Phase 3 Treatment Trial in Recently Infected Asymptomatic Patients Showed REGEN-COV™ (casirivimab with imdevimab) Significantly Reduced Progression to Symptomatic COVID-19

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Second Phase 3 trial undertaken in collaboration with NIAID to announce results today, both using subcutaneous administration of REGEN-COV in asymptomatic individuals without prior COVID-19 infection

Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive data from a Phase 3 trial (2069B) of recently infected asymptomatic COVID-19 patients, evaluating REGEN-COV™ (casirivimab with imdevimab) 1,200 mg administered via subcutaneous (SC) administration. REGEN-COV reduced the overall risk of progressing to symptomatic COVID-19 by 31% (primary endpoint), and by 76% after the third day. The trial also demonstrated that REGEN-COV shortened symptom duration and markedly reduced viral levels.

The Phase 3 trial is the second to report results today, which was jointly run with the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). The trial enrolled 204 individuals without any COVID-19 symptoms who tested positive for SARS-CoV-2 but did not have anti-virus antibodies at baseline, and were randomized to receive either 1 dose of REGEN-COV (1,200 mg) or placebo.

"COVID-19 transmission often occurs via infected people who do not yet have symptoms, so it is critical that we rapidly diagnose and treat these individuals for their own health and to prevent transmission," said Katharine Bar, M.D., co-principal investigator of the trial and Assistant Professor of Medicine, Infectious Diseases, Hospital of the University of Pennsylvania. "These data pave the way for REGEN-COV to be used before patients become symptomatic, with a more convenient subcutaneous administration."

The trial met all primary and key secondary endpoints. In addition to reducing the risk of symptomatic infections, the total number of weeks patients experienced symptoms was nearly cut in half (45%) with REGEN-COV, and the viral burden was reduced by more than 90%. While not included in the initial analysis plan, researchers also found that 0 REGEN-COV patients and 6 placebo patients were either hospitalized or visited the emergency room because of COVID-19 during the 29-day efficacy assessment period.

The data build on previously announced results from the Phase 3 outcomes (2067) and Phase 2 virology (20145) trials in non-hospitalized COVID-19 patients. The Phase 3 outcomes trial in high-risk symptomatic outpatients showed that REGEN-COV (2,400 mg and 1,200 mg administered intravenously [IV]) reduced hospitalization or death by 70%. The Phase 2 virology trial in low-risk outpatients showed that all REGEN-COV doses studied had similar efficacy in rapidly reducing viral load (IV: 2,400 mg, 1,200 mg, 600 mg and 300 mg; SC: 1,200 mg and 600 mg).

"These Phase 3 data provide even more evidence that REGEN-COV, this time given to asymptomatic patients via convenient injections, can change the course of COVID-19 infection in non-hospitalized patients," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. "In this trial, the REGEN-COV antibody cocktail effectively prevented asymptomatic patients from becoming symptomatic, and rapidly lowered their viral load."

TABLE: Key Results from Phase 3 Treatment Trial in Asymptomatic Infected Individuals[1]

	REGEN-COV (single 1,200 mg dose)	**Placebo**
	n=100	n=104
Risk of symptomatic SARS-CoV-2 infection		
Overall risk reduction through day 29 (primary endpoint)		
Risk reduction	31% (p=0.0380)	
# of patients with events	29 (29%)	44 (42%)
Overall risk reduction after day 3 (days 4-29)[2,3]		
Risk reduction	76% (nominal p=0.0007)	
# of patients with events	5 (5%)	22 (21%)
Symptoms, viral load and COVID-19 related events		

Total weeks with symptoms		
Reduction	45% (p=0.0273)	
Total # of weeks (cumulative for all patients in each arm)	90	170
Total weeks with high viral load (>10^4 copies/mL)		
Reduction	40% (p=0.001)	
Total # of weeks (cumulative for all patients in each arm)	48	82
COVID-19 related hospitalizations or emergency room (ER) visits[3]		
Reduction	100% (nominal p=0.029)	
# of patients with events	0 (0%)	6 (6%)

1. 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
2. Does not include results from days 1-3, when events were similar between treatment groups
3. These analyses were not part of the pre-planned statistical analysis plan, so p-values are nominal

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 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 and 1% (n=1) of placebo patients. No patients from either group withdrew from the trial due to AEs, and there were no deaths.

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 treatment trial, 35% were Latino/Hispanic and 5% were Black/African American. In total, 32% had at least 1 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, 32% were obese and 34% were aged ³50 years (median age: 41 years; range: 12-87 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 the 1,200 mg subcutaneous dose of REGEN-COV will be included in the EUA for REGEN-COV based on the data discussed in this press release or otherwise; 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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