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): **September 26, 2018**

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.)

45 Sidney Street **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 September 26, 2018, Blueprint Medicines Corporation issued a press release announcing the presentation and publication of two clinical cases demonstrating proof-of-concept for BLU-667 in combination with osimertinib (Tagrisso®) in treatment-resistant, EGFR-mutant non-small cell lung cancer. A copy of the press release is furnished 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, 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 September 26, 2018

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: September 26, 2018

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

Blueprint Medicines Announces Proof-of-Concept Data Showing Combination of BLU-667 and Osimertinib Overcame Treatment Resistance in Two Patients with EGFR-Mutant, Non-Small Cell Lung Cancer and an Acquired RET Fusion

-- Data presented at Late-Breaking Clinical Session of IASLC World Conference on Lung Cancer, and simultaneously published in Cancer Discovery --

CAMBRIDGE, Mass., September 26, 2018 – Blueprint Medicines Corporation (NASDAQ: BPMC), a leader in discovering and developing targeted kinase medicines for patients with genomically defined diseases, today announced the presentation and publication of two clinical cases demonstrating proof-of-concept for BLU-667 in combination with osimertinib (Tagrisso®) in treatment-resistant, EGFR-mutant non-small cell lung cancer (NSCLC). In both cases, the combined agents overcame resistance to standard treatment due to an acquired RET fusion, resulting in significant tumor reductions. The data are being presented today in a late-breaking oral presentation at the International Association for the Study of Lung Cancer 19th World Conference on Lung Cancer (WCLC) and published online in *Cancer Discovery*.

“The combination of two highly selective agents — BLU-667 and osimertinib — has the potential to become an important new tool to overcome treatment resistance in a subset of patients with EGFR-mutant, non-small cell lung cancer,” said Lecia V. Sequist, M.D., Ph.D., medical oncologist, Massachusetts General Hospital Cancer Center and Associate Professor of Medicine, Harvard Medical School, and senior author of the oral presentation and paper. “We found that two pre-treated patients with advanced disease, who acquired RET fusions resulting in resistance to standard therapy, each showed a meaningful response only eight weeks after initiating the combination regimen. These results are highly encouraging and support further study of BLU-667 in combination with osimertinib in additional patients.”

BLU-667 is an investigational precision therapy designed to potently and selectively inhibit RET alterations including resistance mutations. It is currently being evaluated in the global Phase 1 ARROW clinical trial in patients with RET-altered NSCLC, medullary thyroid cancer (MTC) and other solid tumors.

Data Highlights
The WCLC presentation and *Cancer Discovery* article included preclinical data and two clinical cases highlighting the potential of combining BLU-667 and osimertinib to overcome treatment resistance in EGFR-mutant NSCLC.

The clinical cases included two patients treated with BLU-667 and osimertinib under investigator-sponsored protocols. The patients had advanced EGFR-mutant NSCLC that progressed on standard targeted therapy, with an acquired RET fusion identified via lung biopsy. Radiographic scans after eight weeks showed both patients experienced a partial response (both pending confirmation), with each achieving a 78 percent reduction in target tumors per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. The combination was well tolerated, and all reported adverse events were Grade 1 or 2. Both patients continue to receive treatment as of September 26, 2018.

Based on these data, Blueprint Medicines plans to explore opportunities to evaluate the combination of BLU-667 and osimertinib in additional patients with treatment-resistant, EGFR-mutant NSCLC harboring a RET fusion.

The paper, titled, “Landscape of acquired resistance to osimertinib in EGFR-mutant NSCLC and clinical validation of combined EGFR and RET inhibition with osimertinib and BLU-667 for acquired RET fusion,” will be published online in *Cancer Discovery* at 1:30 p.m. ET on September 26, 2018.

About RET-Altered Solid Tumors
RET activating fusions and mutations are a key disease driver in many cancer types, including NSCLC and MTC. RET fusions are implicated in approximately 1 to 2 percent of patients with NSCLC, while RET mutations are implicated in approximately 60 percent of patients with MTC. In addition, oncogenic RET alterations are observed at low frequencies in colorectal, breast, pancreatic and other cancers, and RET fusions have been observed in patients with treatment-resistant, EGFR-mutant NSCLC.

Currently, there are no approved therapies that selectively target RET-driven cancers, though there are several approved multi-kinase inhibitors with RET activity being evaluated in clinical trials. Thus far, clinical activity attributable to RET inhibition has been uncertain for these inhibitors, likely due to insufficient inhibition of RET and off-target toxicities. There is a need for precision therapies that provide durable clinical benefit by selectively targeting RET alterations and resistance mutations.

About BLU-667
BLU-667 is an investigational, once-daily oral precision therapy specifically designed for highly potent and selective targeting of oncogenic RET fusions, mutations and resistance mutations. In preclinical studies, BLU-667 consistently demonstrated sub-nanomolar potency against the most common RET fusions, activating mutations and resistance mutations. In addition, BLU-667 demonstrated markedly improved selectivity for RET compared to approved multi-kinase inhibitors, including more than 80-fold improved potency for RET versus VEGFR2. By suppressing primary and secondary mutants, BLU-667 has the potential to overcome and prevent the emergence of clinical resistance. This approach is expected to enable durable clinical responses across the range of RET alterations, with a favorable safety profile.

In April 2018, Blueprint Medicines presented proof-of-concept data from its ongoing Phase 1 ARROW clinical trial of BLU-667 in patients with RET-altered NSCLC, MTC and other advanced solid tumors at the American Association for Cancer Research (AACR) Annual Meeting. The data showed broad and robust clinical activity across multiple tumor types and RET genotypes, including in patients whose disease had progressed on prior multi-kinase therapy. Radiographic tumor reductions were observed in 84 percent of patients with RET-altered solid tumors and measurable target lesions. The data also showed that BLU-667 was generally well-tolerated, and most adverse events reported by investigators were Grade 1. Global enrollment in the dose expansion portion of the Phase 1 ARROW clinical trial is ongoing.

Patients and physicians interested in the ARROW clinical trial can contact the Blueprint Medicines study director at arrow@blueprintmedicines.com or 1-617-714-6707. Additional details are also available at www.arrowtrial.com or www.clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT03037385).

BLU-667 was discovered by Blueprint Medicine’s research team based on its proprietary compound library. The company is developing BLU-667 for the treatment of people with RET-altered NSCLC, MTC and other solid tumors. Blueprint Medicines has an exclusive collaboration and license agreement with CStone Pharmaceuticals for the development and commercialization of BLU-667 and certain other drug

candidates in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains development and commercial rights for BLU-667 in the rest of the world.

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 disease driven by the abnormal activation of kinases. Blueprint Medicines is advancing multiple 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.

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-667, including plans to explore opportunities to evaluate the combination of BLU-667 and osimertinib in additional patients with treatment-resistant, EGFR-mutant NSCLC harboring a RET fusion; expectations regarding the potential benefits of BLU-667 in treating patients with RET-altered cancers, including patients with treatment-resistant, EGFR-mutant NSCLC; expectations regarding the potential benefits of treatment with BLU-667 in combination with other therapies, including osimertinib; 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 avapritinib, BLU-554, BLU-667 and BLU-782; 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; actions of 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 for FGFR4-driven hepatocellular carcinoma, avapritinib for PDGFRα D842V-driven gastrointestinal stromal tumors and advanced systemic mastocytosis and BLU-667 for RET-driven non-small cell lung cancer; the success of Blueprint Medicines' current and future collaborations, including its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. and its collaboration with CStone Pharmaceuticals. 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 June 30, 2018, as filed with the Securities and Exchange Commission (SEC) on August 1, 2018, and any other filings that Blueprint Medicines has made or 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.

Except as required by law, Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements.

Tagrisso® is a registered trademark of AstraZeneca plc. All other trademarks and trade names in this press release are the property of Blueprint Medicines Corporation.

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