# Quality hits at lightning speed – hit identification at Evotec

**Discover how an optimised hit identification strategy, integrating advanced tools – including AI and machine learning – can provide the best possible chemical starting points. Explore how Evotec's collaborative approach is key to identifying high-quality hits at lightning speed, saving on costs and time, while reducing the risk of attrition**

**Hit identification is one of the first, yet arguably most important, steps in drug discovery and development. An optimised hit identification strategy will ensure well-characterised, high-quality hits progress to hit-to-lead optimisation and beyond. This saves on the time and resources spent in later stages of drug discovery and development, and reduces the risk of attrition.**

However, with an infinite number of potential chemical starting points, hit identification is a challenging endeavour. Each strategy requires the careful consideration of several elements, including the compound library, screening approaches, primary assay, and methods for hit triage and validation.

A collaborative approach drawing on cross-disciplinary expertise is essential. This includes specialised knowledge in biochemistry, cellular biology, computational chemistry, in vitro biology and medicinal chemistry. Moreover, each hit identification strategy must be tailored to meet the campaign's specific requirements, including the disease area, target, and time and budget allocations. Given the complexity of hit identification, partnering with a specialist organisation such as Evotec can significantly improve outcomes. Here we show how Evotec develops an optimised hit identification strategy with its partners, providing diverse and innovative support to maximise chances of success.

## Developing a winning hit identification strategy

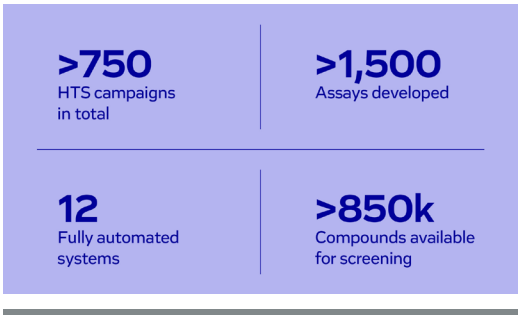
### *Using a high-quality compound library*

Quality, diversity and novelty are essential characteristics when selecting a chemical screening library. Evotec exemplifies this, offering a curated compound library of over 850,000 compounds. The expansive chemical library is comprised of 400,000 lead-like compounds, including maximally diverse 'islands of similarity', fragments, compounds with bio-annotation, natural products, natural product-derived semi-synthetic compounds, and macrocycles.

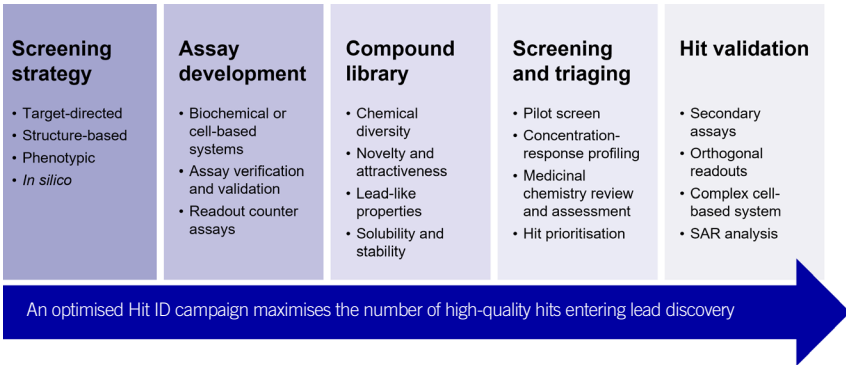
Evotec libraries are continuously evolving to raise the potential of hit identification. This includes the recent incorporation of small molecules targeting RNAs, in addition to molecular glues, covalent binders and splicing modulators. If desired, partners can also screen their own libraries of any size, including large sets of hits derived from virtual screening, or smaller, more target-directed libraries.

### *Optimising hit screening, triaging and validation*

High-throughput screening (HTS) is an automated, fast and cost-effective way to screen large compound libraries. With a cross-disciplinary team of hit identification experts and cutting-edge facilities, Evotec offers a range of HTS approaches. This includes target-directed, structure-based, in silico, or phenotypic HTS, with experts working closely with partners to select the best approaches for each campaign. Following selection of the screening approaches, the development of primary assays can be a complex and lengthy process. Evotec uses broad disease knowledge and expertise to select the most relevant assay system for each target, ensuring sensitivity, robustness, scalability and




High-throughput screening at Evotec




cost-efficiency. A breadth of different HTS screening platforms is available, including biochemical, cell-based, biophysical, anti-infective, phenotypic and imaging-based HTS, in either 384 or 1,536-well plate formats.

After conducting the pilot screen and primary screen, a range of advanced hit triaging and prioritisation techniques are employed to optimise efficiency and success. These include concentration-response profiling to assess potency and selectivity, and medicinal chemistry assessment to characterise the hits' chemical properties.

Orthogonal assay systems, including cell-based and biophysical, are then used to validate the biological activity of prioritised hits. These are conducted using repurchased fresh powder materials to ensure reproducibility and reliability and minimise the risk of false positives. Additional secondary assays including structure-activity relationship (SAR) and ADME-Tox assays are conducted to further confirm biological activity and assess on-target activity and selectivity.

### *Integrating advanced AI/ML approaches*

Several steps of hit identification can be enhanced with Evotec's cutting-edge computational screening approaches, including artificial intelligence (AI) and machine learning (ML). These approaches are continuously evolving through the adoption of reinforcement learning techniques. Algorithms learn from previous hit screening experiments, narrowing their focus on the most promising chemical spaces.

Firstly, screening collections can be assembled with the support of AI/ML to provide the most efficient coverage of the chemical space. Following this, informed and iterative *in silico* screening approaches can be applied integrating AI/ML algorithms. This provides in-depth interpretation of complex biological systems, which is becoming increasingly important to overcome high attrition rates. The improved hit characterisation provided also broadens the possibilities of hit calling during HTS. Additional putative hits can be considered, including those that are weakly active but represent distinct and interesting chemical series.

AI/ML integration enables the screening of ultra-large compound libraries, with chemical spaces explored more effectively. By aiding the identification of the most promising hits, these virtual screening approaches also mean fewer compounds need to be experimentally tested. Techniques such as AI-driven adaptive sampling can be combined with wet lab screening to rapidly identify high-quality candidates.

From hit screening, optimised hit triaging can be achieved using AI/ML, combining experimental and calculated data. This enables more informed and effective analysis, ensuring well-characterised, high-quality hit series are prioritised for progression.

### Partnering with hit identification pioneers

For over 30 years, Evotec has continued to be at the forefront of hit identification. Combining long-standing experience with leading compound libraries and screening facilities, partners can achieve the best possible chemical starting points. So far, the company has developed over 1,500 assays and has supported over 750 HTS campaigns, with state-of-the-art automated screening systems in Germany and France providing capacity for over 80 campaigns each year.

For Evotec, collaboration is central to the success of each campaign. Championing this, the company works with partners to develop highly tailored and flexible hit identification strategies. These can either be stand-alone services or be integrated into Evotec's drug discovery and development programmes or be part of a strategic collaboration.

Unleash accelerated hit identification with Evotec's high-throughput screening – find out more on our website:

**www.evotec.com/hit-identification!**

evotec

For over 30 years, **Evotec** has offered extensive drug discovery and development solutions, guiding projects from target identification to the clinic. We integrate deep disease understanding, a multimodality approach, advanced technologies, and tailored solutions to enhance the probability of success. Our innovative and flexible approach supports collaboration through stand-alone CRO/CDMO services, integrated drug discovery and development programmes, or strategic partnerships, regardless of your stage in the discovery-development journey. Evotec's sites in Europe and the US offer highly synergistic technologies and services and operate as complementary clusters of excellence.