Vir Biotechnology Publishes New Research Characterizing Variation in the SARS-CoV-2 Spike Protein and Virulence of a Prevalent Immune Evasion Variant, N439K

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– Manuscript highlights the importance of molecular surveillance of SARS-CoV-2 immune evasion and rational design of vaccines and antibody therapies for COVID-19 –

SAN FRANCISCO, Nov. 06, 2020 (GLOBE NEWSWIRE) -- Vir Biotechnology, Inc. (Nasdaq: VIR) today announced the publication of new research demonstrating that the immunodominant SARS-CoV-2 receptor binding motif (RBM) is the least conserved region in the SARS-CoV-2 spike protein, allowing for the occurrence of mutations without disrupting human ACE2 (hACE2) binding, which mediates viral entry. Researchers also characterize the virulence and fitness of N439K, a prevalent variant in the RBM that demonstrated resistance to human neutralizing monoclonal antibodies (mAbs), including one that is currently being evaluated in clinical trials. The manuscript, which was developed by Vir in collaboration with the MRC-University of Glasgow Centre for Virus Research, was published online November 5, 2020 on bioRxiv, and has been submitted to a peer-reviewed journal for future print publication.

“This study shows that the receptor binding motif of SARS-CoV-2, a major target of neutralizing antibodies, is evolving at a higher rate than the rest of the receptor binding domain and spike, and is resilient to change,” said Herbert “Skip” Virgin, M.D., Ph.D., chief scientific officer of Vir. “It is reminiscent of our experience with influenza A, where the mutability of the region targeted by the most potent neutralizing antibodies results in ineffective immunity year-over-year. Our demonstration of a virulent SARS-CoV-2 immune evasion mutant provides a cautionary tale for how we address this pandemic, and indicates the importance of ongoing surveillance for immune evasion mutations in the development of antibodies and vaccines.”

Data analyzed from approximately 130,000 SARS-CoV-2 genomic sequences, alongside evaluation of a published deep mutational scanning of the receptor binding domain (RBD), demonstrated that the RBM has a high degree of structural plasticity that permits significant changes in the amino acid sequence of the RBM, including N439K, while maintaining hACE2 binding.

Researchers also sought to define the clinical and epidemiologic impact, molecular features and immune response to the RBM variant, N439K. The goal was to determine if variants emerging in the pandemic have immune evasion potential. This variant, which was first identified in Scotland in March 2020, has since re-emerged independently in a second lineage and has been observed in 14 countries, including the United States. At the time of manuscript submission, it was the second most common circulating RBD variant.

Based on a review of sequenced viral isolates from 1,918 Scottish patients and clinical outcomes for 1,591 of these patients, N439K demonstrated similar clinical virulence to the wild-type 439N strain, full replication in the upper respiratory tract, the capacity to replicate in cultured cells, and the ability to effectively compete in *in vitro* growth assays with the wild-type virus. These data demonstrate that the virus exhibits fitness despite a mutation in the RBM.

To understand whether and how the N439K mutation might evade immunity, researchers noted that the binding of polyclonal sera to 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.

“These data provide critical evidence that more immune-evasive SARS-CoV-2 variants are likely to emerge, necessitating the updating of vaccines and the development of monoclonal antibodies that are highly resistant to viral escape,” said George Scangos, Ph.D., chief executive officer of Vir. “This is what we had in mind when we designed VIR-7831. By targeting a highly conserved epitope with the potential for a high barrier to resistance, we hoped to evade ongoing mutations and increase the long-term immunity of people exposed to SARS-CoV-2. We look forward to continuing to evaluate the utility of VIR-7831 in the prevention and treatment of COVID-19.”

This study was conducted in collaboration with Professors Emma Thomson, M.D, Ph.D., and David Robertson, Ph.D., and their teams at the MRC-University of Glasgow Centre for Virus Research.

As part of Vir’s ongoing commitment to addressing the COVID-19 pandemic, Vir scientists continue to publish new research designed to enhance the scientific understanding of SARS-CoV-2 and COVID-19. The Company’s most recent publications highlight:

- The mechanisms and risk for antibody-mediated enhancement of disease (Nature, October 2020);
- The identification and characterization of ultra-potent anti-COVID neutralizing mAbs (Science September 2020);
- The nature and half-life of human anti-SARS-CoV-2 antibodies in recovered individuals (Cell, September 2020). This research also showed that the part of the SARS-CoV-2 spike that contains the N439K mutation is a dominant target of the antibody response in many individuals;
- A mAb, S309 (the parent of VIR-7831 and VIR-7832), that covers both SARS-CoV-1 and SARS-CoV-2, which may be useful for the current and future pandemics (Nature, May 2020); and
- How to engineer mAbs with significantly increased efficacy in the treatment and prophylaxis of respiratory viral infections (Nature, April 2020).

About VIR-7831

VIR-7831 is a monoclonal antibody that has shown the ability to neutralize SARS-CoV-2 live virus in vitro and in vivo. The antibody binds to an epitope on SARS-CoV-2 that is shared with SARS-CoV-1 (also known as SARS), indicating that the epitope is highly conserved, which may make it more difficult for resistance to develop. VIR-7831 has been engineered with the potential to enhance lung bioavailability and 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 hepatitis B virus, influenza A, SARS-CoV-2, 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 "potential," "may," "will," "could," "expect," "plan," "anticipate," "believe," "estimate," "goal," "intend," "candidate," "continuing," "developing" 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. Each of these forward-looking statements involves risks and uncertainties. Actual results may differ materially from these forward-looking statements. Forward-looking statements contained in this press release include statements regarding print publication of Vir's research in a peer-reviewed journal, the emergence of SARS-CoV-2 variants, the ability of VIR-7831 to evade mutations and increase long-term immunity and the utility of VIR-7831 in the prevention and treatment of COVID-19. 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 neutralizing SARS-CoV-2, difficulty in collaborating with other companies or government agencies, and challenges in accessing manufacturing capacity. 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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