

# PRECISION THAT MOVES™

Staying one step ahead of disease

JANUARY 2021 COMPANY OVERVIEW



© 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, 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.

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.



2010

## Hopeful foundation

A new precision  
therapy platform

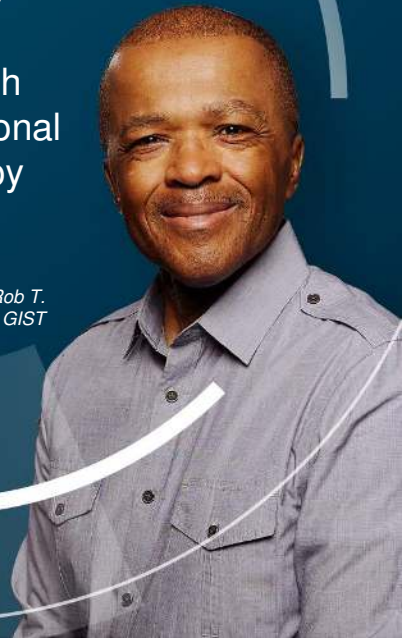


2021

## 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

- ✓ AYAVKIT™ / AYWAKYT® (avapritinib) approved for PDGFRA-driven GIST in the U.S. and Europe<sup>1</sup>
- ✓ GAVRETO™ (pralsetinib) approved for RET-altered NSCLC, MTC and other thyroid cancers in the U.S.<sup>2</sup>
- ✓ 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
  - Double-mutant EGFR inhibitor, for treatment-resistant EGFR-driven NSCLC
  - MAP4K1 inhibitor, under our cancer immunotherapy collaboration with Roche

~\$1.36B IN CASH, CASH EQUIVALENTS AND INVESTMENTS AT END OF Q3 2020



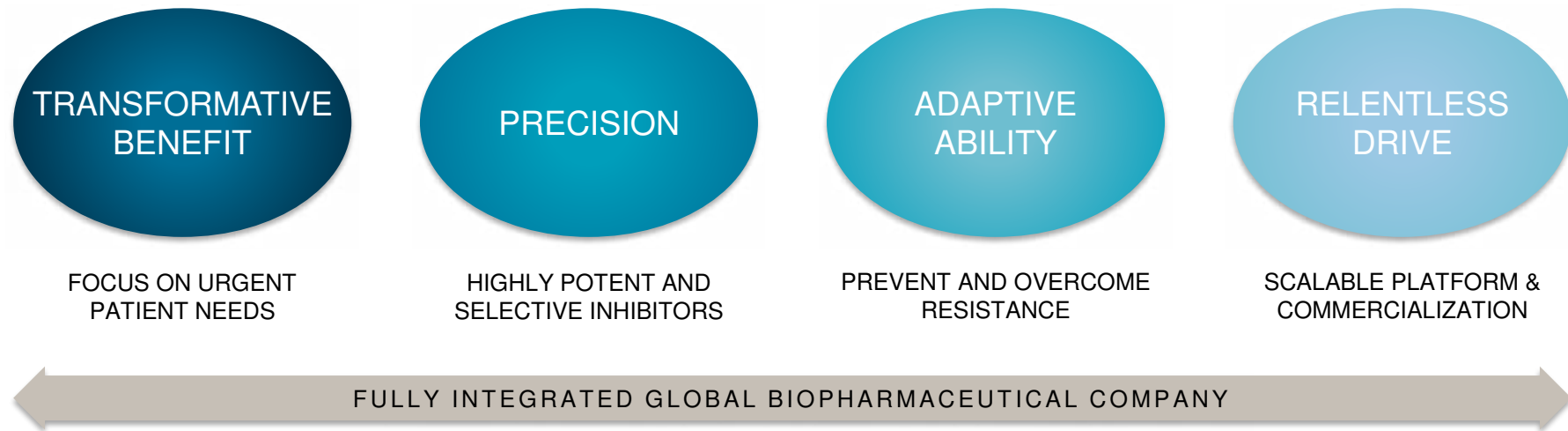
1. AYVAKIT is approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. AVAKYT is approved in Europe for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA D842V mutation. 2. 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. 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.

Not for promotional use.

# Blueprint Medicines' core mission and foundational principles

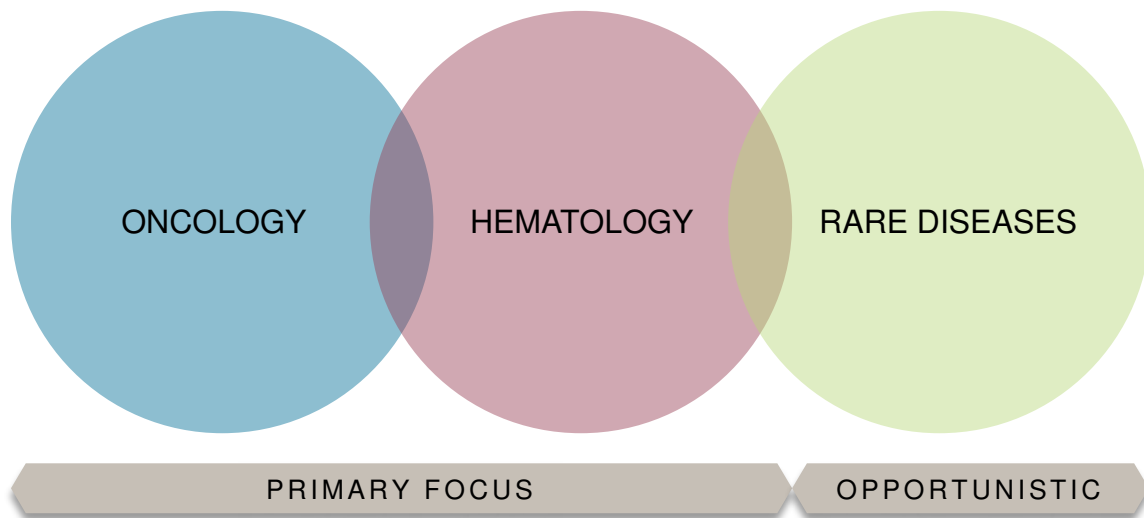
---

**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



	DISCOVERY	EARLY-STAGE DEVELOPMENT	LATE-STAGE DEVELOPMENT	REGULATORY SUBMISSION		APPROVED
AYVAKIT™ (avapritinib) (PDGFRA & KIT)	PDGFRA GIST <sup>1,2,3</sup>					U.S., Europe
	Advanced SM <sup>2</sup>			NDA	MAA	
	Non-advanced SM <sup>2</sup>					
GAVRETO™ (pralsetinib) (RET)	RET+ NSCLC <sup>1,2,4,5</sup>			MAA		U.S.
	RET+ MTC <sup>1,2,4,6</sup>			MAA		U.S.
	RET+ thyroid cancer <sup>1,2,4,6</sup>			MAA		U.S.
	Other RET-altered solid tumors <sup>1,2,4</sup>					
Fisogatinib (FGFR4)	Advanced HCC (+/- sugemalimab) <sup>2</sup>					
BLU-263 (KIT)	Non-advanced SM					
BLU-945 (EGFR+ triple mutant)	EGFR+ NSCLC <sup>1</sup>					
(EGFR+ double mutant)	EGFR+ NSCLC <sup>1</sup>					
(3 undisclosed targets)						
(MAP4K1) <sup>7</sup>						
(1 undisclosed immunokinase target) <sup>7</sup>						

 ongoing or completed  
 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. 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 AVYAKYT® 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; MTC, medullary thyroid cancer; NDA, new drug application; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.



Blueprint Medicines, AYVAKIT, AYVAKYT, GAVRETO and associated logos are trademarks of Blueprint Medicines Corporation.

Updated as of January 11, 2021

Not for promotional use.

# 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 first approved in 2020 with clear pathways for growth



- Approved for unresectable or metastatic PDGFRA exon 18 mutant GIST

## CORE VALUE OPPORTUNITY

- sNDA submitted to FDA for advanced SM in Q4 2020
- Plan to submit MAA to EMA for advanced SM in Q1 2021
- Registrational PIONEER trial in non-advanced SM enrolling
- FDA breakthrough therapy designations granted for advanced SM and moderate to severe indolent SM

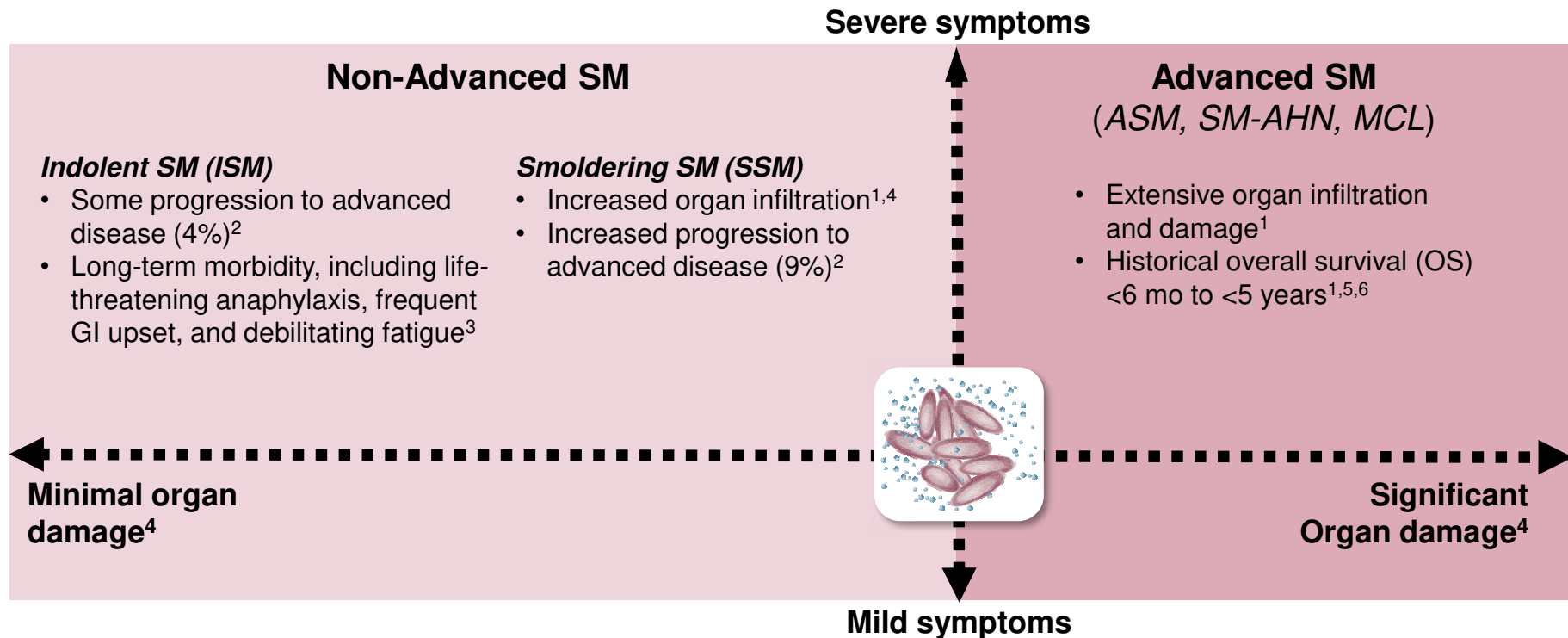


- Approved for advanced or metastatic RET-altered NSCLC, MTC and other thyroid cancers

## GROWTH OPPORTUNITY

- Transformative global collaboration with Roche
  - Ongoing co-commercialization in the U.S.
  - 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

# Systemic mastocytosis is driven by KIT D816V

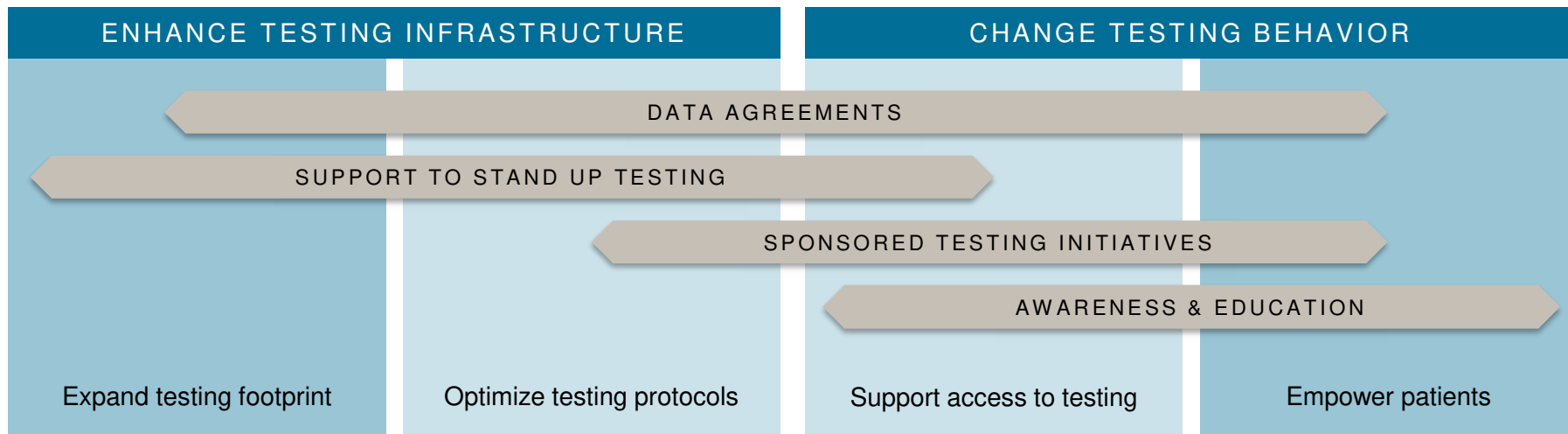


# Significant initial target patient population with additional growth potential



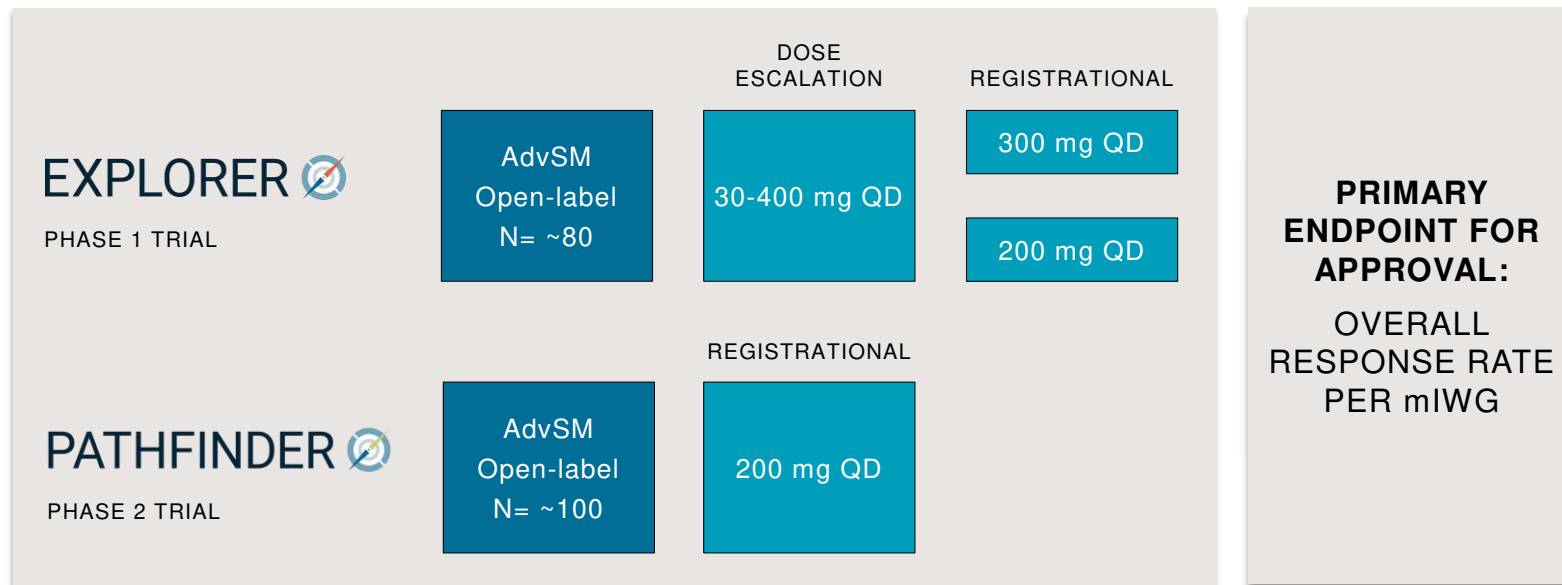
# Pursuing a range of testing initiatives to facilitate SM patient identification

DATA SHOW HIGHLY SENSITIVE DDPCR TESTING DETECTS KIT D816V IN 95% OF PATIENTS<sup>1</sup>



Anticipate highly sensitive ddPCR KIT D816V testing to be widely available in 2021  
at laboratories currently testing ~80% of SM patients in U.S.<sup>2</sup>

# AVYAKIT 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

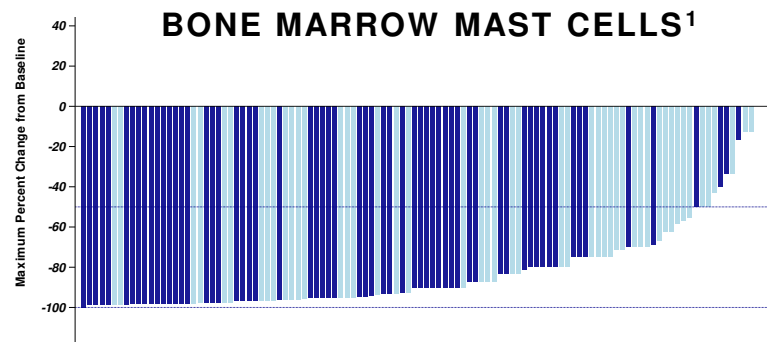
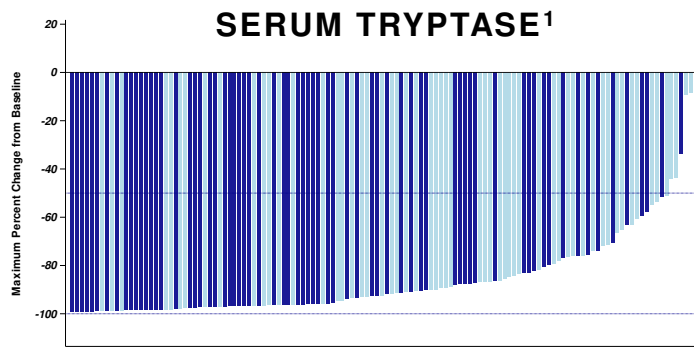
Median follow up:  
27.3 months

Median follow up:  
10.4 months

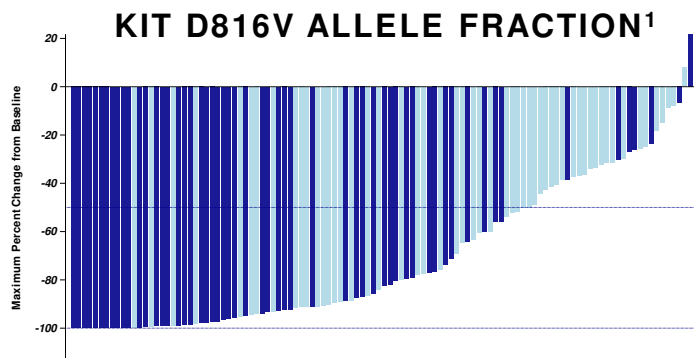
PATHFINDER INTERIM ANALYSIS WAS POSITIVE (P-VALUE=0.0000000016)



# Deep reductions in mast cell burden and resolution of organ damage



■ Explorer  
■ Pathfinder

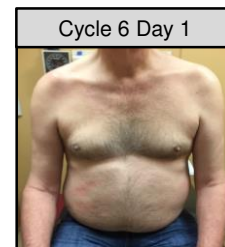


## RESOLUTION OF ORGAN DAMAGE (C-FINDINGS)<sup>2</sup>

Patient with SM-AHN



- 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

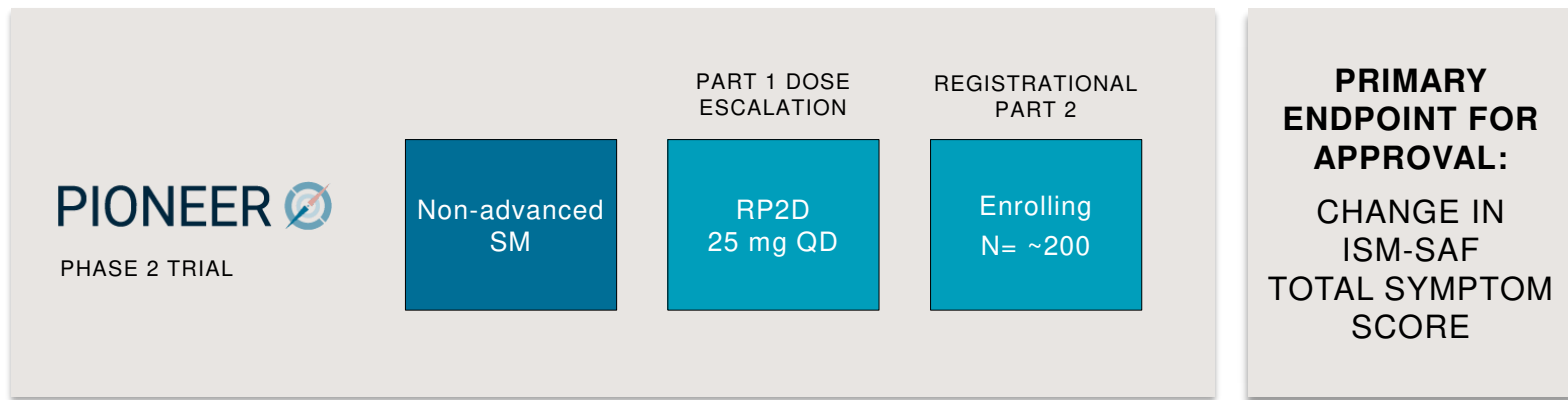
Cognitive effects	10 ( 12.3)	37 ( 25.0)
≥Grade 2	2 (2.5)	13 (8.8)

- 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%)<sup>†</sup>
  - PATHFINDER (n=57): 0<sup>‡</sup>

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.

<sup>†</sup> Both ICB events in EXPLORER patients were Grade 1 and asymptomatic. <sup>‡</sup> 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

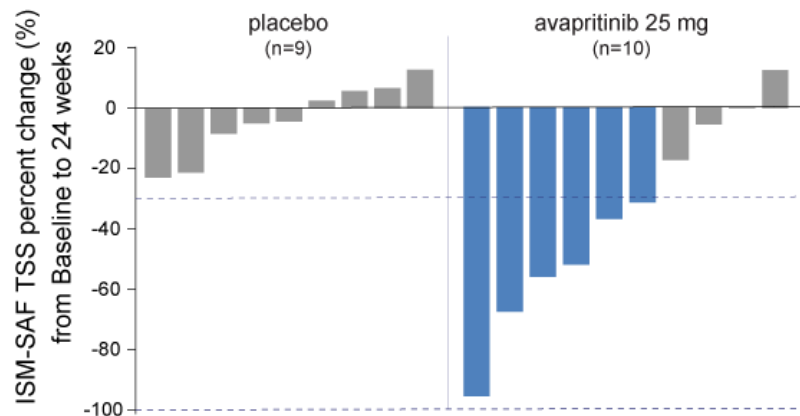
**Key endpoints:** Response rate defined as  $\geq 30\%$  reduction in ISM-SAF total symptom score (primary), measures of mast cell burden, quality of life, concomitant medications

**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

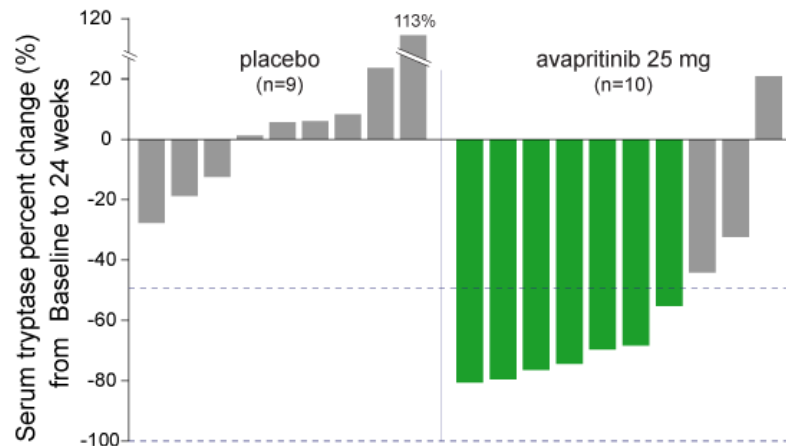


Response rate: 0%

60%

## Part 2 first key secondary endpoint

≥50% tryptase reduction at 24 weeks\*



0%

70%

# Safety results for AYVAKIT 25mg QD are similar to placebo at 16 weeks<sup>1</sup>

AE in >15% of placebo or avapritinib arms			avapritinib	
Preferred term	Placebo n=9		25 mg n=10	
% 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

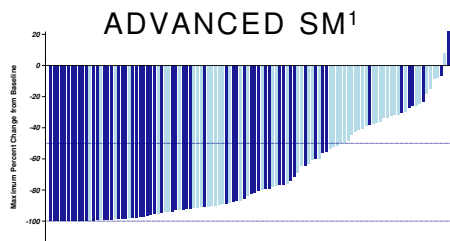
## AVAPRITINIB 25 MG QD

- **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**

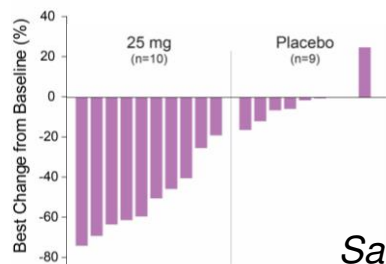
FOLLOW UP AT 24 WEEKS SHOWED NO ≥GRADE 3 AES OR DISCONTINUATIONS DUE TO AES FOR 25 MG QD<sup>2</sup>

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

## REDUCE MAST CELL BURDEN

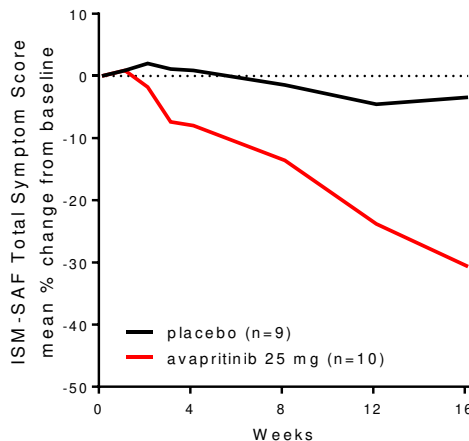


## NON-ADVANCED SM<sup>2</sup>



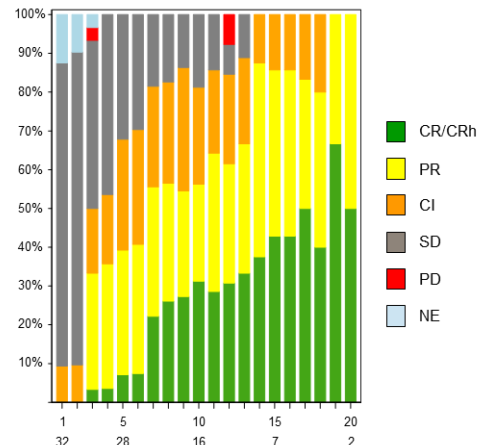
## IMPROVE DISEASE SYMPTOMS

### NON-ADVANCED SM<sup>2</sup>



## INDUCE DEEP AND DURABLE RESPONSES

### ADVANCED SM<sup>1</sup>



*Safety profile enables tailored dosing based on patient need*

# 2021 roadmap for precision medicine leadership

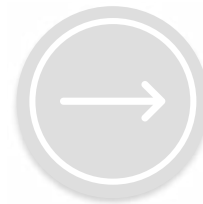
---



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"><li>• Well-tolerated in Phase 1 healthy volunteer trial</li><li>• Plan to initiate Phase 2 trial in non-advanced SM in mid-2021</li></ul>
 BLU-945 (triple-mutant EGFR)	<i>Treatment-resistant EGFR-driven NSCLC</i> <ul style="list-style-type: none"><li>• Presented foundational preclinical data at ESMO 2020</li><li>• Plan to initiate Phase 1 trial in 1H 2021</li></ul>
 (Double-mutant EGFR)	<i>Treatment-resistant EGFR-driven NSCLC</i> <ul style="list-style-type: none"><li>• Plan to present foundational preclinical data in 1H 2021</li><li>• Plan to initiate Phase 1 trial by the end of 2021</li></ul>
 (MAP4K1)	<i>Cancer immunotherapy, under collaboration with Roche</i> <ul style="list-style-type: none"><li>• Plan to present foundational preclinical data in 1H 2021</li></ul>

### INDUSTRY BENCHMARK

**10** precision oncology  
IPOs in 2020

**4** had no clinical assets  
at time of IPO

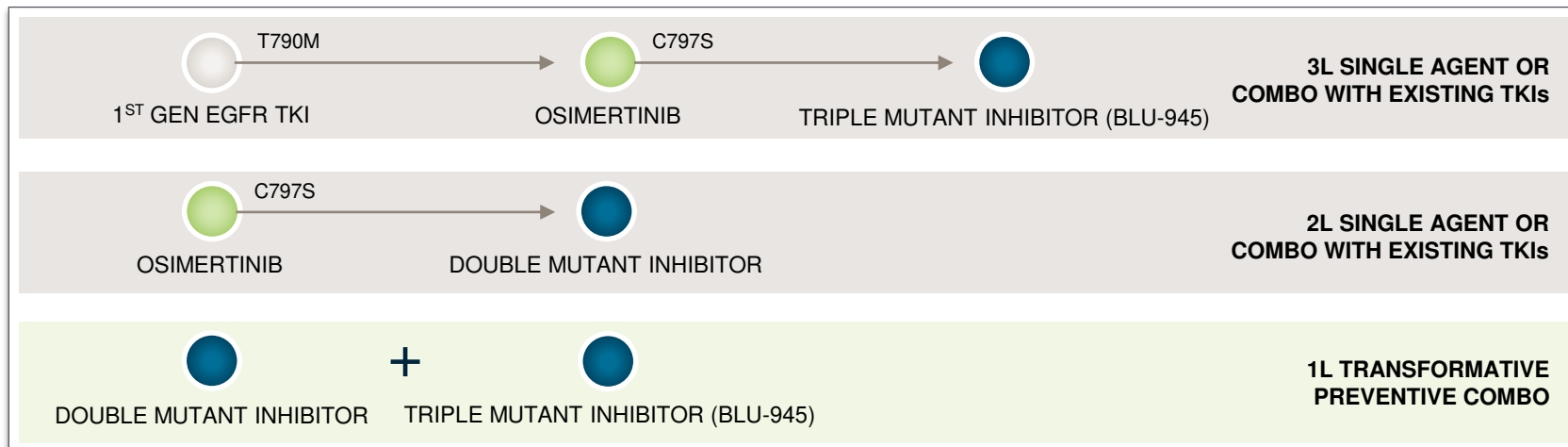
**\$2.3B** mean market  
capitalization<sup>1</sup>

# 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 Asia<sup>1</sup>
- 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 1<sup>st</sup> generation EGFR inhibitors and osimertinib<sup>2</sup>

## 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 IC<sub>50</sub>

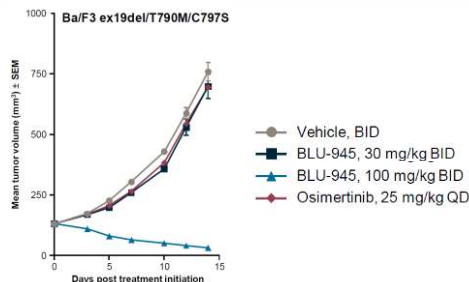
	L858R/ T790M/C797S	ex19del/ T790M/C797S
BLU-945	0.5	0.8
Gefitinib	3921.8	1219.7
Osimertinib	5461.6	649.9

## EXCELLENT SELECTIVITY

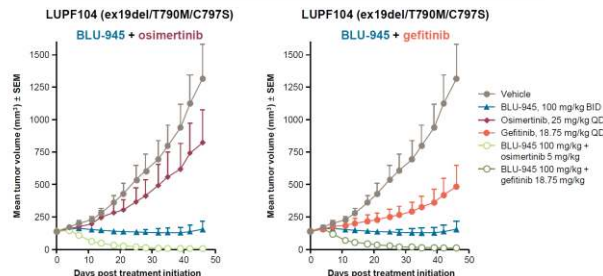
CELLULAR IC<sub>50</sub>

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

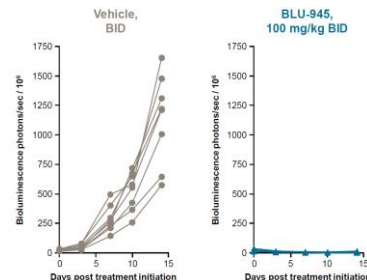
## ROBUST SINGLE AGENT ACTIVITY



## COMBINATION POTENTIAL



## PRECLINICAL CNS ACTIVITY



# 2021 roadmap for precision medicine leadership

---



Accelerate global adoption  
of AYVAKIT and GAVRETO



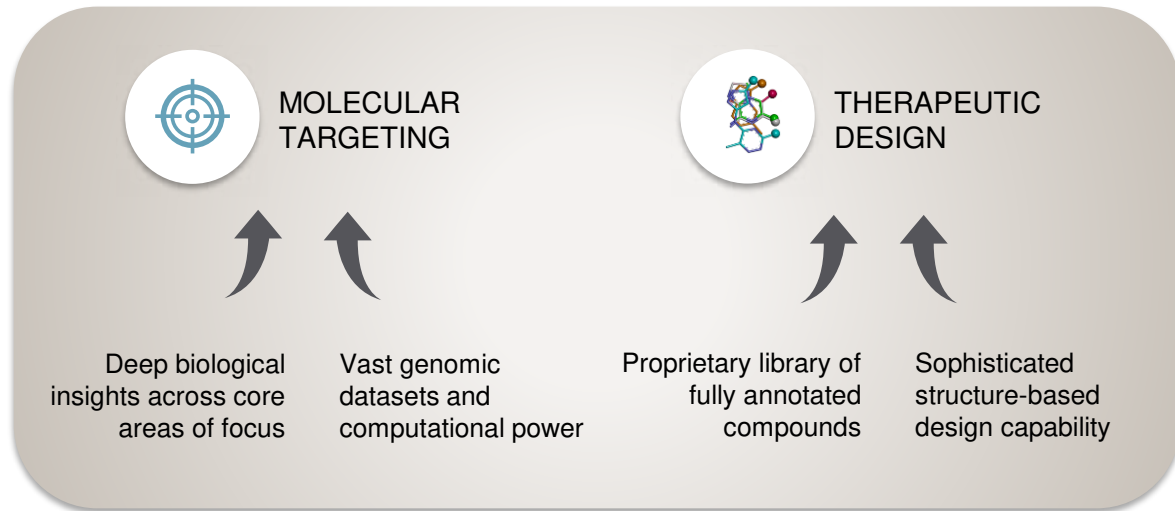
Advance a new wave of  
therapeutic candidates toward  
clinical proof-of-concept



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

# Constant expansion of highly productive research platform

## WORLD-CLASS EXPERTISE IN CATALYTIC KINASE INHIBITION



## PLANNED FUTURE

EXPANDED INTERNAL CAPABILITY  
ACROSS ADDITIONAL  
PRECISION THERAPY MODALITIES

POTENTIAL COMPLEMENTARY  
EXTERNAL INNOVATION

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

- Obtain FDA approval and launch AYVAKIT for advanced SM in the U.S. in 2H 2020
- Submit MAA to EMA for AYVAKIT for advanced SM in Q1 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 and launch 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 double-mutant EGFR inhibitor in EGFR-driven NSCLC by the end of 2021
- Present preclinical data for double-mutant EGFR and MAP4K1 inhibitors in 1H 2021
- Present preclinical data for combo of BLU-945 and double-mutant EGFR inhibitor 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 medicine pipeline.

# Blueprint Medicines is in the strongest financial position in our history

Statement of Operations (unaudited)	Three Months Ended 9/30/2020	Three Months Ended 9/30/2019
Total revenue	\$745.1M	\$9.1M
Collaboration revenue	\$738.8M	\$9.1M
Net product sales	\$6.3M	--
Cost of sales	\$0.1M	--
Research & development expense <sup>1</sup>	\$74.2M	\$81.5M
Selling, general & administrative expense <sup>2</sup>	\$37.4M	\$25.6M
Net income (loss)	\$634.0M	\$(94.3)M
Balance Sheet (unaudited)	9/30/2020	12/31/2019
Cash, cash equivalents and investments	\$1,355.9M	\$548.0M

Based on current operating plans, expect existing cash balance, with anticipated product revenues, to enable self-sustainable financial profile