La valutazione da parte dei pari: una buona pratica al cuore della ricerca scientifica d'eccellenza

Presentazione del volume "Quality Management in Scientific Research" di Antonella Lanati

Pavia, 30 novembre 2018

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FONDAZIONE Telethon

Fondazione Telethon: an Italian charity tackling a global challenge

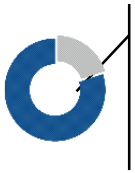
Investing in **RARE GENETIC DISEASES** research by mandate of the patient community since 1990

> 500 M€ invested
> 2,600 research projects and activities
> 570 rare diseases studied
> 11,000 scientific publications

Rare genetic diseases

350 MILLION PEOPLE AFFECTED BY 7,000+ RARE DISEASES WORLDWIDE

LESS THAN 5 OUT OF 10,000 PEOPLE ARE AFFECTED BY EACH RARE DISEASE (in the EU)



80% ARE GENETIC IN ORIGIN

Our mission

To advance biomedical research towards the diagnosis and the cure of muscular dystrophy and other genetic diseases

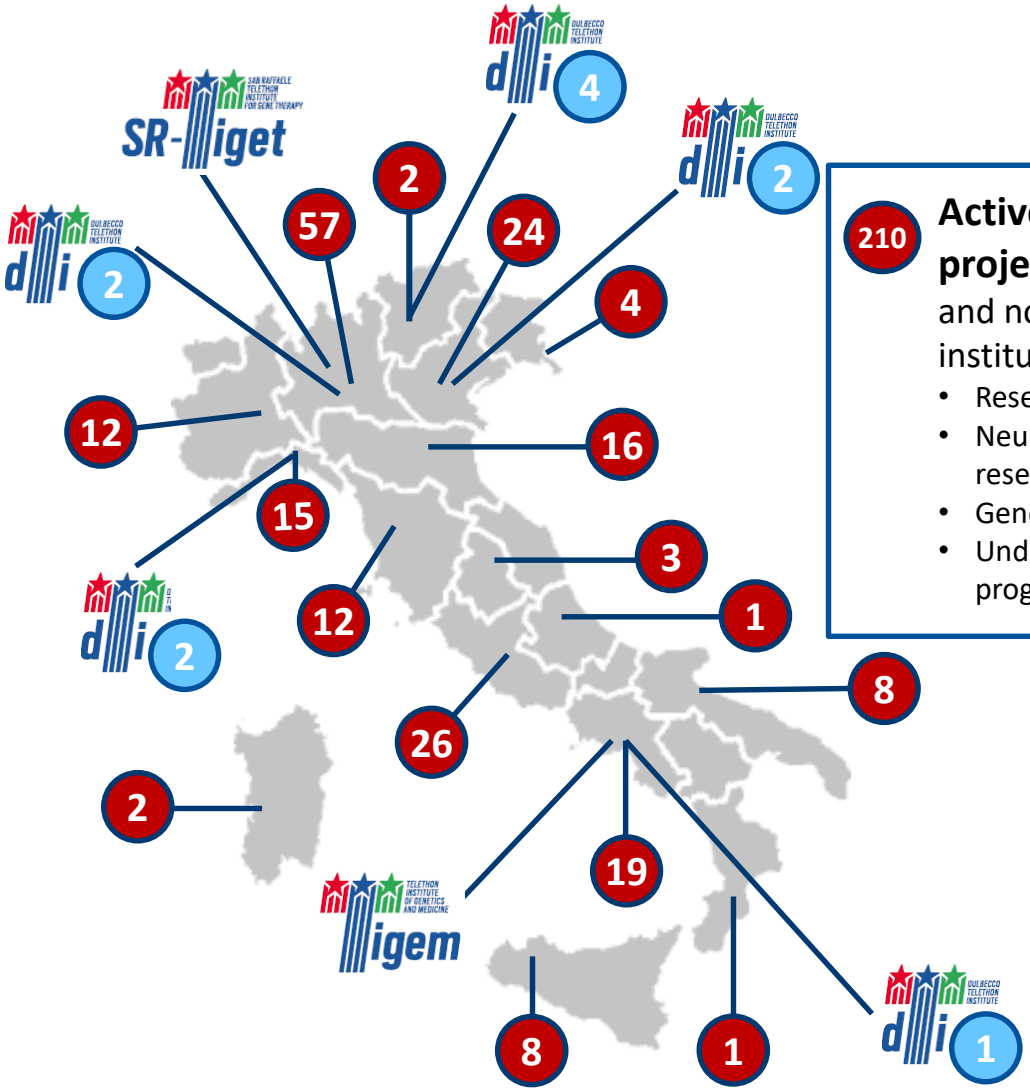
Our vision

To make therapies and diagnostic tools developed from excellent, selected and sustained research available to patients

Fondazione Telethon's research in Italy

Active Telethon projects and institutes

October 2018



210 **Active Telethon projects** at universities and non-profit research institutes

- Research projects
- Neuromuscular clinical research projects
- Genetic biobanks
- Undiagnosed diseases program

Telethon research institutes

11 Active DTI laboratories

The basis of Fondazione Telethon's scientific selection

Peer review's core principles

1. Excellence
2. Impartiality
3. Transparency
4. Appropriateness for purpose
5. Efficiency and speed
6. Confidentiality
7. Ethical and integrity considerations

European peer review guide
European Science Foundation
March 2011

Fondazione Telethon's peer review

- Fund allocation through **peer review** only
- **Regular calls** for applications
- **International scientific committee** (<10% from Italy)
- **External referees** form **abroad** only
- **Plenary review sessions**
- **Complete review reports** fed back to applicants

ISO 9001:2015 certified

Managed by a **professional scientific office** that safeguards the correctness of the process

Responsible research management

Open access/open science

- Mandatory open access for original publications
- Member of the Europe PubMed Central open access network (since 2009)
- Mandatory data sharing in accessible repositories
- Scientific Convention gathering all grantees, open to Patient Organizations

ELSI

- Required compliance with current legislation on ethical issues (patient involvement, animal experiments)
- Collaboration with patient advocacy groups on informed consent documents

Research integrity

- Dedicated policy for intramural research
- Liaison with Host Institutes for extramural research

Measuring the scientific influence of Telethon publications

- 11,000+ scientific publications since 1991
- 2776 papers in the 2013-2017 five-year period

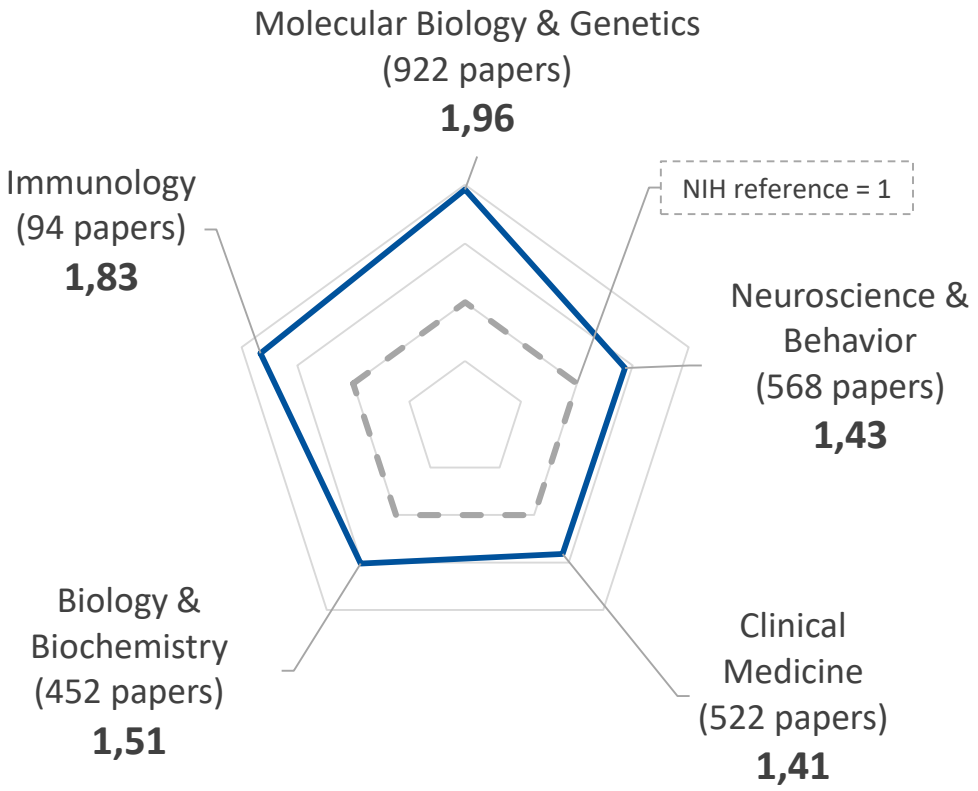
Average **RCR**/Telethon paper 2013-2017: **1,72**

The **Relative Citation Ratio** (**RCR**) is a field-normalized metric that shows the **scientific influence** of one or more articles relative to the average NIH-funded paper

Hutchins BI et al., PLoS Biol 2016

Average RCR of Telethon papers

- **original articles** and **reviews**
- **five major life sciences categories** (95% of all Telethon publications)



Sources: iCite database, November 2018

Driving research towards therapies

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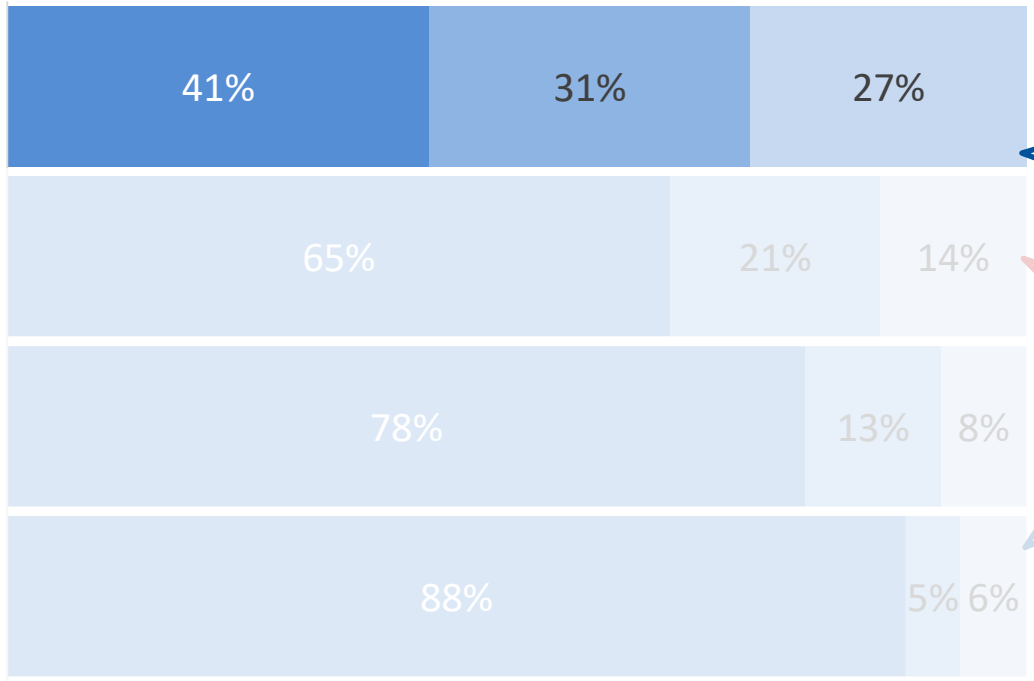
- Disease mechanisms
- Genetic studies

- In vivo/in vitro therapeutic approaches

- Therapeutic trials
- Observational studies

GENETIC DISEASES

Fundamental research → Preclinical research → Clinical research → THERAPIES



2010: first industrial partnership

2006: score on "Impact on Patients"

1995: gene therapy-dedicated investment (SR-TIGET)

May 2016: the first ex-vivo gene therapy treatment approved in the world

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How did we get there?

Strimvelis®

(autologous CD34+ cells transduced to express ADA)

for the treatment of patients with ADA-SCID for whom no suitable HLA-matched related stem cell donor is available

ADA-SCID

- Life-threatening disease
- Often fatal within the child's first years of life
- Incidence : 2-7 per million live births
- Severe immunodeficiency caused by mutated ADA gene
- The ADA enzyme protects developing lymphocytes from death

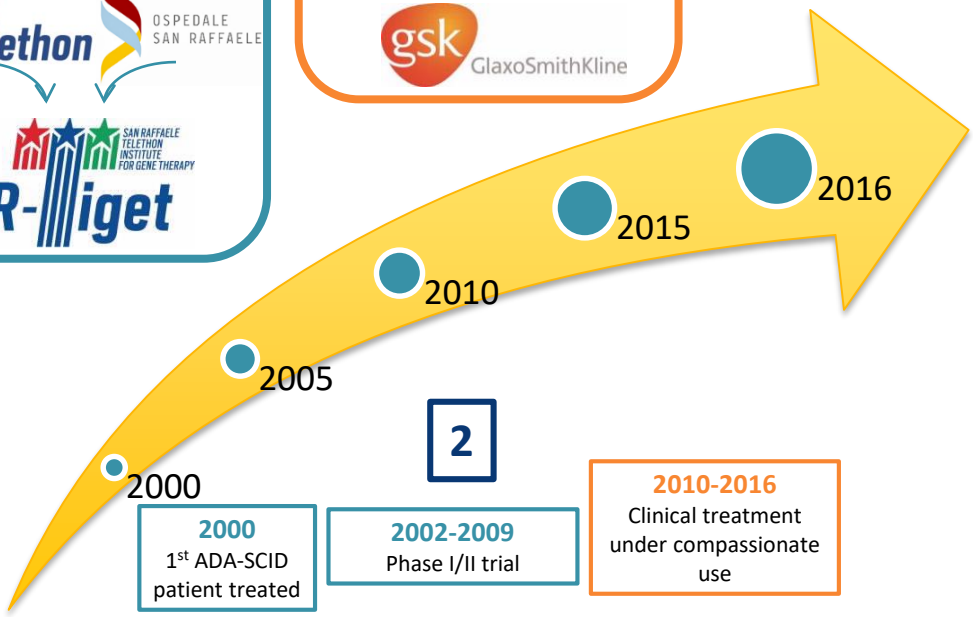
The path to Strimvelis

1

1995
SR-TIGET is founded

2010
Alliance with GSK

2018
GSK license transferred to Orchard therapeutics



May 2016
First ex-vivo gene therapy treatment approved in the world
Strimvelis® (autologous CD34+ cells transduced to express ADA)

2016
Approved by AIFA/Italy

2018
Approved by NICE/England

Market access

ADA-SCID

2

2000
1st ADA-SCID patient treated

2002-2009
Phase I/II trial

2010-2016
Clinical treatment under compassionate use

GMP production at CMO MolMed

GLP-certified laboratories at SR-TIGET

2005
EMA ODD

2007
Protocol Assistance from EMA

2009
FDA ODD

2015
MAA filing at EMA

May 2016
MA by EMA

3

Enabling factors

1. Strategic partnerships
2. Clinical trials supported by GXPS
3. Regulatory activities

Challenges for a charity in the development of an advanced therapy medicinal product (ATMP)

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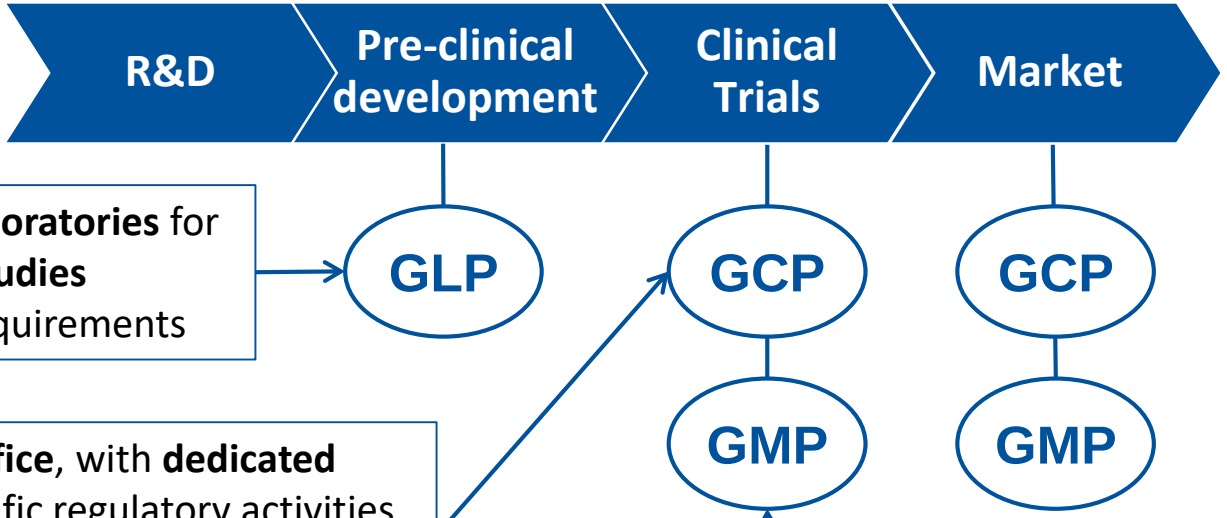
Developing ATMPs entails **complex and innovative trials** that must comply with the general regulatory frame for **Good Standard Practices**



Creation of **GLP-certified laboratories** for the conduct of **pre-clinical studies** compliant with regulatory requirements

Creation of a **Clinical Trial Office**, with **dedicated personnel** in support of specific regulatory activities for ATMP clinical trials and **training** to specialised staff (e.g. clinical nurses, data manager, etc.)

Identification of a GMP-certified **Contract Manufacturing Organisation**; high costs and timing; risk of failure

None of these actions are typical of a charity

Building investment strategies at Fondazione Telethon

A clearly defined evidence-based decision-making process

External bodies

- **Scientific Advisory Board** – made of scientists, pharma and patient representatives – to advise and guide strategic decisions
- **International Scientific Committee** to assess and select the best science to fund

Internal bodies

- **Board of Directors** – including patient representative – to decide on investments
- **Research impact and strategic analysis Unit** to monitor research outcomes and scope trends

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Thank you for your attention!

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