CONTEXT

Lysosomal storage disorders (LSDs), such as Fabry, Gaucher, Hunter, and Sanfilippo diseases are a group of rare diseases that currently lack a definitive cure. LSDs individually occur with incidences of less than 1:100,000; but as a group the incidence is about 1:5,000 - 1:10,000, representing a serious global health problem. Therefore, development of new treatments for this type of rare diseases has become a key priority for European Research policy.

01 TREATMENT OPTIONS

Although most of the LSDs lack an effective and curative treatment, some of them benefit from Enzyme Replacement Therapies (ERTs), based on the administration of the defective enzyme (GLA in the case of Fabry), usually obtained by recombinant biotechnology. The success of ERTs is limited mainly due to the instability and low efficacy of the exogenously administered therapeutic enzyme. There is a continuous effort towards finding new alternative therapeutic approaches that improve the limitations of current ERTs for all these rare diseases, while reducing costs.

02 INNOVATION USING NANOTECHNOLOGY

CIBER has developed and patented an innovative peptide-targeted liposomal nanocarrier for the transport, protection and improvement of the pharmacological properties of biologicals, such as enzymes. A new GLA nanoformulation has been obtained by integrating the enzyme in this novel type of nanocarrier, using Arginine-Glycine-Aspartic acid (RGD) peptide as targeting moiety. This product has shown outstanding enhanced specific enzymatic activity, higher intra-cellular penetration and a higher plasma half-life, compared to free-GLA.

CONSORTIUM

ciber-bbn
Centro de Investigación Biomédica en Red Bioingeniería, Biomateriales y Nanomedicina

JOANNEUM RESEARCH

BIO NANONET

Technion Israel Institute of Technology

DDR
Drug Development & Regulation

AARHUS UNIVERSITY

nanomol Technologies

Praxis Biopraxis Research

LeanBioPro

COVANCE
SOLUTIONS MADE REAL

IN COLLABORATION WITH

CSIC
Consejo Superior de Investigaciones Científicas

Vall d'Hebron Institut de Recerca

UAB
Universitat Autònoma de Barcelona

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SMART4FABRY.EU

SMART4FABRY

SMART FUNCTIONAL GLA-NANOFORMULATION FOR FABRY DISEASE

European Commission | Horizon 2020 European Union funding for Research & Innovation

SMART4FABRY.EU

OBJECTIVES

The aim of the Smart4Fabry project is to obtain a final nanoformulation of GLA enzyme, ready to enter future clinical testing, with a solid pre-clinical proof of concept (PoC) to demonstrate that nano-GLA has a higher targeting of the enzyme to affected organs and a lower clearance rate than free GLA. Our objective is that the new nanoformulation of GLA will allow a significant increase in the efficacy (30-80% higher) compared to the current ERT with non-nanoformulated GLA.

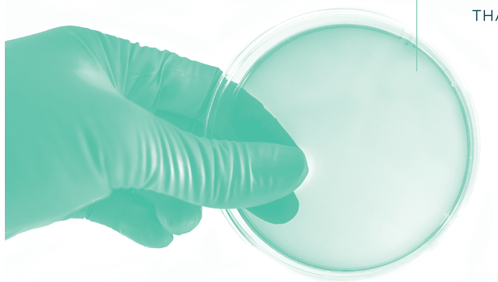
THIS MAIN OBJECTIVE HAS BEEN DIVIDED INTO SEVEN SPECIFIC OBJECTIVES:

- ACHIEVE QUALITY CONTROL OVER THE SELF-ASSEMBLY OF NANO-GLA MOLECULAR COMPONENTS AND ITS PHYSICO-CHEMICAL PARAMETERS.
- PROVIDE A COMPLETE PRE-CLINICAL SAFETY, PK AND TOXICO-LOGICAL PACKAGE FOR THE FINAL GLA-NANOFORMULATION.
- DEVELOP A NANO-GLA CAPABLE OF CROSSING THE BLOOD BRAIN BARRIER.
- CONSTRUCTION AND OPERATION OF A GMP PLANT FOR THE PRODUCTION OF THE QUANTITIES OF NANO-GLA NEEDED FOR REGULATORY PRE-CLINICAL AND FUTURE CLINICAL TRIALS.
- TO PRODUCE GLA WITH ADEQUATE QUALITY CONDITIONS.
- DEVELOPMENT OF THE GLA NANOFORMULATION FOLLOWING THE REQUIREMENTS OF THE PHARMACEUTICAL INDUSTRY AND REGULATORY AUTHORITIES.
- CREATE A REALISTIC EXPLOITATION PLAN AND BUSINESS MODEL, BASED ON EXPERIENCE FROM THE COMPANIES IN THE RARE DISEASES MARKET, IN ORDER TO ENSURE THE TRANSLATION OF THE PROJECT RESULTS TO PATIENTS SUFFERING FROM FABRY DISEASE.

EXPECTED OUTCOMES

Smart4Fabry project execution will have a clear impact on some of the current challenges and trends already identified in Europe as priorities for innovation deployment. Its fulfilment will impact on a major health problem, the need of new therapies for rare diseases, which constitutes a priority societal challenge.

- SMART4FABRY WILL SERVE AS A FIRST DEMONSTRATOR FOR THE COMPLETION OF THE TECHNOLOGY DEVELOPMENT AT PRECLINICAL AND INDUSTRIAL SCALE, OPENING A PATHWAY FOR TAILORED SOLUTIONS FOR OTHER LSDS AND FOR OTHER PATHOLOGIES.
- THE DEVELOPMENT OF NEW THERAPEUTIC SYSTEMS LIKE OUR NEW NANOFORMULATION OF GLA, ABLE TO OVERCOME THE MAIN LIMITATIONS AND PROBLEMS OF CURRENT TREATMENTS, IS A KEY CHALLENGE FOR THE TREATMENT AND IMPROVEMENT OF THE QUALITY OF LIFE OF THE FABRY DISEASE PATIENTS.
- SMART4FABRY STARTS FROM AN ESTABLISHED INNOVATIVE TECHNOLOGY DEVELOPED IN AN ACADEMIC ENVIRONMENT AND WITH POSITIVE RESULTS AT A NON-GLP PRECLINICAL STAGE. THE PROJECT CONNECTS THE NECESSARY HIGH-LEVEL EXPERTISE TO COMPLETE ALL THE DEVELOPMENT CHAIN TO BE READY FOR CLINICAL TESTING.
- SMART4FABRY WILL HAVE A WIDE IMPACT ON IMPROVING THE COMPETITIVENESS OF INDUSTRY. IT WILL HAVE A DIRECT IMPACT AT THE COMPANIES LEVEL, ALLOWING THE GENERATION OF A NEW, HIGHLY COMPETITIVE PRODUCT THAT WILL OPEN NEW MARKETS.



PROJECT STRUCTURE

The work plan for Smart-4-Fabry has been thoroughly designed taking into account the specificities of this project. To respond to the challenge of efficiently organizing the work, Smart-4-Fabry is divided into 9 core work packages (WP), distributed across 4 specific stages.

WP8
DISSEMINATION AND COMMUNICATION ACTIVITIES

WP7
BUSINESS MODEL AND EXPLOITATION ACTIVITIES

WP1
NANOFORMULATION OF THE GLA IN MULTIFUNCTIONAL NANOLIPOSOMES

WP2
PHYSICO-CHEMICAL CHARACTERIZATION TOOLS FOR QUALITY CONTROL

WP4
IN VITRO AND IN VIVO EVALUATION OF GLA NANOFORMULATION

WP11
GLA PRODUCTION

WP3
SCALE-UP AND GMP PRODUCTION

WP5
REGULATORY PRE-CLINICAL STUDIES

WP10
ETHICAL REQUIREMENTS

WP6
CRITICAL REGULATORY ACTIVITIES

WP9
PROJECT MANAGEMENT