VIR-2218 Demonstrates Dose-Dependent and Durable Reductions of Hepatitis B Surface Antigen in Phase 1/2 Trial

April 15, 2020

Company to host a conference call at 2:00 p.m. PT today

SAN FRANCISCO, April 15, 2020 (GLOBE NEWSWIRE) -- Vir Biotechnology, Inc. (NASDAQ: VIR) today announced additional interim data from the ongoing Phase 2 trial in patients and results from the Phase 1 trial in healthy volunteers of VIR-2218, an investigational small interfering ribonucleic acid (siRNA) that mediates RNA interference (RNAi) for the treatment of chronic hepatitis B virus (HBV) infection.

Interim results from the ongoing Phase 2 trial demonstrate that VIR-2218 results in a significant dose-dependent and durable reduction in hepatitis B surface antigen (HBsAg) through Week 24 in patients with chronic HBV who received two doses of VIR-2218, ranging from 20 mg to 200 mg. Similar HBsAg reductions were observed in both HBeAg- and HBeAg+ patients. In addition, VIR-2218 was generally well tolerated, with the majority of treatment emergent adverse events (AEs) reported as mild in severity, and no clinically significant alanine transaminase (ALT) elevations observed.

“The rapid and sustained dose-dependent knockdown of surface antigen observed in this trial with only 2 doses of VIR-2218 is impressive,” said Edward J. 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. “Notably, this response was seen in both the HBeAg- and HBeAg+ patient groups, demonstrating that this single siRNA can knock down HBsAg in patients regardless of the stage of their disease. Novel agents like VIR-2218 that reduce the high viral antigen burden associated with chronic HBV infection will likely become the cornerstone of future functional cure regimens.”

By targeting a conserved region of the HBV genome, VIR-2218 is designed to inhibit the production of all HBV proteins, including HBsAg. Suppression of HBV proteins, particularly HBsAg, is hypothesized to remove the inhibition of T and B cell activity directed against HBV. VIR-2218 was the first siRNA in the clinic to include Alnylam Pharmaceutical, Inc.’s (NASDAQ:ALNY) Enhanced Stabilization Chemistry-Plus (ESC+) technology to enhance stability and minimize off-target activity, which may result in an enhanced therapeutic index.

Dose-dependent HBsAg reductions in HBV patients

In the ongoing Phase 2 trial, virally suppressed patients on nucleos(t)ide reverse transcriptase inhibitor therapy (n=24) received two subcutaneous 20, 50, 100, or 200 mg doses of VIR-2218 on Day 1 and Day 29. At Week 24, the mean change in HBsAg observed with 20, 50, 100, and 200 mg was -0.76 $\log_{10}$, -0.93 $\log_{10}$, -1.23 $\log_{10}$, and -1.43 $\log_{10}$, respectively. Of note, all patients who received the 200 mg dose level achieved a ≥1 $\log_{10}$ reduction in HBsAg, with HBeAg- and HBeAg+ patients achieving similar mean declines. There has been no dose-related trend in the frequency of AEs observed during the trial, with the most common AE being headache (n=6; 25%). No patients discontinued the trial due to an AE.

ESC+ design suggests a potentially improved hepatic safety profile

The Alnylam ESC+ technology incorporated into VIR-2218 is designed to reduce off-target binding while maintaining on-target activity, which is hypothesized to result in an improved hepatic safety profile. In analyses of the in vitro, in vivo and Phase 1 clinical data, the ESC+ siRNA VIR-2218, when compared to the parent compound ALN-HBV, which is not an ESC+ siRNA, was shown to have:

- Improved in vitro specificity by reducing off-target effects on host messenger RNA;
- Decreased propensity to cause ALT elevations in a humanized liver chimeric mouse model; and
- In a cross-study comparison of Phase 1 data, decreased propensity to cause ALT elevations in healthy volunteers at dose levels anticipated to be clinically relevant.

Information on the potential hepatic safety profile of all siRNAs is an important consideration in the HBV patient population, especially those with advanced liver disease.

“We are pleased that the data from our VIR-2218 Phase 1/2 clinical trial continue to support the potential of this molecule to be the backbone of a treatment regimen aimed at the functional cure of chronic HBV infection,” said Phil Pang, M.D., Ph.D., Chief Medical Officer of Vir. “Our next step will be to demonstrate whether knockdown of HbsAg can result in high rates of functional cure when VIR-2218 is given in combination with other agents, which is the goal of our next set of trials. We expect the first of those combination trials – combining VIR-2218 with a shortened course of pegylated interferon - to begin dosing patients in the second half of this year.”

Conference Call Information

Vir will discuss these results via a conference call today at 2:00 p.m. PT (5:00 p.m. ET). The call will include presentation by Dr. Gane, who is the lead investigator for the VIR-2218 trials.

Participant Toll-Free Dial-In Number: +1 (833) 727-9519
Participant International Dial-In Number: +1 (830) 213-7696

A live webcast of the presentation can be accessed under Events & Presentations in the Investors section of the Vir website at www.vir.bio and will be archived there following the presentation for 30 days.

About Hepatitis B

Approximately 290 million people globally are chronically infected with HBV and approximately 900,000 of them die from HBV-associated complications each year. There is a significant unmet medical need for more effective therapies that lead to life-long control of the virus after a finite duration of therapy, which is the definition of a functional cure. For a registrational trial to demonstrate a functional cure, the formal endpoint accepted by the U.S. Food and Drug Administration, or the FDA, is undetectable HBsAg, defined as less than 0.05 international units per milliliter, or IU/ml, as well as HBV DNA less than the lower limit of quantification, in the blood six months after the end of therapy. Currently, a year-long course of PEG-IFN-α is the best available curative therapy. It has a low functional cure rate of approximately three to seven percent. Alternatively, suppressive therapy with nucleotide/nucleoside reverse transcriptase inhibitors, or NRTIs, is commonly used, but patients often require a lifetime of therapy.

About VIR-2218

VIR-2218 is a subcutaneously administered HBV-targeting siRNA that has the potential to stimulate an effective immune response and have direct antiviral activity against HBV. 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 can 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

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 "may," "will," "expect," "plan," "anticipate," "estimate," "intend," "potential" 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 the potential benefits of VIR-2218, the timing of VIR-2218 clinical trials, the potential of ESC+ technology to enhance the safety of siRNAs and statements regarding the potential benefits of Vir's collaboration with Alnylam Pharmaceuticals, Inc. Many factors may cause differences between current expectations and actual results including unexpected safety or efficacy data observed during clinical trials, difficulties in obtaining regulatory approval, challenges in accessing manufacturing capacity, clinical site activation rates or clinical trial enrollment rates, changes in expected or existing competition, delays or disruptions due to the COVID-19 pandemic, 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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