



## Announcement

### NeuroSearch presents additional data from the MermaiHD study with Huntexil® at the 5<sup>th</sup> Annual CHDI Conference on Huntington's disease

Copenhagen, 11 February 2010 – Today, at the 5<sup>th</sup> Annual CHDI Conference on Huntington's disease, held 8 to 11 February in Palm Springs, California, NeuroSearch (NEUR.CO) presented the results from the MermaiHD study, a Phase III study with Huntexil® (pridopidine) for the treatment of Huntington's disease. Top-line results from the study were announced on 3 February 2010 (Announcement no. 01-10),

Presenting as the featured speaker at the conference, Dr. Joakim Tedroff, Head of Clinical Science at NeuroSearch on Wednesday 10 February, 4pm to 5pm PDT (Thursday, 1am to 2am CET) presented the study results, including the following:

- *Efficacy* - Results from the MermaiHD study demonstrate that six months' (26 weeks) treatment with Huntexil® (45 mg BID), in Huntington's patients significantly improves both voluntary movement control, as measured on the primary endpoint, the mMS, and also a broader range of voluntary and involuntary motor symptoms, including dystonia and eye movements. Measured in both the ITT (Intention to treat) and the PP (per protocol, 82% of patients) populations, the improvements seen were highly statistically significant, and thereby the results in the PP population fully confirm the ITT analysis :

Motor scale	Significance level for the PP population	Significance level for the ITT population
Modified Motor Score, mMS	$p < 0.005$	$p < 0.02$
Total Motor Score, TMS	$p < 0.005$	$p < 0.001$
Eye Movements	$p < 0.02$	$p < 0.002$
Dystonia	$p < 0.01$	$p < 0.001$

- *Cognitive testing* – On one of the cognitive measures, the Trail Making test, included in the MermaiHD study as a secondary endpoint, six months treatment with Huntexil® 45mg BID showed a significant improvement (*ITT*;  $p < 0.05$ ).
- *Safety and compliance* – Over the six months of treatment in the study, less than two thirds of all patients reported adverse events. The most frequently observed adverse events were falls, dizziness, Huntington's chorea, diarrhoea, nausea, nasopharyngitis, depression, fatigue and insomnia, occurring at a frequency between 3% and 9% and equally distributed between the active treatment groups and placebo. In total, the study had a high completion rate, and with less than 4% of patients withdrawing from the study due to adverse events:



	Placebo	Huntexil <sup>®</sup> 45 mg QD	Huntexil <sup>®</sup> 45 mg BID
Randomised pts (ITT)	144	148	145
Completers	129 (90%)	143 (97%)	131 (90%)
Withdrawals due to AE	8 (6%)	2 (1%)	7 (5%)
Any adverse event	64%	61%	68%

The study showed no worsening of any disease signs and symptoms, including Huntington's chorea, on which measure both the ITT and the PP analyses showed no difference compared to placebo.

- *Patient demographics* – Patient randomization in the MermaiHD study was successful with patients in the three study arms (Huntexil<sup>®</sup> 45 mg QD; Huntexil<sup>®</sup> 45 mg BID; and placebo) expressing similar demographic characteristics. At baseline, the mean age across the study was 50.6 years, time since diagnose 4.8 years and the mean CAG repeats was 44.7 (between 36 and 63). Out of the total number of randomized patients, 190 (43.5%) were on antipsychotic medication, and 247 (56.5%) were not.

*Insight into the unique pharmacology of Huntexil<sup>®</sup>*

Huntexil<sup>®</sup> (pridopidine) exerts its pharmacological effect via induction of a unique functional modulation of dopamine D2 receptors primarily in the striatum. This functional feature of the compound has recently been published in the European Journal of Pharmacology (2010, issue 628, pp 19-26 by T. Dyhring et al.; *The dopaminergic stabilizers pridopidine (ACR16) and (-)-OSU6162 display dopamine D2 receptor antagonism and fast receptor dissociation properties.*

Further, *in vivo* studies have shown that Huntexil<sup>®</sup> strengthens the glutamate function in the cortex, an effect most likely to be mediated by the release of dopamine and consequently D1 activation.

Huntington's disease is associated with dopaminergic dysfunction and disruptive corticostriatal circuitry, and the combined effect of Huntexil<sup>®</sup> on both the dopaminergic and glutamatergic systems is believed to account for the observed partial normalization of motor dysfunctions in Huntington patients.

*Conclusions from the MermaiHD study*

In the MermaiHD study, six months' treatment with Huntexil<sup>®</sup> has shown to significantly improve both voluntary and involuntary motor functions, translating into a ½ to 1½ years of set-back in the natural progression of these disease symptoms. Importantly, this improvement is seen without any "therapeutic" disadvantages in terms of worsening of other disease signs or symptoms and with good safety.

Following the results from the MermaiHD study, NeuroSearch has undertaken further in-depth analysis of the results and initiated dialogue with regulatory authorities to discuss the study outcome and plans for market registration of Huntexil<sup>®</sup> as a novel treatment for Huntington's disease.

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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<sup>®</sup> on a number of Huntington's disease parameters.

The study has enrolled 437 patients with Huntington's disease from Austria, Belgium, France, Germany, Italy, Portugal, Spain and the UK. The patients have been randomly allocated to receive treatment with one of two Huntexil<sup>®</sup> doses (45 mg QD or 45 mg BID) or placebo during a six month double-blinded phase. Hereafter, they have been offered to continue into a six month open-label extension phase, in which they receive treatment with Huntexil<sup>®</sup> 45 mg BID only. The last patient completed the double-blinded phase in November 2009, and of the total number of patients having completed six months of randomised treatment, almost 90% have chosen to continue into the open-label extension phase.

The primary study endpoint is voluntary motor function in Huntington patients, measured on *the modified Motor Score (mMS)*. The mMS is defined as the sum score of voluntary motor items from *the Total Motor Score (TMS)*. The TMS is part of the Unified Huntington's Disease Rating Scale (UHDRS) and measures a broader range of motor symptoms, including voluntary motor function (mMS and eye movements) and also involuntary movements such as dystonia and chorea. Further study endpoints include the TMS, cognitive function, behaviour and symptoms of depression and anxiety.

**About Huntington's disease**

Huntington's disease (HD) 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. Patients suffering from HD 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 have a life expectancy of 10 to 20 years.

The disease occurs at a rate of about one in every 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 HD prevalence is lower, and the total number of patients suffering from HD outside North America and Europe is estimated at 30,000 to 35,000. The rate of diagnose also varies among geographic regions.

After symptoms onset the disease progresses without remission and 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.

**About NeuroSearch – Company profile**

NeuroSearch (NEUR) is a Scandinavian biopharmaceutical company listed on NASDAQ OMX Copenhagen A/S. The core business of the company covers the development of novel pharmaceutical agents, 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 Janssen Pharmaceutica, Eli Lilly and Company and GlaxoSmithKline (GSK), and a license collaboration with Abbott. The drug pipeline comprises eight clinical (Phase I-III) development programmes: Huntexil<sup>®</sup> (pridopidine) for Huntington's disease (Phase III), tesofensine for obesity (ready for Phase III), ABT-894 for ADHD (Phase II) in partnership with Abbott, ACR343 for schizophrenia (ready for Phase II), 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 partnership with GSK. In addition, NeuroSearch has a broad portfolio of preclinical drug candidates and holds equity interests in several biotech companies.

