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 non-viral vectors for ocular 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**

The project is in the frame of DM 630/2024 "Innovative PhDs in partnerships with companies"
The partner company is Medivis s.r.l.

LOCATION OF THE RESEARCH ACTIVITY (INSTITUTION/DEPARTMENT):
University of Naples Federico II – Department of Pharmacy
Medivis s.r.l. (Catania-Italy)

TUTOR:
Prof. Fabiana Quaglia

PROPOSED RESEARCH ACTIVITIES:
iRNA-based therapy holds promise in revolutionizing the treatment of ocular diseases, targeting undruggable proteins at a molecular level. Several companies are developing siRNA therapeutics for treating pathologies such as diabetic retinopathy, glaucoma, and age-related macular degeneration (AMD). These diseases are generally chronic and degenerative and sometimes lead to blindness. Nevertheless, the unique features of the eye and the presence of numerous biological barriers (e.g., tear film, water-blood and blood-retinal barriers, ocular clearance, corneal and retinal pigment epithelium, conjunctive/choroidal blood flow) make the development of iRNA delivery strategies urgent.

The project focuses on designing and developing iRNA-loaded nanoparticles tailored to overcome biological barriers of the eye and their formulation as a final product. Topical formulations (anterior segment of the eye) and injectable formulations will be considered.
The first step of the research activity aims to design, develop, and engineer carriers at the nanoscale level. In this context, following the ICH Q8 guidelines on pharmaceutical development, Quality Target Product Profile, Critical Quality Attributes (CQAs), design space will be defined, and the critical variables of the formulation process (CPPs) will be recognized. CQAs of nanoparticles as prepared and in the final formulation, iRNA actual loading/encapsulation efficiency and release kinetics will be screened.
In the second step of the project, biological tests will be carried out on selected prototype formulations. In particular, in vitro tests on different 2D/3D cell cultures (human corneal epithelial cells-HCE or Human Retinal Pigment Epithelium Human Cells -ARPE-19, EpiOcular™) will be performed to verify the toxicity and transfection efficiency of the nanocarriers. The most promising formulations will then be evaluated in animal models. The biocompatibility will be assessed by histological evaluation of animal tissues, followed by immunohistochemical analysis, whereas the transfection efficiency will be evaluated using reporter or animal disease models.