



New England Journal of Medicine Publishes Positive Phase 3 Trial Results for REGEN-COV™ (casirivimab and imdevimab) to Treat COVID-19

September 29, 2021

TARRYTOWN, N.Y., Sept. 29, 2021 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced that the *New England Journal of Medicine (NEJM)* [published](#) positive detailed results from a Phase 3 trial that assessed the ability of REGEN-COV™ (casirivimab and imdevimab) to treat COVID-19 in infected high-risk non-hospitalized patients (outpatients). The trial met its primary and all secondary endpoints and showed treatment with REGEN-COV significantly reduced the risk of hospitalization or death, with a safety profile consistent with previously reported data.

"Results from this *NEJM* publication show that REGEN-COV reduced the risk of hospitalization or death by 70% in high-risk non-hospitalized patients infected with COVID-19," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. "This peer-reviewed publication further supports the growing evidence on REGEN-COV's critical role to improve outcomes for patients, and reduce the significant burden on their communities and healthcare systems during this COVID-19 pandemic."

REGEN-COV is an investigational medicine authorized by the U.S. Food and Drug Administration (FDA) under an emergency use authorization to treat people who are at high risk of serious consequences from COVID-19, including those who are already infected ([non-hospitalized](#)) or those in certain [post-exposure prophylaxis](#) settings.

Regeneron [previously presented](#) initial results from the Phase 3 trial at the 2021 American Thoracic Society International Conference (ATS 2021). In addition, the robust REGEN-COV development program has reported positive Phase 3 trial results across the spectrum of COVID-19 infection, from prevention to hospitalization:

- Prevention of symptomatic infection in both [uninfected](#) and [infected](#) asymptomatic household contacts of SARS-CoV-2 infected individuals
- Treatment of [non-hospitalized](#) patients already infected with SARS-CoV-2 (as detailed in today's publication)
- Treatment of certain patients [hospitalized](#) due to COVID-19 infection, including the [RECOVERY trial](#)

Multiple analyses have shown that the antibody cocktail retains potency against the main variants of concern circulating within the U.S., including Delta (first identified in India), Gamma (first identified in Brazil), Beta (first identified in South Africa) and Mu (first identified in Colombia), with information available in the [Fact Sheet for Healthcare Providers](#). Consequently, REGEN-COV remains available for use across the U.S., and Regeneron will continue actively monitoring the potency of REGEN-COV against emerging variants.

In the U.S., REGEN-COV is available for free to [eligible people](#), as part of a U.S. government funded program and recently, Regeneron [announced](#) a new agreement with the U.S. government to supply an additional 1.4 million 1,200 mg doses of REGEN-COV. Information on how to access REGEN-COV throughout the U.S. is available from the [Department of Health and Human Services](#) and the [National Infusion Center Association](#).

The development and manufacturing of REGEN-COV have been funded in part with federal funds from the Biomedical Advanced Research and Development Authority, 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 Trial

The Phase 3, randomized, double-blind, placebo-controlled trial evaluated REGEN-COV in non-hospitalized adult patients who had detectable SARS-CoV-2 infection when they entered the trial (measured by nasopharyngeal samples by PCR). All patients evaluated for efficacy had at least one risk factor for progressing to severe COVID-19, such as chronic lung disease (including asthma), obesity, cardiovascular disease or being at least 50 years of age. Patients included in this analysis were randomized into three treatment arms: REGEN-COV 2,400 mg (n=1,355), REGEN-COV 1,200 mg (n=736) and placebo (n=1,341 for 2,400 mg comparator, n=748 for 1,200 mg comparator). After receiving one dose when they entered the trial, patients were then followed for 28 days to assess efficacy and safety.

On average, patients included in the efficacy analysis had experienced symptoms for 3 days. Approximately 37% were Hispanic or Latino and 5% were African American. Patients were on average approximately 50 years of age, 52% were female and 48% were male.

About the REGEN-COV Antibody Cocktail

REGEN-COV (casirivimab and imdevimab) is a cocktail of two monoclonal antibodies 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 [Cell](#) and [Science](#).

REGEN-COV has not been approved by the FDA, but is currently [authorized](#) in the U.S. for the treatment and post-exposure prophylaxis in certain high risk individuals. Post-exposure prophylaxis with REGEN-COV is not a substitute for vaccination against COVID-19. REGEN-COV is not authorized for pre-exposure prophylaxis for prevention of COVID-19 or 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. This authorization is for the duration of the declaration that circumstances exist justifying the authorization of the emergency uses under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner. Additional information

about REGEN-COV in the U.S. is below (authorized uses and important safety information).

In August, Regeneron submitted the first of two Biologics License Applications (BLAs) for REGEN-COV. The initial submission included data on the efficacy and safety of REGEN-COV to treat and prevent SARS-CoV-2 infection in non-hospitalized people. The second BLA submission will focus on those hospitalized because of COVID-19, and is expected to be completed later this year.

Emergency or temporary pandemic use authorizations are currently in place in more than 40 countries, including the U.S., several European Union countries, India, Switzerland and Canada, and the antibody cocktail is fully approved in Japan and conditionally approved in the UK.

Regeneron invented REGEN-COV and is [collaborating](#) with Roche to increase global supply, with Roche primarily responsible for development and distribution outside the U.S. Regeneron and Roche 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 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 and imdevimab), Dupixent® (dupilumab), Libtayo® (cemiplimab-rwlc), Praluent® (alirocumab), Kevzara® (sarilumab), Evkeeza® (evinacumab-dgnb) and Inmazeb™ (atoltivimab, maftivimab and odesivimab-ebgn).

AUTHORIZED USES AND IMPORTANT SAFETY INFORMATION

Treatment:

REGEN-COV 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 progression to severe COVID-19, including hospitalization or death

Limitations of Authorized Use (Treatment)

- 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
- 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

Post-Exposure Prophylaxis:

REGEN-COV is authorized in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) for post-exposure prophylaxis of COVID-19 in individuals who are at high risk for progression to severe COVID-19, including hospitalization or death, and are:

- not fully vaccinated **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions including those taking immunosuppressive medications) **and**
 - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC) **or**
 - who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example, nursing homes, prisons)

Limitations of Authorized Use (Post-Exposure Prophylaxis)

- Post-exposure prophylaxis with REGEN-COV is not a substitute for vaccination against COVID-19
- REGEN-COV is not authorized for pre-exposure prophylaxis for prevention of COVID-19

REGEN-COV has not been approved, but has been authorized for emergency use by FDA

These uses are 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 uses 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](#)

Criteria for Identifying High Risk Individuals

Please refer to the Fact Sheet for Healthcare Providers for criteria for identifying high risk individuals

SARS-CoV-2 Viral Variants

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 and 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

- **Contraindication:**

REGEN-COV is contraindicated in individuals with previous severe hypersensitivity reactions, including anaphylaxis, to REGEN-COV

- **Warnings and Precautions:**

- **Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions:** Serious hypersensitivity reactions, including anaphylaxis, have been observed 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. Hypersensitivity reactions occurring more than 24 hours after the infusion have also been reported with the use of REGEN-COV under EUA. Infusion-related reactions, occurring during the infusion and up to 24 hours after the infusion, have been observed with administration of REGEN-COV. These reactions may be severe or life threatening

- **Signs and symptoms of infusion-related reactions may include:** fever, difficulty breathing, reduced oxygen saturation, chills, nausea, arrhythmia (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, vasovagal reactions (e.g., pre-syncope, syncope), dizziness, fatigue and diaphoresis. Consider slowing or stopping the infusion and administer appropriate medications and/or supportive care if an infusion-related reaction occurs

- **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, arrhythmia (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:** 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:**

- **COV-2067 (Treatment):** Infusion-related reactions (adverse event assessed as causally related by the investigator) of grade 2 or higher severity have been observed in 10/4,206 (0.2%) of those who received REGEN-COV at the authorized dose or a higher dose. Three subjects receiving the 8,000 mg dose of REGEN-COV, and one subject receiving the 1,200 mg casirivimab and 1,200 mg imdevimab, had infusion-related reactions (urticaria, pruritus, flushing, pyrexia, shortness of breath, chest tightness, nausea, vomiting, rash) which resulted in permanent discontinuation of the infusion. All events resolved. Anaphylactic reactions have been reported in the clinical program in subjects receiving REGEN-COV. The events began within 1 hour of completion of the infusion, and in at least one case required treatment including epinephrine. The events resolved

- **COV-2069 (Post-exposure prophylaxis):** In subjects who were SARS-CoV-2 negative at baseline (Cohort A), injection site reactions (all grade 1 and 2) occurred in 55 subjects (4%) in the REGEN-COV group and 19 subjects (2%) in the placebo group. The most common signs and symptoms of injection site reactions which occurred in at least 1% of subjects in the REGEN-COV group were erythema and pruritus. Hypersensitivity reactions occurred in 2 subjects (0.2%) in the REGEN-COV group and all hypersensitivity reactions were grade 1 in severity. In subjects who were SARS-CoV-2 positive at baseline (Cohort B), injection site reactions, all of which were grade 1 or 2, occurred in 6 subjects (4%) in the REGEN-COV group and 1 subject (1%) in the placebo group. The most common signs and symptoms of injection site reactions which occurred in at least 1% of subjects in the REGEN-COV group were ecchymosis and erythema

- **COV-2093 (Subcutaneous Dosing):** Injection site reactions occurred in 12% and 4% of subjects following single dose administration in the REGEN-COV and placebo groups, respectively. Remaining safety finding following subcutaneous administration in the REGEN-COV group were similar to the safety findings observed with intravenous administration in COV-2067. With repeat dosing, injection site reactions occurred in 252 subjects (35%) in the REGEN-COV group and 38 subjects (16%) in the placebo group; all injection site reactions were grade 1 or 2 in severity. Hypersensitivity reactions occurred in 8 subjects (1%) in the REGEN-COV group; and all

hypersensitivity reactions were grade 1 or 2 in severity. There were no cases of anaphylaxis

- **Patient Monitoring Recommendations:** Clinically monitor patients during dose administration and observe patients for at least 1 hour after intravenous infusion or subcutaneous dosing is complete
- **Use in Specific Populations:**
 - **Pregnancy:** There are insufficient data to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. REGEN-COV should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus
 - **Lactation:** There are no available data on the presence of casirivimab and/or imdevimab in human milk or animal milk, the effects on the breastfed infant, or the effects of the drug on milk production. 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, hematologic conditions, 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 being developed by Regeneron and/or its collaborators (collectively, "Regeneron's Product Candidates") and research and clinical programs now underway or planned, including without limitation the development program relating to the REGEN-COV™ (casirivimab and imdevimab) antibody cocktail; the utilization, market acceptance, and commercial success of Regeneron's Products and Regeneron's Product Candidates (such as REGEN-COV), including the impact of recommendations, guidelines, or studies (whether conducted by Regeneron or others and whether mandated or voluntary), such as the study discussed in this press release, on any of the foregoing or any potential regulatory approval of Regeneron's Products and Regeneron's Product Candidates; 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, including based on the Biologics License Applications filed or planned to be filed with the FDA and referenced in this press release) and new indications for Regeneron's Products; 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 Regeneron's Product Candidates (including REGEN-COV) and the impact of the foregoing on Regeneron's ability to supply Regeneron's Products and Regeneron's 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 Regeneron's Product Candidates (such as REGEN-COV) in patients, including serious complications or side effects in connection with the use of Regeneron's Products and Regeneron's Product Candidates in clinical trials; 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 Regeneron's 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 Regeneron's 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 the casirivimab and imdevimab antibody cocktail (known as REGEN-COV in the United States and Ronapreve™ in other countries) and its REGEN-COV supply agreement with the U.S. government referenced in this press release, 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® (afibercept) 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 and its Form 10-Q for the quarterly period

ended June 30, 2021. 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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