National University Cancer Institute, Singapore and MiNA Therapeutics announce initiation of a Phase 1 clinical study of MTL-CEBPA in combination with first-line standard of care in advanced liver cancer

London, United Kingdom, 1 December 2021 – The National University Cancer Institute, Singapore ("NCIS") and MiNA Therapeutics Limited ("MiNA" or the "Company"), the pioneer in small activating RNA therapeutics, announce that the first patient has been dosed in an investigator-sponsored Phase 1 study of MiNA's small activating RNA oligonucleotide, MTL-CEBPA, in combination with first-line standard of care, atezolizumab and bevacizumab, in patients with previously untreated, advanced hepatocellular carcinoma (HCC). Atezolizumab and bevacizumab are being provided by F. Hoffmann-La Roche, Ltd ("Roche") who is also supporting the study.

The study has been designed by Principal Investigator Dr. Cheng Ean Chee, Senior Consultant at the Department of Haematology-Oncology, NCIS and supported by the Singapore Ministry of Health's National Medical Research Council under its Centre Grant programme (CG; NMRC/CG/M005/2017_NCIS). The study will be conducted at NCIS's clinical trial facility with the Haematology-Oncology Research Group (HORG) at the National University Hospital, Singapore.

This is a single-center, Phase 1, open label dose-escalation and dose expansion study of MTL-CEBPA, co-administered with atezolizumab and bevacizumab, in approximately 30 patients with unresectable or advanced HCC who have not previously received systemic therapy. The primary endpoint for the dose escalation phase will be determination of any dose-limiting toxicity, and the primary endpoint of the dose expansion phase will be objective response rate (ORR). The study is expected to read out top-line data in 2023.

Dr Cheng Ean Chee, Senior Consultant at the Department of Haematology-Oncology, NCIS, commented:
"Despite the recent progress of immunotherapies, advanced liver cancer remains a significant unmet medical need. With only 30% of patients benefiting from objective responses to first-line standard of care, new treatment combinations are needed in order to improve patient outcomes. We are excited to evaluate investigational agent MTL-CEBPA in combination with the current standard of care and we are glad to collaborate with MiNA Therapeutics and Roche."

Nagy Habib, Head of R&D at MiNA Therapeutics, commented:
"We are delighted to collaborate with the National University Cancer Institute, Singapore, and Roche to evaluate this new immunotherapy combination. In preclinical and clinical studies, MTL-CEBPA has been reported to improve the anti-tumour activity of leading oncology drugs by counteracting a new cancer immune evasion pathway which causes resistance to those drugs. Based on this data, we believe that MTL-CEBPA combinations have the potential to improve the standard of care significantly in patients with advanced HCC."

Dr Sivabalan Sivanesan, Medical Director at Roche Singapore, commented:
"Roche is both proud and excited to join this investigation of a new treatment combination in advanced HCC. Having established a role in metastatic HCC and other cancers, atezolizumab is currently being investigated in many different cancers including early HCC. With more than 70% of the global liver cancers being diagnosed in Asia, this is an amazing opportunity to study the role of a new combination with atezolizumab in HCC."

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 have been identified as a critical barrier for many therapies to induce clinical responses. 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 their suppressive effect in the tumour micro-environment. MTL-CEBPA is currently in clinical development as a combination therapy for the treatment of advanced liver cancer and advanced solid tumour malignancies.

About atezolizumab and bevacizumab

Atezolizumab is a human monoclonal antibody IgG1 classified as a PD-L1 inhibitor, and functions by binding to PD-L1 and blocking the PD-1/PD-L1 interaction, thus restoring T-cell activation and antitumour responses.[4] Bevacizumab is a recombinant humanized monoclonal IgG1 antibody that binds to and inhibits the biologic activity of human vascular endothelial growth factor (VEGF). [4] The immunomodulatory effect of bevacizumab is expected to increase CD8-positive T-cell recruitment and relieve intratumoral immunosuppression, thereby boosting the effects of atezolizumab.

The results of the phase 3 study of atezolizumab plus bevacizumab vs sorafenib in untreated, advanced HCC patients has been published and an overall survival (OS) benefit was observed with the combination compared to sorafenib.[4] The median OS in the atezolizumab plus bevacizumab group compared to those in sorafenib group was 19.2 mo vs 13.4 mo (HR 0.66, 95% CI: 0.52-0.85; P=0.0009).[7] The trial also reported an updated objective response rate (ORR) of 29.8% with atezolizumab plus bevacizumab vs 11.3 % in sorafenib (per RECIST 1.1).[7] The combination provides the longest survival seen in a front-line phase 3 study in advanced HCC, confirming atezolizumab plus bevacizumab as a standard of care for first line therapy in untreated, advanced HCC.

About hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the seventh most common cancer diagnosed and second most common cause of cancer deaths worldwide.[1] It has an annual incidence of at least 840 000 patients[1,2] with rising incidence in the developed world. HCC is an aggressive tumour that often occurs in the setting of chronic liver disease and cirrhosis and is often diagnosed late in its course, as there are no biomarkers to detect it when it is incipient and potentially curable. Treatment options are divided into surgical therapies and nonsurgical therapies. Curative therapies such as resection, transplantation, or percutaneous therapies benefit only 25% of patients. The majority of patients are not eligible for such therapies because of the extent of their tumour or underlying liver dysfunction. Improving treatment outcomes in patients with advanced stage hepatocellular carcinoma (HCC) requires the development of agents with tolerable safety profiles and the identification of biomarkers capable of predicting tumour response or resistance to treatment. The underlying aetiology for HCC development is often chronic viral infection and inflammation. Recently, the combination of atezolizumab (anti-PDL1) and bevacizumab (anti-VEGF) was approved by the FDA in 2020 for frontline therapy in advanced HCC based on an overall survival benefit compared to sorafenib.[4] This has established atezolizumab and bevacizumab as a standard of care for first line therapy in untreated, unresectable or metastatic HCC. Sorafenib, a multikinase inhibitor, was approved by the FDA and globally in 2007 for treatment of advanced-stage HCC. In the past 4 years, additional systemic therapies have been approved for treatment of advanced HCC including other tyrosine kinase inhibitors such as lenvatinib, regorafenib, and cabozantinib; antibodies against VEGFR2 eg. ramucirumab; and anti-PD1 immunotherapy such as

nivolumab. Overall response and survival benefit of all of these agents have been modest and highlight a need for better treatment in this disease.

About the National University Hospital

The National University Hospital is a tertiary hospital and major referral centre with over 50 medical, surgical and dental specialties, offering a comprehensive suite of specialist care for adults, women and children. It is the only public hospital in Singapore to offer a paediatric kidney and liver transplant programme, in addition to kidney, liver and pancreas transplantation for adults. The hospital was opened on 24 June 1985 as Singapore's first restructured hospital. Each year, the Hospital attends to more than one million patients. As an academic health institution, patient safety and good clinical outcomes are the focus of the Hospital. It plays a key role in the training of doctors, nurses, allied health and other healthcare professionals. Translational research is pivotal in the Hospital's three-pronged focus, and paves the way for new cures and treatment. A member of the National University Health System, it is the principal teaching hospital of the NUS Yong Loo Lin School of Medicine and the NUS Faculty of Dentistry. For more information about NUH, please visit www.nuh.edu.sg.

About National University Cancer Institute, Singapore

The National University Cancer Institute, Singapore (NCIS) offers a broad spectrum of cancer care and management covering both paediatric and adult cancers, with expertise in prevention, screening, diagnosis, treatment, rehabilitation and palliative care. The Institute's strength lies in the multi-disciplinary approach taken to develop a comprehensive and personalised plan for each cancer patient and his or her family. Our award-winning clinician scientists and clinician-investigators conduct translational research and clinical trials, providing patients with access to evidence-based cancer diagnostics, technology and therapies. For more information about NCIS, please visit www.ncis.com.sg.

About MiNA Therapeutics

MiNA Therapeutics is the leader in small activating RNA therapeutics. Harnessing innate mechanisms of gene activation, small activating RNA therapeutics are a revolutionary new class of medicines that can restore or boost normal function in patients' cells. We are advancing a proprietary pipeline of new medicines with an initial focus on cancer and genetic diseases, while collaborating with leading pharmaceutical companies to apply our technology platform across a broad range of 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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III study of atezolizumab (atezo)+ bevacizumab (bev) versus sorafenib (sor) in patients (pts) with unresectable hepatocellular carcinoma (HCC)." (2021): 267-267.

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