BioPharma Services

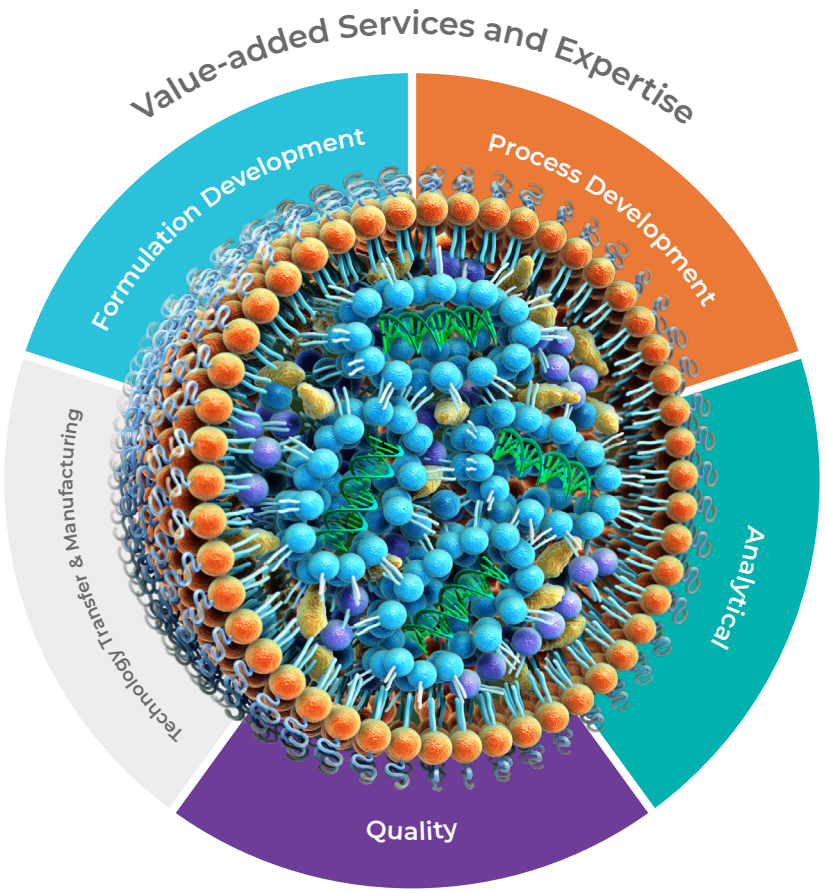
One-Stop-Shop for Advancing mRNA-LNPs from Bench to Clinic

PRECISION NANOSYSTEMS

Create Transformative Medicines™

De-Risk and Accelerate Nanomedicine Development

In a drug development process, genomic medicine can reach its full potential when developers work with a single contract services vendor to avoid delays in tech transfer and losing control over process know-how. This strategy helps achieve successful product development meeting regulatory milestones that require detailed data and formulation know-how to produce the final drug product. The BioPharma Services (BPS) team at Precision NanoSystems provides access to expertise and is a one-stop-shop for superior Lipid Nanoparticle (LNP) technologies and proven expertise in formulation and analytics for successful outcomes for your payload and target applications.



The BPS team offers expert services at every drug development stage, making it possible to identify the critical quality attributes (CQAs) in scale-up, develop drug product specifications and establish critical process parameters (CPPs) for downstream processing operations, such as tangential flow filtration (TFF) and sterile filtration. Our approach of using small-scale systems to model cGMP process reduces the time, cost and risk when transitioning from the R&D phase to GMP manufacturing and streamlines regulatory filings. Using the NanoAssemblr® instruments, the BPS team offers end-to-end LNP formulation services combined with industry-leading quality assurance, analytical, bioassay and quality control capabilities from proof-of-concept studies to preclinical to clinical transition with credible expertise and proven success.

BPS Success Track Record

Precision NanoSystems' BioPharma Services team comprises of experts that bring in their cumulative experience, working with 26 clinical-stage programs producing over 44 GMP batches and contributing to two approved drug products as of 2023.

160+ Contract services projects

15+ Clinical licenses signed for NanoAssemblr and GenVoy™ Technologies

~125 Patents granted or pending to protect proprietary technology platforms

5 Nanomedicine innovation network centers

250+ Active customers

2 cGMP Manufacturing lines under development in Vancouver, Canada

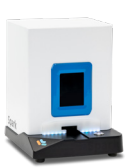
800+ NanoAssemblr instruments installed globally

Your Trusted Partner from Discovery to Clinic

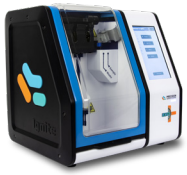
Precision NanoSystems is a global leader in nanoparticle technologies and solutions with the goal of empowering our clients to develop genomic medicines, including mRNA vaccines and therapeutics that define the future of medicine. The BPS team comprises formulation scientists, manufacturing and quality team members who can uniquely deliver a trusted partnership. Leverage our end-to-end LNP formulation technologies, strategies, custom services and genomic medicine expertise to optimize and accelerate drug candidates across applications from discovery to the clinic, thereby maximizing commercial success.

NanoAssemblr® Systems

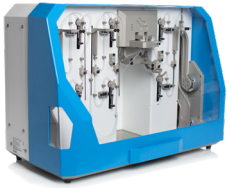
Spark™	Ignite™	Blaze™	NanoAssemblr® commercial formulation system
Rapid screening, *in vitro* studies	Formulation development at bench scale	Process development, CMC, larger animal studies	Configurable for manufacturing under cGMP conditions



Up to 240 uL undiluted



Up to 20 mL undiluted, 20 mL/min



Up to 10 L undiluted, 115 mL/min

Up to 400 L undiluted, 800 mL/min

BioPharma Contract Services

Program Kick Off — Target Product Profie (TPP)

Formulation Screening and Development

- Small scale formulations with your payloads for In vitro testing to select most potent construct
- Perform formulation and process optimization to optimize efficacy, safety and storage stability
- Screen lipid compositions to select best performing compositions
- Perform formulation and process optimization to optimize efficacy, safety and storage stability

Process Development

- Develop and optimize scale-up process for manufacture of drug products at-scale
- Develop and optimize scale-up process for RNA manufacturing using IVT process for best yields and specifications
- Optimize downstream process using intermediate volumes

Technology Transfer & Manufacturing

- Manufacture drug product batches to support GLP studies (Safety/Tox)
- Manufacture cGMP drug product batches to support Phase I/II studies
- Develop and execute stability studies on GLP and cGMP batches

Analytical and Bioassay Services

- Develop and select analytical methods to test defined characteristics of drug substance and drug product against target acceptance criteria
- Develop robust bioassay to evaluate the potency and In vitro gene expression of any drug payload
- Perform routine testing throughout the drug development cycle, selecting optimal compositions from discovery to clinic

Quality

- Perform material and in-process testing to support non-GMP and GMP manufactured products
- Conduct release and stability testing for drug products to GMP standards

Formulation Screening and Development Services

Proof-of-concept studies conducted during the early discovery phase are imperative for a successful drug launch. Our BPS team can help in screening the right nanoparticle formulations for your payloads during the discovery stage. We can help select lipid compositions for your proof-of-concept (POC) studies, formulation development, or optimization of lead formulations to improve safety, efficacy, stability, and process scalability.

Our scientists offer deep technology expertise to solve drug discovery challenges and assist with the following:

- Nanoparticle formulation development of RNA, DNA, peptides and small molecules
- Optimization and process scale-up of existing formulations
- Proof-of-concept/Feasibility studies
- Physico-chemical characterization of nanoparticle formulations
- Analytical method development
- Bioassay development and testing

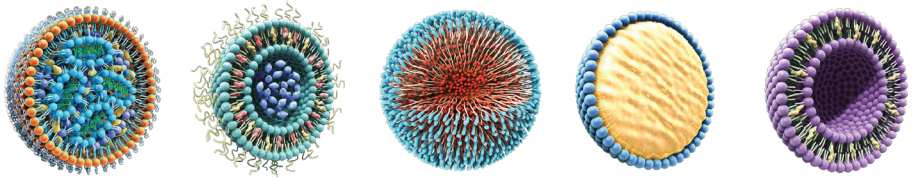
We offer in-house affordable, high-quality, research-grade RNA synthesis that fits your project requirements.

- Custom RNA synthesis
- GMP equivalent grade RNA
- Scalable RNA manufacturing with minimal process optimization

Customized LNP Formulation Services

Leverage our lipid nanoparticle portfolio and GenVoy-ILM™ off-the-shelf Research Use Only (RUO) LNP delivery reagent kits to protect and deliver nucleic acids to target cells, validating payload delivery in preclinical stages using formulations that can be licensed for use in clinical trials.

To maximize the probability of commercial success, BPS offers LNP formulation and ionizable lipid selection expertise to customize fit-for-purpose lipid compositions. Based on years of experience, our lipid mixes are catered to the intended *in vivo/ex vivo* application, rationally designed to maximize performance and efficiency, thereby accelerating drug candidates across applications from discovery to the clinic. We also provide an end-to-end Genomic Medicine Tool Kit that uniquely enables access to our proprietary lipid portfolio, LNP technologies, and expertise to develop any desired lipid nanoparticle formulation.



Biological Assays Capabilities

Our dedicated teams include highly experienced research and development scientists who test formulations for the success of targeted drug products.

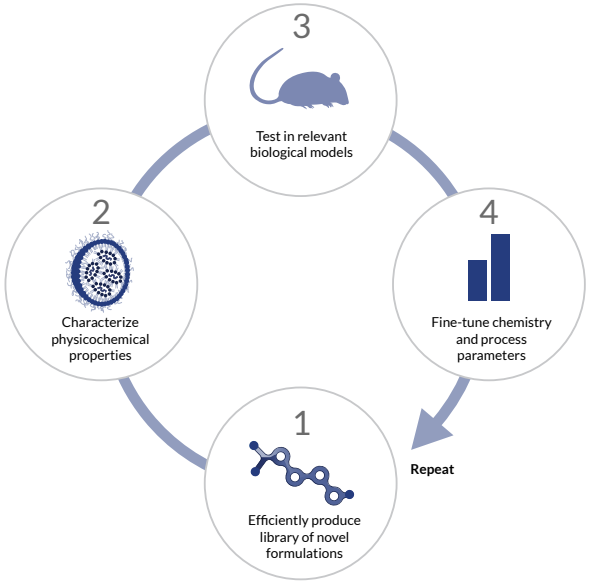
- We develop robust bioassays to evaluate the potency and *in vitro* gene expression of the targeted drug payload during the early development phase.
- We create workflows to screen large numbers of variables to support the formulation and process development.
- We have pre-developed, fast-to-qualify assays for a range of modalities by leveraging our years of experience in designing, optimizing, qualifying, and validating assays with unique APIs and compositions.
- We have expertise with all major lipids, payload design, and lipid-based delivery systems, including lipid nanoparticle and lipopolymeric formulations administration for a wide range of disease applications.

Biological Assay Instrumentation
Cytation 7 cell imaging multi-mode reader, Biospa, and MultiFlo Fx
SDS-PAGE and Jess Automated Western blot
Biotek plate readers (Colorimetric + Luminescence-based assays) Ella automated ELISA
CytoFLEX Flow Cytometer
ELLA - Automated ELISA
RT-qPCR

Quality Management System (QMS)

Precision NanoSystems' Quality Management System (QMS) is aligned with global regulatory requirements such as 21 CFR Parts 210 and 211 to support developing, manufacturing, and testing clinical trial materials. The QMS is based upon the principles outlined in ICH Q10 Pharmaceutical Quality System as well as specific regional GMP requirements.

Quality Assurance provides oversight and approval for GMP activities and works with customers to meet quality and compliance requirements. When GMP activities are in scope, a Quality Agreement is established to define and establish the responsibilities for GMP activities and expectations for documentation and communication between the parties.



Analytical and Physiochemical Characterization

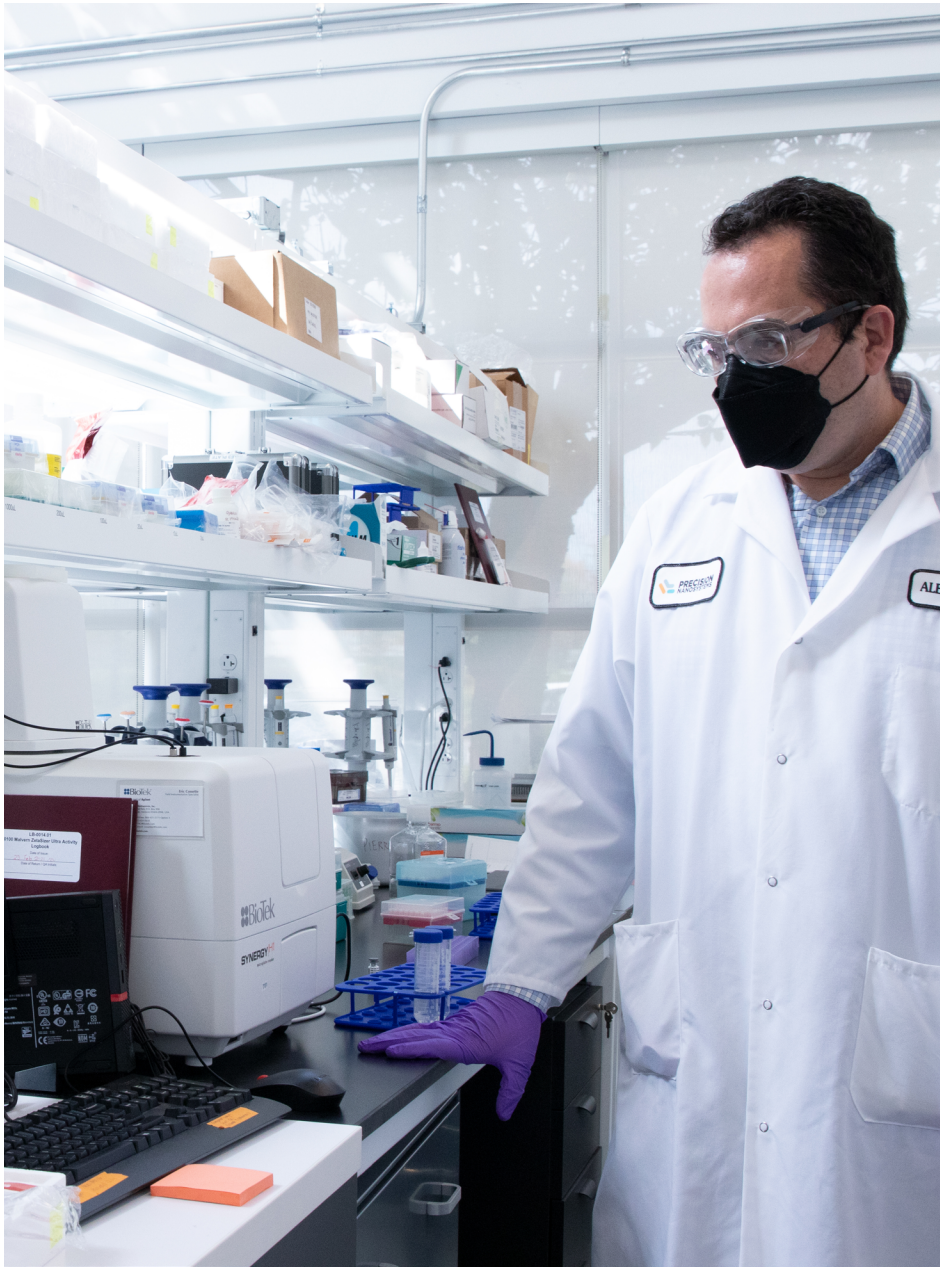
With industry-leading expertise, technical knowledge, and scalable technologies, we develop and apply advanced analytical methodologies to support the characterization of the drug substance, raw materials, and nanoparticle formulation. The analytical development team works across the preclinical, clinical, process development, manufacturing, and quality teams, from selecting lead candidates during formulation and development to ensure specifications of the drug product remain consistent as production is scaled. In addition, we have the analytical instrumentation, technologies, and analytical services for non-viral genomic medicines, including drug product identity confirmation and physical characterization.

Take advantage of our analytical capabilities to perform *In vitro* Potency Assays including lipid and nucleic acid-specific analyses to generate data insights for proof of concept (POC), preclinical, or clinical milestones for accelerated clinical trials.

LNP composition	RNA quality	Payload Design	Encapsulation
Size, PDI, ζ-potential	Quantity	Sequence	Encapsulation efficiency
Stability	Integrity	Production	Nanoparticle structure
Lipid composition	Structure	Biology	
Excipients	Purity	Immunology	

Analytical Instrumentation: We have the following advanced technologies to assess drug substances and products that include particle size analyzers, bioanalyzers, mass spectrometers, liquid chromatographic systems, cryogenic electron microscopes and flow cytometers.

LNP composition	Excipients	Payload Design
Size, PDI, ζ-potential	Quantity	Sequence
Stability	Integrity	Production
Lipid composition	Structure	Biology
Excipients	Purity	Immunology



Quality Control (QC) Support

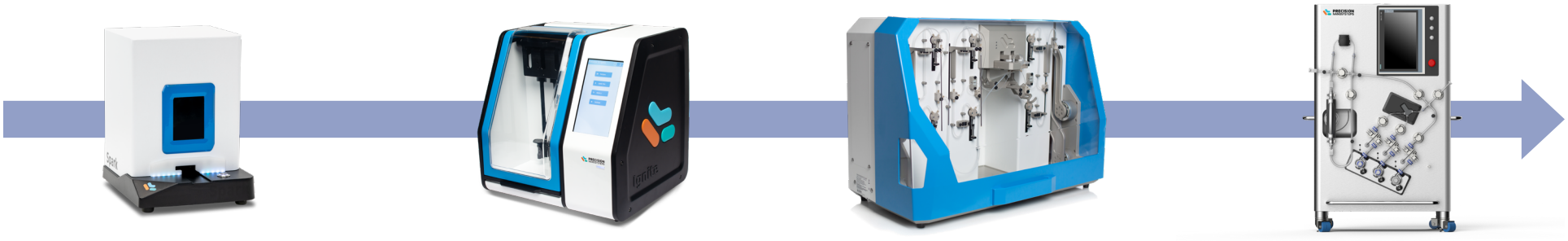
Our QC group is comprised of analytical and microbiology sub-teams that perform a range of testing for raw material and genetic medicine drug product samples. Testing is conducted to support manufacturing processes and ensure defined characteristics meet criteria in pre-clinical studies and clinical trials. Test methods and related SOPs, specifications and protocols are established to define testing, requirements and the studies performed. Samples, standards, data and documents are managed to ensure traceability, compliance and ease of use when preparing regulatory submissions. Our QC group has the expertise to quickly adapt and apply methods and studies to a client program, thereby lowering the barrier to entry and accelerating timelines to take drug products from concept to clinic.

QC Activities and Services:

- Material and drug product specification development
- Raw material sampling and testing
- Drug product release and stability testing
- Test method verification, qualification and validation
- Test method transfer
- Compatibility, dose solution analysis and characterization studies
- Dose solution analysis
- Data and document packages to enable CMC submissions

Tech Transfer to GMP Manufacturing

A robust technology transfer package is key to successfully advancing a molecule toward a clinical trial. We define the manufacturing conditions from early process transfer development to production scale allowing seamless technology and accelerating the clinical and commercial development of nanomedicine drug products.



Spark™

25–250 uL

Ignite™ and Ignite+™

Up to 60 mL

Blaze™ and Blaze+™

Up to 10 L

NanoAssemblr® commercial formulation system

Up to 400 L

Our BPS can take your drug from research through development to regulatory submission with seamless tech transfer and exceptional service. Our tech transfer activities include the following:

- Install and qualify the NanoAssemblr commercial formulation system
- Transfer equipment, materials, and analytical methods to the GMP manufacturing site
- Prepare GMP Master Batch Records
- Prepare demonstration batch at scale on the NanoAssemblr commercial formulation system
- Prepare GLP-Tox batch & perform test article characterization and stability testing
- Manufacture GMP batches for Phase I and II clinical trials
- Provide relevant documentation & on-site training

Chemistry Manufacturing & Controls (CMC) Support

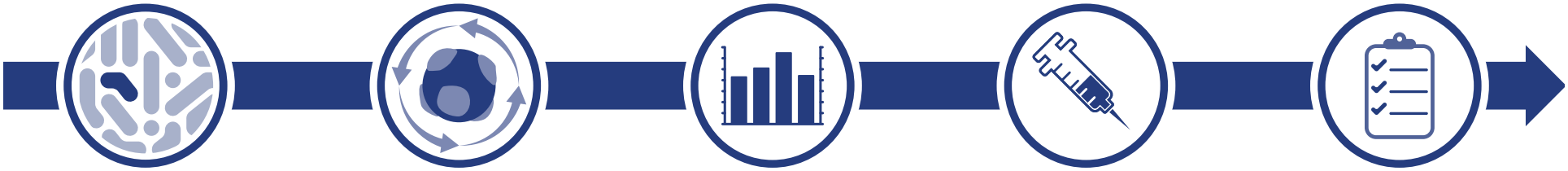
- Provide oversight for the manufacture and testing of engineering and GMP batches
- Data reports for seamless CMC Regulatory Submissions
- Quality & Regulatory support

Clinical Manufacturing

In addition to our formulation and pre-clinical manufacturing expertise we offer consulting services for the following:

- Good Laboratory Practices (GLP) Compliance
- Assay support at contract manufacturing organizations (CMO)
- Technology transfer to CMO: processes, materials, equipment and analytical methods
- Production of engineering and GMP batches in a cleanroom at CMO
- QC GMP testing
- GMP stability program (drug substance-DS & DP)
- Regulatory advice
- Complete documentation support

Preclinical & Clinical Development



Source/Qualify Vendors for Production of GMP Lipids and API (saRNA/RNA)

Optimize Process Parameters to Ensure Robust and Reproducible RNA-LNP Manufacturing Process at Clinical Scale

Qualify Analytical and Bio-Analytical Methods for GMP Lipids, API and RNA-LNP

Develop Raw Material & Drug Product Specifications

Produce GLP/Tox LNP Batches

CMO Activities

Technology Transfer to CMO: Processes, Materials, Equipment and Analytical Methods

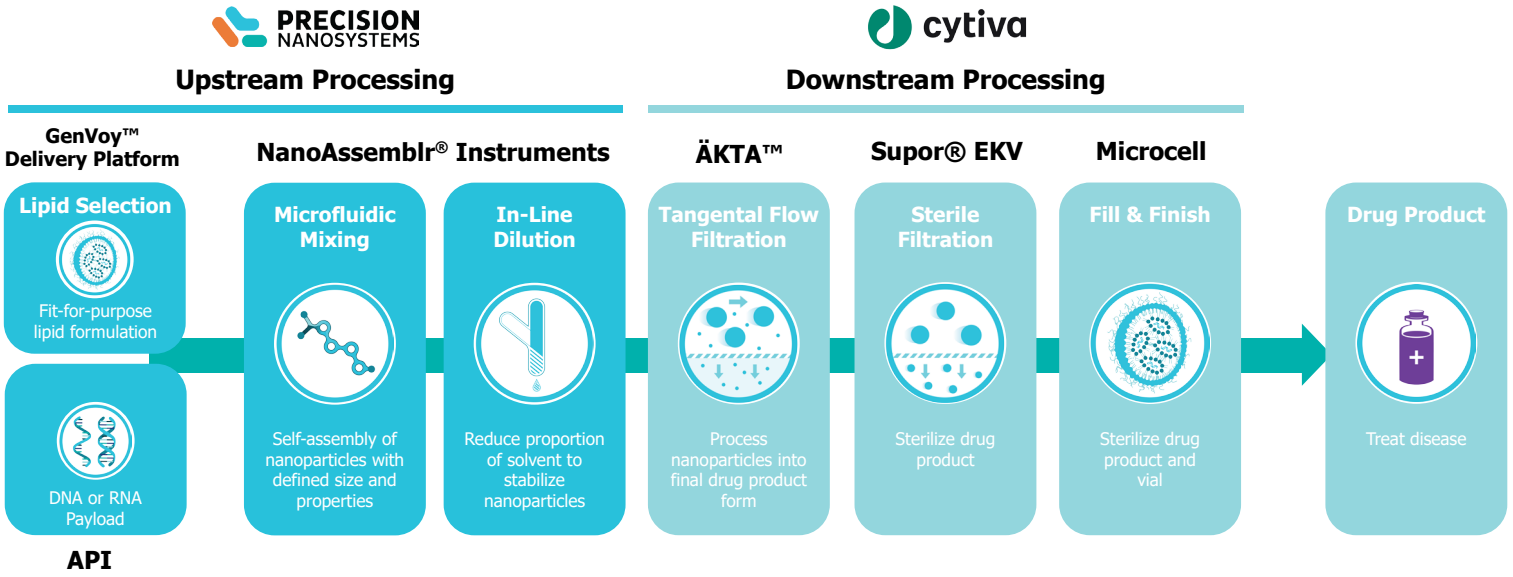
Production of Engineering and GMP batches in Cleanroom at CMO

QC GMP Testing, QA Release, Packaging and Distribution of Finished Product

GMP Stability Program (DS & DP)

About Precision NanoSystems

Precision NanoSystems is a Danaher company. Together with our partners Pall and Cytiva, we offer an end-to-end manufacturing workflow for clinical and commercial nanomedicine production. This versatile solution for commercial manufacturing provides the ability to scale up and scale out a range of facilities.



We are committed to a flexible, individualized approach with a global team of field application scientists for your support. Partner with Precision NanoSystems' BioPharma Services team and get started with a well-defined project plan, milestones, deliverables, and timeline customized to your needs and budget.

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