GSK and Vir Submit Emergency Use Authorization Application to FDA for Intramuscular Administration of Sotrovimab for the Early Treatment of COVID-19

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– If authorized, would provide the option for intramuscular administration of sotrovimab, in addition to currently authorized intravenous administration –

– Submission follows COMET-TAIL Phase 3 data demonstrating that intramuscular administration of sotrovimab was non-inferior and offered similar efficacy to intravenous administration for high-risk populations –

PHILADELPHIA and SAN FRANCISCO, Jan. 13, 2022 (GLOBE NEWSWIRE) -- GlaxoSmithKline plc (LSE/NYSE: GSK) and Vir Biotechnology, Inc. (Nasdaq: VIR) today announced the submission of an application to the US Food and Drug Administration (FDA) requesting an amendment to the Emergency Use Authorization (EUA) for sotrovimab, an investigational monoclonal antibody for the early treatment of COVID-19, to include intramuscular (IM) administration. The EUA for sotrovimab was granted by the FDA in May 2021 as an investigational single-dose intravenous (IV) (500 mg) infusion SARS-CoV-2 monoclonal antibody for the early treatment of COVID-19, and the companies are requesting an expansion to the EUA to also include IM administration (500 mg).

Under the current EUA, sotrovimab can be used for the treatment of mild-to-moderate 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.

This submission is based on the Phase 3, randomized, open-label, non-inferiority COMET-TAIL trial, which achieved its primary endpoint, demonstrating that 500mg IM administration of sotrovimab (n=376) was non-inferior and offered similar efficacy to 500 mg IV administration (n=378) for the early treatment of mild-to-moderate COVID-19 in high-risk, non-hospitalized adults and adolescents. Low rates of serious adverse events (≤1% in both arms) were observed in the headline data.

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 the Sotrovimab Clinical Development Program

- COMET-ICE: a Phase 3, multi-center, double-blind, placebo-controlled trial investigated IV infusion of sotrovimab in adults with mild-to-moderate COVID-19 at high risk of progression to severe disease, who are not hospitalized and not requiring oxygen. The final COMET-ICE trial results in the full trial population of 1,057 participants demonstrated a 79% reduction (adjusted relative risk reduction) ($p<0.001$) in hospitalization for more than 24 hours or death due to any cause by Day 29 compared to placebo, meeting the primary endpoint of the trial. Interim data were published in *The New England Journal of Medicine* on October 27, 2021 and final data were pre-published on November 8, 2021 on *medRxiv*.

- COMET-TAIL: an ongoing Phase 3, randomized, multi-center, open-label, non-inferiority trial of IM versus IV administration of sotrovimab for the early treatment of mild-to-moderate COVID-19 in high-risk non-hospitalized adult and pediatric patients (12 years of age and older). The trial's primary endpoint was met, and headline data demonstrated that 500mg IM-administered sotrovimab was non-inferior and offered similar efficacy to IV administration for high-risk populations. In the IM administration (500mg) arm of the trial, there was a 2.7% rate of progression to hospitalization for more than 24 hours or death through Day 29 of the trial, compared to 1.3% in the IV administration arm (also 500mg). The adjusted difference between the IM and IV arms of the trial was 1.07% with a 95% confidence interval (CI) of -1.25% to 3.39%. The upper bound of the 95% CI is within the predetermined 3.5% non-inferiority margin set for the trial's primary endpoint. Low rates of serious adverse events (≤1% in both arms) were observed in the headline data. The trial originally included three arms: 500mg of sotrovimab given intravenously, and two intramuscular arms, consisting of 500mg and a low dose of 250mg. An independent safety monitoring committee recommended enrollment in the 250mg arm be discontinued after a greater number of hospitalizations in that arm was noted. The 500mg dose arms were recommended to continue with enrollment as planned. The companies plan to submit the complete COMET-TAIL data set to a peer-reviewed journal for publication in the first quarter of 2022.

- COMET-PEAK: a Phase 2, randomized, multi-center, parallel group trial evaluating IV and IM administration of sotrovimab in outpatients with mild-to-moderate COVID-19. The companies plan to submit the full COMET-PEAK data set to a peer-reviewed journal for publication.

- Additionally, GSK and Vir are partnering to investigate the use of sotrovimab in uninfected immunocompromised adults to determine whether sotrovimab can prevent symptomatic COVID-19 infection. GSK and Vir are supporting investigator sponsored studies and fostering scientific collaborations with both experienced investigators and networks, who are involved in the continuum of care of immunocompromised patients, to understand the role sotrovimab for prophylaxis could play in this population. Discussions with regulatory authorities regarding the prophylaxis program will occur in due course.

- Sotrovimab is also being studied by the University of Oxford among patients hospitalized with COVID-19 in the United Kingdom as part of the Randomized Evaluation of COVID-19 Therapy (RECOVERY) Trial.

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 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 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 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 sotrovimab has not been observed in patients hospitalized due to COVID19. 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 (eg, pre-syncope, syncope), dizziness and diaphoresis.

Consider slowing or stopping the infusion and administer appropriate medications and/or supportive care if an infusion-related reaction occurs.

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 (eg, 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
Hypersensitivity adverse reactions have been observed in 2% of patients treated with sotrovimab and 1% with placebo in COMET-ICE.

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). No other treatment-emergent adverse events were reported at a higher rate with sotrovimab compared to placebo.

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 outcome. Sotrovimab should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.

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 organizations.

GSK is collaborating with several organizations 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 3 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, optimized 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 preclinical 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. For more information, please visit 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 2020, GSK's 2021 Q3 Results 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 either through IV or IM administration, Vir's collaboration with GSK, plans to progress regulatory submissions globally, including with the FDA regarding the existing EUA for sotrovimab, planned discussions with other global regulatory agencies, the timing of availability of clinical data, program updates and data disclosures, and the clinical development program for sotrovimab. Many factors may cause differences between current expectations and actual results, including unexpected safety or efficacy data observed during preclinical or clinical studies, challenges in the treatment of hospitalized patients, difficulties in collaborating with other companies or

government agencies, challenges in accessing manufacturing capacity, 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 U.S. 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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