NH001: A Treatment for Cognition Recovery in Brain Injury Patients

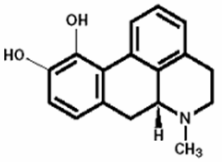
Summary

NH001 is a potent and broad acting dopamine agonist to help regain consciousness, accelerate recovery and improve the functional outcome of patients who remain in a vegetative state (VS) or minimally conscious state (MCS) **weeks to months after** a traumatic brain injury. Currently, there are no approved drugs for this severe, life-threatening indication. In a pilot clinical trial, NH001 demonstrated excellent responses in VS and MCS patients. A Phase II double-blind placebo-controlled trial was initiated under an FDA IND. Issued patents in the USA, Canada & Europe, and Orphan Drug designations in the US & Europe, provide good market protection.

Some salient considerations:

= strategic entry to untapped neurorehab market for an established neuroscience franchise
= lower risk clinical program, based on drug with well-known safety profile
= favorable regulatory path – IND filed under subpart E, orphan designations, FDA clinical grant
= $b range product, marketable by a small sale force, no approved product for indication
= for use 1-4 months post brain injury (and quite distinct by mechanism, pathobiology, clinical trials & marketing from acute tbi indication).

Active Ingredient and Mechanism of Action



Apomorphine HCl

Apomorphine is a broad dopamine agonist active in both D_1 and D_2 class receptors. It is used with syringe injectors for the treatment of hypomobility in advanced Parkinson's disease as a rescue treatment once other less potent drugs have lost efficacy. In patients remaining in a vegetative state or minimally conscious state after a TBI, areas of the brain remain viable, but the connections between functional sections are impaired due to the diffuse axonal injury. Apomorphine stimulates the dopaminergic pathways and promotes integration between distant functional regions of the brain, which results in the regaining of consciousness. Once consciousness is restored, the patient can engage in active rehabilitation. Accelerating the recovery of consciousness helps patients to achieve their best possible functional outcome.

Delivery System

NH001 is delivered subcutaneously, 12 hours per day, through a continuous infusion pump in pre-filled reservoir cartridges. Subcutaneous NH001 is rapidly absorbed and readily crosses the blood–brain barrier, reaching brain concentrations six times higher than in plasma. NH001 is the only dopaminergic agent that can be delivered parenterally, and rapidly achieve and maintain a steady and high brain concentration. NH001 treatment is administered for a period of 2-3 months.

Market

Each year in the U.S., it is estimated that 25,000 to 50,000 patients sustain a traumatic brain injury (TBI) with loss of consciousness for more than 2 weeks. Currently there are no drugs approved for this patient population. The cost of care for severe TBI patients is very high, with the lifetime cost estimated at over $1 million per patient. Most patients are in rehab facilities such that NH001 can be marketed with a small specialty sales force.

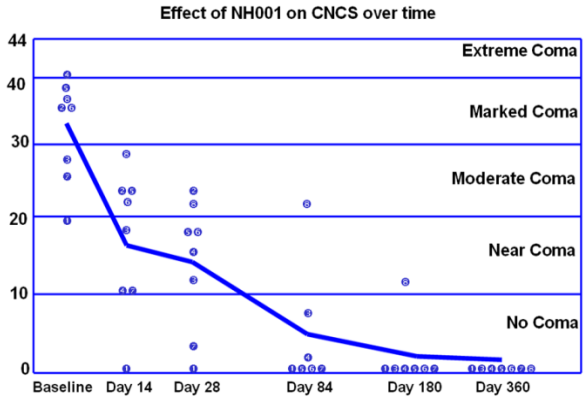
Intellectual Property

NeuroHealing filed and fully owns patents on methods of using NH001 to treat subjects in an altered consciousness state. A patent entitled "*High Potency Dopaminergic Treatment of Neurological Impairment Associated with Brain Injury*" includes claims for formulations containing dopaminergic agents optimized for sc continuous infusion and as a kit attached to an infusion pump. Patents have issued in the United States (No 7,943,632 [with term extension expiring 2028]), Canada (CA2519117), Europe (1 610 796) and Australia (AU2004222307).

NH001 has been granted orphan drug status from the FDA Office of Orphan Products Development. The orphan drug designation covers the use of NH001 for the treatment of patients in a vegetative state or minimally conscious state for up to twelve months following brain injury (TBI or stroke). NH001 has also been designated as an Orphan Drug in Europe by the EMA.

Clinical Data

An open-label clinical trial demonstrated that shortly after NH001 administration patients improved their consciousness levels and were able to start active rehabilitation. Patients in the study fared much better than the expected incident of recovery based on published historical data (see below). These data suggest that NH001 may accelerate the recovery of post-TBI patients and patients may achieve a better long-term functional outcome. Papers reporting these results have been published [Fridman et al, *Brain Injury* (2009) and Fridman et al, *Brain Injury* (2010)].



	Incidence of Recovery *	Responses with NH001
	n=434	n=7
Death	33%	14%
Vegetative State	15%	0%
Severe Disability	28%	29%
Moderate Disability	24%	57%
Good Recovery		

* New England J Medicine 330:1572

Clinical Development Status

NeuroHealing began a phase II double-blind placebo-controlled study in 76 unconscious patients at the Spaulding Rehabilitation Hospital, Harvard Medical School. The PI is Ross Zafonte, Chair of the Dept of Physical Medicine & Rehabilitation at Harvard, VP of Medical Affairs for Spaulding, and a recognized leader in the field of drug treatments for patients with low neurological functioning. The IND was filed under 21CFR601 subpart E: Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses also referred to as 'fast track.' NeuroHealing was awarded an FDA Orphan Drug clinical grant to initiate this trial.

Another study is to begin soon to correlate the observed clinical responses of unconscious patients to NH001 treatment with multimodal neuroimaging assessments (including MRI, PET, EEG).