US Food and Drug Administration Revises Emergency Use Authorization for Sotrovimab Due to Omicron BA.2 Subvariant

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SAN FRANCISCO, March 25, 2022 (GLOBE NEWSWIRE) -- GlaxoSmithKline plc (LSE/NYSE: GSK) and Vir Biotechnology, Inc. (Nasdaq: VIR) today announced that the US Food and Drug Administration has amended the Emergency Use Authorization (EUA) Fact Sheet for sotrovimab, an investigational monoclonal antibody. The FDA has determined that, based on the totality of available evidence, including new live virus data generated by Vir, it is unlikely that the sotrovimab 500 mg dose will be effective against the Omicron BA.2 variant. GSK and Vir are preparing a package of data in support of a higher dose of sotrovimab for the Omicron BA.2 subvariant and will be sharing these data with regulatory and health authorities around the world for discussion.

The FDA has updated its website to exclude sotrovimab use in geographic regions where infection is likely to have been caused by a non-susceptible SARS-CoV-2 variant based on available information, including variant susceptibility to these drugs and regional variant frequency (HHS regions 1 and 2). The FDA will continue to monitor the prevalence of circulating variants and update its website accordingly.

In connection with this announcement, Vir has filed a Current Report on Form 8-K, which can be found at www.sec.gov.

About sotrovimab
Sotrovimab is an investigational SARS-CoV-2 neutralizing monoclonal antibody. The antibody binds to an epitope on SARS-CoV-2 shared with SARS-CoV-1 (the virus that causes SARS), indicating that the epitope is highly conserved, which may make it more difficult for resistance to develop. Sotrovimab, which incorporates Xencor, Inc.'s Xtend™ technology, has also been designed to achieve high concentration in the lungs to ensure optimal penetration into airway tissues affected by SARS-CoV-2 and to have an extended half-life.

About global access to sotrovimab
Sotrovimab is authorized for emergency use in the United States and has been granted a marketing authorization in the European Union (EU), conditional marketing authorization in the UK, provisional marketing authorization in Australia, and conditional marketing authorization in Saudi Arabia. It has also been approved via Japan's Special Approval for Emergency Pathway. Temporary authorizations for sotrovimab have also been granted in several other countries.

Sotrovimab is supplied in several countries worldwide, including through national agreements in the US, UK, Japan, Australia, Canada, Singapore, Switzerland and the United Arab Emirates. Vir and GlaxoSmithKline are also supplying sotrovimab to participating Member States of the EU through a Joint Procurement Agreement with the European Commission. Additional agreements are yet to be disclosed due to confidentiality or regulatory requirements.

Sotrovimab in the United States
The following is a summary of information for sotrovimab. Healthcare providers in the US should review the Fact Sheets for information about the authorized use of sotrovimab and mandatory requirements of the Emergency Use Authorization (EUA). Please see the Food and Drug Administration (FDA) Letter of Authorization, full Fact Sheet for Healthcare Providers and full Fact Sheet for Patients, Parents, and Caregivers.

Sotrovimab has been authorized by the FDA for the emergency use described below. Sotrovimab is not FDA-approved for this use.

Sotrovimab is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of sotrovimab under section 564(b)(1) of the Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Authorized use
The FDA has issued an EUA to permit the emergency use of the unapproved product sotrovimab 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 40kg) 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

- Sotrovimab is not authorized for treatment of mild to moderate COVID-19 in geographic regions where infection is likely to have been caused by a non-susceptible SARS-CoV-2 variant based on available information including variant susceptibility to these drugs and regional variant frequency.
    - FDA's determination and any updates will be available at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs.

Sotrovimab is not authorized for use in adult or pediatric patients who:

- are hospitalized due to COVID-19, OR
- require oxygen therapy and/or respiratory support due to COVID-19, OR
- require an increase in baseline oxygen flow rate and/or respiratory support due to COVID-19 in those on chronic oxygen.

Benefit of treatment with sotrovimab has not been observed in patients hospitalized due to COVID-19. SARS-CoV-2 monoclonal antibodies may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Important Safety Information

CONTRAINDICATIONS
Sotrovimab is contraindicated in patients who have a history of anaphylaxis to sotrovimab or to any of the excipients in the formulation.

WARNINGS AND PRECAUTIONS
There are limited clinical data available for sotrovimab. Serious and unexpected adverse events may occur that have not been previously reported with sotrovimab use.

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions
Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of sotrovimab. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Infusion-related reactions, occurring during the infusion and up to 24 hours after the infusion, have been observed with administration of sotrovimab. These reactions may be severe or life-threatening.

Signs and symptoms of infusion-related reactions may include: fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia (eg, atrial fibrillation, sinus tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, vaso-vagal reactions (e.g., pre-syncope, syncope), dizziness and diaphoresis.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care. Clinically monitor patients for at least 1 hour after completion of the infusion for signs and symptoms of hypersensitivity. Hypersensitivity reactions occurring more than 24 hours after the infusion have also been reported with the use of SARS-CoV-2 monoclonal antibodies under Emergency Use Authorization.

Clinical Worsening After SARS-CoV-2 Monoclonal Antibody Administration
Clinical worsening of COVID-19 after administration of SARS-CoV-2 monoclonal antibody treatment 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 SARS-CoV-2 monoclonal antibody 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 sotrovimab has not been observed in patients hospitalized due to COVID-19. SARS-CoV-2 monoclonal antibodies may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation. Therefore, sotrovimab 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 EVENTS
Infusion-related reactions, including immediate hypersensitivity reactions, were observed in subjects treated with sotrovimab in COMET-ICE (1%) and in COMET-TAIL (<1%). Events reported within 24 hours of study treatment were pyrexia, chills, dizziness, dyspnea, pruritus, rash, and infusion-related reactions; all events were Grade 1 (mild) or Grade 2 (moderate).

Hypersensitivity adverse reactions were observed in 2% of patients treated with sotrovimab in COMET-ICE and in <1% of subjects treated with sotrovimab in COMET-TAIL. All were Grade 1 (mild) or Grade 2 (moderate). One reaction led to temporary pausing of the infusion.

The most common treatment-emergent adverse events observed in the sotrovimab treatment group in COMET-ICE were rash (1%) and diarrhea (2%), all of which were Grade 1 (mild) or Grade 2 (moderate).

USE IN SPECIFIC POPULATIONS
Pregnancy
A pregnancy exposure registry monitors pregnancy outcomes in women exposed to sotrovimab during pregnancy. To enroll, go to https://covid-pr.pregistry.com/ or call 1-800-616-3791 to obtain information about the registry.

There are insufficient data to evaluate a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcome. Sotrovimab should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus. There are maternal and fetal risks associated with untreated COVID-19 in pregnancy.

Lactation
There are no available data on the presence of sotrovimab in human milk, the effects on the breastfed infant or the effects on milk production. Individuals with COVID-19 who are breastfeeding should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

About the GSK and Vir Collaboration
In April 2020, GSK and Vir entered into a collaboration to research and develop solutions for coronaviruses, including SARS-CoV-2, the virus that causes COVID-19. The collaboration uses Vir's proprietary monoclonal antibody platform technology to accelerate existing and identify new anti-viral antibodies that could be used as therapeutic or preventive options to help address the current COVID-19 pandemic and future outbreaks. The companies will leverage GSK's expertise in functional genomics and combine their capabilities in CRISPR screening and artificial intelligence to identify anti-coronavirus compounds that target cellular host genes. They will also apply their combined expertise to research SARS-CoV-2 and other coronavirus vaccines.

GSK Commitment to Tackling COVID-19
GSK's response to COVID-19 has been one of the broadest in the industry, with potential treatments in addition to the Company's vaccine candidates in development with partner organisations.

GSK is collaborating with several organisations on COVID-19 vaccines by providing access to its adjuvant technology. The Company is working with Sanofi SA, Medicago Inc. and SK bioscience Co., Ltd. to develop adjuvanted, protein-based vaccine candidates, and all are now in phase III clinical trials. The use of an adjuvant can be of particular importance in a pandemic since it may reduce the amount of vaccine protein required per dose, allowing more vaccine doses to be produced and contributing to protecting more people in need.

GSK is also working with mRNA specialist CureVac NV to jointly develop next-generation, optimised mRNA vaccines for COVID-19 with the potential to address multiple emerging variants in one vaccine.

GSK is also exploring treatments for COVID-19 patients, collaborating with Vir Biotechnology to investigate monoclonal antibodies that could be used as therapeutic or preventive options for COVID-19.

Vir's Commitment to COVID-19
Vir was founded with the mission of addressing the world's most serious infectious diseases. In 2020, Vir responded rapidly to the COVID-19 pandemic by leveraging our unique scientific insights and industry-leading antibody platform to explore multiple monoclonal antibodies as potential therapeutic or preventive options for COVID-19. Sotrovimab is the first SARS-CoV-2-targeting antibody Vir advanced into the clinic. It was carefully selected for its demonstrated promise in pre-clinical research, including an anticipated high barrier to resistance and potential ability to both block the virus from entering healthy cells and clear infected cells. Vir is continuing to pursue novel therapeutic and prophylactic solutions to combat SARS-CoV-2 and future coronavirus pandemics, both independently and in collaboration with its partners.

About GSK
GSK is a science-led global healthcare company. For further information please visit www.gsk.com/aboutus.

About Vir Biotechnology
Vir Biotechnology is a commercial-stage immunology company focused on combining immunologic insights with cutting-edge technologies to treat and prevent serious infectious diseases. Vir has assembled four technology platforms that are designed to stimulate and enhance the immune system by exploiting critical observations of natural immune processes. Its current development pipeline consists of product candidates targeting COVID-19, hepatitis B virus, influenza A and human immunodeficiency virus. We routinely post information that may be important to investors on our website at www.vir.bio.

GSK Cautionary Statement Regarding Forward-Looking Statements
GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described in the Company's Annual Report on Form 20-F for 2021 and any impacts of the COVID-19 pandemic.

Vir Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "plan," "potential," "aim," "promising" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These forward-looking statements are based on Vir's expectations and assumptions as of the date of this press release. Forward-looking statements contained in this press release include, but are not limited to, statements regarding the ability of sotrovimab to treat and/or prevent COVID-19, Vir's collaboration with GlaxoSmithKline, planned discussions with global regulatory agencies, the timing of availability of pre-clinical data, data disclosures and publications related to sotrovimab. Many factors may cause differences between current expectations and actual results, including unexpected safety or efficacy data observed during pre-clinical or clinical studies, challenges in the treatment of hospitalized patients, difficulties in collaborating with other companies or government agencies, successful development and/or commercialization of alternative product candidates by Vir's competitors, changes in expected or existing competition, delays in or disruptions to Vir's business or clinical trials due to the COVID-19 pandemic, geopolitical changes or other external factors and unexpected litigation or other disputes. Other factors that may cause actual results to differ from those expressed or implied in the forward-looking statements in this press release are discussed in Vir's filings with the US Securities and Exchange Commission, including the section titled "Risk Factors" contained therein. Except as required by law, Vir assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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