Design of a Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study with FNP-223 (oral formulation) in PSP: The PROSPER Study

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PSP Neuroscience Hub

Objective

To describe the design of a Phase 2 trial assessing the efficacy, safety and tolerability of FNP-223 in patients with Progressive Supranuclear Palsy (PSP)

Background

Progressive Supranuclear Palsy (PSP) is a rare neurodegenerative disorder with a mean survival of 7 years after symptom onset[1]. It is characterized by underlying neuronal and glial abnormal tau accumulation in the brain, it is classified as a tauopathy[1]. No effective disease-modifying or neuroprotective therapy for PSP is yet available[1].

FNP-223 is a new oral selective O-GlcNAcase (OGA) inhibitor shown to decrease tau aggregation in preclinical models. Phase I studies have demonstrated favourable safety, pharmacokinetics and brain penetration; it was well tolerated, with no dose-limiting toxicities[2-4].

PROSPER Population

Early patient selection collaborates with FNP-223 mechanism of action[4], preventing tau accumulation.

Study PROSPER
PROGRESSIVE SUPRANUCLEAR PALSY

Key Eligibility Criteria

Inclusion Criteria:

- ✔ Adults (50-80y) with possible or probable PSP-RS (MDS 2017 criteria).[5]
- ✔ PSP symptoms onset ≤3 years.
- ✔ PSPRS score ≤40 and MoCA score ≥23.
- ✔ Able to ambulate independently or with minimal assistance.
- ✔ Study partner required along the trial.

Exclusion Criteria:

- ✔ Score of 3 on any functional domain in the PSP-CDS.
- ✔ Participants with known genetic mutation.
- ✔ Evidence of other neurological disorder that could explain signs of PSP.
- ✔ Primary degenerative diseases other than PSP.

Objectives & Key Endpoints

PROSPER is a phase 2 study to assess the efficacy of FNP-223 to slow the disease progression of PSP

	Objectives	Endpoints
Primary	• To assess the **efficacy** (slow disease progression), **safety & tolerability** of FNP-223 in participants with PSP over 52 weeks.	• Efficacy: **PSPRS change from baseline to 52 weeks.** • Safety: Incidence of **TEAEs, SAEs, vital signs, laboratory evaluations, physical examinations** and **suicidal ideation/ behavior** (C-SSRS).

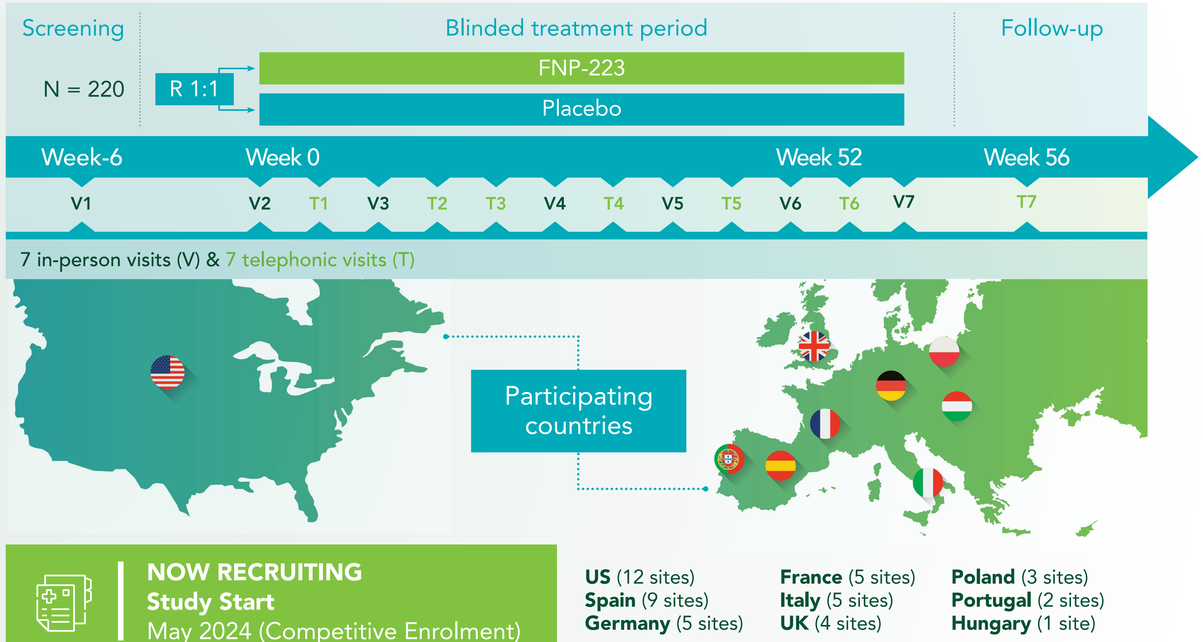
Secondary	• **Key Secondary:** Effects of FNP-223 on **disease severity** assessed by investigator, patient and caregiver through CGI-S.
	• Effects of FNP-223 on **cognitive function** and health-related **quality of life**.
	• **Pharmacokinetic (PK) profile** of FNP-223.
		• Change from baseline to 52w:
		  • Severity: **CGI-S, PGI-S, CaGI-S**.
		  • Functionality: **Slope of decline & subitems PSPRS, PSP-CDS**.
		  • Cognition: **MoCA**.
		  • QoL and daily activities: **PSP-QoL, SE-ADL**.
		• **PK** characterization.

Exploratory	• Effects of FNP-223 on **global and regional brain volumetric changes associated with PSP**[5]. • Effects of FNP-223 on **neurodegeneration biomarkers** in CSF and plasma. • Effects of FNP-223 on **fall** risk assessment.	• Regional Brain volume changes: **volumetric MRI** *(optional)*. • Biomarkers: **CSF** *(optional)* **& Plasma**. • Fall risk: **Electronic diary**.

Study Design

The PROSPER study will randomize 220 participants with PSP to FNP-223 (300mg, oral, 3 times daily) or matched placebo in a 1:1 ratio. Participants will receive double-blind treatment for 52 weeks[6].

PROSPER is a randomized, double-blind, placebo-controlled, phase 2



NOW RECRUITING
Study Start
May 2024 (Competitive Enrolment)

US (12 sites)
Spain (9 sites)
Germany (5 sites)
France (5 sites)
Italy (5 sites)
UK (4 sites)
Poland (3 sites)
Portugal (2 sites)
Hungary (1 site)

Conclusions

- PSP is a rare, serious, neurodegenerative disorder with a mean survival of 7 years after symptom onset.
- There are no effective symptomatic, disease-modifying, or neuroprotective therapies for PSP.
- PROSPER study is an ongoing phase 2 study designed to assess safety, tolerability and efficacy of a dose of 300 mg oral, 3 times daily of FNP-223 in the treatment of participants with PSP for 52 weeks.

C-SSRS: Columbia Suicide Severity Rating Scale; **CaGI-S:** Caregiver Global Impression of Severity scale; **CGI-S:** Clinical Global Impression of Severity scale; **CSF:** cerebrospinal fluid; **MoCA:** Montreal Cognitive Assessment; **MRI:** magnetic resonance imaging; **OGA:** O-GlcNAcase; **PGI-S:** Patient Global Impression of Severity scale; **PK:** pharmacodynamic(s); **PSP:** Progressive Supranuclear Palsy; **PSP-CDS:** Progressive Supranuclear Palsy Clinical Deficits Scale; **PSP-QoL:** Progressive Supranuclear Palsy Quality of Life scale; **PSP-RS:** PSP Richardson Syndrome; **PSPRS:** Progressive Supranuclear Palsy Rating Scale; **R:** Randomization; **SAE:** serious adverse event; **SE-ADL:** Schwab and England Activities of Daily Living Scale; **T:** telephonic visits; **TEAE:** treatment-emergent adverse event; **V:** in person visits.

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