



Nucleic Acid Therapeutics by LGC

Complete journey from discovery to commercialisation

A large, stylized DNA double helix graphic that curves from the top left towards the bottom right. The spheres representing the base pairs are colored in a gradient from light yellow to dark purple. Four white rectangular boxes with colored borders are placed along the curve of the helix, each containing a stage of the drug development process.

DISCOVERY

PRE-CLINICAL
DEVELOPMENT

CLINICAL
DEVELOPMENT

COMMERCIAL

The development of siRNAs, antisense oligonucleotides, aptamers, sgRNAs, miRNAs and other nucleic acid modalities as therapeutics increases the need for support in discovery, pre-clinical development and expert manufacturing capabilities from the laboratory bench to clinical phase studies. Axolabs has created an expert team focused on contract development and manufacture of nucleic acid therapeutics. Our experience provides a unique support from discovery through pre-clinical development to the clinic and even beyond. With three sites in USA and Europe, we offer:

Expertise and scientific excellence

The Axolabs team leverages its world-leading know-how and 20+ years of experience providing high-end pre-clinical solutions and consultancy for nucleic acid therapeutics tailored to the client's specific needs.

Axolabs has world-class bioanalytical capabilities and experience in high-integrity analytical science. Operating to GLP, GCP and cGMP standards, Axolabs also has leading capabilities in CMC of nucleic acid therapeutics.

Together, we have proven expertise in a wide range of therapeutic nucleic acid modalities including antisense and immunostimulatory oligonucleotides, siRNAs, aptamers, microRNAs and microRNA mimics, synthetic mRNAs and guide RNAs for CRISPR applications. We hold proprietary IP on oligonucleotide-based medicines.

We have unique expertise allowing us to support our customers through oligonucleotide therapeutic discovery, development and manufacture, across sites in the USA and Germany.

Services across multiple disciplines from target to clinic and beyond

We deliver integrated solutions for pre-clinical research covering chemistry, biology and analytics of nucleic acid therapeutics, allowing us to provide efficient and validated services towards the successful development of nucleic acid-based therapeutics.

Our capabilities are offered as standalone specialised products or services, or as part of an integrated program customised to your requirements.

High quality manufacturing of nucleic acid therapeutics and related services

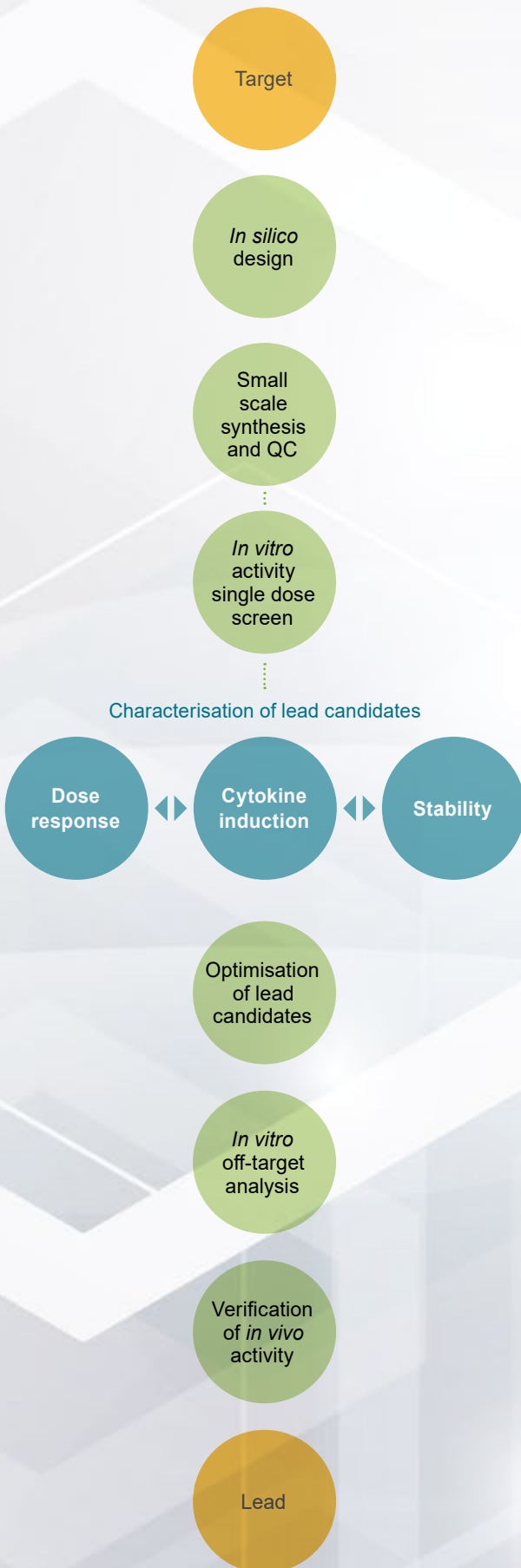
All sites have established quality management systems and specialist manufacturing facilities. Fully traceable documentation can be provided from start to finish.

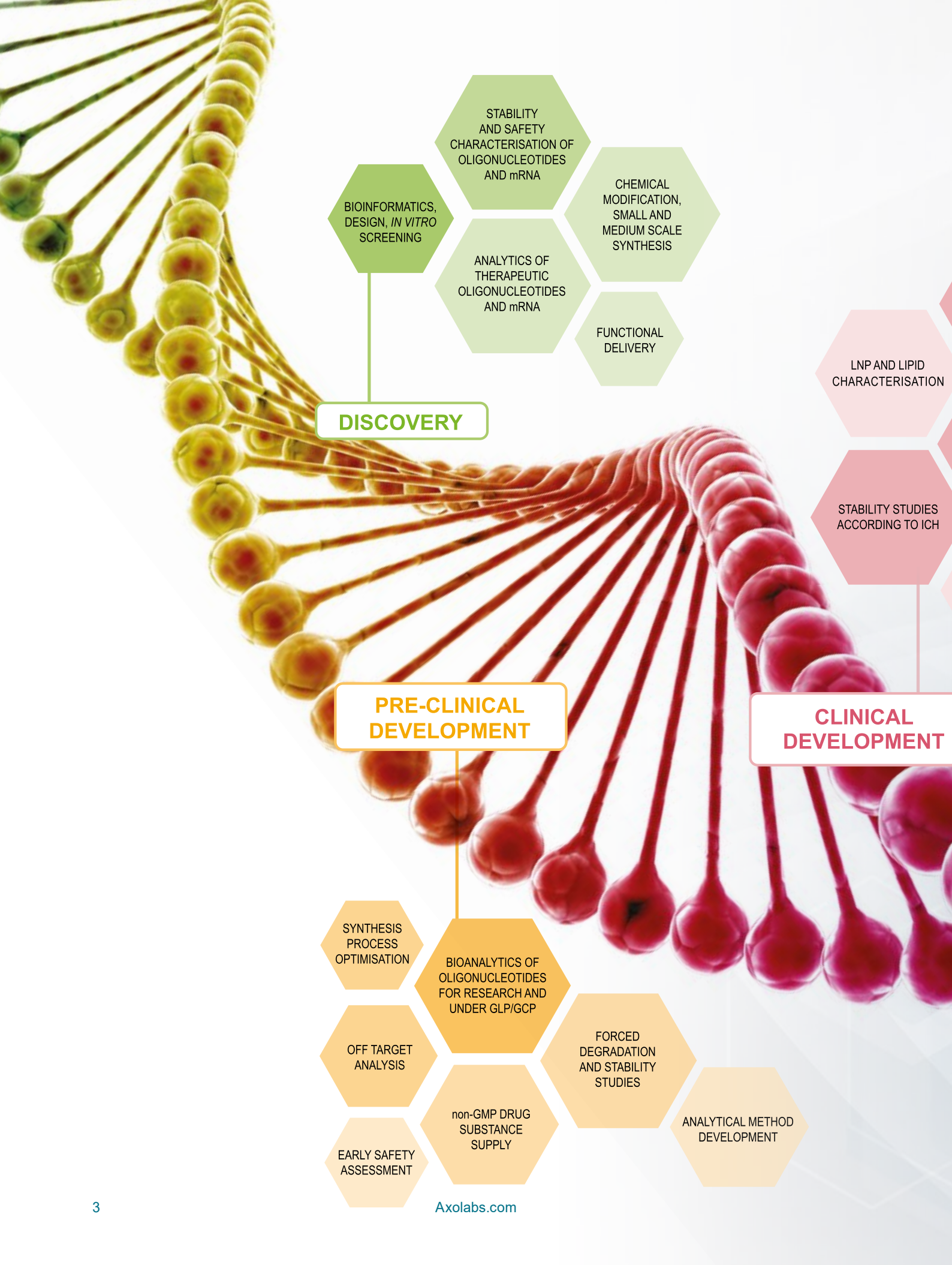
Lead discovery

Our bioinformatics group is experienced in the design of siRNAs, antisense oligonucleotides and other nucleic acid therapeutics modalities. During the *in silico* drug design process, the avoidance of potential off-target effects is taken into account.

In the course of lead identification and optimisation we synthesise a set of suitable drug candidates. With our broad portfolio of capabilities and well established methods, we further select and characterise the best suited nucleic acid drug candidates with respect to stability, safety and other relevant parameters.

With our proprietary lipid platform and our long-standing conjugation expertise, we provide solutions for the functional cellular delivery of various oligonucleotide drugs.





DISCOVERY

BIOINFORMATICS,
DESIGN, *IN VITRO*
SCREENING

STABILITY
AND SAFETY
CHARACTERISATION OF
OLIGONUCLEOTIDES
AND mRNA

ANALYTICS OF
THERAPEUTIC
OLIGONUCLEOTIDES
AND mRNA

CHEMICAL
MODIFICATION,
SMALL AND
MEDIUM SCALE
SYNTHESIS

FUNCTIONAL
DELIVERY

**PRE-CLINICAL
DEVELOPMENT**

SYNTHESIS
PROCESS
OPTIMISATION

BIOANALYTICS OF
OLIGONUCLEOTIDES
FOR RESEARCH AND
UNDER GLP/GCP

OFF TARGET
ANALYSIS

FORCED
DEGRADATION
AND STABILITY
STUDIES

EARLY SAFETY
ASSESSMENT

non-GMP DRUG
SUBSTANCE
SUPPLY

ANALYTICAL METHOD
DEVELOPMENT

**CLINICAL
DEVELOPMENT**

LNP AND LIPID
CHARACTERISATION

STABILITY STUDIES
ACCORDING TO ICH

Supporting you across all areas of development, production and testing



COMMERCIAL AND LATE CLINICAL PHASE

Our manufacturing capabilities

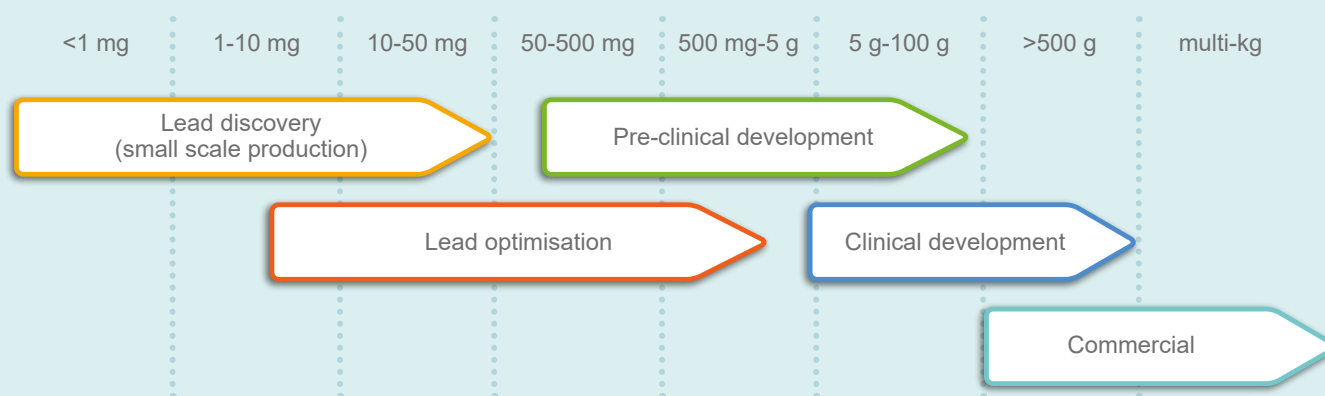
The combination of Axolabs expertise in process development and manufacturing of therapeutic oligonucleotides, with the throughput, scale and GMP capabilities, create combined manufacturing capabilities ideally suited to optimise your oligonucleotides production needs from discovery through clinical development.

We support the discovery process with a large portfolio of chemical modifications and corresponding analytics required to transform

various oligonucleotide modalities into potent and safe drug candidates.

Our expertise includes the synthesis of long RNA/DNA that is mainly used for single guide RNAs for Gene Editing applications and Aptamers.

Our team is also highly experienced in developing analytical methods to optimise GMP manufacturing processes and support CMC dossiers.



Our capabilities include:

Custom small molecule synthesis

Including specialty phosphoramidites, solid supports (CPG), and conjugation reagents (e.g. active esters and click chemistry).

Chemically modified oligonucleotides

Modifications we routinely work with include:

- Large variety of sugar and/or base-modified nucleotides
- Small molecule, lipid, peptide and carbohydrate conjugates (e.g. GalNAc cluster)
- Fluorescent dyes

Long DNA/RNA

Including single guide RNAs for CRISPR/Cas applications and Aptamers.

Custom tailored process optimisation

QbD-based process development to maximise yield, quality, process efficiency and robustness. Technology transfer packages can be provided.

cGMP manufacturing

Production is currently carried out at upgraded Oligopilot-400+ scales (up to multiple hundreds of grams) in controlled laboratories and classified cleanrooms with isolated sub-suites.

Beyond, Axolabs has invested in a capacity expansion for large-scale production of oligonucleotides at the Petaluma and Berlin sites, implementing Oligo Process manufacturing scales (multi-kg), planned to be operational in 2024. We have an ICH Q7-based Quality System and IQ/OQ on all manufacturing and support equipment.

Lipid synthesis

For the LNP formulation of oligonucleotides we offer a set of proprietary clinically verified lipids that we synthesise in various scales and out-license to interested customers.

Analytics, bioanalytics and clinical trial support

We have a variety of state-of-the-art techniques for the physicochemical and thermodynamic characterisation of single and double-stranded oligonucleotides. This also includes:

- Identification of oligonucleotide metabolites (DMPK)
- Characterisation of nucleosides and nucleotides
- Analysis of nucleic acid-protein interactions.

For the growing field of mRNA applications our experts have developed sophisticated methods, to verify critical quality attributes of mRNAs. This includes identity, purity, quantitative cap-structure assessment and poly-A tail characterisation.

Our unique and proprietary assay system for the quantification of oligonucleotides from biological matrices has become the gold standard in pre-clinical and clinical studies to analyse PK and biodistribution of the drug under the standards of GLP/GCP.

Also available GLP compliant assay for the quantitative detection of mRNA therapeutics from various biological matrices.



Oligonucleotide manufacturing

- High-quality synthesis – from discovery to pre-clinical, clinical and commercial stage
- Custom-tailored process development optimisation
- Long RNA/DNA, e.g. for CRISPR/Cas applications
- Chemically modified oligonucleotides and conjugates
- Regulatory documentation
- Impurity markers and reference standards
- Lipid synthesis

Oligonucleotide and nucleic acid analytics

- HPLC and LC/MS for purity and impurity assessment
- Physicochemical and thermodynamic characterisation
- Solid state investigation on lyophilized products
- mRNA characterisation (purity, identity, cap, poly-A, LNP drug product)
- Characterisation of nucleosides and nucleotides raw materials
- Stability determination in biological matrices
- Identification of impurities and metabolites by LC/MS
- Analysis of nucleic acid-protein interactions

Bioanalytical services

- Detection of oligonucleotides from biological matrices
- Quantitative detection of mRNA therapeutics from biological matrices
- GLP/GCP certified test site
- WinNonLin PK parameter analysis
- Biomarkers

Oligonucleotide lead identification

- Bioinformatics assessment for sequence pre-selection
- Drug design and synthesis
- High-throughput *in vitro* screening
- Lead characterisation and optimisation
- *In vivo* efficacy and early safety assessment

Biological and pharmacological tests and analyses

- Cell-based assays for cell function, proliferation and toxicity
- Ligand-receptor interaction and uptake studies/histology
- Flow cytometry
- Protein analysis
- Analysis of mRNA up- and downregulation
- Next generation sequencing
- **Platform for functional cell type-specific delivery of nucleic acid therapeutics**
- *In vivo* efficacy and early safety assessment of oligonucleotide- based therapeutics in wild type mice
- Rational design tailored for specific delivery systems
- Proprietary lipid nanoparticle (LNP) formulations

CMC analytical services

- cGMP release testing of oligonucleotide-based drug substances and drug products
- Forced degradation and stability studies of oligonucleotide-based drug substances and drug products according to ICH guidelines
- Broad analytical capabilities
- Materials science
- IMPD and IND submission support/writing

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