Making Our Mission a Reality

KATE HAVILAND, CHIEF EXECUTIVE OFFICER

J.P. MORGAN HEALTHCARE CONFERENCE

JANUARY 8, 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; 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 development of the company’s current or future drug candidates; 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; 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.

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

2011 – 2021

Establishing leadership in SM

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

2021 – 2023

Accelerating growth

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

2024 – FUTURE

Avapritinib is approved under the trade name AYVAKIT® 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
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
- Compelling clinical profile
- Positive receptivity driving **demand**
- Multiple opportunities for **growth**
AYVAKIT is capturing a blockbuster opportunity in SM

AYVAKIT NET PRODUCT REVENUE ($M)

- $28.6 (Q3 2022)
- $30.1 (Q4 2022)
- $39.1 (Q1 2023)
- $39.9 (Q2 2023)
- $54.2 (Q3 2023)

May 22, 2023: FDA approval for ISM

- 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

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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

**Broad demand** across provider types and channels

- ~60/40% Volume driven by **academic** vs. **community** accounts
- ~50/50% Volume driven by **new vs. existing** prescribers

**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
- ~65% Patients likely to **ask their doctor** about AYVAKIT

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**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**

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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

~32,000
U.S. SM prevalence²

>20% YoY growth

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

#### MAST CELL DISORDERS

**Allergy/inflammation focus:**

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**Oncology focus:**

**SOLID TUMORS**

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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
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

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

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<tr>
<th>Attribute</th>
<th>Ideal Candidate</th>
<th>BLU-808</th>
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<tr>
<td>pKIT / proliferation IC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>&lt; 10 nM pKIT IC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>0.37/1.3 nM</td>
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<tr>
<td>PDGFR / FLT3 selectivity</td>
<td>&gt; 50x / &gt; 50x</td>
<td>&gt;300/&gt;9600</td>
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<tr>
<td>Kinase Selectivity; S(10)</td>
<td>&lt; 0.1</td>
<td>0.042</td>
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<tr>
<td>Drug/Drug Interactions</td>
<td>Low potential</td>
<td>Low potential</td>
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<tr>
<td>Peripherally Restricted</td>
<td>Kpuu &lt; 0.1</td>
<td>Kpuu 0.021</td>
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**IND submission planned for 2Q 2024**

- 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.
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 & EU\(^4\)

Unmet need for an oral therapy that targets core biology

TKI, tyrosine kinase inhibitor; QoL, quality of life; EU\(^4\) includes France, Germany, Italy, Spain

1. Antihistamine refractory, claims-identified patients with CU in the US and EU\(^4\)
Building scale in two focused and exciting areas of science

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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

### PRECLINICAL PROFILE

<table>
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<tr>
<th></th>
<th>BLU-222&lt;sup&gt;1&lt;/sup&gt;</th>
<th>PF-4091&lt;sup&gt;2&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Selectivity score / SI(10)</td>
<td>0.045</td>
<td>0.127</td>
</tr>
<tr>
<td>CDK2 potency / CDK2 enzyme IC&lt;sub&gt;50&lt;/sub&gt; (nM)</td>
<td>2.6</td>
<td>7.2</td>
</tr>
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</table>

### PHASE 1 MONOTHERAPY DOSE ESCALATION DATA

<table>
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<tr>
<th></th>
<th>Patients</th>
<th>Dose range tested</th>
<th>PK (average effective half life)</th>
<th>Treatment emergent adverse events (TEAEs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>27 patients</td>
<td>50 mg – 800 mg BID (MTD not determined)</td>
<td>~12 hrs</td>
<td>No Gr5; 1 Gr4 (hypokalemia; unrelated)</td>
</tr>
<tr>
<td></td>
<td>35 patients</td>
<td>75 mg – 500 mg BID (MTD: 300 mg BID)</td>
<td>~2-3 hrs</td>
<td>1 Gr5 (unrelated); 1 Gr4 (neutropenia)</td>
</tr>
</tbody>
</table>

### HEMATOLOGIC TEAEs

<table>
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<tr>
<th></th>
<th>ALL</th>
<th>GR3</th>
<th>GR4</th>
<th>ALL</th>
<th>GR3</th>
<th>GR4</th>
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<tbody>
<tr>
<td>• Anemia</td>
<td>29.6%</td>
<td>3.7%</td>
<td></td>
<td>45.7%</td>
<td>8.6%</td>
<td></td>
</tr>
<tr>
<td>• Neutropenia</td>
<td>3.7%</td>
<td></td>
<td></td>
<td>28.6%</td>
<td>14.3%</td>
<td>2.9%</td>
</tr>
<tr>
<td>• Thrombocytopenia</td>
<td>3.7%</td>
<td>3.7%</td>
<td></td>
<td>20.0%</td>
<td>2.9%</td>
<td></td>
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<sup>2</sup> 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)

Will provide FY 2023 financials and 2024 AYVAKIT product revenue guidance at Q4/FY 2023 earnings call.

ESTIMATED >$1.5B GLOBAL SM PEAK REVENUE

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:

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