

Blueprint Medicines Announces FDA Approval of GAVRETO™ (pralsetinib) for the Treatment of Adults with Metastatic RET Fusion-Positive Non-Small Cell Lung Cancer

-- GAVRETO, the only once-daily RET-targeted therapy, demonstrated durable efficacy, with complete responses in a subset of patients --

-- Blueprint Medicines and Genentech will co-commercialize GAVRETO in the U.S. --

-- FDA approval underscores Blueprint Medicines' commitment to deliver a portfolio of transformative precision therapies to patients with NSCLC --

-- NDA accepted by FDA for pralsetinib for RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer --

-- Blueprint Medicines to host conference call on Tuesday, September 8, 2020 at 8:00 a.m. ET --

CAMBRIDGE, Mass., September 4, 2020 – Blueprint Medicines Corporation (NASDAQ: BPMC), a precision therapy company focused on genomically defined cancers, rare diseases and cancer immunotherapy, today announced that the U.S. Food and Drug Administration (FDA) has approved GAVRETO™ (pralsetinib) for the treatment of adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test. The approval is based on data from the Phase 1/2 ARROW clinical trial, which showed efficacy for GAVRETO in patients with RET fusion-positive NSCLC with or without prior therapy, and regardless of RET fusion partner or central nervous system involvement. Under Blueprint Medicines' collaboration with Roche, Blueprint Medicines and Genentech, a member of the Roche Group, will co-commercialize GAVRETO in the U.S.

GAVRETO is a once-daily oral RET-targeted therapy developed by Blueprint Medicines. It is designed to selectively and potently inhibit RET alterations that drive many cancer types, including approximately 1 to 2 percent of patients with NSCLC. Currently, RET is one of seven NSCLC biomarkers that can be targeted with an FDA-approved therapy.

"Targeted therapies have dramatically improved care for patients with non-small cell lung cancer driven by oncogenes, including EGFR and ALK, and the approval of the selective RET inhibitor pralsetinib, or GAVRETO, marks another milestone in a paradigm shift toward precision medicine," said Vivek Subbiah, M.D., associate professor of Investigational Cancer Therapeutics and center medical director of the Clinical Center for Targeted Therapy at The University of Texas MD Anderson Cancer Center, and an investigator on the ARROW trial. "Patients treated with GAVRETO had durable clinical responses, with a subset achieving complete responses characterized by the resolution of all target lesions, an uncommon outcome in metastatic lung cancer. We observed this activity with or without prior therapy and regardless of RET fusion partner or the presence of brain metastases. This approval represents an important advance with the potential to change standards of care for patients with RET fusion-positive non-small cell lung cancer, who have historically had limited treatment options."

"GAVRETO is the second breakthrough therapy discovered by Blueprint Medicines that has received FDA approval in 2020, less than 10 years since the company started operations. This progress reflects the power of our scientific platform, our focus on delivering transformative outcomes to patients and our urgency to address important medical needs," said Jeff Albers, Chief Executive Officer of Blueprint Medicines. "We are working with our partner Genentech to rapidly bring GAVRETO to healthcare providers and patients in the U.S., applying our complementary capabilities to support patient identification and access to treatment. Ultimately, we aim to accelerate the identification of patients with RET fusion-positive non-small cell lung cancer and enable them to rapidly access treatment with GAVRETO."

GAVRETO was granted accelerated approval by the FDA¹, and continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. In 87 patients previously treated with platinum-based chemotherapy, the overall response rate (ORR) was 57 percent (95% CI: 46%, 68%) with a 5.7 percent complete response (CR) rate, and the median duration of response (DOR) was not estimable (95% CI: 15.2 months, not estimable). In 27 treatment-naïve patients who were ineligible for platinum-based chemotherapy per the study protocol, the ORR was 70 percent (95% CI: 50%, 86%) with an 11 percent CR rate, and the median DOR was 9.0 months (95% CI: 6.3 months, not estimable). GAVRETO has warnings and precautions of interstitial lung disease/pneumonitis, hypertension, hepatotoxicity, hemorrhagic events, risk of impaired wound healing and risk of embryo-fetal toxicity.

“We applaud therapeutic advancements like GAVRETO that allow lung cancer treatment to be personalized based on the molecular drivers in a person’s tumor,” said Andrea Ferris, President and CEO of LUNGeity. “There are now a number of tumor-specific gene alterations that can be targeted with FDA-approved therapies, reflecting an important inflection point supporting the widespread use of comprehensive biomarker testing. At LUNGeity, we want to empower patients and their families to discuss biomarker testing with clinicians prior to initiating treatment.”

Biomarker testing for RET is the only way to identify patients with metastatic NSCLC who are candidates for treatment with GAVRETO. RET fusions can be identified with available biomarker tests, including next-generation sequencing with tumor tissue or liquid biopsies. In the ARROW trial, RET fusions were detected using next-generation sequencing, FISH or other methods.

Blueprint Medicines and Genentech plan to make GAVRETO available in the U.S. within one week. GAVRETO will be available in a 100 mg dose strength, and the recommended starting dose is 400 mg once daily.

Blueprint Medicines is dedicated to helping patients access treatment with GAVRETO and delivering support throughout their treatment journey. As part of this commitment, Blueprint Medicines is providing YourBlueprint™, a patient support program that offers access and affordability solutions for individuals receiving GAVRETO. For more information, visit YourBlueprint.com or call 1-888-BLUPRNT (1-888-258-7768), Monday to Friday, 8:00 a.m. to 8:00 p.m. ET. Healthcare providers who prescribe GAVRETO can fill out an enrollment form at YourBlueprint.com/HCP to help patients access the support services.

GAVRETO is a cornerstone precision medicine for Blueprint Medicines, supporting its commitment to advance targeted therapies for patients with NSCLC. As previously announced in November 2019, Blueprint Medicines is pursuing two research programs targeting well-characterized resistance mutations in patients with EGFR-driven NSCLC.

New Drug Application Accepted by FDA for the Treatment of RET-Mutant Medullary Thyroid Cancer and RET Fusion-Positive Thyroid Cancer

Blueprint Medicines today announced the FDA has accepted the company’s new drug application (NDA) for pralsetinib for the treatment of patients with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) and RET fusion-positive thyroid cancer. This NDA was accepted for review under the FDA’s Real-Time Oncology Review (RTOR) pilot program, which aims to explore a more efficient review process to ensure safe and effective treatments are available to patients as early as possible. The FDA granted priority review and set an action date of February 28, 2021 under the Prescription Drug User Fee Act.

Conference Call Information

Blueprint Medicines will host a live webcast on Tuesday, September 8, 2020 beginning at 8:00 a.m. ET to discuss the FDA approval of GAVRETO. To access the live call, please dial (855) 728-4793 (domestic) or (503) 343-6666 (international) and refer to conference ID 6266646. A webcast of the conference call will be available under

“Events and Presentations” in the Investors & Media section of Blueprint Medicines’ website at <http://ir.blueprintmedicines.com>. The archived webcast will be available on Blueprint Medicines’ website approximately two hours after the conference call and will be available for 90 days following the call.

About GAVRETO (pralsetinib)

GAVRETO (pralsetinib) is a once-daily oral targeted therapy approved by the FDA for the treatment of adults with metastatic RET fusion-positive NSCLC as detected by an FDA approved test. It is designed to selectively and potently target oncogenic RET alterations. In pre-clinical studies, GAVRETO inhibited RET at lower concentrations than other pharmacologically relevant kinases, including VEGFR2, FGFR2 and JAK2. For more information, visit GAVRETO.com.

GAVRETO is not approved for the treatment of any other indication in the U.S. by the FDA or for any indication in any other jurisdiction by any other health authority.

Blueprint Medicines and Roche are co-developing pralsetinib globally (excluding Greater China) for the treatment of patients with RET-altered NSCLC, various types of thyroid cancer and other solid tumors. The FDA has accepted an NDA for pralsetinib for the treatment of RET-mutant MTC and RET fusion-positive thyroid cancer, and the European Medicines Agency has validated a marketing authorization application for pralsetinib for the treatment of RET fusion-positive NSCLC. The FDA has granted breakthrough therapy designation to pralsetinib for the treatment of RET fusion-positive NSCLC that has progressed following platinum-based chemotherapy and for RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments.

Blueprint Medicines has an exclusive collaboration and license agreement with CStone Pharmaceuticals for the development and commercialization of pralsetinib in Greater China, which encompasses Mainland China, Hong Kong, Macau and Taiwan.

Enrollment is ongoing in the Phase 1/2 ARROW trial, including for patients with various RET fusion-positive solid tumors, and the Phase 3 AcceleRET Lung trial for treatment-naïve patients with RET fusion-positive NSCLC. For more information about pralsetinib clinical trials, visit www.clinicaltrials.gov or www.blueprintclinicaltrials.com.

About RET-Altered Solid Tumors

RET activating fusions and mutations are key disease drivers in many cancer types, including NSCLC and multiple types of thyroid cancer. RET fusions are implicated in approximately 1 to 2 percent of patients with NSCLC and approximately 10 to 20 percent of patients with papillary thyroid cancer, while RET mutations are implicated in approximately 90 percent of patients with advanced MTC. In addition, oncogenic RET fusions are observed at low frequencies in colorectal, breast, pancreatic and other cancers, as well as in patients with treatment-resistant EGFR-mutant NSCLC.

Important Safety Information

Pneumonitis occurred in 10% of patients who received GAVRETO, including 2.7% with Grade 3/4, and 0.5% with fatal reactions. Monitor for pulmonary symptoms indicative of interstitial lung disease (ILD)/pneumonitis. Withhold GAVRETO and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms (e.g., dyspnea, cough, and fever). Withhold, reduce dose or permanently discontinue GAVRETO based on severity of confirmed ILD.

Hypertension occurred in 29% of patients, including Grade 3 hypertension in 14% of patients. Overall, 7% had their dose interrupted and 3.2% had their dose reduced for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate GAVRETO in patients with uncontrolled

hypertension. Optimize blood pressure prior to initiating GAVRETO. Monitor blood pressure after 1 week, at least monthly thereafter and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue GAVRETO based on the severity.

Hepatotoxicity: Serious hepatic adverse reactions occurred in 2.1% of patients treated with GAVRETO. Increased AST occurred in 69% of patients, including Grade 3/4 in 5.4% and increased ALT occurred in 46% of patients, including Grade 3/4 in 6%. The median time to first onset for increased AST was 15 days (range: 5 days to 1.5 years) and increased ALT was 22 days (range: 7 days to 1.7 years). Monitor AST and ALT prior to initiating GAVRETO, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose or permanently discontinue GAVRETO based on severity.

Grade ≥ 3 **hemorrhagic events** occurred in 2.5% of patients treated with GAVRETO including one patient with a fatal hemorrhagic event. Permanently discontinue GAVRETO in patients with severe or life-threatening hemorrhage.

Impaired wound healing can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, GAVRETO has the potential to adversely affect wound healing. Withhold GAVRETO for at least 5 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of GAVRETO after resolution of wound healing complications has not been established.

Based on findings from animal studies and its mechanism of action, GAVRETO can cause **fetal harm** when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with GAVRETO and for 2 weeks after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with GAVRETO and for 1 week after the final dose. Advise women not to breastfeed during treatment with GAVRETO and for 1 week after the final dose.

Common adverse reactions ($\geq 25\%$) were fatigue, constipation, musculoskeletal pain, and hypertension. **Common Grade 3-4 laboratory abnormalities ($\geq 2\%$)** were decreased lymphocytes, decreased neutrophils, decreased phosphate, decreased hemoglobin, decreased sodium, decreased calcium (corrected) and increased alanine aminotransferase (ALT).

Avoid coadministration with **strong CYP3A inhibitors**. Avoid coadministration of GAVRETO with **combined P-gp and strong CYP3A inhibitors**. If coadministration cannot be avoided, reduce the GAVRETO dose. Avoid coadministration of GAVRETO with **strong CYP3A inducers**. If coadministration cannot be avoided, increase the GAVRETO dose.

Please click here to see the full [Prescribing Information](#) for GAVRETO.

About Blueprint Medicines

Blueprint Medicines is a precision therapy company striving to improve human health. With a focus on genomically defined cancers, rare diseases and cancer immunotherapy, we are developing transformational medicines rooted in our leading expertise in protein kinases, which are proven drivers of disease. Our uniquely targeted, scalable approach empowers the rapid design and development of new treatments and increases the likelihood of clinical success. We have two FDA-approved precision therapies and are currently advancing multiple investigational medicines in clinical development, along with a number of research programs. For more information, visit www.BlueprintMedicines.com and follow us on [Twitter](#) (@BlueprintMeds) and [LinkedIn](#).

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 Blueprint Medicines' views with respect to the approval of GAVRETO and the implications of such approval for patients, caregivers and healthcare professionals; expectations regarding the ability to accelerate the identification of patients with RET fusion-positive NSCLC; expectations regarding when GAVRETO will be commercially available in the U.S. and patients' ability to rapidly access treatment with GAVRETO; Blueprint Medicines' plans and ability to provide robust support services for patients prescribed GAVRETO through YourBlueprint; plans for Blueprint Medicines and Roche to expand development of pralsetinib in additional treatment settings; plans, timelines and expectations for interactions with the FDA and other regulatory authorities, including for the separate NDA for pralsetinib for the treatment of patients with RET-mutant MTC and RET fusion-positive thyroid cancer; the potential benefits of Blueprint Medicines' current and future approved drugs or drug candidates in treating patients; and Blueprint Medicines' strategy, goals and anticipated milestones, business plans and focus. The words "aim," "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 impact of the COVID-19 pandemic to Blueprint Medicines' business, operations, strategy, goals and anticipated milestones, including Blueprint Medicines' ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products; Blueprint Medicines' ability and plans in establishing a commercial infrastructure, and successfully launching, marketing and selling current or future approved products, including AYVAKIT™ (avapritinib) and GAVRETO; Blueprint Medicines' ability to successfully expand the approved indications for AYVAKIT and GAVRETO or obtain marketing approval for AYVAKIT and GAVRETO in additional geographies in the future; the delay of any current or planned clinical trials or the development of Blueprint Medicines' current or future drug candidates; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; 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; and the success of Blueprint Medicines' current and future collaborations, partnerships or licensing arrangements, including Blueprint Medicines' global collaboration with Roche for the development and commercialization of pralsetinib. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' filings with the Securities and Exchange Commission (SEC), including Blueprint Medicines' most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q 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.

Reference

¹ GAVRETO™ (pralsetinib) Prescribing Information (U.S.). Blueprint Medicines Corporation, Cambridge, Massachusetts, USA; September 2020.

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