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):

University of Napoli Federico II- Department of Pharmacy

TUTOR:

Prof. Fabiana Quaglia

PROPOSED RESEARCH ACTIVITIES (max 300 words):

This project aims to develop a novel generation of lipid nanoparticles (LNPs) for the delivery of RNAs engineered to improve RNA transfection efficiency and target a specific area in the body. The project is centered on a multidisciplinary approach encompassing Chemistry, Computational methods, Pharmaceutical Technology, Cell Biology, and Pharmacology.
The project is organized into two clusters of activities aimed at i) discovering novel components of LNPs ensuring high transfection efficiency; ii) designing and developing LNPs for precision delivery. In the first research trajectory, we aim to screen a large library of newly synthesized steroidal and ionizable components in collaboration with the PIs of Spoke 8 (Annex 1-WP 8.1-task 8.1.1). The novel components will replace cholesterol and ionizable lipids commonly employed in LNP formulation to identify those molecules able to improve RNA transfection efficiency in a panel of human cells. We will fabricate a library of LNPs with different compositions with a model siRNA and mRNA cargo and test their delivery efficiency in vitro and in vivo. In a parallel research trajectory, we plan to develop a novel generation of LNPs functionalized with targeting

peptides/peptidomimetics designed for precision delivery to organs/tissues (tLNPs). To this purpose, we will focus on the non-covalent functionalization of LNPs with targeting ligands that recognize receptors typically upregulated in pathological conditions. We plan to build a library of tLNPs with different surface features, evaluate both their trafficking in 2D/3D cell cultures and biodistribution in mice, finally linking their chemical identity to biological behaviour. A PoC of the LNPs/tLNPs therapeutic potential will be provided in collaboration with the PIs in Spoke 4 (Annex 1-WP 4.1-task 4.1.1) and Spoke 2 (Annex 1-WP 2.1 and 2.2).