PMN310 Profile Review
November 2026

The following update is intended to provide an update on the development of PMN310 following the recent data release of Acumen Pharmaceuticals' Phase 2 ALTITUDE-AD clinical trial of sabirnetug (ACU193) for the treatment of early Alzheimer's disease.

1) **What is the central hypothesis behind PMN310 and do the Acumen results impact it?**

Our conviction in the oligomer hypothesis remains strong. We believe toxic amyloid-beta oligomers, not plaques, are the principal drivers of pathology that lead to cognitive decline in Alzheimer's disease, and PMN310 is built to target and bind them directly.

The approved therapies provide additional strong evidence of the critical role of toxic oligomers in AD pathology. They reduce amyloid plaque substantially yet deliver only modest clinical benefit. Removing plaque is insufficient, and we believe that gap is the opportunity. Decades of published research identify toxic oligomers as key contributors to synaptic dysfunction, downstream tau pathology and, ultimately, the loss of memory and cognitive function.

PMN310 was engineered to target these toxic, misfolded oligomers with exceptional selectivity. Our goal is not to strip away amyloid deposits. It is to neutralize and clear the toxic species that damage neurons, before that damage progresses.

We believe targeting the right species with the right antibody has the potential to result in greater clinical benefit with a better safety profile. ProMIS' ongoing clinical trial PRECISE-AD is designed to demonstrate this, and these recent data from Acumen do not alter this hypothesis.

2) Do the negative ALTITUDE-AD results change ProMIS' development strategy?

No. Our development plan and anticipated Q1 2027 readout remain unchanged.

3) How is PMN310 differentiated from sabirnetug?

PMN310 and Acumen's sabirnetug are fundamentally different antibodies. PMN310 was engineered to recognize only toxic, misfolded amyloid-beta oligomers while avoiding monomers and plaque. Sabirnetug does not appear to be a selective oligomer binder. Acumen's own data indicate sabirnetug binds multiple targets, including plaque. In our view, its results are not a test of the oligomer hypothesis and have no bearing on PMN310.

Three differences set PMN310 apart:

i. **Selectivity**: Across multiple preclinical studies, PMN310 was shown to bind only toxic amyloid-beta oligomers, not monomers, fibrils or plaque. Sabirnetug, by contrast, has consistently shown broader reactivity, producing significant plaque lowering in its Phase 2 study. That is a fundamentally different binding profile, and it shows up in the safety data.

ii. **Antibody design (isotype)**: PMN310 is built on an IgG1 backbone, the same class as lecanemab and donanemab, so it is designed to both neutralize toxic oligomers and recruit microglia to actively clear them. Sabirnetug uses an IgG2 isotype with minimal effector function, limiting it largely to neutralization (and not clearance). We believe PMN310's ability to engage the brain's immune system to eliminate these pathogenic species is a required therapeutic attribute.

iii. **Safety profile:** The safety profiles are strikingly different. Acumen reported a 10% incidence of ARIA-E, the more serious form of ARIA associated with plaque-binding antibodies, in line with the two marketed drugs. PMN310's 6-month blinded interim analysis showed zero cases of ARIA-E across all ApoE genotypes.

Clinical efficacy is still to be established, but we believe PMN310's differentiated design and the clinical evidence to date can set it apart from other Alzheimer's disease antibodies, sabirnetug included.

4) What is the relevance of IgG1 versus IgG2? Is this an important differentiator and could it help explain sabirnetug's lack of efficacy?

We believe this is an important potential differentiator between PMN310 and sabirnetug. An antibody has two important functions: recognizing its target and determining what happens once that target is bound.

PMN310 is an IgG1 antibody, designed not only to selectively bind and neutralize toxic amyloid-beta oligomers, but also to potentially facilitate their active clearance through the brain's immune cells, including microglia. Lecanemab and donanemab, the two approved antibodies that have shown clinical benefit, are both IgG1.

In contrast, sabirnetug utilizes an IgG2 backbone engineered with reduced immune effector function. While it can bind oligomers, its capacity to recruit immune-mediated clearance mechanisms is substantially reduced. Therefore, sabirnetug may be able to neutralize its target, but it cannot actively clear it, which can effectively limit its therapeutic potential.

5) If oligomers drive cognitive decline, and it is thought that sabirnetug binds at least some oligomers, why did there appear to be little evidence of efficacy?

We will have to see the data in totality before we can understand all effects on efficacy measures. However, binding some oligomers is not the same as removing the toxic ones in sufficient amounts from the brain. We see three potential reasons for sabirnetug's lack of clinical efficacy but, we must stress, we have only seen limited publicly available data. We believe none of these possibilities undermines the oligomer hypothesis.

i. Plaque binding may have distracted the antibody away from its intended target. Sabirnetug produced statistically significant reductions in amyloid plaque at both dose levels at weeks

36 and 76. That appears to be evidence of plaque binding. The brain contains vastly more plaque than soluble oligomers, so an antibody that binds plaque can be heavily absorbed there. This reduces the amount of free antibody available to reach the toxic oligomers it was meant to neutralize. PMN310 was engineered to avoid this. It was designed to not bind monomers, fibrils or plaque, so the antibody that reaches the brain remains available for its toxic oligomer target.

ii. Neutralizing without clearing may not sufficiently reduce the toxic load. As described above, an IgG2 antibody can bind oligomers, but the brain keeps producing them. Without active clearance, the pool of toxic oligomers may never reduce enough to protect synapses.

iii. Not all oligomers are equally toxic. “Oligomer” covers a varied range of amyloid-beta aggregates, and only some of them are in the misfolded toxic forms we believe damage neurons. Binding a broad mix of oligomers is different from precisely targeting the most harmful ones. PMN310 is directed against a conformational feature found only on toxic, misfolded oligomers.

The Acumen trial outcome also reinforces a broader point. Sabirnetug lowered plaque and still showed no clinical benefit. We believe that strengthens the case that plaque removal is not, on its own, sufficient to slow cognitive decline. The opportunity lies in selectively removing the toxic oligomers.

6) What is the status of the PRECISE-AD study and which patient population is enrolled?

Enrollment is complete, with 144 participants. PRECISE-AD is a randomized, double-blind, placebo-controlled Phase 1b study of monthly intravenous PMN310 (5, 10 and 20 mg/kg) over 12 months in patients with mild cognitive impairment due to AD or mild AD (“Early AD”). ProMIS continues to anticipate unblinded 12-month topline results in Q1 2027.

7) What did the PRECISE-AD 6-month blinded interim analysis show?

The blinded interim results presented on July 28, 2026, were encouraging. In 136 evaluable patients at 6 months of treatment, PMN310 showed a favorable safety profile across all ApoE genotypes, with no cases of ARIA-E as of the data cutoff. Results also showed directionally consistent movement in two disease-relevant biomarkers (pTau-217 and MTBR-tau243). Because the analysis was blinded, these changes cannot yet be attributed to PMN310, though the pattern is consistent with what we would expect given the trial’s randomization.

8) What should investors expect from the topline readout?

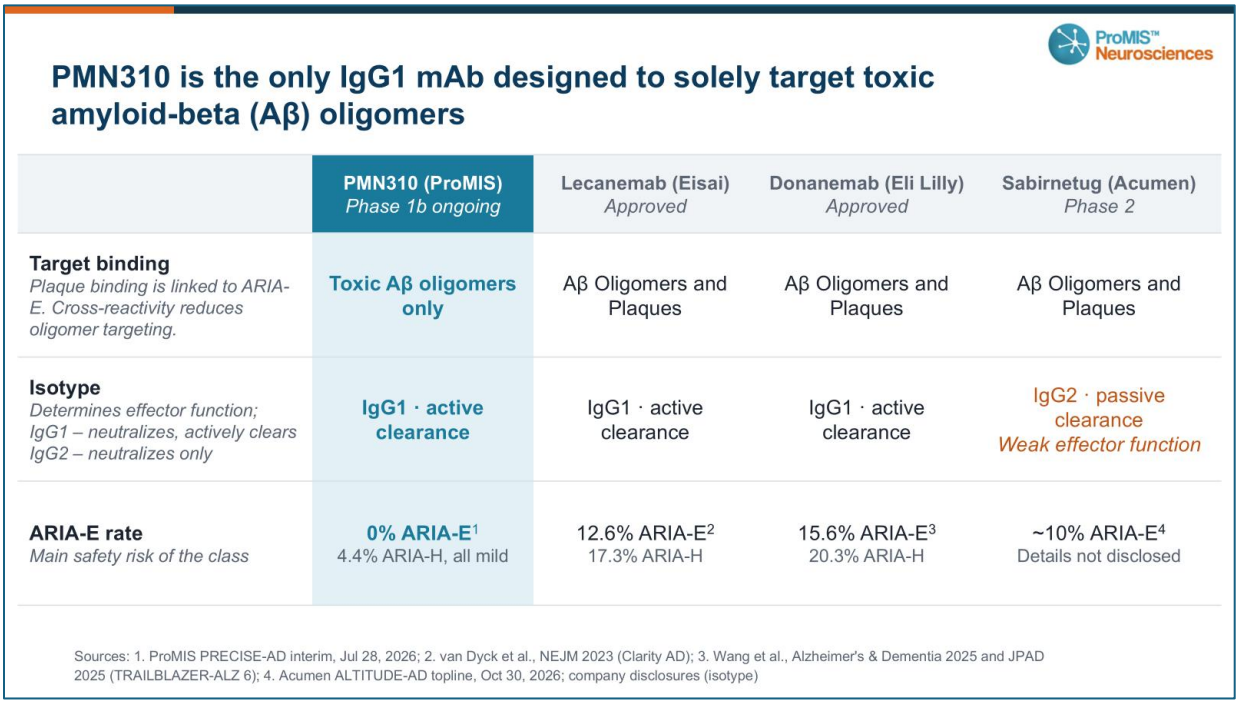
PRECISE-AD was designed to produce a rich, multi-dimensional dataset. Topline results will span four areas: (1) safety, including ARIA incidence and overall side-effect profile; (2) biomarkers,

including measures of tau pathology, inflammation and synaptic function; (3) clinical outcomes, including iADRS and CDR-SB; and (4) mechanism of action, including oligomer levels in CSF and response to treatment. We are looking for a coherent signal across these measures, one that supports a superior risk:benefit profile for PMN310 relative to the approved therapies and sharpens the design of our next trial.

9) What is the company's cash position and runway?

ProMIS is well funded through its key catalyst, completion of the Phase 1b trial. As of our Q2 2026 quarterly report, the company held approximately $53.4 million in cash, providing runway through 2027, well beyond the expected Q1 2027 topline readout.

10) Overview of antibodies:



ProMIS™ Neurosciences

PMN310 is the only IgG1 mAb designed to solely target toxic amyloid-beta (Aβ) oligomers

	PMN310 (ProMIS) *Phase 1b ongoing*	Lecanemab (Eisai) *Approved*	Donanemab (Eli Lilly) *Approved*	Sabirnetug (Acumen) *Phase 2*
Target binding *Plaque binding is linked to ARIA-E. Cross-reactivity reduces oligomer targeting.*	**Toxic Aβ oligomers only**	Aβ Oligomers and Plaques	Aβ Oligomers and Plaques	Aβ Oligomers and Plaques
Isotype *Determines effector function; IgG1 – neutralizes, actively clears IgG2 – neutralizes only*	**IgG1 · active clearance**	IgG1 · active clearance	IgG1 · active clearance	IgG2 · passive clearance *Weak effector function*
ARIA-E rate *Main safety risk of the class*	**0% ARIA-E**[1] 4.4% ARIA-H, all mild	12.6% ARIA-E[2] 17.3% ARIA-H	15.6% ARIA-E[3] 20.3% ARIA-H	~10% ARIA-E[4] Details not disclosed

Sources: 1. ProMIS PRECISE-AD interim, Jul 28, 2026; 2. van Dyck et al., NEJM 2023 (Clarity AD); 3. Wang et al., Alzheimer's & Dementia 2025 and JPAD 2025 (TRAILBLAZER-ALZ 6); 4. Acumen ALTITUDE-AD topline, Oct 30, 2026; company disclosures (isotype)

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Forward Looking Statements

This document contains forward-looking statements within the meaning of applicable securities laws, including statements regarding the design, mechanism of action, safety and potential efficacy of PMN310, including relative to other approved or investigational products; the conduct, timing and results of the PRECISE-AD trial, including the expected release of topline data; the design of future clinical trials; and the Company's cash position and cash runway. Words such as "believe," "expect," "potential," "may," "designed to" and similar expressions identify forward-looking statements.

These statements are based on management's current expectations and assumptions and are subject to risks and uncertainties that could cause actual results to differ materially, including risks related to clinical development, the interpretation of interim and blinded data, regulatory review, competition and financing. Interim and blinded results may not be predictive of final results. Comparisons with other products are not based on head-to-head trials and are subject to differences in trial design and patient populations.

For additional risk factors, see the Company's filings with the U.S. Securities and Exchange Commission and applicable Canadian securities regulators. Forward-looking statements speak only as of the date of this document, and the Company undertakes no obligation to update them except as required by law.