



NodThera Ltd

(“NodThera” or the “Company”)

NodThera is first to demonstrate reduction in neuroinflammation in the clinic with brain penetrant NLRP3 inflammasome inhibitor

- **NT-0796 demonstrates reduction of multiple neuroinflammatory and inflammatory biomarkers in plasma and CSF of elderly volunteers in just 7 days**
- **Individuals with the highest baseline levels of inflammation demonstrate greatest reductions, including reductions in CSF neurofilament light chain (NfL), a key biomarker of neurodegeneration**
- **Recruitment into patient arm of pioneering Phase Ib/IIa study in Parkinson’s disease with extensive biomarker analysis ongoing**

BOSTON, MA, July 11, 2023 – NodThera, a leading clinical-stage biotech developing brain-penetrant NLRP3 inflammasome inhibitors to treat chronic inflammatory diseases, today announces positive, initial data from four subjects in the elderly volunteer stage of its Phase Ib/IIa study evaluating the effects of its lead candidate NT-0796 on inflammatory and disease-specific biomarkers in the blood and cerebrospinal fluid (CSF).

Alan Watt, Chief Executive Officer of NodThera, said: “Taken together, these initial findings represent the first unambiguous demonstration of modulation of neuroinflammation in a human population with an NLRP3 inflammasome inhibitor. In designing our Parkinson’s disease study, we deliberately chose to measure the effects of NT-0796 in an elderly volunteer population as the first stage, since age is a clear factor in increased neuroinflammation.

“Demonstrating such rapid decreases in just 7 days, across a broad range of neuroinflammatory biomarkers in the CSF, particularly NfL, is a striking result, as other drugs have required an extended timeframe of months or even years to show reduction of this biomarker. Our data provide clear validation of our strategy to take highly differentiated brain penetrant molecules into the clinic and justify our confidence in the potential of NT-0796 to treat diseases such as Parkinson’s disease and Alzheimer’s disease.”

Professor Paul Matthews, Head of the Department of Brain Sciences in the Faculty of Medicine of Imperial College London, said: ““These data, while still very preliminary, provide promising evidence of the potential of NLRP3 inhibition to modulate the neuroinflammation associated with Parkinson’s disease. This is an exciting area. Development of molecules based on this concept could lead to a step change in the treatment landscape for neurodegenerative diseases more generally.”

Significant anti-inflammatory effects in both plasma and CSF

Initial data from the ongoing study confirm earlier findings from the completed first-in-human and preclinical studies with NT-0796 showing excellent pharmacokinetics with a novel capsule formulation.

Subjects in the study were cannulated and CSF-sampled on Day 1 (pre-dose) and Day 7 following daily NT-0796 dosing. CSF drug levels were confirmed as consistent with previous observations and a range of inflammatory CSF biomarkers demonstrated meaningful reductions.



Neurofilament light chain (NfL), exclusively synthesised in the central nervous system (CNS), decreased by approximately 25% over 7 days in the most inflamed subject and by 13% on average. NfL is now recognised by the Food and Drug Administration (FDA) as a key biomarker of neuroaxonal damage and neurodegeneration.

A full panel of cytokines, chemokines and adhesion molecules known to be associated with neuroinflammation were determined in the CSF, with the most inflamed individuals again demonstrating the most robust reductions. As previously observed, the most inflamed subjects at baseline showed the largest decreases in key peripheral inflammatory markers, C-reactive protein (CRP) and fibrinogen. Consistent reductions in circulating levels of unstimulated IL-1 β , IL-18 and TNF α were also seen in subjects on Day 7 compared to Day 1.

NodThera's pioneering, biomarker-rich Phase Ib/IIa study in Parkinson's disease, previously announced [in June 2023](#), is currently recruiting into the patient arm of the study. This innovative clinical biomarker panel was designed using the preclinical profile of NT-0796 which demonstrated modulation of cytokines, chemokines and markers of gliosis relevant to neuroinflammatory disease.

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About NodThera

NodThera is a leading clinical-stage biotech developing brain-penetrant NLRP3 inflammasome inhibitors to treat chronic inflammatory diseases. Led by an experienced management team, NodThera is combining a deep understanding of NLRP3 inhibition, pharmaceutical neuroscience expertise and precision molecular chemistry. Its two lead clinical candidates are oral, small molecule NLRP3 inflammasome inhibitors, which have demonstrated differentiated, potentially best-in-class clinical profiles with significant anti-inflammatory effects and the ability to penetrate different areas of the brain, offering distinct opportunities to treat multiple indications. The Company is backed by top-tier investors including 5AM Ventures, Cowen Healthcare Investments, Epidarex Capital, F-Prime Capital, Novo Holdings, Sanofi Ventures and Sofinnova Partners. NodThera is headquartered in Boston, MA, with additional operations in Cambridge, UK and Seattle, WA. Learn more at www.nodthera.com or follow the Company on [LinkedIn](#).