Median DOR

96%
6-month DOR

Top-line ARROW trial data in patients with RET mutated MTC reported on April 1, 2020. Data cutoff: February 13, 2020. NE, not estimable.

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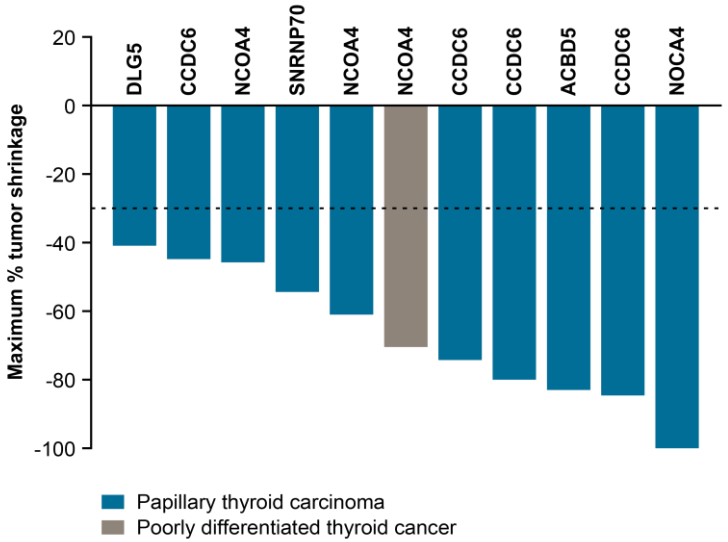
Deep and durable responses in patients with RET fusion+ thyroid cancer

TUMOR SHRINKAGE PER CENTRAL RADIOLOGY



RET FUSION+ THYROID CANCER ALL DOSES (N=11)

91% (95% CI: 59-100%) **ORR**

100% **6-month DOR**

10/11 PATIENTS PREVIOUSLY TREATED WITH SYSTEMIC THERAPY

Data presented at ASCO 2020 virtual annual meeting. Data cutoff: February 13, 2020.

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Pralsetinib is well-tolerated in patients with advanced cancer

- Only 4% discontinued due to treatment-related AEs
- Low ≥Grade 3 hypertension
- Low ≥Grade 3 AST/ALT elevations
- No clinically or statistically significant QT prolongation observed in QT sub-study
- No treatment-related hypersensitivity

Treatment-related adverse events in ≥15% of patients	All patients (N=354)*	
AE preferred term	**Any grade (%)**	**Grade ≥3 (%)**
AST increased	31	2
Anemia	22	8
ALT increased	21	1
Constipation	21	1
Hypertension	20	10
Neutropenia	19	10

Natural history data highlight importance of drug safety profile in advanced cancer patients:
67% of NSCLC patients have ≥1 CV comorbidity, with ~10% experiencing a CV event[1]

Data presented at ASCO 2020 virtual annual meeting. Data cutoff: November 18, 2019. 1. Kocher, et al. Clinical Lung Cancer, 2014. AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CV, cardiovascular; QT, interval between Q and T electrical waves on an electrocardiogram.

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Our plan to deliver a best-in-class selective RET inhibitor to patients

DIFFERENTIATED CLINICAL PROFILE

Data showing deep responses, long-lasting benefit, tolerability and convenience

PATIENT- AND HEALTHCARE PROVIDER-CENTERED APPROACH

Tailored support enabling patient identification, ease of prescribing and ongoing patient management

HIGHLY EXPERIENCED, NIMBLE TEAM

Fully-integrated launch-ready team in place, 2/3 with prior lung cancer experience

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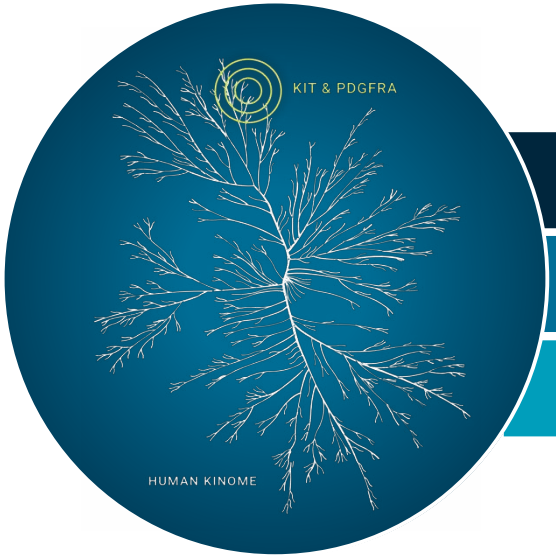
Avapritinib: a precision therapy with broad potential



LATE CLINICAL DEVELOPMENT	U.S. REGULATORY SUBMISSION STATUS
PDGFRA exon 18 mutant GIST	APPROVED[1]
Advanced SM	Q4 2020*
Indolent and smoldering SM	

AVAPRITINIB

POTENT AND HIGHLY SELECTIVE KIT AND PDGFRA INHIBITOR

Anticipate EMA CHMP opinion on avapritinib MAA for PDGFRA D842V GIST in Q3 2020

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. CHMP; EMA Committee for Medicinal Products for Human Use.

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Strong early AYVAKIT execution establishes a foundation for anticipated launches in RET-altered cancers and systemic mastocytosis

With transformative therapies and superior service,
we aim to be recognized as the leader in precision medicine
by hematology/oncology centers of excellence

STRATEGIC IMPERATIVES	ACHIEVEMENTS THROUGH Q1 2020
Drive positive first experiences with AYVAKIT	**>100** unique prescribers, with **~40%** in community setting
Deliver best-in-class patient support	**~80%** of prescriptions processed through YourBlueprint™ **>90%** of commercial and Medicare lives covered at or better than label
Catalyze patient identification	Precision medicine team actively engaged at national and regional levels to drive patient identification across portfolio

$3.5M in net sales achieved in first partial quarter of launch (Q1 2020)

Full prescribing information is available at www.AYVAKIT.com.

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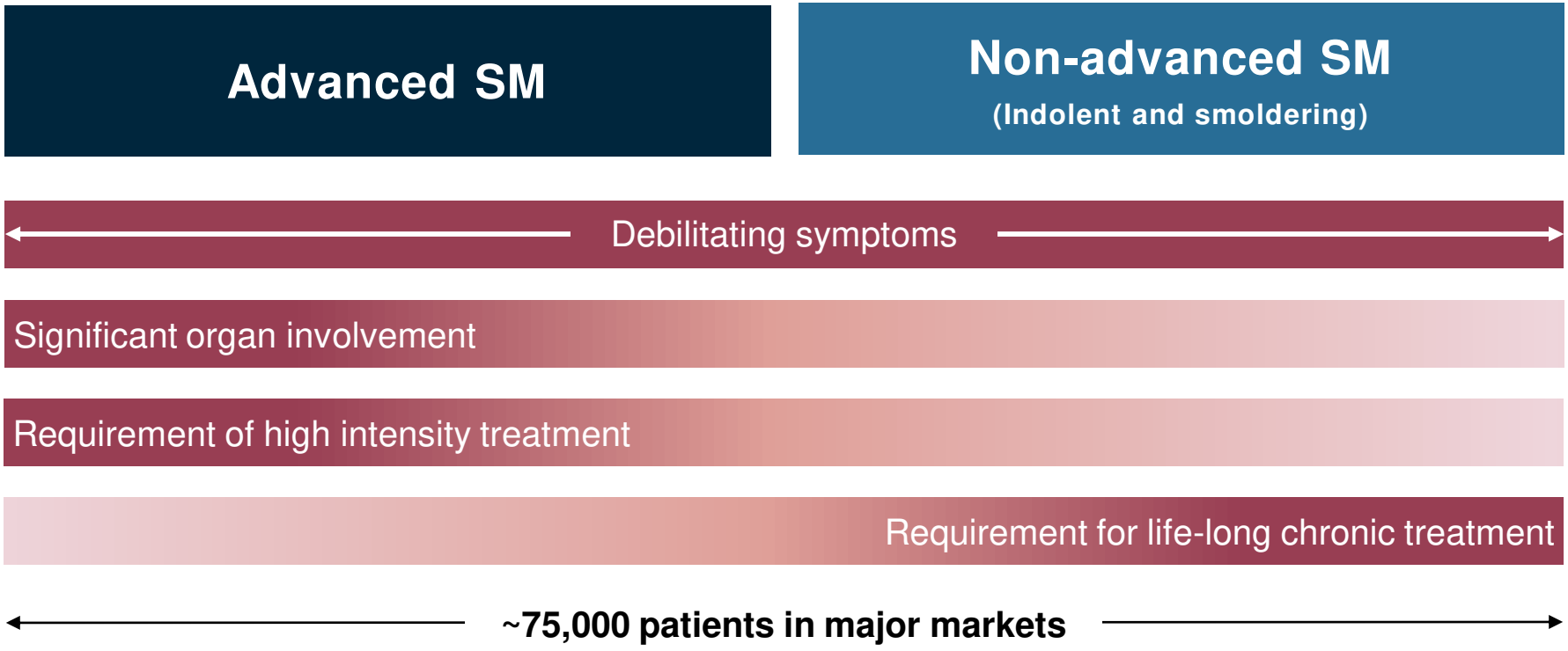
Systemic mastocytosis is one disease driven by KIT D816V



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

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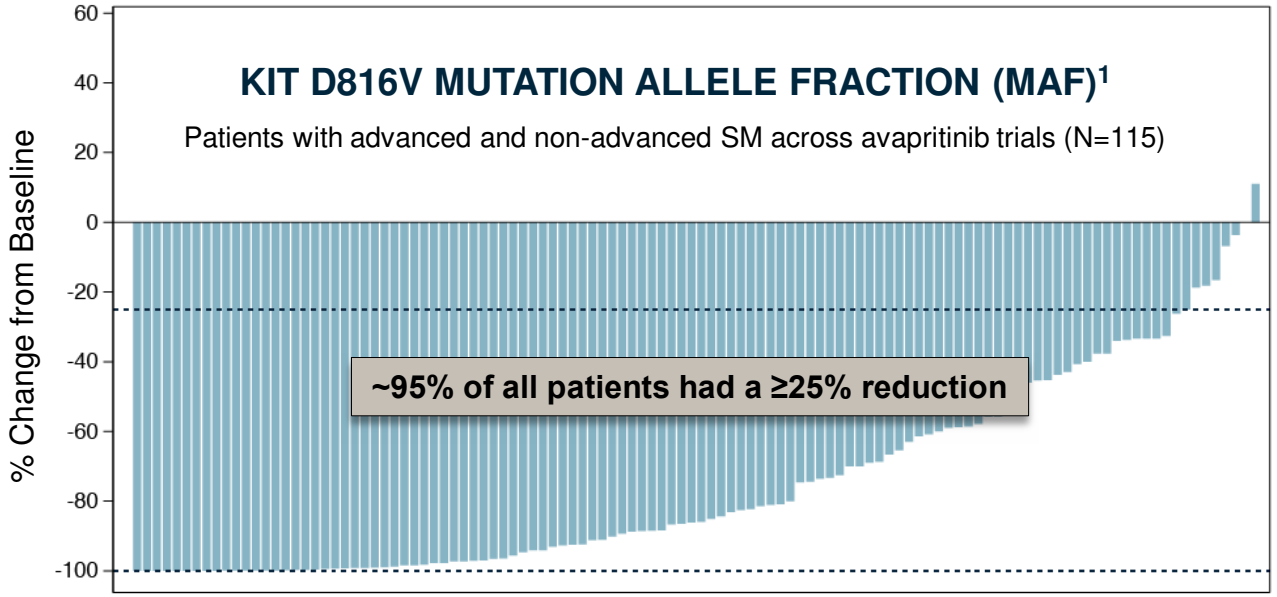
Avapritinib is the only highly potent inhibitor of KIT D816V, the common disease driver across systemic mastocytosis



≥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. MAF, mutant allele fraction.

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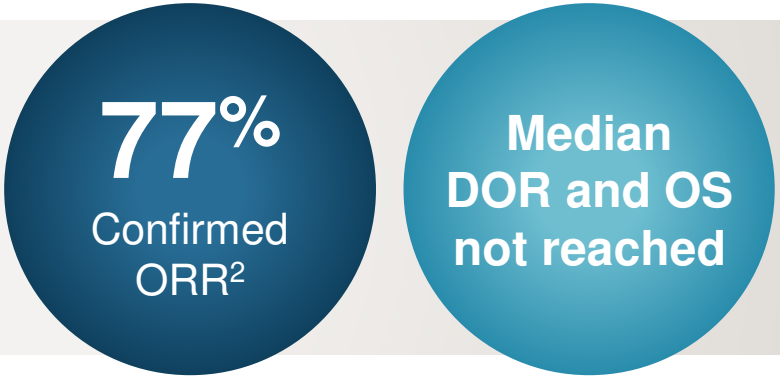
EXPLORER trial results: Remarkable response rate and prolonged duration of response in patients with advanced SM

- 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.

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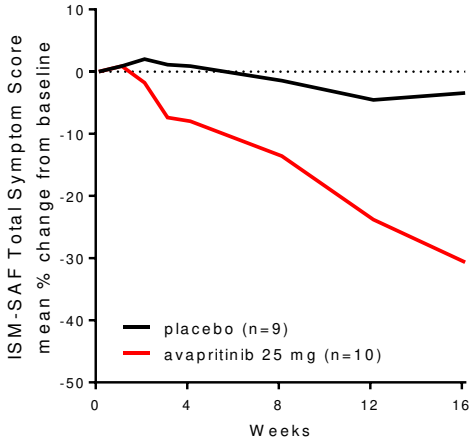
PIONEER trial results: unparalleled clinical profile in patients with indolent SM

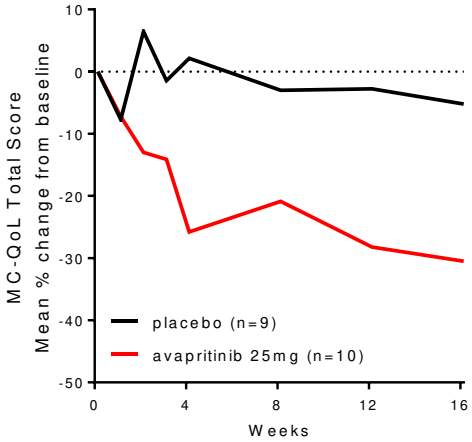
Improves disease symptoms

ISM-SAF total symptom score



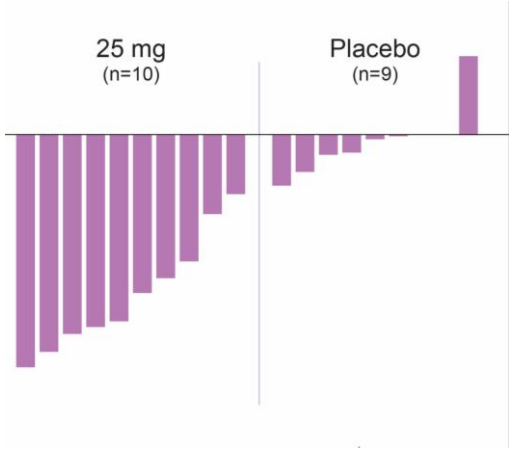
Improves quality of life

MC-QoL total score



Reduces mast cell burden

KIT D816V mutant allele fraction



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. ISM-SAF, indolent systemic mastocytosis – symptom assessment form; MC-QoL, Mastocytosis Quality of Life Questionnaire; QD, once daily.

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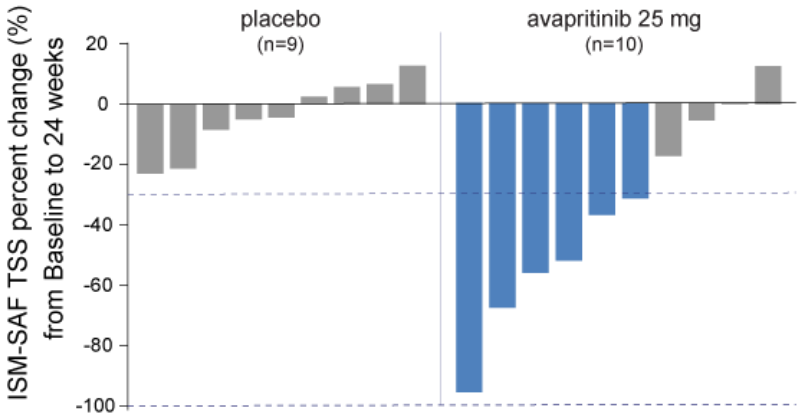
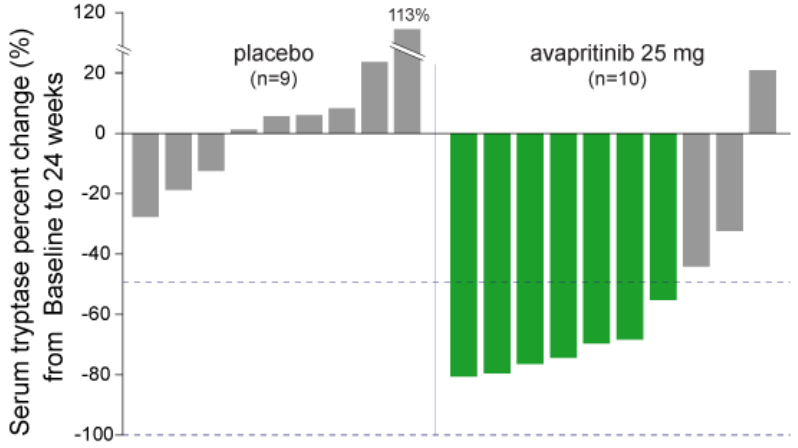
Avapritinib 25 mg QD reduces symptoms and mast cell burden in indolent SM

Part 2 primary endpoint
≥30% reduction in ISM-SAF Total Symptom Score at 24 weeks



Part 2 first key secondary endpoint
≥50% tryptase reduction at 24 weeks*



Response rate: **0%** **60%** **0%** **70%**

Presented at EAACI Virtual 2020 Congress. Data cut-off: March 31, 2020. *24 weeks or last assessment before, if 24 weeks not available. EAACI, European Academy of Allergy and Clinical Immunology.

Not for promotional use.

Safety results for avapritinib 25mg QD are similar to placebo at 16 weeks[1]

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**

Follow up at 24 weeks showed no ≥grade 3 AEs or discontinuations due to AEs for avapritinib 25 mg QD[2]

1. Data presented in March 2020 at AAAAI annual meeting. Data cutoff: December 27, 2019. 2. Data cutoff: March 31, 2020.

Not for promotional use.

PIONEER Part 2 clinical trial design

PIONEER REGISTRATION-ENABLING PART 2

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

Key endpoints: Response rate defined as ≥30% reduction in ISM-SAF total symptom score (primary), measures of mast cell burden, quality of life, concomitant medications

Sample size: ~200 patients

Duration: 24 weeks

Not for promotional use.

Key anticipated corporate milestones through 2H 2020

Q3 2020

- Obtain CHMP opinion from EMA for avapritinib in PDGFRA GIST
- Report top-line EXPLORER and PATHFINDER data for avapritinib in advanced SM

Q4 2020

- Pralsetinib PDUFA action date for RET+ NSCLC NDA
- Submit avapritinib NDA to FDA for advanced SM
- Present BLU-945 preclinical data in resistant EGFR+ NSCLC