PRECISION THAT MOVES™

Staying one step ahead of disease

September 14, 2020

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), GAVRETO™ (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 additional marketing applications for avapritinib and pralsetinib and, if approved, commercializing avapritinib and pralsetinib in additional geographies or for additional indications; the potential benefits of any of the Company's current or future approved drugs or drug candidates in treating patients; the potential benefits of the Company's collaboration with Roche and Genentech for pralsetinib, including anticipated milestone payments and other financial terms of the collaboration agreement; 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 AYVAKIT, GAVRETO or future approved drugs, and launching, marketing and selling AYVAKIT, GAVRETO or future approved drugs; the delay of any current or planned clinical trials or the development of the Company's drug candidates or any 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 AYVAKIT, GAVRETO or any drug candidates it is developing; the Company' ability and plans for maintaining a commercial infrastructure, and successfully launching, marketing and selling AYVAKIT, GAVRETO or future approved drugs; the Company's ability to develop and commercialize companion diagnostic tests for AYVAKIT, GAVRETO or any of the Company's future approved drugs or drug candidates; and the success of the Company's current and future collaborations, partnerships and licenses, including the Company's global collaboration with Roche for the development and commercialization of pralsetinib.

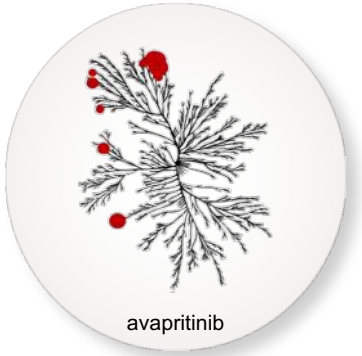
These and other risks and uncertainties are described in greater detail under "Risk Factors" in the Company's filings with the Securities and Exchange Commission ("SEC"), including its most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q, and any other 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.

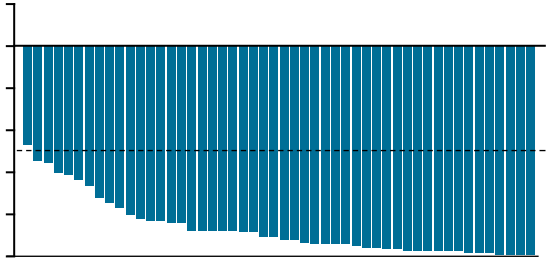
The rapid evolution of Blueprint Medicines

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

HIGHLY SELECTIVE KINASE MEDICINE DISCOVERY PLATFORM



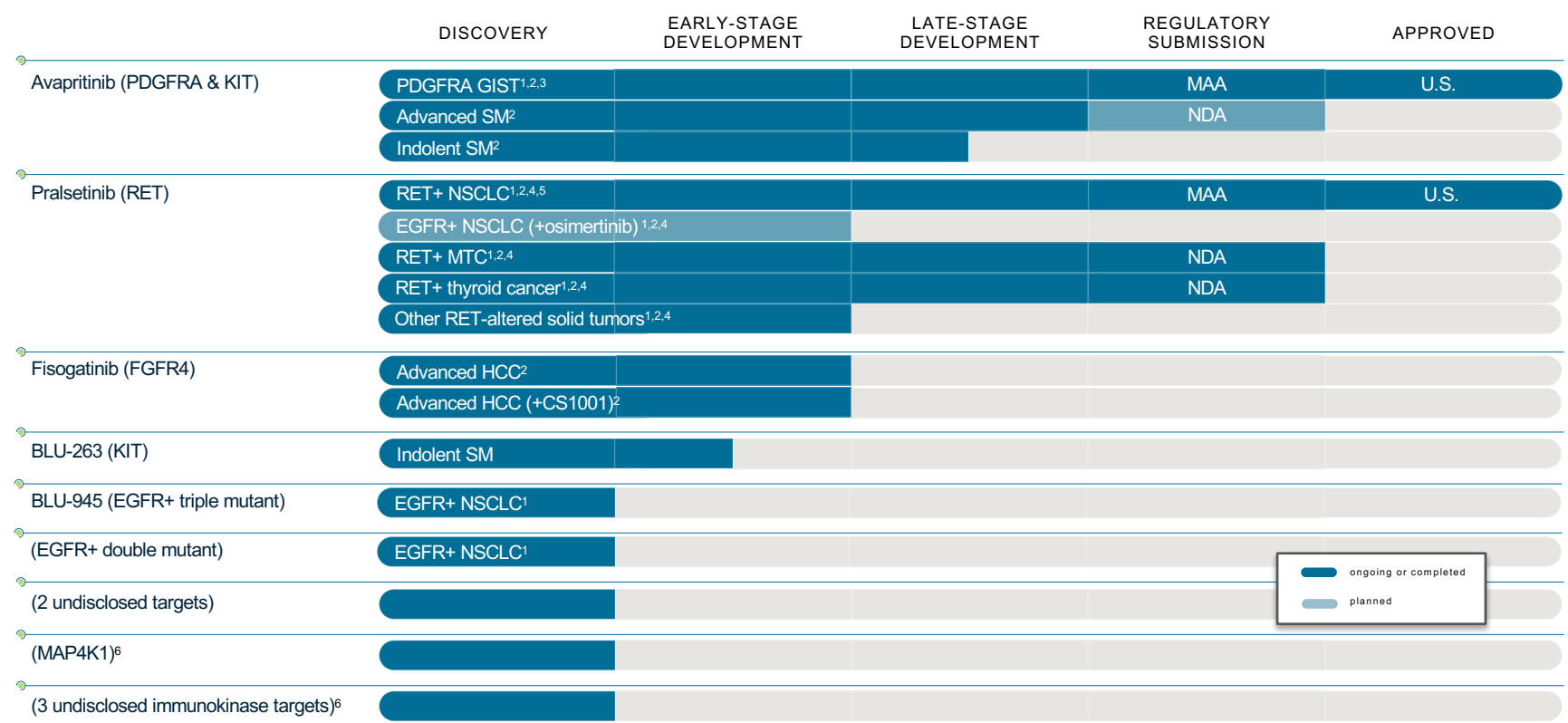
RAPID CLINICAL PROOF-OF-CONCEPT ACROSS MULTIPLE PROGRAMS



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.

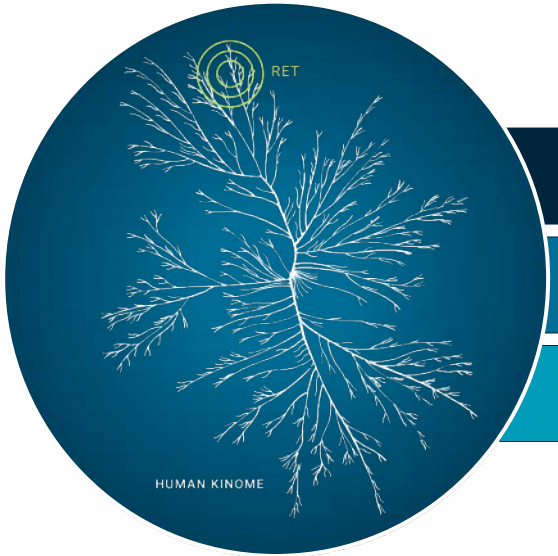


1. Unresectable or metastatic disease. 2. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan. 3. Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring 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. In July 2020, received a positive opinion from the European Medicines Agency's Committee for Medicinal Products for Human Use. 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. Received accelerated approval in the U.S. for the treatment of adults with metastatic RET fusion-positive NSCLC. Continued approval may be contingent on a confirmatory trial. 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 September 4, 2020.

blueprint™ MEDICINES

Pralsetinib: a precision therapy for RET-altered cancers



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

PRALSETINIB

POTENT AND HIGHLY SELECTIVE RET INHIBITOR

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.

Now approved in the United States

GAVRETO is indicated for the treatment of adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test.

Only RET-targeted therapy to offer the convenience of once-daily treatment with a single commercial strength

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. FDA, U.S. Food and Drug Administration; RET, rearranged during transfection.

Not for promotional use.

GAVRETO: a precision therapy that can transform NSCLC patients' lives

GAVRETO™
pralsetinib | 100mg capsules

- Selective and potent mechanism of action inhibiting RET fusions and mutations
- Deep and durable responses regardless of patient baseline characteristics
- Predictable and manageable safety profile that is familiar to oncologists
- Once-daily dosing format that optimizes adherence and ease of dose modification

Accelerated approval of GAVRETO based on Phase 1/2 ARROW trial in patients with RET fusion+ NSCLC

EFFICACY PARAMETER	TREATMENT NAÏVE (N=27)	PRIOR PLATINUM (N=87)
Overall response rate (95% CI)	70% (50%, 86%)	57% (46%, 68%)
Complete response	11%	5.7%
Partial response	59%	52%
Duration of response	n=19	N=50
Median in months (range)	9 (6.3, NE)	NE (15.2, NE)
Patients with DOR ≥ 6-mo (%)	58%	80%

Full prescribing information is available at www.GAVRETO.com. CI, confidence interval; DOR, duration of response; NE, not evaluable.

Not for promotional use.

Safety highlights from GAVRETO prescribing information

MOST COMMON ADVERSE REACTIONS (≥25%; ANY GRADE):[1]

- Fatigue, constipation, musculoskeletal pain and hypertension

MOST COMMON LABORATORY ABNORMALITIES (≥2%; GRADE 3-4):[1]

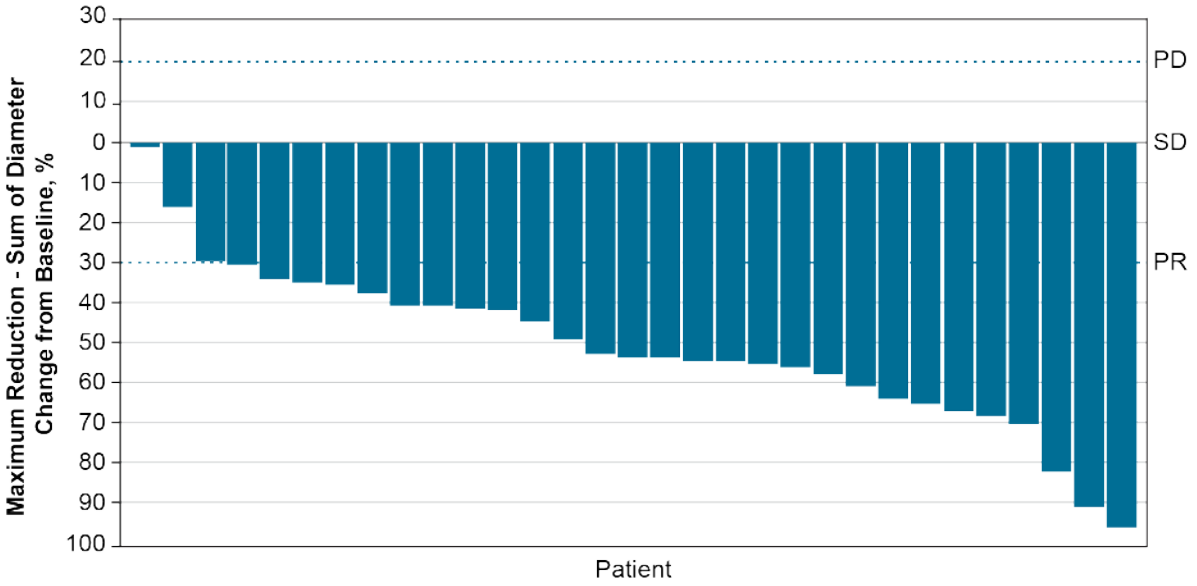
- Decreased lymphocytes, decreased neutrophils, decreased phosphate, decreased hemoglobin, decreased sodium, decreased calcium (corrected) and increased alanine aminotransferase (ALT)

WARNINGS AND PRECAUTIONS:

- Interstitial Lung Disease (ILD)/Pneumonitis
- Hypertension
- Hepatotoxicity
- Hemorrhagic Events
- Risk of Impaired Wound Healing
- Embryo-Fetal Toxicity

High response rates in treatment-naïve NSCLC populations consistent with real-world patients

TUMOR SHRINKAGE PER INVESTIGATOR ASSESSMENTS



OVERALL RESPONSE RATE

TREATMENT-NAÏVE PATIENTS

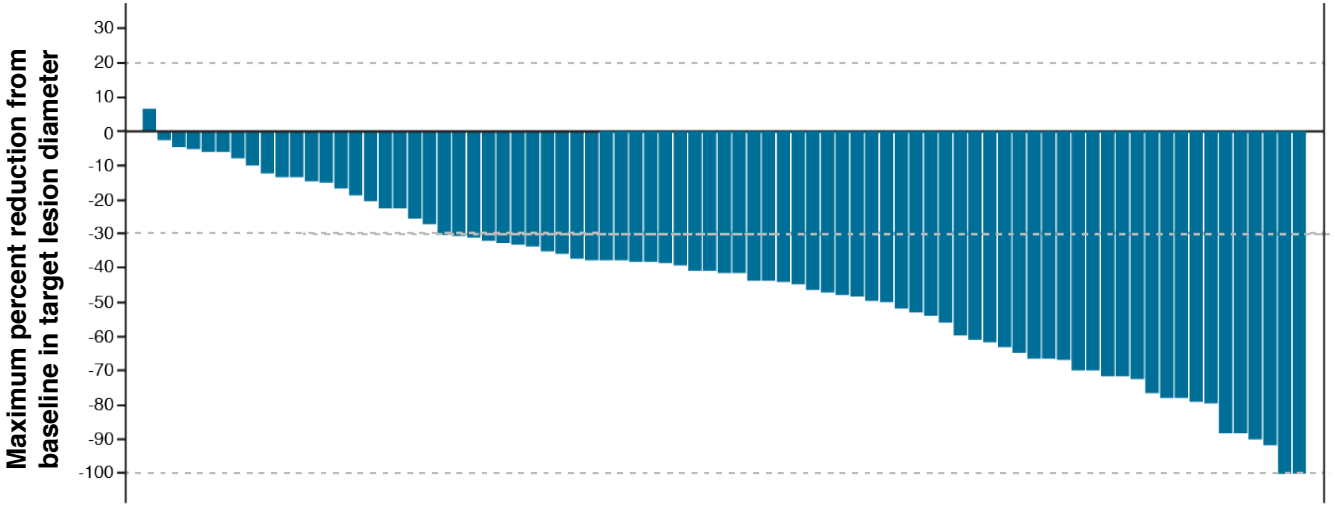
88% **Eligible for standard therapy (n=32)**

Target population for actively enrolling AcceleRET Lung Phase 3 trial in treatment-naïve NSCLC

Patients evaluable for response and enrolled after July 11, 2019. Data cut off: April 24, 2020. Data presented in May 2020 at ASCO 2020 virtual annual meeting.
PD, progressive disease; PR, partial response; SD, stable disease.

Robust clinical activity in MTC patients regardless of prior therapy

TUMOR SHRINKAGE PER CENTRAL RADIOLOGY



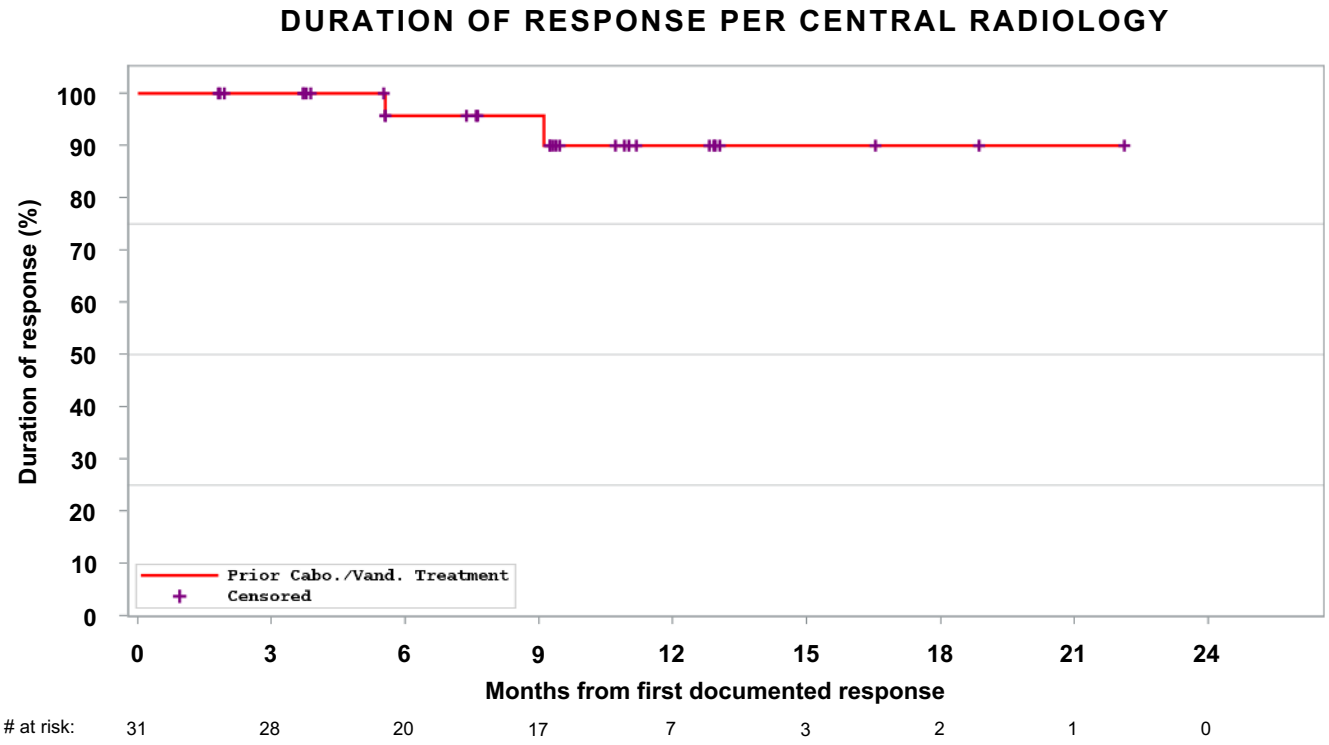
OVERALL RESPONSE RATE

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.

Prolonged duration of response in patients with previously treated MTC



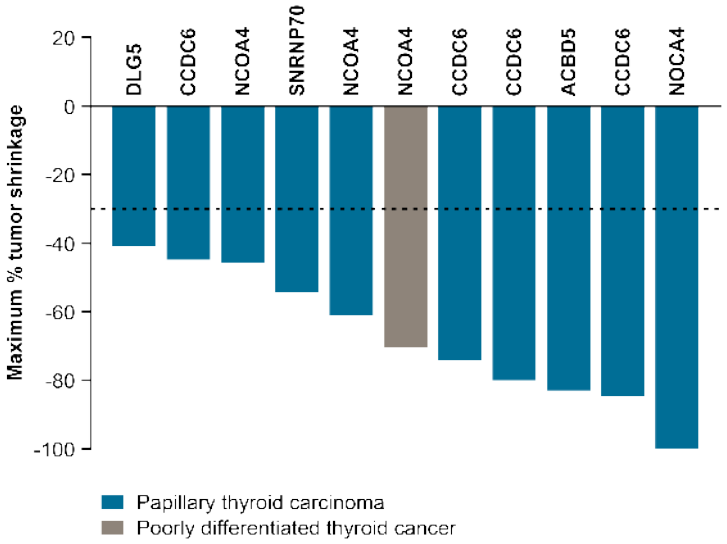
NR
(95% CI: NE-NE)
Median DOR

96%
6-month DOR

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

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

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 • Roche granted exclusive 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 Blueprint Medicines 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.

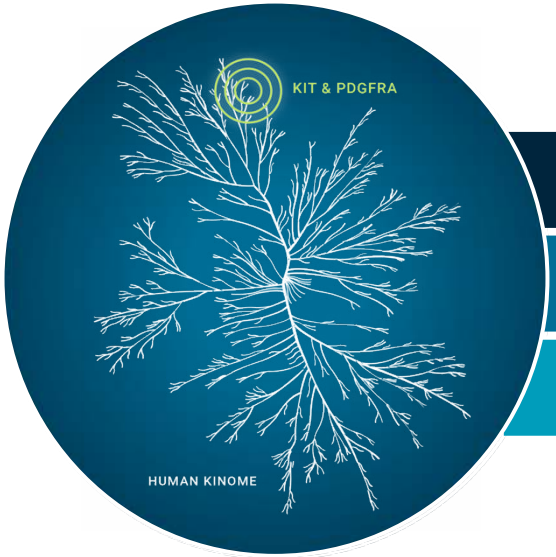
Summary of financial terms

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

UPFRONT	$775M, with $675M in cash and $100M equity investment at $96.57 per share
MILESTONES	Up to $927M in contingent payments, with approximately $90M in potential near-term milestones[2]
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. Blueprint Medicines will receive $40.0 million in specified regulatory and commercialization milestones under the Roche collaboration as a result of FDA approval of GAVRETO (pralsetinib).

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 European Commission decision on avapritinib MAA for PDGFRA D842V GIST by end of September

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 supplemental 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.

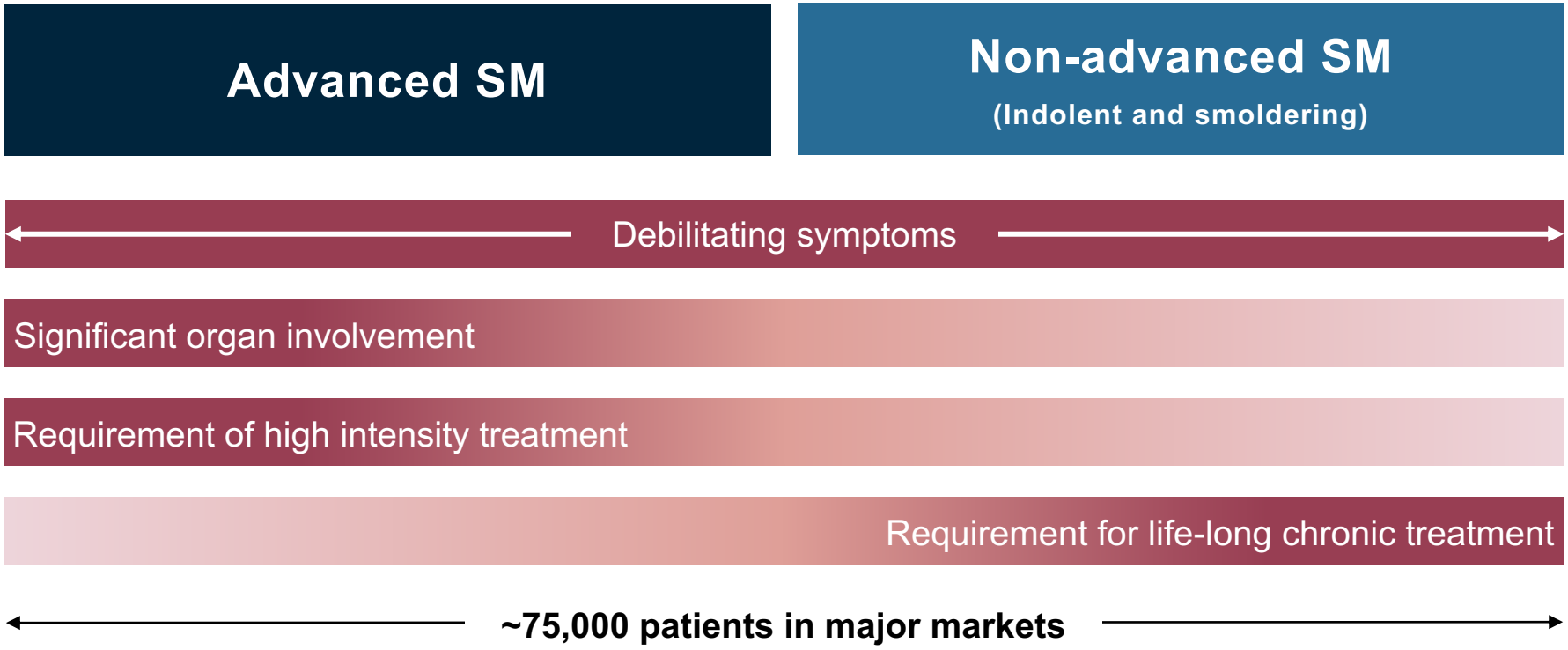
AYVAKIT launch has established a strong foundation for Blueprint Medicines' commercial execution

AYVAKIT™
avapritinib | tablets

- ✓ Establish Blueprint Medicines with key centers of excellence
- ✓ Drive broad access to therapy quickly
- ✓ Support patients to start and stay on therapy
- ✓ Strong field engagement to identify new prescribers and drive patient demand

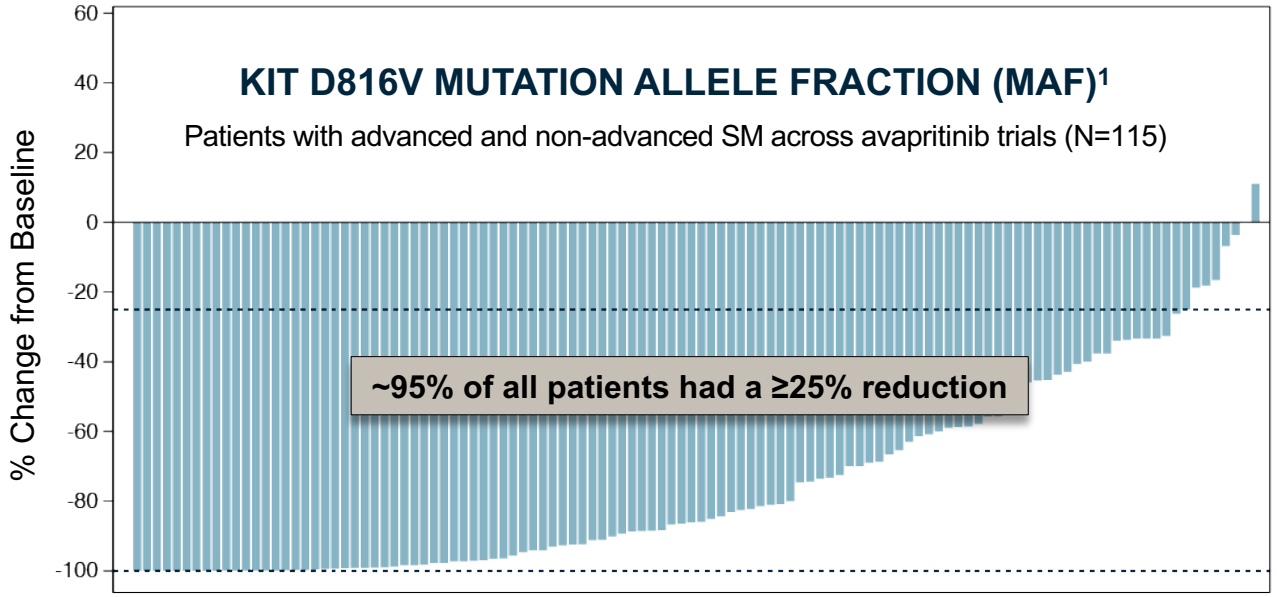
$5.7M in Q2 2020 sales ($9.1M since launch)

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



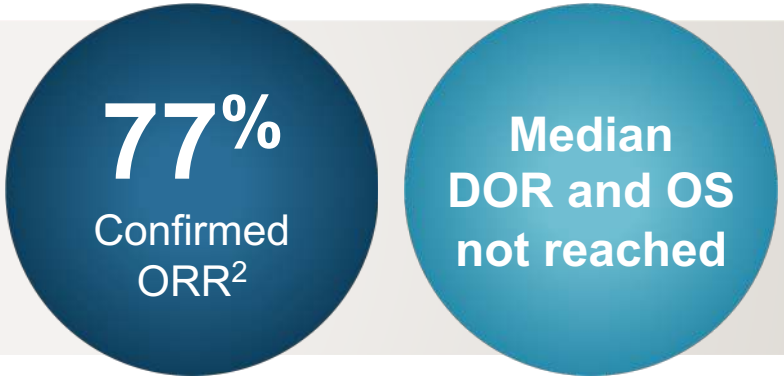
≥25% reduction in KIT D816V MAF is correlated with improved overall survival in advanced SM[2]

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. MAF, mutant allele fraction.

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

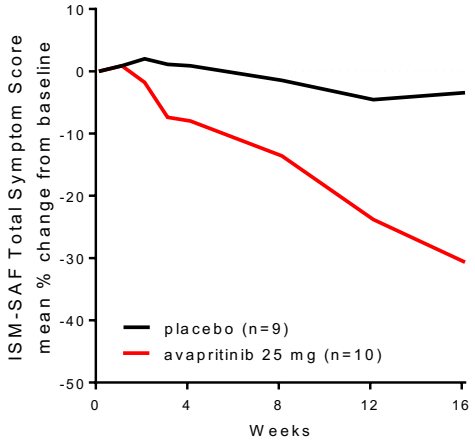
Top-line data for avapritinib from EXPLORER and PATHFINDER expected in Q3 2020

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.

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

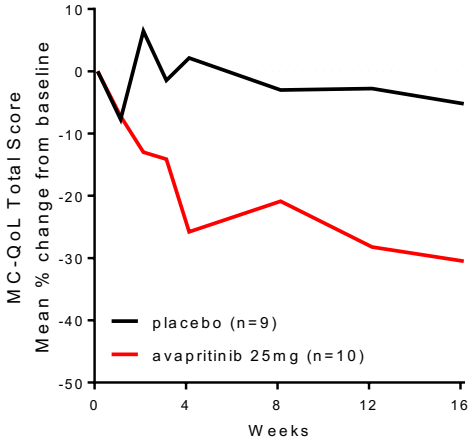
Improves disease symptoms

ISM-SAF total symptom score



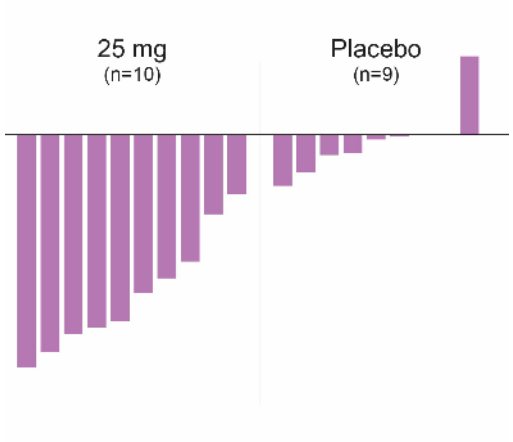
Improves quality of life

MC-QoL total score



Reduces mast cell burden

KIT D816V mutant allele fraction

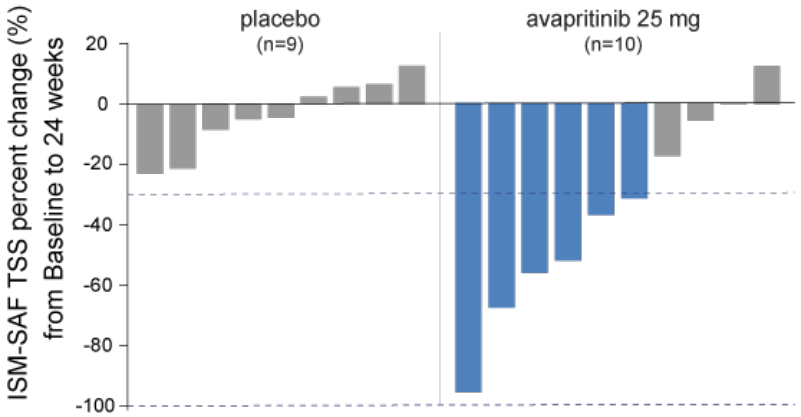


Favorable safety profile supports the selection of avapritinib 25 mg QD as recommended Part 2 dose

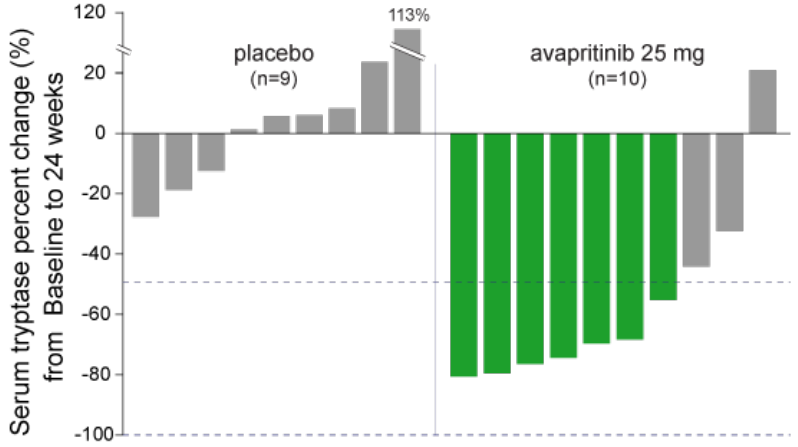
Data reported at AAAAI Annual Meeting in March 2020. Data cutoff: December 27, 2019. ISM-SAF, indolent systemic mastocytosis – symptom assessment form; MC-QoL, Mastocytosis Quality of Life Questionnaire; QD, once daily.

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 in June 2020. Data cutoff: March 31, 2020. *24 weeks or last assessment before, if 24 weeks not available. EAACI, European Academy of Allergy and Clinical Immunology.

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.

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

Second quarter 2020 financial results

Statement of Operations (unaudited)	Three Months Ended 6/30/2020	Three Months Ended 6/30/2019
Total revenue	$8.3M	$5.1M
Collaboration revenue	$2.6M	$5.1M
AYVAKIT net sales	$5.7M	--
Cost of sales	$0.1M	--
Research & development expense[1]	$91.1M	$87.1M
Selling, general & administrative expense[2]	$42.2M	$21.9M
Net loss	$(123.5)M	$(99.7)M

Balance Sheet (unaudited)	6/30/2020	12/31/2019
Cash, cash equivalents and investments	$650.3M[3]	$548.0M

Received $775M in payments under Roche collaboration in Q3 2020

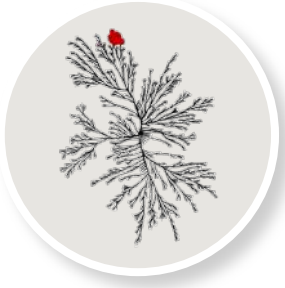
1. Includes stock-based compensation expense of $8.7M in 2020 and $7.5M in 2019. 2. Includes stock-based compensation expense of $10.8M in 2020 and $6.2M in 2019. 3. Does not include $775.0M in upfront payments received under the Roche collaboration for pralsetinib in Q3 2020 or $40.0 million in specified regulatory and commercialization milestones that Blueprint Medicines will receive under the Roche collaboration as a result of FDA approval of GAVRETO (pralsetinib).

Significant progress across portfolio sets up key 2H 2020 milestones

AYVAKIT™ avapritinib | tablets

GAVRETO™ pralsetinib | 100mg capsules

R.S., living with SM



BUILD ON COMMERCIAL MOMENTUM

- ✓Launch GAVRETO for metastatic RET+ NSCLC in the U.S.
- Obtain marketing authorization for avapritinib for PDGFRA D842V mutant GIST in the EU in Q3 2020

ADVANCE REGISTRATION PROGRAMS FOR SM

- ✓Initiate registration-enabling Part 2 of PIONEER trial of avapritinib in ISM
- Report top-line data for avapritinib in advSM in Q3 2020
- Submit supplemental NDA to FDA for avapritinib for advSM in Q4 2020

STRENGTHEN PIPELINE WITH NEW PROGRAMS

- Present preclinical data for BLU-945 at ESMO 2020 Congress

blueprint MEDICINES

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