Investor Update

Basel, 24 May 2017

New data at ATS add to the body of evidence for Roche’s Esbriet (pirfenidone) in idiopathic pulmonary fibrosis (IPF)

- In new post hoc analyses of phase III data, Esbriet reduced the risk of death in patients with more advanced lung function impairment and the risk of respiratory-related hospitalisations as a first progressive event
- In post hoc analysis Esbriet also slowed the progression of breathlessness in patients with less preserved lung function
- In retrospective analysis of real-world data patients on Esbriet had good adherence

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new retrospective data analyses for Esbriet® (pirfenidone) in idiopathic pulmonary fibrosis (IPF) that were presented at the American Thoracic Society (ATS) 2017 International Conference. Three post hoc analyses of the pooled phase III ASCEND and CAPACITY studies indicated that IPF patients treated with Esbriet may experience a reduction in the risk of death,¹ reduction in patient-reported breathlessness, ² and longer progression-free survival (PFS) with fewer respiratory-related hospitalisations compared to placebo.³ In a fourth, real-world analysis of US claims data on
persistence, patients overall had a good adherence. 76.2% of the Esbriet patients persisted on therapy. 

“These data expand our understanding of how Esbriet may help people with IPF by slowing disease progression,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “The data also provide insights on management of IPF in real-world settings.”

In the first post hoc analysis of the pooled phase III studies, Esbriet was associated with a 72% reduction in the risk of all-cause mortality in patients with more advanced lung function impairment over one year compared to placebo (4 versus 12 deaths; HR 0.28 [95% CI 0.09, 0.86]; P = 0.018) and a 56% relative reduction in the proportion of patients with a ≥10% absolute decline in FVC or death at one year compared to placebo.

In the second post hoc analysis of the pooled phase III studies, treatment with Esbriet was associated with reduced progression of breathlessness in patients with moderate lung function impairment, as measured by the University of California, San Diego Shortness of Breath Questionnaire (UCSD-SOBQ). In patients with less preserved lung function (GAP stage II/III), the median UCSD-SOBQ score for patients receiving Esbriet was 9.2, whereas for patients receiving placebo it was 13.0 (median difference −3.67, 95% CI, −6.50, −1.00; p=0.009). In addition, a lower proportion of patients on Esbriet experienced more pronounced increases in UCSD-SOBQ scores at one year.

The third post hoc analysis of the pooled phase III studies was conducted on the effect of Esbriet on disease progression over one year, using a novel
definition of PFS that includes respiratory-related hospitalisations. The novel definition resulted in a hazard ratio of 0.49; (95% CI 0.38, 0.64; p<0.0001) for progression-free survival in favour of Esbriet compared to placebo.\textsuperscript{3} Data recently published in the American Journal of Respiratory and Critical Care Medicine (AJRCCM) also showed retrospectively that Esbriet reduced the risk of respiratory-related hospitalisation compared to placebo (7% vs 12%, HR 0.52, 95% CI 0.36-0.77, p-value=0.001).\textsuperscript{5} Among those hospitalised for any reason, Esbriet was associated with a lower risk of death following hospitalisation.\textsuperscript{5}

Finally, in the first retrospective study of real-world adherence and persistence data with antifibrotic therapies for the treatment of IPF, patients on Esbriet had a high rate of adherence during the follow-up period of the study.\textsuperscript{4} Of the patients on Esbriet, 76.2% persisted on therapy.\textsuperscript{4}

**About idiopathic pulmonary fibrosis**

Idiopathic pulmonary fibrosis (IPF) is a fatal disease caused by irreversible, progressive scarring (fibrosis) of the lungs, which makes breathing difficult and prevents the heart, muscles and vital organs from receiving enough oxygen to work properly.\textsuperscript{6} The disease can advance quickly or slowly, but eventually the lungs will harden and stop working altogether.\textsuperscript{6} People with IPF experience a more rapid decline than most cancer patients; in a recent study, only people with lung and pancreatic cancer were shown to have worse survival.\textsuperscript{7} Approximately 100,000 people in the United States\textsuperscript{8} and 110,000 people in Europe have IPF.\textsuperscript{9} The cause is unknown, and there is no cure. A limited number of people with IPF undergo lung transplantation. IPF
inevitably causes shortness of breath and destruction of healthy lung tissue. Half of IPF people fail to survive just three years following diagnosis, and the five-year survival rate is approximately 20-30%.\(^\text{10}\) IPF typically occurs in people over the age of 45, and tends to affect more men than women.\(^\text{11,12}\)

**About Esbriet**

Esbriet is an oral medicine approved for the treatment of IPF and is available in more than 40 countries worldwide. The mechanism of action of Esbriet is not fully understood, although it is believed to interfere with the production of transforming growth factor (TGF)-beta, a small protein in the body involved in how cells grow and produce scars (fibrosis), and tumour necrosis factor (TNF)-alpha, a small protein that is involved in inflammation. Esbriet has Orphan Drug designation and was approved for use in Europe in 2011 in adults with mild-to-moderate IPF\(^\text{13}\) and in the US in people with IPF in October 2014.\(^\text{14}\) In early 2017, the U.S. Food and Drug Administration (FDA) approved the Esbriet 801 mg and 267 mg tablets as new options for administering the medicine for the treatment of IPF. The new 801 mg tablets, which are now available in the U.S., offer people with IPF a maintenance option for taking Esbriet with fewer pills per day.

Esbriet was initially approved for the treatment of IPF on the basis of the largest clinical trial programme in IPF to date, including three phase III trials (ASCEND and CAPACITY 004 and 006) with a total of 1,247 people with IPF. Esbriet has a well-established safety profile, the most common adverse events being related to the gastrointestinal tract (nausea, diarrhoea, dyspepsia), skin (rash and photosensitivity reaction), as well as fatigue and anorexia.
Esbriet is conditionally recommended for use in people with IPF in the ATS / ERS / JRS / ALAT treatment guidelines published in July 2015. Pirfenidone has been marketed as Pirespa since 2008 in Japan and since 2012 in South Korea by Shionogi & Co Ltd. Under different trade names, pirfenidone is also approved for the treatment of IPF in China, India, Argentina and Mexico. Roche acquired InterMune and its lead asset Esbriet in September 2014 and continues to expand access to Esbriet in more countries worldwide.

**About Roche in Respiratory Diseases**
Roche is committed to transforming care for people with severe respiratory diseases. The Roche Group's nearly 30 years of respiratory experience includes medicines such as Xolair® (omalizumab) in severe asthma marketed by Genentech in the US, Pulmozyme® (dornase alfa) for cystic fibrosis, and Esbriet® (pirfenidone) for idiopathic pulmonary fibrosis. Roche medicines Alecensa® (alectinib), Avastin® (bevacizumab), Tarceva® (erlotinib) and TECENTRIQ® (atezolizumab) are approved for the treatment of specific types of lung cancer.

**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. 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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References
1 Nathan SD, et al. 'Effect of Pirfenidone on All-Cause Mortality (ACM) and Forced Vital Capacity (FVC) in Idiopathic Pulmonary Fibrosis (IPF) Patients With Low FVC and/or Low DLCO: Analysis of Pooled Data From ASCEND and CAPACITY'. Presented at 113th Annual Conference of the American Thoracic Society (ATS), Washington, DC, USA, 19-24 May 2017.
9 European IPF Patient Charter. What is Idiopathic Pulmonary Fibrosis [Internet; cited 2017 May]. Available from: http://www.ipfcharter.org/what-is-ipf/