PLL Therapeutics obtains authorization to start phase I/II trial in Australia for patients with Amyotrophic Lateral Sclerosis (ALS)

- **Australia's Human Research Ethics Committees (HREC) cleared first-in-human study of drug candidate PLL001**
- **PLL001 aims at restoring microbiome and stopping gut from leaking to treat root cause of ALS, not solely symptoms**
- **Lead candidate stems from PLL Therapeutics' polypeptide delivery platform, early-diagnostics and poly-targeted therapeutic approach developed to stabilize autoimmune and neurodegenerative diseases at earliest outset**

Villenave-d'Ornon (near Bordeaux), France, November 19, 2024 – PLL Therapeutics, a biopharmaceutical company developing a groundbreaking polypeptide delivery platform to treat the root cause of autoimmune and neurodegenerative diseases with a focus on restoring gut permeability, today announces it will start a phase I/II clinical study in Australia for patients with Amyotrophic Lateral Sclerosis (ALS). The launch of this ALS study follows the recent approval by the Australian Department of Health, Human Research Ethics Committees (HREC) to evaluate the safety, tolerability, efficacy and pharmacodynamics of PLL001. PLL001 is PLL Therapeutics' (PLL Th) lead candidate for treating the chronicity of this fatal disease linked to the intestines and Blood-Brain Barrier (BBB) and extending patient quality of life.

This phase I/II trial is a multi-center, randomized, double-blind, placebo-controlled study with an optional open-label extension, where eligible trial participants take the active form of the drug without placebo.

Monash Health, the largest public hospital in Melbourne (AU), is the lead clinical site for the enrolment of 12 patients in phase I and 140 in phase II. Trial results will be available in 18 months and will include a six-month milestone.

"PLL Therapeutics is extremely pleased to have obtained approval from the HREC in Australia to conduct a phase I/II study on ALS patients, a fatal disease with a high unmet need for treatment options. We commend the HREC for facilitating a smooth administrative process in obtaining authorization and accessing resources in conjunction with financial incentives," said Jean-Pascal Zambaux, co-founder and CEO of PLL Therapeutics. "Our lead candidate, PLL001, derived from our polypeptide delivery platform, works by replacing in the microbiome a critical compound required to restore the permeability of the gut and Blood-Brain Barrier. This prevents contaminants that are present at the initialization of neurodegenerative diseases from leaking into the brain. Our approach is different as it tackles the triggers underlying leaks in the gut and BBB - not addressing only disease symptoms."

Advancing early-stage diagnostics – a first in ALS

In parallel, PLL Th will conduct an evaluation of its early-stage and companion diagnostics tool. It offers a quick and simple way to detect a neurodegenerative pathology, such as ALS. This diagnostics kit based on serum antibodies is the first-of-its-kind to use biomarkers in the blood to measure the onset of ALS and other neurodegenerative

diseases, which currently rely on an ALSFRS-R Score; a questionnaire-based scale that measures and tracks changes in a person's physical function over time, but has known shortcomings.

During the ALS clinical trial, PLL Th aims to demonstrate the advantages of its unique 'combined' early-diagnostics and therapeutic approach, enabling for the first time, detection and treatment at the onset of the disease, prior to irreversible damage impacting the patient.

ALS, also known as Lou Gehrig's disease, is a rapidly progressive neurodegenerative disorder affecting upper and lower motor neurons, with death resulting mainly from respiratory failure three to five years after symptom onset. Although classified as rare, there are approximately 140,000 new cases diagnosed worldwide each year, representing 384 new cases every day.

Collaborators on this phase I/II study are Australian-based Alithia Lifesciences, a Contract Research Organization and Swiss consultancy firm Copexis. PLL Th anticipates completing patient enrolment before the end of 2024.

About PLL001
PLL Therapeutics' lead candidate, PLL001, consists of several API (Active Pharmaceutical Ingredient) molecules that, when combined, are designed to restore the microbiome and stop the gut from leaking. PLL001 is derived from the company's patented Poly-L-Lysine technology, an effective drug carrier able to transport four Small Chain Fatty Acids (SCFAs) to the epithelium gut cells as well as the Blood-Brain Barrier (BBB). It releases the drug at 'point of use'.

About PLL Therapeutics
PLL Therapeutics, a biopharmaceutical company developing a groundbreaking polypeptide delivery platform, is spearheading a unique early-diagnostics and therapeutic approach for treating the root cause of autoimmune and neurodegenerative diseases. PLL Therapeutics focuses on restoring gut permeability. Its initial indication is Amyotrophic Lateral Sclerosis (ALS), a fatal motor neuron disease. The company's therapy, PLL001, consists of several API (Active Pharmaceutical Ingredient) molecules that, when combined, can heal a leaky gut. PLL Therapeutics' 'poly-targeted' drug therapy aims at destroying the initialization of the disease by combatting, within the gut, the multiple external and internal factors that drive the onset of ALS, while facilitating the development of cells in the microbiota to rebuild the gut barrier. PLL Therapeutics' approach for restoring the microbiome derives from its patented poly-L-lysine technology, an effective drug carrier able to transport several molecules and release the drug at 'point of use' without side effects. The platform will play a key role in the early detection of autoimmune and neurodegenerative diseases (ALS) and proliferative disorders (colon cancer) through specific biomarkers.
Founded in 2019, PLL Therapeutics is led by a highly experienced management team. A phase I/II clinical trial is underway, with a phase IIb planned for 2025. The company is located near Bordeaux, France.
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