DCRT
Dutch
Center for
RNA
Therapeutics

DCRT CHARTER

Version 1.1

16/07/2021

TABLE OF CONTENTS

CONTENTS

1 INTRODUCTION

1.1 PURPOSE OF DCRT CHARTER

The DCRT charter documents the information pertinent to how DCRT (Dutch Center for RNA Therapy) operates and what is aspired. The charter includes the needs, scope, justification, and resource commitment.

2 DCRT OVERVIEW

DCRT (Dutch Center for RNA Therapy) is located in The Netherlands and is a not-for-profit collaboration between Dutch University Medical Centers (UMC's). Currently composed of Leiden University Medical Center (LUMC), Radboud University Medical Center and Erasmus University Medical Center, the aim is to have all UMC's that will be involved in antisense oligonucleotide treatment development for ultra-rare diseases involved in the DCRT – each with different specialties and areas of focus. The domain in which DCRT operates is in the healthcare sector – more specifically in human genetics, RNA therapy, neurology and ophthalmology.

The DCRT board is composed of the following people:

- Annemieke Aartsma-Rus, Professor at Leiden University Medical Center
- Willeke v. Roon-Mom, Associate Professor at Leiden University Medical Center
- Linda van der Graaf, Project Manager at DCRT
- Rob Collin, Professor at Radboud University Medical Center
- Ype Elgersma, Professor at Erasmus MC

The aim of DCRT is to develop personalized antisense oligonucleotides for the treatment of patients with brain and eye diseases.

Antisense oligonucleotides (ASOs) offer an interesting and promising therapeutic option for patients with brain or eye diseases with eligible mutations. Here ASOs can restore or increase production of a missing protein or reduce expression of toxic proteins. Clinical applications have revealed that local delivery of ASOs is well tolerated and effective and that dosing frequency is low (3-4 times per year). However, patients eligible for ASO treatment often carry rare or even unique mutations and as such the pharmaceutical industry is not highly interested.

DCRT is focused primarily on patients within The Netherlands. However, we also aim to collaborate within Europe and around the world to exchange information, support treatment development for unique mutations in other countries, to connect stakeholders and to best collaborate if there is patient support needed.

DCRT was officially launched on February 29 2020 (rare disease day): https://www.lumc.nl/over-het-lumc/nieuws/2020/Februari/rna-therapie/.

Seed funding for one year was provided by the Human Genetics department of the LUMC for one year for both operational costs for DCRT and research into personalized ASO development.

3 JUSTIFICATION

3.1 PURPOSE

The purpose of DCRT is to develop ASO treatments for patients with an eligible mutation, where ASO treatment can improve conditions of the eye or brain and where there is no alternative treatment available. DCRT is a not-for-profit collaboration of academic medical centers that aims to develop these ASOs and provide them to patients at cost.

3.2 FUNDING

Currently DCRT relies on contributions from participating UMCs for running costs and on funding from third parties for ASO development (grants, donations etc).

4 SCOPE

4.1 OBJECTIVES

The objectives of the DCRT are as follows:

- Identify mutations that are eligible for ASO therapy
- Raise awareness with key groups who can refer mutations to us (Dutch clinical geneticists and clinicians, heads of departments and UMC board of directors)
- Collaborate with international counterparts (e.g. everyone foundation, N-of-1+ taskforce of the oligonucleotide therapeutics society)
- Share our learnings so process can be replicated in other centers
- Align with other centers working on similar initiatives
- Treat (at least) a patient with eye and brain disorder in a 3 year time frame

4.2 BOUNDARIES

What is in scope for DCRT:

- Genetic eye and brain disorders with an eligible mutation that is amenable to ASO treatment
- Very rare mutation
- ASO not in development by other similar initiatives
- ASO not in development by a company
- ASO treatment provided under a named patient mechanism

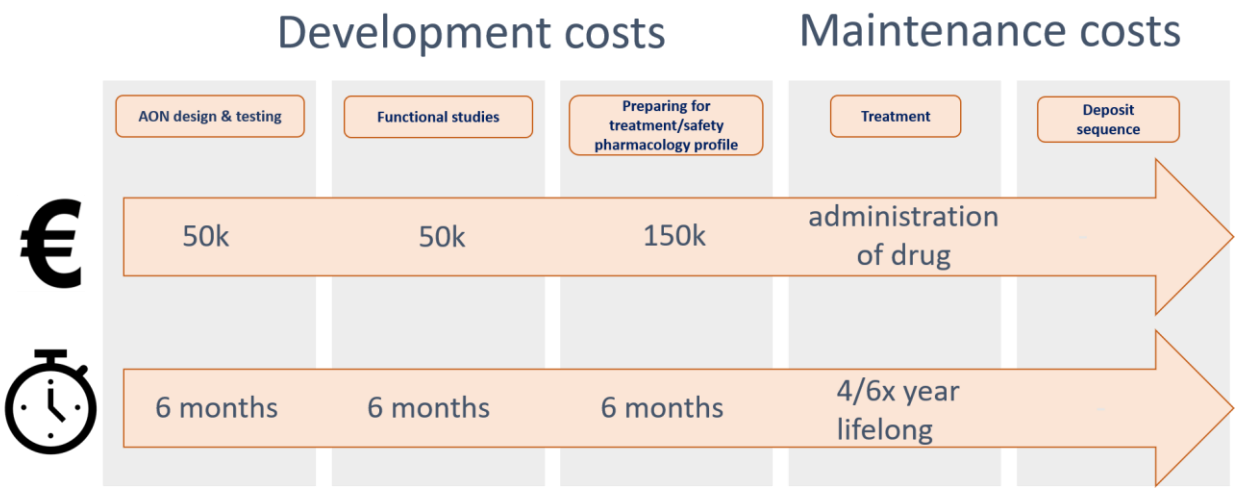
What is out of scope for DCRT:

- Making financial profit
- Patenting or registering an ASO with regulatory bodies

5 DURATION

5.1 TIMELINE

A high-level timeline is provided below:



5.2 EXECUTIVE MILESTONES

The table below lists the high-level Executive Milestones and their estimated completion timeframe.

Executive Milestones	Estimated Completion Timeframe
First patient treated through DCRT	End 2021
DCRT consortium agreement	Mid 2021

6 BUDGET

6.1 FUNDING SOURCE

Seed funding has come from LUMC for one year. From year 2 onwards, running costs will be shared by all partners equally as outlined in the consortium agreement. For ASO development DCRT will rely on funding from third parties.

7 GOVERNANCE

DCRT is governed by a board of directors. The board can consult the scientific advisory board on an at need basis. The board of directors is responsible for the strategy and vision of DCRT and for managing the timeline for the deliverable. The scientific advisory board will provide guidance on issues concerning ethics, scientific feasibility, interactions with patients, interaction with the private sector, regulatory aspects and reimbursement

The board of directors consists of:

1. Annemieke Aartsma-Rus (Leiden University Medical Center)
2. Willeke van Roon-Mom (Leiden University Medical Center)
3. Rob Collin (Radboud University Medical Center)
4. Ype Elgersma (Erasmus Medical Center)

Scientific advisory board:

- Cathalijne van Doorne (European Medicines Agency)
- Mariette Driessens (VSOP – Patiëntenkoepel voor zeldzame en genetische aandoeningen)
- Frits Fallaux (Princess Máxima Center for Pediatric Oncology)
- Richard Geary (Ionis Pharmaceuticals)
- Carla Hollak (University of Amsterdam)
- Bart Leroy (Ghent University Hospital & The Children's Hospital of Philadelphia)
- Anke Pisters - van Roy (medical advisor health insurer CZ), member of the committee assessing expensive add-on medicines (CieBAG) from health insurers in the Netherlands (ZN), member of the Roundtable on Orphan Drugs of the National Health Care Institute (ZINL).
- Ghislaine van Thiel (UMC Utrecht)
- Lonneke Timmers (Zorginstituut Nederland)
- Tim Yu (Boston Children's Hospital)