Media Release

FDA accepts Roche's supplemental biologics license application for Tecentriq plus chemotherapy (Abraxane and carboplatin) for the initial treatment of metastatic non-squamous non-small cell lung cancer

Basel, 17 January 2019 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has accepted the company's supplemental Biologics License Application (sBLA) for Tecentriq® (atezolizumab) in combination with Abraxane® [albumin-bound paclitaxel; *nab*-paclitaxel]) and carboplatin for the initial (first-line) treatment of people with metastatic non-squamous non-small cell lung cancer (NSCLC) who do not have EGFR or ALK genomic tumour aberrations. The FDA is expected to make a decision on approval by 2 September 2019.

"We look forward to working with the FDA in order to bring this Tecentriq-based combination to people with non-squamous non-small cell lung cancer as soon as possible," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "Lung cancer is a challenging disease to treat, and this review takes us one step closer towards offering a new treatment option that has shown a clinically meaningful survival benefit in the treatment of this type of disease."

This sBLA is based on results from the Phase III IMpower130 study, which met its co-primary endpoints of overall survival (OS) and progression-free survival (PFS) in the initial treatment of people with metastatic non-squamous NSCLC.

The FDA recently approved Tecentriq in combination with Avastin, paclitaxel and carboplatin (chemotherapy) for the initial treatment of people with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumour aberrations. Tecentriq is also approved by the FDA to treat people with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should have disease progression on FDA approved therapy for NSCLC harbouring these aberrations prior to receiving Tecentriq.

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 724 people who were randomised in a 2:1 ratio to receive:

- Tecentriq plus *nab*-paclitaxel and carboplatin (Arm A), or
- *Nab*-paclitaxel and carboplatin (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 in Arm A 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 in Arm B 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 following disease progression to receive Tecentriq as monotherapy until further disease progression.

The co-primary endpoints were:

- PFS as determined by the investigator using RECIST v1.1 in people without EGFR or ALK mutations, assessed in the ITT-WT population
- OS in the ITT-WT population

The IMpower130 study met its OS and PFS co-primary endpoints as per the study protocol. The interim analysis showed that Tecentriq plus chemotherapy helped people live significantly longer compared with chemotherapy alone (median 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 (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] Safety for the Tecentriq plus chemotherapy combination appeared consistent with the known safety profiles of the individual medicines, and no new safety signals were identified with the combination. Grade 3-4 treatment-related adverse events (AEs) were reported in 73.2% of people receiving Tecentriq plus chemotherapy compared to 60.3% of people receiving chemotherapy alone.

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

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.

Currently, Roche has nine Phase III lung cancer studies evaluating Tecentriq alone or in combination with other medicines.

Tecentriq is already approved in the European Union, United States and more than 85 countries for people with previously treated metastatic NSCLC and for certain types of untreated or previously treated metastatic urothelial carcinoma (mUC). Tecentriq was also recently approved in the United States for the initial treatment of people with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumour aberrations.

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. 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 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.

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's (ESMO) 2018 Conference on 22 October 2018, Munich, Germany. Abstract #LBA53.
[2] World Health Organization. GLOBOCAN 2018; Lung Cancer: Estimated cancer incidence, mortality and prevalence worldwide. [Internet]: http://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf. Accessed January 2019.
[3] American Cancer Society. What is non-small cell lung cancer? [Internet]: https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html. Accessed January 2019.

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