Vaccitech's VTP-300 induced sustained reductions of surface antigen in patients with chronic hepatitis B both as a monotherapy and in combination with a single low dose of anti-PD-1

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VTP-300 as a monotherapy and in combination with a single administration of low-dose nivolumab was administered, with no treatment-related serious adverse events and infrequent transient transaminitis.

Meaningful, durable reductions of Hepatitis B surface antigen (HBsAg) were seen in some patients who received VTP-300 as either a monotherapy or in combination with a single low dose of nivolumab at the booster dose. Declines were most prominent in patients with lower baseline HBsAg.

All patients who received VTP-300 monotherapy or in combination with low-dose nivolumab and who had a HBsAg decline greater than 0.5 log_{10} had durable reductions of HBsAg until the last measurement (up to eight months after last dose).

A robust T cell response against all encoded antigens, measured by overnight stimulation, was observed following VTP-300 administration, notably for marked CD8+ T cell predominance, which, to our knowledge, has never been achieved by any other immunotherapeutic.

OXFORD, United Kingdom, June 22, 2022 (GLOBE NEWSWIRE) -- Vaccitech plc (NASDAQ: VACC), a clinical-stage biopharmaceutical company engaged in the discovery and development of novel immunotherapeutics and vaccines for the treatment and prevention of infectious diseases, cancer, and autoimmune diseases, today announced an update to the interim analysis of safety and efficacy data from the HBV002 study (NCT04778904), which is being presented as a poster at the 2022 EASL International Liver Congress™ by Professor Ellie Barnes, Professor of Hepatology and Experimental Medicine at the University of Oxford.

The updated analysis, with a data cut-off of May 9th, which now includes 39 patients with at least three months of follow-up, shows that VTP-300 as a monotherapy or in combination with a single low-dose nivolumab at the time of the booster dose was safely administered with no treatment-related serious adverse events and two patients with mild, rapidly resolving transaminitis.

In the VTP-300 monotherapy group, meaningful and durable reductions of HBsAg were seen in all three patients with baseline HBsAg under 50 IU/mL. These three patients had 0.7, 0.7 and 1.4 log_{10} declines two months after the last dose of VTP-300. These dramatic declines have persisted in all three patients at their latest follow-up at five or eight months after the last dose of VTP-300.

For the first eight patients who received VTP-300 in combination with a single low-dose of nivolumab at the time of the booster dose, the mean reduction in HBsAg was over 1 log_{10} at six months, an effect that persisted, with a mean decline of 1.15 log_{10} at eight months after the last dose of VTP-300. The effect was most prominent in patients with baseline HBsAg lower than 1,000 IU/mL. One patient in this group developed a non-detectable HBsAg level, which continued eight months after the last dose of VTP-300.

No reductions ≥1 log_{10} were seen in patients who received two doses of MVA-HBV, or in patients who received low-dose nivolumab with both doses of VTP-300. These two groups were discontinued after interim analysis.

"The immune system is likely a needed component in achieving durable HBsAg loss that could lead to a functional cure for patients with chronic hepatitis B (CHB)," said Dr. Henry Chan, Honorary Clinical Professor, Faculty of Medicine, The Chinese University of Hong Kong. "This exciting initial data supports VTP-300's potential as an immunotherapy that can stimulate an antigen-specific immune response and could be a critical component of a functional cure regimen. I look forward to following future clinical and combination developments." Dr. Henry Chan is a scientific advisor to Vaccitech but not directly involved in the HBV002 study.

A robust T cell response against all encoded antigens (core protein, polymerase and surface antigen), measured by overnight stimulation, was observed following VTP-300 administration, notable for marked CD8+ T cell predominance.

"The robust T cell response and marked, durable HBsAg reduction eight months after VTP-300 administration is remarkable," said Thomas Evans, M.D., Chief Scientific Officer of Vaccitech. "We believe the prominent effect we are observing in patients with lower starting HBsAg levels supports the collaborative study with Arbutus Biopharma's siRNA, AB-729, in which HBsAg has shown to be lowered below 100 IU/mL in a majority of treated patients."

Enrollment in the HBV002 study is complete with 55 patients enrolled. An updated interim analysis for all patients at the six month follow-up timepoint is expected at the end of 2022.

A trial to look at timing of low dose nivolumab and additional doses of the MVA boost component of VTP-300 (NCT05343481) is planned in multiple countries, with the first patient expected to be dosed in the third quarter of 2022.

HBsAg is a hallmark of chronic hepatitis B virus (HBV) infection. Fewer than 10% of patients on current standard of care HBV therapies ever achieve distinct, sustained HBsAg decrease or loss, a state associated with functional cure of the disease. The crux of chronic HBV is the immune system's inability to clear the virus due to insufficient immune priming and/or aberrant immune tolerance due to large quantities of HBV protein expression. Many involved in the field believe it makes sense to combine an immune-stimulating agent with an HBV protein-suppressing agent, to potentially elicit a functional cure to HBV.

Presentation details
Poster Title*:* Phase 1b/2a study of heterologous ChAdOx1-HBV/MVA-HBV therapeutic vaccination (VTP-300) as monotherapy and combined with low-dose nivolumab in virally-suppressed patients with CHB on nucleos(t)ide analogues
Poster Number: SAT-428
Presenter: Ellie Barnes, Professor of Hepatology and Experimental Medicine, Nuffield Department of Medicine, University of Oxford
Abstract: 3328

About HBV002

HBV002 is an open-label trial designed to evaluate the safety, immunogenicity and preliminary efficacy of ChAdOx1-HBV and MVA-HBV (VTP-300), with or without low-dose nivolumab, in patients with chronic HBV with suppressed HBV DNA on nucleos(t)ide therapy.

As of June 22, 2022, 55 patients have been enrolled, and no concerning safety signals or vaccine-related serious adverse events have been reported.

Data from a previous interim analysis of HBV002 presented at the AASLD The Liver Meeting® in November 2021 showed that VTP-300 induced antigen specific T cell responses to all antigens, with elevated responses to core and polymerase, as compared to healthy controls dosed with ChAdOx1-HBV alone in HBV001, who exhibited a greater response to surface antigen. As in the HBV001 results, T cell responses cross-reactive to Genotype D-specific peptides were measured in the majority of patients.

About VTP-300

VTP-300 is a novel immunotherapy, dosed in a prime-boost regimen, whereby the immune system is primed with an adenovirus (ChAdOx1) and boosted with a pox virus (MVA). Both vectors have been modified to improve safety, enhance the immune response they induce and include HBV specific antigens including core, polymerase and surface antigen. Clinical data generated to date has demonstrated this regimen to be generally safe and well-tolerated, that antigen specific T cell responses are stimulated to each antigen and there were meaningful reductions in hepatitis B surface antigen when this regimen is given alone or when given in combination with a low dose of nivolumab at the boost.

About Vaccitech plc.

Vaccitech (“the Company”) is a clinical-stage biopharmaceutical company engaged in the discovery and development primarily of novel immunotherapies for the treatment of chronic infectious diseases, cancer, autoimmunity and diseases where the T cell arm of the immune system is believed to play an important role. The company’s proprietary platforms include modified simian adenoviral vectors (ChAdOx1 and ChAdOx2), other viral vectors including the well-validated Modified Vaccinia Ankara (MVA) and synthetic nano-particle technologies (SNAPvax™ and Syntholytic™). The combination of different technologies in a mix and match approach (heterologous prime-boost) consistently generates significantly higher magnitudes of T cells compared with other technologies and approaches. The company has a broad pipeline of both clinical and preclinical stage therapeutic programs to treat solid tumors, chronic viral infections, as well as a few prophylactic viral vaccine programs. Vaccitech co-invented a COVID-19 vaccine with the University of Oxford, now approved for use in many territories and exclusively licensed worldwide to AstraZeneca through Oxford University Innovation, or OUI. Vaccitech is entitled to receive a share of all milestones and royalty income received by OUI from AstraZeneca.

Forward Looking Statement

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, express or implied statements regarding: the Company’s business plans and objectives, including the clinical trials of ChAdOx1-HBV and the ChAdOx1-HBV/MVA-HBV (VTP-300) and low-dose nivolumab combination, the continued development of VTP-300 and the potential therapeutic effects and expected patient population of VTP-300. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “future,” “potential,” “continue” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on 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: the success, cost and timing of the Company’s product development activities and planned and ongoing clinical trials, the Company’s ability to execute on its strategy, regulatory developments, the Company’s ability to fund its operations and the impact that the current COVID-19 pandemic will have on the Company’s clinical trials and preclinical studies and other risks identified in the Company’s filings with the Securities and Exchange Commission (the “SEC”), including its Annual Report on Form 10-K for the year ended December 31, 2021 and its Quarterly Report on Form 10-Q for the first quarter of 2022 and subsequent filings with the SEC. The Company cautions you not to place undue reliance on any forward- looking statements, which speak only as of the date they are made. The Company expressly disclaims 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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