Media Release

European Commission approves Roche's new Tecentriq-based combination therapy as an initial treatment for most common form of advanced lung cancer

- **The approval of the new Tecentriq-based combination expands treatment options for people across Europe affected by non-squamous non-small cell lung cancer (NSCLC)**
- **Decision based on data showing that the Tecentriq plus chemotherapy combination demonstrated a significant overall survival (OS) and progression-free survival (PFS) benefit**

Basel, 6 September 2019 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Commission has approved and granted marketing authorisation for Tecentriq® (atezolizumab) in combination with chemotherapy (carboplatin and Abraxane® [albumin-bound paclitaxel; nab-paclitaxel]), for the initial (first-line) treatment of adults with metastatic non-squamous non-small cell lung cancer (NSCLC) who do not have EGFR mutant or ALK-positive NSCLC.

"Today's approval marks another advance for people living with non-squamous non-small cell lung cancer, providing a new treatment option for those affected in Europe," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "This Tecentriq-based combination expands treatment options and offers flexibility to physicians when making treatment choices combining immunotherapy with chemotherapy – which is important, given the complexity of lung cancer."

This approval is based on results from the Phase III IMpower130 study, which demonstrated that the Tecentriq combination therapy helped people live significantly longer, compared with chemotherapy alone (median overall survival [OS]=18.6 versus 13.9 months; hazard ratio [HR]=0.79; 95% CI: 0.64–0.98; p=0.033) in the intention-to-treat wild-type (ITT-WT) population.[1] The Tecentriq-based combination also significantly reduced the risk of disease worsening or death (progression-free survival [PFS]) compared with chemotherapy alone (median PFS=7.0 versus 5.5 months; HR=0.64; 95% CI: 0.54–0.77; p<0.0001) in the ITT-WT population.[1] The safety profile of the Tecentriq combination therapy was consistent with that observed in previous studies.

Lung cancer is the leading cause of cancer death globally, and each year 1.76 million people die as a result of the disease, which translates into more than 4,800 deaths worldwide every day.[2] NSCLC is the most prevalent type of lung cancer, accounting for around 85% of all cases.[3]

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

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About the IMpower130 study
IMpower130 is a Phase III, multicentre, open-label, randomised study evaluating the efficacy and safety of Tecentriq in combination with carboplatin and nab-paclitaxel versus chemotherapy (carboplatin and nab-paclitaxel) alone for chemotherapy-naïve patients with stage IV non-squamous NSCLC. The study enrolled 723 people who were randomised (2:1) to receive:

- Tecentriq plus carboplatin and nab-paclitaxel (Arm A), or
- Carboplatin and nab-paclitaxel (Arm B, control arm)

During the treatment-induction phase, people in Arm A received Tecentriq and carboplatin on day 1 of each 21-day cycle, and nab-paclitaxel on days 1, 8 and 15 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit, whichever occurred first. People received Tecentriq during the maintenance treatment phase until loss of clinical benefit was observed.

During the treatment-induction phase, people in Arm B received carboplatin on day 1 and nab-paclitaxel on days 1, 8 and 15 of each 21-day cycle for 4 or 6 cycles or until disease progression, whichever occurred first. People received best supportive care during the maintenance treatment phase. Switch maintenance to pemetrexed was also permitted. People who were consented prior to a protocol revision were given the option to crossover to receive Tecentriq as monotherapy until disease progression.

The co-primary endpoints were:

- PFS, as determined by the investigator using Response Evaluation Criteria in Solid Tumours version 1.1 (RECIST v1.1) in the ITT-WT population
- OS in the ITT-WT population

A summary of the ITT-WT data from the IMpower130 study that support this approval is included below:[1]

- Tecentriq in combination with chemotherapy helped people live significantly longer, compared with chemotherapy alone (median OS=18.6 versus 13.9 months; HR=0.79; 95% CI: 0.64–0.98; p=0.033).
- Tecentriq in combination with chemotherapy significantly reduced the risk of disease worsening or death (PFS) by 36% compared with chemotherapy alone (median PFS=7.0 versus 5.5 months; HR=0.64; 95% CI: 0.54–0.77; p<0.0001).
- Tecentriq in combination with chemotherapy shrank tumours (objective response rate [ORR]) in 49.2% of people (95% CI: 44.49–53.96) compared with 31.9% of people (95% CI: 25.84–38.36) on chemotherapy alone.
- The median duration of response (DoR) for people receiving Tecentriq in combination with chemotherapy was 8.4 months (95%, CI: 6.9–11.8) compared with 6.1 months (95% CI: 5.5–7.9) for people on chemotherapy alone.
- Grade 3–4 treatment-related adverse events (AEs) were reported in 73.2% of people receiving Tecentriq plus chemotherapy compared with 60.3% of people receiving chemotherapy alone. The most common Grade 3–4 AEs in people receiving Tecentriq plus chemotherapy were an abnormal low count of a

certain type of white blood cell (neutropenia, 32.1%), a decrease in red blood cells (anaemia, 29.2%), and a decreased neutrophil count (12.1%).

About NSCLC

Lung cancer is the leading cause of cancer death globally.[2] Each year 1.76 million people die as a result of the disease; this translates into more than 4,800 deaths worldwide every day.[2] Lung cancer can be broadly divided into two major types: NSCLC and small cell lung cancer. NSCLC is the most prevalent type, accounting for around 85% of all cases.[3] NSCLC comprises non-squamous and squamous-cell lung cancer, the squamous form of which is characterised by flat cells covering the airway surface when viewed under a microscope.[3]

About Tecentriq (atezolizumab)

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 (CIT) 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 triple-negative breast cancer.

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 tenth consecutive year, Roche has been recognised as the most sustainable company 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.

References
[1] Capuzzo F et al. IMpower130: Progression-free survival (PFS) and safety analysis from a randomised phase 3 study of carboplatin + nab-paclitaxel (CnP) with or without atezolizumab (atezo) as first-line (1L) therapy in advanced non-squamous NSCLC. Presented at: European Society for Medical Oncology (ESMO) 2018 Conference, 22 October 2018, Munich, Germany. Abstract #LBA53.
[2] World Health Organization. GLOBOCAN 2018; Lung Cancer: Estimated cancer incidence, mortality and prevalence worldwide. Available from: http://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf. Accessed August 2019.
[3] American Cancer Society. What Is Non-Small Cell Lung Cancer? [Internet]: Available from: https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html Accessed August 2019.

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