



New England Journal of Medicine Publishes Positive Initial Regeneron Antibody Cocktail Results in Non-hospitalized Patients with COVID-19

December 17, 2020

TARRYTOWN, N.Y., Dec. 17, 2020 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today announced that the *New England Journal of Medicine* (NEJM) has [published](#) initial clinical data from an ongoing seamless Phase 1/2/3 trial of the antibody cocktail casirivimab and imdevimab in non-hospitalized patients with COVID-19.

"The peer-reviewed *NEJM* publication of our first set of clinical data in recently infected COVID-19 patients showed that casirivimab and imdevimab effectively reduced viral load and the need for medically-attended visits, with the greatest benefit in patients who had not yet mounted their own effective immune response or had high viral load at baseline," said David Weinreich, M.D., Senior Vice President and Head of Global Clinical Development at Regeneron and lead author of the publication. "The investigational cocktail is now available to indicated high-risk U.S. patients under an Emergency Use Authorization, and we also continue a robust clinical development program."

"Building on these initial findings, we were gratified to recently report follow-on data from the next-stage analysis of this ongoing trial, which prospectively replicated these results in a rigorous and statistically significant manner. These follow-on data provided the first definitive prospective evidence demonstrating anti-viral activity for a treatment regimen now available for COVID-19, and also further documented the ability of this treatment to decrease the need for further medical attention," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. "We are continuing to evaluate our antibody cocktail in this outpatient setting, as well as in late-stage trials in hospitalized patients and for prevention of infection, and will continue to share our findings as quickly as possible."

Regeneron previously [announced](#) the initial results featured in this *NEJM* publication from the Phase 1/2 portion of the trial that enrolled 275 patients randomized 1:1:1 to receive 8 grams casirivimab and imdevimab (high-dose, n=90), 2.4 grams casirivimab and imdevimab (low-dose, n=92) or placebo (n=93). Approximately 56% of patients were Latino/Hispanic, 13% were Black/African American and 64% had one or more underlying risk factors for severe COVID-19, including obesity (more than 40%).

Regeneron also subsequently [announced](#) additional prospective results in a total of 799 patients from the trial. In both the initial descriptive analyses of 275 patients, as well as in the following prospective analyses involving a total of 799 patients, a greater effect was observed in patients treated with the antibody cocktail who did not have SARS-CoV-2 antibodies at baseline ('sero-antibody-negative') or who had high viral load at baseline. As would be expected, a much higher proportion of sero-antibody-negative patients had high viral loads when they entered the trial. Additionally, a smaller proportion of antibody cocktail-treated patients required medically-attended visits due to COVID-19 (inclusive of hospitalizations, urgent care or emergency room visits, in-person physician or telemedicine visits) through day 29 compared to placebo; there was an even greater benefit on this endpoint among sero-antibody-negative patients.

In the initial 275 patients, rates of adverse events (AEs) were similar among groups. Serious AEs occurred in 2 placebo patients, 1 low-dose patient and 0 high-dose patients. AEs included infusion-related reactions (1 placebo patient, 0 low-dose patients, 2 high-dose patients) and hypersensitivity reactions (2 placebo patients, 0 low-dose patients, 1 high-dose patient).

About casirivimab and imdevimab

Casirivimab and imdevimab (formerly known as REGN-COV2 or REGEN-COV2) is a cocktail of two monoclonal antibodies (also known as REGN10933 and REGN10987, respectively) and was designed specifically to block infectivity of SARS-CoV-2, the virus that causes COVID-19.

To develop this novel medicine, Regeneron scientists evaluated thousands of fully-human antibodies produced by the company's *VelocImmune*[®] mice, which have been genetically modified to have a human immune system, as well as antibodies identified from humans who have recovered from COVID-19. The two potent, virus-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](#).

The development and manufacturing of the antibody cocktail has been funded in part with federal funds from BARDA under OT number: HHSO100201700020C. Data from the Phase 1/2/3 clinical trial supported an [Emergency Use Authorization](#) for casirivimab and imdevimab administered together, granted by the U.S. Food and Drug Administration (FDA) for the treatment of mild to moderate COVID-19 in patients 12 years of age and older 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. Regeneron continues to increase in-house production of casirivimab and imdevimab, and the company has [partnered](#) with Roche to increase the global supply beginning in 2021. If the therapy proves safe and effective in clinical trials and regulatory approvals are granted, Regeneron will manufacture and distribute it in the U.S., and Roche will develop, manufacture and distribute it outside of the U.S. Once both companies are at full manufacturing capacity in 2021, there are expected to be at least 2 million treatment doses available annually.

AUTHORIZED USE AND IMPORTANT SAFETY INFORMATION

Authorized Emergency Use

Casirivimab and imdevimab injection is an investigational combination therapy and has been authorized by FDA for the emergency use described above. Casirivimab and imdevimab injection is not FDA approved for any use. Safety and effectiveness of casirivimab and imdevimab injection have not yet been established for the treatment of COVID-19.

This authorized use is 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.

Limitations of Authorized Use

- Casirivimab and imdevimab injection 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 casirivimab and imdevimab injection has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19.

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 ≥ 85 th percentile for their age and gender based on CDC growth charts, OR
 - sickle cell disease, OR
 - congenital or acquired heart disease, OR
 - neurodevelopmental disorders, for example, 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.

Warnings and Precautions:

- **Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions:** There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of casirivimab and imdevimab injection. 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 casirivimab and imdevimab injection. Signs and symptoms of infusion related reactions may include fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, and/or dizziness. If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.
- **Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19:** Benefit of treatment with casirivimab and imdevimab injection has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19. Therefore, casirivimab and imdevimab injection is not authorized for use in 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 the casirivimab and imdevimab injection 2,400 mg group, 2 (0.8%) patients in casirivimab and imdevimab injection 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 casirivimab and imdevimab injection), intestinal obstruction and dyspnea (8,000 mg casirivimab and imdevimab injection) and COVID-19, pneumonia and hypoxia (placebo). Casirivimab and imdevimab injection are not authorized at the 8,000 mg dose (4,000 mg casirivimab and 4,000 mg imdevimab).

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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 casirivimab and imdevimab, 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 casirivimab and imdevimab injection in COVID-19 patients who are pregnant. Casirivimab and imdevimab injection therapy should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.
- **Nursing Mothers:** There is currently no clinical experience in use of casirivimab and imdevimab injection 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 casirivimab and imdevimab injection and any potential adverse effects on the breastfed child from casirivimab and imdevimab injection 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 eight FDA-approved treatments and numerous product candidates in development, 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, 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.

Regeneron 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 (including those discussed in this press release), 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 casirivimab and imdevimab (Regeneron's investigational multi-antibody therapy for the treatment and prevention of COVID-19); how long the Emergency Use Authorization ("EUA") granted by the U.S. Food and Drug Administration (the "FDA") for casirivimab and imdevimab 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 casirivimab and imdevimab) and new indications for Regeneron's Products; safety issues resulting from the administration of Regeneron's Products and product candidates (such as casirivimab and imdevimab) in patients, including serious complications or side effects in connection with the use of Regeneron's Products and product candidates in clinical trials (including those discussed in this press release); the ability of Regeneron to manufacture in anticipated quantities Regeneron's Products and product candidates, including casirivimab and imdevimab; the ability of Regeneron to manage supply chains for multiple products and product candidates; 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; 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 trials discussed in this press release, on any potential regulatory approval (including with respect to casirivimab and imdevimab) 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 casirivimab and imdevimab; 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 casirivimab and imdevimab, 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), and Praluent® (alirocumab)), 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, 2019 and its Form 10-Q for the quarterly period ended September 30, 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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