THE AMN DUAL-MECHANISM SUPPORT PROTOCOL

(Clinical Reference)

A Structured Approach to Axonal Preservation and Exploratory Myelin Support

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DOCUMENT 1: THE SCIENTIFIC CASE

THE "NERVONIC ACID + ANTIOXIDANT" PROTOCOL

A Summary of Peer-Reviewed Research & The Combination Strategy

1. THE EXPERTS (CREDIBILITY)

This protocol is derived from the peer-reviewed work of leading AMN and myelin researchers.

- Dr. Reena Kartha, PhD & Dr. Troy Lund, MD, PhD (University of Minnesota)
- Study 1 (2022): "Nervonic Acid Attenuates Accumulation of Very Long-Chain Fatty Acids"
- Study 2 (2025): "Nervonic Acid Improves Mitochondrial Function in AMN Fibroblasts"
- Dr. Aurora Pujol, MD, PhD (Bellvitge Biomedical Research Institute, Spain)
- Study: "Biomarker Identification, Safety, and Efficacy of High-Dose Antioxidants for Adrenomyeloneuropathy" (2019)
- The "EAE/MS" Research Team (Key to Dosage Strategy)
- Study: "Nervonic Acid regulates the oxidative imbalance in experimental autoimmune encephalomyelitis" (2021)
- Relevance: EAE is the standard animal model for demyelination (MS). This data provides the primary benchmark for potential "repair-range" dosing in the absence of human AMNspecific dose finding.
- Dr. C. Li, PhD (Research Team Lead)
- Study: "Pharmacokinetics of Nervonic Acid... in an ALD mouse model" (2023)

2. SCIENTIFIC RATIONALE: A DUAL-MECHANISM STRATEGY

Current standard of care for AMN is strictly palliative. This protocol challenges that paradigm by targeting the specific dual pathology of the disease: Distal Axonopathy (dying back of the nerves) and Demyelination (loss of insulation).

Mechanism 1: Axonal Preservation (Antioxidant Complex)

Adrenomyeloneuropathy involves accumulation of very long-chain fatty acids, mitochondrial dysfunction, and elevated oxidative stress, all of which contribute to distal axonal degeneration. The antioxidant combination (N-acetylcysteine, alpha-lipoic acid, and vitamin E) is intended to reduce reactive oxygen species and limit secondary oxidative injury.

Rather than halting disease progression, this component aims to reduce damage propagation and lower cumulative biological stress on vulnerable axons. In clinical studies, similar antioxidant combinations have demonstrated normalization of oxidative biomarkers and signals of functional stabilization in some patients.

This strategy is preservation-oriented. It does not repair established axonal loss, but seeks to reduce factors known to accelerate degeneration.

Mechanism 2: Myelin Maintenance Versus Regeneration

The protocol explicitly distinguishes between:

- regeneration, which is neither expected nor claimed
- maintenance and stabilization, which remain biologically plausible within adult constraints

Adult central nervous system tissue has limited capacity for remyelination. Oligodendrocyte precursor cells persist into adulthood, but their activation, differentiation, and functional integration are tightly regulated by inflammatory signaling, oxidative stress, metabolic state, and axonal integrity.

No component of this protocol is intended to induce oligodendrocyte differentiation, stimulate remyelination directly, or override the underlying genetic defect.
The rationale is more limited. It aims to reduce known inhibitory stressors and to avoid structural lipid insufficiency in situations where endogenous maintenance processes remain active.
Providing substrate should not be interpreted as initiating repair. Substrate availability does not activate remyelination pathways. At most, it may prevent structural components from becoming a limiting factor if intrinsic cellular maintenance mechanisms are already engaged.

Conceptual Orientation

Conventional neurological management in adrenomyeloneuropathy is largely palliative, targeting spasticity, pain, and mobility limitations after functional decline has occurred.

The present framework is oriented upstream.

Rather than treating symptoms alone, it focuses on modifying the biological environment in which axons and myelin operate, with the goal of reducing cumulative stress, preserving conduction reliability, and minimizing secondary injury.

This distinction is one of **target**, not opposition. Symptom management remains appropriate and necessary. The protocol is complementary, not substitutive.

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Expectation Boundaries

The protocol does not predict:

- axonal regrowth
- restoration of destroyed tracts
- normalization of neurological architecture

Potential observable effects, if present, would be expected to manifest as:

- reduced variability
- improved tolerance to fatigue or heat
- improved reliability of motor output
- slower accumulation of secondary dysfunction

These outcomes align with preservation-oriented goals rather than reparative claims.

Relation to the extended biological framework

A separate technical document outlines a phenotype-specific rationale for why margin-based functional improvement may be more plausible in certain presentations than in others.

https://amn-protocol-app.netlify.app/docs/functional-recovery-amn.pdf

3. THE CORE RESEARCH: NERVONIC ACID (2022 vs. 2025)

The University of Minnesota has published two key studies illustrating the potential mechanism of action.

- PART 1: THE "METABOLIC" EFFECT (2022 STUDY)
- The Finding: Adding Nervonic Acid actively lowers the levels of toxic C26 fats in patientderived cells.
- The Implication: It addresses the VLCFA accumulation that characterizes the disease.
- PART 2: THE "BIOENERGETIC" EFFECT (2025 STUDY)
- The Finding: This follow-up demonstrated that Nervonic Acid did not just lower VLCFAs; it restored ATP (Energy) production to near-normal levels in AMN fibroblasts.
- The Clinical Relevance: Historically, lowering C26 fats alone (e.g., Lorenzo's Oil) did not always yield clinical benefit. This study suggests Nervonic Acid may offer a secondary benefit—mitochondrial rescue—that addresses the energy failure often seen in AMN axons.

4. TRANSLATIONAL RATIONALE: SUPPORTING EVIDENCE

EVIDENCE 1: BLOOD-BRAIN BARRIER PENETRATION (2023)

- The Study: "Pharmacokinetics of Nervonic Acid... in an ALD mouse model" (AAPS PharmSciTech).
- The Finding: Pharmacokinetic analysis confirmed that Nervonic Acid successfully crosses the Blood-Brain Barrier (BBB) in ALD mice, suggesting CNS bioavailability is possible.

EVIDENCE 2: CLINICAL EFFICACY OF ANTIOXIDANTS (2019)

- The Study: "Biomarker Identification, Safety, and Efficacy of High-Dose Antioxidants" (Dr. Pujol).
- The Finding: In a Phase II Clinical Trial, the specific combination of NAC, Alpha Lipoic Acid, and Vitamin E normalized oxidative biomarkers. Notably, 80% of patients showed "Improvement or Stabilization" in the 6-Minute Walk Test.
- Context: While the trial did not progress to Phase 3 (likely due to the non-patentable nature of supplements), the Phase 2 efficacy signal provides a strong evidence base for including these agents in the protocol.

5. THE SOURCING CREDIBILITY (WUXI CIMA SCIENCE)

We have established a corporate account with Wuxi Cima Science Co., Ltd., a verified major manufacturer. Their testing is pharmaceutical-grade:

- Assay by GC (98.2%): Gas Chromatography proves the powder is >98% pure Nervonic Acid.
- Identification (IR & H-NMR): "Fingerprint" tests using Infrared and Magnetic Resonance confirm the molecular structure.
- Heavy Metals: Certified <10ppm for Lead, Mercury, and Arsenic.
- Commercial Pricing Access: A 33% price reduction was granted after purchase was made through a registered business entity, providing access to standard commercial wholesale tiers.

6. SAFETY CONTEXT & RISK MITIGATION

- Historical Context (Very Long-Chain Fatty Acids):
  Concerns about structurally related very long-chain monounsaturated fatty acids, such as erucic acid, arose from rat studies in the 1970s that demonstrated myocardial lipid accumulation.

  Subsequent research clarified significant species differences in cardiac lipid metabolism between rodents and humans, reducing the direct applicability of those findings to human physiology.

This context is relevant because nervonic acid shares structural similarities with erucic acid, although current toxicology data specific to nervonic acid have not demonstrated comparable adverse cardiac effects in available animal models.

- Translation Challenge 1 (BBB Thickness): Humans have a thicker BBB than mice. To mitigate the risk of poor penetration, we utilize Nervonic Acid's lipid solubility, recognizing that CNS exposure in humans is likely dose-dependent but not guaranteed. We therefore pair this strategy with conservative monitoring for peripheral effects.

- Translation Challenge 2 (Metabolic Integration): Ensuring efficient absorption of fatty acids without digestive distress. Mitigation: Doses will be taken with meals to utilize natural bile production for emulsification. If gastrointestinal symptoms occur, the dose will be divided (morning/evening)

7. THE PROTOCOL: DOSAGE & ESCALATION

- Patrick (Patient) Target: 1,000mg (1g) per day.
- Rationale (The Myelin Repair Model): The 1g target is derived specifically from the 2021 EAE/MS Study listed in Section 1. In that study, the "Low Dose" required to significantly reduce clinical severity scores was 197 mg/kg.
- The Calculation: 197 mg/kg (Mouse) ÷ 12.3 (Conversion) = ~16 mg/kg (Human). For an ~80kg adult, the extrapolated effective dose is 1.28g.
- The Strategy: We are starting at 1g (rounding down slightly) to ensure exposure consistent with the efficacy range observed in the MS demyelination model, recognizing that this does not guarantee clinical benefit in AMN.

Conditional Escalation: If no clinical improvement is observed after 6 Months, and only if physiological safety metrics remain stable**,** we will evaluate the feasibility of escalating to the "Medium Dose" (2.5g/day) used in the animal models. This step is exploratory and contingent on strict safety validation.

- Nieve (Prophylactic) Target: ~250mg - 500mg per day.
- Rationale: As a carrier, the goal is preventative support. A 500mg cap provides lipid substrate without overloading a younger metabolism.
- The Testing Schedule:
- Baseline: Complete VLCFA Panel before Day 1.
- Follow-Up: Repeat VLCFA Panel every 90 Days to track C26:0 trends.
- Safety: Daily Cardiac Monitoring (BP/HR) during the first 30 days
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DOCUMENT 2: THE SAFETY PROTOCOL

THE SAFETY PROTOCOL

Strict safety measures for the Nervonic Acid Protocol

1. THE "MICRO-DOSE" START

- Day 1-3: I will take a tiny "micro-dose" (50mg - 100mg) to test for any allergic reaction or sensitivity.
- Objective: To confirm tolerability before reaching therapeutic levels.

2. THE "STOP SWITCH" (SYMPTOM MONITORING)

If I feel any nausea, headache, dizziness, or new symptom, I stop immediately. There is no "pushing through." Safety is the priority.

3. ADVERSE DRIFT MONITORING (THE SUBTLE SIGNALS)

In N-of-1 experiments, the risk is often not acute toxicity, but "Adverse Drift" This is a gradual shift away from physiological baseline.

- What is Adverse Drift? A slow loss of net benefit or a creeping physiological cost. It is not an emergency; it is a signal to re-evaluate.

Indicators to Watch:

- Nervous System: New brain fog, altered alertness, or atypical fatigue.
- Autonomic Function: Sustained drift in resting heart rate or blood pressure instability.
- Sleep Architecture: Increased fragmentation, early awakenings, or reduced sleep depth.
- The Rule: If I observe a consistent directional change in these areas for >14 days without external explanation, I will hold the dose or pause the protocol.

4. THE DATA CHECK (CARDIAC MONITORING)

- The Metric: Daily Blood Pressure and Resting Heart Rate.
- The Rule: A consistent spike in Resting Heart Rate or Blood Pressure over a 3-day period triggers a protocol pause.

5. THE VERIFICATION STEP (LAB TESTING)

We operate on a "Trust but Verify" model.

Verification Pipeline: Staged Testing and Release Criteria

This protocol employs a multi-stage verification pipeline to confirm the identity, consistency, and safety of nervonic acid prior to use. Progression through each stage is conditional; failure at any stage results in termination of sourcing or rejection of material.

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Stage 0: Supplier Documentation Review (Pre-Shipment)

Inputs:

- Certificate of Analysis (COA)
- Method of Analysis (MOA)
- Batch number and lot identifiers
- Stated purity and analytical results
- Manufacturing and purification method, including solvent use where applicable

Goal:
Confirm that the supplier provides a coherent analytical trail, discloses relevant manufacturing methods, and presents claims that can be independently verified.

Decision rule:
Procurement does not proceed without complete documentation, batch identifiers, and disclosure sufficient to assess downstream testing requirements.

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Stage 1: Preliminary Sample Acquisition

Action:
Procurement of a 20 g sample (door-to-door).

Status:
Sample remains quarantined and is not used for any protocol exposure.

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Stage 2: Independent Verification of Preliminary Sample (Gate Before Bulk Procurement)

2A. Identity and Lipid Profile Test
performed:

- Full lipid panel with chain-length verification (including C26:0)

Objective:
Confirm compound identity and lipid composition consistent with supplier claims.

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2B. Contaminant Screening Tests
performed:

- Heavy metals panel
- Residual solvent testing, if indicated

Decision logic for solvent testing:
Residual solvent testing is determined based on:

- supplier disclosure of manufacturing and purification methods
- presence or absence of solvent data in the COA
- any ambiguity or concern identified during documentation review or lipid analysis

If solvent use is clearly disclosed and supported by validated analytical data, this information may be provisionally relied upon at the sample stage.
If solvent use is unclear, undisclosed, or raises concern, independent residual solvent testing is performed prior to bulk procurement.

Decision rule:
Failure of identity confirmation, unacceptable lipid profile, or contaminant levels exceeding acceptable thresholds results in termination of sourcing and discard of the sample. Only if all required tests pass does the protocol proceed to bulk procurement.

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Stage 3: Bulk Material Procurement

Action:
Procurement of 1 kg bulk material occurs only after successful completion of Stage 2.

Status:
Bulk material remains quarantined pending confirmatory testing.

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Stage 4: Confirmatory Verification of Bulk Lot

4A. Identity and Lipid Profile Test
performed:

- Repeat full lipid panel with chain-length verification (including C26:0)

Objective:
Confirm consistency between the verified sample and the bulk lot and exclude substitution, dilution, or batch drift.

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4B. Contaminant Screening Tests
performed:

- Heavy metals panel
- Residual solvent testing, if not previously performed or if batch-to-batch variability is a concern

Decision rule:
Any meaningful deviation from the verified sample profile or contaminant thresholds results in rejection of the bulk material.

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Release Criteria

Material is approved for controlled use under the protocol only if:

- Sample identity and lipid profile pass
- Sample contaminant screening passes
- Bulk identity and lipid profile pass
- Bulk contaminant screening passes

Residual solvent testing is performed either at the sample stage or the bulk stage, depending on supplier disclosure and initial analytical findings, but is not omitted if uncertainty remains.

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Summary

This staged verification approach prioritizes:

- identity confirmation before exposure
- contaminant screening before scale-up
- protection against batch substitution or drift

The pipeline is designed to be conservative, auditable, and responsive to uncertainty rather than assuming completeness of upstream documentation.

6. THE "TEST PILOT" RULE (FOR NIEVE)

Nieve does not take a single milligram until I have been on the full dose for 30 days with zero side effects. I am the Test Pilot; she is the passenger.

DOCUMENT 3: THE FINANCIAL BREAKDOWN

OPTION A: THE RETAIL TRAP (US CAPSULES)

The safe-looking bottle is actually a financial disaster.

Product: Standard Nervous System Support Capsules (Retail - Nervidyne)

Cost: $109.00 USD per bottle plus shipping equals approximately $155.00 CAD

Strength: 240 mg per capsule of Nervonic Acid (unverified purity)

Cost per capsule: $5.17 CAD

PATRICK COST (1 g target)

Dosage: 4 capsules per day (approximately 1 g)

Daily cost: $20.68

Monthly cost: $620.40

Annual cost: $7,548.00

NIEVE COST (0.5 g target)

Dosage: 2 capsules per day

Daily cost: $10.34

Monthly cost: $310.20

Annual cost: $3,774.00

TOTAL FAMILY BILL (RETAIL)

Monthly burn: $930.60

Yearly total: $11,167.00 CAD (recurring every year)

OPTION B: PROCUREMENT STRATEGY (DIRECT SOURCING)

Rather than purchasing a finished consumer product, the raw ingredient is sourced directly and treated analogously to a compounding or pharmacy-grade input. This allows independent verification of identity and lipid composition prior to use and avoids reliance on retail labeling or blended formulations.

Supplier and Pricing Context (WuXi Cima Science)

- Retail quotation (August 2025): $2,230 USD per kg
- Commercial quotation (January 2026): $1,490 USD per kg

By registering Elastic Soda Inc. as a legitimate business entity, access was granted to commercial pricing tiers typically available to research or pharmaceutical partners. No claims are made regarding endorsement or preferential treatment beyond standard wholesale eligibility.

Cost Sequence and Real-World Budget (Ontario, Canada)

1. Preliminary sample acquisition (required)

- Sample size: 20 g
- Quoted cost: $95 USD, door-to-door
- Tax / duty status: unclear (not specified whether HST or customs fees are included) *(This sample is required before committing to bulk procurement.)*

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2. Initial independent lipid testing (required)

Testing performed through *Lipid Labs, Mississauga (Ontario)*

- Test type: Full lipid panel, including chain-length verification (e.g., C26:0)
- Cost: $365 CAD + HST

(Used to confirm identity and lipid profile of the preliminary sample.)

3. Heavy Metal Testing: Practical Cost Estimate (Canada)

For raw lipid or chemical material intended for ingestion (not environmental samples), typical ICP-MS–based heavy metal panels include:

- Lead (Pb)
- Mercury (Hg)
- Arsenic (As)
- Cadmium (Cd)
- Sometimes additional metals depending on the lab

Typical cost range (Ontario / Canada)

- $200–$400 CAD per sample, before tax
- HST (13%) applies in most cases

Most realistic expectation

For a private analytical lab comparable to Lipid Labs:

- ~$250–$350 CAD + HST per test
- All-in estimate: ~$285–$395 CAD

Residual Solvent Testing (If Indicated)

If review of supplier documentation, manufacturing methods, or initial analytical findings raises uncertainty regarding solvent use, independent residual solvent testing will be performed prior to material release.

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4. Bulk raw material procurement

- Quantity: 1 kg
- Cost: $1,490 USD ≈ $2,150 CAD (exchange-rate dependent) Import taxes:
- HST (13 percent): ≈ $280 CAD

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5. Confirmatory independent lipid testing (required)

- Test type: Full lipid panel, including C26:0
- Cost: $365 CAD + HST

(Performed on the received bulk material to confirm consistency with the verified sample.)

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Residual Solvent Testing (If Indicated)

If review of supplier documentation, manufacturing methods, or initial analytical findings raises uncertainty regarding solvent use, independent residual solvent testing will be performed prior to material release.

For raw lipid or chemical materials, residual solvent analysis (e.g., GC-based panels covering common organic solvents) is typically priced as a separate assay.

Estimated cost (Ontario / Canada):

- Approximately $200–$400 CAD per sample, before tax
- HST (13%) applies in most cases

Residual solvent testing is expected to be required at most once per lot (either at the preliminary sample stage or on the bulk material, depending on timing and disclosure) and is therefore treated as a contingent, non-recurring cost rather than a baseline expense.

Contingent costs related to residual solvent testing, if required based on upstream findings, are not included in this baseline estimate and would increase total cost modestly.

Interpretation
This procurement strategy prioritizes verification, traceability, and analytical confirmation over cost minimization. Multiple independent lipid panels are required to confirm both identity and consistency of the material prior to use in an exploratory, non-commercial context. Costs are presented transparently and conservativel.

THE CONSUMPTION COST (1,000,000 mg or 1 kg)

Total fully tested, landed cost (estimate):
≈ $3,750 CAD Cost per gram:
$3,750 ÷ 1,000 g = $3.75 CAD per gram
(Includes sample, dual full lipid panels, import HST, and estimated heavy metal testing.)

PATRICK’S COST (1 g target) Dosage:
1,000 mg powder per day (1 g)

- Daily cost: $3.75
- Monthly cost (30 days): $112.50
- Annual cost: $1,368.75

NIEVE’S COST (0.5 g target) Dosage:
500 mg powder per day (0.5 g)

- Daily cost: $1.88
- Monthly cost (30 days): $56.25
- Annual cost: $684.38

(Per-day and per-person costs are based on the fully tested, landed cost amortized over the full supply.)

TOTAL FAMILY COST (WHOLESALE, DIRECT SOURCING)

- Combined daily burn: $5.63
- Monthly burn: $168.75
- Annual total: $2,053.13 CAD
  (Recurring cost equivalent, assuming ongoing resupply at similar pricing.)

These cost estimates reflect the fully tested, landed cost of Nervonic Acid only. Other baseline supportive supplements and the three components of the antioxidant protocol are already in use and are not included, as their incremental cost to add to Nieve's protocol is modest and not a primary driver of overall expense.

THE INVENTORY BONUS

Because the minimum order is 1 kg (1,000 g), the upfront purchase provides: •
Total daily family usage: 1.5 g/day

- Total supply duration:
  1,000 g ÷ 1.5 g/day ≈ 666 days

➡ Approximately 1.8 years of supply for the family from a single order.

THE VERDICT: BREAK-EVEN POINT

Retail option cost: ≈
$930 CAD per month
Direct sourcing option:
≈ $3,750 CAD upfront **Conclusion**

- Break-even point: ~4 months
- After month 4, the remaining ~1.4 years of supply represent net savings compared to retail pricing.

Estimated 2-year savings:
≈ $18,500–$19,000 CAD, depending on exchange rates and retail price stability.

*The duration of supply depends only on dosage and total quantity purchased, not on procurement or testing costs

DOCUMENT 4: THE INDUSTRY CONTEXT

THE "WHY" & THE "HOW"

A Summary of the Manufacturing History & Industry Safety Data

1. THE "MISSING LINK"

While Western medicine has focused on clinical applications, the Asian pharmaceutical industry has spent 30 years perfecting the extraction and safety profile of Nervonic Acid.

2. THE SOURCE: ACER TRUNCATUM

Our Nervonic Acid is not chemically synthesized. It is extracted from the seed oil of Acer Truncatum (Purpleblow Maple).

- The "Green" Extraction: Research teams at Zhejiang University developed the extraction technology to isolate high-purity Nervonic Acid from this plant, replacing unsustainable shark-derived sources.
- National Recognition: This process was designated a "National Key New Product" by the Chinese Ministry of Science in 2003.

3. INDEPENDENT CONFIRMATION OF MECHANISM

Industry data independently supports the proposed bioenergetic mechanism, demonstrating increased intracellular ATP production under oxidative stress conditions.

The Industry Finding: "Nervonic Acid promotes intracellular ATP production... providing cytoprotection against oxidative stress and preventing mitochondrial damage."

The Significance: This corroborates the University of Minnesota's 2025 findings on mitochondrial rescue.

4. ADDITIONAL SAFETY DATA (ANIMAL TOXICOLOGY)

- The Data: Mice fed a diet containing 0.6% Nervonic Acid for over 3 months showed no toxicity, no liver/kidney damage, and no adverse physical signs.
- Relevance: This supports the safety profile of our 1g/day protocol.

5. DISCLAIMER

Industry data are included for context regarding manufacturing and safety history, but do not substitute for peer-reviewed clinical evidence.

6. SUMMARY

We are sourcing a plant-derived, pharmaceutical-grade isolate of Nervonic Acid produced using extraction technologies developed through decades of national-level research in China on Acer truncatum seed oil.

While much of the historical Chinese research focused on Nervonic-Acid–rich oils and functional food preparations rather than purified isolates, this body of work established the safety profile, biological relevance, and scalable extraction methods that now make high-purity Nervonic Acid feasible.

In parallel, Western academic research is now defining the cellular, metabolic, and bioenergetic effects of isolated Nervonic Acid in disease-relevant models. Together, these lines of research link mature manufacturing capability in the East with emerging mechanistic and efficacy data in the West.

TECHNICAL SUMMARY & INTEGRATION

1. Purpose and Scope

This document presents a structured rationale for the exploratory use of Nervonic Acid as part of a combination strategy for adrenomyeloneuropathy, alongside established antioxidant support. It integrates peer-reviewed cellular, animal, and limited clinical evidence with manufacturing, safety, and sourcing considerations to define a protocol that is evidence-informed, conservative, and explicitly bounded by known limitations.

This is not a claim of clinical efficacy. It is a technical justification for a monitored, hypothesis-driven intervention in the absence of approved disease-modifying therapies.

2. Mechanistic Rationale

The scientific case rests on two complementary pathological targets.

First, Nervonic Acid is proposed as a structural and metabolic substrate relevant to myelin integrity and axonal energy function. Cellular studies in patient-derived models demonstrate reductions in toxic very long-chain fatty acid accumulation and providing structural support of mitochondrial ATP production, addressing both a defining biochemical abnormality and a downstream bioenergetic deficit observed in adrenomyeloneuropathy.

Second, oxidative stress and inflammatory signalling are addressed through a defined antioxidant combination with demonstrated biomarker normalization and functional stabilization in a Phase II clinical context. This component targets damage propagation rather than structural repair.

Together, this two-mechanism model distinguishes between structural support and protection, recognizing that antioxidant strategies have demonstrated meaningful protective and stabilizing effects in humans, while structural or reparative approaches have not yet been directly addressed in clinical trials.

Conceptual Illustration: Damage Containment vs Structural Support

To clarify the dual-mechanism framework, consider the distinction between limiting ongoing injury and addressing structural integrity.

1. Damage Propagation (Oxidative Injury)
Oxidative stress contributes to progressive axonal dysfunction by promoting cumulative cellular damage.

The antioxidant combination (N-acetylcysteine, alpha-lipoic acid, and vitamin E) is intended to reduce reactive oxygen species and limit secondary injury.
This strategy focuses on containing ongoing damage rather than reversing established structural loss.

2. Structural Lipid Availability (Myelin-Associated Support)
Demyelination reflects disruption of lipid-rich membrane architecture. Nervonic acid (C24:1), a long-chain monounsaturated fatty acid enriched in myelin, is proposed as a structural substrate relevant to membrane composition.

Providing substrate does not initiate remyelination or force oligodendrocyte differentiation. However, in the presence of preserved oligodendrocyte and precursor populations, adequate lipid availability may reduce the risk of structural insufficiency during endogenous maintenance processes.

Mechanistic Distinction

This two-mechanism model distinguishes between:

- Protection: Reducing oxidative stress and limiting damage propagation
- Structural Support: Avoiding substrate limitation in myelin-associated lipid biology

Antioxidant strategies have demonstrated biomarker normalization and signals of functional stabilization in humans. Structural lipid supplementation, by contrast, remains mechanistically plausible but has not yet been validated in controlled clinical trials for AMN.

Translational Context

Large-scale clinical trials are typically required before a compound becomes an approved prescription therapy. Phase 3 trials are expensive and are often funded when there is a clear pathway to regulatory exclusivity.

Natural or nutritionally derived compounds may have limited patent protection in their base form. This can reduce commercial incentive for large-scale trials, particularly in rare diseases.

As a result, mechanistic or early-phase findings do not always progress to late-stage clinical validation.

This absence of large trials should not be interpreted as proof of efficacy, nor as evidence of suppression. It reflects structural features of biomedical funding and drug development economics.

The current protocol operates within this translational gap. It applies available cellular, animal, and early human data in a monitored, hypothesis-driven framework, without presuming established clinical benefit.

1. Translation Strategy and Dose Logic

Because human dose-finding studies for isolated Nervonic Acid in adrenomyeloneuropathy do not yet exist, dose selection relies on translational inference from established demyelination models and pharmacokinetic data. These models provide a defensible exposure range rather than a prediction of clinical response.

The selected target dose reflects a conservative alignment with observed efficacy ranges in disease-relevant animal models, adjusted using standard interspecies conversion methods. Escalation beyond this range is conditional, exploratory, and contingent on the absence of adverse physiological drift.

Uncertainty regarding central nervous system exposure in humans is explicitly acknowledged, with the protocol structured to prioritize safety and peripheral monitoring rather than assumed central effects.

2. Safety Framework and Risk Containment

The protocol is designed around the principle that long-term risk is more likely to arise from gradual physiological drift than from acute toxicity. Accordingly, safety measures emphasize continuous monitoring of autonomic markers, sleep patterns, subjective neurological changes, and laboratory indices rather than reliance on short-term tolerance alone.

Historical concerns regarding structurally related fatty acids are addressed through modern understanding of species-specific lipid metabolism and supported by contemporary toxicology data for Nervonic-Acid–enriched diets. These data inform safety boundaries but do not substitute for human clinical outcomes.

For prophylactic use in a younger carrier, an additional safeguard is imposed through delayed initiation and reliance on real-world tolerability data from the primary subject.

3. Manufacturing, Sourcing, and Verification

High-purity Nervonic Acid is obtained through plant-based extraction methods developed and refined through decades of industrial and academic work on *Acer truncatum* seed oil. This manufacturing history supports scalability, purity, and safety but is not presented as evidence of therapeutic efficacy.

Independent verification through third-party analytical testing is required prior to use, ensuring identity and purity beyond manufacturer documentation. This verification step is treated as non-negotiable.

4. Limitations and Boundaries

Several limitations remain unresolved and are acknowledged explicitly:

- **Clinical efficacy in humans with adrenomyeloneuropathy has not Been Established**
- Central nervous system penetration in humans is inferred, not proven.
- Long-term outcomes beyond biochemical and functional proxies are unknown
- Individual variability in lipid handling and neurological response is Expected

Accordingly, this protocol is framed as investigational and adaptive, not definitive.

We are not inventing unsupported theory. We are applying existing mechanistic research in a monitored, hypothesis-driven way, while acknowledging that clinical efficacy remains unproven.

5. Integrated Conclusion

Taken together, the available evidence supports the plausibility of Nervonic Acid as part of a carefully monitored combination strategy addressing both metabolic dysfunction and oxidative injury in adrenomyeloneuropathy. The protocol prioritizes safety discipline, transparency of uncertainty, and verification at each step.

In the absence of approved disease-modifying treatments, this approach represents a rational attempt to align emerging mechanistic evidence with conservative real world application, while remaining open to revision as new data become available.

External Clinical Context

Brain MRI findings were independently reviewed by Dr. Wolfgang Köhler, a neurologist specializing in adrenoleukodystrophy (ALD). He confirmed the presence of cerebral lesions consistent with ALD that appear radiographically arrested at this time.

During discussion, the exploratory nature of this functional tracking approach was shared. While no clinical endorsement was implied, interest was expressed in being kept informed should longitudinal observations yield clinically relevant patterns.

DIGITAL MONITORING & DATA COLLECTION

To ensure strict adherence, safety monitoring, and rigorous data capture, this protocol utilizes a custom-built tracking application. This platform logs daily dosage, qualitative metrics (gait analysis, energy levels), and potential side effects in real-time.

Access The Patient Monitoring Portal: https://elastic-amn-protocol.netlify.app/

REFERENCES

Nervonic Acid, VLCFAs, and AMN / ALD Mechanisms

1. Kartha RV, et al. Nervonic Acid attenuates accumulation of very longchain fatty acids in adrenomyeloneuropathy patient-derived fibroblasts. ***J Lipid Res*. 2022.**
2. Lund TC, Kartha RV, et al. Nervonic Acid improves mitochondrial bioenergetics and ATP production in adrenomyeloneuropathy fibroblasts. ***Biochim Biophys Acta Mol Basis Dis*. 2025.**
3. Kemp S, et al. ABCD1 mutations and the pathophysiology of X-linked adrenoleukodystrophy. ***Biochim Biophys Acta*. 2012.**
4. Pujol A, et al. Oxidative stress and mitochondrial dysfunction in adrenoleukodystrophy. ***Free Radic Biol Med*. 2014.**

Demyelination Models and Dose Translation (EAE / MS)

5. Li C, et al. Nervonic Acid regulates oxidative imbalance and clinical severity in experimental autoimmune encephalomyelitis. ***Neurochem Int*. 2021.**
6. Gold R, et al. Animal models for autoimmune demyelinating disease. ***Nat Rev Neurosci*. 2006.**
7. Reagan-Shaw S, Nihal M, Ahmad N. Dose translation from animal to human studies revisited. ***FASEB J*. 2008.**

Pharmacokinetics and Blood–Brain Barrier Penetration

8. Li C, et al. Pharmacokinetics and tissue distribution of Nervonic Acid in an adrenoleukodystrophy mouse model. ***AAPS PharmSciTech*. 2023.**
9. Banks WA. Characteristics of compounds that cross the blood– brain barrier. ***BMC Neurol*. 2009.**
10. Pardridge WM. Drug transport across the blood–brain barrier. ***J Cereb Blood Flow Metab*. 2012.**

Antioxidant Therapy in AMN

11. Pujol A, et al. Biomarker identification, safety, and efficacy of high-dose antioxidants for adrenomyeloneuropathy. ***Orphanet J Rare Dis*.**

2019.
12. Trushina E, et al. Oxidative stress and mitochondrial dysfunction in neurodegeneration. ***Antioxid Redox Signal*. 2013.**
13. Ziegler DR, et al. Alpha-lipoic acid and mitochondrial redox regulation. ***Biochim Biophys Acta*. 2016.**

Acer truncatum, Extraction, and Manufacturing Context

14. Wu X, et al. Nervonic Acid-rich oil from ***Acer truncatum*: extraction and compositional analysis. *J Am Oil Chem Soc*. 2015.**
15. Zhang Y, et al. Green extraction technology for Nervonic Acid from ***Acer truncatum* seed oil. *Food Chem*. 2017.**
16. Liu R, et al. Nutritional and functional properties of ***Acer truncatum* seed oil. *J Food Sci*. 2018.**
17. Ministry of Science and Technology of the People's Republic of China. National Key New Product designation for ***Acer truncatum* Nervonic Acid extraction technology. 2003.**

Safety, Toxicology, and Lipid Metabolism

18. Beare-Rogers JL, et al. Erucic acid metabolism and myocardial lipidosis: species differences. ***Lipids*. 1974.**
19. Houtsmuller UMT, et al. Effects of dietary very-long-chain fatty acids in humans. ***Am J Clin Nutr*. 1980.**
20. Chen X, et al. Subchronic toxicity evaluation of Nervonic Acidenriched diets in mice. ***Regul Toxicol Pharmacol*. 2019.**
21. EFSA Panel on Dietetic Products. Scientific opinion on long-chain fatty acids and safety thresholds. ***EFSA J*. 2016.**

Supporting Myelin and Lipid Biology

22. Saher G, Simons M. Cholesterol and myelin biogenesis. ***Nat Rev Neurosci*. 2010.**
23. Nave KA, Werner HB. Myelination of the nervous system: mechanisms and functions. ***Annu Rev Cell Dev Biol*. 2014.**
24. Chrast R, et al. Lipid metabolism in myelinating glial cells. ***J Lipid Res*. 2011.**

APPENDIX A: MANUFACTURER CERTIFICATION DATA

1. MOA (Test Method of Nervonic Acid)

Test Method of Nervonic Acid

1. Principle

1.1 Hydrolysis-Extraction Method: The sample undergoes hydrolysis followed by fat extraction with an ether solution. The fat is then saponified and methylated under alkaline conditions to generate fatty acid methyl esters (FAMEs). These are analyzed by capillary column gas chromatography and quantified using the external standard method.

Pure animal and vegetable oil/fat samples undergo direct saponification and fatty acid methylation without prior fat extraction.

1.2 Acetyl Chloride-Methanol Method (Applicable to milk powder and anhydrous milk fat samples with water content < 5%): The fat and free fatty acids are methylated using hydrochloric acid-methanol generated from the reaction of acetyl chloride with methanol. After extraction with toluene, separation and detection are performed by gas chromatography, quantified using the external standard method.

1.3 Transesterification Method (Applicable to oils/fats with free fatty acid content ≤ 2%): The oil/fat is dissolved in isooctane. Potassium hydroxide methanol solution is added for transesterification methylation. After the reaction is complete, sodium bisulfate is added to neutralize the remaining potassium hydroxide. Fatty acid content is determined using the external standard method.

2. Reagents and Materials

Unless otherwise specified, all reagents used in this method are of analytical grade, and water is Grade I water as specified in GB/T6682.

2.1 Reagents
2.1.1 Hydrochloric acid (HCl).
2.1.2 Ammonia solution ($NH_3 \cdot H_2O$).
2.1.3 Pyrogallic acid ($C_6H_6O_3$).
2.1.4 Diethyl ether ($C_4H_{10}O$).
2.1.5 Petroleum ether: Boiling range 30°C ~ 60°C.
2.1.6 Ethanol (C_2H_6O) (95%).
2.1.7 Methanol (CH_3OH): Chromatographic grade.
2.1.8 Sodium hydroxide (NaOH).
2.1.9 n-Heptane ($CH_3(CH_2)_5CH_3$): Chromatographic grade.

ed for 3 months.
solution: Select the corresponding
of fatty acids to be analyzed in the
priate concentrations using toluene

es
tion Detector (FID).
y polar stationary phase of
internal diameter 0.25 mm, film

ure control range 40°C ~ 100°C.

pe): 15 mL.

ration should be avoided. Solid or
nder/pulverizer. Liquid samples are
y -18°C, thaw before analysis.

od)
le portion of 0.1 g ~ 10 g (precise to
of fat) into a 250 mL flat-bottomed
few boiling chips, then 2 mL of 95%
ethod based on the sample type.

ose): Add 10 mL of hydrochloric acid
water bath for 40 min, shaking every

mmonia solution, mix well. Place in a
. Cool.
monia solution, hydrolyze 20 min at
tion, continue hydrolysis for 20 min.

Cool.

4.2.3 Fat Extraction: Add 10 mL of 95% ethanol to hydrolysate, mix. Transfer to separatory funnel, rinse with 50 mL ether-petroleum ether mixture, shake 5 min, settle 10 min. Collect ether layer. Repeat extraction 3 times. Combine extracts, evaporate to dryness using rotary evaporator.

4.2.4 Fat Saponification and Fatty Acid Methylation: Add 8 mL of 2% sodium hydroxide methanol solution to fat extract, reflux at 80°C±1°C until oil drops disappear. Add 7 mL of 15% boron trifluoride methanol solution through condenser, reflux 2 min. Cool. Add 10-30 mL n-heptane, shake 2 min. Add saturated NaCl solution, settle. Transfer ~5 mL upper layer to tube with 3-5 g anhydrous Na_2SO_4, shake, settle. Use supernatant for GC.

- For pure oils/fats: Proceed directly to saponification/methylation without prior fat extraction.

4.3 Sample Pretreatment (Acetyl Chloride-Methanol Method)

4.3.1 Sample Weighing: Accurately weigh milk powder (0.5 g) or anhydrous milk fat (0.2 g) into a dry 15 mL screw-thread glass tube. Add 5.0 mL toluene.

4.3.2 Preparation of Sample Test Solution: Add 6 mL of 10% acetyl chloride methanol solution, purge with N_2, tighten cap. Shake, place in 80°C±1°C bath for 2 h, shaking every 20 min. Cool. Transfer to 50 mL centrifuge tube, rinse tube 3 times with 3 mL sodium carbonate solution (6%), combine washings. Centrifuge at 5000 r/min for 5 min. Use supernatant for GC.

4.4 Sample Pretreatment (Transesterification Method)

4.4.1 Sample Weighing: Weigh 60.0 mg sample (precise to 0.1 mg) into a stoppered test tube.

4.4.2 Methyl Ester Preparation: Add 4 mL isooctane to dissolve sample (warm if needed). Add 200 μL potassium hydroxide methanol solution (2 mol/L), stopper, shake vigorously 30 s. Let stand until clear. Add ~1 g sodium bisulfate, shake to neutralize. After salt precipitates, transfer upper solution for GC.

4.5 Preparation of Standard Test Solution

Accurately pipette 0.5 mL of the fatty acid triacylglycerol standard working solution and perform the same pretreatment steps as described in section 4.4.2.

4.6 Chromatographic Determination

4.6.1 Chromatographic Reference Conditions:

a) Capillary column: poly(cyanopropyl)siloxane, 100 m × 0.25 mm, 0.2 μm film.

b) Injector: 270°C.

c) Detector (FID): 280°C.

d) Oven: 100°C (hold 13 min) → 180°C @ 10°C/min (hold 6 min) → 200°C @ 1°C/min (hold 20 min) → 230°C @ 4°C/min (hold 10.5 min).

e) Carrier gas: Helium.

f) Split ratio: 100:1.

g) Injection volume: 1.0 μL.

h) Performance: Theoretical plates (n) ≥ 2000/m, resolution (R) ≥ 1.25.

4.6.2 Injection: Inject the standard test solution and sample test solutions separately under the above conditions.

5. Calculation

5.1 Content of Each Fatty Acid

Quantify using chromatographic peak area. The content of each fatty acid in the sample is calculated as:

$$X_i = \frac{A_i \times m_{Si} \times F_{TG_i\text{-}FA_i}}{A_{Si} \times m} \times 100$$

Where:

X_i = Content of fatty acid i in sample, g/100g

A_i = Peak area of fatty acid methyl ester i in sample test solution

m_{Si} = Mass of reference standard in the pipetted volume of fatty acid triacylglycerol standard working solution used for standard test solution preparation, mg

$F_{TG_i\text{-}FA_i}$ = Conversion factor from fatty acid triacylglycerol to fatty acid (see Appendix D of GB 5009.168-2016)

A_{Si} = Peak area of fatty acid i in standard test solution

m = Mass of sample weighed, mg

5.2 Total Fatty Acid Content

$$X_{Total\,FA} = \sum X_i$$

Where:

$X_{Total\ FA}$ = Total fatty acid content in sample, g/100g

X_i = Content of each fatty acid in the sample, g/100g

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Certificate of Analysis

Product and Batch Information			
Product Name:	Nervonic Acid	Country of Origin:	P.R. China
CAS No.:	506-37-6	Molecular Weight:	366.62
Molecular Formular:	$C_{24}H_{46}O_2$	Batch:	CS-NA-251128
Manufacture Date:	Nov 28, 2025.	Expired Date:	Nov 27, 2027.

Item	Specification	Result	Test Method
Active Ingredeints			
Assay(%)	NLT98.0%	98.20%	GC
Physical Control			
Appearance	Crystal Powder	Complies	Visual
Color	White to Off white	Complies	Visual
Identification	Positive	Complies	IR&1H NMR
Melting Point(°C)	41.0-43.8°C	42.8-42.5°C	Melting cryoscope
Loss on Drying	3.0% Max	0.13%	CP%
Chemical Control			
Heavy metals	NMT 10PPM	Conforms	CP%
Arsenic (As)	NMT 1PPM	Conforms	CP%
Mercury (Hg)	NMT 0.5PPM	Conforms	CP%
Cadmium (Cd)	NMT 1PPM	Conforms	CP%
Solvent Residue	NMT 10PPM	Conforms	CP%
Microbiological Control			
Total Plate Count	1000cfu/g Max	Conforms	CP%
Yeast & Mold	100cfu/g Max	Conforms	CP%
E.Coli	Negative/10g	Conforms	CP%
Salmonella sp.	Negative/25g	Conforms	CP%
Staph Aureus	Negative/10g	Conforms	CP%
Packing and Storage			
Packing	20kg/ fibre drum double-deck plastic bag inside		
Storage	Store in a well-closed container away from [illegible] light.		
Shelf Life	2 years if sealed and stored properly.		

QC Passed

2. **COA (Certificate of Analysis)**

3. **Chromatogram (Raw DataSource: Shimadzu LabSolutions Analysis Report**