NEUROSEARCH

NeuroSearch A/S
Pederstrupvej 93
DK - 2750 Ballerup
Denmark
Telephone: +45 4460 8000
Telefax: +45 4460 8080
ns@neurosearch.dk
www.neurosearch.com
CVR No: DK-12 54 61 06

**Announcement**

**NeuroSearch announces breakthrough tesofensine results from clinical Phase IIb study in obesity ("TIPO-1")**

*- Average weight loss of 12.6% and 11.2%, respectively, seen in the two highest dose groups after 24 weeks treatment with tesofensine*

NeuroSearch has concluded a Phase IIb Proof-of-Concept and dose finding study ("TIPO-1") with its drug candidate tesofensine for the treatment of obesity with very positive results. Data from the study in 203 patients show that 24 weeks' treatment with 0.25 mg, 0.5 mg and 1 mg tesofensine resulted in a dose-dependent average weight loss of 6.5%, 11.2% and 12.6%, respectively (against a weight loss of 2.0% in the placebo group). In all treatment groups, the primary endpoints were met with high statistical significance ($p < 0.0001$).

| **TIPO-1 results** | Placebo | Tesofensine 0.25 mg | Tesofensine 0.5 mg | Tesofensine 1.0 mg |
|---|---|---|---|---|
| ITT* population | 52 | 52 | 50 | 49 |
| Mean weight at base line (kg) | 103.2 | 101.7 | 100.1 | 101.3 |
| **Average relative weight loss** | **2.0%** | **6.5%**** | **11.2%**** | **12.6%**** |
| **Average absolute weight loss (kg)** | **2.2** | **6.7**** | **11.3**** | **12.8**** |

* All patients enrolled in the study (ITT = Intention to treat)

** Statistically significantly different from placebo ($p < 0.0001$)

Secondary end-points, including relative change (reduction) in BMI (Body Mass Index ($kg/m^2$)) as well as feeling of satiety and appetite were also met ($p < 0.0001$ for BMI). In the two highest dose groups (0.5 mg and 1.0 mg), treatment with tesofensine led to an average reduction in the patients' BMI of 4.

Further, results from the TIPO-1 study showed that tesofensine has a good safety profile and was well tolerated. The most frequently reported adverse events were mostly mild to moderate, and included dry mouth, sleep disturbances, nausea, constipation and diarrhoea. In line with tesofensine's pharmacological profile, there was a tendency towards an increased number of adverse event observations in the highest dose groups (0.5 mg and 1.0 mg). A similar pattern was observed when measuring cardiovascular effects, with slight increases in heart rate and blood pressure. However, no clinically relevant cardiovascular adverse events or changes in either blood pressure or pulse were seen, according to FDA criteria.

The number of patients discontinuing the study was 42 (21%) which was lower than expected (33%). The highest numbers of patients discontinuing were observed in the placebo group and in the highest dose group (1.0 mg).

<u>Conclusions from the TIPO-1 study</u>

*The results of the TIPO-1 study show a clear dose-dependent weight reducing effect of tesofensine with a marked and clinically relevant effect already at the lowest dosing (0.25 mg).*

The placebo adjusted weight loss of approx. 10% seen in both of the two highest dose groups (0.5 mg and 1.0 mg) is highly superior to the efficacy of any marketed drug for obesity management. The strong effect in both the low and the middle dose combined with a generally well-tolerated high dose leaves a highly promising therapeutic window for tesofensine.

The combined clinical safety data base from five individual studies with tesofensine now counts approximately 1,000 patients exposed to relevant therapeutic doses. This safety backing together with the breakthrough weight-loss results from the TIPO-1 study as well as weight-loss data from previous clinical studies support the preparation for a pivotal clinical Phase III programme with tesofensine for the treatment of obesity with a clear guidance for final dosing regimes.

Flemming Pedersen, CEO of NeuroSearch, commented:

"*We are very excited about these robust results, which demonstrate that tesofensine holds promising potential to be leading the next generation of drugs that can offer a more efficacious and safe medical option in the struggle against obesity. Bearing from this, tesofensine may also offer a preventive treatment of other serious conditions relating from obesity such as type 2 diabetes. Tesofensine is a result of NeuroSearch's dedicated drug development efforts and we are very pleased to be able to announce a major step forward in bringing this novel product to the market.*"

Professor, MD, Dr.Med.Sci. Arne Astrup***, Head of Department of Human Nutrition at University of Copenhagen Faculty of Life Sciences, who was leading the Danish multi-centre TIPO-1 study of tesofensine, commented:

*"Current anti-obesity medications on the market produce a weight loss that is 3-5 kg greater than placebo over 6 months, and the major pharmaceutical companies have for several years been struggling to develop drugs that produce a 6-8 kg weight loss. Therefore, I was thrilled to see that the tesofensine trial actually produced a weight loss of approx. 10 kg more than placebo, without major safety concerns. If tesofensine will prove to live up to this weight loss effect in 12 months' Phase III trials, thereby opening a whole new dimension in obesity management that can effectively compete with gastric surgery, this drug will definitely set a new standard in obesity treatment."*

*** Conflict-of-interest statement: Professor, MD, Dr.Med.Sci. Arne Astrup is principal investigator in the TIPO-1 study and chairman of NeuroSearch's Scientific Advisory Board for this programme. NeuroSearch pays a fee for these services. Arne Astrup has informed NeuroSearch that he holds 452 shares in NeuroSearch.

## TIPO-1 – Study design

The TIPO-1 Phase IIb Proof-of-Concept study was conducted as a parallel-group, double-blind, placebo-controlled study in five centres in Denmark including a total of 203 patients with obesity. Selection criteria in the study were a BMI of 30-40 and an age between 18 and 65 years. Patients were randomly selected to receive daily treatment of 0.25 mg, 0.5 mg or 1.0 mg tesofensine or placebo. The treatment period was 24 weeks with a two weeks' lead-in and an eight weeks' follow-up period. From the beginning of the lead-in period and until the end of the follow-up period, all patients in the study followed the same reduced-calorie diet and the same exercise programme.

## Ongoing tesofensine studies (TIPO-2 and TIPO-4)

NeuroSearch is also conducting a human metabolic study with tesofensine ("TIPO-2"), to evaluate the drug candidate's direct effect on metabolic parameters such as insulin, glucose and cholesterol levels. The TIPO-2 study was initiated in November 2006 with planned enrolment of a total of 32 patients. Results are expected in Q4 of 2007.

Further, in June 2007 NeuroSearch initiated an open-label Phase II extension study, TIPO-4, with tesofensine, offering all patients having concluded 24 weeks' treatment in TIPO-1 with tesofensine or placebo another six months of treatment. In TIPO-4, the dosing of tesofensine is 0.5 mg daily for all patients with the possibility to increase to 1.0 mg daily according to tolerance and efficacy. The aim of TIPO-4 is continuously to evaluate tesofensine's safety profile and tolerability as well as to generate additional observations on maintenance of effect (weight reduction) for a total of up to 12 months. The patients in TIPO-4 will follow the same diet and exercise programme as in TIPO-1. To date, almost 90% of the patients having completed TIPO-1 have chosen to continue tesofensine treatment in TIPO-4. Results from TIPO-4 are expected in the 1st half of 2008.

The results from the TIPO-1 Phase II Proof-of-Concept study with tesofensine does not change NeuroSearch's financial expectation for 2007 of a loss in the range of DKK 230-250 million before recognition of associates and other equity interests.

Asger Aamund
Chairman of the Board

**Conference call**

NeuroSearch will host a conference call today, 17 September 2007 at 2:00 p.m. Copenhagen time (8:00 a.m. Eastern Time) to discuss the results from the TIPO-1 study with tesofensine. Participating in the call will be CEO Flemming Pedersen, Chief Medicinal Officer Dieter Meier and VP, Director of IR & Corporate Communications Hanne Leth Hillman. The conference call will be conducted in English and can be accessed by dialing +44 (0)20 7162 0025. Prior to the conference call, a powerpoint-presentation will be available at NeuroSearch's website www.neurosearch.com.

**Contact persons**:

Flemming Pedersen, CEO, phone: +45 4460 8214 or +45 2148 0118

Hanne Leth Hillman, Vice President, Director of Investor Relations & Corporate Communications, phone: +45 4460 8212 or +45 4017 5103

Tesofensine background

Tesofensine is a triple monoamine re-uptake inhibitor, i.e. a compound that blocks the re-uptake of the neurotransmitters serotonin, dopamine and nor-adrenaline in the brain with no direct effect on the monoamine receptors. The mechanism of action behind this class of compounds is very well described. Serotonin, dopamine and nor-adrenaline are all involved in the brain's central regulation of food intake, metabolic control and in subsequent weight control. Tesofensine's relative impact on the three monoamine systems is believed to induce weight reduction through both a reduction in appetite and an effect in the metabolic centre in the brain leading to increased thermogenesis.

NeuroSearch has conducted a preclinical study with tesofensine in Diet Induced Obese (DIO) rats showing that tesofensine elicits a sustained weight-loss of approximately 10%. This compares favourably to the maximal effect of approximately 8% and 4% observed with sibutramine (Reductil®) and rimonabant (Acomplia®),

respectively, which have been used as reference compounds in the study. The weight reduction induced by tesofensine involved a clinical relevant loss of both abdominal and subcutaneous fat stores. Furthermore, a strong reduction in blood cholesterol and triglycerides was observed after chronic treatment with tesofensine. Importantly, also the insulin sensitivity was found to be significantly increased in the animals treated with tesofensine, suggesting a better regulation of glucose metabolism in obese and diabetic animals.

Obesity - clinical condition

Obesity is characterised by severe excess weight in the form of fat and is defined on the basis of a measure referred to as Body Mass Index (BMI). A BMI of more than 30 is referred to as clinical obesity, while a BMI of between 25 and 30 expresses overweight. According to the World Health Organization (WHO), obesity has reached epidemic proportions globally, with up to 1.6 billion adults (over 15 years old) overweight and at least 400 million of them clinically obese.

According to the American Obesity Association (Obesity Fact Sheet), patients with obesity are at risk of developing one or more serious medical conditions, which can cause poor health and premature death. Obesity has been found to be the largest environmental influence on the prevalence of diabetes and it complicates the management of type 2 diabetes by increasing insulin resistance and glucose intolerance, which makes the medical treatment for type 2 diabetes less effective. Approximate 90% of individuals with type 2 diabetes are reported to be overweight or obese. In addition, obesity increases the risk of cardiovascular disease, and is a major risk factor for heart attack. Over 75 per cent of hypertension cases are reported to be directly attributed to obesity. A weight loss of as little as 5 per cent can reduce high blood sugar and blood cholesterol.

NeuroSearch (NEUR) is a Scandinavian biopharmaceutical company listed on the OMX Nordic Exchange Copenhagen A/S. Our core business covers the development of novel drugs, based on a broad and well-established drug discovery platform focusing on ion channels and CNS disorders. A substantial part of the company's activities are partner financed through a broad alliance with GlaxoSmithKline (GSK) and collaborations with among others Abbott and Astellas. The drug pipeline comprises 11 clinical (Phase I-III) development programmes: ACR16 in Huntington's disease (in preparation for Phase III), tesofensine in obesity/type 2 diabetes (Phase II), NS2359 in depression (Phase II) and ADHD (Phase II) in partnership with GSK, NS1209 in epilepsy and pain (Phase II), ABT-894 in ADHD (Phase II) and pain (Phase II) in partnership with Abbott, ACR16 in schizophrenia (Phase I) in partnership with Astellas, ACR325 in bipolar disorder (Phase I) and ABT-107 as well as ABT-560 for the treatment of various CNS diseases – both (Phase I) in collaboration with Abbott. In addition, NeuroSearch has a broad portfolio of preclinical drug candidates and holds equity interests in several biotech companies.