NeuroHealing is a private, clinical stage company developing innovative treatments for specialty indications based on repositioning neurologically active compounds. We use proprietary novel formulation and drug delivery strategies to reposition approved small molecule drugs. To date, three different products have been conceived, developed, patented and tested in human studies.

NeuroHealing is guided by an experienced management team and advisory boards. Elkan Gamzu is acting Head of Clinical Trials for NeuroHealing. Dr. Gamzu has worked in the biopharmaceutical industry since 1971, in discovery with Hoffmann-La Roche, in clinical management and drug development with Warner-Lambert, where as VP, Drug Development, he had responsibility for the development of Cognex, the first drug approved for Alzheimer’s, and Neurontin. Dr. Gamzu served as CEO of Cambridge Neuroscience and as Interim VP of Development Project Leadership for Millennium Pharmaceuticals. He was a co-founder of BioPharmAnalysis, a company offering due diligence services. He has been the medical monitor for Phase I-III studies in PD, Alzheimer’s Disease, epilepsy, depression, cognition, TBI, stroke, insomnia, and pain disorders and has presented before the FDA and a number of European regulatory agencies.

NeuroHealing works with a network of manufacturers, regulatory consultants, CROs and clinical consultants. Santiago Perez-Lloret, MD, PhD is a clinical pharmacologist and pharmacoepidemiologist with expertise in Parkinson’s Disease non-motor symptoms including sialorrhea. Dr Perez-Lloret was an investigator for the NH004-2 PD study and is an advisor for the NH004-3 study on issues related to protocol design, regulatory documentation, site logistics, data collection and data analysis.

NeuroHealing’ CEO is Neal M. Farber, PhD who has over 30 years experience in the biotech industry in research, product development and company building.

**Opportunity Overview**

NH004 is a novel treatment to control the symptoms of sialorrhea (excessive drooling) in patients suffering from Parkinson’s disease and other motor disorders. NH004’s active ingredient is the anticholinergic drug tropicamide, delivered in a thin film designed to adhere and slowly dissolve within the oral cavity to allow the drug to reach the underlying salivary gland, thereby reducing saliva secretions. The advantages of NH004 include local bioavailability with low systemic exposure, rapid onset of action and, importantly, convenience of use for patients. Currently, there are no approved therapies to treat sialorrhea for these patients.

Tropicamide is a synthetic anticholinergic agent acting as a non-selective blockage to muscarinic receptors. It is FDA approved as an ophthalmic solution for diagnostic procedures and surgeries. In sialorrhea, tropicamide acts by blocking the acetylcholine receptors of the salivary glands. A short-acting anticholinergic agent, tropicamide (plasma half-life of 30 min) has the potential to reduce saliva secretion without the side effects associated with long-acting cholinergic blockers.

NH004 contains tropicamide formulated in a novel and convenient drug delivery means known as thin films or “thin strips,” modeled on Listerine PocketPaks® breath strips, with two significant modifications: the film used in NH004 is formulated with a muco-adhesive property to adhere to the oral mucosa and allow the drug to be absorbed locally near the submandibular salivary gland. After placement in the mouth, the film dissolves slowly over a 60-90 minute period. An attractive feature of NH004 films is the ability to readily modify the amount of the drug and excipients (such as flavors) or change the dissolution rate, and thereby differentiate a spectrum of products.

Sialorrhea is one of the major non-motor complaints in patients suffering from various neurological impairments, including Parkinson’s disease, cerebral palsy, ALS, Huntington’s, stroke and traumatic brain injury. Sialorrhea is often described by these patients a significant disabling social problem of their disease and not discussed due to the embarrassing nature of the condition. Depending on its severity, drooling can result in medical disability, impaired speech or serious eating difficulties.

Existing approaches to treating sialorrhea are not satisfactory. These include surgical procedures, prosthetic devices, botulinum toxin injections, systemic anticholinergic drugs, and speech and behavioral therapy. No single therapy satisfactorily resolves
sialorrhea in all patients. There are also several ‘off label’ drug approaches to treat sialorrhea, including atropine and glycopyrrolate. Each of these treatments has several shortcomings impeding their use and they have not gained any general acceptance.

NeuroHealing performed a comparative study to assess the pk and toxicity of tropicamide following a single dose via topical ocular (eye), oral (mouth), or intra-oral (a muco-adhesive thin film placed inside the mouth) administration in rabbits. Tropicamide was absorbed most rapidly after topical ocular administration with the highest $C_{\text{max}}$ value and the shortest plasma $T_{\text{max}}$ value compared to the other routes of administration. Systemic exposure, both in terms of $C_{\text{max}}$ and AUC, were 40% lower for the NH004 films than for the ophthalmic administration, strongly suggesting that NH004 film administration would be at least as safe as the standard ophthalmic administration of tropicamide.

### Details of MJFF Grant

NeuroHealing has been awarded two grants from the MJFF to conduct two NH004 clinical studies.

The first study, designed NH004-2 ([www.clinicaltrials.gov/show/NCT00761137](http://www.clinicaltrials.gov/show/NCT00761137)) was a double-blind Phase IIa single-administration dose-finding study conducted at the doctor’s office setting testing NH004 in PD patients complaining of sialorrhea. This study found that a 1 mg dose was the most effective and that the NH004 films provided better relief from sialorrhea than films with placebo. The results have been published (Lloret SP, et al, “A double-blind, placebo-controlled, randomized, crossover pilot study of the safety and efficacy of multiple doses of intra-oral tropicamide films for the short-term relief of sialorrhea”, J Neurol Sci 2011).

No adverse events were observed in the NH004-2 trial, thus providing a justification for home administration of multiple NH004 films per day.

The second follow-on NH004-3 study is designed to demonstrate that NH004 films at the dose of 1 mg provide better short term relief from sialorrhea symptoms in Parkinson’s disease patients than the placebo films when the films are taken twice a day, in a home setting, over a period of one week.

### Results and Potential Next Steps

NeuroHealing’s NH004 clinical studies have demonstrated encouraging results. In Parkinson’s patients complaining of sialorrhea, a clinically effective reduction of saliva was observed with no side effects or complications.

NeuroHealing has conducted a phase IIa, dose response, double-blind, placebo-controlled, crossover study testing NH004 in PD patients. PD patients complaining of sialorrhea were randomized to receive treatment with three doses of NH004 and placebo. Results of this study showed that NH004 produced a reduction in drooling, as determined by two outcomes measurements. No adverse events were detected in any of the treatment sequences. Results have been published.

Based on the findings of this single-administration dose-finding study, another study is about to begin to demonstrate that NH004 films provide better relief from sialorrhea than placebo in Parkinson’s patients when taken twice a day over a period of one week.

NeuroHealing is seeking a partner to enable the rapid completion of the NH004-3 study and begin the required approval studies. Sialorrhea clinical trials have a number of advantages including: outpatient basis, short time frame for efficacy testing, and established clinical outcome measures. NH004 development will require two Phase III studies, which can be done in parallel in approximately a years’ time. This opportunity would be ideal for a company (1) with a development & marketing presence in PD or movement disorders, (2) expanding in the specialty pharma area, or (3) interested in novel intra-orally deliverable drug means.

### Intellectual Property Status

NeuroHealing owns patent applications for the NH004 film composition and uses of intra-orally delivered tropicamide and other anticholinergics. The first issued patent (2006206252AU) in this family includes claims for compositions for the treatment of sialorrhea. The company also has know-how related to the manufacture and delivery of muco-adhesive slow-dissolving thin strips containing anticholinergic agents.

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For additional information, please contact: ResearchPartnerships@michaeljfox.org