New phase III data shows investigational antibody cocktail casirivimab and imdevimab reduced hospitalisation or death by 70% in non-hospitalised patients with COVID-19

- **Investigational antibody cocktail of casirivimab and imdevimab also significantly shortened the duration of symptoms by four days**
- **The 2,400 mg and 1,200 mg doses tested in the phase III study had similar efficacy across all endpoints**
- **Companion dose-ranging phase II trial showed significant and comparable viral reductions for a range of doses of casirivimab and imdevimab**
- **The combination of casirivimab and imdevimab is the only monoclonal antibody treatment to retain potency against key emerging variants, based on the recently updated EUA guidance from the U.S. FDA[1]**

Basel, 23 March 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today confirmed positive topline results from the largest trial to date assessing a COVID-19 treatment in infected non-hospitalised patients (n=4,567; REGN-COV 2067). The phase III outcomes trial in high-risk non-hospitalised patients with COVID-19 met its primary endpoint, showing the investigational antibody cocktail of casirivimab and imdevimab significantly reduced the risk of hospitalisation or death by 70% (1,200 mg intravenously [IV]) and 71% (2,400 mg IV) compared to placebo.

Casirivimab and imdevimab also met all key secondary endpoints in the phase III REGN-COV 2067 trial, including the ability to reduce symptom duration from 14 to 10 days (median numbers). In addition, a companion phase II trial (REGN-COV 20145) in low risk symptomatic or asymptomatic non-hospitalised patients with COVID-19 showed significant and comparable viral load reductions across doses ranging from 300 to 2,400 mg.

“Today's results show the important medical benefit casirivimab and imdevimab may provide to people with COVID-19 by significantly reducing their risk of hospitalisation and death,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “New infections continue to rise globally with over three million reported cases last week, so this investigational antibody cocktail may offer hope as a potential new therapy to high-risk patients - particularly in light of recent evidence showing that casirivimab and imdevimab together retain activity against key emerging variants. Together with our partner Regeneron, we are grateful to the patients and investigators who have participated in ongoing clinical trials and look forward to discussing the growing body of evidence with health authorities and to bringing the treatment to as many people as possible."

In addition to these trials in non-hospitalised patients, the investigational antibody cocktail of casirivimab and imdevimab is currently being studied in a phase II/III clinical trial for the treatment of COVID-19 in hospitalised patients, the phase III open label RECOVERY trial of hospitalised patients in the UK, and a

phase III trial for the prevention of COVID-19 in household contacts of infected individuals. As of March 2021, approximately more than 25,000 people have participated in casirivimab and imdevimab clinical trials.

Detailed results from both trials (REGN-COV 2067 and REGN-COV 20145) will be shared with regulatory authorities and submitted for peer review as soon as possible. Regeneron will share new data with the 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. Earlier this year, the EMA's Committee for Medicinal Products for Human Use 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.

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

Key results from phase III REGN-COV 2067 trial in non-hospitalised patients[1-3]

	1,200 mg IV n=736	**Placebo n=748**	**2,400 mg IV n=1,355**	**Placebo n=1,314**
Patients with ≥1 COVID-19-related hospitalization or death through day 29				
Risk reduction	**70% (p=0.0024)**		**71% (p<0.0001)**	
Number of patients with events	**7 (1.0%)**	**24 (3.2%)**	**18 (1.3%)**	**62 (4.6%)**
Time to COVID-19 symptom resolution				
Median reduction (days)	**4 (p<0.0001)**		**4 (p<0.0001)**	
Median (days)	**10**	**14**	**10**	**14**

1. Based on the mFAS population, which includes all randomised patients with a positive SARS-CoV-2 RT-qPCR test from NP swabs at randomisation and ≥1 risk factor for severe COVID-19.

2. The formal hierarchical analysis first evaluated 2,400 mg dose versus concurrent placebo and then evaluated 1,200 mg dose versus concurrent placebo.

3. Based on phase I/II analyses showing that the 8,000 mg and 2,400 mg doses were indistinguishable, the phase III protocol was amended to compare 2,400 mg and 1,200 mg versus placebo, and 8,000 mg data were converted to a descriptive analysis.

A safety assessment was conducted on all available patient data up to day 169, and identified no new safety signals. Serious adverse events (SAEs) were largely related to COVID-19 and occurred in 1.1% of patients in the 1,200 mg group, 1.3% in the 2,400 mg group and 4.0% in the placebo groups. There was one death in the 1,200 mg group (n=827), one death in the 2,400 mg group (n=1,849) and five deaths in the placebo groups (n=1,843).

All patients in this analysis had at least one risk factor, including obesity (58%), age 50 years (51%) and cardiovascular disease, including hypertension (36%). Approximately 35% of patients were Latino/Hispanic, 5% were Black/African American and the median age was 50 years (range: 18-96 years). The phase III REGN-COV 2067 trial in non-hospitalised patients was previously amended to stop enrollment in the placebo group, following a recommendation from the Independent Data Monitoring Committee, which found clear efficacy for both doses.

About the REGN-COV 2067 trial
REGN-COV 2067 [NCT04425629] is a phase I-III adaptive, randomised, placebo-controlled, double-blind, clinical trial to evaluate the efficacy, safety and tolerability of casirivimab and imdevimab compared to placebo for the treatment of non-hospitalised adult patients with COVID-19. The objective of the confirmatory phase III trial in 4,567 patients was to prospectively demonstrate clinically significant effect on risk of COVID-19 hospitalisation or all-cause death in high-risk non-hospitalised patients, and confirm safety. The trial also prospectively evaluated potential benefit on symptom duration. The patient population included adult, non-hospitalised patients with COVID-19 with a symptom onset ≤7 days from randomisation. Patients were SARS-CoV-2 confirmed by molecular testing ≤72 hours from randomisation and not on any putative COVID-19 therapies. The trial design originally compared 8,000 mg and 2,400 mg versus placebo, and was amended to evaluate 2,400 mg and 1,200 mg versus placebo.

Initial data from the phase II portion of the study met primary and key secondary endpoints, showing a reduction in viral load and a decrease in medically-attended visits in non-hospitalised patients with COVID-19. These data were from two analyses of 799 symptomatic patients who received either casirivimab and imdevimab or placebo added to standard of care. The investigational antibody cocktail was also generally found to be well-tolerated.

About the REGN-COV 20145 trial
REGN-COV 20145 [NCT04666441] is a phase II randomised study to assess the antiviral effect of casirivimab and imdevimab across different intravenous and subcutaneous doses compared to placebo in 803 non-hospitalised low risk and asymptomatic adult patients with COVID-19. The primary endpoint is time-weighted average daily change from baseline in viral load, with key secondary endpoints including additional

indicators of virology efficacy, safety and tolerability, concentrations of the antibodies in serum over time and the immunogenicity of the antibody cocktail against placebo. All tested doses met the primary endpoint, rapidly and significantly reducing patients' viral load (log10 copies/mL) compared to placebo ($p<0.001$), with all doses demonstrating similar efficacy.

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 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). They have 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 and in a phase III trial for the prevention of COVID-19. 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.

References

[1] U.S. Food and Drug Administration: Fact sheet for health care providers Emergency Use Authorization (EUA) of REGEN-COV2™ (casirivimab with imdevimab) [Internet; cited March 2021] Available from: https://www.fda.gov/media/145611/download

Roche Group Media Relations
Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

Dr. Nicolas Dunant
Phone: +41 61 687 05 17

Patrick Barth
Phone: +41 61 688 44 86

Dr. Daniel Grotzky
Phone: +41 61 688 31 10

Karsten Kleine
Phone: +41 61 682 28 31

Nina Mählitz
Phone: +41 79 327 54 74

Nathalie Meetz
Phone: +41 61 687 43 05

Dr. Barbara von Schnurbein
Phone: +41 61 687 89 67

Roche Investor Relations

Dr. Karl Mahler
Phone: +41 61 68-78503
e-mail: karl.mahler@roche.com

Jon Kaspar Bayard
Phone: +41 61 68-83894
e-mail: jon_kaspar.bayard@roche.com

Dr. Sabine Borngräber
Phone: +41 61 68-88027

Dr. Bruno Eschli
Phone: +41 61 68-75284

e-mail: sabine.borngraeber@roche.com

e-mail: bruno.eschli@roche.com

Dr. Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Dr. Gerard Tobin
Phone: +41 61 68-72942
e-mail: gerard.tobin@roche.com

Investor Relations North America

Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com

Dr. Lisa Tuomi
Phone: +1 650 467 8737
e-mail: tuomi.lisa@gene.com