

Roche provides update on phase III studies of etrolizumab in people with moderately to severely active ulcerative colitis

- **Etrolizumab met its primary endpoint of inducing remission versus placebo for people with ulcerative colitis in only two of three studies**
- **Etrolizumab failed to meet its primary endpoint versus placebo as maintenance therapy in people with ulcerative colitis**
- **Analyses of these data are ongoing to better understand the results**
- **Pivotal phase III study of etrolizumab in Crohn's disease is ongoing**
- **Roche is studying additional investigational medicines in inflammatory bowel diseases**

Basel, 10 August 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced topline results from its phase III study programme evaluating the investigational medicine etrolizumab in people with moderately to severely active ulcerative colitis. Mixed results were seen in studies evaluating etrolizumab as an induction therapy, and both studies evaluating etrolizumab as a maintenance therapy failed to meet their primary endpoints, showing no significant difference in the proportion of people achieving remission with subcutaneous etrolizumab versus placebo.

In the HIBISCUS I induction study, in people without prior anti-tumour necrosis factor (anti-TNF) treatment, etrolizumab met the primary endpoint. In contrast, the HIBISCUS II induction study, which also included people without prior anti-TNF treatment, did not meet its primary endpoint. In the HICKORY study, in people with prior anti-TNF treatment, etrolizumab met the primary endpoint at induction but not at maintenance. In the LAUREL maintenance study in people without prior anti-TNF treatment, etrolizumab failed to meet its primary endpoint. The safety profile of etrolizumab was consistent with previous studies and no major safety issues were identified in the four phase III clinical trials reported to date.

“We are disappointed with these results, because we know that people with ulcerative colitis need new treatment options,” said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. “We are fully analysing these data to learn more about how we might address the needs of people with this devastating disease. These studies were part of the largest clinical trial programme ever undertaken in inflammatory bowel diseases, and we thank all the patients, investigators and healthcare professionals for their participation.”

Further analyses of the data, including secondary endpoints, are ongoing and will be submitted for presentation at upcoming medical meetings.

Etrolizumab continues to be studied as an investigational induction and maintenance treatment in people with moderately to severely active Crohn's disease with and without prior anti-TNF treatment in a global phase III study (BERGAMOT) and open-label extension and safety monitoring study (JUNIPER), involving more than 1,100 people with Crohn's disease. In addition, Roche is studying other investigational medicines

in inflammatory bowel diseases and is committed to further understanding this disease.

About inflammatory bowel diseases and ulcerative colitis

Inflammatory bowel diseases (IBD) are a group of chronic gastrointestinal disorders affecting almost 7 million people worldwide.¹ The two main types of IBD are ulcerative colitis (mainly affecting the colon and rectum) and Crohn's disease (affecting the entire gastrointestinal tract).^{2,3} Patients can experience unpredictable symptoms that include abdominal pain and cramping, frequent and urgent bowel movements, diarrhoea, leakage, rectal bleeding, weight loss, energy loss and fatigue.^{2,3} About 80% of all individuals with IBD do not experience lasting remission, which can have a long-term impact on quality of life and leave many feeling like they have little control over their daily lives.⁴

Ulcerative colitis is most commonly diagnosed in young people aged 15 to 30 years, affecting them over the course of their entire future lives.⁵ Up to a quarter of people with ulcerative colitis will require a colectomy within 10 years of diagnosis, in which all or part of the colon is removed.⁶

About etrolizumab

Etrolizumab is the first investigational dual anti-integrin studied in inflammatory bowel diseases (IBD). It is designed to target IBD on two fronts by selectively inhibiting $\alpha 4\beta 7$ and $\alpha E\beta 7$ to control both trafficking of immune cells into the gut and their inflammatory effects on the gut lining.⁷

About the etrolizumab study programme

Etrolizumab is being studied in the largest clinical trial programme in inflammatory bowel diseases to date, comprised of eight randomised-controlled and open-label trials.⁸⁻¹⁵ The landmark study programme includes more than 3,100 patients across six phase III studies, plus two open-label extension (OLE) and safety monitoring studies for ulcerative colitis and Crohn's disease, spanning more than 40 countries globally, including head-to-head trials against the most common current treatments.

The etrolizumab study programme consists of:

- **Phase III HIBISCUS I and II:** Two identical, randomised, double-blind, double-dummy, placebo-controlled, multicentre studies evaluating the efficacy (induction of remission) and safety of etrolizumab versus adalimumab and placebo in patients with moderately to severely active ulcerative colitis who have not been previously treated with anti-tumour necrosis factor (anti-TNF) agents^{8,9}
- **Phase III LAUREL:** Randomised, double-blind, placebo-controlled, multicentre study evaluating the efficacy (maintenance of remission) and safety of etrolizumab in patients with moderately to severely active ulcerative colitis who have not been previously treated with anti-TNF agents¹⁰
- **Phase III GARDENIA:** Randomised, multicentre double-blind, double-dummy study evaluating the efficacy (sustained remission) and safety of etrolizumab versus infliximab in patients with moderately to severely active ulcerative colitis who have not been previously treated with anti-TNF agents¹¹
- **Phase III HICKORY:** Double-blind, placebo-controlled, multicentre study evaluating the efficacy and safety of etrolizumab during induction and maintenance in patients with moderately to severely active ulcerative colitis who have been previously treated with anti-TNF agents¹²

- **COTTONWOOD study:** An open-label extension and safety monitoring study of patients with moderately to severely ulcerative colitis previously enrolled in etrolizumab phase II/III studies¹³
- **Phase III BERGAMOT:** A phase III, randomised, double-blind, placebo-controlled, multicentre study evaluating the efficacy and safety of etrolizumab as an induction and maintenance treatment in patients with moderately to severely active Crohn's disease¹⁴
- **JUNIPER study:** An open-label extension and safety monitoring study of patients with moderately to severely active Crohn's disease previously enrolled in the etrolizumab phase III BERGAMOT study¹⁵

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.

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