Guard Therapeutics provides updated information on the phase 2 study AKITA

Guard Therapeutics [GUARD] provides updated timelines and additional details on the plan for data analysis in the clinical phase 2 study AKITA, which aims to evaluate the kidney-protective effect of the investigational drug RMC-035 in connection with open heart surgery. The previously reported interim analysis focused on acute drug effects including the incidence of acute kidney injury within 72 hours after surgery. Data collection and analysis for evaluation of efficacy continues for the planned 90-day period for subjects in the study.

- *Data collection continues as planned for up to 90 days after surgery in all 177 dosed patients.*
- *The last patient visit in the study is anticipated to occur in mid-July*
- *Important analyses of already collected blood and urine samples will be conducted before the last patient visit.*
- *Locking of the complete database (encompassing all 177 patients dosed) is expected to occur no later than September, at which point overall outcomes and conclusions from the study are expected to be presented. These will also guide further development of RMC-035.*
- *Full study results are expected to be available in October.*

On April 14th, the company announced that patient recruitment for the AKITA study had been terminated in accordance with a recommendation from an independent Data Monitoring Committee, following a pre-defined interim analysis involving 134 of the planned 268 patients. The interim analysis focused on the acute treatment effect of RMC-035, particularly the study's primary endpoint, which is the incidence of acute kidney injury within 72 hours of the first dose, according to guidelines established by the scientific organization Kidney Disease: Improving Global Outcomes (KDIGO).

Several important secondary outcomes were not analyzed in the interim analysis. These include, among others, the severity and duration of acute kidney injury, changes in kidney function from baseline before surgery to day 30 and 90 after surgery, as well as major adverse kidney events (MAKE) at the same time points. MAKE is a composite endpoint of death, dialysis, or >25% reduction in eGFR (estimated glomerular filtration rate) compared to baseline before surgery.

The planned size of the study, including a total of 268 patients, was estimated based on achieving a positive outcome with statistical significance for the primary (acute) endpoint. However, for understanding potential treatment effects of RMC-035, several important secondary endpoints can be evaluated with relatively good statistical power with fewer than 268 patients. In total, 177 patients have been randomized and dosed in the AKITA study, which consequently provides a comprehensive data set for both analyzing key secondary endpoints and conducting extensive subgroup analyses, such as patients with or without chronic kidney disease.

Continued data collection and analysis of blood and urine samples
The AKITA study is an exploratory proof-of-concept phase 2 trial designed to identify relevant

efficacy signals of RMC-035 in order to guide its further development. Therefore, there are no formal requirements for the primary efficacy endpoint to be met to advance the project to the next development stage if clinically relevant treatment effects are observed. It should also be noted that the primary (acute) endpoint in the study is a surrogate (predictor) for the regulatory relevant endpoint of MAKE at 90 days after surgery. Therefore, it is the treatment effect in stable phase at 90 days after surgery that will be evaluated by key regulatory authorities, including the US FDA, for market approval and is expected to contribute to a high commercial value.

Against this background, the company decided to continue data collection up to 90 days after surgery for all patients who have been dosed in the study. The main purpose is to maximize the amount of data, particularly regarding kidney function, in stable phase after surgery and at the time point that the FDA has defined as relevant for market approval. This means that data collection from the last patient in the study will end in mid-July.

In parallel with the continued data collection, the company has also decided to analyze blood and urine samples that have already been collected during the study. This particularly includes plasma concentrations of RMC-035 for pharmacokinetic analyses and biomarkers in urine for the identification of possible early cell damage in the kidney. The analyses are expected to provide important information regarding both the efficacy and safety of RMC-035 linked to its plasma concentrations.

Analysis of existing data before locking the final database
The normal procedure in a double-blind and randomized clinical trial is not to unblind any results until the full database has been locked for further changes. This is to maintain the integrity and validity of the data and to prevent bias in how already known results can affect ongoing data collection and registration of new data points.

Since recruitment in the AKITA study has ended due to a low probability of reaching the primary (acute) efficacy endpoint, the company has initiated a very limited and carefully controlled unblinding process at treatment group level (but not at individual patient level) based on existing and incomplete data. The purpose is to be able to initiate analyses and assessments of existing data with the highest possible data integrity before data collection is complete and the final database is locked.

Timeline
The company currently expects to communicate preliminary analyses and overall conclusions after full database lock in September. These results will guide the decision on further development of RMC-035.

The overall top-line results of the study are expected to be available in October.

About RMC-035
RMC-035 is a first-in-class investigational drug that consists of a recombinant and modified variant of the endogenous protein alpha-1-microglobulin. Its mechanism of action includes protection of cells and their mitochondria against injury caused by ischemia and elevated levels of the oxygen-

binding and toxic protein heme. Robust treatment effects of RMC-035 have been observed in several different preclinical disease models. RMC-035 primarily targets the kidneys and is being developed as an intravenous kidney-protective treatment for patients at high risk of developing acute kidney injuries.

RMC-035 has received an IND approval from the US Food and Drug Administration (FDA) for the treatment of cardiac surgery-associated AKI. The FDA has also granted RMC-035 Fast Track Designation for reducing the risk of an irreversible loss of kidney function, initiation of kidney replacement therapy or death following open-chest cardiac surgery in patients who are at increased risk for AKI. RMC-035 is currently being evaluated in the global phase 2 clinical trial AKITA for the prevention and treatment of AKI in open heart surgery. Positive results of the ongoing phase 1b study in kidney transplantation were announced on 20 March 2023.

About the AKITA study
AKITA is a global, randomized, double-blind, and placebo-controlled phase 2 clinical trial that aims to evaluate the kidney-protective effect of RMC-035 in patients who are at increased risk of developing acute kidney injuries during open-heart surgery. The study is being conducted at nearly 30 trial centers in both Europe and North America. The primary outcome measure of the study includes the occurrence of acute kidney injury (AKI) 72 hours after heart surgery, according to the internationally accepted KDIGO guidelines, as well as the evaluation of the drug candidate's safety profile during a 90-day follow-up period.

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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.

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Attachments

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