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 THERAPUETICS 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):

Department of Pharmacy, University of Salerno

TUTOR: Prof. Pasquale Del Gaudio

PROPOSED RESEARCH ACTIVITIES (max 300 words):

The research focuses on developing a novel biocompatible delivery platform (DP) for efficient siRNA delivery in the treatment of cancer disease. The primary objective is to address the existing challenges associated with siRNA delivery, including poor biopharmaceutical characteristics, chemical/enzymatic instability *in vivo*, limited cellular penetration, and non-specific distribution. To achieve this, the modification of natural polymers with positive charges and specific targeting ligands is an advantageous way to create a tailored DP capable of recognizing specific cellular receptors.
The methodology entails using a natural polymer as the basis for the DP by grafting a cationic moiety for siRNA interaction and a hydrophobic portions for supramolecular assembly and control over siRNA release, to achieve efficient delivery of siRNA and potentially co-deliver anticancer agents. To ensure targeted delivery and maximum uptake by cancer cells, the DP will be decorated with selected active targeting agents.
The project's main results will encompass two key aspects. First, the development and validation of an experimental design to functionalize the starting polymer with the desired moieties will be conducted. This will involve identifying optimal synthetic routes that are high-yielding, versatile for various functional substances, easy to apply, and environmentally friendly.

The second main result will involve the optimization of nanocarrier selection and prototype manufacturing. Through this process, relevant parameters of the siRNA-targeted nanocarriers will be identified and optimized to maximize their performance.

The efficacy, safety, and distribution of the nanocarriers will be demonstrated in tissue and organoid models appropriate for cancer research, exploiting forefront analytical solutions such as integrated advanced imaging and MS strategies, able to screen downstream events following the administration of the targeted siRNA DPs. The proposed activities will significantly contribute to cancer therapeutics research, providing a basis for further studies and advancements in the field.