UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): July 28, 2026

PROMIS NEUROSCIENCES INC.

(Exact name of registrant as specified in its charter)

Ontario, Canada	**001-41429**	**98-0647155**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
Suite 200, 1920 Yonge Street, Toronto, Ontario		**M4S 3E2**
(Address of principal executive offices)		**(Zip Code)**

Registrant's telephone number, including area code: (416) 847-6898

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange on Which Registered**
Common Shares, no par value per share	PMN	The Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter)

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On July 28, 2026, ProMIS Neurosciences Inc. (the "Company") issued a press release (the "Press Release") titled "ProMIS Neurosciences Reports Positive Blinded Six-Month Interim Safety and Biomarker Data for PMN310 in the PRECISE-AD Phase 1b Alzheimer's Disease Trial." A copy of the Press Release is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Also, on July 28, 2026 at 8:00 a.m. E.T., the Company will host a virtual webinar featuring key opinion leaders Dr. Will Mantyh, Associate Professor with Tenure, University of Minnesota Medical School and Dr. Michael Weiner, Professor Emeritus, University of California, San Francisco, to discuss the Company's six-month blinded interim data from the PRECISE-AD Phase 1b trial evaluating PMN310 in patients with early Alzheimer's disease. A copy of the presentation from the event will be available in the "Investors" section of the Company's website at https://www.promisneurosciences.com/ and is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information included under Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.1 and 99.2 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, and shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On July 28, 2026, the Company issued the Press Release. The update is summarized below.

In the blinded interim analysis evaluating 136 AD patients, PMN310 was observed to have a favorable safety profile across all genotypes, with no cases of amyloid-related imaging abnormalities-edema (ARIA-E) reported as of the data cutoff date, and early, directionally consistent movement in disease-relevant biomarkers potentially reflective of the randomization pattern. The trial remains blinded and ongoing with topline 12-month results expected in the first quarter of 2027.

Interim Highlights

- **Favorable safety profile across all genotypes:** No ARIA-E and 4.4% total ARIA (all mild and asymptomatic, consisting of only amyloid-related imaging abnormalities-microhemorrhages (ARIA-H)), with no treatment-related serious adverse events and no drug-related discontinuations at the interim.
- **Same profile in high-risk APOE4 carriers:** No ARIA-E observed in any genotype in a population that included 61% APOE4 carriers, of which 11% were homozygotes, a group underserved by approved amyloid-directed therapies.
- **Early biomarker movement consistent with target engagement:** On a blinded basis, a majority of patients showed reductions in disease-relevant biomarkers against expected increases in natural-history trajectories: 68.5% of patients had a decline from baseline (change ≤ 0) in plasma pTau217 and 62.5% had a decline in CSF MTBR-tau243, consistent with a potential beneficial drug effect and potentially reflective of the trial's 3:1 active-to-placebo randomization. These are blinded interim biomarker observations, meaning treatment allocations between drug and placebo groups are not known at this time. These observed biomarker trends are not a determination of efficacy, and trends in biomarkers may not ultimately be reflective of clinical effects.
- **Differentiated, oligomer-selective mechanism:** PMN310 is designed to selectively bind toxic amyloid-beta oligomers while avoiding plaque, a mechanism intended to decouple potential efficacy from ARIA risk.
- **Clear path forward:** Unblinded 12-month topline data expected Q1 2027, including efficacy data.

Forward-Looking Statements

This Current Report on Form 8-K 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. 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 PRECISE-AD Phase 1b clinical trial, the interpretation and significance of the blinded six-month interim safety and biomarker data (including ARIA, pTau217 , and MTBR-tau243 findings), target engagement, the expected timing and nature of topline clinical data of PMN310, its mechanism of action and potential benefits, and the Company's development plans. 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 early results or interim results may not be indicative of future results and that blinded, pooled data may not reflect the effect of PMN310 once unblinded. 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, 2025 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release Issued by ProMIS Neurosciences Inc. on July 28, 2026.
99.2	Slide presentation of ProMIS Neurosciences Inc.
104	Cover Page Interactive Data File (embedded within Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PROMIS NEUROSCIENCES INC.

Date: July 28, 2026

By: /s/ Neil Warma
Name: Neil Warma
Title: Chief Executive Officer

Exhibit 99.1

ProMIS Neurosciences Reports Positive Blinded Six-Month Interim Safety and Biomarker Data for PMN310 in the PRECISE-AD Phase 1b Alzheimer's Disease Trial

No ARIA-E observed across all genotypes, including APOE4 homozygotes

ARIA-H tracking background rates

Early biomarker movement consistent with target engagement

12-month topline results expected in Q1 2027

Cambridge, Massachusetts, July 28, 2026 (GLOBE NEWSWIRE) — ProMIS Neurosciences Inc. (Nasdaq: PMN), a clinical-stage biopharmaceutical company developing therapeutics that selectively target toxic misfolded proteins in neurodegenerative diseases, today announced positive blinded six-month interim safety and biomarker results from PRECISE-AD, the Phase 1b trial of its lead drug candidate, PMN310, in patients with mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease (AD).

In the blinded interim analysis evaluating 136 AD patients, PMN310 was observed to have a favorable safety profile across all genotypes, with no cases of amyloid-related imaging abnormalities-edema (ARIA-E) reported as of the data cutoff date, and early, directionally consistent movement in disease-relevant biomarkers potentially reflective of the randomization pattern. The trial remains blinded and ongoing with topline 12-month results expected in the first quarter of 2027.

Interim Highlights

- **Favorable safety profile across all genotypes:** No ARIA-E and 4.4% total ARIA (all mild and asymptomatic, consisting of only amyloid-related imaging abnormalities-microhemorrhages (ARIA-H)), with no treatment-related serious adverse events and no drug-related discontinuations at the interim.

- **Same profile in high-risk APOE4 carriers:** No ARIA-E observed in any genotype in a population that included 61% APOE4 carriers, of which 11% were homozygotes, a group underserved by approved amyloid-directed therapies.

- **Early biomarker movement consistent with target engagement:** On a blinded basis, a majority of patients showed reductions in disease-relevant biomarkers against expected increases in natural-history trajectories: 68.5% of patients had a decline from baseline (change ≤ 0) in plasma pTau217 and 62.5% had a decline in CSF MTBR-tau243, consistent with a potential beneficial drug effect and potentially reflective of the trial's 3:1 active-to-placebo randomization. These are blinded interim biomarker observations, meaning treatment allocations between drug and placebo groups are not known at this time. These observed biomarker trends are not a determination of efficacy, and trends in biomarkers may not ultimately be reflective of clinical effects.

- **Differentiated, oligomer-selective mechanism:** PMN310 is designed to selectively bind toxic amyloid-beta oligomers while avoiding plaque, a mechanism intended to decouple potential efficacy from ARIA risk.

- **Clear path forward:** Unblinded 12-month topline data expected Q1 2027, including efficacy data.

“These interim data reinforce our central thesis: by selectively targeting toxic oligomers, PMN310 has the potential to deliver the benefits of amyloid-directed therapy without the ARIA burden that has constrained this class of drugs,” said Neil Warma, Chief Executive Officer of ProMIS Neurosciences. “The absence of ARIA-E, an overall favorable safety profile, and early biomarker movement together align with our expectations based on our prior studies. We look forward to our 12-month topline readout in the first quarter of 2027.”

Dr. Will Mantyh, a behavioral neurologist at the University of Minnesota, said, “In real-world practice, ARIA risk is the central prescribing barrier: clinicians, patients, and health systems must contend with the issues of safety monitoring, identification, and sometimes emergent neurological treatment of ARIA. A profile with low incidence of total ARIA, including no ARIA-E, would be a game-changer. Just as importantly, plasma pTau217 and CSF MTBR-tau243 are among the most informative fluid biomarkers we have for tracking Alzheimer’s biology; seeing early, coherent movement in both is highly encouraging before a definitive readout.”

ProMIS will host a live webinar today to discuss these results.

Webinar Details

Date: July 28, 2026

Time: 8:00–9:00 a.m. ET

Speakers (ProMIS): Neil Warma, Chief Executive Officer, and Dr. Larry Altstiel, Chief Medical Officer

Featured Key Opinion Leaders: Dr. Will Mantyh and Dr. Michael Weiner

Registration: https://lifescievents.com/event/it38tlq/

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

PMN310, ProMIS’ lead product candidate for the treatment of AD, is a humanized IgG1 monoclonal antibody designed to selectively target only the toxic oligomers of amyloid-beta (AβOs), believed to be among the earliest and most damaging drivers of Alzheimer’s disease, while avoiding binding to amyloid plaques and vascular deposits. This selectivity may reduce or eliminate the risk of amyloid-related imaging abnormalities (ARIA), including brain swelling (ARIA-E) and microhemorrhages (ARIA-H), which are commonly associated with plaque-binding antibodies. PMN310 was granted Fast Track Designation by the U.S. Food and Drug Administration in July 2025.

Based on encouraging results from a Phase 1a trial (NCT06105528) in healthy volunteers, ProMIS initiated the PRECISE-AD Phase 1b trial to evaluate PMN310 in patients with mild cognitive impairment due to AD or mild AD. PRECISE-AD (NCT06750432) is a randomized, double-blind, placebo-controlled study evaluating the safety, tolerability, and pharmacokinetics of multiple ascending doses (5, 10, and 20 mg/kg) of intravenous PMN310. The study has completed enrollment of 144 participants across the three dosing cohorts who are being treated for twelve months. It is designed to provide meaningful insight into the effects of PMN310 on biomarkers and clinical outcomes.

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 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).

Forward-Looking Statements

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For further information:

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PRECISE-AD · PMN310 · PHASE 1b

BLINDED 6-MONTH INTERIM ANALYSIS

Safety & Biomarker Assessment Update

Blinded Interim Analysis
Topline results expected Q1 2027

LEGAL · DISCLOSURES

Forward-Looking Statements & Disclaimers

This slide deck may contain certain forward-looking information and "forward-looking statements" that are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Such information involves known and unknown risks, uncertainties and other factors that may cause actual results, performance or achievements to be materially different from those implied by statements herein, and therefore these statements should not be read as guarantees of future performance or results. Such forward-looking statements include, among others, statements pertaining to the ProMIS Neurosciences Inc.'s (the "Company") PRECISE-AD Phase 1b clinical trial, target engagement and biomarker findings, the results and nature of the blinded interim clinical data of PMN310 and anticipated topline clinical data of PMN310, its mechanism of action and potential benefits and the Company's development plans and anticipated milestone timing, among other factors. Forward-looking information is based on a number of opinions, assumptions and estimates that, while considered reasonable by the Company as of the date of this slide deck, 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 the results of early clinical trials are not necessarily predictive of future results with PMN310 and the Company's ability to fund its operations. 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, 2025 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.

Data presented as of July 22, 2026

Blinded Interim Analysis
Topline results expected Q1 2027

ProMIS™ Neurosciences

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Presenters & KOL Participants

ProMIS™ Neurosciences

PRESENTERS

Neil Warma
President & CEO
ProMIS Neurosciences

Dr. Larry Altstiel
Chief Medical Officer
(M.D., Ph.D.)
ProMIS Neurosciences

KEY OPINION LEADER

Dr. Will Mantyh

Behavioral Neurologist
University of Minnesota

Focused on early detection and diagnosis of Alzheimer's and related neurodegenerative diseases. Develops blood and imaging biomarkers to bring new blood tests to real-world and underrepresented patient populations. A tenured Associate Professor at the University of Minnesota, he leads a $3.7M NIH R01 bringing Alzheimer's blood tests to Native American communities. His honors include the AAN's Robert W. Katzman Award and the Fesler-Lampert Chair.

KEY OPINION LEADER

Dr. Michael Weiner

Professor Emeritus, UCSF
Principal Investigator, ADNI*

Principal Investigator of ADNI, the world's largest observational Alzheimer's study, and founder of the Brain Health Registry. A pioneer in MRI/MRS development who helped bring nuclear magnetic resonance imaging into clinical use, he has published over 1,030 peer-reviewed articles. His honors include the Alzheimer's Association's Nancy and Ronald Reagan Award, the AAN's Potamkin Prize, and the Henry Wisniewski Lifetime Achievement Award (2021).

*Alzheimer's Disease Neuroimaging

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COMPANY SNAPSHOT

Clinical-stage biotechnology company with a pipeline designed to selectively target specific, disease-causing misfolded proteins

Unique selectivity may create potential to address the unmet need for safer, more efficacious therapies.

PMN : NASDAQ · Cambridge, MA

TOP-LINE DATA	**Early Q1 2027** PRECISE-AD Phase 1b readout
PEAK SALES POTENTIAL	**>$10B** PMN310 in early Alzheimer's
FINANCIAL	**Up to $175M raised** Cash through 2027 · A-list syndicate
LEADERSHIP	**Global development team** Deep neuroscience domain experience
DIFFERENTIATION	**Oligomer-selective by design** Aim to reduce ARIA and improve clinical efficacy

TRIAL MILESTONES

Execution on Track, Progressing Quickly Toward Topline Results

BLINDED 6-MONTH INTERIM · EARLY Q3 2026

- Trial design & execution overview
- Safety observations & ARIA snapshot
- Directional trend on key biomarker
- Patient demographics

UNBLINDED 12-MONTH TOPLINE RESULTS · EARLY 2027

- Active vs. placebo group comparisons
- Safety, biomarker & efficacy analysis
- Clinical endpoints: cognition change
- Imaging results

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PRECISE-AD Study Design
&
Patient Demographics

TRIAL DEMOGRAPHICS AND DESIGN

PRECISE-AD: Phase 1b Trial Design

KEY STUDY PARAMETERS & PATIENT DEMOGRAPHICS

Study	**PRECISE-AD · Phase 1b**
Agent	**PMN310 - humanized IgG1 mAb**
Patient population	**Mild Cognitive Impairment (MCI) due to AD / early AD**
Total enrolled	**144 patients**
Safety-evaluable	**136 patients**
Mean age	**73.3 years**
Sex	**58% F · 42% M**
Race	**White 69% · Hispanic 24% · Black 6% · Asian 1%**
APOE4 carriers	**50% heterozygotes · 11% homozygotes**

RANDOMIZATION · 3:1 DRUG TO PLACEBO

136 patients
Safety-Evaluable

- **Drug (~75%)**
- **Placebo (~25%)**

DOSE COHORTS · MULTIPLE ASCENDING DOSE
12 MONTHLY IV INFUSIONS

Cohort 1	Cohort 2	Cohort 3
350 mg (5 mg/kg)	**700 mg** (10 mg/kg)	**1400 mg** (20 mg/kg)

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Subjects Evaluated to Confirm Mild Cognitive Impairment (MCI) due to AD or Early AD

CONFIRMATION CRITERIA

	Clinical Criteria	NIA-AA criteria: MCI due to AD or mild AD dementia
100%	**Amyloid-Positive**	Confirmed on PET imaging
	Cognitive Staging	MMSE* 20–30 & CDR Global 0.5–1.0 confirm early-stage AD
	Plasma Biomarker	p-tau217/Aβ42 ratio positive, consistent with AD pathology

*Mini-Mental State Examination, 30-point questionnaire

TRIAL DEMOGRAPHICS

PRECISE-AD: Enrollment Consistent with Real World AD Population

PRECISE-AD PATIENT POPULATION

11% — **APOE4/4 Homozygous**
Highest ARIA-risk subgroup with plaque-binding therapies

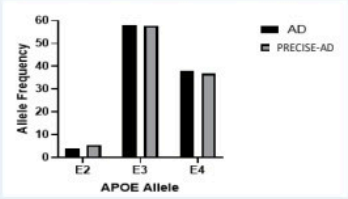
50% — **APOE4 Carrier (1 allele)**
E2/E4, E3/E4, E4/E3 and E4/E2 combined

61% — **Total APOE4 Carriers**
Any participant with ≥1 APOE4 allele

WHY THIS MATTERS

- ✓ **Representative population, including highest ARIA-risk patients**
- ✓ **Treatment options may open for ~15% of AD patients** who are APOE4 homozygotes, the group current therapies largely exclude.

APOE allele frequency: trial vs. reference AD population



In Hardy-Weinberg Equilibrium

Observed APOE genotype frequencies match those expected under Hardy-Weinberg equilibrium ($p > 0.05$), confirming a genetically representative sample with no enrollment selection bias.

Source: AD population genotype percentage and allele frequencies; Yamazaki et al. Nat Rev Neurol 2019

SAFETY

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Many Patients are Currently Well Beyond 6 Months of Treatment

- All patients have been treated for at least 6 months. Many (~49%) have completed all 12 doses
- 144 subjects were enrolled, 136 have been included in this safety analysis
- Safety data is reported as of July 22, 2026 for all patients
- Biomarker data presented through the 6-month time point

MRI is performed at baseline, 2, 4, 6, 9 and 12 months per protocol; ARIA incidence reflects all scans completed as of the interim cutoff. Follow-up distribution shown; illustrative of assessment maturity.

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Blinded Safety Assessment

INTERIM SAFETY · 6-MONTH BLINDED

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Favorable Safety Data, Observed Across Key Measures

6-month blinded interim · N = 144 dosed, 136 safety-evaluable · a representative population

0.0% ARIA-E

The most severe treatment driven form of ARIA

No treatment-related serious AEs

Across all genotypes

No treatment-related discontinuations

Low overall dropout rate to date

4.4% total ARIA

In-line with placebo-range ARIA-H, all mild, asymptomatic, non-serious

Minimal infusion reactions

A recognized liability of approved anti-amyloids and brain-shuttle candidates.
PRECISE-AD: one non-serious event, non-systemic, dosing continued.

APOE4 carriers included

61% carry ≥1 APOE4 allele

11% ε4/ε4 homozygotes — the highest ARIA-risk group

✓ **No ARIA-E in any genotype**

ARIA detection using **Susceptibility-Weighted Imaging (SWI)** for increased sensitivity.

6-month blinded. Infusion-reaction comparators: lecanemab 26.4% (CLARITY AD, van Dyck NEJM 2023); donanemab 8.7% (TRAILBLAZER-ALZ 2, Sims JAMA 2023). Descriptive comparison only. No head-to-head studies have been conducted to compare PMN310 with approved products or other product candidates in development.

TIME-MATCHED SAFETY

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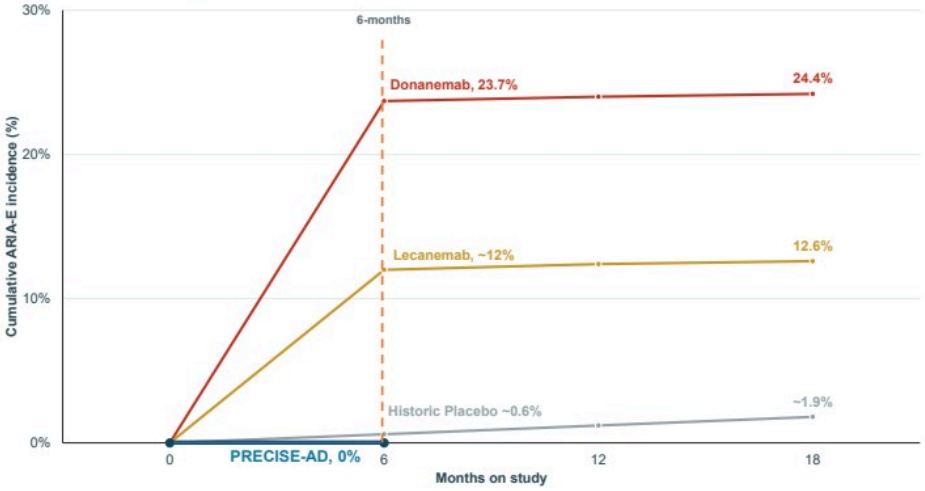
Cumulative ARIA-E Over Time: Zero Edema Observed First 6 Months

ARIA-E (the most serious ARIA type) has been observed to occur almost entirely in the first six months of dosing.
Comparator ARIA-E plateaus after the first few months; rates are time-matched to published data where available, with ~ indicating values estimated between published time points.



AT 6 MONTHS

Time-matched to estimated or published 6-month rates

Donanemab	23.7%
Lecanemab	~12%
Historic, third-party placebo data (avg across both trials)	~0.6%*
PRECISE-AD	**0%**

Illustrative cross-trial comparison — not head-to-head; ~ denotes values estimated between published time points.

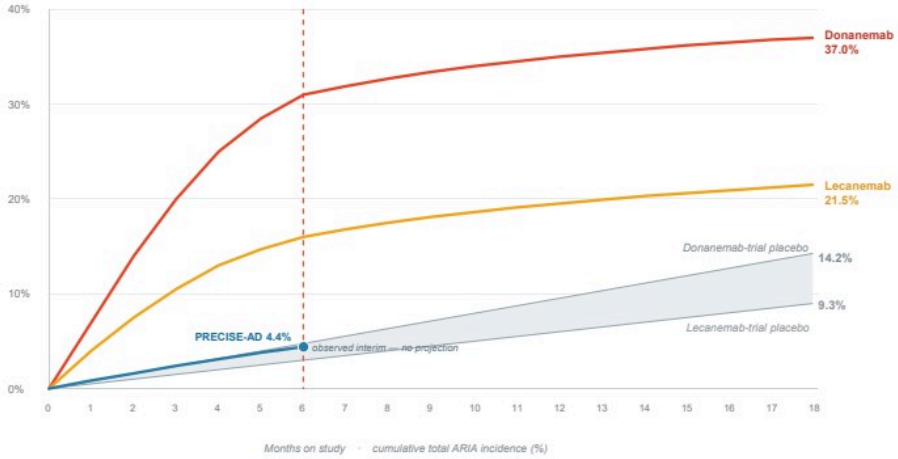
* Placebo: 6-mo ARIA-E (~0.6%) is ProMIS-calculated by linear accrual — (6/18) × ~1.9%, the average of the two trials' 18-mo placebo rates (1.7% and 2.1%). Lecanemab: 12.6% treated / 1.7% placebo ARIA-E at 18 mo; 6-mo (~12%) approximated from this front-loaded cumulative (van Dyck et al., NEJM 2023;388:9–21). Donanemab, TRAILBLAZER-ALZ 2: 24.0% treated / 2.1% placebo over 76 wk (Sims et al., JAMA 2023;330:512–527). Donanemab standard regimen, TRAILBLAZER-ALZ 6: 23.7% ARIA-E at wk 24 (6 mo), 24.2% at 76 wk (Wang et al., Alzheimer's & Dementia 2025;21:e70062); pooled standard-dosing 18-mo ~24.4%. PRECISE-AD: blinded pooled cohort (active + placebo, 3:1); 0/136 ARIA-E at 6-mo interim — observed, not projected.

TIME-MATCHED SAFETY

Cumulative Total ARIA Over Time: Blinded PRECISE-AD Data Tracks the Placebo Range Reported in Other Trials

Approved anti-amyloids accrue ARIA steeply in the first months of dosing, with 90%+ ARIA-E occurring in the first 6 months.

Comparator rates are time-matched to published data where available, with ~ indicating values estimated between published time points.



AT 6 MONTHS

**Calculated based on published data*

Donanemab	*~31%
Lecanemab	*~16%
Historic, third-party placebo data (both trials)	*~3-5%
PRECISE-AD	**4.4%**

MODELED SHAPE, ACTUAL ENDPOINTS — comparator and placebo curves are reconstructed from published trial time-course; trial-end values are as reported. Illustrative, not a head-to-head comparison.

Any ARIA (ARIA-E and/or ARIA-H): Lecanemab 21.5% / 9.3% placebo at 18 mo (van Dyck, NEJM 2023); Donanemab 37.0% / 14.2% placebo, TRAILBLAZER-ALZ 2 ~76 wk (Sims, JAMA 2023; Zimmer, JAMA Neurol 2025). 6-mo points calculated from the published time-course (>90% of ARIA-E within 6 mo): Donanemab ~31%, Lecanemab ~16%, placebo ~3–5%; placebo accrues linearly to reported endpoints. PRECISE-AD: blinded pooled cohort (active + placebo, 3:1); 4.4% total ARIA (6/136) at 6-mo interim — observed, not projected.

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APOE4: Higher-risk Patient Population for ARIA-E

ARIA risk rises sharply with APOE4 carrier status. Approved drugs carry boxed warnings and the worst risk/benefit profile, especially for homozygotes, who represent ~15% of patients.

ARIA-E rates at 6 months by APOE4 genotype

Genotype	Lecanemab*	PMN310
Noncarrier	~5%	0%
APOE4 Heterozygote	~10%	0%
APOE4 Homozygote	~30%	0%

~61% of the PRECISE-AD population were APOE4 carriers. No ARIA-E events were reported in any study participants to date.

A low ARIA-E profile across genotypes could help address a significant barrier to treating higher risk patients.

*Lecanemab data (van Dyck CH, Sperling R, Johnson K, et al. Long-term safety and efficacy of lecanemab in early Alzheimer's disease: Results from the clarity AD open-label extension study. Alzheimer's Dement. 2025; 21:e70905);

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Blinded Biomarker Assessment

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Two complementary biomarkers: plasma pTau217 and CSF MTBR-tau243

Presenting 6-month blinded interim data on two biomarkers chosen to bracket the disease cascade.

UPSTREAM · PLASMA · AMYLOID-DRIVEN

Plasma pTau217

The earliest-moving, best-validated plasma marker of AD pathology. It rises before clinical change, predicts 12-month clinical outcome, and is a key plasma biomarker in current diagnostic criteria, potentially the marker most likely to show an early drug effect by 6 months.

DOWNSTREAM · CSF · TANGLE-SPECIFIC

CSF MTBR-tau243

A CSF marker specific for insoluble tau tangles, the pathology most tightly linked to tau-PET and cognitive decline. It captures the downstream, disease-driving process that amyloid-oriented markers do not.

Rationale

Bracketing the disease cascade triggered by amyloid-beta oligomers**:** pTau217 reports upstream, amyloid-beta-driven tau phosphorylation; MTBR-tau243 reports the ensuing downstream tangle accumulation. A favorable move in both is far stronger evidence of a potential drug effect than either alone.

BIOMARKER RATIONALE

pTau217: early blood-based readout of AD biology

6-month pTau217 is a sensitive early signal, not a standalone efficacy claim. Potential to inform dose selection and bridge to later clinical outcomes.

What it measures

Disease progression: a downstream marker of amyloid-positive AD pathology and tau pathway activation.

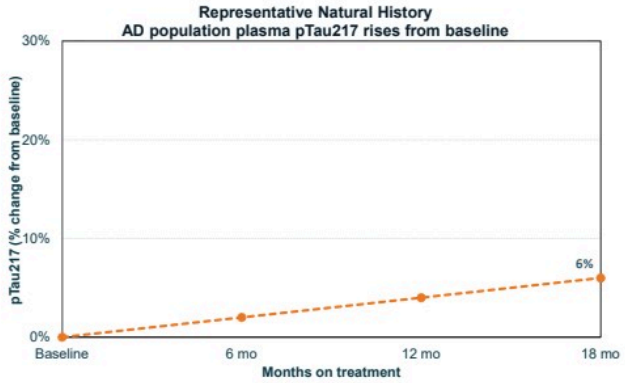
Why it matters

In untreated (placebo) patients, pTau217 rises ~6% over 18 months.

A decline in pTau217 would be an encouraging sign, indicating biological / pharmacodynamic activity and is potentially supportive of disease modification.

Predictive ability

Recent Pentara / ProMIS analysis found 6-month plasma pTau treatment effects correlated with later CDR-SB effects and showed ~2.6× larger effect size than CDR-SB.



Placebo arm — donanemab Phase 2 (TRAILBLAZER-ALZ), ~76 weeks; Pontecorvo et al., JAMA Neurology 2022. Interim time points illustrative.

Refs: Pontecorvo et al., JAMA Neurology 2022 (TRAILBLAZER-ALZ Ph2 placebo-arm natural history); Leveraging recent advances in plasma biomarkers to optimize early proof of concept trials in Alzheimer's disease." Alzheimer's & Dementia: Translational Research & Clinical Interventions (TRC), 2025. DOI 10.1002/trc2.70183.

6-MONTH BLINDED ANALYSIS · PLASMA

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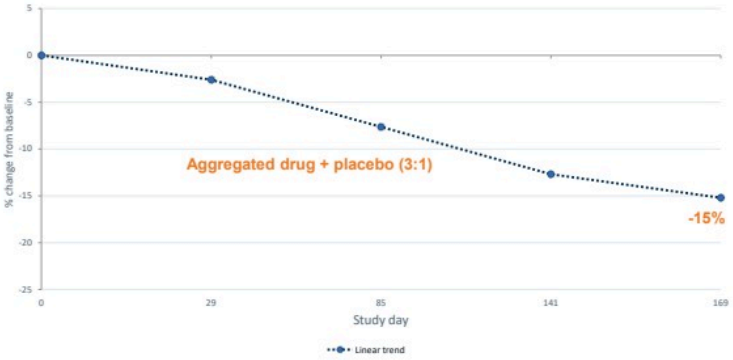
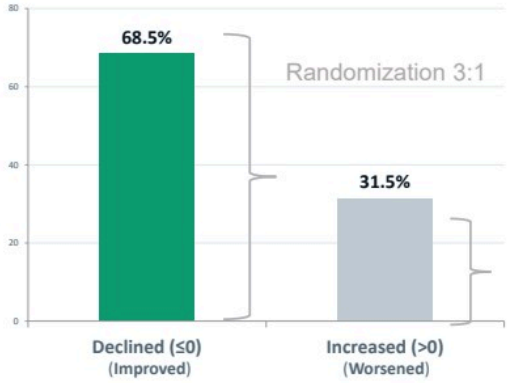
PRECISE-AD RESULTS: Plasma pTau217 declined steadily through Day 169

PRECISE-AD Mean % change from baseline over time



PRECISE-AD patients with a day-169 decline



Why this is compelling at 6 months

Untreated pTau217 rises as the disease progresses. The **15% decline shown in the PRECISE-AD** data (including both PMN and placebo treated patients) indicates a possible early treatment-associated reversal. Although responder data remains blinded, the ~68% responder fraction closely aligns with the 75% active allocation in the 3:1 design based on a prior ProMIS analysis. A 6-month pT217 change could be an early leading indicator of benefit and a predictor of 12-month clinical outcome (Pentara/ProMIS).

Ref: "Leveraging recent advances in plasma biomarkers to optimize early proof of concept trials in Alzheimer's disease." Alzheimer's & Dementia: Translational Research & Clinical Interventions (TRCI), 2025. DOI 10.1002/trc2.70183.

BIOMARKER RATIONALE

CSF MTBR-tau243: tangle-specific marker of AD pathology

What it measures

A CSF marker of tauopathy, the pathology most closely tied to symptoms.

Why it's strong

Correlates with tau-tangle burden and cognition comparable to tau-PET, and more strongly than other CSF markers.

Tau pathology tends to become more evident as patients become symptomatic.

Why it tracks change

Tau tangles correlate with cognitive decline. MTRB-tau243 rises as tangles accumulate and moves in step with disease progression over time.

This biomarker tends to respond more slowly than pTau217.

Natural history progression

What the published evidence supports

Time matched longitudinal data for CSF MTBR-tau243 is limited but has been shown to steeply increase as the disease progresses:

- As a tangle-specific marker, it is elevated at more advanced disease stages.[1]
- Closely related tau markers, notably p-tau217, increase measurably over time across the AD continuum.

In untreated patients, MTBR-tau243 is therefore expected to trend upward. A downward trend with treatment would indicate a possible drug effect.

[1] Horie et al., Nature Medicine 2023; BioFINDER-2 n = 448; Knight ADRC n = 219.

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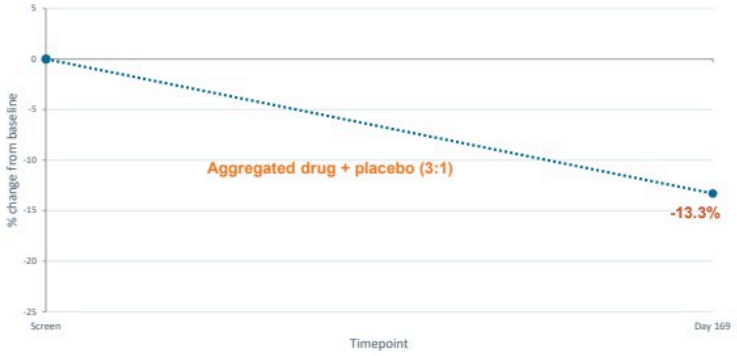
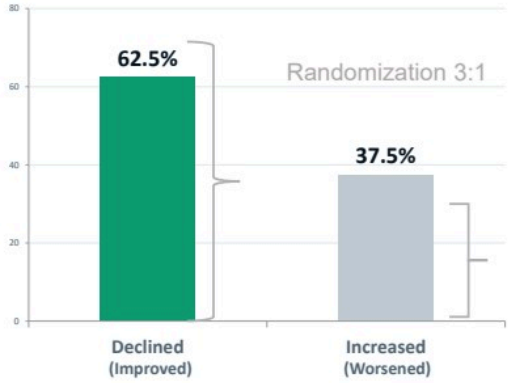
PRECISE-AD RESULTS: CSF MTBR-tau243 declined steadily through Day 169

PRECISE-AD Mean % change, screen → Day 169



PRECISE-AD: Patients with a Day-169 decline



Why this matters at 6 months

MTBR-tau243 is **tangle-specific** and normally **rises** as aggregates accumulate, so a downward move is a favorable, disease-relevant signal. Across the trial participants, it declined on average (-13.3%) and in the majority of patients. The effect is early, not yet powered for significance, but its direction, **against a rising natural history**, is the meaningful result and is directionally consistent with the upstream plasma pT217 decline and tracks the 3:1 randomization pattern.

BIOMARKER SUMMARY

Two biomarkers, one coherent 6-month signal

UPSTREAM · PLASMA

pT217 declined through Day 169

A steady overall decline of 15% vs baseline with ~68% of all patients showing a reduction, indicating potential improvement. This tracks the 75% (3:1) randomization pattern, in a blinded analysis. A meaningful reversal versus a rising natural history.

DOWNSTREAM · CSF

MTBR-tau243 declined through Day 169

This tangle-specific marker declined by 13.3% in the blinded and aggregated analysis with ~62% of all patients showing a reduction, indicating potential improvement. This closely aligns with the 3:1 randomization. This is an early signal, but opposite the usual biomarker increase expected in AD progression.

The takeaway

Upstream (amyloid-beta-driven pT217) and downstream (tangle-specific MTBR-tau243) markers both moved in a favorable direction at 6 months, against a natural history of rising levels. Although data remain blinded, this suggests an early, biologically coherent signal suggesting disease modification.

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Summary & Conclusions

CONCLUSION

A Differentiated, Precision Approach to Alzheimer's — With a Clear Path Forward

PRECISE-AD's blinded interim analysis shows favorable safety data and early, mechanism-consistent biomarker signals, supporting a differentiated approach for patients underserved by approved anti-amyloid therapies.

01

DIFFERENTIATED MECHANISM

Oligomer-selective by design. PMN310 is engineered to bind toxic amyloid-β oligomers while avoiding plaque, decoupling efficacy from the ARIA liability that defines the approved class.

02

FAVORABLE SAFETY PROFILE

Zero ARIA-E; 4.4% total ARIA — all mild, asymptomatic ARIA-H. Zero treatment-related SAEs and zero drug-related discontinuations, minimal (n=1) drug-related infusion reactions as of data cutoff date.

03

TARGET ENGAGEMENT WITH RELEVANT BIOMARKERS

Coherent, biologically aligned signal. Upstream plasma pTau217 declined significantly (~69% of patients, tracking 3:1 randomization) and downstream CSF MTBR-tau243 moved favorably (~63% of patients declined), both opposite a rising natural history.

04

OPENING ACCESS TO APOE4 CARRIERS

No ARIA-E in any genotype. With 61% APOE4 carriers and 11% homozygotes enrolled, a favorable safety profile could remove the class's single biggest barrier, especially for the patients at highest risk.

05

POTENTIAL IN PRECLINICAL AD

A safety profile suited to earlier intervention. A placebo-level ARIA profile makes PMN310 a strong candidate to move upstream into preclinical AD, where prevention has the greatest impact, but tolerability is paramount.

Topline results early Q1 2027

Favorable safety profile

No ARIA-E, zero SAEs — across all genotypes.

Early biomarker signals

Directional trends consistent with potential target engagement.

Oligomer-selective MOA

Designed to decouple efficacy from ARIA liability with precision selectivity.

PMN : NASDAQ · Cambridge, MA

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