

## **Update of Internal Projects**

- **KB5359 has been discontinued for further development**
- **KB2115 shows statistically significant efficacy on LDL cholesterol, triglycerides and other risk factors in the first phase II study**
- **A second phase II clinical study with KB2115 in combination with statins is planned to be initiated during the autumn of 2007**
- **A clinical trials application has been filed for initiation of phase I clinical trials with KB3305**
- **Optimization of selective ER beta agonists for the purpose of selecting a candidate drug is ongoing**

### **Selective Thyromimetics for Dyslipidemia**

The dyslipidemia market is the largest pharmaceutical market segment in the world with sales around \$ 30 billion. High LDL cholesterol levels are strongly associated with the risk for cardiovascular disease. The market trend is to more efficiently lower LDL cholesterol levels and larger doses of statins as well as combination therapies are being introduced. New drugs with a new mechanism of action, like KB2115, that can be used alone or in combination with statins are required to reach treatment targets.

Karo Bio is a leader in development of selective thyromimetics. The most advanced compound KB2115 has completed the first phase II study in patients with dyslipidemia. The successful outcome of this study was briefly communicated in June this year. In essence, the study showed that KB2115 is efficacious and well tolerated. KB2115 induced a statistically significant lowering of LDL-cholesterol, as well as Apo B/Apo A-1 ratio (a risk factor that strongly correlates with myocardial infarction), triglycerides and the independent risk factor lipoprotein (a). The thyroid hormone homeostasis was preserved and there were no negative effects on the heart, bone metabolism or muscle parameters. Small, transient, and dose dependent effects on liver enzymes were noted and these effects are considered to be benign and not related to underlying toxicology. All side effects were reversible over the time of the study. The phase II study results will be further presented at different scientific meetings. The first presentation will be made at the upcoming DALM (Drugs Affecting Lipid Metabolism) meeting in New York, October 4-7, 2007. During the autumn, Karo Bio will also initiate an additional phase II study with KB2115 given concomitantly with statins.

KB5359 is a follow up compound to KB2115. Karo Bio recently communicated that toxicological findings in the 28 day toxicology studies in rats and dogs requires further examination. This investigation has now been concluded and Karo Bio has decided that KB5359 shall not be further developed. The toxicological findings observed with KB5359 are considered to be compound specific and not related to selective thyromimetics as a class of compounds. Karo Bio has an extensive compound library

and the possibility to identify a new compound for further development will be explored.

**Type 2 Diabetes**

KB3305 is a liver targeted glucocorticoid antagonist intended for treatment of type 2 diabetes. This new mechanism of action for the treatment of type II diabetes is promising and a number of studies have confirmed that the hepatic glucose production is elevated in type II diabetics. KB3305 is efficacious and safe in a number of animal models. New and improved pharmaceutical formulations have been developed and the plan is to initiate phase I clinical studies during the second half of this year. A clinical trials application for the first phase I study has been filed. The plan is to conduct the first clinical studies in three parts. First, single ascending doses will be given to healthy volunteers followed by multiple ascending doses. The third part of this study sequence is multiple doses given to patients with type 2 diabetes. This will ensure preliminary data on efficacy and safety in the target population.

**Selective ER beta agonists**

The discovery of ER beta has opened a number of new therapeutic possibilities. Estrogen affects mood and behavior and the Estrogen Receptor beta in particular appears to be mediating these effects. Karo Bio has shown that effects of ER beta selective compounds can be obtained in animal anti-depression models. There are also evidence for ER beta effects in inflammatory conditions and in cancer. Currently, highly selective compounds are undergoing optimization towards improved bioavailability. Karo Bio is evaluating additional clinical applications for its compounds.

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**Facts about Karo Bio**

*Karo Bio is a drug discovery and development company specializing in nuclear receptors for the development of novel pharmaceuticals with focus on metabolic diseases. Karo Bio has two clinical and five preclinical projects.*

*The company has expanded from being a drug discovery company by adding in-house preclinical and clinical development resources and competence for development of drugs to treat metabolic diseases. The company has a strong project portfolio with innovative molecules that primarily targets diseases such as diabetes, atherosclerosis and dyslipidemia. In all of these areas there are significant market opportunities and a growing need for new pharmaceuticals with new mechanisms of action.*

*In addition to the proprietary projects Karo Bio has two strategic collaborations with international pharmaceutical companies and one biotech collaboration for development of innovative therapies for the treatment of common diseases.*

*Karo Bio is listed on the OMX Nordic Exchange Stockholm AB since 1998 (Reuters: KARO.ST).*

This press release is also available online at: [www.karobio.com](http://www.karobio.com) and [www.waymaker.net](http://www.waymaker.net).