EMA Issues Advice on Regeneron's Antibody Cocktail (casirivimab with imdevimab) for Certain COVID-19 Patients

February 26, 2021 at 6:46 AM EST

TARRYTOWN, N.Y., Feb. 26, 2021 /PRNewswire/ --

EU member states can utilize the positive CHMP opinion when making national decisions about use of the antibody cocktail, prior to a potential future EMA market authorization

Regeneron has collaborated with Roche to develop and manufacture the antibody cocktail; Roche is responsible ex-U.S. and has already begun distribution in the EU

Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has issued a positive opinion for the company's investigational COVID-19 antibody cocktail (casirivimab with imdevimab). The CHMP recommends that the antibody cocktail, known as REGEN-COV™ in the U.S., can be used to treat confirmed COVID-19 in patients who do not require supplemental oxygen and who are at high risk of progressing to severe COVID-19.

"Today's endorsement by the EU's leading scientific body for medicines helps bring our antibody cocktail one step closer to even more COVID-19 patients who could benefit from it," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. "Our collaborator Roche is already in active discussions with a number of European countries following release of our data in non-hospitalized patients that showed the antibody cocktail significantly reduced virus levels within days of treatment, which was associated with significantly fewer medical visits. This is supported by preclinical data that show that our antibody cocktail effectively neutralizes emerging strains of the virus, which are becoming increasingly common in Europe and around the world."

The CHMP recommendation provides a harmonized, European Union (EU)-level opinion on the efficacy, quality and safety of the antibody cocktail, which can be used by EU member states when making decisions on the possible use of the antibody cocktail at a national level prior to a market authorization. Under Article 5(3) of Regulation EC 726/2004, the CHMP assessed available data in non-hospitalized patients ("outpatients") with COVID-19 as well as supportive data from other settings.

The CHMP's review took place in parallel to the EMA's ongoing rolling review process, which is used to speed up the formal marketing application assessment of a promising medicine during a public health emergency. Once finalized it will be the basis for an EU marketing authorization for the antibody cocktail. Regeneron, together with Roche, continues to work closely with the EMA as it undertakes its rolling review.

Regeneron is collaborating with Roche to increase global supply of the antibody cocktail. 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., with the first Roche-manufactured doses already being distributed. 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.

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 Antibody Cocktail

The antibody cocktail, known as REGEN-COV (casirivimab with imdevimab) in the U.S., consists of two monoclonal antibodies (also known as REGN10933 and REGN10987) and was designed specifically to block infectivity of SARS-CoV-2, the virus that causes 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*.

In November 2020, REGEN-COV received Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration (FDA) for the treatment of 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. The clinical evidence from Regeneron's outpatient trial suggests that monoclonal antibodies such as casirivimab and imdevimab have the greatest benefit when given early after diagnosis and in patients who are seronegative and/or who have high viral load. 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.

REGEN-COV continues to be evaluated in clinical trials in multiple settings for COVID-19: in non-hospitalized and certain hospitalized patients, including the open-label RECOVERY trial of hospitalized patients in the UK, and a trial for the prevention of COVID-19 in household contacts of infected individuals. As of February 2021, approximately 23,000 people have participated in clinical trials involving REGEN-COV. Lower doses of REGEN-COV are also being studied with the aim of increasing the number of patients who could potentially be treated if the cocktail is approved.

REGEN-COV was invented using Regeneron's *VelocImmune*® technology that 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 multiple antibodies including 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) is an investigational combination therapy and has been authorized by FDA for the emergency use described above. REGEN-COV is not FDA approved for any use and its safety and effectiveness has 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

-- 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.

-- 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.

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.

-- Nursing Mothers: 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, 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, 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 and imdevimab antibody cocktail); 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, including the impact of the positive opinion issued by the European Medicines Agency's Committee for Medicinal Products for Human Use discussed in this press release on any potential regulatory approval of REGEN-COV; 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 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 studies discussed or referenced 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).

Regeneron Contacts:

Media Relations	**Investor Relations**
Sarah Cornhill	Vesna Tosic
media@regeneron.com	investor@regeneron.com

View original content:http://www.prnewswire.com/news-releases/ema-issues-advice-on-regenerons-antibody-cocktail-casirivimab-with-imdevimab-for-certain-covid-19-patients-301236407.html

SOURCE Regeneron Pharmaceuticals, Inc.