PRECISION THAT MOVES™
Staying one step ahead of disease

July 20, 2020

Linnea, living with lung cancer

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Forward-looking statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. 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. In this presentation, forward-looking statements include, without limitation, statements regarding the plans, strategies, timelines and expectations of Blueprint Medicines Corporation (the "Company") for the preclinical and clinical development and commercialization of AYVAKIT™ (avapritinib), pralsetinib and other current or future drug candidates; plans, timing, design, initiation, enrollment, expectations and announcement of results for the Company's ongoing and planned clinical trials; plans and timelines for submitting marketing applications for avapritinib and pralsetinib and, if approved, commercializing avapritinib in additional geographies or for additional indications or pralsetinib; the potential benefits of any of the Company's current or future approved drugs or drug candidates in treating patients; the collaboration agreement among the Company, Roche and Genentech, including anticipated upfront, milestone and other payments, equity investment and other financial terms of the collaboration agreement; plans to develop a next-generation RET inhibitor; plans and timelines for submitting additional marketing applications for pralsetinib and, if approved, commercializing pralsetinib; plans to expand investment in systemic mastocytosis and pipeline programs; expectations regarding the Company's existing, cash, cash equivalents and investments, including expectations for achieving a self-sustainable financial profile and a reduced reliance on capital markets; and the Company's strategy, goals and anticipated milestones, 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 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 drugs, and launching, marketing and selling current or future approved drugs; the delay of any current or planned clinical trials or the development of the Company's drug candidates or the licensed drug candidate; the Company's advancement of multiple early-stage efforts; the Company's ability to successfully demonstrate the efficacy and safety 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; actions or decisions of regulatory agencies or authorities, which may affect the initiation, timing and progress of clinical trials or marketing applications; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing or AYVAKIT; the Company's ability and plans for maintaining a commercial infrastructure, and successfully launching, marketing and selling its current or future approved drugs; the Company's ability to develop and commercialize companion diagnostic tests for any of the Company's current or future approved drugs or drug candidates; and the success of the Company's current and future collaborations, partnerships and licenses.

These and other risks and uncertainties are described in greater detail under "Risk Factors" in the Company's filings with the Securities and Exchange Commission ("SEC"). Including its most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q, and any other filings it 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 its 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.

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The rapid evolution of Blueprint Medicines

**IMAGINING A NEW PLATFORM**
- 2011 – 2014

**BUILDING THE PIPELINE**
- 2015 – 2019

**REALIZING THE VISION**
- 2020 – FUTURE

**HIGHLY SELECTIVE KINASE MEDICINE DISCOVERY PLATFORM**

**RAPID CLINICAL PROOF-OF-CONCEPT ACROSS MULTIPLE PROGRAMS**

- Avapritinib in advanced systemic mastocytosis: change in serum tryptase

**Integration**
- Integrated commercialization
- Indication expansion
- Therapeutic area leadership
- Innovative kinase biology


Not for promotional use.
<table>
<thead>
<tr>
<th>DISCOVERY</th>
<th>EARLY-STAGE DEVELOPMENT</th>
<th>LATE-STAGE DEVELOPMENT</th>
<th>REGULATORY SUBMISSION</th>
<th>APPROVED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avapritinib (KIT &amp; PDGFRA)</td>
<td>PDGFRA GIST&lt;sup&gt;1,2,3&lt;/sup&gt;</td>
<td>MAA</td>
<td>U.S.</td>
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<tr>
<td></td>
<td>Advanced SM&lt;sup&gt;2&lt;/sup&gt;</td>
<td>NDA</td>
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<tr>
<td></td>
<td>Indolent SM&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>Pralsetinib (RET)</td>
<td>RET+ NSCLC&lt;sup&gt;1,2,4&lt;/sup&gt;</td>
<td>NDA</td>
<td>NDA / MAA&lt;sup&gt;5&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>EGFR+ NSCLC (+osimertinib) &lt;sup&gt;1,2,4&lt;/sup&gt;</td>
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<td>RET+ MTC&lt;sup&gt;1,2,4&lt;/sup&gt;</td>
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<tr>
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<td>RET+ thyroid cancer&lt;sup&gt;1,2,4&lt;/sup&gt;</td>
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<td>NDA</td>
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<td>Other RET-altered solid tumors&lt;sup&gt;1,2,4&lt;/sup&gt;</td>
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<tr>
<td>Fisogatinib (FGFR4)</td>
<td>Advanced HCC&lt;sup&gt;2&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>Advanced HCC (+CS1001)&lt;sup&gt;2&lt;/sup&gt;</td>
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<tr>
<td>BLU-263 (KIT)</td>
<td>Indolent SM</td>
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<tr>
<td>BLU-945 (EGFR+ triple mutant)</td>
<td>EGFR+ NSCLC&lt;sup&gt;1&lt;/sup&gt;</td>
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<tr>
<td>(EGFR+ double mutant)</td>
<td>EGFR+ NSCLC&lt;sup&gt;1&lt;/sup&gt;</td>
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<tr>
<td>(2 undisclosed targets)</td>
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<tr>
<td>(MAP4K1)&lt;sup&gt;6&lt;/sup&gt;</td>
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<tr>
<td>(3 undisclosed immunokinase targets)&lt;sup&gt;6&lt;/sup&gt;</td>
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</tbody>
</table>

1. Unresectable or metastatic disease. 2. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, pralsetinib and fsgatinib in Mainland China, Hong Kong, Macau and Taiwan. 3. Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. The proposed indication for the MAA is unresectable or metastatic GIST harboring a PDGFRA D842V mutation. 4. In collaboration with Roche. Blueprint Medicines and Roche have co-exclusive rights to develop and commercialize pralsetinib in the U.S., and Roche has exclusive rights to develop and commercialize pralsetinib outside the U.S., excluding the CStone territory. 5. The proposed indication for the MAA is locally advanced or metastatic RET fusion-positive NSCLC previously treated with platinum-based chemotherapy. 6. In collaboration with Roche. Blueprint Medicines has U.S. commercial rights for up to two programs. Roche has worldwide commercialization rights for up to two programs and ex-U.S. commercialization rights for up to two programs. GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; MAA, marketing authorization application; MTC, medullary thyroid cancer; NDA, new drug application; NSCLC, non small cell lung cancer; SM, systemic mastocytosis.

Updated as of July 14, 2020.
Pralsetinib: an investigational precision therapy for RET-altered cancers

POTENT AND HIGHLY SELECTIVE RET INHIBITOR

PRALSETINIB

LATE CLINICAL DEVELOPMENT

U.S. REGULATORY SUBMISSION STATUS

RET+ NSCLC
Submitted

RET+ thyroid cancer
Submitted

Other RET+ solid tumors

NDA for RET+ NSCLC granted priority review with November 23, 2020 PDUFA action date

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Pralsetinib’s rapid development path reflects our precision therapy expertise and culture of urgency and efficiency

~3 YEARS FROM FIRST PATIENT DOSED TO NDA SUBMISSION

2017
First patient dosed

2018
Clinical POC data presented at AACR

2019
Granted FDA breakthrough therapy designation
Expansion trial data presented at ASCO

2020
NDA submitted to FDA for RET+ NSCLC
MAA submitted to EMA for RET+ NSCLC
NDA submitted to FDA for RET+ thyroid cancers
NSCLC registration data presented at ASCO

AACR, American Academy of Cancer Research Annual Meeting; ASCO, American Society of Clinical Oncology Annual Meeting; EMA, European Medicines Agency; FDA, U.S. Food and Drug Administration; PDUFA, Prescription Drug User Fee Act; POC, proof of concept.

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Blueprint Medicines and Roche: a transformative partnership for pralsetinib

**STRATEGIC IMPERATIVES**

1. Bring pralsetinib faster to more patients globally
2. Continue to build best-in-class precision medicine capabilities
3. Transform the company with path to financial independence

**COLLABORATION STRUCTURE & IMPACT**

- Co-commercialize pralsetinib in the U.S., equally sharing responsibilities, profits and losses
- Grant Roche license to commercialize pralsetinib outside of the U.S., excluding Greater China\(^1\)
- Co-develop pralsetinib globally, expanding into new treatment settings
- Explore co-development of a next-generation selective RET inhibitor
- Reduce reliance on capital markets to finance company
- Expand investment in systemic mastocytosis and pipeline programs

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1. Greater China comprises Mainland China, Hong Kong, Macau and Taiwan.
Summary of financial terms

2ND LARGEST BIOPHARMACEUTICAL COLLABORATION IN 2020 TO DATE

**UPFRONT**
$775M, with $675M in cash and $100M equity investment at $96.57 per share

**MILESTONES**
Up to $927M in contingent payments, with approximately $90M in potential near-term milestones

**ROYALTIES**
Tiered high-teens to mid-twenties on aggregate net sales outside U.S.

**U.S. P&L**
Companies to equally share profits and losses

**DEVELOPMENT**
Costs shared 45% Blueprint / 55% Roche up to pre-specified limit, then % reduction for Blueprint

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1. Based on upfront payment. Source: company information, third party press releases and SEC filings. 2. Closing for a minority portion of the equity investment is subject to the expiration or termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions.

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RET alterations: oncogenic drivers lacking a targeted therapeutic approach

Non-small cell lung cancer:
~1-2% RET fusions\textsuperscript{1,2}

Advanced medullary thyroid cancer:
~90% RET mutations\textsuperscript{3}

Papillary thyroid cancer:
~10-20% RET fusions\textsuperscript{4}

Multiple other tumor types
<1% RET-altered, including:\textsuperscript{5,6}
- esophageal
- pancreatic
- breast
- melanoma
- colorectal
- leukemia

Robust clinical activity in NSCLC patients regardless of prior therapy

Data presented at ASCO 2020 virtual annual meeting. Data cutoff: November 18, 2019. 1. Two responses pending confirmation at the time of data cutoff were subsequently confirmed. CI, confidence interval.

12% complete response rate in patients with no prior systemic therapy

Data presented at ASCO 2020 virtual annual meeting. Data cutoff: November 18, 2019. 1. Two responses pending confirmation at the time of data cutoff were subsequently confirmed. CI, confidence interval.

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Prolonged duration of response in NSCLC patients regardless of prior therapy

DURATION OF RESPONSE PER CENTRAL RADIOLOGY

Data presented at ASCO 2020 virtual annual meeting. Data cutoff: November 18, 2019. CR, complete response; PR, partial response. NR, not reached.

Median DOR: 11.3 months (95% CI: 11.3 m - NR)
6-month DOR: 86%
Responders on treatment: 74%

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Robust clinical activity in MTC patients regardless of prior therapy

TUMOR SHRINKAGE PER CENTRAL RADIOLOGY

OVERALL RESPONSE RATE

| Tumor shrinkage in 99% of patients regardless of prior therapy |


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Prolonged duration of response in patients with previously treated MTC


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Deep and durable responses in patients with RET fusion+ thyroid cancer


TUMOR SHRINKAGE PER CENTRAL RADIOLOGY

ORR
91%
(95% CI: 59-100%)

6-month DOR
100%

RET FUSION+ THYROID CANCER
ALL DOSES (N=11)

10/11 patients previously treated with systemic therapy


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Pralsetinib is well-tolerated in patients with advanced cancer

- Only 4% discontinued due to treatment-related AEs
- Low ≥Grade 3 hypertension
- Low ≥Grade 3 AST/ALT elevations
- No clinically or statistically significant QT prolongation observed in QT sub-study
- No treatment-related hypersensitivity

### Treatment-related adverse events in ≥15% of patients

<table>
<thead>
<tr>
<th>AE preferred term</th>
<th>Any grade (%)</th>
<th>Grade ≥3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST increased</td>
<td>31</td>
<td>2</td>
</tr>
<tr>
<td>Anemia</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>ALT increased</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>Constipation</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>19</td>
<td>10</td>
</tr>
</tbody>
</table>

• Only 4% discontinued due to treatment-related AEs
• Low ≥Grade 3 hypertension
• Low ≥Grade 3 AST/ALT elevations
• No clinically or statistically significant QT prolongation observed in QT sub-study
• No treatment-related hypersensitivity

**Natural history data highlight importance of drug safety profile in advanced cancer patients:**

67% of NSCLC patients have ≥1 CV comorbidity, with ~10% experiencing a CV event

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Our plan to deliver a best-in-class selective RET inhibitor to patients

**DIFFERENTIATED CLINICAL PROFILE**

Data showing deep responses, long-lasting benefit, tolerability and convenience

**PATIENT- AND HEALTHCARE PROVIDER-CENTERED APPROACH**

Tailored support enabling patient identification, ease of prescribing and ongoing patient management

**HIGHLY EXPERIENCED, NIMBLE TEAM**

Fully-integrated launch-ready team in place, 2/3 with prior lung cancer experience
Avapritinib: a precision therapy with broad potential

**Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations.**

**Planned NDA submission. Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com) (CSTI). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content. CHMP; EMA Committee for Medicinal Products for Human Use.**

**Anticipate EMA CHMP opinion on avapritinib MAA for PDGFRA D842V GIST in Q3 2020**

**Anticipate EMA CHMP opinion on avapritinib MAA for PDGFRA D842V GIST in Q3 2020**

1. Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations.

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Strong early AYVAKIT execution establishes a foundation for anticipated launches in RET-altered cancers and systemic mastocytosis

With transformative therapies and superior service, we aim to be recognized as the leader in precision medicine by hematology/oncology centers of excellence

<table>
<thead>
<tr>
<th>STRATEGIC IMPERATIVES</th>
<th>ACHIEVEMENTS THROUGH Q1 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drive positive first experiences with AYVAKIT</td>
<td>&gt;100 unique prescribers, with ~40% in community setting</td>
</tr>
<tr>
<td>Deliver best-in-class patient support</td>
<td>~80% of prescriptions processed through YourBlueprint™</td>
</tr>
<tr>
<td></td>
<td>&gt;90% of commercial and Medicare lives covered at or better than label</td>
</tr>
<tr>
<td>Catalyze patient identification</td>
<td>Precision medicine team actively engaged at national and regional levels to drive patient identification across portfolio</td>
</tr>
</tbody>
</table>

$3.5M in net sales achieved in first partial quarter of launch (Q1 2020)

Full prescribing information is available at www.AYVAKIT.com.

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Systemic mastocytosis is one disease driven by KIT D816V

**Advanced SM**

- Debilitating symptoms
- Significant organ involvement
- Requirement of high intensity treatment

**Non-advanced SM** (Indolent and smoldering)

- Requirement for life-long chronic treatment

~75,000 patients in major markets

Patient numbers in major markets based on estimated prevalence for advanced, indolent and smoldering systemic mastocytosis in the US, EU5 and Japan.

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Avapritinib is the only highly potent inhibitor of KIT D816V, the common disease driver across systemic mastocytosis.


KIT D816V MUTATION ALLELE FRACTION (MAF)¹

Patients with advanced and non-advanced SM across avapritinib trials (N=115)

~95% of all patients had a ≥25% reduction

≥25% reduction in KIT D816V MAF is correlated with improved overall survival in advanced SM²


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EXPLORER trial results: Remarkable response rate and prolonged duration of response in patients with advanced SM

- FDA breakthrough therapy designation
- Robust activity across all disease subtypes
- Median follow up of 21 months with ongoing treatment up to ~3.5 years

BEST RESPONSE PER IWG-MRT-ECNM CRITERIA
ALL DOSES (N=48)

77% Confirmed ORR
Median DOR and OS not reached

SAFETY
ALL DOSES (N=80)

- Avapritinib was generally well-tolerated, and most AEs were grade 1 or 2
- Most common treatment-emergent AEs were periorbital edema, anemia, diarrhea, fatigue, peripheral edema, nausea, thrombocytopenia, vomiting and cognitive effects
- Across all doses, 6 patients discontinued treatment due to treatment-related AEs

1. EXPLORER trial data reported on December 8, 2019. Data cutoff: August 30, 2019. 2. ORR defined as complete remission with full or partial recovery of peripheral blood counts, partial remission or clinical improvement. 3. Avapritinib granted Breakthrough Therapy Designation for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia. 4. After the data cutoff date, one patient with SM and an associated hematologic neoplasm (SM-AHN) of myelodysplastic syndrome had a Grade 5 intracranial bleed. At the time of the bleeding event, the patient had severe thrombocytopenia and experienced a serious injury involving head trauma. DOR, duration of response; OS, overall survival.

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PIONEER trial results: unparalleled clinical profile in patients with indolent SM

**Improves disease symptoms**

ISM-SAF total symptom score

**Improves quality of life**

MC-QoL total score

**Reduces mast cell burden**

KIT D816V mutant allele fraction

Favorable safety profile supports the selection of avapritinib 25 mg QD as recommended Part 2 dose


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Avapritinib 25 mg QD reduces symptoms and mast cell burden in indolent SM

Presented at EAACI Virtual 2020 Congress. Data cut-off: March 31, 2020. *24 weeks or last assessment before, if 24 weeks not available. EAACI, European Academy of Allergy and Clinical Immunology.

Part 2 primary endpoint
≥30% reduction in ISM-SAF Total Symptom Score at 24 weeks

Part 2 first key secondary endpoint
≥50% tryptase reduction at 24 weeks*

Response rate: 0% 60% 0% 70%
Safety results for avapritinib 25mg QD are similar to placebo at 16 weeks

<table>
<thead>
<tr>
<th>Preferred term</th>
<th>Placebo (n=9)</th>
<th>avapritinib (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of subjects with ≥1 AE</td>
<td>any grade</td>
<td>grade 3</td>
</tr>
<tr>
<td>Nausea</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>11</td>
<td>0</td>
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<tr>
<td>Diarrhea</td>
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<tr>
<td>Fatigue</td>
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<td>Face edema</td>
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<td>0</td>
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<td>Periorbital edema</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bone Pain</td>
<td>22</td>
<td>0</td>
</tr>
</tbody>
</table>

AVAPRITINIB 25 MG QD

- No patients had serious AEs
  - 2 patients treated with placebo had serious AEs, 1 with psychogenic seizure and 1 with diffuse cutaneous mastocytosis
- No patients had dose modifications
- No patients discontinued due to AEs

Follow up at 24 weeks showed no ≥grade 3 AEs or discontinuations due to AEs for avapritinib 25 mg QD

PIONEER Registration-enabling Part 2

Design: Randomized, double-blind, placebo-controlled treatment period, followed by open-label expansion

Key endpoints: Response rate defined as ≥30% reduction in ISM-ASF total symptom score (primary), measures of mast cell burden, quality of life, concomitant medications

Sample size: ~200 patients

Duration: 24 weeks
Key anticipated corporate milestones through 2H 2020

**Q3 2020**

- Obtain CHMP opinion from EMA for avapritinib in PDGFRA GIST
- Report top-line EXPLORER and PATHFINDER data for avapritinib in advanced SM

**Q4 2020**

- Pralsetinib PDUFA action date for RET+ NSCLC NDA
- Submit avapritinib NDA to FDA for advanced SM
- Present BLU-945 preclinical data in resistant EGFR+ NSCLC