Guard Therapeutics reports robust efficacy of RMC-035 in Phase 2 (AKITA) and advances clinical development program

- Statistically significant and clinically relevant improvement of long-term kidney function (compared to placebo)
- Statistically significant and clinically relevant reduction of Major Adverse Kidney Events (MAKE) on Day 90, i.e. the primary endpoint in a future registrational Phase 3 study as required by regulatory agencies
- Guard Therapeutics will host an investor webcast on September 19, 2023, 14:00 CET.

Guard Therapeutics [GUARD], a biotechnology company specializing in kidney diseases, today announced top-line results from its Phase 2 clinical study AKITA, evaluating RMC-035 for the prevention of kidney injury in open-heart surgery. In line with previous communication patient recruitment was prematurely stopped, and as expected the primary (short-term) endpoint, incidence of acute kidney injury (AKI) within 72 hours after surgery, was not reached. Importantly though, pre-defined secondary endpoints demonstrated the intended long-term benefit of RMC-035 with improved kidney function compared to placebo. These results clearly support advancement in the clinical development program and highlight the potential of RMC-035 as a novel short-term treatment for kidney protection.

"We are very excited by the results of this Phase 2 trial with RMC-035. Whereas the chosen primary (acute) endpoint AKI failed, it is important to note that AKI merely serves as a short-term prognostic indicator of clinically relevant outcomes, including long-term kidney function and Major Adverse Kidney Events (MAKE). The actual efficacy of RMC-035 assessed by these hard clinical outcomes is far above expectations and makes the chosen primary endpoint, AKI, irrelevant in this context," said Tobias Agervald, CEO at Guard Therapeutics.

"The study has clearly demonstrated the efficacy signals needed to advance the project towards a future pivotal study. With these results we are back on track, strengthened in our confidence to establish a new and unique treatment for the prevention of kidney injuries in heart surgery and proceed with the clinical development of RMC-035 as planned. We are eagerly awaiting further discussions with regulatory authorities, and we look forward to providing more information about the clinical pathway shortly", Tobias Agervald continued.

"The top-line results from Guard Therapeutics' Phase 2 clinical trial AKITA with RMC-035 are very exciting, as they represent a potential breakthrough for the protection of kidney function in open-heart surgery. The consistency between improved kidney function and MAKE reduction in the stable phase after surgery is compelling because these outcome measures offer distinct perspectives on assessing the kidney-protective treatment effect. As the lead investigator of the AKITA trial, I am eager to see the compound's further development progress and ultimate contribution to improving patient outcomes," said Prof. Dr. Alexander Zarbock.

Key findings:

The AKITA study is a randomized, double-blind, placebo-controlled Phase 2 study of RMC-035 in patients undergoing open-heart surgery and at increased risk to develop kidney injuries. A total of 177 patients were randomized and dosed in the study (89 in the RMC-035 group, 88 in the placebo group). Patients were followed for 90 days after surgery.

Of note: The study was powered by a pre-defined alpha level of 0.1, meaning all p-values below 0.1 are statistically significant.

Primary endpoint (AKI within 72 hours after surgery):

- AKI rate was 50.6% for RMC-035 versus 39.8% for placebo (relative risk [RR]=1.30, p=0.12).
- AKI rate in the pre-defined subgroup of patients having a better kidney function at the time of surgery (estimated glomerular filtration rate [eGFR] ≥60 mL/min/1.73m2) and who received the higher start dose of 1.3 mg/kg (n=112; 63%):
    - 56.4% for RMC-035 versus 35.1% for placebo (RR=1.66, p=0.01)
- AKI rate in the pre-defined subgroup with worse kidney function at the time of surgery (eGFR <60 mL/min/1.73m2) and who received the lower start dose of 0.65 mg/kg (n=65; 37%):
    - 41.2% for RMC-035 versus 48.4% for placebo (RR=0.85, p=0.57).

Based on the primary endpoint analysis, a key learning going forward concerns identification of the most appropriate RMC-035 dose. Notably, the overall higher AKI rate for subjects on RMC-035 treatment was driven by the higher RMC-035 start dose in the subgroup of eGFR ≥60 mL/min/1.73m2, which caused an acute (within 12 hours) drug-induced increase in serum creatinine. This directly explains the higher AKI rate (and potentially failure to meet the primary endpoint) since an acute increase in creatinine, although reversible, triggers AKI per definition. Hence, the conclusion, and the basis for the Data Monitoring Committee (DMC) recommendation to discontinue further patient enrolment, are linked to a too high dose of RMC-035.

Secondary endpoints (to assess long-term kidney function):

eGFR change from baseline (before surgery):

- In the total study population, the difference in eGFR change from baseline on Day 90 for RMC-035 versus placebo was 4.3 mL/min/1.73m2 (p=0.06), in favor of RMC-035
    - This effect was greater in the subgroup of patients with eGFR <60 mL/min/1.73m2 who had received the lower RMC-035 dose: 7.9 mL/min/1.73m2 (p=0.05)
    - The effect was weaker in the subgroup of patients with eGFR ≥60 mL/min/1.73m2 who received the higher start dose: 2.3 mL/min/1.73m2 (p=0.41)

Major Adverse Kidney Events (MAKE):

- The number of MAKE events on Day 90 was significantly reduced with RMC-035 treatment: 6.7% for RMC-035 vs 15.9% for placebo (relative risk 0.41 (p=0.047)). This effect was consistent across the two eGFR subgroups and in a sensitivity analysis using a combination of creatinine and cystatin C for eGFR assessment.

The company considers the overall improved long-term kidney function (eGFR) with RMC-035 treatment as clinically relevant and predictive of the efficacy in a registrational Phase 3 clinical study required to support a future marketing authorization application/new drug application. In particular, the more pronounced effect in patients with lower kidney function (eGFR <60 mL/min/1.73m2) is remarkable given that generally these patients have a diagnosis of chronic kidney disease (CKD). Since the stronger treatment effect in this subgroup is likely to be attributed to the lower start dose (i.e. not causing an acute creatinine increase and higher AKI rate), the observed eGFR effect in the full AKITA study population may be underestimated in relation to the potentially achievable effect with an optimized dose of RMC-035.

Importantly, the MAKE endpoint on Day 90, which was successfully met with statistical significance in this study, is the expected primary endpoint in a pivotal Phase 3 study as required by the U.S. Food and Drug Administration (FDA). This composite endpoint captures an irreversible loss of kidney function (i.e., a disease-modifying effect) and includes any of the following components: death, post-surgery dialysis treatment, or ≥25% reduction in eGFR compared to baseline. The MAKE reduction is consistent with the observed improvement of eGFR, providing clear support for the kidney-protective effect of RMC-035.

Safety:
The safety profile of RMC-035 was consistent with earlier clinical trials, and reported adverse events were in line with expectations for patients undergoing open-heart surgery. Of note, adverse events reported with a higher frequency in the RMC-035 group compared to placebo indicated the presence of so-called infusion-related reactions (IRRs), which were mostly mild to moderate and typically occurred after the fourth or fifth (final) dose administration.

Investor webcast September 19, 2023, 14:00 (Europe/Stockholm)
Based on these important top-line results supporting continued development of RMC-035, the company will host an open webcast on September 19 at 14:00 pm CET. Registration to this webcast is available here: https://financialhearings.com/event/47345

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About Guard Therapeutics

Guard Therapeutics is a Swedish biotech company that identifies and develops new therapies for diseases with a great medical need for more effective treatments. The company's investigational drug RMC-035 is being developed as a kidney protective treatment in connection with open heart surgery and kidney transplantation. Guard Therapeutics is listed on Nasdaq First North Growth Market Stockholm.

Certified Adviser is Svensk Kapitalmarknadsgranskning AB, www.skmg.se.

About RMC-035

RMC-035 represents a completely new class of drugs (first-in-class) and consists of a recombinant and modified variant of the endogenous protein alpha-1-microglobulin. The investigational drug has the ability to protect cells and their mitochondria from damage caused by oxygen deprivation and elevated levels of the oxygen-binding and toxic protein heme. Favorable treatment effects of RMC-035 have been observed in several preclinical disease models. RMC-035 has a natural affinity for the kidneys and is primarily being developed as an intravenous kidney protective treatment for patients at high risk of developing acute kidney injury (AKI).

RMC-035 has obtained an Investigational New Drug (IND) clearance by the U.S. Food and Drug Administration (FDA) for the treatment of AKI in open-heart surgery. Additionally, RMC-035 has been granted Fast Track Designation by the FDA to reduce the risk of irreversible loss of kidney function, the need for dialysis treatment, or death after open-heart surgery in patients at elevated risk of AKI. In addition to open-heart surgery, a second development program with RMC-035 was initiated with a recently completed Phase 1b clinical study in patients undergoing kidney transplantation.

About the AKITA study

AKITA is a global, randomized, double-blind, and placebo-controlled Phase 2 clinical study aimed at evaluating the kidney protective effect of the company's investigational drug, RMC-035, in patients at an increased risk of developing acute kidney injury (AKI) associated with open-heart surgery. The AKITA study involves approximately 30 investigational sites in both Europe and North America. The primary outcome measures of the study include the incidence of AKI within 72 hours after completion of heart surgery, according to the internationally recognized KDIGO guidelines, as well as the evaluation of the investigational drug's safety profile during a 90-day follow-up period.

This information is information that Guard Therapeutics 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 2023-09-19 08:00 CEST.

Image Attachments

CEO Tobias Agervald

Attachments

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