PLL Therapeutics enrolls first patient in phase I/II trial of drug candidate PLL001 for Amyotrophic Lateral Sclerosis (ALS)

- **Multi-stage Australian study will evaluate safety of PLL001 in 12 ALS patients, testing three different doses along with placebo**
- **140 ALS patients will participate in second stage of study to test efficacy of PLL001**
- **Trial will also evaluate world's very first early-stage diagnostics paired with poly-targeted therapeutic approach, bringing promise of new standard to combat ALS from onset**

Villenave-d'Ornon (near Bordeaux), France, April 15, 2025 – PLL Therapeutics, a biopharmaceutical company developing a groundbreaking polypeptide delivery platform to treat the root cause of autoimmune and neurodegenerative diseases, today announces the enrollment of the first patient in its phase I/II clinical trial for treating Amyotrophic Lateral Sclerosis (ALS), a fatal disease. Enrollment in phase I commenced in Australia at Monash Health, one of the largest hospitals in Melbourne.

The phase I/II multi-stage study will recruit 12 patients in the first stage, testing three different doses of PLL001 given by subcutaneous injection, alongside a placebo. This trial will last five months, with results anticipated by mid-2025.

A six to 12-month study of 140 ALS patients will follow as a second stage, encompassing various subtypes of ALS: sporadic, familial, bulbar or spinal, with all participants meeting rigorous inclusion criteria, including ALSFRS-R (ALS Functional Rating Scale) and TRICALS (Treatment Research Initiative to Cure ALS).

"This phase I/II clinical trial represents a critical step in addressing ALS at its earliest stages, prior to irreversible damage," said Jean-Pascal Zambaux, co-founder and CEO of PLL Therapeutics. "The study of our lead candidate, PLL001, marks a significant milestone in the path to delivering innovative solutions for ALS patients, particularly through a unique approach that combines early-stage diagnostics with a groundbreaking therapy, offering hope for meaningful results. This first enrollment solidifies our mission to advance ALS treatment through early intervention."

Unique treatment tackles root cause of ALS

The lead candidate under study, PLL001, is designed to address ALS at its onset and slow or halt disease progression. Derived from PLL Therapeutics' polypeptide delivery platform, PLL Therapeutics' approach differs as a treatment because, rather than solely addressing disease symptoms, it tackles the triggers of the disease - underlying leaks in the gut and the Blood-Brain Barrier (BBB).

World first early-stage ALS diagnostics biomarker, also under study
In parallel, the study provides an opportunity to conduct large-scale blood sampling to evaluate the efficiency of PLL Therapeutics' diagnostics kit based on serum antibodies; the first-of-its-kind to use biomarkers in the blood to measure the onset of ALS, as well as monitor patients during treatment.

PLL Therapeutics is conducting the clinical trial in collaboration with Alithia Lifesciences, an Australian Contract Research Organization, and Copexis, a Swiss consultancy firm.

Preliminary phase I results will be available at the end of the first stage of the trial, mid-2025; phase II recruitment will start in July with the aim of obtaining initial assessments within six months of the study.

About ALS
Amyotrophic Lateral Sclerosis (ALS) is a rapidly progressive neurodegenerative disorder, with death resulting mainly from respiratory failure three to five years after symptom onset. There are no effective drugs against this progressive disease. There is also currently no method available to definitively diagnose ALS, which makes critical the development of PLL Therapeutics' early-stage blood biomarker test, also under evaluation in this study.

About PLL001
Lead candidate, PLL001, is a poly-targeted therapy consisting of several APIs (Active Pharmaceutical Ingredients) that, when combined, are able to restore the microbiome and stop the gut from leaking toxins into the bloodstream. The underlying premise is that the origin of ALS and other auto-immune or neurodegenerative diseases lies in the intestine. Therefore, there is a need to protect the gut and restore gut integrity to prevent progression of the disease. PLL001 is derived from PLL Therapeutics' patented Poly-L-Lysine drug transport system, which successfully delivers four Small Chain Fatty Acids (SCFAs) - known to be effective against ALS' neuro-inflammatory and neurodegenerative pathways - to the epithelium gut cells and the Blood-Brain Barrier (BBB). It releases the drug at the 'point of use'.

About PLL Therapeutics
PLL Therapeutics, a biopharmaceutical company developing a groundbreaking polypeptide delivery platform, is spearheading a unique early-stage diagnostics and therapeutic approach for treating the root cause of autoimmune and neurodegenerative diseases. PLL Therapeutics focuses on restoring gut integrity. Its initial indication is Amyotrophic Lateral Sclerosis (ALS), a fatal motor neuron disease. The company's lead candidate is PLL001, a 'poly-targeted' drug therapy aimed at destroying the initialization of the disease. PLL Therapeutics' approach 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. The company is located near Bordeaux, France.
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