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): **November 29, 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 8.01 Other Events.

On November 30, 2016, Blueprint Medicines Corporation (the "Company") issued a press release announcing 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. BLU-285 is an orally available, potent and highly selective inhibitor that targets D842V mutant PDGFRα and Exon 17 mutant KIT. The Company is presenting the data on Thursday, December 1, 2016, in an oral presentation at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Munich, Germany (the "EORTC-NCI-AACR Symposium"). A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference.

In addition, on November 29, 2016 at the EORTC-NCI-AACR Symposium, the Company presented data from the dose escalation stage of its ongoing Phase 1 clinical trial evaluating BLU-554 for the treatment of advanced hepatocellular carcinoma. BLU-554 is an orally available, potent and highly selective inhibitor that targets the kinase FGFR4. A copy of the poster presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release issued by Blueprint Medicines Corporation on November 30, 2016
99.2	Poster presentation by Blueprint Medicines Corporation on November 29, 2016 at the EORTC-NCI-AACR Symposium

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: November 30, 2016

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

EXHIBIT INDEX

Exhibit No.	Description
99.1	Press release issued by Blueprint Medicines Corporation on November 30, 2016
99.2	Poster presentation by Blueprint Medicines Corporation on November 29, 2016 at the EORTC-NCI-AACR Symposium

Blueprint Medicines Announces Proof-of-Concept Data from Phase 1 Clinical Trial of BLU-285 in Patients with Advanced Gastrointestinal Stromal Tumors

– Favorable Safety and Tolerability Profile –
– Tumor Reduction Observed in Both PDGFRα-Driven and KIT-Driven Patients –
– Blueprint Medicines to Host Investor Conference Call and Webcast on December 1, 2016 at 12:30 p.m. ET –

CAMBRIDGE, Mass., November 30, 2016 – Blueprint Medicines Corporation (NASDAQ: BPMC), a leader in discovering and developing targeted kinase medicines for patients with genomically defined diseases, today announced data from its ongoing Phase 1 clinical trial evaluating BLU-285, an investigational medicine for the treatment of patients with advanced gastrointestinal stromal tumors (GIST). These data provide proof-of-concept for BLU-285, a potent, highly selective inhibitor of D842V mutant PDGFRα and Exon 17 mutant KIT. The data will be presented on Thursday, December 1, 2016 at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Munich, Germany (EORTC-NCI-AACR).

“The clinical activity observed to date in the dose escalation portion of this Phase 1 study is promising,” said Michael Heinrich, M.D., Oregon Health & Science University, an investigator for the clinical trial. “Advanced GIST is a devastating illness, marked by rapid disease progression. Seeing tumor shrinkage in 14 out of 15 PDGFRα-driven GIST patients at this point in the study is notable. I am also excited to see tumor shrinkage in four out of the six KIT-driven GIST patients treated at the higher dose levels, indicating the potential for increased clinical activity as we continue to dose-escalate. Given these encouraging early data for this investigational medicine, I believe BLU-285 could be transformative for patients with advanced GIST.”

“These data help to validate Blueprint Medicines’ ability to craft targeted kinase inhibitors and to achieve rapid proof-of-concept for our investigational therapies in genomically-defined populations,” said Andy Boral, M.D., Chief Medical Officer at Blueprint Medicines. “We are encouraged by the early evidence of clinical activity, with the majority of patients achieving stable disease or a partial response, and some patients having durable tumor reduction lasting at least eight months. I am also pleased that BLU-285 has been well-tolerated to date and that the pharmacokinetic profile supports once daily dosing. We continue to believe that BLU-285 has the potential to significantly impact the treatment paradigm for patients with GIST.”

Data from the Ongoing Phase 1 Clinical Trial

BLU-285 is currently being evaluated in the dose escalation stage of a Phase 1 clinical trial in patients with unresectable PDGFRα-driven GIST and patients with treatment-resistant KIT-driven GIST. As of the data cutoff date of November 1, 2016, 36 patients had been treated in the dose escalation portion of the Phase 1 clinical trial at seven dose levels (ranging from 30 mg once daily (QD) to 400 mg QD), including 18 patients with PDGFRα-driven GIST and 18 patients with KIT-driven GIST. The median age was 61 (ranging from 41 to 77), and the median number of prior tyrosine-kinase inhibitor (TKI) regimens was 3.5 (ranging from zero to 12).

Preliminary pharmacokinetic analysis demonstrated relatively rapid absorption of BLU-285 and a mean half-life of over 24 hours that supports once daily dosing.

Preliminary Safety Data

As of the data cutoff date of November 1, 2016, BLU-285 was observed to be well-tolerated at all doses. The majority of adverse events (AEs) reported by investigators were Grade 1 or 2. Across all grades, AEs reported by investigators most commonly included nausea (42%), vomiting (33%), peripheral edema (31%), fatigue (28%) and constipation (22%). Investigators reported treatment-related Grade 3 AEs in three patients: nausea and vomiting (one patient); anemia and intratumoral hemorrhage (one patient); and hypophosphatemia (one patient). No dose-limiting toxicities or drug-related Grade 4 or 5 AEs were reported, and no patients discontinued BLU-285 due to treatment-related adverse events. A maximum tolerated dose (MTD) has not been reached, and enrollment in the dose escalation portion of the Phase 1 clinical trial is ongoing.

Preliminary Clinical Activity Data

As of the data cutoff date of November 1, 2016, 28 patients in the first six cohorts of the dose escalation portion of the clinical trial (at doses ranging from 30 mg QD to 300 mg QD) had completed at least two 28-day dosing cycles and were evaluable for response assessment. CT and MRI imaging was used to measure clinical activity by Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1.

- In PDGFRα-driven GIST, investigators observed radiographic tumor reduction in 14 of 15 evaluable patients with six patients achieving a partial response (PR) by RECIST (five confirmed, one unconfirmed). Tumor reduction was observed at the first dose level in the PDGFRα-driven subgroup of advanced GIST.

- In KIT-driven GIST, investigators observed radiographic tumor reduction in five of the 13 evaluable patients, including one who achieved a PR by RECIST (confirmed). At the higher dose levels (greater than or equal to 135 mg), four out of six patients had tumor reduction, including the patient with a PR, suggesting increased clinical activity with increased dose. Tumor shrinkage was first observed at the fourth dose level in the KIT-driven subgroup of advanced GIST.

- Among all 36 patients treated, 27 patients remained on BLU-285, including all 18 patients with PDGFRα-driven GIST, with a duration of treatment ranging from 0.8 months to 12.3 months.

- Nine patients discontinued treatment with BLU-285 due to progressive disease.

Clinical Development Plans for BLU-285 in GIST

Based on the favorable safety profile and encouraging clinical activity observed to date in the Phase 1 clinical trial for BLU-285 for the treatment of advanced GIST, Blueprint Medicines will continue to enroll patients in the dose escalation portion of this clinical trial until a MTD or a lower recommended dose for further clinical evaluation has been established. Enrollment in the expansion cohorts for this Phase 1 clinical trial is expected to begin in the first half of 2017. Blueprint Medicines plans to enroll approximately 35 patients with advanced GIST in the expansion cohorts. We also plan to accelerate our evaluation of expanded development options for BLU-285 in GIST, including opportunities to move to earlier lines of therapy and possible combinations.

In January 2016, the U.S. Food and Drug Administration (FDA) granted orphan drug designation to BLU-285 for the treatment of GIST, and in October 2016, the FDA 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 with the PDGFRα D842V mutation regardless of prior therapy. Blueprint Medicines plans to seek regulatory guidance on potential pathways for expedited clinical development of BLU-285 for the treatment of advanced GIST.

Conference Call Information

Blueprint Medicines will host a conference call and webcast on Thursday, December 1, 2016 at 12:30 p.m. ET (6:30 p.m. CET) to discuss the preliminary clinical data for BLU-285 in GIST. The data will be presented on December 1, 2016 by Michael Heinrich, M.D., Oregon Health & Science University, in an oral presentation, "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)," (Abstract 6LBA) at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Munich, Germany at 4:00 p.m. CET (10:00 a.m. ET). As part of the conference call and webcast, Blueprint Medicines will also be discussing the preliminary data from the dose escalation portion of its Phase 1 clinical trial for BLU-554, an investigational medicine in development for patients with advanced hepatocellular carcinoma, which was presented in a poster presentation at EORTC-NCI-AACR.

To participate in the conference call, please dial 1-855-728-4793 (domestic) or 1-503-343-6666 (international) and refer to conference ID 10770449. A live webcast of the presentation will also be available under "Events and Presentations" in the Investors section of Blueprint Medicines' website at http://ir.blueprintmedicines.com. A replay of the webcast will be available approximately two hours after the conference call and will be available for 30 days following the call.

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

Blueprint Medicines' Phase 1 clinical trial for BLU-285 for the treatment of patients with unresectable PDGFRα-driven GIST and treatment-resistant KIT-driven GIST is designed to evaluate the safety and tolerability of BLU-285 in multiple ascending doses with the goal of establishing an MTD or a lower recommended dose. All patients are tested retrospectively for both PDGFRα D842 and KIT mutational status. Once the MTD is reached, or a recommended dose is established, Blueprint Medicines plans to open expansion cohorts for patients with a PDGFRα D842 mutation, regardless of line of therapy, and for patients who have received imatinib and at least one other KIT-directed TKI, clinically selecting for patients with KIT-driven GIST who have a KIT Exon 17 mutation. Secondary objectives include assessing response rate by RECIST version 1.1 criteria commonly used to measure clinical responses in solid tumors, the pharmacokinetics of BLU-285 and allelic burden using circulating tumor DNA. The Phase 1 clinical trial is designed to enroll approximately 60 patients, including approximately 25 patients during dose escalation and approximately 35 additional patients in expansion cohorts, at multiple sites in the United States, European Union and Asia. Please refer to www.clinicaltrials.gov for additional details related to this Phase 1 clinical trial (NCT02508532). For more information, please contact the study director for 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-driven GIST, and progression can occur 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 D842V mutant PDGFRα and Exon 17 mutant KIT. 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 Blueprint Medicines retains worldwide development and commercialization rights for BLU-285.

About Blueprint Medicines

Blueprint Medicines is developing a new generation of targeted 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 three programs in clinical development for subsets of patients with gastrointestinal stromal tumors, hepatocellular carcinoma and systemic mastocytosis, as well as multiple programs in research and preclinical development.

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; our ability to implement our clinical development plans for BLU-285 for the treatment of advanced GIST; our ability to enroll patients in our ongoing Phase 1 clinical trial for BLU-285 in advanced GIST; 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 product candidates, including BLU-285 and BLU-554; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the efficacy and safety of its drug product candidates; the preclinical and clinical results for Blueprint Medicines' drug product candidates, which may not support further development of such drug product candidates; and actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Blueprint Medicines' ability to develop and commercialize companion diagnostics for its current and future drug candidates, including companion diagnostics 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 September 30, 2016, as filed with the Securities and Exchange Commission (SEC) on November 10, 2016, 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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Poster
P076A

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

Hypothesis and objectives

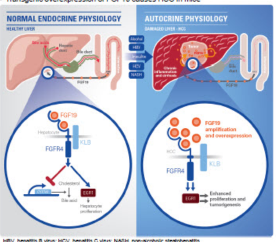
- A Phase I study was initiated in advanced HCC to explore the hypothesis that targeting FGFR4 will have therapeutic benefit in HCC driven by the FGFR4 ligand, FGF19
- The key objectives were to determine the maximum tolerated dose (MTD) and to evaluate the safety, pharmacokinetics (PK), pharmacodynamics (PD) and preliminary anti-tumor activity of BLU-554, an investigational, potent, highly-selective, oral FGFR4 inhibitor

HCC – a worldwide medical need[1]

- >700,000 new cases/year; 600,000 deaths/year
- Sorafenib, standard of care for advanced disease, provides a response rate of ~2% and median survival <11 months
- Viral and non-viral etiologies are well known, but molecular drivers are largely undefined; consequently, there are no molecular diagnostics to guide patient care

FGF19 identified as a potential HCC driver[1–5]

- ~5% of HCCs have genomic amplification of the FGF19/CCND1 locus (Immunohistochemistry [IHC]+ Fluorescent In Situ Hybridization [FISH]+)
- ~25% of HCCs overexpress FGF19 in the absence of genomic amplification (IHC+ FISH-)
- Transgenic overexpression of FGF19 causes HCC in mice


NORMAL ENDOCRINE PHYSIOLOGY
HEALTHY LIVER
AUTOCRINE PHYSIOLOGY
DAMAGED LIVER - HCC
Alcohol
HBV
Insults
HCV
NASH
FGF19
Hepatocyte
KLB
FGFR4
Cholesterol
Bile acid
EGR1
Hepatocyte proliferation
FGF19 amplification and overexpression
HCC
Enhanced proliferation and tumorigenesis

HBV, hepatitis B virus; HCV, hepatitis C virus; NASH, non-alcoholic steatohepatitis

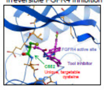
- Normal liver does not express FGF19, but expresses high levels of FGFR4 and klotho-beta (KLB). FGF19 produced by the ileum acts in an endocrine fashion on the liver to initiate signaling (left panel)
- HCC retains high levels of FGFR4/KLB and remains poised to bind FGF19. Aberrant FGF19 expression in HCC promotes autocrine signaling (right panel)

Methods

- Patients were given BLU-554 orally, once daily (QD) on a 4-week cycle following a 3+3 design. Adverse events (AEs), PK and PD were assessed. Baseline tumor FGF19 expression was analyzed via IHC as a marker of pathway activation. FISH was assessed retrospectively. Response was determined by RECIST 1.1 every 8 weeks
- All data are preliminary and based on a cut-off of November 7, 2016

BLU-554

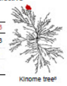
Irreversible FGFR4 inhibition



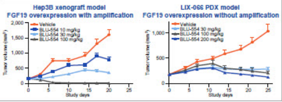
Highly potent and selective

Inhibitor[6,7]	IC_{50} (nM) FGFR4	IC_{50} (nM) FGFR1–3
BLU-554	5	624–2203
AZD4547*	160	0.2–2.5
NVP-BGJ398*	60	0.9–1.4

*Pan FGFR inhibitors



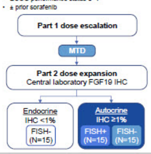
Kinome tree[8]


Hep3B xenograft model
FGF19 overexpression with amplification
Vehicle
BLU-554 10 mg/kg
BLU-554 30 mg/kg
BLU-554 100 mg/kg
Tumor volume (mm³)
Study days
LIX-066 PDX model
FGF19 overexpression without amplification
Vehicle
BLU-554 30 mg/kg
BLU-554 100 mg/kg
BLU-554 200 mg/kg

Phase I study design

Key inclusion criteria

- Unresectable HCC
- Child-Pugh class A with no clinically apparent ascites
- ECOG performance status 0–1
- ± prior sorafenib



Part 1 dose escalation

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

- 3+3 dose escalation with FGF19+ patient enrichment via additional accrual to dose levels declared safe
- MTD defined as 600 mg QD
- Dose expansion now enrolling

Baseline demographics and characteristics

- 25 patients were enrolled over 12 months; 7 (28%) patients remain on study
- 18 (72%) patients discontinued BLU-554:
  - 15 due to disease progression, 2 due to AEs, 1 due to investigator's decision

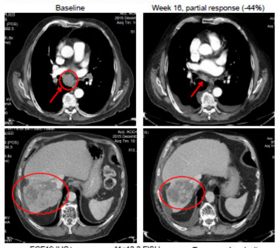
Characteristic, n (%)	Total (N=25)	Characteristic, n (%)	Total (N=25)
Mean age, years (range)	61 (19–81)	**FGF19 FISH**	
Gender		FISH+	1 (4)*
Male	19 (76)	FISH-	13 (52)
Etiology		Unknown	11 (44)
Non-viral	4 (16)	**Prior therapy**	
HBV	8 (32)	Surgical resection	14 (56)
HCV	4 (16)	Radiotherapy	6 (24)
Other/unknown	9 (36)	TACE/embolization	10 (40)
Metastatic disease		Kinase inhibitor	20 (80)
Yes	17 (68)	Sorafenib	19 (76)
FGF19 IHC		Systemic therapy	23 (92)
IHC ≥1% (IHC+)	10 (40)		
IHC <1% (IHC-)	10 (40)		
Unknown	5 (20)		

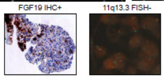
*CN=4, low level copy number gain; TACE, transarterial chemoembolization

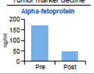
Proof-of-concept

Case study 1 (280 mg)

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

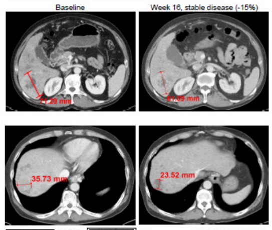


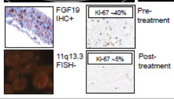


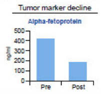


Case study 2 (600 mg)

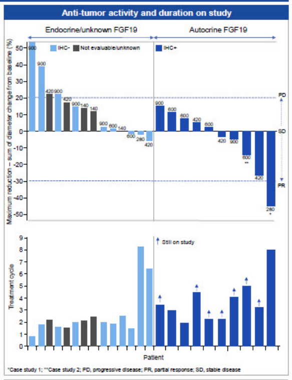
- 64 year old male; HBV-related HCC; Barcelona clinic liver cancer stage C with macrovascular invasion; prior sorafenib; ongoing at cycle 6







Anti-tumor activity and duration on study



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

Safety

Adverse events

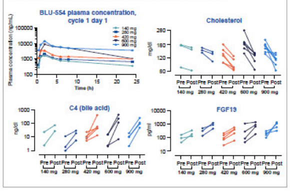
- 2 patients experienced dose-limiting toxicities at 900 mg:
  - Grade 3 abdominal pain; Grade 3 fatigue lasting more than 7 days
- 2 patients discontinued BLU-554 due to treatment-related toxicity:
  - Grade 3 hemorrhage; Grade 4 AST increase
- 17 patients had Grade ≥3 AEs which were treatment-related in 12 patients
- AEs occurring in >15% of patients are summarized in the table below

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

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase

Pharmacokinetics and pharmacodynamics

- PK shows rapid absorption (T_{max} ~1–3 hours) and half-life of ~10 hours
- Exposure increases over the 140–900 mg dose range with significant AUC overlap between 600 and 900 mg dose levels
- Blood PD markers show pathway engagement at all dose levels



Conclusions

- 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 partial response
  - 7 of 10 FGF19 IHC+ patients remain on study
- The QD MTD and recommended dose for expansion (600 mg) provides tolerability, pathway modulation, and exposure in the expected therapeutic range based on xenograft models
- FGF19 IHC data suggest potential for autocrine FGF19-FGFR4 pathway activation in approximately 30% of HCC patients
- Part 2 dose expansion underway with central laboratory FGF19 IHC and FISH testing to better define responsive patient population(s) based on pathway status

Acknowledgments
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