Media Release

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FDA grants Roche's Cancer Immunotherapy Atezolizumab priority review for advanced bladder cancer

Roche Group (SIX: RO, ROG; OTCQX: RHHBY), today announced that the U.S. Food and Drug Administration (FDA) has accepted the company's Biologics License Application (BLA) and granted Priority Review for atezolizumab (anti-PDL1; MPDL3280A) for the treatment of people with locally advanced or metastatic urothelial carcinoma (mUC) who had disease progression during or following platinum-based chemotherapy in the metastatic setting, or whose disease worsened within 12 months of receiving platinum-based chemotherapy before surgery (neoadjuvant) or after surgery (adjuvant). Urothelial carcinoma accounts for 90 percent of all bladder cancers and can also be found in the renal pelvis, ureter and urethra.

"Atezolizumab was granted Priority Review designation based on results of the IMvigor 210 study, which showed the medicine shrank tumors in a type of advanced bladder cancer, and the majority responding to treatment continued to respond after nearly a year of follow up," said Sandra Horning, M.D., Chief Medical Officer and Head of Global Product Development. "The treatment options available for advanced bladder cancer are very limited, and we are committed to working with the FDA to bring the first anti-PDL1 cancer immunotherapy to people with this disease as quickly as possible."

A Priority Review designation is granted to medicines that the FDA has determined to have the potential to provide significant improvements in the safety and effectiveness of the treatment, prevention or diagnosis of a serious disease. Atezolizumab was granted Breakthrough Therapy Designation by the FDA in May 2014 for the treatment of people whose metastatic bladder cancer expresses the protein PD-L1 (programmed death ligand-1). 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 that people have access to them through FDA approval as soon as possible. The BLA submission for atezolizumab is based on results of the IMvigor 210 Phase II study, and the FDA will make a decision on approval by Sept. 12, 2016. Atezolizumab is also being studied in a number of other cancers.

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About the IMvigor 210 study

IMvigor 210 is an open-label, multicenter, single-arm Phase II study that evaluated the safety and efficacy of atezolizumab in people with locally advanced or mUC, regardless of PD-L1 expression. People in the study whose disease had progressed during or following previous treatment with a platinum-based chemotherapy regimen (n=311) received a 1200-mg intravenous dose of atezolizumab on day one of 21-day cycles until loss of clinical benefit. The primary endpoint of the study was objective response rate (ORR) as assessed by an independent review facility (IRF) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Secondary endpoints included duration of response (DOR), overall survival, progression-free survival and safety.

In an updated analysis based on 11.7 months of median follow up, atezolizumab shrank tumors (ORR) in 15 percent (95 percent CI: 11, 19) of people evaluable for efficacy and safety (n=310) whose disease progressed after platinum-based chemotherapy. Atezolizumab shrank tumors in 26 percent (95 percent CI: 18, 36) of people whose disease had medium and high levels of PD-L1 expression (n=100). Median DOR was not reached at the time of analysis; with a median duration of follow up of 11.7 months, 84 percent (38/45) of people had an ongoing response. The most common Grade 3 to 4 treatment-related adverse events included: fatigue (2 percent), decreased appetite, fever (pyrexia), anemia, enzymes in the blood (ALT and AST increase), joint pain (arthralgia), difficulty breathing (dyspnea), inflammation of the lung wall (pneumonitis), inflammation of the lining of the colon (colitis), hypertension and hypotension (all 1 percent). There were no treatment-related Grade 5 adverse events.

In addition to IMvigor 210, Genentech has an ongoing, confirmatory Phase III study (IMvigor 211), which compares atezolizumab to chemotherapy in people whose bladder cancer has progressed on at least one prior platinum-containing regimen.

About metastatic urothelial cancer

According to the American Cancer Society (ACS), it is estimated that more than 76,000 Americans will be diagnosed with bladder cancer in 2016, and about 11 percent of new diagnoses are made when bladder cancer is in advanced stages. There is a dramatic difference in survival rates between early and advanced bladder cancer. The ACS estimates that approximately 96 percent of people will live five or more years when diagnosed with the earliest stage of the disease, compared to 39 percent when diagnosed in advanced stages (stage III-IV) of the disease. Men are about three to four times more likely to get bladder cancer during their lifetime than women.

About atezolizumab

Atezolizumab (also known as MPDL3280A; anti-PDL1) is an investigational monoclonal antibody designed to bind with a protein called programmed death ligand-1 (PD-L1). Atezolizumab is designed to directly bind to PD-L1 expressed on tumor cells and tumor-infiltrating immune cells, blocking its interactions with PD-1 and B7.1 receptors. By inhibiting PD-L1, atezolizumab may enable the activation of T cells. Atezolizumab 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

The aim of personalised cancer immunotherapy (PCI) is to provide individual patients with treatment options that are tailored to their specific needs. Our PCI research and development programme comprises more than 20 investigational candidates, eight of which are in clinical trials. All studies include the prospective evaluation of biomarkers to determine which people may be appropriate candidates for our medicines. In the case of atezolizumab (also known as MPDL3280A), PCI begins with the PD-L1 (programmed death ligand-1) IHC assay based on the SP142 antibody developed by Roche Tissue Diagnostics. The goal of PD-L1 as a biomarker is to identify those people most likely to experience clinical benefit with atezolizumab as a single agent and those who may be appropriate candidates for combination therapies; the purpose is not to exclude patients from atezolizumab therapy, but rather to enable the design of combinations that will provide the greatest chance for transformative responses. The ability to combine atezolizumab with multiple chemotherapies may provide new treatment options to people across a broad range of tumours regardless of their level of PD-L1 expression.

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives.

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. 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.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. 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 seven years in a row by the Dow Jones Sustainability Indices.

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2015 employed more than 91,700 people worldwide. In 2015, Roche invested CHF 9.3 billion in R&D and posted sales of CHF 48.1 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.

Find out more about Roche in oncology here:
www.roche.com/research_and_development/what_we_are_working_on/oncology.htm

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