SERVICE GUIDE

Hit Discovery Research Enablement Service

Find more diverse hits, faster

Enable your drug discovery program with Schrödinger's unrivaled technologies and deep expertise. We'll give your hit discovery campaigns the best chances of success by leveraging our team of experts and our most advanced technologies for ultra-large virtual screening and rigorous rescoring at scale.

Best suited for companies and teams:

- Who want to leverage Schrödinger's advanced physics-based methods and expertise
- Who need to move quickly to hit program milestones
- In need of burst virtual screening capabilities for hit identification

Best suited for projects:

- With a well identified target and binding pocket
- With sufficient structural information available

Schrödinger

Propel your discovery program with unrivaled technologies and expertise

Benefit from the full impact of Schrodinger's hit discovery capabilities

- Our team of experts use extensively validated screening and rescoring workflows that leverage Schrödinger's latest technologies deployed at scale
- Service includes all computing, licensing, and service hours to perform a cutting-edge hit identification campaign with no upfront licensing or hardware costs

Maximize novelty and diversity by screening billions of compounds

- Screen commercial libraries of >5 billion compounds (or >300M for fragments screens) using both structure- and ligand-based approaches simultaneously to maximize the number of unique hits identified
- Explore the largest commercially available libraries for rapid and reliable procurement, including Enamine REAL and WuXi LabNetwork
- Efficiently screen your proprietary or sculpted libraries to explore alternative chemical spaces

Obtain more and higher quality hits with unique rescoring technologies

- Promising compounds are rescored with unmatched accuracy using AB-FEP+ amplified by machine learning
- Accurately identify more diverse and potent hits, requiring fewer compounds to be purchased and assayed

Pay based on the success of your campaign

- Because we are confident in our platform and our expertise, we offer a risk-sharing model where a significant portion of the cost is tied to your success
- You own all intellectual property generated by or derived from this service

From Feasibility Study to Purchase List

Schrödinger has over 20 years of scientific experience in developing industry-leading virtual screening technologies which are used broadly in pharmaceutical companies worldwide.

Through continuous methodology development effort combined with extensive deployment in active drug discovery programs across diverse targets, our team of computational experts have optimized an advanced virtual screening workflow offered in the Hit Discovery Research Enablement Service.

Feasibility Study includes an in-depth evaluation of the structural data available, a detailed characterization of the target binding pocket, and a pilot study to confirm performance and optimal technology settings. Project-specific criteria such as desired property space, specific undesired chemical groups, and requirements for novelty are also assessed.

Feasibility Study

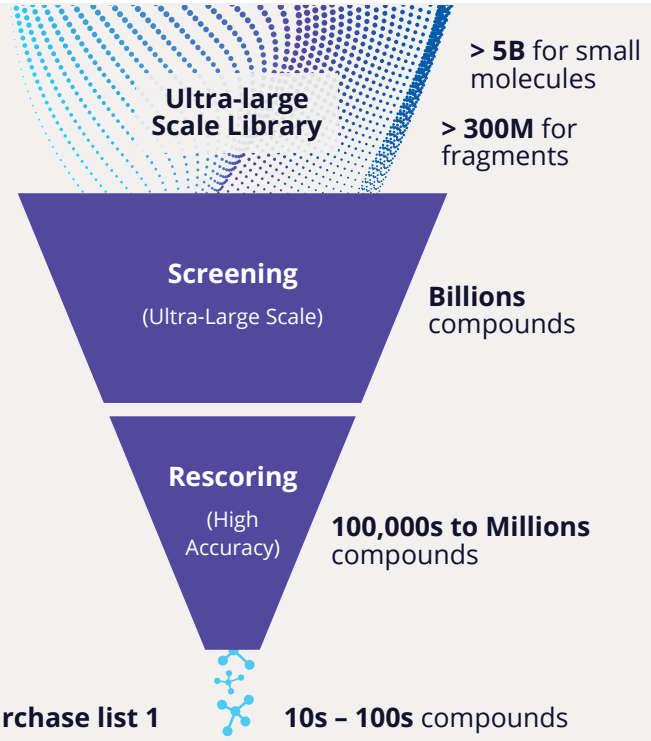
Phase I consists of two successive workflows:

Ultra-large scale screening of billions of virtual compounds using both advanced structure-based and ligand-based approaches in parallel, specifically machine learning enhanced docking (Active Learning-Glide) and high-throughput ligand evaluation (GPU Shape).

Rescoring uses unique computational technologies to improve the number and potency of hits. It includes a proprietary enhanced docking method for reducing false positives and improving poses via water-based scoring (Wscore), followed by an absolute binding FEP method for accurate affinity prediction on diverse sets (AB-FEP+).

The result is an initial purchase list.

Phase I
Large Scale Virtual Screen



Purchase list 1 **10s – 100s** compounds

Experimental Testing (Not Included in Service)

Phase II:

Hit expansion facilitates exploration of SAR around selected confirmed hits, using FEP+ for prioritization, in order to rapidly optimize affinity. The result is a second purchase list for each confirmed hit pursued.

Phase II
Hit Expansion

Purchase list 2

Scientifically-validated solutions for virtual screening

- Efficient Exploration of Chemical Space with Docking and Deep Learning. Yang et al. *J. Chem. Theory Comput.* 2021, 17(11), 7106-7119.
- Enhancing Hit Discovery in Virtual Screening through Absolute Protein–Ligand Binding Free-Energy Calculations. Chen et al. *J. Chem. Inf. Model.* 2023, 63, 10, 3171–3185.
- Benchmarking Refined and Unrefined AlphaFold2 Structures for Hit Discovery. Zhang et al. *J. Chem. Inf. Model.* 2023, 63, 6, 1656–1667.
- WScore: A Flexible and Accurate Treatment of Explicit Water Molecules in Ligand–Receptor Docking. Murphy et al. *J. Med. Chem.* 2016, 59, 9, 4364–4384.

Speak with an expert to advance your hit discovery program

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