Making Our Mission a Reality

CORPORATE DECK
NOVEMBER 2024

Adrianne Clinton
patient living with systemic mastocytosis

Forward-Looking Statements

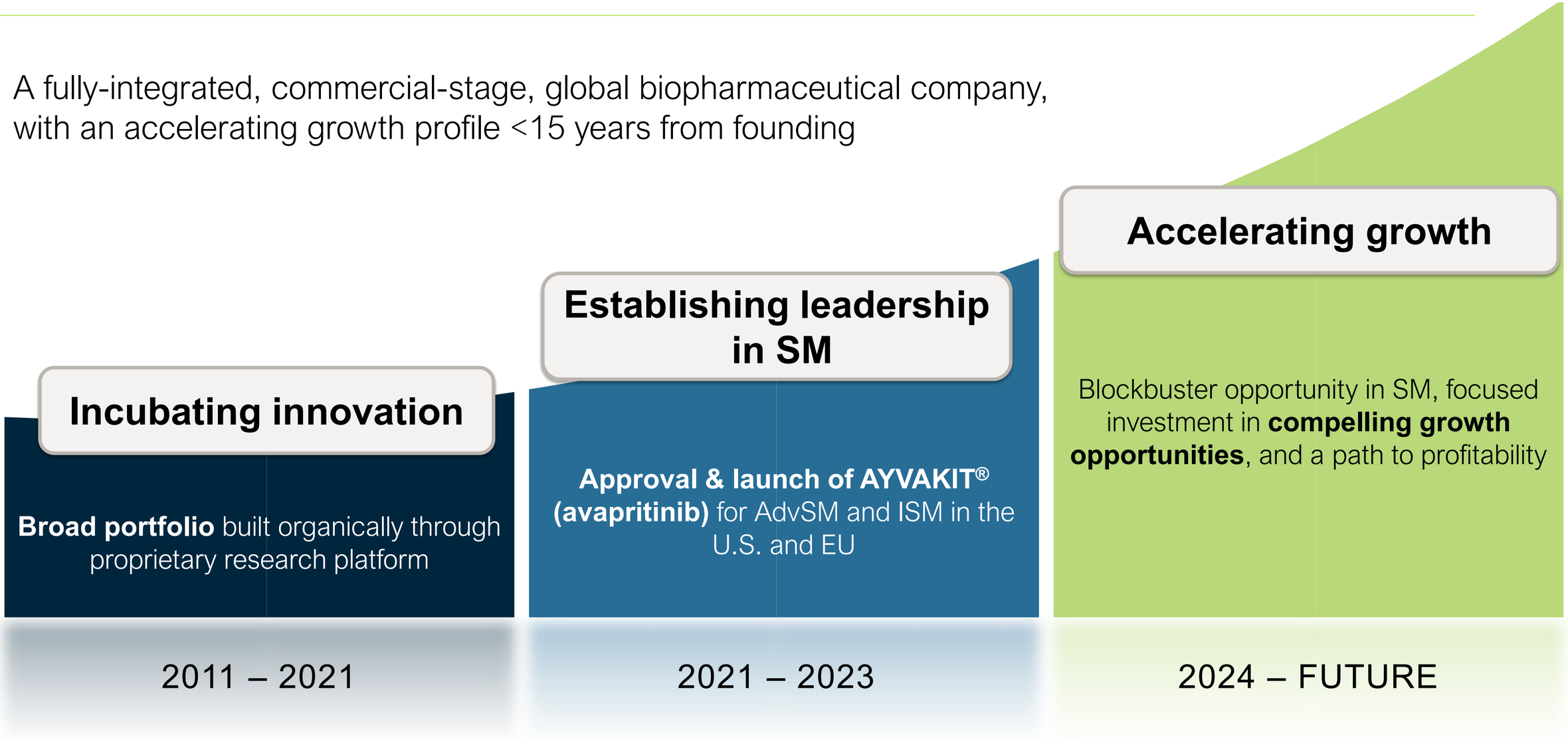
This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, strategies, timelines and expectations for the company's operations, including its growth strategies, opportunities and expectations for 2024 and beyond; the company's expectations regarding continued growth in the breadth and depth of prescribing for AYVAKIT; statements regarding the company's current or future approved drugs and drug candidates, including AYVAKIT's potential to achieve more than $2 billion in peak sales and to capture a blockbuster market opportunity in SM; the company's development plans and expectations regarding BLU-808, including its potential as a first- and best-in-class treatment for mast cell disorders, including chronic urticaria, as well as other potential related allergic-inflammatory indications; expectations related to the markets for the company's current or future approved drugs and drug candidates, including expectations regarding the size or scale of patient opportunities that its current or future approved drugs and drug candidates could address; the company's plans to initiate registration-enabling Part 2 of the HARBOR trial in ISM and to complete Phase 1 combination dose escalation for BLU-222 to inform registration plans, each in the second half of 2024; other plans and expectations for elenestinib, BLU-808, BLU-222 and the company's other current or future approved drugs and drug candidates, including timelines for clinical trials and regulatory submissions; the potential benefits of any of the company's current or future approved drugs or drug candidates in treating patients; statements related to the company's liquidity and capital position, product revenues, financial performance, strategy, goals and anticipated milestones, business plans and focus, including expectations regarding its revenue ramp, run-rate, continued decline in operating expenses and cash burn, and path to profitability.

The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "opportunity," "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 risk that the marketing and sale of AYVAKIT/ AYVAKYT or any future approved drugs may be unsuccessful or less successful than anticipated, or that AYVAKIT/ AYVAKYT may not gain market acceptance by physicians, patients, third-party payors and others in the medical community; the risk that the market opportunities for AYVAKIT/ AYVAKYT or the company's drug candidates are smaller than it estimates or that any approval it obtains may be based on a narrower definition of the patient population that it anticipates; the risk of delay of any current or planned clinical trials or the development of the company's current or future drug candidates; risks related to 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 risk that preclinical and clinical results for the company's 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 risk that 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; the risk that actions of regulatory agencies may affect the company's approved drugs or its current or future drug candidates, including affecting the initiation, timing and progress of clinical trials; risks related to the company's ability to obtain, maintain and enforce patent and other intellectual property protection for its products and current or future drug candidates it is developing; risks related to the success of the company's current and future collaborations, financing arrangements, partnerships, licensing and other arrangements; risks related to the company's liquidity and financial position, including the risk that it may be unable to generate sufficient future product revenues to maintain a self-sustainable financial profile and to achieve profitability; and risks related to the accuracy of the company's estimates of revenues, expenses and capital requirements. 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

Blueprint Medicines Q3 2024 highlights

Driving AYVAKIT® (avapritinib) Revenue Growth

Achieved $128.2M in AYVAKIT revenue in Q3, representing >135% YoY growth

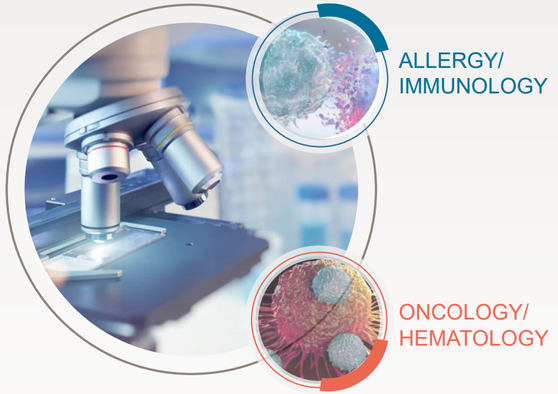
Raising AYVAKIT revenue guidance to **$475-$480M** for 2024

Continued strength across revenue drivers

Maintaining Financial Strength

Strong and **durable financial position** with $882.4M in cash

A financial profile that enables us to **invest sustainably in innovation**



Building a Synergistic R&D Portfolio

Leveraging **mast cell expertise** to expand R&D in allergy and inflammation

On track to initiate registration-enabling **HARBOR Part 2 study** of elenestinib in ISM by end of year 2024

Advancing BLU-808 HV study with data expected in early 2025

YoY, year-over year; R&D, research and development; HV, healthy volunteer; ISM, indolent systemic mastocytosis

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 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

Long-term safety to 25 months with no new safety signals, including at 50mg, presented at EAACI 2024

Range of Doses

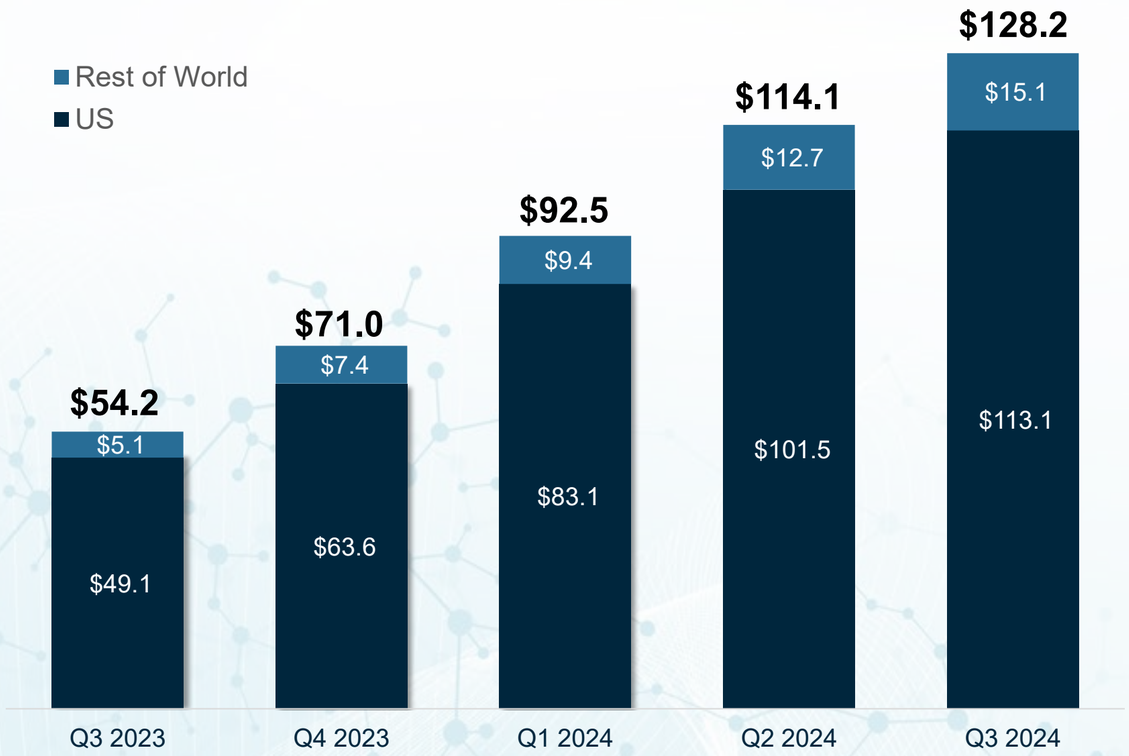
Multiple dose strengths meet the medical needs across a spectrum of SM patients

AYVAKIT®
avapritinib | tablets

1. Sabato et al, EAACI 2024

AYVAKIT revenue has grown more than 135% year-over-year

AYVAKIT Global Net Revenues ($, Millions)



AYVAKIT® avapritinib | tablets

Q3 highlights

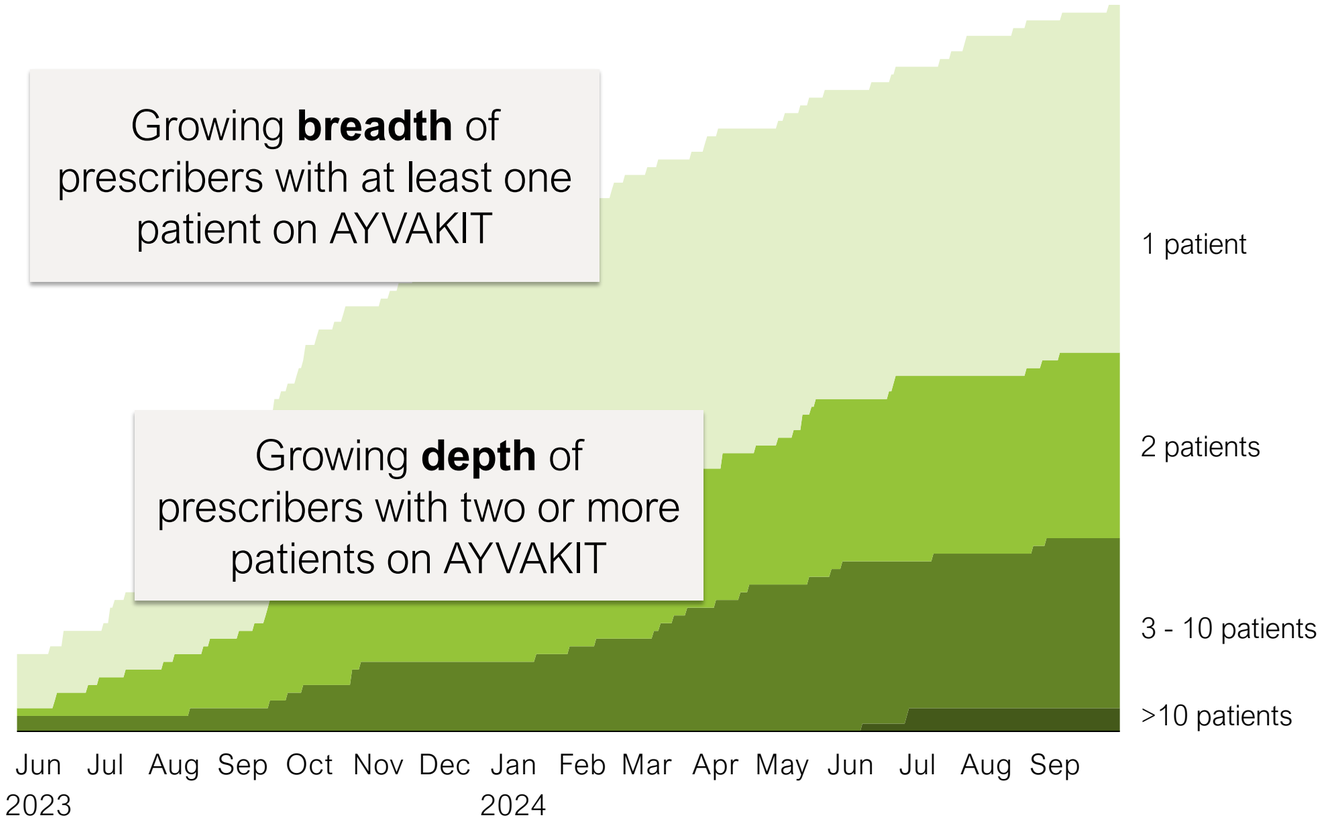
- Strong and steady growth in patients on therapy, driven by new patient starts and low discontinuation rates
- Continued high compliance
- Trend towards multi-year duration of therapy
- Free goods <20% since ISM approval
- Strong international performance, including ISM launch in Germany

AYVAKIT net product revenue guidance updated to $475-$480M for FY 2024

Total revenue may differ from United States plus Rest of World revenue due to rounding.

Driving breadth and depth with significant headroom for future growth

GROWING BREADTH AND DEPTH AMONG TOP 400 TREATERS BY SM PATIENT VOLUME

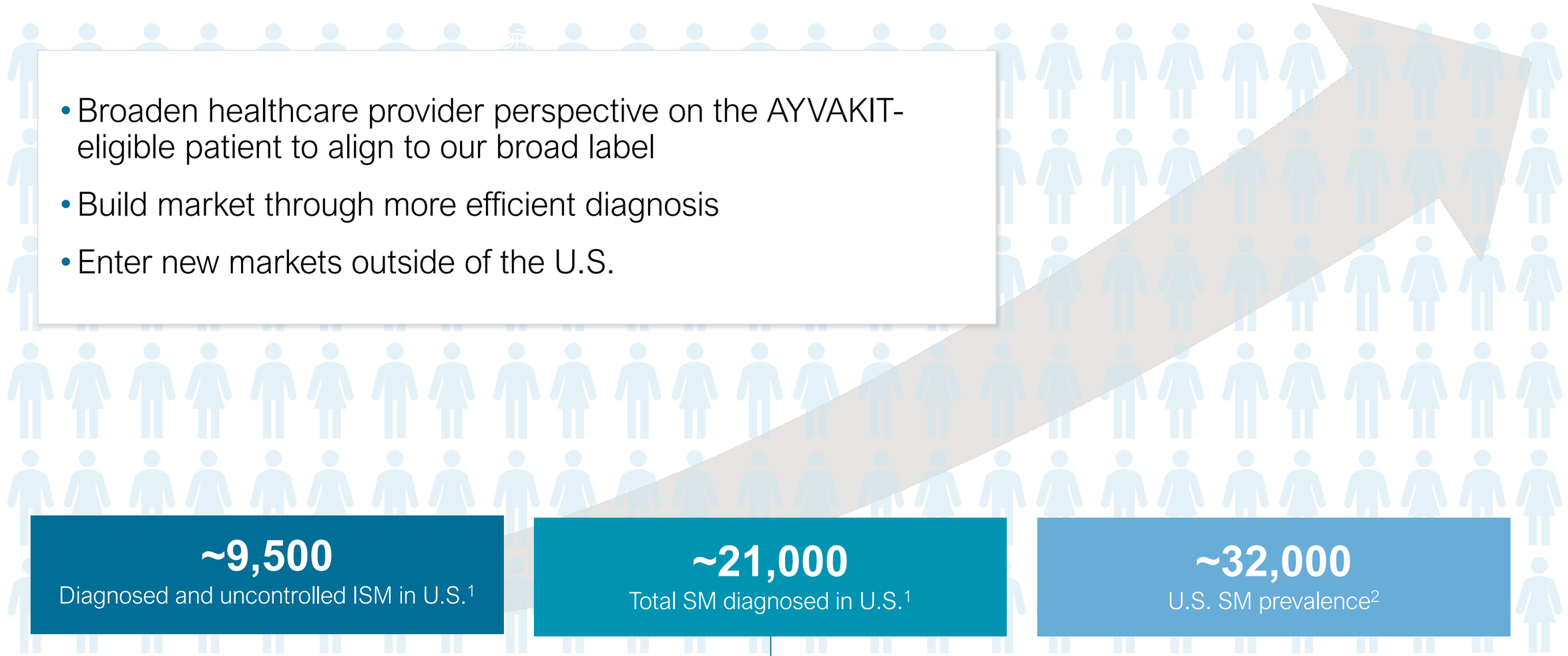


- ✓ Continued growth in breadth and depth of prescriber base, with **significant opportunity for expansion**
- ✓ Differential diagnosis from other diseases that share similar symptom burden, indicative of the **broadening aperture of who may be a candidate** for AYVAKIT
- ✓ Even split in community and academic prescribing, signaling **reach beyond centers of excellence**

1. Blueprint Medicines data on file. Cumulative 25 mg AYVAKIT prescribers within the top 400 targets since ISM approval in May 2023. Data based upon SP/HUB prescriptions which represent ~70% of total AYVAKIT volume in U.S.

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]

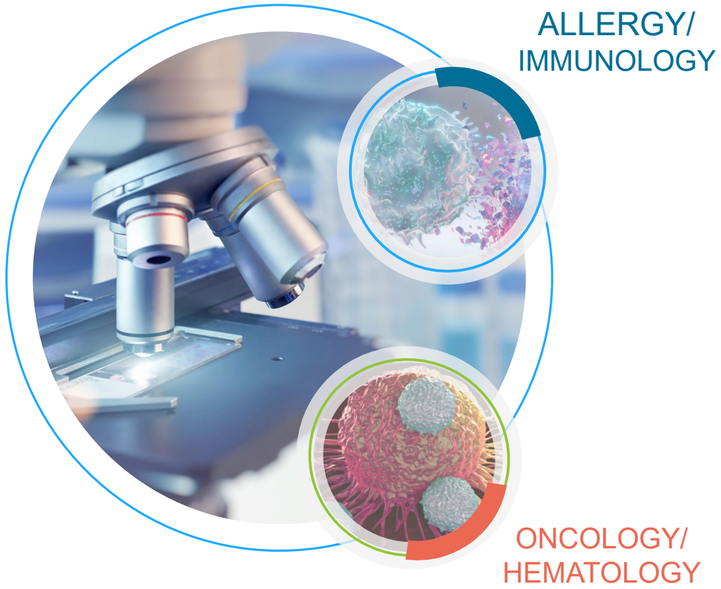
>20% YoY growth

~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

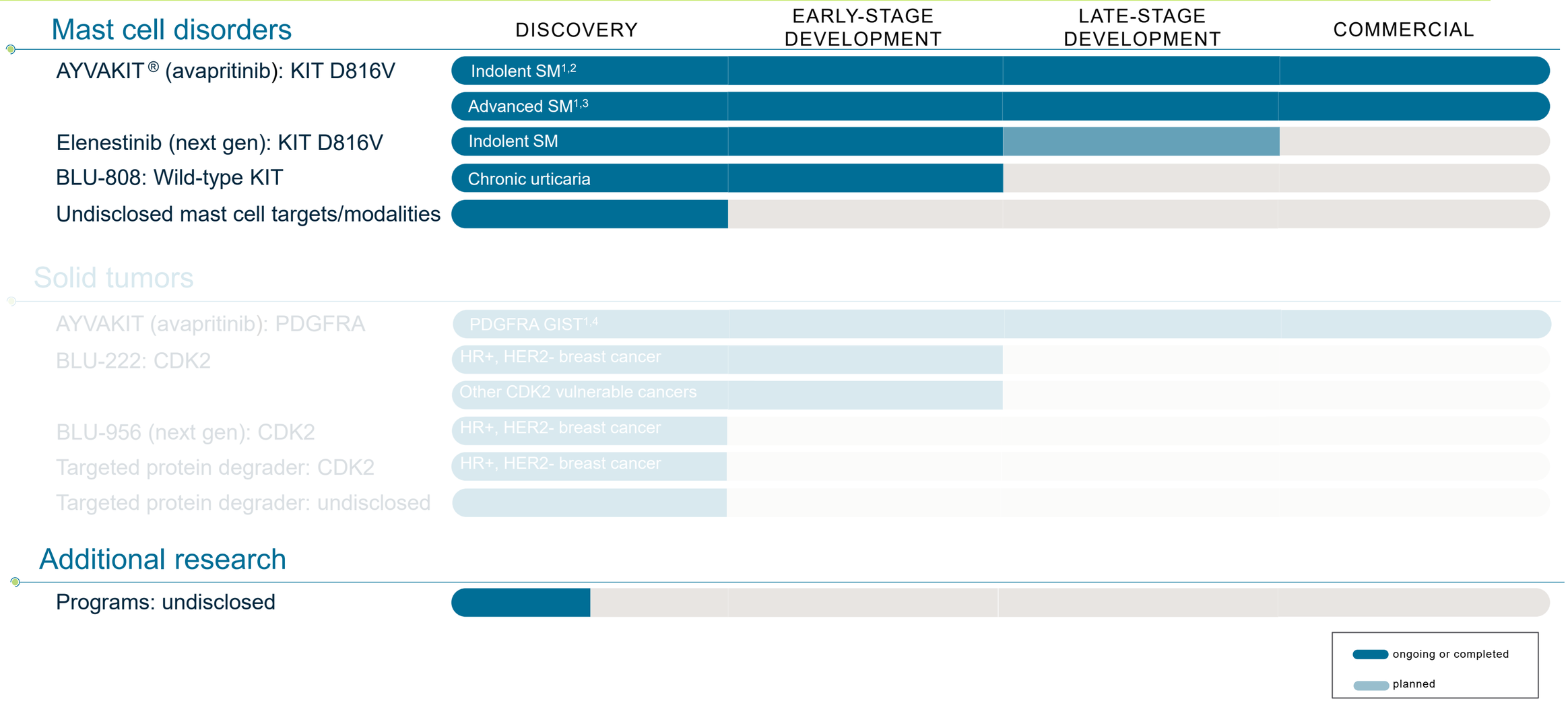


Investing in Sustainable Innovation

Focused investment to drive long-term growth

Maintaining Financial Strength

Blueprint Medicines pipeline



1. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib in Greater China. 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 advanced SM, including 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. 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 PDGFRA D842V mutation. GIST = gastrointestinal stromal tumors. SM = systemic mastocytosis.

Updated as of August 1, 2024.

Scientific leadership in KIT biology

MUTATED KIT

AYVAKIT® avapritinib | tablets

KIT D816V inhibitor
(Systemic mastocytosis)

IDRX-73*

KIT exon 13 inhibitor
(Gastrointestinal stromal tumor)

WILD-TYPE KIT

Elenestinib

Next-generation
KIT D816V inhibitor
(Systemic mastocytosis)

BLU-808

Wild-type KIT inhibitor
(Mast cell-mediated diseases)

1 approved and 3 clinical-stage highly selective and potent KIT inhibitors designed by Blueprint scientists

* IDRX-73, formerly known as BLU-654, was out-licensed to IDRx in 2022.

Growing mountain of data demonstrates commitment to community to advance understanding of SM disease and treatment

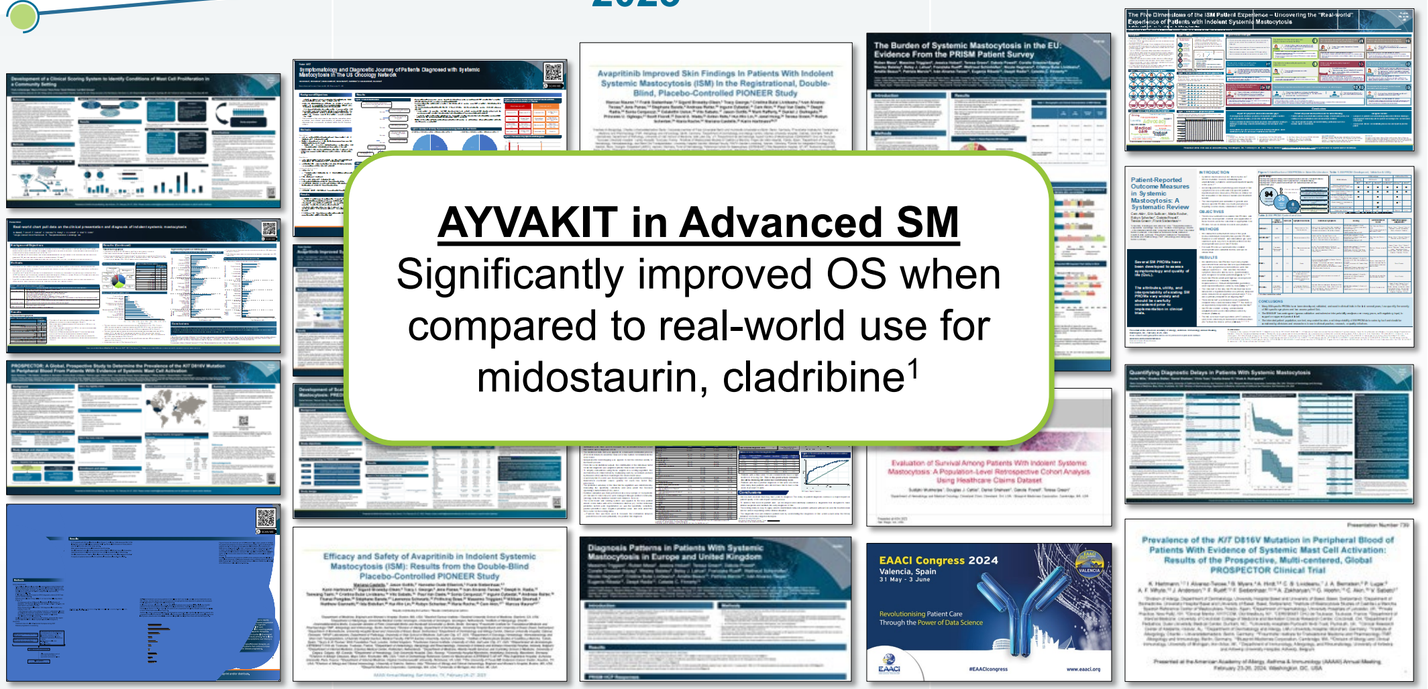
Pivotal PIONEER data for AYVAKIT in ISM

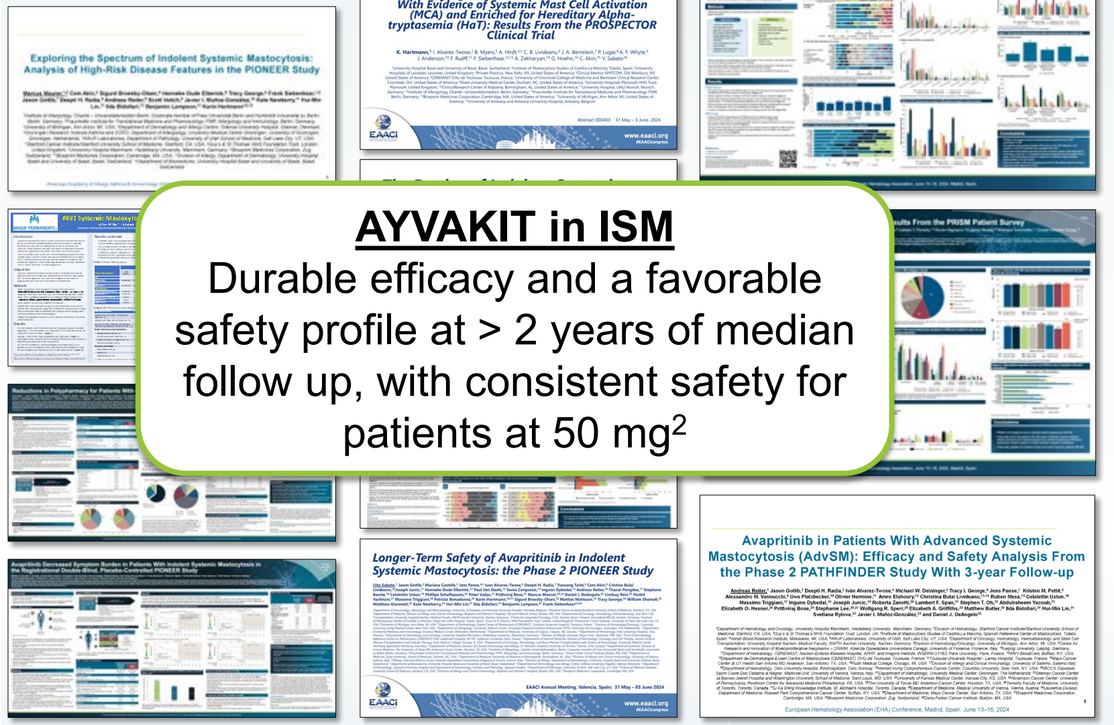
AYVAKIT ISM approval (US)

AYVAKYT ISM approval (EU)

Half-billion-dollar revenue run rate

Q1 Q2 Q3 Q4 **2023** Q1 Q2 Q3 **2024**





AYVAKIT in Advanced SM

Significantly improved OS when compared to real-world use for midostaurin, cladribine[1]

AYVAKIT in ISM

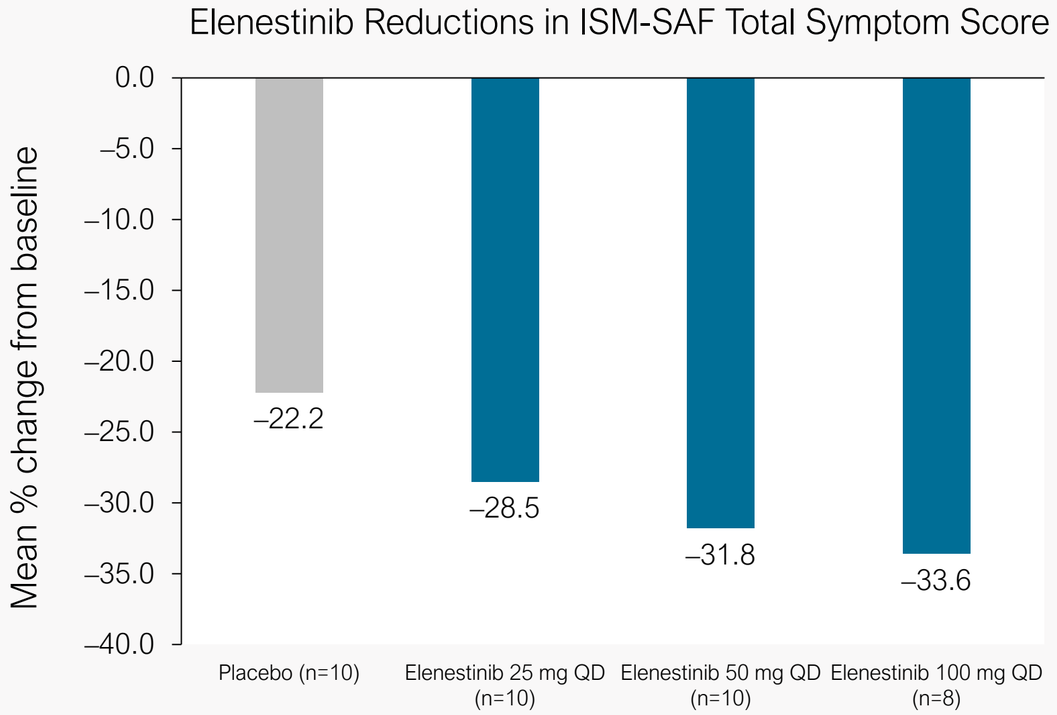
Durable efficacy and a favorable safety profile at > 2 years of median follow up, with consistent safety for patients at 50 mg[2]

1. Reiter et al. EHA Hybrid Congress, June 2022. 2. Sabato et al. EAACI Annual Meeting, June 2024.

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

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

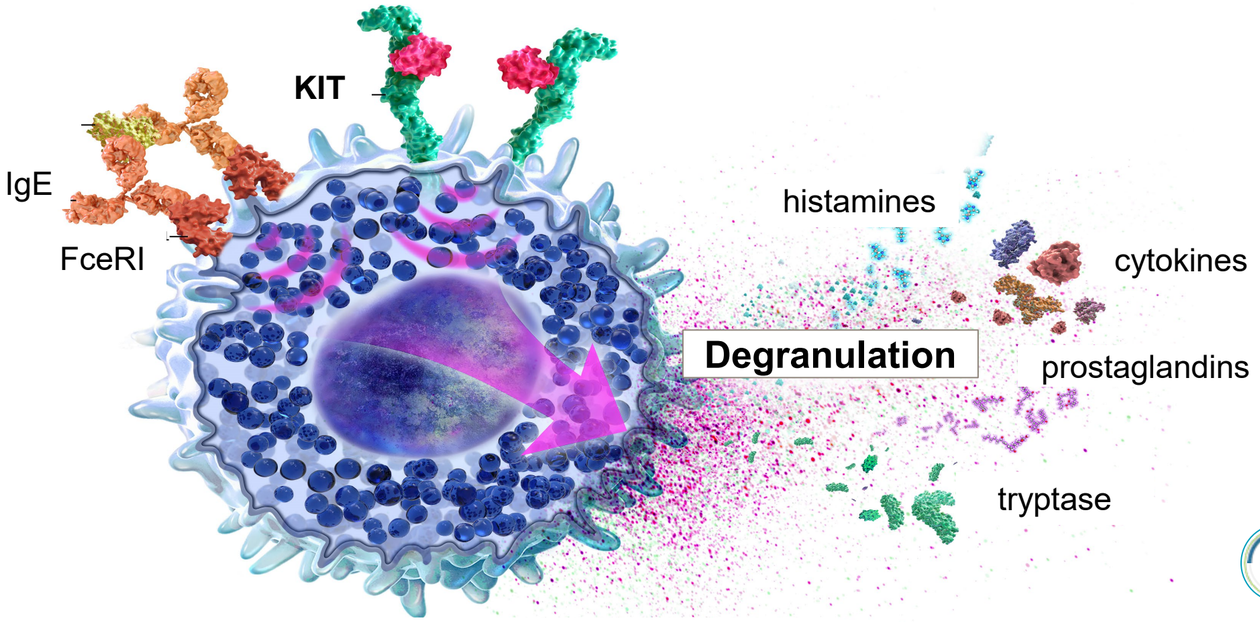
- **Well-tolerated** with no treatment discontinuations due to AEs; most AEs Grade 1/2
- **Improved disease-related symptoms** as assessed by the validated ISM-SAF
- Reduced multiple **biomarkers of mast cell burden**
- Robust clinical activity and favorable tolerability observed across doses



On track to initiate Part 2 of the HARBOR trial in ISM in 2H

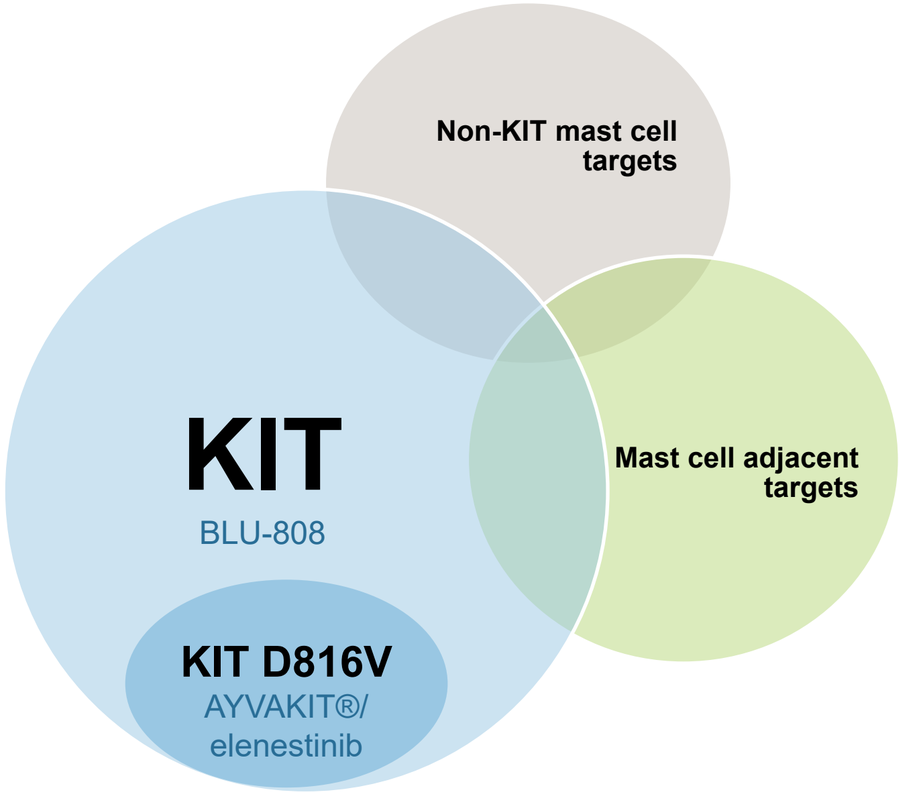
1. Tashi T. Et al. Presented at ASH 2023.

Mast cells are core drivers in a range of inflammatory diseases



Mast cell

- **Central effector cell** in many inflammatory diseases
- Activation leads to release of multiple classes of inflammatory molecules with a broad range of physiological effects
- KIT is a clinically validated **master control switch** for mast cells



- Monotherapy opportunities to inhibit wtKIT, a primary mast cell target
- Opportunities for novel regimens of combination approaches at intersections between therapeutic targets

Proprietary image; AVYAKIT® avapritinib

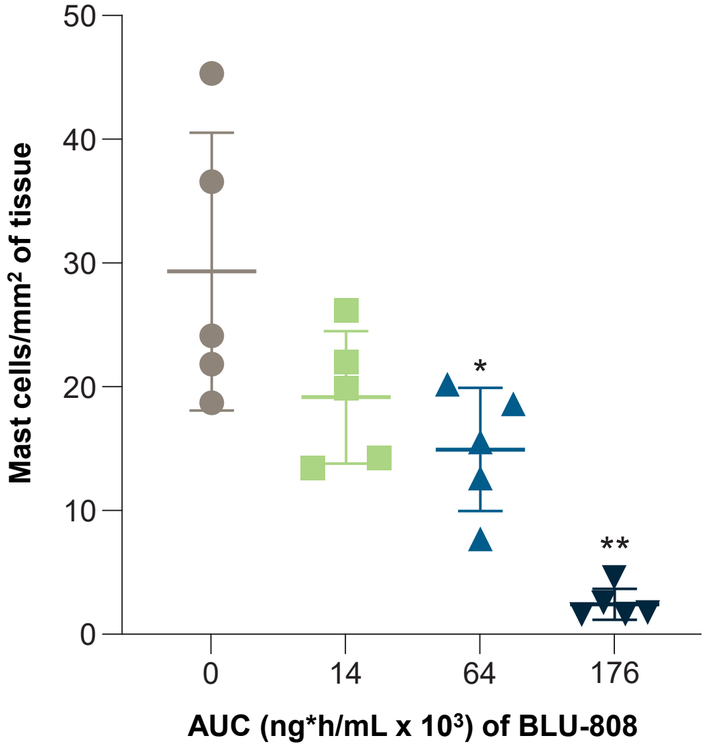
Wild-type KIT inhibitor BLU-808 has first- and best-in-class potential

	BLU-808
Potency	
pKIT cellular IC_{50} (nM)	0.37
WT KIT-dependent proliferation IC_{50} (nM)	1.3
Human-derived $CD34^+$ mast cells: inhibition of CD63 extracellular expression IC_{50} (nM)	2.7
Human-derived $CD34^+$ mast cells: inhibition of histamine degranulation IC_{50} (nM)	8.6
Selectivity	
S(10) @ 3 μM	0.042
PDGFRA / PDGFRB / FLT3 cellular selectivity[a]	>300x/>400x/>9600x
CSF1R Kd selectivity	>800x
Brain penetrance ($Kp_{u,u}$)	0.021
Preclinical PK supports once daily oral dosing	

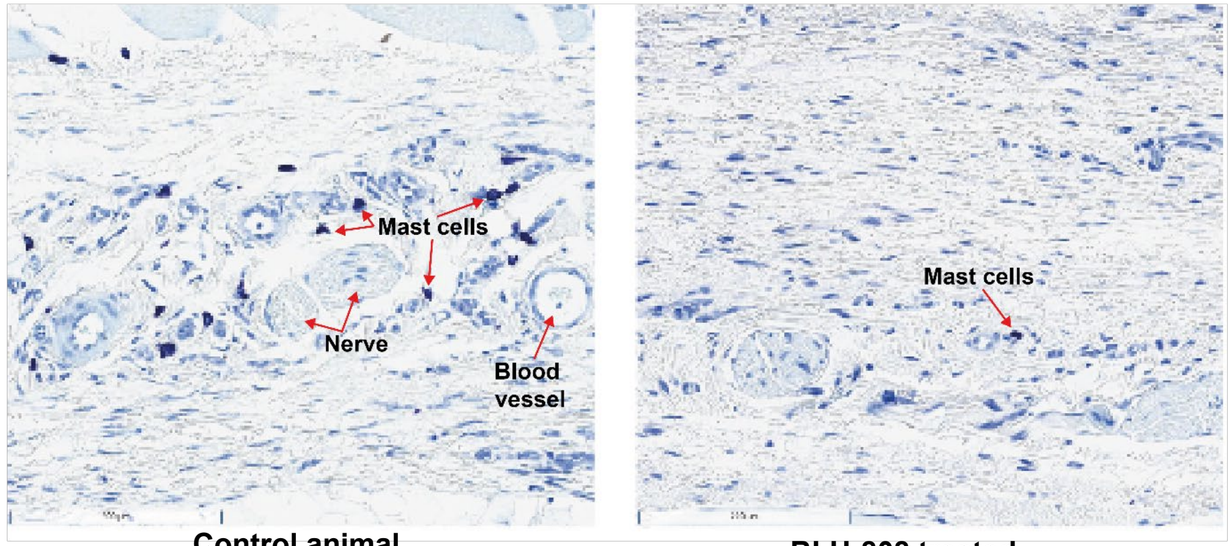
BLU-808 healthy volunteer study initiated

[a]Determined in a cellular assay. CSF1R, colony stimulating factor 1 receptor; FLT3, FMS-like tyrosine kinase 3; IC_{50}, half-maximal inhibitory concentration; PDGFRA/B, platelet-derived growth factor receptor alpha/beta; pKIT, phosphorylated KIT; S(10) @ 3 μM, selectivity score at a concentration of 3 μM; $Kp_{u,u}$, unbound brain to plasma partition

BLU-808 can decrease mast cells in an exposure-dependent manner



Total mast cell % reduction from control:	--	35%	49%	92%

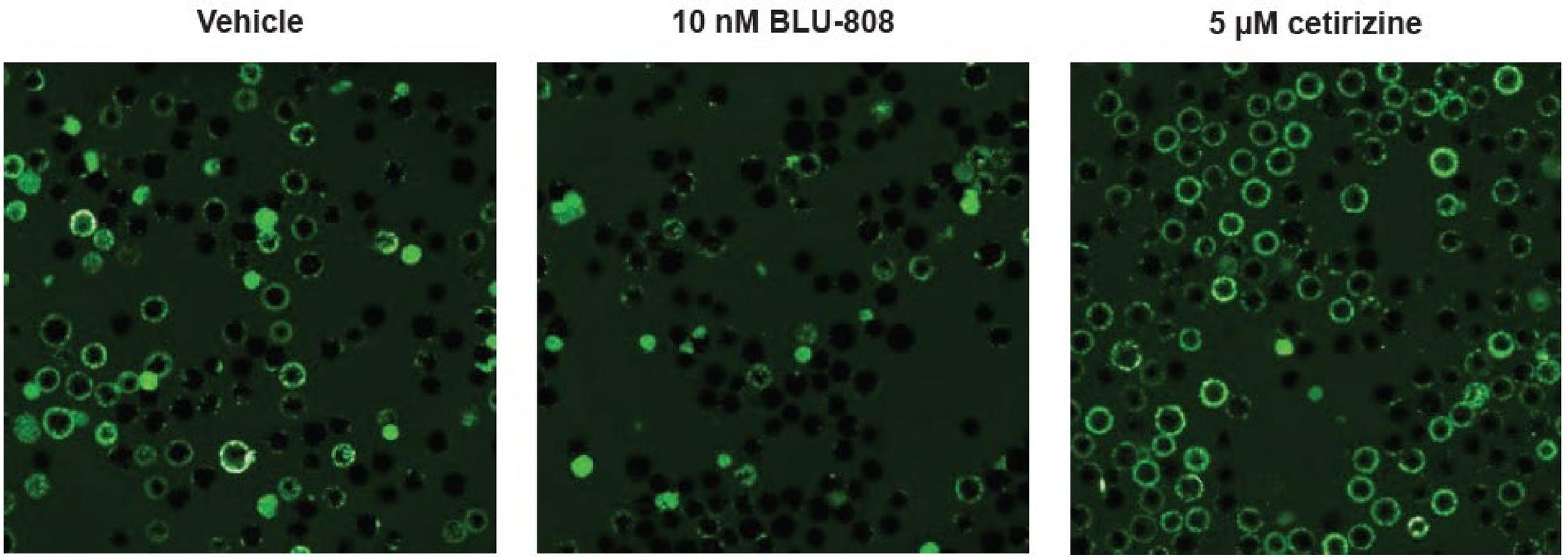


Haired skin: Subcutis at high magnification, toluidine blue staining

- BLU-808 was administered for 7 days at different specific doses in rats
- Mast cells were quantified by toluidine blue staining and showed a dose-dependent reduction
- *In vivo* data in mouse model of asthma also support dose-dependent response

Grassian, A et al, AAAAI 2024; AUC, area under curve. *, P<0.05; **, P<0.005; all per two-way analysis of variance with Tukey's correction for multiple comparisons. Horizontal lines represent mean and standard deviation.

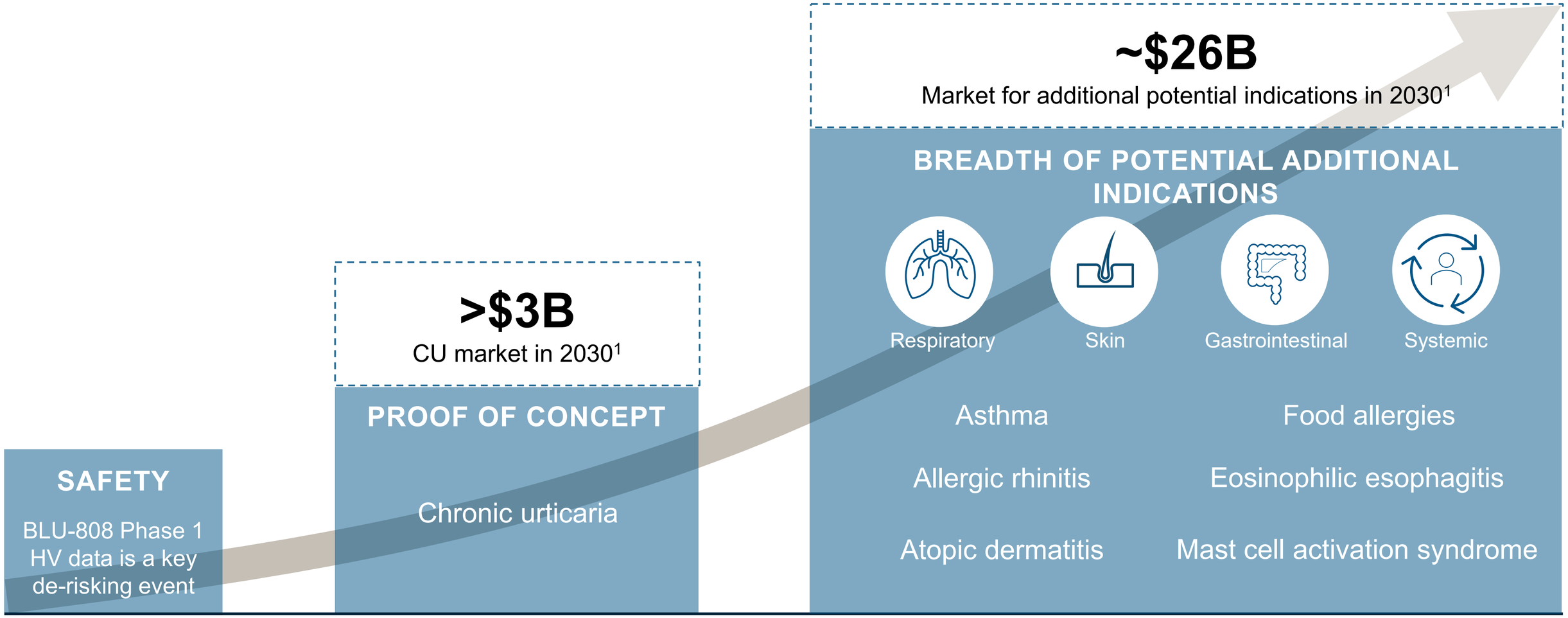
BLU-808 inhibits degranulation of human-derived CD34+ mast cells



- **BLU-808 targets the source of histamine and other mediators by preventing mast cell degranulation**
  - Mast cells were labeled in green to visualize degranulation. Following stimulation, the increase in green fluorescence indicated that degranulation occurred in mast cells treated with vehicle and 5 µM cetirizine, however BLU-808 inhibited degranulation, as shown by reduced fluorescence intensity.
  - Cetirizine, a control here, is an antihistamine that does not affect degranulation in mast cells at lower concentrations[1,2]

Grassian, A et al, AAAAI 2024; IgE, immunoglobulin E. 1. Church DS et al. *World Allergy Organ J*. 2011;4:S22–S27; 2. Fujimura R et al. *Drug Discov Ther*. 2022;16:245–250.

Mast cell diseases represent significant and growing market opportunity



1. Forecasted sales of approved therapies and projected approved therapies in listed indications in 2030, as reported by EvaluatePharma

On track to complete anticipated portfolio milestones in 2024

In addition to achieving **AYVAKIT revenue of $475-480M**, 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	☑
	BLU-808	IND submission	☑
	Elenestinib	Initiate registration-enabling Part 2 of the HARBOR trial in ISM	On track for EOY
Solid tumors	BLU-222	Present data in combination with ribociclib and fulvestrant for HR+/HER2- breast cancer	☑
		Complete Phase 1 combination dose escalation for BLU-222 by end of year to inform registration plans.	On track for EOY

- Expect to present data from the healthy volunteer study of BLU-808, our oral wild-type KIT inhibitor for chronic urticaria and other mast cell diseases, in early 2025

ISM, indolent systemic mastocytosis; IND, investigational new drug; EOY, end of year

Three key growth drivers in 2024

Capturing a Blockbuster Opportunity

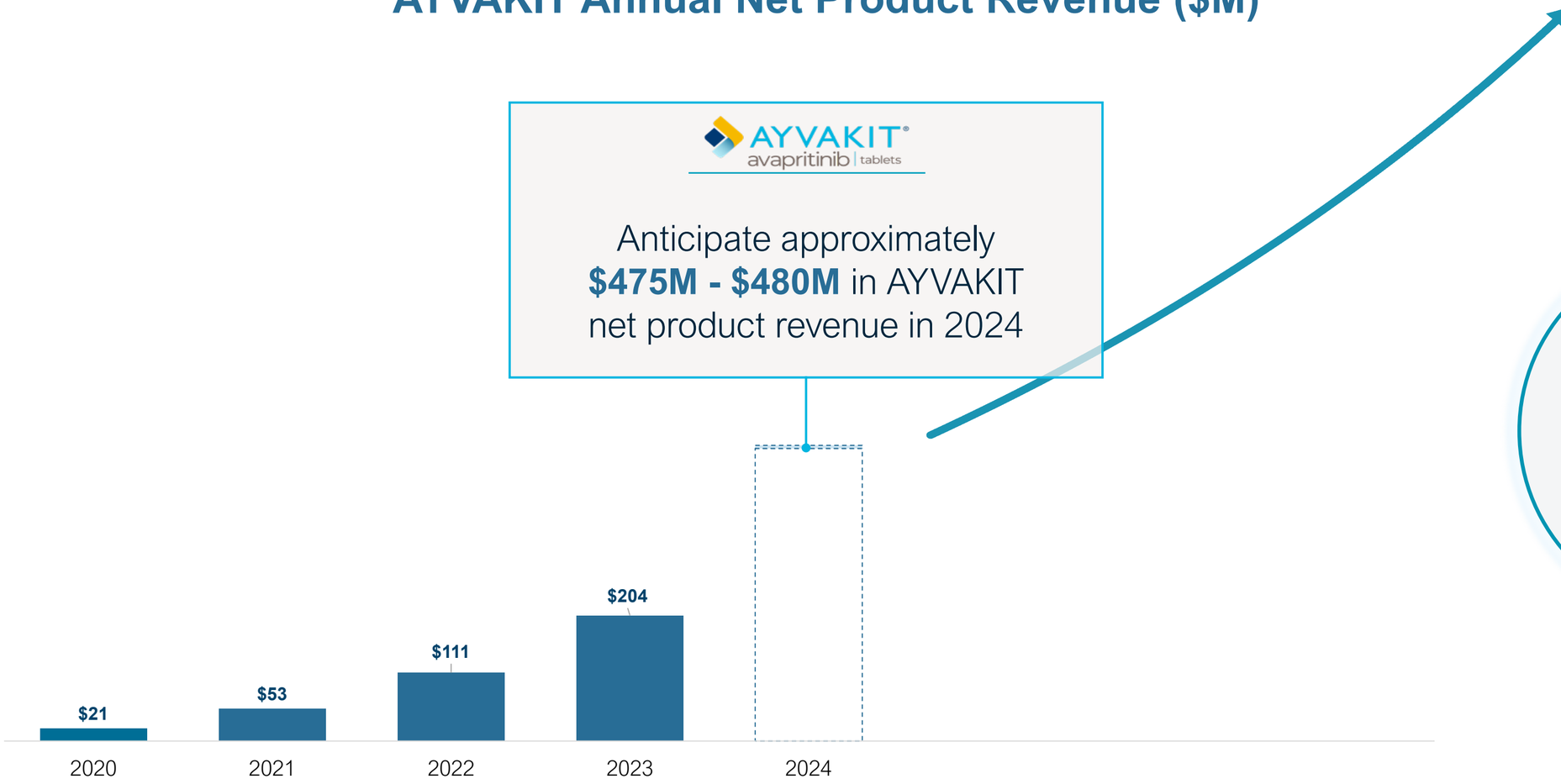
Investing in Sustainable Innovation

Maintaining Financial Strength

Durable capital position with a clear path to profitability

AYVAKIT is now on a half-billion-dollar run-rate

AYVAKIT Annual Net Product Revenue ($M)



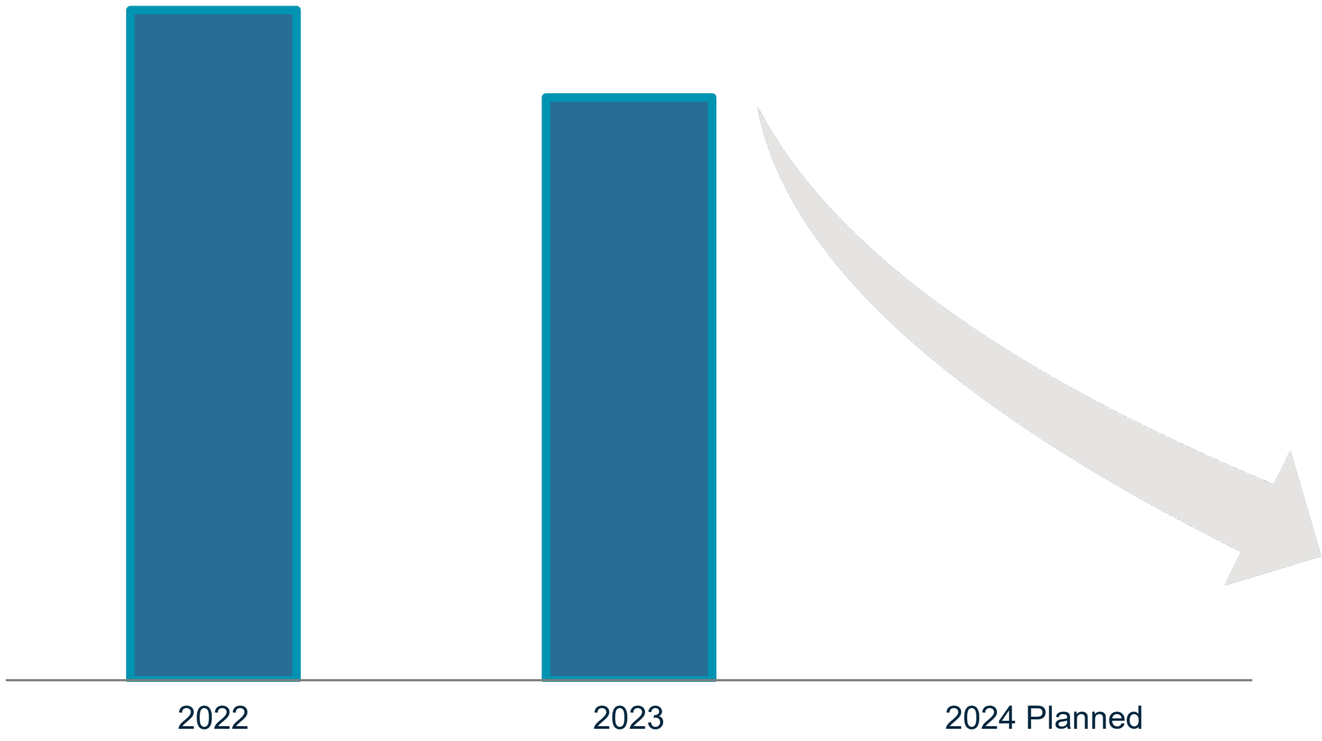
ESTIMATED ~$2B GLOBAL SM PEAK REVENUE

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

Expect operating expenses and cash burn will continue to decline in 2024

- Anticipate **$475 - $480 million in 2024** AYVAKIT revenue on path to **blockbuster opportunity**
- Prioritized capital allocation and continued **reduction in R&D opex**
- **Increasing SG&A operating leverage** from commercial infrastructure
- **Declining cash burn** and durable capital position on **path to profitability**

Operating Cash Burn Will Continue to Decline in 2024+



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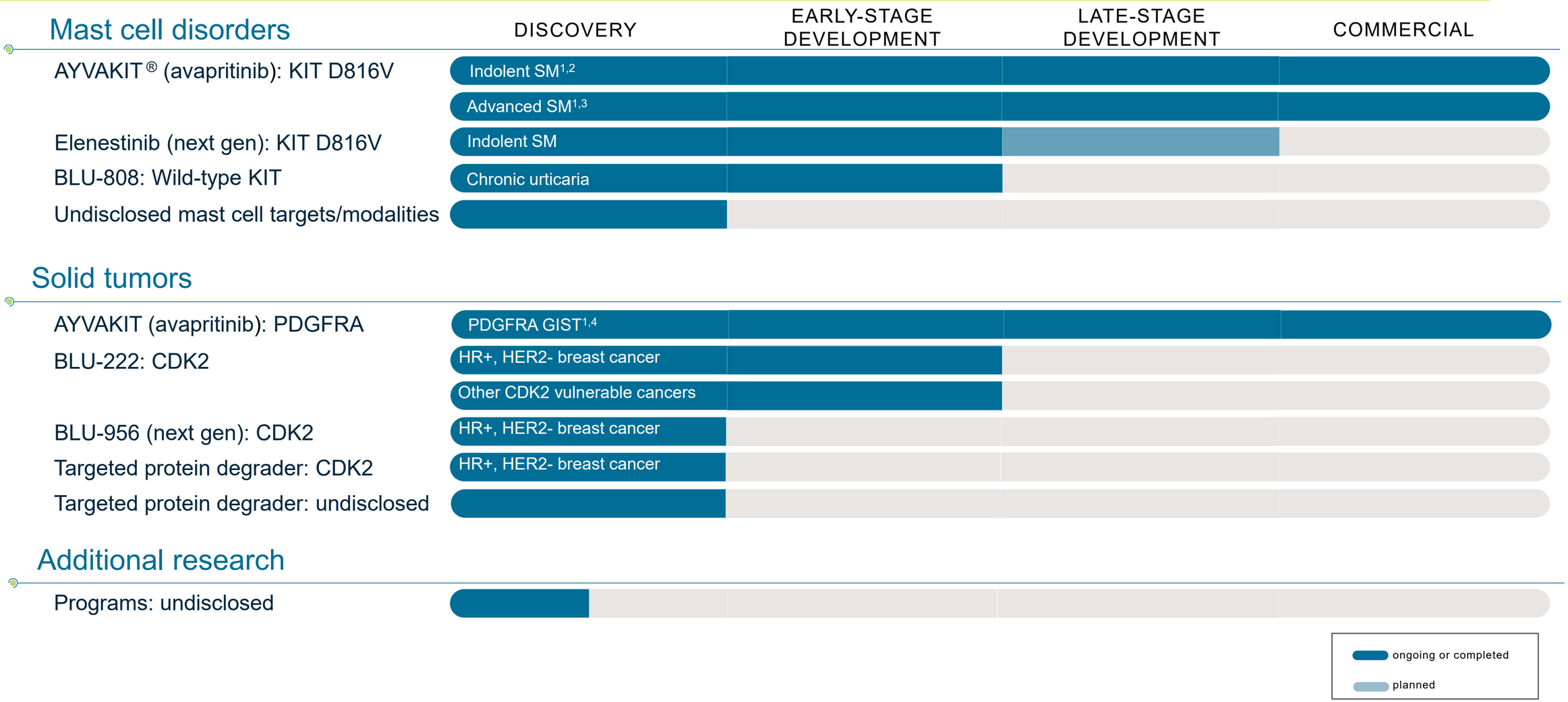
Blueprint positioned to accelerate our business growth in 2024 and beyond

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 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



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Updated as of August 1, 2024.