

## **FDA grants Breakthrough Therapy Designation for Roche's Esbriet (pirfenidone) in unclassifiable interstitial lung disease**

- **There are currently no FDA-approved treatments for unclassifiable ILD (uILD), a debilitating, severe respiratory condition**
- **The designation is based on results from a Phase II trial, which suggested Esbriet slowed disease progression in patients with uILD<sup>[1]</sup> at 24 weeks.**

Basel, 3 March 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation (BTD) to Esbriet® (pirfenidone) for adults with unclassifiable interstitial lung disease (uILD). The designation was granted based on data from a Phase II trial, which studied the efficacy and safety of Esbriet in uILD<sup>[1]</sup>. The study represented the first randomised controlled trial to exclusively enroll patients with progressive fibrosing uILD.

“Today’s milestone for Esbriet builds on our continued commitment to improving the standard of care for people living with fibrotic lung diseases,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “We look forward to discussing the data with the FDA with the hope of bringing our important medicine to those with uILD who are currently without a treatment option.”

ILD is a term that broadly describes a diverse group of more than 200 types of rare pulmonary diseases. While ILDs share similar features, including cough and shortness of breath, each ILD has different causes, treatment approaches, and outlooks.<sup>[2]</sup> Approximately 10% of people living with ILD reviewed by a multidisciplinary team cannot be given a definitive diagnosis, even after a thorough investigation, and in these cases, patients are categorised as having uILD<sup>[3,4]</sup>.

The Phase II data supporting Breakthrough Designation were recently presented as a late-breaking abstract at the 2019 European Respiratory Society’s annual meeting and simultaneously published in *The Lancet Respiratory Medicine*<sup>[5,6]</sup>. The data suggested Esbriet slowed disease progression and supported its efficacy on a number of lung function parameters including forced vital capacity (FVC), in people with uILD. The safety and tolerability profile of Esbriet in people with uILD was comparable with that observed in Phase III trials in people with idiopathic pulmonary fibrosis (IPF).

Breakthrough Therapy Designation is designed to accelerate the development and review of medicines intended to treat serious or life-threatening conditions with preliminary evidence that indicates they may demonstrate a substantial improvement over existing therapies. This is the 33rd Breakthrough Therapy Designation for Roche’s portfolio of medicines.

### **About the Phase II study**

This international, multicentre, double-blind, randomised, placebo-controlled Phase II trial at 70 centres<sup>[5]</sup> included patients (aged  $\geq 18$ -85 years) with progressive fibrosing uILD, a percent predicted forced vital capacity (FVC) of 45% or higher and percent predicted carbon monoxide diffusing capacity (DLco) of 30% or higher, more than 10% fibrosis on high-resolution CT, and a high-resolution CT from the previous 12 months.<sup>[5]</sup>

The primary endpoint was mean predicted change in FVC from baseline over 24 weeks, measured by daily home spirometry.<sup>[5]</sup> Secondary endpoints were change in FVC measured by site spirometry, proportion of patients who had a more than 5% or more than 10% absolute or relative decline in percent predicted FVC measured by clinic-based spirometry, change in percent predicted DLco, change in 6-min walk distance (6MWD), change in University of California San Diego-Shortness of Breath Questionnaire (UCSD-SOBQ) score, change in Leicester Cough Questionnaire score, change in cough visual analogue scale, and changes in total and subscores of the St George's Respiratory Questionnaire (SGRQ), all of which were compared with baseline.<sup>[5]</sup>

Analysis of the primary endpoint was affected by intraindividual variability in home spirometry values, which prevented application of the prespecified statistical model to the primary endpoint assessment. Over 24 weeks, predicted median change in FVC measured by home spirometry was -87.7 mL (Q1-Q3 -338.1 to 148.6) in the pirfenidone group versus -157.1 mL (-370.9 to 70.1) in the placebo group. Over 24 weeks, predicted mean change in FVC measured by site spirometry was lower in patients given pirfenidone than placebo (treatment difference 95.3 mL,  $p=0.002$ ). Results for DLco and 6MWD generally trended in favour of pirfenidone treatment. Adverse event reporting reflected the known safety profile of pirfenidone. The most common treatment-related treatment-emergent adverse events were gastrointestinal disorders (47% in the pirfenidone group vs 26% in the placebo group), fatigue (13% vs 10%), and rash (10% vs 7%). Pirfenidone treatment was associated with less loss to lung function and exercise capacity compared with placebo over 24 weeks. The results of this study suggest that patients with progressive fibrosing uILD may benefit from pirfenidone therapy.

### **About Esbriet**

Esbriet is an oral medicine approved for the treatment of IPF and is available in more than 60 countries worldwide. Esbriet has Orphan Drug designation and was approved for use in Europe in 2011 in adults with mild-to-moderate IPF<sup>[7]</sup> and in the US in people with IPF in October 2014<sup>[8]</sup>. In early 2017, the US 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 US, offer people with IPF a maintenance option for taking Esbriet with fewer pills per day.

Esbriet is approved in Europe for the treatment of IPF on the basis of four Phase III, multicentre, randomised, double-blind, placebo-controlled studies in patients with IPF. Three of the Phase III studies (ASCEND<sup>[9]</sup> and CAPACITY 004 and 006<sup>[10]</sup>) were multinational, and one (SP3<sup>[11]</sup>) was conducted in Japan. Esbriet has an 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. Serious AEs, including elevated liver enzymes and drug-induced liver injury, photosensitivity reactions, and

gastrointestinal disorders, have been reported with Esbriet.

### **About Roche in Respiratory Diseases**

Our goal is to help improve the lives of people with severe respiratory diseases. With nearly 30 years of experience in this area, the recent acquisition of Promedior advances our ambition to transform care for people with severe respiratory diseases. Roche has delivered the first approved treatment for cystic fibrosis (Pulmozyme), the first biological therapy in allergic asthma and chronic idiopathic urticaria (Xolair) and the first approved medicine for idiopathic pulmonary fibrosis (IPF; Esbriet). Promedior's Phase III-ready asset PRM-151 received US FDA Breakthrough Therapy Designation based on Phase II trial results that suggested PRM-151 to be the first molecule in IPF to show a slowing of decline in lung function, when used in combination with standard of care (SoC) therapies, compared to SoC therapies alone. Roche's 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. 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 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 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](http://www.roche.com).

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### **Roche Investor Relations**

Dr. Karl Mahler

Phone: +41 61 68-78503

e-mail: [karl.mahler@roche.com](mailto:karl.mahler@roche.com)

Jon Kaspar Bayard

Phone: +41 61 68-83894

e-mail: [jon\\_kaspar.bayard@roche.com](mailto:jon_kaspar.bayard@roche.com)

Dr. Sabine Borngräber

Phone: +41 61 68-88027

e-mail: [sabine.borngraeber@roche.com](mailto:sabine.borngraeber@roche.com)

Dr. Bruno Eschli

Phone: +41 61 68-75284

e-mail: [bruno.eschli@roche.com](mailto:bruno.eschli@roche.com)

Dr. Birgit Masjost

Phone: +41 61 68-84814

e-mail: [birgit.masjost@roche.com](mailto:birgit.masjost@roche.com)

Dr. Gerard Tobin

Phone: +41 61 68-72942

e-mail: [gerard.tobin@roche.com](mailto:gerard.tobin@roche.com)

### **Investor Relations North America**

Loren Kalm

Phone: +1 650 225 3217

e-mail: [kalm.loren@gene.com](mailto:kalm.loren@gene.com)

Dr. Lisa Tuomi

Phone: +1 650 467 8737

e-mail: [tuomi.lisa@gene.com](mailto:tuomi.lisa@gene.com)