



Preclinical Data Highlight the Significant Antigenic Shift of the Omicron SARS-CoV-2 Variant and its Effect on the Neutralizing Activity of Monoclonal Antibodies, Convalescent Antibodies and Vaccine-Elicited Antibodies

December 14, 2021

– Data demonstrate sotrovimab, developed by Vir in conjunction with GlaxoSmithKline, continues to retain in vitro neutralizing activity against all tested variants of concern, including Omicron –

SAN FRANCISCO, Dec. 14, 2021 (GLOBE NEWSWIRE) -- Vir Biotechnology, Inc. (Nasdaq: VIR) today announced new preclinical data, published to the preprint server [bioRxiv](https://www.biorxiv.org/), demonstrating the impact of the significant antigenic shift of the new SARS-CoV-2 Omicron variant (B.1.1.529). A significant reduction in plasma neutralizing activity was observed against Omicron in sera from vaccinated and convalescent individuals. Researchers also tested the in vitro neutralizing activity of 44 monoclonal antibodies (mAbs) (eight of which are currently authorized or approved). Data demonstrate that sotrovimab and five other preclinical mAbs, developed by Vir in conjunction with GlaxoSmithKline, retained their in vitro neutralizing activity against Omicron.

These preclinical results were generated through pseudo-virus testing, and support recent pre-published findings from [Vir researchers](#)¹, as well as other [independent laboratories and institutions](#)². These data confirm Omicron's immune evasion and its impact on the neutralizing activity of the majority of tested monoclonal antibody therapies that target the receptor binding motif and other areas of the spike protein that are more prone to mutate.

"While we work to better understand the potential impact of the significant number of mutations in the Omicron variant and its anticipated trajectory, it is encouraging to see such a high level of consistency across a rapidly growing body of preclinical data generated from both industry and academia," said Herbert "Skip" Virgin, M.D., Ph.D., executive vice president of research and chief scientific officer for Vir Biotechnology. "These results, together with new data from external sources, continue to validate our approach of targeting a highly conserved region of the spike protein. We believe this strategy is responsible for sotrovimab's ability to maintain activity against all tested variants of concern and interest, including Omicron. We look forward to applying these learnings to our ongoing efforts to address both current and future pandemics."

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.

Preclinical data, published in [bioRxiv](https://www.biorxiv.org/), demonstrate that sotrovimab retains activity against all currently tested variants of concern and interest of the SARS-CoV-2 virus as defined by WHO, plus others, including but not limited to Delta (B.1.617.2), Delta Plus (AY.1 or AY.2), Mu (B.1.621) and Omicron (B.1.1.529).

About the sotrovimab clinical development program

- **COMET-ICE:** a Phase 3, multi-center, double-blind, placebo-controlled trial investigated an intravenous (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 all-cause 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](https://www.medrxiv.org/).
- **COMET-TAIL:** a Phase 3, randomized, multi-center, open-label, non-inferiority trial of intramuscular (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 500 mg intramuscularly administered sotrovimab was non-inferior, and offered similar efficacy and a comparable safety profile to 500 mg intravenous administration for high-risk populations. The companies plan to submit the complete COMET-TAIL data set to a peer-reviewed journal for publication in the first quarter of 2022, and look forward to working with regulatory authorities to help make this new option available to appropriate patients with COVID-19.
- **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. Data available to date from open-label Part B of the trial (500mg IV vs. 500mg IM) demonstrated equivalence on the virological response between the IM and IV arms. The companies plan to submit the complete COMET-PEAK data set to a peer-reviewed journal for publication in due course.

- GSK and Vir are also partnering to assess the use of sotrovimab in uninfected immunocompromised adults to determine whether sotrovimab can prevent symptomatic COVID-19 infection. GSK and Vir support investigator-sponsored studies and foster scientific collaborations with experienced investigators and networks 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.

About global access to sotrovimab

Sotrovimab is authorized for emergency use in the United States. *Xevudy* (sotrovimab) received a [positive scientific opinion](#) under Article 5(3) of Regulation 726/2004 from the Committee for Human Medicinal Products in the EU, conditional marketing authorization in Great Britain, provisional marketing authorization in Australia and conditional marketing authorization in Saudi Arabia. It has been approved via the Special Approval for Emergency Pathway in Japan. Temporary authorizations for sotrovimab have been granted in a dozen countries.

GSK and Vir also recently submitted the Marketing Authorization Application to the European Medicines Agency for *Xevudy* for the treatment of adults and adolescents (aged 12 years and over and weighing at least 40kg) with coronavirus disease 2019 (COVID-19) who do not require oxygen supplementation and who are at risk of progressing to severe COVID-19.

Sotrovimab is supplied in several countries worldwide, including through national agreements in the United States, United Kingdom, Japan, Australia, Canada, Singapore, Switzerland and the United Arab Emirates. The companies have also signed a Joint Procurement Agreement with the European Commission to supply doses of sotrovimab to participating Member States of the EU. Additional agreements are yet to be announced 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 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 US 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 USC § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Authorized Use

The US FDA has issued an Emergency Use Authorization (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 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

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 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 (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.

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 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.

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, the clinical development program for sotrovimab and the ability of sotrovimab to maintain activity against circulating variants of concern and interest, including Omicron. 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 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.

Reference

¹Cathcart AL, Havenar-Daughton C, Lempp FA, et al. The dual function monoclonal antibodies VIR-7831 and VIR-7832 demonstrate potent in vitro and in vivo activity against SARS-CoV-2. [bioRxiv](https://doi.org/10.1101/2021.05.11.446444). 2021. ²Cao YR, Wang J, Jian F, et al. B.1.1.529 escapes the majority of SARS-CoV-2 neutralizing antibodies of diverse epitopes. [bioRxiv](https://doi.org/10.1101/2021.05.11.446444). 2021.

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Source: Vir Biotechnology, Inc.