Vir Biotechnology Announces New Data Highlighting the Importance of Targeting Conserved Regions of the SARS-CoV-2 Spike Protein in the Development of Therapeutics

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– Scientists continuing to advance critical research on mechanisms of immune evasion exemplified by emerging SARS-CoV-2 variants –

– Study identifies the N-terminal domain of the SARS-CoV-2 spike protein as a target of potent neutralizing antibodies, but a target that can vary –

– Separate research results published in *Cell* characterize the virulence and antibody response to N439K, a prevalent variant of the SARS-CoV-2 receptor binding motif –

SAN FRANCISCO, Feb. 01, 2021 (GLOBE NEWSWIRE) -- Vir Biotechnology, Inc. (Nasdaq: VIR) today announced the publication of new research characterizing a novel site of vulnerability on the SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) spike protein – specifically the N-terminal domain (NTD). The study findings were made available online on bioRxiv on January 14, 2021 and have been submitted to a peer-reviewed journal for future print publication. This manuscript, together with data on immune evasion by mutations elsewhere in the spike protein published by scientists in *Cell*, begin to paint a comprehensive picture of the mechanisms that SARS-CoV-2 may utilize to evade immunity. Collectively, these data indicate the importance of carefully targeting conserved regions of the spike for vaccines and clinical monoclonal antibodies.

The receptor binding motif (RBM) of SARS-CoV-2, the region of the receptor binding domain (RBD) that interacts with the SARS-CoV-2 receptor, is a common target of COVID-19 natural and vaccine-induced immune responses, as well as monoclonal antibodies. However, recently published research has characterized the frequent occurrence of mutations within the RBM, highlighting the need for targeting alternate sites within the spike protein.

“This new research indicates the NTD is another site on the SARS-CoV-2 spike protein that, like the RBM, contains mutations as well as deletions in emerging variants,” said Davide Corti, Ph.D., senior vice president of antibody research for Vir. “Mutations in these immunodominant domains can evade natural immune responses and are of concern for vaccines and for therapeutic monoclonal antibodies targeting these regions. This underscores the need to advance therapies that have a high barrier to resistance.”

Little is known about neutralizing antibodies that bind to the NTD and their contribution to protection from infection and disease. In this new study, researchers at Vir, the University of Washington and other universities in the United States and Europe isolated and extensively characterized 41 human monoclonal antibodies that recognize the SARS-CoV-2 NTD. A subset of these NTD-specific monoclonal antibodies neutralize SARS-CoV-2 with potency similar to potential best-in-class monoclonal antibodies that target the RBD. Notably, several new SARS-CoV-2 genetic variants, including the widely prevalent variants identified in South Africa and the UK, were found to possess frequent mutations in the NTD.

These new findings build upon recent research published in *Cell* by Vir scientists in collaboration with colleagues at MRC-University of Glasgow Centre for Virus Research, which demonstrate the RBM of the SARS-CoV-2 spike protein – a major target of neutralizing monoclonal antibodies – is particularly variable.

“Our ongoing effort to characterize the SARS-CoV-2 spike protein is proving ever more critical as new variants continue to emerge. These new findings reinforce the approach we have taken with our monoclonal antibody, VIR-7831, which is currently in Phase 3 trials,” said George Scangos, Ph.D., chief executive officer of Vir. “By targeting a very conserved region of the RBD, VIR-7831 was designed to be effective against SARS-CoV-2 and variants that might emerge in this outbreak or future outbreaks of related viruses.”

The findings published in *Cell* characterize the virulence, fitness, clinical and epidemiologic impact, molecular features and immune response to N439K, a prevalent RBM variant of the SARS-CoV-2 spike protein first identified in Scotland in March 2020. Since then, a second lineage has independently emerged in other European countries, which, by January 2021, was detected in more than 30 countries across the globe. Although N439K variants are not believed to be more virulent or transmissible than the original SARS-CoV-2 strain, this research is the first to demonstrate mutations that maintain viral fitness can evade immunity.

To understand whether and how the N439K mutation might evade immunity, researchers in the findings published in *Cell* noted the binding of polyclonal sera to the SARS-CoV-2 spike was reduced by the mutation in a sizeable fraction of the 445 samples obtained from recovered individuals. Additionally, out of 144 human neutralizing mAbs isolated from individuals who recovered from SARS-CoV-2 infection early in the pandemic, a significant number failed to efficiently recognize N439K. When tested across four clinical-stage antibodies – S309 (the precursor of VIR-7831), LY-CoV555, REGN10933 and REGN10987 – S309, which targets a non-RBM epitope, LY-CoV555 and REGN10933 were capable of neutralizing the N439K variant.

About VIR-7831
VIR-7831 is an investigational dual-action monoclonal antibody. Preclinical data suggest it has the potential to both block viral entry into healthy cells and an enhanced ability to clear infected cells. The antibody binds to an epitope on SARS-CoV-2 that is shared with SARS-CoV (the virus which causes SARS), indicating that the epitope is highly conserved, which may make it more difficult for resistance to develop. VIR-7831 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.

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 SARS-CoV-2, hepatitis B virus, influenza A, human immunodeficiency virus and tuberculosis. 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 statements regarding print publication of Vir's research in a peer-reviewed journal, the emergence of new SARS-CoV-2 variants, the identification of N-terminal domain as a target of potent neutralizing antibodies, the importance of advancing therapies that have a high barrier to resistance and the potential ability of VIR-7831 to evade such variants in the protection and treatment of COVID-19 and in the prevention of future pandemics of related coronaviruses. 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 our competitors, changes in expected or existing competition, delays in or disruptions to our business or clinical trials due to the COVID-19 pandemic, geopolitical changes or other external factors, and unexpected litigation or other disputes.

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