



# Recent, Current and Future Treatment Trials in PSP

**Lawrence I. Golbe, MD**

**Chief Clinical Officer**  
**Chair, Scientific Advisory Board**  
*CurePSP*  
*New York, NY*

**Emeritus Professor of Neurology**  
*Rutgers Robert Wood Johnson*  
*Medical School*  
*New Brunswick, New Jersey*

# “Treatment”

## A Dictionary

(Red: to be discussed now)



### Symptomatic/Palliative

- Symptomatic/palliative
  - **Addresses symptoms only**
- Examples for PSP:
  - L-DOPA for slowness/stiffness
  - sleeping meds
  - bladder control meds

### Neuroprotective/Preventive

- Primary: Prevents disease from developing in healthy people
- **Secondary: Slows or halts worsening in people with the disease**

### Curative

- Reversing the disease progression OR
- Halting progression with repair of existing damage

Past double-blind neuroprotection trials in PSP  
 None showed benefit in slowing progression.



Drug	Year	Mechanism	Comments
Riluzole	2009	Multiple possible mechanisms	Slows progression of ALS slightly
Davunetide	2014	Trophic factor (stimulates brain cell growth)	
Tideglusib <sup>T</sup>	2014	Inhibits tau phosphorylation by GSK3-β	Only MRI showed mild benefit
Rasagiline	2016	Monoamine oxidase inhibitor; trophic factor	Approved for symptoms of PD
Valproic acid <sup>T</sup>	2016	Inhibits tau phosphorylation by GSK3-β	Poorly tolerated
TPI-287	2019	Stabilizes microtubules	Related to taxol, a cancer drug
Young plasma	2020	Cell signaling; others?	
Salsalate acid <sup>T</sup>	2020	Reduces tau acetylation	NSAID approved in Europe
Gosuranemab <sup>T</sup>	2021	Monoclonal antibody vs tau N-terminal	PASSPORT study
Tilavonemab <sup>T</sup>	2021	Monoclonal antibody vs tau N-terminal	ARISE study
RT-001	2023	Protects membrane lipids vs free radicals	Deuterated linoleic acid

<sup>T</sup> = tau-protein-directed

## Active NEUROPROTECTION Trials in PSP (Slide 1 of 2)



Treatment	Sponsor	Phase	Mechanism	Location(s)	Dosing route	Still recruiting?	Comments
<b>Fasudil</b>	Woolsey	2a	Rho kinase inhibitor (indirectly reduces p-tau)	UCSF	Oral	No	Completion 11/2023; N = 15; open-label; PSP and CBS
<b>TPN-101</b>	Transposon	2a	Reverse transcriptase inhibitor (anti-inflammatory)	Boca Raton, FL Farmington Hills, MI Las Vegas, NV Gainesville, FL Englewood, CO	Oral	No	30 patients on drug, 10 on placebo; analysis completion 7/2023
<b>NIO-752</b>	Novartis	1	Anti-sense oligonucleotide reduces tau production	<b>Southampton</b> 4 in US 5 in Germany 2 in Canada	Intra-thecal infusion	Yes	4 infusions over 3 months; Completion in May 2024

## Active NEUROPROTECTION trials in PSP (Slide 2 of 2)



Treatment	Sponsor	Phase	Mechanism	Location(s)	Dosing route	Still recruiting?	Comments
<b>RT-001</b>	BioJiva (product from Retrotope)	1b	Reduces lipid peroxidation, enhancing mitochondrial activity	Munich, Germany	Oral	No	Di-deuterated linoleic acid ester. Early Phase 1 showed benefit but Phase 1b trial did not. Early trial in ALS was positive.
<b>AZP2006</b>	AlzProtect	1	Neurotrophin inducer	3 in France	Oral solution	No	~24 patients on drug, 12 on placebo
<b>Bepranemab</b>	UCB	1	Monoclonal anti-C-terminal tau antibody	11 European sites, including <b>Southampton</b>	IV	No	N = 25; double-blind
<b>Sodium selenate</b>	Govt of Australia	2	Reduces phospho-tau	6 sites in Australia	Oral	Yes	Recruiting

## Active SYMPTOMATIC trials in PSP (Slide 1 of 2)



Treatment	Sponsor	Phase	Mechanism	Location(s)	Dosing route	Still recruiting?	Comments
<b>Atomoxetine (Strattera)</b>	Cambridge University	2a	Inhibits presynaptic NE re-uptake	Cambridge, UK	Oral	Yes	For anxiety; Noradrenaline for PSP Syndromes (NORAPS).
<b>Suvorexant (Belsomra) and zolpidem (Ambien)</b>	UCSF; US Dept of Veterans' Affairs	4	2 approved sleep aids never before evaluated in PSP	All evaluations are remote; US only	Oral	Yes	For sleep; Completion in May 2024.
<b>Expiratory muscle strength training</b>	Kliniken Beelitz	N/A	Exercise	3 in Germany		Yes	For dysphagia; 4R tauopathies, MSA and PD; 2-week training program; N=75
<b>Physical therapy</b>	Univ of Innsbruck	N/A	Exercise	Innsbruck, Austria		Yes	For gait; Double-blind; N=180; MSA-P, PD, PSP

## Active SYMPTOMATIC Trials in PSP (Slide 2 of 2)

Treatment	Sponsor	Phase	Mechanism	Location(s)	Dosing route	Still recruiting ?	Comments
Transcranial magnetic stimulation	Oregon Health & Science U; NIH	N/A	Unclear	Portland OR	Non-invasive magnetic field	Yes	Completion in June 2026
Transcranial magnetic stimulation	Monash University	N/A	Unclear	Melbourne, Aust.	Non-invasive magnetic field	Yes	?
Transcranial direct current stimulation	Univ of Salerno	2	Unclear	U of Salerno, Italy		Yes	For motor and cognitive symptoms; Double-blind with sham; N=24
Spinal cord stimulation	Huashan Hospital, Shanghai	1	Unclear; Epidural implant	Shanghai, China		Yes	Open label; N=10

# Possible Near-Future Clinical Treatment Trials in PSP

Geographical locations not yet known



Treatment	Sponsor	Phase	Mechanism	Location(s)	Comments
<b>ASN120290</b>	Asceneuron	1	Reduces tau misfolding and aggregation by inhibiting O-GlcNAcase, enhancing attachment of N-acetyl glucosamine to tau.	?	Company's plans not yet formed.
<b>MP-101</b>	Mitochon	1	Mitochondrial decoupler; reduces reactive oxygen species	?	Company is planning a Phase 1 trial.
<b>Tolfenamic acid</b>	NeuroTau	1 and 2a	NSAID (COX inhibitor) reduces tau production	Cleveland Clinic (Las Vegas)	Double-blind; 12 week duration. Company not yet ready to proceed with trial.