Making Our Mission a Reality

CORPORATE DECK
MAY 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 future business growth, including its 2024 growth strategy and its mast cell disorders strategy; the company’s expectations for continued growth in breadth and depth of prescribing for AYVAKIT; 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; estimates of market opportunities in systemic mastocytosis, chronic urticaria, other mast cell diseases, and for CDK4/6 inhibitors; whether any of the company’s product candidates will address unmet medical needs; the reduction of the company’s operating expenses and cash burn; 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; 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,” “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, risks and uncertainties related to 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, and commercial supply of current or future approved products; the company’s ability and plans to continue to expand its commercial infrastructure and successfully launch, market and sell current or future approved products; the company’s ability to obtain marketing approval for AYVAKIT/AYVAKYT in additional geographies in the future; the rate and degree of market acceptance of AYVAKIT/AYVAKYT and any future drug candidates for which we receive marketing approval; 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 successfully expand its operations, research platform and portfolio of therapeutic candidates, and the timing and costs thereof; the success of the company’s current and future collaborations, financing arrangements, partnerships or licensing arrangements; and 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. Blueprint Medicines, AYVAKIT, AYVAKYT and associated logos are trademarks of Blueprint Medicines Corporation.
The accelerating growth profile of Blueprint Medicines

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

- **Incubating innovation**
  - Broad portfolio built organically through proprietary research platform

- **Establishing leadership in SM**
  - Approval & launch of AYVAKIT® (avapritinib) for AdvSM and ISM in the U.S. and EU

- **Accelerating growth**
  - Blockbuster opportunity in SM, focused investment in compelling growth opportunities, and a path to profitability

2011 – 2021

2021 – 2023

2024 – FUTURE

Avapritinib is approved under the trade name AYVAKIT® in Europe. AdvSM, advanced systemic mastocytosis; ISM, indolent systemic mastocytosis; SM, systemic mastocytosis.
Achieved $92.5M in AYVAKIT revenue, in Q1, representing >135% YoY growth

Raising AYVAKIT revenue guidance to $390-$410M for 2024

Continued strength across revenue drivers, including patient demand

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

On track to submit BLU-808 IND in Q2

ASCO data to show BLU-222 is the first investigational CDK2 inhibitor to demonstrate combination safety with an approved CDK4/6 inhibitor

Strong and durable financial position with $735.6M in cash at end of 1Q 2024

Continued opex reduction and decline in cash burn
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 out to 18 months with no new safety signals presented at AAAAI 2024

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

1. Gianatti et al, AAAAI 2024
AYVAKIT revenue has grown more than 135% year-over-year

AYVAKIT Global Net Revenues ($, Millions)

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Revenues ($, Millions)</th>
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</thead>
<tbody>
<tr>
<td>Q1 2023</td>
<td>$39.1</td>
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<tr>
<td>Q2 2023</td>
<td>$39.9</td>
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<td>Q3 2023</td>
<td>$54.2</td>
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<td>Q4 2023</td>
<td>$71.0</td>
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<td>Q1 2024</td>
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US Launch
- Strong and steady patient demand
- Growth in commercial patients; free goods ~20% since ISM approval
- Advanced SM duration of therapy trending at ~25 months; early days of ISM trending longer
- Majority of patients on therapy today have ISM

EU Launch
- Strong start in Germany

ISM approval marks clear revenue inflection for AYVAKIT

EMA, European Medicines Agency; DOT, duration of therapy
Driving breadth and depth with significant headroom for future growth

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

Growing **breadth** of prescribers with at least one patient on AYVAKIT

Growing **depth** of prescribers with two or more patients on AYVAKIT

- Continued **growth in overall breadth of prescribing**, including allergists
- **~50/50%** split in prescribing at **academic vs. community** accounts
- **45/55%** of volume driven by **new vs. existing prescribers**
- **~70%** of new SM starts at 25 mg dose

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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

~32,000
U.S. SM prevalence²

>20% YoY growth


Not for promotional use
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**

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Not for promotional use
Scientific leadership in KIT biology

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

**MUTATED KIT**

- **KIT D816V inhibitor**
  - (Systemic mastocytosis)
  - *IDRX-73*, formerly known as BLU-654, was out-licensed to IDRx in 2022.

**Elenestinib**

- Next-generation KIT D816V inhibitor
  - (Systemic mastocytosis)

**WILD-TYPE KIT**

- **BLU-808**
  - Wild-type KIT inhibitor
  - (Mast cell-mediated diseases)

- **KIT D816V inhibitor**
  - (Systemic mastocytosis)

1 approved and 3 clinical-stage highly selective and potent KIT inhibitors designed by Blueprint scientists.
Elenestinib, an investigational next-generation, potent, selective KIT D816V inhibitor

HARBOR PART 1 TRIAL RESULTS PRESENTED AT ASH 2023¹:

- **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

Mean % change from baseline

- Placebo (n=10)
- Elenestinib 25 mg QD (n=10)
- Elenestinib 50 mg QD (n=10)
- Elenestinib 100 mg QD (n=8)

Elenestinib Reductions in ISM-SAF Total Symptom Score

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

Mast cells are core drivers in a range of inflammatory diseases

- **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

Proprietary image; AVYAKIT® avapritinib

- Monotherapy opportunities to inhibit wtKIT, a primary mast cell target
- Opportunities for novel regimens of combination approaches at intersections between therapeutic targets
Wild-type KIT inhibitor BLU-808 has first- and best-in-class potential

<table>
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<tr>
<td><strong>Potency</strong></td>
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<tr>
<td>pKIT cellular IC₅₀ (nM)</td>
<td>0.37</td>
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<td>WT KIT-dependent proliferation IC₅₀ (nM)</td>
<td>1.3</td>
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<tr>
<td>Human-derived CD34⁺ mast cells: inhibition of CD63 extracellular expression IC₅₀ (nM)</td>
<td>2.7</td>
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<tr>
<td>Human-derived CD34⁺ mast cells: inhibition of histamine degranulation IC₅₀ (nM)</td>
<td>8.6</td>
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<tr>
<td><strong>Selectivity</strong></td>
<td></td>
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<tr>
<td>S(10) @ 3 μM</td>
<td>0.042</td>
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<tr>
<td>PDGFRA / PDGFRB / FLT3 cellular selectivityᵃ</td>
<td>&gt;300x/&gt;400x/&gt;9600x</td>
</tr>
<tr>
<td>CSF1R Kd selectivity</td>
<td>&gt;800x</td>
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<tr>
<td>Brain penetrance (Kpu,u)</td>
<td>0.021</td>
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<tr>
<td><strong>Preclinical PK supports once daily oral dosing</strong></td>
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IND submission on-track for Q2 2024, then plan to initiate HV study

ᵃ Determined in a cellular assay. CSF1R, colony stimulating factor 1 receptor; FLT3, FMS-like tyrosine kinase 3; IC₅₀, 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; Kpu,u, unbound brain to plasma partition
BLU-808 inhibits activation of human-derived CD34+ mast cells

Decreased CD63 expression and histamine release in treated human-derived CD34+ mast cells stimulated with IgE and anti-IgE

BLU-808 is potent in two human-derived CD34+ mast cell assays

- BLU-808 inhibits the expression of CD63 at the cell surface, which is a marker of mast cell degranulation
- Inhibition of histamine release shows that BLU-808 can reduce degranulation and subsequent release of inflammatory molecules

Grassian, A et al, AAAAI 2024
BLU-808 can decrease mast cells in an exposure-dependent manner

- 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 concentrations1,2

Mast cell diseases represent significant and growing market opportunity

**SAFETY**

BLU-808 Phase 1 HV data is a key de-risking event

**PROOF OF CONCEPT**

Chronic urticaria

**>$3B CU market in 2030**

**>$26B**

Market for additional potential indications in 2030

**BREADTH OF POTENTIAL ADDITIONAL INDICATIONS**

- Asthma
- Food allergies
- Allergic rhinitis
- Eosinophilic esophagitis
- Atopic dermatitis
- Mast cell activation syndrome

1. Forecasted sales of approved therapies and projected approved therapies in listed indications in 2030, as reported by EvaluatePharma
## Building scale in two focused and exciting areas of science

### PROGRAMS AND TARGETS

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

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

**Large market** with significant unmet need

$10B+

Global sales of CDK4/6 inhibitors for HR+/HER2-negative 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

Selective CDK2 inhibition has historically been challenging to achieve

First safety and early clinical activity data in combination with an approved CDK4/6 inhibitor at ASCO 2024

CDK, cyclin-dependent kinase; HR+, hormone receptor positive; HER2-, human epidermal growth factor receptor 2 negative; SOC, standard of care
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 net product revenue anticipated to approximately double in 2024

AYVAKIT Annual Net Product Revenue ($M)

Anticipate approximately $390M - $410M in AYVAKIT net product revenue in 2024

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 $390 - $410 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+

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:

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<th>Milestone</th>
<th>Timing</th>
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<tr>
<td>Mast cell disorders</td>
<td>AYVAKIT</td>
<td>Present long-term safety and efficacy data from PIONEER trial in ISM</td>
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<td>Elenestinib</td>
<td>Initiate registration-enabling Part 2 of the HARBOR trial in ISM</td>
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<td>Solid tumors</td>
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<td>Provide update on registration plan for HR+/HER2-breast cancer</td>
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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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<td>BLU-956 (next gen)</td>
<td>CDK2</td>
<td>HR⁺ / HER2- breast cancer</td>
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<td>Targeted protein degrader</td>
<td>CDK2</td>
<td>HR⁺ / HER2- breast cancer</td>
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<tr>
<td>Targeted protein degrader</td>
<td>Undisclosed</td>
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<tr>
<td>Additional programs</td>
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<td>Global</td>
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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 (AYVAKITY®) for adults with unresectable or metastatic GIST harboring the PDGFRA D842V 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 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. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib in Greater China. Updated as of January 8, 2024.