Arbutus' Imdusiran with Short Course Interferon Achieves Sustained Undetectable HBsAg, a Necessity for HBV Functional Cure

June 5, 2024

At the end of treatment, 33.3% of patients receiving imdusiran for 48 weeks, interferon (IFN) for 24 weeks and ongoing nucleoside analogue (NA) therapy achieved undetectable levels of HBsAg that were maintained in 100% of these patients 24 weeks after completing imdusiran and IFN treatment

Of the patients who have stopped all therapy, six still have undetectable levels of HBsAg and HBV DNA, with two of these patients reaching 12 weeks off all therapy

All six patients have seroconverted and have high titers of anti-HBsAg antibodies

These new Phase 2a data were presented at the European Association for the Study of the Liver (EASL) Congress 2024

WARMINSTER, Pa., June 05, 2024 (GLOBE NEWSWIRE) -- Arbutus Biopharma Corporation (Nasdaq: ABUS) ("Arbutus" or the "Company"), a clinical-stage biopharmaceutical company leveraging its extensive virology expertise to develop a functional cure for people with chronic hepatitis B virus (cHBV) infection, today announced new data from its Phase 2a clinical trial IM-PROVE I (AB-729-201) showing that imdusiran, the Company's RNAi therapeutic, and 24 weeks of pegylated interferon alfa-2α (IFN), a standard-of-care immunomodulator, added to ongoing nucleos(t)ide analogue (NA) therapy, reduced HBsAg levels and led to sustained HBsAg loss in some patients with cHBV during and after treatment. These data were presented today in the Viral Hepatitis B and D: New therapies, unapproved therapies or strategies poster session, and will be featured during a poster tour on Thursday, June 6, 2024, at the European Association for the Study of the Liver (EASL) Congress.

Select key data from this Phase 2a clinical trial include:

- Some patients who received either 48 or 24 weeks of imdusiran and 24 weeks of IFN with their ongoing NA therapy achieved undetectable HBsAg at the end-of-treatment (EOT) (33.3%, n=4/12; and 23.1%, n=3/13, respectively) that was sustained 24 weeks after completing imdusiran and IFN treatment (33.3%, n=4/12 and 15.4%, n=2/13, respectively). All six patients with sustained HBsAg loss have seroconverted with high anti-HBsAg antibody levels (43.8 to >1,000 mIU/mL suggestive of immune control) and are being followed for maintenance of both undetectable levels of HBsAg and HBV DNA for 24 weeks while off all therapy to assess for a functional cure.
- Two of the six patients have reached 12 weeks off all therapy while maintaining both undetectable levels of HBsAg and HBV DNA. The remaining four patients are at various timepoints less than 12 weeks off therapy with undetectable levels of HBsAg and HBV DNA.
- A total of 21 patients from across the four treatment cohorts have discontinued all therapy and are in the follow-up period. One patient that received 12 weeks of IFN treatment with imdusiran and NA therapy has maintained undetectable levels of HBsAg and HBV DNA while off all therapy for six months, thereby achieving a functional cure.

"These data are impressive with robust HBsAg response rates that are sustained after end-of-treatment in patients receiving imdusiran and IFN," commented Professor Man-Fung Yuen, D.Sc., M.D., Ph.D., Chief of the Division of Gastroenterology and Hepatology, the University of Hong Kong, who presented the data at the Congress. "Unlike other RNAi candidates in development that have been evaluated in combination with IFN, in this trial, imdusiran was administered less frequently, at a lower dose, and when combined with a shorter 24-week course of IFN, achieved undetectable HBsAg that is sustained after end of treatment and into early off-treatment follow-up. This trial evaluated small groups of patients, yet there is reason to believe that the combination of imdusiran and IFN could potentially lead to a functional cure in those patients that remain off all therapy. These data are extremely important for the HBV community, and I look forward to continuing to follow the patients who have discontinued all treatment."

To confirm undetectable HBsAg measured by the trial assay (lower limit of quantitation of 0.05 IU/mL), the Abbott HBsAg Next Qualitative assay, an ultrasensitive, research use only assay with a detection limit of 0.005 IU/mL, was utilized. The Next Assay confirmed HBsAg loss in six of the seven patients at EOT, and those six maintained HBsAg loss for 24 weeks after completing imdusiran and IFN treatment.

These data from the IM-PROVE I trial suggest that the combination of imdusiran and 24 weeks of IFN was generally safe and well-tolerated. There were no serious adverse events (SAEs) related to imdusiran or IFN, and no adverse events (AEs) leading to discontinuation. The most common imdusiran-related treatment emergent adverse events (TEAEs) were transient ALT elevations and injection site bruising. The IFN-related TEAEs were consistent with the known safety profile of IFN.

"There is a significant need for a functional cure for the more than 250 million patients chronically infected with HBV worldwide," commented Dr. Karen Sims, Chief Medical Officer of Arbutus Biopharma. "These data further support our belief that lowering surface antigen with imdusiran and incorporating an immunomodulator in the treatment regimen has the potential to provide a functional cure for patients with cHBV. We look forward to following the progress of these patients as well as those in our other Phase 2a trials evaluating imdusiran with other immunomodulators."

The poster that was presented at EASL Congress 2024 can be accessed through the Arbutus website under Publications.

IM-PROVE I Trial Details

The IM-PROVE I Phase 2a clinical trial (AB-729-201; NCT04980482) enrolled 43 HBeAg-negative, NA-suppressed patients with cHBV infection. After a 24-week lead-in with imdusiran (60 mg every 8 weeks) added to ongoing NA therapy, patients were randomized into one of the following four cohorts:

A1: Imdusiran + NA + IFN weekly for 24 weeks (n=12)

A2: NA + IFN weekly for 24 weeks (n=13)

B1: Imdusiran + NA + IFN weekly for 12 weeks (n=8)

B2: NA + IFN weekly for 12 weeks (n=10)

After completion of the IFN treatment period (Week 52 for cohorts A1 and A2 and Week 40 for cohorts B1 and B2), patients underwent a 24-week follow-up period on NA therapy alone and were then assessed for discontinuation of NA therapy. Patients with ALT levels less than two times the upper limit of normal, undetectable HBV DNA, and HBsAg <100 IU/mL at two consecutive visits at least 24 weeks after the last dose of imdusiran, qualified to discontinue all therapy and will be followed for at least 48 weeks. Safety, antiviral and immunologic assessments were obtained throughout the treatment and follow-up periods. HBsAg was assessed via Roche Cobas Elecsys HBsAg II assay (lower limit of quantitation [LLOQ] = 0.05 IU/mL) and results <LLOQ were analyzed by Abbott HBsAg Next Qualitative assay (detection limit = 0.005 IU/mL).

About Imdusiran (AB-729)

Imdusiran is an RNA interference (RNAi) therapeutic specifically designed to reduce all HBV viral proteins and antigens including hepatitis B surface antigen, which is thought to be a key prerequisite to enable reawakening of a patient's immune system to respond to the virus. Imdusiran targets hepatocytes using Arbutus' novel covalently conjugated N-Acetylgalactosamine (GalNAc) delivery technology enabling subcutaneous delivery. Clinical data generated thus far has shown single and multiple doses of imdusiran to be generally safe and well-tolerated, while also providing meaningful reductions in hepatitis B surface antigen and hepatitis B DNA. Imdusiran is currently in multiple Phase 2a clinical trials.

About HBV

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). HBV can cause chronic infection which leads to a higher risk of death from cirrhosis and liver cancer. Chronic HBV infection represents a significant unmet medical need. The World Health Organization estimates that over 250 million people worldwide suffer from chronic HBV infection, while other estimates indicate that approximately 2.4 million people in the United States suffer from chronic HBV infection. Approximately 820,000 people die every year from complications related to chronic HBV infection despite the availability of effective vaccines and current treatment options.

About Arbutus

Arbutus Biopharma Corporation (Nasdaq: ABUS) is a clinical-stage biopharmaceutical company leveraging its extensive virology expertise to identify and develop novel therapeutics with distinct mechanisms of action, which can be combined to provide a functional cure for patients with chronic hepatitis B virus (cHBV). We believe the key to success in developing a functional cure involves suppressing HBV DNA, reducing surface antigen, and boosting HBV-specific immune responses. Our pipeline of internally developed, proprietary compounds includes an RNAi therapeutic, imdusiran (AB-729), and an oral PD-L1 inhibitor, AB-101. Imdusiran has generated meaningful clinical data demonstrating an impact on both surface antigen reduction and reawakening of the HBV-specific immune response. Imdusiran is currently in three Phase 2a combination clinical trials. AB-101 is currently being evaluated in a Phase 1a/1b clinical trial. For more information, visit www.arbutusbio.com.

Forward-Looking Statements and Information

This press release contains forward-looking statements within the meaning of the Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, and forward-looking information within the meaning of Canadian securities laws (collectively, forward-looking statements). Forward-looking statements in this press release include statements about the potential to lead to a functional cure for HBV, our future development plans for our product candidates; the expected results of our clinical development plans and clinical trials with respect to our product candidates; our expectations with respect to the release of data from our clinical trials and the expected timing thereof; and the potential for our product candidates to achieve success in clinical trials.

With respect to the forward-looking statements contained in this press release, Arbutus has made numerous assumptions regarding, among other things: the effectiveness and timeliness of preclinical studies and clinical trials, and the usefulness of the data; the timeliness of regulatory approvals; the continued demand for Arbutus' assets; and the stability of economic and market conditions. While Arbutus considers these assumptions to be reasonable, these assumptions are inherently subject to significant business, economic, competitive, market and social uncertainties and contingencies.

Additionally, there are known and unknown risk factors which could cause Arbutus' actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements contained herein. Known risk factors include, among others: anticipated pre-clinical studies and clinical trials may be more costly or take longer to complete than anticipated, and may never be initiated or completed, or may not generate results that warrant future development of the tested product candidate; Arbutus may elect to change its strategy regarding its product candidates and clinical development activities; Arbutus may not receive the necessary regulatory approvals for the clinical development of Arbutus' products; economic and market conditions may worsen; market shifts may require a change in strategic focus.

A more complete discussion of the risks and uncertainties facing Arbutus appears in Arbutus' Annual Report on Form 10-K, Arbutus' Quarterly Reports on Form 10-Q and Arbutus' continuous and periodic disclosure filings, which are available at www.sedar.com and at www.sec.gov. All forward-looking statements herein are qualified in their entirety by this cautionary statement, and Arbutus disclaims any obligation to revise or update any such forward-looking statements or to publicly announce the result of any revisions to any of the forward-looking statements contained herein to reflect future results, events or developments, except as required by law.

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