NUVISAN

DRUG DISCOVERY

De-risking projects

How we can support to de-risk your project

Successful drug discovery requires both state-of-the-art technology platforms and in-depth expertise of all disciplines involved along the value chain.

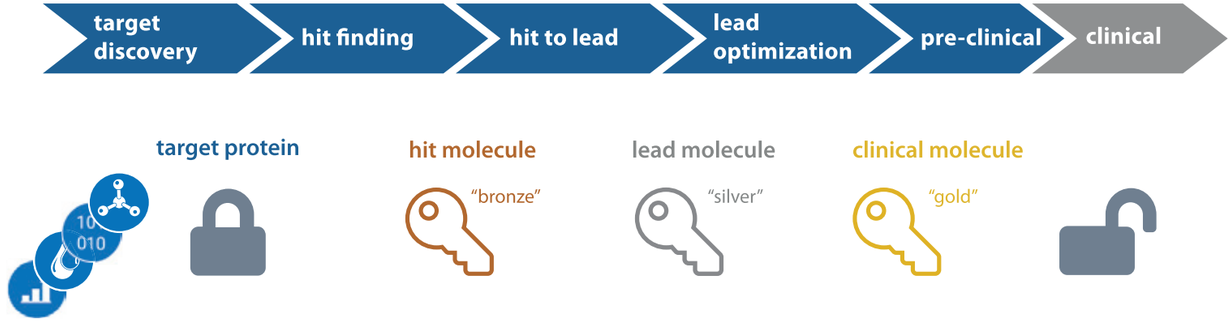
On average, our scientists have more than 20 years of experience in pharmaceutical research, covering a wide range of technologies from target discovery up to pre-clinical candidate generation and characterization.

SOLVING POTENTIAL LIABILITES AT **NUVISAN**

Whether target engagement, DMPK, or safety issues - we empower you to overcome potential liabilities

As increasing attrition rates in drug discovery over recent decades indicate, there are various risks driving the success or failure of a drug discovery campaign. Potential liabilities could be linked to the validation of the target and disease hypothesis, target pharmacology, missing target engagement, toxicology, safety findings, and / or efficacy issues.

An organization with in-depth experience, efficient processes to deliver in line with specific needs, and all necessary technologies under one roof is a major success factor for these challenging tasks. We are happy to provide custom-made solutions for your entire project, subprojects, or a specific question.

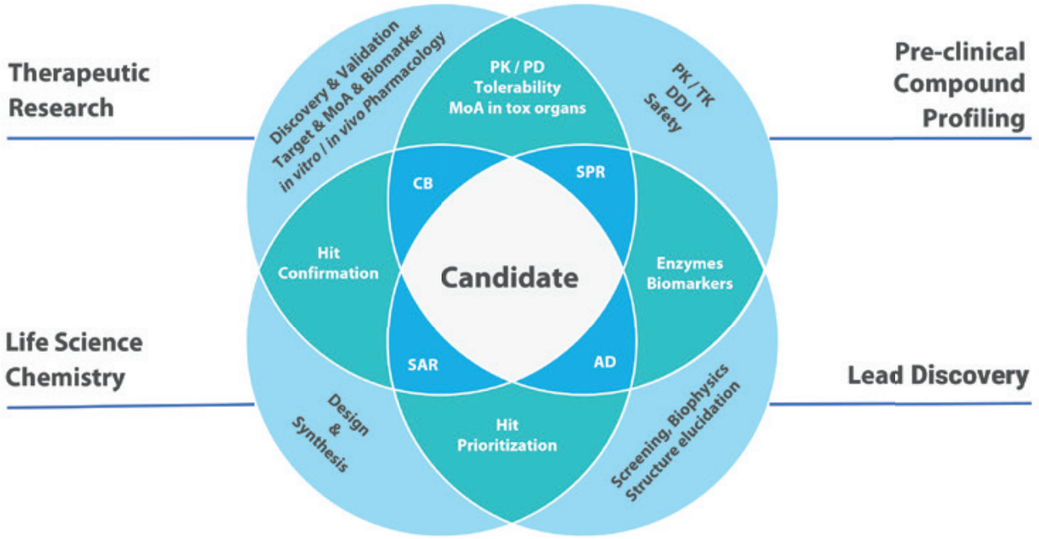


Identify a disease-relevant target ("lock") → Find a first tool compound → Optimize tool further to lead → Develop lead to clinical candidate

We provide solutions for:

Fully integrated turnkey projects | Sub-projects | Individual questions

Drug discovery under one roof, enabling collaborative de-risking strategies for your projects



AD: Assay development
CB: Chemical biology
DDI: Drug-Drug Interactions
PD: Pharmacodynamics
PK: Pharmacokinetics
SAR: Structure-activity relationship
SPR: Structure-pharmacokinetics relationship
TK: Toxicokinetics

A broad range of expertise and tools to optimize and de-risk your R&D project

Examples to de-risk / optimize — R&D project portfolios along the drug discovery path

Target validation	Target engagement	Right molecule	ADMET	Clinical safety	Efficacy	Strategy
Compehensive target validation capabilities CRISPR/Cas RNAi approaches Bioinformatics Chemical probes Improved target understanding	***Broad variety of biophysical methods*** (Ce)TSA SPR ITC Mass spectrometry MST Experience in target deconvolution from phenotypic screens to enable target-based approaches	***Molecule expertise*** Design & synthesize new leads HTS & comprehensive data analysis Pre-clinical compound characterization with prediction of human PK, dose (PK/PD), DDI-potential, and tolerability	***Various methods to identify potential risks*** Physicochemical characterization Various assay panels to assess cross-reactivities Determination of metabolites and their effects Extensive expertise in life science chemistry to remove unwanted side reactivities or unfavorable properties Monitoring of genotoxicity, hERG reactivity, setup of further project-specific models Performing early exploratory *in vivo* rodent toxicology studies	***Monitoring of potentially relevant liabilities*** at very early stage to eliminate candidate-related safety issues Assessment of PK/PD & prediction of human efficacy dose Evaluation of safe starting dose for first-in-human studies	***Defining the most promising patient cohort*** using predicitive biomarkers, resistance data etc.	***Positioning and re-positioning assets***

FINDING THE RIGHT DRUG CANDIDATE

An early identification of potential molecular liabilities is key for a successful project outcome. Various lead series are analyzed and prioritized during lead discovery and hit-to-lead phase to select the best starting point and avoid multi-parameter optimization. The interplay of DMPK, pharmacology, toxicology, and chemistry is essential to identify and characterize a suitable lead compound to also test a target hypothesis *in vivo*. Along the path, tailor-made screening trees are defined to optimize parameters in rapid learning cycles, overcome identified risks (e.g. potency, selectivity, metabolic stability, solubility), and lastly determine a suitable candidate for further pre-clinical development.

Improve the chances of a successful clinical phase by a thorough translational understanding of your drug candidate. Prediction of human PK, identification of factors driving efficacy with PK/PD studies, and a safety evaluation (e.g. explorative 2-week toxicology study in rodents) support de-risking of late stage drug candidates in lead optimization.

IDENTIFY AND OVERCOME ADME-RELATED DEVELOPMENT RISKS

- Permeability assays to assess absorption risks
- Metabolic stability assays to overcome insufficient exposure and high clearance
- Prediction of drug-drug interaction potential by inhibition and induction studies of CYP P450 enzymes as perpetrator and victim
- Metabolite ID studies to identify metabolism-related soft-spots, risks associated with formation of reactive metabolite species, and disproportionate drug metabolites

OUR CORE ASSETS

Multidisciplinary teams with more than 20 years of experience in successfully de-risking pharma research projects

Best-in-class capabilities for *in vitro*, *in vivo,* and *ex vivo* studies with close collaboration of all disciplines at one site

Large spectrum of disease models for efficacy testing across indications

State-of-the-art platform for ADMET profiling

Close collaboration with life science chemistry experts for compound optimization

Strong translational research for biomarker identification, definition of indication space, and patient selection criteria

Successful drug discovery

Successful drug discovery requires both state-of-the-art technology platforms and in-depth expertise of all functions involved along the value chain. NUVISAN ICB is very well positioned to provide both. On average, our co-workers have more than 20 years of experience in pharmaceutical research and we cover a wide range of technologies from target discovery to pre-clinical candidate under one roof.

We offer to bring our integrated expertise from all drug discovery functions to the table: due to the various reasons of failure that may arise throughout a drug discovery campaign we provide you with the integrated expertise in the areas of therapeutic research (pharmacology), lead discovery, life science chemistry, and pre-clinical compound profiling (DMPK and toxicology).

De-risking by an in-depth understanding of target biology

- Cell-based studies to investigate the consequences of target modulation by chemical probes and CRISPR/Cas9 in functional assays.
- *In silico* and experimental analysis on target expression to identify tissues with a liability to undesired effects.
- Next generation sequencing to monitor changes in gene expression upon target modulation, identify affected pathways, and putative risk signals.
- Single cell sequencing to resolve cell types with high target expression and differential response to target modulation by your molecules.
- Identification of pharmacodynamic biomarker candidates.
- Proof of concept by mode-of-action analyses *ex vivo*.
- Translational research to characterize potential indication space / market size.

De-risking by an in-depth understanding of your compound's characteristics

- *In vivo* disease models to identify pharmacodynamic drivers of efficacy.
- Smart read-outs in pharmacodynamic studies to address potential side effects early.
- Asset-centric PK/PD analyses to determine PD biomarkers, providing data for estimated human dose and estimated human biologically effective dose.
- Combinability analysis of your molecule: mode-of-action-based predictions, *in vitro* and *in vivo* combination studies, CYP induction / inhibition studies.

De-risking by in-depth characterization of ADMET properties

- *In vitro* DMPK assays, e.g. metabolic stability, CYP profiling, permeability, metabolite ID, phenotyping of drug metabolizing enzymes.
- *In vivo* DMPK studies in rodents and non-rodents (e.g. dog, minipig) by various administration routes; single compound or cassette dosing.
- Safety profiling *in vitro* with e.g., ames, micronucleus test, phototoxicity.
- Safety profiling *in vivo* in rodents with clinical pathology endpoints, toxicokinetics, and histopathological diagnostics spatially resolved.
- MALDI-MS imaging for spatially resolved analysis of e.g. drug and metabolite distribution, effects on endogenous molecules such as biomarkers.

De-risking and optimizing molecules by their physicochemical properties

- Lipophiliciy (logD)
- Solubility (media, pH, formulations)
- Ionization (pKa)
- Stability (media, pH, stress, oxidative, light)

Highlights

Comprehensive target de-risking platform including CRISPR/Cas9, single cell/next generation sequencing, bioinformatics, advanced cellular, and *in vivo* efficacy models

Smart drug development de-risking by in-depth understanding of PK/PD relationships and mode-of-action in relevant disease models *in vitro* and *in vivo*

Comprehensive asset de-risking by physicochemical and pharmacochemical optimization

MALDI-MS imaging platform for spatially resolved qualitative and quantitative analysis of e.g. drug and metabolite distribution in tissue of your interest

Decades of successful pharma track record from target validation to IND-ready asset characterization packages

NUVISAN

YOUR PARTNER OF CHOICE

All relevant technologies and competences combined in one team

ONE TEAM

Seamless transition of projects along the drug discovery value chain

Quick turnaround times through close co-localization

Unified data and compound handling standards

ONE PARTNER

Fully integrated drug discovery and development team along the value chain and beyond

Programs or part of programs to be handled by one partner

Integrated or selected services out of one hand

ONE SOLUTION

High caliber drug discovery and development team available to drive challenging programs

Long-term drug discovery experience and knowledge in one integrated team

High-end technology and competence portfolio to deliver on challenging tasks

NUVISAN

YOUR SCIENTIFIC CRO / CDMO PARTNER

NUVISAN is a fully integrated CRO / CDMO offering all solutions from drug discovery to proof of concept in patients including: target identification, high-throughput screening, compound profiling, pre-clinical DMPK, toxicology, API synthesis, formulation development, pharmaceutical analysis, and clinical trials in healthy volunteers and patient populations.

With capabilities distributed over 6 locations in Europe, a presence in Latin America, and more than 40 years of experience, we deliver high-quality solutions certified by various accreditations and inspections (e.g. BfArM, EMA, FDA, ANVISA, ANSES, AAALAC, GLP, GMP, CIR).

40 **A trusted scientific partner**
With a 40-year track record of customer satisfaction

A wide range of expertise
A unique, comprehensive and, integrated offer from target identification to clinical trials

A data-focused expert
Our top priority is to ensure accurate, reliable, and consistent data quality

A flexible service provider
Fast turnaround ability and strong responsiveness to change

Enquire now

Whether you need support in specific areas only or need a more comprehensive offer, NUVISAN can tailor a solution to fit your specific requirements.

If you have any questions or need more information, please reach out to us:

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