Pioneering the Science of Time

BLUEPRINT MEDICINES
COMPANY OVERVIEW

SEPTEMBER 2022
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, to submit a supplemental new drug application (sNDA) to the U.S. Food and Drug Administration (FDA) for AYVAKIT in non-advanced SM, with a subsequent submission of a type II variation marketing authorization application to the European Medicines Agency (EMA); plans and timing for presenting detailed data from the PIONEER trial of AYVAKIT in patients with non-advanced SM, and, expectations regarding the potential benefits of AYVAKIT in treating patients with non-advanced SM; statements regarding plans and expectations for Blueprint Medicines' current or future approved drugs and drug candidates; the potential benefits of any of Blueprint Medicines’ current or future approved drugs or drug candidates in treating patients; and Blueprint Medicines' 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 report, including, without limitation, risks and uncertainties related to the impact of the COVID-19 pandemic to Blueprint Medicines' business, operations, strategy, goals and anticipated milestones, including Blueprint Medicines' 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; Blueprint Medicines’ ability and plans in continuing to establish and expand a commercial infrastructure, and successfully launching, marketing and selling current or future approved products; Blueprint Medicines’ ability to successfully expand the approved indications for AYVAKIT/AYVAKYT and GAVRETO 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 Blueprint Medicines’ current or future drug candidates; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' 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 Blueprint Medicines' 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; Blueprint Medicines' ability to obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT, GAVRETO or any drug candidates it is developing; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for AYVAKIT/AYVAKYT, GAVRETO or any of its current and future drug candidates; Blueprint Medicines' ability to successfully expand its operations, research platform and portfolio of therapeutic candidates, and the timing and costs thereof; and the success of Blueprint Medicines' current and future collaborations, partnerships or licensing arrangements. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' filings with the Securities and Exchange Commission (SEC), including Blueprint Medicines' 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 Blueprint Medicines has made or may make with the SEC in the future. Any forward-looking statements contained in this presentation represent Blueprint Medicines' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements.

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Blueprint Medicines is a global leader in precision therapy

AYVAKIT is approved for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and adult patients with advanced SM, including aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia. GAVRETO is approved for the treatment of adult patients with RET-fusion positive NSCLC, adult and pediatric patients with advanced or metastatic RET-mutant medullary thyroid cancer who require systemic therapy and adult, and pediatric patients with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory. FDA, U.S. Food and Drug Administration; GIST, gastrointestinal stromal tumor; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

Ongoing global collaboration with Roche and Genentech for the development and commercialization of GAVRETO

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OUR FIRST DECADE OF ACHIEVEMENT

2 internally discovered medicines

FDA & EMA approved across 5 indications

within 10 years, and with

5 breakthrough therapy designations

3
Diverse drivers uniquely position Blueprint Medicines for long-term growth as a leading global precision therapy company.

SHORT-TERM


MID-TERM

- Positive topline PIONEER trial data for AYVAKIT in non-advSM supports sNDA submission to FDA in Q4 2022 and potential U.S. launch in 2023.

LONG-TERM

- Early clinical datasets for BLU-945, BLU-701 and BLU-451 in EGFRm NSCLC anticipated through 1H 2023.
- Initial clinical data for BLU-222 in breast cancer and other CDK2-vulnerable cancers anticipated in 1H 2023.

PLAN TO SHARE GO-TO-MARKET PLAN FOR AYVAKIT IN NON-ADVSM AND R&D VISION AT INVESTOR DAY ON NOVEMBER 1, 2022

advSM, advanced systemic mastocytosis; EGFRm, EGFR mutant; FDA, U.S. Food and Drug Administration; non-advSM, non-advanced SM; NSCLC, non-small cell lung cancer.

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Driving near-term value in systemic mastocytosis
AYVAKIT is the current standard of care for advanced SM in the U.S.

GLOBAL NET REVENUES ($, MILLIONS) BY FULL QUARTER SINCE ADVANCED SM LAUNCH

Q3 2021: $17.3  Q4 2021: $20.0  Q1 2022: $23.8  Q2 2022: $28.5

Q2 2022 U.S. PERFORMANCE METRICS

- >50% share of all advanced SM patients being treated
- >70% share of new patient starts and switches
- ~300 new accounts since advanced SM approval; 46 new accounts activated in Q2

ANTICIPATE $115 TO $130 MILLION IN AYVAKIT NET PRODUCT REVENUES IN 2022


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Retrospective analysis showed longer OS in AYVAKIT patients, including in SM-AHN where clinical practice has historically prioritized AHN treatment

OS AMONG PATIENTS WITH SM-AHN TREATED WITH AYVAKIT VS. BAT\textsuperscript{1}

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Number at risk</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
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</thead>
<tbody>
<tr>
<td>Avapritinib</td>
<td>119</td>
<td>76</td>
<td>39</td>
<td>16</td>
<td>10</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>BAT</td>
<td>121</td>
<td>71</td>
<td>44</td>
<td>28</td>
<td>15</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Proportion free of event

Time (months)

Log-rank P value

\( < 0.001 \)

OS OF PATIENTS WITH ADVSM TREATED WITH AYVAKIT VS. MIDOSTAURIN OR CLADRIBINE\textsuperscript{2}

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Number at risk</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVA</td>
<td>176</td>
<td>110</td>
<td>56</td>
<td>28</td>
<td>19</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>MIDO</td>
<td>59</td>
<td>66</td>
<td>45</td>
<td>34</td>
<td>24</td>
<td>15</td>
<td>10</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>CLAD</td>
<td>49</td>
<td>35</td>
<td>22</td>
<td>17</td>
<td>9</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Proportion free of event

Time (months)

Log-rank P value

AVA vs. MIDO: \( < 0.001 \)
AVA vs. CLAD: \( < 0.001 \)

A multi-center, global, observational, retrospective chart review study was conducted at 6 study sites (4 European, 2 US) to identify and collect data from AdvSM patients who received BAT. SM-AHN patients were identified using inclusion/exclusion criteria similar to the EXPLORER and PATHFINDER trials. The follow-up times for the midostaurin, cladribine, and BAT cohorts were truncated to match the maximum follow-up time of the avapritinib cohort. 1. Reiter et al. Overall Survival in Patients with Systemic Mastocytosis with Associated Hematologic Neoplasm Treated with Avapritinib Versus Best Available Therapy. Presented at EHA 2022. Abstract #P1013. 2. Reiter et al. Overall Survival in Patients with Advanced Systemic Receiving Avapritinib Versus Midostaurin or Cladrabine. Presented at EHA 2022. Abstract #P1014 BAT, best available therapy; KM, Kaplan-Meier; OS, overall survival; AdvSM, advanced systemic mastocytosis; AVA, AYVAKIT; MIDO, midostaurin; CLAD, cladribine; SM-AHN, systemic mastocytosis with associated hematologic neoplasm
Non-advanced SM patients have high medical need despite available therapies\(^1\)

**SYSTEMIC MASTOCYTOSIS SYMPTOMS\(^2\)**

- Brain fog
- Pruritis, flushing and pigmented skin lesions
- Life-threatening organ infiltration and damage
- Unpredictable, life-threatening anaphylaxis
- Debilitating fatigue
- GI upset with vomiting, diarrhea and nausea

75% of patients have taken **4+ classes of therapies** to address significant symptom burden\(^1\)

>80% of patients report **limitations in their work and/or daily activities**\(^1\)

83% of patients are **frustrated at lack of treatment options** that do not address the underlying driver of disease\(^4\)

95% of SM cases driven by the **KIT D816V mutation**

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Not for promotional use.
Non-advanced SM represents a significant medical need, and is a potential blockbuster opportunity for AYVAKIT.

STEADY GROWTH IN DIAGNOSED PATIENTS

Diagnosed SM Patients Observed in U.S. Claims

~60% OF NON-ADVANCED SM PATIENTS WITH SIGNIFICANT POLYPHARMACY

Diagnosed Non-Advanced SM Patients with Observed Treatment Experience

~7.5K MODERATE-SEVERE NON-ADVANCED SM PATIENTS

U.S. Prevalence vs. Current Addressable Market

1. Reported data represent estimations. Analysis based on US claims data from Komodo Health. SM, systemic mastocytosis; TKI, tyrosine kinase inhibitor; A/I, allergist/immunologist.

Not for promotional use.
Largest clinical trial to date conducted in non-advanced SM

Randomize 2:1

AYVAKIT 25 mg QD + BSC

Placebo QD + BSC (Control)

Primary endpoint

Mean change in TSS at 24 weeks

Rollover (Part 3)

AYVAKIT 25 mg QD + BSC

Eligibility

• Age ≥18 years
• ISM confirmed by central pathology review
• No restriction on prior therapy
• Moderate-to-severe symptoms

Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>AYVAKIT</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled</td>
<td>141</td>
<td>71</td>
</tr>
<tr>
<td>TSS score, mean (SD)</td>
<td>50.2 (19.1)</td>
<td>52.4 (19.8)</td>
</tr>
</tbody>
</table>

• Similar between AYVAKIT and control arms
• Consistent with PIONEER Part 1
• Median BSC across both arms was 3 (range 0 – 11)

Data cutoff as of June 23, 2022. QD, once daily; BSC, best supportive care; TSS, total symptom score; SD, standard deviation

Not for promotional use.
AYVAKIT demonstrated highly significant and clinically meaningful impact on the primary and all key secondary endpoints.

### CLINICAL OUTCOME MEASURES

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>P VALUE&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Endpoint</strong></td>
<td></td>
</tr>
<tr>
<td>Mean Change in TSS</td>
<td>0.003</td>
</tr>
<tr>
<td>≥30% Reduction in TSS</td>
<td>0.009</td>
</tr>
<tr>
<td>≥50% Reduction in TSS</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>Secondary Endpoints</strong></td>
<td></td>
</tr>
<tr>
<td>Mean Change in Most Severe Symptom Score</td>
<td>0.015</td>
</tr>
<tr>
<td>≥50% Reduction in Serum Tryptase</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>≥50% Reduction in KIT D816V VAF</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>≥50% Reduction in Bone Marrow MC Aggregates</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data cutoff as of June 23, 2022. 1. One-sided p-value < 0.025 indicates statistical significance. 2. For secondary endpoints, reductions in TSS and objective measures of mast cell burden represent proportion of patients with ≥30% and ≥50% reductions. All endpoints are key secondary endpoints, with the exception of “Mean Change in Most Severe Symptom Score”, which is an additional secondary endpoint. TSS, total symptom score; VAF, variant allele fraction; MC, mast cell.

Not for promotional use.
Decreases in patient-reported symptoms and objective measures of disease burden

<table>
<thead>
<tr>
<th>Mean Change in TSS [95 % CI]</th>
<th>AYVAKIT</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>PART 3: 48 weeks(^1)</td>
<td>-20.2 [-24.7 – 15.7]</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>≥50% Reduction in Serum Tryptase [95% CI]</th>
<th>AYVAKIT</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>PART 2: 24 weeks</td>
<td>53.9% [45.3 – 62.3]</td>
<td>0.0% [0.0 – 5.1]</td>
</tr>
</tbody>
</table>

\(^1\) After 24 weeks, all patients had the option to cross over into Part 3 and receive treatment with AYVAKIT 25 mg QD. TSS, total symptom score; CI, confidence interval.

Rapid and further deepening in mean TSS reduction observed in Part 3 when control switched over to receive AYVAKIT

Not for promotional use.
AYVAKIT was well-tolerated with a safety profile favorable to control

<table>
<thead>
<tr>
<th></th>
<th>AYVAKIT</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs, n (%)</td>
<td>128 (90.8)</td>
<td>66 (93.0)</td>
</tr>
<tr>
<td>SAEs, n (%)</td>
<td>7 (5.0)</td>
<td>8 (11.3)</td>
</tr>
<tr>
<td>Discontinuation due to TRAEs, n (%)</td>
<td>1 (0.7)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

**TRAEs in ≥5% of AYVAKIT patients, by preferred term**

<table>
<thead>
<tr>
<th></th>
<th>AYVAKIT</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache, n (%)</td>
<td>11 (7.8)</td>
<td>7 (9.9)</td>
</tr>
<tr>
<td>Nausea, n (%)</td>
<td>9 (6.4)</td>
<td>6 (8.5)</td>
</tr>
<tr>
<td>Peripheral edema, n (%)</td>
<td>9 (6.4)</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Periorbital edema, n (%)</td>
<td>9 (6.4)</td>
<td>2 (2.8)</td>
</tr>
</tbody>
</table>

- No ICB events
- Lower rate of cognitive effect AEs\(^1\) reported for AYVAKIT (2.8%) vs. control (4.2%)
- No Grade 3 cognitive effect AEs\(^1\) for AYVAKIT (0%) vs. control (1.4%)
- In the AYVAKIT arm, 93.0% of edema AEs were Grade 1, with remainder Grade 2
- Higher Part 2 completion rate for AYVAKIT (96.5%) vs. control (93.0%)

Data cutoff as of June 23, 2022. 1. Cognitive effect AEs refer to 17 pooled terms identified across AYVAKIT clinical studies. AE, adverse event; SAE, serious adverse event; TRAE, treatment-related adverse event; ICB, intracranial bleed

Not for promotional use.
Driving long-term value in EGFRm lung cancer and CDK2-vulnerable breast cancer
Opportunities for our next-generation EGFR precision therapies

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EGFR-MUTANT NSCLC
ESTIMATED INCIDENT PATIENTS PER YEAR

1L

\[\sim 59,000 \text{ PATIENTS}^1\]

<table>
<thead>
<tr>
<th></th>
<th>Ex19del: (~33,000)</th>
<th>L858R: (~26,000)</th>
</tr>
</thead>
</table>

>70% OF PATIENTS PROGRESS TO 2L

2L+

\[\sim 43,000 \text{ PATIENTS}\]

<table>
<thead>
<tr>
<th></th>
<th>Ex19del: (~24,000)</th>
<th>L858R: (~19,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>On-target resistance (e.g., C797S, T790M)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off-target/unknown resistance</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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OPPORTUNITIES

Enhance activity on L858R activating mutation

Prevent or treat on-target resistance

Treat off-target resistance with well-tolerated combos

Prevent or treat brain mets with enhanced CNS penetration

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Not for promotional use.
Our portfolio of EGFR therapies is purpose-built to address medical needs

TREATMENT GOALS

Effectively block the EGFR pathway

Establish 2L+ SOC with combinations that treat on- and off-target resistance

BLUEPRINT MEDICINES EGFR PORTFOLIO

BLU-945

- Potent EGFR mutation coverage:
  - LR and LR/CS
  - TM and TM/CS regardless of activating mutation
  - Potential for broader coverage at higher exposures
- Highly selective over wild-type EGFR

BLU-701

- Potent EGFR mutation coverage:
  - Ex19del and LR
  - CS regardless of activating mutation
- Highly CNS penetrant

BLU-451

- Potent inhibitor of all common Ex20ins and other uncommon activation mutations
- Highly selective over wild-type EGFR
- CNS penetrant

CS, C797S resistance mutation; Ex20in, activating exon 20 insertion mutations; LR, L858R activating mutation; TM, T790M resistance mutation.
BLU-945 potency and selectivity enable wide therapeutic index and broad EGFR coverage, with promising early clinical monotherapy data

DOSE-DEPENDENT REDUCTIONS IN ctDNA...

In the 400 mg cohort, all detectable T790M and C797S alleles showed reduction, including three that fell below the limit of detection (clearance)

...AND ANTI-TUMOR ACTIVITY, WITH TUMOR SHRINKAGE REPORTED AT DOSES ≥200 MG QD

GENERALLY WELL-TOLERATED†, WITH NO SIGNIFICANT ADVERSE EVENTS ASSOCIATED WITH WILD-TYPE EGFR INHIBITION

*One patient had two different DNA mutations in C797S. Note: reductions in individual variant allele fractions as shown; therefore, patients with multiple mutations may be represented on both plots. All T790M and C797S allele fractions with available baseline and C1D15 data are shown. Increases of greater than 100% were truncated at 100 †Patients with measurable target lesions at baseline with post-baseline scans (investigator assessed). An unconfirmed PR is a PR in which tumor reduction ≥30% has occurred but has not yet been confirmed via a subsequent scan. Most common AEs by preferred term in ≥10% of patients included nausea, headache, fatigue, cough, dyspnea, vomiting, hyponatremia, dry mouth, and anemia. ctDNA, circulating tumor DNA; C, cycle; D, day; F1LCDx, FoundationOne Liquid CDx assay; QD, once daily; CR, complete remission; PD, progressive disease; PR, partial remission; SD, stable disease; EOT, end of treatment. As of the data cut-off (March 9, 2022), 33 patients have been treated with BLU-945 at 25–400 mg once daily (QD) in the first 5 cohorts.
Phase 1/2 trials to rapidly generate data in broad populations, informing development and registration strategies

PLANNED INITIATION OF PHASE 1/2 SYMPHONY / HARMONY TRIAL COHORTS

1L

<table>
<thead>
<tr>
<th>Phase</th>
<th>Treatment</th>
<th>Biomarker</th>
<th>2022</th>
<th>2023</th>
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<tbody>
<tr>
<td>Q2</td>
<td>945 + osi</td>
<td>LR</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>945</td>
<td>LR + CS +/- TM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2L+</td>
<td>945 + osi</td>
<td>LR</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>701 + osi</td>
<td>LR</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>701</td>
<td>LR + CS +/- TM</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>945 + chemo</td>
<td>LR</td>
<td>2H 2022</td>
<td>2023</td>
</tr>
<tr>
<td></td>
<td>945 + ADC</td>
<td>LR</td>
<td>2023</td>
<td>2023</td>
</tr>
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</table>

Not for promotional use.
Opportunity to impact the treatment paradigm for more than 100K patients across multiple CDK2-vulnerable cancers

**CDK-CYCLIN COMPLEXES REGULATE THE CELL CYCLE**

- CDK1 Cyclin A/B
- CDK4/6 Cyclin D
- CDK2 Cyclin E
- CDK2 Cyclin A
- Cyclin A/B
- Cyclin D
- Cyclin E
- DNA SYNTHESIS
- G1
- G2
- M
- CELL DIVISION

**ABERRANT CYCLIN E (CCNE1) DRIVES CELL PROLIFERATION**

**ER+/HER2- BREAST CANCER**

<table>
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<tbody>
<tr>
<td>Sales ($, billions)</td>
<td>$0.7</td>
<td>$2.1</td>
<td>$3.2</td>
<td>$4.6</td>
<td>$6.0</td>
<td>$7.0</td>
<td>$7.7</td>
</tr>
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</table>

**CDK4/6 INHIBITOR GLOBAL SALES ($, BILLIONS)**

**CCNE1-AMPLIFIED TUMORS**

- Uterine: 40%
- Ovarian: 30%
- Stomach: 20%
- Esophageal: 10%
- Uterine: 10%
- Lung: 10%
- Breast: 0%

**FREQUENCY OF CCNE1 AMPLIFICATION**

2. Data from company reports.
3. CCNE1 amplification frequency represented as percentage of total patient samples. Data from the National Cancer Institute’s The Cancer Genome Atlas Program (www.cancer.gov/tcga).
4. CDK, cyclin dependent kinases; ER+/HER2-, estrogen receptor-positive, HER2-negative.

Not for promotional use.
BLU-222 is advancing toward clinical proof-of-concept

PHASE 1/2 TRIAL OF BLU-222
IN CDK2 VULNERABLE CANCERS

PHASE 1 DOSE ESCALATION
(NOW ENROLLING)

Multiple dose cohorts*

*Includes monotherapy and combination regimens

- Safety
- Preliminary clinical activity
- Patient selection strategy

PHASE 2 EXPANSION
(PLANNED)

RP2D

- Combo with ER antagonist – ER+/HER2- breast
- Combo with CDK4/6i + ER antagonist – ER+/HER2- breast
- Monotherapy – CCNE1 tumors
- Combo with chemotherapy – CCNE1 tumors
- Monotherapy – multiple other CCNE1 tumors (basket cohort)

PHASE 1/2 VELA TRIAL OF BLU-222 INITIATED IN Q1 2022 AND FIRST PATIENT DOSED

CCNE1, cyclin E; CDK4/6i, CDK4/6 inhibitor; ER, estrogen receptor.

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Research platform expansion to drive innovation & expand productivity

Consolidate precision medicine platforms with combination of internal and external innovation

EXPANSION AIMS TO DOUBLE THE HISTORIC OUTPUT OF OUR DISCOVERY ENGINE BY 2025

YESTERDAY

KINASE PLATFORM

CURRENT CAPABILITIES

LIBRARY & NEW TARGET DISCOVERY EXPANSION

TODAY

KINASE PLATFORM

NEw PLATFORMS

TARGETED PROTEIN DEGRADATION

FUTURE

INTEGRATED PLATFORM

ENHANCED PRODUCTIVITY

COMPLEMENTARY & SCALABLE

NEW TARGET CLASSES

Consolidate precision medicine platforms with combination of internal and external innovation

EXPANSION AIMS TO DOUBLE THE HISTORIC OUTPUT OF OUR DISCOVERY ENGINE BY 2025

Current capabilities

Library & new target discovery expansion

Targeted protein degradation

Integrated platform

Enhanced productivity

Complementary & scalable

New target classes

Not for promotional use.
Business development plays a key role in our company's value creation and long-term portfolio growth.

Global Strategic Partnerships
Access complementary expertise to maximize program value and global impact on patients

Geographic Expansion
Pioneering early development partnerships in China; expanding to additional key markets through regional distributors

Buy-Side Transactions
Tap into external innovations to complement organic portfolio build

Program Partnerships
Tap into external resources & expertise to enhance internal programs

Over $1.1B earned to-date inclusive of upfront, milestones and royalties

2015: Discovery collaboration on FOP*
2016: Global I/O research collaboration
2018: Greater China partnering on 3 clinical programs
2019: WW out-license of BLU-782 for FOP*
2020: Global collaboration of GAVRETO®
2021: Greater China partnering on 2 preclinical programs
2021: Distribution agreement for AYVAKIT™ in Israel
2022: Distribution agreement for AYVAKIT™ in 14 Central Eastern European countries
2022: Global collaboration of GAVRETO®
2022: Acquisition for its EGFR Exon20 program
2022: Research collaboration on targeted protein degradation
2022: Translational research collaboration on CDK2
2022: Supply agreement for osimertinib
2018: Greater China partnering on 3 clinical programs

Not for promotional use.

* Fibrodysplasia ossificans progressiva
Strong financial position bolstered by diversity of revenue sources and growing product revenue

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Total revenue</td>
<td>$36.5M</td>
<td>$27.3M</td>
<td>$99.3M</td>
<td>$48.9M</td>
</tr>
<tr>
<td>Net product sales</td>
<td>$28.5M</td>
<td>$11.4M</td>
<td>$52.3M</td>
<td>$20.4M</td>
</tr>
<tr>
<td>Collaboration revenue</td>
<td>$8.0M</td>
<td>$15.9M</td>
<td>$47.0M</td>
<td>$28.5M</td>
</tr>
<tr>
<td>Cost of sales</td>
<td>$4.9M</td>
<td>$6.5M</td>
<td>$10.0M</td>
<td>$6.6M</td>
</tr>
<tr>
<td>Collaboration loss sharing</td>
<td>$2.1M</td>
<td>--</td>
<td>$5.4M</td>
<td>--</td>
</tr>
<tr>
<td>Research &amp; development expense ¹</td>
<td>$128.5M</td>
<td>$80.0M</td>
<td>$231.6M</td>
<td>$159.7M</td>
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<tr>
<td>Selling, general &amp; admin expense ²</td>
<td>$58.7M</td>
<td>$49.3M</td>
<td>$115.7M</td>
<td>$91.3M</td>
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<tr>
<td>Net Loss</td>
<td>$(159.7)M</td>
<td>$(108.4)M</td>
<td>$(265.7)M</td>
<td>$(208.2)M</td>
</tr>
</tbody>
</table>

**Balance Sheet (unaudited)**

<table>
<thead>
<tr>
<th></th>
<th>6/30/2022</th>
<th>12/31/2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash, cash equivalents, and investments³</td>
<td>$947.2M</td>
<td>1,034.6M</td>
</tr>
</tbody>
</table>

$947.2 MILLION IN CASH, CASH EQUIVALENTS, AND MARKETABLE SECURITIES, EXCLUDING $400M GROSS PROCEEDS FROM OUR RECENT FINANCING THAT CLOSED IN JULY

¹. Includes stock-based compensation expense of $10.5M and $10.5M in the three months ended 6/30/22 and 6/30/21, respectively, and $20.5M and $19.4M in the six months ended 6/30/22 and 6/30/21, respectively. 2. Includes stock-based compensation expense of $14.9M and $13.8M in the three months ended 6/30/22 and 6/30/21, respectively, and $28.2M and $25.6M in the six months ended 6/30/22 and 6/30/21 respectively. 3. In addition, in July 2022, we received total cash payments of $400.0 million in gross proceeds related to our financing agreement that closed in July.

Not for promotional use.
# Summary of upcoming portfolio milestones

<table>
<thead>
<tr>
<th>Program / activity</th>
<th>Area of focus</th>
<th>Milestone</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>AYVAKIT</td>
<td>Non-advanced SM</td>
<td>Submit sNDA to FDA</td>
<td>Q4 2022</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Submit type 2 variation MAA to EMA</td>
<td>1H 2023</td>
</tr>
<tr>
<td>BLU-263</td>
<td>Non-advanced SM</td>
<td>Report top-line HARBOR Part 1 data</td>
<td>Q4 2022</td>
</tr>
<tr>
<td>BLU-945</td>
<td>EGFRm NSCLC</td>
<td>Report initial dose escalation data for BLU-945 and osimertinib combo with focus on safety results</td>
<td>Q4 2022</td>
</tr>
<tr>
<td>BLU-701</td>
<td>EGFRm NSCLC</td>
<td>Report initial dose escalation data with focus on safety, pharmacokinetics and ctDNA results</td>
<td>Q4 2022</td>
</tr>
<tr>
<td>BLU-451</td>
<td>EGFRex20m NSCLC</td>
<td>Report dose escalation data</td>
<td>1H 2023</td>
</tr>
<tr>
<td>BLU-222</td>
<td>CDK2-vulnerable breast and other cancers</td>
<td>Report dose escalation data</td>
<td>1H 2023</td>
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</tbody>
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