Docusign Envelope ID: A58B7630-049D-8009-808E-DB1DEA66611A

Parley Combination Therapy (LOOT)

Review Decision Letter · RDL-2026-001 · Decided August 26, 2026

Legal basis: SB 535 (69th Leg., Ch. 621) · ARM 37.106.3301-3325

Montana ETRB

APPROVED WITH CONDITIONS

Applicant	Parley Neurotech, Inc. (Denver, CO)
Treatment	Parley Combination Therapy (LOOT): clemastine fumarate equivalent to 12 mg/day clemastine base during week 1 (16.08 mg/day clemastine fumarate) and 8 mg/day clemastine base during weeks 2-4 (10.72 mg/day clemastine fumarate) plus engineered sound delivered by consumer headphones; 4-week course
Indication	Age-related central auditory processing disorder (CAPD)
Submission	First submission: June 17, 2026; request for further information completed: August 21, 2026
Review meeting	August 26, 2026, 12:00-2:00 pm MT. Quorum confirmed; conflict-of-interest declarations (none) confirmed on the record; Applicant session and Q&A minuted; deliberation and vote in closed session.
Decision	**APPROVED WITH CONDITIONS. Vote: 5 for, 0 against**
Effectiveness	This RDL was approved by the Board. The approval is effective upon (a) written confirmation of concordance with the Conditions by the Chair, under the process approved by the Board in this RDL, and (b) becomes effective for use at a given ETC upon that ETC's valid designation of this ETRB (Submission Agreement 4.9).

1. Treatment summary

A four-week, patient-administered combination of oral clemastine fumarate at the remyelination-targeted dose and daily engineered-sound listening sessions streamed to consumer headphones, intended to promote remyelination in the central auditory pathway. The drug component completed Phase 1 in its original FDA development and remains under investigation in the Applicant's combination trial (CAPD-LOOT, NCT07304024) under IND 178,635; FDA authorized the combination protocol by Study May Proceed letter. Delivery contemplates prescription by the treating physician with administration outside the ETC under ARM 37.106.3325.

2. Conditions of approval (binding; Submission Agreement 4.7)

Condition 1 - Informed consent revisions

The Applicant shall revise the Informed Consent Form and verbal-consent script to: (a) disclose the TRAP-MS progressive-MS safety signal with the Applicant's population-specific contextualization; (b) accurately preserve the prescribing clinician's discretion to require an EKG, in-person examination, or laboratory studies, and remove the statement that the medicine's safety in humans is already established; (c) provide that both the written ICF and the recorded verbal consent are captured for every patient; and (d) provide attestation of the written consent consistent with 50-12-105(3), MCA.

Condition 2 - Pre-treatment assessments that differ from the FDA IND

The Applicant and the ETC shall incorporate into the protocol and patient-facing information guidelines to the treating clinician related to potential individual risks associated with the higher dose of clemastine included in the experimental intervention. Specifically, these guidelines should recommend that the treating clinician:

(1) Assess whether the patient does not meet applicable renal, hepatic, or hematologic exclusion criteria. This assessment may rely on sufficiently recent laboratory results available in the patient's medical record when, in the clinician's judgment, those results adequately establish eligibility. CBC, CMP, or other appropriate laboratory testing should be obtained when existing clinical information is insufficient to make that determination.

(2) Assess the patient for cardiac conditions and medications that could materially increase the risk associated with clemastine, including clinically significant QT prolongation. A sufficiently recent ECG available in the medical record may be used when, in the clinician's judgment, it adequately establishes eligibility. A new ECG should be obtained when existing clinical information is insufficient to assess relevant cardiac risk.

(3) Evaluate the patient's age and frailty with respect to risk of falls, given the potential for the treatment to cause sedation or dizziness. If this is considered a significant risk, the prescribing physician should consider reducing the clemastine dose, particularly during the initial phase of the treatment period.

The Applicant and the ETC shall address the Conditions in writing. The Chair confirms concordance in writing without reconvening the Board; upon confirmation, the approval takes effect subject to ETC designation.

3. Required determinations (ARM 37.106.3316(6))

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Determination	Finding	Board position	Basis (summary)
Statutory qualification (50-12-102(1), MCA)	Met (reasonable grounds)	Unanimous	Based on the Applicant's signed eligibility certification and supporting record, under counsel's written framework of Aug 18, 2026.
Safety standards equivalent to or higher than recognized regulatory authorities (16(6)(a)(i))	Met subject to satisfactory resolution of Condition 2	Unanimous	Dose regimen supported by ReBUILD, the ReCOVER loading-dose design precedent, and ongoing IND 178,635 exposure; removal of IND-protocol EKG and in-person examination addressed via Condition 2 and preserved clinician discretion.
Informed consent comprehensive and understandable (16(6)(a)(ii))	Met subject to satisfactory resolution of Condition 1	Unanimous	ICF strong overall; the additions and corrections in Condition 1 are required before consent materials are final.
Risk-benefit demonstrates a reasonable safety profile (16(6)(a)(iii))	Met subject to satisfactory resolution of Condition 2	Unanimous	Older-adult anticholinergic burden (AGS Beers Criteria class) weighed against exclusion criteria, the driving restriction, concomitant-medication screening, and the short 4-week course.
Alternative treatments appropriately evaluated (16(6)(a)(iv))	Met	Unanimous	Protocol establishes adequate per-patient procedures: documented alternatives evaluation in the consent and eligibility process per 50-12-104, MCA.
Risk level and outside-ETC administration (16(6)(f))	Risk level: Low. Safe for administration outside an ETC, subject to the approved protocol and applicable conditions.	Unanimous, with Condition 2	Oral take-home drug plus consumer-headset audio; risk profile consistent with patient self-administration under the protocol's monitoring, driving restriction, and AE-reporting pathways.

Statutory qualification recital: the Company and the Board determined, in reliance on the Applicant's signed eligibility certification and supporting record and on counsel's written guidance dated August 18, 2026, that reasonable grounds exist for treating the requirements of 50-12-102(1), MCA as satisfied. Another reasonable interpretation does not, by itself, preclude approval.

4. Principal matters deliberated

(1) Dose-support chain: the week-1 loading dose exceeds the ReBUILD-tested dose; the Board weighed the ReCOVER design precedent, accumulating IND exposure, and the short course. (2) Older-adult anticholinergic burden: clemastine's class appears in the AGS Beers Criteria for adults 65 and older; mitigations reviewed included exclusion criteria, concomitant-medication screening, and the driving restriction. (3) Removal of IND-protocol safeguards (EKG, in-person examination): resolved through Condition 2 and the preserved discretion of the prescribing clinician. (4) TRAP-MS pyroptosis signal: disclosed to the Board; patient-facing disclosure required through Condition 1. (5) Statutory qualification of the combination: resolved at the reasonable-grounds standard under counsel's framework. Not all deliberations are recorded here, only the most substantial; per-member vote rationales are preserved in the Review Record.

5. Continuing obligations

The Applicant shall report Serious Adverse Events to the Board within 24 hours and other Adverse Events within 3 business days (Submission Agreement 9.2.2); the ETC reports SAEs to the department within five days, with adverse-event data reported to this Board simultaneously (ARM 37.106.3317(1), (4)). Material amendments require prior Board review (9.3). Annual continuing review applies (9.4). Outcome data are collected and shared per the approved protocol's outcome dataset. Records of this review are preserved for at least five years (16(6)(d)).

6. Disclaimers and reliance

This approval reflects the Board's professional judgment on the record submitted. It is not FDA approval or clearance, is not a determination of efficacy or therapeutic benefit, is not medical advice or a recommendation to any patient, and is not a warranty that the treatment is safe (Submission Agreement 8.2-8.4). Responsibility for development, manufacture, supply, and clinical delivery rests with the Applicant, the ETC, and treating providers.

Montana ETRB

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Matt Kaeberlein
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Matt Kaeberlein, PhD - Chair, for the Board

8/30/2026

Date