Evotec offers unique proteomics services to address key issues in drug and biomarker discovery. We continuously advance our capabilities in mass spectrometry-based proteomics to ensure unrivalled comprehensiveness and data quality when analyzing cells, animal models and patient samples.

This involves:
- Highly optimised experimental strategies tailored to different proteomics applications and project needs
- Industry-leading capabilities in high-end quantitative mass spectrometry
- Experience and infrastructure to analyse the enormous amounts of data generated in large-scale proteomics projects
- Advanced statistics and bioinformatics for systems-wide data analysis
- In-depth data interpretation to extract relevant drug target and mode-of-action information from proteomics experiments
- Extensive track record to deliver high-quality results within agreed timelines

Evotec’s chemical proteomics methods such as Evotec Cellular Target Profiling™ reveal cellular drug targets and selectivity in an unbiased manner. Other Evotec proteomics technologies record protein modification and expression on a proteome-wide scale for drug mode-of-action analysis or biomarker discovery efforts. Thus,
our platform offers highly innovative solutions that can be leveraged across the entire drug discovery and development pipeline.

**QUANTITATIVE CHEMICAL PROTEOMICS**
Evotec scientists have pioneered chemical proteomics applications for the identification of cellular small molecule targets. The basic concept involves functional immobilisation of an appropriate linker derivative of a drug, followed by affinity purification of target proteins from cell or tissue extracts and finally their identification by MS analysis. Unlike other competitor technologies, our Evotec Cellular Target Profiling™ technology captures target specificity and affinity information by quantifying target binding across defined sets of affinity purification and drug competition experiments.

Evotec Cellular Target Profiling™
- Reveals and verifies specific cellular targets of a drug by quantitative mass spectrometry
- Determines target-specific dissociation constants for the compound studied, ranking targets according to their likely physiological relevance
- Performs selectivity analysis on a proteome-wide scale against native, post-translationally modified proteins in the presence of cellular co-factors and complex partners
- Has an extensive, non-target class restricted track record in successful profiling of diverse small molecule compounds

Selectivity data about cellular on- and off-target liabilities is particularly useful to inform decisions at various stages of drug development, for example in the lead optimisation phase or in the pre-clinic candidate selection process. Moreover, chemical proteomics enables target deconvolution of bioactive compounds identified in phenotypic screens. Cellular target identification is the crucial step to enable further drug optimisation and development. Evotec Cellular Target Profiling™ perfectly complements Evotec’s medicinal chemistry and high-content screening capabilities to deliver new drugs and targets across many therapeutic areas.

**Evotec Cellular Target Profiling™ key elements**

1. A lysate of the cell line or tissue of interest is prepared.
2. A linker derivative of the test compound is immobilised on sepharose beads and used to enrich compound target proteins.
3. Competition assays with the free test compound and (4) quantitative mass spectrometry analysis reveal the compound’s affinity profile, (5) ranking all protein targets according to their \( K_d \) values for free compound.
Evotec’s proteomics platform for global protein modification analysis permits the identification and quantification of more than 10,000 phosphorylation sites, 1,000 lysine acetylation sites or 5,000 ubiquitylation sites in a single experiment, which may be performed in cells, tissues or patient samples. Accurate quantification is enabled by differential isotope labelling, while highly optimised peptide enrichment and analysis on fast, sensitive and accurate mass spectrometers ensure highest coverage. Evotec’s platform provides highly reliable results, both for in-depth bioinformatics involving enrichment, cluster, network and motif analyses, as well as for expert data interpretation on the level of site-specific changes.

Our quantitative phosphoproteomics (PhosphoScout®) enables the unbiased and comprehensive investigation of signalling pathways, to delineate the cellular modes of action for kinase inhibitors. Typical applications include:

- Identification of specific pharmacodynamic read-outs for therapeutic kinase inhibition
- Selection of lead compounds or pre-clinical candidates with maximal on- and minimal off-target activity in cellular conditions, either as single agents or in combination with other drugs
- Monitoring phosphoproteome regulation in different biological models to shed light on factors underlying differential biological activity of lead compounds or pre-clinical candidates

In addition to PhosphoScout®, Evotec’s acetylomics and ubiquitomics platforms offer similar applications for HDAC and E3 ligase inhibitors using highly optimised workflows with regard to sensitivity and selectivity. As a result, these technology platforms enable comprehensive mode of action studies in the biologically relevant context.

**GLOBAL PROTEOME PROFILING AND BIOMARKER DISCOVERY**

Evotec offers industry-leading platforms for comprehensive protein expression profiling allowing unbiased, proteome-wide target and biomarker discovery on the functional protein level. Depending on the application and required throughput, tailored proteome analysis workflows are available:

- Deep proteome profiling for detection of up to 10,000 proteins from cell or tissue samples upon efficient peptide pre-fractionation
- Single-shot proteome profiling to a depth of 5,000 proteins in cell or
tissue lysate, enabling comparative proteome analysis across 100+ samples

- Comprehensive analysis of any type of biological material, including formalin-fixed paraffin-embedded (“FFPE”) solid tumor samples and body fluids such as plasma and CSF

- Targeted mass spectrometry analysis by Multiple Reaction Monitoring (“MRM”) fully established at Evotec for follow-up validation experiments

Both the expertise and the data processing infrastructure are in place for accurate quantification across many different samples, such as whole panels of cell lines, xenograft models or patient tissue samples. Such data, together with drug response information, provides a unique basis for the discovery of predictive protein biomarkers, arguably one of the most exciting proteomics applications in future medicine.

**EVOTEC’S THREE-TIER STRATEGY TO SUPPORT ONCOLOGY BIOMARKER DISCOVERY**

Evotec technologies cover the entire biomarker discovery phase including elaborate bioinformatics for the identification and verification of predictive multivariate markers, so-called protein signatures. These capabilities have been demonstrated in various cancer-related projects, delivering response prediction signatures in lung cancer cell lines, mouse xenograft models and leukemia patients.

In conclusion, Evotec offers an integrated and unique platform of innovative proteomics technologies for drug and biomarker discovery. Moreover, Evotec is constantly investing in R&D activities dedicated to advance its high-end proteomics capabilities and maintain industry leadership in the years to come.