PRESS RELEASE

EU-supported Private-Public Consortium Exscalate4CoV[1]: Raloxifene proposed for clinical trials after tests show it inhibits SARS-CoV-2 in vitro/in cells

As stated in a consortium agreement with European Commission, the results obtained from Exscalate4CoV are protected by Intellectual Property to promote universal access.

All scientific data produced by the consortium will be released in open domain.

18 June 2020 - Exscalate4CoV, the private-public consortium supported by the EU's Horizon 2020 programme for research and innovation, led by Dompé farmaceutici and currently representing 18 partners, has requested access to clinical trials for the use of Raloxifene in Covid 19 patients.

Raloxifene, already proven effective against Mers and Sars in precliinical tests, has been indicated as effective against Sars-Cov2 by the "in-silico" research conducted by the consortium which has shown efficacy in countering the replication of the virus in cells. The IP for its use against Sars-Cov2 has already been protected on May 6 2020 in the name Dompé farmaceutici, Fraunhofer Institute and KU Leuven, to facilitate the largest possible access. Raloxifene would be used in mildly symptomatic Covid19 patients to halt the spread of infection.

Raloxifene is currently on the market for the treatment of a osteoporosis and is well-tolerated with a known safety profile. The compound is a marketed drug and has been approved by the EMA for clinical use. The consortium is discussing with EMA the fastest path to clinical trials in humans.

This result emerged from the first virtual (in silico) screening conducted on the Consortium's supercomputers of more than 400.000 molecules (safe-in-man drugs and natural products) made available by Dompé farmaceutici and the partner Fraunhofer (IME) to the Consortium. The molecules were prioritized if in clinical stage or already on the market. 7.000 molecules with certain promising characteristics were tested.

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[1] The Exscalate4Cov (www.exscalate4cov.eu) consortium, supported by the the EU's Horizon 2020 programme for research and innovation, is coordinated by Dompé farmaceutici, and composed by 18 member institutions from seven European countries: Politecnico di Milano (Dept. of Electronics, Information and Bioengineering), Consorzio Interuniversitario CINECA (Supercomputing Innovation and Applications), Università degli Studi di Milano (Department of Pharmaceutical Sciences), International Institute of Molecular and Cell Biology in Warsaw (Warsaw, Poland), KU Leuven, Elettra Sincrotrone Trieste, Fraunhofer Institute for Molecular Biology and Applied Ecology, BSC Barcelona Supercomputing Centre, Forschungszentrum Jülich, Università degli Studi Federico II di Napoli (Department of Pharmacy), Università degli Studi di Cagliari, SIB Swiss Institute of Bioinformatics, KTH Royal Institute of Technology (Department of Applied Physics), Associazione Big Data, Istituto Nazionale di Fisica Nucleare (INFN), Istituto nazionale per le malattie infettive Lazzaro Spallanzani and Chelonia Applied Science.

At the core of the project is Exscalate (EXaSCale smArt pLatform Against paThogEns), at present the most powerful2 (and cost-efficient) intelligent supercomputing platform in the world. Exscalate leverages a "chemical library" of 500 billion molecules, thanks to a processing capacity of more than 3 million molecules per second. Exscalate4Cov's drug screening process matches massive supercomputing resources of more than 122 Petaflops from four major EU machines (Cineca's Marconi - 50 Petaflops; ENI's HPC5 - 51,7 Petaflops, and Barcelona Supercomputing Center's MareNostrum4 -13.7 Petaflops, Julich's Juwels - 7 Petaflops) with the contribution of the 40 kcores INFN-CNAF computing center and with some of the continent's best computational and life science research labs to counter international pandemics faster and more efficiently. This enormous effort will receive experimental validation by the capabilities of consortium partners, both in direction of structural complexes elucidation and in the direction of mechanistic elucidation at biochemical and cellular levels.
For the second phase of testing, Exscalate4CoV consortium's work continues to use high-performance computing (HPC) platform and aims to find highly specific novel molecules for the development of post-emergency solutions for SARS-CoV-2. As stated in the consortium agreement with the European Commission, the results obtained from Exscalate4Cov are protected by Intellectual Property. The Commission supported this Consortium with a grant of **€ 3 million** the European Union's Horizon 2020 research and innovation programme under grant agreement No 101003551. The aim of E4C is twofold: to identify molecules capable of targeting the new coronavirus (SARS-CoV-2) and to develop a tool effective for countering future pandemics. More specifically, E4C aims to:

- Establish a **sustainable example** for a rapid scientific answer to any future pandemic scenario. The model leverages a rapid and effective High Performance Computing platform for the generation and analysis of 3D models (provided by SIB's SWISS-MODEL service) and experimental 3D X-ray structures of protein targets from pandemic pathogens

- Drive **a fast virtual identification of known drugs** (repurposing) or proprietary/commercial **candidate molecules** to be further experimentally characterized;

- Define a workflow scheme for **biochemical and cellular screening test to validate the candidate molecules** in previous points and assure, through phenotypic and genomic assays;

- **Prepare, together with EMA, a development plan for successful candidates** for direct "first-in-human" studies or for further testing in animals for bridging studies;

- Identify **SARS-CoV-2 genomic regions** involved in host adaptation, pathogenicity and mutations.

[2] This performance exceeds by far the current "state of the art" technology which is also the subject of a recent article in *Nature* (6 February 2019, https://www.nature.com/articles/s41586-019-0917-9https://www.nature.com/articles/s41586-019-0917-9(www.nature.com/articles/s41586-019-0917-9) whereby a "chemical library" of 138 million molecules of a single target has been reached, with a processing capacity of less than 2 thousand molecules per second.