CELLERON THERAPEUTICS

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Celleron Therapeutics reports 3-year survival data from Phase II clinical trial in MSS colorectal cancer patients treated with zabadinostat and nivolumab combination

Oxford, UK, 29 June 2022 – Celleron Therapeutics, the UK-based company developing innovative precision cancer medicines, announced today a 3-year survival rate of 7.3% in late-stage micro-satellite stable colorectal cancer patients in their Phase II clinical trial, following treatment with zabadinostat (a potentially best-in-class HDAC inhibitor) and nivolumab (an immune checkpoint inhibitor commonly used to treat MSI CRC but has no activity in MSS CRC).

The Phase II clinical trial (CAROSELL study) investigates the effect of zabadinostat (formerly CXD101) in combination with nivolumab in MSS colorectal cancer, which does not respond to immune checkpoint inhibitors (ICI) alone. The clinical strategy is well supported by scientific evidence showing how zabadinostat upregulates genes involved in antigen presentation and activity of natural killer cells, thus attracting cytotoxic T-cells to tumours and killing cells through the immune system; in essence, "turning cold tumours hot".

Following a dose confirmation safety run-in, which showed no treatment-induced toxicity, a Phase II recommended dose (P2RD) of zabadinostat and nivolumab was selected for further investigation. The patients in the study had advanced or metastatic disease, having relapsed after at least two previous lines of therapy.

Enrolment to the Phase II study was completed in May 2019, and all ongoing subjects have completed study treatment. Of 46 evaluable MSS CRC subjects, 22 (48%) exhibited durable disease control (stable disease plus partial response). Post-treatment survival analysis is still ongoing, with surviving patients now under standard of care. The median Overall Survival (OS) was 7 months. Of all patients treated, 8/55 (14.5%) remained in survival 2 years from first dose. To date, 4/55 (7.3%) patients continue to survive past the three-year follow-up point.

Safety wise, the study combination was well tolerated. The most frequent observed Adverse Events were fatigue, nausea, and cytopenia. All AEs were manageable. There were no deaths or discontinuations from the study due to adverse drug reactions.

In consideration to the mechanism of action, clinical activity and safety, the results in this Phase II study suggest that zabadinostat plus nivolumab may be a superior treatment in advanced MSS CRC than marketed products, such as Lonsurf and Stivarga.

David Kerr, CMO of Celleron Therapeutics, and Professor of Cancer Medicine at the University of Oxford, commented:

"We are pleased to continue seeing evidence that zabadinostat and nivolumab may prolong survival in very late-stage cancer patients, with some surviving past three years, the significance of which cannot be understated. This Phase II study not only strengthens the argument that zabadinostat is a clinically viable drug, but perhaps also the best-in-class treatment for cold tumours, such as MSS CRC which do not respond to treatment with immune checkpoint drugs. We remain dedicated to deploying zabadinostat as a precision medicine, maximising clinical benefit by using immune biomarkers to improve selection of patients – a key deliverable of our upcoming Phase III study".

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About Colorectal Cancer

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 is 10% for those with advanced metastatic disease (Stage IV).

Surgery is indicated for localised 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, immune checkpoint inhibitors (ICI) 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.

About Celleron Therapeutics Limited

Celleron Therapeutics is a precision cancer medicine company advancing a pipeline of clinical and pre-clinical assets to treat unmet oncology 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 targeted 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 cancers effectively but also to improve patients' quality of life by the reduction of side effects.

Celleron has global license partnerships with AstraZeneca and Roche. The company secured investment in 2016 from a consortium of South Korean investors; and in 2020 spun out an affiliate company, SynOx Therapeutics. For more information, see **www.cellerontherapeutics.com**

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About Zabadinostsat

Zabadinostat (formerly 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 recognition.

A global Phase III clinical trial of zabadinostat, as MSS CRC combination therapy with an immune checkpoint inhibitor is scheduled to start in 2022.

The European Medicines Agency (EMA) has previously granted zabadinostat 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 Phase II PTCL trial in China is due to start in 2022.