Roche’s investigational immunotherapy MPDL3280A doubled the likelihood of survival compared with chemotherapy in people with a specific type of lung cancer

- Results indicated PD-L1 expression correlated with how well people with previously treated, advanced non-small cell lung cancer (NSCLC) did on MPDL3280A

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced interim results from a global, randomised Phase II study (POPLAR) in people with previously treated NSCLC. The study showed the investigational cancer immunotherapy MPDL3280A (anti-PDL1) doubled the likelihood of survival (overall survival [OS]; HR=0.47) in people whose cancer expressed the highest levels of PD-L1 (programmed death ligand-1) compared with docetaxel chemotherapy. An improvement in survival was also observed in people who had medium and high (HR=0.56) or any level of PD-L1 expression (HR=0.63), as characterised by a test being developed by Roche. MPDL3280A was generally well tolerated and adverse events were consistent with what has been previously reported for MPDL3280A in NSCLC. Updated results will be presented in an oral session at the 51st Annual Meeting of the American Society of Clinical Oncology (ASCO).

“In our study of MPDL3280A in previously treated lung cancer, the amount of PD-L1 expressed by a person’s cancer correlated with improvement in survival,” said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. “The goal of PD-L1 as a biomarker is to identify people most likely to experience improved overall survival with MPDL3280A alone and which people may be appropriate candidates for a combination of medicines.”

In February 2015, MPDL3280A received Breakthrough Therapy Designation from the FDA for the treatment of people whose NSCLC expresses PD-L1 and who progressed 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 the interim data from POPLAR with the FDA as part of Breakthrough Therapy Designation in lung cancer. Roche currently has three Phase II and six Phase III studies of MPDL3280A ongoing in various kinds of lung cancer.
About the POPLAR study

Interim results of the POPLAR study will be presented by Alexander I. Spira, M.D., Ph.D., F.A.C.P, Virginia Cancer Specialists Research Institute; U.S. Oncology Research (Abstract #8010) on Sunday, May 31, 4:42–5:54 P.M. CDT.

*Efficacy, safety and predictive biomarker results from a randomised phase II study comparing MPDL3280A vs docetaxel in 2L/3L NSCLC (POPLAR).*

The Phase II study enrolled 287 patients with previously treated, advanced NSCLC. The primary endpoint was OS; secondary endpoints included progression-free survival (PFS), overall response rate (ORR) and safety. Patients were stratified by PD-L1 expression on tumour-infiltrating immune cells (IC), histology and prior lines of therapy. PD-L1 expression was assessed on both tumour cells (TC) and IC; and patients were scored as TC 0, 1, 2, or 3 and IC 0, 1, 2, or 3 with an immunohistochemistry (IHC) test.

<table>
<thead>
<tr>
<th>Overall survival results (primary endpoint)</th>
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<tbody>
<tr>
<td>Study group</td>
</tr>
<tr>
<td>n=</td>
</tr>
<tr>
<td>Median OS (months)</td>
</tr>
<tr>
<td>HR* (95% CI)</td>
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</tbody>
</table>

CI: confidence interval; Doc: docetaxel; HR: hazard ratio; IC: immune cell; ITT: intention to treat; MPDL: MPDL3280A; NR: not reached; OS: overall survival; TC: tumour cell.

*Stratified HR for ITT and unstratified HR for subgroups.
### Progression-free survival (secondary endpoint)

<table>
<thead>
<tr>
<th>Study group</th>
<th>TC3 or IC3 (high)</th>
<th>TC2/3 or IC2/3 (medium and high)</th>
<th>TC1/2/3 or IC1/2/3 (any expression)</th>
<th>TC0 and IC0</th>
<th>ITT (All Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=</td>
<td>MPDL 24</td>
<td>Doc 23</td>
<td>MPDL 50</td>
<td>Doc 55</td>
<td>MPDL 93</td>
</tr>
<tr>
<td>Median PFS (months)</td>
<td>9.7</td>
<td>3.9</td>
<td>4.0</td>
<td>2.8</td>
<td>3.3</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.56 (0.28, 1.11)</td>
<td>0.70 (0.45, 1.08)</td>
<td>0.87 (0.63, 1.20)</td>
<td>1.15 (0.72, 1.82)</td>
<td>0.96 (0.76, 1.20)</td>
</tr>
</tbody>
</table>

### Overall response rate (secondary endpoint)

| ORR (%) | 38 | 13 | 22 | 15 | 18 | 18 | 8 | 10 | 15 | 15 |

HR: hazard ratio; ITT: intention to treat; NR, not reached. *Stratified HR for ITT and unstratified HR for subgroups.

Fewer people receiving MPDL3280A experienced Grade 3 to 5 adverse events compared to docetaxel (44 percent vs. 56 percent). More respiratory events were reported for MPDL3280A. The median length of treatment with MPDL3280A was 3.7 months compared to 2.1 months for chemotherapy. Other immune related adverse events in the MPDL3280A arm included increase of enzyme levels in the blood (asparate and alanine aminotransferase; 4% each), inflammation in the lining of the colon (colitis; 1%), inflammation of the liver (hepatitis; 1%) and lung tissue (pneumonitis; 2%).

**About MPDL3280A**

MPDL3280A (also known as anti-PDL1 and RG7446) is an investigational monoclonal antibody designed to interfere with a protein called PD-L1. MPDL3280A is designed to target PD-L1 expressed on tumour cells and tumour-infiltrating immune cells, preventing it from binding to PD-1 and B7.1 on the surface of T cells. By inhibiting PD-L1, MPDL3280A may enable the activation of T cells, restoring their ability to effectively detect and attack tumour cells.

**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, which means 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% 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 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 in our effort to bring innovative treatment options that help a person’s own immune system fight cancer. Our Personalised Cancer Immunotherapy research and development programme comprises more than 20 investigational candidates, seven of which are in clinical trials. All studies include the evaluation of biomarkers to help identify the right treatment approach for each patient.

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 biotech 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 frontrunner 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-eight 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 roche.com.

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http://www.roche.com/research_and_development/what_we_are_working_on/oncology.htm

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References
1. Spira A et al., Efficacy, safety and predictive biomarker results from a randomized phase II study comparing MPDL3280A vs docetaxel in 2L/3L NSCLC (POPLAR), Abstract number: #8010. 31 May 2015, 4:42–5:54 CDT, Chicago, United States.