December 1, 2020

To Patients and Patient Advocacy Groups,

We are excited to share that we have now received approval from the United States Food and Drug Administration (FDA) for GAVRETO™ (pralsetinib) to treat certain cancers caused by abnormal rearranged during transfection (RET) gene in adults and children 12 years of age and older with advanced medullary thyroid cancer (MTC) or MTC that has spread who require a medicine by mouth or injection (systemic therapy), and adults and children 12 years of age and older with advanced thyroid cancer or thyroid cancer that has spread who require a medicine by mouth or injection (systemic therapy) and who have received radioactive iodine and it did not work or is no longer working. GAVRETO was previously approved (Sept 4, 2020) by the FDA for the treatment of adult patients with RET fusion-positive non-small cell lung cancer (NSCLC) that has spread. These indications are approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trial(s). These approvals enable access to therapy for many patients outside of clinical trials in the U.S.

All of us at Blueprint Medicines would like to extend our deepest thanks to the ARROW study (BLU-667-1101 or NCT03037385) participants from around the world for their participation in this clinical study. We understand that being a part of a clinical study can be challenging in many ways, and we recognize and appreciate the commitment patients and their families have made to these research efforts. It is solely due to patients’ bravery and commitment to participating in clinical studies that we can develop and bring new treatment options to more patients. We also thank the investigators and clinical site staff who have supported and continue to support this study.

We are also incredibly grateful to patient advocacy organizations for their invaluable collaboration and insights, and their commitment to supporting and advocating for patients throughout their diagnosis, biomarker identification, and treatment journeys.

Information about GAVRETO can be found in the following websites:

- Product website: [https://www.GAVRETO.com](https://www.GAVRETO.com)
- U.S. Prescribing information: [https://www.blueprintmedicines.com/uspi/GAVRETO.pdf](https://www.blueprintmedicines.com/uspi/GAVRETO.pdf)

In the U.S., we have a dedicated patient support and financial assistance program called YourBlueprint™ for eligible individuals. For more information, visit [https://yourblueprint.com/](https://yourblueprint.com/).
This approval in the U.S. does not affect access to drug for current participants in the ARROW and AcceleRET Lung studies, and study visits will continue as planned for the remainder of their trial participation. Outside the U.S., Blueprint Medicines’ Pre-Approval Access Program remains open for eligible patients.

Patients are at the center of Blueprint Medicines’ mission of discovering, developing, and delivering innovative medicines that address significant medical needs. Our global collaborations will help us advance the development of pralsetinib to address the needs of patients around the world more quickly and in the context of multiple treatment settings. We are thankful to be a part of the lung cancer, thyroid cancer, and other cancer communities and look forward to continuing to advance treatment and patient care for patients with RET altered cancers.

Wishing you all the best,

Andy Boral, M.D., PhD.
Chief Medical Officer, Blueprint Medicines

IMPORTANT SAFETY INFORMATION

GAVRETO may cause serious side effects, including

**Lung Problems:** GAVRETO may cause severe or life-threatening inflammation of the lungs during treatment, that can lead to death. Tell your healthcare provider right away if you have any new or worsening symptoms, including shortness of breath, cough, or fever.

**High blood pressure (hypertension):** High blood pressure is common with GAVRETO and may sometimes be severe. You should check your blood pressure regularly during treatment with GAVRETO. Tell your healthcare provider if you have increased blood pressure readings or get any symptoms of high blood pressure, including confusion, dizziness, headaches, chest pain or shortness of breath.

**Liver problems:** Liver problems (increased liver function blood test results) can happen during treatment with GAVRETO and may sometimes be serious. Your healthcare provider will do blood tests before and during treatment with GAVRETO to check you for liver problems. Tell your healthcare provider right away if you get any signs or symptoms of liver problem during treatment, including yellowing of your skin or the white part of your eyes (jaundice), loss of appetite, nausea or vomiting, dark “tea-colored” urine, pain on the upper right side of your stomach area, sleepiness, bleeding or bruising.

**Bleeding problems:** GAVRETO can cause bleeding which can be serious and cause death. Tell your healthcare provider if you have any signs or symptoms of bleeding during treatment, including vomiting blood or if your vomit looks like coffee-grounds, unusual vaginal bleeding, nose bleeds that happen often, pink or brown urine, drowsiness or difficulty being awakened, red or black (looks like tar) stools, confusion,
coughing up blood or blood clots, headache, unusual bleeding or bruising of your skin, change in speech, or menstrual bleeding that is heavier than normal.

**Tumor lysis syndrome (TLS):** TLS is caused by a fast breakdown of cancer cells. TLS can cause you to have kidney failure and the need for dialysis treatment, an abnormal heartbeat, and may sometimes lead to hospitalization. Your healthcare provider may do blood tests to check you for TLS. You should stay well hydrated during treatment with GAVRETO. Call your healthcare provider or get emergency medical help right away if you develop any of these symptoms during treatment with GAVRETO: nausea, shortness of breath, vomiting, muscle cramps, weakness, seizures or swelling.

**Risk of wound healing problems:** Wounds may not heal properly during treatment with GAVRETO. Tell your healthcare provider if you plan to have any surgery before or during treatment with GAVRETO. You should not take GAVRETO for at least 5 days before surgery. Your healthcare provider should tell you when you may start taking GAVRETO again after surgery.

**Before taking GAVRETO, tell your healthcare provider about all of your medical conditions, including if you:**

- have lung or breathing problems other than lung cancer.
- have high blood pressure
- have bleeding problems
- plan to have surgery
- are pregnant or plan to become pregnant. GAVRETO can harm your unborn baby.

Females who are able to become pregnant:

- Your healthcare provider will do a pregnancy test before you start GAVRETO.
- Should use an effective form of non-hormonal birth control (contraception) during treatment with GAVRETO and for 2 weeks after the final dose of GAVRETO.
- Birth control methods that contain hormones (such as birth control pills, injections or transdermal system patches) may not work as well during treatment with GAVRETO.
- Talk to your healthcare provider about birth control methods that may be right for you during this time.
- Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with GAVRETO.

Males with female partners who are able to become pregnant should use effective birth control (contraception) during treatment and for 1 week after your final dose of GAVRETO.

- are breastfeeding or plan to breastfeed. It is not known if GAVRETO passes into your breast milk. Do not breastfeed during treatment and for 1 week after your last dose of GAVRETO.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. GAVRETO may affect the way other medicines work, and other medicines may affect how GAVRETO works.
The most common side effects of GAVRETO include: constipation, decreased levels of phosphate in the blood, high blood pressure, decreased levels of calcium in the blood, tiredness, decreased levels of body salt (sodium) in the blood, muscle and joint pain, diarrhea, abnormal liver function blood tests, and decreased white blood cell, red blood cell, and platelet counts.

GAVRETO may affect fertility in males and females, which may affect your ability to have children. Talk to your healthcare provider if this is a concern for you.

These are not all of the possible side effects of GAVRETO. Call your doctor for medical advice about side effects. You are encouraged to report side effects to the FDA. Visit FDA MedWatch or call 1-800-FDA-1088.

Please see the full Prescribing Information and Patient Information for GAVRETO.