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Celleron Therapeutics CXD101 and nivolumab combination therapy CAROSELL clears initial Phase II clinical trial efficacy hurdle in MSS CRC patients.

Oxford, UK, 16 April 2019 - Celleron Therapeutics, the UK-based company developing personalised medicines for cancer patients, announced today the successful proof-of-concept efficacy read-out from their UK Phase II clinical trial, testing the immune-oncology agent nivolumab in combination with their novel epigenetic regulator CXD101, in patients suffering from advanced micro-satellite stable colorectal cancer (MSS CRC).

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%. 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.

Surgery is indicated for localized disease, whilst chemotherapy has been the standard management for patients with metastatic colorectal cancer. Two agents have been approved for third line management of advanced colorectal cancer, namely regorafenib and Trifluridine-tipiracil hydrochloride (Lonsurf).

A subset (5%) of colorectal cancers is characterized with deficient DNA mismatch repair (dMMR or microsatellite instability, MSI). These tumours tend to have a high expression of checkpoint proteins (PD-1 and PD-L1), which interfere

with the body's normal anti-tumour T-cell response. By disabling these proteins, checkpoint inhibitors such as nivolumab allow the immune system to function properly, and T-cells to kill tumour cells.

However, for the greater majority of patients with a normal Mismatch Repair proficient expression, the microsatellite phenotype is stable (MSS), antigen presentation is believed to be much decreased, and the tumour is thus resistant to checkpoint inhibition. Most MSS patients will ultimately relapse or become resistant to chemotherapy. Thus there remains a very significant unmet clinical need to find novel agents, singly and/or in combination, for the treatment of these late-stage patients.

Celleron's Phase II clinical trial is testing the effect of CXD101 in combination with nivolumab in MSS colorectal cancer, which typically does not respond to IO agents alone (the CAROSELL Study). The clinical trial strategy rests on compelling preclinical results which provide novel insights into how CXD101 and IO drugs work together to re-engage recognition of tumours by the immune system.

Reflecting a successful Phase Ib safety study, a Phase II combination dose of CXD101 and nivolumab was selected for further investigation. The patients studied had advanced or metastatic disease, having relapsed after at least two previous lines of therapy.

In the first 16 MSS CRC subjects treated, 8 (50%) exhibited disease control at 6 weeks, as determined by CT scan tumour measurements (iRECIST). This compares favourably with the reported disease control rates of marketed products such as regorafenib (41%) and Lonsurf (44%).

This represents a successful efficacy read-out at Phase II Stage 1, and the CAROSELL Study will now continue through Stage 2, to treat a total of 55 subjects.

Professor David Kerr CBE, Founder and Chief Medical Officer, Celleron Therapeutics and Professor of Cancer Medicine, University of Oxford commented:

"There is good evidence to suggest that disease stabilisation and control can lead to improved survival in patients such as ours, who have progressed despite receiving all conventional chemotherapy. Further trials will be required, but this early read out is most encouraging."

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

"We are excited by these encouraging Phase II clinical trial results which add to the continuing evidence that CXD101 is a clinically viable drug with wide utility in clinically unmet disease".

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About Celleron Therapeutics

Celleron Therapeutics is a biopharma advancing a clinical and pre-clinical pipeline of precision therapies for different cancer indications. The company is a spin-out from Oxford University and located on the Oxford Science Park, UK. Celleron Therapeutics 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.

Celleron Therapeutics' focus is on those cancers where there is still an unmet need for long-term disease control. It is hoped that not only will patients volunteering for our clinical trials benefit directly, but the results from these studies will ultimately allow the general use of more effective, safer medicines. Our goal is not only to treat cancer, but improve quality of life during therapy by reduction of side effects.

Celleron has a global license partnership with Astra Zeneca and is also initiating new trials in China. The company secured investment in 2016 from a consortium of South Korean investors. For more information see www.cellerontherapeutics.com

About CXD101

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 (histone–deacetylase [HDAC] inhibitor) and reactivates the patient's immune system so that cancer cells can no longer evade immune recognition.

The European Medicines Agency (EMA) has previously granted CXD101 Orphan Drug Designation as single agent therapy, based upon early-phase trial efficacy seen in relapsed or refractory Peripheral T-Cell Lymphoma (PTCL) patients. A PTCL Phase II trial is scheduled to start late 2019 in China.

Celleron Therapeutics are also exclusively financing an investigator-led Phase Ib/II clinical trial in diffuse large B-cell lymphoma (DLBCL) patients who have failed on chemotherapy, called the PLACARD Study. Study subjects would receive and CXD101 and an undisclosed immune-oncology drug together. The

immune-oncology drug will be provided to the Investigator by a large undisclosed pharma manufacturer.