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Kancera presents the statistical analysis of top line data from the FRACTAL study

Kancera AB (Kancera) has previously reported the initial top line results from the FRACTAL study and today Kancera presents the statistical analyses that confirm that:

- **the primary objective was met, by showing that KAND567 was safe and well tolerated in high-risk ST-elevation myocardial infarction patients,**
- **the secondary objective was met, by demonstrating signals of cardio-protective effects,**
- **these signals of cardio-protective effects are clinically relevant as they are markers for commonly used efficacy endpoints in myocardial infarction pivotal studies.**

In December 2023, Kancera reported the initial top line results from the FRACTAL study, an exploratory phase IIa, randomized, two-armed parallel-group, placebo-controlled, double-blind, multi-centre trial of KAND567 in high-risk ST-elevation myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention.

Kancera reported that both the primary objective, to demonstrate safety and tolerability, and the secondary objective, to demonstrate signals of cardio-protective effects, were met. The top line results were based on the primary analysis report from the Newcastle University, Kancera's collaboration partner in the study. Since then, Kancera has received the complete study database, validated the results and conducted additional statistical analyses. Kancera today presents the results of the statistical analyses, including analyses on sub-group level of the previously reported top line results.

Primary endpoints confirm a favorable safety profile in STEMI patients

In total, 71 patients were recruited to the study and included in the evaluation of the primary endpoints. 37 patients were randomized into the KAND567 group and 34 patients into the placebo group. The evaluation of primary endpoints showed that:

- the number of adverse events in the two groups did not differ: 23 (62%) in the KAND567 group compared to 24 (71%) in the placebo group,
- the number of serious adverse events in the two groups did not differ: 12 (32%) in the KAND567 group compared to 11 (32%) in the placebo group,
- no adverse events or serious adverse events were considered to be related to administration of KAND567.

Secondary endpoints and immune markers confirm pharmacological effect and support for a maintained immune function

Administration of KAND567:

- resulted in an effective engagement of the targeted fractalkine axis, e.g. seen as:
  - a statistically significant reduction of CX3CR1, i.e. the fractalkine receptor, on the cell surface on targeted immune cells over time in the KAND567 group compared to the placebo group (p ranging from <0.001-0.02 depending on time point),
  - a statistically significant increase of free CX3CL1, i.e. the fractalkine ligand, in blood plasma over time ($p<0.05$),
- did not change the levels of main sub-types of leukocytes, indicating that the general immune function is maintained.

Secondary and exploratory endpoints provide signals of cardio-protective effects

Administration of KAND567 resulted in the following numerical signals of cardio-protective effects:

Intramyocardial (IM) hemorrhage (secondary endpoint)

29 patients in the KAND567 group and 28 in the placebo group were assessed on IM hemorrhage on Day 3 by magnetic resonance imaging (MRI), showing:

- a trend of reduced frequency of IM hemorrhage in the KAND567 group compared to the placebo group (N=16, 57% and N= 11, 38% in the KAND567 and placebo group respectively, p=0.19). The level of IM hemorrhage in the placebo group is in line with prior studies in high-risk STEMI patients[1].

Infarction size (secondary endpoint)

For subgroup analysis of infarctions size in patients without IM hemorrhage, 15 patients in the KAND567 group and 11 in the placebo group were included in the analysis of Day 90 MRI data showing:

- a more pronounced decrease of infarction size* in all patients without IM hemorrhage at Day 90, and that
- this decrease was numerically larger in the KAND567 group (p=0,15).

Left ventricular (LV) thrombosis (exploratory endpoint)

37 patients in the KAND567 group and 34 placebo group were assessed on LV thrombosis on Day 3 and Day 90 by MRI or echocardiography, showing:

- a statistically significant reduction of LV thrombosis in the KAND567 group compared to the placebo group (2.7% and 17,6% respectively, p=0.05). The level of LV thrombosis in the placebo group is in line with prior studies in high-risk STEMI[2].

Number of patients included in the respective analyses varies depending on available data at different time-points.
* GAD5-SD (%), Late gadolinium-enhanced MRI was used at Day 90 to compare infarction size in patients administered placebo or KAND567 using a thresholding of 5 standard deviations above the mean signal intensity from normal myocardium.

Signals of effects are markers for efficacy endpoints commonly used in pivotal studies

Kancera has in previous clinical studies demonstrated safety and tolerability and pharmacological engagement of the fractalkine axis in severely inflamed patients. The FRACTAL study has now confirmed these results in high-risk STEMI patients. With demonstrated pharmacological effect, i.e. *proof-of-mechanism* in human, and a confirmed favorable safety profile, Kancera has reached an important development milestone, which overall contributes to a reduced risk and increased the probability of success going forward towards market approval.

Further, Kancera believes that the signals of cardio-protective effects demonstrated, increase the probability that KAND567 will meet future product registration efficacy endpoints, as the FRACTAL results are fully aligned with well-established integrated parts of "Major Adverse Cardiovascular Events (MACE)"[3], which commonly defines endpoints in pivotal studies:

- Reduced IM hemorrhage is strongly associated with, and an independent marker of, a lower risk of heart failure.
- Reduced LV thrombosis is strongly associated with a lower risk of systemic embolism, including stroke.

"*The signals of cardio-protective effects seen in the FRACTAL study are very encouraging, as they are established markers for the anticipated efficacy endpoints in upcoming phase IIb/III studies*", says Peter Selin, CEO of Kancera AB and continues: "*The 30 day and one year mortality in STEMI patients have been unchanged during the past 10 years and remain high at 7% and 11%, respectively. There is currently no therapeutic approach addressing the excessive inflammation that we believe may be the root cause for this very high residual risk of death. Thus, our drug candidate has the potential to become first in class and revolutionize the therapy for these patients. We believe that the FRACTAL results create a very strong basis for the continued development of KAND567 in cardiovascular diseases.*"

The way forward for KAND567 in cardiovascular diseases

Kancera will continue to conduct detailed analyses of data from the FRACTAL study, with the aim to identify markers of effects that can be used to design upcoming pivotal studies for product registration. Additional findings are planned to be reported during the second quarter 2024.

In parallel with the continued detailed analysis of data, Kancera is taking actions to advance the KAND567 development program in cardiovascular diseases, with specific focus on activities that are on the "critical path" for start of the next clinical study, which Kancera expects to be a combined phase IIb/III trial for product registration.

Based on previous pivotal studies in the same disease and patient setting, Kancera expects that regulatory authorities and payors will request primary efficacy endpoints that are focusing on patient outcomes. As described above, this is typically measured through follow up of Major Adverse Cardiovascular Events (MACE). Kancera's preliminary primary efficacy endpoint in a combined phase IIb/III pivotal study is a composite of cardiovascular death, heart failure, non-fatal MI or stroke, measured as relative risk reduction and absolute risk reduction compared to placebo.

About the FRACTAL study

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 the 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, 37 and 34 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.

For further information

Please refer to CEO Peter Selin and CSO Thomas Olin's presentation of the FRACTAL study results, available on Kancera's website: www.kancera.com/en/investor-relations/presentations/

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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.

References

1. Impact of Intramyocardial Hemorrhage on Clinical Outcomes in ST-Elevation Myocardial Infarction: A Systematic Review and Meta-analysis https://doi.org/10.1016/j.jscai.2022.100444
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