



**Nobody wins alone.
Public-private collaboration for a new European
leadership in health and life sciences.**

Marcello Allegretti

Chief Scientific Officer, Dompé farmaceutici SpA



Pharmaceutical companies in Italy

67,000 people work in the pharmaceutical industry and 146 thousand in allied industries.

Gender equality is a fact: **43%** of the personnel are **women**.

Each year registers a new record in **R&D investments: € 1.6 bn** of which over **€ 700 m** dedicated to **clinical research**.

In the next 5 years the pharmaceutical companies will invest over \$ 1,500 bn worldwide in R&D.



Source: Facts & Figures Farmindustria – 31.10.2020



Invention
is not an individual achievement
but **a shared effort**
of diverse minds

Sergio Dompé, Executive President Dompé farmaceutici

Our Open Innovation Ecosystem



Proprietary

Drug Design and Discovery Platform

Our **Exscalate** proprietary system covers all **development phases of new synthetic molecules**, to **identify new drugs** leveraging some of the top EU supercomputing, AI and life science resources.

Early Clinical Development Platform

The integration with the Design and Discovery Platform allows us to develop a wide pipeline of products targeting **novel pathways** with innovative **mechanism of action**.

Our research benefits of an open network of international collaborations, connecting more than 300 centers and universities.

Network





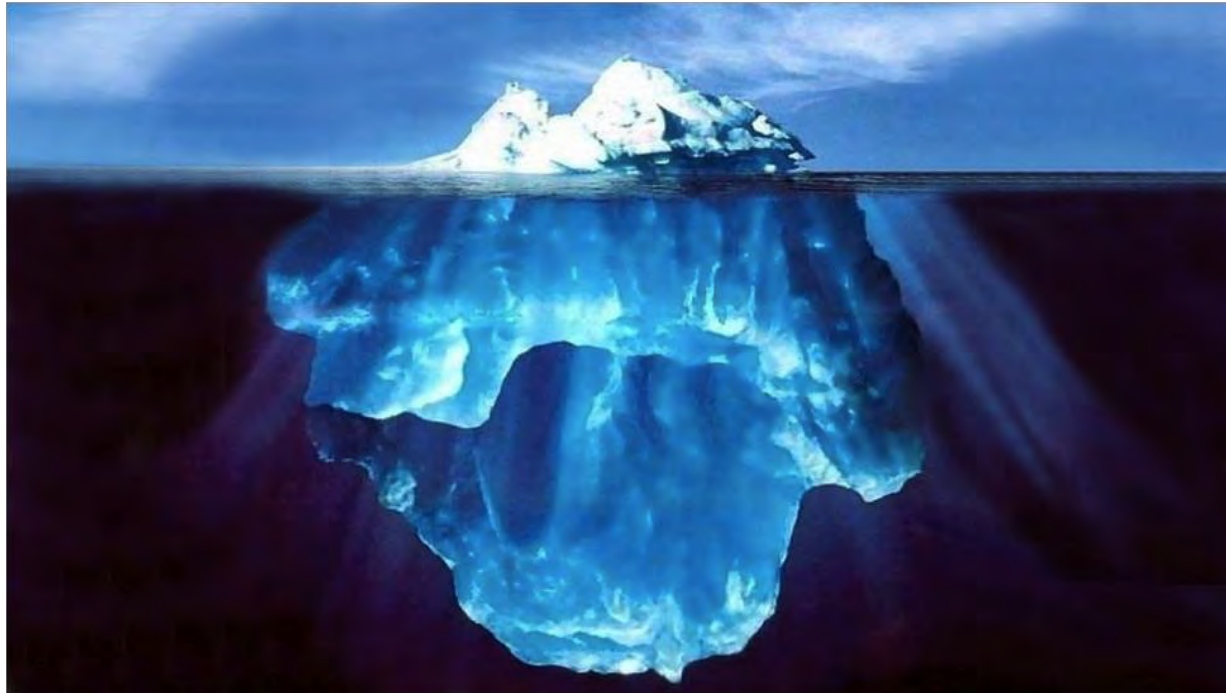
Neurotrophins

A unique breakthrough

Dompé in Ophthalmology - rhNGF



recombinant human Nerve Growth Factor



“The history of NGF can be compared to the discovery of a sunken continent revealed by its emerging top”

Rita Levi Montalcini (Nobel Prize in Medicine-1986)

Anabasis key events



Rapid Progress in 12 Months



Feb 2012: Dompé completes Anabasis's acquisition

2011 Sept.: succesful transfer to Dompé and scale up of manufacturing process

2011 Jan.: Dompé acquires 49% of Anabasis

2010: In-licence manufacturing process from Scil Ag

2009: Anabasis starts operations

2009: NGF glaucoma study - *PNAS, 2009*

2005: NGF reaches the posterior segment of the eye - *IOVS, 2005*

1998: First report on the therapeutic effect in NK - *NEJM, 1998*

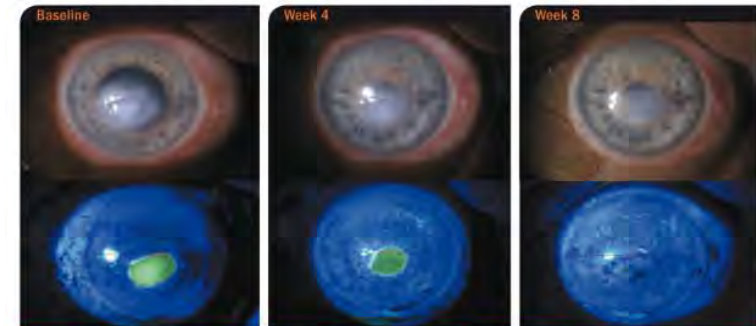
2017 rhNGF as a Treatment



- Oxervate is the first-ever application of a human NGF as drug or treatment, and is the first-ever topical biologic medication approved in ophthalmology.
- The first treatment specifically indicated for neurotrophic keratitis (NK).
- The first drug with a mechanism of action that targets the root pathology of the disease.

Ophthalmology Times

New era for rare corneal disorder



IN VIEW: Healing of a neurotrophic corneal ulcer in a patient treated with cenergermin, viewed under white light (top row) and with fluorescein staining under cobalt-blue light (bottom row). (Bonini S, Lambiase A, Rama P et al, for the Reparo Study Group. Phase II randomized, double-masked, vehicle-controlled trial of recombinant human nerve growth factor for neurotrophic keratitis. *Ophthalmology*. 2018;125:1332-43. Permalink: <https://doi.org/10.1016/j.ophtha.2018.02.022>. © 2018 by the American Academy of Ophthalmology; reproduced under Creative Commons license CC BY-NC-ND 4.0)

Healing of a neurotrophic corneal ulcer in a patient treated with cenergermin, viewed under white light (top row) and with fluorescein staining under cobalt-blue light (bottom row). (Bonini S, Lambiase A, Rama P, et al, for the Reparo Study Group. Phase II randomized, double-masked, vehicle-controlled trial of recombinant human nerve growth factor for neurotrophic keratitis. *Ophthalmology*. 2018;125:1332-43. Permalink: <https://doi.org/10.1016/j.ophtha.2018.02.022>. © 2018 by the American Academy of Ophthalmology; reproduced under Creative Commons license CC BY-NC-ND 4.0)

By Cheryl Guttman Krader
Sep 24, 2018

2020: A New Frontier in Ophthalmology





nature

nature > scientific reports > articles > article

SCIENTIFIC REPORTS

Article | [Open Access](#) | Published: 25 February 2020

Topical recombinant human Nerve growth factor (rh-NGF) is neuroprotective to retinal ganglion cells by targeting secondary degeneration

Li Guo , Benjamin M. Davis, Nivedita Ravindran, Joana Galvao, Neel Kapoor, Nasrin Haamedi, Ehtesham Shamsher, Vy Luong, Elena Fico & M. Francesca Cordeiro 

In March 2020 new research provided experimental evidence of the effectiveness of Dompé’s rh-NGF as treatment against optic nerve degeneration with **“potential in multiple indications in patients, including those affected by glaucomatous optic neuropathy”**.

Glaucoma represents **the leading cause of global irreversible blindness**, affecting over **60.5 million** people, a figure set to double by 2040.



Exscalate

World's fastest molecule screening system

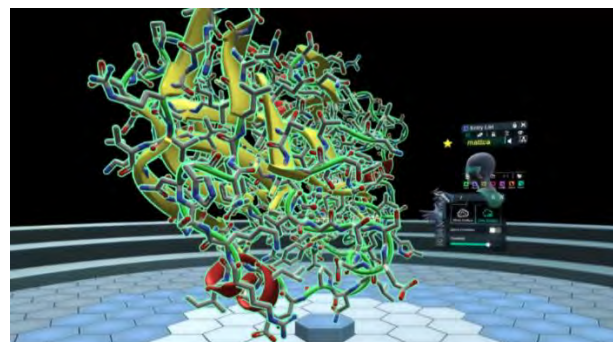
Exscalate: World's fastest molecule screening system



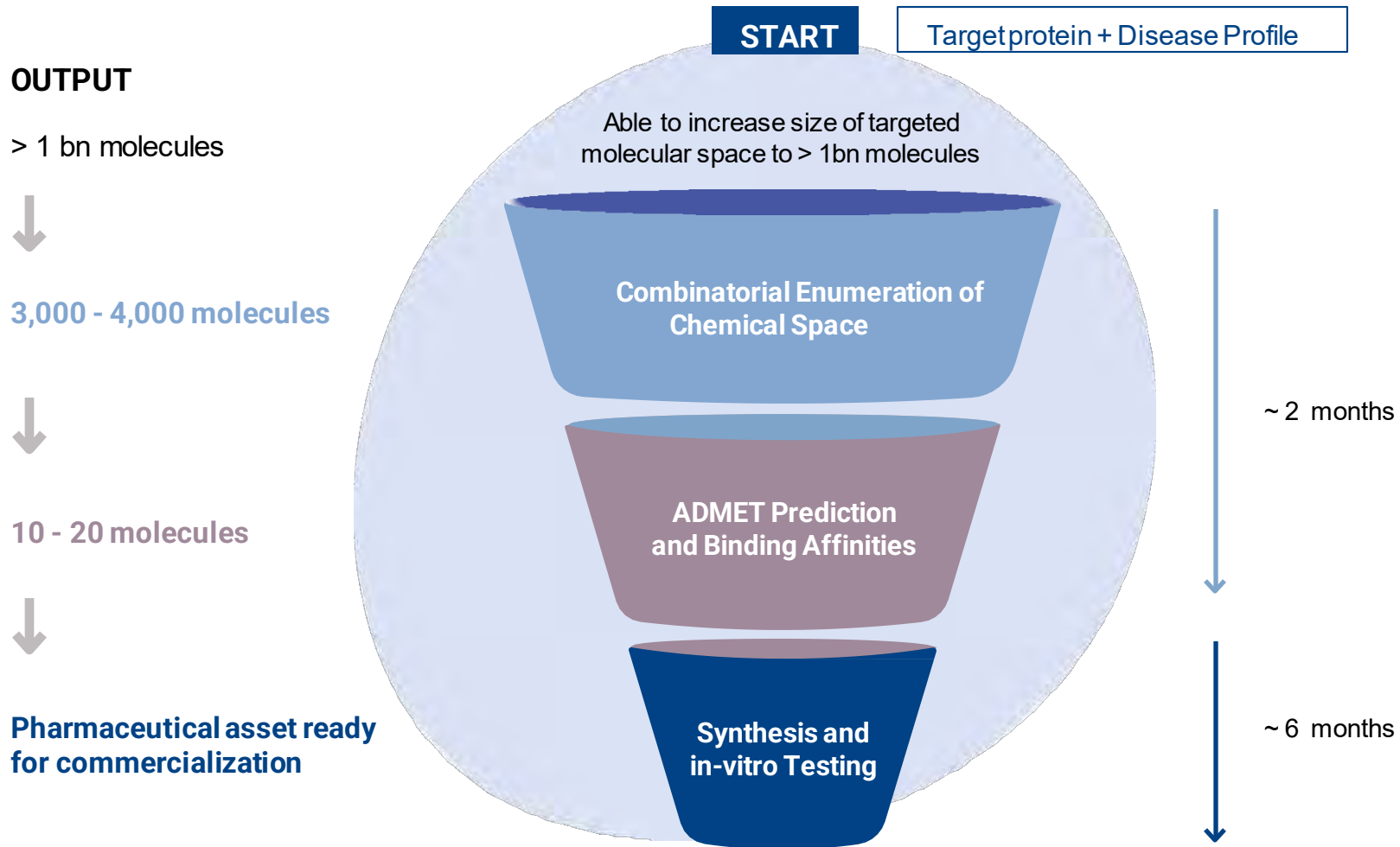
EXSCALATE

SHAPING THE FUTURE
OF DRUG DISCOVERY

- One of the most advanced intelligent supercomputing platform;
- Only AI-enabled drug discovery platform developed leveraging a Pharma Company deep knowledge;
- Unique combination of **computational power** and **polypharmacology** predictions;
- Unprecedented power to revolutionize industry standards, dramatically reducing time from target to candidate identification.



How does the platform work



WHY EXSCALATE IS DIFFERENT

Explore, as never before,
structure and dynamics
of biological systems and link
those to function in
seconds instead of months.



→ Quality

The platform identifies lead molecule candidates from a targeted, large and diverse virtual library of trillions molecules and assesses their quality and disease relevant drug likeness

→ Speed

Leads are evaluated using the structural information of the pharmaceutical target and a set of physicochemical constraints, such as Absorption, Distribution, Metabolism, Excretion and Toxicity (ADMET)

Scalability



Our LiGen technology grants code portability, readiness for synthesis and in-vitro testing

→ Open to the scientific community to drive innovation

Exscalate platform open to researchers and outstanding projects for any target disease.
Calls for proposal always open on specific target.
Partnerships open to reach the market at the speed of light.

COVID-19 case study



E4C is the public-private consortium backed by the European Commission's H2020 program. It currently represents the most advanced center of competence aimed at fighting the coronavirus by combining the best supercomputing resources and artificial intelligence with state-of-the-art experimental facilities up through clinical validation.

Exscalate, on which E4C runs, adopted a repurposing approach to identify active, ready to use in humans drugs. The drug-like and natural product subgroups of the tangible chemical space database have been tested against twelve Covid-19 proteins for a total of 15 binding sites.

One drug has been selected for its overall characteristics: Raloxifene. Raloxifene has been characterized in-vitro and in-vivo and it's now in clinical testing in Italy, just six months from the first computational screening. Additionally, three other back-up molecules validated to inhibit ACE2 are now in preclinical testing.



EXSCALATE
4COV

SPIKE MUTANTS

MEDIATE



EXSCALATE4COV: 18 Partners
(>200 EU Researchers involved)

SARS-COV2 Druggable Proteome

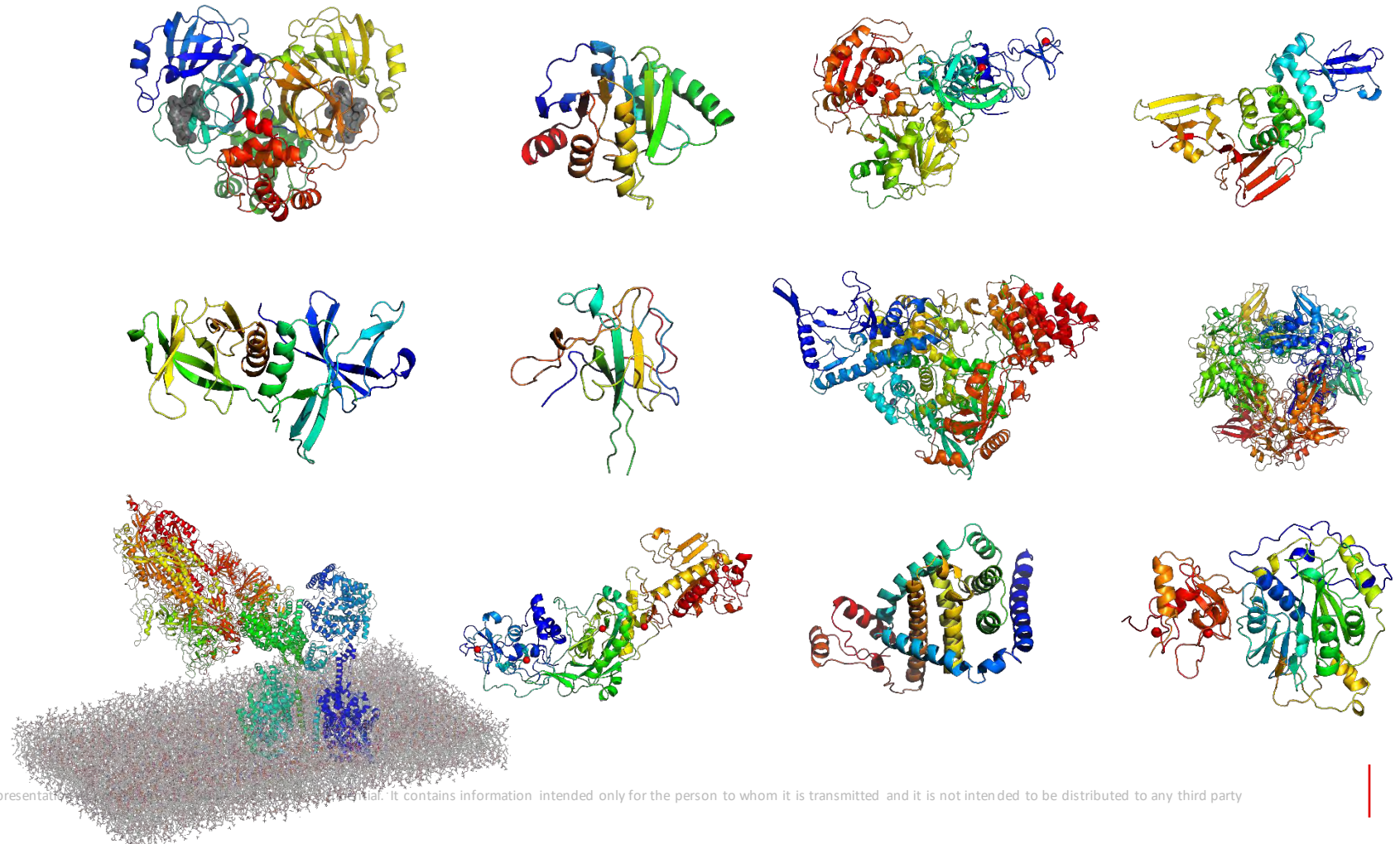


X-Ray, Homology Models,
DeepMind AlfaFold

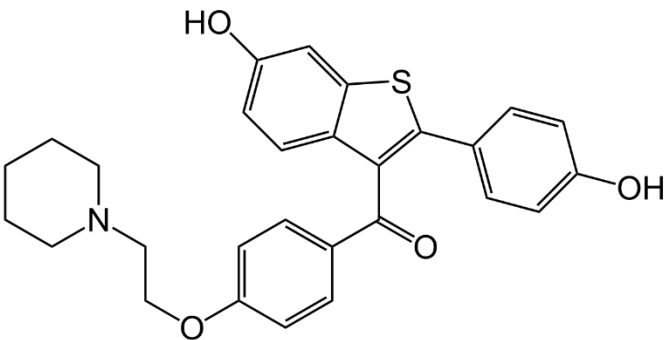
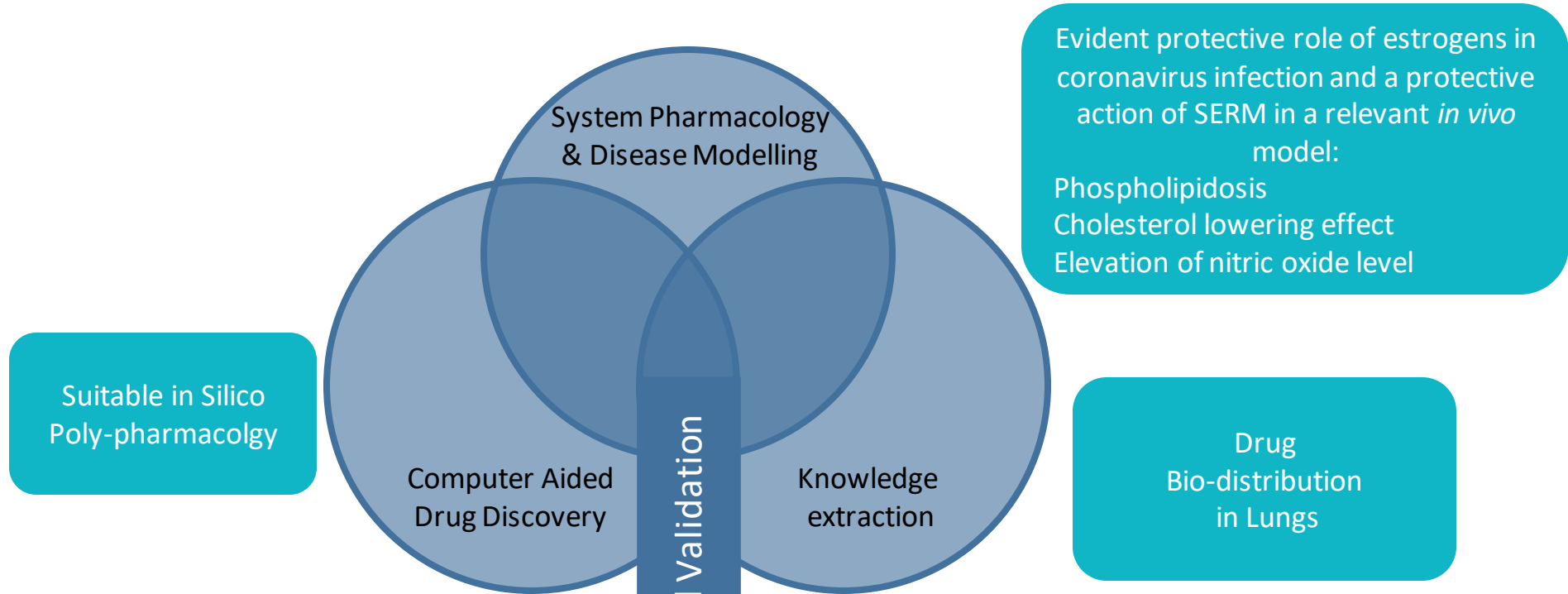
25 proteins (12 Targets)
(40 Homology models)

10 μ Sec Molecular Dynamics
GROMACS 2020

Frame Selection By Principal
Component Analysis (PCA) &
Markov state models (MSMs)



First Outcome of the E4C Project: Raloxifene



Clinical Trial

MEDIATE initiative: Crowdsource virtual screening collection from the pharma computational chemistry & AI/ML communities



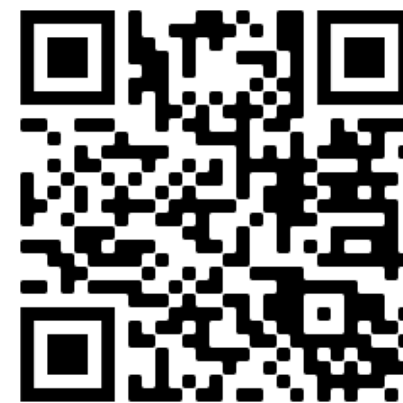
Requested by the EU commission to support the EU research of the research groups not already involved in H2020 projects

EXSCALATE
4COV

Home Actions Data Results

MEDIATE
MolEcular Docking AT home

You find them. We test them. Everyone wins.



<https://mediate.exscalate4cov.eu/>



MEDIATE initiative: Workflow

1. EXSCALATE4COV will make available
 - Chemical libraries and 3D structure of the SARS-COV-2 proteins
 - 3D structure of the SARS-COV-2 Non structural proteins and 10 μ secs Molecular Dynamics Simulations with the Characterization of all orthosteric and allosteric binding sites
 - > 20,000 experimental data to train in silico models
 - >1 Trillion docking simulation results
 - 10,000,000 CPU(GPU) time to run the simulation on the CINECA
 - web portal to collect the community results
- MEDIATE Outcomes
 - Generated a global model for the prioritization of the compounds
 - Knowledge used to acquire up to 10000 novel molecules
 - Experimentally tested in biological tests
 - Progressing the best candidate up a clinical trial validation



Project Results in Numbers



1

Approved clinical trials: RALOXIFENE



3

Clinical Candidates



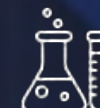
348

Molecules found to be active in experimental assays



20.000

Biological experiments performed



4

Biological assays developed



>1 Trillion

Molecules simulated



45

Proteins simulated in molecular dynamics experiments



>60 million calculation hours

Used for molecular dynamics simulations



35

Crystallographic structures generated



15

Number of publications



3

Number of patents



18

Number of partners



30

League members



€ 3+1* milioni

Project budget



>23.000

Results for "exscalate4cov" in Google Search

**EXSCALATE
4COV**



Think of the future ahead of you,
think about what you can do
and don't fear a thing.

Rita Levi Montalcini, Nobel Laureate

