Basel, 27 September 2015

Two positive studies of Roche’s investigational cancer immunotherapy atezolizumab in specific type of lung cancer presented at 2015 European Cancer Congress

• Phase 2 study POPLAR study demonstrated statistically significant survival benefit compared to chemotherapy
• PD-L1 expression correlated with how well people did on atezolizumab
• Data will be submitted to global health authorities, including the US Food and Drug Administration (FDA)

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from two phase II studies that evaluated the investigational cancer immunotherapy atezolizumab (anti-PDL1; MPDL3280A) in people with advanced non-small cell lung cancer (NSCLC). In the randomised phase II study, POPLAR, atezolizumab met its primary endpoint and showed a statistically significant survival benefit compared to chemotherapy (HR=0.54; p=0.014) in people with recurrent NSCLC whose tumours expressed medium and high levels of PD-L1, which corresponded with people living 7.7 months longer than people who received docetaxel chemotherapy. A separate, single-arm phase II study, BIRCH, met its primary endpoint and showed that atezolizumab shrank tumours (objective response rate, ORR) in up to 27 percent (p=0.0001) of people whose disease had progressed on prior medicines and also expressed the highest levels of PD-L1. Median survival had not yet been reached. In both studies of atezolizumab, adverse events (AEs) were consistent with those observed in previous studies.

“Results from both of our studies in non-small cell lung cancer showed that measuring PD-L1 may help identify people most likely to respond to atezolizumab, and the majority of responses continued when these data were assessed,” said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. “Durable responses are meaningful for people whose cancer has progressed on other medicines, and we plan to submit these results to global health authorities to bring this potential new option to people as soon as possible”.

In February 2015, atezolizumab received Breakthrough Therapy Designation from the US Food and Drug
Administration (FDA) for the treatment of people whose NSCLC expresses PD-L1 and whose disease worsened during or after standard treatments (e.g. platinum-based chemotherapy and appropriate targeted therapy for EGFR mutation-positive or ALK-positive disease). Roche is discussing these NSCLC data from POPLAR and BIRCH with the FDA as part of its Breakthrough Therapy Designation and with other health authorities around the world. Roche currently has seven ongoing phase III studies of atezolizumab alone or in combination with other medicines for various types of lung cancer.

**About the POPLAR study**

Full results of the POPLAR study will be presented by Johan Vansteenkiste, University Hospital Leuven, Leuven, Belgium (Abstract #14LBA) on Sunday, 27 September, 09:15 CET.

*Atezolizumab monotherapy vs docetaxel in 2L/3L non-small cell lung cancer: Primary analyses for efficacy, safety and predictive biomarkers from a randomized phase II study (POPLAR)*

POPLAR is a multicentre, open-label, randomised phase II study evaluating the efficacy and safety of atezolizumab compared with docetaxel in people with recurrent locally advanced or metastatic NSCLC. Patients were randomised to receive either atezolizumab 1200 mg intravenously every three weeks or docetaxel 75 mg/m² intravenously every three weeks. Treatment with atezolizumab may have been continued as long as people were experiencing clinical benefit as assessed by the investigator, i.e. in the absence of unacceptable toxicity or symptomatic deterioration attributed to disease progression. The study enrolled 287 people with previously treated, advanced NSCLC. The primary endpoint was overall survival (OS); secondary endpoints included progression free survival (PFS), ORR and safety. People were stratified by PD-L1 expression on tumour-infiltrating immune cells (ICs), histology and prior lines of therapy. PD-L1 expression was assessed for both tumour cells (TCs) and ICs; people were scored as TC0, 1, 2 or 3 and IC0, 1, 2 or 3 with an immunohistochemistry (IHC) test being developed by Roche Diagnostics.
Interim results of the BIRCH study will be presented by Benjamin Besse, Institut Gustave Roussy, Villejuif, France and Paris Sud University, France (Abstract #16LBA) on Sunday, 27 September, 09:35 Central European Time (CET).

Phase II, single-arm trial (BIRCH) of atezolizumab as first-line or subsequent therapy for locally advanced or metastatic, PDL1-selected NSCLC
BIRCH is an open-label, multicentre, single-arm phase II study that evaluated the safety and efficacy of atezolizumab in 667 people with locally advanced or metastatic NSCLC whose disease expressed PD-L1. PD-L1 expression was assessed for both TCs and tumour-infiltrating ICs with an investigational immunohistochemistry test (IHC) being developed by Roche Diagnostics. Eligibility criteria included people whose tumours were determined to express PD-L1 with an IHC score of TC2/3 or IC2/3. People in the study received a 1200 mg intravenous dose of atezolizumab every three weeks. The primary endpoint of the study was the ORR assessed by independent review facility per RECIST v1.1. Secondary endpoints included duration of response, OS, PFS and safety.

### BIRCH Efficacy Data

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<tr>
<td></td>
<td>TC3 or IC3 (high)</td>
<td>TC2/3 or IC2/3 (medium and high)</td>
<td>TC3 or IC3 (high)</td>
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<tr>
<td>n=</td>
<td>65</td>
<td>139</td>
<td>122</td>
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<tr>
<td>ORR, % (95% CI)</td>
<td>26 (16, 39)</td>
<td>19 (13, 27)</td>
<td>24 (17, 32)</td>
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More than 61% of people whose tumours expressed the highest level of PD-L1 continued to respond at time data was assessed.

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<td>TC3 or IC3 (high)</td>
<td>TC2/3 or IC2/3 (medium and high)</td>
<td>TC3 or IC3 (high)</td>
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<td>6-mo PFS, % (95% CI)</td>
<td>48 (35, 61)</td>
<td>46 (37, 55)</td>
<td>34 (26, 43)</td>
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<tr>
<td>6-mo OS, % (95% CI)</td>
<td>79 (69, 89)</td>
<td>82 (75, 88)</td>
<td>80 (72, 87)</td>
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### Safety (N=659)

- Adverse events were consistent with those observed in previous studies of atezolizumab.
- Eleven percent of people experienced Grade 3-4 treatment related AEs.
- The most common treatment-related AEs were fatigue, diarrhea, nausea, itching (pruritus), fever (pyrexia), decreased appetite, weakness (asthenia), rash and joint pain (arthralgia).

*Confirmed; †IRF. CI: confidence interval; IC: immune cell; IRF: independent review facility; ORR: objective response rate; OS: overall survival; TC: tumour cell.

### About atezolizumab

Atezolizumab (anti-PDL1; MPDL3280A) is an investigational monoclonal antibody designed to interfere with a protein called PD-L1. Atezolizumab is designed to target PD-L1 expressed on TCs and tumour-infiltrating ICs, preventing it from binding to PD-1 and B7.1 on the surface of T cells. By inhibiting PDL1, atezolizumab may activate T cells.
All studies of atezolizumab include the evaluation of an investigational IHC test that uses the antibody SP142 to measure PD-L1 expression on both TCs and tumour-infiltrating ICs. The goal of PD-L1 as a biomarker is to identify those people most likely to benefit when treated with atezolizumab alone, and to determine which people may benefit most from a combination of atezolizumab and another medicine. There are 11 ongoing or planned phase III studies of atezolizumab across certain kinds of lung, kidney, breast and bladder cancers.

**About non-small cell lung cancer**

Lung cancer is the leading cause of cancer death globally. Each year 1.59 million people die as a result of the disease; this translates into more than 4,350 deaths worldwide every day. 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 percent of all cases.

**About Roche in lung cancer**

Lung cancer is a major area of focus and investment for Roche, and we are committed to developing new approaches, medicines and tests that can help people with this deadly disease. Our goal is to provide an effective treatment option for every person diagnosed with lung cancer. We currently have three approved medicines to treat certain kinds of lung cancer and more than 10 medicines being developed to target the most common genetic drivers of lung cancer or to boost the immune system to combat the disease.

**About Roche in personalised cancer immunotherapy**

For more than 30 years, Roche has been developing medicines with the goal to redefine treatment in oncology. Today, we’re investing more than ever to bring personalised cancer immunotherapy (PCI) to people with cancer. The goal of PCI is to provide each person with a treatment tailored to harness his or her own immune system to fight cancer. Roche is studying more than 20 investigational medicines, seven of which are in clinical trials. In every study we are evaluating biomarkers to identify which people may be appropriate candidates for our medicines.

**About Roche**

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world’s largest biotechnology company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in *in vitro* diagnostics and tissue-based cancer diagnostics, and a front runner in diabetes management. Roche’s personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible
improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. 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 chemotherapy.

In 2014 the Roche Group employed 88,500 people worldwide, invested 8.9 billion Swiss Francs in R&D and posted sales of 47.5 billion Swiss Francs. 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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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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