UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): **June 5, 2017**

Blueprint Medicines Corporation
(Exact name of registrant as specified in its charter)

Delaware	**001-37359**	**26-3632015**
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

38 Sidney Street, Suite 200 **Cambridge, Massachusetts**	**02139**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(617) 374-7580**

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☑

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☑

Item 7.01 Regulation FD Disclosure.

On June 5, 2017, Blueprint Medicines Corporation (the "Company") issued a press release announcing new data from its ongoing Phase 1 clinical trial evaluating BLU-285 for the treatment of advanced gastrointestinal stromal tumors ("GIST"). The press release also announced that the U.S. Food and Drug Administration has granted Breakthrough Therapy Designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation. The data were presented on Monday, June 5, 2017 in an oral presentation at the 2017 American Society of Clinical Oncology ("ASCO") Annual Meeting in Chicago, Illinois. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K, and a copy of the presentation at the ASCO Annual Meeting is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

In addition, on June 5, 2017, the Company hosted an investor event and live webcast to discuss the data presented at the ASCO Annual Meeting. A copy of the presentation from the investor event is furnished as Exhibit 99.3 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.1, 99.2 and 99.3, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release issued by Blueprint Medicines Corporation on June 5, 2017
99.2	Presentation by Blueprint Medicines Corporation at the ASCO Annual Meeting on June 5, 2017
99.3	Presentation by Blueprint Medicines Corporation at investor event on June 5, 2017

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

BLUEPRINT MEDICINES CORPORATION

Date: June 6, 2017

By: /s/ Tracey L. McCain
Tracey L. McCain
Chief Legal Officer

EXHIBIT INDEX

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Blueprint Medicines Announces New Phase 1 Clinical Data for BLU-285 in Advanced Gastrointestinal Stromal Tumors and Plans to Pursue Expedited Development in Patients with a PDGFRα D842V Mutation

– BLU-285 receives Breakthrough Therapy Designation for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation –
– Encouraging clinical activity demonstrated in multiple GIST patient populations, including preliminary evidence of prolonged progression free survival –
– Blueprint Medicines to host investor event and webcast on Monday, June 5, 2017 –

CAMBRIDGE, Mass., June 5, 2017 /PRNewswire/ – Blueprint Medicines Corporation (NASDAQ:BPMC), a leader in discovering and developing targeted kinase medicines for patients with genomically defined diseases, today announced new Phase 1 clinical data and outlined registration plans for BLU-285, a potent and highly selective PDGFRα and KIT inhibitor in development as a potential treatment for patients with advanced gastrointestinal stromal tumors (GIST). In patients with PDGFRα-driven GIST harboring a D842 mutation, the data showed an objective response rate (ORR) of 60 percent and an estimated 9-month progression free survival (PFS) of 87 percent. Among patients with treatment-resistant KIT-driven GIST, tumor reduction was observed in eight of 14 evaluable patients treated at dose levels of at least 300 mg once daily (QD). BLU-285 was well tolerated, and most adverse events (AEs) reported by investigators were Grade 1 or 2. The data will be presented today in an oral presentation during the "GIST: Imatinib and Beyond" session from 1:15 to 2:45 p.m. CT (Abstract 11011) at the 2017 ASCO Annual Meeting in Chicago.

Blueprint Medicines also announced today that the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation to BLU-285 for the treatment of patients with unresectable or metastatic PDGFRα D842V-driven GIST, and the Company plans to pursue expedited development of BLU-285 in this population. Based on feedback from the FDA at a recent End-of-Phase 1 meeting, additional data from the expansion portion of the ongoing Phase 1 clinical trial of BLU-285 may be sufficient to support a New Drug Application (NDA) for the treatment of patients with PDGFRα D842V-driven GIST. Blueprint Medicines currently estimates it will complete enrollment of the PDGFRα D842V expansion cohort, which is expected to include approximately 50 patients, by the middle of 2018. The Company also plans to initiate a global, pivotal Phase 3 clinical trial of BLU-285 in the first half of 2018, with the goal of supporting the registration of BLU-285 in a broader GIST patient population.

"Advanced GIST is a devastating disease marked by rapid disease progression, and patients with PDGFRα-driven GIST and treatment-resistant KIT-driven GIST have limited or no effective treatments," said Michael Heinrich, M.D., Oregon Health & Science University, an investigator on the clinical trial. "The new data announced today reinforce the clinical potential of BLU-285 in these populations. High response rates and prolonged progression free survival suggest BLU-285 has the potential to transform the treatment of PDGFRα D842-driven GIST. In addition, BLU-285 showed very encouraging anti-tumor activity in the treatment-resistant KIT-driven GIST population with a complex mutational burden, for whom disease control is a major treatment goal. Together, these results support efforts to expand the clinical development of BLU-285, including into earlier lines of GIST treatment."

“Blueprint Medicines is committed to advancing BLU-285 as swiftly as possible with the goal of addressing the significant medical need in advanced GIST,” said Andy Boral, M.D., Chief Medical Officer at Blueprint Medicines. “Based on the updated BLU-285 clinical data and our recent interactions with the FDA, we believe we have paths forward in PDGFRα D842-driven GIST and treatment-resistant KIT-driven GIST. Importantly, the FDA is open to considering additional data from our ongoing Phase 1 clinical study as the basis for an NDA for BLU-285 in PDGFRα D842V-driven GIST. These developments bring us closer to achieving our vision of rapidly delivering targeted kinase medicines to patients with genomically defined diseases.”

New Data from the Ongoing Phase 1 Clinical Trial of BLU-285 in Advanced GIST

BLU-285 is currently being evaluated in a Phase 1 clinical trial in patients with unresectable PDGFRα-driven GIST and patients with treatment-resistant KIT-driven GIST. Following completion of the dose escalation portion of the trial and determination of the maximum tolerated dose (MTD), Blueprint Medicines initiated the expansion portion of the trial in the first quarter of 2017.

As of the data cutoff date of April 28, 2017, 72 patients had been treated with BLU-285 in the dose escalation and expansion portions of the Phase 1 clinical trial, at eight dose levels (ranging from 30 mg QD to 600 mg QD), including 32 patients with PDGFRα-driven GIST and 40 patients with KIT-driven GIST. The median number of prior tyrosine-kinase inhibitor (TKI) regimens was 1.5 for patients with PDGFRα-driven GIST (ranging from zero to six), and four for patients with KIT-driven GIST (ranging from two to 11). Among patients with KIT-driven GIST, 36 patients (90 percent) had been treated with at least three prior TKI regimens, including 34 patients (85 percent) who had been previously treated with regorafenib.

Pharmacokinetic (PK) data demonstrated a mean half-life of more than 24 hours, supporting a once-daily dosing regimen. Consistent with previously reported preclinical data, PK data from the ongoing clinical trial suggested that exposure at dose levels ranging from 300 to 400 mg QD confers activity against a broad spectrum of disease-driving mutations.

Safety Data

As of the data cutoff date, BLU-285 was observed to be well-tolerated. Most AEs reported by investigators were Grade 1 or 2. Across all grades, AEs reported by investigators most commonly included nausea (60 percent), fatigue (53 percent), vomiting (42 percent), periorbital edema (36 percent), diarrhea (33 percent), and peripheral edema (31 percent). Investigators reported treatment-related Grade ≥3 AEs in 18 patients (25 percent). Grade ≥3 AEs occurring in two or more patients included fatigue, hypophosphatemia, anemia, nausea, vomiting and hyperbilirubinemia. Two patients experienced dose-limiting toxicities at 600 mg QD (Grade 2 hyperbilirubinemia in one patient; Grade 2 rash, Grade 2 hypertension and Grade 2 memory impairment all in one patient), leading to the determination of 400 mg QD as the MTD. Only one patient discontinued treatment with BLU-285 due to a drug-related toxicity (Grade 3 hyperbilirubinemia). An additional 20 patients discontinued treatment, including 19 patients due to progressive disease and one patient due to the investigator’s decision. Among all 72 enrolled patients, 51 remained on the trial as of the data cutoff date.

Clinical Activity Data

As of the data cutoff date, 26 patients with PDGFRα-driven GIST were evaluable for response assessment, including 23 patients with a D842V mutation, two patients with other D842 mutations, and one patient

with an exon 14 mutation who was excluded from analyses of clinical activity. In addition, 25 patients with KIT-driven GIST were evaluable for response assessment. Patients were evaluable if they had at least one centrally reviewed radiographic scan, and all reported data are based on blinded central radiographic review as per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Radiographic scans were also assessed by Choi criteria, a supportive method of response assessment in soft tissue sarcoma. An additional 21 enrolled patients had not been evaluated for response by the data cutoff date.

PDGFRα D842-driven GIST

- Radiographic tumor reductions were observed in 25 of 25 evaluable patients with PDGFRα D842-driven GIST.
- By RECIST criteria, 15 patients had a partial response (PR) (12 confirmed, three pending confirmation), and 10 patients had stable disease (SD), representing a preliminary objective response rate (ORR) of 60 percent and a disease control rate (DCR) of 100 percent.
- By Choi criteria, 25 patients had a PR, representing an ORR of 100 percent.
- Median PFS was not reached and 9-month PFS was estimated to be 87 percent. In contrast, historical data showed a zero percent ORR and median PFS of 2.8 months in patients with PDGFRα D842V–driven GIST treated with imatinib.[1]

Treatment-resistant KIT-driven GIST

- Radiographic tumor reductions were observed in 10 of 25 evaluable patients, including patients with complex genotypes involving primary and secondary KIT mutations (e.g., mutations in exons 8, 9, 11, 13, 17 and 18).
- In patients treated at dose levels of at least 300 mg QD, eight of 14 patients had tumor reductions per RECIST, including one patient who achieved a PR.
- By RECIST criteria, two patients had a PR (one confirmed, one pending confirmation), and 12 patients had SD, representing a preliminary ORR of eight percent and a DCR of 56 percent.
- By Choi criteria, eight patients had a PR, and six patients had SD, representing a preliminary ORR of 32 percent and a DCR of 56 percent.
- Median PFS among patients treated at dose levels of at least 300 mg QD was 9.3 months. In contrast, historical data showed a zero percent ORR and median PFS of 1.8 months in patients with TKI-resistant advanced GIST re-treated with imatinib in a third-line or later setting.[2]

Investor Event and Webcast Information

Blueprint Medicines will host an investor event on Monday, June 5, 2017 beginning at 6:00 p.m. CT (7:00 p.m. ET) in Chicago to review the updated clinical data for BLU-285 in GIST. Formal presentations and the live webcast will begin at 6:30 p.m. CT (7:30 p.m. ET). The event can be accessed by dialing 1-855-728-4793 (domestic) or 1-503-343-6666 (international) and providing the passcode 13676007. A live webcast will also be available under “Events & Presentations” in the Investors section of Blueprint Medicines’ website at http://ir.blueprintmedicines.com. The archived webcast will be available on Blueprint Medicines’ website approximately two hours after the event concludes and will be available for 30 days following the event.

Informational Webinar for the GIST Patient Community

Blueprint Medicines will host an informational webinar for the GIST patient community on Thursday, June 22, 2017 beginning at 12:00 p.m. ET. To participate in the webinar, please dial 1-855-880-1246 (domestic) or 1-408-638-0968 (international) and refer to webinar ID 855 846 509. A live webcast of the presentation will be available at www.blueprintmedicines.com in the "Patients" section of Blueprint Medicines' website under "Patient Community Events." The archived webcast will be available on Blueprint Medicines' website approximately one day after the webinar and will be available for 30 days following the webinar.

About the Phase 1 Clinical Trial for BLU-285 in PDGFRα-Driven and KIT-Driven GIST

The Phase 1 clinical trial of BLU-285 is designed to evaluate the safety and tolerability of BLU-285 in adults with advanced GIST. The trial consists of two parts, a dose-escalation portion and an expansion portion. The dose-escalation portion is complete, and the MTD has been determined to be 400 mg QD. The expansion portion is actively enrolling patients in two defined cohorts, including a cohort of patients with a PDGFRα D842V mutation, regardless of line of therapy, and a cohort of patients who have received imatinib and at least one other KIT-directed TKI. Trial objectives include assessing response, pharmacokinetics and pharmacodynamic measures. The two expansion cohorts of the trial are designed to enroll approximately 100 patients at multiple sites in the United States, United Kingdom and European Union. Please refer to www.clinicaltrials.gov for additional details related to this Phase 1 clinical trial (NCT02508532). Patients and physicians may contact the study director for more information about this Phase 1 clinical trial at studydirector@blueprintmedicines.com.

About GIST

GIST is the most common sarcoma, or tumor of bone or connective tissue, of the gastrointestinal (GI) tract. Tumors arise from cells in the wall of the GI tract and occur most often in the stomach or small intestine. Most patients are diagnosed between the ages of 50-80, and diagnosis is typically triggered by GI bleeding, incidental findings during surgery or imaging and, in rare cases, tumor rupture or GI obstruction. Approximately 80 percent of GIST patients have KIT-driven GIST, and Blueprint Medicines estimates that KIT exon 17 mutations occur in approximately 90 percent of GIST patients with KIT-driven GIST following treatment with at least two TKIs. Approximately five percent of all advanced GIST cases are driven by D842V mutant PDGFRα. Patients diagnosed with GIST at an early stage may undergo surgery. For patients with KIT-driven GIST, treatment with the currently approved frontline therapy typically leads to treatment resistance and disease progression. Treatment options for KIT-driven GIST patients whose disease progresses or develops resistance are currently limited, with approved therapies providing a progression free survival of up to six months and a response rate between five percent and seven percent. There are no effective treatment options for patients with PDGFRα D842V-driven GIST, and progression often occurs in as little as three months with available treatment options.

About BLU-285

BLU-285 is an orally available, potent and highly selective inhibitor of PDGFRα and KIT. Preclinical data have shown that BLU-285 is active across a broad spectrum of PDGFRα and KIT mutations, including PDGFRα D842V and KIT exon 17 mutations for which there are limited or no effective treatment options. Blueprint Medicines is initially developing BLU-285, an investigational medicine, for the treatment of patients with advanced GIST and advanced systemic mastocytosis. BLU-285 was discovered by Blueprint

Medicines' research team leveraging its proprietary compound library, and the Company retains worldwide development and commercialization rights for BLU-285.

In June 2017, BLU-285 received Breakthrough Therapy Designation from the U.S. Food and Drug Administration (FDA) for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation. The FDA's Breakthrough Therapy Designation is intended to expedite the development and review of a drug candidate intended to treat a serious or life-threatening disease or condition, when preliminary clinical evidence indicates that the drug candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Previously, the FDA granted orphan drug designation to BLU-285 for the treatment of GIST. The FDA also granted Fast Track designation to BLU-285 for the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second TKI and for the treatment of patients with unresectable or metastatic GIST in patients with the PDGFRα D842V mutation regardless of prior therapy.

About Blueprint Medicines

Blueprint Medicines is developing a new generation of targeted and potent kinase medicines to improve the lives of patients with genomically defined diseases. Its approach is rooted in a deep understanding of the genetic blueprint of cancer and other diseases driven by the abnormal activation of kinases. Blueprint Medicines is advancing four programs in clinical development for subsets of patients with gastrointestinal stromal tumors, hepatocellular carcinoma, systemic mastocytosis, non-small cell lung cancer, medullary thyroid cancer and other advanced solid tumors, as well as multiple programs in research and preclinical development. For more information, please visit www.blueprintmedicines.com.

References

[1] Cassier PA, Fumagalli E, Rutkowski P, et al. Outcome of Patients with Platelet-Derived Growth Factor Receptor Alpha–Mutated Gastrointestinal Stromal Tumors in the Tyrosine Kinase Inhibitor Era. Clin Cancer Res. 2012;18(16):4458–64.

[2] Kang YK, Ryu MH, Ryoo BY, et al. Resumption of imatinib to control metastatic or unresectable gastrointestinal stromal tumours after failure of imatinib and sunitinib (RIGHT): a randomised, placebo-controlled, phase 3 trial. Lancet Oncol. 2013;14(12):1175–82.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans and timelines for the clinical development of BLU-285, including plans and timelines for pursuing expedited development in patients with a PDGFRα D842V mutation and plans and timelines for the initiation of a global, pivotal Phase 3 clinical trial of BLU-285; Blueprint Medicines' ability to implement its clinical development plans for BLU-285 in advanced GIST; Blueprint Medicines' ability to enroll patients in its ongoing Phase 1 clinical trial for BLU-285 in advanced GIST and expectations regarding the completion of enrollment of the PDGFRα D842V expansion cohort; expectations regarding current and future interactions with the U.S. Food and Drug Administration (FDA) and the impact of Breakthrough Therapy Designation on the development of BLU-285; and Blueprint Medicines' strategy, business plans and focus. 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. Any forward-looking statements in this press release 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 press release, including, without limitation, risks and uncertainties related to the delay of any current or planned clinical trials or the development of Blueprint Medicines' drug candidates, including BLU-285, BLU-554 and BLU-667; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates; the preclinical and clinical results for Blueprint Medicines' drug candidates, which may not support further development of such drug candidates; and actions of the FDA or other regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for its current and future drug candidates, including companion diagnostic tests for BLU-554 with Ventana Medical Systems, Inc. and for BLU-285 with QIAGEN Manchester Limited; and the success of Blueprint Medicines' rare genetic disease collaboration with Alexion Pharma Holding and its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' Quarterly Report on Form 10-Q for the quarter ended March 31, 2017, as filed with the Securities and Exchange Commission (SEC) on May 3, 2017, and other filings that Blueprint Medicines may make with the SEC in the future. Any forward-looking statements contained in this press release 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. Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements.

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GIST: imatinib and beyond

Clinical activity of BLU-285 in advanced gastrointestinal stromal tumor (GIST)

Michael Heinrich[1], Robin Jones[2], Margaret von Mehren[3], Patrick Schoffski[4], Sebastian Bauer[5], Olivier Mir[6], Philippe Cassier[7], Ferry Eskens[8], Hongliang Shi[9], Terri Alvarez-Diez[9], Oleg Schmidt-Kittler[9], Mary Ellen Healy[9], Beni Wolf[9], Suzanne George[10]

[1]Oregon Health & Sciences University, Oregon, USA; [2]Royal Marsden Hospital/Institute of Cancer Research, London, UK; [3]Fox Chase Cancer Center, Pennsylvania, USA; [4]Leuven Cancer Institute, Leuven, Belgium; [5]University of Essen, Essen, Germany; [6]Institut Gustave Roussy, Paris, France; [7]Centre Leon Berard, Lyon, France; [8] Erasmus MC Cancer Institute, Rotterdam, Netherlands; [9]Blueprint Medicines Corporation, Massachusetts, USA; [10]Dana-Farber Cancer Institute, Massachusetts, USA

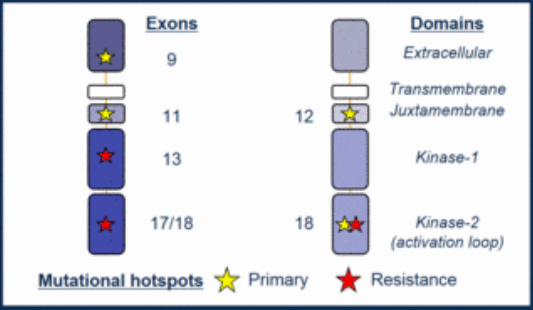
PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Abstract no: 11011 Presented by: Dr. Michael Heinrich

Disclosures

- BLU-285 is an investigational agent currently in development by Blueprint Medicines Corporation (Blueprint Medicines)
- Dr. Michael Heinrich is an investigator for Blueprint Medicines' ongoing Phase 1 studies in unresectable gastrointestinal stromal tumor
- Dr. Michael Heinrich has the following disclosures:
  - Consultant: Blueprint Medicines, Novartis, MolecularMD
  - Equity interest: MolecularMD
  - Research funding: Blueprint Medicines, Deciphera, Ariad
  - Expert testimony: Novartis
  - Patents: four patents on diagnosis and treatment of PDGFRα-mutant GIST

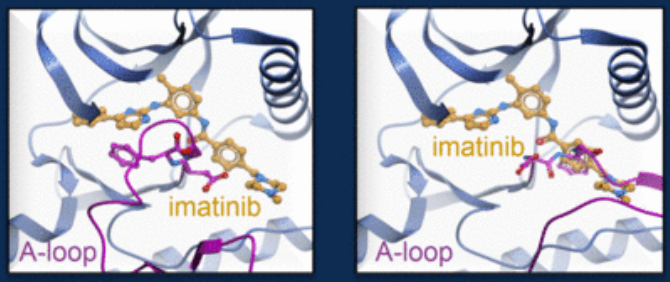
Imatinib revolutionized Gastrointestinal Stromal Tumor (GIST) treatment

KIT PDGFRα



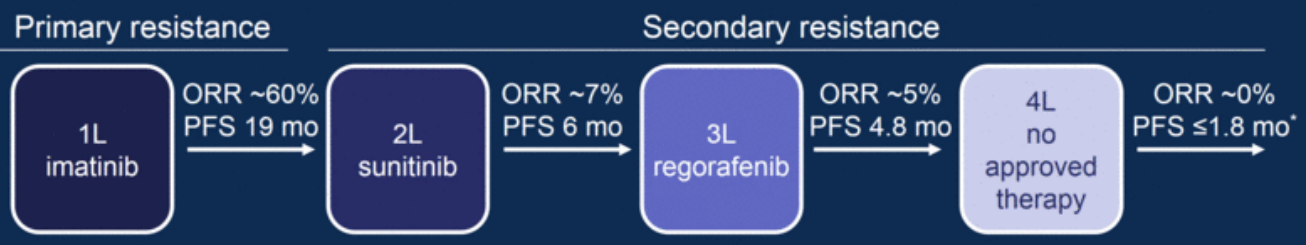
- KIT mutations drive ~75–80% of GIST
- PDGFRα mutations drive ~5–10% of GIST

KIT



- Imatinib binds the inactive kinase conformation and inhibits many primary mutants
- Imatinib is a highly effective first-line GIST therapy

Beyond imatinib, there are no highly effective therapies[1–6]

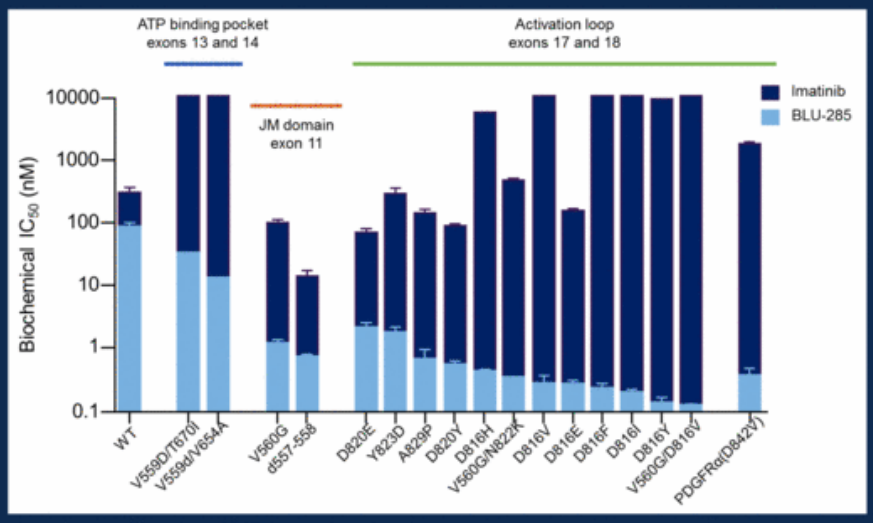


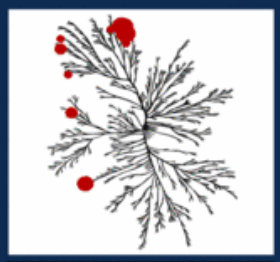
	Prevalence[7,8]	
Resistance mutation	**Primary**	**Secondary**
PDGFRα D842V	**~5–6%**	**Rare**
KIT exon 17/18	**~1%**	**2L ~23% ≥3L ~90%**
KIT exon 13	**N/A**	**2L ~40%**

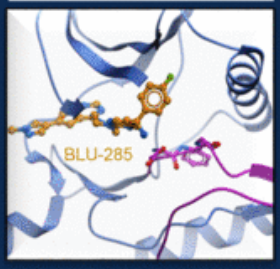
- Primary and secondary mutations cause therapeutic resistance
- Approved agents are ineffective against PDGFRα D842V

*Imatinib re-challenged

BLU-285: highly potent and selective targeting of KIT/PDGFRα GIST mutants





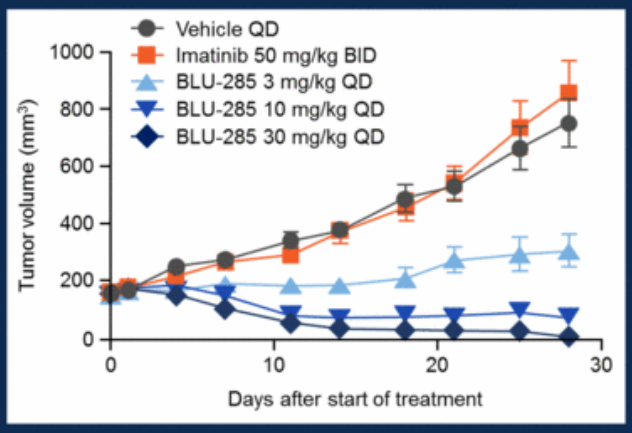


- High kinome selectivity*
- Binds active conformation

*Image reproduced courtesy of CSTI (www.cellsignal.com)

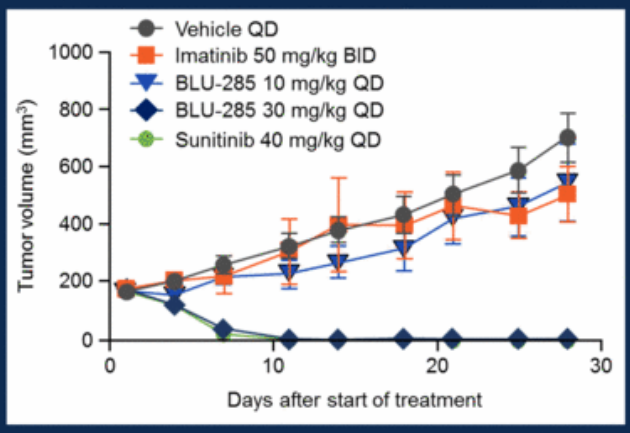
BLU-285: highly active against imatinib-resistant GIST patient derived xenografts

KIT exon 11/17 mutant



- Tumor regression at 10 and 30 mg/kg QD

KIT exon 11/13 mutant

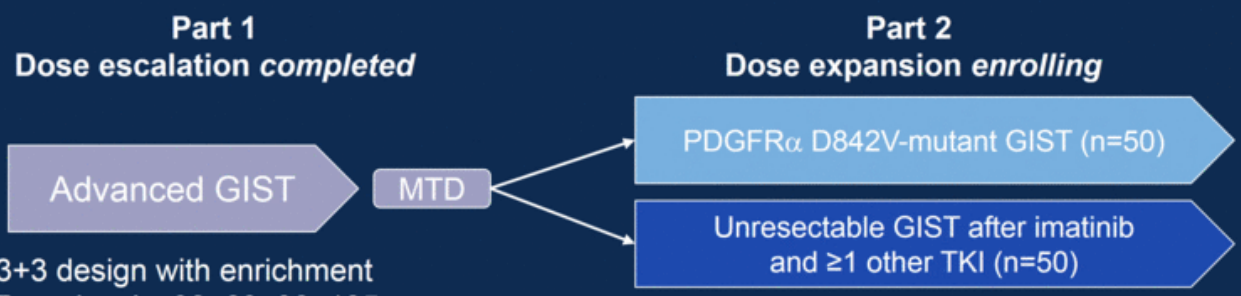


- Tumor regression at 30 mg/kg QD

BLU-285 Phase 1 study

Key objectives

- Part 1: MTD, safety, pharmacokinetics, ctDNA analyses, anti-tumor activity
- Part 2: response rate, duration of response, safety



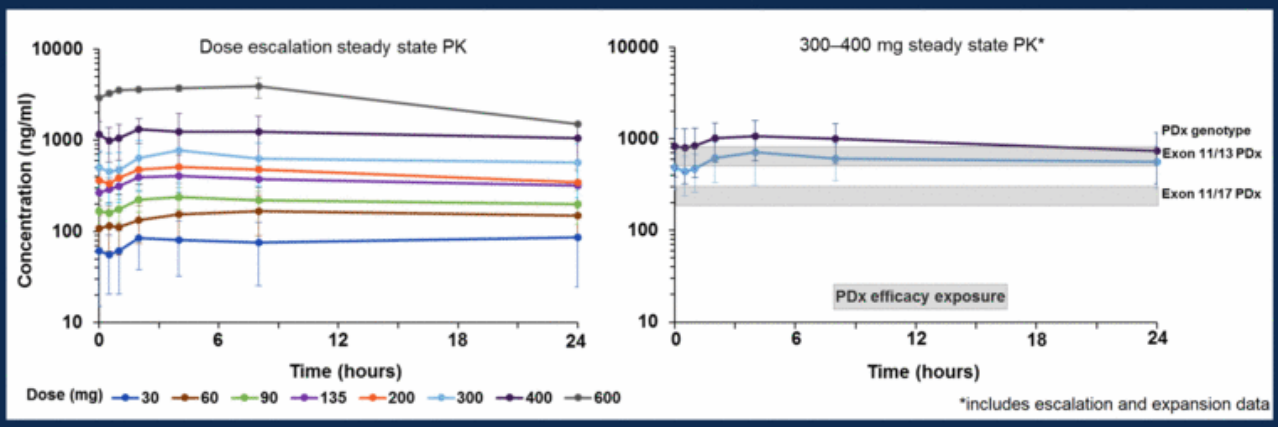
- 3+3 design with enrichment
- Dose levels: 30, 60, 90, 135, 200, 300, 400 and 600 mg QD
- MTD determined to be 400 mg PO QD

Demography and baseline patient characteristics

Parameter	All patients, N=72	
Age (years), median (range)	61 (25–85)	
	n (%)	
GIST subtype		
KIT mutant	40 (56)	
PDGFRα mutant	32 (44)	
Metastatic disease	69 (96)	
Largest target lesion size (cm)		
≤5	18 (25)	
>5–≤10	25 (35)	
>10	29 (40)	
No. prior kinase inhibitors	PDGFRα	KIT
Median (range)	1.5 (0–6)	4 (2–11)
≥3	10 (31)	36 (90)
Prior regorafenib	8 (25)	34 (85)

Data are preliminary and based on a cut off date of 28 April 2017

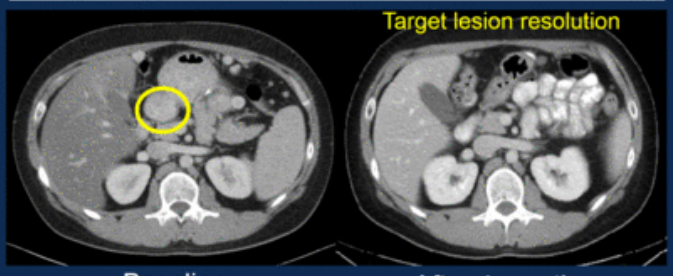
BLU-285 pharmacokinetics support QD dosing and broad mutational coverage



- Relatively rapid absorption Tmax ~2–8 hours and long half-life >24 hours
- Exposure at the 300 and 400 (MTD) mg provides broad coverage of primary and secondary KIT/PDGFRα mutations based on patient derived xenografts (PDX)

Radiographic response per RECIST 1.1 in PDGFRα D842V-mutant GIST

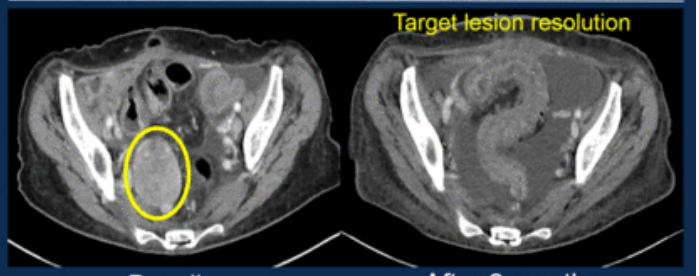
BLU-285 300 mg (dose escalation)



Baseline | After 4 months

- Ongoing at cycle 5
- Prior imatinib and sunitinib
- Confirmed PR, -63% target sum

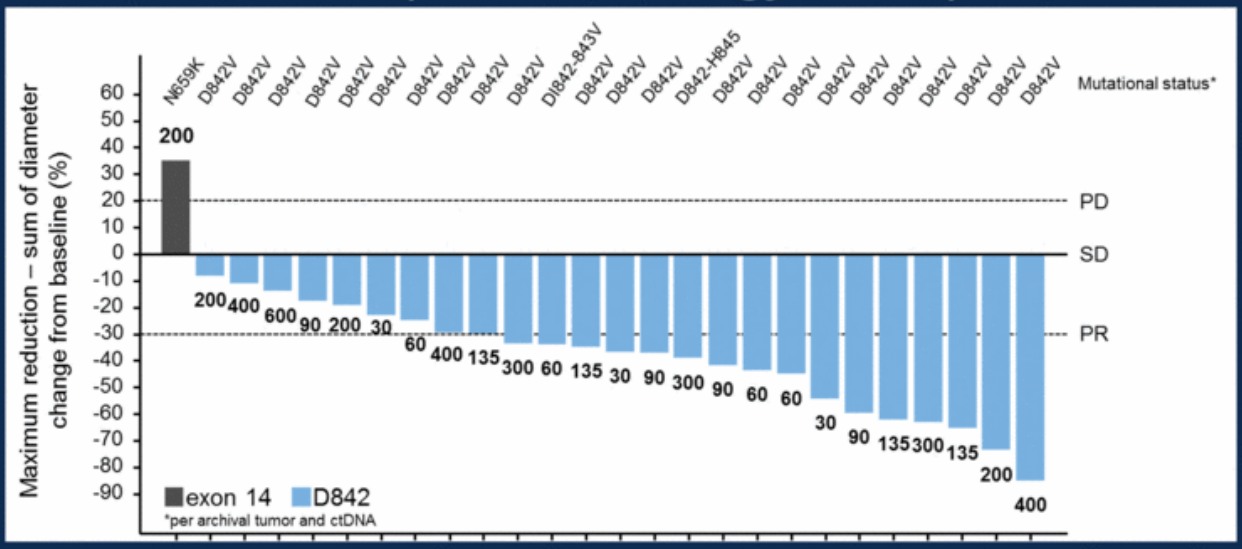
BLU-285 400 mg (dose expansion)



Baseline | After 2 months

- Ongoing at cycle 3
- Prior imatinib
- PR (pending confirmation), -85% target sum

Tumor regression across all dose levels in PDGFRα D842-mutant GIST (central radiology review)



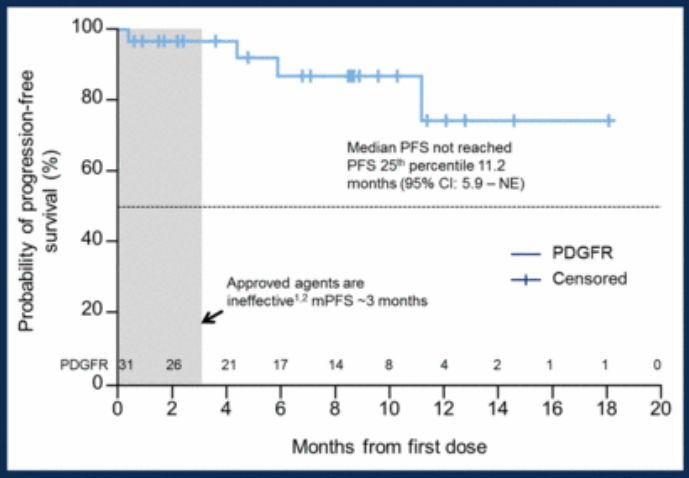
High response rate and prolonged PFS in PDGFRα D842-mutant GIST

Central radiographic review

Best response (N=25)	Choi Criteria n (%)	RECIST 1.1 n (%)
PR	25 (100%)	15* (60%)
SD	0	10 (40%)
DCR (PR + SD)	25 (100%)	25 (100%)
PD	0	0

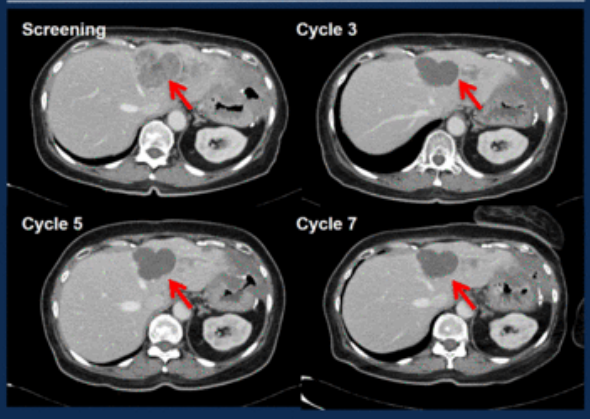
* 12 confirmed, 3 pending confirmation

- Approved agents are ineffective[1,2]
  - ORR ~0%



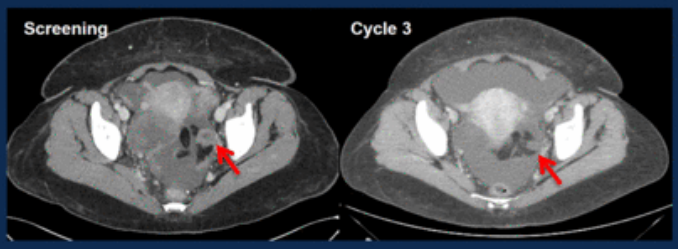
Radiographic response in heavily pre-treated KIT-mutant GIST

BLU-285 300 mg (dose escalation)



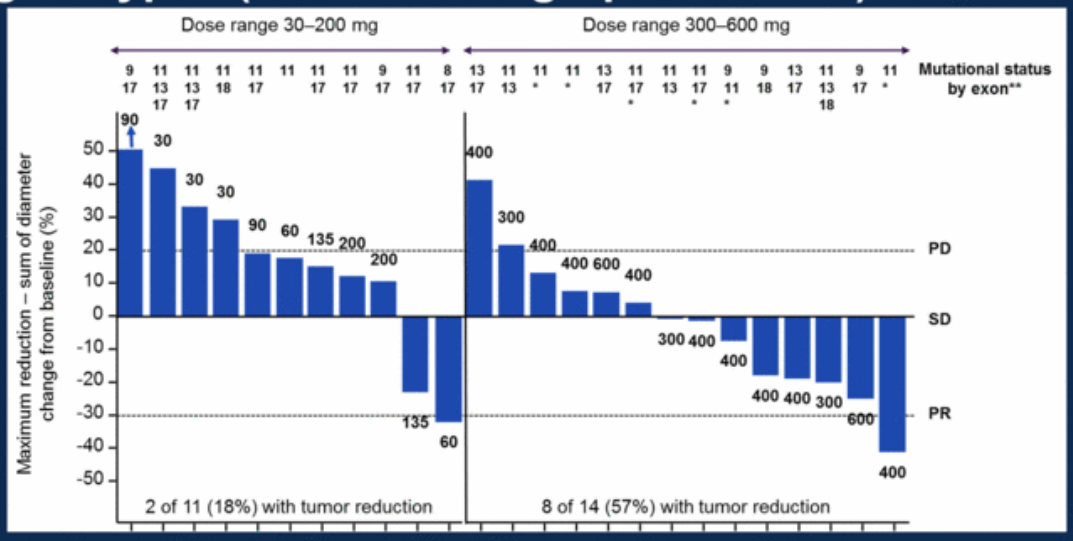
- Ongoing at cycle 12
- 6 prior TKIs; exon 11, 13, and 18 mutations
- CHOI PR (density -53%); RECIST SD (-21%)

BLU-285 400 mg (dose expansion)



- Ongoing at cycle 4
- 5 prior TKIs; 1° exon 11 mutation; ctDNA pending
- CHOI PR (density -76%); RECIST PR (-41%)

Dose-dependent tumor reduction across multiple KIT genotypes (central radiographic review)



*ctDNA results pending

**per archival tumor and ctDNA

Important clinical activity in heavily pre-treated KIT-mutant GIST

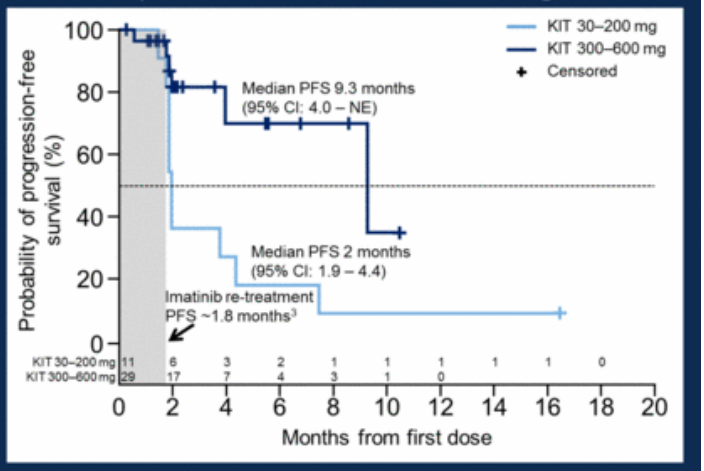
Central radiographic review

Best response (N=25)	Choi Criteria n (%)	RECIST 1.1 n (%)
PR	8 (32)	2* (8)
SD	6 (24)	12 (48)
DCR (PR + SD)	14 (56)	14 (56)
PD	11 (44)	11 (44)

* 1 confirmed, 1 pending confirmation

- Beyond third-line regorafenib there are no approved therapies
  - Imatinib re-treatment in ≥third-line GIST[3]
    - ORR ~0%

↑ PFS with BLU-285 ≥300 mg



Adverse events (AE) associated with BLU-285

Safety population, N=72		Severity, n (%)			
AEs in ≥20% of patients	n (%)	Grade 1	Grade 2	Grade 3	Grade 4/5
Nausea	43 (60)	31 (43)	9 (13)	3 (4)	0
Fatigue	38 (53)	16 (22)	16 (22)	6 (8)	0
Vomiting	30 (42)	21 (29)	6 (8)	3 (4)	0
Periorbital edema	26 (36)	22 (31)	4 (6)	0	0
Diarrhea	24 (33)	19 (26)	4 (6)	1 (1)	0
Edema peripheral	22 (31)	18 (25)	4 (6)	0	0
Decreased appetite	20 (28)	15 (21)	4 (6)	1 (1)	0
Anemia	18 (25)	4 (6)	8 (11)	6 (8)	0
Lacrimation increased	17 (24)	12 (17)	5 (7)	0	0
Dizziness	16 (22)	13 (18)	3 (4)	0	0

- 18 (25%) patients had Grade (G) ≥3 treatment-related (Fatigue [8%], hypophosphatemia [6%], anemia [4%], nausea, vomiting, hyperbilirubinemia [3% each])
- DLT in 2 patients at 600 mg: 1 G2 hyperbilirubinemia; 1 G2 rash, hypertension, memory impairment
- BLU-285 discontinuations: disease progression n=19, treatment-related toxicity (G3 hyperbilirubinemia) n=1, and investigator's decision n=1

Conclusions

- BLU-285 is well tolerated on a QD schedule at doses up to the MTD of 400 mg
- Exposure at 300–400 mg QD provides broad coverage of primary and secondary KIT / PDGFRα mutants
- BLU-285 has strong clinical activity in PDGFRα D842-mutant GIST with an ORR of 60% per central review and median PFS not reached
  - Potential expedited paths for approval are being evaluated
- BLU-285 demonstrates important anti-tumor activity including radiographic response and prolonged PFS in heavily pre-treated, KIT-mutant GIST at doses of 300–400 mg QD
  - Based on these encouraging data, planning is underway for a Phase 3 randomized study of BLU-285 in third-line GIST

Acknowledgments

We thank the participating patients, their families, all study co-investigators, and research coordinators at the following institutions:

- Oregon Health & Sciences University
- Royal Marsden Hospital/Institute for Cancer Research
- Leuven Cancer Institute
- University of Essen
- Fox Chase Cancer Center
- Erasmus MC Cancer Institute
- Centre Leon Berard
- Institut Gustave Roussy
- Dana-Farber Cancer Institute

We also thank Sarah Jackson, PhD, of iMed Comms, an Ashfield company, who provided editorial writing support funded by Blueprint Medicines

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blueprint MEDICINES
Advances in GIST
2017 ASCO Annual Meeting
Monday, June 5, 2017

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 clinical development of BLU-285, BLU-554 and BLU-667 and the ability of Blueprint Medicines Corporation (the "Company") to implement those clinical development plans; the potential benefits of the Company's current and future drug candidates in treating patients; plans and timelines for regulatory submissions, filings or discussions; 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 future collaborations, if any, with strategic partners; the future financial performance of the Company; expectations regarding potential milestones in 2017; 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 future clinical trials or the development of the Company's drug candidates, including BLU-285, BLU-554 and BLU-667; 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 current or future 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 diagnostics for its current and future drug candidates, including a companion diagnostic for BLU-554 with Vantaa Medical Systems, Inc. and a companion diagnostic for BLU-285 with QIAGEN Manchester Limited; and the success of the Company's rare genetic disease collaboration with Alexion Pharma Holding and its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc.

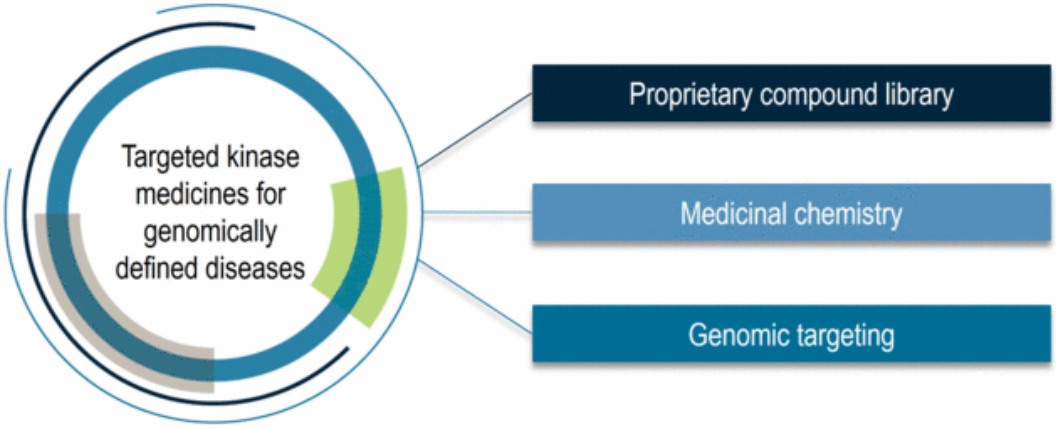
These and other risks and uncertainties are described in greater detail under "Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2017, as filed with the Securities and Exchange Commission ("SEC") on May 3, 2017, and any other filings the Company may make with 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.

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.

Agenda

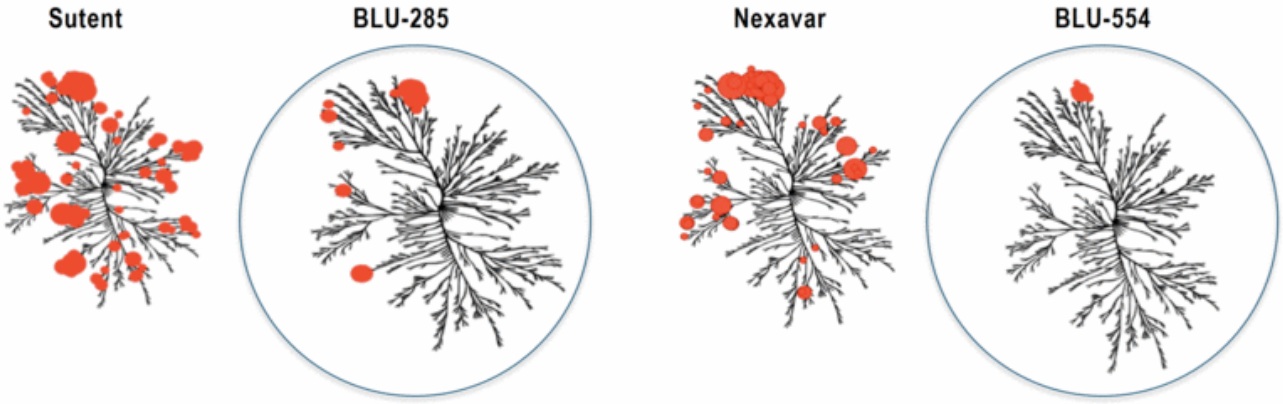
Welcome	Jeff Albers, Chief Executive Officer, Blueprint Medicines
Overview of BLU-285 in GIST	Andy Boral, MD, Chief Medical Officer, Blueprint Medicines
Phase 1 clinical trial results	Michael Heinrich, MD, Professor, Oregon Health and Science University
Proposed registration path	Andy Boral, MD, Chief Medical Officer, Blueprint Medicines
Question and answer session	Michael C. Heinrich, MD, Professor, Oregon Health and Science University Jeff Albers, Chief Executive Officer, Blueprint Medicines Andy Boral, MD, Chief Medical Officer, Blueprint Medicines
Closing remarks	Jeff Albers, Chief Executive Officer, Blueprint Medicines

A blueprint for a healthier tomorrow



Discovery platform for exquisitely selective kinase inhibitors, matched to specific molecular drivers of disease, with rapid path to clinical proof-of-concept

A new way of looking at kinase medicines



We aim to design and develop **highly targeted kinase medicines** with improved potency, less off-target activity, and a high probability of clinical success

Kinome illustration reproduced courtesy of CSTI (cellsignal.com). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content; IO, immuno-oncology

Three major areas of focus

Genomically defined cancers	Rare diseases	Cancer immunotherapy
Oncogenic kinases resulting from tumor genetic alterations	Abnormally activated kinases due to rare genetic alterations	Intracellular immunokinases involved in tumor immunity
• BLU-285 gastrointestinal stromal tumors • BLU-554 hepatocellular carcinoma • BLU-667 RET-altered cancers	• BLU-285 systemic mastocytosis • Alexion collaboration (1 target)	• Roche collaboration (up to 5 targets)

blueprint MEDICINES

Robust pipeline of diverse clinical stage assets

DRUG CANDIDATE	DISCOVERY	PRECLINICAL	CLINICAL	COMMERCIAL RIGHTS
BLU-285 Inhibitor of KIT, including exon 17 mutations, and PDGFRα, including the D842V mutation			PHASE 1 - PDGFRα-DRIVEN GIST PHASE 1 - KIT-DRIVEN GIST PHASE 1 – SYSTEMIC MASTOCYTOSIS	
BLU-554 Inhibitor of FGFR4			PHASE 1 – HEPATOCELLULAR CARCINOMA	
BLU-667 Inhibitor of RET fusions, mutations and resistant mutants			PHASE 1 – NSCLC & THYROID*	
PRKACA Inhibitor of PRKACA fusions			FLC	
Cancer immunotherapy Immunokinases			UP TO 5 PROGRAMS, STAGE UNDISCLOSED**	Roche
Rare genetic disease			TARGET AND DEVELOPMENT STAGE UNDISCLOSED	ALEXION

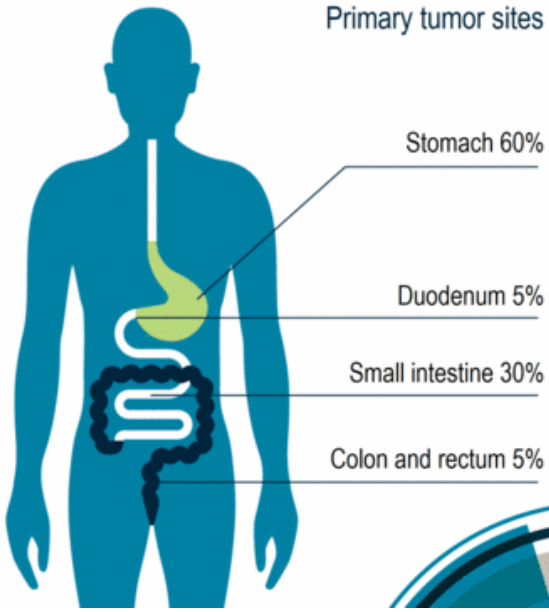
FLC, Fibrolamellar carcinoma; GIST, advanced gastrointestinal stromal tumors; NSCLC, non-small cell lung cancer. All Phase 1 clinical trials are in advanced disease.
*Phase 1 trial includes a basket cohort that consists of other advanced solid tumors with RET alterations.
**Blueprint Medicines has U.S. 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.

BLU-285 Drug Discovery Overview

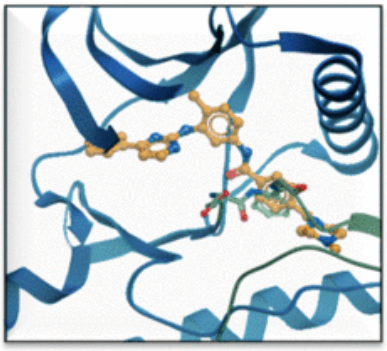
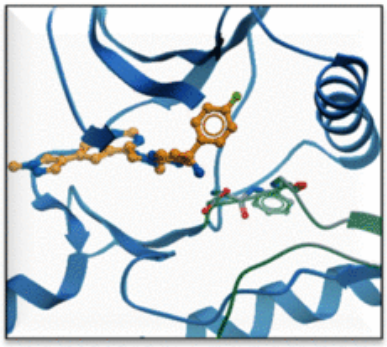
Andy Boral, M.D.
Chief Medical Officer

Gastrointestinal stromal tumors (GIST)

- Typically presents as stomach or intestinal mass
- Metastases in liver, peritoneum and other distant sites
- Mutant receptor tyrosine kinases are key disease drivers
  - PDGFRα ~5-10%
  - KIT ~75-80%
- Beyond imatinib, no highly effective treatments



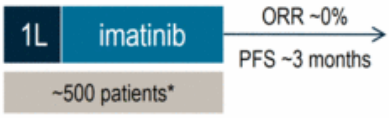
PDGFRα and KIT activation loop mutations stabilize the kinase active conformation, blocking binding of type 2 inhibitors

	Imatinib	BLU-285
Kinase in active conformation		

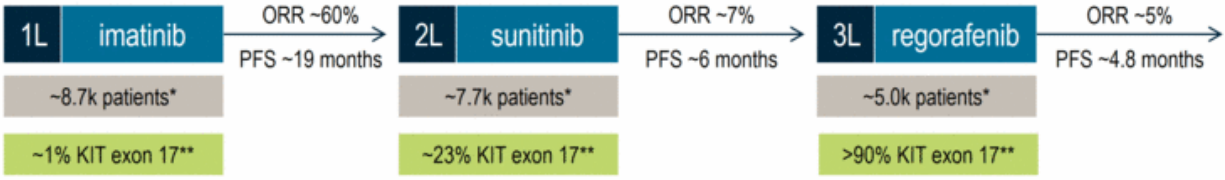
- Imatinib is a type 2 multikinase inhibitor that cannot bind the kinase active conformation due to a steric clash
- BLU-285 is a type 1 selective PDGFRα/KIT inhibitor that binds to the kinase active conformation

Currently available therapies do not effectively address activation loop mutations

PDGFRα D842V



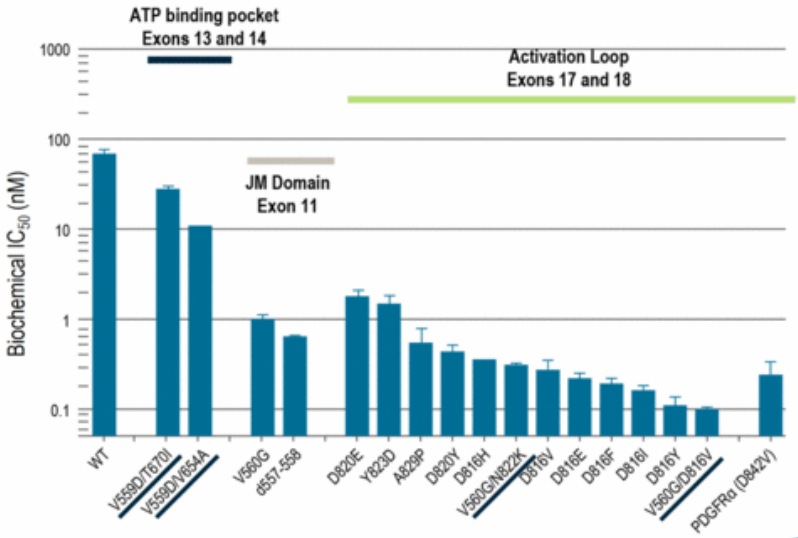
ALL GIST



*Estimated incidence for GIST patients in major markets (US, EU5 and Japan).
**Estimated frequency of Exon 17 activation loop mutations.

Promising preclinical data supported initiation of a Phase 1 clinical trial of BLU-285 in advanced GIST

- Most potent biochemical activity against activation loop mutants
- Biochemical activity across a broad PDGFRα and KIT mutational spectrum



Data previously presented in April 2017 at the AACR Annual Meeting

Updated Phase 1 clinical trial results

Michael C. Heinrich, M.D.
Oregon Health & Sciences University (OHSU)

GIST: imatinib and beyond

Clinical activity of BLU-285 in advanced gastrointestinal stromal tumor (GIST)

Michael Heinrich[1], Robin Jones[2], Margaret von Mehren[3], Patrick Schoffski[4], Sebastian Bauer[5], Olivier Mir[6], Philippe Cassier[7], Ferry Eskens[8], Hongliang Shi[9], Terri Alvarez-Diez[9], Oleg Schmidt-Kittler[9], Mary Ellen Healy[9], Beni Wolf[9], Suzanne George[10]

[1]Oregon Health & Sciences University, Oregon, USA; [2]Royal Marsden Hospital/Institute of Cancer Research, London, UK; [3]Fox Chase Cancer Center, Pennsylvania, USA; [4]Leuven Cancer Institute, Leuven, Belgium; [5]University of Essen, Essen, Germany; [6]Institut Gustave Roussy, Paris, France; [7]Centre Leon Berard, Lyon, France; [8] Erasmus MC Cancer Institute, Rotterdam, Netherlands; [9]Blueprint Medicines Corporation, Massachusetts, USA; [10]Dana-Farber Cancer Institute, Massachusetts, USA

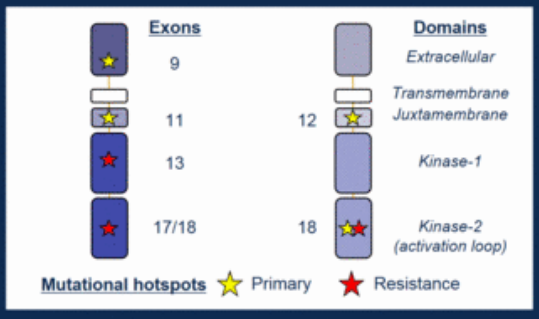
PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Abstract no: 11011 Presented by: Dr. Michael Heinrich

Disclosures

- BLU-285 is an investigational agent currently in development by Blueprint Medicines Corporation (Blueprint Medicines)
- Dr. Michael Heinrich is an investigator for Blueprint Medicines' ongoing Phase 1 studies in unresectable gastrointestinal stromal tumor
- Dr. Michael Heinrich has the following disclosures:
  - Consultant: Blueprint Medicines, Novartis, MolecularMD
  - Equity interest: MolecularMD
  - Research funding: Blueprint Medicines, Deciphera, Ariad
  - Expert testimony: Novartis
  - Patents: four patents on diagnosis and treatment of PDGFRα-mutant GIST

Imatinib revolutionized Gastrointestinal Stromal Tumor (GIST) treatment

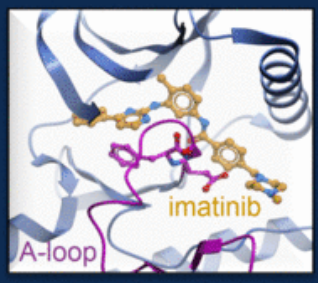
KIT PDGFRα



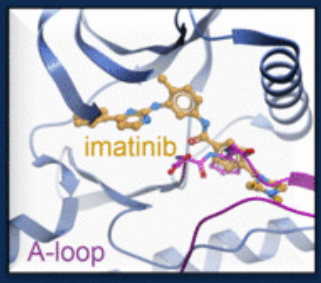
- KIT mutations drive ~75–80% of GIST
- PDGFRα mutations drive ~5–10% of GIST

KIT

Inactive conformation

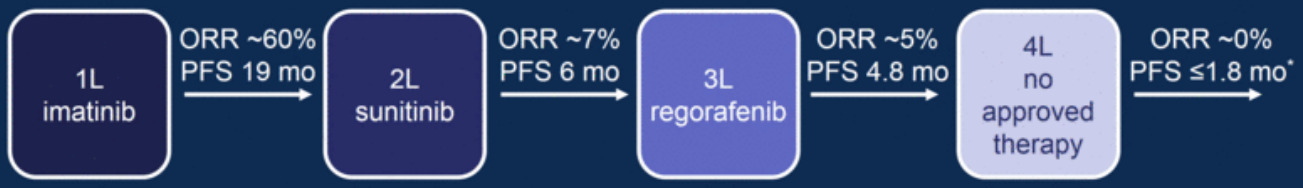


Active conformation



- Imatinib binds the inactive kinase conformation and inhibits many primary mutants
- Imatinib is a highly effective first-line GIST therapy

Beyond imatinib, there are no highly effective therapies[1–6]

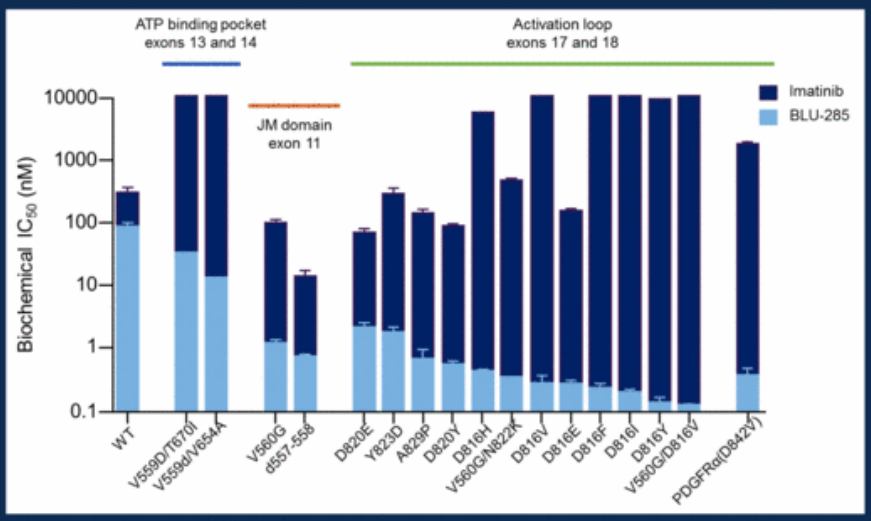


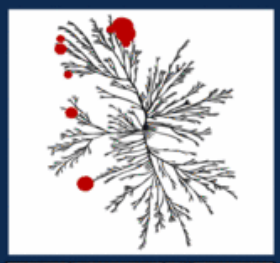
	Prevalence[7,8]	
Resistance mutation	**Primary**	**Secondary**
PDGFRα D842V	~5–6%	Rare
KIT exon 17/18	~1%	2L ~23% ≥3L ~90%
KIT exon 13	N/A	2L ~40%

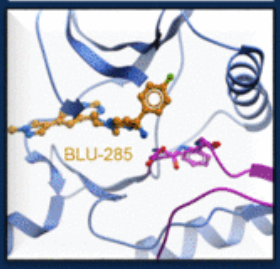
- Primary and secondary mutations cause therapeutic resistance
- Approved agents are ineffective against PDGFRα D842V

*Imatinib re-challenged

BLU-285: highly potent and selective targeting of KIT/PDGFRα GIST mutants





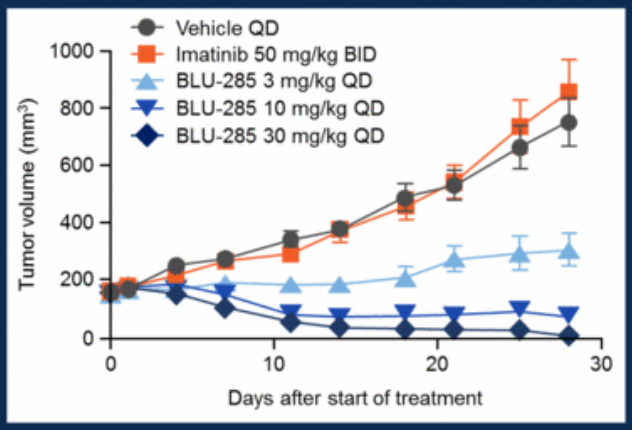


- High kinome selectivity*
- Binds active conformation

*Image reproduced courtesy of CSTI (www.cellsignal.com)

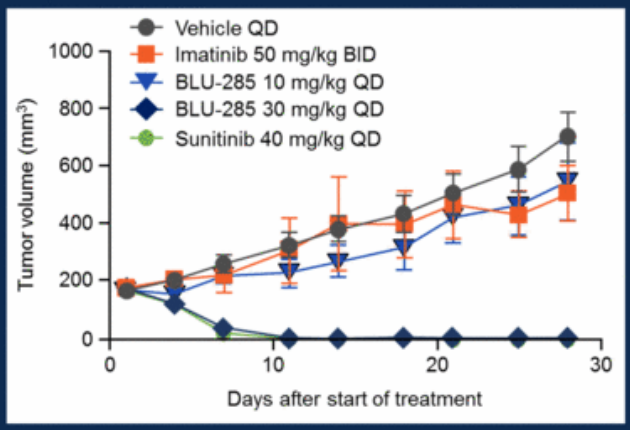
BLU-285: highly active against imatinib-resistant GIST patient derived xenografts

KIT exon 11/17 mutant



- Tumor regression at 10 and 30 mg/kg QD

KIT exon 11/13 mutant

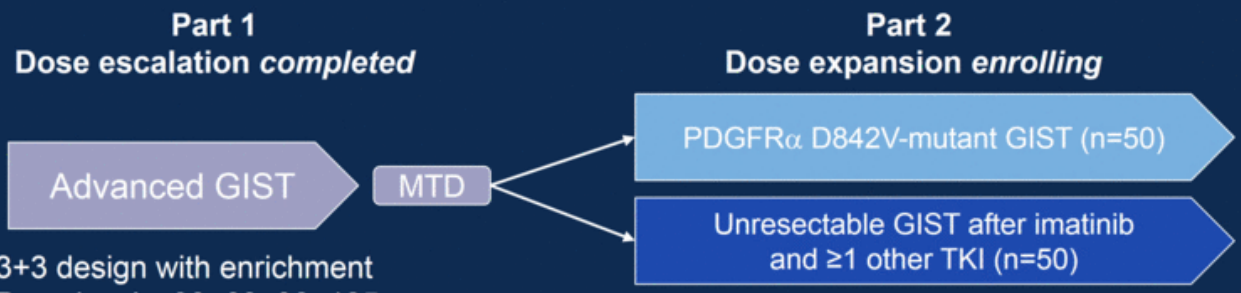


- Tumor regression at 30 mg/kg QD

BLU-285 Phase 1 study

Key objectives

- Part 1: MTD, safety, pharmacokinetics, ctDNA analyses, anti-tumor activity
- Part 2: response rate, duration of response, safety



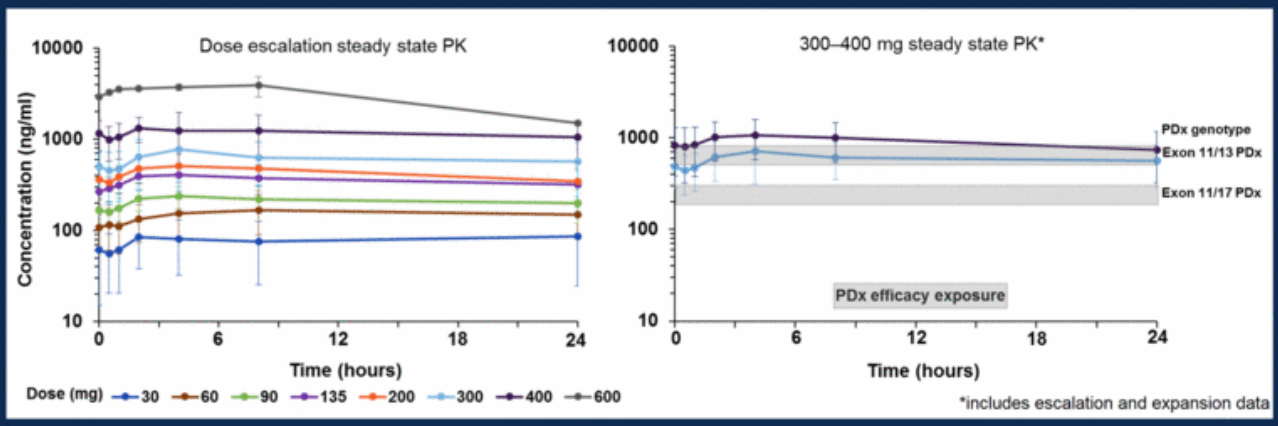
- 3+3 design with enrichment
- Dose levels: 30, 60, 90, 135, 200, 300, 400 and 600 mg QD
- MTD determined to be 400 mg PO QD

Demography and baseline patient characteristics

Parameter	All patients, N=72	
Age (years), median (range)	61 (25–85)	
	n (%)	
GIST subtype		
KIT mutant	40 (56)	
PDGFRα mutant	32 (44)	
Metastatic disease	69 (96)	
Largest target lesion size (cm)		
≤5	18 (25)	
>5–≤10	25 (35)	
>10	29 (40)	
No. prior kinase inhibitors	PDGFRα	KIT
Median (range)	1.5 (0–6)	4 (2–11)
≥3	10 (31)	36 (90)
Prior regorafenib	8 (25)	34 (85)

Data are preliminary and based on a cut off date of 28 April 2017

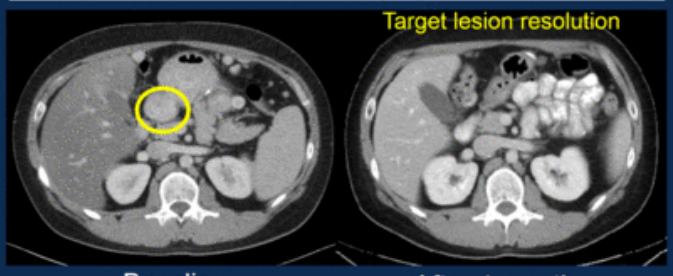
BLU-285 pharmacokinetics support QD dosing and broad mutational coverage



- Relatively rapid absorption Tmax ~2–8 hours and long half-life >24 hours
- Exposure at the 300 and 400 (MTD) mg provides broad coverage of primary and secondary KIT/PDGFRα mutations based on patient derived xenografts (PDX)

Radiographic response per RECIST 1.1 in PDGFRα D842V-mutant GIST

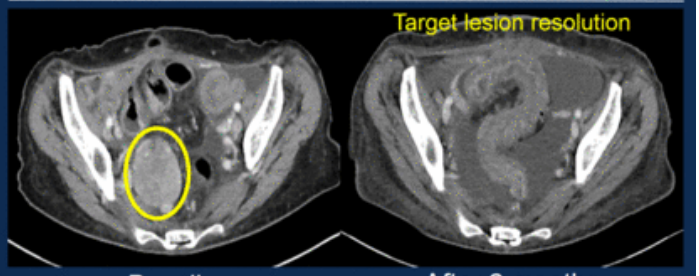
BLU-285 300 mg (dose escalation)



Baseline | After 4 months

- Ongoing at cycle 5
- Prior imatinib and sunitinib
- Confirmed PR, -63% target sum

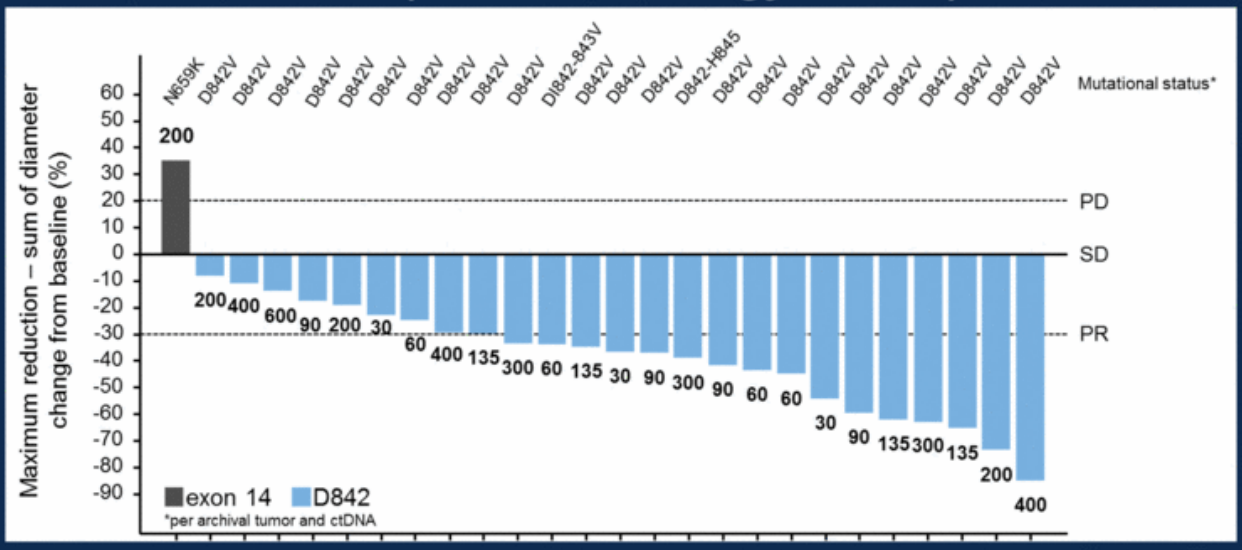
BLU-285 400 mg (dose expansion)



Baseline | After 2 months

- Ongoing at cycle 3
- Prior imatinib
- PR (pending confirmation), -85% target sum

Tumor regression across all dose levels in PDGFRα D842-mutant GIST (central radiology review)



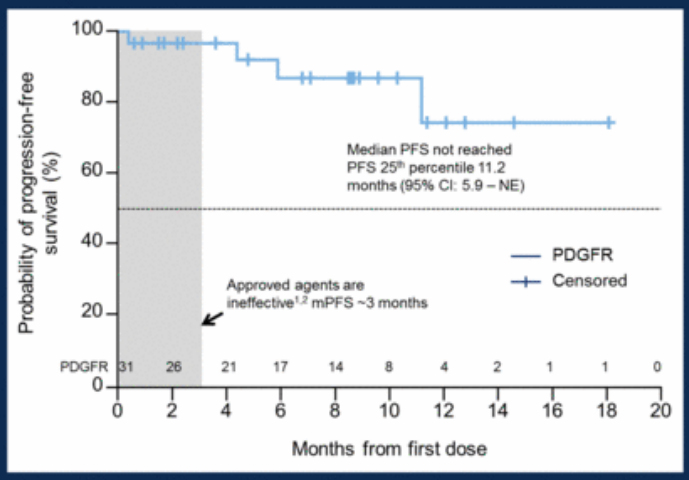
High response rate and prolonged PFS in PDGFRα D842-mutant GIST

Central radiographic review

Best response (N=25)	Choi Criteria n (%)	RECIST 1.1 n (%)
PR	25 (100%)	15* (60%)
SD	0	10 (40%)
DCR (PR + SD)	25 (100%)	25 (100%)
PD	0	0

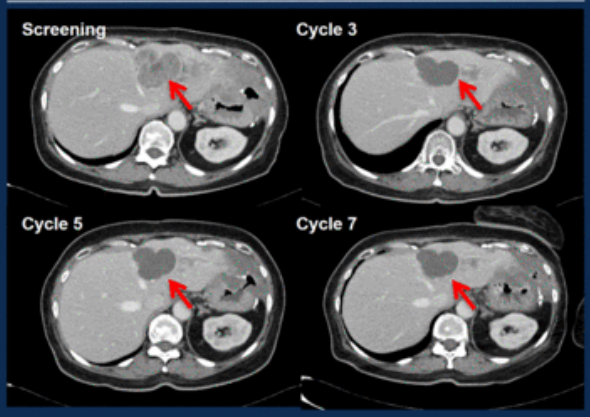
* 12 confirmed, 3 pending confirmation

- Approved agents are ineffective[1,2]
  - ORR ~0%



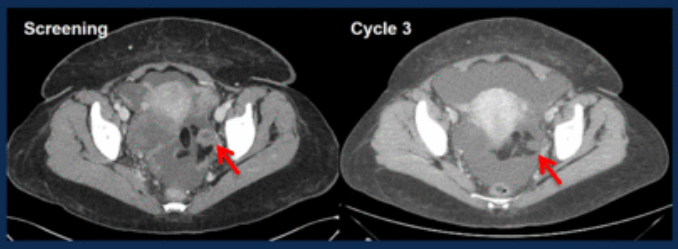
Radiographic response in heavily pre-treated KIT-mutant GIST

BLU-285 300 mg (dose escalation)



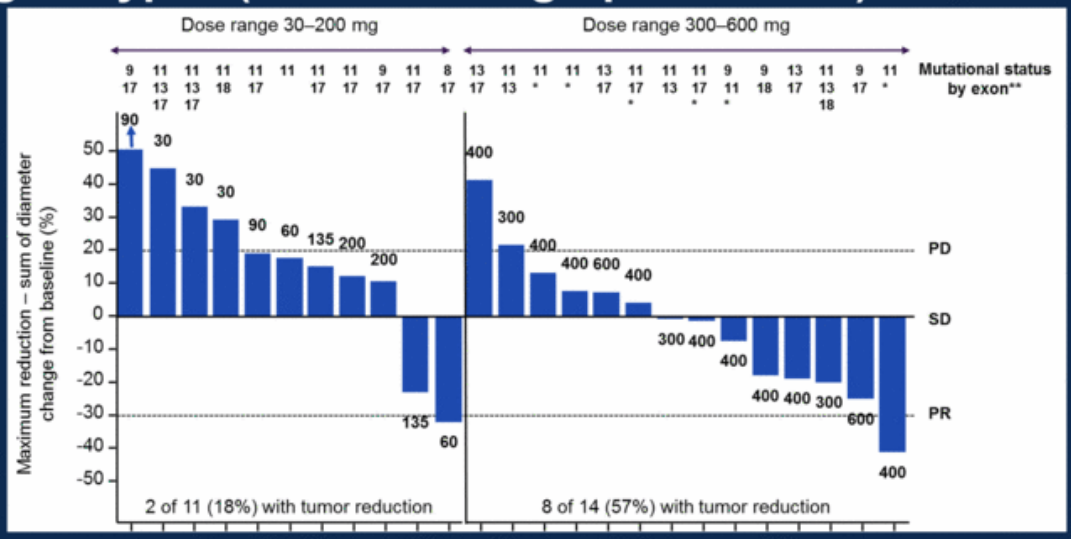
- Ongoing at cycle 12
- 6 prior TKIs; exon 11, 13, and 18 mutations
- CHOI PR (density -53%); RECIST SD (-21%)

BLU-285 400 mg (dose expansion)



- Ongoing at cycle 4
- 5 prior TKIs; 1° exon 11 mutation; ctDNA pending
- CHOI PR (density -76%); RECIST PR (-41%)

Dose-dependent tumor reduction across multiple KIT genotypes (central radiographic review)



*ctDNA results pending

**per archival tumor and ctDNA

Important clinical activity in heavily pre-treated KIT-mutant GIST

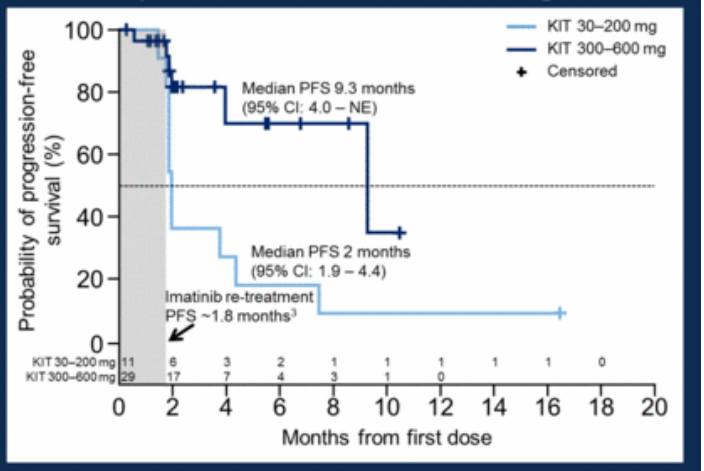
Central radiographic review

Best response (N=25)	Choi Criteria n (%)	RECIST 1.1 n (%)
PR	8 (32)	2* (8)
SD	6 (24)	12 (48)
DCR (PR + SD)	14 (56)	14 (56)
PD	11 (44)	11 (44)

* 1 confirmed, 1 pending confirmation

- Beyond third-line regorafenib there are no approved therapies
  - Imatinib re-treatment in ≥third-line GIST[3]
    - ORR ~0%

↑ PFS with BLU-285 ≥300 mg



Adverse events (AE) associated with BLU-285

Safety population, N=72		Severity, n (%)			
AEs in ≥20% of patients	n (%)	Grade 1	Grade 2	Grade 3	Grade 4/5
Nausea	43 (60)	31 (43)	9 (13)	3 (4)	0
Fatigue	38 (53)	16 (22)	16 (22)	6 (8)	0
Vomiting	30 (42)	21 (29)	6 (8)	3 (4)	0
Periorbital edema	26 (36)	22 (31)	4 (6)	0	0
Diarrhea	24 (33)	19 (26)	4 (6)	1 (1)	0
Edema peripheral	22 (31)	18 (25)	4 (6)	0	0
Decreased appetite	20 (28)	15 (21)	4 (6)	1 (1)	0
Anemia	18 (25)	4 (6)	8 (11)	6 (8)	0
Lacrimation increased	17 (24)	12 (17)	5 (7)	0	0
Dizziness	16 (22)	13 (18)	3 (4)	0	0

- 18 (25%) patients had Grade (G) ≥3 treatment-related (Fatigue [8%], hypophosphatemia [6%], anemia [4%], nausea, vomiting, hyperbilirubinemia [3% each])
- DLT in 2 patients at 600 mg: 1 G2 hyperbilirubinemia; 1 G2 rash, hypertension, memory impairment
- BLU-285 discontinuations: disease progression n=19, treatment-related toxicity (G3 hyperbilirubinemia) n=1, and investigator's decision n=1

Conclusions

- BLU-285 is well tolerated on a QD schedule at doses up to the MTD of 400 mg
- Exposure at 300–400 mg QD provides broad coverage of primary and secondary KIT / PDGFRα mutants
- BLU-285 has strong clinical activity in PDGFRα D842-mutant GIST with an ORR of 60% per central review and median PFS not reached
  - Potential expedited paths for approval are being evaluated
- BLU-285 demonstrates important anti-tumor activity including radiographic response and prolonged PFS in heavily pre-treated, KIT-mutant GIST at doses of 300–400 mg QD
  - Based on these encouraging data, planning is underway for a Phase 3 randomized study of BLU-285 in third-line GIST

Acknowledgments

We thank the participating patients, their families, all study co-investigators, and research coordinators at the following institutions:

- Oregon Health & Sciences University
- Royal Marsden Hospital/Institute for Cancer Research
- Leuven Cancer Institute
- University of Essen
- Fox Chase Cancer Center
- Erasmus MC Cancer Institute
- Centre Leon Berard
- Institut Gustave Roussy
- Dana-Farber Cancer Institute

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3. Kang et al. *Lancet Oncol*. 2013;14(12):1175–82
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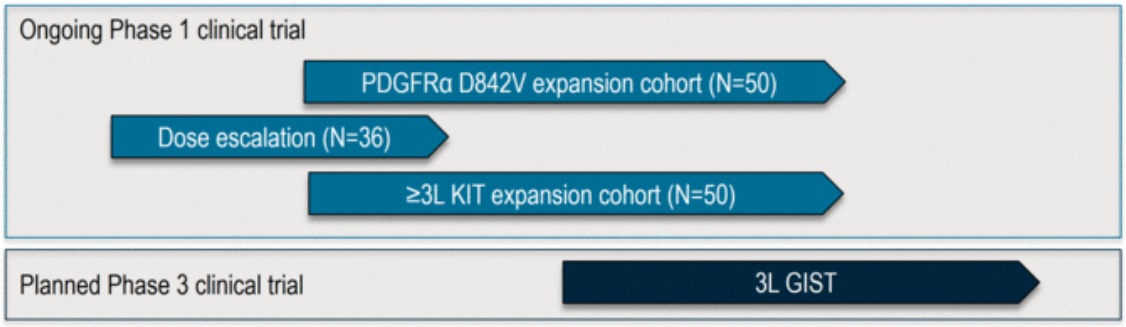
8. Barnett and Heinrich. *Am Soc Clin Onc* Ed Book. 2012;663

Proposed registration path

Andy Boral, M.D.
Chief Medical Officer

BLU-285 clinical development program in advanced GIST



Breakthrough Therapy Designation granted for treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation

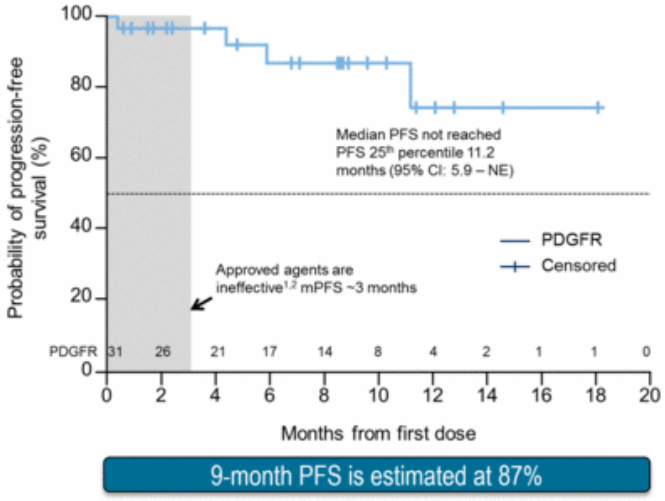
Strong clinical activity in PDGFRα D842V-driven GIST supports expedited approach to clinical development

Central Radiographic Review

Best Response	Choi Criteria (N = 25)	mRECIST 1.1 (N = 25)
PR	25 (100%)	15* (60%)
SD	0	10 (40%)
DCR (PR + SD)	25 (100%)	25 (100%)
PD	0	0

* 12 confirmed, 3 pending confirmation

- Approved agents are ineffective**
  - ORR ~ 0%



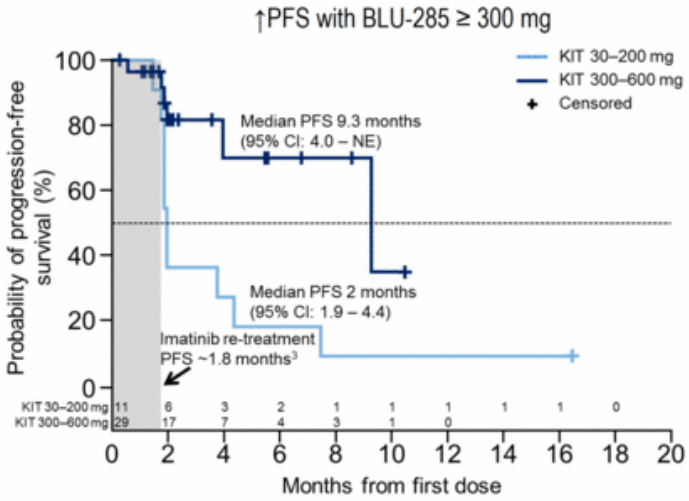
9-month PFS is estimated at 87%

**Cassier CCR (2012); Yoo Can Res Treat (2015).

Preliminary FDA feedback supports potentially expedited approval path for BLU-285 in PDGFRα D842V-driven GIST

- Breakthrough Therapy Designation granted for treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation
- FDA is open to considering additional data from ongoing Phase 1 trial as basis for New Drug Application in PDGFRα D842V-driven GIST
- Phase 1 trial accrual continues with 32 PDGFRα-driven GIST patients enrolled as of April 28, 2017 including 12 at 300-400 mg QD dose levels
  - Estimate expansion cohort enrollment complete by mid-year 2018

Prolonged progression free survival demonstrated in 5L KIT-driven GIST



Prior kinase inhibitor treatment

- Median of 4 therapies
- 90% had ≥3 therapies
- 85% had regorafenib

Regorafenib PFS in 3L

- ~4.8 months

Stable disease is clinically important to patients and physicians

Encouraging clinical activity supports advancing clinical development of BLU-285 into earlier lines of treatment

- Potential Phase 3 trial design:
  - Population: 3L GIST
  - Comparator: regorafenib, with option to cross-over to BLU-285
  - Primary endpoint: PFS
  - Trial sites: global
- Investigators and expert advisors are enthusiastic for 3L approach
- Interactions with global regulatory authorities planned
- Trial initiation planned in 1H 2018

Progress in advanced GIST represents a foundation for a broader vision

Question & Answer Session

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Closing Remarks

Jeff Albers
Chief Executive Officer

Robust pipeline of diverse clinical stage assets

DRUG CANDIDATE	DISCOVERY / PRECLINICAL / CLINICAL	COMMERCIAL RIGHTS
BLU-285 Inhibitor of KIT, including exon 17 mutations, and PDGFRα, including the D842V mutation	PHASE 1 - PDGFRα-DRIVEN GIST PHASE 1 - KIT-DRIVEN GIST PHASE 1 – SYSTEMIC MASTOCYTOSIS	
BLU-554 Inhibitor of FGFR4	PHASE 1 – HEPATOCELLULAR CARCINOMA	
BLU-667 Inhibitor of RET fusions, mutations and resistant mutants	PHASE 1 – NSCLC & THYROID*	
PRKACA Inhibitor of PRKACA fusions	FLC	
Cancer immunotherapy Immunokinases	UP TO 5 PROGRAMS, STAGE UNDISCLOSED**	Roche
Rare genetic disease	TARGET AND DEVELOPMENT STAGE UNDISCLOSED	ALEXION

FLC, Fibrolamellar carcinoma; GIST, advanced gastrointestinal stromal tumors; NSCLC, non-small cell lung cancer. All Phase 1 clinical trials are in advanced disease.
*Phase 1 trial includes a basket cohort that consists of other advanced solid tumors with RET alterations.
**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.

With maturing datasets, additional clinical data updates for BLU-285 and BLU-554 are expected in 2H 2017

	BLU-285 in systemic mastocytosis	BLU-554 in hepatocellular carcinoma
Opportunity	• Poor prognosis and limited effective treatments • KIT D816V mutation is a key driver in 90-95% • ~4.1k advanced SM patients with KIT D816V mutation in major markets*	• 700k new cases and 600k deaths annually • Abnormally activated FGFR4 pathway in ~30% of HCC patients • ~26.9k FGFR4+ HCC patients in major markets*
Previously presented Phase 1 data**	• Encouraging clinical activity, including at lower dose levels • Marked decreases in mast cell burden and improved patient symptoms • Well tolerated to date; dose escalation ongoing	• Evidence of increased clinical activity in biomarker-selected population • Well tolerated at doses up to 600 mg QD; dose expansion ongoing

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*Estimated prevalence for advanced SM in major markets (US, EU5 and Japan). Estimated incidence for 1L and 2L FGFR4+ HCC in major markets.
**SM data previously presented in December 2016 at the American Society of Hematology Annual Meeting. HCC data previously presented in December 2016 at the EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium.


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Thank you