Making Our Mission a Reality

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J.P. MORGAN HEALTHCARE CONFERENCE
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Adrianne Clinton
patient living with systemic mastocytosis

Forward-Looking Statements

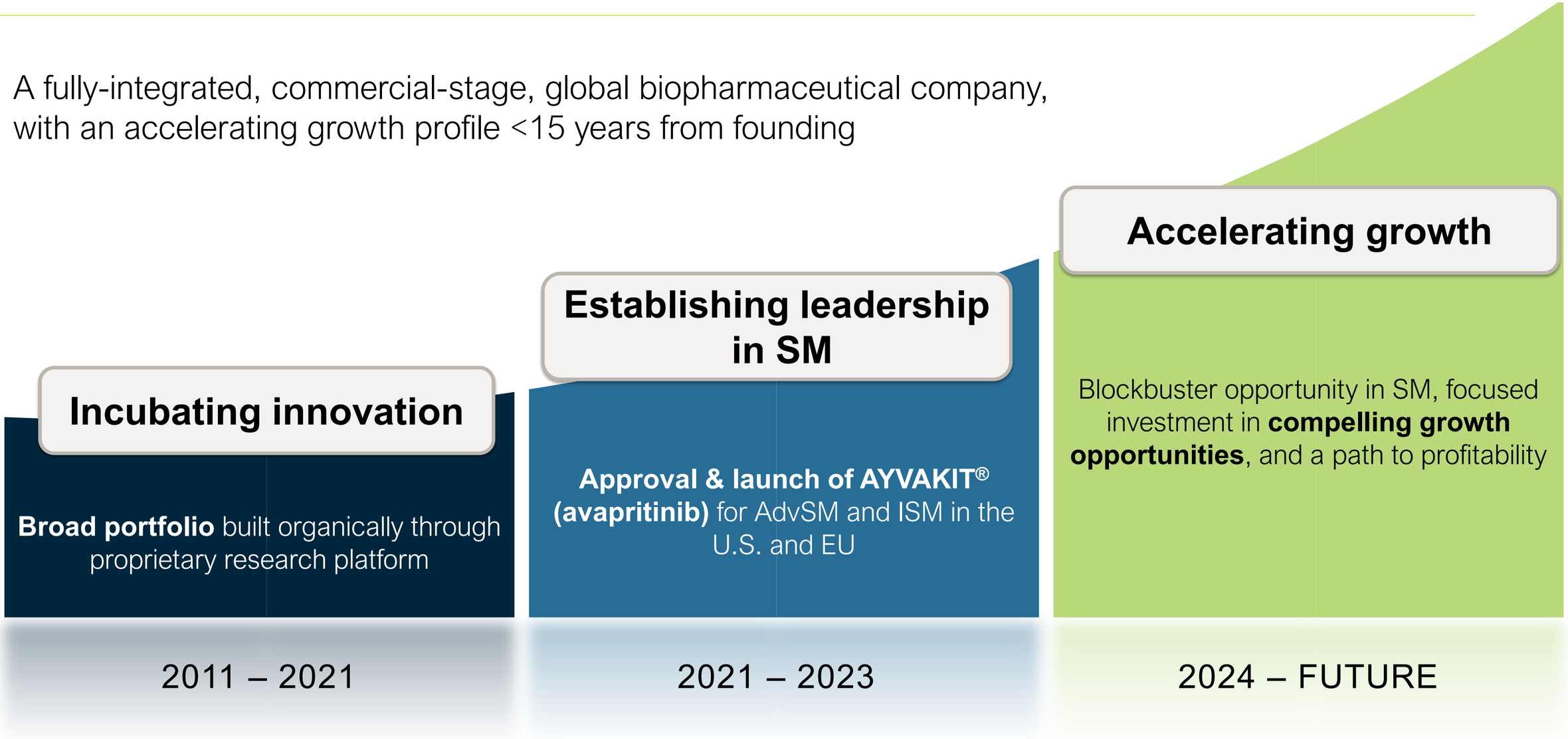
This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, strategies, timelines and expectations for the company's future business growth, including its 2024 growth strategy; AYVAKIT's potential to capture a blockbuster market 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 needs; reduction of 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 benefits of any of the company's current or future approved drugs or drug candidates in treating patients; and the company's 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, the company's ability and plans in continuing to expand 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 AYVAKIT/AYVAKYT 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 the company's current or future drug candidates; the company's advancement of multiple early-stage efforts; the company's 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 the company's 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; 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; the company's 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 successfully expand its operations, research platform and portfolio of therapeutic candidates, and the timing and costs thereof; and the success of the company's current and future collaborations, financing arrangements, partnerships or licensing arrangements; and 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 products, and launching, marketing and selling current or future approved products. These and other risks and uncertainties 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 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 the company has made or may make with the SEC in the future. 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. Accordingly, readers are cautioned not to place undue reliance on these forward-looking 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 other data about the company's industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of the company's future performance and the future performance of the markets in which the company operates are necessarily subject to a high degree of uncertainty and risk.

The 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

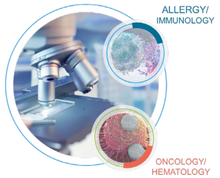
Delivering business growth in 2024 and beyond

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** with AYVAKIT launch in SM



Focused investment in compelling growth opportunities with potential to be significant value drivers

Durable capital position allows for independence from capital markets

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

Maintaining Financial Strength

AYVAKIT has a unique and multidimensional value proposition

Blockbuster market opportunity

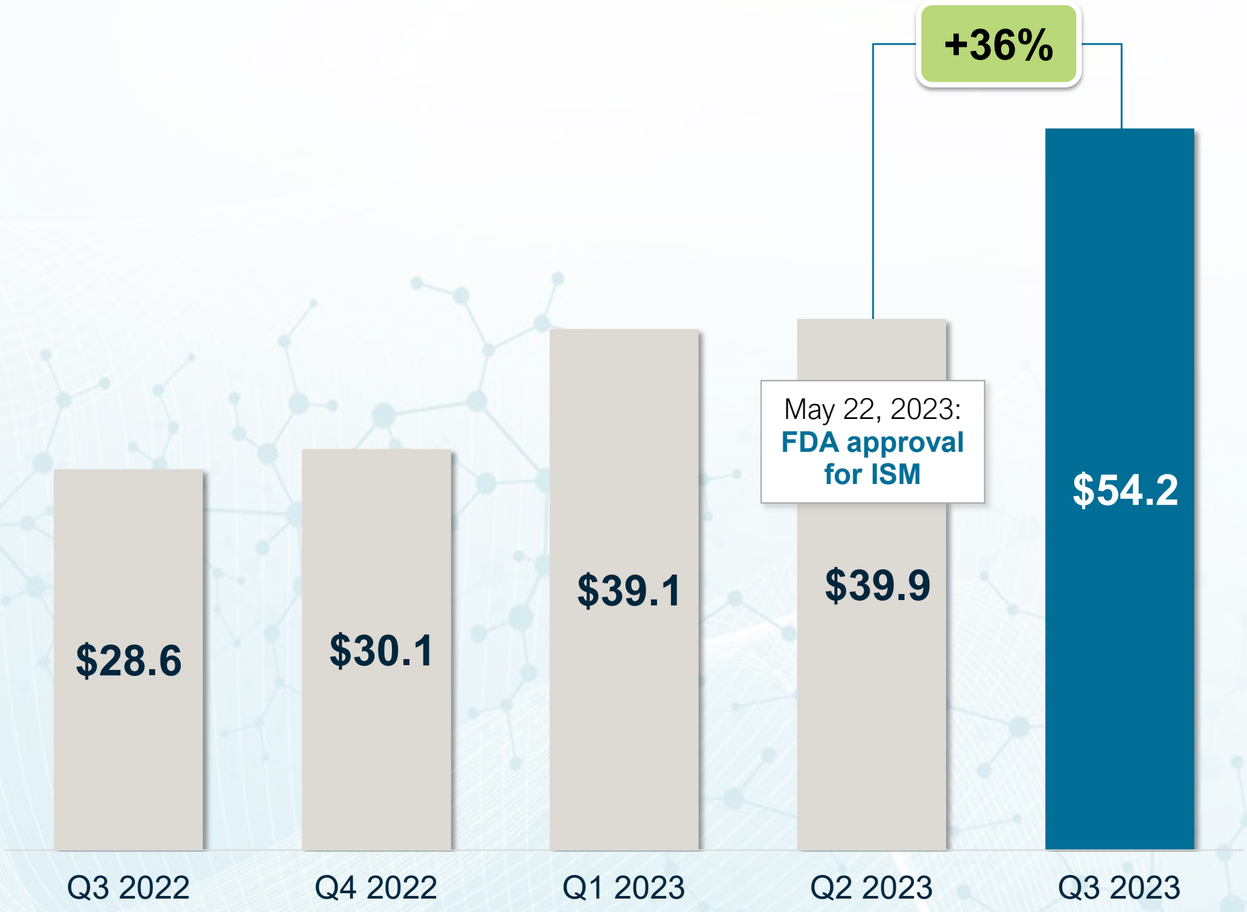
Positive receptivity driving **demand**

Compelling clinical profile

Multiple opportunities for **growth**

AYVAKIT is capturing a blockbuster opportunity in SM

AYVAKIT NET PRODUCT REVENUE ($M)



- Significantly larger population with potential for **chronic duration of treatment** in ISM
- High-margin specialty drug with **tractable call points**
- **Durable growth** expected into next decade with long IP protection
- **First and only** approved therapy to treat the underlying driver of disease

IP, intellectual property

AYVAKIT provides durable symptom control with a well-tolerated, once-daily pill

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

AYVAKIT®
avapritinib | tablets

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 trajectory

~60/40%

Volume driven by **new vs. existing** prescribers

Volume driven by **academic vs. community** accounts

~50/50%

Broad demand across provider types and channels

Commercial and medical execution driving **awareness**

70+ SM **publications**

230+ Educational **speaker programs**

300+ Regional SM **conferences**

3.5X

Growth in patient unaided **AYVAKIT awareness** vs. prior to launch

Patients likely to **ask their doctor** about AYVAKIT

~65%

Ease of **access**

~95% **Conversion rate** from prescription to shipment

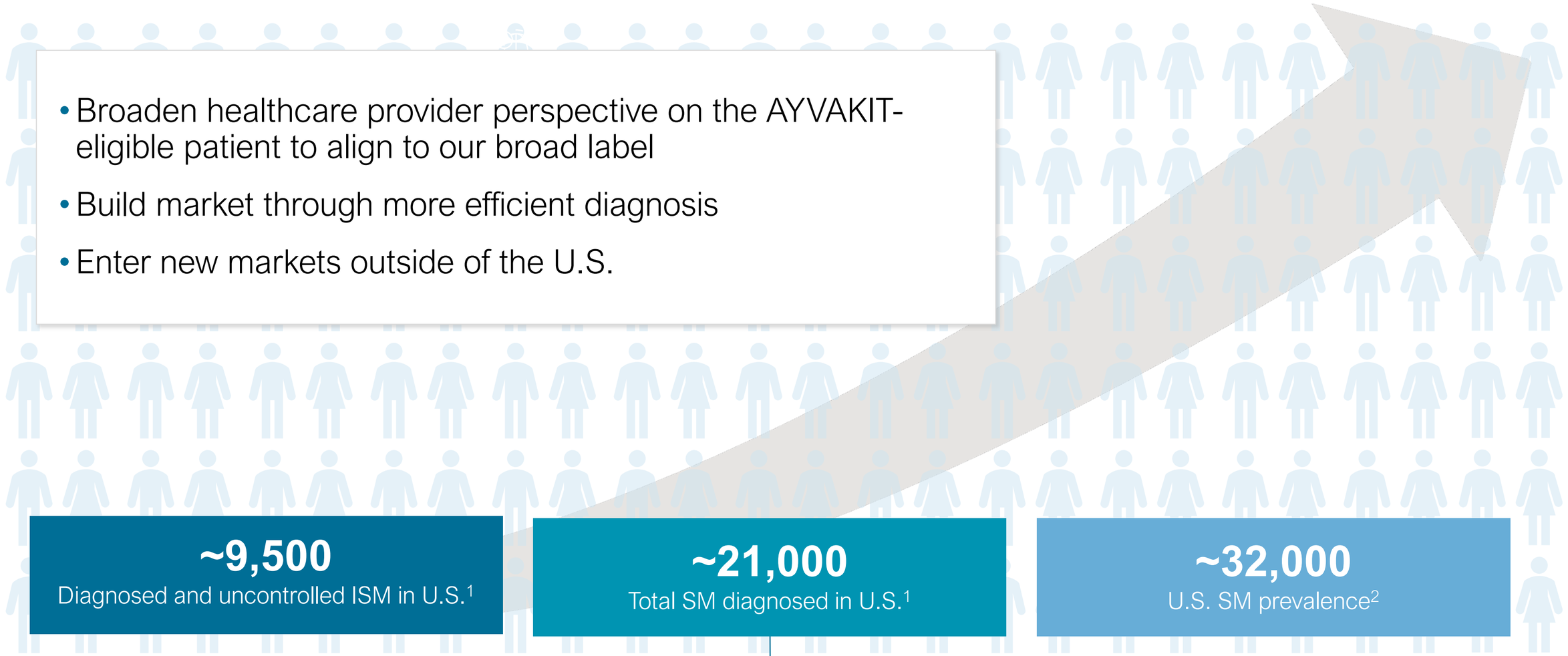
< 10 Days **time to fill** for majority of patients

>95% Percent of lives with **broad coverage to label**

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]

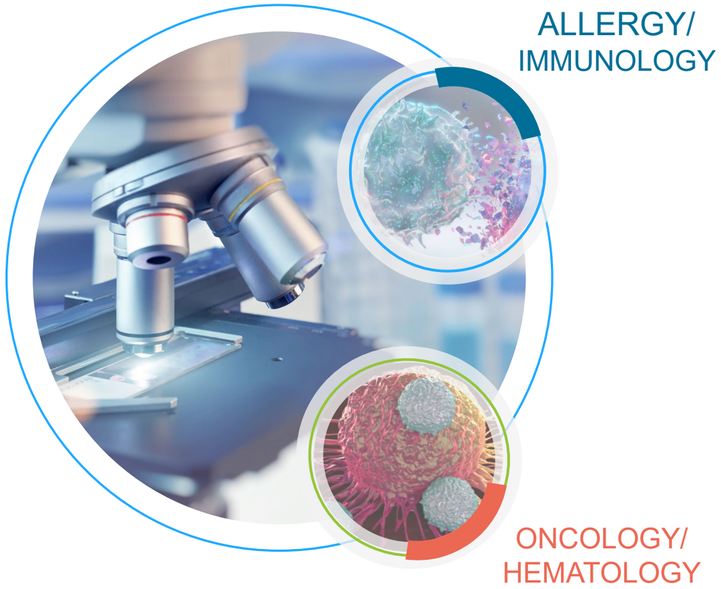
>20% YoY growth

~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

Maintaining Financial Strength

Building scale in two focused and exciting areas of science

Allergy/inflammation focus:

MAST CELL DISORDERS

Oncology focus:

SOLID TUMORS

PROGRAM	TARGET	DISCOVERY	CLINICAL	COMMERCIAL	RIGHTS
AYVAKIT® (avapritinib)[1]	KIT D816V	Indolent SM[2] Advanced SM[3]			Global excluding Greater China[4]
Elenestinib (next gen)	KIT D816V	Indolent SM			Global
BLU-808	Wild-type KIT	Chronic urticaria			
Additional undisclosed mast cell targets/modalities					
BLU-222	CDK2	HR+ / HER2- breast cancer Other CDK2 vulnerable cancers			Ongoing partnering discussions
BLU-956 (next gen)	CDK2	HR+ / HER2- breast cancer			
Targeted protein degrader	CDK2	HR+ / HER2- breast cancer			Global
Targeted protein degrader	Undisclosed				
Additional programs	Undisclosed				Global

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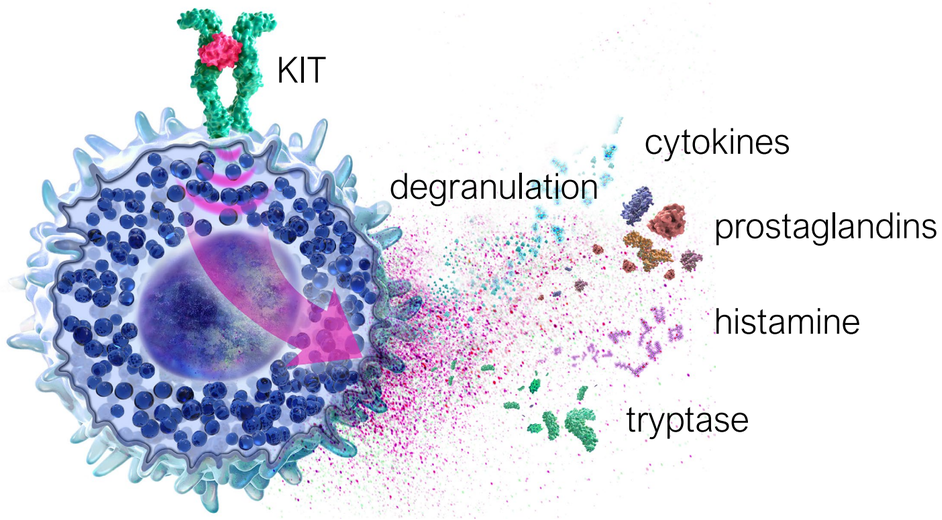
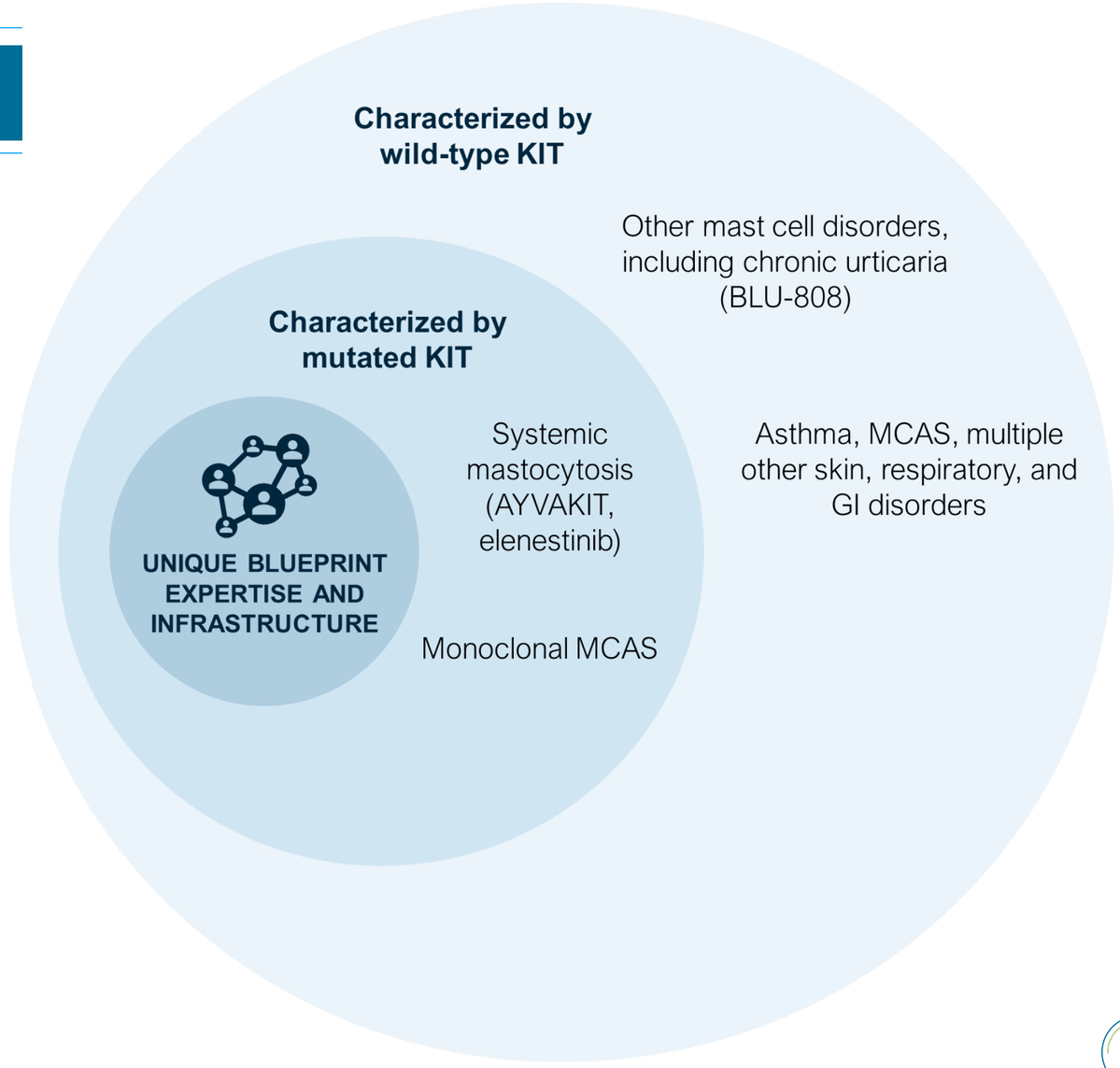
Mast cells are core drivers of biology in a range of inflammatory diseases

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

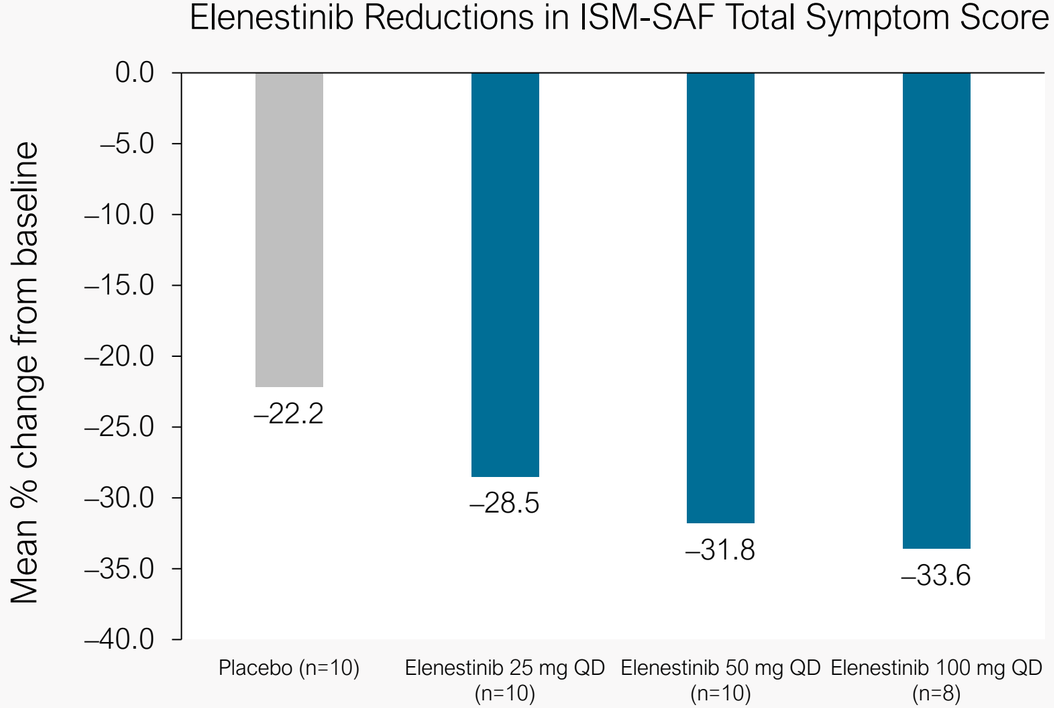


MCAS, mast cell activation syndrom; GI, gastrointestinal

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

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

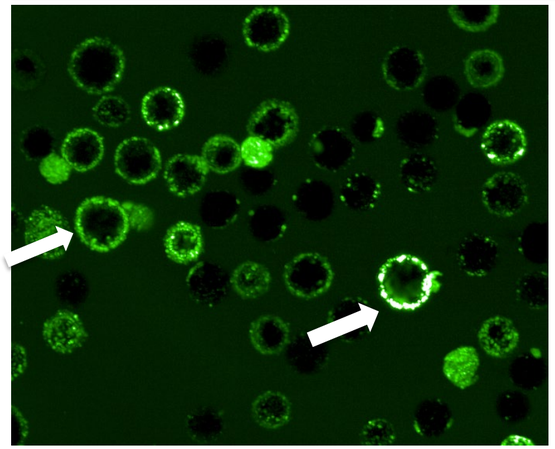


1. Tashi T. Et al. Presented at ASH 2023.

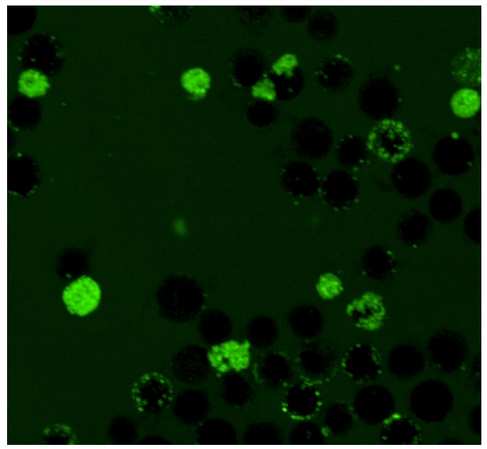
Wild-type KIT inhibitor BLU-808 has first- and best-in-class, pipeline in a pill potential

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

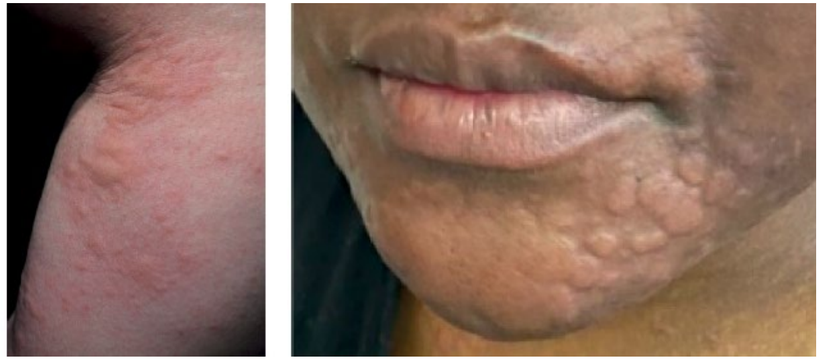


10 nM BLU-808

- 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 medical needs



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 burden and QoL impact due to itching, hives, swelling and related anxiety, sleep loss

~680K patients in US & EU4[1]

Unmet need for an oral therapy that targets core biology

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	RIGHTS
Allergy/inflammation focus: **MAST CELL DISORDERS**	AYVAKIT® (avapritinib)[1]	KIT D816V	Indolent SM[2] Advanced SM[3]			Global excluding Greater China[4]
	Elenestinib (next gen)	KIT D816V	Indolent SM			Global
	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			Ongoing partnering discussions
	BLU-956 (next gen)	CDK2	HR+ / HER2- breast cancer			
	Targeted protein degrader	CDK2	HR+ / HER2- breast cancer			Global
	Targeted protein degrader	Undisclosed				
	Additional programs	Undisclosed				Global

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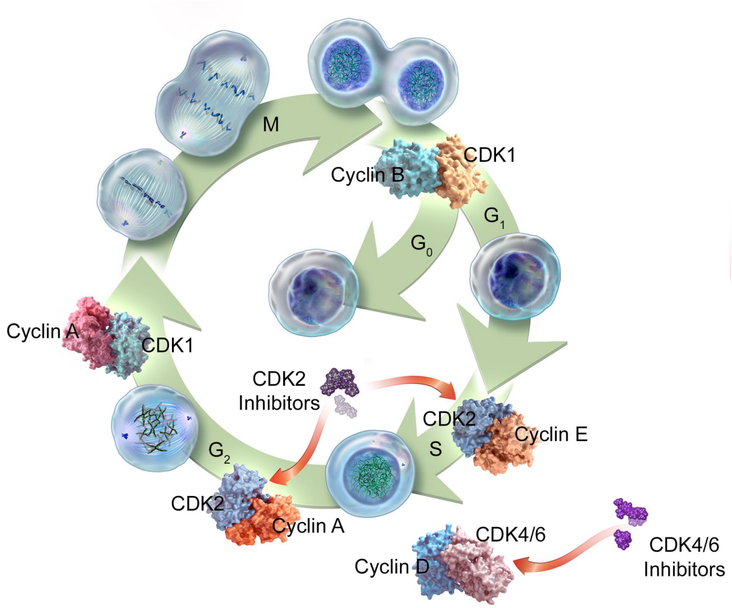
With BLU-222, we have solved the selectivity challenge of CDK2 inhibition

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 program to **drive value**

- Prevent and address CDK4/6 resistance as backbone of combination therapy
- Highly selective approach minimizing off-target toxicity to enable combination partner of choice
- Next-generation assets to maximize long-term value

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 of CDK2

	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: 300 mg BID)		
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 (neutropenia)		
HEMATOLOGIC TEAEs	**ALL**	**GR3**	**GR4**	**ALL**	**GR3**	**GR4**
• Anemia	29.6%	3.7%		45.7%	8.6%	
• Neutropenia	3.7%			28.6%	14.3%	2.9%
• Thrombocytopenia	3.7%	3.7%		20.0%	2.9%	

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

Maintaining Financial Strength

Durable capital position with a clear path to profitability

AYVAKIT is capturing a blockbuster opportunity in SM

AYVAKIT Annual Net Product Revenue ($M)

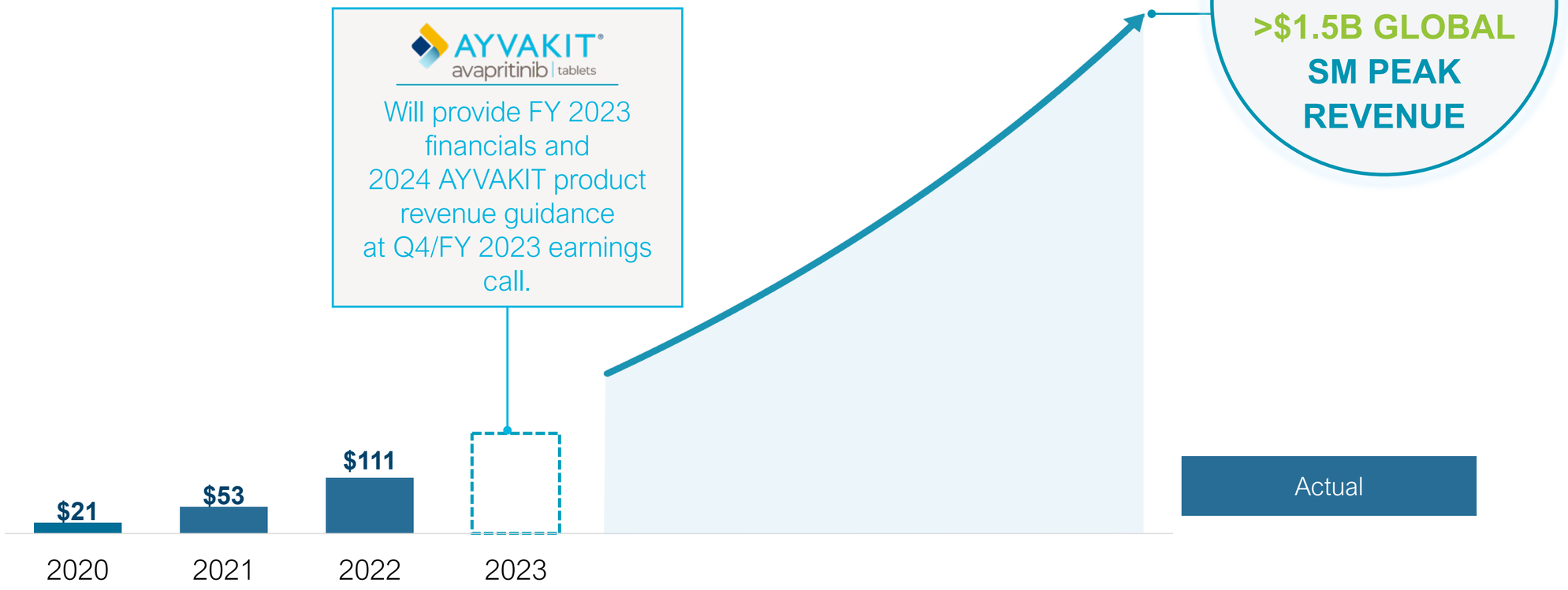


Figure is provided as a graphical representation and is not intended as financial guidance.

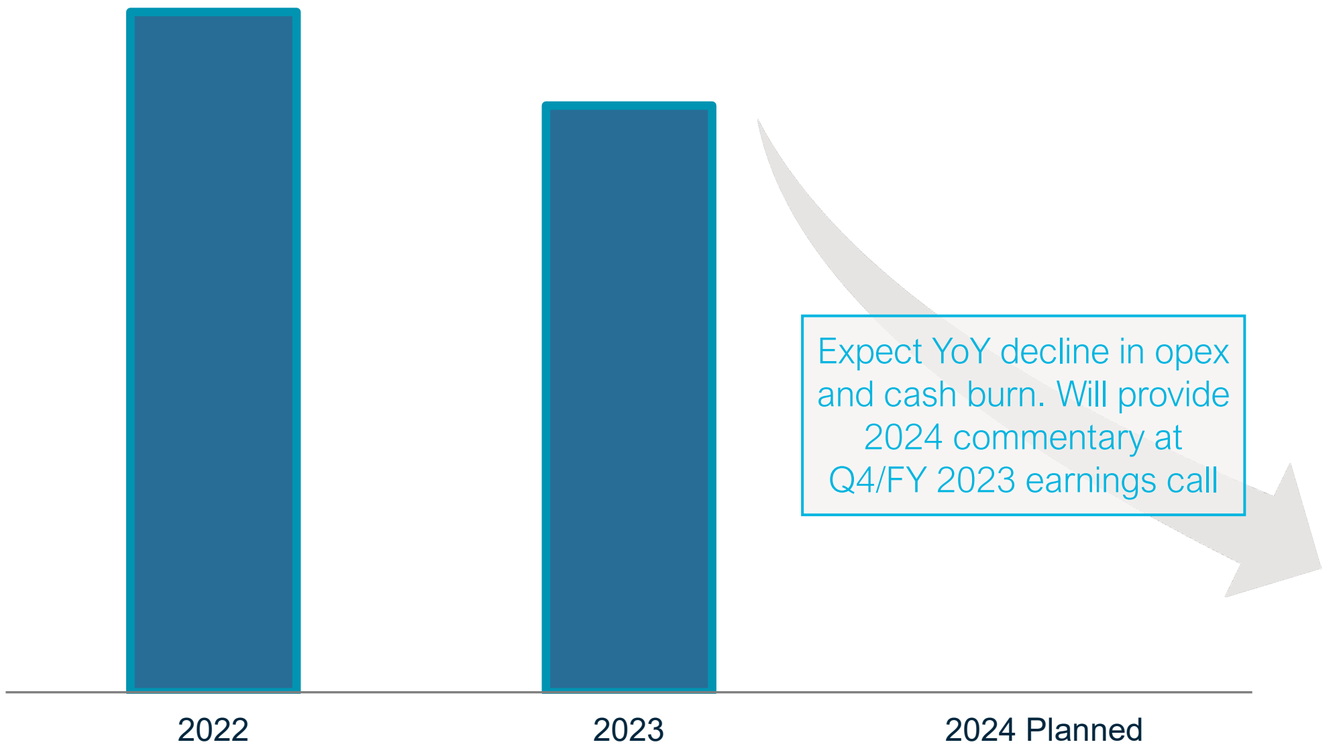
Portfolio prioritization driving continued operating expense reduction

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 Decline in 2024+



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 guidance.

Key anticipated portfolio milestones in 2024

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

Area	Program	Milestone	Timing
Mast cell disorders	AYVAKIT	Present long-term safety and efficacy data from PIONEER trial in ISM	1H 2024
	BLU-808	IND submission	2Q 2024
	Elenestinib	Initiate registration-enabling Part 2 of the HARBOR trial in ISM	2H 2024
Solid tumors	BLU-222	Present data in combination with ribociclib and fulvestrant for HR+/HER2- breast cancer	1H 2024
		Provide update on registration plan for HR+/HER2- breast cancer	2H 2024

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 biology and 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 capital position while also investing in opportunities for longer term growth.

Blueprint Medicines pipeline

Allergy/inflammation focus:

MAST CELL DISORDERS

Oncology focus:

SOLID TUMORS

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