Media Release

Phase III PEMPHIX study shows Roche's MabThera/Rituxan (rituximab) superior to mycophenolate mofetil in patients with pemphigus vulgaris

- **40% of patients with pemphigus vulgaris (PV) achieved sustained complete remission, without the use of steroids for 16 weeks or more, when treated with MabThera/Rituxan compared to 9.5% of patients on mycophenolate mofetil**
- **Study reinforces efficacy and safety of MabThera/Rituxan for treatment of PV, a rare autoimmune condition characterised by blistering of the skin and mucous membranes**
- **Full data of the 52-week treatment period presented at 28th Congress of the European Academy of Dermatology and Venereology (EADV) in Madrid**

Basel, 14 October 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced data from the Phase III PEMPHIX study evaluating the efficacy and safety of MabThera®/Rituxan® (rituximab) compared to mycophenolate mofetil (MMF) in adults with moderate to severe pemphigus vulgaris (PV).[1] The study met the primary endpoint at Week 52 and demonstrated that MabThera/Rituxan is superior to MMF, with 40.3% of patients treated with MabThera/Rituxan achieving sustained complete remission (CR) without the use of steroids for 16 consecutive weeks or more, compared to 9.5% in the MMF arm ($p<0.0001$). All secondary endpoints were statistically significant in favour of MabThera/Rituxan: lower cumulative oral corticosteroid dose (mean difference: 1595 mg; $p=0.0005$), fewer flares (6 vs 44, $p<0.0001$), a greater likelihood of sustained CR (hazard ratio [HR]=4.83; $p=0.0003$), a lesser likelihood of flare (HR=0.15; $p<0.0001$) and a greater improvement in the Dermatology Life Quality Index (DLQI) at week 52 (estimated mean change from baseline -8.87 vs -6.00, $p=0.0012$) compared to the MMF arm. Adverse events were generally consistent with those seen in previous MabThera/Rituxan clinical studies in PV and other approved autoimmune indications. Results were presented as a late-breaking oral presentation at the 28th Congress of the European Academy of Dermatology and Venereology in Madrid, Spain on 12 October, at 09:00-09:15 CEST (Presentation D3T01.1C).

"The approval of MabThera/Rituxan for the treatment of pemphigus vulgaris was the first major advancement in the treatment of this rare, serious disease in more than 60 years," said Levi Garraway, MD, PhD, Roche's Chief Medical Officer and Head of Global Product Development. "The PEMPHIX study showed that 40 percent of people in the study could achieve complete remission from painful blistering without the need for corticosteroids for 16 weeks or more and that Mabthera/Rituxan may be a superior treatment option to mycophenolate mofetil."

The study is ongoing, with patients participating in a 48-week safety follow-up period after treatment completion or discontinuation.

PV is a rare, serious and potentially life-threatening condition characterised by progressive painful blistering of the skin and mucous membranes. MMF is a commonly used, unapproved treatment for PV that is recommended in published treatment guidelines.[2] MabThera/Rituxan became the first biologic therapy for

PV when it was approved by the FDA in June 2018 and the European Commission in March 2019. These approvals were based on data from the Roche-supported Ritux 3 clinical trial. The PEMPHIX study provides additional clinical evidence of the effectiveness of MabThera/Rituxan for PV.

About the PEMPHIX study
PEMPHIX is a phase III, randomised, double-blind, double-dummy, active-comparator, parallel-arm, international, multicentre study (NCT02383589) designed to evaluate the efficacy and safety of MabThera/Rituxan compared with mycophenolate mofetil (MMF) in patients with moderate to severe active pemphigus vulgaris requiring 60-120 mg/day oral prednisone (or equivalent). Participants were randomly assigned to receive MabThera/Rituxan plus MMF placebo or MabThera/Rituxan placebo plus MMF for 52 weeks, in combination with 60 or 80 mg oral prednisone, with the aim of tapering to 0 mg/day by Week 24. MabThera/Rituxan was administered at a dose of 1000 mg via IV infusion on day 1 and 15, with a repeat administration on days 168 and 182. MMF was administered at a dose of 2 grams orally daily (starting at 1 g/day on Day 1 and titrated to achieve a goal of 2 g/day by Week 2). The primary endpoint at Week 52 was the percentage of participants who achieved sustained complete remission without experiencing treatment failure. Sustained complete remission was defined as achieving healing of lesions with no new active lesions (i.e., Pemphigus Disease Area Index activity score of 0) while on 0 mg/day prednisone or equivalent, and maintaining this response for at least 16 consecutive weeks, during the 52-week treatment period. Secondary endpoints were cumulative oral corticosteroid dose, number of disease flares, time to sustained complete remission, time to disease flare and health-related quality of life, as measured by the Dermatology Life Quality Index.

About pemphigus vulgaris
Pemphigus vulgaris is an autoimmune, blistering disease, affecting the skin and mucous membranes.[3] It is the most common type of a group of autoimmune disorders collectively called pemphigus.[4] It is estimated that around three in every 100,000 people are diagnosed with this disease globally.[5]

About MabThera/Rituxan in Immunology
MabThera (Rituxan in the US) is indicated for the treatment of four autoimmune conditions.
MabThera/Rituxan is indicated for the treatment of adults with moderate to severe pemphigus vulgaris (PV).
MabThera/Rituxan in combination with glucocorticoids, is indicated for the treatment of granulomatosis with polyangiitis (Wegener's granulomatosis, GPA) and microscopic polyangiitis (MPA) in adults. In the US, Rituxan, in combination with glucocorticoids, is also indicated for the treatment of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) in paediatric patients 2 years of age and older.
MabThera/Rituxan in combination with methotrexate, is indicated for the treatment of adults with severe active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to other disease-modifying anti-rheumatic drugs (DMARD), including one or more tumour necrosis factor (TNF) inhibitor therapies. MabThera/Rituxan is not indicated in children less than 2 years of age with GPA or MPA, or in children with conditions outside of GPA and MPA.

About Roche in rheumatology and beyond
For more than 50 years, Roche has followed the science to pioneer medicines for immune-mediated rheumatic diseases. First-in-class anti-IL-6 receptor therapy Actemra®/RoActemra® (tocilizumab) has treated more than one million people with debilitating conditions, such as rheumatoid arthritis (RA), polyarticular and systemic juvenile idiopathic arthritis, giant cell arteritis and chimeric antigen receptor T-cell-induced cytokine release syndrome. MabThera®/Rituxan® (rituximab), which targets CD20, has significant clinical and real-world experience treating rheumatic conditions including RA, granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). Roche aims to provide solutions for people that need new treatments most, particularly those with severe or life-threatening conditions and limited treatment options. Our pipeline consists of treatments designed to target immune pathways including a glycoengineered type II anti-CD20 antibody in lupus nephritis.

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. More than 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 eleventh consecutive year, Roche has been recognised as one of the most sustainable companies 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 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 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

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Roche Group Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com
- Nicolas Dunant (Head)
- Patrick Barth
- Daniel Grotzky
- Karsten Kleine
- Nathalie Meetz
- Barbara von Schnurbein