Vir Biotechnology Presents New Data Evaluating the Potential for VIR-2218 and VIR-3434 as Therapies for Chronic Hepatitis B and Hepatitis D

June 24, 2023

– Data from two ongoing clinical trials in people living with chronic hepatitis B infection suggest the combination of an antiviral with an immunomodulator can achieve rapid and deep declines in hepatitis B virus surface antigen (HBsAg) and higher rates of HBsAg loss compared to antivirals or immunomodulators alone –

– Preclinical data suggest the potential of VIR-2218 and VIR-3434 as treatment for the chronic suppression of hepatitis D virus infection –

SAN FRANCISCO, June 24, 2023 (GLOBE NEWSWIRE) -- Vir Biotechnology, Inc. (Nasdaq: VIR) today announced new data from its robust hepatitis B and D virus (HBV and HDV) portfolio that were presented at the EASL ™ (European Association for the Study of the Liver) Congress.

Data presented in a late-breaker oral presentation from a Phase 2 clinical trial demonstrated that when VIR-2218, an investigational small interfering ribonucleic acid (siRNA), was given for 24 or 48 weeks on top of a course of up to 48 weeks of pegylated interferon alpha (PEG-IFN-α) (cohorts 4 and 5 combined), 16% (5/31) achieved sustained HBsAg loss 24 weeks following the end of treatment.

“While based on small numbers, this is one of the highest rates of off-treatment response observed to-date and strongly supports the hypothesis that adding an siRNA to an immunomodulator has the potential to result in functional cure rates higher than historically seen with PEG-IFN-α alone,” said Professor Man-Fung Yuen, M.D., Ph.D., D.Sc., Chief of the Division of Gastroenterology and Hepatology, the University of Hong Kong, Li Shu Fan Medical Foundation Professor in Medicine.

In a poster presentation, new pharmacokinetics (PK) data support the safety, tolerability and antiviral activity of a 300 mg dose of VIR-3434, an investigational monoclonal antibody, which is being evaluated for the treatment of chronic HBV and HDV infection across multiple ongoing clinical trials. In addition, preclinical data presented in a separate poster showed evidence of antiviral efficacy of VIR-2218 and VIR-3434 against HDV infection by demonstrating reduced levels of HBsAg, HDV and HBV viremia *in vivo* with the parental molecule of VIR-3434 as well as reduced HBV antigens and secreted infectious HDV virions *in vitro* with both single and combination therapies of VIR-2218 and VIR-3434. These data further support the clinical development of these investigational medicines for the treatment of HDV.

“I am very excited by the progress we are making toward our goal of achieving HBV functional cure. Our data to-date with VIR-2218 and PEG-IFN- α support our hypothesis of using a cocktail of antivirals combined with immunomodulators. I am very much looking forward to learning how much impact VIR-3434, our vaccinal monoclonal antibody, will have – either as a replacement for PEG-IFN-α, or as an add on to VIR-2218 and PEG-IFN-α,” said Carey Hwang, M.D., Ph.D., Vir’s Senior Vice President, Clinical Research, Head of Chronic Infection. “Separately, our preclinical data strongly support the development of VIR-2218 and VIR-3434, either alone or in combination, to chronically suppress HDV viremia.”

Summary of EASL Congress 2023 Presentations

Late-Breaker Oral Presentation – VIR-2218 with or without PEG-IFN-α

Safety and efficacy of VIR-2218 with or without pegylated interferon alfa in virally-suppressed participants with chronic hepatitis B virus infection: post-treatment follow-up (presentation #LBO-02)

Presenter: Man-Fung Yuen, M.D., Ph.D., D.Sc., Chief of the Division of Gastroenterology and Hepatology, the University of Hong Kong, Li Shu Fan Medical Foundation Professor in Medicine.

Phase 2 follow-up data from an open-label, clinical trial (NCT04412863) evaluating VIR-2218 with or without PEG-IFN-α in virally-suppressed participants with chronic HBV demonstrated:

- In participants receiving VIR-2218 for 24 or 48 weeks plus up to 48 weeks of PEG-IFN-α (cohorts 4 and 5 combined), 26% (8/31) achieved HBsAg loss at the end of treatment and 16% (5/31) sustained HBsAg loss 24 weeks after the end of treatment.
- Across all cohorts, the four participants with anti-HBs titers >500 mIU/mL at the end of treatment achieved a sustained HBsAg loss at 24 weeks after the end of treatment, suggesting the potential use of anti-HBs titers as an on-treatment biomarker of off-treatment sustained response.
- Treatment with VIR-2218 alone and in combination with PEG-IFN-α was generally well tolerated. The majority of adverse events were consistent with the known effects of PEG-IFN-α and resolved after the end of treatment. No serious adverse events related to VIR-2218 were reported.

Oral Presentation – VIR-2218 in Combination with VIR-3434

Safety and antiviral activity of short-duration combinations of the investigational small interfering ribonucleic acid (siRNA) VIR-2218 with the neutralizing, vaccinal monoclonal antibody VIR-3434: post-treatment follow-up from the Phase 2 MARCH trial (presentation #OS-031)

Presenter: Edward Gane, M.D., Professor of Medicine at the University of Auckland, New Zealand, and Chief Hepatologist, Transplant Physician and

Deputy Director of the New Zealand Liver Transplant Unit at Auckland City Hospital

In Part A of the MARCH trial (NCT04856085), participants were treated with short-duration combination therapy with VIR-2218 and VIR-3434 for 5 or 12 weeks. Preliminary 48-week post-treatment safety, tolerability and antiviral activity data demonstrated:

- As previously shown, the combination of VIR-2218 and VIR-3434 resulted in a 2.7-3.1 $\log_{10}$ IU/mL decline in HBsAg levels at the end of treatment. As expected, no participants achieved on-treatment or off-treatment HBsAg loss, consistent with the short duration of combination therapy administered to these participants. Importantly, these short-duration cohorts informed the protocol for Part B, which is designed to evaluate whether VIR-3434 and VIR-2218, given with or without PEG-IFN-α for 24 to 48 weeks, can result in a functional cure for chronic HBV infection.
- The majority of participants met the criteria for discontinuing nucleotide reverse transcriptase inhibitor (NRTI) therapy because they achieved all of the following: HBsAg <100 log10 IU/mL and ≥1 log10 IU/mL reduction from baseline HBsAg level; HBV DNA <LLOQ; HBeAg-negative and ALT ≤2 times the upper limit of normal. Of those participants, 67% (4/6) remained off NRTI therapy as of the last available follow up.
- Combination treatment with VIR-2218 and VIR-3434 was generally well tolerated and was associated primarily with mild adverse events. All treatment-related adverse events were Grade 1, with no study discontinuations.

Poster Presentations – VIR-2218, VIR-3434

VIR-2218 and VIR-3434 therapy is efficacious in preclinical models of hepatitis delta virus infection (poster #TOP-109)

Presenter: Florian Lempp, Ph.D., Director, Virology, Vir Biotechnology

Preclinical *in vivo* and *in vitro* models evaluating the efficacy of VIR-2218 and VIR-3434 for the treatment of HDV infection showed:

- VIR-3434 targets the conserved antigenic loop within HBsAg present on both HBV and HDV virions and neutralized HDV infection with >10,000-fold higher potency than HBV-specific immunoglobulins *in vitro*.
- *In vivo*, the parental molecule of VIR-3434 reduced the levels of HBsAg, HDV and HBV viremia in HBV/HDV-coinfected liver-chimeric mice.
- Single and combination treatments with VIR-2218 and VIR-3434 of HBV/HDV-coinfected primary human hepatocytes *in vitro* reduced HBV antigens as well as secreted infectious HDV virions. Evaluation of such *in vivo* combinations is currently ongoing.

Single dose pharmacokinetics of VIR-3434, a novel neutralizing monoclonal antibody, in participants with chronic hepatitis B virus infection (poster #SAT-177)

Presenter: Sneha V. Gupta, Ph.D., Director, Clinical Pharmacology, Vir Biotechnology

A randomized, double-blind, placebo-controlled, Phase 1 single-ascending dose study (NCT05484206) evaluating the safety, tolerability, antiviral activity and PK of VIR-3434 in patients with chronic HBV infection demonstrated:

- Consistent with prior studies, the highest and most durable free VIR-3434 exposure was observed with the 300 mg dose, regardless of baseline HBsAg level. Other doses studied included 6 mg, 18 mg and 75 mg.
- Baseline HBsAg had a moderate impact in free VIR-3434 PK exposure, with lower PK exposures in participants with higher baseline HBsAg, which is suggestive of target-mediated drug disposition.
- VIR-3434 has a shorter terminal half-life and was cleared faster in participants with higher baseline HBsAg. At the 300 mg dose level, median apparent clearance was 609 mL/day in participants with HBsAg ≤3,000 IU/mL versus 883 mL/day in participants with >3,000 IU/mL.

Treatment eligibility and initiation among chronic hepatitis B patients in a real-world setting in the United States (poster #WED-141)

Presenter: Mark A. Schmidt, Ph.D., M.P.H., Infectious Disease Epidemiologist, Kaiser Permanente Center for Health Research

A retrospective analysis using electronic medical records from two healthcare delivery systems in the U.S. from January 1, 2000, to December 31, 2021, looking at treatment eligibility and time to treatment initiation among patients with chronic HBV infection showed:

- Among all 3,283 patients with untreated chronic HBV infection at cohort entry, 343 (10%) initiated treatment during the study period.
- Only 60% of those defined as treatment-eligible initiated chronic HBV treatment, although the median time for treatment to be initiated was within a year of being determined eligible.
- For untreated patients with chronic HBV infection who are not in a well-defined immunological disease state (“grey area”) entering care, healthcare providers can expect roughly 20% will become treatment eligible, and of these, half will progress in about a year.

The EASL presentations can be accessed under Events & Presentations in the Investors section of the Vir website here.

About Chronic Hepatitis B
Chronic hepatitis B virus (HBV) infection remains an urgent global public health challenge associated with significant morbidity and mortality.

Approximately 300 million people around the world are living with HBV, and approximately 900,000 of them die from associated complications each year. These patients are significantly underserved by existing therapies with low functional cure rates, lifelong daily therapy and/or poor tolerability. Vir is working to achieve a functional cure for the millions of people with HBV around the world through its broad and differentiated portfolio.

About Chronic Hepatitis D
Chronic hepatitis D virus (HDV) infection occurs as a simultaneous co-infection or super-infection with hepatitis B virus (HBV). An estimated 12 million people globally are infected with HDV, representing approximately 5% of those infected with HBV. HDV-HBV co-infection is considered the most severe form of chronic viral hepatitis due to more rapid progression toward hepatocellular carcinoma and liver-related death.

About VIR-2218
VIR-2218 is an investigational subcutaneously administered HBV-targeting siRNA that Vir believes has the potential to stimulate an effective immune response and have direct antiviral activity against hepatitis B virus (HBV) and hepatitis D virus (HDV). It is the first siRNA in the clinic to include Enhanced Stabilization Chemistry Plus (ESC+) technology to enhance stability and minimize off-target activity, which potentially could result in an increased therapeutic index. VIR-2218 is the first asset in the Company's collaboration with Alnylam Pharmaceuticals, Inc. to enter clinical trials.

About VIR-3434
VIR-3434 is an investigational subcutaneously administered antibody designed to block entry of hepatitis B and hepatitis D viruses (HBV and HDV) into hepatocytes and to reduce the level of virions and subviral particles in the blood. VIR-3434, which incorporates Xencor's Xtend™ and other Fc technologies, has been engineered to potentially function as a T cell vaccine against HBV and HDV, as well as to have an extended half-life.

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 and D viruses, influenza A and human immunodeficiency virus. Vir routinely posts information that may be important to investors on its website.

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," "expect," "anticipate," "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 Vir's strategy and plans; the potential clinical effects of VIR-2218 and VIR-3434; preliminary data of VIR-2218 in combination with VIR-3434; the potential benefits, safety and efficacy of VIR-2218, VIR-3434, VIR-2218 in combination with VIR-3434 and VIR-2218 and VIR-3434 in combination with PEG-IFNα; the initial results of the MARCH clinical trial evaluating the combination of VIR-2218 and VIR-3434; Vir's expectations related to the potential success of its current and future clinical development programs for HBV and HDV; Vir's plans and expectations for its HBV portfolio; and risks and uncertainties associated with drug development and commercialization. Many important factors may cause differences between current expectations and actual results, including the MARCH trial or in data readouts; the occurrence of adverse safety events; risks of unexpected costs, delays or other unexpected hurdles; difficulties in collaborating with other companies; 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. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical trials may not be indicative of full results or results from later-stage or larger-scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or the scientific data presented. 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.

Contact: Carly Scaduto Senior Director, Media Relations cscaduto@vir.bio +1-314-368-5189