Media Release

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FDA grants Roche's TECENTRIQ® (atezolizumab) accelerated approval as initial treatment for certain people with advanced bladder cancer

- **First and only cancer immunotherapy approved in advanced bladder cancer as initial treatment for those unable to receive cisplatin chemotherapy**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) granted accelerated approval to TECENTRIQ® (atezolizumab) for the treatment of people with locally advanced or metastatic urothelial carcinoma (mUC) who are not eligible for cisplatin chemotherapy. TECENTRIQ was previously approved for people with locally advanced or mUC who have disease progression during or following any platinum-containing chemotherapy, or within 12 months of receiving chemotherapy before surgery (neoadjuvant) or after surgery (adjuvant). Bladder cancer is the most common type of urothelial carcinoma, and up to half of all people with the advanced form of the disease are unable to receive cisplatin chemotherapy as an initial treatment and therefore have a high unmet medical need. Urothelial carcinoma also includes cancers of the urethra, ureters and renal pelvis.

"We are pleased that TECENTRIQ will now be available to more people with advanced bladder cancer, including those who are unable to receive initial treatment with a standard chemotherapy", said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. "TECENTRIQ was the first cancer immunotherapy approved by the FDA for people with advanced bladder cancer and has become a standard of care in those whose disease has progressed after receiving other medicines, either before or after surgery, or after their disease has spread."

The FDA's Accelerated Approval Program allows conditional approval of a medicine that fills an unmet medical need for a serious condition, based on early evidence suggesting clinical benefit. The indication for TECENTRIQ is approved under accelerated approval based on tumour response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Today's approval of TECENTRIQ is based on the Phase II IMvigor210 study.

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This is the third approval for TECENTRIQ in under a year in the US. TECENTRIQ is also approved for the treatment of people with metastatic non-small cell lung cancer (NSCLC) who have disease progression during or following platinum-containing chemotherapy, and have progressed on an appropriate FDA-approved targeted therapy if their tumour has EGFR or ALK gene abnormalities.

About the IMvigor210 study

IMvigor210 is an open-label, multicentre, single-arm Phase II study that evaluated the safety and efficacy of TECENTRIQ in people with locally advanced or metastatic urothelial carcinoma (mUC), regardless of PD-L1 expression. People in the study were enrolled into one of two cohorts. This accelerated approval is based on results from Cohort 1, which consisted of 119 people with locally advanced or mUC who were ineligible for cisplatin-containing chemotherapy and were either previously untreated or had disease progression at least 12 months after neoadjuvant or adjuvant chemotherapy. People in this cohort received a 1200-mg intravenous dose of TECENTRIQ every three weeks until either unacceptable toxicity or disease progression. The primary endpoint of the study was objective response rate (ORR).

A summary of the efficacy data from the IMvigor210 study that supports this accelerated approval is included below.

	All patients	**PD-L1 expression subgroups**	
	n=119	PD-L1 expression of < 5% in ICs[1] (n=87)	PD-L1 expression of ≥ 5% in ICs[1] (n=32)
Number of IRF-assessed Confirmed responders	28	19	9
Objective response rate (ORR; %) (95% CI)	23.5 (16.2–32.2)	21.8 (13.7–32.0)	28.1 (13.8–46.8)
Complete response (CR)(%)	6.7	6.9	6.3
Partial response (PR)(%)	16.8	14.9	21.9
Median DoR, months (range)	Not reached (3.7–16.6+)	Not reached (3.7–16.6+)	Not reached (8.1–15.6+)

+ Denotes a censored value

[1] PD-L1 expression in tumour-infiltrating immune cells (ICs)

The most common Grade 3–4 adverse reactions (≥ 2%) were: fatigue (8%), urinary tract infection (5%), anaemia (7%), diarrhoea (5%), increase in the level of creatinine in the blood (5%), intestinal obstruction (partial or complete blockage of the bowel), increase of the liver enzyme alanine transaminase (4%), hyponatraemia (low blood sodium level; 15%), decreased appetite (3%), sepsis (blood infection), back/neck pain (3%), renal failure and hypotension (low blood pressure). Five people (4.2%) experienced either sepsis, cardiac arrest, myocardial infarction, respiratory failure or respiratory distress, which led to death. TECENTRIQ was discontinued for adverse reactions in 4.2% (5) of the 119 patients.

Roche is evaluating TECENTRIQ in a confirmatory Phase III study (IMvigor211), which compares TECENTRIQ to chemotherapy as initial treatment in people with a specific type of advanced bladder cancer and in people whose bladder cancer has progressed on at least one prior platinum-containing regimen.

About metastatic urothelial carcinoma

Metastatic urothelial cancer (mUC) is associated with a poor prognosis and limited treatment options. It is a disease that has seen no major advances for more than 30 years outside of the US. UC is the ninth most common cancer worldwide, with 430,000 new cases diagnosed in 2012, and it results in approximately 145,000 deaths globally each year. Men are three times more likely to suffer from UC, compared with women, and the disease is three times more common in developed countries than in less developed countries.

About TECENTRIQ® (atezolizumab)

TECENTRIQ is a monoclonal antibody designed to bind with a protein called PD-L1. TECENTRIQ is designed to bind to 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 may also affect normal cells.

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.

About personalised cancer immunotherapy (PCI)

The aim of personalised cancer immunotherapy (PCI) is to provide patients and physicians with treatment options tailored to the specific immune biology associated with a person's individual tumour. The purpose is to inform treatment strategies that provide the greatest number of people with a chance for transformative benefit. PCI encompasses the search for reliable biomarkers that correlates with clinical benefit either as a monotherapy or in combination, along any of the seven steps in the cancer immunity cycle and across a broad range of tumour types. Fitting the right combination treatment strategies through immune biology profiling of the tumour, also known as phenotypes is one other way in which we are able to personalise treatments.The Roche PCI research and development programme comprises more than 20 investigational candidates, twelve of which are in clinical trials.

PCI is an essential component of how Roche delivers on the broader commitment to personalised healthcare. 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 for improving patient access to medical innovations by working with all relevant stakeholders. Twenty-nine 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 eight 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 2016 employed more than 94,000 people worldwide. In 2016, Roche invested CHF 9.9 billion in R&D and posted sales of CHF 50.6 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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