pharmAI

The Chemical Universe at Your Hands

Focused Library Screening

Rapid Identification of Novel PDE2 Inhibitors

To demonstrate pharmAI's unique accelerated hit finding service in drug discovery we performed a focused library screening in search for potential binders to cGMP-dependent 3',5'-cyclic phosphodiesterase (PDE2).

In a first step, from an HTS library of almost two million compounds, pharmAI's *DiscoveryEngine* scored 125 compounds, spread across the chemical space. These 125 compounds were validated *in vitro* by our partner 2bind. **Seven** compounds where shown to bind to PDE2 (**a hit rate of almost 6%**) of which **three** had affinities in the lower micromolar range.

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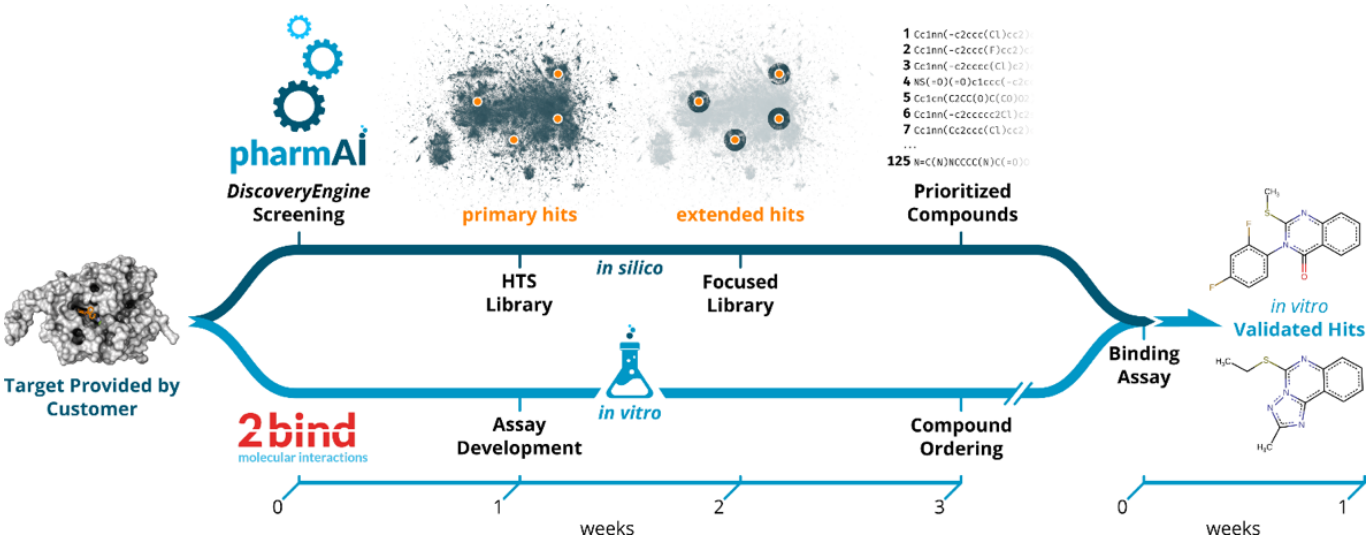
in cooperation with 2bind GmbH, Regensburg, Germany

PharmAI's Focused Library Service: 25x higher hit rate than competitors.

Focused Library Screening

pharmAI's and 2Bind's combination of AI-based drug screening with state-of-the-art biophysics allows a ground-breaking novel methodology for identification of hits to become drug candidates. A typical focused library screening project can be completed within ***4 weeks***, allowing *in silico* and *in vitro* pipelines to run instantaneously in parallel.



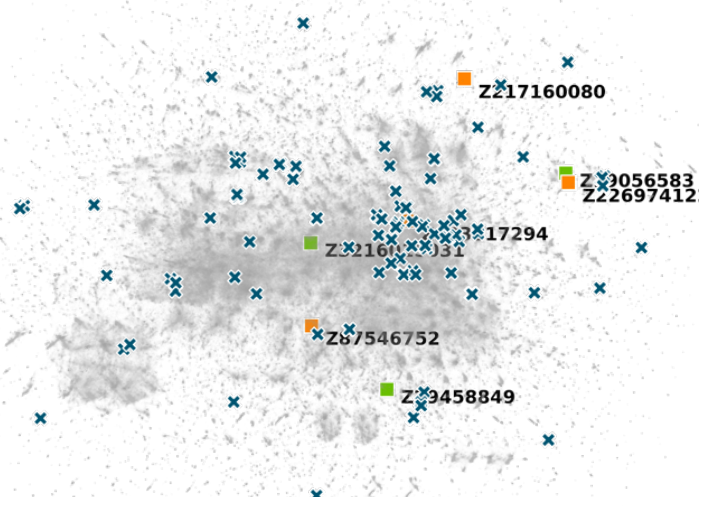
Workflow of the PharmAI·2bind focused library service. Upon the definition of the target, *in silico* and *in vitro* pipelines are launched in parallel. The pharmAI *DiscoveryEngine* delivers a prioritized selection of compounds from the desired HTS library, called the Focused Library. These compounds are then tested *in vitro* and validated hits are delivered to the customer.

PharmAI's Focused Library covers the full chemical diversity with high scaffold diversity.

Scaffold Diversification

pharmAI's hit finding algorithm utilizes the ***full diversity*** of the initial HTS library for optimized scaffold diversification. In the search for binders to PDE2, our algorithm suggested 125 hits (✕), distributed over the HTS library space (●) consisting of over 2M compounds.

The *in vitro* results validated 7 positive predictions (***strong*** and ***weak binders***), confirming the *in silico* results.

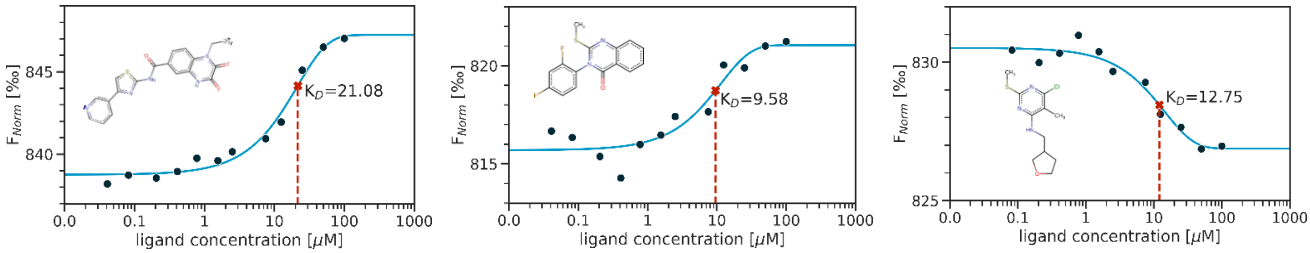


The chemical HTS space (●), *in silico* hits (x), validated *in vitro* strong binders (■) and weak binders (■)

In vitro validated binders have a high scaffold diversity.

High Binding Affinity

The qualitative results of pharmAI's methodology – validated using MicroScale Thermophoresis (MST) from 2bind – are show in the figures below. Despite the focused library screening, the diversity in the initial HTS library is fully taken into account, resulting in binders covering a large chemical space.



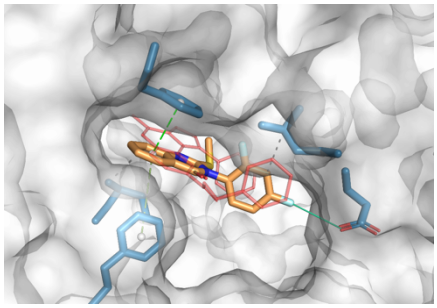
The results for the three best hits from MST measurements. Despite the focused library of 125 compounds initially used, the binders are diversified.

PharmAI provides a wider range of services.

From Hit to Lead

pharmAI can further help you to optimize the initial hits by providing services including but not limited to:

- Docking
- Molecular Dynamics
- Chemoinformatic Analyses



Docking pose of the top identified compound Z19056583 to the binding site of PDE2

Detailed Case Study Publication

Kaiser, F., Plach, M.G., Schubert, T. and Haupt, V.J. (2020). *Focus Your Screening Library: Rapid Identification of Novel PDE2 Inhibitors with in silico Driven Library Prioritization and MicroScale Thermophoresis*. bioRxiV, doi:10.1101/2020.04.22.021360 https://www.biorxiv.org/content/10.1101/2020.04.22.021360v1

Interested?

Contact us today and we will tell you more on how PharmAI can help you accelerate your drug discovery process!

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