UPDATE: On 12/23/21, IMFN updated the distribution of REGEN-COV. Please refer to the FDA, CDC and your state and local health authorities for additional guidance.

LEARN MORE

OUR COVID-19 ANTIBODY PROGRAM

REGEN-COV® (casirivimab and imdevimab) eligibility and access sites

Ongoing clinical and preclinical research

Peer-reviewed research

Our antibody combination approach to infectious disease

Regeneron is applying our 30 years of scientific and technology expertise to combat the COVID-19 pandemic. We feel uniquely positioned to face this public health threat given our proprietary VelocIMmice® technologies and our track record against infectious diseases such as Ebola. We have moved REGEN-COV® (casirivimab and imdevimab) from discovery to late-stage clinical development and regulatory review in record time.

REGEN-COV® (casirivimab and imdevimab) eligibility and access sites

Note: Due to the large reduction of pseudotyped VLP neutralization activity against spike protein from the B.1.1.529/BA.1 (Omicron; South Africa origin) variant, it is unlikely that casirivimab and imdevimab together will be active against this variant.

Treatment:
The U.S. Food and Drug Administration (FDA) has *granted an Emergency Use Authorization* (EUA) for REGEN-COV® (casirivimab and imdevimab) 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 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 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)
- 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)

- 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 been approved but has been authorized for emergency use by the 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.

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.
- There are other authorized treatments available and healthcare providers should choose an authorized therapeutic option with activity against the circulating variants in their state, territory, or US jurisdiction. Current frequency data are available at: https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-proportions.html.

Healthcare providers should review the Fact Sheet for Healthcare Providers for information on the authorized uses of REGEN-COV.

Please see below for Important Safety Information.

Accessing antibody medicines:

The U.S. government has made our investigational antibody therapy, REGEN-COV, for COVID-19 free to patients who qualify under the Emergency Use Authorization parameters issued by the FDA. Patients with commercial insurance may be subject to a co-pay/co-insurance cost for the drug's administration. Currently, there is no cost for the drug's administration for patients with Medicare or Medicaid insurance. Click for more information.

The U.S. government has signed multiple agreements with Regeneron for the purchase of nearly three million doses of REGEN-COV with doses from the most recent agreement to be delivered by January 2022.

For healthcare providers interested in ordering REGEN-COV, it is best to contact your state's department of health for specific ordering instructions.

CONTACT OUR MEDICAL INFORMATION TEAM	HEALTH AND HUMAN SERVICES (HHS) ANTIBODY THERAPEUTIC LOCATOR	NATIONAL INFUSION CENTER ASSOCIATION (NICA)

ADDITIONAL RESOURCES FOR PATIENTS AND PROVIDERS >

Regeneron is collaborating with Roche to increase global supply of REGEN-COV. Regeneron is responsible for manufacturing REGEN-COV for the U.S. and Roche is responsible for manufacturing 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. For ex-U.S. inquiries please contact medinfo.roche.com.

REGEN-COV is recommended in COVID-19 treatment guidelines, including Infectious Diseases Society of America (IDSA), National Institutes of Health (NIH), and World Health Organization (WHO).

Peer-reviewed research

Clinical

- New England Journal of Medicine: *"REGEN-COV Antibody Combination and Outcomes in Outpatients with COVID-19"* described results from a Phase 3 trial showing that REGEN-COV significantly reduced the risk of hospitalization or death in infected high-risk mild to moderate disease in patients not hospitalized for COVID-19 and a safety profile consistent with previously reported data.
- New England Journal of Medicine: *"Subcutaneous REGEN-COV Antibody Combination to Prevent COVID-19"* reported that subcutaneous REGEN-COV prevented COVID-19 infection among household contacts of SARS-CoV-2 infected individuals, across the risk arm of symptomatic infections, and no dose-limiting toxicities were observed.
- New England Journal of Medicine: *"REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with COVID-19"* reported an initial cohort data from a Phase 1/2/3 trial of REGEN-COV in non-hospitalized patients with COVID-19, which showed a reduced viral load and the need for medically attended visits, with the rates of adverse events similar across doses and placebo groups.

Preclinical

- Cell: *"The Monoclonal Antibody Combination REGN-COV Protects Against SARS-CoV-2 Mutational Escape in Preclinical and Human Studies"* showed that REGEN-COV retained neutralization potency against current variants of concern/interest and that treatment with REGEN-COV in humans did not lead to emergence of viral variants.
- Science: *"Antibody Cocktail to SARS-Cov-2 Spike Protein Prevents Rapid Mutational Escape Seen with Individual Antibodies"* demonstrated that, under pressure from individual antibodies, mutant viruses were rapidly selected that evaded the blocking function of all individual antibodies tested, including antibodies that potently bind to highly-conserved regions on the spike protein. However, escape mutants could not be efficiently generated following exposure to the REGEN-COV cocktail since it utilized two antibodies that can simultaneously bind to distinct regions of the virus. The clinical significance of these findings is unknown.
- Science: *"Studies in Humanized Mice and Convalescent Humans Yield a SARS-CoV-2 Antibody Cocktail"* described Regeneron's parallel efforts using both humanized VelocImmune® mice and blood samples from convalescent COVID-19 patients to generate a large and diverse collection of antibodies targeting multiple different regions of the critical receptor binding domain of the SARS-CoV-2 spike protein.
- Science: *"REGN-COV2 Antibody Cocktail Prevents and Treats SARS-CoV-2 Infection in Rhesus Macaques and Hamsters"* demonstrated the efficacy of REGEN-COV in non-human primates and hamsters, and showed its ability to reduce virus load in lower and upper airways and decrease virus-induced pathological impact.

Ongoing clinical and preclinical research

See if you qualify for a REGEN-COV clinical trial by calling (844) 734-6643

We are studying REGEN-COV in multiple patient populations for the potential treatment and prevention of COVID-19. We are sharing data from these ongoing clinical trials as quickly as possible with the public and regulatory authorities.

Data is available on REGEN-COV in various patient populations:

Hospitalized patients: Data from a Phase 2/3 study assessed REGEN-COV in patients hospitalized with COVID-19 who required low-flow or no supplemental oxygen. The separate, nearly 1,000 patient UK RECOVERY study assessed REGEN-COV's ability to reduce risk of death in patients hospitalized with COVID-19 with a broad range of severity.

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.
- There are other authorized treatments available and healthcare providers should choose an authorized therapeutic option with activity against the circulating variants in their state, territory, or US jurisdiction. Current frequency data are available at: https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-proportions.html

Monitor SARS-CoV-2 variants with Regeneron's COVID-19 Dashboard
Refreshed daily with new genomes and associated patient metadata.
FIND OUT MORE

Our antibody combination approach to infectious disease

Regeneron's infectious disease programs have led to an approved medicine for Ebola, an emergency use authorized medicine for COVID-19, and an investigational medicine for Middle East Respiratory Syndrome (MERS). In each case, we have taken a strategic multi-antibody 'cocktail' approach.

Our COVID-19-related discovery efforts started in early 2020, when we utilized our VelocImMice® technologies to produce and evaluate hundreds of virus-neutralizing antibodies from genetically engineered mice. Knowing from the beginning that we would take a combination approach, we also identified similarly-performing antibodies from human COVID-19 survivors in order to maximize the pool of potential candidates. By June, we had selected and progressed the two potent, complementary and non-competing antibodies, casirivimab and imdevimab, into large-scale manufacturing and clinical trials.

Viruses, by their nature, mutate over time leading to variant forms. With two (or more) complementary antibodies in one therapeutic, even if one antibody has reduced potency in response to a certain strain the risk of the combination losing efficacy is diminished since the virus would need to mutate in multiple distinct locations to evade both antibodies. In the case of REGEN-COV for COVID-19, casirivimab and imdevimab bind tightly and non-competitively to different, non-overlapping parts of the spike protein of the SARS-CoV-2 virus, thereby blocking the virus' ability to infect healthy cells.

We have hundreds of additional investigational, neutralizing antibodies in our labs that could form new combinations that might be useful against future variants, and we are evaluating potential next steps with these novel early-stage candidates.

The REGEN-COV antibody cocktail was prospectively designed so that if variants arose affecting one component, the other component could compensate and still allow for potent neutralizing activity. In fact, as reported in Science in June 2020, Regeneron scientists predicted the key mutation that has since appeared in the SARS-CoV-2 variants first identified in South Africa and Brazil. Further showed that this mutation would lower potency of the casirivimab antibody, but be compensated for by the strong potency of the imdevimab antibody.

George D. Yancopoulos, MD, PhD
President and Chief Scientific Officer

Our technologies
From discovery to large-scale manufacturing, our VelocImMice® technologies uniquely enable our discovery and development efforts.
LEARN ABOUT OUR TECHNOLOGIES

2020 was a challenging year for everyone. Our founder, CEO and president, Len Schleifer, MD, PhD, reflects that weathered over COVID-19 work, what we accomplished and what is yet to come.
READ HIS PERSPECTIVE

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

- Contraindications
  - 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. 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, wakefulness, 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 received 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 reported 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 (1.4%) 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 and 2. 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 3 subjects (1.4%) in the REGEN-COV group and 0 subjects 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 erythematous and erythema
  - COV-2093 (Subcutaneous Dosing): Injection site reactions occurred in 12% and 6% 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 of REGEN-COV. With repeat dosing, injection site reactions occurred in 252 subjects (35%) in the REGEN-COV group and 38 subjects (10%) in the placebo group. Injection site reactions were all grade 1 or 2 in intensity. 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.

Reporting Adverse Events:

- The prescribing healthcare provider and/or the provider's designee are responsible for mandatory reporting of ALL MEDICATION ERRORS and ALL SERIOUS ADVERSE EVENTS potentially related to REGEN-COV. These adverse events must be reported within 7 calendar days from the onset of the event
- Healthcare facilities and providers must report dispensing of monoclonal and demonstrate adequate utilization via data reported through HHS Protect, Telehealing or National Healthcare Safety Network (NHSN) as directed by the U.S. Department of Health and Human Services
- **MedWatch adverse event reports can be submitted to the FDA here, by submitting a postage-paid Form FDA 3500 and returning by mail/fax, or by calling 1-800-FDA-1088 to request a reporting form.** In addition, please provide a copy of all FDA MedWatch forms to Regeneron Pharmaceuticals, Inc via fax (1-888-876-2736) or email (medical.information@regeneron.com)

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