Roche announces FDA approval of Gavreto (pralsetinib) for people with advanced or metastatic RET-mutant and RET fusion-positive thyroid cancers

Basel, 2 December 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) has approved Gavreto™ (pralsetinib) for the treatment of adult and paediatric patients 12 years of age and older with advanced or metastatic rearranged during transfection (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). These indications were approved under the FDA's accelerated approval programme based on data from the phase I/II ARROW study. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

"We are proud to partner with Blueprint Medicines to bring this important new option to people with certain types of RET-altered thyroid cancer," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Gavreto is now approved across multiple RET-altered tumour types, underscoring our commitment to advancing personalised healthcare with treatments that target the underlying biology of each person's cancer."

Approximately 10-20% of people with papillary thyroid cancer (the most common type of thyroid cancer)[1] have RET fusion-positive tumours,[2] and roughly 90% of people with advanced MTC (a rare form of thyroid cancer) carry RET mutations.[3] Biomarker testing for RET fusions and mutations can help identify people who are eligible for treatment with Gavreto.

The approvals are based on results from the phase I/II ARROW study, which demonstrated durable clinical activity in people with or without prior therapy and regardless of RET alteration genotypes.[4] Treatment with Gavreto led to an overall response rate (ORR) of 60% (95% CI: 46%, 73%) in 55 people with RET-mutant metastatic MTC previously treated with cabozantinib and/or vandetanib, and the median duration of response (DoR) was not reached (95% CI: 15.1 months, not estimable).[2] In 29 people with cabozantinib- and vandetanib-naïve RET-mutant advanced MTC who were determined to be not eligible for standard therapies, the ORR was 66% (95% CI: 46%, 82%), and the median DoR was not reached (95% CI: not estimable, not estimable).[4] In nine people with RET fusion-positive metastatic thyroid cancer, Gavreto demonstrated an ORR of 89% (95% CI: 52%, 100%), and the median DoR was not reached (95% CI: not estimable, not estimable).[4] In ARROW trial patients across RET-altered tumour types, the most common adverse reactions (≥25%) were constipation, increased blood pressure (hypertension), fatigue, musculoskeletal pain and diarrhoea.[4]

The FDA reviewed and approved the application under its Real-Time Oncology Review (RTOR) pilot programme, which aims to explore a more efficient review process to ensure safe and effective treatments are available to patients as early as possible. In September, the FDA also granted accelerated approval to Gavreto for the treatment of adults with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) as

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detected by an FDA approved test. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. In addition, the FDA granted Breakthrough Therapy Designation to Gavreto for the treatment of RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments and for RET fusion-positive NSCLC that has progressed following platinum-based chemotherapy.

Gavreto is a once-daily, oral precision therapy designed to selectively target RET alterations, including fusions and mutations.

About the ARROW study[5]
ARROW (NCT03037385) is a phase I/II, open-label, first-in-human study designed to evaluate the safety, tolerability and efficacy of Gavreto, administered orally in people with rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC), RET-mutant medullary thyroid cancer (MTC), RET fusion-positive thyroid cancer and other RET-altered solid tumours. The trial consists of two parts: a dose escalation portion, which is complete, and an expansion portion in people treated with 400 mg of Gavreto, once-daily. ARROW is being conducted at multiple sites across the United States, European Union and Asia.

About RET-altered cancers
RET gene alterations, such as fusions and mutations, are key disease drivers in many types of cancer, including NSCLC and several types of thyroid cancers. Approximately 10-20% of people with papillary thyroid cancer (the most common type of thyroid cancer)[1] have RET fusion-positive tumours,[2] and roughly 90% of people with advanced MTC (a rare form of thyroid cancer) carry RET mutations.[3] In NSCLC, RET fusions represent approximately 1-2% of patients.[6] Oncogenic RET fusions also are observed at low frequencies in cholangiocarcinoma, colorectal, neuroendocrine, ovarian, pancreatic and thymus cancers.

About Gavreto
Gavreto is a once-daily, oral precision therapy designed to selectively target RET alterations, including fusions and mutations, regardless of the tissue of origin. Preclinical data have shown that Gavreto inhibits primary RET fusions and mutations that cause cancer in subsets of patients, as well as secondary RET mutations predicted to drive resistance to treatment. Blueprint Medicines and Roche are co-developing Gavreto for the treatment of patients with various types of RET-altered cancers.

Blueprint Medicines and Roche are co-developing Gavreto globally, excluding Greater China.* Blueprint Medicines and Genentech, a wholly owned member of the Roche Group, will co-commercialise Gavreto in the US and Roche has exclusive commercialisation rights for Gavreto outside of the US, excluding Greater China.*

* Greater China encompasses Mainland China, Hong Kong, Macau and Taiwan.

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the twelfth consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 billion. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

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