Vir Biotechnology Announces New Research Demonstrating Novel Mechanisms by Which SARS-CoV-2 Enters Host Cells

April 8, 2021

– Growing body of evidence suggests monoclonal antibodies that target a conserved epitope have the potential to be highly effective against SARS-CoV-2 and associated known mutations –

– Newly identified cell surface proteins play a role in SARS-CoV-2 infection and determine how certain classes of antibodies work –

SAN FRANCISCO, April 08, 2021 (GLOBE NEWSWIRE) -- Vir Biotechnology, Inc. (Nasdaq: VIR) today announced the publication of new preclinical research highlighting novel mechanisms by which SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) enters host cells and identifying how auxiliary receptors may impact the clinical efficacy of monoclonal antibodies (mAbs). The research highlights the distinct mechanism of action of non-receptor-binding motif (RBM)-targeting antibodies, such as VIR-7831 and VIR-7832, the Company's investigational SARS-CoV-2 mAbs that target a conserved non-RBM site within the receptor binding domain (RBD).

While prior literature has shown that SARS-CoV-2 infection is mediated by the virus binding to the ACE-2 entry receptor, findings from this research, posted on BioRxiv, highlight the importance of three additional auxiliary receptors that enhance infection mediated by the ACE-2 receptor. This new study addresses the role of DC-SIGN and L-SIGN lectins in infection and further identifies the SIGLEC1 lectin as a new participant in infection. SIGLEC1 is of particular importance because it is highly expressed and associated with SARS-CoV-2 in macrophages – an inflammatory cell type that is prominent in the lungs of patients with severe COVID-19. These cells can bind to infectious SARS-CoV-2 and present the virus to another cell to establish infection in that second cell. These auxiliary receptors also play an important role in modulating the neutralizing activity of different classes of spike-specific antibodies and may contribute to viral dissemination in the most severe COVID-19 cases.

This study addresses another important aspect related to the influence of the experimental methods used in measuring the neutralizing activity of different classes of spike-specific antibodies. Cells that overexpress ACE-2 at levels in excess of normal cells are widely used in neutralization assays because they can be infected with high efficiency. While these cell lines effectively measure the neutralizing activity of antibodies that target the RBM of the SARS-CoV-2 spike protein, they inadequately measure the neutralizing activity of non-RBM antibodies, as well as antibodies that target the N-terminal domain (NTD) of the spike. The NTD is a major target of human immunity to SARS-CoV-2. This observation indicates the significant limitations of the use of cells overexpressing ACE-2 for studies of mAbs and measuring serum neutralizing antibodies elicited by vaccination or infection.

When tested in more physiologic conditions, with cells expressing low levels of ACE-2 together with lectin receptors, non-RBM antibodies showed an enhanced ability to block viral infection. S309 (the precursor to VIR-7831 and VIR-7832), which targets a conserved non-RBM site within the RBD, showed enhanced neutralizing activity, reaching 100% neutralization. In contrast, antibodies that target the RBM were less effective in preventing infection. Additionally, a subset of the RBM-targeting antibodies analyzed in the study, including three clinical-stage antibodies, were shown to promote cell-cell fusion driven by the SARS-CoV-2 spike protein, potentially promoting cell-to-cell spread of the infection.

"As we continue to advance research that elucidates the mechanisms of SARS-CoV-2 infection, including the development of the disease and immunity to infection, one consistent finding of this study appears to be that certain classes of mAbs have potential advantages at blocking auxiliary receptor-enhanced infection," said Herbert "Skip" Virgin, M.D., Ph.D., chief scientific officer of Vir. "These data, together with recent studies showing an 85% reduction in hospitalization and death in high-risk outpatients receiving VIR-7831 compared to placebo and promising performance against SARS-CoV-2 variants in the lab, add to the growing body of evidence suggesting that antibodies that bind to a conserved non-RBM site of the virus are well suited to help treat and/or prevent COVID-19 infection and have the potential to address both current and future mutations."

VIR-7831 and VIR-7832 are investigational compounds, not approved by the U.S. Food and Drug Administration or any other regulatory authority.

About VIR-7831
VIR-7831 is an investigational dual-action SARS-CoV-2 monoclonal antibody. Preclinical data suggest it has the potential to both block viral entry into healthy cells and clear infected cells. The antibody binds to an epitope on SARS-CoV-2 that is 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. VIR-7831, which incorporates Xencor's Xtend™ technology, also has 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.

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About Vir Biotechnology
Vir Biotechnology is a clinical-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.

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 timing of availability of program updates and data disclosures related to VIR-7831 and VIR-7832, the ability of VIR-7831 and VIR-7832 to treat and/or prevent COVID-19, the ability of VIR-7831 to neutralize the SARS-CoV-2 live virus, and the ability of VIR-7831 and VIR-7832 to maintain activity against variant strains of the virus. 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 in 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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Source: Vir Biotechnology, Inc.