

## **FDA grants Breakthrough Therapy Designation for Roche's Tecentriq in combination with Avastin as first-line treatment for advanced or metastatic hepatocellular carcinoma (HCC)**

Basel, 18 July 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for Tecentriq® (atezolizumab) in combination with Avastin® (bevacizumab) as an initial (first-line) treatment for people with advanced or metastatic hepatocellular carcinoma (HCC), the most common form of liver cancer. The designation is based on data from a Phase Ib study assessing the safety and clinical activity of the combination of Tecentriq and Avastin.

“Hepatocellular carcinoma is an aggressive cancer with limited treatment options and a major cause of cancer deaths worldwide,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “Preliminary data from the combination of Tecentriq and Avastin in this disease are promising and we look forward to working with health authorities to make this potential treatment regimen available to people with hepatocellular carcinoma as soon as possible.”

Breakthrough Therapy Designation is designed to expedite the development and review of medicines intended to treat serious or life-threatening diseases and to help ensure people have access to them through FDA approval as soon as possible. This is the 22nd Breakthrough Therapy Designation for Roche’s portfolio of medicines and the 3rd for Tecentriq.

Roche presented data from a Phase Ib study in HCC at the American Society of Clinical Oncology (ASCO) Annual Meeting, in June 2018. These data showed that after a median follow-up of 10.3 months, responses (independent review facility (IRF) per RECIST v1.1) were seen in 15 (65 percent) of 23 efficacy-evaluable patients. Responses were seen in all subgroups, including on the basis of the cause of their disease (etiology: Hepatitis B, Hepatitis C, and non-viral), region (Asia excl. Japan or Japan/US), baseline alpha-fetoprotein levels (high/low) or spread of tumour beyond the liver (yes/no). Assessment by investigators (INV) assessed per RECIST v1.1 demonstrated a response rate of 61 percent (14 out of 23 patients). Median progression free survival (PFS), duration of response (DOR), time to progression (TTP) and overall survival (OS) have not yet been reached after a median follow-up of 10.3 months; results will be presented at a future medical congress when updated data from an expanded cohort are available. In the safety-evaluable population (n=43), 28 percent of patients (n=12) experienced Grade 3-4 treatment-related adverse events and no treatment-related Grade 5 adverse events were observed. No new safety signals were identified beyond the established safety profiles for the individual medicines. Roche provided additional data per FDA request and the Breakthrough Therapy Designation has been granted based on the totality of these data.

Earlier this year, Roche initiated IMbrave150 (NCT03434379), an open-label, multicentre, randomised Phase III study investigating the combination of Tecentriq and Avastin versus sorafenib in people with previously-untreated (first-line) locally advanced, unresectable or metastatic HCC. This study is currently enrolling. Further information about the trial can be found on [clinicaltrials.gov](https://clinicaltrials.gov).

#### **About the Phase Ib study (NCT02715531)**

This Phase Ib, open-label, multicentre study is evaluating the safety and clinical activity of a number of cancer immunotherapy combinations in different solid tumours, including Tecentriq and Avastin in patients with advanced, unresectable or metastatic first-line HCC (Arm A). Participants in Arm A receive Tecentriq (1200 mg) and Avastin (15 mg/kg) intravenously (IV) every three weeks until loss of clinical benefit or unacceptable toxicity. The primary objectives of Arm A are to assess the clinical activity, based on objective response rate (ORR) assessment by independent review facility (IRF) per RECIST v1.1 and to assess the safety and tolerability of the combination. Secondary efficacy endpoints include objective response rate (ORR) by investigator assessment (INV), as well as progression-free survival (PFS), duration of response (DOR), time to progression (TTP) all by INV and IRF per RECIST v1.1; and overall survival (OS).

#### **About Hepatocellular Carcinoma (HCC)**

Liver cancer is the second most common cause of cancer death globally<sup>[1]</sup> and HCC is the most common primary malignancy of the liver. Globally, HCC is the fifth most common cancer in men and the seventh most common cancer among women, with over half a million new cases diagnosed annually<sup>[1]</sup>. HCC develops predominantly in those people with cirrhosis due to chronic hepatitis B or C<sup>[2]</sup>.

#### **About IMbrave150 (NCT03434379)**

IMbrave150 is a Phase III, multicentre, randomised, open-label study enrolling approximately 480 people with untreated advanced, unresectable or metastatic HCC 2:1 to receive the combination of Tecentriq and Avastin or sorafenib. Tecentriq will be administered IV, 1200mg on day 1 of each 21-day cycle and Avastin will be administered IV, 15mg/kg on day 1 of each 21-day cycle. Sorafenib will be administered by mouth, 400mg twice per day, on days 1-21 of each 21-day cycle. Participants will 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 OS and investigator-assessed ORR. Secondary endpoints include investigator-assessed PFS, TTP, DOR and IRF-assessed ORR, PFS, TTP and DOR.

#### **About the Tecentriq® (atezolizumab) and Avastin® (bevacizumab) 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® (atezolizumab)**

Tecentriq is a monoclonal antibody designed to bind with a protein called PD-L1 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 has the potential to be used as a foundational combination partner with cancer immunotherapies, targeted medicines and various chemotherapies across a broad range of cancers.

Tecentriq is already approved in the European Union, United States and more than 70 countries for people with previously treated metastatic NSCLC and for certain types of untreated or previously treated metastatic urothelial carcinoma (mUC).

### **About Avastin® (bevacizumab)**

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](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. 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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 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](http://www.roche.com).

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## References

[1] Ferlay J et al. GLOBOCAN 2012, Liver Cancer: Estimated Incidence, Mortality and Prevalence Worldwide 2012.

<http://globocan.iarc.fr/old/FactSheets/cancers/liver-new.asp>. Accessed May 2018.

[2] Raza A and Sood GK. Hepatocellular carcinoma review: Current treatment, and evidence-based medicine. World J Gastroenterol.2014; 20(15): 4115-4127.

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