Developing Treatments for Rare Diseases: Fondazione Telethon's Model

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Head of Technology Transfer
Research & Development

9 February 2018 - The University of Tokyo


EVERY MINUTE OF EVERY DAY,
TEN CHILDREN AROUND THE WORLD
ARE BORN WITH A RARE GENETIC DISEASE.
TOMMASO IS ONE OF THEM.

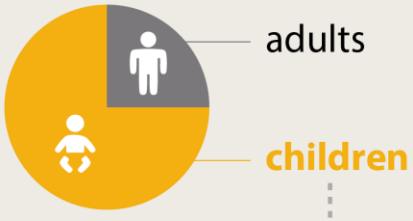
1 in 17 people in the world develop a rare disease at some point in their lives

That's 350,000,000
people with rare diseases

3,500,000

30,000,000

30,000,000



of rare diseases
are **genetic** in origin

of rare diseases have
no drug treatment

of sick **children**
never reach 5th birthday

7,000 different types of rare diseases and disorders

Who we are: Mission & Vision

- **Fondazione Telethon** is a **major Italian biomedical charity** focused on **genetic diseases**
- **Founded in 1990** at the behest of a group of **patients**
- Supported through **fundraising**

OUR MISSION

Advance biomedical research towards the cure of genetic diseases

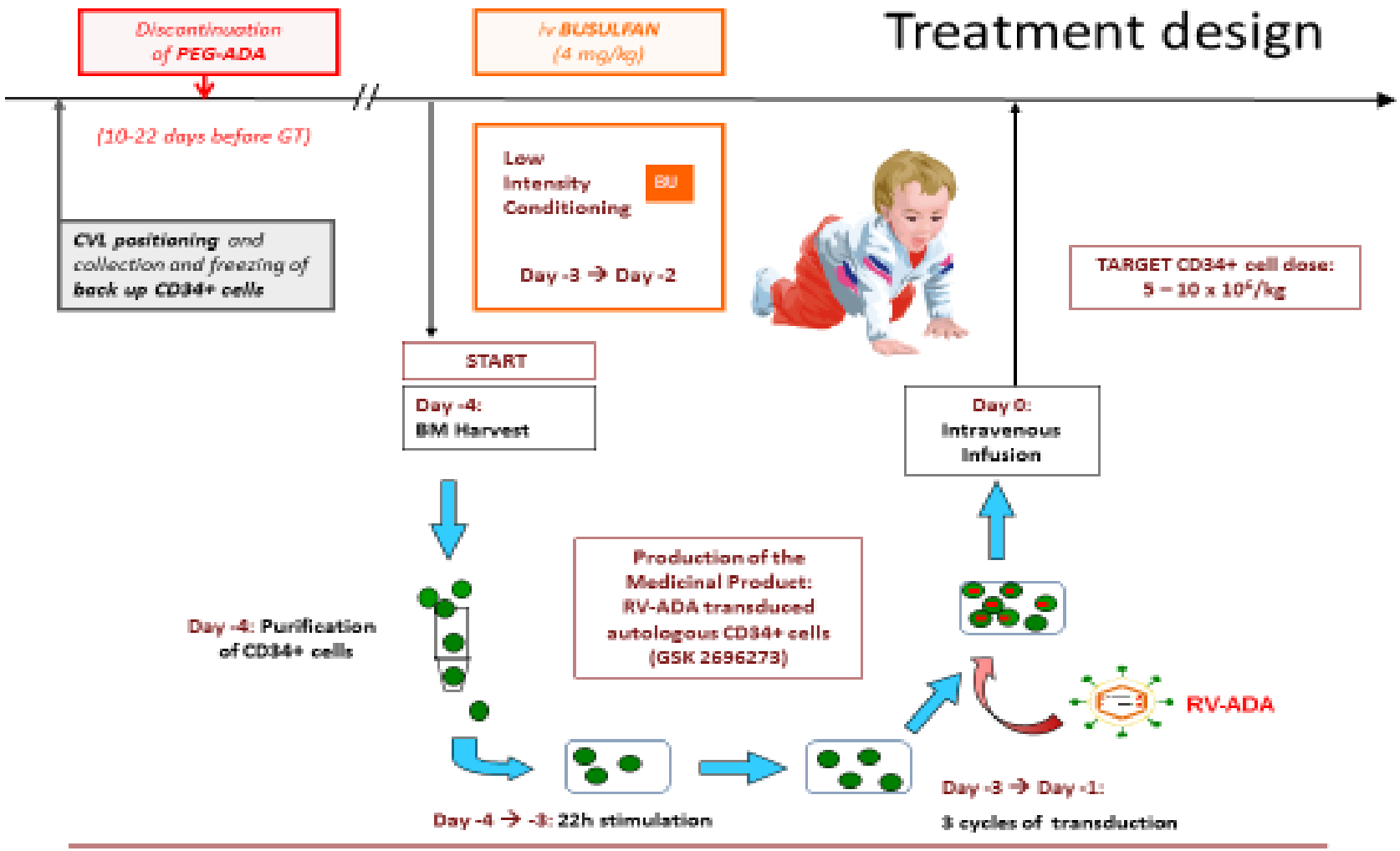
498 M€ research investment
2,629 research grants
10.615 papers published
1,611 PIs awarded
571 genetic diseases studied

OUR VISION

Convert the results of excellent, selected and sustained research into available therapies

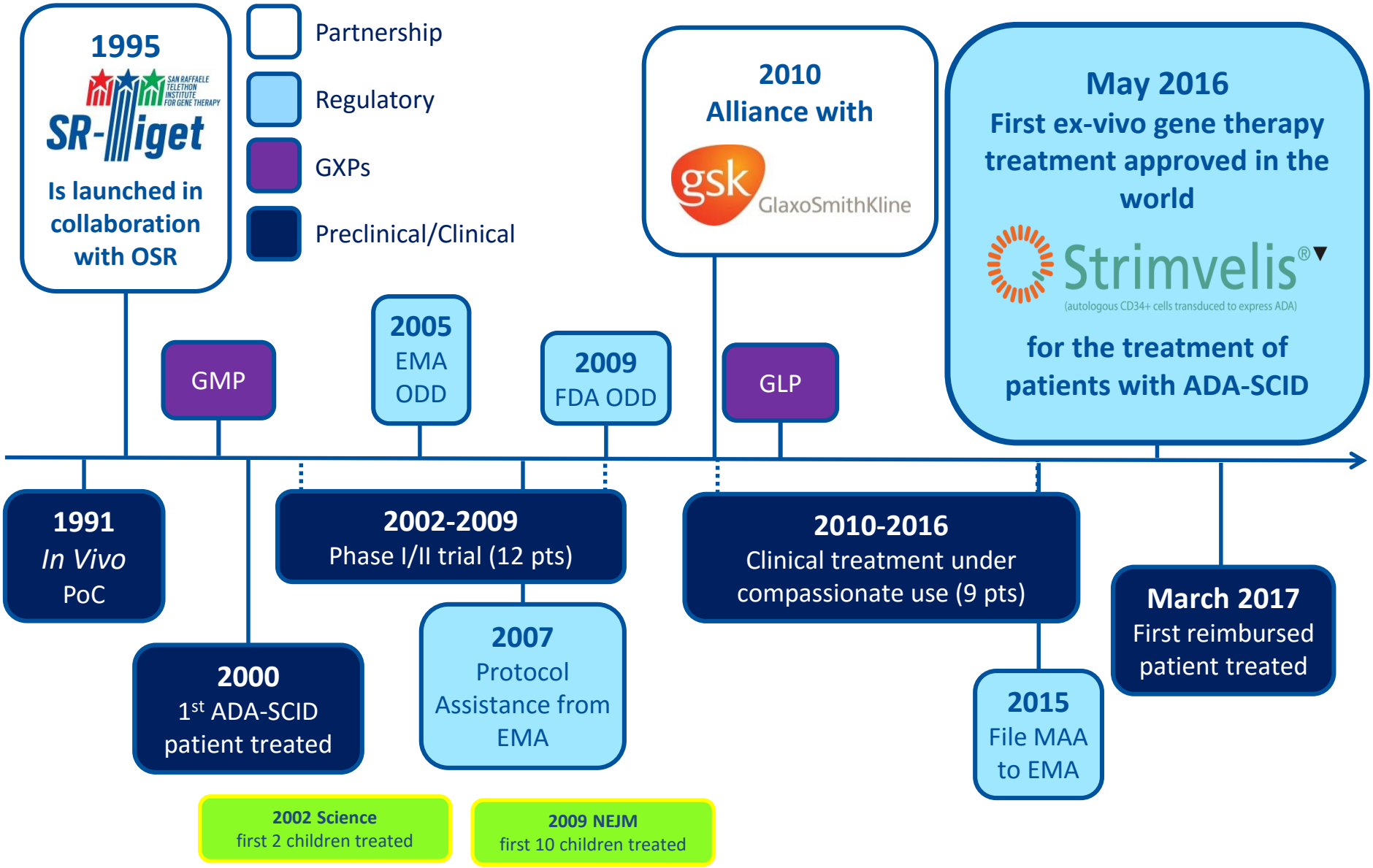
9 active clinical trials
79 patients treated
1 Therapy on the market

ADA SCID severe combined immunodeficiency ex vivo gene therapy



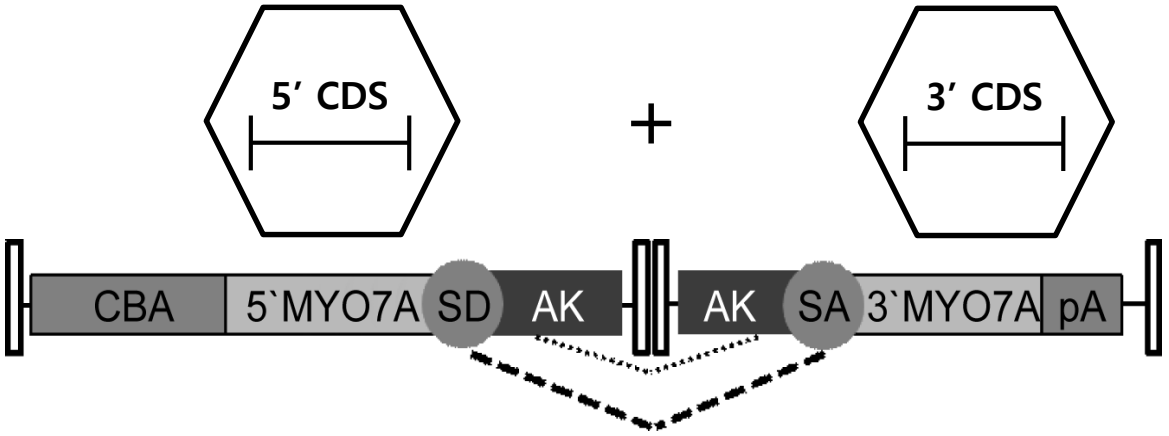
Aiuti A. et al. Science 2002; Aiuti A. et al. NEJM 2009; Cicalese MP, Ferrua F. et al. Blood 2016

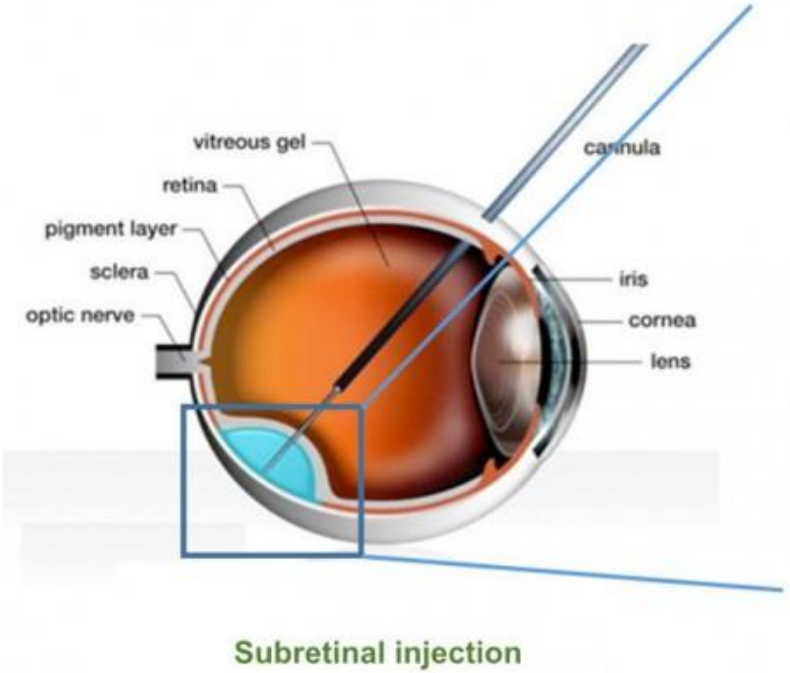
Strimvelis® as a collaborative model

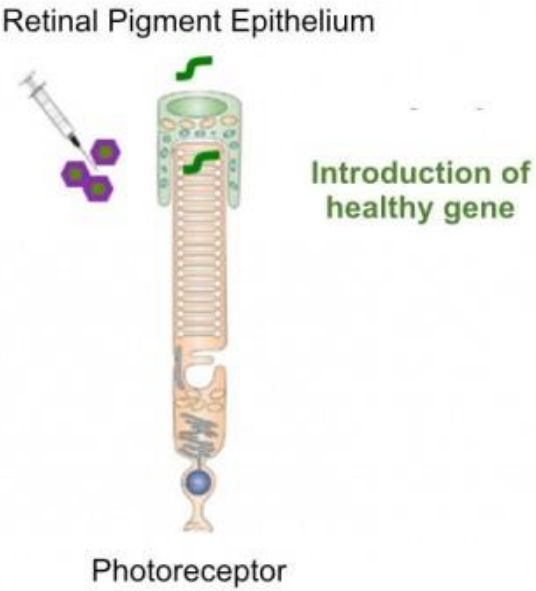


USHER IB retinitis pigmentosa gene therapy

Dual Vector System







USHER IB
as a non-profit collaborative approach

[PROJECT] **RETGENTX** - Overcoming the challenge of large gene transfer for the therapy of inherited retinal diseases
ID: 282085
Start date: 2012-01-01, **End date:** 2016-12-31
Inherited retinal diseases (IRDs) cause blindness in over 200,000 individuals in Europe. The majority are due to mutations in genes expressed in photoreceptors (PR) in the retina. We have recently demonstrated the safety and efficacy of gene therapy for IRDs in patients with ...
Programme: FP7-IDEAS-ERC
Record Number: 101700
Last updated on: 2016-07-11
Booklet

5 years Discovery (2011-2016)

[PROGETTO] **GeneVision** - Developing a cure for retinitis pigmentosa due to Usher syndrome
ID: 755075
Data di inizio: 2017-04-01, **Termine:** 2018-09-30
The GeneVision proof-of-concept project spins from a major discovery made by the principle investigator (PI) within the RetGeneTx ERC project demonstrating that dual AAV vectors expand AAV DNA transfer capacity in the retina thus allowing delivery of genes whose size cannot be...
Programme: H2020-EU.1.1.
Record Number: 209693
Last updated on: 2017-03-27
Booklet

18 months Translation (2016-2017)

RESEARCH & INNOVATION
Participant Portal

TOPIC : New therapies for rare diseases

Topic identifier:	SC1-PM-08-2017		
Publication date:	14 October 2015		
Types of action:	RIA Research and Innovation action		
DeadlineModel:	two-stage	**Deadline:**	04 October 2016 17:00:00
Opening date:	28 July 2016	**2nd stage Deadline:**	11 April 2017 17:00:00

Time Zone : (Brussels time)

5 years First-in-human (2018-2020): consortium of expertise including clinical centres, CRO and CMO

Enabling factors for transformative research

- **Excellent fundamental and pre-clinical research**
  - Stringent selection system (funding to max. top 20% proposals)
  - Adequate funding

Evaluation of projects by independent reviewers, on the basis of the American NIH model.
The process is managed by internal Research Program Managers

- **Identifying projects with translational potential**
  - Monitoring research progression and results
  - Intellectual property protection and technology transfer

- **Effective translational research**
  - Management of clinical trials
  - Management of regulatory affairs
  - Competences in drug development

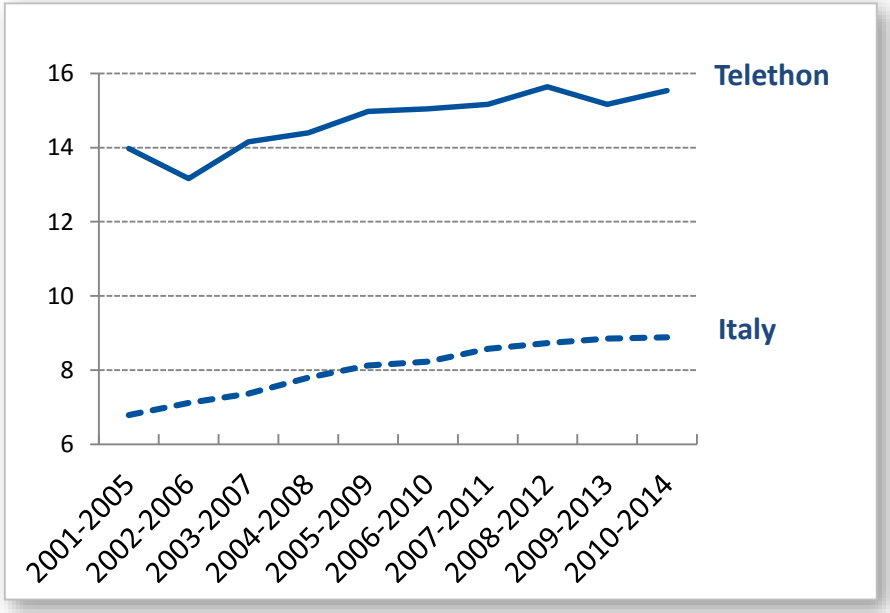
We finance excellent research: Our selection method & our impact

Peer review selection:

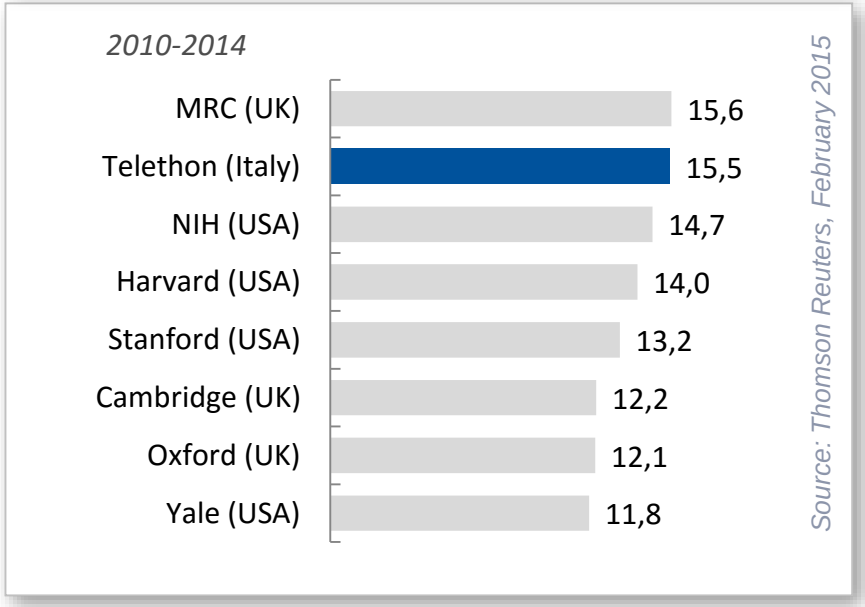
Application > Project Submission > Scientific Evaluation > Plenary Evaluation Session > Project Selection > Feedback to researchers

52% of all ERC grants won in Italy in Life Sciences to Telethon scientists

NATIONAL COMPARISON



INTER-INSTITUTIONAL COMPARISONS



Citation index *– Average number of citations/paper*, 5-yr time windows*

*** Original papers and reviews in the major biomedical research areas** (Biology and Biochemistry, Clinical Medicine, Immunology, Molecular Biology and Genetics, Neuroscience)

Telethon supports its own institutes in Italy as well as the Italian research system

3 Telethon Institutes + **187** laboratories in Research Institutes, Clinical Centers and Academias

INTRAMURAL research

TELETHON INSTITUTE OF GENETICS AND MEDICINE – tigem
Group leaders: 16
Staff: 210

TELETHON INSTITUTE FOR GENE THERAPY – tiget
Group leaders: 12
Staff: 186

DULBECCO TELETHON INSTITUTE – dti
Group Leaders: 11

EXTRAMURAL research

ISTITUTO ITALIANO DI TECNOLOGIA

National Research Council of Italy

UNIVERSITY OF TRENTO

IFOM

SAPIENZA UNIVERSITÀ DI ROMA

INGM ISTITUTO NAZIONALE GENETICA MOLECOLARE "Romeo ed Enrica Invernizzi"

IEO European Institute of Oncology

EMBL European Molecular Biology Laboratory

FONDAZIONE I.R.C.C.S. ISTITUTO NEUROLOGICO CARLO BESTA

UNIVERSITÀ DEGLI STUDI DI MILANO

Università degli Studi di Pavia

OSPEDALE SAN RAFFAELE

UNIVERSITÀ VITA-SALUTE SAN RAFFAELE

TLS TOSCANA LIFE SCIENCES

UNIVERSITÀ DEGLI STUDI DI PADOVA

ce in ge BIOTECNOLOGIE AVANZATE

UNIVERSITÀ DEGLI STUDI DI GENOVA

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Group le… … p Leaders: 11

Staff: 21…

- ✓ FOCUS
- ✓ CRITICAL MASS
- ✓PEER REVIWED
- ✓IP OWNERSHIP

EXTRAMURAL research

ISTITUTO ITALIANO DI TECN…

UNIVE… OF TRI…

- ✓ FLEXIBILITY
- ✓ OPPORTUNITIES
- ✓PEER REVIEWED

EMBL

…titute of Oncology

DEGLI STUDI DI MILANO

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- **Identifying projects with translational potential**
  - Monitoring research progression and results
  - Intellectual property protection and technology transfer

Research progresses are monitored by internal Research Program Managers.
Support for IP protection and industrial partnerships from the internal TTO.

⇩

- Effective translational research
  - Management of clinical trials
  - Management of regulatory affairs
  - Competences in drug development

We team with industrial partners: Our Major Alliances

	Start year	Institute	Scope	Deal Structure
GlaxoSmithKline	2010	TIGET	Retroviral-based ex vivo gene therapy for **ADA-SCID,** and lentivirus bsaed for **WAS, MLD, beta thalassemia** and 3 other diseases.	Upfront:10M€ MS & Royalties
BIOMARIN	2011	TIGEM	Small molecule drug candidates for **Lysosomal Storage disorders** and **neurodegenerative diseases**	R&D MS Royalties
Shire	2012	TIGEM	Gene therapy and small molecule approach for the treatment of **Lysosomal Storage disorders** and **neurodegenerative diseases**	R&D: 17,5M€ MS & Royalties
biogen idec	2014	TIGET	Lentivirus-based gene therapy for **blood disorders**	Upfront R&D MS & Royalties
editas MEDICINE	2016	TIGET	Genome editing of **hematopoietic stem cell (HSC)** and **T cell therapies**	**Undisclosed**
BIOMARIN	2016	TIGEM	**Undisclosed**	**Undisclosed**

The pillars of Telethon's industrial agreements

All agreements between Telethon and industrial Partners

- Safeguard **research independence** of Telethon investigators
- Retain **intellectual property rights**
- Mandate **commitment in developing therapies**
- Imply **return of any IP** and **results co-developed**, in case the Partner does not pursue therapy development

- ➢ Provide **funding** in support of the research in the collaboration programs
- ➢ Supply **additional funding** through milestones/royalties, in support of further research activities

An invited commentary on Fondazione Telethon

EMBO Molecular Medicine, 2 February 2017

Commentary

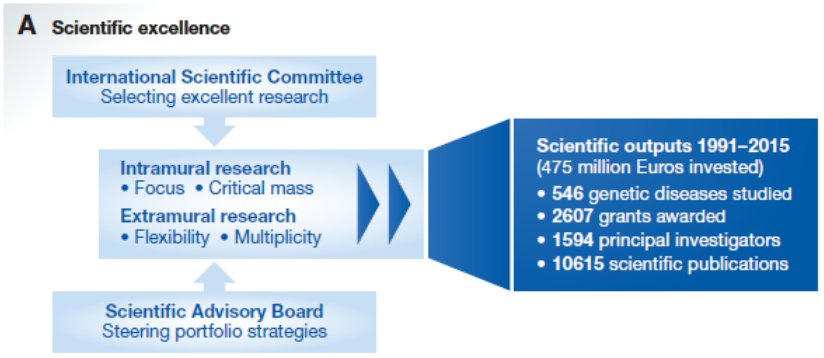
OPEN ACCESS

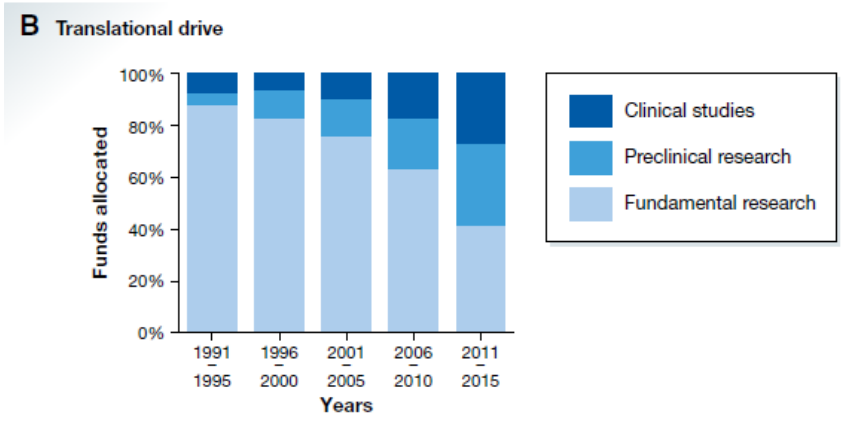
EMBO Molecular Medicine

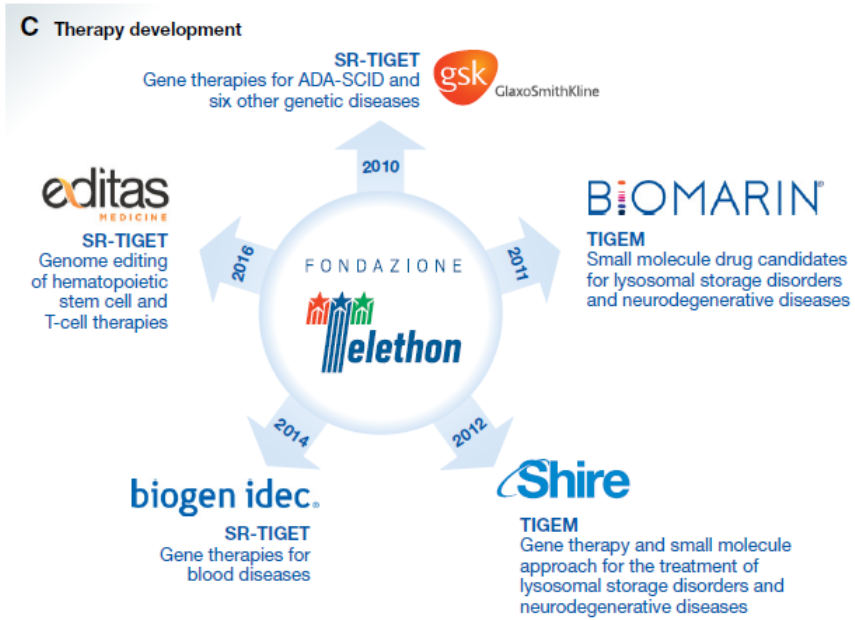
Patient-driven search for rare disease therapies: the Fondazione Telethon success story and the strategy leading to Strimvelis

Lucia Monaco & Lucia Faccio

Figure 1. The pillars of Fondazione Telethon's commitment to research.
(A) Scientific excellence is safeguarded by the rigorous and transparent selection of the best research projects by an international scientific committee and by the steering of the research portfolio by an expert scientific advisory board, which contribute to the constant increase of Fondazione Telethon's scientific outputs. (B) Translational drive is exerted by constantly steering research toward clinical applications and has gradually shifted research investments from fundamental research to pre-clinical and clinical studies. Research costs exclude unallocable costs such as intramural fixed costs, open-access fees. Source: Fondazione Telethon's TRic database. (C) The development of therapies requires partnerships with biotech/pharma companies. Five major alliances have been achieved by Fondazione Telethon in the past 6 years for the major research areas in its intramural institutes SR-TIGET and TIGEM. For SR-TIGET, partnerships are co-signed by Fondazione Telethon and the San Raffaele Hospital in Milan.







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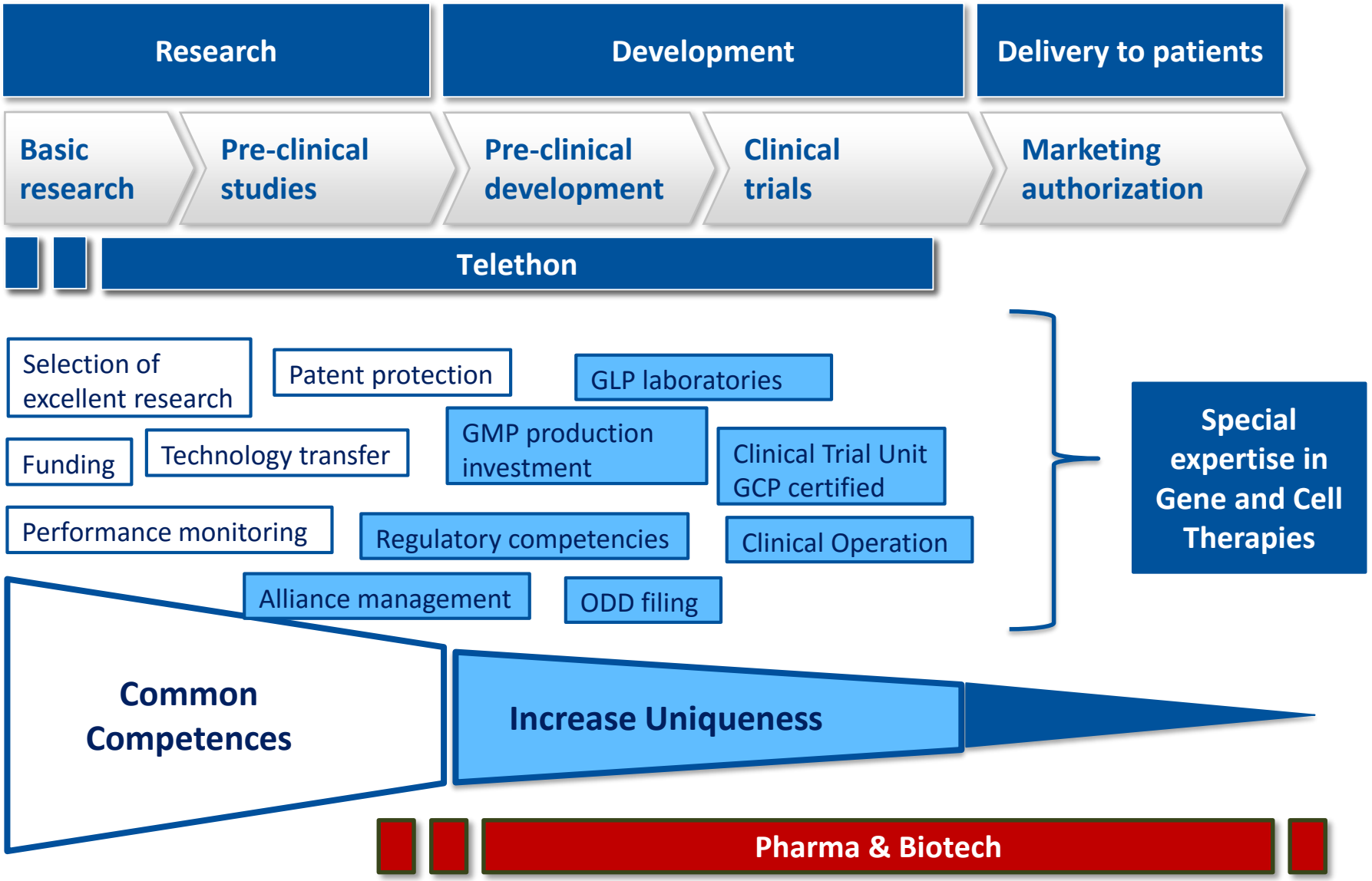
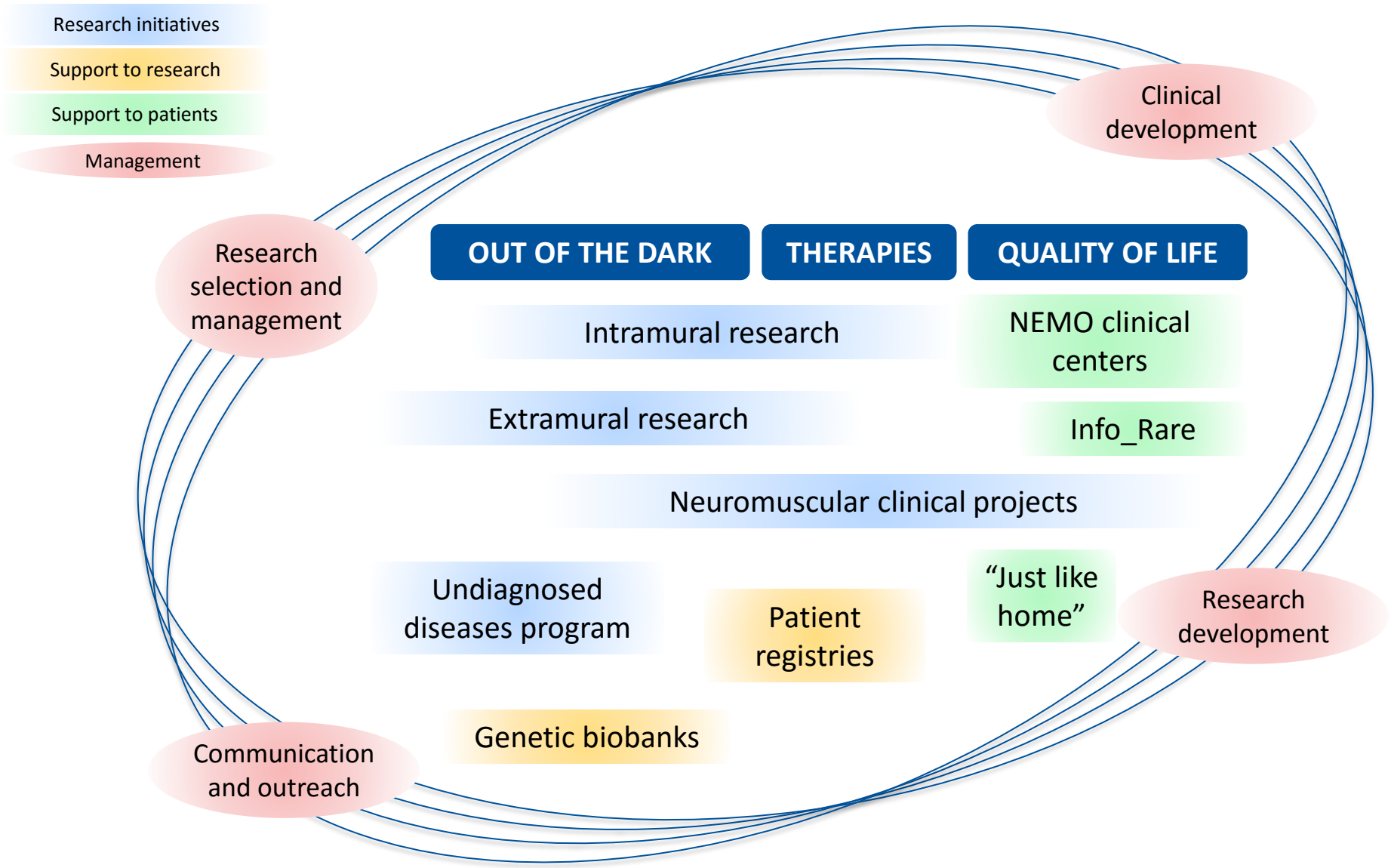
A dedicated team manages activities relevant for clinical trial and postmarketing drug use as well as established industrial alliances that are moving toward clinic.

We have built relevant expertise: Telethon's translational competences



Rare disorders require more efforts: Telethon's initiatives



Support to research

1. **NEUROMUSCOLAR DISEASES PATIENTS REGISTRY**: The alliance among Telethon Foundation and 5 patient association allowed the set up of a registry to collect patients information, their genetic and clinical infromation with the final goal of improving knowledge on the diseases, thus helping both fundamental and clinical research and ultimately the development of a therapy.

   6 registries and more than 2000 subscriptions.

2. **THE TELETHON NETWORK OF GENETIC BIOBANKS** (http://biobanknetwork.telethon.it/) has been founded in 2008 by 7 Biobanks supported by Telethon Foundation, whose purpose is to collect, preserve and offer to the Scientific Community biological samples and related clinical data from individuals affected by genetic diseases, from their relatives or from healthy control individuals.

   At present, the Network is constituted of 11 Biobanks.

3. **THE TELETHON UNDIAGNOSED DISEASE PROGRAM** is a pilot project that aims at finding a diagnosis of patients affected by unknown genetic diseases. It is the first Italian initiative and is relevant for pedriatic disorders.

   At present, clinical diagnosis in 14 casees; molecular diagnosis in 32 cases

Support to patients

1. **INFO_RARE**: information service for people, patients, care givers, physicians who need clear and certified information on genetic rare disease (diagnosis, centers of reference, referred patient organizations).

   11750 queries since 1998.

2. **TELETHON PATIENT ORGANIZATIONS NETWORK**: Since its foundation, Telethon Foundation has been working with Italian patient organizations in order to support research toward the cure.

   At the moment 190 patient organizations are part of this network

3. **"COME A CASA" –> "JUST LIKE HOME"**: program to facilitate access to the therapies developed by Fondazione Telethon, providing economic, logistic, emotional, cultural, legal support to patients and patients' families.

   8 families (participating to clinical trials) hosted in the 2017

4. **NEMO CLINICAL CENTERS**: Fondazione Telethon has been supporting the development of the NEMO project leading, so far, to the creation of three centers (North, Centre and South of Italy) that provide the most advanced standards of care for neuromuscular patients.

   25220 health services in 2016

Conclusions

- **Fondazione Telethon** acts as a **research funding agency**
- We are accountable towards **patients affected by rare genetic diseases**
- **Excellent research** is a mandatory **tool** to reach our goal of providing **therapies** for rare genetic diseases
- We cannot assure success of research results, but **we guarantee full commitment** towards our goals by engaging **all competences** required

Thank you!

FONDAZIONE Telethon