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Celleron Therapeutics Data Committee approves continuation of CXD101 and nivolumab combination therapy CAROSELL Phase II clinical trial in MSS CRC patients

Oxford, UK, 17 Jun 2019 - Celleron Therapeutics, a UK-based company developing personalised medicines for cancer patients, announced today approval by a Data and Safety Monitoring Committee for continuation of the UK Phase II clinical trial (CAROSELL) 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 pre-clinical 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 without toxicity, 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.

The CAROSELL Data Safety and Monitoring Committee (DSMC) met on 12th June 2019 to review the ongoing Phase II data.

The DSMC provides medical oversight in the conduct of the trial. Specifically, during the study the DSMC's functions are: To be responsible for safeguarding the interests of trial subjects; to monitor evidence for treatment harm vs therapeutic benefit; and to confirm the acceptability of study continuation.

The DSMC reviewed summarised reports of tumour CT scans, and adverse drug reaction listings.

Interim analysis of the first cohort of 16 MSS CRC subjects treated saw that 8 (50%) exhibited disease control at 6 weeks, as determined by CT scan tumour measurements (iRECIST). It was noted that this trend appears to be continuing at 6 weeks for subsequently enrolled subjects; with unconfirmed DCR at approximately 54%. Anecdotal cases of extended stable disease were discussed, together with a limited but notable group of subjects with partial responses (>30% tumour shrinkage).

This compares favourably with the reported disease control rates of marketed products such as regorafenib (41%) and Lonsurf (44%).

On safety: adverse drug reactions appear to be following the pattern seen in Phase I for CXD101 and were generally tolerable. There was discussion over why there were not any reports of colitis, as would be expected with a PD-1 inhibitor such as nivolumab in this population. It was commented that underlying anti-

inflammatory mechanisms should be investigated in future trials to understand better if this is a feature of the drug combination.

The DSMC members unanimously agreed that the study should continue, based on encouraging efficacy results coupled with an acceptable safety profile. The committee will meet again in September 2019 to review 12-week tumour measurements for all 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 very pleased with the Committee's conclusions. Our CAROSELL trial continues to show encouraging clinical activity in a very difficult to treat cancer. CXD101's impressive safety profile is reassuring. We look forward to expanding the drug's clinical utility".

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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 to 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 have an ongoing Phase II clinical trial investigating the effectiveness of CXD101 in combination with an immune oncology agent, against a type of colorectal cancer (microsatellite stable) which typically does not respond to IO agents alone (CAROSELL Study). The clinical trial strategy rests on compelling pre-clinical results which provide novel insights into how CXD101 and IO drugs work together to re-engage recognition of tumours by the immune system. The trial will also allow exploration of a range of new biomarkers to help select those patients likely to benefit most from combination therapy.

Celleron Therapeutics is 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.

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