



## Announcement

**The HART study with Huntexil<sup>®</sup> shows significant effect on total motor function in patients with Huntington's disease although it did not meet the primary endpoint after 12 weeks of treatment**

- *The primary endpoint, the modified Motor Score, mMS, measuring voluntary motor function, showed an improvement of 1.2 points ( $p=0.078$ )*
- *The secondary endpoint, the Total Motor Score, TMS, measuring all motor symptoms of the disease, showed an improvement of 2.8 points ( $p=0.039$ )*
- *A statistically significant dose-response relationship was shown for Huntexil<sup>®</sup> on both the primary (mMS) and the secondary endpoint (TMS)*
- *The results support the good safety and tolerability profile of Huntexil<sup>®</sup>*
- *Results are consistent with the results from the MermaiHD study*
- *NeuroSearch will consult with regulatory authorities to define the best strategy for obtaining marketing approval for Huntexil<sup>®</sup>*

Copenhagen, 14 October 2010 – Today, NeuroSearch A/S (NEUR) announced the first results from the 12-week randomised, double-blinded, placebo-controlled Phase II HART study with Huntexil<sup>®</sup> (pridopidine), a novel treatment for Huntington's disease.

The HART study was conducted in 28 centres across the United States and Canada and enrolled a total of 227 patients, who were randomised to treatment with three different doses of Huntexil<sup>®</sup> (10 mg, 22.5 mg or 45 mg – all twice daily) or placebo.

The primary endpoint of the HART study was the change from baseline at 12-weeks on the modified Motor Score, mMS, a subscale of the UHDRS (the Unified Huntington's Disease Rating Scale) Total Motor Score, TMS. For the Huntexil<sup>®</sup> 45 mg twice daily dose group, the effect versus placebo on the mMS did not reach significance, but on the secondary endpoint, the TMS, the change from baseline at week 12 was statistically significant. For both the mMS and the TMS, a statistically significant improvement in the change from baseline was seen with increasing dose, thus demonstrating an important dose-response relationship for Huntexil<sup>®</sup>.

Importantly, the effect sizes for both the mMS and the TMS seen in the HART study are consistent with those seen in the MermaiHD study (see table):

**Table: Huntexil® (45 mg twice daily) – effect on mMS and TMS (mean change versus placebo; p-value)**

	The HART study*	The MermaiHD study at 12 weeks**	The MermaiHD study at 26 weeks***
mMS	-1.2 ( $p=0.078$ )	-0.6 ( $p=0.2$ )	-1.0 ( $p=0.042$ )
TMS	-2.8 ( $p=0.039$ )	-2.0 ( $p=0.032$ )	-3.0 ( $p=0.004$ )

\* ANCOVA (ITT, LOCF) adjustment for baseline score, age, treatment

\*\* MMRM (ITT, OC) adjustment for baseline score, neuroleptics (yes/no), gender, treatment, week and interaction between treatment and week

\*\*\* ANCOVA (ITT, LOCF) adjustment for baseline score, neuroleptics (yes/no), gender, treatment

In the HART study, Huntexil® 45 mg twice daily also showed significant effects on the patients' balance and gait as well as hand movements. For the TMS motor domains for eye movements, dystonia and chorea, positive trends were observed. In general, these results also show consistency with the observations in the MermaiHD study.

The endpoints for cognition, affective symptoms and generalised function/well-being did not show any statistically significant changes.

In the HART study, Huntexil® was found safe and well tolerated, and the most frequently reported adverse events across all treatment groups were falls, headache, diarrhoea and nausea with no apparent pattern related to active treatment. The adverse event findings were consistent with the observations in the MermaiHD study. Compliance with study medication was high across the study.

Treatment was discontinued due to adverse events for 7% of patients, and nine serious adverse events (recurrent breast cancer, suicidal ideation, depression, bipolar disorder, adjustment disorder, testicular torsion and three episodes of convulsions) were reported in six patients. No dose-dependent clinical patterns related to active treatment were observed.

Dr. Karl Kieburtz, University of Rochester Medical Center, Rochester, New York, the US, Primary Investigator on the HART study, commented:

*"I find the results of the HART study encouraging as they provide additional support for the efficacy of pridopidine (Huntexil®) while helping also to demonstrate its benign safety profile in patients with Huntington's disease. Pridopidine is the first drug ever to target both the voluntary and involuntary motor features of this disease."*

Patrik Dahlen, CEO of NeuroSearch, added:

*"We are highly encouraged by the supportive HART study outcome and we look forward to taking the next steps towards our goal of establishing Huntexil® as a new and better treatment option for patients with Huntington's disease."*

NeuroSearch is very encouraged by the strong trend in improvement on mMS, as well as the significant improvement on TMS and other secondary motor endpoints seen with Huntexil® in the HART study. This, together with the significant dose-response relationship on both endpoints provide strong support to previous clinical findings, demonstrating that the drug has beneficial and relevant effects on core motor functions in patients with Huntington's disease. Further, the efficacy of Huntexil has been shown to be associated with a good safety profile.

In the coming weeks, additional study analyses will be undertaken, including meta-analyses of data from both the HART and the MermaiHD studies. When the evaluation of all available clinical data is completed, NeuroSearch plans to engage in dialogue with regulatory authorities in North America and in Europe with a view to discussing the best way forward to obtaining marketing approvals for Huntexil® as a novel treatment for Huntington's disease.

NeuroSearch holds all commercial rights to Huntexil®, and the company is on a continuous basis evaluating the best commercial options for the drug in North America, Europe and the rest of the world.

The HART results do not change the company's financial guidance for 2010 of a loss before financials and other shares of results of approximately DKK 350 million.

Patrik Dahlen  
CEO

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### Conference call

NeuroSearch will host a conference call tomorrow, Friday 15 October, 11:30 am to 12:00 local time (10:30 to 11:00 am UK time/5:30 to 6:00 am EST) to further present and discuss the HART results. Participating in the call will be CEO Patrik Dahlen, Dr. Nicholas Waters, CEO of NeuroSearch Sweden AB and Hanne Leth Hillman, VP and Director of IR & Capital Market Relations. The telephone 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.

### About Huntexil® (pridopidine)

Pridopidine acts as a dopaminergic stabiliser and is the first compound in a new class of pharmaceutical agents, *dopidines* to have demonstrated clinical effect. Dopidines have the unique ability to stabilise the dopaminergic system, i.e., to either enhance or inhibit dopamine dependent functions in the brain, depending on the initial level of dopaminergic activity.

Pridopidine inhibits dopamine activation of the D2 receptor with a preference towards the high affinity (activated) receptor state and has no detectable agonist activity on this receptor. *In vivo*, pridopidine strengthens glutamate function in the frontal cortex, which may add to the agent's powerful behavioural effects in states of excessively high dopamine activity or excessively low glutamate activity, while not affecting behaviour under normal conditions. Together, these findings suggest that pridopidine stabilises psychomotor activity in states of hypo- and hyperactivity by means of functional D2 antagonism and strengthening of cortical glutamate functions.

### About Huntington's disease

Huntington's disease is a highly disabling, fatal and incurable 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 is hereditary and every child of someone with Huntington's disease has a 50% chance of inheriting the disease.

Patients with Huntington's disease experience a wide variety of symptoms, which typically can be grouped into three categories: *motor dysfunction* includes loss of muscle co-ordination, parkinsonism, chorea, dystonia, and abnormal gait and posture, which can markedly impair patients' daily functioning. *Impaired executive and cognitive functions* lead to loss of organizational and planning skills, and *psychiatric changes*, such as depression and anxiety, are typical; manic and psychotic symptoms can also be present. The onset of symptoms is typically around 35–45 years of age, after which patients deteriorate gradually and have a life expectancy of 10–20 years.

Patients with Huntington's disease will eventually require full-time care, and the therapy area has high unmet medical needs. No cure or effective treatment is available and only a limited number of novel drugs are in development. The prevalence of Huntington's disease is about 1: 10 000 in most western countries, corresponding to an estimated 70 000 affected patients in North America and Europe combined. In other parts of the world, the prevalence varies substantially and is generally lower.

#### **About NeuroSearch**

NeuroSearch A/S is a leading CNS focused and European based biopharmaceutical company listed on NASDAQ OMX Copenhagen A/S (NEUR). The company's core business is development of novel drugs to treat diseases of the central nervous system, and the pipeline comprises eight products in clinical development (Phase I-III). These include Huntexil<sup>®</sup> (pridopidine), a unique orphan drug in Phase III development for the treatment of Huntington's disease, and tesofensine ready for Phase III development as a novel drug to treat obesity.

NeuroSearch is founded on a well-established drug discovery platform in the field of ion channels and monoamine transporters, ensuring the continuous production of novel preclinical development candidates. The company has strategic drug discovery and development alliances with Janssen Pharmaceutica and Eli Lilly as well as a licence collaboration with Abbott. Further, NeuroSearch has equity interests in a number of private companies in the Life Science industry.

