Blueprint Medicines

Driving growth and innovation with operational excellence

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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 2025 and beyond; the company's expectations regarding its estimated peak revenue for AYVAKIT and the systemic mastocytosis market; continued growth in the breadth and depth of prescribing for AYVAKIT; the company's development plans and expectations regarding BLU-808, including its potential treatment for mast cell disorders, 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; statements regarding anticipated clinical milestones; 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, run-rate, financial performance, strategy, goals and anticipated milestones, business plans and focus, including expectations regarding its 2025 capital allocation strategy, its anticipated 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.

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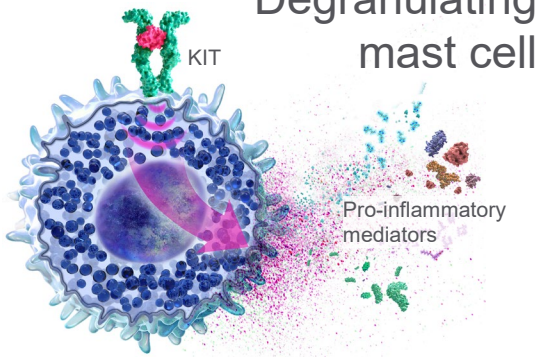
Targeting the mast cell to fundamentally change the treatment of allergic and inflammatory diseases

Degranulating mast cell

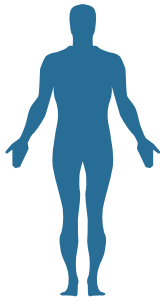


AYVAKIT® avapritinib | tablets

+

elenestinib

BLU-808, oral wtKIT inhibitor for mast cell diseases



- Skin
- Respiratory
- Gastrointestinal
- Systemic

Clinical-stage therapy with multibillion-dollar pipeline-in-a-product potential

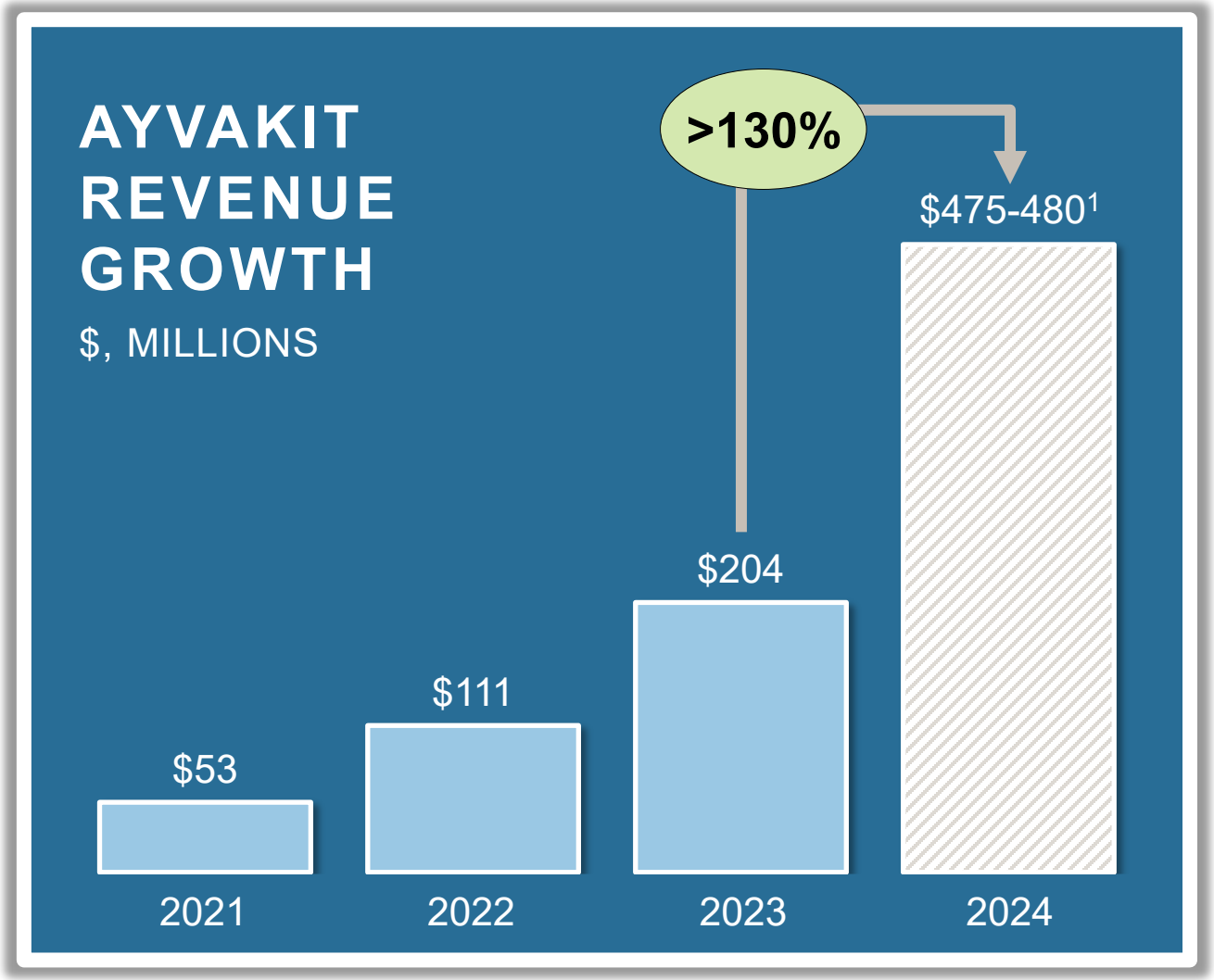
$4B estimated peak systemic mastocytosis franchise revenue

$2B estimated AYVAKIT revenue by 2030

Nearly 15 years of scientific leadership in mast cell biology

wtKIT, wild-type KIT.

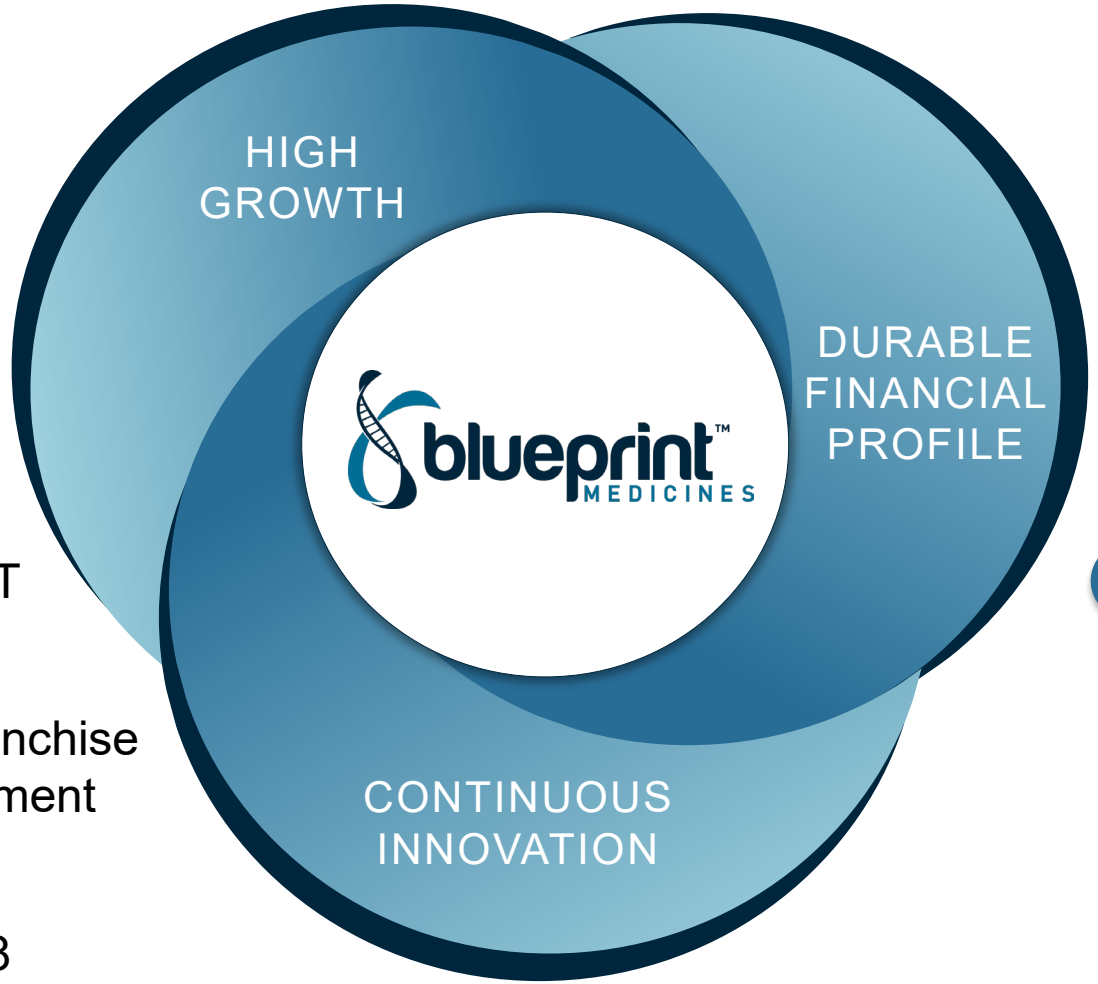
Looking back at a year of achievement in 2024



- Achieved inflection in AYVAKIT revenue toward multibillion-dollar peak potential
- Expanded global reach with AYVAKYT® reimbursed in 15 countries to date
- Initiated registrational Phase 3 study of elenestinib in ISM
- Submitted BLU-808 IND to FDA and completed healthy volunteer trial
- Strengthened financial profile, with >50% reduction in anticipated cash burn[1]

[1] Based on 2024 revenue guidance. Plan to report Q4 and full-year 2024 financial results in February 2025. FDA, U.S. Food and Drug Administration; IND, investigational new drug application; ISM, indolent systemic mastocytosis.

Our core growth drivers in 2025



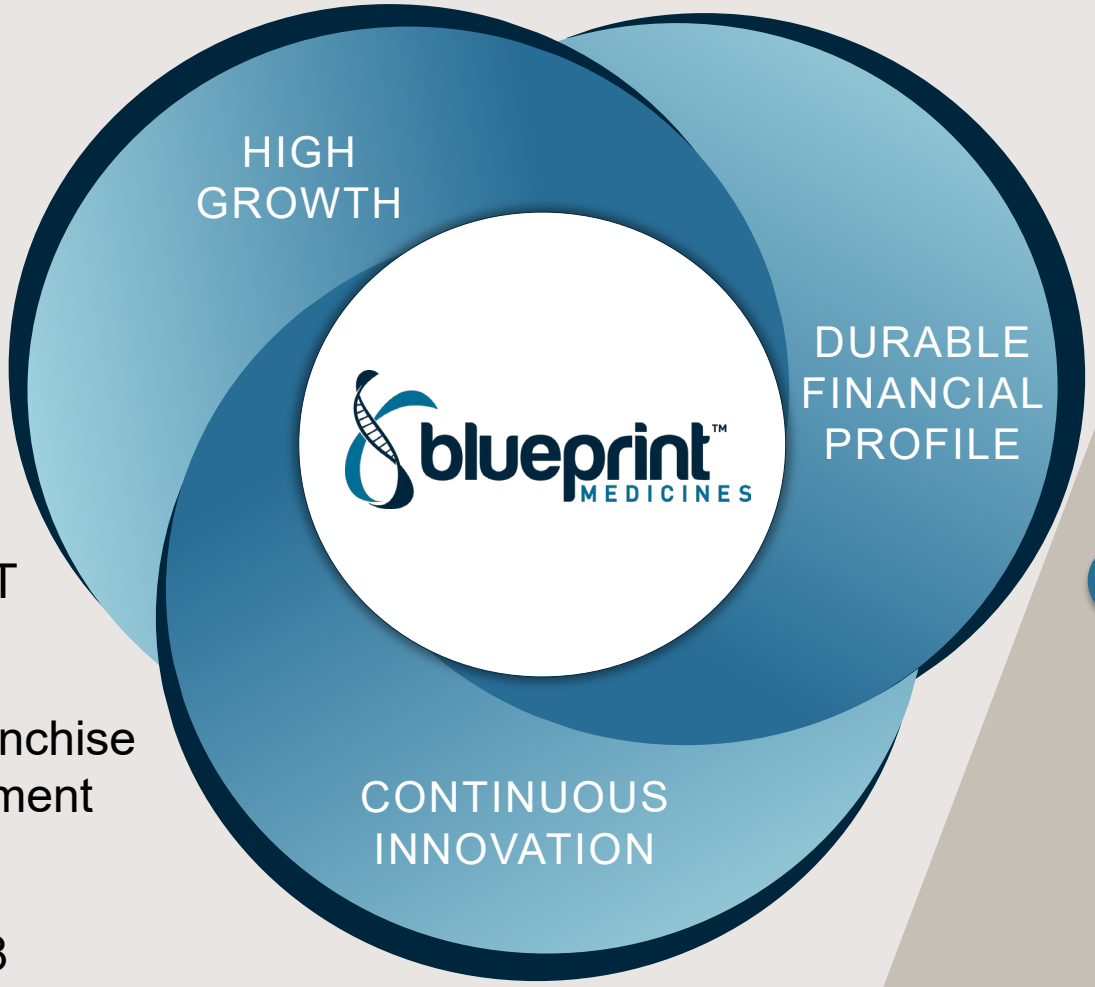
- Drive continued AYVAKIT revenue growth
- Extend long-term SM franchise with elenestinib development
- Accelerate and expand development of BLU-808
- Advance R&D innovation to fuel long-term growth

SM, systemic mastocytosis.

Our capital allocation strategy aligns with core growth drivers

80%

2025 capital allocation



- Drive continued AYVAKIT revenue growth
- Extend long-term SM franchise with elenestinib development
- Accelerate and expand development of BLU-808

- Advance R&D innovation to fuel long-term growth

20%

2025 capital allocation

SM, systemic mastocytosis.

We’re hearing life-changing stories with AYVAKIT

“I think it was just the hope to be done with all this sort of cumbersome palliative care.

I just wanted to feel better.

The goal for me was to start cutting out all that stuff from my life and get back to living.

Sometimes I reflect now and think wow. I feel way better than I did before.

AYVAKIT streamlines and simplifies my life and plans.”

– Andrew, AYVAKIT patient

Systemic mastocytosis is a fast-growing rare disease market

LARGE, GROWING MARKET OPPORTUNITY

Increase in diagnosed SM patients

- ~25K patients observable in U.S. claims data today[1]

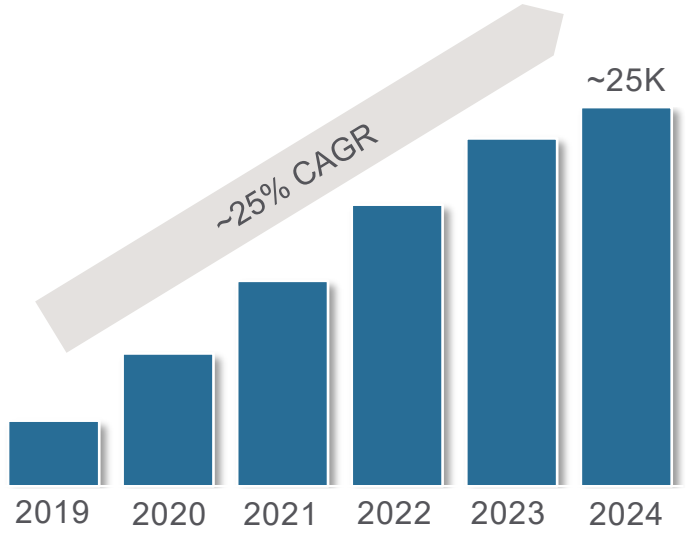
Widening lens on who is an AYVAKIT patient

- Supported by growing body of long-term safety & efficacy data

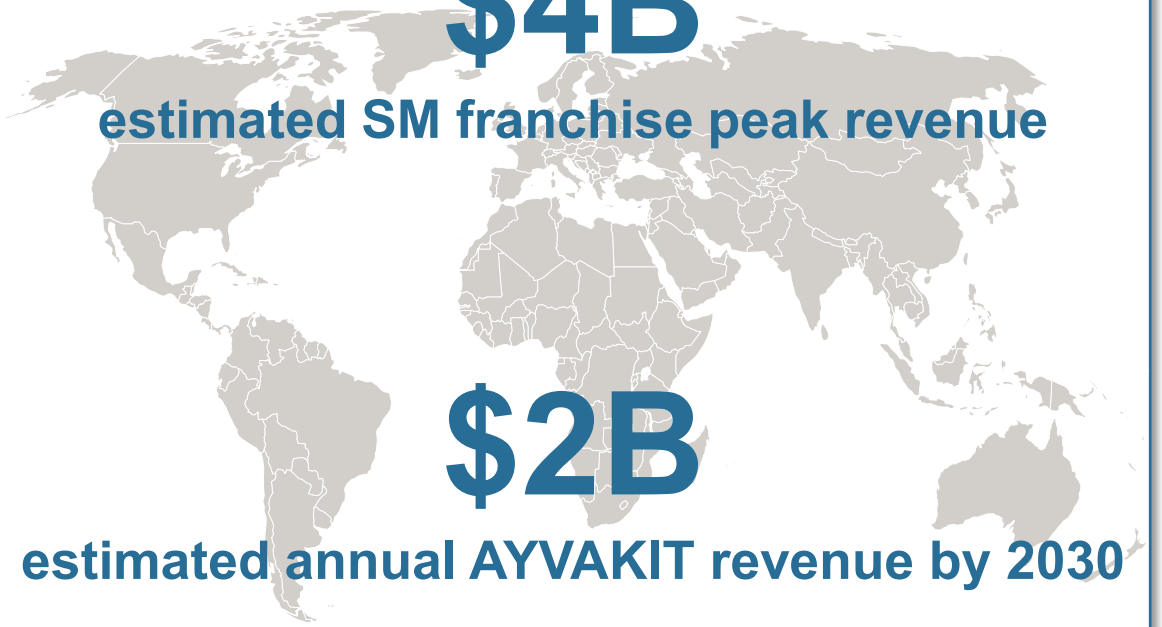
Higher estimated SM prevalence

- 2x prior estimate, based on recent large independent study[2]

OBSERVABLE SM PATIENTS IN U.S. CLAIMS DATA[1]



GLOBAL SM REVENUE POTENTIAL



$4B

estimated SM franchise peak revenue

$2B

estimated annual AYVAKIT revenue by 2030

[1] Internal Blueprint Medicines analyses of U.S. claims data. [2] Bergstrom et al; Acta Oncologica (2024). CAGR, compound annual growth rate.

Building off AYVAKIT's strong launch to drive growth to peak

STRONG LAUNCH (TODAY)

- Strong and steady new patient starts
- Significant, growing number of patients on AYVAKIT
- Trend toward multi-year duration of therapy
- Growing breadth and depth of prescribing in hem/onc and A/I specialties
- Robust payer coverage and fast time to fill

PEAK POTENTIAL (FUTURE)

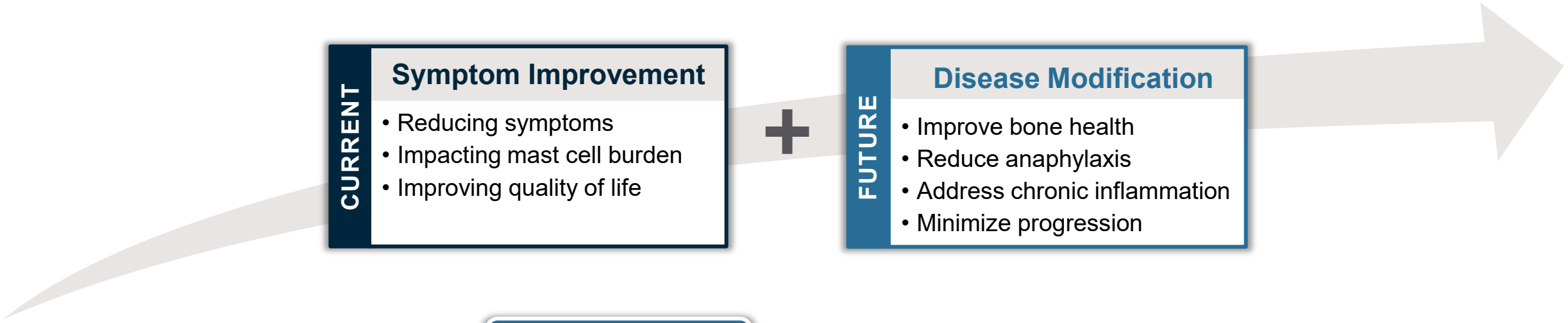
- Reach a wider group of providers and specialties, including derm and GI
- Optimized diagnosis and care championed by an empowered global SM community
- More patients activated to seek out AYVAKIT
- Disease control redefined with long-term data on AYVAKIT and real-world SM burden
- Continued global geographic expansion

Planned 2025 investments

- Incremental field force expansion
- New HCP and patient initiatives
- Additional data generation

A/I, allergy/immunology; derm, dermatology; GI, gastroenterology; HCP, healthcare provider; hem/onc, hematology/oncology.

Driving innovation with elenestinib to extend SM franchise lifecycle



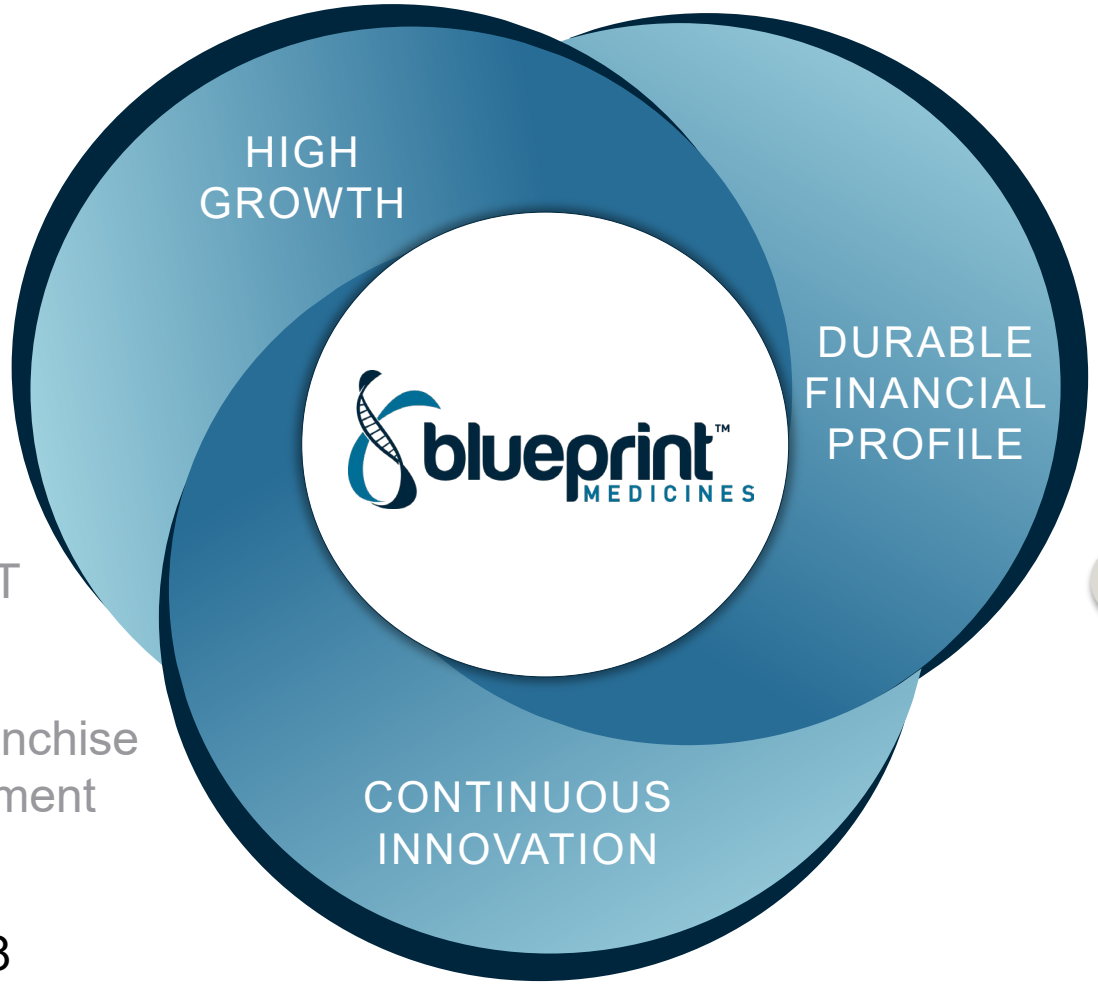
HARBOR Registrational Trial of elenestinib, a next-gen KIT D816V inhibitor, in patients with ISM

Primary endpoint	Mean change in ISM-SAF TSS from baseline, leveraging AYVAKIT precedent
Novel endpoints	Reduction in anaphylaxis frequency, improvement in bone health, additional biomarkers
Multiple doses	Two active arms, 75 & 100 mg elenestinib selected based on Part 1 data, versus placebo

Registrational Phase 3 HARBOR trial initiated in Q4 2024

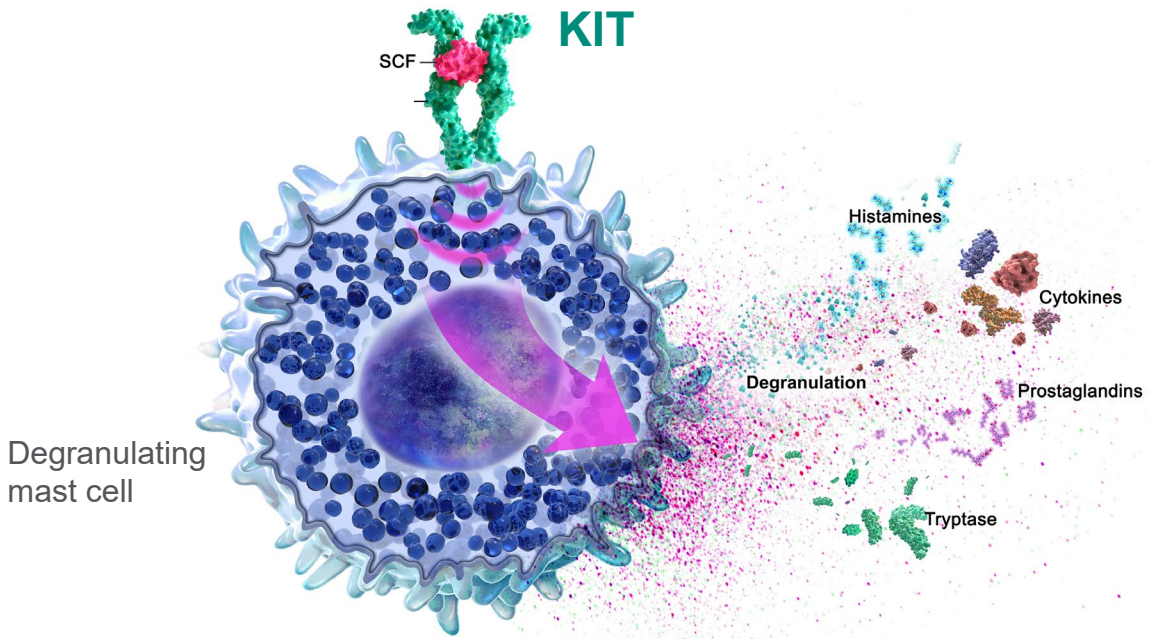
ISM-SAF, indolent systemic mastocytosis symptom assessment form. TSS, total symptom score.

Our core growth drivers in 2025



- Drive continued AYVAKIT revenue growth
- Extend long-term SM franchise with elenestinib development
- **Accelerate and expand development of BLU-808**
- Advance R&D innovation to fuel long-term growth

BLU-808 targets wild-type KIT (wtKIT), the master regulator of the mast cell



VALIDATED TARGET

- KIT is the **master regulator** of mast cell activity
- Activation **triggers an inflammatory response** and broad symptomology
- Inhibition proven to have therapeutic effects

UNMET NEED

- **Highly potent and selective oral wtKIT inhibitor**
- **Once-daily** dosing
- **Wide therapeutic index** enabling tunable approach to optimize benefit-risk

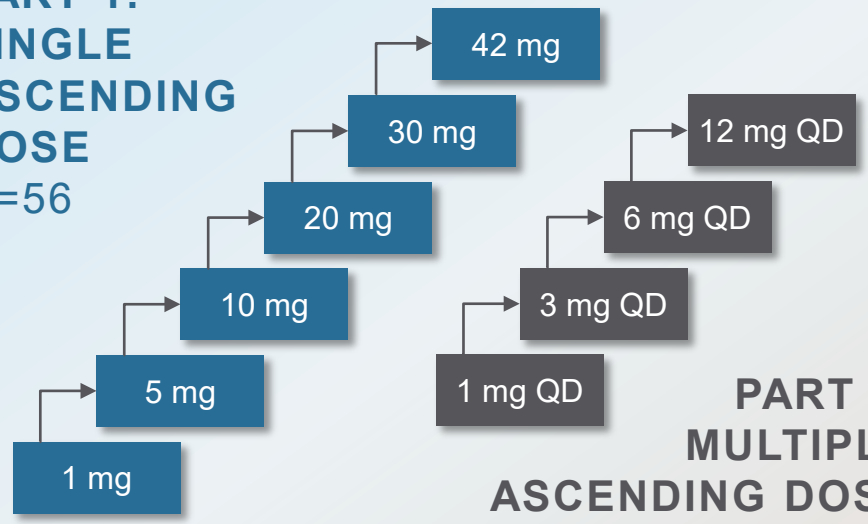
BLU-808 designed to be a best-in-class oral, once-daily wtKIT inhibitor

BLU-808 OPTIMIZED PROFILE[1]	
POTENCY	
pKIT cellular IC_{50} (nM)	0.37
WT KIT-dependent proliferation IC_{50} (nM)	1.3
Inhibition of CD63 extracellular expression IC_{50} (nM)	2.7
Inhibition of histamine degranulation IC_{50} (nM)	8.6
SELECTIVITY	
S(10) @ 3 µM	0.042
PDGFRA selectivity	>300x
PDGFRB selectivity	>400x
FLT3 selectivity	>9600x
CSF1R Kd selectivity	>800x
Brain penetrance ($Kp_{u,u}$)	0.021

PHASE 1 HEALTHY VOLUNTEER STUDY

To support tunable dosing potential and meaningful therapeutic differentiation

PART 1: SINGLE ASCENDING DOSE
N=56



PART 2: MULTIPLE ASCENDING DOSE
N=31[2]
Daily (QD) dosing; 14 days + follow-up

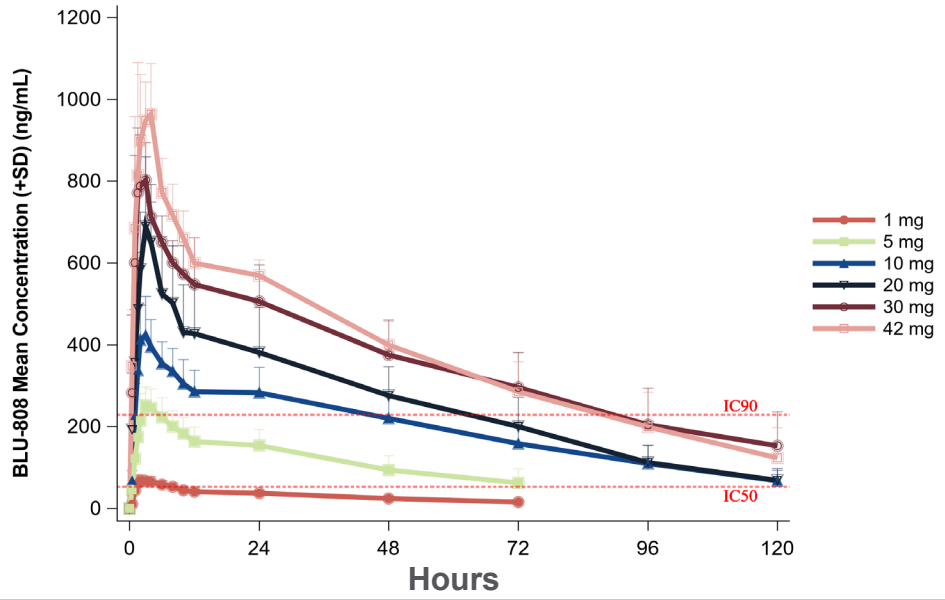
Assessments: safety, pharmacokinetics, & pharmacodynamics

[1] Grassian, A. et al. Presentation at AAAAI (2024). In single ascending dose (SAD) study, 42 mg was selected to achieve 50% greater exposure over 30 mg, based on preclinical data.
[2]Two patients did not complete the protocol including one subject in the placebo cohort who was removed at Day 12 due to violation of study site policy and one subject in the 6 mg cohort who was found to be ineligible at Day 8 due to a medical history of benign ethnic neutropenia and was removed. All available data for both subjects are included.

Single ascending dose (SAD)

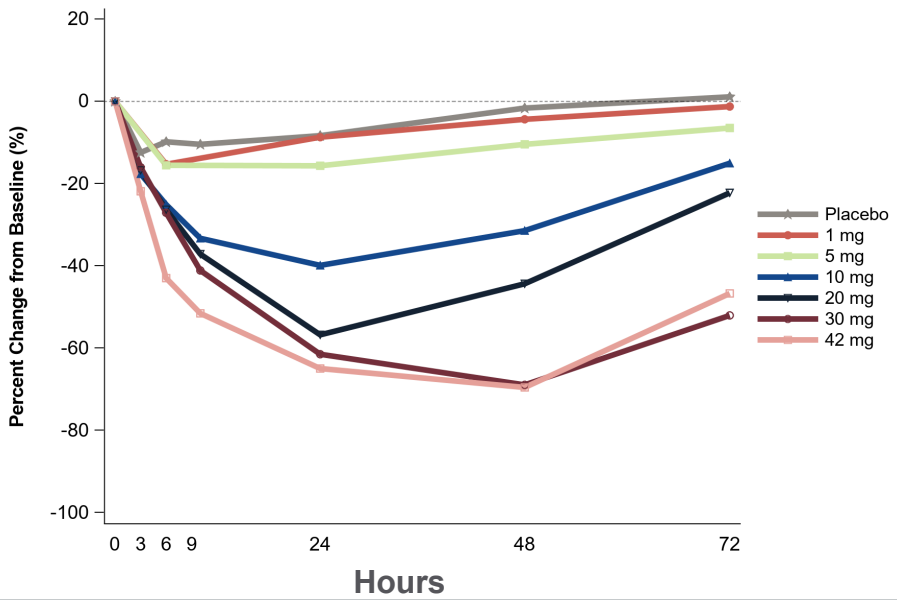
Dose-dependent PK and tryptase response with single BLU-808 dose

SINGLE DOSE PHARMACOKINETICS (N=56)



- $T_{1/2}$ ~40 hours supports **once-daily dosing**
- **Low PK variability** (%CV ~30%)
- **No food effect**

CHANGE IN SERUM TRYPTASE (N=56)



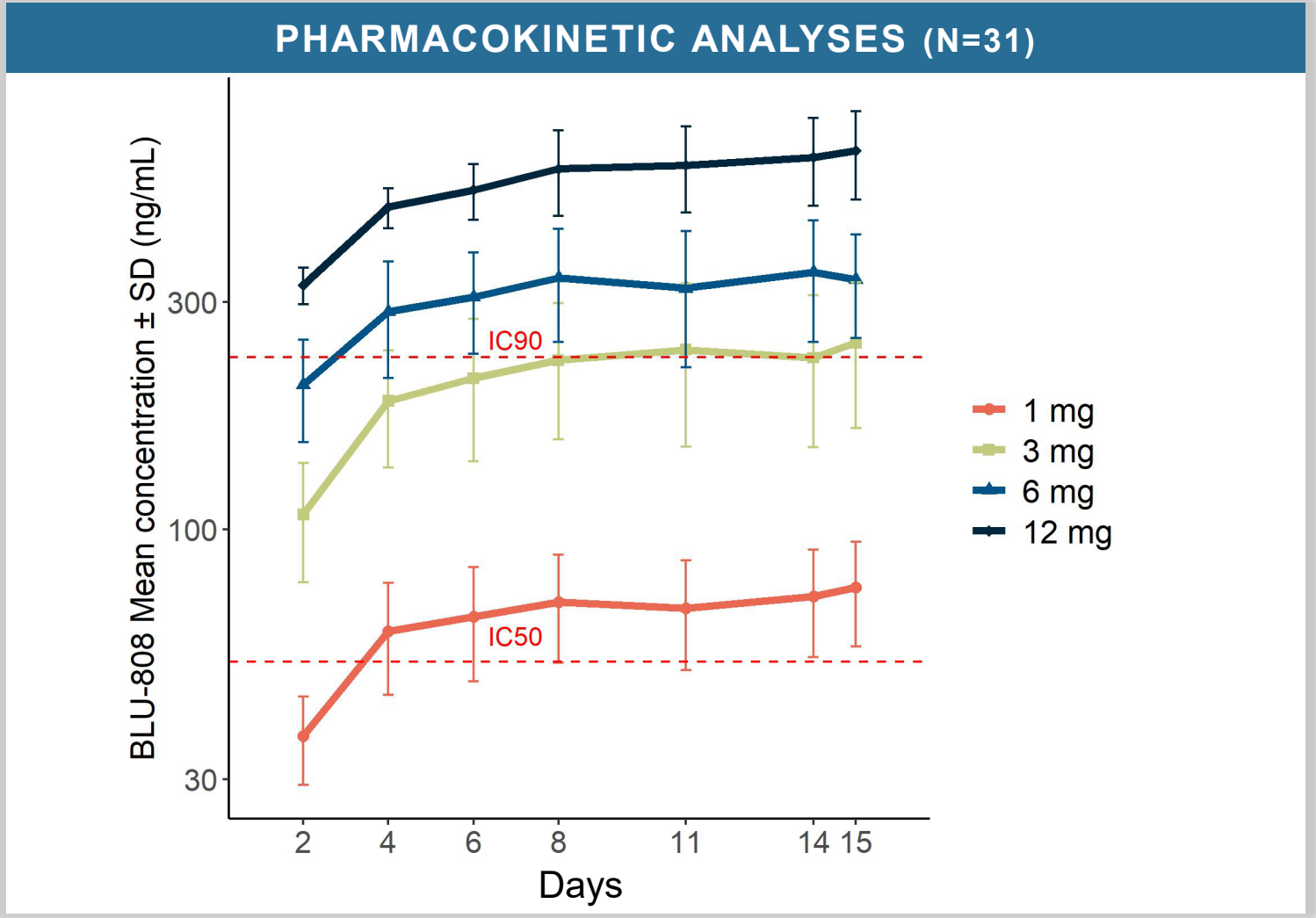
- **Dose-dependent serum tryptase decrease**
- Single dose of BLU-808 reduced serum tryptase by more than 60%

Single doses of BLU-808 were well-tolerated (1-42 mg), with no significant changes in labs, including AST/ALT

IC50, predicted 50% inhibitory concentration based on cellular proliferation assays; IC90, predicted 90% inhibitory concentration based on cellular proliferation assays; AST, aspartate aminotransferase; ALT, alanine aminotransferase; PK, pharmacokinetics; $T_{1/2}$, terminal half-life; %CV, coefficient of variation (percent); SD, standard deviation.
Tryptase values below lower limit of quantification (LLOQ; 1ng/mL) were imputed at 0 ng/mL.

Multiple ascending dose (MAD)

Consistent, dose-dependent PK with multiple BLU-808 doses

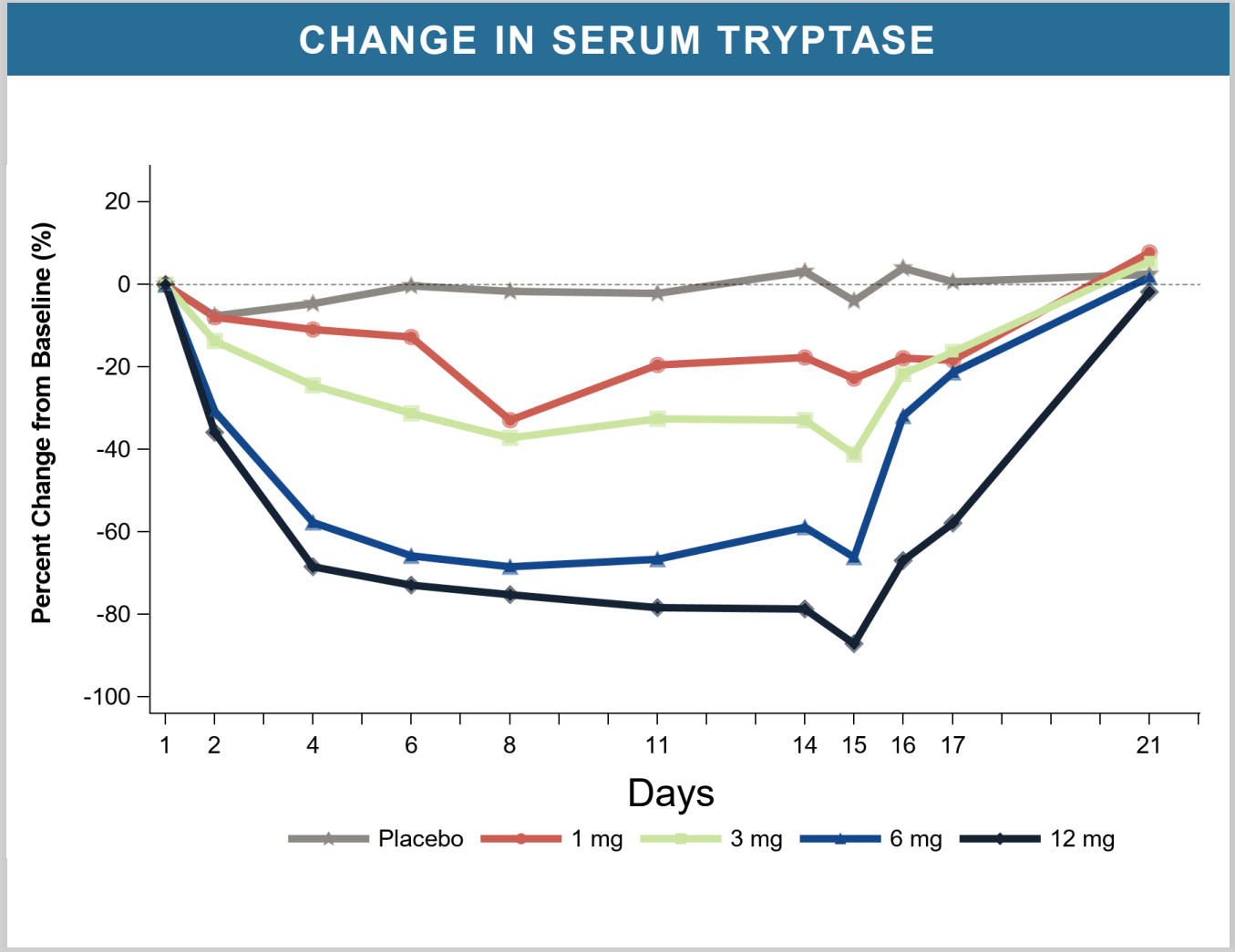


- Sustained target coverage with **once-daily dosing** at all doses
- Doses ≥ 3mg reached **concentrations above IC_{90}**
- **Low variability** (<30% CV)

IC50, predicted 50% inhibitory concentration based on cellular proliferation assays; IC90, predicted 90% inhibitory concentration based on cellular proliferation assays. %CV, coefficient of variation (percent).

Multiple ascending dose (MAD)

Rapid, robust and sustained tryptase responses with multiple BLU-808 doses



- **Dose-dependent** reductions exceeding 80%

Dose	Change in serum tryptase	
	Reduction at Day 15	Participants reaching LLOQ
Placebo (n=8)	-4%	0
1 mg (n=6)	-23%	1/6
3 mg (n=6)	-41%	1/6
6 mg (n=6)	-66%	3/6
12 mg (n=4)[a]	-87%	3/4

Tryptase values below lower limit of quantification (LLOQ; 1 ng/mL) were imputed at 0 ng/mL.
[a]One participant in the 12 mg cohort had undetectable tryptase levels at baseline and was not included in the tryptase analysis.

Multiple doses of BLU-808 were well-tolerated

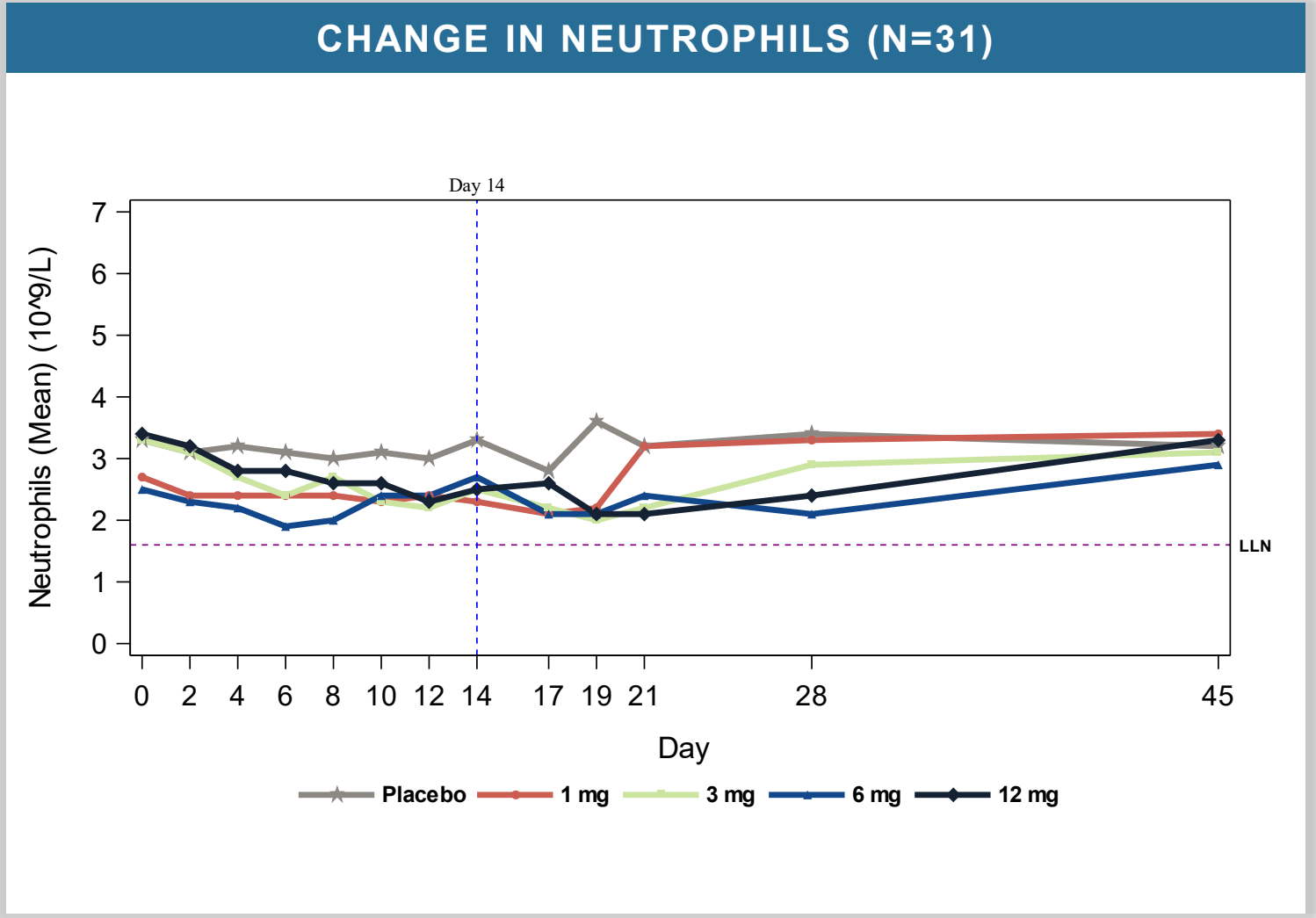
	TEAEs REPORTED IN ≥2 PARTICIPANTS (MAD, N=31)									
	Placebo (n=8)		1 mg (n=6)		3 mg (n=6)		6 mg (n=6)		12 mg (n=5)	
	Gr 1	Gr 2+	Gr 1	Gr 2+	Gr 1	Gr 2+	Gr 1	Gr 2+	Gr 1	Gr 2+
Hair color change	0	0	0	0	0	0	4	0	3	0
Constipation	1	1	0	0	2	0	0	0	2	0
Headache	1	0	2	0	0	0	0	0	1	0
Pruritus	1	0	0	0	0	0	1	0	1	0
Fatigue	1	0	1	0	0	0	0	0	0	0
Rash	0	0	0	0	0	0	2	0	0	0

- All TEAEs in patients treated with BLU-808 were reported as Grade 1
- No serious AEs and no discontinuations or dose modifications due to AEs were reported
- Dose-dependent hair color changes reported: none at 1 and 3 mg, minor and isolated at 6 mg, more noticeable at 12 mg
- No significant changes in laboratory measures, including AST/ALT, were reported

Constipation (1), headache (all), pruritus (1), and rash (1) reported as unrelated to treatment.
Three participants experienced AEs with blood draw at 12 mg vessel puncture site pain, 2 of them with lightheadedness. One patient at 6 mg was found to be ineligible for study at Day 8 due to medical history of benign ethnic neutropenia and was removed. One placebo patient was removed at Day 12 due to study site policy.
AE; adverse event; TEAE, treatment-emergent AE.

Multiple ascending dose (MAD)

No significant changes in neutrophil counts



- Neutrophil counts generally stable across all doses
- No adverse events reported related to neutrophil values

LLN, lower limit of normal

Data show BLU-808 has a tunable profile for optimizing benefit-risk

- Highly potent and selective
- Well-tolerated safety profile
- Wide therapeutic window
- Rapid, sustained tryptase reductions
- Low, once-daily oral dosing
- No food effect

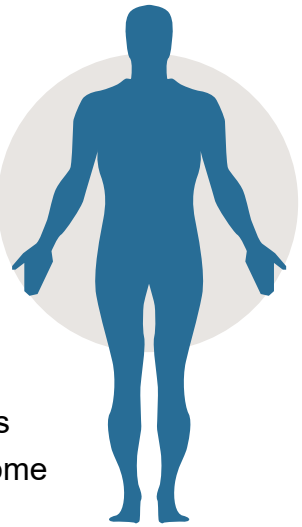
DIALING IN CLINICAL ACTIVITY

MANAGING ON TARGET ADVERSE EVENTS

- Multiple clinically active and well-tolerated BLU-808 doses enable titratability
- BLU-808's clinical profile supports broad optionality across indications
- Successful AYVAKIT development in SM informs our approach to BLU-808

Multiple clinical data milestones anticipated in 2025 and beyond

UNIVERSE OF ALLERGIC & INFLAMMATORY DISEASES



Respiratory
- Allergic asthma
- Allergic rhinitis
- Allergic conjunctivitis
- Nasal polyps
- COPD

Skin
- Chronic urticaria
- Psoriasis
- Atopic dermatitis

Gastrointestinal
- Eosinophilic disorders
- Irritable bowel syndrome
- Food allergy

Multi-system
- Mast cell activation syndrome (MCAS)

PLUS OTHERS…

BLU-808 PROOF-OF-CONCEPT STRATEGY

Move rapidly into areas where targeting KIT has been de-risked

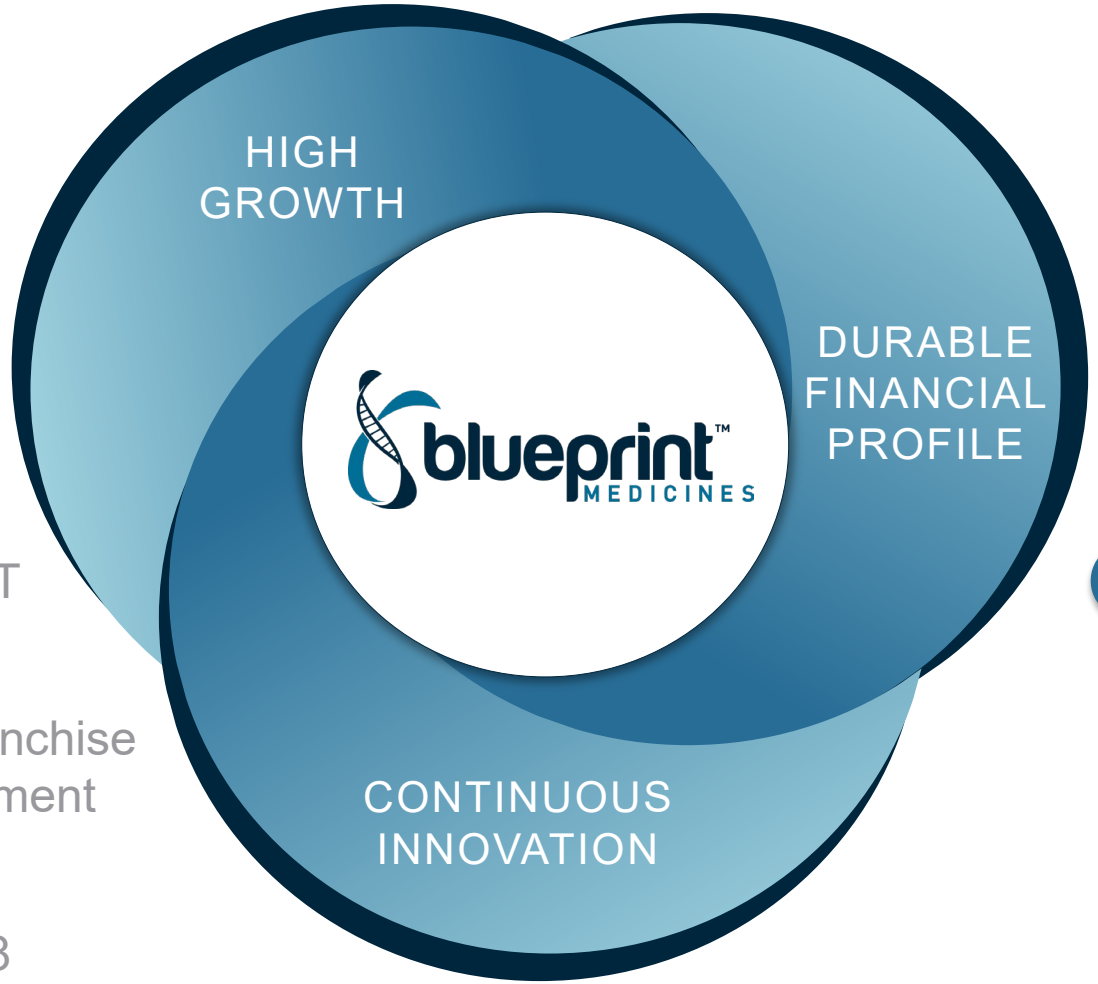
- Chronic spontaneous urticaria
- Chronic inducible urticaria

Explore other biology across organ systems to unlock broader potential

- Allergic asthma
- Allergic rhinitis
- Allergic conjunctivitis
- Mast cell activation syndrome (ISM adjacent)

COPD, chronic obstructive pulmonary disease.

Our core growth drivers in 2025

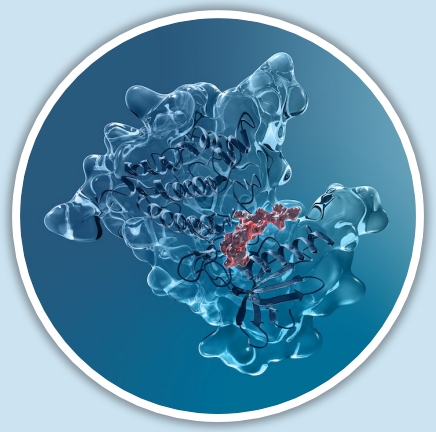


- Drive continued AYVAKIT revenue growth
- Extend long term SM franchise with elenestinib development
- Accelerate and expand development of BLU-808
- Advance R&D innovation to fuel long-term growth

Highly productive research engine has nominated 17 candidates to date

INTEGRATED RESEARCH APPROACH

Small molecule inhibitors



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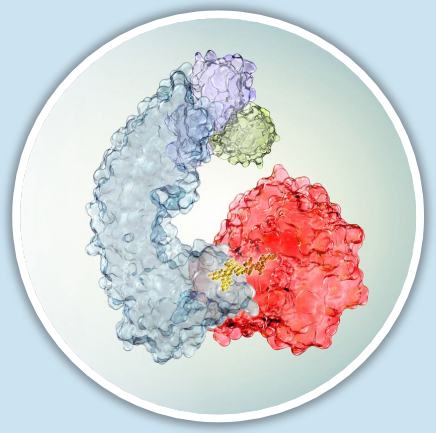


Targeted protein degraders

- Prioritize **large opportunities** with **transformative potential**
- Pursue **clear biology** where **early data can derisk** future investment
- **Integrate R&D and commercial** to drive significant, sustainable growth
- Leverage the **best modality** for each target

AREAS OF FOCUS

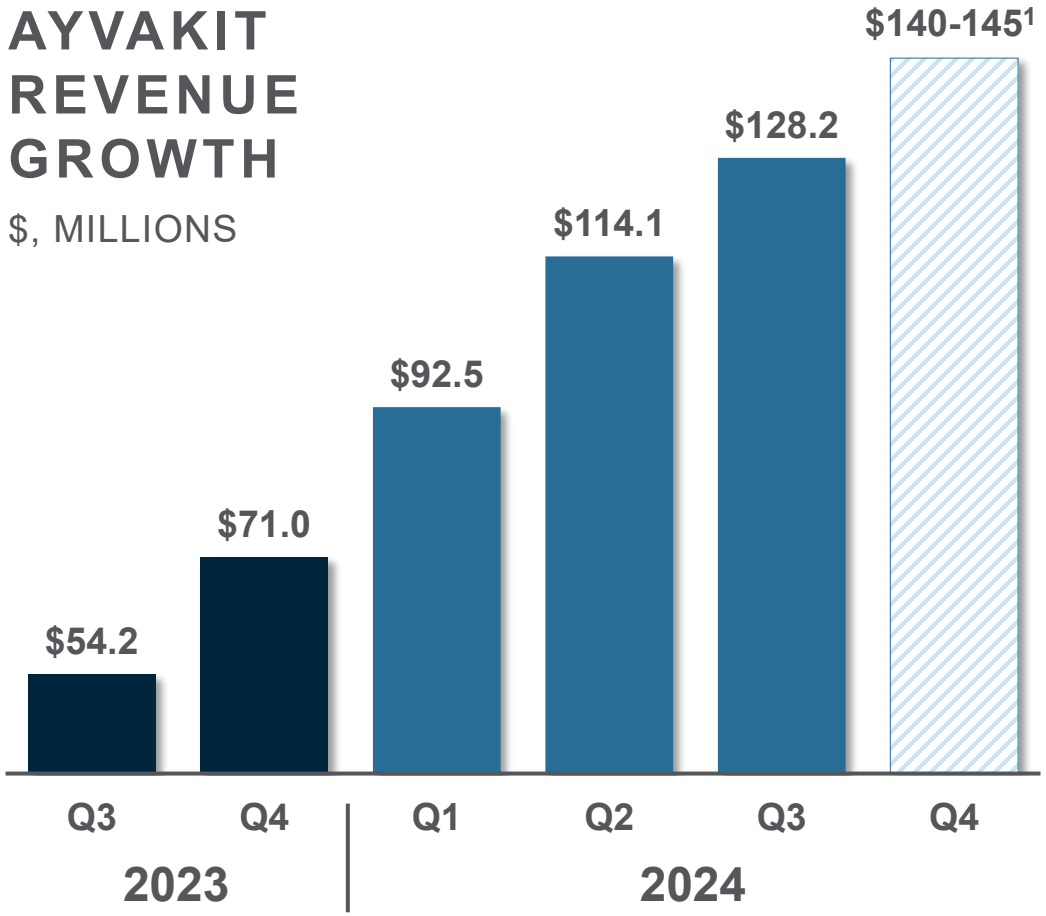
► ALLERGY / INFLAMMATION

Undisclosed mast cell targets and modalities

► ONCOLOGY / HEMATOLOGY

CDK2 and CDK4 degrader programs

We're on the path to sustainability as we continue to invest in innovation



Plan to report Q4 and full-year 2024 financial results in February 2025

$475 – 480 million

2024 AYVAKIT revenue guidance

>50% reduction

in anticipated cash burn in 2024 over prior year[1]

$882.4 million

cash and cash equivalents at end of Q3 2024

anticipate ~$80M in proceeds from GSK acquisition of IDRx due to equity stake, upon closing

[1] Based on 2024 revenue guidance.

2025 strategic priorities to unlock the next stage of growth

STRATEGIC PRIORITY	GOAL	1H 2025	2H 2025
Grow leadership in systemic mastocytosis	Deliver continued strong and steady AYVAKIT revenue growth	●	
	Present additional long-term data from PIONEER trial of AYVAKIT	●	
	Achieve reimbursement of AYVAKYT in ≥20 countries overall	●	
	Activate sites and drive enrollment of HARBOR trial of elenestinib	●	
Achieve BLU-808 clinical proof-of-concept	Present Phase 1 healthy volunteer trial results	✓	
	Initiate POC trials in CSU, CindU, AR and AC	●	
	Initiate POC trials in allergic asthma and MCAS		●
Drive research innovation	Nominate 2 development candidates, including first protein degrader		●

AC, allergic conjunctivitis; AR, allergic rhinitis; CindU, chronic inducible urticaria; CSU, chronic spontaneous urticaria, MCAS, mast cell activation syndrome; POC, proof of concept

Blueprint Medicines

Driving growth and innovation with operational excellence