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Results of a six-month study combining Roche's Esbriet with nintedanib in patients with IPF presented at ERS

- **New study combining Esbriet (pirfenidone) and nintedanib showing similar safety profile for the combination treatment to that expected for each treatment alone**
- **A second, retrospective, post-hoc, analysis suggests that treatment with Esbriet may be associated with a reduction of multiple progression events as well as reduction of deaths after one or more progression events**
- **In a third study, in which real-world data from over 1,000 European patients was analysed, no new safety signals were observed**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced results of a six month study combining Esbriet (pirfenidone) and nintedanib treatment, showing a similar safety profile for the combination treatment to that expected for each treatment alone.¹ The majority of the 89 patients included in the study tolerated the combination treatment. The study further suggested that over the six month period, lung function change from baseline was small, and quality of life scores did not deteriorate in patients who completed the 6 months of combination treatment. Data were presented at the European Respiratory Society (ERS) congress 9-13 September in Milan, Italy.

“IPF is a devastating condition that progressively scars the lungs, leads to deteriorating lung function and makes it difficult to breathe,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “This study data assesses a combination treatment regimen where it was shown that the combination, based on Esbriet, was well tolerated”.

The majority of patients with IPF will be treated with either Esbriet or nintedanib. However, robust information regarding the safety and tolerability of the combination therapy was not available up until now.

For the combination study patients were given a stable dose of Esbriet for at least 16 weeks before initiation of nintedanib. 16.9% of patients experienced at least one treatment-emergent adverse event (TEAE) related to Esbriet only, compared to 74.2% of patients who experienced at least one TEAE that investigators attributed as related to nintedanib only. Importantly, combining Esbriet and nintedanib for 24 weeks did not reveal a different safety profile to that expected for either treatment alone.

Important efficacy parameters routinely assessed when measuring lung function in IPF, such as change from baseline forced vital capacity (FVC), diffusing capacity of the lungs for carbon monoxide (DLco) and King's brief interstitial lung disease (K-BILD) score, were assessed at 24 weeks as exploratory endpoints in the study. The results support Esbriet's known efficacy profile and suggest stability over time in K-BILD parameters in patients completing the 6 months combination treatment.

In a second new, post-hoc, analysis of pooled phase III trial studies, treatment with Esbriet showed that the number of progression events was reduced when patients received treatment with Esbriet compared to placebo (188/624 vs 106/623, $P < 0.0001$).² Progression events were defined as relative decline in % predicted FVC $\geq 10\%$, absolute decline in 6MWD ≥ 50 m; respiratory hospitalization, or death from any cause. There was also reduced mortality following one progression event when patients were treated with Esbriet, compared to placebo (39/624 vs 13/623, $P=0.0002$). These data support the continuation of treatment with Esbriet in case of disease progression.

A third study, involving real-world post-authorisation safety data from over 1,000 European patients receiving treatment with Esbriet and followed for up to 2 years, was also presented at ERS. The data of this real-world study showed that occurrence of adverse drug reactions (ADRs) was consistent with the known safety profile of Esbriet, with no new safety signals observed.³

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.⁴ The disease can advance quickly or slowly, but eventually the lungs will harden and stop working altogether.⁴ 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.⁵

Approximately 100,000 people in the United States⁶ and 110,000 people in Europe have IPF.⁷ 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. Untreated, half of IPF people fail to survive just three years following diagnosis, and the five-year survival rate is approximately 20-30%.⁸ IPF typically occurs in people over the age of 45, and tends to affect more men than women.^{9, 10}

About Esbriet

Esbriet is an oral medicine approved for the treatment of IPF and is available in approximately 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 IPF¹¹ and in the US in people with IPF in October 2014.¹² In 2017, the U.S. Food and Drug Administration (FDA) and the European Commission 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 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 2015.¹³ 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. 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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine 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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