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): **December 1, 2016**

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:

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

Item 7.01 Regulation FD Disclosure.

On December 1, 2016, Blueprint Medicines Corporation hosted an investor conference call and live webcast to discuss initial data from the dose escalation stage of its ongoing Phase 1 clinical trial evaluating BLU-554 for the treatment of advanced hepatocellular carcinoma and initial data from the dose escalation stage of its ongoing Phase 1 clinical trial evaluating BLU-285 for the treatment of advanced gastrointestinal stromal tumors. These data were presented at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Munich, Germany on November 29, 2016 and December 1, 2016, respectively. BLU-554 is an orally available, potent and highly selective inhibitor that targets the kinase FGFR4. BLU-285 is an orally available, potent and highly selective inhibitor that targets D842V mutant PDGFRα and Exon 17 mutant KIT. A copy of the slide presentation from the conference call is attached as Exhibit 99.1 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1 attached hereto, 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	Slide presentation by Blueprint Medicines Corporation on December 1, 2016

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.

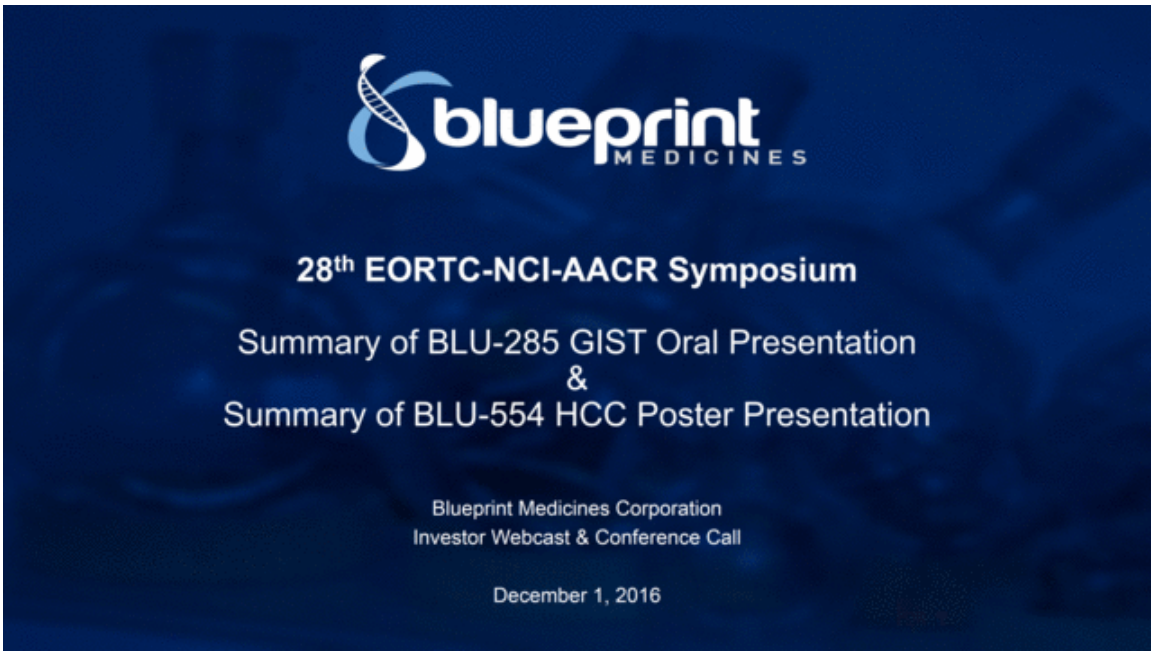
BLUEPRINT MEDICINES CORPORATION

Date: December 1, 2016

By: /s/ Jeffrey W. Albers
Jeffrey W. Albers
Chief Executive Officer

EXHIBIT INDEX

Exhibit No.	Description
99.1	Slide presentation by Blueprint Medicines Corporation on December 1, 2016


blueprint
MEDICINES
28th EORTC-NCI-AACR Symposium
Summary of BLU-285 GIST Oral Presentation
&
Summary of BLU-554 HCC Poster Presentation
Blueprint Medicines Corporation
Investor Webcast & Conference Call
December 1, 2016

Conference Call Participants

Jeff Albers
Chief Executive Officer, Blueprint Medicines

Andy Boral, M.D.
Chief Medical Officer, Blueprint Medicines

Michael Heinrich, M.D.
Oregon Health & Sciences University

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 our ability to implement those clinical development plans; the potential benefits of our current and future drug candidates in treating patients; the timing of regulatory submissions or filings; plans and timelines for the development of companion diagnostics for BLU-285 and BLU-554; plans and timelines for current or future discovery programs; the future financial performance of Blueprint Medicines Corporation (the "Company"); 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 Ventana 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 September 30, 2016, as filed with the Securities and Exchange Commission ("SEC") on November 10, 2016, 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.

Combining Biology and Chemistry Expertise to Unlock the Potential of Kinase Therapies

Proprietary Compound Library

- Unique collection of small molecule kinase inhibitors
- Provides high-quality medicinal chemistry starting points
- Ability to craft drug candidates to previously difficult targets

Target Discovery Engine

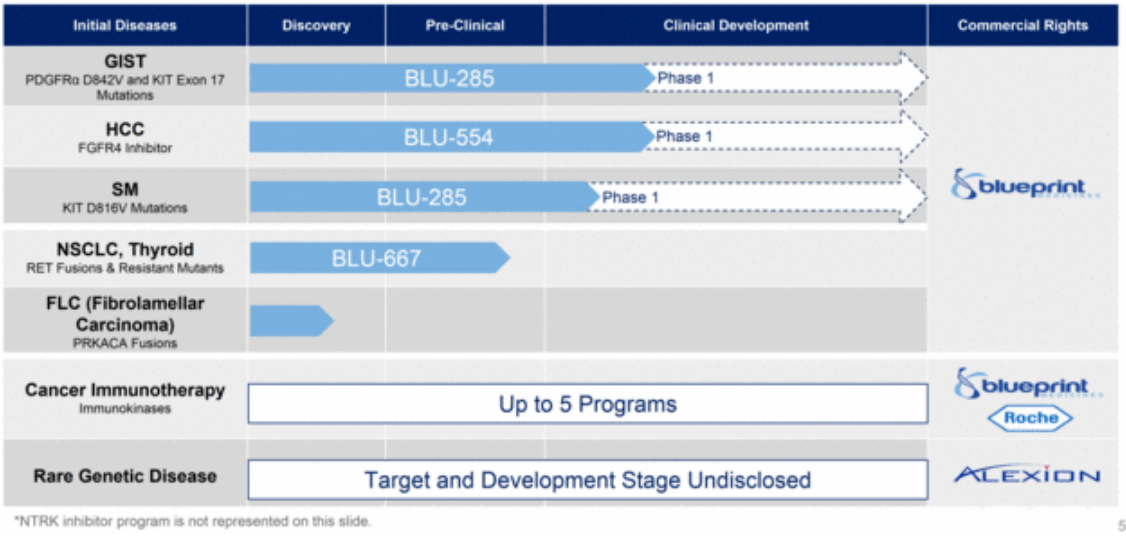
- New insights into the biology of kinases as disease drivers
- Identification of new drug targets from Kinases of Unknown Biology (KUBs)
- Precision target product profiles

Highly selective and potent kinase inhibitor drug candidates:

- BLU-285 – Inhibitor of KIT Exon 17 and PDGFRa D842V mutations
- BLU-554 – Inhibitor of FGFR4
- BLU-667 – Inhibitor of RET fusions and predicted resistance mutations

Kinome illustration reproduced courtesy of CSTI (www.cellsignal.com). The foregoing website is maintained by CSTI, and Blueprint is not responsible for its content.

Robust Portfolio with Diverse Clinical Stage Assets



*NTRK inhibitor program is not represented on this slide.

Preliminary safety and activity in a first-in-human Phase 1 study of BLU-285, a potent, highly selective inhibitor of KIT and PDGFRα activation loop mutants in advanced gastrointestinal stromal tumor (GIST)

Michael Heinrich[1], Robin Jones[2], Patrick Schoffski[3], Sebastian Bauer[4], Margaret von Mehren[5], Ferry Eskens[6], Philippe Cassier[7], Olivier Mir[8], Hongliang Shi[9], Terri Alvarez-Diez[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]Leuven Cancer Institute, Leuven, Belgium; [4]University of Essen, Essen, Germany; [5]Fox Chase Cancer Center, Pennsylvania, USA; [6]Erasmus MC Cancer Institute, Rotterdam, Netherlands; [7]Centre Leon Berard, Lyon, France; [8]Institut Gustave Roussy, Paris, France; [9]Blueprint Medicines Corporation, Massachusetts, USA; [10]Dana-Farber Cancer Institute, Massachusetts, USA

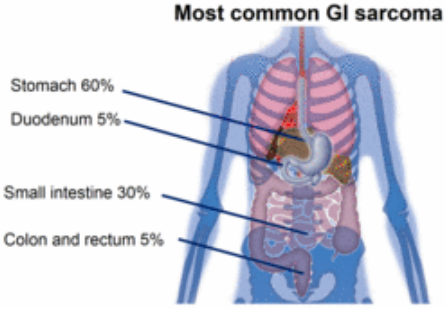
EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium, Munich, Germany, 01 Dec 2016

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 study 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

Gastrointestinal Stromal Tumor (GIST)

Most common GI sarcoma



- Cancer of the interstitial cells of Cajal
- Primary tumor usually presents as a stomach or intestinal mass
- Metastatic recurrences spread to liver, peritoneum, and other distant sites
- Chemotherapy has no impact

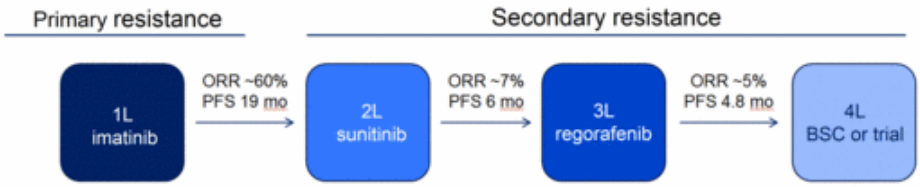
Activating RTK mutations drive metastatic GIST

KIT ~ 80% PDGFRα ~ 8%

- Primary mutational hotspots ☆
  - KIT Exons 9 or 11
  - PDGFRα D842V Exons 12 and 18
- Resistance mutations ★
  - KIT Exons 13 and 17
  - PDGFRα D842V Exon 18

GI, gastrointestinal; JM, juxtamembrane; KIT, receptor tyrosine kinase protein; PDGFRα, platelet-derived growth factor receptor; RTK, receptor tyrosine kinase; TM, transmembrane
Barnett & Heinrich (2012) Am Soc Clin Oncol Educ Book;663; Nowain et al (2005) J Gastroen Heptol;20:818; Dematteo et al (2000) Ann Surg;231:51;
Plumb et al (2013) Clin Radiol;68:770; Joensuu (2006) 17 Suppl 10:x280

Advanced GIST has high medical need



	Prevalence	
Resistance mutation	**Primary**	**Secondary**
KIT Exon 17	~ 1%	2L ~ 20% 3L ~ 90%
PDGFRα D842V	~ 5-6%	rare

- Activation loop mutations are associated with resistance to therapy
- Approved agents are ineffective against PDGFRα D842V
  - ORR ~ 0%
  - mPFS ~ 3 months

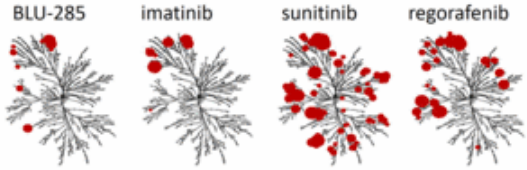
mPFS, median progression-free survival; ORR, objective response rate; PFS, progression-free survival

Cassier (2012) CCR;*18:4458*; Yoo (2016) Can Res Treat;48:546; Corless (2005) JCO;*23:5357*; Barnett and Heinrich (2012) Am Soc Clin Onc Ed Book: 663; Demetri (2006) Lancet;*368:1329*; Demetri (2013) Lancet;*381:295-302*

BLU-285 is a highly potent and selective inhibitor of KIT and PDGFRα activation loop mutants

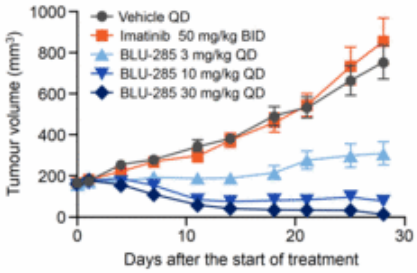
Biochemical profiles

	Activation loop		JM domain/ activation loop
	Exon 18	Exon 17	Exon 11/17
Compound	**PDGFRα D842V IC_{50} nM**	**KIT D816V IC_{50} nM**	**KIT V560G/D816V IC_{50} nM**
BLU-285	0.24	0.27	0.10
imatinib	759	8150	6145
sunitinib	120	207	97.2
regorafenib	810	3640	1685



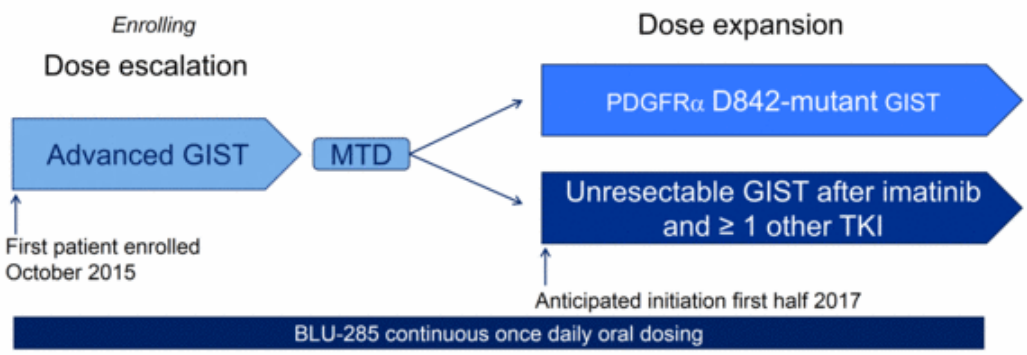
BID, twice daily; IC_{50}, half maximal inhibitory concentration; PDX, patient derived xenograft; QD, once daily
Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com)

Tumor regression in KIT exon 11/17* mutant GIST PDX



*del556-558/Y823D

BLU-285 Phase 1 study



- Primary objectives – determine the MTD and RP2D, and assess safety and tolerability
- Secondary objectives – PK, mutational status, anti-tumor activity

MTD, maximum tolerated dose; PK, pharmacokinetics; RP2D, recommended Phase 2 dose; TKI, tyrosine-kinase inhibitor
NCT02508532

Demography and baseline patient characteristics

Parameter	All patients, N = 36
Age (years), median (range)	61 (41 – 77)
	n (%)
GIST subtype	
KIT mutant	18 (50)
PDGFRα mutant	18 (50)
Metastatic Disease	35 (97)
Largest target lesion size (cm)	
≤ 5	8 (22)
> 5 – ≤ 10	12 (33)
> 10	14 (39)
pending	2 (6)
#Prior TKI, median (range)	3.5 (0 – 12)
≤ 2	12 (33)
> 2	24 (67)

Data are preliminary and based on a cut off date of 1 November 2016

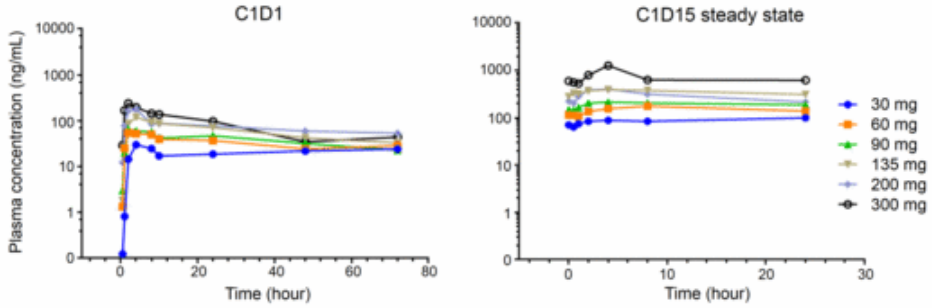
Initial dose escalation results

- Patients with unresectable GIST
  - Prior imatinib and ≥ 1 TKI
  - PDGFRα D842 mutation regardless of prior therapy
- 3 + 3 dose escalation with additional accrual to dose levels declared safe at a dose escalation meeting
- 36 patients enrolled over 12 months
- MTD has not been reached

BLU-285 mg/day	Patients treated by dose N = 36
30	3 + 2 enrichment
60	3 + 3 enrichment
90	3 + 3 enrichment
135	3 + 3 enrichment
200	3 + 2 enrichment
300	3 + 1 enrichment
400	4

- 75% (n=27) of patients remain on treatment, range 0.8 – 12.3 months
- All PDGFRα patients remain on treatment
- 9 patients off treatment (all due to progressive disease)

BLU-285 pharmacokinetics support once daily dosing

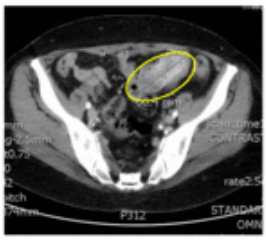


- Half-life > 24 hour, supporting QD dosing
- Relatively rapid absorption: T_{max} ~ 2 – 8 hr
- Accumulation in plasma: 2.5 – 4.7 -fold after 15 days
- Exposure at 300 mg is at low end of predicted therapeutic range based on KIT Exon 17 mutant xenograft studies

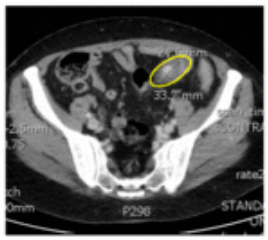
C1D1, Cycle 1 Day 1; C1D15, Cycle 1 Day 15; T_{max}, time at which C_{max} is observed; QD, once daily

Radiographic response per RECIST 1.1 in PDGFRα D842V GIST (dose level 1, 30 mg)

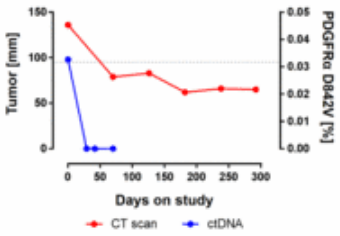
Baseline



After 8 weeks, partial response (-42%)



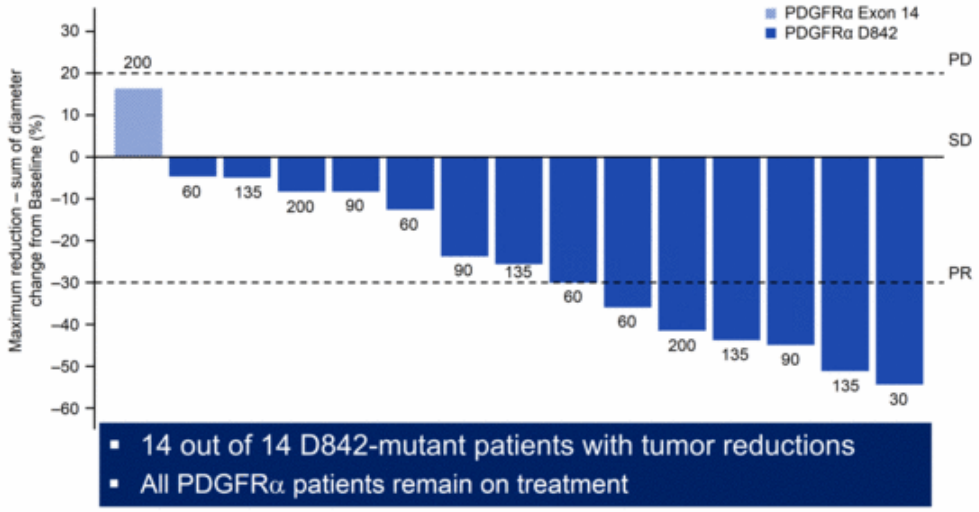
Rapid PDGFRα D842V ct-DNA decline



- *65 yo female, Primary Gastric GIST, PDGFRα D842V*
  - Previous surgical de-bulking: stomach; peritoneal metastases x 2; colon
  - Prior response to crenolanib followed by progression
  - Progression on prior dasatinib (no response)
  - Ongoing at Cycle 13 with confirmed partial response (-52% per RECIST 1.1)

CT, computerized tomography; ct-DNA, circulating tumor DNA; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors

Strong clinical activity against PDGFRα D842-mutant GIST at all dose levels

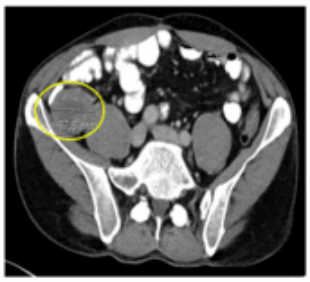


- 14 out of 14 D842-mutant patients with tumor reductions
- All PDGFRα patients remain on treatment

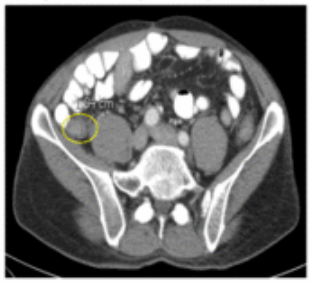
The values above/below the bars denote the dose level (mg) QD received by each patient
SD, stable disease; PD, progressive disease; PR, partial response

Radiographic response per RECIST 1.1 in heavily pretreated KIT Exon 11/17 GIST (dose level 4, 135 mg)

Baseline

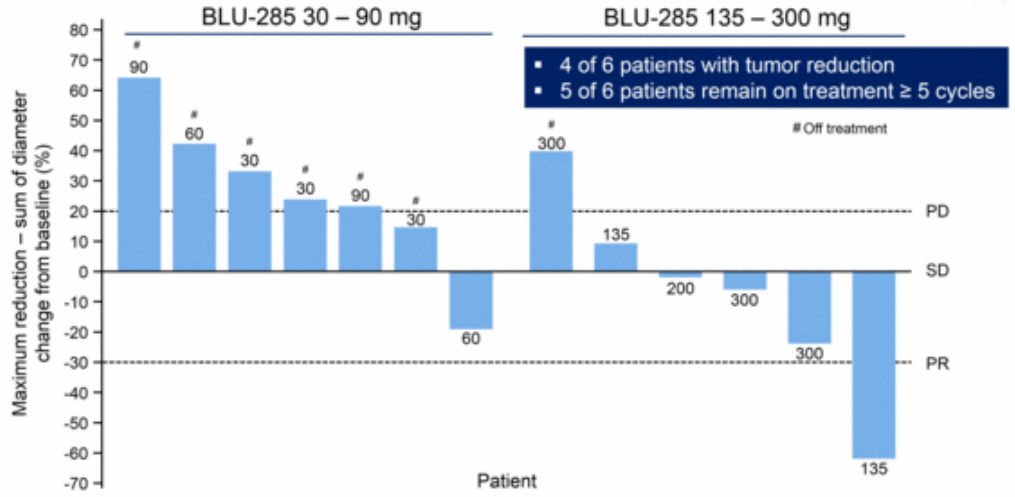


After 24 weeks,
partial response (-62%)



- 57 year old male, KIT Exon 11 (delWK557-8)/Exon 17 (D816V) mutations
  - Prior imatinib, sunitinib, nilotinib, sorafenib, imatinib + BKM120
  - Ongoing at Cycle 8 with confirmed partial response per RECIST 1.1

KIT GIST - early dose-response relationship



NB: The values above/below the bars denote the dose level (mg) QD received by each patient

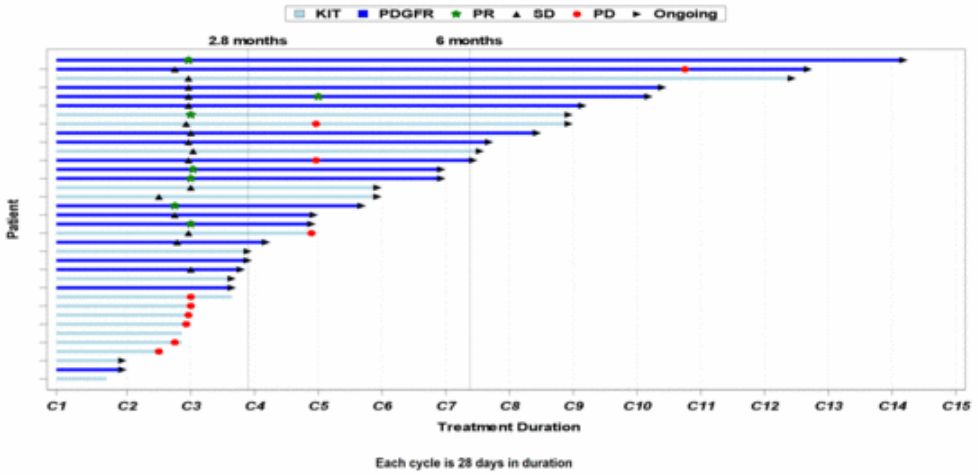
Best radiographic response with BLU-285 per RECIST 1.1

Best response (per investigator)	PDGFRα N=15 n (%)	KIT N=13 n (%)	Total N=28 n (%)
PR	6 (40)	1 (8)	7 (25)
SD	9 (60)	6 (46)	15 (54)
DCR (PR +SD)	15 (100)	7 (54)	22 (79)
PD	0	6 (46)	6 (21)

- Of 7 partial responses, 6 confirmed; 1 pending (still on treatment)

DCR, disease control rate

BLU-285: GIST treatment duration



Adverse events associated with BLU-285

- No DLTs or treatment-related Grade 4 – 5 AEs
- No patient discontinued BLU-285 due to treatment-related toxicity
- 11 (31%) patients had Grade 3 or higher AEs; of these, 3 were considered treatment-related:
  - 1 patient with Grade 3 nausea and vomiting
  - 1 patient with Grade 3 anemia and intratumoral hemorrhage
  - 1 patient with Grade 3 hypophosphatemia
- AEs occurring in ≥ 20% of patients
  - Nausea (42%)
  - Vomiting (33%)
  - Peripheral edema (31%)
  - Fatigue (28%)
  - Constipation (22%)

AE, adverse event; DLT, dose limiting toxicity

Summary

- BLU-285 has been well tolerated on a QD schedule at doses of 30 – 400 mg
- Half-life > 24 hours, supports QD dosing
- BLU-285 demonstrates strong clinical activity in PDGFRα D842-mutant GIST at all dose levels
- Significant anti-tumor activity in TKI-resistant, KIT-mutant GIST observed at doses ≥ 135 mg with tumor reduction in 4 of 6 patients, including 1 PR
- Dose escalation continues with the goal of maximizing clinical activity in KIT-mutant GIST and to define the MTD and RP2D
- Anticipate initiation of expansion cohorts in first half of 2017

Acknowledgments

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

First-in-human study of BLU-554, a potent, highly selective FGFR4 inhibitor designed for hepatocellular carcinoma (HCC) with FGFR4 pathway activation

Richard Kim[1], Sunil Sharma[2], Tim Meyer[3], Debashis Sarker[4], Teresa Macarulla[5], Max Sung[6], Su Pin Choo[7], Hongliang Shi[8], Oleg Schmidt-Kittler[8], Corinne Clifford[8], Beni Wolf[8], Yoon-Koo Kang[9], Josep Llovet[6]

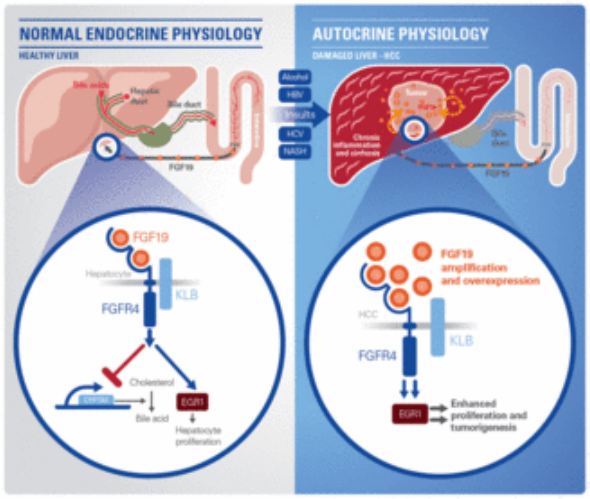
[1]Moffitt Cancer Center, Tampa, Florida, USA; [2]Huntsman Cancer Center, Salt Lake City, Utah, USA; [3]UCL Cancer Institute, London, UK; [4]Guy's Hospital, London, UK; [5]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [6]Mount Sinai Medical Center, New York, USA; [7]National Cancer Center Singapore, Singapore; [8]Blueprint Medicines, Cambridge, Massachusetts, USA, [9]Asan Medical Center, Seoul, South Korea

EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium,
Munich, Germany,
29 Nov 2016

The FGFR4 signaling pathway is a promising new driver for a molecularly targeted therapy for HCC

Clinical Opportunity
▪ Liver cancer, most often HCC, is 2nd leading cause of cancer death worldwide
▪ Sorafenib only approved drug, no approved 2nd line therapy   ▪ Response rate ~2%; median time to progression 3-6 months
▪ Approximately 30% of HCC patients estimated to have abnormally active FGFR4 pathway, a validated driver
▪ No genomically targeted therapies available

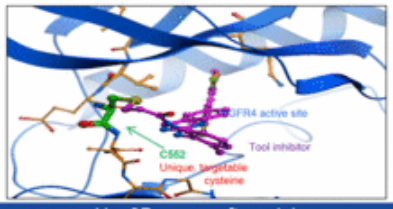
FGFR4 activation may result from FGF19 being expressed by either endocrine or autocrine physiology



HBV, hepatitis B virus; HCV, hepatitis C virus; NASH, nonalcoholic steatohepatitis; KLB, Klotho-β

BLU-554 is a potent and highly selective inhibitor of FGFR4

Irreversible FGFR4 inhibition



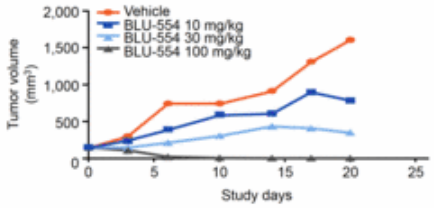
Potent and Highly Selective

Inhibitor	IC_{50} (nM) FGFR4	FGFR1-3
BLU-554	**5**	**624-2203**
AZD4547*	160	0.2-2.5
NVP-BGJ398*	60	0.9-1.4

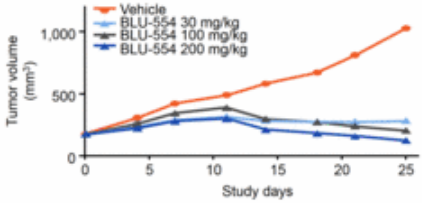
*Pan FGFR inhibitors

BLU-554

Hep3B xenograft model
FGF19 overexpression with amplification

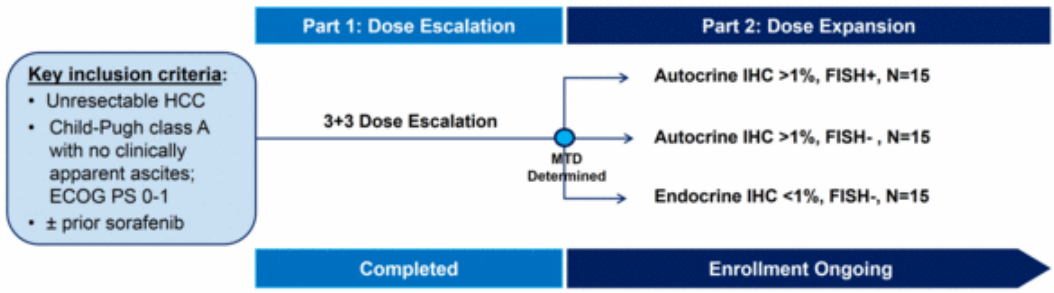


LIX-066 xenograft model
FGF19 overexpression without amplification



*Hagel M et al (2015) Cancer Discovery 5: 424–37; Gavine PR et al (2012) Cancer Res: 72:2045
Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com)

BLU-554 Phase 1 study



- Primary objectives – determine MTD and RP2D, assess safety and tolerability
- Secondary objectives – PK, biomarker status, anti-tumor activity

IHC, immunohistochemistry; FISH, fluorescence in situ hybridization; MTD, maximum tolerated dose; PK, pharmacokinetics; RP2D, recommended Phase 2 dose
NCT02508467

Demography and baseline patient characteristics

Parameter	All patients, N = 25
Age (years), median (range)	61 (19 – 81)
	n (%)
Gender – Male	19 (76)
Etiology	
Non-viral	4 (16)
HBV	8 (32)
HCV	4 (16)
Other/unknown	9 (36)
Metastatic Disease	17 (68)
FGF19 IHC	
IHC ≥ 1% (IHC+)	10 (40)
IHC < 1% (IHC-)	10 (40)
Unknown	5 (20)
FGF19 FISH	
FISH+	1 (4)*
FISH-	13 (52)
Unknown	11 (44)
Prior Therapy	
Surgical Resection	14 (56)
Radiotherapy	6 (24)
TACE / embolization	10 (40)
Kinase Inhibitor	20 (80)
sorafenib	19 (76)
Systemic Therapy	23 (92)

*CN=4, low level copy number gain; TACE, transarterial chemoembolization
Data are preliminary and based on a cut off date of November 7, 2016

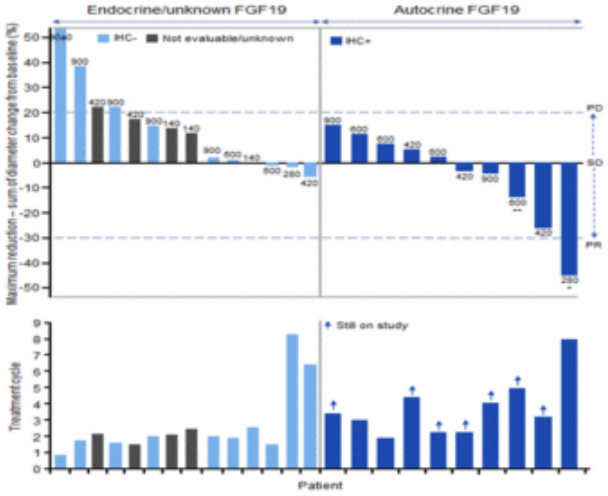
Initial dose escalation results

BLU-554 mg/day	Patients treated by dose N = 25	DLT
140	3	0
280	3	0
420	3 + 3 enrichment	0
600	3 + 3 enrichment	0
900	7	2

- Patients with unresectable HCC ± prior sorafenib
- 3 + 3 dose escalation with additional accrual to previous dose levels
- 25 patients enrolled over 12 months
- MTD defined as 600 mg QD

DLT, dose limiting toxicity; QD, once daily

Five of 10 FGF19 IHC+ patients with radiographic tumor shrinkage



- 25 patients in the first 5 dose escalation cohorts were evaluable for clinical activity (doses ranging from 140 mg -900 mg QD)
- 12 patients had SD, including 7 patients with tumor reduction that did not reach the threshold of 30% tumor reduction for a PR per RECIST
- 7 of 10 FGF19+ patients remain on treatment as of the data cutoff
- Duration of treatment ranging from 0.8 to 7.6 months

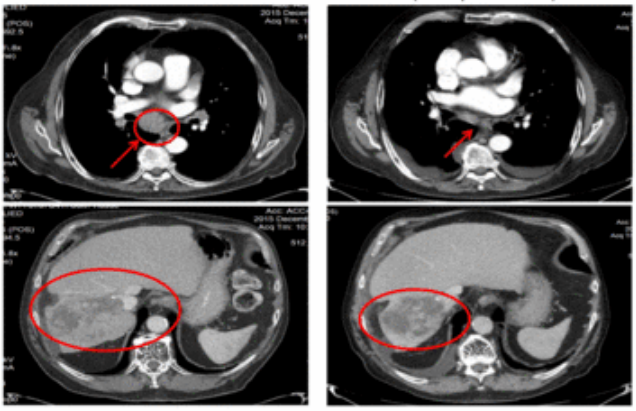
PD, progressive disease; PR, partial response; SD, stable disease
* Case study 1; ** Case study 2

Case study 1: Radiographic response per RECIST in patient with alcohol-related cirrhosis and advanced HCC (dose level 2, 280 mg)

81 year old male; alcohol-related cirrhosis and metastatic HCC; prior radiation therapy; sorafenib; remained on treatment for 8 cycles

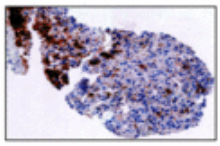
Baseline

Week 16, confirmed partial response (-44% per RECIST)

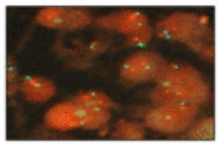


RECIST, Response Evaluation Criteria in Solid Tumors

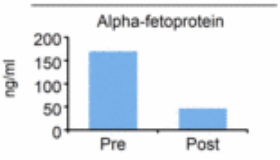
FGF19 IHC+



11q13.3 FISH-

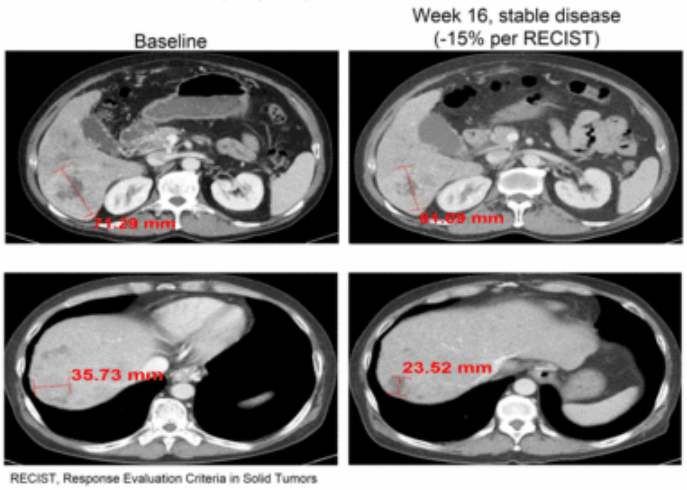


Tumor marker decline

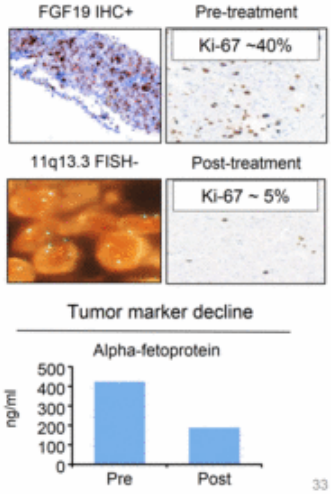


Case study 2: Radiographic response per RECIST in patient with HBV-related advanced HCC (dose level 4, 600 mg)

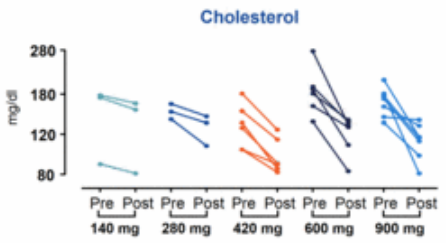
64 year old male; HBV-related HCC; BCLC stage C with macrovascular invasion; prior sorafenib; ongoing at cycle 6

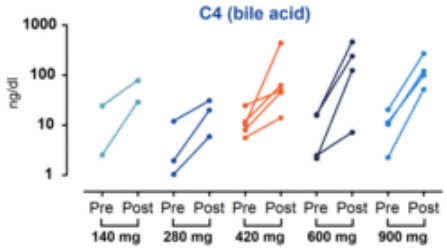


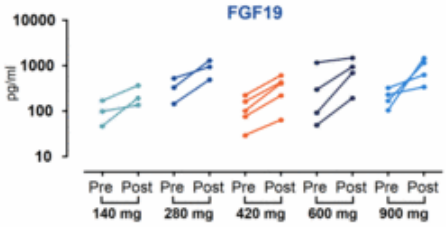
RECIST, Response Evaluation Criteria in Solid Tumors



Blood pharmacodynamic markers demonstrated FGFR4 pathway inhibition at all doses





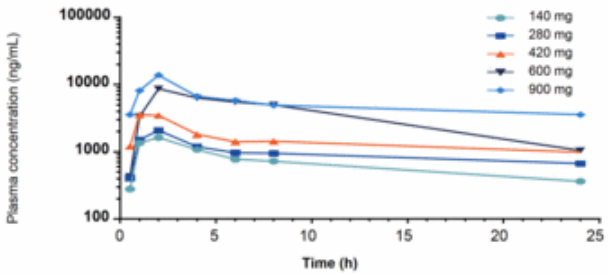


Effects on metabolic pathways downstream of FGFR4:

- Decreases in cholesterol
- Increases in C4, the bile acid precursor
- Feedback upregulation of the FGF19 ligand in blood

BLU-554 pharmacokinetics

BLU-554 plasma concentration: cycle 1, day 1



- Half-life of ~10 hours
- Rapid absorption: T_{max} ~1–3 hours
- Exposure increases over the 140–900 mg dose range with significant AUC overlap between 600 and 900 mg dose levels

AUC, area under the curve
Each cycle is 28 days in duration

Adverse events associated with BLU-554

- 2 (8%) patients experienced DLTs at 900 mg:
  - Grade 3 abdominal pain (1 patient); Grade 3 fatigue (1 patient)
- 2 (8%) patients discontinued BLU-554 due to treatment-related toxicity:
  - Grade 3 hemorrhage (1 patient); Grade 4 AST increase (1 patient)
- 17 (68%) patients had AEs of Grade 3 or greater, of which AEs in 12 (48%) patients were treatment-related

Adverse Events Occurring in >15% of Patients

AE Category # (%)	Any Grade	Grade 3 or Higher
Diarrhea	18 (72)	2 (8)
Nausea	11 (44)	0
Abdominal pain	10 (40)	3 (12)
Vomiting	10 (40)	0
Fatigue	9 (36)	2 (8)
ALT increased	8 (32)	3 (12)
AST increased	7 (28)	4 (16)
Decreased appetite	6 (24)	0
Anemia	5 (20)	5 (20)
ALP increased	5 (20)	0
Dyspnea	5 (20)	1 (4)
Peripheral edema	5 (20)	1 (4)
Maculo-papular rash	5 (20)	1 (4)
Bilirubin increased	4 (16)	1 (4)
Hyperhidrosis	4 (16)	0
Hyponatraemia	4 (16)	2 (8)
Lymphocytes decreased	4 (16)	3 (12)

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase

Summary

- Proof-of-concept established for highly selective targeting of FGFR4 with BLU-554 in advanced HCC
  - 5 of 10 FGF19 IHC+ patients with radiographic tumor shrinkage, including 1 confirmed PR
  - 7 of 10 FGF19 IHC+ patients remain on treatment
- MTD and recommended dose for expansion (600 mg QD) provides tolerability, pathway modulation and exposure within expected therapeutic range based on xenograft models
- Screening experience with IHC assay supports estimate of FGF19-FGFR4 pathway activation in approximately 30% of HCC patients
- Part 2 dose expansion initiated with central laboratory FGF19 IHC and FISH testing and goal of better defining responsive patient population(s) based on pathway status

Next steps

- BLU-285 in GIST
  - Continue dose escalation to define an MTD and to maximize clinical activity in KIT-driven patients
  - Increase the cohort sizes in the expansion to evaluate the potential of BLU-285 as a single agent therapy in PDGFRα-driven and KIT-driven GIST
  - Seek guidance from the FDA on the development path forward, including any possibilities for expedited clinical development of BLU-285 for the treatment of advanced GIST
  - Accelerate the evaluation of expanded development options, including opportunities to move to earlier lines of therapy and possible combinations
- BLU-554 in HCC
  - Continue enrollment in the expansion to define the patient population(s), based on their biomarker status, that may respond to BLU-554 as a single agent therapy
  - Accelerate the evaluation of expanded development options, including opportunities to move to earlier lines of therapy and possible combinations


blueprint
MEDICINES
Questions & Answers