



Blueprint Medicines Announces FDA Approval of GAVRETO™ (pralsetinib) for the Treatment of Patients with Advanced or Metastatic RET-Mutant and RET Fusion-Positive Thyroid Cancer

-- Once-daily treatment with GAVRETO demonstrated robust efficacy in patients with RET-altered thyroid cancers, including prolonged duration of response --

-- Expands GAVRETO label following initial approval for RET fusion-positive non-small cell lung cancer in September 2020 --

-- Blueprint Medicines and Genentech are co-commercializing GAVRETO in the U.S. --

CAMBRIDGE, Mass., December 1, 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 patients with RET-altered thyroid cancers. The accelerated approval expands the labeled indications for GAVRETO to include adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy, or with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). Developed by Blueprint Medicines, GAVRETO is a once-daily oral precision therapy designed to potently and selectively target RET alterations that drive multiple tumor types. GAVRETO is jointly commercialized in the U.S. by Blueprint Medicines and Genentech, a wholly owned member of the Roche Group, under Blueprint Medicines' collaboration with Roche.

In the Phase 1/2 ARROW trial, GAVRETO showed durable efficacy and was generally well-tolerated in patients with RET-altered thyroid cancers with or without prior systemic therapy. Earlier this year, the FDA granted accelerated approval to GAVRETO for the treatment of adults with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test.

"With this approval, Blueprint Medicines has achieved four marketing authorizations this year across our lead programs, making real our vision to bring transformative precision therapies to patients globally," said Jeff Albers, Chief Executive Officer of Blueprint Medicines. "Today's approval also builds further momentum toward bringing GAVRETO to a wide range of patients with RET-altered cancers. Now, as we work with our partner Genentech to rapidly deliver GAVRETO to patients with RET-altered non-small cell lung cancer and thyroid cancers, we continue to explore the potential of GAVRETO to address additional tumor types and treatment settings."

"Traditionally, we have treated patients with RET-altered thyroid cancers with multi-kinase inhibitors, non-selective therapies with modest efficacy and clinically significant side effects. The FDA approval of pralsetinib (GAVRETO), a once-daily RET-targeted therapy, advances the standard of care for these patients," said Mimi Hu, M.D., professor in the Department of Endocrine Neoplasia and Hormonal Disorders at The University of Texas MD Anderson Cancer Center, and an investigator on the ARROW trial. "As a clinical researcher with a focus on thyroid cancer, I am encouraged by the safety profile and durable responses shown by GAVRETO in RET-altered thyroid cancers in both treatment-naïve and previously treated patients."

This approval is based on efficacy and safety results from the ARROW trial.¹ In 55 patients with RET-mutant MTC previously treated with cabozantinib or vandetanib, the overall response rate (ORR) was 60 percent (95% CI: 46%, 73%), and the median duration of response (DOR) was not reached (95% CI: 15.1 months, not estimable). In 29 cabozantinib and vandetanib-naïve patients with RET-mutant MTC who were not candidates for standard systemic therapy per the study protocol, the ORR was 66 percent (95% CI: 46%, 82%), and the median DOR was not reached (95% CI: not estimable, not estimable). In addition, the ORR was 89 percent (95% CI: 52%, 100%) in nine patients with RET fusion-positive thyroid cancer, and the median DOR was not reached (95% CI: not estimable, not estimable). In ARROW trial patients across RET-altered tumor types, the most common adverse reactions (≥25%) were constipation, hypertension, fatigue, musculoskeletal pain and diarrhea.

The continued approval of GAVRETO for advanced or metastatic RET-altered thyroid cancers may be contingent upon verification and description of clinical benefit in confirmatory trials. The FDA approved these additional indications for GAVRETO under its Real-Time

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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 approval of GAVRETO has the potential to address important medical needs for patients with RET-altered thyroid cancers, and reflects a shift in care toward precision medicines designed to target the underlying driver of disease,” said Gary Bloom, executive director of ThyCa: Thyroid Cancer Survivors’ Association (www.thyca.org). “We are excited that the emergence of targeted therapies like GAVRETO, combined with the expanded use of biomarker testing, may dramatically improve treatment for the RET-altered thyroid cancer community. At ThyCa, we are committed to advancing awareness of these promising areas of clinical research, educating our members on the importance of biomarker testing and offering support for those impacted by the disease.”

Biomarker testing for RET enables clinicians to identify patients who are candidates for treatment with GAVRETO. RET alterations can be identified with available biomarker tests, including next-generation sequencing with tumor tissue or liquid biopsies.

Blueprint Medicines is dedicated to helping patients access 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.

About GAVRETO (pralsetinib)

GAVRETO (pralsetinib) is a once-daily oral targeted therapy approved by the FDA for the treatment of three indications: adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA approved test, adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant MTC who require systemic therapy, and adults and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

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.

GAVRETO is designed to selectively and potently target oncogenic RET alterations, including secondary RET mutations predicted to drive resistance to treatment. 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.

Blueprint Medicines and Roche are co-developing GAVRETO globally (excluding Greater China) for the treatment of patients with RET-altered NSCLC, various types of thyroid cancer and other solid tumors. The European Medicines Agency validated a marketing authorization application for GAVRETO for the treatment of RET fusion-positive NSCLC. The FDA granted breakthrough therapy designation to GAVRETO 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 GAVRETO 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 in the Phase 3 AcceleRET Lung trial for treatment-naïve patients with RET fusion-positive NSCLC. For more information about GAVRETO 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

Interstitial Lung Disease (ILD)/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 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 aspartate aminotransferase (AST) occurred in 69% of patients, including Grade 3/4 in 5% and increased alanine aminotransferase (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 \geq 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.

Tumor Lysis Syndrome (TLS): Cases of TLS have been reported in patients with medullary thyroid carcinoma receiving GAVRETO. Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated.

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 constipation, hypertension, fatigue, musculoskeletal pain and diarrhea. **Common Grade 3/4 laboratory abnormalities (\geq 2%)** were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate,

decreased calcium (corrected), decreased sodium, increased AST, increased ALT, decreased platelets and increased alkaline phosphatase.

Avoid coadministration of GAVRETO with **strong CYP3A inhibitors or 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 approved precision therapies and are currently advancing multiple investigational medicines in clinical and pre-clinical development, along with a number of earlier-stage 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 FDA approval of GAVRETO and the implications of such approval for patients, caregivers and healthcare professionals; expectations regarding patients' ability to rapidly access treatment with GAVRETO; Blueprint Medicines' plans and ability to provide robust support services for patients prescribed GAVRETO through YourBlueprint; the potential benefits of Blueprint Medicines' current and future approved drugs or drug candidates in treating patients, including expectations regarding the potential of GAVRETO to address additional tumor types and treatment settings; 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 continuing to establish and maintain a commercial infrastructure, and successfully launching, marketing and selling current or future approved products; Blueprint Medicines' ability to successfully expand the approved indications for AYVAKIT™/AYVAKYT® (avapritinib) and GAVRETO or obtain marketing approval for AYVAKIT/AYVAKYT 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 obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT, GAVRETO or any drug candidates it is developing; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for AYVAKIT/AYVAKYT, GAVRETO or any of its current and future drug candidates; and the success of Blueprint Medicines' current and future collaborations, partnerships or licensing arrangements. 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; December 2020.

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