



NodThera Ltd

(“NodThera” or the “Company”)

NodThera announces first patients dosed in a Phase Ib/IIa cardiovascular risk trial of NLRP3 inflammasome inhibitor NT-0796

- **Aberrant NLRP3 activation is recognised as a critical driver of cardiometabolic disease**
- **A Phase Ib/IIa trial of lead candidate NT-0796 will assess inflammatory biomarkers and other cardiometabolic endpoints in an inflamed obese population**
- **Sub-cohort will examine potential of NLRP3 modulation to reduce neuroinflammation as a contributor to cardiometabolic disease in these patients**

BOSTON, MA, October 16, 2023 - NodThera, a leading clinical-stage biotech developing brain-penetrant NLRP3 inhibitors to treat chronic inflammatory diseases, today announces that the first patients have been dosed in a Phase Ib/IIa clinical trial evaluating the potential of its lead candidate, NT-0796, to assess cardiometabolic biomarkers in obese patients with risk factors for atherosclerotic cardiovascular disease. This follows the U.S. Food and Drug Administration’s (FDA) ‘safe to proceed’ letter in response to the Company’s Investigational New Drug (IND) application.

The NLRP3 inflammasome is a highly validated drug target that plays a pivotal role in controlling inflammatory diseases. NLRP3 activation is recognised as a critical driver of cardiometabolic disease with strong data supporting a role in atherosclerosis, myocardial infarction and heart failure.

Emerging evidence also suggests that NLRP3 activation can drive neuroinflammation (reactive gliosis) leading to dysregulated storage of body fat, energy utilisation and obesity. NodThera’s trial of its brain-penetrant candidate NT-0796 will explore the potential of central NLRP3 inhibition in the brain to reduce gliosis and other consequences of obesity.

The randomised, double-blind, placebo-controlled Phase Ib/IIa trial will evaluate the pharmacokinetic and pharmacodynamic (PK/PD) profile of NT-0796 in inflamed obese patients over 28 days. Up to 60 patients will be enrolled and randomised into two cohorts receiving either NT-0796 or placebo. The study’s primary endpoint is the change in baseline to Day 28 of high-sensitivity C-reactive protein (CRP) levels, a key peripheral inflammatory marker and known predictor of risk of developing atherosclerotic cardiovascular (CV) disease. Secondary endpoints include multiple inflammatory and CV-risk specific biomarkers.

Alan Watt, Chief Executive Officer of NodThera, said: “Atherosclerosis is the leading cause of death in Western populations and inflammation is increasingly recognised as playing a major role in all stages of the disease. Modulation of the NLRP3 inflammasome consequently holds great potential for the development of novel treatment approaches. Our strategy at NodThera has been to develop small molecule NLRP3 inhibitors that penetrate both tissues and brain, not just for treating neurological disease but for treating the central components of peripheral disease that are caused by neurological dysfunction.

“Novel in-house preclinical findings have confirmed the importance of inhibiting brain NLRP3 in cardiometabolic disease models. In evaluating an obese population at high risk of cardiovascular



disease we aim to assess the impact of NLRP3 inhibition on both peripheral inflammation and reactive gliosis, both of which contribute to cardiometabolic dysfunction.”

An earlier first-in-human study of NT-0796 has confirmed the candidate’s excellent PK/PD profile, brain penetration and anti-inflammatory effects in healthy subjects. A Phase Ib/IIa study in Parkinson’s disease patients is ongoing following NT-0796’s demonstration of a reduction of multiple neuroinflammatory and inflammatory biomarkers in plasma and cerebrospinal fluid (CSF) of elderly volunteers.

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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](#).