Arbutus and Barinthus Bio Announce New Data from the IM-PROVE II Trial Showing that the Addition of Nivolumab Increased Rates of HBsAg Loss in People with Chronic Hepatitis B

November 15, 2024

Significantly greater mean declines in HBsAg levels (p <0.017) were seen in those receiving imdusiran, VTP-300 and low-dose nivolumab compared to other cohorts assessed previously

23% of participants receiving imdusiran, VTP-300 and low-dose nivolumab reached HBsAg loss by Week 48

WARMINSTER, Pa. and OXFORD, United Kingdom, 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 infection, and Barinthus Biotherapeutics plc (NASDAQ: BRNS), a clinical-stage biopharmaceutical company developing novel immunotherapeutic candidates that guide T cells to control disease, today announced new preliminary data from the Phase 2a IM-PROVE II clinical trial (AB-729-202) of people with chronic hepatitis B virus (cHBV) at the American Association for the Study of Liver Diseases (AASLD) – The Liver Meeting® 2024.

The new data are from an additional cohort of participants (Group C) who received repeat doses of imdusiran, Arbutus' RNAi therapeutic, followed by Barinthus Bio's T-cell stimulating immunotherapeutic, VTP-300, with or without low-dose nivolumab, an anti-PD-1 monoclonal antibody. The data indicated that Group C participants receiving nivolumab experienced increased rates of HBsAg loss (defined as HBsAg <LLOQ [0.05 IU/mL]) compared to Group A and B participants who received imdusiran and VTP-300 or placebo. The data from Groups A and B were previously presented at the European Association for the Study of the Liver (EASL) Congress in June 2024.

Group C enrolled a total of 22 non-cirrhotic, virally suppressed cHBV participants with HBsAg ≥100 to <5,000 IU/mL at screening who were on stable nucleos(t)ide analogue (NUC) therapy for ≥12 months. Thirteen of these participants were eligible to receive low-dose nivolumab and nine participants were not eligible, based on the trial criteria.

The preliminary data from Group C included data to Week 48 (20/22 participants) and showed the following:

- Imdusiran lead-in treatment led to a mean decline from baseline in HBsAg consistent with data from Groups A and B.
- Significantly greater mean declines in HBsAg levels (p <0.017) were seen in Group C participants who received imdusiran and VTP-300 with nivolumab, at Week 48 compared with Groups A and B and Group C without nivolumab.
- 23% of participants (3/13) in the group receiving imdusiran, VTP-300 and low-dose nivolumab achieved HBsAg loss by Week 48.
- Increases in soluble immune biomarkers associated with immune checkpoint proteins, inflammation, and T-cell activation were observed in participants who had HBsAg loss at any point through Week 48.
- The Group C treatment regimen with nivolumab was generally well tolerated and did not result in any immune-related adverse events.

"These data demonstrated the impact of the combination of an immune stimulant such as VTP-300 and a low dose of the checkpoint inhibitor nivolumab in helping participants reach HBsAg loss," said Dr. Leon Hooftman, Chief Medical Officer of Barinthus Bio. "While these are early data, the imdusiran, VTP-300 and low-dose nivolumab regimen is promising and is consistent with the data we are seeing from our HBV003 trial of VTP-300 plus low-dose nivolumab."

"These data continue to support our belief that lowering surface antigen is key to promoting HBV-specific immune reawakening," commented Dr. Karen Sims, Chief Medical Officer of Arbutus Biopharma. "In this trial, imdusiran provided meaningful reductions in HBsAg prior to treatment with the immunomodulatory agents VTP-300 and low dose nivolumab, leading to improved response rates with this combination."

The poster from the presentation at AASLD 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 participants that were on stable NUC therapy in Groups A and B. These participants received imdusiran (60mg every 8 weeks) for 24 weeks with on-going NUC therapy and were then randomized to receive either VTP-300 (Group A) or placebo (Group B) at Weeks 26 and 30 (and conditionally at Week 38 if they experienced a >0.5 log10 decline in HBsAg between Weeks 26 and 34).

This trial was amended to include an additional cohort (Group C) which enrolled 22 participants, 13 of which were eligible to receive imdusiran (60mg every 8 weeks) for 24 weeks with ongoing NUC therapy followed by VTP-300 at Weeks 26 and 30 plus up to two low doses of nivolumab (0.3 mg/kg), an approved PD-1 monoclonal antibody at Week 30. The remaining 9 participants received the imdusiran/NUC/VTP-300 regimen without nivolumab. Participants could receive a second dose of VTP-300 ± low-dose nivolumab at Week 38 if their HBsAg was ≥10 IU/mL at Week 34.

Upon completion of the treatment period at Week 48, all participants who met certain criteria could discontinue NUC therapy and be followed for an additional 48 weeks. Those who did not meet the criteria continued on NUC therapy for an additional 24 weeks of follow-up.

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 VTP-300

VTP-300 is an immunotherapeutic candidate consisting of an initial dose using the ChAdOx vector and a secondary dose(s) using the MVA vector, both encoding multiple HBsAg, including full-length surface, modified polymerase, and core antigens. VTP-300 is the first antigen-specific immunotherapy that has been shown to induce sustained reductions in HBsAg. Barinthus Bio is studying VTP-300 in combination with other agents, including siRNA and low-dose anti-PD-1 antibodies, to control the infection, and counterbalance the immune suppression and T cell exhaustion in the liver caused by chronic HBV infection.

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 generated meaningful clinical data demonstrating an impact on both surface antigen reduction and reawakening of the HBV-specific immune response. Imdusiran is currently in two 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.

About Barinthus Bio

Barinthus Biotherapeutics (Nasdaq: BRNS) is a clinical-stage biopharmaceutical company developing novel immunotherapeutic candidates designed to guide the immune system to overcome chronic infectious diseases and autoimmunity. Helping people living with serious diseases and their families is the guiding principle at the heart of Barinthus Bio. With a focused pipeline built around its proprietary platform technologies, Barinthus Bio is advancing immunotherapeutic product candidates in infectious diseases and autoimmunity, including: VTP-300, that utilizing its ChAdOx/MVA platform designed as a potential component of a functional cure for chronic HBV infection and VTP-1000, utilizing our SNAP-Tolerance Immunotherapy (SNAP-TI) platform and is designed to treat people with celiac disease. Barinthus Bio is also conducting a Phase 1 clinical trial for VTP-850, a second-generation immunotherapeutic candidate designed to treat recurrent prostate cancer. Barinthus Bio's differentiated technology platforms and therapeutic approach, coupled with deep scientific expertise and focus on clinical development, uniquely positions the company to navigate towards delivering treatments that improve the lives of people with chronic infectious diseases and autoimmunity. For more information, visit www.barinthusbio.com.

Arbutus 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 Arbutus' future development plans for its product candidates; the expected cost, timing and results of its clinical development plans and clinical trials with respect to Arbutus' product candidates; Arbutus' expectations with respect to the release of data from its clinical trials and the expected timing thereof; Arbutus' expectations and goals for its collaborations with third parties and any potential benefits related thereto; 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, including uncertainties and contingencies related to patent litigation matters.

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; Arbutus may not realize the anticipated benefits from its recent organizational changes; Arbutus may incur additional unexpected expenses in connection with the organizational changes; Arbutus may experience additional employee turnover as a result of the organizational changes; uncertainties associated with litigation generally and patent litigation specifically; and Arbutus and its collaborators may never realize the expected benefits of the collaborations; and 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.

Barinthus Bio's Forward Looking Statements

This press release contains forward-looking statements regarding Barinthus Bio within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, which can generally be identified as such by use of the words "may," "will," "plan," "forward," "encouraging," "believe," "potential," "expect," and similar expressions, although not all forward-looking statements contain these identifying words. These forward-looking statements

include, without limitation, express or implied statements regarding our future expectations, plans and prospects, including our product development activities and clinical trials, including timing for readouts of any preliminary, interim or final data or next steps for any of our programs, and our ability to develop and advance our current and future product candidates and programs. Any forward-looking statements in this press release are based on our management's current expectations and beliefs and are subject to numerous risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks and uncertainties related to the success, cost and timing of our pipeline development activities and planned and ongoing clinical trials, including the risk that the timing for preliminary, interim or final data or initiation of our clinical trials may be delayed, the risk that interim or topline data may not reflect final data or results, our ability to execute on our strategy, regulatory developments, the risk that we may not achieve the anticipated benefits of our pipeline prioritization and corporate restructuring, our ability to fund our operations and access capital, our cash runway, including the risk that our estimate of our cash runway may be incorrect, global economic uncertainty, including disruptions in the banking industry, the conflicts in Ukraine, Israel and Gaza, and other risks identified in our filings with the Securities and Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2023, our Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. We caution you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. We expressly disclaim any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

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