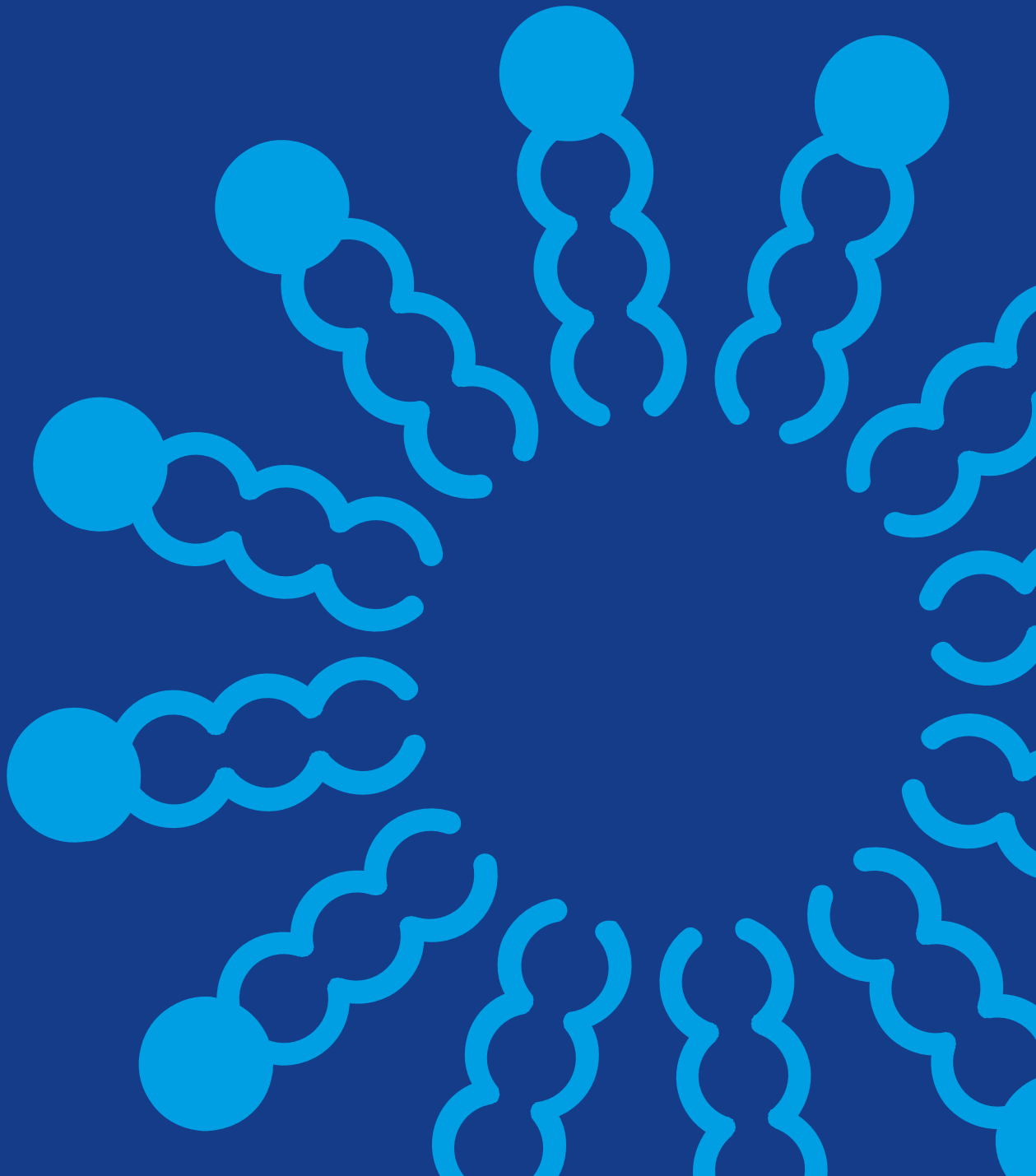


# Lipids & Carbohydrates

Technology Platform





Looking for rapid scale-up services?

Looking for a supplier to help reduce your Scope 3 sustainability targets?

Need labelled lipids for your initial discovery works or pharmacokinetics studies?

Searching for one partner for drug substance & drug product from early-stage to global commercial supply?

Expect proven process knowledge from pre-clinical to commercial?

Looking for an experienced partner to industrialize your SFC purification processes up to commercial-scale?

Searching a supplier that can ensure sustainable, consistent, and high quality from R&D to commercial?

Need regulatory support for your filing or access to our DMFs for your key lipids?



**The right partner is one partner.** Working and coordinating with several providers can be demanding and time consuming when outsourcing a project. No matter where your project starts, Cordenpharma is the partner you need for a fully-integrated solution spanning the complete product life cycle at all stages, from preclinical to commercial, supported by dedicated regulatory and project management services. A straightforward communication with

one supplier alleviates the need for excess resources required to manage multiple providers. Our organizational structure provides you with one point of contact to help navigate your way to project completion. Through our network of integrated cGMP facilities across Europe and the US organized under six Technology Platforms, we have fostered an efficient exchange between API & Drug Product teams to decrease your development time to market.

# Your Benefits – Our Strengths

**Scientific Expertise**  
Your project will benefit from our efficient, time-saving development of thousands of process steps using six-sigma.

**Fast & Lean Process Development Approach**

**Targeting from Design to Commercial**  
Access to our proven lipid & peptide expertise for the design, development, and manufacturing of your lipo-peptides for targeting modalities.

**Lipid Expertise**

**Fully-integrated Offering for Lipid Supply, LNP Formulation, Aseptic Fill & Finish**  
Get access to our state-of-the-art R&D LNP Lab for formulation screening and select the most suitable lipids from our broad portfolio. Benefit from scale up into GMP manufacturing directly at the Fill & Finish facility.

**Lipid Nano-Particle (LNP) Technology**

**Unique Purification Capabilities**  
Take advantage of the largest capacity of complex lipids available globally through our SFC concept, a unique technique that reduces your scope 3 sustainability targets.

**Go Green, Go Large**

**Foster Entrepreneurial Spirit**

**Flexibility & Transparency**  
Benefit from our collaborative commitment to react with flexibility & transparency to your changing needs.

**Focus on Patient Safety**

**Our Motto is Quality**  
Rely on the integrity of our robust quality & regulatory compliance standards at the foundation of every step your project takes, from initial process development through product delivery and beyond.

**Ingenuity at Work**

**Thinking Outside the Box**  
Grow from our scientific passion and ingenuity in finding new ways to solve complex problems that help you take the most efficient path to reach your project goals.

**Access to Broad Manufacturing Capabilities**

**Lipid & Carbohydrate Complexity**  
Receive adaptable support for multiple programs at any scale & stage of (functional) excipient and / or API development & commercialization.

**Quality Is the Foundation of Every Step Your Project Takes**  
Rely on the integrity of our robust quality, regulatory compliance & manufacturing standards from initial process development through product delivery, supported by substantial global regulatory & filing experience (EMA, FDA, PMDA).

**Focus on Reliable Safety Expertise**

**Transparent Communication**  
Work closely with our dedicated project management teams to receive regular project updates, gain continual access to your batch records and reach your defined target.

**Continuous Exchange & Knowledge Sharing**



**Your Goal is our Goal.** We turn our strengths into your benefits by keeping in mind that your goal is our goal: to produce high quality pharmaceutical medicines through efficient, lean processes with reduced times to market.

# Your Full-Service CDMO for a Global Market

## Secure Your Supply Chain with our Fully-Integrated Solution



CordenPharma is the partner you need for a Fully Integrated Supply solution spanning your complete product life cycle at all stages, from sourcing of raw materials to secure your supply chain, through preclinical & commercial development and manufacturing of GMP starting materials, APIs, finished dosage Drug Products & Packaging > resulting in reduced time & cost. Your project is all the while supported by dedicated regulatory & project management expertise at every step along your outsourcing path.

## The Lipid & Carbohydrates Platform: A Driving Force for the Creation of New Complex Modalities

CordenPharma stands as a global CDMO leader in pioneering lipid-based products for research and pharmaceutical development. With a remarkable track record of over three decades, CordenPharma has collaborated extensively with the research, pharmaceutical, and diagnostic sectors, delivering cutting-edge solutions that push the boundaries of science and contribute to enhancing and saving lives. Our unwavering commitment to quality across all our products and services forms the bedrock of our esteemed reputation.

At CordenPharma, we are driven by a deep passion for pure lipids and the extraordinary benefits they bring to our customers. This fuels our continuous pursuit of innovation, expanding our diverse portfolio with remarkable products that positively impacts our customers and the lives of their patients. Our adaptability and responsiveness to dynamic market needs empower us to creatively transform challenges into solutions, to support and nurture pharma innovators' complex modalities for the development of their groundbreaking medicines.

The essence of our dedication to customers lies not just in what we do, but how we do it. It all starts with assembling a team of foremost lipid technology experts, collaborating through the discovery process in a synergistic manner. From your project's inception, we provide ex-

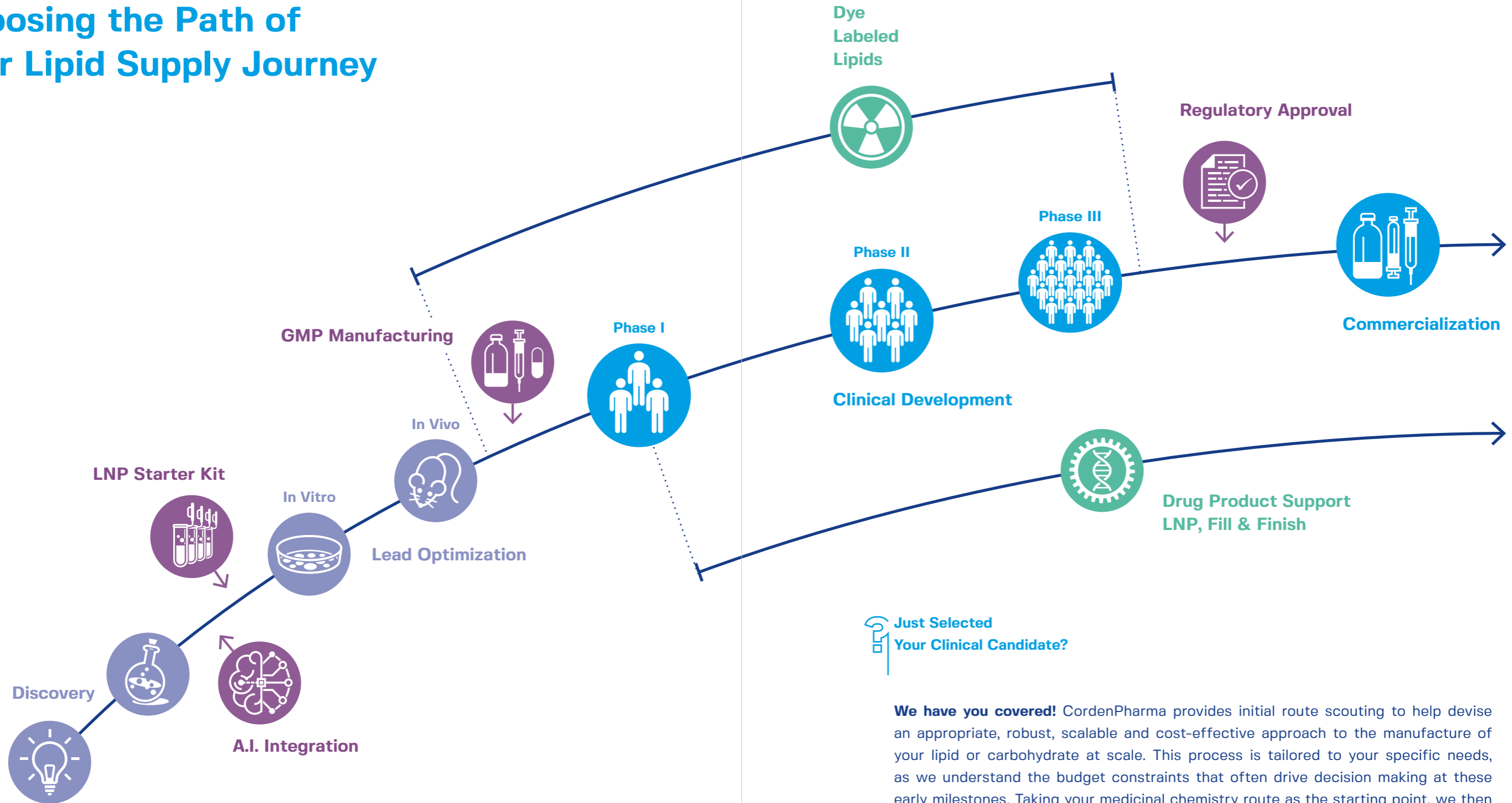


pert technical partnerships in product design, where our wealth of knowledge is seamlessly transferred into a cGMP manufacturing environment, employing safe and sustainable practices to support clinical development. Driven by our unwavering integrity, we remain steadfast in maintaining the highest standards of quality across our services, workforce, and entire organization.

The heart of our Lipids & Carbohydrates Platform lies in our people. With highly-trained staff leveraging proven methods and procedures to ensure the excellence of your final lipid-based products, each project is meticulously supported by our specialized Quality, Analytical, and Regulatory teams, adhering to stringent specifications. At CordenPharma, we recruit the finest talents, equip them with the best technology, and empower them to excel. As a result, many of our pioneering lipid synthesis processes and products are brought to life through our customers, supported by the passion and commitment of our dedicated team members.



# Choosing the Path of Your Lipid Supply Journey



**We have you covered!** CordenPharma provides initial route scouting to help devise an appropriate, robust, scalable and cost-effective approach to the manufacture of your lipid or carbohydrate at scale. This process is tailored to your specific needs, as we understand the budget constraints that often drive decision making at these early milestones. Taking your medicinal chemistry route as the starting point, we then perform a criticality analysis to identify potential stumbling blocks for the scale-up including safety concerns, price drivers, green chemistry options, atom economy and isolation challenges, and then devise a customized development plan to address your exact needs to safely execute the process at scale.

With recently expanded small-scale production facilities comprised of movable and interchangeable equipment, our aim is to provide a highly flexible manufacturing space geared towards meeting your wide-ranging requirements and aggressive timelines.



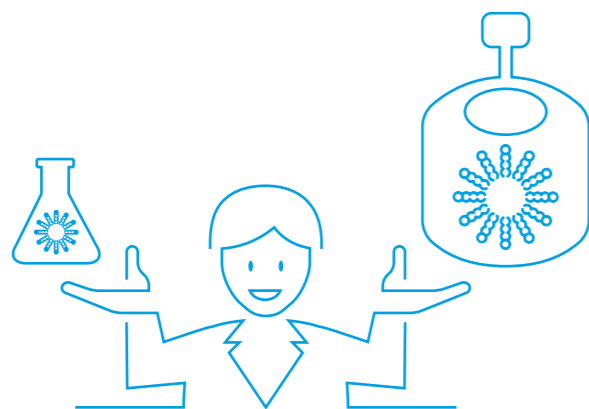
Large-scale lipid production at CordenPharma Switzerland, Liestal (CH).



Analytical testing of custom lipids at CordenPharma Switzerland, Liestal (CH).

## **Already Demonstrated Your Process at Scale? Looking For a New Manufacturing Site?**

**We have you covered!** With API manufacturing sites in both Europe and the US, different geographic locations depending upon your preference, requirements or strategies, our network allows for a continuum of scales available from low kilos to metric ton demands. Whether you may initially only be projecting small annual demands of a few kilos or progress towards large-scale commercialization in the clinic with a sudden annual demand growing in orders of magnitude – no issue! Through an internal technology transfer system, our team can seamlessly transfer your process between sites to execute on a scale-up in minimal timeframe to keep your program on track.



## **Full-Service Offering**

To stimulate and support your research, CordenPharma has introduced several tools designed for ADME – CMPK activities (Radiolabeled compounds, lipids conjugated to a dye).

We also provide full Lipid NanoParticle (LNP) support from R&D to GMP at our CordenPharma Caponago (IT) site, which is adaptable with your own internal resources and competences.

Based on our experience with LNP formulation and our longstanding track record in manufacturing catalog lipids, CordenPharma now offers LNP Starter Kits, which provide a tailored mix of four effective lipids (ionizable, Pegylated, phospholipids and Cholesterol) in a suitable ratio, that are readily available online.

## **Regulatory Support**

Our local Regulatory teams at each manufacturing site are adept at managing and fulfilling the expectations of global regulatory agencies, including letters of authorization to our existing DMFs or support in the preparation of your CMS section.

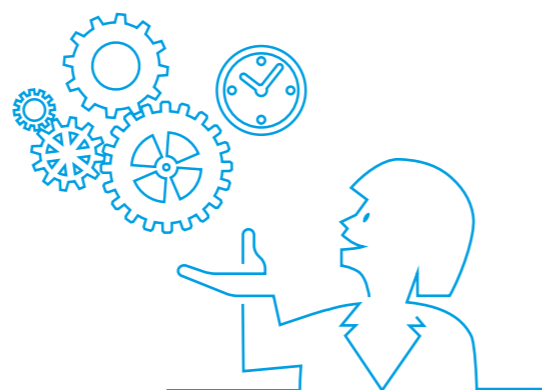
# Lipids & Carbohydrates Production

## CordenPharma Lipids

To support the rising demand for production of liposomal drugs using phospholipid excipients, CordenPharma draws upon an impressive history of excellence in providing specialized functionalities such as longer shelf-life to render a competitive advantage to your API formulations. With a strong market position in synthetic Lipid process development, scale-up and large-scale manufacturing, including custom & standard lipids, we hold several Drug Master Files (DMFs) to even further expand your access to a broad range of lipid products & services.

### Our Lipids Offering

- Highly efficient, quality excipients
- Adherence to the latest guidelines of the International Pharmaceutical Excipient Council (IPEC)
- cGMP certified supplier of high quality liposomal excipients
- Aid development of target delivery drugs
- Emphasis on Quality by Design (QbD) & Process Analytical Technology (PAT) for controlled raw materials & lower net costs
- Comply with Pharmacopeia standards: USP, BP, EU & IP (where a monography is established)
- Comply with the GMP API requirements (Eudralex Vol 4, part II)
- Bovine Spongiform Encephalopathy (BSE) & Transmissible Spongiform Encephalopathies (TSEs) free certification
- Well-established specification sheets, quality control & test procedures
- Functionality with lot-to-lot consistency



Scan me  
for more info

## CordenPharma Carbohydrates

With over a decade of experience in the field of carbohydrate molecules, CordenPharma has gained specialized expertise in complex oligosaccharides. Our carbohydrate portfolio includes multi-kg manufacturing of innovative carbohydrate products for monosaccharide building blocks, GalNAc and conjugates such as glycolipids, phosphatidyl inositols and glycopeptides.

Our complex carbohydrate know-how has been successfully demonstrated on several multi-kg cGMP manufacturing scales, delivering very high quality products showing lot-to-lot consistency, with processes developed according to Quality by Design (QbD) and a manufacturing approach supported by Process Analytical Technology (PAT). Unique back integration of non-GMP raw materials to support your carbohydrate projects is also available.

### Our Carbohydrate Offering

- Synthesis & manufacturing of complex & conjugated carbohydrates
- Purification capabilities by Flash Chromatography (LPLC & MPLC): Biotage 15 & 40 cm cartridges, large-scale glass flash columns (40 cm ID)
- Preparative HPLC columns (10 cm – 100 cm ID)
- Nanofiltration, aqueous & organic solvent removal -permeate flow up to 60 l / hour at pressure up to 40 bar (ATEX)

CordenPharma Switzerland performing the final carbohydrate purification step to reach the expected 99% purity.



# LNP Starter Kit

**Lipid Nanoparticle (LNP) Starter Kits** are important for effective mRNA formulation in the development of mRNA-based therapeutics, such as mRNA vaccines or gene therapies. The starter kits provide researchers and developers with the essential components needed to create and optimize their own LNPs for mRNA delivery. The benefits of CordenPharma's LNP starter kits include:

- **Customization & Optimization:** LNP starter kits offer flexibility for researchers to customize and optimize the lipid composition and formulation parameters according to the specific requirements of their mRNA-based therapeutic. This is crucial for achieving optimal delivery efficiency and minimizing potential side effects. CordenPharma's lipids are of high purity, and will be available at larger scale once your program progresses through clinical phases.



- **Cost-Effectiveness:** Developing LNPs in-house using starter kits can be more cost-effective than purchasing pre-made LNP because researchers can adjust the formulation to match their needs and scale up the production as necessary.
- **Research & Development:** LNP starter kits enable researchers to experiment with various lipid components and ratios, helping them understand how different formulations affect LNP stability, biodistribution, cellular uptake, and gene expression.
- **Intellectual Property Control:** Creating custom LNPs using starter kits allows research organizations and companies to maintain control over their formulation processes, potentially protecting their Intellectual Property.
- **Tailored Therapeutic Applications:** Different therapeutic applications may require specific LNP formulations. Starter kits enable the development of LNPs tailored for different target cells, tissues, and therapeutic objectives.
- **Iterative Improvement:** Starter kits facilitate iterative optimization, enabling researchers to refine LNP formulations over time for improved delivery efficiency, stability, and safety.
- **Rapid Prototyping:** Researchers can rapidly prototype LNPs using starter kits to test hypotheses and gather initial data before committing to larger-scale production.

**It's important to note** that while LNP starter kits provide valuable tools, working with LNPs and mRNA formulations requires specialized knowledge and expertise. Safety, stability, and efficacy considerations are crucial, and regulatory standards must be met for clinical applications. Therefore, researchers often collaborate with CordenPharma's experts to ensure the successful development of their mRNA-based therapeutics. Several kits consisting of CordenPharma lipids are ready-available in our online catalog.

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for more info



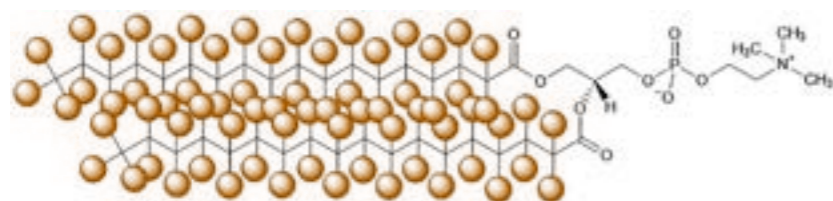


## ADME – DMPK Tools

**ADME (Absorption, Distribution, Metabolism & Excretion)** – It is a fundamental concept in pharmacology and drug development, encompassing the processes that a drug undergoes within the body from the time of administration to its elimination. Understanding the ADME properties of a drug is crucial for assessing its pharmacokinetics and pharmacodynamics, which in turn influence its effectiveness and safety, and helps researchers and pharmaceutical innovators predict how the drug will behave in the human body. This information is vital for determining appropriate dosing regimens, assessing potential drug-drug interactions, and ensuring the drug's safety and efficacy. ADME studies are conducted during preclinical and clinical development phases to gather data on how the drug is processed within the body and how it affects different tissues and systems.

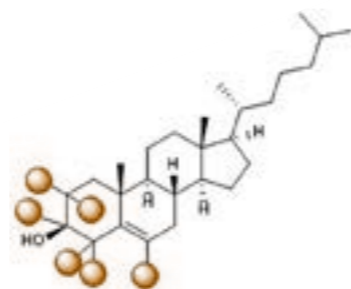
Radio-labelled compounds are excellent investigative tools, widely used to carry out ADME studies during drug discovery and development stages. For in vivo studies, radiolabeled compounds are employed to investigate the extent of absorption, bioavailability, tissue distribution, mass balance, routes of excretion, pre-systemic metabolism and to elucidate metabolites formed.

### DSPC-d70



**DMPK (Drug Metabolism & Pharmacokinetics) studies** help researchers and pharmaceutical companies optimize drug candidates, understand potential drug-drug interactions, establish appropriate dosing regimens, and predict a drug's behavior in humans based on preclinical studies. This information is vital for ensuring drug safety and efficacy before entering clinical trials, and eventually reaching the market.

**At CordenPharma** have developed labelled lipids (examples: deuterated lipids like d6-Cholesterol, d70-DSPC) to support your drug development. By using our labelled lipids for the creation of LNP (Lipid NanoParticle) formulations, you can track the precise location of your LNP in the subject body, including the organs being targeted and the biodistribution of the formulation, followed by the secretion of the lipid components. Further benefits such as In Vitro Assay development, high throughput screening, quantification, and validation of assays, as well as non-invasive imaging are all possible thanks to our special labelled lipids.



Cholesterol-d6

## Supercritical Fluid Chromatography (SFC)

**Supercritical Fluid Chromatography (SFC)** is a chromatographic technique that employs supercritical fluids such as carbon dioxide as the mobile phase to separate and analyze compounds. The application area of SFC has expanded tremendously over the last years, and more polar analytes such as biomolecules have become accessible. The growing interest in biopharmaceuticals and associated regulatory requirements demand alternative analytical tools. The orthogonal nature of Supercritical Fluid Chromatography, compared to reverse-phase liquid chromatography, meets these needs and makes it a useful option during research and development. Furthermore, the inherent scalability of SFC with limited environmental foot-

print makes it ideal for the production of large-scale chromatography to produce ultra-high purity compounds in an economical fashion.

CordenPharma has invested massively to support the expansion of specialty lipids production in CordenPharma Chenôve (FR) and CordenPharma Switzerland, which are essential for newly developed cell and gene therapies, as well as siRNA and miRNA programs. However, these commercial lipid quantities also require the highest purity levels possible. Through the application of SFC on a large scale, we are now able to offer large-scale, high purity lipid production at CordenPharma Chenôve in France using this revolutionary technique.

CordenPharma's SFC 1500 (PIC Solution) technology for lipids purification at CordenPharma Chenôve.

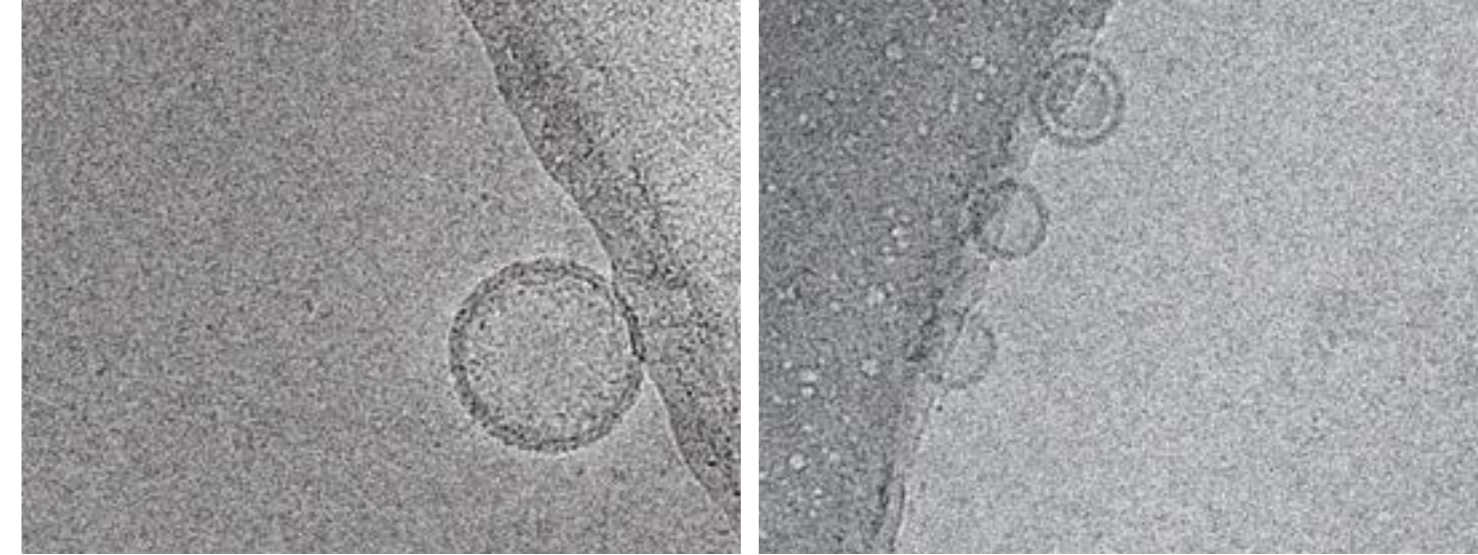
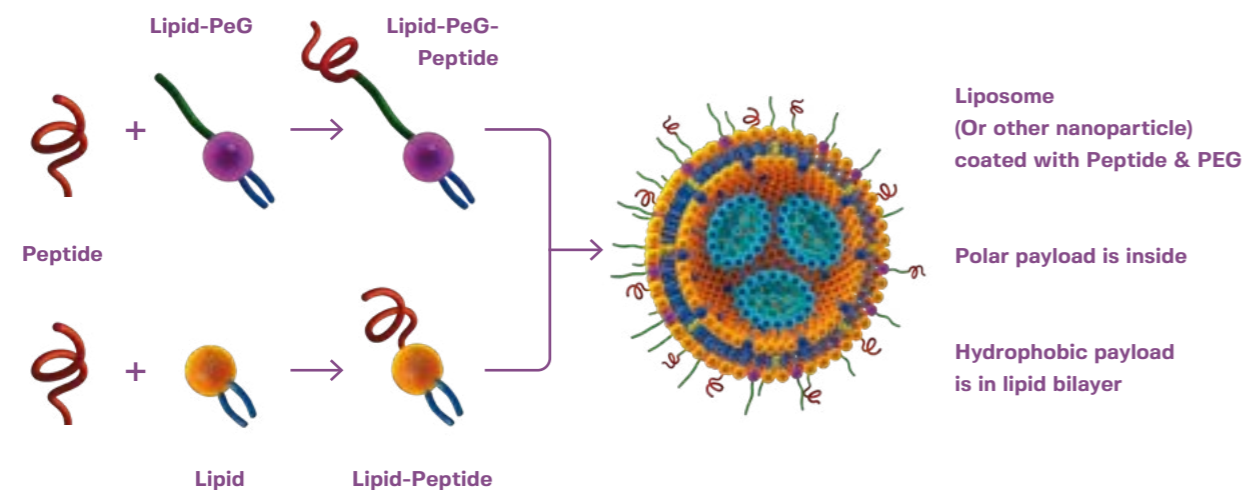


# Targeting Specific Organs with Coated LNPs

Over the past two years, the potential and practical application of messenger RNA (mRNA) technology has been vividly demonstrated through the creation of multiple COVID-19 vaccines utilizing SARS-CoV-2 mRNA encapsulated in Lipid NanoParticles (LNPs). The remarkable utilization of LNP technology for delivering mRNA-encoded antigens into cells has sparked discussions about potential applications in other therapies. LNPs have emerged as the most promising delivery method for a range of medical advancements, including new vaccines, protein replacement therapies, genome editing, cancer immunotherapies, and more.

Traditional LNPs consist of four key molecules that CordenPharma produces at all scales: an ionizable amino lipid for nucleic acid binding and endosomal escape facilitation, an amphipathic phospholipid to promote fusion with cell and endosomal membranes, BotaniChol® (cholesterol from plant origin) for LNP stability, and a polyethylene glycol (PEG) lipid for improved colloidal stability and reduced clearance by the reticuloendothelial system.

While traditional LNPs have proven safe and effective, their usage has largely been confined to intramuscular and intravenous administration, mainly targeting liver hepatocytes. This is due to their physiochemical resemblance to very-low-density lipoprotein, and their tendency to adsorb apolipoprotein E in blood

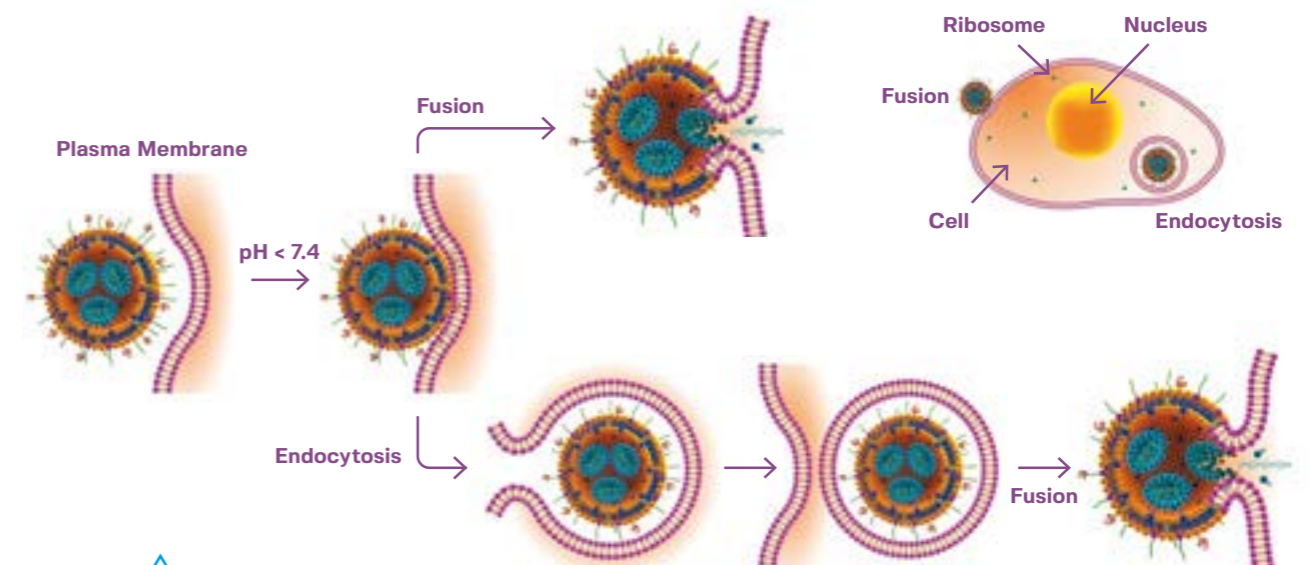


Scanning Electron Microscope images of LNPs from CordenPharma Caponago (IT).

plasma, resulting in accumulation in the liver and uptake into hepatocytes via the low-density lipoprotein receptor. Designing LNPs predictably and rationally for delivering nucleic acids to tissues outside the liver remains a significant challenge that must be addressed to fully unlock the potential of LNP technologies across diverse therapeutic settings.

In response to this challenge, we have introduced a methodology known as Selective Organ Targeting (SORT), which involves the systematic engineering of nanoparticles to precisely deliver therapeutic molecules to both hepatic and extrahepatic tissues. These SORT LNPs incorporate an additional lipo-peptide that aids in redirecting LNPs and enhancing cellular uptake in target organs through an inherent targeting mechanism of action. These effects can be tailored and adjusted based on the chemistry and quantity of the included lipo-peptide.

Thanks to this unique expertise, our scientists can adjust either the lipid and / or the peptide sequence to produce the optimal outcome.



Targeting & Fusion of Peptide-coated LNPs

## Lipids Blend by Spray Drying

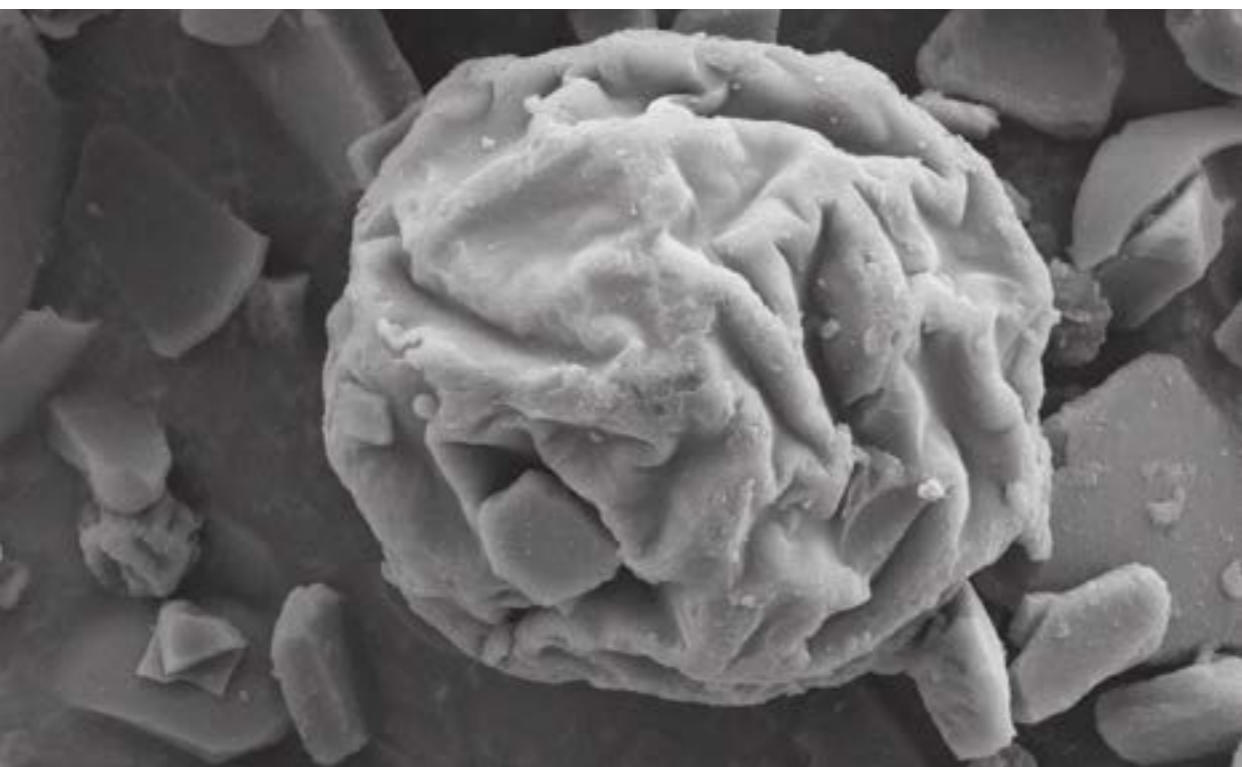
The **spray-drying technique** has proven highly effective in microencapsulating bioactive molecules like enzymes, flavors, and drugs. It is also widely used in preparing drug delivery systems using diverse biodegradable polymers. Much like supercritical fluid precipitation, spray drying is considered a modern one-step method for producing small particles suitable for pulmonary administration.

CordenPharma has successfully prepared amorphous structures of free peptides and drugs. This is achieved by using solutions of pure compounds or, more commonly, in combination with sugars as additional excipients. Amorphous solids hold significance for pharmaceutical materials due to their heightened solubility, quicker dissolution rates, and sometimes superior compression characteristics compared to their crystalline counterparts.

Recent innovations have introduced novel methods for liposome preparation, including freeze drying, stable plurilamellar vesicles, and dry, free-flowing granular products. Despite these advancements, the bulk production of liposomes remains limited. To address this, the spray drying technique has been utilized to stabilize preformed liposomes and their contents during storage. This approach scales well for bulk preparation of dried lipid mixtures for secondary liposome production. Notably, spray-dried phospholipids exhibit promise as efficient drug carriers, effectively safeguarding the structural integrity, stability, and functionality of active materials like DNA.

At CordenPharma, our expertise and advanced equipment enable comprehensive support from early development to commercial production. Our focus lies in understanding the operational variables and mixture composition that influence the structural, thermodynamic, and physical properties of dried particles.

Scanning Electron Microscope image of spray dried particle from CordenPharma Brussels (BE).

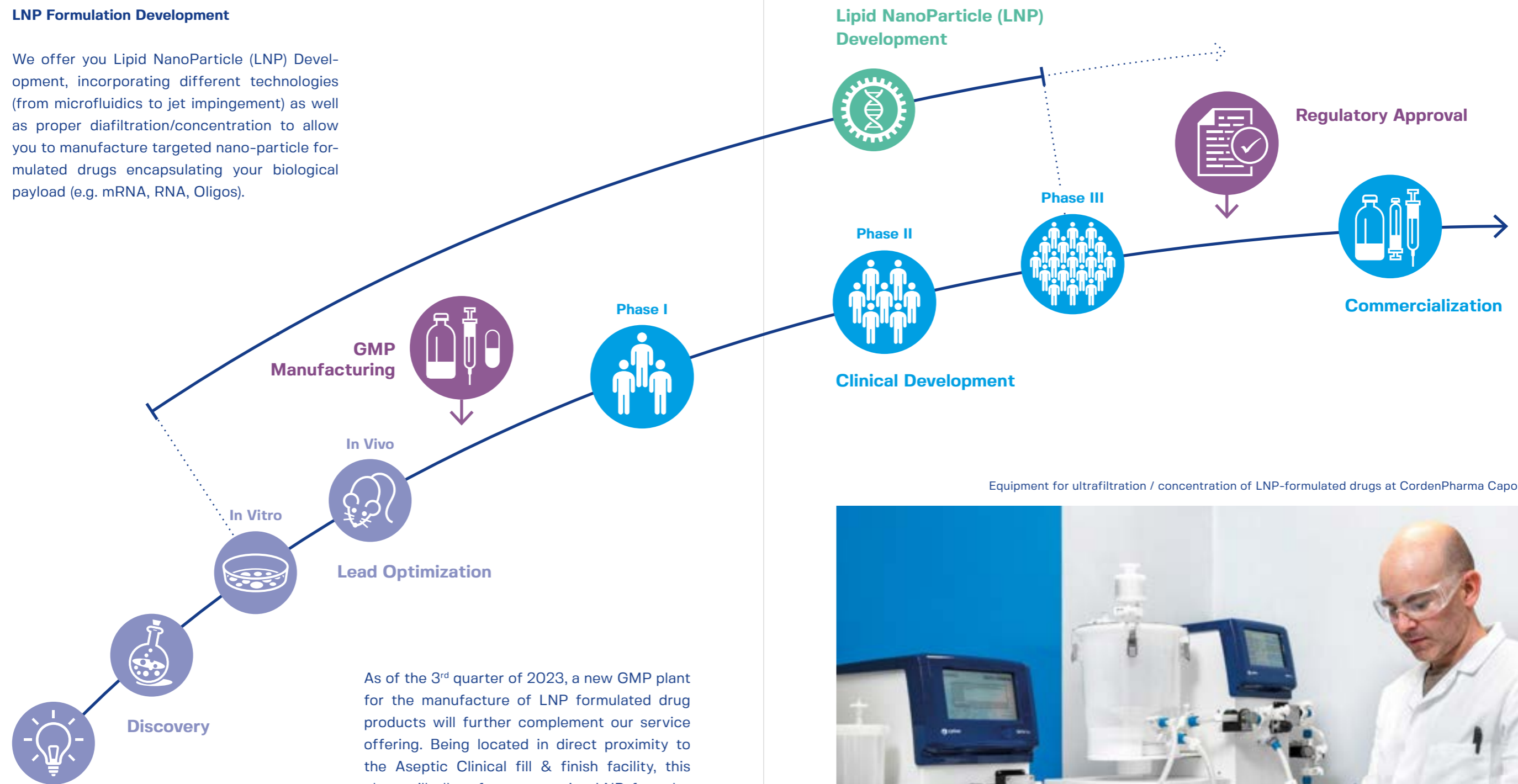


Spray drying process at CordenPharma Brussels (BE).

# LNP – Preclinical to Manufacturing

## LNP Formulation Development

We offer you Lipid NanoParticle (LNP) Development, incorporating different technologies (from microfluidics to jet impingement) as well as proper diafiltration/concentration to allow you to manufacture targeted nano-particle formulated drugs encapsulating your biological payload (e.g. mRNA, RNA, Oligos).



As of the 3<sup>rd</sup> quarter of 2023, a new GMP plant for the manufacture of LNP formulated drug products will further complement our service offering. Being located in direct proximity to the Aseptic Clinical fill & finish facility, this plant will allow for consecutive LNP formulation as well as batch filling, and thus minimize the production time for your clinical material.

Equipment for ultrafiltration / concentration of LNP-formulated drugs at CordenPharma Caponago (IT).



# Quality & Compliance First

**Our commitment to seek** the highest standards of Quality & Compliance First is the backbone of all our activities and projects. We make no compromises in this area. We have and continue to invest heavily in compliance programs, with the objective to meet and surpass applicable regulatory requirements & legislations. Our focus on quality & compliance will be ongoing, with budgeted investment in improvements such as compliance-enhancing IT solutions.




## CordenPharma Continuous Improvement Program

You will benefit from the ongoing support of CordenPharma's Continuous Improvement Program, based on the consistent completion of corrective and preventive actions arising from self-initiated proactive third party group-wide gap assessments, agency inspections, as well as internal, annual corporate & customer audits. This approach enables us to not only meet, but surpass general requirements needed to see your project through to completion.

## CordenPharma Global Compliance Team

The CordenPharma Global Compliance Team systematically interprets these continuous improvement program audit and assessment results on your behalf to generate corporate policies and global standards enabling employees at all levels to comply with current applicable guidelines and legislations in their daily activities.

Corporate compliance standards & policies are then implemented at all CordenPharma sites globally, with the objective of complete harmonization to foster transparency and straightforward communication, both internally and externally with our customers. The whole organization works together, from the Executive Leadership Team and Facility Managing Directors to the Marketing & Sales team and operators, to make sure all employees effectively comply with implemented policies, Standard Operating Procedures (SOPs), master work instructions, plans & forms to meet all the requirements for your pharmaceutical success.

Market	Agency	Caponago (IT)	Brussels (BE)	Chenôve (FR)	Liestal (CH)
	EMA, EU local	●	●	●	●
	FDA	●	●	●	●
	PMDA	●	●	●	●
	TGA	●		●	
	Health Canada	●		●	●
	ANVISA	●	●		





## Our Manufacturing Sites

Manufacturing Sites	Products	Services
<ul style="list-style-type: none"> <li>CordenPharma Caponago, IT</li> </ul>	Injectable Drug Products	<ul style="list-style-type: none"> <li>→ Injectable Drug Products</li> <li>→ Fill &amp; Finish</li> <li>→ LNP Formulation</li> </ul>
<ul style="list-style-type: none"> <li>CordenPharma Chenôve, FR</li> </ul>	Integrated Lipid Excipients Supply	<ul style="list-style-type: none"> <li>→ Botanichol® (Non-Animal Cholesterol)</li> <li>→ Phospholipids, Custom Lipids</li> <li>→ SFC Purification R&amp;D to Commercial</li> </ul>
<ul style="list-style-type: none"> <li>CordenPharma Switzerland, Liestal, CH</li> </ul>	Integrated Lipid Excipients Supply	<ul style="list-style-type: none"> <li>→ Standard &amp; Custom Lipids</li> <li>→ SFC Purification R&amp;D and GMP</li> <li>→ LNP Starter Kit</li> <li>→ Labelled Lipids</li> </ul>
<ul style="list-style-type: none"> <li>CordenPharma Brussels, BE</li> </ul>	Integrated Lipid Excipients Supply	<ul style="list-style-type: none"> <li>→ Standard &amp; Custom Lipids</li> <li>→ Spray Drying of lipid Mix</li> </ul>

# CordenPharma

## International

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4051 Basel  
Switzerland

[cordenpharma.com](http://cordenpharma.com)



Peptides



Lipids &  
Carbohydrates



Highly Potent  
& Oncology



Injectables



Small Molecules



Oligonucleotides