PNRR Missione 4, Componente 2, Investimento 1.4 "Potenziamento strutture di ricerca e creazione di "campioni nazionali di R&S" su alcune Key Enabling Technologies"
Iniziativa finanziata dall'Unione europea –- NextGenerationEU.
National Center for Gene Therapy and Drugs based on RNA Technology
Sviluppo di terapia genica e farmaci con tecnologia a RNA
Codice progetto MUR: **CN00000041** – CUP UNINA: **E63C22000940007**

Doctorate of National Interest

RNA THERAPEUTICS AND GENE THERAPY

SELECT ONE OF THE FOLLOWING RESEARCH AREA:

☐ **Mechanisms of Diseases and Drug Target Identification**

☒ **Design and Delivery of New Gene Therapy and RNA-Based Medicines**

☐ **Validation and Safety in Preclinical and Clinical Studies**

LOCATION OF THE RESEARCH ACTIVITY (INSTITUTION/DEPARTMENT):

CEINGE -Biotecnologie Avanzate Franco Salvatore-

Via G. Salvatore 486 - 80145 Napoli, Italy

TUTOR:

Prof Alessandro Fraldi, PhD

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PROPOSED RESEARCH ACTIVITIES (max 300 words):

Sanfilippo syndrome is a rare hereditary disorder characterized by severe involvement of the central nervous system (CNS). To date, there are no effective therapies for the treatment of CNS pathology in Sanfilippo patients. Furthermore, there is low availability of biomarkers useful for monitoring the disease that makes it more difficult to evaluate the effectiveness of new treatments. The purpose of this project is:

1) In patients affected by Sanfilippo, some proteins, known as amyloid-like proteins, are prone to aggregate generating toxic deposits in the cells of various tissues, including the CNS. The inhibition of this aggregation through the systemic injection of a molecule known as CLR01 in a Sanfilippo mouse model can effectively protect against neurodegeneration by reducing neuroinflammation. In this project we want to study the synergistic potential of a treatment in which the systemic injection of CLR01 is combined with a gene therapy protocol based on the use of viral vectors (AAV) for the brain delivery of sulfamidase gene, which is defective in Sanfilippo A patients.

2) To identify new biomarkers for Sanfilippo Syndrome. These new biomarkers will be based on the evaluation of amyloid proteins in the blood and CSF samples. By profiling the amyloid proteome in blood and CSF samples, we want to explore in the next future the possibility of using the amyloid storage burden as predictive marker to develop more precise and effective therapies for Sanfilippo patients.

Overall, the results of this project will be useful for the future clinical transfer of innovative therapies for Sanfilippo Syndrome.