Phase III prevention trial showed subcutaneous administration of investigational antibody cocktail casirivimab and imdevimab reduced risk of symptomatic COVID-19 infections by 81%

- **Among individuals who still experienced symptomatic infections, those who received casirivimab and imdevimab were able to clear the virus faster and had much shorter symptom duration**
- **In a cohort of recently-infected asymptomatic patients, casirivimab and imdevimab reduced the overall risk of progressing to symptomatic COVID-19 by 31%**
- **Detailed results will be shared with regulatory authorities including the EMA and the FDA**

Basel, 12 April 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today confirmed positive results from the phase III REGN-COV 2069 trial assessing the ability of the investigational antibody cocktail casirivimab and imdevimab to reduce the risk and burden of COVID-19 infection among household contacts of SARS-CoV-2 infected individuals. The trial, which was jointly run with the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), met its primary and key secondary endpoints. It showed that the subcutaneous administration of casirivimab and imdevimab reduced the risk of symptomatic infections by 81% in those who were not infected when they entered the trial. In addition, individuals treated with casirivimab and imdevimab who still experienced a symptomatic infection resolved their symptoms on average within one week, compared to three weeks with placebo. No new or serious safety signals were observed.

"Today's data confirm the potential dual value of casirivimab and imdevimab to reduce household COVID-19 infections and to decrease the disease burden in those who do become infected, when given as a subcutaneous option," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Although vaccinations are increasing globally, there remains a critical unmet need worldwide to prevent infections and provide immediate protection from COVID-19 between close contacts. This is why we are excited to bring this data to health authorities with the goal of making the combination available to more people as soon as possible."

The phase III, double-blind, placebo-controlled trial assessed the effect of casirivimab and imdevimab on individuals without SARS-CoV-2 antibodies or any COVID-19 symptoms, who lived in the same household as an individual who tested positive to SARS-CoV-2 within the prior four days. It included 1,505 people who were not infected with SARS-CoV-2 at baseline and received either one dose of casirivimab with imdevimab (1,200 mg) or placebo, administered as subcutaneous injections.

In addition, the multi-part study evaluated the antibody cocktail in a cohort of 204 recently infected asymptomatic patients randomised to receive either one dose of casirivimab and imdevimab (1,200 mg subcutaneous administration) or placebo. In this cohort, casirivimab and imdevimab reduced the overall risk of progressing to symptomatic COVID-19 by 31%.

Detailed results from the trial will be shared with regulatory authorities as soon as possible. Regeneron will share new data with the United States (U.S.) Food and Drug Administration (FDA) and Roche and Regeneron will continue to work with the European Medicines Agency (EMA) and other health authorities across the globe.

The antibody cocktail continues to be evaluated in clinical trials in multiple settings for COVID-19: in non-hospitalised and certain hospitalised patients, including the open-label RECOVERY trial of hospitalised patients in the UK. As of April 2021, more than 25,000 people have participated in clinical trials involving casirivimab and imdevimab.

In these exceptional times, Roche stands together with society, governments, healthcare providers and all those working to overcome the pandemic.

Table 1: Key results from phase III prevention cohort in uninfected individuals*

	Casirivimab and imdevimab (1,200 mg subcutaneous dose)	**Placebo**
	n=753	**n=752**
Proportion of subjects with symptomatic SARS-CoV-2 infections through day 29 (primary endpoint)		
Risk reduction	**81% (p<0.0001)**	
# of patients with events	**11 (1.5%)**	**59 (7.8%)**
Symptoms and viral load		
Total weeks with symptoms		
Reduction	**93% (p<0.0001)**	
Total # of weeks (cumulative for all individuals in each arm)	**13**	**188**

# of weeks with symptoms (mean) in symptomatic individuals	**1.2**	**3.2**
Total weeks with high viral load (>10^4 copies/mL)		
Reduction	**90% (p<0.0001)**	
Total # of weeks (cumulative for all individuals in each arm)	**14**	**136**
# of weeks with high viral load (mean) in qPCR positive subjects	**0.4**	**1.3**

***Individuals without any COVID-19 symptoms who lived in the same household as an individual who tested positive to SARS-CoV-2 within the prior four days. Based on the seronegative modified Full Analysis Set population, which includes all randomized subjects without evidence of current or prior SARS-CoV-2 infection (i.e., a negative RT-qPCR test and a negative antibody test) at randomization.**

Adverse events (AEs) occurred in 20% (n=265 out of 1,311) of REGEN-COV participants and 29% (n=379 out of 1,306) of placebo participants, and serious AEs occurred in 1% (n=10) of REGEN-COV participants and 1% (n=15) of placebo participants. There were 0 REGEN-COV participants and 4 placebo participants who were either hospitalized or visited the emergency room because of COVID-19 during the 29-day efficacy assessment period. Injection site reactions, all of which were grades 1-2, occurred in 4% (n=55) of REGEN-COV participants and 2% (n=19) of placebo participants. No individuals from either group withdrew from the trial due to AEs, and none of the deaths in the trial (2 REGEN-COV, 2 placebo) were attributed to COVID-19 or study drug.

Table 2: Key results from phase III treatment cohort in asymptomatic infected individuals

	Casirivimab and imdevimab (single 1,200 mg dose)	Placebo
	n=100	n=104
Proportion of subjects with symptomatic SARS-CoV-2 infections through day 29 (primary endpoint)		
Risk reduction	31% (p=0.0380)	
# of patients with events (cumulative for all individuals in each arm)	29 (29%)	44 (42%)
Symptoms, viral load and COVID-19 related events		
Total weeks with symptoms		
Reduction	45% (p=0.0273)	
Total # of weeks (cumulative for all individuals in each arm)	90	170
Total weeks with high viral load (>10^4 copies/mL)		
Reduction	40% (p=0.001)	
Total # of weeks	48	82

Based on the seronegative modified Full Analysis Set population, which includes all randomized asymptomatic patients who were SARS-CoV-2 positive but had no evidence of prior infection (i.e., a positive RT-qPCR test and a negative antibody test) at randomization

Adverse events (AEs) occurred in 34% (n=52 out of 155) of REGEN-COV patients and 48% (n=75 out of 156) of placebo patients, and serious AEs occurred in 0% (n=0) of REGEN-COV patients and 3% (n=4) of placebo patients. Injection site reactions, all of which were grades 1-2, occurred in 4% (n=6) of REGEN-COV patients and 1% (n=1) of placebo patients. No patients from either group withdrew from the trial due to AEs, and there were no deaths.

About REGN-COV 2069
REGN-COV 2069 is a phase III, randomised, double-blind, placebo-controlled multi-part study assessing the efficacy and safety of casirivimab and imdevimab in preventing symptomatic infection in household contacts of individuals infected with COVID-19.

In January 2021, initial data from the trial showed that there was a reduction in overall infections seen with casirivimab and imdevimab within the first week, with approximately 50% lower overall rates of infection (symptomatic and asymptomatic) and 100% prevention of symptomatic infections. Casirivimab and imdevimab showed efficacy when administered via a low-dose (1,200 mg) subcutaneous route.

In the safety assessment of these patients, adverse events occurred more frequently in participants on placebo during the efficacy analysis period (12% in the casirivimab and imdevimab group and 18% in the placebo group) and during the follow-up period (11% in the casirivimab and imdevimab group and 20% in the placebo group).

About casirivimab and imdevimab
Casirivimab and imdevimab is a cocktail of two monoclonal antibodies (also known as REGN10933 and REGN10987, respectively) and was designed by Regeneron scientists to block infectivity of SARS-CoV-2, the virus that causes COVID-19. They evaluated thousands of fully-human antibodies produced by the company's proprietary VelocImmune® mice, which have been genetically modified to have a human immune system, as well as antibodies identified from humans who have recovered from COVID-19.

The two potent, virus-neutralising antibodies casirivimab and imdevimab are believed to bind non-competitively to the critical receptor binding domain of the virus's spike protein, which is hypothesised to diminish the ability of mutant viruses to escape treatment and to protect against spike variants that may arise in the human population, as detailed in Science publications.

The cocktail of casirivimab and imdevimab has not been granted a marketing authorisation by any health authority. In November 2020, the antibody cocktail was authorised by the United States (U.S.) Food and Drug Administration (FDA) under an Emergency Use Authorization (EUA) for the treatment of mild to moderate COVID-19 in adults and paediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalisation. The US EUA is temporary and does not take the place of the formal biologics license application (BLA) submission, review and approval process.

In February 2021, the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) issued a scientific opinion under Article 5(3) of Regulation 726/2004 supporting the use of casirivimab and imdevimab as a treatment option for patients with confirmed COVID-19 who do not require oxygen supplementation and who are at high risk of progressing to severe COVID-19. The scientific opinion can be considered by EU member states when making decisions on the use of medicines at a national level before a formal authorisation is issued. The review under Article 5(3) was separate, but ran in parallel to the rolling review of casirivimab and imdevimab, which is currently ongoing by the EMA.

Casirivimab and imdevimab's development, manufacturing and clinical trials have been funded in part by the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response at the US Department of Health and Human Services under OT number: HHSO100201700020C.

About U.S. FDA EUA status

Casirivimab and imdevimab have not been Food and Drug Administration (FDA) cleared or approved in the United States (US). It has been authorised by the FDA under an Emergency Use Authorization (EUA) during the current public health emergency for the treatment of mild to moderate COVID-19 in adults and paediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalisation. Please see the Fact Sheet for Healthcare Providers for more information, including important safety information. The cocktail is only authorised for the duration of the declaration that circumstances exist justifying the authorisation of the emergency use under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb3(b)(1), unless the declaration is terminated or authorisation revoked sooner.

About Roche's response to the COVID-19 pandemic

As a leading healthcare company we are doing all we can to support countries in their fight against COVID-19 and minimising its impact. We have developed a growing number of diagnostic solutions that help to detect and diagnose the infection, as well as providing digital support to healthcare systems. We also continue to identify, develop and support potential therapies which can play a role in treating the disease.

The impact of COVID-19 goes beyond those who contract it. That is why we are working with healthcare providers, laboratories, authorities and organisations to help make sure patients continue to receive the tests, treatment and care they need during these challenging times. Building on a longstanding tradition of partnerships, we are working together with governments and others to make healthcare stronger and more sustainable in the future.

Reliable, high-quality testing is essential to help healthcare systems overcome this pandemic and Roche has so far launched 16 diagnostics solutions to help minimise the impact of COVID-19. As soon as the novel SARS-CoV-2 virus was sequenced in early 2020, we got to work. On 13 March 2020 we became the first

company to receive U.S. Food and Drug Administration (FDA) Emergency Use Authorization (EUA) for a high-volume molecular test to detect the virus. Since then, we have continued to add a range of diagnostics solutions to our global portfolio to help in the fight against COVID-19. In addition to the gold standard PCR test, we have developed antigen tests to help diagnose the virus in settings where there is limited molecular laboratory infrastructure, rapid antigen where the virus can be detected on the spot, tests that can test for both flu and COVID-19 at the same time, both high throughput and at the point of care, and tests that can detect virus antibodies that can help monitor the spread of the virus and can also support in vaccine development. On 16 March 2021 the SARS-CoV-2 variant test was launched, designed to detect key spike mutations.

Aside from these tests we have also looked at how we can support care for patients who have COVID-19, receiving an FDA EUA for the Elecsys® IL-6 test to assist in identifying severe inflammatory response in patients with confirmed COVID-19, as well as launching Roche v-TAC, a digital algorithm that could help simplify the screening, diagnosis and monitoring of respiratory-compromised patients with COVID-19. Roche is working closely with governments and health authorities around the world, and has significantly increased production to support availability of tests globally.

Roche is actively involved in understanding the potential of the existing portfolio and is researching options for the future. In 2020, Roche entered into a number of new partnerships, including with Gilead, Regeneron and Atea, to develop, manufacture and distribute molecules that can potentially both treat and prevent COVID-19.

In October, Roche announced a partnership with Atea Pharmaceuticals to jointly develop the investigational compound AT-527. If approved, Atea will distribute AT-527 in the United States (US) and Roche will be responsible for global manufacturing and distribution outside the US. Atea's compound has the potential to be the first oral antiviral to treat COVID-19 patients outside the hospital setting as well as in the hospital. Its anticipated formulation (pill) could allow for large-scale manufacturing and may help to facilitate access to a broad patient population.

In November, our partner Regeneron received FDA EUA for casirivimab and imdevimab, its investigational antiviral antibody combination, for the treatment of recently diagnosed patients with mild to moderate COVID-19 who are at high risk of progressing to severe COVID-19 and/or hospitalisation. The antibody cocktail is currently being studied in two phase I-III adaptive clinical trials for the treatment of COVID-19 and in a phase III trial for the prevention of the disease. As part of the global partnership with Regeneron, we are committing a significant amount of manufacturing capacity and are working to expand supply of this antibody combination beyond the US to as many people as possible.

In addition, we are exploring the potential of our investigational molecules and existing portfolio: For example, Roche has initiated three global phase III clinical trials investigating the safety and efficacy of Actemra/RoActemra in COVID-19 associated pneumonia (COVACTA, EMPACTA and REMDACTA).

Following initial interactions with health authorities, Roche will continue to monitor the evolving clinical evidence for Actemra/RoActemra in this setting.

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 twelfth 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 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 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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