UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): **January 8, 2024**

Blueprint Medicines Corporation
(Exact name of registrant as specified in its charter)

Delaware	**001-37359**	**26-3632015**
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

45 Sidney Street **Cambridge, Massachusetts** (Address of principal executive offices)	**02139** (Zip Code)

Registrant's telephone number, including area code: **(617) 374-7580**

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	BPMC	Nasdaq Global Select Market

Item 7.01 Regulation FD Disclosure.

On January 8, 2024, Blueprint Medicines Corporation (the "Company") issued a press release providing a business update, including its 2024 outlook. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

Also on January 8, 2024, the Company updated its corporate presentation to reflect certain business and strategic updates. The Company intends to use this presentation in meetings with members of the investment community and others from time to time, including its presentation by management at the 42nd Annual J.P. Morgan Healthcare Conference on January 8, 2024 at 10:30 a.m. PT (1:30 pm ET). A copy of the presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated by reference herein. A live webcast of the presentation and will be available on the "Events and Presentations" section of the Company's website at http://ir.blueprintmedicines.com.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1 and 99.2 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release issued by Blueprint Medicines Corporation on January 8, 2024
99.2	Corporate slide presentation of Blueprint Medicines Corporation dated January 8, 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 101)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

BLUEPRINT MEDICINES CORPORATION

Date: January 8, 2024

By: /s/ Kathryn Haviland
Kathryn Haviland
Chief Executive Officer

Exhibit 99.1

Blueprint Medicines Highlights 2024 Corporate Strategy and Business Priorities at 42nd Annual J.P. Morgan Healthcare Conference

-- AYVAKIT® (avapritinib) launch in indolent systemic mastocytosis to drive strong revenue growth in 2024, with ongoing U.S. launch and recent EU approval --

-- Expanding mast cell disease leadership with oral wild-type KIT inhibitor, BLU-808, advancing into clinical development; IND submission planned in Q2 2024 --

-- Maintaining durable cash position through focused investment and global commercial execution --

-- Kate Haviland, Chief Executive Officer, to present at J.P. Morgan conference today at 10:30 a.m. PT (1:30 p.m. ET) --

SAN FRANCISCO, Calif., Jan. 8, 2024 /PR Newswire/ -- Blueprint Medicines Corporation (Nasdaq: BPMC) today outlined its 2024 corporate strategy to deliver accelerated revenue growth, sustainable research and development, and a clear path to profitability.

Kate Haviland, Chief Executive Officer of Blueprint Medicines, said:

"As we enter 2024, AYVAKIT's early launch success in indolent systemic mastocytosis has grown our conviction that AYVAKIT has the potential to be a multi-billion-dollar therapy that will drive long-term growth into the next decade. We know that the first few quarters of a launch are critical in defining the trajectory of a new medicine, and we have built a strong foundation for success with AYVAKIT as we continue to drive growth in the U.S**.** and expand our launch in Europe this year.

Throughout 2023, we also made significant progress across our research and development pipeline enabling us to focus investments on our most promising programs. A core component of our growth strategy is to build on our leadership position in SM by expanding to other allergic-inflammatory diseases where mast cells play a core role in the biology, and we have integrated infrastructure that we can efficiently scale. Across our portfolio, we are investing in our most compelling opportunities to deliver innovative, life-changing medicines to patients, while maintaining a strong and sustainable financial profile."

Focused investment strategy in 2024 to drive long-term growth and maintain durable cash position

1. Prioritized programs for investment

Blueprint Medicines is building portfolio scale in therapeutic areas where there are significant medical needs in large patient populations and the company has a deep understanding of biological pathways, a potential to drive best-in-class efficacy and an ability to leverage expertise and infrastructure.

Mast cell diseases

- Extend the company's leadership position in systemic mastocytosis with the ongoing launch of AYVAKIT in the U.S. and EU and continued development of the next-generation KIT D816V inhibitor elenestinib.
- Expand into larger patient populations with allergic-inflammatory diseases with BLU-808, an oral wild-type KIT inhibitor, including chronic urticaria and other diseases where mast cells are core to the biology.

Breast cancer and other solid tumors

- Advance combination development of BLU-222, a highly selective CDK2 inhibitor with best-in-class potential, in HR+/HER2- breast cancer based on positive previously reported monotherapy clinical data.
- Progress ongoing strategic partnership discussions to maximize the potential of BLU-222 as a backbone combination therapy in HR+/HER2- breast cancer and other CDK2-vulnerable cancers.
- Advance additional programs including BLU-956, a next-generation CDK2 inhibitor development candidate nominated in 2023, and targeted protein degrader research programs for CDK2 and an undisclosed target to support long-term lifecycle management.

2. De-prioritized programs

Blueprint Medicines is discontinuing investment in specific programs, based on the evolving external landscape, emerging clinical data and partnering considerations.

Lung cancer

- Discontinue further investment in the early clinical-stage therapies BLU-945 and BLU-451 for EGFR-mutant NSCLC and explore strategic options, including potential out-licensing, based on the evolving external landscape and emerging clinical data.
- In February 2023, Blueprint Medicines announced Roche's decision to terminate the global collaboration agreement for GAVRETO® (pralsetinib). Given Blueprint Medicines' lack of global infrastructure in lung and thyroid cancer, the company has decided to discontinue global development and marketing of GAVRETO in territories excluding the U.S. and Greater China. The companies will continue working on transition and wind-down activities anticipated to begin in the first quarter of 2024; further information on product discontinuation timing to be provided in the near future.
- Blueprint Medicines has identified a potential alternate partner for GAVRETO in the U.S. and is continuing to work with the involved parties to define a scenario that enables continued availability of GAVRETO in the U.S.
- Blueprint Medicines expects the wind-down of the Roche collaboration for GAVRETO will result in significantly lower year-over-year operating expenses related to GAVRETO in 2024 and will not affect the $175 million upfront payment received under a 2022 financing agreement with Royalty Pharma.

As a result of continued strategic portfolio prioritization, Blueprint Medicines expects a year-over-year decline in operating expenses in 2024. The company plans to provide financial guidance for 2024, including anticipated AYVAKIT revenue, when it reports fourth quarter and full-year 2023 financial results in February 2024.

2024 Corporate Milestones

The company's anticipated 2024 corporate milestones include:

Mast cell diseases

- Present long-term safety and efficacy data from the PIONEER trial of AYVAKIT in indolent SM (ISM) in the first half of 2024.
- Submit an investigational new drug (IND) application for BLU-808 in the second quarter of 2024.
- Initiate the registration-enabling Part 2 of the HARBOR trial of elenestinib in ISM in the second half of 2024.

Breast cancer and other solid tumors

- Continue ongoing strategic business development discussions.
- Present data for BLU-222 in combination with ribociclib and fulvestrant in patients with HR+/HER2- breast cancer in the first half of 2024.
- Provide update on BLU-222 registration plan in HR+/HER2- breast cancer in the second half of 2024.

J.P. Morgan Healthcare Conference Presentation Information

Kate Haviland, Chief Executive Officer of Blueprint Medicines, will present a company overview and 2024 outlook at the 42nd Annual J.P. Morgan Healthcare Conference on Monday, January 8 at 10:30 a.m. PT / 1:30 p.m. ET. A live webcast of the presentation and Q&A breakout session will be available by visiting the "Events and Presentations" section of Blueprint Medicines' website at http://ir.blueprintmedicines.com. A replay of the webcast will be archived on Blueprint Medicines' website for 30 days following the presentation.

About Blueprint Medicines

Blueprint Medicines is a global precision therapy company that invents life-changing medicines. Applying an approach that is both precise and agile, we create therapies that selectively target the root cause of disease, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. Today, we have brought our approved medicines to patients in the United States and Europe, and we are globally advancing multiple programs for mast cell disorders, including systemic mastocytosis and chronic urticaria, breast cancer and other solid tumors. For more information, visit www.BlueprintMedicines.com and follow us on X (formerly Twitter; @BlueprintMeds) and LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding Blueprint Medicines' views with respect to AYVAKIT's potential to be a multi-billion-dollar therapy; the continued growth of AYVAKIT in the U.S. and the expansion of AYVAKYT's launch in Europe; the expansion of Blueprint Medicines' mast cell disease franchise with the development of BLU-808; the advancement of its clinical development of BLU-222, preclinical development of BLU-956 and progression of targeted protein degrader research programs for CDK2; plans, strategies, timelines and expectations for Blueprint Medicines' current or future approved drugs and drug candidates; the potential benefits of any of Blueprint Medicines' current or future approved drugs or drug candidates in treating patients; and Blueprint Medicines' financial performance, strategy, goals and anticipated milestones, business plans, outlook 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 press release 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 press release, including, without limitation: preliminary activity and safety data may not be representative of more mature data; the risk of delay of any current or planned clinical trials or the development of Blueprint Medicines' current or future drug candidates; risks related to 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; preclinical and clinical results for Blueprint Medicines' drug candidates 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 may be delayed or slower than anticipated; actions of regulatory agencies may affect the initiation, timing and progress of clinical trials; the success of Blueprint Medicines' current and future collaborations, financing arrangements, partnerships or licensing arrangements may impact Blueprint Medicines' ability to capitalize on the market potential of its approved drugs and drug candidates; and risks related to Blueprint Medicines' ability to obtain, maintain and enforce patent and other intellectual property protection for its products and current or future drug candidates it is developing. 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 press release 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.

Trademarks

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blueprint™ MEDICINES

Making Our Mission a Reality

KATE HAVILAND, CHIEF EXECUTIVE OFFICER

J.P. MORGAN HEALTHCARE CONFERENCE
JANUARY 8, 2024

Adrianne Clinton
patient living with system

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 limita regarding plans, strategies, timelines and expectations for the company's future business growth, including its 2024 growth strategy; AYVAKIT's potential to capture a blo opportunity in SM; whether BLU-808 has first- and best-in-class, pipeline in a pill potential; whether any of the company's product candidates will address unmet medical nee the company's cash burn in 2024; statements regarding plans and expectations for the company's current or future approved drugs and drug candidates; the potential bene company's current or future approved drugs or drug candidates in treating patients; and the company's financial performance, strategy, goals and anticipated milestones, bu focus.

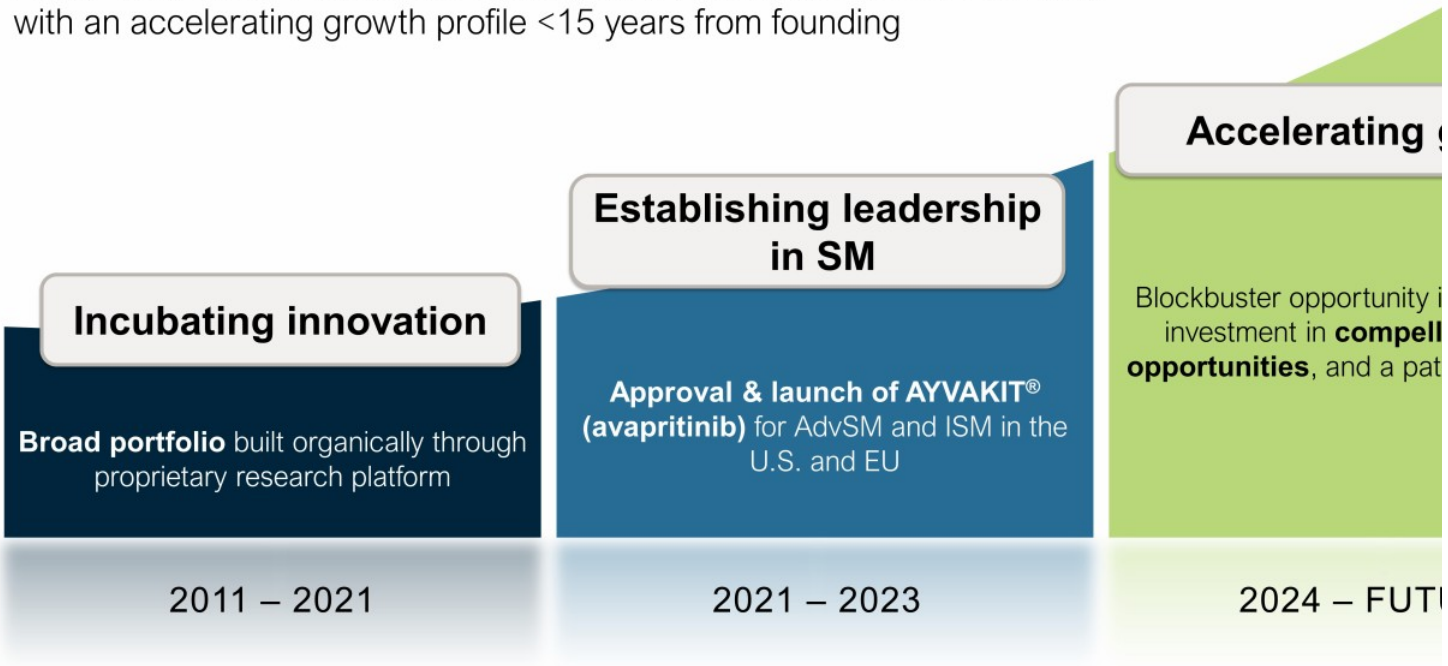
The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "tar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking sta 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 eve differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, the company's ability and plans expand a commercial infrastructure, and successfully launching, marketing and selling current or future approved products; the company's ability to successfully expar indications for AYVAKIT/AYVAKYT or obtain marketing approval for AYVAKIT/AYVAKYT in additional geographies in the future; the delay of any current or planned clini development of the company's current or future drug candidates; the company's advancement of multiple early-stage efforts; the company's ability to successfully demonstrat 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 the company's drug candidates, which 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 submissio 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 pro trials; the company's ability to obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT or any drug candidates it is developing ability to develop and commercialize companion diagnostic tests for AYVAKIT/AYVAKYT or any of its current and future drug candidates; the company's ability to succes operations, research platform and portfolio of therapeutic candidates, and the timing and costs thereof; and the success of the company's current and future collabor arrangements, partnerships or licensing arrangements; and risks and uncertainties related to the impact of the COVID-19 pandemic to the company's business, operations, str anticipated milestones, including the company's ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products. These and other risks a are described in greater detail in the section entitled "Risk Factors" in the company's filings with the Securities and Exchange Commission (SEC), including the company's mo Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q and any other filings that the company has made or may make with the SEC ir 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 statements contained in this presentation as a result of new information, future events or otherwise. Accordingly, readers are cautioned not to place undue reliance on these statements.

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 othe 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, a 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 uncertaint

blueprint™ MEDICINES

The accelerating growth profile of Blueprint Medicines

A fully-integrated, commercial-stage, global biopharmaceutical company, with an accelerating growth profile <15 years from founding



Avapritinib is approved under the trade name AYVAKYT® in Europe. AdvSM, advanced systemic mastocytosis; ISM, indolent systemic mastocytosis; SM, systemic mastocytosis

Delivering business growth in 2024 and beyond

2023 Accomplishments

- Launched AYVAKIT in ISM
- Delivered four Phase 1 clinical datasets informing future investment
- Nominated 3 DCs, including oral wild-type KIT inhibitor BLU-808
- Continued decline in operating expenses

2024 Growth Strategy

Significant **revenue growth** AYVAKIT launch in SM

Focused investment in co growth opportunities with po significant value drivers

Durable capital position a independence from capital r

blueprint MEDICINES

DC, development candidate

Three key growth drivers in 2024

Capturing a Blockbuster Opportunity

Strong and steady global launch delivering growth well into the next decade

Investing in Sustainable Innovation

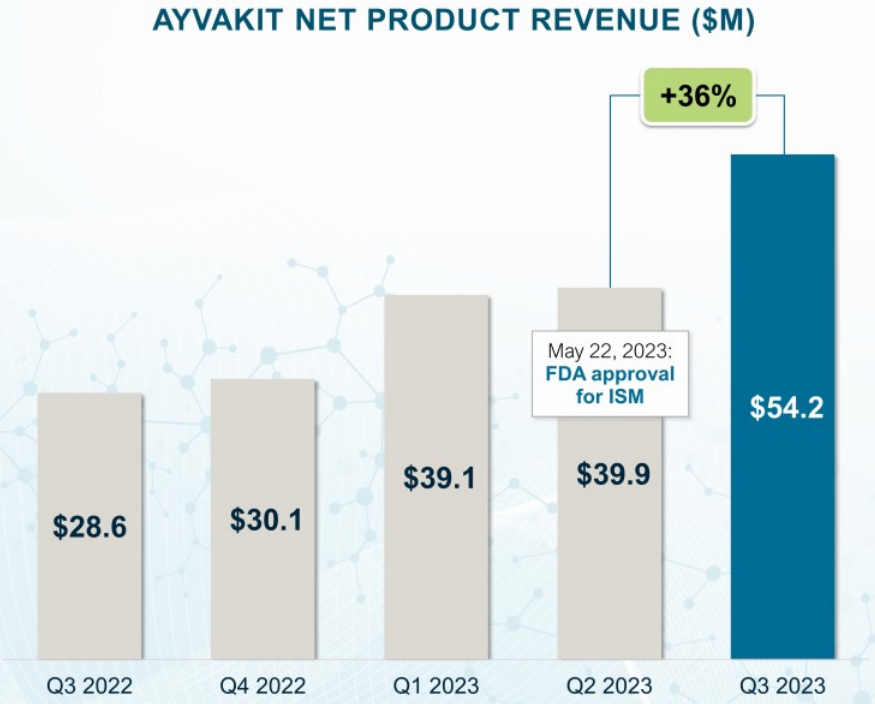
Maintai Financial S

blueprint MEDICINES

AYVAKIT has a unique and multidimensional value proposition

blueprint MEDICINES

AYVAKIT is capturing a blockbuster opportunity in SM



- Significantly larger population for **chronic duration of trea**
- High-margin specialty drug w **call points**
- **Durable growth** expected in decade with long IP protectio
- **First and only** approved the the underlying driver of diseas

IP, intellectual property

AYVAKIT provides durable symptom control with a well-tolerated, onc

Broad and Durable Efficacy

Improvement across broad range of skin, gastrointestinal, neurocognitive, and other symptoms

Safety Profile Supporting Chronic Treatment

Treatment durations up to 4+ years in PIONEER[1]; long-term safety data to be presented in 2024

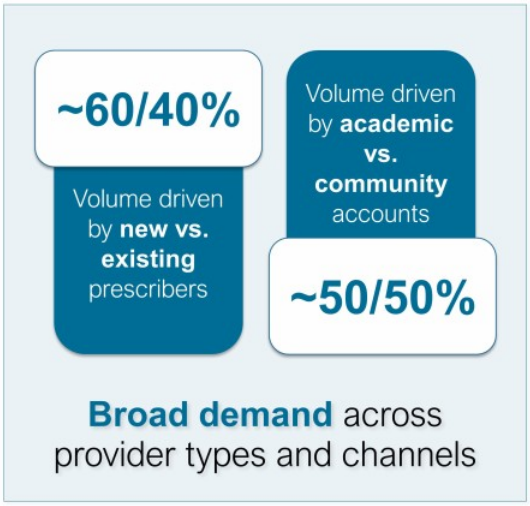
Range of Doses

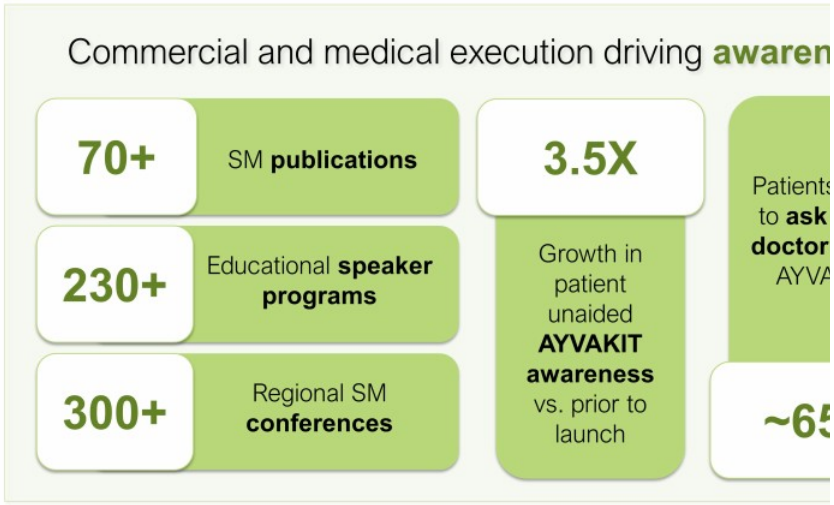
Multiple dose strengths meet the medical needs across a spectrum of SM patients

AYVA
avapritinib

1. Blueprint Medicines data on file. As of November 2023, the median duration of therapy in PIONEER (n=251) was 25.1 months (range: 0.2 - 52.9 months).

Strong foundation and breadth of execution fuel near-term growth traj





1. Blueprint Medicines data on file. Percentages are based upon new SM patient starts in Q3 2023 visible in the SP/HUB channel, which reflects the majority of AYVAKIT volume.

Significant headroom for upside opportunity with growing SM market

- Broaden healthcare provider perspective on the AYVAKIT-eligible patient to align to our broad label
- Build market through more efficient diagnosis
- Enter new markets outside of the U.S.

~9,500
Diagnosed and uncontrolled ISM in U.S.[1]

~21,000
Total SM diagnosed in U.S.[1]

>20% YoY growth

~32,000
U.S. SM prevalence[2]

1. Blueprint Medicines data on file, based upon visibility of unique patients in US claims data. 2. Cohen et al 2014.

Three key growth drivers in 2024

Capturing a Blockbuster Opportunity

Investing in Sustainable Innovation

Focused investment to drive long-term growth

Maintai Financial S

blueprint MEDICINES

Building scale in two focused and exciting areas of science

	PROGRAM	TARGET	DISCOVERY	CLINICAL	COMMERCIAL
Allergy/inflammation focus: **MAST CELL DISORDERS**	AYVAKIT® (avapritinib)[1]	KIT D816V		Indolent SM[2]	
				Advanced SM[3]	
	Elenestinib (next gen)	KIT D816V		Indolent SM	
	BLU-808	Wild-type KIT		Chronic urticaria	
	Additional undisclosed mast cell targets/modalities				
Oncology focus: **SOLID TUMORS**	BLU-222	CDK2		HR+ / HER2- breast cancer	
				Other CDK2 vulnerable cancers	
	BLU-956 (next gen)	CDK2		HR+ / HER2- breast cancer	
	Targeted protein degrader	CDK2		HR+ / HER2- breast cancer	
	Targeted protein degrader	Undisclosed			
	Additional programs	Undisclosed			

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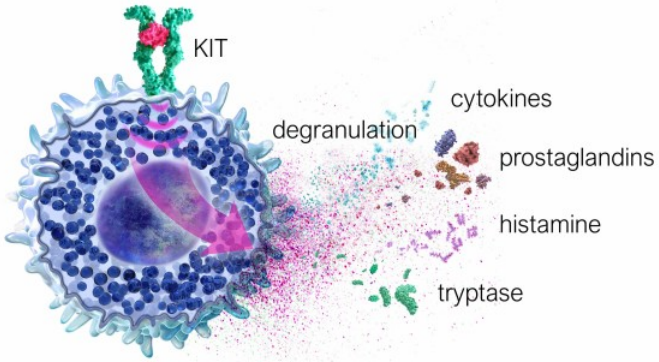
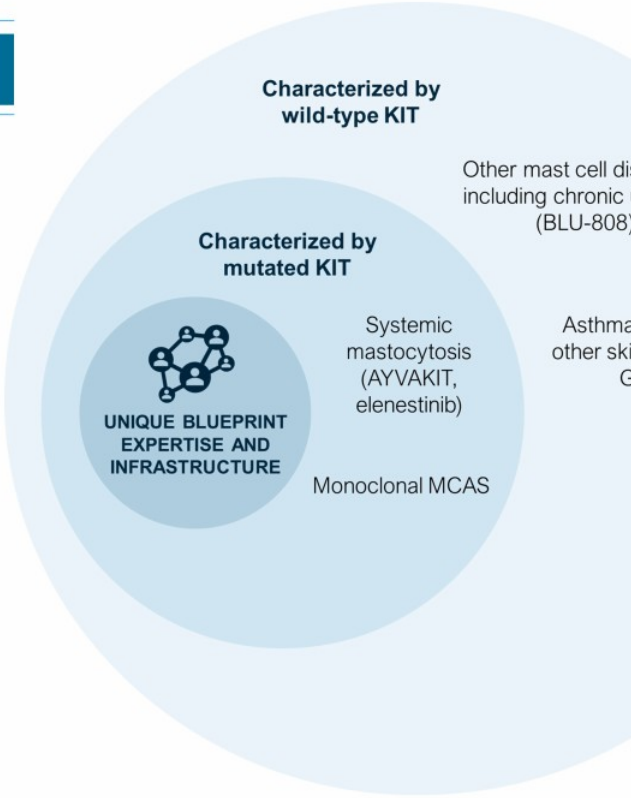
1. Also approved in the U.S. for adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. Approved in Europe (AYVAKYT®) for adults with unresectable or metastatic GIST harboring the PDG mutation. 2. Approved in the U.S. for adults with indolent SM. Approved in Europe (AYVAKYT) for adults with indolent SM with moderate to severe symptoms inadequately controlled on symptomatic treatment. 3. Approved in the U.S. for adults with advanc aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL). Approved in Europe (AYVAKYT®) for adults with ASM, SM-AHN or MCL, after at least one systemic therapy. 4. CStone Pharmaceuticals has develop and commercialize avapritinib in Greater China. Updated as of January 8, 2024.

Mast cells are core drivers of biology in a range of inflammator

KIT is a clinically validated **mast cell target**



- KIT-mediated signaling plays a central role in survival, proliferation, and activation of mast cells
- When degranulation occurs, release of inflammatory molecules leads to a broad range of physiological effects

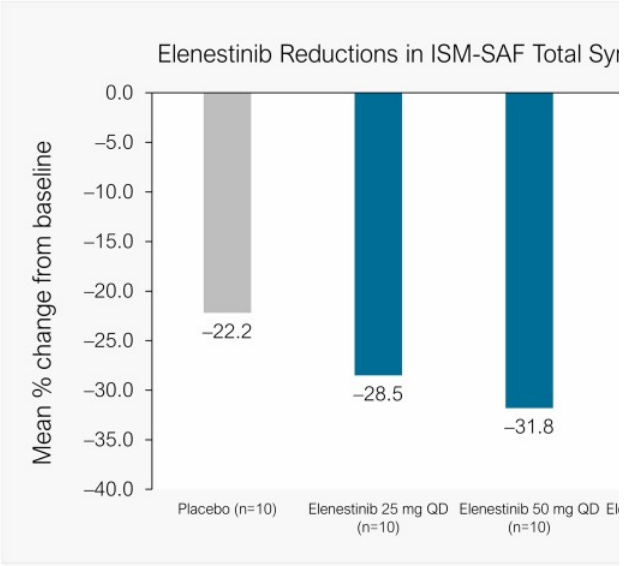


MCAS, mast cell activation syndrom; GI, gastrointestinal

Elenestinib, an investigational next-generation, potent, selective KIT D816V ir

HARBOR PART 1 TRIAL RESULTS PRESENTED AT ASH 2023[1]:

- **Well-tolerated** with no treatment discontinuations due to AEs; most AEs Grade 1/2
- **Improved disease-related symptoms** as assessed by the validated ISM-SAF
- Reduced multiple **biomarkers of mast cell burden**
- Robust clinical activity and favorable tolerability observed across doses

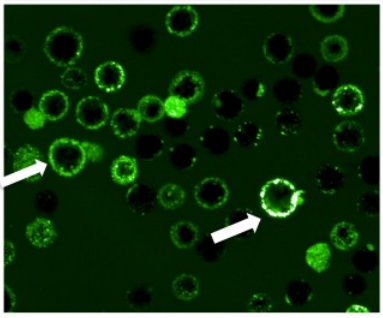


1. Tashi T. Et al. Presented at ASH 2023.

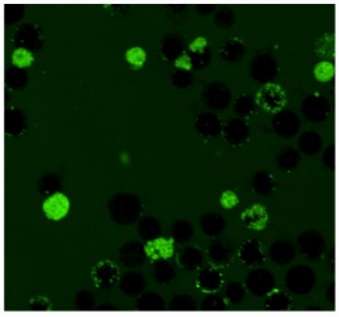
Wild-type KIT inhibitor BLU-808 has first- and best-in-class, pipeline i pill potential

Attribute	Ideal Candidate	BLU-808
pKIT / proliferation IC_{50}	< 10 nM pKIT IC_{50}	0.37/1.3 nM
PDGFR / FLT3 selectivity	> 50x / > 50x	>300/>9600
Kinase Selectivity; S(10)	< 0.1	0.042
Drug/Drug Interactions	Low potential	Low potential
Peripherally Restricted	Kpuu < 0.1	Kpuu 0.021

IND submission planned for 2Q 2024



Vehicle

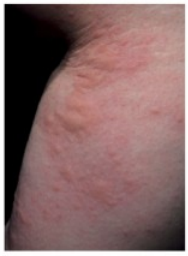


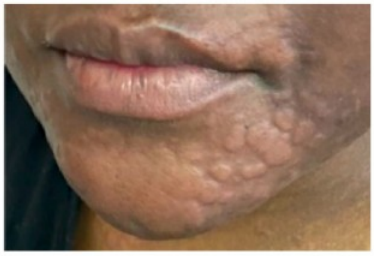
10 nM BLU-808

- Preclinical treatment with BLU-808 inhibits degranulation, **targeting an underlying cause of inflammatory disease**.
- Images are frame capture from videos available at the QR code.

PDGFR, platelet-derived growth factor receptor; FLT3, fms-like tyrosine kinase 3; Kpuu, unbound partition coefficient; IgE, immunoglobulin E; IND, investigational new drug

Targeting KIT with an oral therapy to address significant unmet medic





Typical presentation of hives or wheals, a common symptom in **chronic urticaria**[1]

Disease Biology Driven by Mast Cells

Target Validation

wtKIT inhibition has established clinical proof-of-concept in chronic urticaria

Approach

Small molecule TKI; opportunity to drive market expansion with an oral regimen

Opportunity

Significant disease burde
impact due to itching, hives
related anxiety, slee

~680K patients in US

Unmet need for an oral t
targets core biol

TKI, tyrosine kinase inhibitor; QoL, quality of life; EU4 includes France, Germany, Italy, Spain
1. Antihistamine refractory, claims-identified patients with CU in the US and EU4

Building scale in two focused and exciting areas of science

	PROGRAM	TARGET	DISCOVERY	CLINICAL	COMMERCIAL
Allergy/inflammation focus: **MAST CELL DISORDERS**	AYVAKIT® (avapritinib)[1]	KIT D816V		Indolent SM[2]	
				Advanced SM[3]	
	Elenestinib (next gen)	KIT D816V		Indolent SM	
	BLU-808	Wild-type KIT		Chronic urticaria	
	Additional undisclosed mast cell targets/modalities				
Oncology focus: **SOLID TUMORS**	BLU-222	CDK2		HR+ / HER2- breast cancer	
				Other CDK2 vulnerable cancers	
	BLU-956 (next gen)	CDK2		HR+ / HER2- breast cancer	
	Targeted protein degrader	CDK2		HR+ / HER2- breast cancer	
	Targeted protein degrader	Undisclosed			
	Additional programs	Undisclosed			

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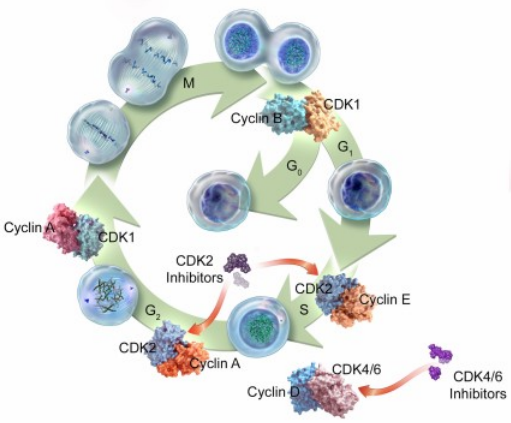
1. Also approved in the U.S. for adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. Approved in Europe (AYVAKYT®) for adults with unresectable or metastatic GIST harboring the PDG mutation. 2. Approved in the U.S. for adults with indolent SM. Approved in Europe (AYVAKYT) for adults with indolent SM with moderate to severe symptoms inadequately controlled on symptomatic treatment. 3. Approved in the U.S. for adults with advanc aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL). Approved in Europe (AYVAKYT®) for adults with ASM, SM-AHN or MCL, after at least one systemic therapy. 4. CStone Pharmaceuticals has develop and commercialize avapritinib in Greater China. Updated as of January 8, 2024.

With BLU-222, we have solved the selectivity challenge of CDK2 inhibition

CDK2 is a **clinically validated** cell cycle target



Selective CDK2 inhibition has historically been challenging to achieve

Large market with **significant unmet need**

$10B+

Global sales of CDK4/6 inhibitors for HR+/HER2- breast cancer in 2023

Comprehensive **drive va**

- Prevent and ad CDK4/6 resista backbone of co therapy
- Highly selective minimizing off-t to enable comb partner of choic
- Next-generatio maximize long-

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CDK, cyclin-dependent kinase; HR+, hormone receptor positive; HER2-, human epidermal growth factor receptor 2 negative; SOC, standard of care

BLU-222 has the potential to be the first and best-in-class selective inhibitor c

	BLU-222[1]			PF-4091[2]	
PRECLINICAL PROFILE					
Selectivity score / SI(10)	0.045			0.127	
CDK2 potency / CDK2 enzyme IC_{50} (nM)	2.6			7.2	
PHASE 1 MONOTHERAPY DOSE ESCALATION DATA					
Patients	27 patients			35 patients	
Dose range tested	50 mg – 800 mg BID (MTD not determined)			75 mg – 500 mg BID (MTD:	
PK (average effective half life)	~12 hrs			~2-3 hrs	
Treatment emergent adverse events (TEAEs)	No Gr5; 1 Gr4 (hypokalemia; unrelated)			1 Gr5 (unrelated); 1 Gr4 (ne	
HEMATOLOGIC TEAEs	**ALL**	**GR3**	**GR4**	**ALL**	**GR3**
• Anemia	29.6%	3.7%		45.7%	8.6%
• Neutropenia	3.7%			28.6%	14.3%
• Thrombocytopenia	3.7%	3.7%		20.0%	2.9%

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1. Patel, M.R. et al, ASCO 2023 and Blueprint data on file. Data cut April 25, 2023. 2. Yap, T.A. et al, ASCO 2023

Three key growth drivers in 2024

Capturing a Blockbuster Opportunity

Investing in Sustainable Innovation

Maintai Financial S

Durable capital posi
path to pro

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AYVAKIT is capturing a blockbuster opportunity in SM

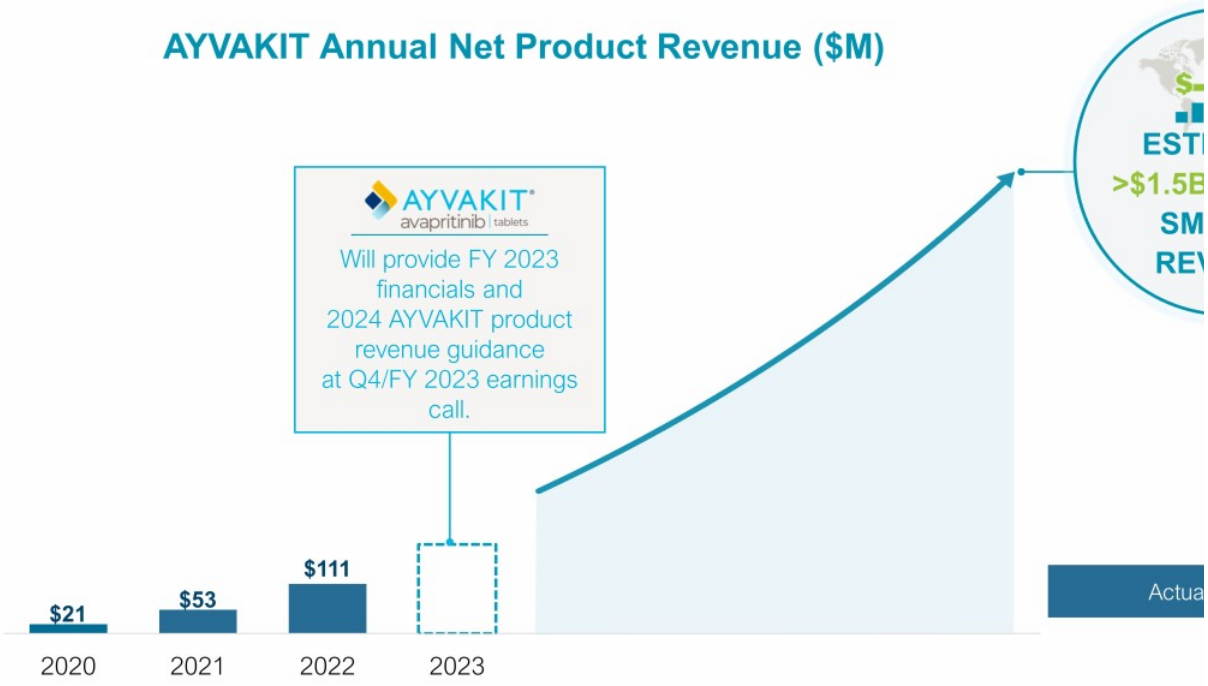


Figure is provided as a graphical representation and is not intended as financial guidance.

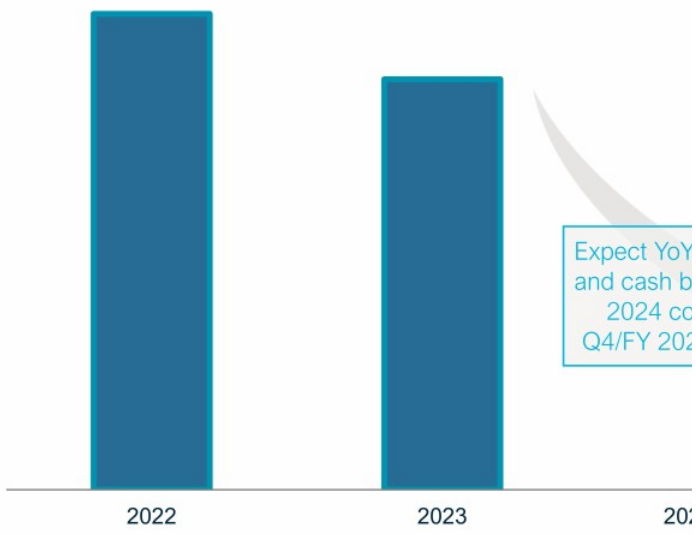
Portfolio prioritization driving continued operating expense reduction

Continued reduction in opex

- Deprioritized investment decisions (e.g., EGFR) support anticipated opex reduction
- Plan for continued opex reduction while still investing sustainably, allocating capital toward highest priority programs

AYVAKIT revenue growth and opex reductions will drive **continued decline in cash burn**

Operating Cash Burn will Continue to Decli



Operating cash burn for 2023 is based upon unaudited results, to be announced at Q4/FY 2023 financial and operating results call in February 2024. Figure is provided as a graphical representation and is not intended as financial gui

Key anticipated portfolio milestones in 2024

In addition to **AYVAKIT revenue growth**, Blueprint expects the following data-related milestones in 2024:

Area	Program	Milestone	Ti
Mast cell disorders	AYVAKIT	Present long-term safety and efficacy data from PIONEER trial in ISM	1H
	BLU-808	IND submission	2C
	Elenestinib	Initiate registration-enabling Part 2 of the HARBOR trial in ISM	2H
Solid tumors	BLU-222	Present data in combination with ribociclib and fulvestrant for HR+/HER2- breast cancer	1H
		Provide update on registration plan for HR+/HER2- breast cancer	2H

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Blueprint positioned to accelerate our business growth in 2024 and beyond

AYVAKIT is capturing a blockbuster opportunity in SM.
AYVAKIT in SM is one of the most exciting rare disease launches happening today.

Focused investment in growth opportunities that leverage our expertise.
Pursuing exciting areas of science at the nexus of our deep understanding of core biol
our business strategy to drive growth through leverage and scale.

On the path to profitability.
With ramping revenues and a focused spending plan we are maintaining a durable cap
while also investing in opportunities for longer term growth.

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Blueprint Medicines pipeline

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