NUVISAN

Your partner of choice
in bringing
therapeutics to life

THE SCIENCE CRO

Fully integrated solutions

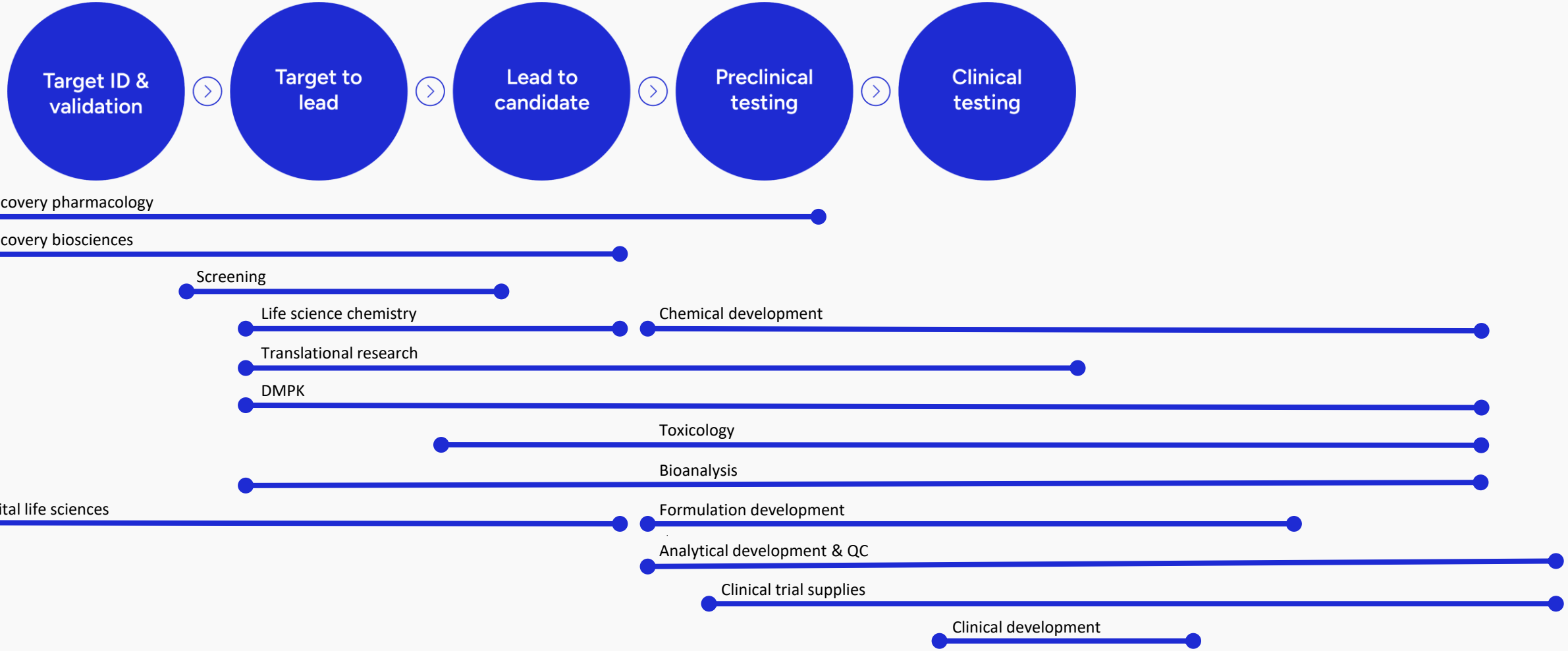
From target to patient

- EU-based company with > 40 years of experience, short communication paths, quick turnaround & unified molecule and data handling standards
- One partner to move your assets with seamless transition of unique, high-quality, & tailored integrated solutions along R&D value chain

NUVISAN
The Science CRO

Drug discovery

Drug development



Our History

NUVISAN
The Science CRO

Global division fully formed last year with long history of expertise and acquisitions

1863

Campbell Brothers established as a small Australia based chemical company in 1863.

1952

Listed on the Australian Stock Exchange (ASX) in 1952.

2000's

Expanded into North America, Africa and Europe in the early 2000s and the Middle East in the early 2010s.

Local GMP Pharmaceutical capabilities

2017-2024

Accelerated the incursion into the Life Sciences diversification with focused acquisition and greenfield startup in food and pharma in 2017 onward.

Pharmaceutical expansion in Mexico, India, Denmark, UK, Brazil, US, Sweden
B&PC acquisitions in US and Brazil

2024

ALS acquires 100% of Nuvisan

ALS Global Pharmaceutical division formed – and first joint strategy meeting held Q3 2024

2021

Nuvisan partners with ALS as CRO/CDMO provider in central Europe

1979

LAB Bioanalytical CRO founded

2010

Founding of Nuvisan GmbH

2011- 2020

Pharma R&D acquisitions

MSD
Merck R&D
Galderma R&D
Bayer R&D

Our sites in Europe

NUVISAN
The Science CRO

Formerly: BAYER · MSD · MERCK · GALDERMA

Berlin (GER)

Lead discovery
MedChem
Pharmacology
DMPK
Toxicology

Neu-Ulm (GER)

Bioanalysis
Pharma testing
Clinical trials
Clinical trial supplies
Safety lab

Waltrop (GER)

Pharma analysis
Small molecules
Biologics
TDS & polymers

Grafing (GER)

DMPK
ADME
BioT + MetID
Bioanalysis
Radiosynthesis

Sophia (FRA)

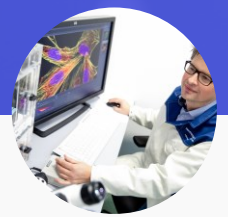
API synthesis
Formulation development
Manufacturing
Pharma analysis
Clinical trial supplies
Bioanalysis

Drug discovery — **Drug development**

Drug discovery

From target to lead

Pharmacology



Target validation

In vitro biology

In vivo pharmacology

Functional genomics

Therapeutic areas

Pharmacology

Target validation

- Bioinformatics in silico target analysis
- Indication space assessment, positioning & expansion
- Cell engineering tools
- CRISPR screening
- Target deconvolution
- Strategy development

Functional genomics

- Next-generation & single-cell sequencing
- CRISPR/RNAi platform
- Expression analysis
- Bioinformatics services

In vitro biology

- Cellular assays & assay development
- Cell line generation
- iPSC platform
- Ex vivo assays
- Virus biology
- Flow cytometry, IHC & microscopy units

In vivo pharmacology

- Efficacy & PD studies
- Disease models
- Ex vivo analysis
- Imaging capabilities
- Model development

Therapeutic areas

- Oncology
- Dermatology
- Inflammatory/autoimmune diseases
- Fibrotic diseases
- Contraception
- Women‘s health
- Neurology/pain
- Metabolic diseases/aging
- Cardiology/pulmonary diseases

Translational research

Biomarkers

Biomarker discovery

Biomarker assay development

Biomarker technologies

Clinical translation of biomarkers

Translational research

Biomarker discovery

- Target/mode-of-action based or hypothesis free global biomarker discovery approaches
- Proof-of-concept studies in vitro & in vivo
- Demonstration of target engagement & pharmacodynamic effects
- Correlation of predictive biomarkers & response

Biomarker technologies

- Next-generation & single-cell sequencing
- Immunohistochemistry
- In situ hybridisation
- Flow cytometry & cytokine/chemokine platform
- Real-Time PCR/automated Western Blot
- In vivo imaging platform

Biomarker assay development

- Project tailored in vitro & in vivo models for PK/PD assessment
- Assays in target & surrogate tissue
- Assay optimisation & fit-for-purpose validation
- Analysis of preclinical & clinical samples

Clinical translation of biomarkers

- Human tumor & normal tissue biobank
- Indication profiling to support phase 1 target patient population
- Reverse translation of biomarker read-outs from clinical trials

Biosciences

Protein sciences

Assays

High-content analysis

Bophysics

Mass spectrometry

Structural biology

Biosciences

Protein sciences

- Customised molecular biology service
- Multi-parallel expression optimisation (*E.coli*, insect & mammalian cells)
- High quality protein production for assays, structural biology & biophysics
- Protein QC (MS, fSEC, aSEC, nDSF, DLS)
- Membrane protein platform

Assays

- Assay development incl. tool generation (stable cell lines)
- Biochemical, cellular & high content assays
- Binding & enzyme activity assays
- Adaptation to ultra high-throughput

High-content analysis

- Phenotypic & multiplexed HTS
- SMOL & CRISPR libraries
- Eukaryotic cells (animal, fungi, plant), bacteria & 2D and 3D cell systems
- Single time points & live-cell kinetics

Biophysics

- Versatile platform: SPR, TSA, nDSF, NMR, ITC, DLS, MST
- Hit characterisation, kinetic profiling & SAR support
- Mode-of-action & target engagement
- Biophysical fragment screening (SPR, TSA, NMR)

Mass spectrometry

- High-throughput (HT) MS (rapidFire MS & MALDI-MS)
- Intact mass measurement
- Native mass spectrometry
- Targeted metabolomics
- Proteomics & peptide mapping

Structural biology

- X-ray determination & analysis
- High-throughput platform for multi-target crystallisation
- Cryo-EM, NMR
- HT crystallography (HTX) for fragment screening
- Small molecule structure determination

Compound screening

Libraries

High-throughput screening

Fragment screening

Virtual screening

Screening

Libraries

- 3 million small molecule library (access to pharma library)
- Different subsets & focused libraries (e.g. 290k / 820k / 2.4 million compounds)
- High chemical diversity, > 70 % proprietary

High-throughput screening

- Biochemical, biophysical, cellular with up to 300,000 tests/day
- Mass spectromety HTS (MALDI-HTOF, RapidFire)
- Best-in-class high content analysis (HCA) screening platform
- > 20 yrs of pharma HTS experience (> 10 clinical cpds)
- State-of-the-art screening data management

Fragment screening

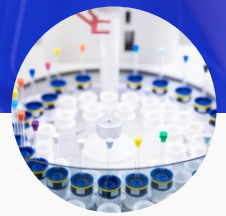
- Biophysical screening (SPR, TSA, NMR) of customised library (~ 2k Ro3 fragments)
- X-ray screening of customised library (~ 900 fragments @500 mM DMSO)
- 1° screen/hit confirmation → hit validation → fragment-to-lead

Virtual screening

- Internal library (3 million small molecules)
- External libraries (100k - > 1b)
- In silico virtual screening
- Target / ligand data mining
- Hit expansion

Chemistry

Design
& synthesis



Analytics
& purification

Scale-up
& special
technologies

Microbiological
chemistry

Compound
logistics

Physchem

Chemistry

Design & synthesis

- Decades of Medchem experience from hit assessment to clinical compound
- ID of new leads for challenging targets
- Multi-parameter optimisation of molecules (hit-to-lead, lead-to-candidate)
- SMOLs, probes & new modalities (incl. PROTAC®s)

Purification & analytics

- Separation technology platform (from < 1 mg up to 1 kg)
- Chiral separation incl. SFC
- NMR, MS & OPT expertise for structure services
- Ligand-protein interaction analysis via NMR & MS

Scale up & special technologies

- Large-scale synthesis of API or intermediates incl. route optimisation
- High pressure reactions, photochemistry, hydrogenation, carbonylation

Microbiological chemistry

- Biotransformation & protein/plasmid production
- Integration in Nuvisan metabolite discovery platform
- Metabolite identification, screening, synthesis & characterisation

Compound logistics

- Collection, storage, plating & shipping of compounds
- Building block collection for fast synthetic diversity

Physchem

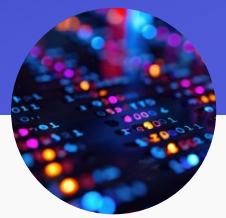
- Solubility
- Lipophilicity
- Stability
- Crystallinity (XRPD) & pKa

Digital life sciences

Life science datasets

Molecular modelling

Cheminformatics & machine learning



Omics data analysis & bioinformatics

Digital life sciences

Life science datasets

- ~1b in vitro & in vivo data points connected to 3 million well-characterised compounds from > 1 decade of research
- HTS, physicochemical, biochemical, pharmacological, pharmacokinetic & toxicological data
- Digital technologies & data mining

Cheminformatics & machine learning

- Fingerprint, substructure & similarity search
- ML models for ADME end points
- QSAR predictions
- Clustering & SAR
- Chemical space analysis
- R-group decomposition & visualisation, activity cliffs

Molecular modelling

- Virtual screening
- Structure-based design
- Pharmacophore- & ligand shape-based screen
- Scaffold hopping
- Molecular docking
- Molecular dynamics & free energy calculation

Omics data analysis & bioinformatics

- Interpretation of transcriptomics, genomics, epigenomics (single-cell & bulk next-generation sequencing)/spatial profiling/pooled, arrayed & single-cell CRISPR screens
- Microscopy image analysis at single-cell resolution
- In silico target & indication space evaluation
- Literature & database mining

DMPK

Discovery & development

In Vitro PK & DDI

In vivo DMPK

Biotransformation & MET ID

Consultancy services

Isotope chemistry

DMPK (discovery & development)

In vitro PK & DDI

- In vitro ADMET assay panel for research (HT) & IND-enabling PK characterization
- In vitro HT assays with custom protocols
- Investigation of absorption, distribution, metabolism, excretion (ADME) with radio- /non-labeled material
- DDI profiling (victim & perpetrator) & assessment of transporter proteins & metabolising enzymes

In vivo DMPK

- PK in rodents & dogs, single compound & cassette dosing, different admin routes
- Microsurgical rodent models e.g. cannulation of bile duct & portal vein, lymph sampling, femoralis admin
- Absorption, metabolism & excretion (mass balance studies incl. bile excretion & expired air)
- Quantitative tissue distribution incl. placental transfer
- According to GLP upon request

Biotransformation & MetID

- In vitro & in vivo metabolite profiling, quantification & structure elucidation in various matrices
- Analysis of clinical trial samples (metabolite “scouting”, relative & absolute quantitation, profiling & metabolite ID in hADME)

Consultancy services

- DMPK consultancy through all R&D phases
- Human PK predictions & DDI evaluations
- Project management, DMPK representation
- Scientific writing (IND/IMPD, IB, briefing books, reports)

Isotope Chemistry

- ^{14}C & ^{3}H radiosynthesis
- Synthesis of stable labeled compounds (^{2}H, ^{13}C, ^{15}N)
- Manufacturing & QC of radiolabeled APIs according to EU-GMP guidelines
- Reanalysis & repurification of APIs
- Dedicated storage for radioactive APIs (^{14}C & ^{3}H)

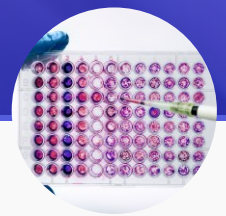
Best practice in animal welfare

(discovery & development)

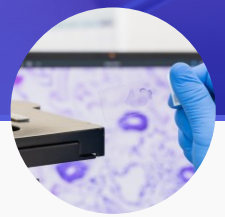
- We believe that humane care & use of animals is a key element of high-quality science
- Our high standards are confirmed by continuous positive feedback from client audits, authorities & full AAALAC accreditation at all sites working with animals
- In addition to complying with legal requirements, we strive to continuously improve our practices & husbandry conditions in the interest of animal welfare

Toxicology

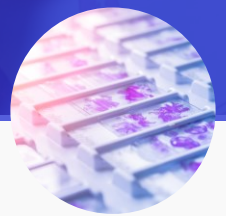
Discovery & Development



In vitro toxicology



In vivo toxicology*



Toxicologic pathology*

Clinical pathology*

Formulation*

Toxicology (discovery & development)

In vitro toxicology

- Genotoxicity: Bacterial reverse mutation & mammalian Cell/erythrocyte micronucleus test, mammalian erythrocyte, pig-a gene mutation & in vivo mammalian alkaline comet assay
- Skin toxicity: skin irritation (corrosion & sensitisation) assays & NRU 3T3 phototoxicity test
- Cardiac safety (ion channel screenings)

In vivo toxicology*

- Via strategic partner (AAALAC+)
- Rodents + non-rodents
- Non-GLP and GLP

Toxicologic pathology*

- Via strategic partner (AAALAC+)

Clinical pathology*

- Via strategic partner (AAALAC+)

Formulation*

- Via strategic partner (AAALAC+)

Drug development

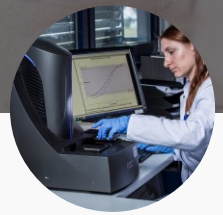
From preclinical candidate to patient

Bioanalysis

Discovery & development

LC-MS assays

Ligand-binding assays



Cell-based assays

Bioanalysis (discovery & development)

LC-MS

- Method development & validation (> 100 assays / yr)
- Dedicated large molecule & new modality assay development team
- > 250 non-proprietary assays
- Experienced in VAMS, peptide analysis, PROTAC®s, chiral separations & ion mobility chromatography
- Support from discovery PK throughout non-clinical GLP & clinical development; all biological matrices

Cell-based assays

- Support of cell-based assays & cell preparations (lysates & cryopreservation)
- Fully equipped cell culture laboratory
- State-of-the-art flow cytometry (BD FACSLyric)

Ligand-binding assays

- Support of PK & immunogenicity studies (ADA & NAb), biomarkers & biosimilars
- Fully validated systems incl. MSD QuickPlex SQ 120, Gyrolab xPlore & xPand, Tecan M200 ELISA Reader
- Experience with various tissues (using Precellys tissue homogeniser)

- All assays validated according to applicable international guidelines
- Fully validated Watson LIMS incl. immunogenicity module covering validation studies as well
- GLP, ANVISA, S1 license (GMO), BSL2 certification (pathogenic / infectious samples)
- Co-location with Phase I clinic

Clinical development

Early clinical development

Phase 2-3, clinical efficacy trials

Clinical trial services

Clinical & regulatory consulting

Clinical development

Early clinical development

- Clinical trials:
  - First-in-man (SAD/MAD)
  - Pharmacokinetic (incl. PK, BA/BE, DDI)
  - Special safety (e.g. TQT trials)
  - PK/PD
  - Proof-of-concept
  - First-to-patient (Phase 1b)
  - Exploratory in patients with PK/PD endpoints

Clinical trial services

- Project management
- Clinical trial supply management
- Data management
- Medical writing
- Biostatistical & bioanalytical evaluation
- Regulatory support
- Clinical monitoring

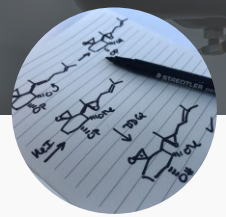
Phase 2-3, clinical efficacy trials

- Phase II clinical trials with complex endpoints at few specialised sites
- Large-scale phase 2 or 3 clinical trials in a multi-center setting
- Special expertise & track record in therapeutic area respiratory

Clinical & regulatory consulting

- Setup of clinical trial concepts & development plans
- Regulatory consulting
- Advice on clinical-pharmacological questions

Chemical development



Process research & development

GMP batch manufacturing

Solid phase investigations

Impurities ID & assessment

Chemical development

Process research & development

- Fast, efficient route evaluation, selection & scale-up
- Co-localised process development & kg batch manufacturing of preclinical & clinical supplies
- Production of 1 - 10 kg batches (intermediate/API) incl. impurity control for preclinical studies

GMP batch manufacturing

- Advancing of candidate from preclinical through phase I / IIa by scale-up in GMP Kilo Lab
- Starting material definition, analytical method validation & PGI assessments, informal & full ICH stability studies & CoA

Solid phase investigations

- Selection & control of API solid state
- Identification of new solid forms of small organic molecules (e.g. polymorphs, salts, co-crystals, or amorphous forms)
- Polymorph & salt screening, solubility curves, filtration assessments

Impurities ID & assessment

- Isolation, identification, synthesis & assessment of unknown impurities (higher than ICH legislation, 0.1 %)
- Analysis of degradation pathways
- Identification of potential ingredient interactions for dossier examination by regulatory agencies

- GMP compliance
- Tox & GMP batches up to 10 kg
- HPAPI up to OEL 0.1 µg/m^3
- Prep-HPLC/SFC, high-res MS, 400 MHz NMR
- State-of-the-art laboratory

Formulation development

Focus on semi-solids & liquids

Consulting & technology development

Preformulation

Prototype development

Formulation selection & preliminary process

Formulation development

Consulting & technology development

- Project evaluation, product development planning & troubleshooting
- Technology assessment
- IP creation & patent strategy
- Strategic life-cycle management

Prototype development

- Target product profile & formulation strategy
- Excipient selection & function justification
- Prototyping for optimised formulation parameters
- Stability/API release & skin delivery/tolerance customised to disease/sensory assessment/microstructure characterisation

Preformulation

- Solubility & compatibility profiling (single solvents & solvent blends)
- Assessment of key formulation parameters incl. pH, temperature & oxidation
- Rational residual composition design to optimise solubility & skin delivery

Formulation selection & preliminary process

- Robust & de-risked formulation selection of lead & backup candidates & regulatory compliance, stability
- In vitro release & skin permeation testing (IVRT/IVPT)
- In vitro (irritation, inflammation), & in vivo models, imaging (AP-MALDI-MS)*
- Preliminary assessment of critical process parameters to support scale up

- R&D of topical formulations for pharmaceutical & OTC dermatological treatments & complementary consumer products
- Conception & creation from TPP, preformulation to formulation selection & transition into scale-up, clinical development & QbD.
- 10 g – 10 kg capacity
- HPAPI up to OEL 0.1 µg/m3 (OEB5)
- Other delivery routes, incl. oral liquids (see slide 44)

*atmospheric pressure-Matrix-assisted laser desorption/ionization-mass spectrometry

Analytical development & QC

Full service

Method development & validation

Release & QC testing

Stability testing

Analytical development & QC

Full service

- Specifications tailored to project stage
- Small & large molecules
- Dosage forms: solid, semi-solid, liquids
- Highly potent APIs up to HHB5 (OEL > 1 µg/m^3)
- GMP certified & FDA inspected

Method development & validation

- Analytical continuum DS/DP
- Forced degradation studies
- Container closure integrity testing (blue dye, headspace analysis, high voltage leakage detection)
- Break-loose/glide-force testing
- Rheology platform & in vitro release testing

Release & QC testing

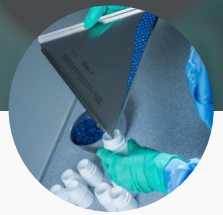
- QC testing of drug substances & products
- Support to preformulation, formulation & scale-up
- Cleaning validation methods
- Non-sterile microbial testing with preservative efficacy & microbial limit tests (USP & Eur Ph)
- In-house QP release

Stability testing

- Stability chambers, climate cabinets & stand-alone stability storage
- Zone I to IV, ICH compliance
- 320 m^3 of storage with rooms from - 70 → + 60 °C
- Temperature, light & humidity controlled
- Cycling, photostability & transportation studies

Clinical trial supplies

Manufacturing



Packaging
& labelling

Logistics &
depot solutions

Supporting
services

Clinical trial supplies

Manufacturing

- Solid oral forms, esp.:
  - Automatic capsule filling, incl. over-encapsulation
  - Tablet pressing (matching placebos)
- Creams, lotions, ointments & oral solutions
  - 10 & 50 kg tank with 5 kg/25 kg melting vessel
- Handling of high potent APIs

Packaging & labelling

- Primary packaging of non-sterile products
- Blistering (PVC/Alu, Alu/Alu, Aclar) & wallet packs
- Secondary packaging & labeling at:
  - Ambient/2 - 8°C/- 20°C/on dry ice
- Blinding solutions for, e.g., PFS, inhalers, tubes
- Packaging of light-sensitive products

Logistics & depot solutions

- > 700 m^2 clean rooms for manufacturing & primary packaging
- 6 walk-in refrigerators & 2 walk-in freezers
- Global distribution
- Worldwide depot network
- Reconciliation & destruction

Supporting services

- Import & QP services (incl. blood products & vaccines)
- Creation of randomization lists & emergency envelopes
- In-house label printing, all types of labels
- Comparator sourcing incl. decommissioning
- Handling of controlled substances

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