Phase 3 Prevention Trial Showed 81% Reduced Risk of Symptomatic SARS-CoV-2 Infections with Subcutaneous Administration of REGEN-COV™ (casirivimab with imdevimab)

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REGEN-COV rapidly protected household contacts from exposure to SARS-CoV-2 at home, with 72% protection against symptomatic infections in the first week, and 93% in subsequent weeks

Among individuals who developed symptomatic infections, REGEN-COV recipients cleared the virus faster and had much shorter symptom duration

Regeneron will share data with U.S. FDA and request EUA expansion to include COVID prevention for appropriate populations, using a 1,200 mg subcutaneous dose

Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive results from a Phase 3 trial (2069A) assessing the ability of REGEN-COV™ (casirivimab with 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, showing that REGEN-COV 1,200 mg administered subcutaneously (SC) reduced the risk of symptomatic infections by 81% in those who were not infected when they entered the trial.

"These data suggest that REGEN-COV can complement widespread vaccination strategies, particularly for those at high risk of infection. Importantly, to date REGEN-COV has been shown *in vitro* to retain its potency against emerging COVID-19 variants of concern," said Myron Cohen, M.D., who leads the monoclonal antibody efforts for the NIH-sponsored COVID Prevention Network (CoVPN) and is Director of the Institute for Global Health & Infectious Diseases at the University of North Carolina at Chapel Hill. "Despite standard precautions to reduce transmission, nearly 10% of unvaccinated individuals living with an infected person developed symptomatic infections if they did not receive REGEN-COV. If authorized, convenient subcutaneous administration of REGEN-COV could help control outbreaks in high-risk settings where individuals have not yet been vaccinated, including individual households and group living settings."

The Phase 3, double-blind, placebo-controlled trial assessed the effect of REGEN-COV on uninfected individuals without anti-SARS-CoV-2 antibodies or any COVID-19 symptoms, who lived in the same household as an individual who tested positive for SARS-CoV-2 within the prior 4 days. The trial enrolled 1,505 people who were not infected with SARS-CoV-2 at baseline and randomized to receive either 1 dose of REGEN-COV (1,200 mg) or placebo, administered as SC injections.

"These findings are very encouraging and suggest that REGEN-COV is highly effective at preventing symptomatic COVID-19 in household contacts of SARS-CoV-2 infected individuals," said Dan H. Barouch, M.D., Ph.D., co-principal investigator of the trial and Director of the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center and Professor of Medicine at Harvard Medical School. "The rapid and robust protection, together with the subcutaneous route of administration, support the practical utility of these antibodies in protecting against COVID-19 in multiple settings, including after high-risk exposures. These antibodies may be particularly useful in individuals who are not yet vaccinated, and may also have potential in those who are immunosuppressed and may not respond well to vaccines."

On average, individuals treated with REGEN-COV who experienced a symptomatic infection resolved their symptoms in 1 week, compared to 3 weeks with placebo. Infected individuals also cleared the virus faster with REGEN-COV.

"With more than 60,000 Americans continuing to be diagnosed with COVID-19 every day, the REGEN-COV antibody cocktail may help provide immediate protection to unvaccinated people who are exposed to the virus, and we are also working to understand its potential to provide ongoing protection for immunocompromised patients who may not respond well to vaccines," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. "We thank the individuals, investigators and our collaborators involved in the trial, and look forward to rapidly discussing these results with regulatory authorities."

TABLE: Key Results from Phase 3 Trial for the Prevention of COVID-19 in Uninfected Individuals[1]

	REGEN-COV (single 1,200 mg dose)	**Placebo**
	n=753	n=752
Risk of symptomatic SARS-CoV-2 infection		
Through day 29 (primary endpoint)		
Risk reduction	81% (p<0.0001)	
# of patients with events	11 (1.5%)	59 (7.8%)
Within 1 week[2]		
Risk reduction	72% (nominal p=0.0002)	
# of individuals with events	9 (1.2%)	32 (4.3%)

Post-1 week[2]		
Risk reduction	93% (nominal p<0.0001)	
# of individuals with events	2 (0.3%)	27 (3.6%)
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 (average) 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 (average) in qPCR positive subjects	0.4	1.3

1. 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
2. These analyses were not part of the pre-planned statistical analysis plan, so p-values are nominal

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 and 1% (n=15) of placebo participants. There were 0 REGEN-COV 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 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.

REGEN-COV continues to be evaluated in clinical trials in multiple settings for COVID-19: for the prevention of COVID-19 in household contacts of infected individuals, and in non-hospitalized and certain hospitalized patients, including the open-label RECOVERY trial of hospitalized patients in the UK. As of April 2021, more than 25,000 people have participated in clinical trials involving REGEN-COV.

The development and manufacturing of REGEN-COV have been funded in part with federal funds from the Biomedical Advanced Research and Development Authority (BARDA), part of the U.S. Department of Health and Human Services, Office of the Assistant Secretary for Preparedness and Response, under OT number: HHSO100201700020C.

About the Multi-part Phase 3 Trial
To qualify for the joint Regeneron/NIAID multi-part Phase 3 trial, all participants were enrolled without any COVID-19 symptoms (asymptomatic) and lived in the same household as an individual who tested positive for SARS-CoV-2 within the prior 4 days. All participants were tested for SARS-CoV-2 at baseline using a RT-qPCR test from nasopharyngeal swabs. Participants with a negative test result joined the prevention trial (2069A) and participants with a positive test result joined the treatment trial (2069B).

All participants were then randomized (1:1) to receive either 1 dose of REGEN-COV (1,200 mg) or placebo, administered via 4 SC injections.

Among participants enrolled in the prevention trial, 41% were Latino/Hispanic and 9% were Black/African American. In total, 31% of participants had at least one known factor that put them at high risk of suffering severe consequences from COVID-19, as defined in the REGEN-COV fact sheet. In addition, 33% were obese and 38% were aged ³50 years (median age: 44 years; range: 12-92 years).

About the REGEN-COV Antibody Cocktail
REGEN-COV (casirivimab with imdevimab) is a cocktail of two monoclonal antibodies (also known as REGN10933 and REGN10987) that was designed specifically to block infectivity of SARS-CoV-2, the virus that causes COVID-19, using Regeneron's proprietary *VelocImmune*® and *VelociSuite*® technologies. The two potent, virus-neutralizing antibodies that form the cocktail bind non-competitively to the critical receptor binding domain of the virus's spike protein, which diminishes the ability of mutant viruses to escape treatment and protects against spike variants that have arisen in the human population, as detailed in *Science*.

Under an EUA issued by the U.S. Food and Drug Administration (FDA), REGEN-COV is currently available in the U.S. to treat mild-to-moderate COVID-19 in adults, as well as in pediatric patients at least 12 years of age and weighing at least 40 kg, who have received positive results of direct SARS-CoV-2 viral testing and are at high risk for progressing to severe COVID-19 and/or hospitalization. REGEN-COV has not been approved by the FDA but has been authorized for emergency use. This use is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

REGEN-COV is currently authorized and available in a 2,400 mg IV dose, with infusion times as short as 20 minutes. The criteria for 'high-risk' patients are described in the Fact Sheet for Healthcare Providers. In the U.S., REGEN-COV is not authorized for use in patients who are hospitalized due to COVID-19 or require oxygen therapy, or for people currently using chronic oxygen therapy because of an underlying comorbidity who require an increase in baseline oxygen flow rate due to COVID-19.

Under this EUA, REGEN-COV is available throughout the U.S. – information on availability in your area is available from the Department of Health and Human Services and the National Infusion Center Association.

Regeneron is collaborating with Roche to increase global supply of REGEN-COV. Regeneron is responsible for development and distribution of the treatment in the U.S., and Roche is primarily responsible for development and distribution outside the U.S. The companies share a commitment to making the antibody cocktail available to COVID-19 patients around the globe and will support access in low- and lower-middle-income countries through drug donations to be made in partnership with public health organizations.

About Regeneron's *VelocImmune* Technology

Regeneron's *VelocImmune* technology utilizes a proprietary genetically engineered mouse platform endowed with a genetically humanized immune system to produce optimized fully human antibodies. When Regeneron's co-Founder, President and Chief Scientific Officer George D. Yancopoulos was a graduate student with his mentor Frederick W. Alt in 1985, they were the first to envision making such a genetically humanized mouse, and Regeneron has spent decades inventing and developing *VelocImmune* and related *VelociSuite* technologies. Dr. Yancopoulos and his team have used *VelocImmune* technology to create approximately a quarter of all original, FDA-approved fully human monoclonal antibodies currently available. This includes REGEN-COV™ (casirivimab with imdevimab), Dupixent® (dupilumab), Libtayo® (cemiplimab-rwlc), Praluent® (alirocumab), Kevzara® (sarilumab), Evkeeza™ (evinacumab-dgnb) and Inmazeb™ (atoltivimab, maftivimab and odesivimab-ebgn).

AUTHORIZED USE AND IMPORTANT SAFETY INFORMATION

Authorized Emergency Use

REGEN-COV, (casirivimab with imdevimab to be administered together) is authorized for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric 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 hospitalization. [see Limitations of Authorized Use]

- REGEN-COV has not been approved, but has been authorized for emergency use by FDA
- This use is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner
- Healthcare providers should review the **Fact Sheet for Healthcare Providers** for information on the authorized use of REGEN-COV and mandatory requirements of the EUA and must comply with the requirements of the EUA. The **FDA Letter of Authorization** is available for reference**,** as well as the **Dear Healthcare Provider Letter** and **Patient Fact Sheet**

Limitations of Authorized Use

- REGEN-COV (casirivimab with imdevimab) is not authorized for use in patients:
  - who are hospitalized due to COVID-19, OR
  - who require oxygen therapy due to COVID-19, OR
  - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity
- Benefit of treatment with REGEN-COV has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as REGEN-COV, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Definition of High-Risk Patients

High-risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders (e.g., cerebral palsy), OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

Circulating SARS-CoV-2 viral variants may be associated with resistance to monoclonal antibodies. Healthcare providers should review the Antiviral Resistance information in Section 15 of the Fact Sheet for details regarding specific variants and resistance, and refer to the CDC website (https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html) as well as information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions.

IMPORTANT SAFETY INFORMATION

REGEN-COV (casirivimab with imdevimab) is an unapproved investigational therapy, and there are limited clinical data available. Serious and unexpected adverse events may occur that have not been previously reported with REGEN-COV use.

Warnings and Precautions:

- **Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions:** There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of REGEN-COV. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy. Infusion-related reactions have been observed with administration of REGEN-COV.
    - **Signs and symptoms of infusion related reactions may include** fever, difficulty breathing, reduced oxygen saturation, chills, nausea, arrythmia (e.g., atrial fibrillation, tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness, fatigue and diaphoresis. If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care
- **Clinical Worsening After REGEN-COV Administration**: Clinical worsening of COVID-19 after administration of REGEN-COV has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrythmia (e.g., atrial fibrillation, tachycardia, bradycardia), fatigue, and altered mental status. Some of these events required hospitalization. It is not known if these events were related to REGEN-COV use or were due to progression of COVID-19.
- **Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19:** Benefit of treatment with REGEN-COV has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as REGEN-COV, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high-flow oxygen or mechanical ventilation. Therefore, REGEN-COV is not authorized for use in patients who are hospitalized due to COVID-19, OR who require oxygen therapy due to COVID-19, OR who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

Adverse Reactions:

- Serious adverse events (SAEs) were reported in 4 (1.6%) patients in REGEN-COV 2,400 mg group, 2 (0.8%) patients in REGEN-COV 8,000 mg group and 6 (2.3%) patients in the placebo group. None of the SAEs were considered to be related to study drug. SAEs that were reported as Grade 3 or 4 adverse events were pneumonia, hyperglycemia, nausea and vomiting (2,400 mg REGEN-COV), intestinal obstruction and dyspnea (8,000 mg REGEN-COV) and COVID-19, pneumonia and hypoxia (placebo). **REGEN-COV is not authorized at the 8,000 mg dose (4,000 mg casirivimab and 4,000 mg imdevimab).**
- One anaphylactic reaction was reported in the clinical program. The event began within 1 hour of completion of the infusion, and required treatment including epinephrine. The event resolved. Infusion-related reactions, of Grade 2 or higher severity, were reported in 4 subjects (1.5%) in the 8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab) arm. These infusion-related reactions events were moderate in severity; and include pyrexia, chills, urticaria, pruritus, abdominal pain, and flushing. One infusion-related reaction (nausea) was reported in the placebo arm and none were reported in the 2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab) arm. In two subjects receiving the 8,000 mg dose of REGEN-COV, the infusion-related reactions (urticaria, pruritus, flushing, pyrexia, shortness of breath, chest tightness, nausea, vomiting) resulted in permanent discontinuation of the infusion. All events resolved.

Patient Monitoring Recommendations: Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.

Use in Specific Populations:

- **Pregnancy:** There is currently limited clinical experience in the use of REGEN-COV in COVID-19 patients who are pregnant. REGEN-COV therapy should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.
- **Lactation:** There is currently no clinical experience in use of REGEN-COV in COVID-19 patients who are breastfeeding. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for REGEN-COV and any potential adverse effects on the breastfed child from REGEN-COV or from the underlying maternal condition.

About Regeneron

Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for over 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to nine FDA-approved treatments and numerous product candidates in development, almost all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, pain, hematology, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite* technologies, such as *VelocImmune*, which uses unique genetically humanized mice to produce optimized fully human antibodies and bispecific antibodies, and through ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world. For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

Forward-Looking Statements and Use of Digital Media

This press release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, and suppliers and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs, Regeneron's ability to manage its supply chain, net product sales of products marketed or otherwise commercialized by Regeneron and/or its collaborators (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of Regeneron's Products and product candidates and research and clinical programs now underway or planned, including without limitation the development program relating to REGEN-COV™ (casirivimab with imdevimab) antibody cocktail; how long the Emergency Use Authorization ("EUA") granted by the U.S. Food and Drug Administration (the "FDA") for REGEN-COV will remain in effect and whether the EUA is revoked by the FDA based on its determination that the underlying health emergency no longer exists or warrants such authorization or other reasons; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's product candidates (such as REGEN-COV) and new indications for Regeneron's Products; whether, based on the data discussed in this press release or otherwise, the EUA for REGEN-COV will be expanded to include COVID-19 prevention for appropriate populations and/or include the 1,200 mg subcutaneous dose of REGEN-COV; the ability of Regeneron's collaborators, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and product candidates (including REGEN-COV) and the impact of the foregoing on Regeneron's ability to supply its Products and product candidates (including REGEN-COV); the ability of Regeneron to manage supply chains for multiple products and product candidates; safety issues resulting from the administration of Regeneron's Products and product candidates (such as REGEN-COV) in patients, including serious complications or side effects in connection with the use of Regeneron's Products and product candidates in clinical trials; uncertainty of market acceptance and commercial success of Regeneron's Products and product candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) (including the study discussed in this press release) on any potential regulatory approval (including with respect to REGEN-COV) and/or the commercial success of Regeneron's Products and product candidates; determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize Regeneron's Products and product candidates, including without limitation REGEN-COV; ongoing regulatory obligations and oversight impacting Regeneron's Products, research and clinical programs, and business, including those relating to patient privacy; the availability and extent of reimbursement of Regeneron's Products from third-party payers, including private payer healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid; coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and product candidates; the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license, collaboration, or supply agreement, including Regeneron's agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), as well as Regeneron's collaboration with Roche relating to REGEN-COV, to be cancelled or terminated; and risks associated with intellectual property of other parties and pending or future litigation relating thereto (including without limitation the patent litigation and other related proceedings relating to EYLEA® (aflibercept) Injection, Dupixent® (dupilumab), Praluent® (alirocumab), and REGEN-COV), other litigation and other proceedings and government investigations relating to the Company and/or its operations, the ultimate outcome of any such proceedings and investigations, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition. A more complete description of these and other material risks can be found in Regeneron's filings with the U.S. Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2020. Any forward-looking statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any forward-looking statements made by Regeneron. Regeneron does not undertake any obligation to update (publicly or otherwise) any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

Regeneron uses its media and investor relations website and social media outlets to publish important information about the Company, including information that may be deemed material to investors. Financial and other information about Regeneron is routinely posted and is accessible on Regeneron's media and investor relations website (http://newsroom.regeneron.com) and its Twitter feed (http://twitter.com/regeneron).

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