

PRECISION THAT MOVES™

Staying one step ahead of disease

February 25, 2021



© 2021 Blueprint Medicines Corporation

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 2021 goals and anticipated milestones for Blueprint Medicines Corporation (the "Company"); plans, strategies, timelines and expectations for the Company's current or future approved drugs and drug candidates, including timelines for marketing applications and approvals, commercialization activities, the initiation of clinical trials, or results of ongoing and planned clinical trials; the potential benefits of any of the Company's current or future approved drugs or drug candidates in treating patients; 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 Company's ability and plans in establishing a commercial infrastructure, and successfully launching, marketing and selling current or future approved products; the Company's ability to successfully expand the approved indications for AYWAKIT™/AYVAKYT® (avapritinib) and GAVRETO™ (pralsetinib) or obtain marketing approval for AYWAKIT/AYVAKYT in additional geographies in the future; 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 AYWAKIT/AYVAKYT, GAVRETO or any drug candidates it is developing; 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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2011

Hopeful foundation

A new precision
therapy platform

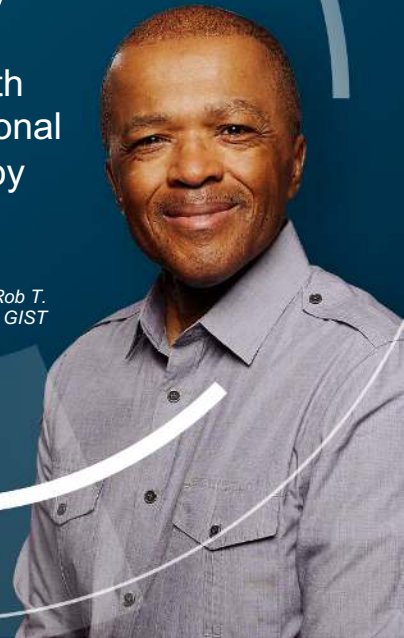


2021

Hopeful reality

~2,600 patients treated with
an approved or investigational
Blueprint Medicines therapy

Rob T.
Living with GIST



2020: a transformational year for Blueprint Medicines

Build commercial momentum

- ✓ AYVAKIT™ / AYVAKYT® (avapritinib) approved for PDGFRA-driven GIST in the U.S. and Europe¹
- ✓ GAVRETO™ (pralsetinib) approved for RET-altered NSCLC and thyroid cancers, including MTC, in the U.S.²
- ✓ Initiated transformational global collaboration with Roche to develop and commercialize GAVRETO

Advance registration program for SM

- ✓ Submitted sNDA to FDA for AYVAKIT for the treatment of advanced systemic mastocytosis (SM)
- ✓ Initiated global enrollment of registration-enabling Part 2 of PIONEER trial of AYVAKIT in non-advanced SM
- ✓ Received FDA breakthrough therapy designation for AYVAKIT for moderate to severe indolent SM

Strengthen pipeline with new programs

- ✓ Nominated four new development candidates since Q4 2019
 - BLU-263, a next-generation KIT inhibitor, for non-advanced SM and other KIT-driven disorders
 - BLU-945, a triple-mutant EGFR inhibitor, for treatment-resistant EGFR-driven NSCLC
 - BLU-701, a double-mutant EGFR inhibitor, for treatment-resistant EGFR-driven NSCLC
 - MAP4K1 inhibitor, under our cancer immunotherapy collaboration with Roche

~\$1.5B IN CASH, CASH EQUIVALENTS AND MARKETABLE SECURITIES AT END OF 2020

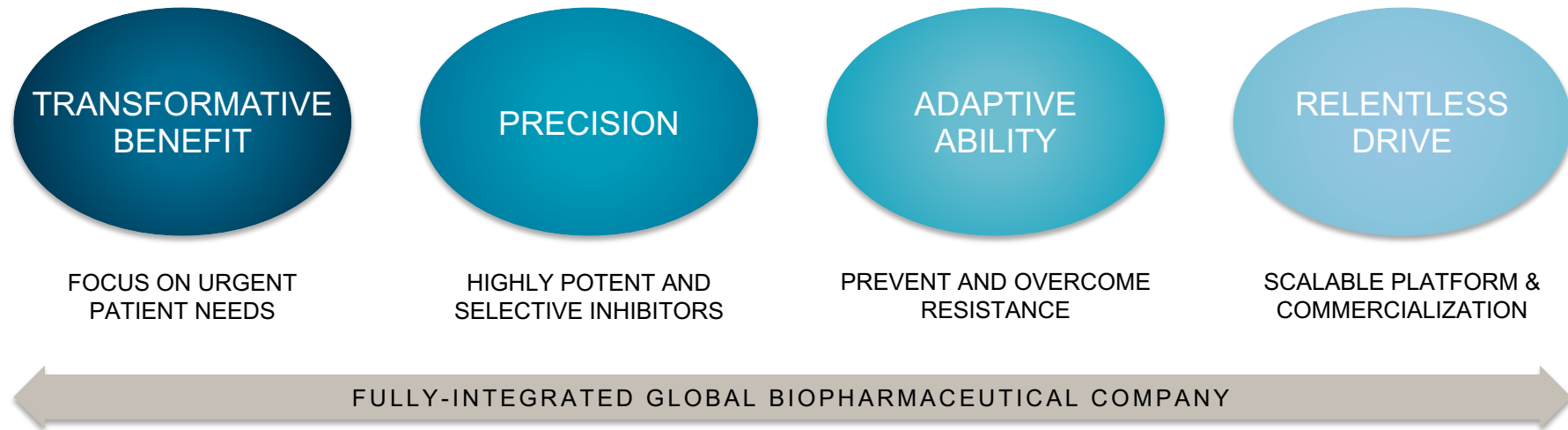


1. AYVAKIT is approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. AYVAKYT is approved in Europe for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA D842V mutation. 2. GAVRETO is approved in the U.S. for adults with metastatic RET fusion-positive NSCLC, adult and pediatric patients with advanced or metastatic RET-mutant MTC who require systemic therapy, and adult and pediatric patients with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory. Continued approval may be contingent on confirmatory trials. FDA, U.S. Food and Drug Administration; GIST, gastrointestinal stromal tumor; MTC, medullary thyroid cancer; NSCLC, non-small cell lung cancer; sNDA, supplemental new drug application.

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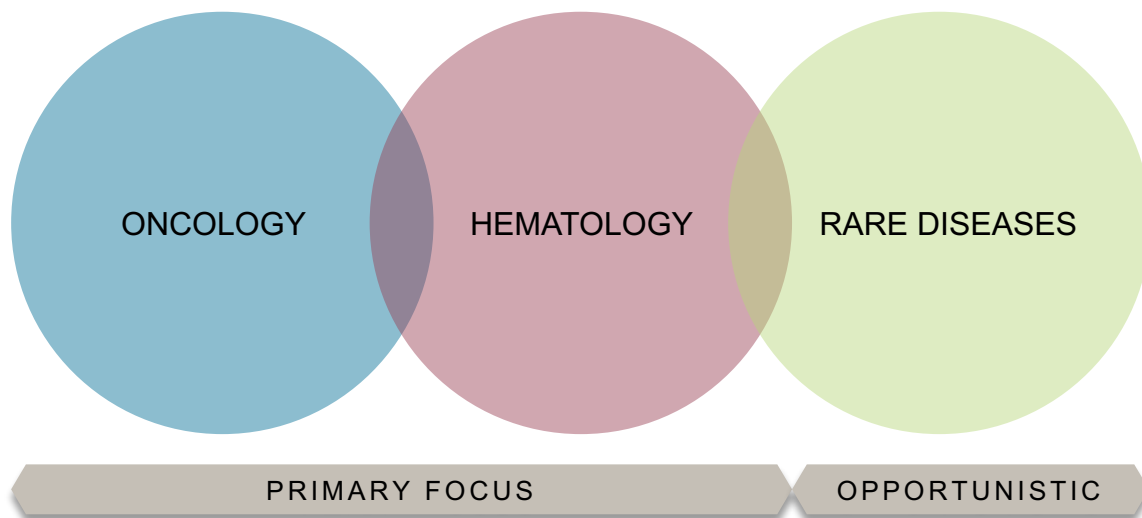
Blueprint Medicines' core mission and foundational principles

We aim to make real the promise of precision therapy to improve and extend life for as many people with cancer and hematologic disorders as possible



A leader in precision oncology and hematology

PORTFOLIO AREAS OF FOCUS



THERAPEUTIC AREA LEADERSHIP

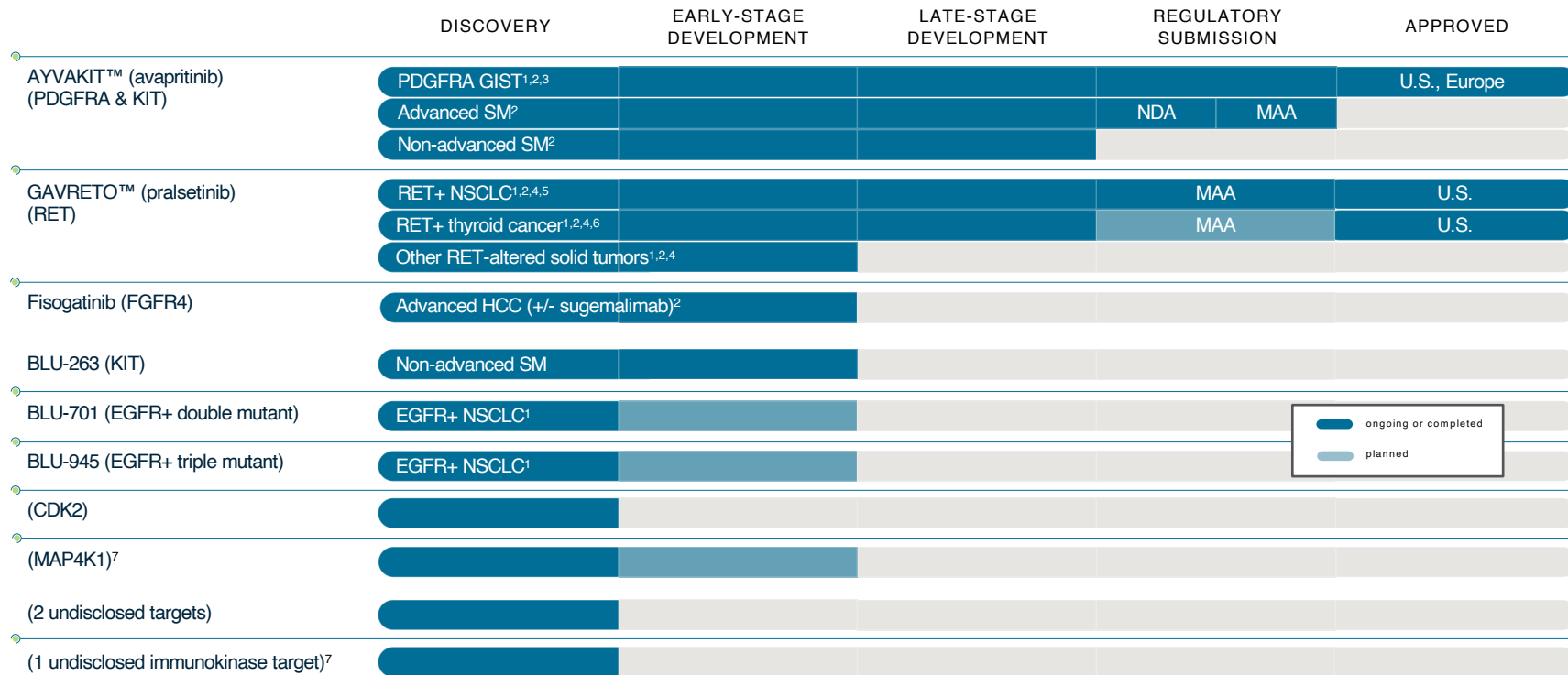


SYSTEMIC MASTOCYTOSIS



LUNG CANCER

Following 4 regulatory approvals in 2020, we now aim to advance our next wave of transformative precision therapies toward clinical proof-of-concept



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. Received conditional marketing authorization in Europe under the brand name AYVAKYT® for the treatment of adults with unresectable or metastatic GIST harboring the 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. 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. Received accelerated approval in the U.S. for the treatment of patients with advanced or metastatic RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer. Continued approval may be contingent on confirmatory trials. 7. In collaboration with Roche. For one of the programs, Blueprint Medicines has U.S. commercial rights and Roche has ex-U.S. commercialization rights. For one of the programs, Roche has worldwide commercialization rights. GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; MAA, marketing authorization application; NDA, new drug application; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

2021 roadmap for precision medicine leadership



**Accelerate global adoption
of AYVAKIT and GAVRETO**



**Advance a new wave of
therapeutic candidates toward
clinical proof-of-concept**



**Further expand the company's
precision therapy pipeline**

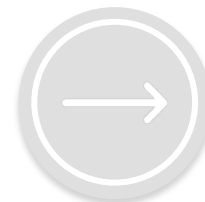
2021 roadmap for precision medicine leadership



Accelerate global adoption of AYVAKIT and GAVRETO



Advance a new wave of therapeutic candidates toward clinical proof-of-concept



Further expand the company's precision therapy pipeline

Two precision therapies approved in 2020 that are poised for growth



- Approved for unresectable or metastatic PDGFRA GIST



- Approved for advanced or metastatic RET-altered NSCLC, MTC and other thyroid cancers¹

KEY PRIORITIES AND AREAS OF GROWTH

- Prepare for anticipated launch in advanced SM in mid-2021
 - sNDA accepted by FDA; PDUFA date June 16, 2021
 - MAA submitted to EMA in Q1 2021
- Potential launch in non-advanced SM in 2022
 - Registrational PIONEER trial enrolling
- FDA breakthrough therapy designations granted for advanced SM and moderate to severe indolent SM

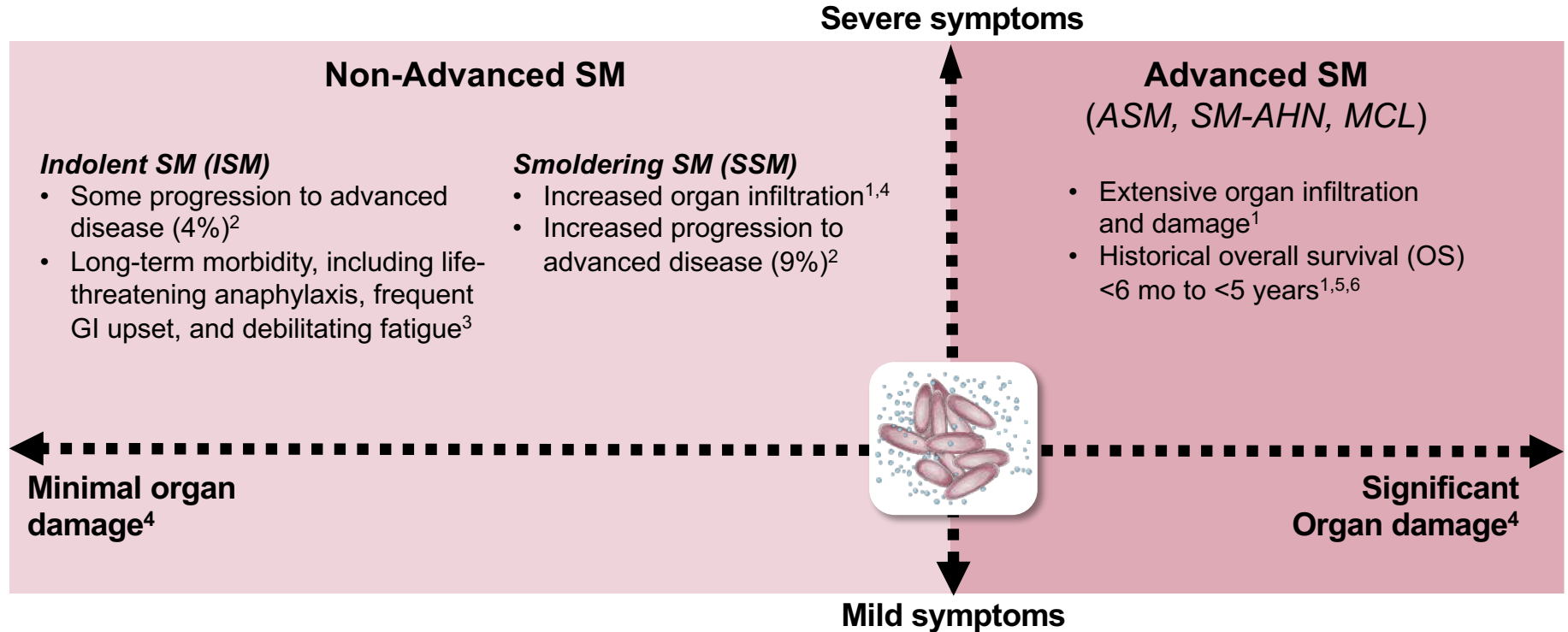
KEY PRIORITIES AND AREAS OF GROWTH

- Continue to advance ongoing U.S. launch, with focus on share of new patient starts and volume of identified patients
- MAA for RET fusion+ NSCLC under review by EMA
- Plan to submit marketing applications across multiple additional global geographies
- Plan to develop in additional treatment settings



1. In collaboration with Roche. Blueprint Medicines and Roche have co-exclusive rights to develop and commercialize GAVRETO in the U.S., and Roche has exclusive rights to develop and commercialize pralsetinib outside the U.S., excluding Greater China.

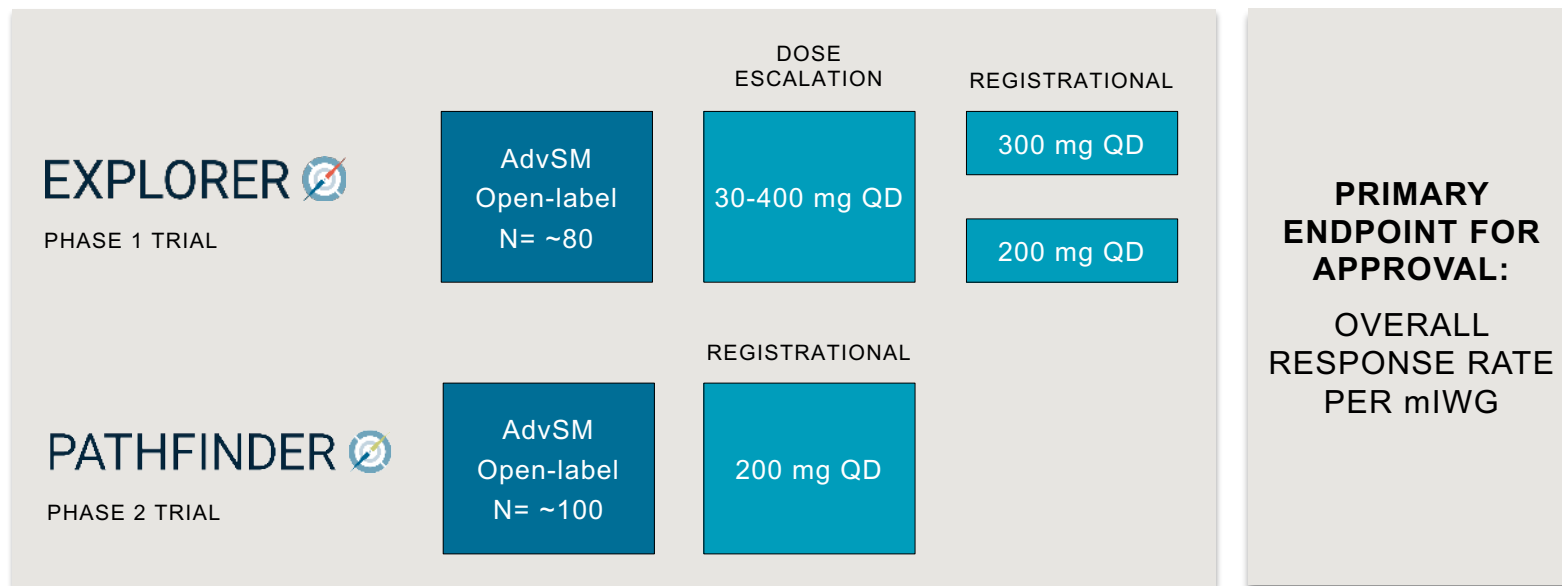
Systemic mastocytosis is driven by KIT D816V



Significant initial target patient population with additional growth potential



AYVAKIT registration program in advanced systemic mastocytosis



Consistently high ORRs and prolonged duration of response across trials

EXPLORER 

PATHFINDER 

200 MG QD
POOLED GROUP

ORR (CR+CRh+PR+CI)	75.5% (61.7- 86.2)	75.0 (56.6 – 88.5)
CR+CRh	35.8%	18.8%
mDOR (months)	38.3 (21.7 - NE)	NE (NE - NE)
mOS (months)	NE (46.9 - NE)	NE



68.2%
18.2%

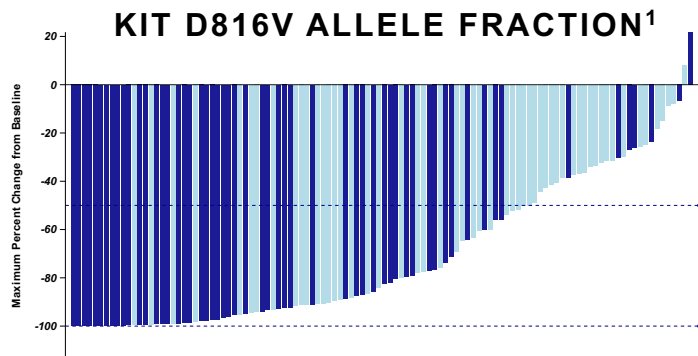
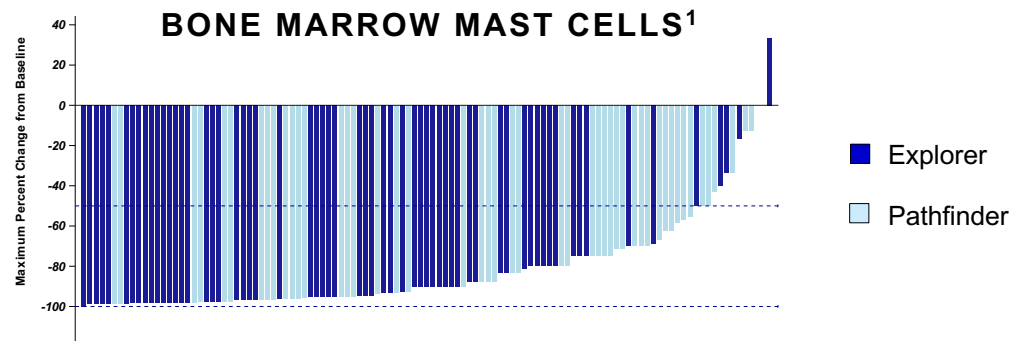
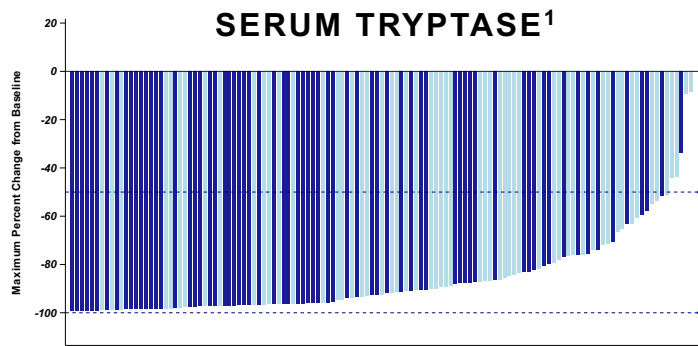
Median follow up:
10.4 months

Median follow up:
27.3 months

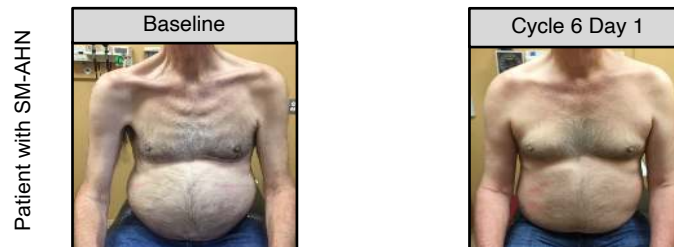
Median follow up:
10.4 months

PATHFINDER INTERIM ANALYSIS WAS POSITIVE (P-VALUE=0.000000016)

Deep reductions in mast cell burden and resolution of organ damage



RESOLUTION OF ORGAN DAMAGE (C-FINDINGS)²



- Weight loss of >50 pounds
- Hypoalbuminemia (2.3 mg/dL)
- Ascites with paracentesis (15 L/week)

- All weight gained back
- Albumin normalized
- Ascites resolved

AYVAKIT demonstrated improved tolerability at 200 mg QD

Treatment Emergent AEs ≥ 20%, All Grades*	200 mg n=81 (%)	All doses N=148 (%)
Peripheral Edema	39 (48.1)	65 (43.9)
Periorbital Edema	32 (39.5)	81 (54.7)
Thrombocytopenia	28 (34.6)	55 (37.2)
Anemia	26 (32.1)	65 (43.9)
Diarrhea	23 (28.4)	53 (35.8)
Nausea	20 (24.7)	49 (33.1)
Fatigue	15 (18.5)	44 (29.7)
Vomiting	15 (18.5)	42 (28.4)

* Most common AEs in patients treated at 200mg in EXPLORER and PATHFINDER

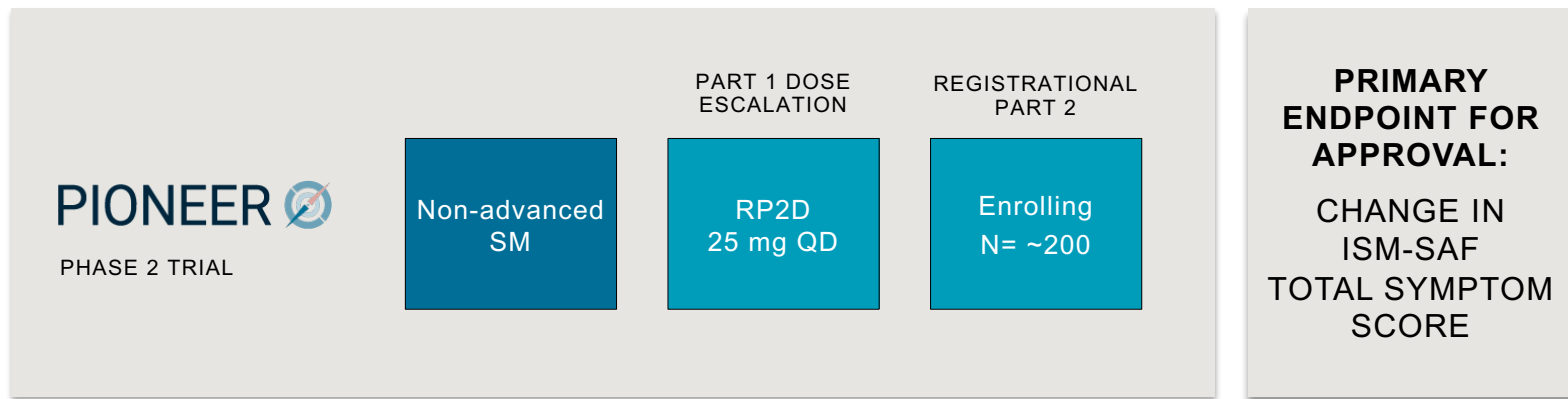
Cognitive effects	10 (12.3)	37 (25.0)
≥Grade 2	2 (2.5)	13 (8.8)

- Overall, 8.1% of patients discontinued treatment due to treatment-related AEs
- ICB risk mitigations implemented
 - Starting dose of 200 mg QD
 - Exclusion criteria for pre-existing severe thrombocytopenia
 - Increased platelet monitoring
 - Mandatory dose interruption for severe thrombocytopenia
- ICB events in patients without pre-existing severe thrombocytopenia
 - Pooled 200 mg group (n=76): 2 (2.6%)[†]
 - PATHFINDER (n=57): 0[‡]

Top-line EXPLORER and PATHFINDER data presented in September 2020. Data cutoff: May 27, 2020 for EXPLORER and June 23, 2020 for PATHFINDER, with response assessments per central review completed in September 2020.

[†] Both ICB events in EXPLORER patients were Grade 1 and asymptomatic. [‡] 1 ICB event occurred in a PATHFINDER patient with pre-existing severe thrombocytopenia prior to exclusion of such patients for 1/62 (1.6%) overall. AE, adverse event; ICB, intracranial bleed.

Plan to complete enrollment of registrational Part 2 of PIONEER trial of AYVAKIT in non-advanced SM in mid-2021



PIONEER REGISTRATION-ENABLING PART 2

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

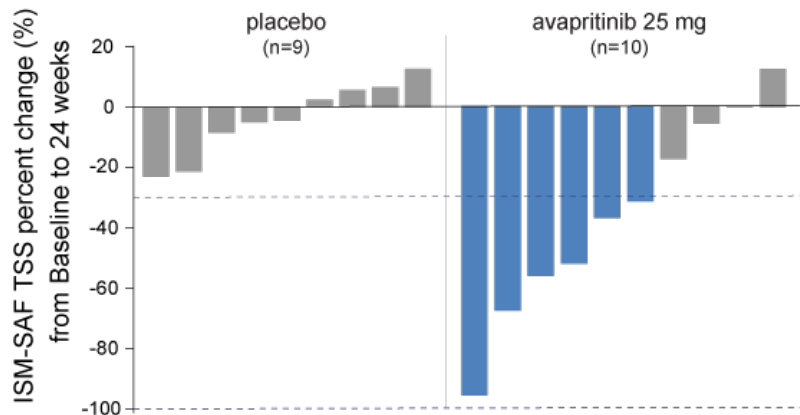
Key endpoints: Response rate defined as $\geq 30\%$ reduction in ISM-SAF total symptom score (primary), measures of mast cell burden, quality of life, concomitant medications

Duration: 24 weeks

PIONEER Part 1 data showed AYVAKIT 25 mg QD reduces symptoms and mast cell burden in non-advanced SM

Part 2 primary endpoint

≥30% reduction in ISM-SAF Total Symptom Score at 24 weeks

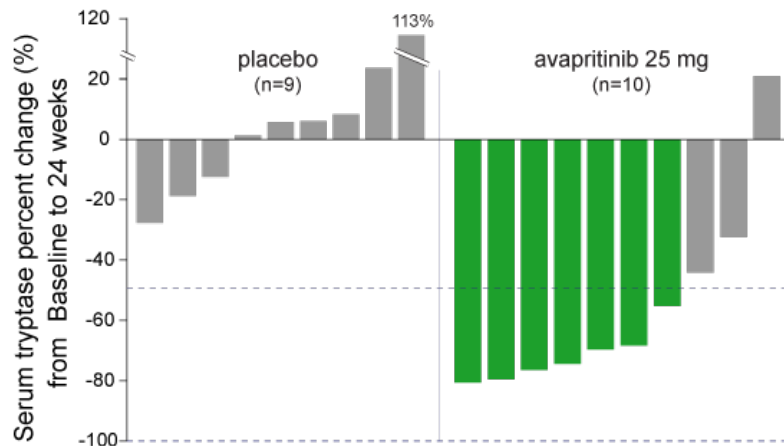


Response rate: **0%**

60%

Part 2 first key secondary endpoint

≥50% tryptase reduction at 24 weeks*



Response rate: **0%**

70%



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

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Safety results for AYVAKIT 25mg QD are similar to placebo at 16 weeks¹

Preferred term	Placebo n=9		avapritinib 25 mg n=10	
	any grade	grade 3	any grade	grade 3
% of subjects with ≥1 AE	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**

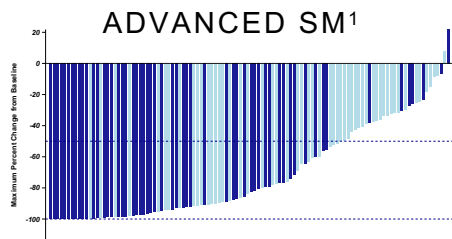
FOLLOW UP AT 24 WEEKS SHOWED NO ≥GRADE 3 AES OR DISCONTINUATIONS DUE TO AES FOR 25 MG QD²



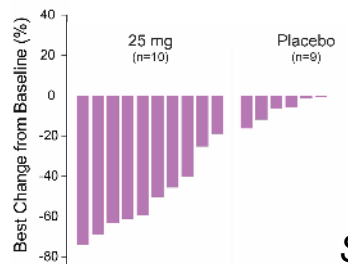
1. Data presented in March 2020 at AAAAI annual meeting. Data cutoff: December 27, 2019. 2. Data cutoff: March 31, 2020.

AYVAKIT is the only clinically validated, highly potent inhibitor of KIT D816V, the genetic driver of SM

REDUCE MAST CELL BURDEN

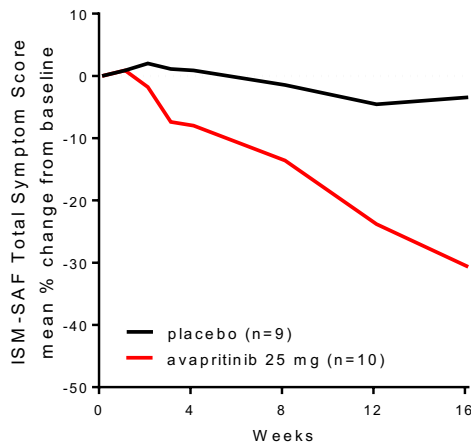


NON-ADVANCED SM²



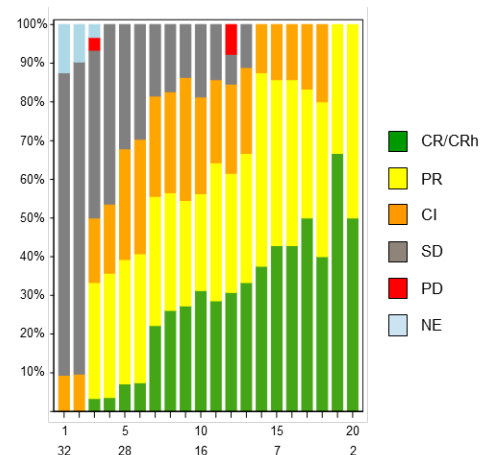
IMPROVE DISEASE SYMPTOMS

NON-ADVANCED SM²



INDUCE DEEP AND DURABLE RESPONSES

ADVANCED SM¹



Safety profile enables tailored dosing based on patient need



1. Top-line EXPLORER and PATHFINDER data presented in September 2020. Data cutoff: May 27, 2020 for EXPLORER and June 23, 2020 for PATHFINDER, with response assessments per central review completed in September 2020.

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

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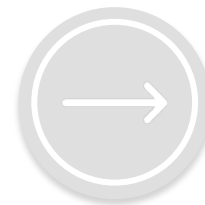
2021 roadmap for precision medicine leadership



Accelerate global adoption of AYVAKIT and GAVRETO







Advance a new wave of therapeutic candidates toward clinical proof-of-concept



Further expand the company's precision therapy pipeline

Multiple additional opportunities for transformative medicines

4 DEVELOPMENT CANDIDATES NOMINATED SINCE Q4 2019

PROGRAM (TARGET)	DESCRIPTION / STATUS
 BLU-263 (KIT D816V)	<i>Non-advanced SM and other mast cell disorders</i> <ul style="list-style-type: none">• Well-tolerated in Phase 1 healthy volunteer trial• Plan to initiate Phase 2 trial in non-advanced SM in mid-2021
 BLU-945 (triple-mutant EGFR)	<i>Treatment-resistant EGFR-driven NSCLC</i> <ul style="list-style-type: none">• Presented foundational preclinical data at ESMO 2020• Plan to initiate Phase 1 trial in 1H 2021
 BLU-701 (double-mutant EGFR)	<i>Treatment-resistant EGFR-driven NSCLC</i> <ul style="list-style-type: none">• Plan to present foundational preclinical data in 1H 2021• Plan to initiate Phase 1 trial in the second half of 2021
 (MAP4K1)	<i>Cancer immunotherapy, under collaboration with Roche</i> <ul style="list-style-type: none">• Plan to present foundational preclinical data in 1H 2021

INDUSTRY BENCHMARK

10 precision oncology IPOs in 2020

4 had no clinical assets at time of IPO

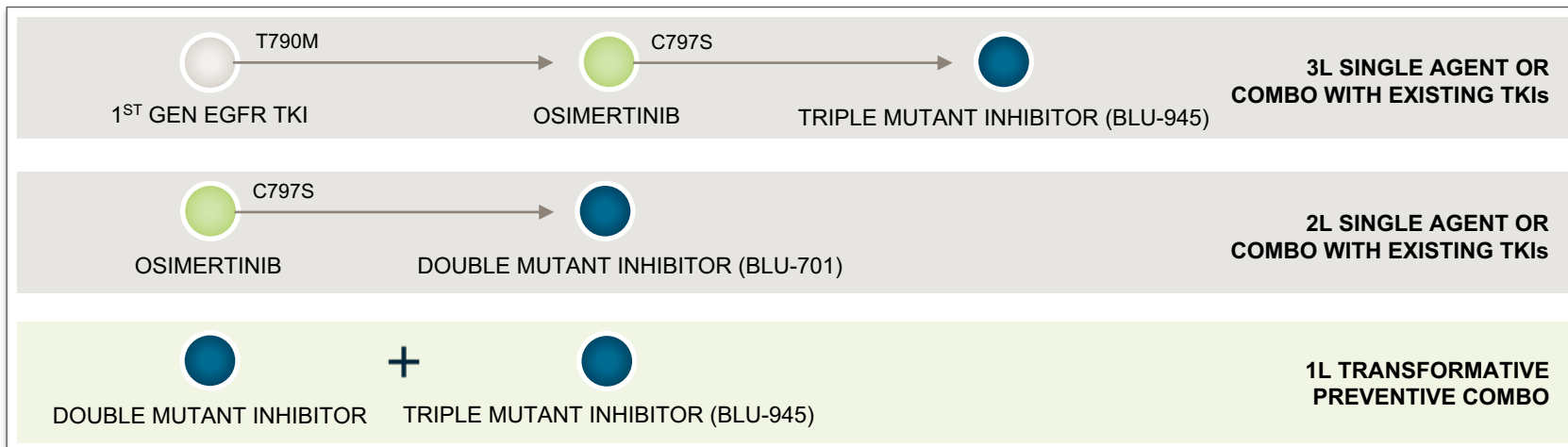
\$2.3B mean market capitalization¹

Our vision for transforming treatment of EGFR+ NSCLC



- Primary EGFR mutation frequency in NSCLC: ~10-15% in the U.S. and Europe; ~40-50% in Asia¹
- While current therapies have revolutionized care, treatment resistance is a significant, emerging medical need
- T790M and C797S are most common on-target resistance mutations to 1st generation EGFR inhibitors and osimertinib²

POTENTIAL FOR PROLONGED CLINICAL BENEFIT WITH TRANSFORMATIVE 1L PREVENTIVE COMBO



Foundational BLU-945 preclinical data presented at ESMO 2020 support initiation of clinical development in 1H 2021

SUBNANOMOLAR POTENCY

BIOCHEMICAL IC₅₀

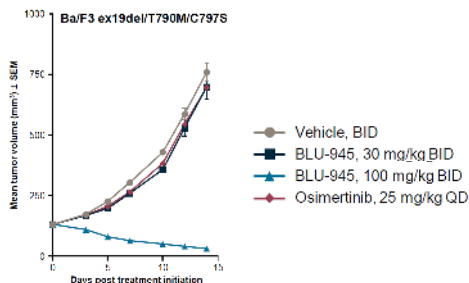
	L858R/ T790M/C797S	ex19del/ T790M/C797S
BLU-945	0.5	0.8
Gefitinib	3921.8	1219.7
Osimertinib	5461.6	649.9

EXCELLENT SELECTIVITY

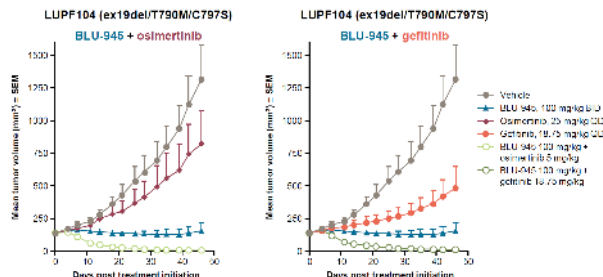
CELLULAR IC₅₀

	EGFR wild-type (A431 cell line)
BLU-945	544.4
Gefitinib	16.5
Osimertinib	115.9

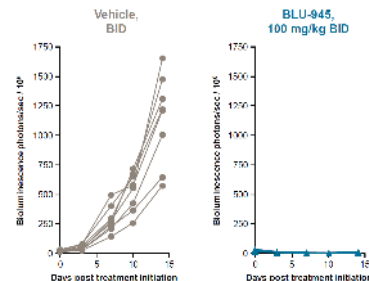
ROBUST SINGLE AGENT ACTIVITY



COMBINATION POTENTIAL



PRECLINICAL CNS ACTIVITY



2021 roadmap for precision medicine leadership



Accelerate global adoption of AYVAKIT and GAVRETO



Advance a new wave of therapeutic candidates toward clinical proof-of-concept

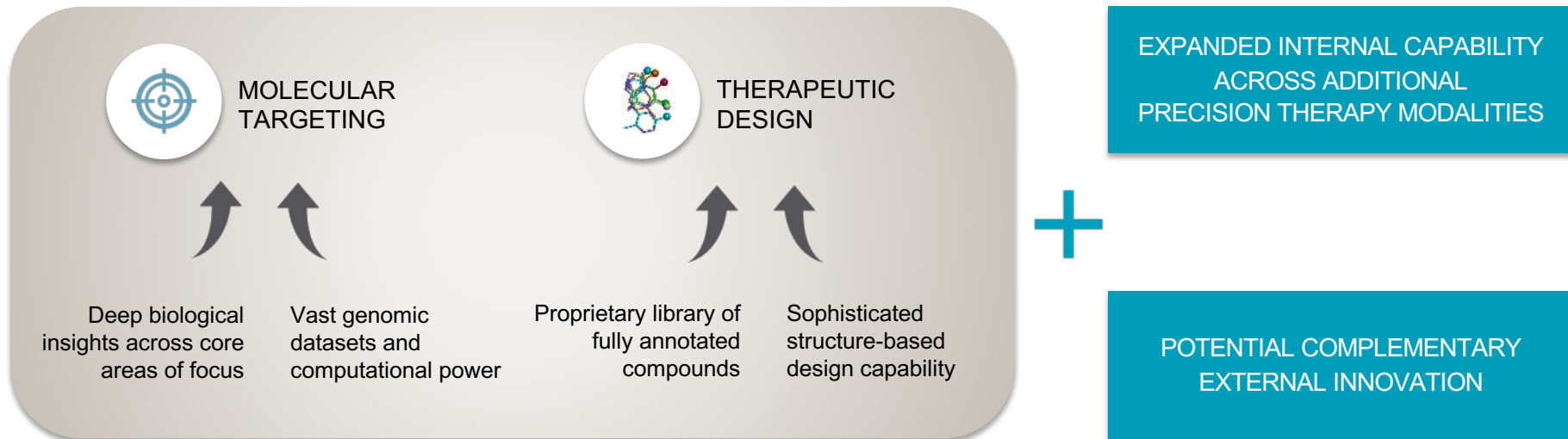


Further expand the company's precision therapy pipeline

Constant expansion of highly productive research platform

WORLD-CLASS EXPERTISE IN CATALYTIC KINASE INHIBITION

PLANNED FUTURE



PLAN TO EXPAND PIPELINE WITH ONE OR MORE DEVELOPMENT CANDIDATES

2021 roadmap for precision medicine leadership: strategies and key goals



Accelerate global adoption of
AYVAKIT and GAVRETO

- ✓ Submitted MAA to EMA for AYVAKYT for advanced SM in Q1 2021
- Obtain FDA approval AYVAKIT for advanced SM in the U.S. in 1H 2021
- Present registrational PATHINDER trial data for AYVAKIT in advanced SM in 1H 2021
- Complete enrollment of registration-enabling PIONEER trial in mid-2021
- Obtain EMA approval GAVRETO for RET fusion-positive NSCLC in 1H 2021
- Submit MAA to EMA for GAVRETO for RET-altered thyroid cancers in 2H 2021
- Initiate GAVRETO cohort in Roche's TAPISTRY tumor-agnostic platform trial in 2H 2021
- Submit multiple marketing applications for GAVRETO across multiple additional geographies



Advance a new wave of
therapeutic candidates toward
clinical proof-of-concept

- Initiate Phase 2 HARBOR trial of BLU-263 in non-advanced SM in mid-2021
- Initiate Phase 1 trial of BLU-945 in EGFR-driven NSCLC in 1H 2021
- Initiate Phase 1 trial of BLU-701 in EGFR-driven NSCLC in 2H 2021
- Present preclinical data for BLU-701 and MAP4K1 inhibitors in 1H 2021
- Present preclinical data for combo of BLU-945 and BLU-701 in 2H 2021



Further expand the company's
precision therapy pipeline

- Expand pipeline with one or more development candidates
- Pursue external opportunities to complement the company's precision therapy pipeline

Blueprint Medicines is in the strongest financial position in our history

Statement of Operations (unaudited)	Three Months Ended 12/31/2020	Three Months Ended 12/31/2019	FY Ended 12/31/2020	FY Ended 12/31/2019
Total revenue	\$34.1M	\$51.5M	\$793.7M	\$66.5M
Collaboration revenue	\$27.4M	\$51.5M	\$771.6M	\$66.5M
Net product sales	\$6.7M	--	\$22.1M	--
Cost of sales	\$0.1M	--	\$0.4M	--
Research & development expense ¹	\$77.4M	\$88.6M	\$326.9M	\$331.5M
Selling, general & admin expense ²	\$42.5M	\$32.3M	\$157.7M	\$96.4M
Net income (loss)	\$(85.7)M	\$(66.3)M	\$313.9M	\$(347.7)M

Balance Sheet (unaudited)	12/31/2020	12/31/2019
Cash, cash equivalents and investments	\$1,549.7M	\$548.0M



1. Includes stock-based compensation expense of \$8.5M and \$7.6M in the three months ended 12/31/20 and 12/31/19, respectively, and \$33.6M and \$28.6M in the FY ended 12/31/20 and 12/31/19, respectively. 2. Includes stock-based compensation expense of \$11.0M and \$8.1M in the three months ended 12/31/20 and 12/31/19, respectively, and \$41.9M and \$26.1M in the FY ended 12/31/20 and 12/31/19, respectively