evotec

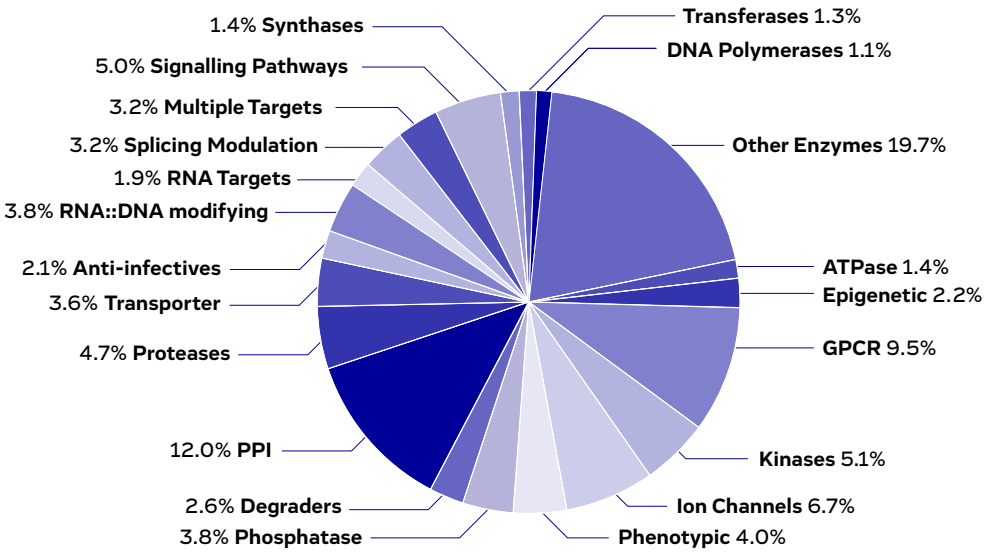
Quality Hits at Lightning Speed

Accelerated Hit Finding Through Innovative Screening Approaches in Vast Chemical Spaces

Experience

- Established in 1993 with proven success in Hit ID
- Strong knowledge of disease biology
- Extensive range of innovative technologies and platforms
- Track record in performing both standalone HTS and integrated drug discovery projects
- Wealth of experience in an expansive range of target classes
- Expansion into PPIs and RNA targeting small molecules, degraders, molecular glues, covalent binders
- Multi-disciplinary team of biologists, automation and data scientists, medicinal chemists and drug hunters overviewing projects

Target Classes and Modalities



Proven Success

- Developed >1,500 biochemical and cell-based assays
- Completed >750 high throughput screening campaigns
- >85% success rate in generating novel, validated and chemically tractable hits

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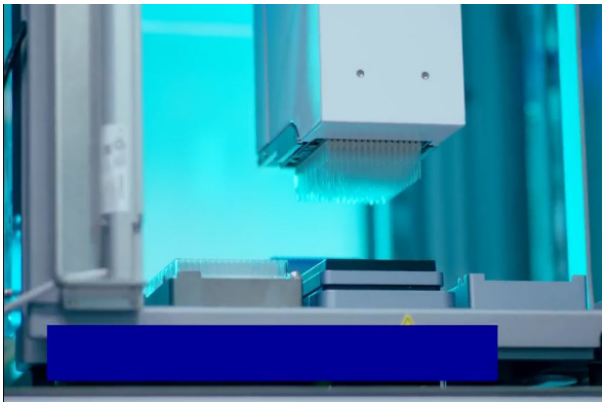
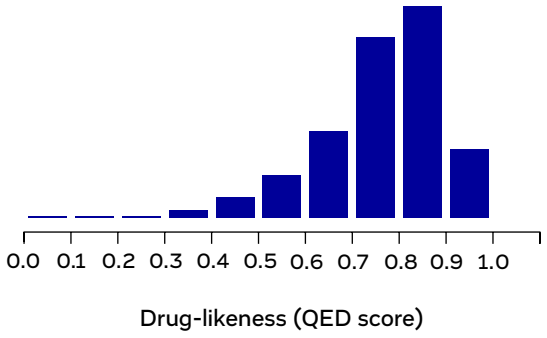
Technologies and Platforms

- State-of-the-art facilities in Europe and US
- Industrialized processes for rapid and robust data generation and analysis
- Expansive range of biochemical, bio-physical, cell-based and microbial assays
- Industry leading *in silico* and AI/ML-enabled screening capabilities



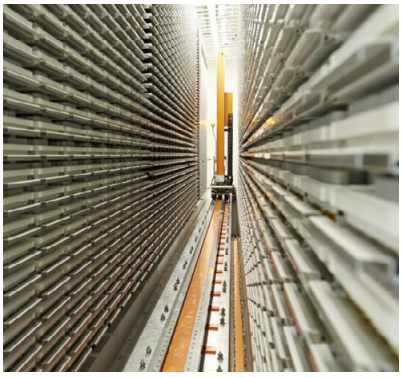
Compound Collection

- Maximally diverse and carefully curated libraries of >850,000 lead-like compounds and 25,000 fragments
- Chemical space and target space focused libraries
- Routine QC testing to confirm compound integrity and purity
- Single and pooled compound libraries optimized for Affinity Selection Mass Spectometry (ASMS) screening
- Through Evotec's collaboration with X-Chem, access to over 150 billion drug-like compounds from X-Chem's diverse collection of non-covalent and covalent DNA-encoded libraries
- Access to 48 million commercial compounds through 800+ catalogues of global suppliers
- Rapid access to >70 billion on-demand 'synthetically accessible' compounds



Compound Management

- World leading compound management facilities co-located with HTS facilities
- Library management with fast order fulfilment and worldwide delivery
- Inert or dry atmosphere and low temperature storage and processing options
- Multi-format plating and reformatting (milli to nanolitre volumes)
- Titian Mosaic infrastructure for sample tracking and management



Evotec's Compound Collection

Evotec's screening library is differentiated by its **quality, diversity** and **novelty.** It has a confirmed track record for delivering **high-quality, diverse** and **tractable** hit compounds for medicinal chemistry optimization.

Collection of
> 850,000
IP-free lead-like compounds

Collection of
~ 25,000
fragments

Access to
> 150 billion
DEL compounds

- Over 850,000 IP-free lead-like compounds
  - 800,000 maximally diverse compounds including 50,000 'ligand efficiency' compounds
  - 25,000 fragments
  - 5,000 compounds with known bio-annotation
  - 30,000 natural products and semi-synthetic derivatives
  - 2,000 macrocycles
  - 5,000 Cys directed covalent library
  - 1,200 RNA-focussed binders
- Carefully curated to fuel groundbreaking discoveries
- Single and pooled compound libraries optimized for Affinity Selection Mass Spectrometry (ASMS) screening
- Through collaboration with X-Chem, access to over 150 billion drug-like compounds from X-Chem's diverse collections of non-covalent and covalent DNA-encoded libraries
- Access to 48 million commercial compounds available through 800+ catalogues of global suppliers
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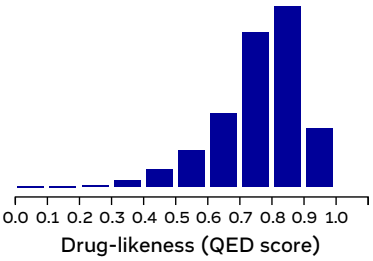
Third Party Collections

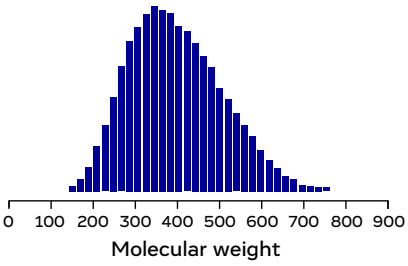
Evotec can also screen:

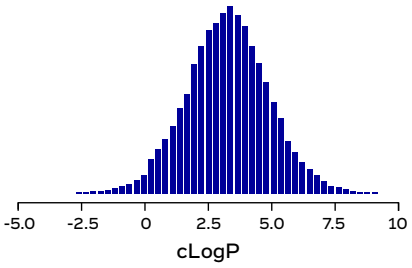
- customer libraries of any size
- virtual screening derived hits
- smaller, more target-directed libraries

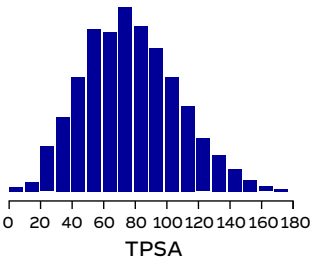
Characteristics of Evotec's Compound Collection

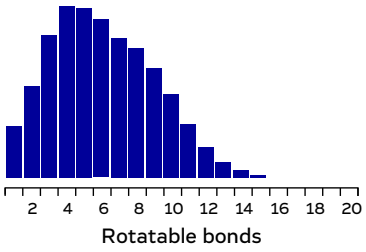
Evotec's high-quality collection of >850,000 compounds exhibits a high degree of drug-likeness as assessed by QED score and other physicochemical properties, ensuring the best possible chance of success.

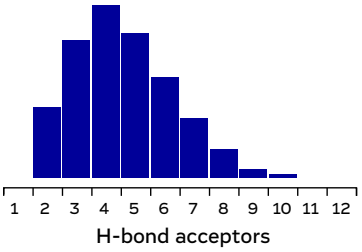


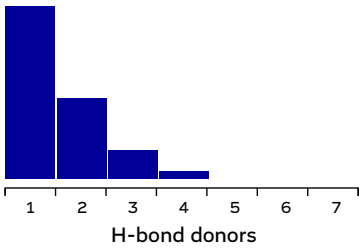












Quality Control

Maintaining quality is vital to ensure the generation of high-quality screening data. In addition to characterizing new compounds added to the collection, routine quality control is performed on our compound collection to ensure quality over time. These include:

- Confirmation of compound integrity/identity by mass spectrometry
- Purity assessment: UV-purity detection at 215 nm (optionally expanded to 200–400 nm) and, if required, ELSD detection

Compound Management

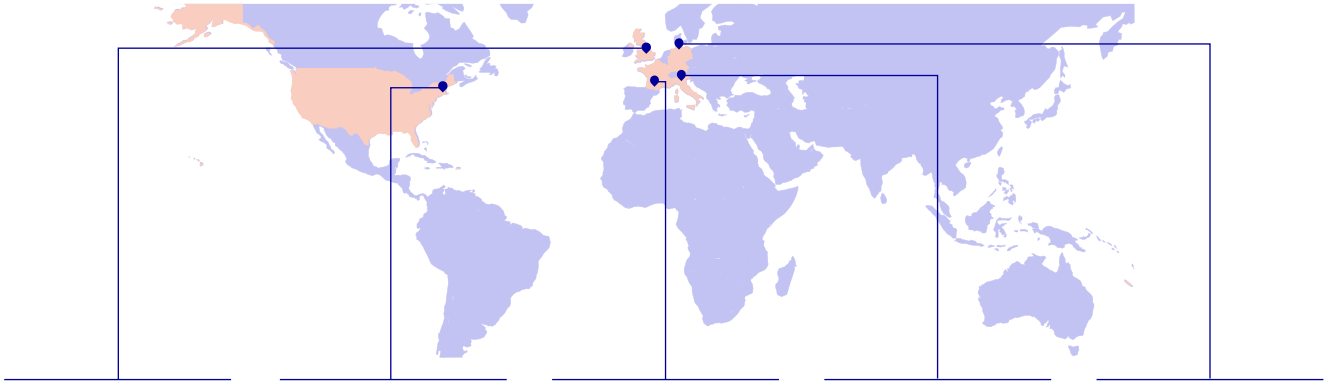
- World leading compound management facilities (7 global sites)
- Library management with fast order fulfilment and worldwide delivery
- Inert or dry atmosphere and low temperature storage and processing options
- Multi-format plating and reformatting (milli to nanolitre volumes)
- Titian Mosaic infrastructure for sample tracking and management

Sample Management: Enhancing Project Value with Our Services

With over 20 years of experience, Evotec's sample management is one of the industry's largest groups, providing comprehensive services from compound reception and storage to preparation and delivery for both internal and external customers

- Cost effective compound identification, selection, and procurement
- High-throughput compound analysis
- Multi-format plating and reformatting (milli- to nano-litre volumes)
- Inert or dry atmosphere and low temperature storage and processing
- Fast order fulfillment and worldwide delivery
- Multi-site disaster recovery and business continuity
- Access to compound collections of some of its partners through an open innovation strategy
- Co-localization of activities such as chemistry, biology, HTS, DMKP and research informatics
- Strong knowledge of IT tools (Mosaic, ordering tool) and state-of-the-art compound management equipment
- Experienced project leaders with a strong track record of managing in-house and remote (in-source to client site) projects for pharma, biotech and nonprofit organizations

A strong worldwide sample management network: 7 locations, 150+ collaborators



Abingdon, UK
Cyprotex, UK

Branford, CT, USA,
Princeton, NJ, USA

Toulouse, France

Verona, Italy

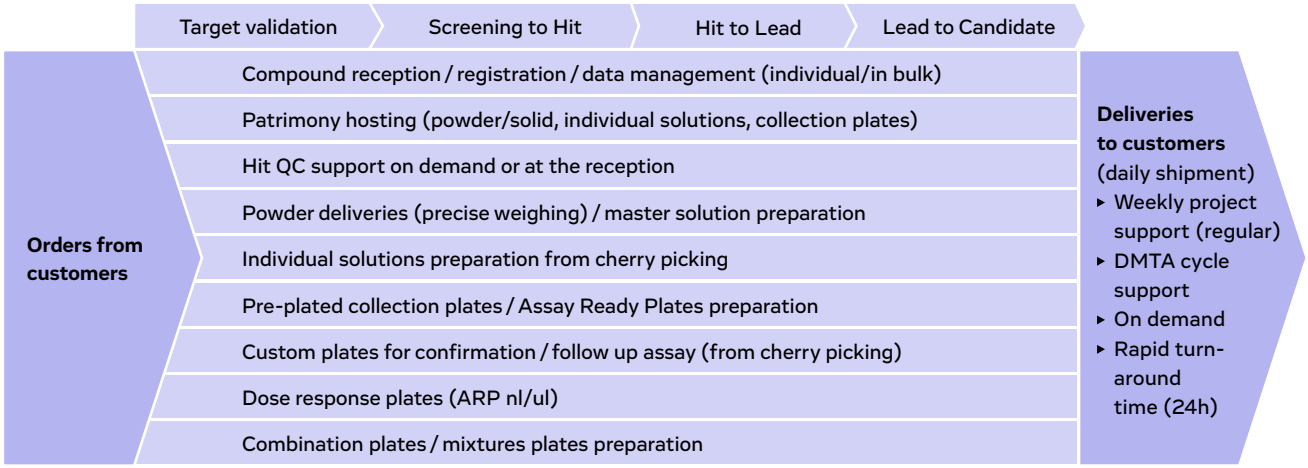
Hamburg, Germany

Significant statistics/metrics (2023)

Storage capacity >23+ M samples*	Global job activity (annually; all tasks) 43+ M	Rework analysis < 5%	>36M compounds prepared and delivered**	>12 000 shipments

* all sites, RT, +4°C, -20°C, -80°C
** powder delivery, master solution, custom plates, ARP, collection plates, dose response plates
*** >98% success in delivery times

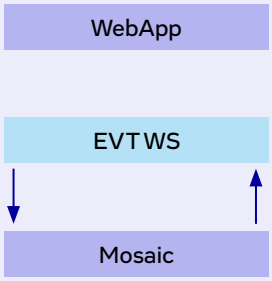
Qualified processes supporting all sample management activities: Storage, preparation and delivery of compound and biosamples



Operations are managed in a state-of-the-art facility with controlled compound flow, temperature, and humidity. The facility is equipped with fire detection and extinguishing systems, as well as access control.

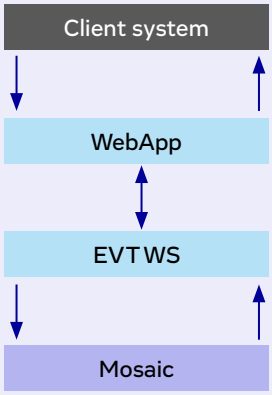
3 technical options to integrate the customer IT environment with the Evotec IT environment (Mosaic, Web services/RIO)

Standard solutions: WebApp



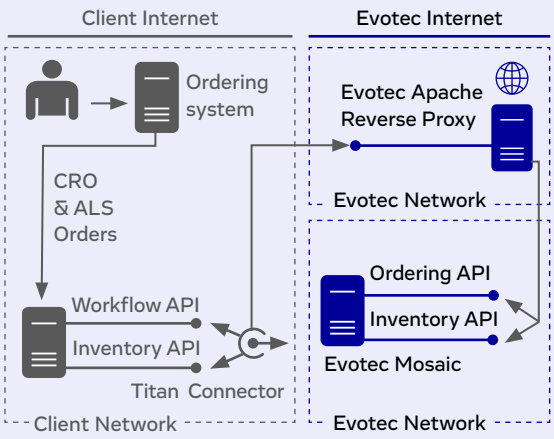
- User access available on demand
- User friendly interface
- Supported and upgraded by Evotec

Integrated solutions: WebServices



- Web services connected
- Supported by Evotec and clients
- Integration step (Project-based approach)

Fully integrated solution: Mosaic to Mosaic connection



- Maintained by Titian
- Integration step needed (Project-based approach)

Learn more:

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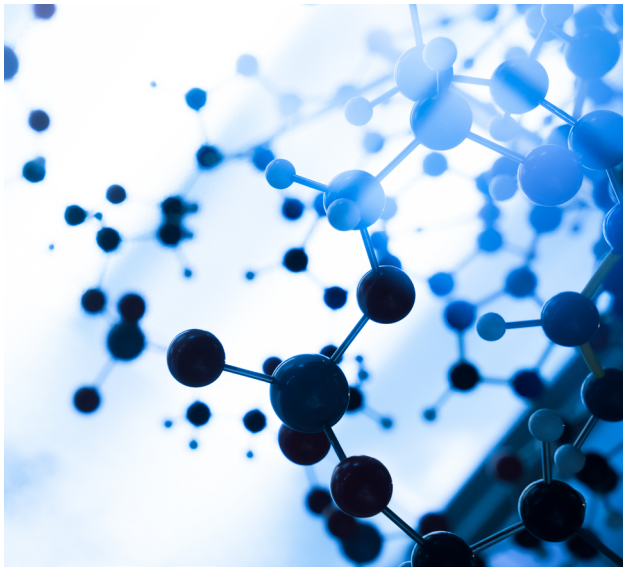
Covalent Drug Discovery

Covalent drugs offer new avenues for treating diseases that were otherwise considered untreatable. These drugs act by binding covalently to target proteins, leading to prolonged therapeutic effects, high potency and the ability to overcome drug resistance. Traditionally, concerns have been raised over potential off-target effects and toxicity, however, with advances in technologies and drug design, it has been possible to improve the selectivity profile of covalent drugs and to reduce the risk of adverse effects. In this respect, the use of covalent approaches have been valuable in characterizing the interactions between small molecules and their protein targets, typically those directed at cysteine residues.

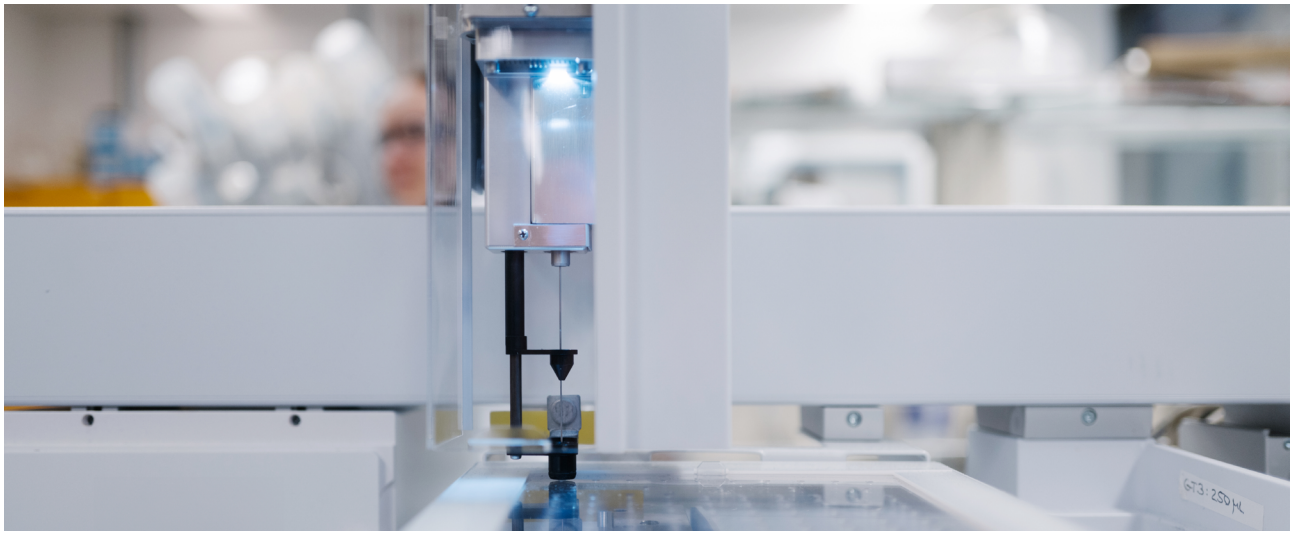
Advantages of Covalent Drugs

- **High Potency:** The combination of optimized binding affinity and covalent attachment of drug results in higher potency compared to reversible drugs, making them more effective at lower concentrations.
- **Prolonged Action:** Covalent drugs provide a sustained therapeutic effect due to the nature of their high potency, reducing the need for frequent dosing.
- **Selective Targeting:** Advances in drug design have improved the selectivity of covalent drugs, minimizing off-target effects and reducing the risk of adverse reactions.
- **Overcoming Resistance:** Covalent drugs can target proteins that have developed resistance to non-covalent inhibitors, offering new treatment options for resistant diseases.



Challenges in Covalent Drug Discovery

- **Complex Development Process:** Developing covalent drugs involves sophisticated techniques and methodologies, making the process more complex and resource-intensive.
- **Toxicity Concerns:** The irreversible nature of covalent binding can lead to off-target effects, which may cause toxicity. Ensuring high specificity in drug design is crucial to mitigate these risks.
- **Regulatory Hurdles:** Due to potential toxicity and the irreversible nature of covalent binding, obtaining regulatory approval can be challenging. Rigorous testing and validation are required to ensure safety and efficacy.



Why choose Evotec?

- **High quality covalent library**

– 5k carefully curated reactive compounds with MedChem properties

– Cysteine-directed covalent library (mainly acrylamides) with extension for other reactive amino acid residues

– Optimized library for storage and stability including regular LC/MS QC

– Access to commercially available compound sources through network of preferred suppliers

- **Advanced technology**

– Curation and handling of specifically designed covalent library

– High-throughput MS-based technologies for intact protein and peptide attenuation screening

– Cutting-edge chemoproteomics for screening covalent libraries in their native context to identify new starting points for drug discovery and assess off-target effects by selectively modifying proteins and studying their functions

– Industrialized processes for rapid and robust data generation and analysis

– Industry leading *in silico* and AI/ML-enabled screening capabilities

Strategies to Identify Covalent Small Molecule Hit Compounds

Ligand First Approach

- Addition of reactive functional groups to existing ligands
- Enables potent and selective inhibition of target proteins
- Successful in the discovery of EGFR and BTK inhibitors used in cancer treatment

Electrophile First Approach

- Electrophilic fragment-based approach to identify hits from small libraries of less complex molecules
- Generates viable chemical starting points even for barely tractable targets
- Successful in the discovery of KRAS(G12C) and SARS-CoV-2 inhibitors

Biophysics Services

Evotec has a strong background in biophysics and has established a comprehensive biophysics platform supporting hit identification, structural biology, protein science and *in vitro* biology activities.

Capabilities

Biosensor-based Services

- Surface Plasmon Resonance (SPR) for soluble proteins
- Grating Coupled Interferometry for membrane proteins

Mass Spectrometry Services

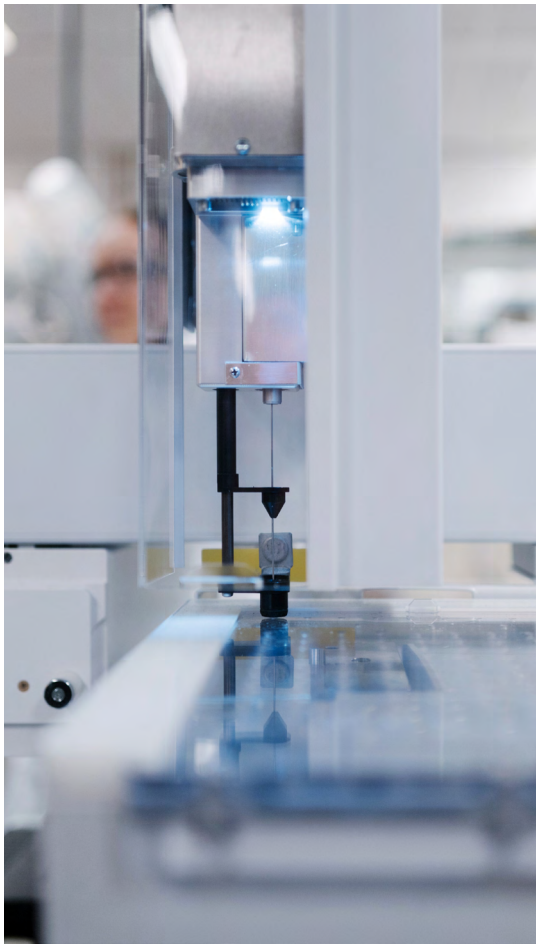
- Targeted MS approaches using RapidFire® High Throughput MS System (RFMS) & Acoustic Ejection MS (AEMS)
- Affinity Selection MS (ASMS)
- Intact protein screening coupled to to RFMS & native MS combined with Size Exclusion Chromatography (SEC-MS)
- Hydrogen-Deuterium Exchange MS (HDX-MS)
- UPLC-MS for quality control and assessment of purity and identity and UPLC-MS/MS for quantitative analysis

NMR-based Services

- Protein-observed
- Ligand-observed

Orthogonal Technologies

- Differential Scanning Fluorimetry (DSF)
- Microscale Thermophoresis (MST)
- Nephelometry



Application

Evotec's advanced biophysics platforms deliver robust data on binding, structural and functional information or kinetic profiling of target engagement for various modalities including small molecules, biologics or RNA-based approaches

Why choose Evotec?

Experience

- Established in 1993, Evotec has laboratories in the USA and Europe
- At Evotec, the biophysics unit and related functions have a vast wealth of experience to guide you in your drug discovery journey

Platforms and Capabilities

- Evotec offers a comprehensive range of capabilities and platforms
- By investing heavily in its screening infrastructure, Evotec ensures robust data is delivered rapidly using highly automated systems
- Biophysical screening services
  - Screening of lead-like collections up to 400,000 compounds with RFMS, AEMS or ASMS
  - Screening of fragment collections (3,000 & 20,000 fragments or 3rd party) with SPR, GCI, NMR or DSF
  - Screening of covalent libraries (5,000 Evotec covalent compounds or 3rd party library)
- Biophysical profiling services
  - Small molecule binders against protein and RNA targets:
    - SPR and GCI-based including kinetic characterization
    - DSF and MST-based binding interaction
  - Small molecule inhibitors with RFMS- technology
  - Biologics based binders (antibodies, Fabs, mini-proteins) with SPR- technology
    - On target binding with kinetic profile
    - Off target panel (FcRn) with kinetic profile
- Support of integrative structural biology and protein QC
  - Epitope binning with HDX-MS or protein-observed NMR
  - NMR-assignments
  - Characterization of protein flexibility with NMR or HDX-MS
  - Secondary structure determination with NMR or CD
  - Thermal denaturation assays with DSF or nanoDSF
  - Validation of protein-protein interactions with SPR or MST

Flexible Consultative Approach

- Evotec offers a flexible service with dedicated project managers and full access to scientific experts
- Careful scientific and operational planning determines the optimal screening strategy to ensure project success
- Both integrated projects and standalone services are supported

Compound Collection

- Carefully curated collection of >850,000 maximally diverse lead-like compounds plus 25,000 fragments
- Access to 48 million commercial compounds through 800+ catalogues of global suppliers
- Through collaboration with X-Chem, access to >150 billion drug-like compounds from X-Chem's DNA encoded libraries
- External access to virtual 'synthetically accessible' library in excess of 70 billion compounds

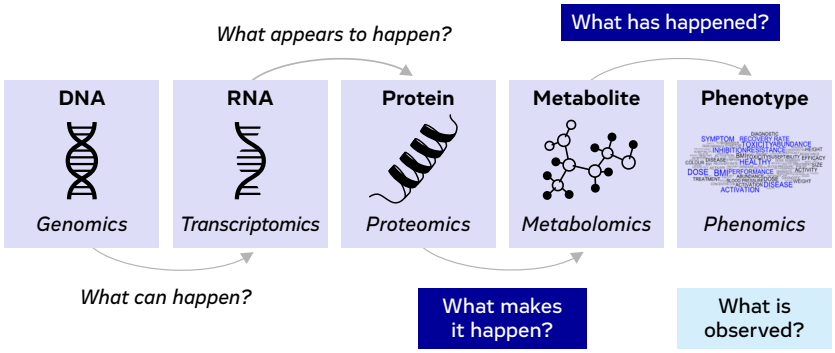
Proteomics & Metabolomics

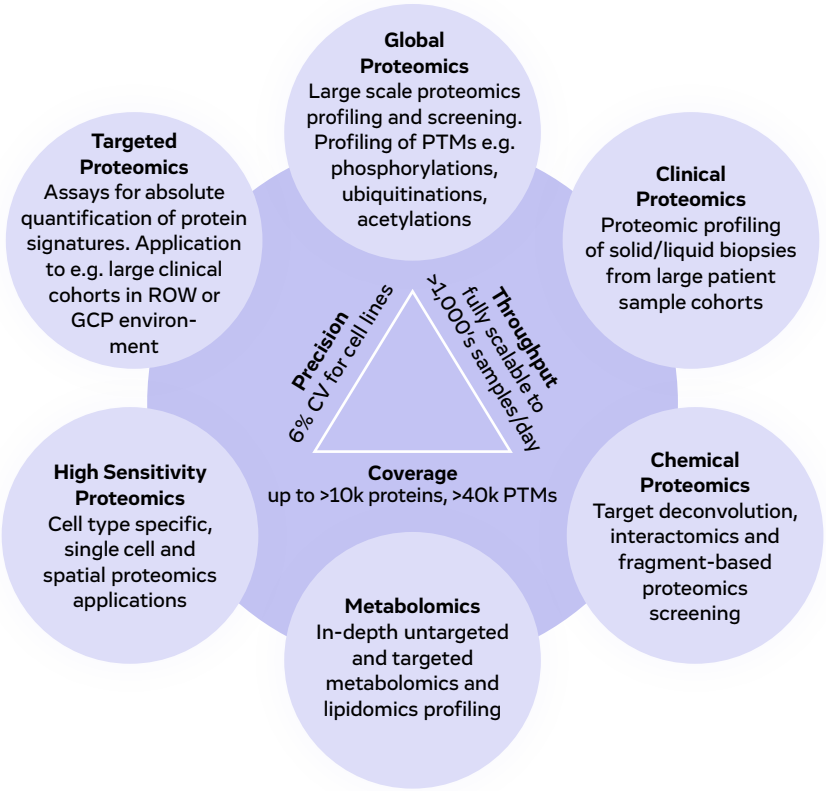
High-Throughput, Quantitative Mass Spectrometry Platforms to Support Data-Driven Drug Discovery

Evotec is one of the world-leaders in the field of industrialized mass-spectrometry-based proteomics & metabolomics with more than 20 years of experience in drug and biomarker discovery operating more than 50 MS instruments generating >1.5 B data points p.a.

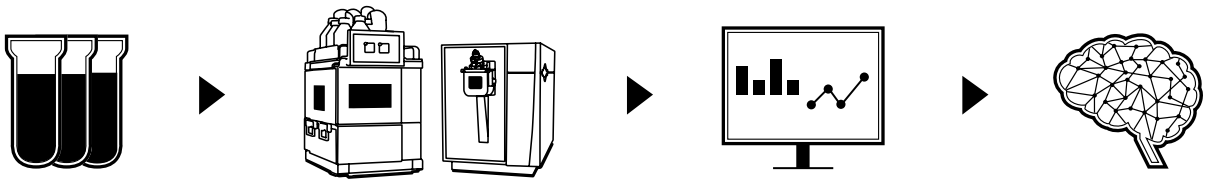
Unique technological offering

Platforms and custom-tailored services to understand what is driving disease biology and drug effects at unprecedented coverage, throughput and precision.





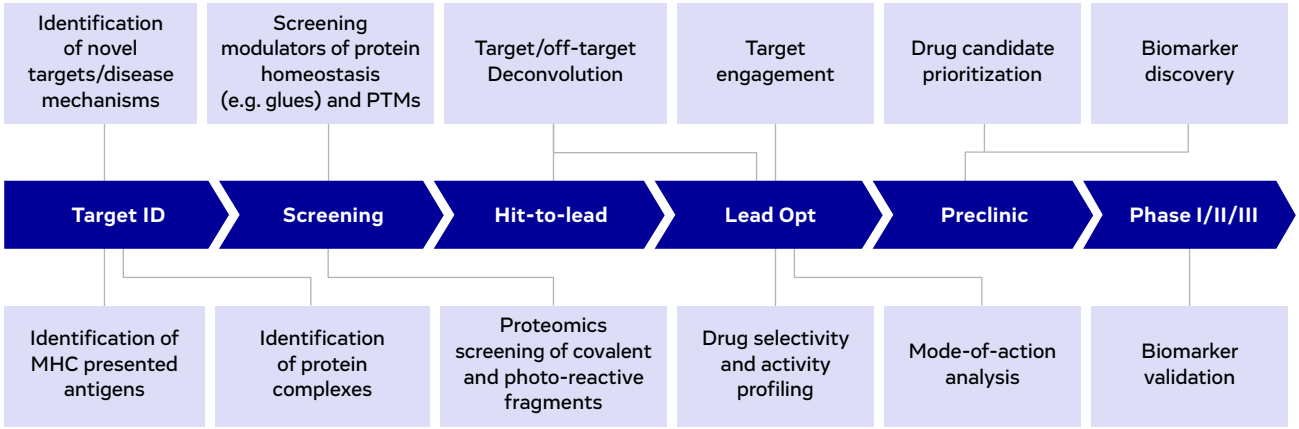
Proteomics & Metabolomics Workflow



Sample preparation | Data generation | Data analysis | Data integration

State-of-the-art highly automated sample preparation workflows combined with latest LC-MS instrumentation and acquisition modes feeding into dedicated, in-house developed, bioinformatics solutions for data analysis and full MultiOmics data integration in Evotec's PanHunter suite.

Data-Driven Drug Discovery



Extensive track record applying Evotec's proteomics & metabolomics platforms across the whole drug discovery and development pipeline to accelerate data driven drug discovery.

Evotec Proteomic & Metabolomic Solutions

- **Fit for Purpose:** Highly optimized experimental strategies tailored to different applications and project needs
- **High-End:** Industry-leading capabilities in high-end quantitative mass spectrometry
- **High-Throughput:** Industrialized, QMS supported process enables analysis of 1,000s of samples with constant high quality
- **Data Infrastructure:** Experience and infrastructure to analyze the enormous amounts of data generated in large-scale studies
- **Advanced Bioinformatics:** Advanced statistics and bioinformatics for systems-wide data analysis and in-depth data interpretation
- **Quality and Reporting:** Extensive track record to deliver high quality and actionable results within agreed timelines

Learn more:

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