Second Quarter 2022 Financial and Operating Results

August 2, 2022

Blueprint Medicines call participants

PREPARED REMARKS

Introduction and business review	**Kate Haviland**, Chief Executive Officer
Commercial updates	**Philina Lee, PhD,** Chief Commercial Officer
Clinical updates	**Becker Hewes, MD,** Chief Medical Officer
Second quarter 2022 financial results	**Mike Landsittel**, Chief Financial Officer
Upcoming data milestones and catalysts	**Christy Rossi**, Chief Operating Officer
Q&A	**All**

Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, strategies, timelines and expectations for interactions with the FDA and other regulatory authorities; plans and timelines to update the primary endpoint of the registrational PIONEER trial of AYVAKIT in patients with non-advanced SM; expectations regarding the potential benefits of AYVAKIT in treating patients with non-advanced SM; and the potential benefits of Blueprint Medicines' collaborations; and Blueprint Medicines' financial performance, strategy, goals and anticipated milestones, business plans and focus. 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. Any forward-looking statements in this presentation are based on management’s current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, risks and uncertainties related to the impact of the COVID-19 pandemic to Blueprint Medicines’ business, operations, strategy, goals and anticipated milestones, including Blueprint Medicines’ 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 products, and launching, marketing and selling current or future approved products; Blueprint Medicines’ ability and plans in continuing to establish and expand a commercial infrastructure, and successfully launching, marketing and selling current or future approved products; Blueprint Medicines’ ability to successfully expand the approved indications for AYVAKIT/AYVAKYT and GAVRETO or obtain marketing approval for AYVAKIT/AYVAKYT in additional geographies in the future; the delay of any current or planned clinical trials or the development of Blueprint Medicines’ current or future drug candidates; Blueprint Medicines’ advancement of multiple early-stage efforts; Blueprint Medicines’ ability to successfully demonstrate the safety and efficacy of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; the preclinical and clinical results for Blueprint Medicines’ drug candidates, which may not support further development of such drug candidates either as monotherapies or in combination with other agents or may impact the anticipated timing of data or regulatory submissions; the timing of the initiation of clinical trials and trial cohorts at clinical trial sites and patient enrollment rates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Blueprint Medicines’ ability to obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT, GAVRETO or any drug candidates it is developing; Blueprint Medicines’ ability to develop and commercialize companion diagnostic tests for AYVAKIT/AYVAKYT, GAVRETO or any of its current and future drug candidates; Blueprint Medicines' ability to successfully expand its operations, research platform and portfolio of therapeutic candidates, and the timing and costs thereof; Blueprint Medicines' ability to realize the anticipated benefits of its executive leadership transition plan; and the success of Blueprint Medicines’ current and future collaborations, financing arrangements, partnerships or licensing arrangements. These and other risks and uncertainties are described in greater detail in the section entitled “Risk Factors” in Blueprint Medicines’ filings with the Securities and Exchange Commission (SEC), including Blueprint Medicines’ most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q and any other filings that Blueprint Medicines has made or may make with the SEC in the future. Any forward-looking statements contained in this presentation represent Blueprint Medicines’ views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements.

Blueprint Medicines second quarter 2022 highlights

EXECUTING ACROSS OUR PORTFOLIO AS WE BUILD THE WORLD'S LEADING PRECISION THERAPY COMPANY

Strong global commercial launch execution for AYVAKIT® in advanced SM, with **$28.5M in net product revenues**

Multiple pipeline programs accelerating toward value-driving data inflection points

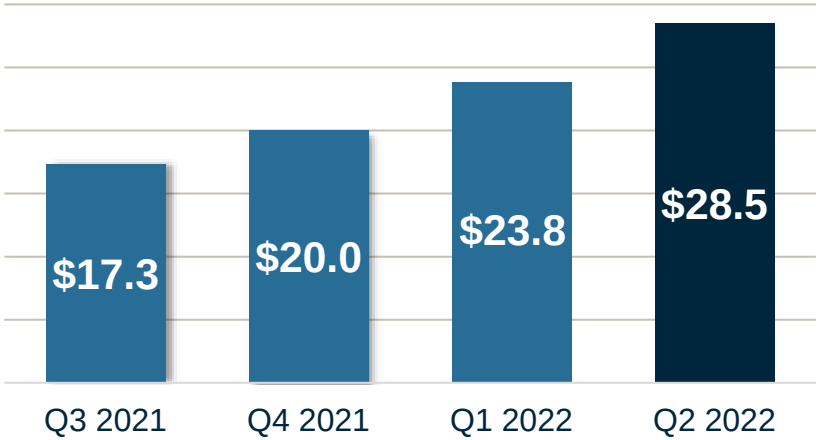
Operational flexibility and path to financial independence, with well over **$1B in cash on balance sheet today**

INVESTOR DAY ON NOVEMBER 1, 2022 IN NEW YORK, NY

SM, systemic mastocytosis

AYVAKIT is now the standard of care for advanced SM

GLOBAL NET REVENUES ($, MILLIONS) BY FULL QUARTER SINCE ADVANCED SM LAUNCH



Q2 2022 U.S. PERFORMANCE METRICS[1]

- **>50%** share of all advanced SM patients being treated
- **>70%** share of new patient starts and switches
- **~300** new accounts since advanced SM approval; **46** new accounts activated in Q2

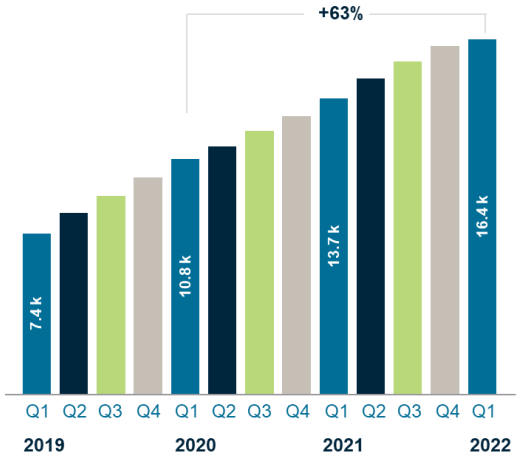
REITERATING GUIDANCE OF $115 TO $130 MILLION IN AYVAKIT NET PRODUCT REVENUES IN 2022

1. Reported data represent estimations. Analysis based on US claims data from Komodo Health. SM, systemic mastocytosis

Non-advanced SM represents a significant medical need, and is a potential blockbuster opportunity for AYVAKIT

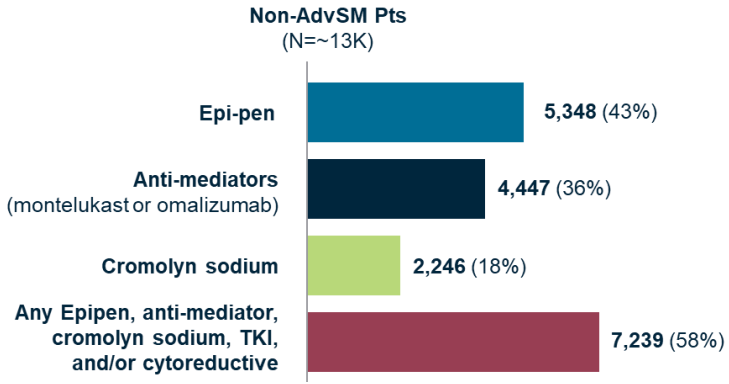
STEADY GROWTH IN DIAGNOSED PATIENTS

Diagnosed SM Patients Observed in US Claims[1]



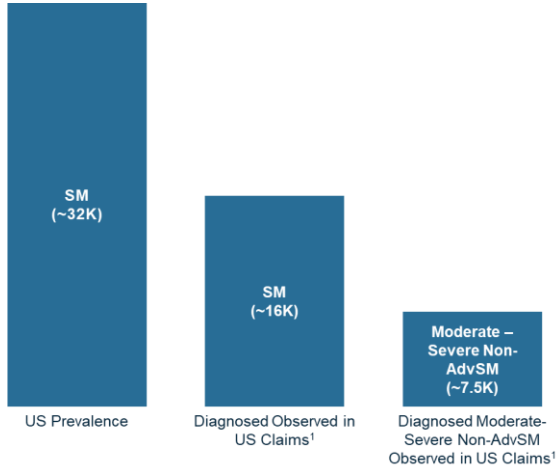
~60% OF NON-ADVANCED SM PATIENTS WITH **SIGNIFICANT POLYPHARMACY**

Diagnosed Non-Advanced SM Patients with Observed Treatment Experience[1]



~7.5K MODERATE-SEVERE NON-ADVANCED SM PATIENTS

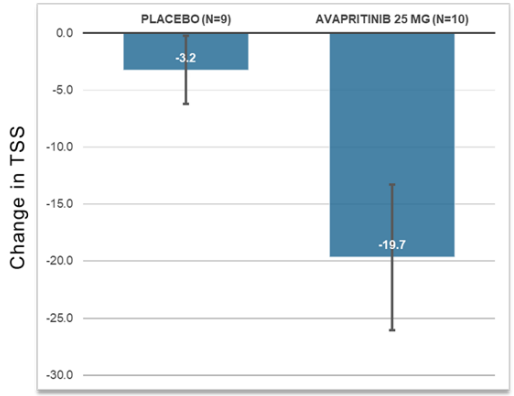
US Prevalence vs. Current Addressable Market



1. Reported data represent estimations. Analysis based on US claims data from Komodo Health. SM, systemic mastocytosis; TKI, tyrosine kinase inhibitor; A/I, allergist/immunologist

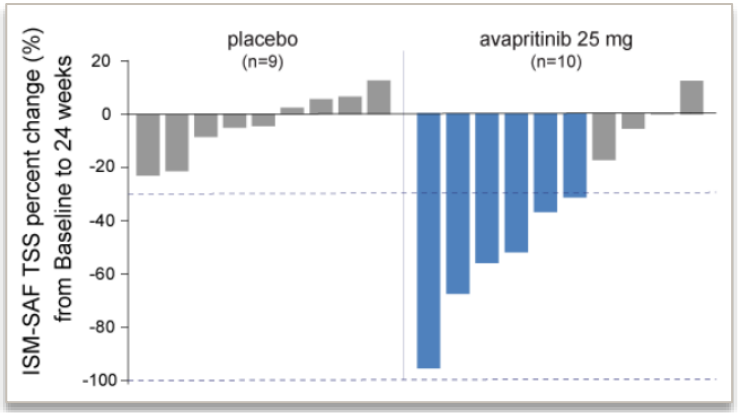
Mean change in TSS and proportion of patients with percent decrease in TSS are correlated in PIONEER Part 1

PIONEER PART 1
MEAN CHANGE IN TSS AT 24 WEEKS[1]
AVAPRITINIB 25 MG VS. PLACEBO (+/- SE)



16.5-point difference in mean TSS reduction
between AYVAKIT vs. placebo

PIONEER PART 1
≥ 30% REDUCTION IN TSS AT 24 WEEKS[2]
AVAPRITINIB 25 MG VS. PLACEBO



60% of AYVAKIT patients **with ≥ 30% reduction in TSS**

FOR PART 2, EXPECT 7 – 10 POINT DIFFERENCE IN MEAN TSS REDUCTION TO BE ASSOCIATED WITH AT LEAST 1/3 OF PATIENTS WITH ≥ 30% REDUCTION IN TSS

1. PIONEER Part 1. Based upon a data cutoff of March 31, 2020. 2. Hartmann K. et al. Avapritinib reduces cutaneous symptoms and mast cell burden in patients with indolent systemic mastocytosis in the PIONEER study. Presented at the European Academy of Allergy Clinical Immunology Annual Meeting. June 2020. Based upon a data cutoff of March 31, 2020. TSS, total symptom score; SE, standard error

Value-driving data milestones and catalysts

EXPAND GLOBAL SM LEADERSHIP				
AYVAKIT® avapritinib | tablets	Advanced SM	EMA approval and launch in EU	✓	Q1 2022
		Global commercial execution	✓	Ongoing 2022
PIONEER	Avapritinib in non-advanced SM	Present topline, registration-enabling Part 2 data		August 2022
		Submit sNDA for non-advanced SM		2H 2022
HARBOR	BLU-263 in non-advanced SM	Initial clinical data		2H 2022
ADVANCE EGFR-MUTANT NSCLC PROGRAMS TOWARD REGISTRATION				
Symphony	BLU-945 monotherapy and combinations	Initial monotherapy clinical data	✓	Q2 2022
		Updated monotherapy data (incl. RP2D)		2H 2022
		Initial combination data with osimertinib (incl. safety, early translation, and early clinical activity)		2H 2022
Harmony	BLU-701 monotherapy and combinations	Initial clinical data		2H 2022
Concerto	BLU-451 monotherapy	Initial clinical data		1H 2023
ADVANCE CDK2-VULNERABLE BREAST, OVARIAN, ENDOMETRIAL, AND OTHER CANCER PROGRAMS TOWARD REGISTRATION				
Vela	BLU-222 monotherapy and combinations	Initial clinical data		1H 2023
GROW R&D PIPELINE				
		Nominate two new development candidates	✓ (1 of 2)	2H 2022

Does not include partnered programs, including GAVRETO® (pralsetinib) in partnership with Roche/Genentech and CStone; nor ex-US milestones for AYVAKIT in partnership with CStone EMA, European Medicines Agency; sNDA, supplemental new drug application; SM, systemic mastocytosis; RP2D, recommended phase 2 dose

Strong financial position bolstered by diversity of revenue and growing product revenue

Statement of Operations (unaudited)	Three Months Ended 6/30/2022	Three Months Ended 6/30/2021	Six Months Ended 6/30/2022	Six Months Ended 6/30/2021
Total revenue	$36.5M	$27.3M	$99.3M	$48.9M
Net product sales	$28.5M	$11.4M	$52.3M	$20.4M
Collaboration revenue	$8.0M	$15.9M	$47.0M	$28.5M
Cost of sales	$4.9M	$6.5M	$10.0M	$6.6M
Collaboration loss sharing	$2.1M	--	$5.4M	--
Research & development expense[1]	$128.5M	$80.0M	$231.6M	$159.7M
Selling, general & admin expense[2]	$58.7M	$49.3M	$115.7M	$91.3M
Net Loss	$(159.7)M	$(108.4)M	$(265.7)M	$(208.2)M
Balance Sheet (unaudited)			**6/30/2022**	**12/31/2021**
Cash, cash equivalents, and investments[3]			$947.2M	1,034.6M

$947.2 MILLION IN CASH, CASH EQUIVALENTS, AND MARKETABLE SECURITIES, EXCLUDING $400M GROSS PROCEEDS FROM OUR RECENT FINANCING THAT CLOSED IN JULY

1. Includes stock-based compensation expense of $10.5M and $10.5M in the three months ended 6/30/22 and 6/30/21, respectively, and $20.5M and $19.4M in the six months ended 6/30/22 and 6/30/21, respectively. 2. Includes stock-based compensation expense of $14.9M and $13.8M in the three months ended 6/30/22 and 6/30/21, respectively, and $28.2M and $25.6M in the six months ended 6/30/22 and 6/30/21 respectively. 3. In addition, in July 2022, we received total cash payments of $400.0 million in gross proceeds related to our financing agreement that closed in July.

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Thank you