# 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 28, 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**<br>**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 November 28, 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-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 press release is attached as Exhibit 99.1 to this Current Report on Form 8-K. The Company is presenting the data on Tuesday, November 29, 2016, in a poster presentation at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Munich, Germany.

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 | Press release issued by Blueprint Medicines Corporation on November 28, 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: November 29, 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 28, 2016 |

**Blueprint Medicines Announces Proof-of-Concept Data from Global Phase 1 Clinical Trial of BLU-554 in Patients with Advanced Hepatocellular Carcinoma**

*– Radiographic Tumor Reduction Observed in 5 of 10 Patients with FGFR4 Pathway Activation –*
*– MTD Determined and Biomarker-Selected Dose Expansion Initiated –*
*– Blueprint Medicines to Host Investor Conference Call and Webcast on Thursday, December 1, at 12:30 p.m. ET –*

CAMBRIDGE, Mass., November 28, 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 trial evaluating BLU-554, an investigational medicine for the treatment of advanced hepatocellular carcinoma (HCC). Blueprint Medicines is developing BLU-554 as a potent, highly selective inhibitor of fibroblast growth factor receptor 4 (FGFR4). The data are being presented on Tuesday, November 29, 2016, at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Munich, Germany.

"We desperately need new treatment options for patients with liver cancer, the second leading cause of cancer deaths worldwide," said Richard Kim, M.D., Moffitt Cancer Center, an investigator for the study. "Unlike many other tumor types, there are no biomarker-driven targeted therapies currently approved for HCC, the most common form of liver cancer. These preliminary data are exciting as they suggest BLU-554 may offer the first targeted therapy in a biomarker-defined group of patients with advanced HCC. I am excited to evaluate BLU-554 in the expansion portion of the Phase 1 clinical trial, where we are prospectively selecting patients for FGFR4 pathway activation."

"We are very encouraged to see early anti-tumor activity in patients with confirmed FGF19 overexpression and consistent evidence of FGFR4 pathway modulation during the dose escalation part of this first-in-human clinical trial," said Andy Boral, M.D., Chief Medical Officer of Blueprint Medicines. "Now that we have demonstrated proof-of-concept, determined the maximum tolerated dose (MTD), and implemented FGF19 biomarker screening globally, we can move rapidly to enroll patients in the expansion part of the study to more fully evaluate the activity of BLU-554 in patients with advanced HCC."

**Data from the Ongoing Global Phase 1 Clinical Trial**

BLU-554 was evaluated in the dose escalation stage of a Phase 1 clinical trial in patients with advanced HCC. As of the data cutoff date of November 7, 2016, 25 patients had been treated in the dose escalation portion of the Phase 1 clinical trial at five dose levels (ranging from 140 mg once daily (QD) to 900 mg QD), with the majority of patients having previously received sorafenib. The study was designed to retroactively assess patient biopsies for FGFR4 pathway activation after enrollment by evaluating levels of FGF19, the protein that activates FGFR4, using an investigational immunohistochemistry (IHC) assay. Prospective screening of patients with the investigational IHC assay was implemented during dose escalation, enabling enrollment of enrichment patients with confirmed FGF19 overexpression which resulted in a larger number than anticipated of biomarker positive patients being enrolled. Blueprint Medicines has initiated the expansion portion of the Phase 1 clinical trial, and enrollment is ongoing.

Pharmacokinetic (PK) data across all dose levels showed rapid oral absorption, a mean half-life of approximately ten hours, and exposure in the expected therapeutic range based on HCC xenograft models.

Pharmacodynamic (PD) data demonstrated FGFR4 pathway inhibition with BLU-554, as evidenced by effects on metabolic pathways downstream of FGFR4, with increases in the bile acid precursor C4, decreases in cholesterol, and feedback upregulation of the ligand FGF19 in blood.

*Preliminary Safety Data*

As of the data cutoff date of November 7, 2016, the majority of adverse events (AEs) reported by investigators were Grade 1 or 2 and most commonly included diarrhea (72%), nausea (44%), abdominal pain (40%), vomiting (40%), fatigue (36%), transaminase elevation (ALT 32% and AST 28%) and decreased appetite (24%). Treatment with BLU-554 demonstrated acceptable tolerability below 900mg. Investigators reported Grade 3 or higher AEs in 17 patients. Grade 3 or worse AEs occurring in three or more patients included anemia, elevated transaminases (AST and ALT), abdominal pain and decreased lymphocytes. Two patients experienced dose-limiting toxicities at 900 mg (Grade 3 abdominal pain and Grade 3 fatigue), defining 600 mg QD as the MTD. Only two patients discontinued treatment with BLU-554 due to drug-related toxicities, including Grade 4 increased AST and Grade 3 hemorrhage. The case of Grade 3 hemorrhage occurred in a patient treated at 900 mg, above the MTD.

*Preliminary Clinical Activity Data*

As of the data cutoff date of November 7, 2016, 25 patients in the first five cohorts of the dose escalation portion of the clinical trial (at doses ranging from 140 mg QD to 900 mg QD) were evaluable for clinical activity.

- One patient had a confirmed partial response (PR), and remained on the clinical trial for eight 28-day dosing cycles. Twelve patients had stable disease (SD), including seven who had tumor reduction but did not reach the threshold for a PR.

- Of ten evaluable patients with FGF19 overexpression in their tumors, five had radiographic tumor reduction, including one patient with a confirmed PR. Seven of the ten patients with FGF19 overexpression remain on treatment as of the data cutoff.

- Among all 25 evaluable patients, seven patients remain on treatment as of the data cutoff, with a duration of treatment ranging from 0.8 to 7.6 months.

- Eighteen patients discontinued treatment with BLU-554, including 15 patients due to disease progression, two patients due to treatment-related AEs and one patient due to the investigator's decision.

**Clinical Development Plans for BLU-554**

Blueprint Medicines has initiated enrollment of the biomarker-selected expansion cohorts at the maximum tolerated dose of 600 mg QD. In the expansion, patients will be prospectively evaluated for tumor expression of FGF19 using an investigational IHC assay. We plan to enroll approximately 45 patients in three subsets. Two subsets of patients will be selected to have tumors that overexpress FGF19

(confirmed by IHC), which indicates autocrine physiology, where FGF19 is produced by the tumor cells in the liver. One of the patient subsets with tumors that overexpress FGF19 will also have FGF19 gene amplification (confirmed by fluorescence in situ hybridization). The third subset of patients will be selected to have tumor FGF19 expression less than 1% by the IHC assay, which indicates normal endocrine physiology, where FGF19 is produced by the intestine.

**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-554 in HCC. The data will be presented on Tuesday, November 29, 2016 by Richard Kim, M.D., Moffitt Cancer Center, in a poster presentation, "First-in-Human Study of BLU-554, a Potent, Highly-Selective FGFR4 Inhibitor Designed for Hepatocellular Carcinoma (HCC) with FGFR4 Pathway Activation," (Abstract 105A) at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Munich, Germany (EORTC-NCI-AACR). The poster is included in the Molecular Targeted Agents I session from 5:45 a.m. – 12:30 p.m. ET (11:45 a.m. – 6:30 p.m. CET). 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-285 in unresectable PDGFRα-driven and treatment-resistant KIT-driven gastrointestinal stromal tumors, which will be presented in a late-breaking oral presentation at EORTC-NCI-AACR on December 1, 2016, and the abstract and data will remain embargoed until December 1, 2016 at 12:01 a.m. CET (November 30, 2016 at 6:01 p.m. ET).

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 Global Phase 1 Clinical Trial for BLU-554 in Advanced HCC**

Blueprint Medicines' Phase 1 clinical trial for BLU-554 is designed to evaluate the safety and tolerability of BLU-554 in multiple ascending doses in patients with advanced HCC. Enrollment in the dose-escalation portion of the Phase 1 clinical trial has been completed, and the maximum tolerated dose (MTD) has been determined to be 600 mg QD. Blueprint Medicines has initiated enrollment of the expansion portion of the Phase 1 clinical trial in three defined cohorts at the MTD. The primary objective of the expansion portion of the Phase 1 clinical trial is to continue to evaluate the safety and tolerability of BLU-554. Secondary objectives include assessing clinical activity by Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) criteria, as well as evaluating the pharmacokinetics of BLU-554 and pharmacodynamic markers of BLU-554 activity. The expansion portion of the Phase 1 clinical trial is designed to enroll approximately 45 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. For more information, please contact the study director for this Phase 1 clinical trial at studydirector@blueprintmedicines.com.

**About HCC**

Liver cancer is the second leading cause of cancer-related deaths worldwide, with HCC accounting for most liver cancers. In the United States, HCC is the fastest rising cause of cancer-related death. Over the

past two decades, the incidence of HCC has tripled while the five-year survival rate has remained below 12%. The highest incidence of HCC occurs in regions with endemic hepatitis B virus, including Southeast Asia and sub-Saharan Africa. Treatment options for patients with advanced HCC are limited, with the currently approved first line therapy providing a time to progression that is less than six months and overall survival that is typically less than one year. FGF19 is the ligand that activates FGFR4, which Blueprint Medicines estimates is aberrantly activated in approximately 30% of patients with HCC. FGF19 and FGFR4 promote hepatocyte proliferation and regulate bile acid homeostasis in the liver.

**About BLU-554**

BLU-554 is an orally available, potent, highly selective and irreversible inhibitor of the kinase FGFR4, while sparing the other three FGFR paralogs. Blueprint Medicines is initially developing BLU-554, an investigational medicine, for the treatment of patients with advanced HCC. BLU-554 was discovered by Blueprint Medicines' research team, and Blueprint Medicines retains worldwide development and commercialization rights for BLU-554.

**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. For more information, please visit www.blueprintmedicines.com.

**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-554; our ability to implement our clinical development plans for BLU-554 for the treatment of advanced HCC; our ability to enroll patients in our ongoing Phase 1 clinical trial for BLU-554 in advanced HCC; 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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