



NodThera Ltd

("NodThera" or the "Company")

NodThera announces positive first-in-human data for two brain penetrant NLRP3 inflammasome inhibitors

- **Oral, small molecule, clinical candidates NT-0249 and NT-0796 demonstrate differentiated, potentially best-in-class clinical profiles with significant anti-inflammatory effects**
- **Proven to penetrate different areas of the brain, providing opportunity to treat multiple indications**
- **Pioneering, biomarker-rich Parkinson's disease study now underway with NT-0796**

BOSTON, MA, June 20, 2023 – NodThera, a leading clinical-stage biotech developing brain-penetrant NLRP3 inflammasome inhibitors to treat chronic inflammatory diseases, today announces positive data from first-in-human studies of its lead therapeutic candidates, NT-0249 and NT-0796, and provides an update on the Company's priority clinical development programme.

In the studies, both candidates were shown to clearly inhibit the NLRP3 inflammasome, a highly validated drug target that plays a pivotal role in controlling inflammatory diseases. The differentiated design characteristics of each candidate enabled them to penetrate different areas of the brain for optimal drug distribution in a range of NLRP3-driven diseases.

Brain penetration and anti-inflammatory effects across both clinical programmes

Data from the recently completed multiple-ascending dose (MAD) cohorts of **NT-0249's** first-in-human study confirm a potentially best-in-class pharmacokinetic/ pharmacodynamic (PK/PD) profile, suitable for once-daily dosing. NT-0249 demonstrated significant anti-inflammatory effects in healthy volunteers, with reductions in key inflammatory biomarkers, C-reactive protein (CRP) and fibrinogen, that were maintained throughout treatment. Levels of NT-0249 measured in the cerebrospinal fluid (CSF) additionally demonstrated high levels of brain penetration.

Findings from the completed first-in-human study of **NT-0796**, initially disclosed in September 2022, also confirm an excellent PK/PD profile, brain penetration and anti-inflammatory effects in healthy volunteers.

Both candidates were well tolerated, treatment emergent effects were predominantly mild and there were no serious adverse events (SAEs).

Priority development programme underway in Parkinson's disease

Development of NT-0796 is now progressing in a pioneering, biomarker-rich Phase Ib/IIa study in Parkinson's disease. The study is exploring the candidate's effect on inflammatory and disease-specific biomarkers in the blood and CSF using an innovative clinical biomarker panel, designed using the preclinical profile of NT-0796 on cytokines, chemokines and markers of microgliosis and astrogliosis relevant to NLRP3 inhibition.

The initial stage of the study, in healthy, elderly volunteers, is already underway, investigating a modified formulation of the drug candidate designed for use in the upcoming patient arm of the study.



Alan Watt, Chief Executive Officer of NodThera, said: “As the burden of non-communicable diseases continues to rise globally, targeting chronic low-grade inflammation, through selective modulation of the NLRP3 inflammasome, holds enormous potential for the treatment of these diseases. Our strategy to design highly differentiated and brain penetrant molecules, which combines a deep understanding of NLRP3 inhibition, pharmaceutical neuroscience expertise and precision molecular design, is delivering on the promise that NLRP3 inflammasome modulation can change the treatment paradigm for chronic peripheral and neurodegenerative diseases. These excellent clinical data from both clinical candidates reinforce our confidence that NodThera has the clinical tools to address these challenges.”

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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](#).