MHSRS 2026

NANOPHARMA SOLUTIONS

Nasal Riluzole for Acute TBI

William Martin | bill@nanopharmasolutions.com

Acknowledgements

Contributing on behalf of Transforma Bio, Inc. f/k/a Nano PharmaSolutions, Inc.

- Kay Olmstead, CEO

Disclosures

William Martin discloses the following relationships

- Consultant (Interim COO) for Transforma Bio, Inc. f/k/a Nano PharmaSolutions, Inc.
- Owner of pharmaceutical advisory firm WKM BIO Consulting, LLC (dba Point Forward Bio)

Kay Olmstead, PhD discloses the following relationship

- Employee (CEO / founder) of Transforma Bio, Inc. f/k/a Nano PharmaSolutions, Inc.

TBI Unmet Need:
Early therapeutic intervention

Within minutes of impact, a self-amplifying injury cascade is set in motion — *the earliest ionic and excitotoxic events are the most reversible.*

Pathologic Na^+ influx[1]	Glutamate release[2]	Calcium overload[3]	Neuro-inflammation[4]	Cerebral edema[5]
SECONDS	SECONDS–MINUTES	MINUTES	HOURS–DAYS	HOURS–DAYS
Membrane mechanoporation → depolarization	NMDA / AMPA over-activation	Enzyme cascades, mitochondrial failure	Microglial activation, cytokine release	Cytotoxic → vasogenic swelling, ↑ ICP

GOLDEN HOUR — injury cascade still interruptible → **Secondary injury entrenched →**

Early intervention in the golden hour targets the upstream, reversible triggers — before neuroinflammation and cerebral edema become self-sustaining.

Riluzole: multi-modal neuroprotective agent ideal for prevention of injury cascade

Oral riluzole — FDA-approved 1st-line therapy for ALS · well-characterized human safety profile

MECHANISMS OF ACTION

- **Use-dependent Na^+-channel blockade**[6]
- **↓ Presynaptic glutamate release**[7]
- **↑ Astrocytic glutamate clearance (GLT-1 / EAAT2)**[8]
- **TREK-1 / TRAAK K^+-channel activation**[9]

CONFER NEUROPROTECTION

1. **Ischemia / excitotoxic injury**[10,11]
2. **Oxidative stress**[12,13,14]
3. **Inflammatory / glial stress**[15,16,17]
4. **Brain swelling / BBB injury**[18,19,20]

Single-dose safety: riluzole's established ALS profile carries minimal acute risk — its principal chronic caution (transient hepatic enzyme elevation)[16] is largely irrelevant to one-time field dosing; acute-SCI trials showed no rise in adverse events or mortality vs placebo.[21,22]

Riluzole: role in trauma-related neuroprotection

Reproducible neuroprotection across acute CNS trauma · consistent benefit in TBI and SCI models

TRAUMATIC BRAIN INJURY — rat models[23,24]

Lesion volume ↓ ~44%

+ improved neurological function (lateral fluid-percussion model)

First dose: 15 min

↓ Motor & cognitive deficits

+ reduced regional cerebral edema & histologic cell damage (n = 109)

First dose: 15 min

SPINAL CORD INJURY — human evidence[21,25]

First Phase III RCT — RISCIS

Acute cervical tSCI (AIS A–C, dosed < 12 h); favorable neurological outcomes

First dose: <12h

Pooled meta-analysis (5 studies)

↑ ASIA motor & AIS conversion;

safe — no rise in AEs or mortality vs control

First dose: 12 – 96h

Therapeutic window 1–6 h post-injury[26]
in TBI models — consistent with an acute, field-rescue treatment concept.

Riluzole: first randomized trial in TBI

The first randomized controlled trial of riluzole in acute traumatic brain injury.

Severe-TBI RCT — n = 160 (GCS ≤ 8) - *Shojaei et al. BMC Neurol. 2026;26(1):379.*[22]

Design: adjunctive riluzole (50 mg) vs placebo + guideline-based standard care.

Result: primary cognitive endpoint (MoCA, day 28) trended in riluzole's favor

functional outcomes, edema progression and length of stay were comparable.

Safety: safe — no drug-related serious adverse events.

Timing: median time to initial dosing ~9 h; authors note benefit may require optimized timing, dosing and patient selection.

This trial's ~9 h median dosing fell outside the ideal window for riluzole TBI treatment. **Rapid, field-deployable delivery of riluzole can treat within that window to minimize brain injury threat to the force, maintain readiness, and preserve operational effectiveness.**

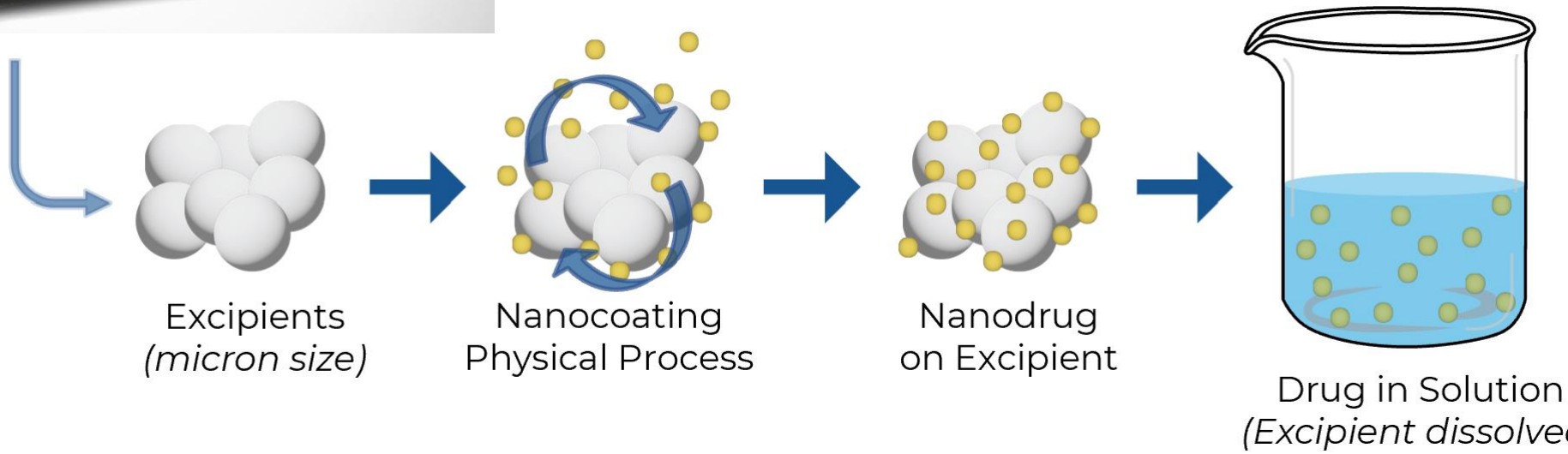
Opportunity:
Rapid Field-deployable Riluzole for TBI

- **Goal:** Easy-to-use fast-acting riluzole / device with good SWaP characteristics
- **Nasal riluzole offers:**
  - ✓ **Safety** when administered acutely – reduce the diagnostic / decision-making burden
  - ✓ **Non-oral** dosage form for unconscious victims
  - ✓ **Needle-free** delivery that can be administered without extensive preparation or training
  - ✓ **Portable** and shelf-stable system without complex storage requirements
- **Obstacle:** Riluzole's poor solubility limits routes of administration (e.g.; oral, IV)

Improving solubility of riluzole for nasal administration
will allow for potential field-deployable neuroprotection that prevents long-term damage and faster return-to-duty

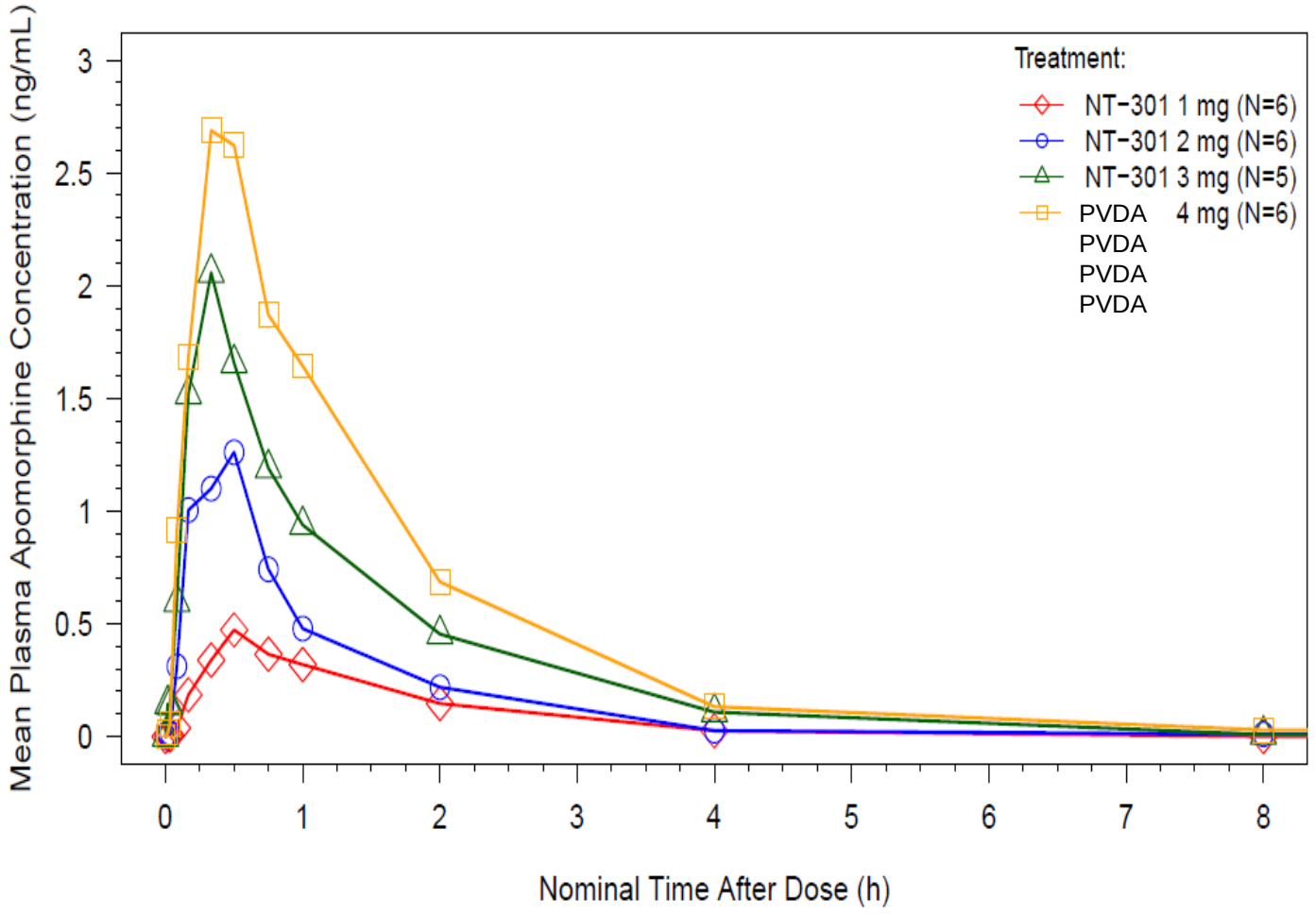
Solution:
Solvent-free Physical Vapor Deposition (PVD)

Using **high vacuum** to evaporate drugs, nano-coating of drugs on sugar spheres *(excipient drug carrier granule)*



Clinically validated technology:
Nasal PVD apomorphine Ph1 data

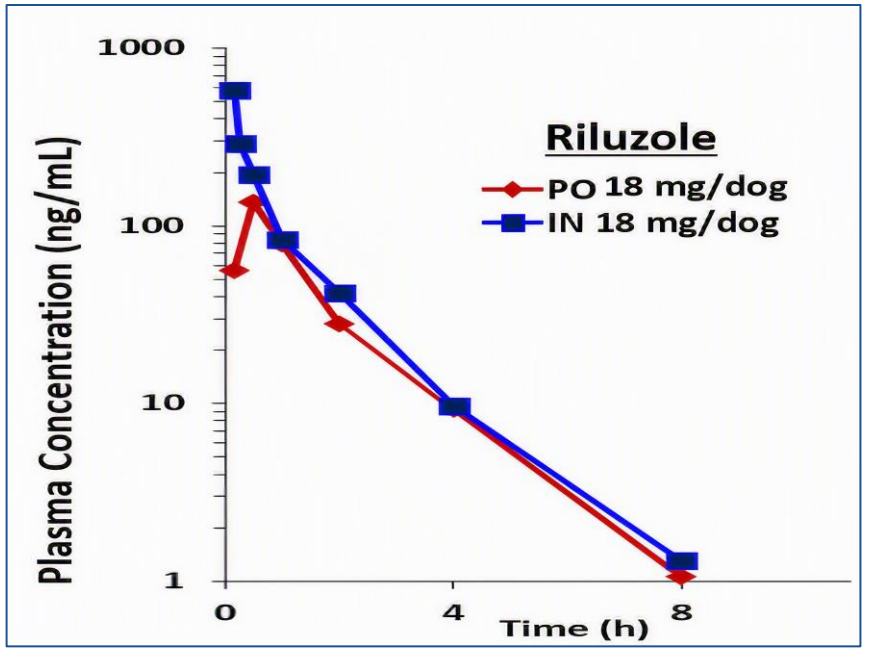
- PVD apomorphine dry powder nasal spray (PVDA)
- Fast absorption (T_{max} 20 min)
- Dose proportional absorption
- No significant AEs



PVD riluzole:
Single-use nasal spray

- **Better bioavailability** of riluzole than oral route in dogs
- **Human factor** is negligible for single-dose dry powder nasal delivery
- **Small and Portable** – using a commercially available TLR5 device
- **Stable** at room temp.

- Nasal T_{max} of less than 15 minutes (earliest-sampled timepoint) vs oral T_{max} of 30 minutes
- Nasal **AUC** 1.8x of oral



Riluzole nanosizing approaches:
Stability for field use / transport / storage

PVD nanosized dry powder has inherent advantages for portable field-stable use

	PVD dry powder spray	Aqueous solution nasal spray
Chemical stability	▪ Eliminates water, slowing degradation	▪ Vulnerable to aqueous hydrolysis, chemical oxidation of riluzole, or microbial growth
Mechanical stability	▪ Phase stable – cannot "cream" or "break"	▪ Extreme environmental changes can cause separation
Thermal stability	▪ Immune to phase separation from freezing or heating	▪ Can break at extreme temperatures due to surfactant desolvation

PVD Dry powder nasal spray is the ideal dose-form for long-term deployment in extreme conditions – validating with further stability data

Next Steps:
PVD riluzole nasal spray path to IND

1. Optimize riluzole nanosizing & formulation stability (target 20% w/w) and analytical release-testing methods, incl. pre- and post-actuation particle size and aerodynamic performance — **6 mo**
2. Conduct a GLP 30-day nasal safety & toxicokinetic rat study supporting the 505(b)(2) route-of-administration change — **7 mo**
3. Tech transfer and manufacture GMP clinical supplies and placebo, with release and stability testing per USP<601> — **8 mo**
4. Prepare and submit an initial IND application following a pre-IND FDA consultation

Primary technical risks – scalable nanosizing, formulation stability, dose consistency, and nasal absorption variability – are mitigated through Quality-by-Design process control, validated analytical methods, stress-condition stability testing, GLP toxicology, and early FDA engagement for regulatory alignment.

Management Team

Kay Olmstead

CEO: PhD, MBA

Successfully led 5 drugs through FDA approval

DR. S. Shrewsbury

Interim CMO

Medical Affairs
Glaxo, Chiron, Impel, etc.

Bill Martin

COO: MBA

Cofounder of multiple Life Science Startups

Justin Cho

CBO: PhD

CEO of IAPB
Early-stage incubator

Strong Technical Team & Business Development

La Jolla Pharmaceutical · Conatus Pharmaceuticals · Santarus, Inc. · KIST · Intercept · Tocagen · MAP Pharmaceuticals, Inc. · Impel Pharmaceuticals · Corthera · Syndax · adynxx · BCG

Clinical Team

DR. M. Fehlings

Department of Surgery
Univ. of Toronto

Deb Gessner

Regulatory Lead
for 3 Approved Drugs

Kelsey Satterly

Intranasal CNS drug and PD expertise

Mira Huyghe

Clinical Lead
for 2 Approved Drugs

Track record of success in 505(b)(2) development

Neuroprotection at the Point of Injury

- PVD riluzole – clear mechanistic rationale for early therapeutic neuroprotective intervention
- Rapid intervention during the golden hour 1–2 hr after injury
- Needle-free battlefield administration of single-use spray
- Portable and Stable – SWaP characteristics
- Designed for Austere and Prolonged field care environment
- TRL 5 Component validated in relevant environment

The military is uniquely positioned to evaluate early neuroprotective interventions, given access to time-critical combat casualty populations and established emergency research infrastructure.

References

1. Wolf JA, et al. J Neurosci. 2001;21(6):1923–1930.
2. Yi JH, Hazell AS. Neurochem Int. 2006;48(5):394–403.
3. Weber JT. Front Pharmacol. 2012;3:60.
4. Shao F, et al. Front Aging Neurosci. 2022;14:825086.
5. Jha RM, Kochanek PM, Simard JM. Neuropharmacology. 2019;145(Pt B):230–246.
6. Benoît E, Escande D. Pflugers Arch. 1991;419(6):603–609.
7. Chéramy A, et al. Neurosci Lett. 1992;147(2):209–212.
8. Carbone M, Duty S, Rattray M. Neurochem Int. 2012;60(1):31–38.
9. Duprat F, et al. Mol Pharmacol. 2000;57(5):906–912.
10. Pratt J, et al. Neurosci Lett. 1992;140(2):225–230.
11. Mottet I, et al. MAGMA. 1997;5(3):185–191.
12. Wang et al. Int J Clin Exp Med. 2018.
13. Carbone M, Duty S, Rattray M. Neurochem Int. 2012;60(1):31–38.
14. Liu AY, et al. J Biol Chem. 2011;286(4):2785–2794.
15. Kyllo T, et al. Front Pharmacol. 2024;15:1466953.
16. Carbone M, Duty S, Rattray M. BMC Neurosci. 2012;13:38.
17. McIntosh TK, et al. J Neurotrauma. 1996;13(12):767–780.
18. Bareyre F, et al. J Neurotrauma. 1997;14(11):839–849
19. Stover JF, et al. J Neurotrauma. 2000;17(12):1171–1178.
20. Rilutek (riluzole) prescribing information. Covis Pharma; 2016.
21. Fehlings MG, et al. J Neurotrauma. 2023;40(17–18):1878–1888.
22. Shojaei SH, et al. BMC Neurol. 2026;26(1):379.
23. Wahl F, et al. Brain Res. 1997;756(1–2):247–255.
24. McIntosh TK, et al. J Neurotrauma. 1996;13(12):767–780.
25. Weisbrod LJ, et al. Neurotrauma Rep. 2024;5(1).
26. Wahl F, et al. Acta Neurochir Suppl. 1999;73.

Nasal riluzole for acute TBI