Media Release

FDA approves Roche's Tecentriq in combination with Avastin for people with the most common form of liver cancer

- **Tecentriq in combination with Avastin is the first and only cancer immunotherapy regimen approved for the treatment of unresectable or metastatic hepatocellular carcinoma**
- **Tecentriq combination improved overall survival and progression-free survival compared to the previous standard of care**
- **Application approved under FDA's Project Orbis initiative and Real-Time Oncology Review pilot programme**

Basel, 2 June 2020 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has approved Tecentriq® (atezolizumab) in combination with Avastin® (bevacizumab) for the treatment of people with unresectable or metastatic hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

"We're excited that today's approval of Tecentriq in combination with Avastin for unresectable or metastatic hepatocellular carcinoma brings a cancer immunotherapy option to people with this aggressive form of liver cancer," said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development. "The application was reviewed under the FDA's Real-Time Oncology Review pilot and Project Orbis initiative, helping to bring this new treatment option rapidly to patients in the United States and around the world."

"The results of the IMbrave150 study are really transformative for patients with advanced liver cancer, one of the few cancers with a rising death rate and limited options in the first-line setting," said Dr Richard Finn, Professor of Medicine at the David Geffen School of Medicine at UCLA and Director of the Signal Transduction and Therapeutics Program at the UCLA Jonsson Comprehensive Cancer Center. "For the first-time we have a regimen that markedly improves survival over sorafenib, the standard of care for first-line hepatocellular carcinoma since 2007, and offers patients the opportunity for improved disease control with a favourable tolerability profile."

The review of this application was conducted under the FDA's Project Orbis initiative, which provides a framework for concurrent submission and review of oncology medicines among international partners. According to the FDA, collaboration among international regulators may allow patients with cancer to receive earlier access to products in other countries where there may be significant delays in regulatory submissions.[1] Simultaneous applications were submitted to regulators in the United States, Australia, Canada and Singapore under Project Orbis. Additionally, the FDA rapidly 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.

F. Hoffmann-La Roche Ltd 4070 Basel Switzerland
Group Communications Roche Group Media Relations
Tel. +41 61 688 88 88 www.roche.com

The approval was based on results from 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. IMbrave150 is the first Phase III cancer immunotherapy study to show an improvement in OS and PFS in people with unresectable or metastatic HCC compared with sorafenib. Serious adverse reactions (Grade 3-4) occurred in 38% of people in the Tecentriq and Avastin arm. The most frequent serious adverse reactions (≥2%) were bleeding in the gastrointestinal tract, infections and fever. These results were published in the New England Journal of Medicine on 14 May 2020.

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 or metastatic 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 disease progression or unacceptable toxicity. The two primary endpoints were OS and independent review facility (IRF)-assessed PFS per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1). Additional study endpoints were IRF-assessed overall response rate (ORR) per RECIST and mRECIST.

About hepatocellular carcinoma
HCC is an aggressive cancer with limited treatment options and is a major cause of cancer deaths worldwide.[2] Every year, more than 750,000 people worldwide are diagnosed with HCC,[2,3] with the majority of cases in Asia and almost half of all cases in China.[3,4] 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.[5-7] HCC develops predominantly in people with cirrhosis due to chronic hepatitis (B or C) or alcohol consumption, and typically presents at an advanced stage.[2] The prognosis for unresectable HCC remains poor, with few systemic therapeutic options and a 1-year survival rate of less than 50% following diagnosis.[8]

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. In the US, Tecentriq in combination with Avastin is approved for people with unresectable or metastatic HCC.

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
Roche's rigorous pursuit of groundbreaking science has contributed to major therapeutic and diagnostic advances in oncology over the last 50 years, and today, realising the full potential of cancer immunotherapy is a major area of focus. With over 20 molecules in development, Roche is investigating the potential benefits of immunotherapy alone, and in combination with chemotherapy, targeted therapies or other immunotherapies with the goal of providing each person with a treatment tailored to harness their own unique immune system to attack their cancer. Our scientific expertise, coupled with innovative pipeline and extensive partnerships, gives us the confidence to continue pursuing the vision of finding a cure for cancer by ensuring the right treatment for the right patient at the right time.

In addition to Roche's approved PD-L1 checkpoint inhibitor, Tecentriq® (atezolizumab), Roche's broad cancer immunotherapy pipeline includes other checkpoint inhibitors, such as tiragolumab, a novel cancer immunotherapy designed to bind to TIGIT, individualised neoantigen therapies and T-cell bispecific antibodies. To learn more about Roche's scientific-led 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 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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Roche Group Media Relations
Phone: +41 61 688 8888 / e-mail: media.relations@roche.com
- Nicolas Dunant (Head)
- Patrick Barth
- Daniel Grotzky
- Karsten Kleine
- Nathalie Meetz
- Barbara von Schnurbein