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ProMIS Neurosciences Announces New Peer-Reviewed Publication Highlighting Selective Targeting of Toxic Oligomers for Potential Clinical Benefit and Reduced ARIA Risk

Results support the potential of PMN310 to improve outcomes by selectively targeting oligomers and avoiding binding to monomer and plaque

ProMIS on track to complete enrollment in PRECISE-AD trial in Alzheimer's disease by end of 2025 with planned Q2 2026 interim readout

Cambridge, Massachusetts, Dec. 10, 2025 (GLOBE NEWSWIRE) -- ProMIS Neurosciences Inc. (Nasdaq: PMN), a clinical-stage biotechnology company focused on the generation and development of antibody therapeutics and vaccines targeting toxic misfolded proteins in neurodegenerative diseases, such as Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS) and Parkinson's disease (PD), today announced a publication in the peer-reviewed journal *Alzheimer's & Dementia: Translational Research & Clinical Interventions*. entitled, *"Relationship between efficacy and preferential targeting ofsoluble Aβ aggregates."* The paper can be accessed at the following link: http://dx.doi.org/10.1002/trc2.70184.

Amyloid beta (A*β*) is known to play a role in the pathogenesis of AD, and certain approved and marketed Aβ-directed antibodies have achieved slowing of cognitive decline in AD. The results and analysis from the study announced today highlight the importance of targeting soluble toxic A*β* aggregates as supported by the observed retrospective correlation between selectivity for soluble toxic oligomers and reported clinical efficacy and the potential for attenuation of amyloid-related imaging abnormalities (ARIA), an adverse side effect of current anti-amyloid antibody therapies.

"This new publication reinforces the critical importance of selectively targeting toxic Aβ oligomers, believed to be the hallmark drivers of Alzheimer's pathology," said Neil Warma, Chief Executive Officer of ProMIS Neurosciences. "We believe PMN310 has the potential to deliver a meaningful advance in both clinical outcomes and quality of life for patients and caregivers, and with our 6-month interim readout from our ongoing PRECISE-AD clinical trial expected in Q2 2026 and top-line results expected in Q4 2026, we look forward to providing clinical data evaluating our approach next year."

In this study, a side-by-side comparison of the binding profile of various *Aβ*-targeted antibodies to A*β* species, including monomers, low- and high-molecular-weight AD brain oligomers, and plaque was conducted and compared with known clinical outcomes.

1. Key Findings and Implications for PMN310: Antibody Specificity for Toxic Oligomers May Provide Greater Potency

- In the studies conducted, clinical efficacy across Aβ antibodies correlated strongly with the ability to bind toxic oligomers even in the presence of overwhelming monomer concentrations, which otherwise divert antibody activity away from pathogenic species.

- PMN310 showed the highest resistance to monomer competition among all antibodies tested, preserving oligomer binding while pan-Aβ antibodies lost activity in in vitro models. This suggests that a higher proportion of each dose of PMN310 could be available to reach the relevant toxic targets, which could potentially translate into clinical benefit in patients.

- In AD mouse studies, this oligomer selectivity translated into complete protection of spatial memory, restoring performance to normal wild-type levels, reinforcing the mechanistic rationale.

2. PMN310's Lack of Plaque or Vascular Deposit Binding Suggests a Possible Lower Risk of ARIA

- ARIA is strongly associated with antibody binding to insoluble plaque and vascular amyloid deposits. Antibodies such as donanemab, aducanumab, and lecanemab showed significant plaque binding and correspondingly increased ARIA rates. In contrast, PMN310 exhibited no detectable plaque binding across concentrations tested, aligning with its engineered specificity for misfolded, soluble oligomers, not fibrils.

- Consistent with this mechanism, high-dose chronic administration of PMN310 in plaque-bearing mice (800 mg/kg for 26 weeks) produced no microhemorrhages on microscopic examination of brain tissue.

- Together, these findings provide preclinical evidence supporting a possible reduced ARIA risk.

3. PMN310 Is Positioned to Test the Oligomer Hypothesis Without Confounding Cross-Reactivity

- All other antibodies tested in the study appeared to bind monomers and/or plaque to varying degrees. PMN310 was the only antibody in the study showing strict specificity for toxic soluble oligomers while avoiding monomers and plaque.

- This positions the ongoing PRECISE-AD study to potentially become the first clinical test of oligomer-only targeting, which may clarify the relative contributions of oligomers vs plaque to cognitive decline, an important scientific inflection point for the field.

"This publication provides further evidence, supported experimentally and clinically, that selective targeting of toxic A*β* oligomers has the potential to increase efficacy by focusing the dose of antibody on the most relevant toxic A*β* species and improve safety by reducing the risk of ARIA associated with plaque binding which has been a significant side effect of current A*β*-directed antibodies," said Johanne Kaplan, PhD, Chief Development Officer of ProMIS Neurosciences.

About ProMIS Neurosciences Inc.

ProMIS Neurosciences is a clinical-stage biotechnology company committed to the discovery and development of therapeutic antibodies and vaccines selective for toxic oligomers associated with the development and progression of neurodegenerative and other misfolded protein diseases. The Company's proprietary target discovery engine, EpiSelect™, has been shown to predict novel targets known as Disease Specific Epitopes (DSEs) on the molecular surface of misfolded proteins that cause neurodegenerative and other misfolded protein diseases, including Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), multiple system atrophy (MSA), and Parkinson's Disease (PD). ProMIS has offices in Cambridge, Massachusetts (USA) and Toronto, Ontario (CAN).

About PMN310 and the PRECISE-AD Trial for Alzheimer's Disease (AD)

PMN310, the Company's lead product candidate for the treatment of AD, is a humanized monoclonal antibody that has been designed to selectively target only the toxic oligomers, avoiding plaque, thereby potentially reducing or eliminating amyloid-related imaging abnormalities (ARIA) liability. In addition, because PMN310 may not be limited by off-target binding or side effects, PMN310 could potentially offer an improved efficacy profile over other amyloid-directed antibody therapeutics. PMN310 was granted Fast Track designation by the U.S. Food and Drug Administration in July 2025.

Based on the encouraging results from the Phase 1a trial (NCT06105528) of PMN310, ProMIS initiated PRECISE-AD, a Phase 1b clinical trial in AD patients with targeted enrollment of 128 AD patients. PRECISE-AD (NCT06750432) is a randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability and pharmacokinetics of multiple ascending doses (5, 10, 20 mg/kg) of intravenous PMN310 in patients with Mild Cognitive Impairment due to AD and mild AD (Stage 3 and Stage 4 AD). PRECISE-AD will be the first study to examine the effects of a monoclonal antibody directed solely against toxic amyloid-beta oligomers on biomarkers associated with AD pathology and clinical outcomes. Safety will be a primary outcome of the study with particular emphasis on assessing whether, as a non-plaque binder, PMN310 may have a reduced risk of ARIA. The study is powered to provide 95% confidence for detection of ARIA. The study has been designed with a sample size intended to provide sufficient power to provide meaningful insight into effects of PMN310 on biomarkers and clinical outcomes. A blinded 6-month interim analysis is expected in Q2 2026 with final top line data expected in Q4 2026.

Forward Looking Statements

This press release contains forward-looking statements that are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Certain information in this news release constitutes forward-looking statements and forward-looking information (collectively, "forward-looking information") within the meaning of applicable securities laws. In some cases, but not necessarily in all cases, forward-looking information can be identified by the use of forward-looking terminology such as "plans", "pleased to", "look forward to", "potential to", "targets", "expects" or "does not expect", "is expected", "excited about", "an opportunity exists", "is positioned", "estimates", "intends", "assumes", "anticipates" or "does not anticipate" or "believes", or variations of such words and phrases or state that certain actions, events or results "may", "could", "would", "might", "will" or "will be taken", "occur" or

“be achieved”. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances contain forward-looking information. Specifically, this news release contains forward-looking information relating to the Company’s preclinical data and retrospective clinical analysis, the Company’s progress and expectations for its Phase 1b clinical trial in AD patients, including planned timing for completion and anticipated data readout of interim results in the second quarter of 2026, the potential for such studies to provide the first proof-of-concept data for PMN310, the potential for PMN310 to positively benefit patients with AD and to be a more effective and well-tolerated option, the targeting of toxic misfolded proteins in neurodegenerative diseases that the Company believes may directly address fundamental AD pathology (including the belief and understanding that toxic amyloid-beta oligomers are a major driver of AD) and have greater therapeutic potential due to reduction of off-target activity. Statements containing forward-looking information are not historical facts but instead represent management's current expectations, estimates and projections regarding the future of our business, future plans, strategies, projections, anticipated events and trends, the economy and other future conditions. Forward-looking information is necessarily based on a number of opinions, assumptions and estimates that, while considered reasonable by the Company as of the date of this news release, are subject to known and unknown risks, uncertainties and assumptions and other factors that may cause the actual results, level of activity, performance or achievements to be materially different from those expressed or implied by such forward-looking information, including, but not limited to, the risk that preclinical and retrospective clinical analyses described in the Alzheimer’s & Dementia: Translational Research & Clinical Interventions publication will not be predictive of clinical results for PMN310, the risk that enrollment may not continue at the current rate, that clinical results or early results may not be indicative of future results, the Company’s ability to retain and recognize the incentives conferred by Fast Track Designation for PMN310, the Company’s ability to fund its operations and continue as a going concern, its accumulated deficit and the expectation for continued losses and future financial results. Important factors that could cause actual results to differ materially from those indicated in the forward-looking information include, among others, the factors discussed throughout the “Risk Factors” section of the Company's most recently filed Annual Report on Form 10-K for the year ended December 31, 2024 and in its subsequent filings filed with the United States Securities and Exchange Commission. Except as required by applicable securities laws, the Company undertakes no obligation to publicly update any forward-looking information, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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