Arbutus' Imdusiran Achieves Functional Cure in cHBV Patients when Combined with a Short Course of Interferon

November 15, 2024

50% of patients who had baseline HBsAg levels less than 1000 IU/mL achieved functional cure in Cohort A1 of the IM-PROVE I Phase 2a clinical trial

Overall, in Cohort A1, 25% of patients achieved functional cure

Data to be presented in late-breaker poster session at AASLD – The Liver Meeting® on Monday, November 18, 2024

WARMINSTER, Pa., Nov. 15, 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 IM-PROVE I Phase 2a clinical trial (AB-729-201) showing that six doses of imdusiran, the Company's RNAi therapeutic candidate, and 24 weeks of pegylated interferon alfa-2α (IFN), a standard-of-care immunomodulator, added to ongoing nucleos(t)ide analogue (NA) therapy, led to a functional cure rate of 50% (3/6) in HBeAg-negative patients with baseline HBsAg levels less than 1000 IU/mL, and an overall functional cure rate of 25% (3/12). Patients with HBsAg levels less than 1000 IU/mL represent a significant portion of the cHBV population. These data will be presented as a late-breaker poster presentation on November 18, 2024 at The American Association for the Study of Liver Diseases (AASLD) – The Liver Meeting® 2024.

"For the first time, we are seeing a meaningful percentage of HBV patients functionally cured with an RNAi therapeutic and interferon," commented Professor Man-Fung Yuen, D.Sc., M.D., Ph.D., Chief of the Division of Gastroenterology and Hepatology, the University of Hong Kong and Principal Investigator of the IM-PROVE I clinical trial, who will present the data at AASLD. "While 48 weeks of interferon can be used as a standard of care treatment for HBV patients, historically less than 10% of patients experience a functional cure. Here, with the combination of imdusiran and 24 weeks of interferon, we see a 50% functional cure rate in HBV patients with HBsAg less than 1000 IU/mL at baseline and a 25% functional cure rate overall. In addition, I was pleased to see that this regimen with a short course of interferon was generally safe and well-tolerated. These data are extremely impressive and provide hope for the millions of HBV patients worldwide and the medical community that a finite curative treatment is possible with imdusiran and interferon."

Key data from patients in Cohort A1 that received 6 doses of imdusiran plus 24 weeks of IFN in addition to ongoing NA therapy include:

- 50% of patients (3/6) with baseline HBsAg <1000 IU/mL achieved a functional cure (defined as sustained HBsAg loss and HBV DNA less than the lower limit of quantification (LLOQ) 24 weeks off all treatment (including NAs), with or without hepatitis B surface antibodies (anti-HBs)).
- Overall, 25% of patients (3/12) achieved a functional cure.
- Those patients that achieved a functional cure also seroconverted with anti-HBs levels increasing as patients lost HBsAg.
- The combination of imdusiran and 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 late-breaker poster, titled, "IM-PROVE I: Imdusiran in Combination with Short Courses of Pegylated Interferon Alfa-2a in Virally Suppressed, HBeAg Negative Subjects with Chronic HBV (cHBV) Infection Leads to Functional Cure", is available on the Company's website and provides the complete data set for all four cohorts of patients dosed in this clinical trial.

Additional immune activation data in those patients in Cohort A1 that achieved a functional cure will be presented by Dr. Emily Thi, Senior Director, Immunobiology and Biomarkers Research at Arbutus Biopharma in a poster titled, "Soluble Immune Biomarker Profiling of Chronic Hepatitis B Subjects Treated with Imdusiran in Combination with Pegylated Interferon Alfa Reveals Phases of Immune Activation." The data in this poster show that patients in Cohort A1 had greater increases in favorable immune biomarkers than those in other cohorts. Functionally cured patients and those with baseline HBsAg <1000 IU/mL had elevations of key immune biomarkers during the imdusiran lead-in, IFN treatment and follow-up periods, suggesting immune activation induced by imdusiran plus IFN treatment.

"We are extremely excited to have functionally cured these patients with the imdusiran and interferon treatment regimen. 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. "Excess production of surface antigen is believed to contribute to host immune exhaustion, resulting in inadequate immune response and failure to suppress the virus. These data support our belief that lowering surface antigen with imdusiran and incorporating an immunomodulator in the treatment regimen provides a functional cure in some patients with cHBV. We thank all the patients and investigators who participated in this clinical trial."

All of the above posters that will be presented at AASLD – The Liver Meeting can be accessed through the Arbutus website under Publications.

IM-PROVE I CLINICAL 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, 4 doses) added to ongoing NA therapy, patients were randomized into one of the following four cohorts: Cohort A1: imdusiran (2 doses) + NA + IFN weekly for 24 weeks (n=12), Cohort A2: NA + IFN weekly for 24 weeks (n=13), Cohort B1:

Imdusiran (1 dose) + NA + IFN weekly for 12 weeks (n=8) and Cohort 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.

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. In a Phase 2a clinical trial, imdusiran achieved meaningful functional cure rates in patients with cHBV when combined with pegylated interferon alfa-2α and nucleos(t)ide analogue therapy. Additional clinical data generated thus far has shown imdusiran to be generally safe and well-tolerated, while also providing meaningful reductions in hepatitis B surface antigen and hepatitis B DNA. Plans are underway to advance imdusiran into a Phase 2b clinical trial.

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 million people in the United States suffer from chronic HBV infection. Approximately 1.1 million 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 develop novel therapeutics with distinct mechanisms of action, which can potentially be combined to provide a functional cure for patients with chronic hepatitis B virus (cHBV). Arbutus believes the key to success in developing a functional cure involves suppressing HBV DNA, reducing surface antigen, and boosting HBV-specific immune responses. Arbutus' pipeline of internally developed, proprietary compounds includes an RNAi therapeutic, imdusiran (AB-729), and an oral PD-L1 inhibitor, AB-101. Imdusiran has achieved meaningful functional cure rates in patients with cHBV when administered as combination therapy. Plans are underway to advance imdusiran into a Phase 2b clinical trial. 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 IM-PROVE I Phase 2a clinical trial data; the potential for finite curative treatment to be possible with imdusiran, interferon and NA therapy; the IM-PROVE I Phase 2a clinical trial data supporting Arbutus' belief that lowering surface antigen with imdusiran and incorporating an immunomodulator in the treatment regimen combined with ongoing NA therapy provides a functional cure in some patients with cHBV; the potential to lead to a functional cure for HBV; Arbutus' future development plans for its product candidates; the expected results of Arbutus' clinical development plans and clinical trials with respect to its product candidates; Arbutus' expectations with respect to the release of data from its clinical trials and the expected timing thereof; and the potential for Arbutus' 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.

Contact Information

Investors and Media

Lisa M. Caperelli
Vice President, Investor Relations
Phone: 215-206-1822
Email: lcaperelli@arbutusbio.com