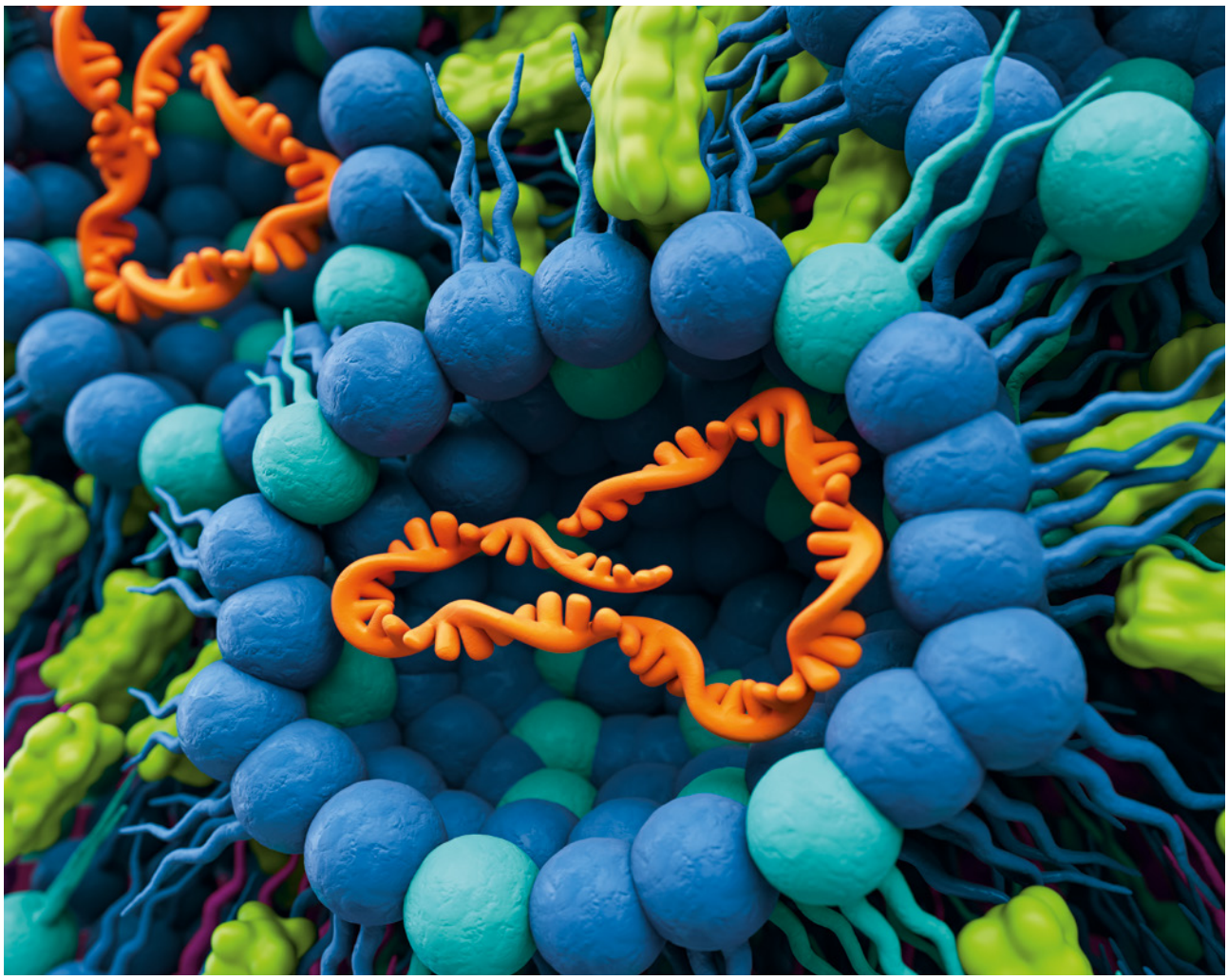
Lipid-based delivery of nucleic acids

Your global CDMO for advanced drug delivery



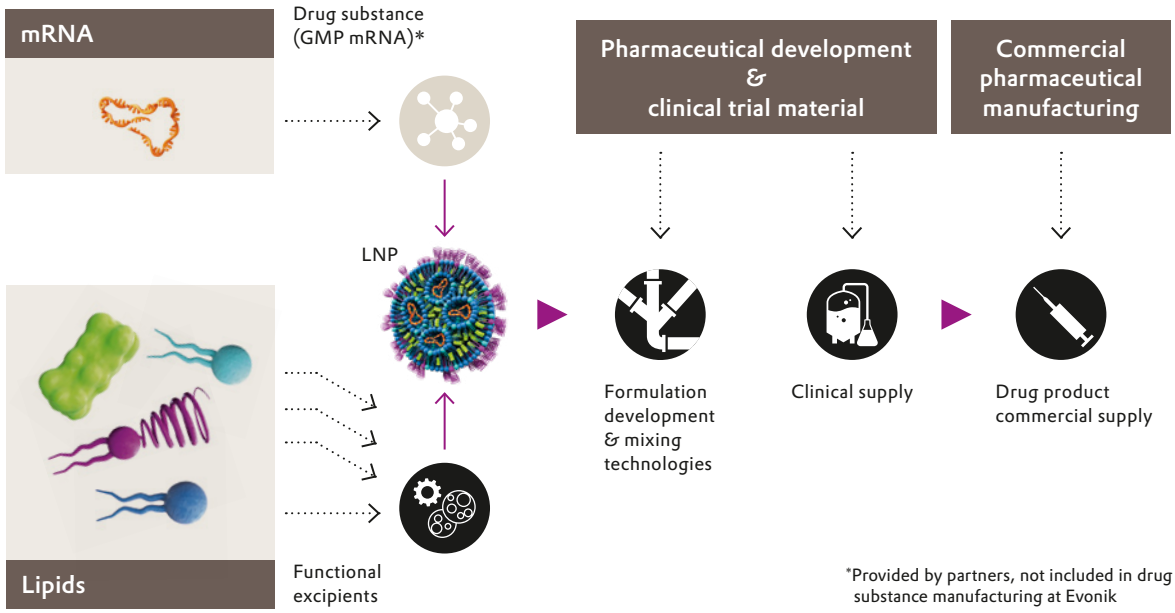
EVONIK
Leading Beyond Chemistry

Your preferred partner for advancing gene delivery and mRNA technologies

Genetic technologies are rapidly evolving and have great potential to treat a range of acquired and hereditary diseases, from cancer and metabolic disorders to infectious diseases. As a partner to many of the world's largest and most innovative pharmaceutical and biotechnology companies, Evonik's Health Care business line is ideally placed to help you realize the potential of gene therapies.

We are a fully integrated solutions provider for advanced drug delivery and can support any stage of the drug development process, from the manufacturing of pharmaceutical excipients to the development of innovative formulations, as well as the production of clinical and commercial drug products.

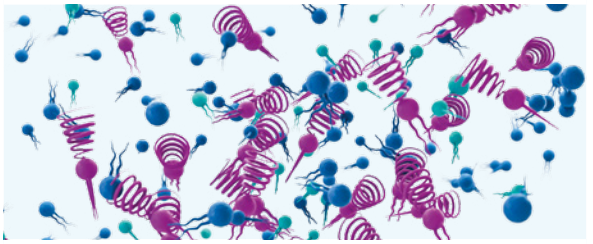
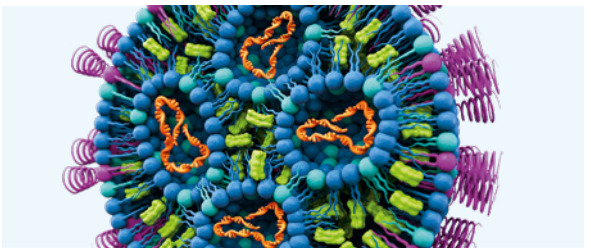
How Evonik contributes to the value chain of mRNA-LNP therapeutics



Fueling the growth of advanced biopharmaceuticals

- Nucleic acid-based therapeutics
- Anticancer agents
- Synthetic vaccines: peptide and protein-based
- Ligand-targeted formulations
- Drug combinations

We support customers with end-to-end CDMO services for nucleic acid therapeutics

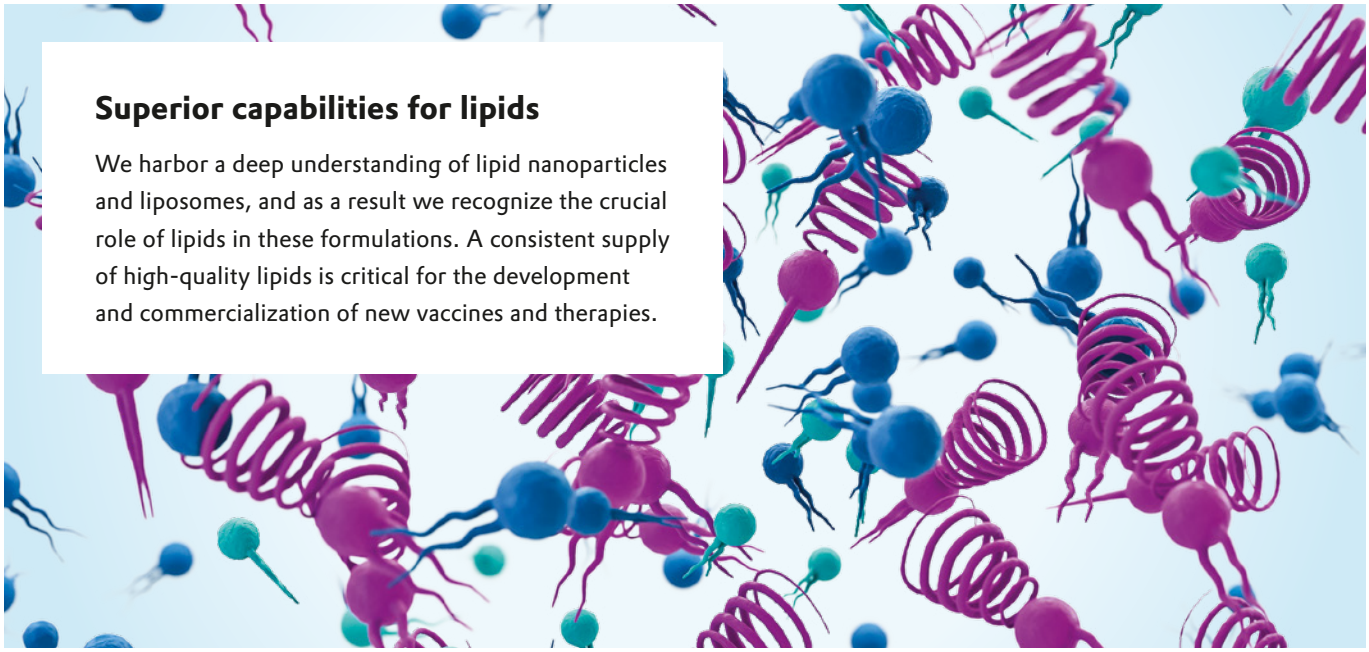
Excipients and biomaterials		**PLG excipients, plant-derived cholesterol, recombinant collagen**
Drug delivery technologies		**A delivery leader for liposomes, nano-and microparticles and drug-loaded implants**
Formulation and process development		**Seamless support from concept to commercial, including extrusion and micromixing**
cGMP drug manufacturing		**High-quality clinical and commercial production at North American sites**
Aseptic filling		**Semi- and automated vial filling of powders, liquids and suspensions**

We build on our expertise in parenteral excipients, formulation, and contract manufacturing

- Integrated CDMO for gene therapies
- Specialized in complex parenterals
- Involved in many mRNA projects including multiple COVID-19 vaccines

CONTACT US
healthcare@evonik.com

An experienced provider of novel and established functional excipients



Superior capabilities for lipids

We harbor a deep understanding of lipid nanoparticles and liposomes, and as a result we recognize the crucial role of lipids in these formulations. A consistent supply of high-quality lipids is critical for the development and commercialization of new vaccines and therapies.

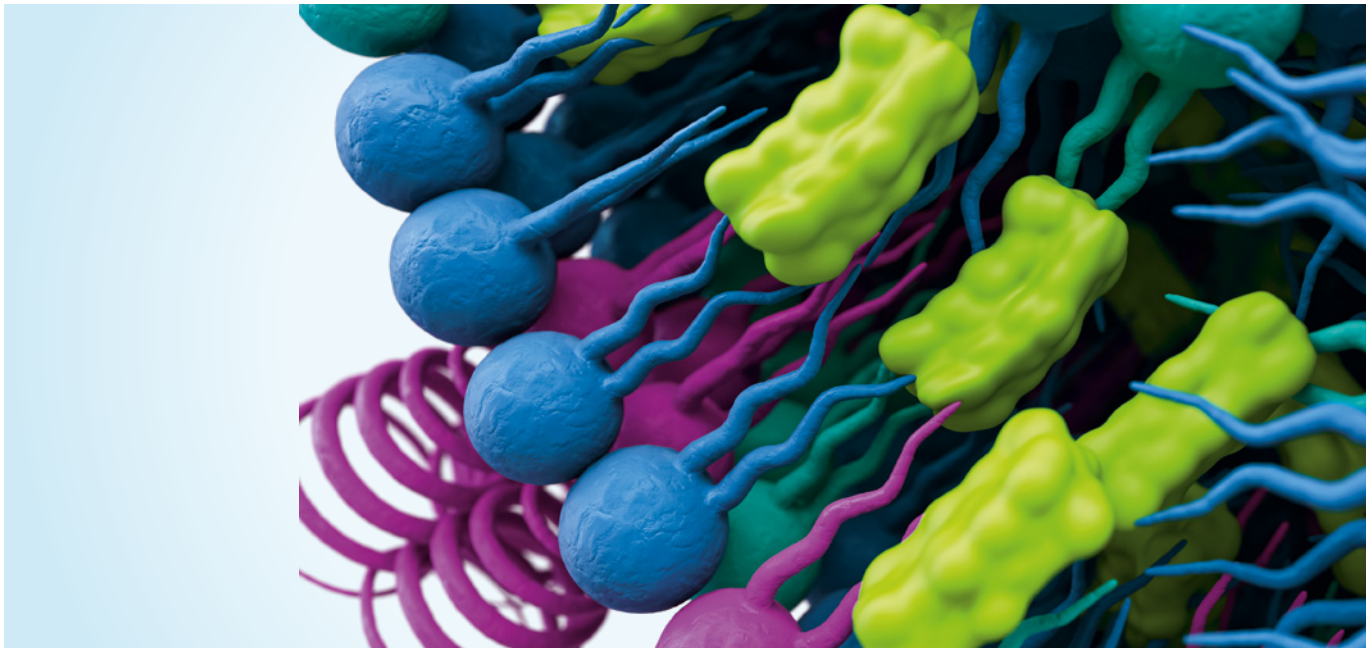
Meeting your need for custom lipids

We support our clients with custom lipid projects by combining this understanding with decades of expertise in process development, analytics, scale up, validation and GMP manufacturing. Regardless of your current scale and requirements, Evonik can support with non-GMP and GMP capabilities from small-scale through large-scale production.

As an integrated solution provider, we combine all these capabilities in one package, at any scale

- Chemical process R&D
- Flow chemistry
- PEGs (polyethylene glycol) and mPEGs (methoxy-PEG)
- Purification technology
- Particle engineering
- Analytical services

Stable supply of plant-derived synthetic cholesterol



PhytoChol® provides you with the following advantages

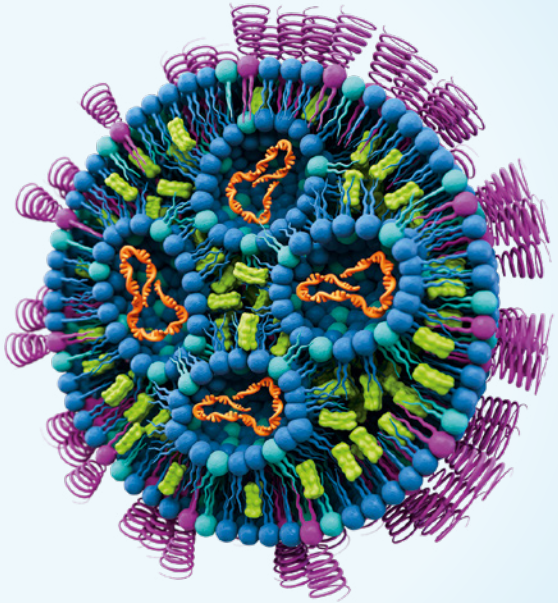
- Non-animal derived
- Secure and stable supply
- Large-scale manufacturing
- High purity
- vegetal-derived
- Ultra-low endotoxin
- USP-NF, Ph. Eur. and JP compliant

PhytoChol®

A leader in formulation technologies for nucleic acid therapeutics

Seamless support for your formulation and processing needs

As a specialist CDMO for lipid-based drug delivery systems for almost 30 years, we have an unparalleled track record in early-stage development, process development and scale up, and analytical characterization. With a broad base of pharmaceutical and biotech customers across the world, we have accumulated extensive expertise across all classes of pharmaceuticals, including nucleic acid therapies and other advanced nanomedicines.



Lipid-based particles are a versatile formulation platform

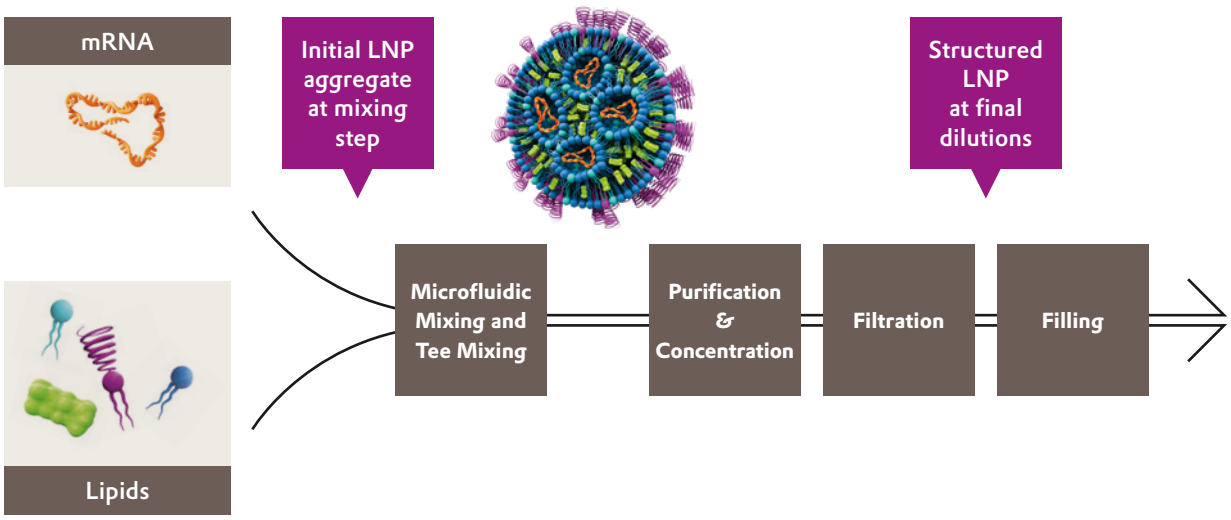
- Decreased toxicity / side effects and improved safety
- Increased efficacy
- A well-studied technology; proven in humans

Typical composition of a lipid nanoparticle
Nucleic acid payload is encapsulated in lipids

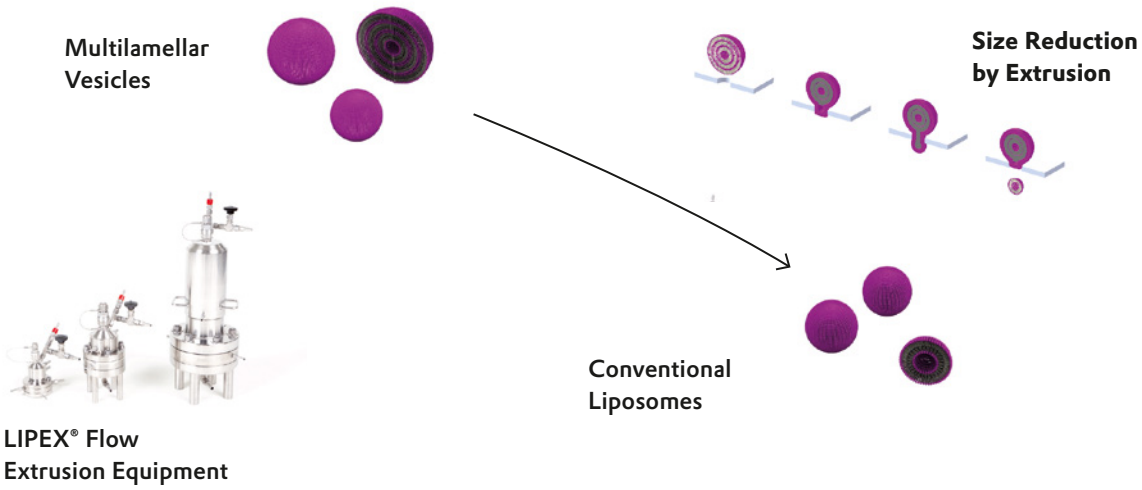
Nucleic Acid		▪ The active payload
Cholesterol		▪ ~38.5 % ▪ Improves stability of LNPs and improves overall encapsulation of payload; affects transfection efficiency
Ionizable Cationic Lipid		▪ ~50 % ▪ Complexes the nucleic acid ▪ Destabilizes the endosome
PEG Lipid		▪ ~1.5 % ▪ Stabilizes LNPs during formation and controls particle size
Structural Lipid		▪ ~10 % ▪ Examples or DSPC or DOPE ▪ Required for overall stability

We use two key processes to manufacture lipid-based drug delivery systems at a large scale

LNP formulation



Liposome formulation



Advantages of our integrated formulation services

- More than 25 years' experience developing lipid-based delivery systems
- Significant experience formulating nucleic acid-based drugs
- Enhancement of solubility and bioavailability of high potency APIs through encapsulation in a lipid carrier
- Seamless transition from scale up through clinical manufacturing
- Comprehensive analytical services to accompany R&D, toxicology, clinical and commercial manufacturing
- LIPEX® extruders ranging from benchtop to commercial production scale to support conventional liposomal formulations

Advanced cGMP manufacturing and fill-finish capabilities

Versatile and reliable filling lines and cGMP manufacturing can enable the production of highly potent drug products, as well as vaccines, gene therapy technologies and personalized medicine. As the number of drug products requiring advanced drug delivery technologies increases, the need to address manufacturing challenges becomes crucial.

We operate a global network of development and manufacturing sites

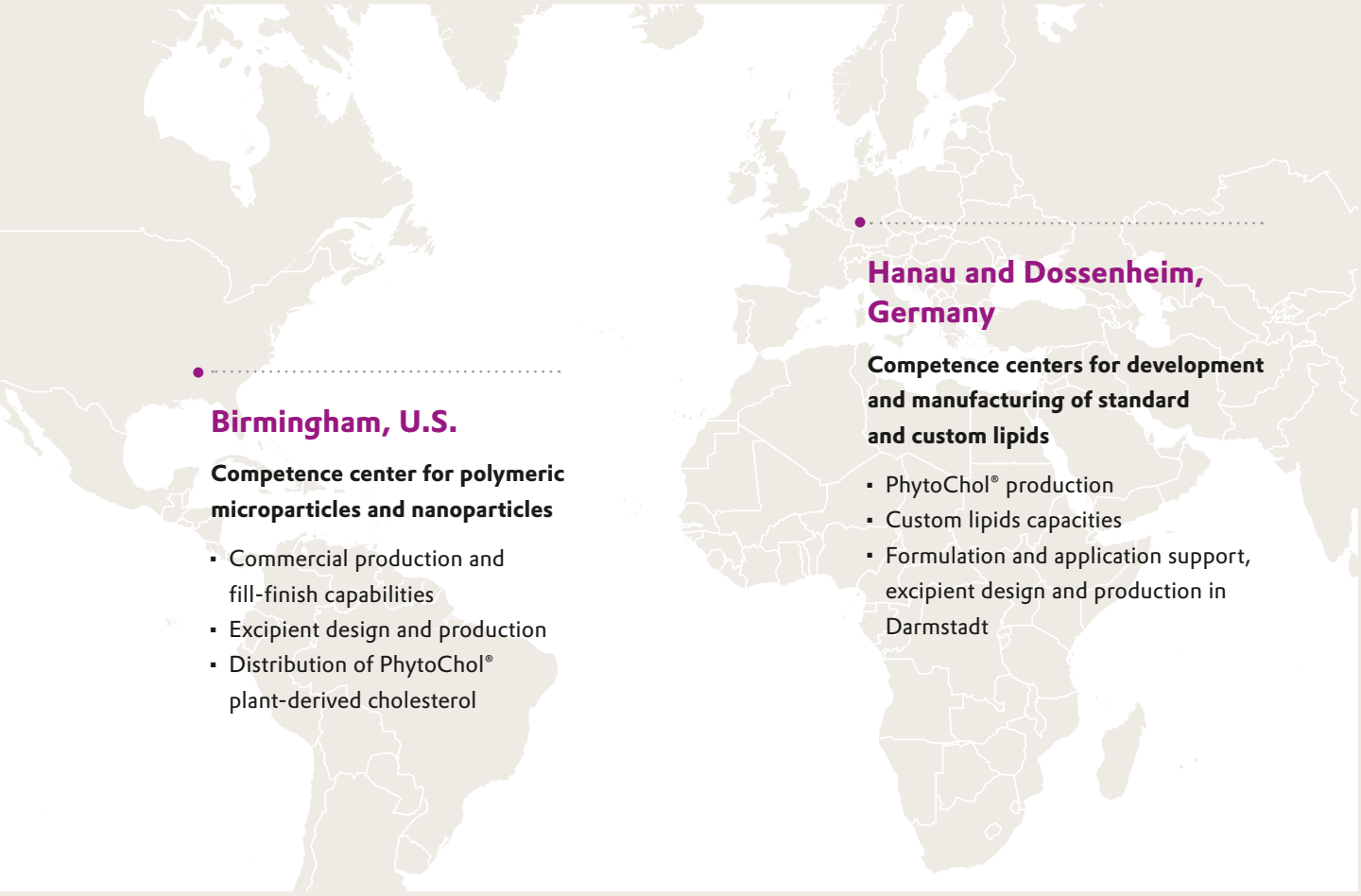
- cGMP production for clinical batches and commercial products
- Specializing in advanced parenteral dosage forms such as liposomes, lipid nanoparticles, and micelles
- Full support in process development, engineering and scale-up
- Aseptic fill/finish, performed in Grade A isolators
- Fully integrated, automated commercial filling line, and filling lines for clinical batches
- Encapsulation of small molecules, peptides, and proteins for systemic or localized drug delivery
- Scalable extrusion technologies for manufacturing of conventional liposomes
- Handling of high potency drug substances to > 0.1 µg/m^3 (OEL)

Vancouver, Canada

Competence center for liposomes and nanoparticles

- LIPEX® extruders
- Formulation and process development
- Clinical manufacturing

	R&D	Pre-clinical	Phase I
Development and cGMP Manufacturing Services	Formulation feasibility	Formulation development	
	Process identification	Process development	
	Developmental stability	Test article supply IND-enabling stability	
	Lead candidate identification		
Analytical Services	Method development		
	Analytical characterization support		
Process Equipment	Extruders < 100 mL	Extruders < 800 mL	



Birmingham, U.S.

Competence center for polymeric microparticles and nanoparticles

- Commercial production and fill-finish capabilities
- Excipient design and production
- Distribution of PhytoChol® plant-derived cholesterol

Hanau and Dossenheim, Germany

Competence centers for development and manufacturing of standard and custom lipids

- PhytoChol® production
- Custom lipids capacities
- Formulation and application support, excipient design and production in Darmstadt

	Phase II	Phase III	Commercial
Formulation optimization			Lifecycle management
Process optimization, scale up, QbD		Process performance qualification (PPQ)	
Clinical cGMP production and aseptic filling			Commercial cGMP production and aseptic filling
Technology transfer and scale-up			
Phase-specific method transfer, qualification and validation to ICH guidelines			
Drug product release testing and stability studies			
Client-owned and dedicated extrusion equipment			Custom extruders
Microfluidics and micro-mixing devices			

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