precision at scale™

JUNE 2023
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OUR MISSION

Make real the promise of precision therapy to extend and improve life for as many patients as possible

Suki
patient with indolent systemic mastocytosis
Blueprint’s strategy to achieve Precision at Scale by 2027

**APPROACH**

1. Start with genetic drivers of disease
2. Design highly potent and selective medicines
3. Select the right patients
4. Drive transformative outcomes with high POS

**FOCUS**

- Mast cell disorders
- Lung cancer
- Breast cancer

**ASPIRATION**
Blueprint has a compelling value proposition

1. FOUNDATION OF SUCCESS
   Differentiated scientific platform, development and business execution

2. COMMERCIAL PORTFOLIO
   Doubled product revenue in 2022

3. NEAR-TERM REVENUE GROWTH
   Expansion into indolent SM, a ~15x larger patient opportunity

4. ROBUST CLINICAL PIPELINE
   Diverse set of programs targeting compelling peak revenue opportunities
Blueprint’s proven track record of R&D success

- **14** development candidates nominated
- **80%** success rate from IND to clinical POC
- **5** breakthrough therapy designations
- **~4** years from IND to first approval
- **2** approved medicines
- **6** FDA approved indications

**Note:**
- FDA, Food and Drug Administration.
- IND, investigational new drug application.
- POC, proof-of-concept.
Our scientific platform is a competitive advantage

SELECTIVE SMALL MOLECULE PRECISION THERAPIES

DURABILITY
Potent target inhibition leading to rapid and deep responses

TOLERABILITY
Limit side effects driven by off-target activity

COMBINABILITY
Combine therapies to shut down disease drivers and resistance
Consistent business execution resulting in balance sheet strength and diversity of revenue

BLUEPRINT MEDICINES NET REVENUE ($M)

- Nearly $1B in cash
- Strong product revenue growth anticipated over the next few years

**2023 Guidance**

- Anticipate $135 million to $145 million in AYVAKIT net product revenues for advanced SM and GIST, as well as additional revenue growth driven by expansion into ISM
- Anticipate $40 million to $50 million in collaboration revenues from existing collaborations

**AYVAKIT® Sales**

- 45 in 2018
- 67 in 2019
- 21 in 2020
- 53 in 2021
- 180 in 2022

**Collaboration / Other Revenue**

- 0 in 2018
- 0 in 2019
- 21 in 2020
- 127 in 2021
- 93 in 2022

**Sources of Collaboration / Other Revenue**

1 Includes Gavreto sales booked as revenue in 2020 and 2021. 2 Includes Roche collaboration payments.
Strong track record of business development enabling corporate strategy

2015:
- Discovery collaboration on FOP

2016:
- Global I/O research collaboration

2018:
- Greater China collaboration on FOP

2019:
- WW out-license of BLU-782 for FOP

2020:
- Global collaboration of GAVRETO®

2021:
- Greater China partnering on 2 preclinical programs
- Distribution agreement for AYVAKIT® in Israel
- Distribution agreement for AYVAKIT™ in 14 Central Eastern European countries
- Greater China partnering on 3 clinical programs
- Acquisition for its EGFR Exon20 program
- Translational research collaboration on CDK2
- Distribution agreement of BLU-654 for GIST
- Global partnering on 3 clinical programs

2022:
- WW out-license of BLU-654 for GIST
- Global collaboration of GAVRETO®
- Research collaboration on targeted protein degradation
- Supply agreement for osimertinib

>$1.1B of capital brought in to-date inclusive of upfront, milestones and royalties

FOP, fibrodysplasia ossificans progressiva. GIST, gastrointestinal stromal tumor. I/O, immunotherapy; WW, worldwide.
Strong foundation of enterprise capabilities and infrastructure

- **KNOWLEDGE & LEADERSHIP**: Precision medicine and therapeutic area leadership
- **EXPERIENCED TEAM**: Track record of bringing innovation from discovery to commercial
- **GLOBAL INFRASTRUCTURE**: Established U.S. and EU operations, with global partner network
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Commercial portfolio of transformative medicines

AYVAKIT®
avapritinib tablets

GAVRETO®
pralsetinib capsules
AYVAKIT is the first precision therapy to target the underlying cause of SM

~540 patient years of SM clinical data demonstrating:

- Reduced mast cell burden
- Improved disease symptoms
- Improved quality of life
- Deep and durable clinical responses
- Positive benefit-risk profile
- One pill, once daily dosing

Estimate ≥$1.5 billion peak revenue opportunity in SM
AYVAKIT is the standard of care for advanced SM in the U.S.

AYVAKIT NET REVENUE GROWTH

- 2x growth from FY '20 to FY '22
- FY '20: $21.2M
- FY '21: $53.0M
- FY '22: $111.0M

AVYAKIT is the preferred treatment for advanced SM
- >75% of new patient starts / switches

Total number of patients on therapy continues to grow
- ~520 total patients on therapy

Increasing healthcare provider experience
- ~460 new U.S. accounts since advanced SM approval

Favorable patient access achieved
- 100% coverage with rapid average time to fill of 4.9 days

FY '20 FY '21 FY '22

* SM-AHN, SM with an associated hematologic neoplasm.
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Now approved and available for patients with ISM

FIRST AND ONLY FDA APPROVED TREATMENT FOR ISM
AYVAKIT prescribing information for ISM

1. AYVAKIT is not recommended for the treatment of patients with ISM with platelet counts of less than 50 X 10^9/L.

**Broad indication for the treatment of adult patients with ISM¹**

**Significant improvement in SM symptoms and objective measures of pathologic disease**

**Favorable safety profile with <1% discontinuing due to adverse reactions**
AYVAKIT’s broad ISM indication unlocks blockbuster potential

**CORE OPPORTUNITY**

~7,500 diagnosed and treated patients with moderate to severe ISM

**GROWTH OPPORTUNITY**

Additional diagnosed patients with ISM and estimated undiagnosed ISM patients

AYVAKIT has the potential to reach many ISM patients over time with a broad indication, widening HCP view on candidates for AYVAKIT therapy, and increased diagnosis.
AYVAKIT’s label enables a highly compelling promotional narrative

- High disease burden
- Targets primary disease driver
- Improved symptoms
- Reduced mast cell burden
- Favorable safety profile
- Convenient once-daily dose

STRONGLY RESONATED WITH MULTIPLE HCP SPECIALTIES IN MARKET RESEARCH
We’re committed to helping patients access AYVAKIT

25 MG DOSE IS AVAILABLE NOW

All approved doses are in the channel today

STRONG FOUNDATION OF PAYER COVERAGE

100% payer coverage for all AYVAKIT NDCs, including 25mg

PROVEN ACCESS SUPPORT

Award-winning patient support program minimizes OOP cost and streamlines payer approvals
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Pipeline targeting prevalent diseases with high medical need

**MAST CELL DISORDERS**

- **AYVAKIT**: KIT D816V
- **Elenestinib**: KIT D816V\(^1\)
- **Research**: wild-type KIT

**LUNG CANCER**

- **GAVRETO**: RET
- **BLU-945**: EGFR
- **BLU-525**: EGFR
- **BLU-451**: EGFR exon 20

**BREAST CANCER**

- **BLU-222**: CDK2

Multiple additional undisclosed research programs in areas of medical need

1 Elenestinib was formerly known as BLU-263.
Comprehensive and modular EGFR portfolio strategy

**FULL SPECTRUM COVERAGE**\(^1\) OF EGFR DRIVERS\(^2\)

**BLU-945**
- More potent on L858R than ex19del
- Covers T790M and C797X resistance
- Selectivity profile: best-in-class potential

**BLU-525**
- Potent coverage of L858R and ex19del
- Covers C797X resistance
- CNS penetration: best-in-class potential

**BLU-451**
- Potent coverage of all common ex20ins, plus atypical mutations (e.g., G719X, L861Q, etc.)
- CNS penetration: best-in-class potential

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Randomized SYMPHONY trial expansion designed to de-risk combination development in 1L EGFR L858R mutant NSCLC

ONGOING DOSE ESCALATION
• Late-line EGFR mutant NSCLC

BLU-945 + osimertinib → RP2D → R → Osimertinib

PLANNED EXPANSION
• 1L EGFR L858R mutant NSCLC

BLU-945 + osimertinib

Our goal is to establish BLU-222 as the essential component of treatment paradigms for cancers vulnerable to CDK2 inhibition

TARGET PRIMARY DRIVERS
2L+ CCNE1-driven tumors

TARGET RESISTANCE MECHANISMS
2L+ CDK4/6i resistant HR+ / HER2- mBC

TRANSFORM TREATMENT PARADIGMS
1L combinations in lead indications

EXPAND INTO OTHER POPULATIONS
CDK2 inhibition across broader tumor types

VELA trial dose escalation data, including RP2D, translational and initial combination safety, anticipated in 1H 2023
Blueprint is uniquely positioned with a diversity of significant growth drivers

- **SYSTEMIC MASTOCYTOSIS**
- **LUNG CANCER**
- **BREAST CANCER**

> $1.5B estimated global peak revenue opportunity\(^1\)

~ $5B osimertinib global sales in 2021\(^2\)

~ $8B CDK4/6 inhibitor global sales in 2021\(^2\)

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\(^1\) Blueprint Medicines estimate. 2 Based on company reports.
### Progress against key anticipated portfolio milestones in 2023

<table>
<thead>
<tr>
<th>Area</th>
<th>Program</th>
<th>Milestone</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mast cell disorders</strong></td>
<td>AYVAKIT</td>
<td>Present registrational PIONEER trial data in indolent SM at AAAAI Annual Meeting</td>
<td>✔</td>
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<tr>
<td></td>
<td>AYVAKYT</td>
<td>Achieve EMA validation of a type II variation MAA for indolent SM</td>
<td>✔</td>
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<tr>
<td></td>
<td>AYVAKIT</td>
<td>Achieve FDA approval and initiate U.S. launch in indolent SM</td>
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<tr>
<td>Research</td>
<td></td>
<td>Nominate a development candidate targeting wild-type KIT for chronic urticaria</td>
<td>Mid 2023</td>
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<tr>
<td>Elenestinib</td>
<td></td>
<td>Present Part 1 HARBOR trial data in indolent SM</td>
<td>2H 2023</td>
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<tr>
<td><strong>EGFRm NSCLC</strong></td>
<td>BLU-525</td>
<td>Submit IND to FDA</td>
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<tr>
<td></td>
<td>BLU-451</td>
<td>Present initial CONCERTO trial dose escalation data in EGFR exon 20 NSCLC</td>
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<tr>
<td><strong>CDK2 vulnerable cancers</strong></td>
<td>BLU-222</td>
<td>Present initial VELA trial dose escalation data</td>
<td>✔</td>
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</tbody>
</table>

**SM, systemic mastocytosis; AAAAI, American Academy of Allergy, Asthma & Immunology; EMA, European Medicines Agency; MAA, marketing authorization application; FDA, U.S. Food and Drug Administration; IND, investigational new drug; NSCLC, non-small cell lung cancer**
Blueprint 2027: Doubling our impact, in half the time

<table>
<thead>
<tr>
<th>Category</th>
<th>2011-2022</th>
<th>Planned 2022-2027</th>
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<tr>
<td>Approved medicines</td>
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<td>4+</td>
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<tr>
<td>Disease leadership areas</td>
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<td>3+</td>
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<tr>
<td>Late-stage clinical programs</td>
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<td>4+</td>
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<tr>
<td>Research platforms</td>
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<td>2</td>
</tr>
<tr>
<td>Cumulative development candidates</td>
<td>14</td>
<td>25+</td>
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</table>
precision at scale™
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<tr>
<th>Mast cell disorders</th>
<th>DISCOVERY</th>
<th>EARLY-STAGE DEVELOPMENT</th>
<th>LATE-STAGE DEVELOPMENT</th>
<th>REGULATORY SUBMISSION</th>
<th>APPROVED</th>
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<tr>
<td>CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib and pralsetinib in Greater China.</td>
<td>Advanced SM</td>
<td>Indolent SM</td>
<td></td>
<td>U.S., Europe</td>
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<td></td>
<td></td>
<td>Indolent SM</td>
<td></td>
<td>U.S.</td>
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<tr>
<td>Elenestinib (BLU-263): KIT</td>
<td>Indolent SM</td>
<td>Chronic urticaria</td>
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<tr>
<td>Wild-type KIT research program</td>
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<tr>
<th>Lung cancer</th>
<th>DISCOVERY</th>
<th>EARLY-STAGE DEVELOPMENT</th>
<th>LATE-STAGE DEVELOPMENT</th>
<th>REGULATORY SUBMISSION</th>
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<tbody>
<tr>
<td>GAVRETO® (pralsetinib): RET</td>
<td>RET+ NSCLC</td>
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<td>U.S., Europe</td>
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<tr>
<td>BLU-945: EGFR</td>
<td>EGFR+ NSCLC</td>
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<td>BLU-525: EGFR</td>
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<td>BLU-451: EGFR exon 20 insertions</td>
<td>EGFR+ NSCLC</td>
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<th>Breast cancer</th>
<th>DISCOVERY</th>
<th>EARLY-STAGE DEVELOPMENT</th>
<th>LATE-STAGE DEVELOPMENT</th>
<th>REGULATORY SUBMISSION</th>
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<td>BLU-222: CDK2</td>
<td>ER+/HER2- breast cancer</td>
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<th>Additional genomically defined cancers</th>
<th>DISCOVERY</th>
<th>EARLY-STAGE DEVELOPMENT</th>
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<td>AYVAKIT: PDGFRA</td>
<td>PDGFRA GIST</td>
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<td>U.S., Europe</td>
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<td>GAVRETO: RET</td>
<td>RET+ thyroid cancer</td>
<td>Other RET+ solid tumors</td>
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<td>U.S.</td>
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<tr>
<td>BLU-222: CDK2</td>
<td>CDK2-vulnerable cancers</td>
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<th>Cancer immunotherapy</th>
<th>DISCOVERY</th>
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<tr>
<td>BLU-852: MAP4K1</td>
<td>Advanced cancers</td>
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<tr>
<th>Multiple undisclosed research programs</th>
<th>DISCOVERY</th>
<th>EARLY-STAGE DEVELOPMENT</th>
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1. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib and pralsetinib in Greater China. 2. 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 (AYVAKIT®) for adults with ASM, SM-AHN or MCL, after at least one systemic therapy. 3. Approved in the U.S. for adults with indolent SM. 4. In collaboration with Roche. 5. Received U.S. accelerated approval for adults with metastatic RET fusion-positive NSCLC. Received conditional marketing authorization in Europe for adults with advanced RET fusion-positive NSCLC not previously treated with a RET inhibitor. 6. Zai Lab has exclusive rights to develop and commercialize BLU-945 and BLU-525 in Greater China. 7. 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 (AYVAKIT®) for adults with unresectable or metastatic GIST harboring the PDGFRA D842V mutation. 8. Received U.S. accelerated approval for advanced or metastatic RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer.

Not for promotional use.  Updated as of May 22, 2023.