Roche receives positive CHMP opinion for Gavreto® (pralsetinib) for the treatment of adults with RET fusion-positive advanced non-small cell lung cancer

- **Gavreto showed robust and durable clinical responses in people with NSCLC with RET fusions**
- **If approved, Gavreto will be the first and only targeted treatment approved by the EMA that includes first-line treatment of people with RET fusion-positive advanced NSCLC**

Basel, 17 September 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended the approval of Gavreto® (pralsetinib) as a monotherapy for the treatment of adult patients with rearranged during transfection (RET) fusion-positive advanced non-small cell lung cancer (NSCLC) not previously treated with a RET inhibitor.

"This positive CHMP opinion for Gavreto represents another important step towards our goal of providing effective therapeutics that target genomic drivers of disease for as many cancer patients as possible," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Advances in personalised medicine also underscore the importance of tumour genomic profiling to identify patients who may benefit from targeted therapies."

RET alterations are key disease drivers in many cancer types, including NSCLC and multiple types of thyroid cancer. RET fusion-positive NSCLC affects approximately 37,500 people worldwide each year and the disease often affects those who least expect it;[1,2,3] RET fusion-positive NSCLC is often identified in younger people with a minimal to no history of smoking.[3] These cancers also typically represent a high unmet need, due to limitations associated with standard therapies.[4,5,6] Biomarker testing for these fusions is the most effective way to identify people with advanced NSCLC who are eligible for treatment with Gavreto. Gavreto is a highly selective, potent, and CNS-penetrant RET inhibitor and, together with Alecensa® (alectinib) and Rozlytrek® (entrectinib), is part of Roche's portfolio of targeted treatments for NSCLC. Together, they offer personalised treatment options for almost one in ten people with advanced NSCLC.[7]

The CHMP recommendation is based on the results of the phase I/II ARROW study, in which Gavreto demonstrated rapid, potent, and durable clinical activity in patients with advanced RET fusion-positive NSCLC.[8] A final decision regarding the approval of Gavreto is expected from the European Commission in the coming months.

Gavreto has also shown activity across multiple solid tumour types, reflecting tumour-agnostic potential.[9] In September 2020, the U.S. Food and Drug Administration (FDA) approved Gavreto for the treatment of adults with metastatic RET fusion-positive NSCLC, and in December 2020 it was approved for the treatment of adult and paediatric patients 12 years of age and older with advanced RET-altered thyroid cancers. Gavreto has since been approved in Canada, mainland China and Switzerland. In the European Union, the

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MAA for Gavreto for the treatment of adults with RET fusion-positive NSCLC is ongoing, and a submission for RET-altered thyroid cancers is planned. Regulatory submissions for these indications are underway in multiple countries worldwide.

Blueprint Medicines and Roche are co-developing Gavreto globally, with the exception of certain territories in Asia, including China.* Blueprint Medicines and Genentech, a wholly owned member of the Roche Group, are commercialising Gavreto in the US and Roche has exclusive commercialisation rights for Gavreto outside of the US, with the exception of certain territories in Asia, including China.*

*CStone Pharmaceuticals retains all rights to the development and commercialisation of Gavreto in these territories under its existing collaboration with Blueprint Medicines.

About the ARROW study[10]
ARROW is an ongoing 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, RET fusion-positive thyroid cancer and other RET-altered solid tumours. ARROW is being conducted at multiple sites across the United States, Europe and Asia.

An update from the ARROW study was presented at the American Society of Clinical Oncology (ASCO) 2021 Virtual Scientific Programme, 4-8 June.[11] In 126 patients with RET fusion-positive NSCLC who previously received platinum-based chemotherapy, Gavreto demonstrated an overall response rate (ORR) of 62% (95% CI: 53%, 70%), a clinical benefit rate (CBR) of 74% (95% CI: 65%, 81%), and a disease control rate (DCR) of 91% (95% CI: 85%, 96%). Median progression-free survival (PFS) was 16.5 months (95% CI: 10.5 months, 24.1 months). In 68 treatment-naïve patients, the confirmed ORR was 79% (95% CI: 68%, 88%), the CBR was 82% (95% CI: 71%, 91%), and the DCR was 93% (95% CI: 84%, 98%). Median PFS was 13.0 months (95% CI: 9.1 months, not reached (NR)). In 25 treatment-naïve patients who were enrolled after eligibility criteria were revised, to allow candidates for platinum-based therapy, the confirmed ORR was 88% (95% CI: 69%, 98%), the CBR was 88% (95% CI: 69%, 98%), and the DCR was 96% (95% CI: 80%, 100%). Median PFS was not reached. In addition, Gavreto was well-tolerated; of the 471 ARROW trial patients across RET-altered tumour types, the most common (≥ 25%) treatment-related adverse events were neutropenia, increased liver enzymes (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]), anaemia, white blood cell count decrease, high blood pressure (hypertension) and lack of energy (asthenia).

About rearranged during transfection (RET)-altered cancers
RET gene alterations, such as fusions and mutations, are key disease drivers in many types of cancer, including non-small cell lung cancer (NSCLC) and several types of thyroid cancers. There are approximately 2.21 million cases of lung cancer diagnosed each year worldwide,[1] of which approximately 1.8 million are NSCLC and RET fusions are present in approximately 1-2% of these patients,[2,3] meaning RET fusion-positive NSCLC affects up to 37,500 people each year. Additionally, approximately 10-20% of people with papillary thyroid cancer (the most common type of thyroid cancer) have RET fusion-positive tumours,[12]

and roughly 90% of people with advanced medullary thyroid cancer (a rare form of thyroid cancer) carry RET mutations.[13] Oncogenic RET fusions also are observed at low frequencies in cholangiocarcinoma, colorectal, neuroendocrine, ovarian, pancreatic and thymus cancers.

About Gavreto® (pralsetinib)
Gavreto is a once-daily, oral targeted treatment designed to selectively target rearranged during transfection (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 people with various types of RET-altered cancers.

About Roche in lung cancer
Lung cancer is a major area of focus and investment for Roche, and we are committed to developing new approaches, medicines and tests that can help people with this deadly disease. Our goal is to provide an effective treatment option for every person diagnosed with lung cancer. We currently have six approved medicines to treat certain kinds of lung cancer and more than ten medicines being developed to target the most common genetic drivers of lung cancer or to boost the immune system to combat the disease.

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, as well as growing capabilities in the area of data-driven medical insights help Roche deliver truly personalised healthcare. Roche is working with partners across the healthcare sector to provide the best care for each person.

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. In recent years, Roche has invested in genomic profiling and real-world data partnerships and has become an industry-leading partner for medical insights.

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 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 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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