Media Release

Roche's Tecentriq in combination with Avastin shows encouraging results in Phase Ib study of people with unresectable hepatocellular carcinoma

- **The study showed a confirmed objective response rate of 36% for people treated with the Tecentriq and Avastin combination in unresectable hepatocellular carcinoma who have not received prior systemic therapy**
- **The combination of Tecentriq and Avastin was shown to reduce the risk of disease worsening or death by 45% compared with Tecentriq monotherapy**
- **Data from the Phase Ib cancer immunotherapy combination study will be presented at the European Society for Medical Oncology (ESMO) 2019 congress on Friday 27 September at 14:00**

Basel, 27 September 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) will today present results from a Phase Ib study evaluating the efficacy and safety of Tecentriq® (atezolizumab) in combination with Avastin® (bevacizumab) as a treatment for people with unresectable hepatocellular carcinoma (HCC), the most common form of liver cancer, who have not received prior systemic therapy. [1]

Data from the non-randomised Tecentriq and Avastin cohort (Arm A) showed clinically meaningful and durable responses after a median follow-up of 12.4 months, with a confirmed objective response rate (ORR) of 36% (95% CI 26–46) by central review per RECIST v1.1. The data also showed that 12% of people had a complete response to treatment and a median duration of response (DOR) was not yet reached. Median progression-free survival (PFS), by central review per RECIST v1.1, a secondary efficacy endpoint in the study, was 7.3 months (95% CI 5.4–9.9). [2] Safety for the combination of Tecentriq and Avastin appeared to be consistent with the known safety profile of the individual medicines. No new safety signals were identified.

For the randomised portion of the study (Arm F), evaluating the combination approach with Tecentriq and Avastin versus Tecentriq alone, the primary efficacy endpoint of PFS as assessed by central review per RECIST v1.1 was met, with the combination reducing the risk of disease worsening or death by 45% compared with Tecentriq monotherapy. After a median follow-up of 6.6 months, the results demonstrate the superiority of the combination of Tecentriq and Avastin over Tecentriq monotherapy (hazard ratio =0.55, 80% CI 0.40–0.74, p=0.0108). Median PFS in the Tecentriq and Avastin arm was 5.6 months (95% CI 3.6–7.4) compared with 3.4 months (95% CI 1.9–5.2) in the Tecentriq monotherapy arm. [2] Additional secondary endpoints of Arm F are being evaluated and at this time the data remain immature. Safety for both cohorts in Arm F appeared to be consistent with the known safety profile of the individual medicines. No new safety signals were identified.

"We are encouraged by these latest results, which show promising progression-free survival and confirmed objective response rates in people with unresectable hepatocellular carcinoma, a disease for which the unmet

medical need is particularly great," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "These data strengthen our belief in the combination of Tecentriq and Avastin in this common form of liver cancer and we look forward to the results from our Phase III study, IMbrave150."

The data (Abstract #LBA39) will be presented at 14:15 in the Proffered Paper session (14:00–15:30) in the Madrid Auditorium (Hall 2), at ESMO on Friday 27 September.

In July 2018, the US Food and Drug Administration (FDA) granted Breakthrough Therapy Designation (BTD) for Tecentriq in combination with Avastin as an initial (first-line) treatment for advanced or metastatic HCC based on data from this Phase Ib study.

Earlier this year, enrolment was completed for IMbrave150 (NCT03434379), an open-label, multicentre, randomised Phase III study investigating the combination of Tecentriq and Avastin versus sorafenib in people with unresectable HCC who have not received prior systemic therapy. The study is expected to read out later this year.

Roche has an extensive clinical trial development programme for Tecentriq, with studies ongoing or planned, including multiple 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 GO30140 study (NCT02715531)

GO30140 is an open-label, multicentre Phase Ib study evaluating the safety and efficacy of Tecentriq (anti-PD-L1 antibody) administered in combination with Avastin and/or other treatments in people with solid tumours, including HCC. In Arms A and F of the study, people with unresectable HCC who had not received prior systemic therapy were eligible for enrolment. All patients in Arm A received Tecentriq and Avastin. Patients in Arm F were randomised 1:1 to receive Tecentriq and Avastin or Tecentriq monotherapy. Patients on the combination received Tecentriq (1200 mg) and Avastin (15 mg/kg) intravenously every 3 weeks, while those in the monotherapy cohort received Tecentriq (1200 mg) intravenously every 3 weeks. In all cohorts, treatment continued until unacceptable toxicity or loss of clinical benefit. Primary endpoints were ORR (Arm A) and PFS (Arm F) by central review per RECIST v1.1, and safety (both arms).

About hepatocellular carcinoma (HCC)

HCC is an aggressive cancer with limited treatment options and is a major cause of cancer deaths worldwide.[1] The disease affects over 750,000 people every year,[1,3] with the majority of cases in Asia and almost half of all cases in China.[3,4] 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 limited, with few systemic therapeutic options and a 1-year survival rate of less than 50% following diagnosis. [5]

About IMbrave150 (NCT03434379)

IMbrave150 is a global Phase III, multicentre, open-label study of 480 people with unresectable HCC who have not received prior systemic therapy. People are randomised 2:1 to receive the combination of Tecentriq and Avastin or sorafenib. Tecentriq is administered intravenously, 1200 mg on day 1 of each 21-day cycle, and Avastin is administered intravenously, 15 mg/kg on day 1 of each 21-day cycle. Sorafenib is administered by mouth, 400 mg twice per day, on days 1–21 of each 21-day cycle. People receive the combination or the control arm treatment until unacceptable toxicity or loss of clinical benefit as determined by the investigator. Co-primary endpoints are overall survival (OS) and PFS by central review per RECIST v1.1. Secondary endpoints include ORR, PFS, time to progression (TTP) and DOR all assessed by the investigator per RECIST v1.1 and HCC mRECIST, as well as ORR, TTP and DOR by central review per RECIST v1.1, along with time to deterioration (TTD) in patient-reported global health status/quality of life (GHS/QoL).

About the Tecentriq and Avastin combination

There is a strong scientific rationale to support the use of Tecentriq and 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 (metastasize).

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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References

[1] Llovet J et al. Hepatocellular carcinoma. Nat Rev Dis Primers. 2016;2:16018.
[2] Lee MS et al. Randomised Efficacy and Safety Results For Atezolizumab (Atezo) + Bevacizumab (Bev) in Patients (pts) With Previously Untreated, Unresectable Hepatocellular Carcinoma (HCC). LBA39. ESMO 2019, 27 September–1 October, Barcelona, Spain. Presented at 14:15 in the Proffered Paper session (14:00–15:30) in the Madrid Auditorium (Hall 2) on Friday 27 September.
[3] World Health Organisation: Globocan 2018 – Liver cancer factsheet. [Internet; cited 19 August 2019] Available from: http://gco.iarc.fr/today/data/factsheets/cancers/11-Liver-fact-sheet.pdf
[4] World Health Organisation: Globocan 2018 – China factsheet. [Internet; cited 19 August 2019] Available from: http://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf
[5] Giannini G et al. Prognosis of untreated hepatocellular carcinoma. Hepatology. 2015;61(1):184-190.

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