**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**
**New polymeric/lipid platforms for the combined delivery of nucleic acids and enzymes**

**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):**

Department of Pharmaceutical and Pharmacological Sciences

**TUTOR:**

Paolo Caliceti

**PROPOSED RESEARCH ACTIVITIES (max 300 words):**
The research project is aimed at exploiting new polymeric/lipid platforms for the combined delivery of nucleic acids and enzymes. In particular, the study will focus on formation of polyplexes with nucleic acids, namely mRNA or silencing short ONs (siRNA etc) which can be incorporated into lipid particles, SLN or liposomes, for multifunctional behavior. Lipid nanoparticles can be decorated with targeting agents to achieve selective delivery to specific cells by active recognition and tissue tropism, favoring the cell up-take. Polymers can stabilize the nucleic acids increasing the loading into the nanoparticles. Furthermore, polymers can be up-graded with lysosomal escaping moieties to release of the nucleic acid into the cytoplasm and intracellular targeting agents to yield specific delivery into intracellular organelles such as mitochondria or nucleus. In this project, the above reported platform will be exploited to simultaneous delivery of guide ONs and caspase9 expressing mRNA or directly the

enzyme to yield a single carrier delivering both functional molecules. This technology is expected to provide a new CRISPR strategy with enhanced performance. Polymeric platforms that will be used in this study will be “head-to-tail” oligocationic polymers that have been developing in the proponent laboratory. A library of polymers that showed to be per se performing systems for nucleic acid delivery will be properly modified for this scope. The lipopolyplexes will be generated by microfulidfic technology which exploits the know how of the proponent for formulation of lipoplexes with tailored biopharmaceutical profoiles