

# NeuroBo Pharmaceuticals

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## Novel therapies with multi-modal effects for treatment of neurodegenerative conditions

In its neurodegenerative disease therapeutic pipeline, NeuroBo Pharmaceuticals has a phase 3-ready drug candidate, NB-01, in development for painful diabetic neuropathy and a number of other indications, as well as an investigational new drug (IND)-ready candidate, NB-02, that targets Alzheimer's disease and tauopathies.

Drugs approved to treat neurodegenerative conditions address symptoms of disease but not the underlying pathology, and are often accompanied by unwanted side effects. NeuroBo Pharmaceuticals, based in Boston, MA addresses complex diseases, including neuropathic pain, inherently caused by multiple pathways, with a multi-modal drug approach that targets more than one of these pathways, while leveraging favorable adverse event profiles.

NeuroBo, founded in 2017, has assembled an experienced management team hailing from various organizations within the pharmaceutical, diabetes and biotechnology industries. Roy Freeman, a professor of neurology at Harvard Medical School, has been closely involved with the company as founder and chairman of the Scientific Advisory Board.

### Neuropathic pain

Diabetes and cancer chemotherapy are among the leading causes of neuropathic pain. Diabetic neuropathic pain, also known as painful diabetic neuropathy (PDN), affects 8.4 million patients with diabetes worldwide. Symptoms range from a dull tingling to a debilitating pain, and are accompanied by related effects, such as limited mobility and poor sleep. PDN impacts significantly both the quality of life of diabetic patients and the cost of healthcare. At present, the three approved therapies for neuropathic pain, and others used off-label, are only effective in about half of the treated patients and results in only a limited reduction in pain. These patients also have high rates of non-compliance because of adverse side effects, and many patients are ultimately treated with opioids.

"Painful diabetic neuropathy is a multi-target disease with a complex pathophysiology. Currently available drugs are sub-optimal, poorly tolerated and do not address the underlying pain-causing nerve damage," said NeuroBo's CMO Mark Versavel. "We believe our lead candidate, NB-01, has the potential to significantly benefit many patients suffering from this condition."

The active ingredients in NeuroBo's NB-01 are derived from two species of the plant genus *Dioscorea* that have been used in traditional Chinese medicine for centuries. Researchers at the Korean pharmaceutical company, Dong-A ST (from which NB-01 was licensed), developed a potent oral drug formulation as an extract from these plants. Since then, NeuroBo has identified approximately 60 compounds in the drug that fall into 8 structural classes, including saponins (glycosides), curcuminoids and rosmarinic acids, which appear to have known pharmacologic effects in painful diabetic neuropathy. NB-01 adheres to the

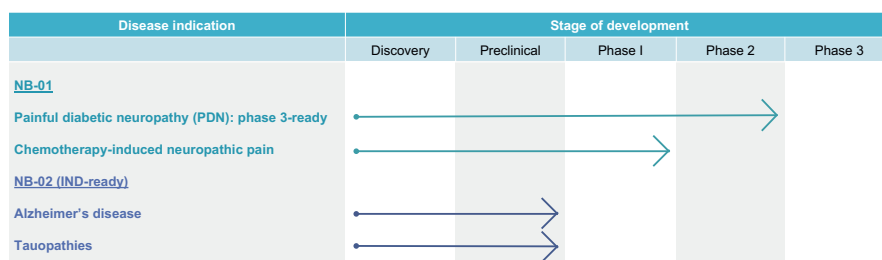


Fig. 1 | The clinical development pipeline at NeuroBo Pharmaceuticals. IND, investigational new drug.

US Food and Drug Administration (FDA) drug guidelines for the manufacture of natural product-based drug compounds, which require certain marker compounds to monitor batch-to-batch consistency. The final drug product falls under the FDA's Center for Drug Evaluation and Research (CDER) guidelines and is treated like any other drug undergoing development.

### Pre-clinical characterization

Extensive preclinical studies in rodents have shown that NB-01 increases endogenous levels of the neurotrophin, nerve growth factor (NGF), which promotes nerve repair. In addition, the drug is anti-inflammatory (reducing TNF and IL-6 levels) and decreases advanced glycation end products (AGEs), which are elevated in diabetes-related complications and can cause cell injury. Phase 3 trials of NB-01 in diabetic neuropathic pain are scheduled to start by mid-2020.

NB-01 is patent protected for peripheral neuropathic pain, including that caused by chemotherapy. Chemotherapy-induced peripheral neuropathy (CIPN) is a common side effect of chemotherapeutic agents that can potentially limit dosage during patient treatment and affects quality of life in cancer survivors. Improved long-term survival of cancer patients has led to an increase in the prevalence of CIPN. With further development, NB-01 could play an important role in the large oncology market.

### Alzheimer's disease and tauopathies

Alzheimer's disease is among the most challenging neurodegenerative conditions today. Despite a global prevalence of 10.6 million people, currently available therapies are ineffective in slowing progression and focus on managing symptoms, largely via acetyl cholinesterase (AChE) inhibition.

NeuroBo's second drug candidate, NB-02, is currently investigational new drug (IND)-ready as a potentially disease-modifying treatment for Alzheimer's disease and tauopathies (Fig. 1). As with NB-01, NB-02 is a

natural product derived from a plant species and the peel of a fungus, extracted and developed as an oral formulation optimized for AChE inhibition. In pre-clinical studies, NB-02 has demonstrated inhibitory effects on cholinesterase activity, amyloid toxicity, plaque deposition and tau phosphorylation. Animal studies also show improved cognitive endpoints in transgenic mouse models. Both acute and short-term toxicity studies required for IND submission have been completed for NB-02 and the company is planning for a phase 1 human study in late 2020.

In addition to Alzheimer's disease, NB-02 has broad patent protection for neurodegenerative diseases and is expected to greatly benefit those suffering from other tauopathies, such as progressive supranuclear palsy (PSP). Additional tau-related disease conditions are also being explored that would benefit from synergistic pTau and amyloid inhibition.

### Partnerships

In July 2019 NeuroBo Pharmaceuticals announced a merger with Gemphire Therapeutics, a Nasdaq-listed company. The combined company will keep the NeuroBo name and will focus on developing NB-01 and NB-02.

"NeuroBo will continue to explore strategic partnerships and further financing opportunities to advance its pipeline programs," said CEO John L. Brooks III. "Our multi-target pharmaceutical candidates incorporate a unique approach that has the potential to bring life-changing therapies to patients suffering from a range of neurodegenerative diseases."

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