



Announcement

NeuroSearch A/S announces the results of additional assessment and analysis of data from the Phase III MermaiHD study with Huntexil® in Huntington's disease

- **Further assessment of data from the study shows that the significance value for the primary study endpoint, the modified Motor Score (mMS) of $p=0.042$ did not meet the pre-specified level of $p<0.025$. With inclusion of the clinically relevant CAGn adjustment, the p-value is <0.02 as previously communicated**
- **This revised statistical conclusion is isolated to the primary endpoint, and there are no changes to the previously communicated results for other endpoints**
- **Overall, the data confirm that Huntexil® has a unique and clinically meaningful effect on global motor function in Huntington's patients with a good safety profile**
- **The regulatory strategy for Huntexil® is unchanged, and NeuroSearch will initiate dialogue with regulatory authorities based on the MermaiHD study results**

Copenhagen, 28 April 2010 – NeuroSearch (NEUR) has completed additional data assessment and analyses of the MermaiHD study, a European Phase III study with Huntexil® in Huntington's disease.

Overall, the additional assessments and analyses confirm the clinical top-line results as previously communicated in Announcement no. 01-10 on 3 February 2010, namely that

- Huntexil® significantly improves motor function in Huntington patients
- Huntexil® demonstrates positive effects on both voluntary and involuntary motor symptoms
- Huntexil® was very well tolerated with an adverse event profile similar to placebo

The conclusion regarding the primary endpoint, the mMS with a significance level of $p<0.02$, which was communicated as part of the top-line results, was based on a clinically relevant baseline covariate adjustment for differences in patients' genetic disposition, i.e. the length of CAG repeats (CAGn) in the diseased gene sequence. This adjustment is judged to be clinically important and appropriate in ensuring a more meaningful representation of the data set. Based on this assessment, the primary endpoint for the MermaiHD study was concluded to be met ($p<0.025$).

The adjustment for individual differences in patients' CAGn x treatment was pre-specified in the study protocol as a sensitivity analysis but not as part of the main effects model for the primary analysis. In view of this, the statistical results have been re-assessed, demonstrating a formal p-value of 0.042 for the primary endpoint, the mMS, and consequently indicating that the study did not reach the $p<0.025$ significance level (Bonferroni adjustment) as pre-defined in the study protocol. As adjustments for CAGn are recommended for the analysis of clinical studies in Huntington's disease,



NeuroSearch will include the CAGn covariate adjusted analysis in the presentation of the MermaiHD study results to regulatory authorities.

Overall, in the MermaiHD study, 26 weeks treatment with Huntexil® (45 mg twice daily) led to significant improvements of patients motor function measured on both mMS and TMS (the Total Motor Score) as compared to placebo. The statistical significance outcomes are summarised below for both endpoints as measured in the ITT (Intention to Treat) population and the PP (Per Protocol) population (the 82% of the patients who completed the study in compliance with the study protocol):

ITT (Intention to Treat) population

Huntexil® (45 mg twice daily) vs placebo	Main effects model ¹⁾	+CAGn x trt ^{2)*}	+CAGn x age ^{3)*}
mMS	p = 0.042	p < 0.02	p < 0.01
TMS	p = 0.004	p < 0.001	p < 0.001

PP (Per Protocol) population:

Huntexil® (45 mg twice daily) vs placebo	Main effects model ¹⁾	+CAGn x trt ^{2)*}	+CAGn x age ^{3)*}
mMS	p = 0.014	p < 0.005	p < 0.005
TMS	p < 0.01	p < 0.0025	p < 0.001

- 1) Main effects model: ANCOVA including baseline mMS/TMS score, neuroleptic cotreatment and gender as covariates
- 2) Main model plus CAGn x treatment as baseline covariate
- 3) Main model plus CAGn x age as baseline covariates
- * CAG values not yet available for 44 patients (of which 13 in the placebo group, 18 in the 45 mg once daily group and 13 in the 45 mg twice daily dose group)

The additional data assessment generally confirms the consistency and robustness of the results and supports the overall positive clinical outcome of the MermaiHD study, including the following positive findings:

- Huntexil® demonstrates a superior treatment effect in patients with an elevated CAGn score (considered a surrogate marker for rate of progression and disease prognosis)
- The significant improvements observed in mMS are driven primarily by positive effects on fine motor skills, gait and balance
- Positive effects were also observed in certain cognitive and functional domains
- Significant benefit was observed on the independence scale in patients with higher CAGn scores

In the study, Huntexil® also demonstrated a very good safety profile and was shown to have no significant disadvantages in terms of worsening of other disease signs or symptoms. The further data analysis also showed that there were no significant changes in vital signs between the treatment groups.

Conclusions and next steps

The revised statistics do not change the overall clinical evidence from the MermaiHD study demonstrating that Huntexil® offers clinically meaningful improvements to Huntington patients across a broad range of motor symptoms without worsening any other disease signs and symptoms and thus shows promise in being a uniquely efficacious and well tolerated therapeutic option. NeuroSearch continues to plan for initial interactions with regulatory authorities based on the results from the MermaiHD study.



Telephone conference

NeuroSearch will conduct a telephone conference today at 10 am DK time (9 am UK time and 4am US time) in connection also with the release of the company's interim report for Q1 2010. Participating in the conference will be CEO Flemming Pedersen, Vice President and CFO Anita Milland and Vice President and Director of IR & Capital Market Relations Hanne Leth Hillman. The conference will be conducted in English and the dial-in numbers are UK and International: +44 207 509 5139, US: +1 718 354 1226, and DK: +45 3271 4767.

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About the MermaiHD study

The MermaiHD study is a randomised, double-blinded and placebo-controlled Phase III study conducted at 32 clinical centres across Europe to examine the effects of Huntexil[®] on a number of Huntington's disease parameters. The study included 437 patients with Huntington's disease from Austria, Belgium, France, Germany, Italy, Portugal, Spain and the UK.

In the study, patients were randomly allocated to receive treatment with one of two Huntexil[®] doses (45 mg. once or twice daily) or placebo during a 26-week period. Patients completing the randomised phase have been offered to continue into a 26-week open-label extension phase, in which they receive treatment with 45 mg. Huntexil[®] twice daily, only.

The primary study endpoint is voluntary motor function in Huntington patients, measured on *the modified Motor Score (mMS)*, which is defined as the sum score of voluntary motor items (items 4-10 and items 13-15) from *the Total Motor Score (TMS)*, The TMS includes 15 items of motor assessment and comprises the motor part of the Unified Huntington's Disease Rating Scale (UHDRS), including both voluntary motor function (mMS and eye movements) and involuntary movements such as dystonia and chorea. TMS is also included as endpoint in the MermaiHD study. Other endpoints include cognitive function, behaviour and symptoms of depression and anxiety.

About Huntington's disease

Huntington's disease is a highly disabling, hereditary neurodegenerative genetic disorder, which leads to damage of the nerve cells in certain areas of the brain including the basal ganglia and the cerebral cortex.

The disease has a prevalence of about 1: 10,000 in most western countries with an estimated 70,000 affected patients in North America and Europe combined. In other parts of the world, the disease prevalence varies substantially among geographic regions and is generally lower. The total number of patients outside North America and Europe is estimated to be in the range of 30,000 to 35,000.

Patients with Huntington's disease experience a wide variety of symptoms typically grouped into three categories: motor, cognitive and psychiatric symptoms. The onset of symptoms is typically around 35 and 45 years of age, and patients hereafter deteriorate gradually with a life expectancy of 10 to 20 years.

Eventually every person with Huntington's disease will require full-time care. Huntington's disease represents high unmet medical needs, as there is currently no cure or effective treatment available and only a limited number of novel drugs in development.

NeuroSearch – Company profile

NeuroSearch (NEUR) is a Scandinavian biopharmaceutical company listed on NASDAQ OMX Copenhagen A/S. The company's core business covers the development of novel drugs, based on a broad and well-established drug discovery platform focusing on ion channels and central nervous system (CNS) disorders. A substantial share of the activities is partner financed through





strategic alliances with Eli Lilly and Janssen and a license collaboration with Abbott. The drug pipeline comprises eight clinical (Phase I-III) development programmes: Huntexil[®] for Huntington's disease (Phase III), tesofensine for obesity (Phase III), ABT-894 for ADHD (Phase II) in partnership with Abbott, ACR343 for schizophrenia (Phase II ready), ACR325 to treat dyskinesias in Parkinson's disease (Phase Ib), ABT-560 for the treatment of cognitive dysfunctions (Phase I) in collaboration with Abbott, NSD-788 for anxiety/depression (Phase I) and NSD-721 for social anxiety disorder (Phase I). In addition, NeuroSearch has a broad portfolio of preclinical drug candidates and holds equity interests in several biotech companies.