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Announcement

NeuroSearch reports final results from the TIPO-2 study with tesofensine in obesity

- ***Results show that tesofensine's outstanding efficacy in weight reduction is obtained through both appetite suppression and a favourable impact on energy and fat metabolism***
- ***The positive results strongly support tesofensine's potential as a superior new treatment of obesity and type 2 diabetes***

NeuroSearch has concluded the detailed evaluation of the data from TIPO-2, a human metabolic study with tesofensine, a monoamine reuptake inhibitor, in development for the treatment of obesity and type 2 diabetes. The results show that tesofensine significantly increases feelings of satiety and decreases the desire to eat while impacting favourably also on energy expenditure and fat metabolism in overweight and obese subjects. These synergistic effects are likely to help explain the outstanding efficacy of tesofensine in body weight management observed in both TIPO-2 (placebo-controlled mean weight loss of 1.8 kg after 14 days) and other clinical studies, including TIPO-1 (placebo-controlled mean weight loss of 9.2 kg after 24 weeks), and TIPO-4 (additional mean weight loss of approx. 4 kg after 24 weeks' treatment extension to TIPO-1).

TIPO-2 was designed as a randomised, double-blinded, placebo-controlled, parallel-group study, in which 32 overweight and obese subjects with a BMI (Body Mass Index (kg/m^2)) of 28-35 were treated for 14 days with either tesofensine (with an accelerated daily dosing scheme of up to 1 mg exposure) or placebo. The aim of the study was to evaluate tesofensine's effect on selected metabolic parameters by means of measurement of energy expenditure, fat oxidation and subjective appetite sensation (visual analogue scales (VAS) scores), DEXA scanning, and biochemical blood analyses.

Main conclusions from the evaluation of tesofensine's metabolic effects in TIPO-2:

- *Tesofensine reduces appetite sensations*
  In line with earlier clinical data from TIPO-1, the subjective appetite sensations measured after 14 days' treatment in TIPO-2 showed that subjects in the tesofensine treated group had an increased feeling of satiety with less desire to eat than subjects in the placebo group ($p<0.05$).

- *Tesofensine significantly increases fat oxidation and reduces fat tissue*
  In the tesofensine treated group, 24-hour fat oxidation was increased by 15% ($p<0.05$), while, reassuringly, 24-hour protein oxidation was lower compared with the placebo group ($p<0.05$). Also, results from DEXA scanning show a statistically significantly greater loss of fat tissue in the tesofensine treated subjects than under placebo ($p<0.01$).

- *Tesofensine increases levels of adiponectin and improves insulin sensitivity*
  The significant loss of fat in the tesofensine-treated subjects was also reflected in a higher level of adiponectin in their blood. Adiponectin is a peptide hormone

secreted exclusively by fat cells (adipocytes). Adiponectin decreases free fatty acids in the blood (plasma triglycerides) and increases glucose metabolism by improved insulin sensitivity, thereby also playing an important role in the treatment of type 2 diabetes.

- *Tesofensine increases energy expenditure at rest*

  After 14 days, a significant increase of 6% in night time energy expenditure was observed in the tesofensine treated group compared with placebo ($p<0.05$). The observed increase could not be explained by differences in body weight or spontaneous physical activity, indicating a direct effect of tesofensine on energy expenditure at rest.

The synergistic effects of tesofensine as observed in TIPO-2 with positive modulation of appetite sensations combined with increased energy expenditure and fat metabolism are likely to explain the pronounced effect on body weight (fat tissue reduction) and with improved glucose metabolism observed both in the present and previous studies. In line with the data from TIPO-1 where approximately 80% of the observed weight loss was related to body fat reduction, the detailed results from TIPO-2 show that tesofensine exerts its effect on energy metabolism via loss of fat and not by increased muscle degradation or other catabolic effects in the organism.

Hence, the findings from TIPO-2 strongly support tesofensine's potential as a superior new treatment of obesity and type 2 diabetes.

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