NewAmsterdam Pharma Presents Positive Data from BROADWAY Trial Demonstrating Statistically Significant Reductions in Key Alzheimer's Disease Biomarkers at AAIC 2025

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-- Pre-specified analysis shows obicetrapib significantly reduced absolute levels of plasma p-tau217, a key biomarker of Alzheimer's disease pathology, in both the full analysis set (p=0.0019) and in ApoE4 carriers (p=0.0215), supporting CETP inhibition as a potential novel, upstream approach to Alzheimer's prevention –

-- In APOE4/E4 carriers, the highest risk category for Alzheimer's disease, obicetrapib reduced p-tau217 levels by 20.5%, over 12 months, compared to placebo (p=0.010) --

-- Results build on obicetrapib's cardiometabolic profile, including multiple clinical trials demonstrating reductions in LDL-C, small dense LDL particles, Lipoprotein(a), and biomarkers associated with diabetes and kidney function –

NAARDEN, the Netherlands and MIAMI, July 30, 2025 (GLOBE NEWSWIRE) -- NewAmsterdam Pharma Company N.V. (Nasdaq: NAMS or "NewAmsterdam" or the "Company"), a late-stage, clinical biopharmaceutical company developing oral, non-statin medicines for patients at risk of cardiovascular disease ("CVD") with elevated low-density lipoprotein cholesterol ("LDL-C"), for whom existing therapies are not sufficiently effective or well-tolerated, today announced full data from the prespecified Alzheimer's disease ("AD") biomarker analysis in the BROADWAY clinical trial (NCT05142722). The data were presented today during a Developing Topics oral session at the 2025 Alzheimer's Association International Conference ("AAIC") in Toronto.

The BROADWAY trial was primarily designed as a pivotal Phase 3 trial to evaluate LDL-C lowering efficacy of obicetrapib, a potent CETP inhibitor, in adult patients with established atherosclerotic cardiovascular disease ("ASCVD") and/or heterozygous familial hypercholesterolemia ("HeFH"), whose LDL-C is not adequately controlled, despite being on maximally tolerated lipid-lowering therapy. In connection with this trial, a prespecified analysis evaluated the effect of obicetrapib on plasma biomarkers of AD in 1,515 patients with established ASCVD and/or HeFH whose ApoE status was able to be determined, including 367 ApoE4 carriers. Safety in this population was not evaluated independently from the overall BROADWAY study population, where obicetrapib was observed to be well-tolerated, with safety results comparable to placebo.

ApoE4 is both a risk factor for CVD and AD where ApoE4 carriers generally exhibit higher levels of LDL-C, Lp(a), and reduced cholesterol transport and clearance. Treatment with obicetrapib 10 mg daily for 12 months resulted in statistically significant lower absolute changes in plasma p-tau217, a key biomarker of AD pathology, in both the analysis set (p=0.0019) and in ApoE4 carriers (p=0.0215). Favorable trends were also observed across additional biomarkers, including neurofilament light chain ("NFL"), glial fibrillary acidic protein ("GFAP"), p-tau181, and the Aβ42/40 ratio, in the full analysis set and in ApoE4 carriers, with the greatest effect generally observed in carriers of two E4 proteins.

Percent change in AD biomarkers among E4/E4 carriers versus placebo (n=29)

Biomarker	p-tau217	NFL	GFAP	p-tau181	Aβ42/40	p-tau217/ (Aβ42/40)
Mean % Change	-20.48%	-17.31%	-15.24%	-13.67%	-7.96%	-22.65%
p-value	*0.010*	*0.020*	*0.006*	*0.06*	*0.013*	*0.032*

"Alzheimer's disease remains a devastating global health challenge, with no effective preventive treatments available," said Michael Davidson, M.D., Chief Executive Officer of NewAmsterdam Pharma. "Obicetrapib, our investigational once-daily oral therapy, shows promise by significantly slowing the progression of, and in some instances decreasing, plasma levels of p-tau217, a key Alzheimer's biomarker, in this analysis. This is especially important in ApoE4 gene carriers—a group that represents over a quarter of the population and faces a heightened risk for this disease. Combined with its LDL-C lowering benefits observed in multiple clinical trials, obicetrapib may offer a unique opportunity to reduce both neurodegenerative and heart disease risks."

Percent change in p-tau217 progression by subgroup versus placebo

Biomarker	Full Analysis Set	ApoE4 Carriers	ApoE4, Age ≥ 60	ApoE4, Age ≥ 70	ApoE4/E4
n=	1515	367	283	139	29
Mean % Change	-2.99%	-5.74%	-5.40%	-8.39%	-20.48%
p-value	*0.019*	*0.022*	*0.06*	*0.039*	*0.010*

One of the first biomarkers to provide evidence of neurodegeneration is p-tau217, which can begin to increase more than 20 years before onset of cognitive impairment. In addition, p-tau217 has shown significantly higher accuracy in assessing AD than alternative plasma- or MRI-based analyses, and its performance does not significantly differ from key CSF- or PET-based measures. NFL and GFAP biomarkers are also considered predictive of neurodegeneration and elevated levels in the blood have been associated with AD progression and pathology. These results build on NewAmsterdam's Phase 2a proof of concept trial and preclinical data, which showed reductions in brain cholesterol metabolites and stabilization of AD biomarkers in ApoE4 carriers.

"These results advance our understanding of how upstream lipid modulation may influence Alzheimer's disease risk, especially in individuals carrying

the ApoE4 protein," said Philip Scheltens, M.D., Ph.D., Professor Emeritus at Amsterdam UMC. "With more than 25% of the population carrying one or two copies of ApoE4 and no approved preventative therapies, interventions that can slow AD associated biomarker progression may offer a promising path toward delaying or modifying disease onset and progression in this high-risk group."

"Today's findings mark an important early step in linking lipid biology and cardiometabolic medicine to neurodegeneration," said John Kastelein, M.D., Ph.D., FESC, Chief Scientific Officer of NewAmsterdam Pharma. "Obicetrapib's ability to reduce not only p-tau217 in ApoE4 carriers, a well-characterized and defined group, but also multiple additional important AD biomarkers would add a compelling new dimension to its therapeutic profile. Coupled with effects on LDL-C, small dense LDL particles, Lp(a), and metabolic biomarkers observed in multiple clinical trials, these data highlight obicetrapib's potential to address the converging pathways of cardiovascular and neurovascular disease with a single, oral therapy."

The Company looks forward to discussing these results with regulatory authorities to determine potential next steps.

Conference Call and Webcast Information

NewAmsterdam will host a live webcast and conference call at 10:00 a.m. ET on July 30, 2025 to review the full AD biomarker data presented at AAIC. To access the live webcast, participants may register here. The live webcast will be available under the "Events & Presentations" section of the Investor Relations page of the Company's website at ir.newamsterdampharma.com.

To participate via telephone, please register in advance here. Upon registration, all telephone participants will receive a confirmation email detailing how to join the conference call, including the dial-in number along with a unique passcode and registrant ID that can be used to access the call. While not required, it is recommended that participants join the call ten minutes prior to the scheduled start. An archived replay of the webcast will be available on NewAmsterdam's website following the live event.

Design of the Pivotal Phase 3 BROADWAY Clinical Trial

The 52-week, global, pivotal, Phase 3, randomized, double-blind, placebo-controlled multicenter trial evaluated the efficacy and safety of 10 mg obicetrapib compared to placebo as an adjunct to maximally tolerated lipid-lowering therapies in patients with ASCVD and/or HeFH whose LDL-C is not adequately controlled. The trial was conducted at sites in North America, Europe, Asia and Australia. A total of 2,530 patients were randomized 2:1 to receive 10 mg obicetrapib or placebo dosed as a once-daily oral treatment, with or without food for 52 weeks. The mean baseline LDL-C for enrolled patients in the obicetrapib arm was approximately 100 mg/dL despite high intensity statin use reported by nearly 70% of patients during screening. Females comprised approximately 34% of the trial population and the median age of participants at baseline was 65 years.

The primary endpoint was LS mean percent change from baseline in LDL-C of obicetrapib 10 mg compared to placebo after 84 days which showed a reduction of 33% with imputation. Secondary endpoints also included percent changes from baseline of obicetrapib 10 mg compared to placebo in ApoB, Lp(a), ApoA1, HDL-C, non-HDL-C, total cholesterol, and triglycerides at day 84, and on LDL-C levels at days 180 and 365. Other exploratory outcome measures included time from randomization until the first confirmed occurrence of MACE in the obicetrapib arm compared to placebo. The trial also evaluated the safety and tolerability profile of obicetrapib.

Alzheimer's Analysis

In BROADWAY, a pre-specified AD analysis was designed to assess plasma AD biomarkers in patients enrolled in the BROADWAY trial and evaluated the effects of longer duration of therapy (12 months) with a prespecified population of ApoE3/4 or 4/4 carriers, based on phenotypic analysis. The analysis included 1,515 patients, including 367 ApoE4 carriers, whose ApoE status was able to be determined. Because this analysis was based on a subset of patients from BROADWAY (which was designed to evaluate LDL-C reductions in an ASCVD and/or HeFH population), the AD analysis was not controlled for baseline differences between the treatment and placebo population. The primary outcome measure was p-tau217 absolute and percent change over 12 months, among patients with baseline and end of study datapoints above the lower limit of quantitation. Additional outcome measures included NFL, GFAP, p-tau181, and Aβ42/40 ratio absolute and percent change over 12 months. NewAmsterdam observed statistically significant lower absolute changes in p-tau217 compared to placebo over 12 months in both the full analysis set (p=0.0019; n= 1,515) and in ApoE4 carriers (p=0.0215; n=367). Although a safety analysis was not performed in the AD study population, in BROADWAY obicetrapib was observed to be well-tolerated, with safety results comparable to placebo.

Design of the Phase 2a Alzheimer's Trial

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-hydroxycholestrol in both plasma and cerebrospinal fluid. 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.

About Obicetrapib

Obicetrapib is a novel, oral, low-dose CETP inhibitor that NewAmsterdam is developing to overcome the limitations of current LDL-lowering treatments. In each of the Company's Phase 2 trials, ROSE2, TULIP, ROSE, and OCEAN, as well as the Company's Phase 3 BROOKLYN, BROADWAY and TANDEM trials, 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. The Company commenced the Phase 3 PREVAIL cardiovascular outcomes trial in March 2022, which is designed to assess the potential of obicetrapib to reduce occurrences of MACE. The Company completed enrollment of PREVAIL in April 2024 and randomized over 9,500 patients. Commercialization rights of obicetrapib in Europe, either as a monotherapy or as part of a fixed-dose combination with ezetimibe, have been exclusively granted to the Menarini Group, an Italy-based, leading international pharmaceutical and diagnostics company.

About NewAmsterdam

NewAmsterdam Pharma (Nasdaq: NAMS) is a late-stage biopharmaceutical company whose mission is to improve patient care in populations with metabolic diseases where currently approved therapies have not been adequate or well tolerated. We seek to fill a significant unmet need for a safe, well-tolerated and convenient LDL-lowering therapy. In multiple phase 3 trials, NewAmsterdam is investigating obicetrapib, an oral, low-dose and once-daily CETP inhibitor, alone or as a fixed-dose combination with ezetimibe, as LDL-C lowering therapies to be used as an adjunct to statin therapy for patients at risk of CVD with elevated LDL-C, for whom existing therapies are not sufficiently effective or well tolerated.

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 therapeutic potential of obicetrapib including, without limitation, its potential to reduce neurodegenerative and heart disease risks; the potential for obicetrapib to favorably impact AD biomarkers and the potential benefits of doing so; the Company's plans to discuss the results of the AD analysis with regulatory authorities to determine potential next steps; the Company's clinical trials and the timing relating thereto; and the timing and forums for announcing data. 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 obicetrapib and the timing of expected regulatory and business milestones; whether results of the AD analysis and other early studies will be indicative of the results of later clinical trials; whether projections regarding clinical outcomes will reflect actual results in future clinical trials or clinical use of obicetrapib, if approved; the potential for varying interpretations of the results of the AD analysis; the impact of competitive product candidates; and those risks, uncertainties and other factors discussed under the caption "Item 1A. Risk Factors" and elsewhere in the Company's most recent Form 10-K, Form 10-Q and other public filings with the Securities and Exchange Commission - which are available at www.sec.gov. 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 obicetrapib; risks associated with the Company's efforts to commercialize obicetrapib; 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 and prospects; intellectual property related claims; the Company's ability to attract and retain qualified personnel; and ability to continue to source the raw materials for obicetrapib and manufacturer final product. 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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