Avapritinib update for the GIST patient and caregiver community

Stephen Miller, PhD
Vice President, Translational Medicine
Blueprint Medicines

LIFE FEST
JULY 14, 2018
Forward-looking statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. The words “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.

In this presentation, forward-looking statements include, without limitation, statements about plans and timelines for the development of avapritinib, BLU-554, BLU-667 and BLU-782 and the ability of Blueprint Medicines Corporation (the “Company”) to implement those clinical development plans; plans and timelines for reporting data for the Company's current or future clinical trials; the potential benefits of the Company's current and future drug candidates in treating patients; plans and timelines for regulatory submissions, filings or discussions, including a first New Drug Application for avapritinib for the treatment of PDGFRα D842V-driven gastrointestinal stromal tumors (“GIST”); plans and timelines for the development and commercialization of companion diagnostics for the Company's current or future drug candidates; plans and timelines for current or future discovery programs; plans and timelines for any current or future collaborations with strategic partners; and the Company’s strategy, business plans and focus. The Company has based these forward-looking statements on management’s current expectations, assumptions, estimates and projections.

While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks, uncertainties and other important factors, many of which are beyond the Company’s control and may cause actual results, performance or achievements to differ materially from those expressed or implied by any forward-looking statements. These risks and uncertainties include, without limitation, risks and uncertainties related to the delay of any current or planned clinical trials or the development of the Company's drug candidates, including avapritinib, BLU-554, BLU-667 and BLU-782; the Company's advancement of multiple early-stage efforts; the Company's ability to successfully demonstrate the efficacy and safety of its drug candidates; the preclinical and clinical results for the Company's drug candidates, which may not support further development of such drug candidates; actions or decisions of regulatory agencies or authorities, 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 any drug candidates it is developing; the Company's ability to develop and commercialize companion diagnostic tests for its current and future drug candidates, including companion diagnostic tests for BLU-554 for FGFR4-driven hepatocellular carcinoma, avapritinib for PDGFRα D842V-driven GIST and BLU-667 for RET-driven non-small cell lung cancer; and the success of the Company’s current and future collaborations, including its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. and its collaboration with CStone Pharmaceuticals.

These and other risks and uncertainties are described in greater detail under “Risk Factors” in the Company’s Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, as filed with the Securities and Exchange Commission (“SEC”) on May 2, 2018, and any other filings the Company has made or may make with the SEC in the future. The Company cannot guarantee future results, outcomes, levels of activity, performance, developments, or achievements, and there can be no assurance that the Company’s expectations, intentions, anticipations, beliefs, or projections will result or be achieved or accomplished. 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.
Introduction to Blueprint Medicines

- Based in Cambridge, Mass.
- ~150+ employees strong
- Founded by the team who discovered and developed Gleevec® (imatinib)
- Developing targeted kinase medicines for patients with genomically defined diseases
- Culture of urgency to develop medicines for underserved patients
A new way of looking at kinase medicines

**Highly selective kinase medicines** offer potential for improved potency, less off-target activity and increased probability of clinical success.

### SELECTIVE
- AVAPRITINIB

### NON-SELECTIVE
- SUTENT® (SUNITINIB)
- RYDAPT® (MIDOSTAURIN)

Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. ([www.cellsignal.com](http://www.cellsignal.com)) (CSTI). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.
# Realizing our vision for Blueprint Medicines

### Drug Candidate (Target)

<table>
<thead>
<tr>
<th>Drug Candidate (Target)</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Phase 1-2</th>
<th>Pivotal</th>
<th>Commercial Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>avapritinib (KIT &amp; PDGFRα)</td>
<td>Phase 1 NAVIGATOR – Advanced PDGFRA-driven GIST</td>
<td>Phase 1 NAVIGATOR – Advanced 3L+ (KIT-driven) GIST</td>
<td>Phase 1 NAVIGATOR – 2L (KIT-driven) GIST</td>
<td>Phase 3 VOYAGER – Advanced 3L GIST</td>
<td>Phase 1 EXPLORER – Advanced systemic mastocytosis (SM)</td>
</tr>
<tr>
<td>BLU-554 (FGFR4)</td>
<td>Phase 1 – Advanced hepatocellular carcinoma</td>
<td></td>
<td></td>
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<tr>
<td>BLU-667 (RET)</td>
<td>Phase 1 ARROW – Advanced NSCLC, thyroid and other cancers¹</td>
<td></td>
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<td></td>
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<tr>
<td>BLU-782 (ALK2)</td>
<td>Fibrodyplasia ossificans progressiva</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3 undisclosed kinase targets</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Immunokinase targets</td>
<td>Up to 5 cancer immunotherapy programs; development stage undisclosed</td>
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</tbody>
</table>

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1. ARROW trial includes a basket cohort that consists of other advanced solid tumors with RET alterations.
2. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, BLU-554 and BLU-667 in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains all rights in the rest of the world.
3. Blueprint Medicines has U.S. commercial rights for up to two programs. Roche has worldwide commercialization rights for up to three programs and ex-U.S. commercialization rights for up to two programs.
Most GIST cases are caused by mutations in KIT or PDGFRA

- KIT mutations drive about 75-80% of GIST
- PDGFRA mutations drive about 5-10% of GIST

Primary GIST tumor sites:
- Stomach 60%
- Duodenum 5%
- Small intestine 30%
- Colon and rectum 5%
Beyond Gleevec® (imatinib), there are no highly effective therapies for patients with advanced GIST

<table>
<thead>
<tr>
<th></th>
<th>Gleevec® (imatinib)</th>
<th>Sutent® (sunitinib)</th>
<th>Stivarga® (regorafenib)</th>
<th>No approved treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1L</strong></td>
<td>~60%</td>
<td>~7%</td>
<td>~5%</td>
<td>~0% (^1)</td>
</tr>
<tr>
<td><strong>ORR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PFS</strong></td>
<td>19 months</td>
<td>6 months</td>
<td>4.8 months</td>
<td>1.8 months (^1)</td>
</tr>
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</table>

All FDA approved treatments are ineffective against PDGFRα D842V-driven GIST

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1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line; ORR, overall response rate; PFS, progression free survival

Avapritinib (formerly known as BLU-285)

- Experimental medicine
- Potent and selective inhibitor of KIT and PDGFRA
- Currently being evaluated in clinical trials for advanced GIST and advanced systemic mastocytosis
- Oral medication taken by mouth once a day
- Granted FDA Breakthrough Therapy Designation for the treatment of PDGFRα D842V-driven GIST
KIT and PDGFRA are increasingly activated in patients with GIST

- Avapritinib is uniquely designed to bind to the active “on” conformation of KIT and PDGFRA
  - This design enables potent inhibition of primary and secondary mutants that shift the kinase towards its active conformation
- Current treatments only bind to the inactive “off” conformation
Avapritinib potently inhibits the spectrum of clinically relevant KIT and PDGFRA mutations in advanced GIST

<table>
<thead>
<tr>
<th>Mutation Description</th>
<th>BLU-285 IC&lt;sub&gt;50&lt;/sub&gt;</th>
<th>Imatinib IC&lt;sub&gt;50&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>KIT Exon 11 deletion</td>
<td>0.6 nM</td>
<td>12 nM</td>
</tr>
<tr>
<td>KIT Exon 11 V560G</td>
<td>1 nM</td>
<td>87 nM</td>
</tr>
<tr>
<td>KIT Exon 11/13</td>
<td>11 nM</td>
<td>9160 nM</td>
</tr>
<tr>
<td>KIT Exon 11/14</td>
<td>28 nM</td>
<td>19650 nM</td>
</tr>
<tr>
<td>KIT Exon 17</td>
<td>&lt;2 nM</td>
<td>60–12750 nM</td>
</tr>
<tr>
<td>KIT Exon 17 D816V</td>
<td>0.27 nM</td>
<td>8150 nM</td>
</tr>
<tr>
<td>PDGFRα Exon 18 D842V</td>
<td>0.24 nM</td>
<td>759 nM</td>
</tr>
</tbody>
</table>

nM, nanomolar
Evans EK et al. Sci Transl Med. 2017 Nov 1;9(414).
Clinical activity of BLU-285, a highly potent and selective KIT/PDGFRα inhibitor designed to treat gastrointestinal stromal tumor (GIST)

Michael Heinrich1, Robin Jones2, Margaret von Mehren3, Patrick Schoffski4, Sebastian Bauer5, Olivier Mir6, Philippe A. Cassier7, Ferry Eskens8, Hongliang Shi9, Terri Alvarez-Diez9, Oleg Schmidt-Kittler9, Mary Ellen Healy9, Beni B. Wolf9, Suzanne George10

1Knight Cancer Institute, OHSU, Portland, OR, USA; 2Royal Marsden Hospital/Institute of Cancer Research, London, UK; 3Fox Chase Cancer Center, Temple University Health System, Philadelphia, USA; 4University Hospitals Leuven, Department of General Medical Oncology, Leuven Cancer Institute, Leuven, Belgium; 5West German Cancer Center, University Hospital, Essen, Germany; 6Gustave Roussy, Villejuif, France; 7Centre Leon Berard, Lyon, France; 8Erasmus MC Cancer Institute, Rotterdam, Netherlands; 9Blueprint Medicines, Cambridge, MA, USA; 10Dana-Farber Cancer Center, Boston, MA, USA

Abstract no. 2803523, CTOS 2017 Maui, Hawaii. Presented by Dr. Michael Heinrich

Connective Tissue Oncology Society 2017 Annual Meeting
November 8-11, 2017
Maui, Hawaii
Tumor reduction and prolonged progression free survival observed in patients with advanced GIST


**KIT-driven GIST (median 4 prior therapies)**

- Median progression free survival of 11.5 months

**PDGFRα D842-driven GIST**

- Median progression free survival not reached
- 78% of patients had not progressed at 12 months

77% disease control rate
17% overall response rate

100% disease control rate
71% overall response rate

N=30 patients
300–400 mg once daily
2 responses pending confirmation

N=31 patients
4 responses pending confirmation
Avapritinib has been generally well tolerated in patients with GIST

• Most adverse events were Grade 1 or 2 (mild or moderate)

• Only 6 patients (5%) discontinued treatment with avapritinib due to adverse events

• Regardless of severity or relationship to treatment with avapritinib, the most common adverse events occurring in 25% or more patients included:
  
  o Nausea (56%), fatigue (53%), periorbital edema (43%), vomiting (41%), peripheral edema (34%), anemia (31%), diarrhea (31%), increased lacrimation (30%), cognitive effects (30%), decreased appetite (28%)

• Treatment-related ≥Grade 3 (severe) adverse events were reported in 39 patients (34%)

AE, adverse event. Data previously presented in November 2017 at the CTOS Annual Meeting. Data cutoff: October 11, 2017. Cognitive effects are an aggregated category of individual cognitive events, each of which was observed in fewer than 20% of patients.
Phase 1 NAVIGATOR clinical trial now enrolling patients with 2L GIST

Design
- Open-label, Phase 1 clinical trial
- All enrolled patients receive avapritinib

Eligibility
- Aged 18 years or older
- Metastatic and/or unresectable GIST
- Have received Gleevec® (imatinib) or are intolerant to imatinib

Key endpoints: overall response rate, duration of response, safety

More Information
- Website: www.NavigatorStudy.com
- Email: studydirector@blueprintmedicines.com

Part 1 complete
- Open-label dose escalation (3+3)
- avapritinib 300 mg once daily

Part 2 ongoing
- PDGFRα D842V (n= ~50) fully enrolled
- 3L+ GIST (n= ~100) fully enrolled
- 2L GIST (n= ~50) enrolling
Phase 1 NAVIGATOR U.S. trial sites now enrolling patients with 2L GIST

Active

Additional trial sites active in Europe, United Kingdom, and Asia

- Oregon Health and Science University
  Portland, OR
- Sarcoma Oncology Center
  Santa Monica, CA
- MD Anderson Cancer Center
  Houston, TX
- Dana-Farber Cancer Institute
  Boston, MA
- Memorial Sloan Kettering Cancer Center
  New York, NY
- Fox Chase Cancer Center
  Philadelphia, PA
- Sylvester Comprehensive Cancer Center
  Miami, FL

A travel support program is available to qualifying patients and caregivers and includes reimbursement of eligible local and long-distance travel and lodging.
Phase 3 VOYAGER clinical trial now enrolling patients with 3L and 4L GIST

**Design**
- Open-label, randomized, Phase 3 clinical trial
- Patients randomized to receive either avapritinib or Stivarga® (regorafenib)
- Patients assigned to receive regorafenib may cross over to receive avapritinib following confirmed disease progression

**Eligibility**
- Aged 18 years or older
- Metastatic and/or unresectable GIST
- Have received Gleevec® (imatinib) and 1 or 2 other tyrosine kinase inhibitors

**More Information**
- Website: www.VoyagerTrial.com
- Email: studydirector@blueprintmedicines.com

- **Randomized**
  - avapritinib (n= 230)
    - 300 mg once daily
  - Stivarga® (regorafenib) (n= 230)
    - 160 mg once daily for 3 out of every 4 weeks

Primary endpoint: progression free survival
A travel support program is available to qualifying patients and caregivers and includes reimbursement of eligible local and long-distance travel and lodging.
Summary of key avapritinib updates

- Granted FDA Breakthrough Therapy Designation for the treatment of PDGFRα D842V-driven GIST

- Completed enrollment of cohorts for patients with PDGFRα D842V-driven GIST and 3L+ (KIT-driven GIST) in Phase 1 NAVIGATOR clinical trial
  - Additional cohort for patients with 2L GIST is actively enrolling

- Initiated Phase 3 VOYAGER clinical trial for patients with 3L and 4L GIST

- Plan to report updated data from the NAVIGATOR trial in the second half of 2018

- Plan to submit a New Drug Application for the approval of avapritinib for the treatment of patients with PDGFRα D842V-driven GIST in the first half of 2019
Questions and Answers

Clinical trial inquiries:
studydirector@blueprintmedicines.com