Barinthus Bio's VTP-300 Trials Demonstrate Ability to Achieve Undetectable HBsAg levels and Statistical Significance in Lowering HBsAg Levels in People with Chronic Hepatitis B

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- *In the HBV003 trial, 67% of participants had HBsAg <10 IU/mL and 19% of participants had undetectable HBsAg when assessed for NUC discontinuation (end of treatment) or later, and 76% of participants were eligible for nucleos(t)ide analogue (NUC) therapy discontinuation.*
- *In the IM-PROVE II trial, conducted in partnership with Arbutus Biopharma, a statistically significant difference was observed in HBsAg levels between the VTP-300 treatment and placebo groups at 24-weeks post-*end of treatment (*EOT) and 84% of participants who received VTP-300 discontinued standard of care (SoC) NUC therapy vs 53% receiving placebo.*

OXFORD, United Kingdom, June 06, 2024 (GLOBE NEWSWIRE) -- Barinthus Biotherapeutics plc (NASDAQ: BRNS), a biopharmaceutical company developing novel T cell immunotherapeutic candidates, today announced the presentation of updated data from two clinical trials in people with chronic hepatitis B (CHB) at the European Association for the Study of the Liver (EASL) Congress 2024. The presentations include updated interim data from the Phase 2b clinical trial (HBV003), as well as new interim EOT data from the Phase 2a clinical trial (IM-PROVE II, AB-729-202) in partnership with Arbutus Biopharma (NASDAQ: ABUS), both in people with CHB receiving ongoing SoC NUC therapy.

Interim HBV003 data: VTP-300 and Low-dose Nivolumab
Interim data from the HBV003 trial indicate that treatment with VTP-300 and low-dose nivolumab is generally well-tolerated and sustained HBsAg declines were observed across all groups, with some participants reaching undetectable levels of HBsAg. As of the data cutoff on April 15, 2024, 91 out of a planned 120 virally suppressed patients with CHB on stable NUC therapy were enrolled in the trial, 40 of whom had screening HBsAg ≤200 IU/mL as per the study protocol amendment in 2023 and 21 of whom had been assessed for NUC discontinuation. Participants reaching Day 169 were assessed to confirm if they were eligible to discontinue NUC therapy in line with the study criteria. Data presented focuses on participants with baseline HBsAg ≤200 IU/mL:

- 76% of assessed participants (n=16/21) were eligible for NUC discontinuation at EOT, 7 of these discontinued.
  - 71% (n=5/7) remained off NUC therapy, up to 44 weeks post-discontinuation in one case.
- 19% of participants (n=4/21) across the groups assessed for NUC discontinuation, had undetectable HBsAg at any time.
  - This has been maintained for ≥16 weeks in 2 cases.
- 67% of participants (n=14/21) across all groups assessed for NUC discontinuation had HBsAg <10 IU/mL at Week 24 or later.
- Robust T cell responses as measured by IFNy ELISpot were observed to all encoded antigens.
- There were no Serious Adverse Events (SAEs), Grade 3 or 4 Adverse Events (AEs) related to treatment. There was one treatment discontinuation due to an AE. The most common treatment-related AE was thyroid dysfunction, reported in 9% of participants (n=8/91) with normal Thyroid Function Tests reported in 7 of 8 (88%) at last recorded visit. Transient alanine transaminase (ALT) elevations occurred in 14 participants through to Day 85.

“With the majority of patients assessed reaching very low levels of HBsAg and eligibility for NUC discontinuation, we believe these data are further evidence that VTP-300 could be a critical component of a functional cure regimen,” said Bill Enright, Chief Executive Officer of Barinthus Bio. “At the time of the data cut and analysis, the most advanced participant had undetectable levels of HBsAg and HBV DNA for more than five months and had been able to remain off NUC therapy for 44 weeks, further highlighting the potential of VTP-300 in reshaping the chronic HBV treatment landscape.”

“People with Hepatitis B currently require life-long therapy and may still progress to liver failure or liver cancer, which is a slowly developing and often-devastating process,” said Prof. Man-Fung Yuen, Chief of Division of Gastroenterology and Hepatology, Queen Mary Hospital, University of Hong Kong, Hong Kong. “I'm encouraged by the potential of VTP-300 to provide sustained viral suppression and what may ultimately be a potential functional cure, which would allow patients to stop taking life-long therapies and halt progression of liver failure or cancer.”

End of Treatment IM-PROVE interim data: imdusiran and VTP-300
Data from IM-PROVE II as of the data cutoff on April 12, 2024, indicate that treatment with imdusiran, Arbutus’ RNAi therapeutic candidate, followed by Barinthus Bio's T-cell stimulating immunotherapeutic candidate, VTP-300, was generally well-tolerated and observed to maintain low HBsAg levels during the post-treatment follow-up period. 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 EASL Congress.

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

- Robust reductions of HBsAg were observed during the imdusiran lead-in period with 95% of patients achieving HBsAg <100 IU/mL before undergoing dosing in the VTP-300 treatment or placebo groups.
- At 24-weeks post-EOT, there was a significant difference ($p<0.05$) in HBsAg levels between the VTP-300 treatment group (n=5) and placebo (n=6).
- 94% of participants (n=18/19) in the VTP-300 treatment group achieved HBsAg levels of <100 IU/mL and 36% had <10 IU/mL (n=7/19) at EOT (Week 48) compared to the placebo group, 84% (n=16/19) and 21% (n=4/19), respectively.
  - Similarly, at 24-weeks post-EOT (Week 72), the VTP-300 treatment group had lower HBsAg levels with 80% of

participants at <100 IU/mL (n=4/5) and 60% at <10 IU/mL (n=3/5) than the placebo group, 16% (n=1/6) and 0% (n=0/6), respectively.

- 84% of participants (n=16/19) in the VTP-300 treatment group met criteria at EOT (Week 48) to discontinue NUC therapy vs 52% in the placebo group (n=10/19).
- In the VTP-300 treatment group, 20% of participants (n=1/5) achieved undetectable HBsAg at 24-weeks post-EOT and a further 20% of participants (n=1/5) had a >1.5$\log_{10}$ decline between the last two visits during the NUC therapy discontinuation follow-up period.
- Treatment with imdusiran and VTP-300 was generally well-tolerated. There were no reported SAEs, Grade 3 or 4 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 NUC therapy in CHB patients meaningfully reduces HBsAg after the end of the treatment period. I am impressed with the number of patients that qualified to stop NUC therapy in the VTP-300 group and the clear separation in HBsAg levels between the treatment group and placebo at Week 72.”

“The data clearly showed the role of VTP-300 in maintaining low HBsAg levels and the therapeutic potential of this specific combination approach, with imdusiran, to lower and maintain low levels of HBsAg,” said Dr. Nadege Pelletier, Chief Scientific Officer of Barinthus Bio. “As we continue to monitor HBsAg declines in the VTP-300 treatment group we are eager to see the next data cut in the fourth quarter of the year, which we expect will include data from the triple combination approach, including nivolumab. Understanding the impact of nivolumab could take us another step closer to a potential hepatitis B functional cure regimen.”

The slides from the poster and oral presentations at EASL 2024 can be found on the Barinthus Bio website under the Events & Presentation page.

About the HBV003 Trial
The HBV003 trial is designed to obtain critical information on treatment dosing regimen with patients receiving VTP-300 and low-dose (LD) nivolumab. All Groups received ChAdOx at Day 1; Groups 1 & 2 received MVA with nivolumab at Day 29; Group 2 was dosed again with MVA and nivolumab at Day 85; Group 3 received only MVA at Day 29, nivolumab at Day 36, and a conditional second MVA dose at Day 85 to evaluate anti-PD-1 inhibition timing. The conditional MVA dose was administered if participants had HBsAg ≥10 IU/mL. In 2023, the study inclusion criteria was amended from people with CHB with HBsAg ≥10 and <4,000 IU/mL to ≥10 and ≤200 IU/mL, as strongest responses were observed in participants with HBsAg ≤200 IU/ml.

About the IM-PROVE II Trial
The IM-PROVE II (AB-729-202) Phase 2a clinical trial initially enrolled 40 non-cirrhotic, virally suppressed CHB patients that were on stable NUC-therapy. The patients initially received imdusiran (60mg every 8 weeks) for 24 weeks with on-going NUC-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, 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 NUC-therapy and were 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.

This trial has been amended to include an additional cohort of 20 patients that will receive imdusiran plus NUC-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 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 HBV
Globally it is estimated that there are approximately 254 million people living with chronic HBV infection.[1] This includes up to 2.4 million in the U.S. and 10.6 million in Europe, with the highest prevalence in East Asia and Africa.[1,2] Approximately 1.1 million people died from HBV and related complications in 2022, such as liver cirrhosis and hepatocellular carcinoma.[1] Due to low HBV diagnosis rates, only 13% of people living with chronic hepatitis B are aware of their infection and less than 3% had received antiviral treatment at the end of 2022.[1]

About Barinthus Biotherapeutics
Barinthus Bio is a clinical-stage biopharmaceutical company developing novel T cell immunotherapeutic candidates designed to guide the immune system to overcome chronic infectious diseases, autoimmunity and cancer. Helping people living with serious diseases and their families is the guiding principle at the heart of Barinthus Bio. With a broad pipeline, built around three proprietary platform technologies: ChAdOx, MVA and SNAP, Barinthus Bio is advancing a pipeline of four product candidates across a diverse range of therapeutic areas, including: VTP-300, an immunotherapeutic candidate designed as a potential component of a functional cure for chronic HBV infection; VTP-200, a non-surgical product candidate for persistent high-risk human papillomavirus (HPV); VTP-1000, an autoimmune candidate designed to utilize the SNAP-Tolerance Immunotherapy (TI) platform to treat patients with celiac disease; and VTP-850, a second-generation immunotherapeutic candidate designed to treat recurrent prostate cancer. Barinthus Bio’s proven scientific expertise, diverse portfolio and focus on pipeline development uniquely positions the company to navigate towards delivering treatments for people with infectious diseases, autoimmunity and cancers that have a significant impact on their everyday lives. For more information, visit www.barinthusbio.com.

References

1. WHO, Global hepatitis report 2024.
2. Hepatitis B Foundation, What is Hepatitis B?, 2023.

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,” 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 product development activities and clinical trials, including timing for readouts of any interim data or next steps for any of our programs, including VTP-300 and the HBV003 trial, the timing for readouts for the IM-PROVE II trial of our collaboration partner, Arbutus, the tolerability or potential benefits of VTP-300 or imdusiran, 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, our ability to execute on our strategy, regulatory developments, our ability to fund our operations and access capital, the risk that interim or topline data may not reflect final data or results, global economic uncertainty, including disruptions in the banking industry, the conflict in Ukraine, the conflict in Israel and Gaza, and other risks identified in our filings with the Securities and Exchange Commission (the "SEC"), 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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