NanoAssemblr® Commercial Formulation System

Single-use system for clinical and commercial production of lipid nanoparticles

PRECISION NANOSYSTEMS
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NanoAssemblr® Commercial Formulation System

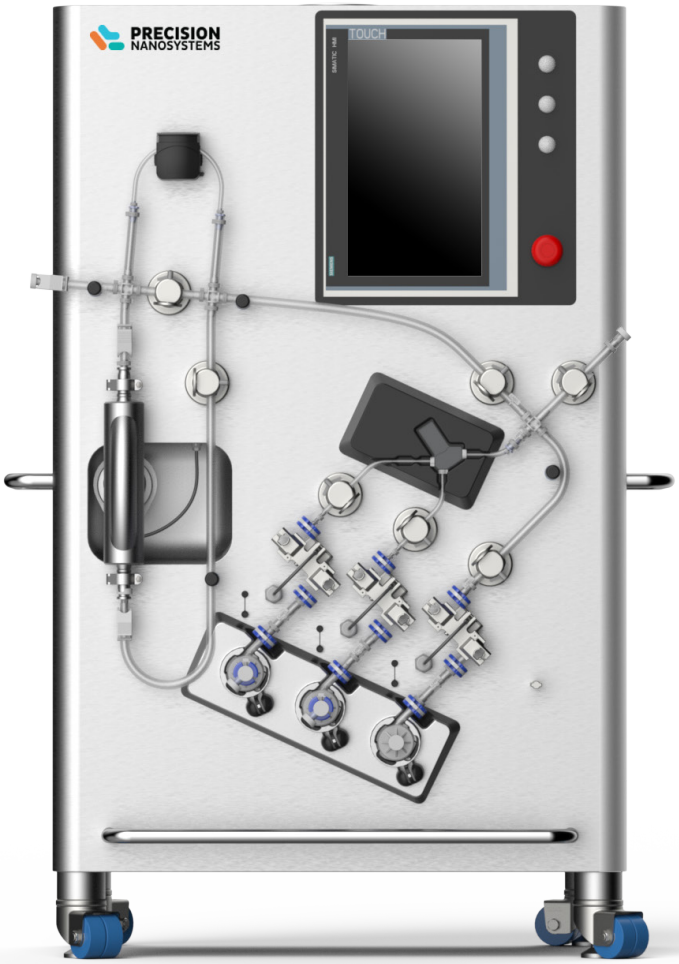
The NanoAssemblr® commercial formulation system is an automated, single-use system for the clinical and commercial production of lipid nanoparticles (LNPs) under cGMP conditions. Designed for efficient changeover and robust manufacturing processes, the system enables operational flexibility and standardized manufacturing of genomic medicines.

System Overview

The NanoAssemblr commercial formulation system supports an automated workflow of priming, calibration, formulation, and in-line dilution to simplify GMP manufacturing of mRNA-LNP drug products. Its intuitive software interface enables 21 CFR Part 11 compliance* and electronic batch records that capture in-process monitoring of flow rate and pump speed. The system uses scalable NxGen™ technology and low-pulsation pumps for precise control of mixing parameters, resulting in consistent flow rates from 6 to 48 L/h that produce homogenous and reproducible nanoparticles.

The single-use flow path minimizes the need for sanitizing and performing cleaning validation, enabling efficient changeover between production runs while minimizing the risk of cross-contamination. The flow kit can be easily installed, calibrated, and ready for formulation in less than 60 minutes.

The system is also ATEX (ATmosphères EXplosibles) and IECEx** (International Electrotechnical Commission System for Certification to Standards Relating to Equipment for Use in Explosive Atmospheres) rated for use in hazardous locations to ensure safety when handling flammable solvents during LNP formulation.



*Pending third party audit

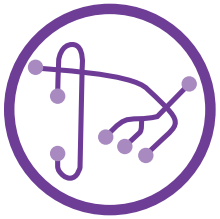
**Pending final certification

Scalable Single-Use Platform with Built-in Automation

The NanoAssemblr commercial formulation system enables standardized manufacturing workflows through scalable single-use technology, built-in automation, regulatory-compliant software, and materials traceability.

Automated

- Electronic batch records
- In-process monitoring of flow rate
- Workflow for priming, calibration, formulation, and in-line dilution

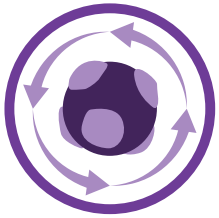


Single-use Technology

- Single-use flow kit reduces the risk of cross-contamination between batches and campaigns
- Enables multi-product manufacturing in GMP facilities

Regulatory Compliant

- Intuitive software interface enables 21 CFR Part 11 compliance*
- ATEX and IECEx** rated for use with flammable solvents
- Extractables report for single-use flow kit



Reproducible

- NxGen architecture and low-pulsation pumps enable efficient mixing and consistent flow rates
- Particles maintain CQAs for a robust manufacturing process

Scalable

- NxGen™ technology accelerates scale-up and minimizes process development
- Direct transfer of CPPs from clinical development to commercial manufacturing

Qualification & Expertise

- Installation and qualification with on-site IOQ
- Leverage Precision NanoSystems' technical knowledge and LNP expertise

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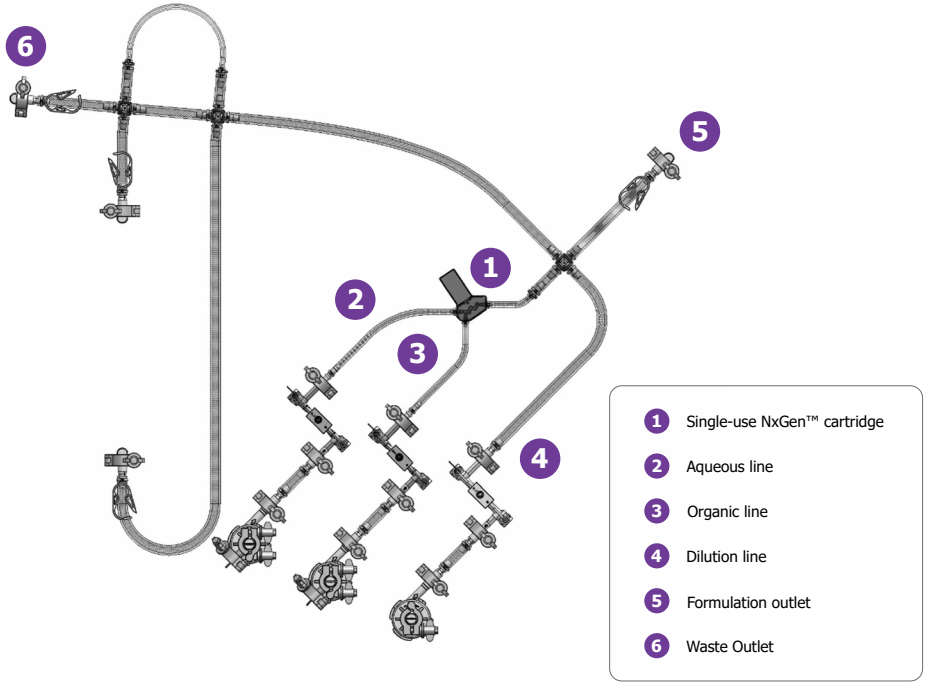
Single-Use Flow Kit

The single-use flow kit includes the NxGen cartridge, pump heads, flow meters, and flow path. Composed of biocompatible and animal-derived ingredient free materials, the flow kits are assembled in a cleanroom, packed in double bags, and gamma-irradiated (25.0 to 45.0 kGy) for bioburden reduction before delivery.

The flow kit can be easily installed and ready for formulation in less than 60 minutes, supporting efficient changeover between production batches and products during manufacturing. The intuitive software guides the user through the installation of the flow kit and the entire process workflow, reducing the risk of user error. Discarding the flow path following each run minimizes the risk of cross-contamination, enabling the manufacture of multiple mRNA products within the same facility.

Validation guides, certificates of quality, and extractables data are available for the NxGen commercial manufacturing flow kit. The flow kit is also available as a limited multi-use flow kit for research and development, including the production of engineering batches.



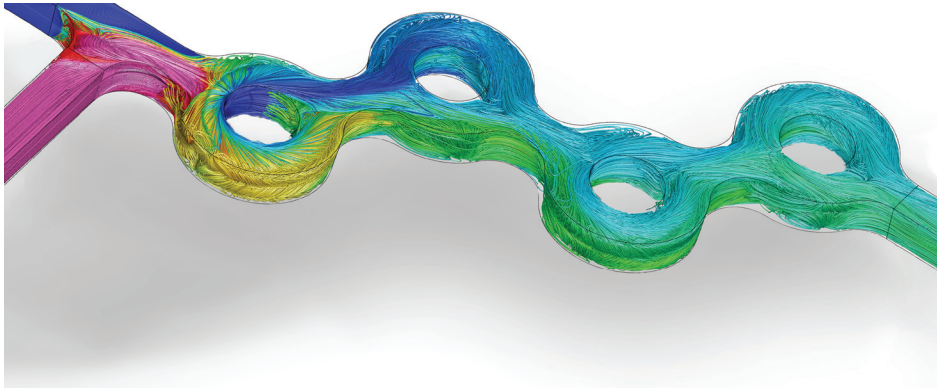
Schematic of the single-use flow path. The flow kit includes the NxGen cartridge, pump heads, flow meters, and flow path.

FLOW KIT	DESCRIPTION	INTENDED USE
NxGen™ commercial manufacturing flow kit 12 L/h	Single-use manufacturing flow kit for flow rates from 6 to 12 L/h	Manufacturing under cGMP conditions
NxGen™ commercial manufacturing flow kit 48 L/h	Single-use manufacturing flow kit for flow rates from 24 to 48 L/h	
NxGen™ commercial development flow kit 12 L/h	Limited multi-use development flow kit for flow rates from 6 to 12 L/h	Research and development, including engineering batches
NxGen™ commercial development flow kit 48 L/h	Limited multi-use development flow kit for flow rates from 24 to 48 L/h	

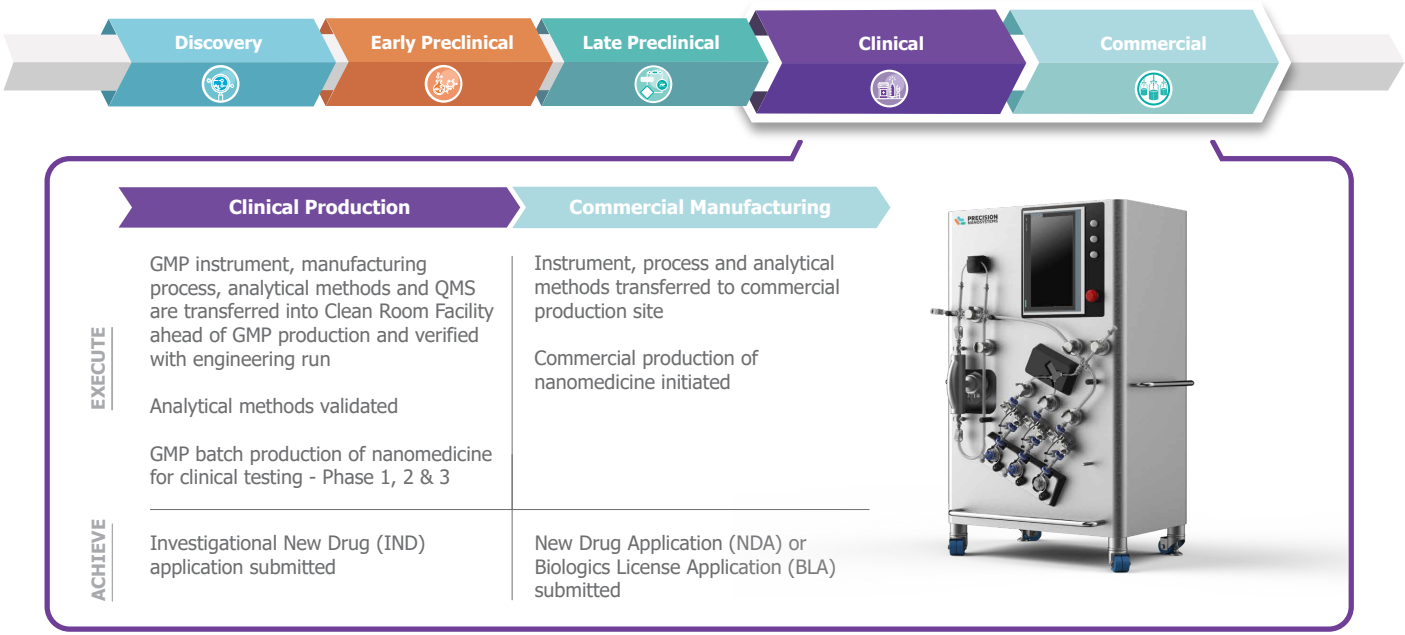
Scalable NxGen™ Technology

NxGen technology enables controlled and reproducible mixing conditions for precise assembly of LNPs using the scalable NxGen architecture, which is present throughout the NanoAssemblr family of systems. This enables the transfer of critical process parameters and ensures consistent critical quality attributes (CQAs) during scale-up from process development to clinical production and commercial manufacturing.

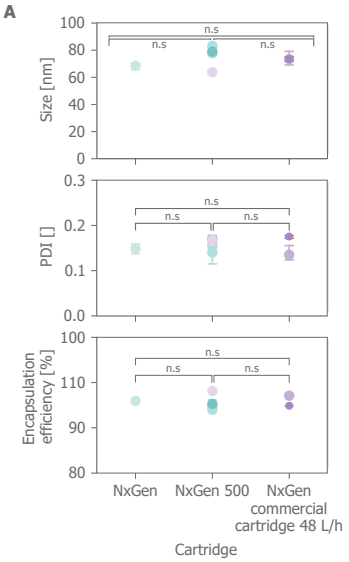
NxGen mixers feature unique toroidal structures within the flow route that reduce the mixing time and increase process consistency by increasing the contact area between fluids.

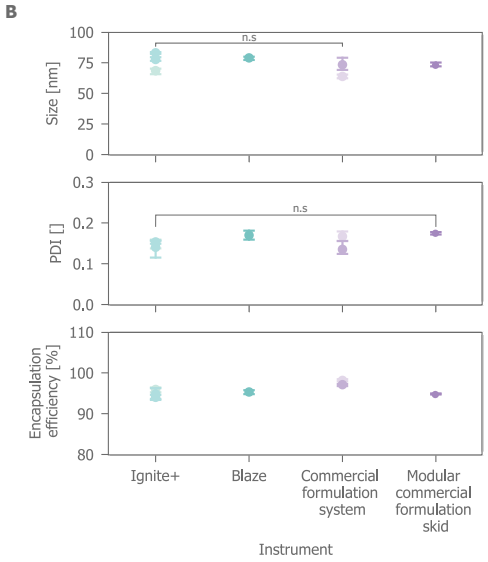


NxGen technology allows for controlled mixing and the production of nanoparticles across a wide range of flow rates. Computational fluid dynamic simulation modeling the mixing of water (blue) and ethanol (pink) in the NxGen commercial cartridge 48 L/h.



Maintain Critical Quality Attributes from Preclinical Development to Commercial Manufacturing

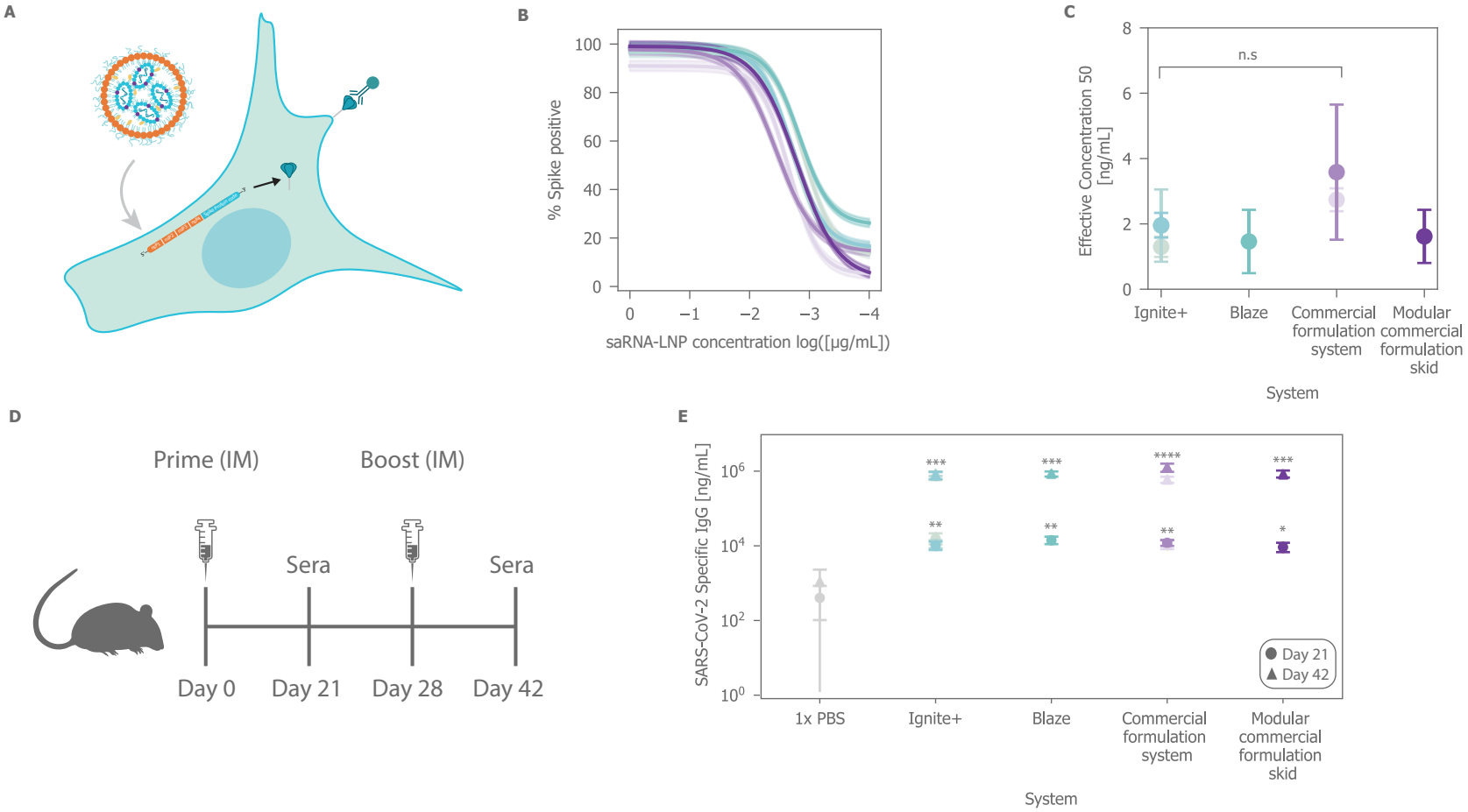




Condition	Development stage	NanoAssemblr® system	NxGen mixer cartridge	Total flow rate [L/h]	Batch volume [mL]	RNA Encapsulated [mg]
1	Early preclinical	Ignite+	NxGen	0.72	30	1.1
2	Early preclinical	Ignite+	NxGen 500	6.9	30	1.1
3	Early preclinical	Ignite+	NxGen 500	12	30	1.1
4	Late preclinical	Blaze	NxGen 500	6.9	30	1.1
5	Clinical and commercial production	Commercial formulation system	NxGen commercial cartridge 12 L/h [Nxgen 500]	12	100	3.3
6	Clinical and commercial production	Commercial formulation system	NxGen commercial cartridge 48 L/h	48	100	3.3
7	Commercial manufacturing	Modular commercial formulation skid	NxGen commercial cartridge 48 L/h	48	150	5.0

Self-amplifying RNA (saRNA)-LNPs prepared using NxGen technology maintain physicochemical characteristics throughout scale-up to commercial manufacturing. Size, polydispersity index (PDI), and encapsulation efficiency are consistent using **A)** the NxGen, NxGen 500, and NxGen commercial cartridge 48 L/h and **B)** from Ignite+ for early preclinical development through to the commercial formulation system for clinical and commercial manufacturing. Error bars are 1 standard deviation and comparison values are from a *post-hoc* Tukey test after one-way ANOVA.

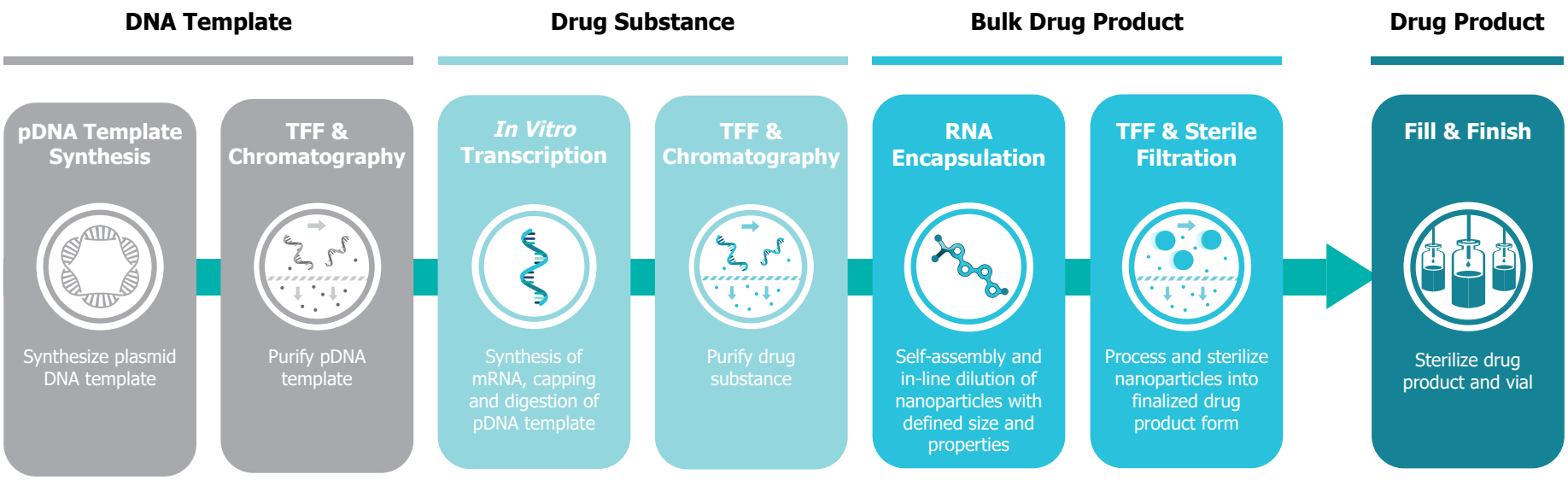
Transfer Manufacturing Processes and Minimize Process Development



saRNA-LNPs are biologically potent *in vitro* and *in vivo*, inducing expression of SARS-CoV-2 antigen and robust immune responses. A) BHK 570 cells were transfected with decreasing amounts of saRNA-LNPs and **B)** the percentage of cells expressing SARS-CoV-2 spike protein was measured using an anti-spike conjugated AlexaFluor488 antibody with 95% confidence intervals in shaded areas. **C)** EC_{50} values were similar across systems. Error bars represent 95% confidence intervals. **D)** BALB/c mice were used for a 42-day prime and boost dose study. **E)** Robust SARS-CoV-2-specific IgG responses in serum were observed at day 21 and 42 post-injection for each condition. Error bars are 1 standard deviation. 1x PBS vs instrument comparison p-value for a given time point using *post-hoc* Tukey test after one-way ANOVA ($p \leq .05$: *, $p \leq .01$: **, $p \leq .001$: ***, $p \leq .0001$: ****).

Integrated mRNA Manufacturing Solutions at Any Scale

Access technologies for a complete mRNA manufacturing workflow to maximize efficiency and increase manufacturing agility at any scale, from pDNA template synthesis to LNP encapsulation and fill-finish of mRNA-LNP drug products.



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Specifications

NanoAssemblr Commercial Formulation System

PARAMETER	INSTRUMENT SPECIFICATION
Supply voltage	100–240 V AC, 50/60 Hz
Compressed air pressure	6.0–8.0 bar g
Dimensions (approximate)	120 x 80 x 170 cm
Weight (approximate)	270 kg

NxGen Manufacturing and Development Flow Kits

PARAMETER	NXGEN™ FLOW KIT 12 L/H	NXGEN™ FLOW KIT 48 L/H
Total flow rate	6 to 12 L/h	24 to 48 L/h
Flow rate ratios (FRR)	1:1 to 5:1 FRR range is dependent on recipe flow rates	
Dilution ratio	1:1 to 10:1	1:1 to 8:1
Undiluted volume	0.5–100 L	0.5–400 L
Diluted volume	Up to 1100 L	Up to 3600 L
Fluid temperature	5°C to 45°C	

Ordering Information

INSTRUMENT AND FLOW KITS		PRODUCT CODE	DESCRIPTION
	**NanoAssemblr® commercial formulation system**	1002276	Single-use formulation system for clinical and commercial production - ATEX/IECEx** HazLoc rated system
	**NxGen™ commercial manufacturing flow kit 12 L/h**	1002279	Single-use manufacturing flow kit for flow rates of up to 12 L/h
	NxGen™ commercial manufacturing flow kit 48 L/h	1002280	Single-use manufacturing flow kit for flow rates of up to 48 L/h
	NxGen™ commercial development flow kit 12 L/h	1002277	Multi-use development flow kit for flow rates of up to 12 L/h
	NxGen™ commercial development flow kit 48 L/h	1002278	Multi-use development flow kit for flow rates of up to 48 L/h

***Pending final certification*

About Precision NanoSystems

Precision NanoSystems is a global leader ushering in the next wave of genomic medicines in infectious diseases, cancer and rare diseases. We work with the world's leading drug developers to understand disease and create the therapeutics and vaccines that will define the future of medicine. Precision NanoSystems offers proprietary technology platforms and comprehensive expertise to enable researchers to translate disease biology insights into non-viral genomic medicines.

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