Cancer Research UK and VOLT open squamous oesophageal cancer cohort in immunotherapeutic trial

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OXFORD and LONDON, UK, 11 March 2024 – Cancer Research UK's Centre for Drug Development and Vaccitech Oncology Limited (VOLT), a strategic collaboration between Barinthus Biotherapeutics Plc and the Ludwig Institute for Cancer Research, have opened a new cohort in the Phase 1/2a MAGE clinical trial to assess the VTP-600 immunotherapeutic in treating squamous oesophageal cancer.

VTP-600 is designed to enable T cell-mediated anti-cancer activity by delivering genes that encode cancer-associated proteins – in this case MAGE-A3 and NY-ESO-1 antigens, both of which were discovered and clinically validated by the Ludwig Institute for Cancer Research. VTP-600 is designed to deliver these genes to antigen-presenting cells (dendritic cells), potentially leading to the generation of cytotoxic T cells that specifically target and kill cancer cells expressing these antigens.

The MAGE trial first opened as a collaboration between Cancer Research UK and VOLT in January 2022 to determine the safety and initial efficacy of VTP-600 given in combination with chemotherapy and anti-PD-1 treatment to patients with non-small cell lung cancer. Immune checkpoint inhibitors, such as anti-PD-1, are also approved for the treatment of advanced oesophageal cancers, of which squamous oesophageal cancer also expresses the highest rates of MAGE-A3 and NY-ESO-1 antigens. The trial has therefore been amended to include a cohort of up to 17 of these patients. Because squamous oesophageal cancer is suitable for biopsy, we believe that the trial will enable us to observe changes in T cell immunity both in the periphery and in the tumour microenvironment between pre- and post-VTP-600 treatment.

The MAGE trial is led by Fiona Blackhall, Professor of Thoracic Oncology and Honorary Consultant in Medical Oncology, at The Christie NHS Foundation Trust, and the first two sites for this cohort are at St James's University Hospital, Leeds, and the Beatson West of Scotland Cancer Centre, Glasgow. The squamous oesophageal cohort will be led by Eileen Parkes, Associate Professor in Innate Tumour Immunology and Oxford's Experimental Cancer Medicine Centre (ECMC) Lead. More information on the clinical trial can be found at NCT04908111.

Dr Lars Erwig, Director of Drug Development at Cancer Research UK, said: "It is promising to see the MAGE trial expand to a new cohort of patients. As squamous oesophageal tumours have an unmet medical need and poor long-term outcomes, it is vital that we continue to support treatment trials for these patients. If successful, this could open up development into additional tumour types, allowing more patients to benefit from cancer immunotherapy."

Professor Fiona Blackhall, Chief investigator for the MAGE clinical trial, said: "It is exciting to be able to open the MAGE trial to patients with squamous oesophageal cancer. Patients with squamous oesophageal cancer have a limited long-term survival and there is a need to find better treatments. The plan is to open this cohort in 10–12 hospitals across the UK to ensure as many patients as possible can have access to the trial."

Associate Professor Eileen Parkes, lead of the squamous oesophageal cohort for the MAGE clinical trial, said: "Squamous cell cancer of the oesophagus is a devastating disease where we urgently need new treatments. The MAGE trial will investigate delivering proteins that are commonly increased in these cancers using a cutting-edge immunotherapy approach to stimulate short- and long-term immune responses, which was first proposed by researchers at the University of Oxford. We are excited to be opening this study across the UK and enrolling the first patients with squamous oesophageal cancer on this trial. Our goal remains to improve treatments for people with cancer."

Bill Enright, Barinthus Bio CEO, said, "We are incredibly pleased with the initiation of a new cohort targeting squamous oesophageal cancer using VTP-600, our immunotherapy product candidate that is designed to engage the immune system to attack cancer cells. Oesophagus cancer is a challenging disease - the sixth most common cause of cancer death in the world - with overall poor survival rates. With this collaboration and new cohort in the MAGE trial, our hope is to clinically advance a new treatment option to improve survival rates for this aggressive disease."

Notes to editors

About VTP-600 and the Phase 1/2a MAGE trial
VTP-600 is a cancer immunotherapeutic product candidate comprising three components (ChAdOx1-MAGEA3-NYESO, MVA-MAGEA3, and MVA-NYESO), which are administered sequentially depending on the patient's tumour antigen expression. VTP-600 is designed based on Barinthus Bio's proprietary viral vector antigen-delivery platforms ChAdOx1 and MVA. The ChAdOx1 component is designed to induce a T cell response specific to MAGE-A3 and NY-ESO-1, which are antigens expressed by tumour cells in some cancers, including squamous oesophageal cancer. MAGE-A3 and NY-ESO-1 have been shown to be expressed, respectively, in 42–63% and 19-41% of squamous oesophageal cancers.

Patients in the MAGE trial with a tumour expressing only MAGE-A3 will receive the ChAdOx1-MAGEA3-NYESO initial dose, followed by a MVA dose encoding MAGE-A3, which is expected to improve the size and duration of the induced immune response. Patients in the MAGE trial with a tumour expressing both MAGE-A3 and NY-ESO-1 will get the same initial ChAdOx1-MAGEA3-NYESO dose followed by both MVA-MAGEA3 and MVA-NYESO, with the potential for additional doses depending upon status.

About oesophageal cancer
Cancer of the oesophagus is the eighth most commonly diagnosed cancer and the sixth most common cause of cancer death in the world. Five-year survival rates are low, in the range of 10–30%, for most countries. The annual incidence of oesophageal cancer in the UK is 14.0 per 100,000 of the population with around 9,300 new oesophageal cancer cases in the UK every year. Two histologic types account for the majority of oesophageal cancers: adenocarcinoma and squamous cell carcinoma, with the highest rates of MAGE-A3 and NY-ESO-1 expression being observed in squamous oesophageal cancers. Adenocarcinomas typically start in the lower oesophagus and squamous cell carcinoma can develop throughout the oesophagus.

About Cancer Research UK's Centre for Drug Development
Cancer Research UK has an impressive record of developing novel treatments for cancer. The Cancer Research UK Centre for Drug Development has been pioneering the development of new cancer treatments for 30 years, taking over 160 potential new anti-cancer agents into clinical trials in

patients. It currently has a portfolio of 16 new anti-cancer agents in preclinical development, Phase 1 or early Phase 2 clinical trials. Six of these new agents have made it to market, including temozolomide for brain cancer, abiraterone for prostate cancer and rucaparib for ovarian cancer. Two other drugs are in late development Phase 3 trials. Thirteen agents remain in active development with the potential to reach the market.
www.cruk.org.uk/cdd

About VOLT
Vaccitech Oncology Limited (VOLT) is a strategic collaboration between Barinthus Biotherapeutics plc, a clinical-stage T cell immunotherapy company developing products to treat and prevent cancer, autoimmunity and infectious diseases, and The Ludwig Institute for Cancer Research (Ludwig), an international non-profit organisation that conducts innovative cancer research to prevent, detect and control cancer.

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 antigen-delivery platforms: 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, a tolerance 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.

About Ludwig Cancer Research
Ludwig Cancer Research is an international collaborative network of acclaimed scientists that has pioneered cancer research and landmark discovery for 50 years. Ludwig combines basic science with the ability to translate its discoveries and conduct clinical trials to accelerate the development of new cancer diagnostics and therapies. Since 1971, Ludwig has invested nearly $3 billion in life-changing science through the not-for-profit Ludwig Institute for Cancer Research and the six U.S.-based Ludwig Centers. To learn more, visit www.ludwigcancerresearch.org.

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: Barinthus Bio's plans and strategy with respect to its pipeline and product candidates, including VTP-600 and the Phase 1/2a MAGE trial, and the potential benefits of VTP-600 for the treatment of oesophageal cancer. Any forward-looking statements in this press release are based on Barinthus Bio 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 Barinthus Bio's pipeline development activities and planned and ongoing clinical trials, Barinthus Bio's ability to execute on its strategy, regulatory developments, Barinthus Bio's ability to fund its operations and access capital, global economic uncertainty, including disruptions in the banking industry, the conflict in Ukraine, and the conflict in Israel and Gaza, and other risks identified in Barinthus Bio's filings with the Securities and Exchange Commission (the "SEC"), including its Annual Report on Form 10-K for the year ended December 31, 2022, its Quarterly Reports on Form 10-Q and subsequent filings with the SEC. Barinthus Bio cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. Barinthus Bio 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.