NUVISAN

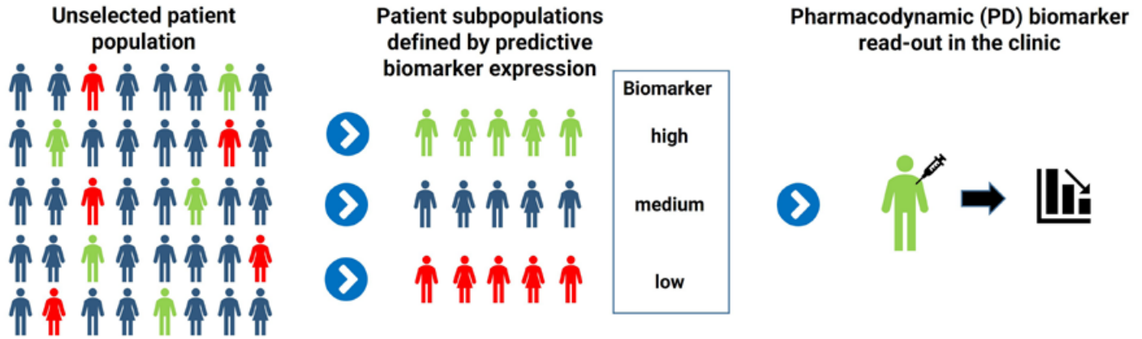
DRUG DISCOVERY

Biomarker Services

Integrated biomarker services from discovery to the clinic

Biomarkers support the de-risking of your project and increase the chances of success at the transition stage from discovery into the clinic. Our team of specialists identifies and validates the most promising biomarkers for your asset.

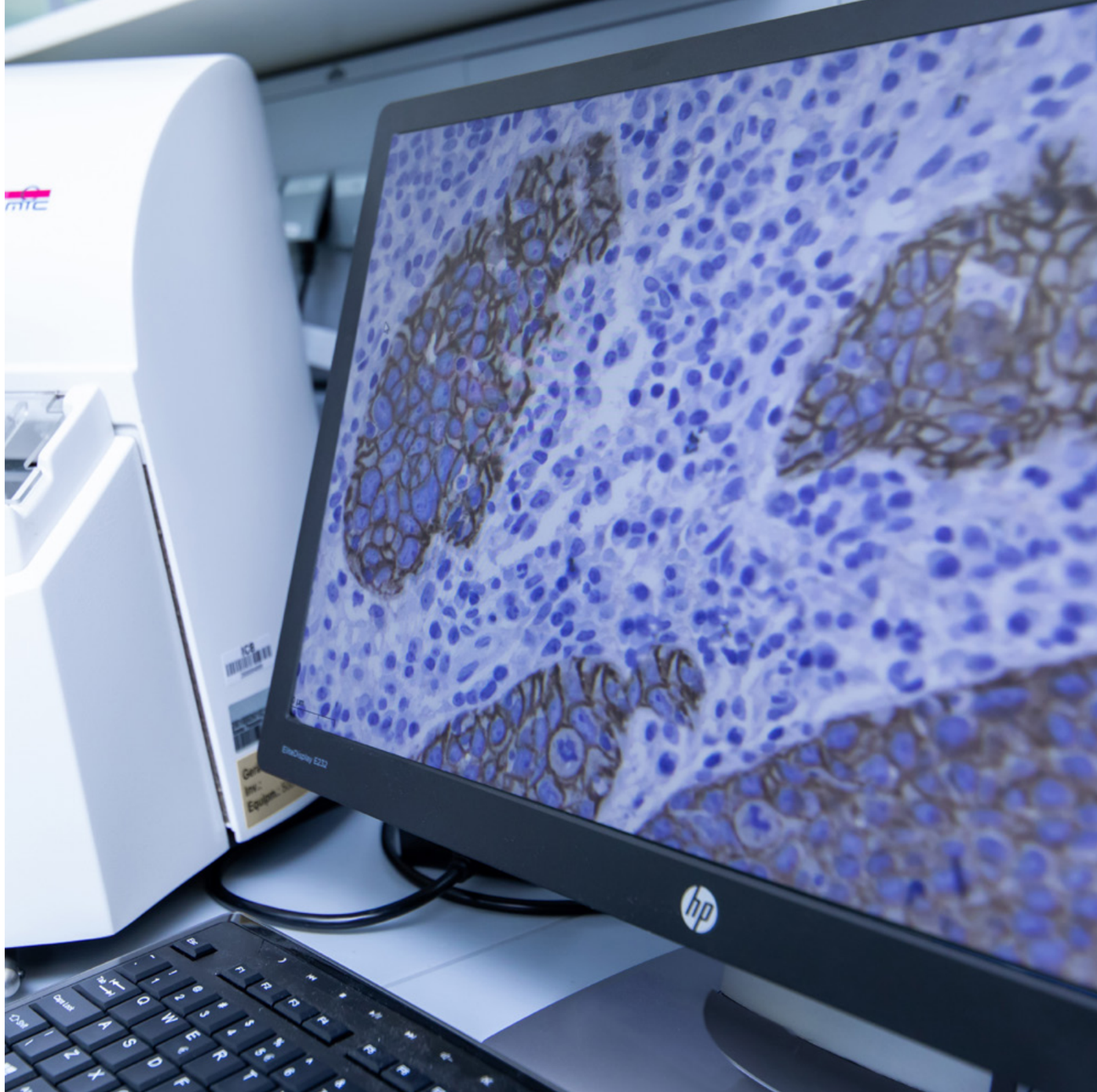
Our key expertise is in biomarker discovery and development of pharmacodynamic / target engagement biomarkers in target organs and surrogate tissues and predictive biomarkers guiding clinical target patient population refinement.



BIOMARKER SERVICES AT **NUVISAN** ICB

Biomarkers from bench to clinic and back

- Integrated biomarker services covering the entire drug discovery value chain from pre-clinical biomarker discovery and validation, robust assay development, target patient population refinement all the way to biomarker analysis of clinical samples.
- Identification and validation of pharmacodynamic biomarkers in target organs and surrogate tissues.
- *In vivo* PK / PD and biomarker studies for subsequent *ex vivo* validation of PD biomarker candidates. Correlation of drug exposure to efficacy and PD biomarker modulation for mechanistic modelling.
- Identification of predictive biomarkers guiding target patient population refinement through combined *in silico*, *in vitro* and *in vivo* studies.
- In-house biobank of human normal and disease (e.g. cancer) tissues to support profiling of the drug target or predictive biomarker expression using clinically relevant assays.
- Reverse translation and refinement of biomarker candidates through biomarker analysis of clinical trial samples.



OUR BIOMARKER SERVICES AT A GLANCE

Experienced biomarker scientists / staff with decade-long pharma industry background

Expansive knowledge in a wide range of therapeutic areas and modalities

Proven track record of successfully translating drug discovery programs into the clinic

State-of-the-art *in vitro* and *in vivo* facilities fully equipped to support all aspects of biomarker discovery and development

Platforms:
Gene & protein expression
Histology / IHC / RNAscope™
CRISPR / Cas9
NGS / single cell sequencing
Flow cytometry
In vivo PK / PD & biomarker studies
Tissue biobank

OUR BIOMARKER TECHNOLOGY PLATFORMS

Our biomarker discovery services include complementary technologies such as unbiased global and hypothesis-driven approaches

- Next-generation sequencing (incl. single cell sequencing)
- Mass spectrometry-based proteomics
- Multiplex protein analysis platforms
- Multicolor flow cytometry
- Cytokine profiling
- Immunohistochemistry incl. digital imaging and semi-automated analysis
- *In situ* hybridization (RNAscope™)
- Western blot (Simple Western)
- qRT-PCR
- *Ex vivo* assays in target organs and surrogate tissues
- Project-tailored *in vitro* and *in vivo* models for PK / PD assessment
- Human tumor and normal tissue biobank for the assessment of target or predictive biomarker prevalence using clinically relevant assays
- In-house board-certified pathologists for histology assessments and H-Score
- *In silico* / bioinformatics analysis

Pharmacodynamic biomarkers

Pharmacodynamic (PD) biomarkers are molecular indicators of drug effects on the target in an organism. A PD biomarker can be used to examine the link between drug regimen, target effect, and biological tumor response.

Our approach:
Identification and validation of pharmacodynamic biomarkers and PK / PD studies, to support clinical dose prediction and demonstrate relevant exposure levels in clinical studies.

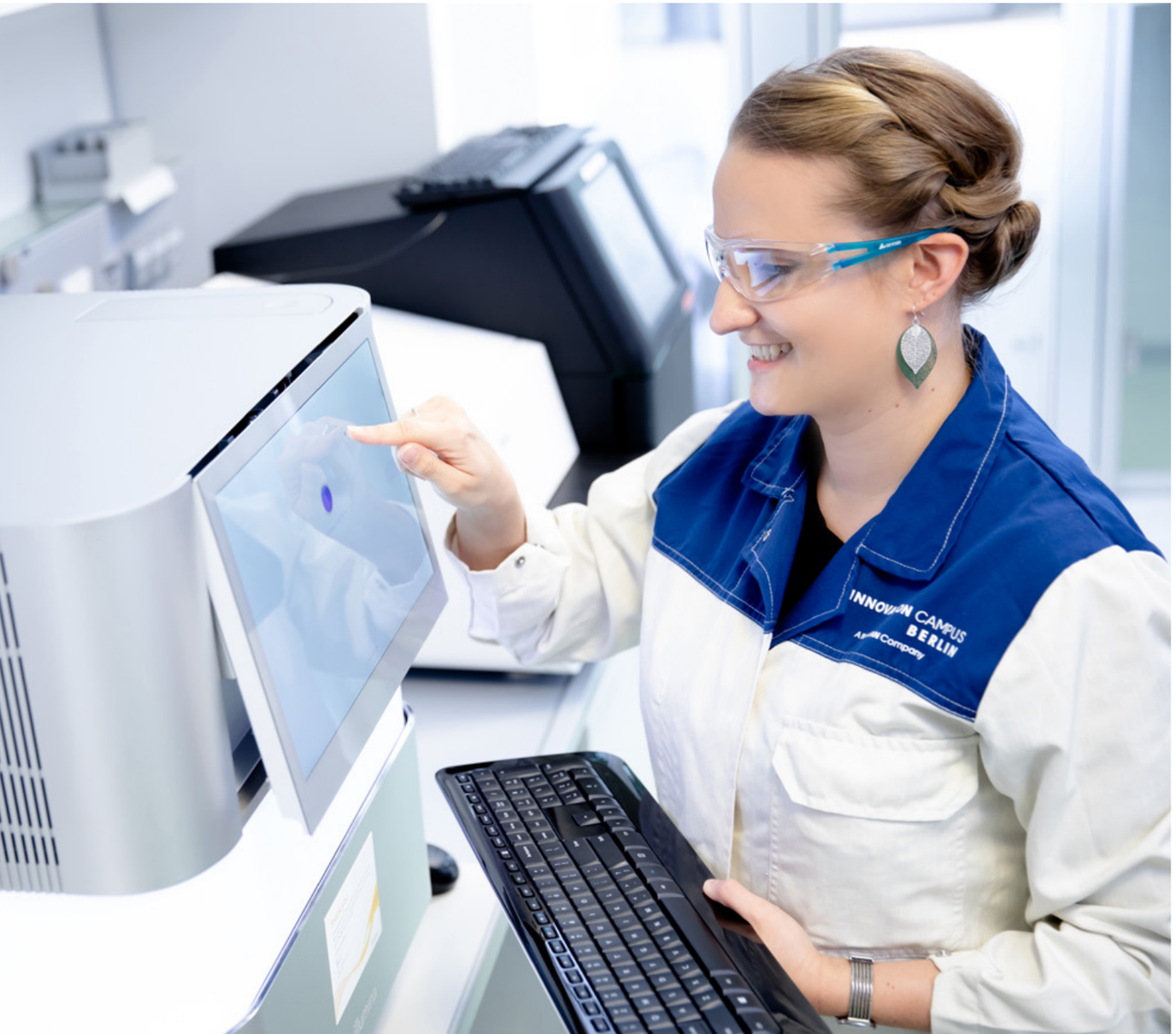
These goals are best achieved using blood-based biomarkers, which are more readily available.

We routinely use multicolor flow cytometry to characterize blood cell populations, phosphoproteins / protein expression in peripheral blood cells and qRT-PCR to monitor transcriptional regulation of biomarkers in blood cells.

ELISA / MSD assays are our methods of choice for the quantification of soluble biomarkers in plasma or serum samples.

Tumor-tissue based detection of PD biomarkers is accomplished via our automated IHC platform and subsequent digital image quantification.

Histopathology assessment and H-Score by in-house board-certified pathologist available.



Predictive biomarkers

Predictive biomarkers provide a forecast of the potential for a patient to respond to specific treatments. Targeted therapies require selection of eligible patients, and the identification of suitable indications is key for clinical trial success.

Our approach:
Identification of predictive biomarker candidates based on focused exploration of the mode-of-action of the drug candidate or by unbiased global cell line panel profiling and bioinformatic analysis of responders and non-responders.

Validation of predictive biomarker candidates in *in vitro* knock-out cell lines and in *in vivo* efficacy studies.

For indication profiling and patient selection, immunohistochemistry (IHC) remains the gold standard to detect target expression in tumor samples.

We offer broad indication profiling by using comprehensive sample collections comprising the most relevant tumor indications along with clinically relevant assays.

If the target protein cannot be profiled, RNA *in situ* hybridization (RNAscope™) is a well-established alternative for characterization of preclinical and clinical samples.

Automated imaging platform and subsequent digital image quantification. Histopathology assessment and H-Score by in-house board-certified pathologist available.

Our single cell sequencing platform

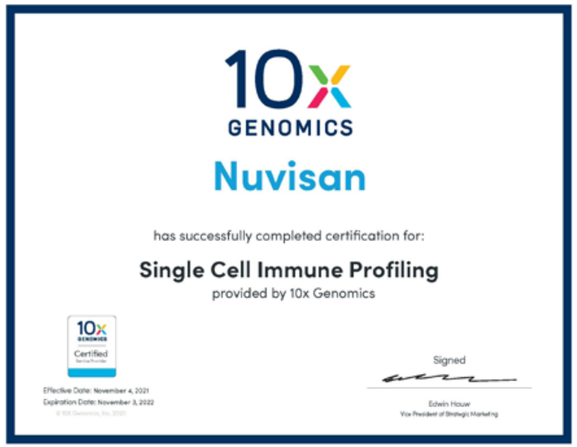
Whole genome expression profiling of thousands of individual cells in parallel.

At NUVISAN, we use single cell sequencing to identify novel targets and biomarkers and can analyse the mode-of-action of development compounds at unprecedented resolution.

NUVISAN single cell sequencing offers integrated services to customers including

- Experimental design
- Professional execution in the lab
- In-house NGS sequencing
- State-of-the-art bioinformatic analysis

NUVISAN single cell sequencing is a certified as service provider for 10x Genomics.

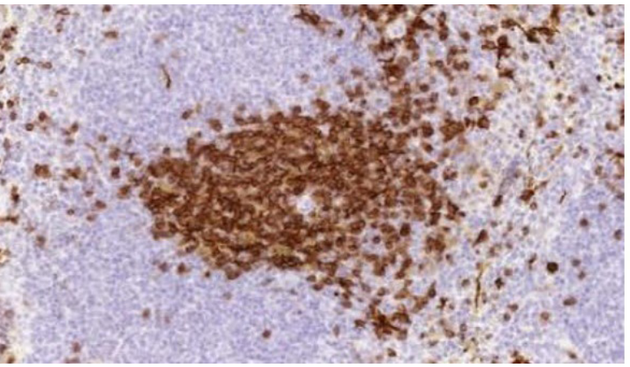


Our histology platform

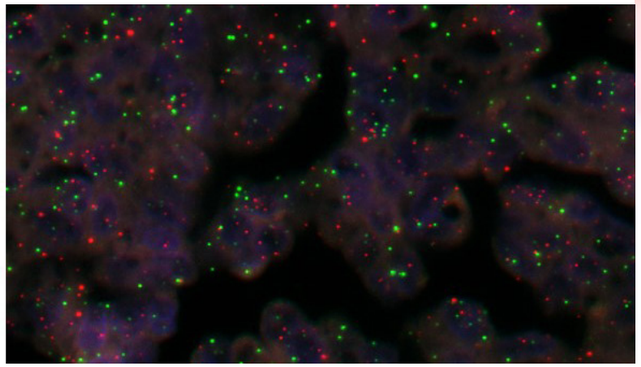
Immunohistochemistry and *in situ* hybridization (RNAscope™) biomarker assay development.

We perform robust assay development and fit-for-purpose validation:

- Reagent specificity & sensitivity
- Assay specificity & sensitivity
- Assay optimization (antibody dilution, retrieval method)
- Assay suitability for *in vivo* and clinical samples
- Assay performance (reproducibility & robustness)



IHC (Chromogenic staining)



RNAscope™ Fluorescence multiplex staining

Our flow cytometry platform

Multicolor flow cytometry is the method of choice to assess biomarkers in blood samples.

We offer comprehensive panels to characterize immune cell populations for immuno-oncology and inflammatory diseases.

Our experienced staff operates various multi-color flow cytometers:

- Phospho-flow assays
- Immunophenotyping
- Receptor quantification
- Receptor occupancy assays
- Rare cell detection

Fit for purpose assay validation comprising specificity, range of detection, pre-analytics, sample stability, reproducibility.

Our *in vivo* pharmacology platform

In vivo PK/PD and biomarker studies for *ex vivo* validation of PD biomarker candidates, correlation of drug exposure to efficacy, and PD biomarker modulation for mechanistic modelling.

Cell line derived syngeneic and xenogeneic models:

- Subcutaneous models
- Orthotopic models
  - Brain, pancreas, liver, colon, kidney, other organs
  - Hematological (liquid) and bone marrow (intrafemural) tumor models
  - Available in tumor bearing mice and rats

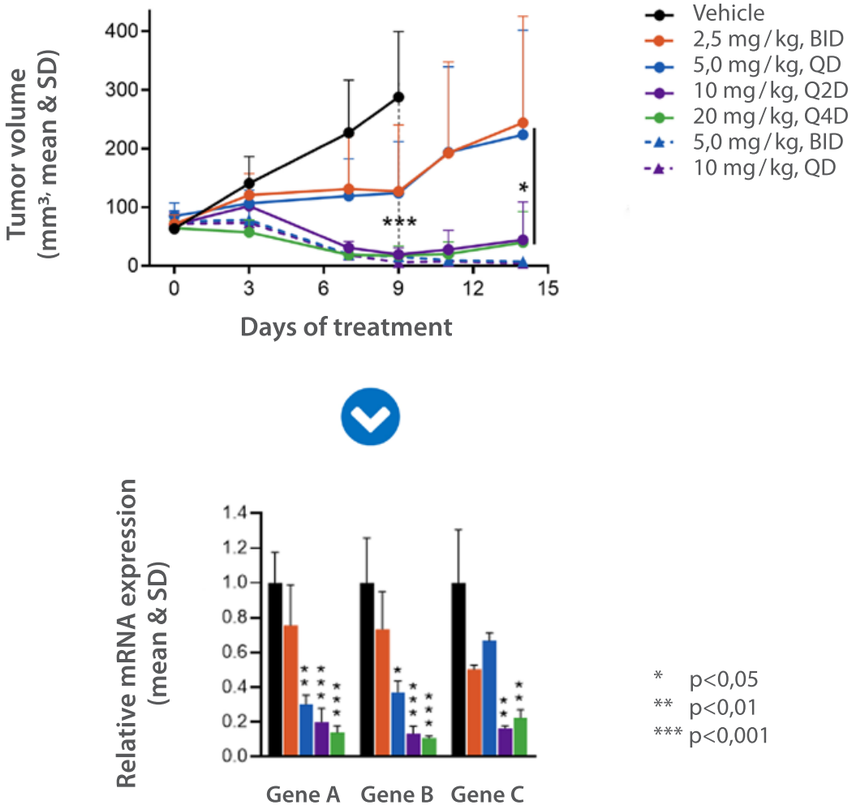
Treatments:

- SMOLs, biologics, SoC, radiation, combinations
- Assessment of different formulations
- Various routes (sc, ip, im, po, iv) and timelines (bolus, infusion) of application
- Various treatment schedules

Analysis/readout:

- PK/PD (Biomarker) assessment
  - *Ex vivo* analysis of tumor and other solid tissues (such as IHC, NGS, RNA / DNA analyses, flow cytometry)
  - *Ex vivo* analysis of bodily fluids (cytokine profiling, flow cytometry in blood, urine)
  - Immune cell profiling by flow cytometry
  - Immune cell infiltration by IHC / RNAscope

PK/PD xenograft study in mouse



Our biobank

Make use of our in-house biobank of human tumor and normal tissue to support profiling of drug target and predictive Biomarker expression using clinically relevant assays.

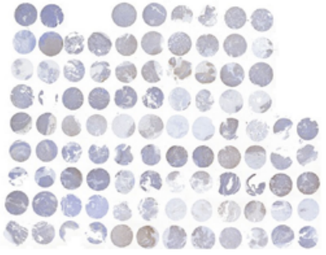
Predictive biomarkers for precision medicine: tumor indication profiling to assess the clinical option space.

Targeted therapies require selection of eligible patients. Biomarkers increase the chance of success in the clinic and help de-risk projects.

We have a collection of tissue microarrays (TMAs) of most relevant tumor indications that enable an assessment for prevalence and expression of your predictive biomarker candidates. These results can be used for a refinement of the target patient population, positioning of your asset, and planning of early clinical trials.

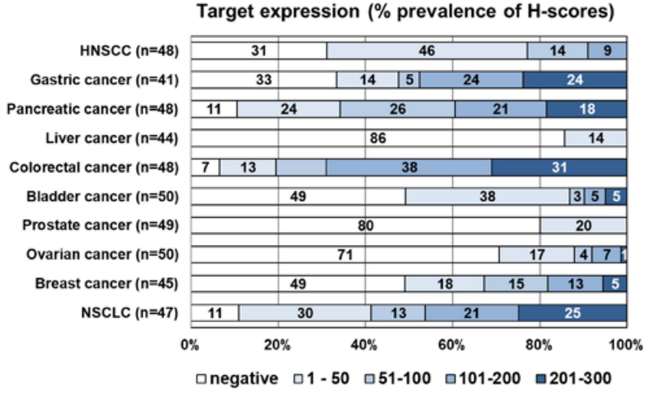
We also offer tissue microarrays (TMAs) of normal tissues, which can be used to pre-evaluate potential side effects in normal organs based on target expression.

Profiling of human tumor samples for predictive biomarker expression



- ✓ In-house biobank of human tumor TMAs
- ✓ Histopathology assessment and H-Score by in-house pathologist / automated quantification

Selection of biomarker-positive tumor indications for Phase 1 trials



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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Mail: hello@nuvisan.com
Web: www.nuvisan.com

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