First patient dosed in randomised Phase 2 clinical trial of MTL-CEBPA in patients with advanced liver cancer

OUTREACH-2 study evaluating MTL-CEBPA in combination with sorafenib, in comparison to sorafenib alone, in up to 150 patients

Builds on strong proof-of-concept data from Phase 1b study in same indication

Data read-out expected in early 2024

London, United Kingdom, 25 January 2022 – MiNA Therapeutics Limited ("MiNA" or the "Company"), the pioneer in small activating RNA (RNAa) therapeutics, announces that it has dosed the first patient in a global Phase 2 clinical trial (OUTREACH-2) of MTL-CEBPA in combination with second line standard of care sorafenib (a tyrosine kinase inhibitor (TKI)) in advanced hepatocellular carcinoma (HCC or liver cancer).

OUTREACH-2 is a multi-centre, open-label, randomised study of MTL-CEBPA in combination with sorafenib, compared to sorafenib alone, in TKI-naïve advanced pre-treated HCC patients with viral hepatitis etiology. The study will recruit up to 150 patients globally from centres in the US, Europe, and Asia. OUTREACH-2 is designed to assess further to what extent the MTL-CEBPA and sorafenib combination offers therapeutic advantage compared to sorafenib alone for the treatment of advanced HCC. The study's primary endpoint is progression-free survival by blinded radiological assessment and the study is expected to complete in the first quarter of 2024. If the data from this Phase 2 OUTREACH-2 study are satisfactory to the US Food and Drug Administration (FDA), this could enable an Accelerated Approval of MTL-CEBPA in combination with sorafenib soon thereafter.

Professor Tim Meyer, Professor of Experimental Cancer Medicine at University College London, and Chief Investigator of the study, commented:
"*Advanced liver cancer remains a significant unmet medical need, in particular for those patients who are resistant to front line systematic therapy. This combination treatment demonstrated intriguing signals of activity in a Phase 1b trial, including durable and complete tumour responses. We believe that MTL-CEBPA's immunological activity in the tumour microenvironment enables a greater effectiveness of sorafenib and we are excited to seek to validate those early findings in this Phase 2 clinical trial."*

Robert Habib, CEO of MiNA Therapeutics, commented:
"We are very excited to dose our first patient in the OUTREACH-2 study, which is the first Phase 2 clinical trial of a RNAa therapeutic. MTL-CEBPA has demonstrated its potential to make tumours more susceptible to established anti-cancer therapies, which can significantly improve treatment outcomes for patients. We look forward to building on data from our successful Phase 1b study of the sorafenib combination and to developing MTL-CEBPA more broadly for the benefit of patients."

The study builds on the successful proof-of-concept data from MiNA's first-in-human, Phase 1b clinical trial (OUTREACH) evaluating the safety and tolerability of the therapeutic combination in patients with advanced HCC. The clinical activity observed in OUTREACH, which included durable and complete tumour responses not common with sorafenib alone, suggested that MTL-CEBPA may increase the effectiveness of sorafenib as a second line standard of care for HCC. The OUTREACH study showed that MTL-CEBPA plus sorafenib achieved a complete response rate (CRR) of 13% and an overall response rate (ORR) of 27% in the target population. By comparison sorafenib alone achieved a CRR of <1% and an ORR of 5-11% in recent published studies. The trial protocol has been accepted in an investigational new drug (IND) application by the FDA. The FDA has also granted Orphan Drug Designation for MTL-CEBPA in combination with sorafenib for the treatment of HCC of viral hepatitis etiology who have progressed following prior therapy. As a monotherapy, MTL-CEBPA achieved a CRR of 2% and an ORR of 6%, despite not being intended to target the tumours directly.

As the first ever RNAa therapy to enter the clinic, MTL-CEBPA is being studied as a combination therapy in cancer. The mechanism of action of MTL-CEBPA is to reduce or remove one of the main defence mechanisms by which tumours can resist the immune system, thereby opening the tumour to

attack by the immune system and tumour-targeting drugs. In combination, data suggests that the drug can significantly improve the effectiveness of established cancer treatments by altering the tumour microenvironment in favour of those treatments. It achieves this by using the RNA activation mechanism to boost and restore expression of the C/EBP-α protein to normal levels which, in turn, reduces immune suppression by myeloid cells in which this protein has been down-regulated by the tumour. The drug candidate is also being investigated in an investigator-sponsored Phase 1a/1b study in first-line HCC in combination with first-line standard of care combination atezolizumab and bevacizumab in collaboration with F Hoffman-La Roche Ltd, as well as in an ongoing multi-centre Phase 1b clinical trial in patients with a variety of advanced solid tumours in combination with pembrolizumab, a PD-L1 inhibitor.

About MTL-CEBPA

MTL-CEBPA is the first therapy that specifically up-regulates CCAAT/enhancer binding protein alpha (C/EBP-α), a transcription factor that acts as a master regulator of myeloid cell lineage determination and differentiation. Dysregulated myeloid cells have been implicated in several diseases and in solid tumour cancers these cells have been identified as a critical barrier to induction of clinical response for many therapies. In pre-clinical studies MTL-CEBPA has been shown to improve the anti-tumour activity of cancer therapies by targeting dysregulated myeloid cells and reducing or eliminating their suppressive effect on immune response and therapies in the tumour micro-environment. MTL-CEBPA is currently in clinical development in three different studies as a combination therapy for the treatment of both first- and second-line advanced liver cancer and for a variety of other advanced solid tumour malignancies.

About MiNA Therapeutics

MiNA Therapeutics is the global leader in small activating RNA therapeutics or RNAa. Harnessing innate mechanisms of gene activation, RNAa therapeutics are a revolutionary new class of medicines that can restore or boost normal function of genes and thereby protein-modulated pathways in patients' cells. We are advancing a proprietary pipeline of new medicines with an initial focus on genetic diseases and cancer, while collaborating with leading pharmaceutical companies to apply our technology platform across a broad range of other therapeutic areas. Based on our unique know-how in RNA activation, we are expanding the possibilities of RNA-based medicine for patients. www.minatx.com

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