ENTRY-DM Q&A Factsheet

What is ENTRY-DM?
ENTRY-DM is a doctoral training network focused on developing antisense oligonucleotide (ASO)-based therapies for Myotonic Dystrophy (DM), a rare neuromuscular disease. The project will train 14 doctoral candidates in interdisciplinary research, combining fundamental science, clinical research, and therapeutic development.

What is the goal of ENTRY-DM?
The main goal is to advance ASO-based therapies for DM and to prepare for future clinical trials by addressing disease mechanisms, generating innovative disease models, improving therapeutic strategies, and identifying reliable biomarkers for disease progression.

Who are the key participants?

- **Beneficiaries:**
  - National Institute of Health and Medical Research, INSERM (France)
  - University of Valencia, UVEG (Spain)
  - Institute for Bioengineering of Catalonia, IBEC (Spain)
  - University of Rome Tor Vergata, UTOV (Italy)
  - Radboud University Medical Center, RUMC (Netherlands)
  - Ludwig Maximilian University of Munich, LMU (Germany)
  - Adam Mickiewicz University (Poland)
  - Stem Cells Research Centre, CECS (Paris)
  - Genartis SRL (Italy)
  - Paris City University, UPC (France)
  - Spanish National Research Council, CSIC (Spain)

- **Associated Partners:**
  - Myology Institut Association, AIM (France)
  - European Clinical Research Infrastructure Network, ECRIN (Europe)
  - Arthex Biotech SL (Spain)
  - European Dystrophia Myotonia Association EURO-DyMA (Europe)
  - Virginia Commonwealth University (USA)
  - Biobam Bioinformatics SL (Spain)
  - University of Florida (USA)
  - European infrastructure for translational medicine, EATRIS-ERIC (Netherlands)
  - The Chancellor, Masters and Scholars of the University of Oxford (UK)
  - University of Gothenburg (Sweden)
  - Sanofi S.A. (USA)
  - Myotonic Dystrophy Foundation, MDF (USA)
  - ELIXIR-IT Research Infrastructure (Italy)
  - Sorbonne University (France)
  - Stichting Radboud University, SRU (Netherlands)
  - Université d'Evry-Val-d'Essonne (France)
  - University of Barcelona (Spain)
  - Universita degli Studi di Verona (Italy)

What are the main work packages?

1. **WP1:** Disease mechanisms & innovative model systems.
2. **WP2:** Design of effective ASO-based therapies.
3. **WP3:** Biomarkers of disease progression & therapeutic response.
4. **WP4:** Training & career development for doctoral candidates.
5. **WP5:** Dissemination, exploitation, and communication.
6. **WP6:** Management, recruitment, and sustainability.
7. **WP7:** Ethics requirements.

What are the key objectives?

- **RO1:** Develop human 3D disease models for DM research.
- **RO2:** Design novel ASO-based therapeutic strategies.
- **RO3:** Identify biomarkers for disease progression and clinical trials.

What are the expected results?

- **Innovative Disease Models:** 3D models to study DM.
- **Improved ASO Therapeutics:** Enhanced ASO molecules with better bioavailability and efficacity.
- **Biomarker Discovery:** Identification of biomarkers for disease monitoring and clinical trial readiness.

How will ethical concerns be addressed?

ENTRY-DM will comply with all ethical guidelines for patient involvement, data handling, and clinical trials, with regular reporting from an appointed ethics advisor.

How many doctoral candidates will be recruited to the project?

ENTRY-DM will recruit **14 doctoral candidates** (DCs) to participate in the research and training program.

What kind of projects will the doctoral candidates work on?

The 14 doctoral candidates (DCs) in the **ENTRY-DM** project will work on innovative research projects focused on Myotonic Dystrophy (DM), specifically in the development of antisense oligonucleotide (ASO)-based therapies. Their projects will span various aspects of disease research, therapeutic development, and clinical trial readiness.

What specific projects will the doctoral candidates work on?

The DCs will be involved in the following specific projects within the work packages:

- **WP1 (DM Disease Mechanisms & Model Systems):**
  - Development of 3D disease models, such as muscle-on-chip and neuromuscular junction organoids.
  - Research on the genetics and molecular mechanisms of DM, including investigating RNA foci dynamics and the role of miRNAs in DM1.
- **WP2 (ASO-Based Therapeutic Strategies):**
  - Designing and testing ASO molecules to target the RNA mutations in DM.
  - Investigating ways to improve the internalization and delivery of ASO molecules into cells affected by DM.

  - Identifying new chemical modifications for ASO molecules to enhance efficacy.

- **WP3 (Biomarkers & Clinical Trial Readiness):**
  - Developing biomarkers to monitor the progression of DM and therapeutic responses in patients.
  - Investigating the role of cognitive abilities in patient decision-making and clinical trial participation.
  - Identifying muscle-specific and CNS biomarkers for DM1 and DM2.

What kind of training will the doctoral candidates receive?
The doctoral candidates will receive comprehensive training, including:

- **Scientific Training:** Conducting hands-on research in advanced disease models, ASO development, and biomarker discovery.
- **Career Development:** Support in writing career development plans (CDPs), attending network-wide training, and participating in secondments with partner institutions.
- **Transferable Skills:** Gaining skills in communication, project management, and collaboration across interdisciplinary fields.

How will the doctoral candidates contribute to the project?
The doctoral candidates will conduct independent research under the supervision of experts, contributing to groundbreaking findings in DM therapeutics and clinical research. Their work will directly support the development of ASO-based therapies and the preparation for upcoming clinical trials in DM.

What is the expected impact of their research?
The projects will contribute to:

- **Therapeutic Advancements:** Enhancing ASO therapies, which could lead to the development of effective treatments for DM and other rare diseases.
- **Clinical Readiness:** Identifying biomarkers and disease models that will improve the design and execution of clinical trials.
- **Scientific and Societal Impact:** Contributing to the understanding of DM disease mechanisms and improving the quality of life for patients through new therapeutic strategies.