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ProMIS Neurosciences Announces New Peer-Reviewed Publication Showing Plasma pTau as a Predictive Early Endpoint in Alzheimer's trials, Supporting its Ongoing Phase 1b PRECISE-AD trial with PMN310

Cross-trial analysis supports plasma pTau as a potential early predictor of clinical benefit, reinforcing the biomarker-driven design of ProMIS' PRECISE-AD trial

ProMIS on track to leverage new plasma pTau insights with planned Q2 2026 interim readout

Cambridge, Massachusetts, Dec. 01, 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, *"Leveraging recent advances in plasma biomarkers to optimize early proof of concept trials in Alzheimer's disease."* The paper can be accessed at the following link: http://dx.doi.org/10.1002/trc2.70183.

The analysis, conducted by Pentara Corporation in collaboration with scientists from ProMIS, provides important new evidence that plasma phosphorylated tau (pTau181 and pTau217) can serve as a meaningful primary endpoint in early-stage AD clinical trials, with potential to predict subsequent clinical benefit.

Key Findings from the Publication

Using summary data from several large monoclonal antibody (mAb) trials in early AD, the analysis showed:

- **Strong predictive relationship:** Group level treatment effects on plasma pTau at 6 months were strongly correlated with treatment effects on the Clinical Dementia Rating Sum of Boxes (CDR-SB) at 12 months (correlation ≈ 0.78; statistically significant).
- **Amplified signal, earlier readout compared to clinical outcomes:** The effect size on plasma pTau was ~2.6 times larger than the effect size on CDR-SB, indicating that

biomarker changes can be detected earlier and more robustly than clinical changes.

- **Potential for smaller, more efficient trials:** Simulations suggest that, for drugs with effect sizes similar to those seen with one of the leading mAbs, well-powered proof-of-concept (POC) trials using plasma pTau as a primary endpoint may require as few as ~100 participants.

Together, these findings support the use of plasma pTau as a primary endpoint in early clinical development and as a quantitative bridge to predict future clinical outcomes.

Implications for ProMIS, PMN310, and the PRECISE-AD Trial

ProMIS is currently conducting PRECISE-AD, an ongoing Phase 1b clinical trial of PMN310, its lead amyloid-beta targeting antibody, in patients with early Alzheimer's disease (AD). PMN310 is designed to selectively target toxic amyloid-beta oligomers, the species believed to be a primary driver of synaptic dysfunction and downstream disease pathology, while avoiding binding to monomers or plaque which is associated with higher rates of amyloid-related imaging abnormalities.

The newly published analysis is directly aligned with, and supportive of, key elements of the PRECISE-AD design:

- **Biomarker-centric strategy:** PRECISE-AD incorporates plasma pTau (including pTau217) as a central biomarker endpoint at 6 and 12 months, consistent with the timing and methodology highlighted in the publication.

- **Early readout with potentially predictive value:** By assessing plasma pTau changes as early as 6 months, PRECISE-AD is positioned to generate an early, quantitative signal of disease modification that can be used to model and predict future clinical outcomes.

- **Efficient, de-risking design:** The publication's simulations reinforce that a biomarker-driven Phase 1b trial can be both smaller and faster, while still providing robust information to guide dose selection and go/no-go decisions for future trials including a pivotal Phase 3 trial.

- **Mechanistic fit for PMN310:** Because PMN310 is designed to neutralize toxic oligomers upstream of tau phosphorylation, meaningful reductions in plasma pTau could be expected if PMN310 successfully interrupts this pathogenic cascade.

"This publication provides important validation of the strategy we have adopted at ProMIS which is to use highly sensitive plasma pTau biomarkers as a central pillar of our ongoing Phase 1b AD clinical trial," said Neil Warma Chief Executive Officer of ProMIS Neurosciences. "The ability to link a 6-month plasma readout to later clinical benefit means we can make smarter, earlier decisions about PMN310's development path, while using capital more efficiently. Importantly, we remain on track to assess blinded 6-month biomarker data, including plasma pTau217, from our PRECISE-AD trial in Q2 2026, which we believe will offer an early and meaningful look at PMN310's potential to modify disease biology. This publication significantly strengthens the scientific and investment thesis behind our approach."

“For years, the field has discussed the promise of blood-based biomarkers, but they are now transitioning into practical tools for trial optimization,” added Larry D. Altstiel, M.D., Ph.D., Chief Medical Officer of ProMIS and a co-author on the paper. “Our analysis shows that plasma pTau not only tracks disease biology, but also robustly predicts clinical outcomes across multiple monoclonal antibody trials. For PMN310, which is designed to selectively target the toxic amyloid-beta oligomers that trigger tau phosphorylation, we believe plasma pTau offers a sensitive, biologically aligned readout of drug effect that can inform both dose selection and future Phase 3 planning.”

“By combining data across several large, well-characterized AD trials, we were able to quantify how strongly early plasma pTau changes predicted later clinical outcomes,” said Suzanne Hendrix, Ph.D., CEO of Pentara Corporation and a co-author on the paper. “The magnitude of this relationship, and the fact that the biomarker signal is easier to detect than the clinical signal, make plasma pTau a highly attractive primary endpoint for early proof-of-concept studies. This approach has the potential to reduce trial size and duration while increasing confidence in the decisions sponsors must make as they advance into Phase 3 pivotal studies.”

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.

About Pentara

Pentara Corporation provides statistical expertise and is a leader in the neurodegenerative space. Pentara offers clinical data analysis services to the pharmaceutical and biotechnology industries, including ProMIS. The teams at Pentara have decades of experience in clinical trial experiences, regulatory interactions, and Alzheimer's Disease research. Pentara is headquartered in Salt Lake City, Utah.

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 progress and expectations for its Phase 1b clinical trial in AD patients, including planned timing for completion and anticipated data readout of interim and full results in the second and fourth quarters of 2026, respectively, 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 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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