

## **NewAmsterdam Pharma Announces Initial Data from Phase 2a Clinical Trial Evaluating Obicetrapib in Patients with Early Alzheimer's Disease Who Carry an ApoE4 Mutation**

- Observed reductions of 11% and 12% in 24- and 27-hydroxycholesterol in cerebrospinal fluid ("CSF"), respectively, indicating potential improvement of cholesterol metabolism in the brain --*
- Observed 8% increase in A $\beta$ 42/40 ratio, a key biomarker of AD risk, suggesting improvement in disease pathology --*

**Naarden, the Netherlands and Miami, USA; September 21, 2023** – NewAmsterdam Pharma Company N.V. (Nasdaq: NAMS or "NewAmsterdam" or the "Company"), a clinical-stage biopharmaceutical company developing oral, non-statin medicines for patients at high risk of cardiovascular disease with residual elevation of low-density lipoprotein cholesterol ("LDL-C"), for whom existing therapies are not sufficiently effective or well-tolerated, today announced initial data from its Phase 2a clinical trial evaluating obicetrapib in patients with early Alzheimer's disease ("AD") and at least one copy of the apolipoprotein E4 mutation ("ApoE4").

This Phase 2a trial was designed to explore the effects of obicetrapib on lipid metabolism in the brains of early AD patients who are ApoE4 carriers. Two key biomarkers measured in the trial include 24- and 27-hydroxycholesterol; increases in these oxysterols over time have been observed to lead to a rise in cognitive and related functional impairment. As such, NewAmsterdam believes reductions of 24- and 27-hydroxycholesterol in the CSF may indicate improved cholesterol metabolism in the brain and may lead to improved cognitive function. In addition, the Phase 2a trial assessed the A $\beta$ 42/40 ratio and plasma pTau181, also believed to be biomarkers of AD, with lower levels of A $\beta$ 42/40 and increased levels of pTau181 correlating with a greater risk of AD.

This trial builds on observations from NewAmsterdam's preclinical studies and third-party genetic studies that inhibiting cholesteryl ester transfer protein ("CETP") may protect against ApoE4-associated AD risk by preventing the accumulation of amyloid plaque in the brain through improved cholesterol metabolism and, as a result, potentially slow disease progression.

"These data represent an important first step in determining the role of lipid metabolism in the brain," said Jeffrey Cummings, M.D., Director of the Chambers-Grundy Center for Transformative Neuroscience at the University of Nevada, Las Vegas. "Approximately two thirds of patients with Alzheimer's dementia carry at least one copy of the ApoE4 gene and CETP loss-of-function mutations have been shown to protect against ApoE4-associated AD risk. These data warrant further study of CETP inhibition as a potential mechanism to ameliorate ApoE4-associated AD risk."

### **Initial Data from the Phase 2a Alzheimer's Trial**

"We are encouraged by our initial data, in which we observed reductions in CSF levels of 24- and 27-hydroxycholesterol in the 13 patients treated in the trial. We believe increased CSF levels of these oxysterols may be linked to neuroinflammation and Alzheimer's pathology," said Michael Davidson, M.D., Chief Executive Officer of NewAmsterdam. "We are particularly pleased that this observed reduction in 24- and 27-hydroxycholesterol was paired with an eight percent improvement in the A $\beta$ 42/40 ratio. Based on these initial results, we believe obicetrapib could offer a meaningful advancement for a high-risk patient population with limited available treatment options and look forward to working to further characterize its potential for AD in an efficient, cost-effective manner through our ongoing clinical trials."

The open-label and single-arm trial was designed to assess the pharmacodynamics, pharmacokinetics, safety and tolerability of obicetrapib 10 mg in early AD patients carrying at least one copy of ApoE4. A total of 13 patients were given 10 mg obicetrapib and followed for 24 weeks. NewAmsterdam observed reductions in the levels of 24- and 27-hydroxycholesterol of 11% and 12%, respectively, in the CSF. In addition, an increase of 8% in the A $\beta$ 42/40 ratio in patient's plasma was observed and pTau181 levels were observed to be stable. Overall, obicetrapib was observed to be well-tolerated. No serious adverse events ("AEs") were reported, nor were any AEs considered to be related to the study drug.

“Together, we believe these observations suggest that potent CETP inhibition may offer a novel approach to reducing the risk of AD in ApoE4 carriers. In this small trial, treatment with obicetrapib was observed to reduce levels of 24- and 27-hydrocholesterol and increase the ratio of Aβ42/40 in plasma, supporting our belief that improved brain cholesterol metabolism correlates with removal of amyloid beta peptides which ultimately might lead to improved cognition,” said John Kastelein, M.D., Ph.D., FESC, Chief Scientific Officer of NewAmsterdam.

NewAmsterdam anticipates sharing the full results of this Phase 2a clinical trial in a forthcoming publication or in a presentation at an upcoming medical meeting and plans to seek feedback from the U.S. Food and Drug Administration to inform the potential further development of obicetrapib for the treatment of AD.

### **About Obicetrapib**

Obicetrapib is a novel, oral, low-dose CETP inhibitor that NewAmsterdam is developing to overcome the limitations of current LDL-lowering treatments. The Company believes that obicetrapib has the potential to be a once-daily oral CETP inhibitor for lowering LDL-C, if approved. In the Company’s Phase 2b ROSE trial, obicetrapib demonstrated a 51% lowering of LDL-C from baseline at a 10 mg dose level on top of high-intensity statins and, in the Company’s Phase 2 ROSE2 trial, the combination of a 10 mg dose of obicetrapib and a 10 mg dose of ezetimibe demonstrated a 63% lowering of LDL-C from baseline. In all five of the Company’s Phase 2 trials, ROSE2, TULIP, ROSE, OCEAN, and TA-8995-203, evaluating obicetrapib as monotherapy or combination therapy, the Company observed statistically significant LDL-lowering combined with a side effect profile similar to that of placebo, including no increase in blood pressure or muscle related side effects. Obicetrapib has demonstrated strong tolerability in more than 800 patients with elevated lipid levels (“dyslipidemia”) in NewAmsterdam’s clinical trials to date. The Company is conducting two Phase 3 pivotal trials, BROADWAY and BROOKLYN, to evaluate obicetrapib as a monotherapy used as an adjunct to maximally tolerated lipid-lowering therapies to provide additional LDL-lowering for high-risk cardiovascular disease (“CVD”) patients. The Company began enrolling patients in BROADWAY in January 2022 and in BROOKLYN in July 2022 and completed enrollment of BROOKLYN in April 2023 and BROADWAY in July 2023. The Company also commenced the Phase 3 PREVAIL cardiovascular outcomes trial in March 2022, which is designed to assess the potential of obicetrapib to reduce occurrences of major adverse cardiovascular events, including cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and non-elective coronary revascularization.

### **About NewAmsterdam**

Based in the Netherlands, NewAmsterdam (Nasdaq: NAMS) is a clinical-stage biopharmaceutical company whose mission is to improve patient care in populations with metabolic diseases where currently approved therapies have not been sufficiently adequate or well tolerated. NewAmsterdam seeks to fill a significant unmet need for a safe, cost-effective and convenient LDL-lowering therapy as an adjunct to statins, a class of lipid-lowering medications that are the current standard of care for high-risk CVD patients with high cholesterol. NewAmsterdam is investigating obicetrapib, an oral, low-dose and once-daily CETP inhibitor, as the preferred LDL-C lowering therapy to be used as an adjunct to maximally tolerated statin therapy for high-risk cardiovascular disease patients.

### **Forward-Looking Statements**

Certain statements included in this document that are not historical facts are forward-looking statements for purposes of the safe harbor provisions under the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements generally are accompanied by words such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” “should,” “would,” “plan,” “predict,” “potential,” “seem,” “seek,” “future,” “outlook” and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These forward-looking statements include, but are not limited to, statements regarding the Company’s business and strategic plans, the Company’s commercial opportunity, the therapeutic and curative potential of the Company’s product candidate, the Company’s clinical trials and the timing for

enrolling patients, the timing and forums for announcing data, the achievement and timing of regulatory approvals, and plans for commercialization. These statements are based on various assumptions, whether or not identified in this document, and on the current expectations of the Company's management and are not predictions of actual performance. These forward-looking statements are provided for illustrative purposes only and are not intended to serve as and must not be relied on as a guarantee, an assurance, a prediction, or a definitive statement of fact or probability. Actual events and circumstances are difficult or impossible to predict and may differ from assumptions. Many actual events and circumstances are beyond the control of the Company. These forward-looking statements are subject to a number of risks and uncertainties, including changes in domestic and foreign business, market, financial, political, and legal conditions; risks related to the approval of the Company's product candidate and the timing of expected regulatory and business milestones, including potential commercialization; whether topline, initial or preliminary results from a particular clinical trial will be predictive of the final results of that trial and whether results of early clinical trials will be indicative of the results of later clinical trials; ability to negotiate definitive contractual arrangements with potential customers; the impact of competitive product candidates; ability to obtain sufficient supply of materials; global economic and political conditions, including the Russia-Ukraine conflict; the effects of competition on the Company's future business; and those factors described in the Company's public filings with the Securities Exchange Commission. Additional risks related to the Company's business include, but are not limited to: uncertainty regarding outcomes of the Company's ongoing clinical trials, particularly as they relate to regulatory review and potential approval for its product candidate; risks associated with the Company's efforts to commercialize a product candidate; the Company's ability to negotiate and enter into definitive agreements on favorable terms, if at all; the impact of competing product candidates on the Company's business; intellectual property related claims; the Company's ability to attract and retain qualified personnel; ability to continue to source the raw materials for its product candidate. If any of these risks materialize or the Company's assumptions prove incorrect, actual results could differ materially from the results implied by these forward-looking statements. There may be additional risks that the Company does not presently know or that the Company currently believes are immaterial that could also cause actual results to differ from those contained in the forward-looking statements. In addition, forward-looking statements reflect the Company's expectations, plans, or forecasts of future events and views as of the date of this document and are qualified in their entirety by reference to the cautionary statements herein. The Company anticipates that subsequent events and developments may cause the Company's assessments to change. These forward-looking statements should not be relied upon as representing the Company's assessment as of any date subsequent to the date of this communication. Accordingly, undue reliance should not be placed upon the forward-looking statements. Neither the Company nor any of its affiliates undertakes any obligation to update these forward-looking statements, except as may be required by law.

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