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Kancera reports positive top line results from the FRACTAL study

Kancera AB (publ) today reports the top line results from the FRACTAL study, a double-blinded placebo-controlled, explorative phase IIa study of Kancera's fractalkine blocker KAND567 in high-risk ST-elevation myocardial infarction (STEMI) patients undergoing acute percutaneous coronary intervention (PCI).

- **The study met the primary objective to confirm the favourable safety and tolerability profile of KAND567 in myocardial infarction patients.**

- **In addition, the secondary objective to demonstrate signals of clinically relevant cardio-protective effects was met.**

"*We have demonstrated that KAND567 is safe and tolerable at the dose level expected to be effective for treatment of high-risk STEMI patients when added to standard of care in patients undergoing acute PCI. In addition, we have seen clear signals of heart-protective effects that are clinically relevant and we therefore view the study as successful. We will now intensify our efforts to seek a partner for the continued development of KAND567 in cardiovascular diseases*", says Peter Selin, CEO of Kancera AB.

FRACTAL is an explorative phase IIa, randomized, two-armed parallel-group, placebo-controlled, double-blind, multi-centre trial with the primary objective to evaluate safety and tolerability and the secondary objective to evaluate cardio-protective effects after intravenous and oral administration of KAND567 in STEMI patients undergoing percutaneous coronary intervention. The study has been conducted in collaboration with the Newcastle upon Tyne Hospitals NHS Foundation Trust (NHS), also sponsor of the study and who has compiled the data and provided an end of study report.

In total, 71 patients were recruited to the study and 61 patients completed the required steps to be considered fully evaluable. The selected dosage of KAND567 resulted in an adequate plasma concentration of the drug candidate and expected effect on the fractalkine axis.

The analysis of the primary endpoints based on NHS's end of study report shows

- that KAND567 and placebo had similar safety profiles. Accordingly, the trial oversight committee at NHS concluded that KAND567 met the primary endpoint for safety and tolerability in myocardial infarction patients.

The analysis of the secondary endpoints shows signals of heart-protective effects:

- reduction of intramyocardial hemorrhage incidence (38% in the KAND567 group vs 57% in the placebo group). The level in the placebo group is in line with prior studies in high-risk STEMI and hence the reduction in the KAND567 group is perceived to be clinically relevant as IM hemorrhage is strongly correlated with an increased risk of developing heart failure.
- reduction of left ventricular (LV) thrombosis incidence (3% in the KAND567 group vs 15% in the placebo group). The level in the placebo group is in line with prior studies in high-risk STEMI and hence the reduction in the KAND567 group is perceived to be clinically relevant as LV thrombosis is strongly correlated with an increased risk of cardioembolic stroke or systemic embolism.
- all other markers of cardiac function and integrity were similar between patients receiving KAND567 or placebo, respectively, but all were numerically in favor of the KAND567 group when comparing change Day 3 and Day 90.

Kancera will now conduct detailed analyses of the full study data set and report any potential further significant findings as soon as they become available.

Kancera views the top line results in this explorative phase IIa study as very positive, providing clear signals of cardio-protective effects. In addition to confirming the favourable safety profile, the results support the hypothesis that KAND567 is a “first in class” drug candidate with potential to protect against reperfusion injury by reducing intramyocardial hemorrhage as well as LV thrombus formation. Both factors are strongly related to increased cardiovascular events and mortality risk. The reduced incidence of LV thrombosis was achieved on top of an intensive anticoagulant and antiplatelet therapy. If this overall effect profile can be confirmed in larger pivotal studies, KAND567 has the potential to meet a significant medical need for improved protection of vital organ function in patients undergoing reperfusion treatment such as STEMI or large vessel occlusion stroke.

Kancera now takes action to continue the development of KAND567 for treatment of cardiovascular diseases and has exercised its option according to the clinical trial agreement with NHS to obtain exclusive commercial rights to all study data and results. Kancera will intensify its business development activities with the objective to enter into a partnership for the continued development of KAND567 for treatment of cardiovascular diseases.

About the FRACTAL study design
The FRACTAL study is an explorative clinical phase IIa study of Kancera’s fractalkine-blocking drug candidate KAND567 when added to standard of care in STEMI patients undergoing acute primary percutaneous coronary intervention (PCI), including heparin, glycoprotein IIb/IIIa inhibitors and dual antiplatelet inhibitors. The study, a two-arm, double-blinded and placebo-controlled study, was conducted at the two hospitals: the Freeman Hospital in Newcastle and the James Cook University Hospital in Middlesbrough. Chief Investigator of the study was Professor Ioakim Spyridopoulos, Professor of Cardiology and Cardiovascular Gerontology, Newcastle University and sponsor was the Newcastle upon Tyne Hospitals NHS Foundation Trust.

Participants were randomized (1:1) to receive intravenous infusion of KAND567 for 6 hours, followed by a bridging dose of up to 200mg KAND567 orally after the infusion (bridging dose dependent on the time of primary PCI procedure, followed by 8 doses of 200mg of KAND567, 8 hours apart, or, a matched placebo).

All participants who received any dose of KAND567 or placebo, and for whom any post-dose data were available were included in the safety analysis set. Any participant receiving any dose of KAND567 was treated as if they were allocated to the active arm. Of the 71 patients recruited in total, 35 and 36 patients were randomized to the KAND567 group and placebo group, respectively.

The primary objective was to evaluate safety and tolerability of KAND567, assessed on Adverse Events, Severe Adverse Events and Suspected Unexpected Serious Adverse Reactions, cumulatively for each arm from baseline up to day 90 and on safety laboratory parameters. The secondary objective was to evaluate signs of cardio-protective effects, which has been assessed through a range of inflammatory biomarkers and magnetic resonance imaging (MRI) markers.

About excessive inflammation in connection with myocardial infarction
Myocardial infarction is a leading cause of heart failure and cardiovascular death. The organ damage severity of myocardial infarction is partly dependent on the duration and extent of the primary ischemia, and secondarily due to lack of reperfusion in the microcirculation distal to the culprit lesion treated by primary PCI. Lack of reperfusion in the distal microcirculation despite a re-opened and patent epicardial vessel, is triggered by ischaemia-related damage of endothelial cells and cardiomyocytes, and accumulation and extravasation of blood and immune cells flowing into the microcirculation of the ischemic area; causing a so called reperfusion injury.

Excessive inflammation is suggested to be a major driving force for developing reperfusion injury, leading to adverse healing and remodelling and a final exaggerated extent of myocardial damage, loss of heart function, heart failure, and cardiovascular death.

Activation and migration of immune blood cells and platelets during the immediate reperfusion phase injury is regulated by chemokines, such as fractalkine, and their receptors. Shortly after induction of ischemia, chemokines are released which increases the expression of fractalkine ligand on the endothelium, increasing the capacity for vascular adhesion and infiltration of subsets of T cells and monocytes expressing the fractalkine receptor (CX3CR1). This immune-cell infiltration is correlated with increased risk for complications such as LV thrombosis, microvascular obstruction and intramyocardial hemorrhage, and leads to an increased three-year mortality risk.

Tissue hemorrhage following reperfusion is a dreaded complication in large vessel occlusion stroke with reperfusion with thrombolysis and/or thrombectomy. Significant hemorrhagic conversion of ischemic stroke leading to intracerebral bleeding, which occurs in up to 20% of patients and is strongly associated with worse patient outcomes.

KAND567, by firmly inhibiting the exaggerated acute inflammatory response mediated through the CX3CR1 pathway, may thus be hypothesized to provide organ protection by preventing ischemic thrombus formation and intra-tissue bleeding and thereby improve outcomes for patients undergoing acute reperfusion treatment strategies. This hypothesis will need to be tested in larger studies going forward.

This information is information that Kancera is obliged to make public pursuant to the EU Market Abuse Regulation. The information was submitted for publication, through the agency of the contact persons set out above, at 2023-12-20 08:30 CET.

Further information
The company will present the FRACTAL top line results at 15.00 CET December 20, 2023. Visit Kancera's web page https://kancera.com/en/videos/video-category/presentations/ to see the presentation,

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About Kancera AB (publ)
Kancera is developing a new class of small molecule drugs targeting the fractalkine axis. Kancera's main focus is to develop its candidate drugs for treatment of severe inflammatory diseases and cancer that currently lack effective treatments. The stock is traded on the Nasdaq First North Premier Growth Market. FNCA Sweden AB is the company's Certified Adviser.

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