Finanziato dall'Unione europea NextGenerationEU
Ministero dell'Università e della Ricerca
Italiadomani PIANO NAZIONALE DI RIPRESA E RESILIENZA
Università degli Studi di Napoli Federico II

**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**

**TITLE OF THE RESEARCH PROJECT**
**Development of new RNA-based approaches for the rescue of neurodevelopmental alterations in ADNP haploinsufficiency**

**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):**
Human Technopole, Viale Rita Levi-Montalcini 1, 20157, Milano

**TUTOR:**
Prof. Giuseppe Testa

**PROPOSED RESEARCH ACTIVITIES (max 300 words):**
ADNP syndrome is a neurodevelopmental disorder caused by loss of function mutations in the ADNP gene which manifests with intellectual disabilities and autism spectrum disorder features. The current research project aims to explore the delivery efficiency and efficacy of synthetic mRNAs into 3D neurodevelopmental models to rescue the neurodevelopmental alterations caused by ADNP haploinsufficiency.
Specifically, the candidate will utilize pluripotent stem cells available in our lab to study the impact of ADNP mutation in a multitude of PSC derived *in vitro* models, including neurons and brain organoids. In a second phase, the candidate will explore different approaches for the delivery of RNA-based drugs in such systems and

will perform -omic, molecular biology and imaging analysis to evaluate both the efficiency of drug delivery as well as the efficacy of these drugs in reverting the molecular phenotype caused by ADNP mutations.
Overall, the candidate will learn the bases of human neurodevelopment, pluripotent stem cells (PSCs), PSC-derived brain organoids, Crispr-Cas9 technology and therapeutic RNAs delivery approaches *in vitro*. Moreover, the candidate will have the opportunity to learn and master the principal computational tools used in the analysis of -omic data, including single cell transcriptomics.