TREK-1 INHIBITOR PEPTIDE

PE-22-28

Spadin analog, BL-1028

Molecular Formula	C89H132N24O19S2
Molecular Weight	2097.3 Da
Sequence / Structure	GEGLGLGKEEEEGGLGKEE
Category	TREK-1 Inhibitor Peptide
Available Specifications	2mg vial, 5mg vial (custom order)

1. OVERVIEW

PE-22-28 (also known as Spadin or BL-1028) is a peptide-based TREK-1 (tandem of pore domains in a weakly inducible K channel) inhibitor derived from spider venom. TREK-1 is a mechanosensitive potassium channel implicated in mood regulation and anxiety. PE-22-28 selectively blocks TREK-1, enhancing serotonergic neurotransmission and producing rapid antidepressant effects without monoamine oxidase inhibition.

2. MECHANISM OF ACTION

PE-22-28 inhibits the TREK-1 potassium channel, reducing K+ efflux and increasing neuronal excitability in serotonergic dorsal raphe neurons. This enhances serotonin release and availability in depression-relevant circuits. TREK-1 is also involved in pain modulation; channel inhibition may contribute to analgesic effects. The peptide crosses the blood-brain barrier via carrier-mediated transport.

3. CLINICAL EVIDENCE & RESEARCH

Preclinical studies in rodent depression models show rapid (within 30 minutes) and sustained antidepressant effects with a single injection. Electrophysiology confirms increased serotonergic neuron firing. No tolerance development observed over 28 days of repeated dosing. Phase 1 human trials demonstrate safety and CNS penetration.

4. THERAPEUTIC BENEFITS

- Rapid onset of antidepressant effect (minutes to hours)
- Novel mechanism distinct from SSRIs/SNRIs
- Potential anxiolytic and analgesic properties
- No monoamine oxidase inhibition
- No sexual dysfunction or weight gain
- Reduced suicide risk vs. conventional antidepressants
- No tolerance development with chronic use

5. INDICATIONS

- Major depressive disorder, particularly treatment-resistant cases
- Rapid-onset depression (acute crisis)
- Anxiety disorders (GAD, social anxiety)
- Chronic pain syndromes with comorbid depression
- Post-traumatic stress disorder (PTSD)
- Suicidal ideation or behavior

6. DOSING & ADMINISTRATION PROTOCOL

Indication	Dose	Route	Frequency	Duration
Initial dose	2mg	IV/SC	Once	Single dose
Maintenance	2mg	IV/SC	Once weekly	8 weeks
Chronic therapy	2mg	IV/SC	Twice weekly	Open-ended

Reconstitution

Reconstitute with sterile PBS (pH 7.4) or 0.9% saline. Stable 24 hours at room temperature, 7 days at 2-8°C. Solution should be colorless to pale yellow.

Administration

IV infusion over 10-15 minutes in 10mL PBS. SC injection into abdomen or thigh. Intranasal formulation in development.

Protocol Notes

Antidepressant effects typically manifest within 30 minutes to 4 hours post-administration. Sustained effect extends 24-72 hours. No interactions with conventional antidepressants; may combine for enhanced response.

7. SIDE EFFECTS & SAFETY PROFILE

- Mild headache (transient)
- Dizziness or lightheadedness
- Transient increase in anxiety (paradoxical, rare)
- Sleep disturbance (usually transient)
- Mild nausea
- Injection site reactions (rare)

8. CONTRAINDICATIONS & PRECAUTIONS

- Bipolar disorder (risk of manic induction)
- Active psychosis (may worsen)
- Uncontrolled hypertension
- Recent MI or unstable angina
- Hypersensitivity to peptide products
- Concurrent use of monoamine oxidase inhibitors

Drug Interactions

Safe to combine with SSRIs, SNRIs, tricyclic antidepressants. No significant CYP450 interactions. Avoid simultaneous administration of other TREK inhibitors.

9. STORAGE & HANDLING

Lyophilized: -20°C long-term, 2-8°C short-term. Reconstituted: 24 hours room temperature, 7 days at 2-8°C. Protect from light.

10. KEY REFERENCES

1. Djillani A, et al. Spadin as antidepressant. Neuropharmacology. 2018;138:72-82.
2. Chen X, et al. TREK-1 inhibition produces antidepressant effects. Transl Psychiatry. 2018;8(1):63.
3. Heurteaux C, et al. TREK-1 in mood regulation. Nat Rev Neurosci. 2014;15(3):167-177.
4. Wulff H, et al. Potassium channels in neuropsychiatry. Nature Rev. 2015;16(1):21-36.
5. Calabrese F, et al. Neurobiology of rapid-acting antidepressants. Neuropharmacology. 2017;113:216-225.

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