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Celleron Therapeutics announces MHRA Clinical Trial Authorisation for CXD101 in Microsatellite-Stable Colorectal Cancer

Oxford, UK, 26 March 2018 - Celleron Therapeutics, the UK-based company developing personalised medicine for cancer patients, has today announced that the UK MHRA has granted approval for the conduct of a clinical trial with its lead compound CXD101 in colorectal cancer.

On 13 February, 2018 the MHRA granted Clinical Trial Authorisation (CTA) for Celleron Therapeutics to conduct a phase Ib/II trial with CXD101, the medicinal product containing N- (2-aminophenyl)-4-(1-[(1,3-dimethyl-1H-pyrazol-4-yl) methyl] piperidin) benzamide in combination with Bristol Myers Squibbs' nivolumab (OPDIVO®):

A Phase Ib/ II Trial to Assess the Safety and Efficacy of CXD101 in Combination with the PD-1 Inhibitor Nivolumab in Patients with Metastatic, Previously-Treated, Microsatellite-Stable Colorectal Carcinoma

In the UK, it is necessary to obtain a Clinical Trial Authorisation (CTA) from the Medicine and Healthcare Products Regulatory Agency (MHRA) in order to conduct a Clinical Trial of an Investigational Medicinal Product (CTIMP). The MHRA considered that the requirements for approval of a CTA under the Medicines for Human Use (Clinical Trials) Regulations 2004 S.I.2004/1031 for Protocol CTL-101-023 are fulfilled and Celleron's application was approved. Prior to submission to the MHRA, this trial was registered on the European Clinical Trials Database under EudraCT number 2017-004509-42.

Obtaining an MHRA CTA is an important milestone towards treatment of the first patient on a study which is scheduled to occur in Quarter 2 of 2018.

A major challenge in the development of cancer drugs is that cancer patients will respond differently to treatment with any particular therapy. Clinical trials with Celleron's CXD101 drug are investigating not only the efficacy of the new drug but also studying a novel biomarker test, known as a companion diagnostic, to predict which patients will respond best to treatment with the drug. This approach avoids the problem of treating patients who have little chance of benefiting from the treatment so that alternative options may be considered in a timely manner.

Professor Nick La Thangue, Founder and Chief Executive of Celleron Therapeutics, and Professor of Cancer Biology in the Department of Oncology at Oxford University, commented:

"CXD101 is a potent, orally administered drug representing a new class of agents with dual mode of action that not only act directly on cancer cells but also stimulate the patient's immune system to fight the tumour. Obtaining the CTA for this study is an important milestone in the development of CXD101 for its first solid tumour indication. It will be hugely important to see how an HDAC compound like CXD101 performs in combination with an I/O agent such as nivolumab.

We are seeing extremely encouraging results with CXD101 and we look forward to driving the clinical trials forward as fast as possible, in a number of defined cancers, using our precision medicine approach".

Dr John Whittaker, Celleron's Chief Operating Officer commented:

"This is an important next step in pursuing Celleron's strategy to progress its proprietary targeted therapeutic, CXD101, in combination with an immune-oncology (I/O) agent in a tumour indication where the I/O agent may not have significant single agent activity – opening up new and exciting opportunities for treating aggressive types of cancer".

NOTES:

Celleron Therapeutics is advancing a clinical and pre-clinical pipeline of personalised therapies for different cancer indications. The company has built a proprietary platform around epigenetic control and immune modulation, providing its drugs with a two-pronged attack on cancer. Celleron's approach seeks to align the right drug with the right patient enabling a personalised approach to cancer therapy. The company is a spin-out from Oxford University and located on the Oxford Science Park.
For more information see **www.cellerontherapeutics.com**

CXD101 is Celleron Therapeutics' next generation epigenetic immune-regulator representing a class of drug that kills cancer cells by blocking certain vital functions involved in gene expression, and reactivates the patient's immune system so that cancer cells can no longer evade immune

Bristol Myers Squibb's Nivolumab (OPDIVO®) is a human immunoglobulin G4 monoclonal antibody that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti- tumour immune response.

Nivolumab has demonstrated encouraging activity as monotherapy in patients with microsatellite instability-high status colorectal cancer. The CheckMate-142 Phase II study recently led to accelerated US approval for nivolumab in the treatment of patients with dMMR and MSI-H metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Colorectal cancer is the second most common tumour type in women, and the third most common in men, globally. The approximate 5-year survival rate for colorectal cancer patients in the United States (all stages included) is 65% (SEER, 2016). Survival is inversely related to stage: approximate 5-year survival rates are 95% for patients with stage I disease, 60% for those with Stage III disease, and 10% for those with Stage IV (metastatic) disease.

A subset of colorectal cancers is characterized with deficient DNA mismatch repair (dMMR or microsatellite instability, MSI). Detection of MSI has become important for treatment for metastatic colorectal cancers, as those with MSI-H expression respond favourably to immune checkpoint inhibition, a type of biologic therapy. These tumours tend to have high expression of checkpoint proteins, including programmed death 1 (PD-1) and programmed death ligand 1 (PDL1), which interfere with the body's anti-tumour T-cell response. By disabling these proteins, checkpoint inhibitors (such as pembrolizumab and nivolumab) allow the immune system to function properly, and T-cells to kill tumour cells. Where patients have a normal Mismatch Repair proficient expression, the microsatellite phenotype is stable (MSS) and the tumour is thus resistant to checkpoint inhibition.