Dompé farmaceutici S.p.A.
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EXSCALATE
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Exscalate: supercomputing and artificial intelligence for drug discovery and design

Dompé's Exscalate supercomputing platform is designed to accelerate drug development and is deploying an open innovation approach collaborating with top tier academic institutions, industry players and startups.

Despite tremendous technological advances in drug discovery and medicinal chemistry, the failure rate of new molecular entities remains extremely high, and drug development costly and slow. Dompé, a global biopharmaceutical company with a 130-year legacy of medical innovation, is here to solve the problem. Leveraging strong drug development capabilities and more than 20 years of experience, Dompé has developed the most advanced intelligent supercomputing platform for drug testing, and the largest enumerated chemical library in the world for preclinical and candidate identification, enabling faster, more efficient and inexpensive drug discovery.

"Our virtual screening platform, Exscalate, leverages high-performance computing, big data and artificial intelligence (AI) to perform in silico drug testing and design," explained Andrea R. Beccari, head of discovery platform senior director. "The platform not only has unprecedented speed, quality and scalability, but is also open to the scientific community to drive innovation."

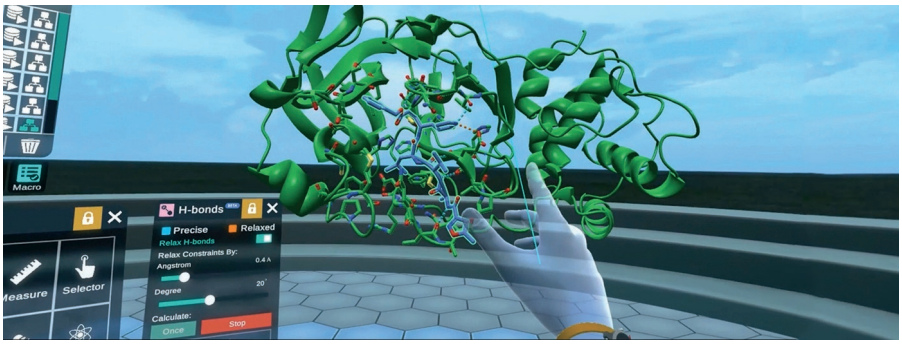

Fig. 1 | A virtual working environment. The platform is capable of evaluating more than three million molecules per second drawing on a 'chemical library' of 2 trillion molecules.

Exscalate

The platform, currently being upgraded at the high performance computing (HPC) exascale, comprises three Dompé-developed complementary modules:

- A tangible chemical space (TCS) consisting of the world's largest virtual ligand library of organic chemistry molecules, and the information required to readily synthesize each of them in a one-step reaction. "Our TCS of 2 trillion molecules is continually expanding and designed to ensure that all de novo molecules are easy to synthesize and empowered by artificial intelligence to extract the maximum knowledge for structure-activity relationships[1]," said Beccari. "The TCS contains annotated libraries, such as safe-in-man drugs (>5K), natural products (>5K), oligopeptides (>5K), and ad hoc libraries of allosteric modulators from the corporate collection."
- A comprehensive therapeutic target database (CTTD) that combines all known annotated druggable targets with decades of studies on protein–ligand and protein–protein interactions. The CTTD is designed to leverage advanced annotations of more than 45,000 binding sites (mainly allosteric)[2] of small molecules and peptides generated by the analysis of large-scale molecular dynamics simulations with protein functional annotation and pathways.
- LiGen, the most powerful in silico simulator on the market. LiGen enables Exscalate to virtually test the binding of 16.5 billion molecules on a target protein—including many conformations of the same protein—in just one hour (Fig. 1). By harnessing the capabilities of some of the top 50 supercomputers in the world, Dompé is able to model long times and large systems with a high level of accuracy. LiGen's HPC simulations increase the quality of expected delivery, reducing time[3] and ensuring transactional clinical success[4].

Dompé has multiple ongoing late-stage clinical trials for several indications with high medical need, such as viral infection, ophthalmology, oncology and immune diseases. "By combining Exscalate's features and our unique know-how in mapping allosteric sites, we are able to attack undruggable targets with novel mechanisms of action," said Beccari. "We improve clinical success rates through drug polypharmacology profiles enabled through the highest quality chemical probes exploited by Exascale AI-driven medicine design."

Partnering with open innovation

Recognizing that collaboration is key to address the challenges of successful drug development, Dompé has long adopted an open innovation approach, partnering with companies, institutions, and research networks, including the European Commission, academic spin-offs and promising biotech companies. "Nobody can win alone," pointed out Marcello Allegretti, chief scientific officer at Dompé farmaceutici. "We are convinced that partnering with the best academic and industrial groups is the most effective way to accelerate excellent research and bring new treatments to patients."

Indeed, by accelerating the identification of highly selective compounds for complex biological targets, Exscalate has proven instrumental in boosting preclinical and clinical candidate selection and supporting de novo drug design and drug repurposing strategies.

In 2020, for example, Exscalate rapidly identified a lead compound for a new target in a dry eye indication, enabling a Harvard Medical School, Boston, spin-off, Aramis Biosciences, to go from zero to phase 2 investigational new drug (IND) approval of a new molecular entity (NME) in only 14 months. Also in 2020, a Dompé-led consortium (Exscalate4CoV) used Exscalate to identify—in a record-breaking four months—a low molecular weight negative allosteric modulator, raloxifene, which successfully entered phase 3 clinical trials against SARS-CoV-2. And in 2021, Dompé struck a multi-program deal with University College London spin-off, Engitix, leveraging Exscalate to develop selective molecules for Engitix-discovered targets in fibrosis and solid tumors.

"The novelty of our business model is that we are ready to accept the challenges of drug discovery, confident that our Exscalate platform will overcome them, promoting a risk sharing approach in collaboration with companies on promising biological targets for indications with high unmet needs," said Gianluca Rossetti, strategic planning, corporate business development senior director at Dompé farmaceutici. "We are now ready to fully deploy an open-innovation approach to research and development by collaborating with top-tier academic institutions, industry players and startups."

1. Manelfi, C. et al. *J. Cheminform.* **13**, 54 (2021).
2. Bocchi, G. et al. Preprint at https://arxiv.org/abs/2202.00451 (2022).
3. Gadioli, D. et al. Preprint at https://arxiv.org/pdf/2110.11644.pdf (2021).
4. https://clinicaltrials.gov/ct2/show/NCT05172050

CONTACT
Guido Romeo, Head of Corporate Communications Director
Dompé farmaceutici S.p.A.
Milan, Italy
Email: info@exscalate.com