Treatment with Arbutus' Imdusiran and VTP-300 Achieves Statistical Significance in Lowering HBsAg Levels

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Data highlighted in oral presentation at the European Association for the Study of the Liver (EASL) Congress

WARMISTER, Pa., June 06, 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, announced new preliminary end-of-treatment (EOT) data from the Phase 2a clinical trial (IM-PROVE II, AB-729-202) in patients receiving ongoing standard-of-care nucleos(t)ide analogue (NA) therapy indicating that treatment with imdusiran, Arbutus' RNAi therapeutic, followed by Barinthus Biotherapeutic's T-cell stimulating immunotherapeutic, VTP-300, was generally safe, well-tolerated and led to maintenance of lower HBsAg levels during the post-treatment follow-up period in patients with cHBV. The data were presented today by Dr. Kosh Agarwal, MD, Consultant Hepatologist and Transplant Physician at the Institute of Liver Studies at King's College Hospital, London, during a session focused on new treatments for viral hepatitis B at the European Association for the Study of the Liver (EASL) Congress.

Dr. Agarwal presented the following data from 38 of 40 patients that were on stable NA therapy throughout the treatment period, received imdusiran (60mg every 8 weeks) for 24 weeks and were then randomized to receive either VTP-300 (treatment arm) or placebo at Weeks 26 and 30:

- Robust reductions of HBsAg were seen during the imdusiran lead-in period (-1.8 $\log_{10}$ by week 26) with 95% of patients achieving HBsAg <100 IU/mL before undergoing dosing in the treatment or placebo arm.
- At 24-weeks post-EOT, there was a significant difference ($p<0.05$) in HBsAg levels between the treatment arm (n=5) and placebo (n=6).
- 94% of patients (n=18/19) in the treatment arm achieved HBsAg levels of <100 IU/mL and 36% (n=7/19) had <10 IU/mL at EOT (Week 48) compared to 84% (n=16/19) and 21% (n=4/19), respectively in the placebo arm.
    - Similarly, at 24-weeks post-EOT (Week 72), the treatment arm had lower HBsAg levels with 80% of patients (n= 4/5) at <100 IU/mL and 60% (n=3/5) at <10 IU/mL compared to the placebo arm with 16% (n=1/6) and 0% (n=0/6), respectively.
- 84% of patients (n=16/19) in the treatment arm met the NA therapy discontinuation criteria and stopped NA treatment after Week 48 compared to 53% (n=10/19) in the placebo arm. One patient in the treatment arm achieved undetectable HBsAg and another had a >1.5 $\log_{10}$ decline between the last two visits during the NA-therapy discontinuation follow-up period.
- Treatment with imdusiran and VTP-300 was generally safe and well-tolerated. There were no Serious Adverse Events (SAEs), Grade 3 or 4 Adverse Events (AEs) or discontinuations due to treatment. The most common treatment-related AEs in two or more patients were injection site-related (both imdusiran and VTP-300) and transient ALT increases (imdusiran).

Dr. Agarwal commented, "These data show that adding imdusiran and VTP-300 to ongoing NA therapy in cHBV patients meaningfully reduces HBsAg after the end of the treatment period. I am impressed with the number of patients that qualified to stop NA therapy in the VTP-300 group and the clear separation in HBsAg levels between the treatment arm and placebo at Week 72."

"Imdusiran consistently provides notable reductions in HBsAg prior to combining with other therapies, such as VTP-300, which may improve the response rates of these immunomodulatory approaches," commented Dr. Karen Sims, Chief Medical Officer of Arbutus Biopharma. "We continue to believe that lowering surface antigen is key to promoting HBV-specific immune reawakening. We are looking forward to the data coming in the second half of this year from the additional arm of this trial evaluating the potential of nivolumab, a PD-1 monoclonal antibody, to further enhance responses to this treatment regimen."

The slides from the oral presentation at EASL 2024 can be accessed through the Arbutus website under Publications.

IM-PROVE II Trial Details

The IM-PROVE II Phase 2a clinical trial initially enrolled 40 non-cirrhotic, virally suppressed cHBV patients that were on stable NA therapy. The patients initially received imdusiran (60mg every 8 weeks) for 24 weeks with on-going NA therapy and were then randomized to receive either VTP-300 or placebo at Weeks 26 and 30 (and conditionally at Week 38 if they experienced a >0.5 $\log_{10}$ decline in HBsAg between Weeks 26 and 34). After completion of the treatment period at Week 48, those patients who met the following criteria: ALT levels less than two times the upper level of normal, HBV DNA less than the lower limit of quantitation, HBsAg <100 IU/mL, and HBeAg negative, discontinued NA therapy and were followed for an additional 48 weeks. Those who did not meet the criteria continued on NA therapy for an additional 24 weeks of follow-up.

This trial has been amended to include an additional cohort of 20 patients that will receive imdusiran plus NA therapy for 24 weeks followed by VTP-300 plus up to two low doses of nivolumab, an approved PD-1 monoclonal antibody. Enrollment is complete in this additional cohort with preliminary data expected in the second half of 2024.

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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