Appendix A: Informed Consent Form (English Translation)

Version Number: 2.0

Version Date: July 12, 2025

Total Pages: 5

Study Title:

A Prospective Study on the Safety, Tolerability, and Efficacy of PDR-001 Injection for Bilateral Stereotactic Subthalamic Nucleus (STN) Clearance of Alpha-Synuclein

Protocol Number: NA

Investigational Site: Department of Neurology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine

Principal Investigator: Dr. Jun Liu

What is the background and purpose of this study?

Parkinson's disease (PD) poses a growing threat to public health, with increasing incidence each year. A major cause of PD is the aggregation of abnormal alpha-synuclein (α-syn), which leads to dopaminergic neuron death. Although siRNA against α-syn offers some neuroprotection, it is limited by low cellular uptake, off-target effects, and short duration.

This study investigates a novel therapeutic method involving a tripeptide (tat-βsyn-deg, also known as PDR-001) targeting α-syn, delivered via an AAV9 vector through bilateral stereotactic subthalamic nucleus (STN) injection. Preclinical studies in mice and monkeys confirmed significant α-syn degradation and motor improvement. The aim is to further test the safety and preliminary efficacy of this gene therapy in humans, a novel shift from symptomatic to disease-modifying treatment.

What will I need to do if I participate?

This trial will enroll 12 patients with primary PD. If you agree to participate:

- You will be assigned a study ID and your medical data will be collected.

- You will undergo stereotactic surgery for PDR-001 injection into the bilateral STN (4 injection targets).

- You will be followed up for 5 years with scale assessments, blood tests (10 ml each), urine tests (10 ml each), MRI and PET imaging.

How will biological samples and data be handled?

All samples and personal data will remain confidential and anonymized using a study ID. Samples will be tested locally and then destroyed. Only authorized research staff may access your information. Regulatory agencies and ethics committees may review your data as needed. No personal data will appear in publications.

Are there risks involved?

PDR-001 is an investigational product. Risks include:

- AAV-related allergic reactions (rash, itching, nausea, shortness of breath, etc.)

- Temporary headache or motor dysfunction at the injection site

This is a Phase I clinical trial aimed at evaluating safety and tolerability.

Are there potential benefits?

You may experience improved motor and non-motor function, quality of life, and reduced burden of disease.

Are there any costs or compensation?

Costs: All treatment and follow-up are covered by study funding.

Compensation: Travel and nutrition support of ¥5,000 each (total ¥10,000).

What if I suffer harm from participation?

You will receive free treatment and/or compensation for study-related injuries. An insurance policy will also be in place since this is a first-in-human trial.

Is my information confidential?

Yes. Personal information and samples are anonymized. Only the study team has access. Regulatory bodies may inspect records. Publications will not include any identifying information.

Do I have to participate?

Participation is voluntary. You may withdraw at any time without penalty or impact on your medical care. The investigator may also terminate your participation if deemed necessary.

Who should I contact for more information?

If you have any questions or feel discomfort during the study, please contact:

Study Contact: Zhang Yi

Phone: 64370045

For ethical concerns, contact:

Ruijin Hospital Ethics Committee

Contact Person: Ms. Zhao

Phone: 64370045-675226

Consent Signature Page

I have read and understood the information provided. I understand that participation is voluntary, and I may withdraw at any time.

- **Participant Name:** _____

- **Signature:** _____

- **Date:** _____/_____/_____

- **Guardian Name (if applicable):** _____

- **Signature:** _____

- **Date:** _____/_____/_____

- **Legal Representative (if applicable):** _____

- **Signature:** _____

- **Date:** _____/_____/_____

- **Witness Name (if participant is illiterate):** _____

- **Signature:** _____

- **Date:** _____/_____/_____

I have explained the contents of this form to the participant, answered all questions fully, and provided a signed copy.

- **Investigator Name:** _____

- **Signature:** _____

- **Date:** _____/_____/_____