Media Release

Roche submits supplemental Biologics License Application to the FDA for Tecentriq in combination with Avastin for the most common form of liver cancer

- **Application is being reviewed under FDA's Real-Time Oncology Review pilot programme**

Basel, 27 January 2020 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced the completion of a supplemental Biologics License Application (sBLA) submission to the US Food and Drug Administration (FDA) for Tecentriq® (atezolizumab) in combination with Avastin® (bevacizumab), for the treatment of people with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy. The FDA is reviewing the application under the Real-Time Oncology Review 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 July 2018, the FDA granted Breakthrough Therapy Designation for Tecentriq in combination with Avastin in HCC based on data from an ongoing Phase Ib trial.

"Liver cancer is the most rapidly increasing cause of cancer-related death in the United States. In the IMbrave150 study, Tecentriq in combination with Avastin became the first treatment in more than a decade to improve overall survival compared with the current standard of care," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We are pleased that these results are being reviewed under the FDA Real-Time Oncology Review pilot programme, and we are working closely with the agency to bring this potential new treatment option to people with unresectable hepatocellular carcinoma as quickly as possible."

This application is based on the results of the Phase III IMbrave150 study, which demonstrated that Tecentriq in combination with Avastin reduced the risk of death (overall survival; OS) by 42% (hazard ratio [HR]=0.58; 95% CI: 0.42-0.79; p=0.0006) and reduced the risk of disease worsening or death (progression-free survival; PFS) by 41% (HR=0.59; 95% CI: 0.47–0.76; p<0.0001), compared with sorafenib. Safety for Tecentriq and Avastin was consistent with the known safety profiles of the individual medicines. The results were presented at the European Society for Medical Oncology (ESMO) Asia Congress in November 2019.

Roche has an extensive development programme for Tecentriq, including multiple ongoing and planned Phase III studies, across several types of lung, genitourinary, skin, breast, gastrointestinal, gynaecological, and head and neck cancers. This includes studies evaluating Tecentriq both alone and in combination with other medicines.

About the IMbrave150 study
IMbrave150 is a global Phase III, multicentre, open-label study of 501 people with unresectable HCC who had not received prior systemic therapy. People were randomised 2:1 to receive the combination of Tecentriq and Avastin or sorafenib. Tecentriq was administered intravenously (IV), 1200 mg on day 1 of each 21-day cycle, and Avastin was administered IV, 15 mg/kg on day 1 of each 21-day cycle. Sorafenib was administered by mouth, 400 mg twice per day, on days 1–21 of each 21-day cycle. People received the combination or the control arm treatment until unacceptable toxicity or loss of clinical benefit as determined by the investigator.

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The two primary endpoints were OS and PFS by independent review facility (IRF) per Response Evaluation Criteria in Solid Tumours Version 1.1 (RECIST v1.1). Additional study endpoints included overall response rate (ORR) and duration of response (DoR), as measured by RECIST v1.1 (investigator-assessed [INV] and IRF) and HCC mRECIST (IRF), as well as patient-reported outcomes (including time to deterioration of patient-reported quality of life), safety and pharmacokinetics.

About hepatocellular carcinoma

HCC, the most common form of liver cancer, is an aggressive cancer with limited treatment options and is a major cause of cancer deaths worldwide.[1] Every year, more than 750,000 people worldwide are diagnosed with HCC,[1,2] with the majority of cases in Asia and almost half of all cases in China.[2,3] In the US, the number of liver cancer cases have more than tripled since 1980 and HCC represents the fastest-rising cause of cancer-related death, while in Europe, liver cancer is also on the rise.[4–6] HCC develops predominantly in people with cirrhosis due to chronic hepatitis (B or C) or alcohol consumption, and typically presents at an advanced stage.[1] The prognosis for unresectable HCC remains poor, with few systemic therapeutic options and a 1-year survival rate of less than 50% following diagnosis.[7]

About the Tecentriq and Avastin combination

There is a strong scientific rationale to support the use of Tecentriq plus Avastin in combination. The Tecentriq and Avastin regimen may enhance the potential of the immune system to combat a broad range of cancers. Avastin, in addition to its established anti-angiogenic effects, may further enhance Tecentriq's ability to restore anti-cancer immunity, by inhibiting vascular endothelial growth factor (VEGF)-related immunosuppression, promoting T-cell tumour infiltration, and enabling priming and activation of T-cell responses against tumour antigens.

About Tecentriq

Tecentriq is a monoclonal antibody designed to bind with a protein called PD-L1, which is expressed on tumour cells and tumour-infiltrating immune cells, blocking its interactions with both PD-1 and B7.1 receptors. By inhibiting PD-L1, Tecentriq may enable the activation of T-cells. Tecentriq is a cancer immunotherapy that has the potential to be used as a foundational combination partner with other immunotherapies, targeted medicines and various chemotherapies across a broad range of cancers. The development of Tecentriq and its clinical programme is based on our greater understanding of how the immune system interacts with tumours and how harnessing a person's immune system combats cancer more effectively.

Tecentriq is approved in the US, EU and countries around the world, either alone or in combination with targeted therapies and/or chemotherapies in various forms of non-small cell and small cell lung cancer, certain types of metastatic urothelial cancer, and in PD-L1-positive metastatic triple-negative breast cancer.

About Avastin
Avastin is a prescription-only medicine that is a solution for intravenous infusion. It is a biologic antibody designed to specifically bind to a protein called VEGF that plays an important role throughout the lifecycle of the tumour to develop and maintain blood vessels, a process known as angiogenesis. Avastin is designed to interfere with the tumour blood supply by directly binding to the VEGF protein to prevent interactions with receptors on blood vessel cells. The tumour blood supply is thought to be critical to a tumour's ability to grow and spread in the body (metastasise).

About Roche in cancer immunotherapy
For more than 50 years, Roche has been developing medicines with the goal to redefine treatment in oncology. Today, we're investing more than ever in our effort to bring innovative treatment options that help a person's own immune system fight cancer.

By applying our seminal research in immune tumour profiling within the framework of the Roche-devised cancer immunity cycle, we are accelerating and expanding the transformative benefits with Tecentriq to a greater number of people living with cancer. Our cancer immunotherapy development programme takes a comprehensive approach in pursuing the goal of restoring cancer immunity to improve outcomes for patients.

To learn more about the Roche approach to cancer immunotherapy please follow this link: http://www.roche.com/research_and_development/what_we_are_working_on/oncology/cancer-immunotherapy.htm

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 eleventh 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 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF

56.8 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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