PRECISION NANOSYSTEMS

Create Transformative Medicines™

# NanoAssemblr® Ignite™ and Ignite+™

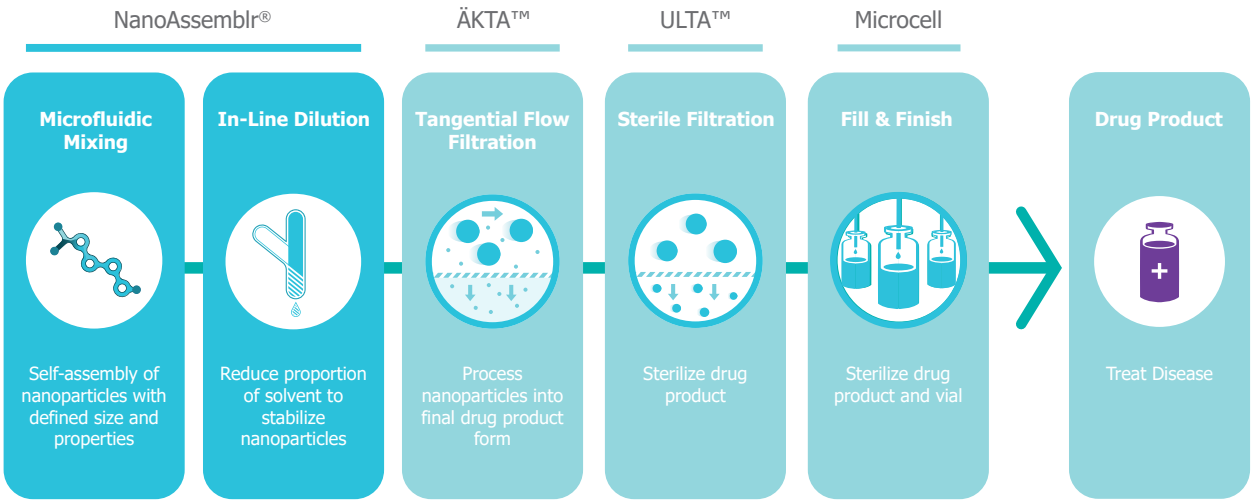
NXGen™ Technology

Power to Advance

# Advance Preclinical Drug Development

## Develop a Robust, Scalable Process from Preclinical to Clinical Development

The NanoAssemblr® Ignite™ and Ignite+™ enable the controlled and precise assembly of lipid nanoparticles (LNPs) by combining optimized precision pumping with the time-invariant mixing of NxGen™ microfluidic technology. By modeling unit operations at scale and maintaining the same process parameters as the NanoAssemblr Blaze and GMP System, Ignite and Ignite+ simplify the transition into clinical development and manufacturing. Incorporating fundamental process steps for scale-up in the earliest stages of preclinical development at low volumes reduces risks, simplifies workflows and accelerates drug development timelines.

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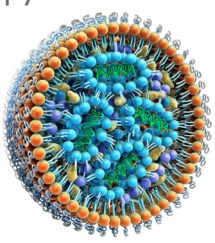
## Simplify Genomic Medicine Development and Scale-Up

Ignite lowers the barrier to developing genomic medicines by providing an intuitive, easy-to-use platform consisting of the Ignite and Ignite+ instruments for preclinical development. Its simple, low-volume workflow results in the automated synthesis of nanomedicines requiring minimal setup and operator training for robust and reproducible formulations. This saves time and reduces raw materials, waste volumes and associated costs, enabling you to expand manufacturing capabilities for a broad range of applications including vaccine development, cell therapy and gene therapy.



# Scale Nanomedicines from Discovery to Commercial Manufacturing


**Excipient Identification** | **Formulation Development** | **Formulation Optimization**

**Ignite**

**Ignite+**

| | | | | |
|---|---|---|---|---|
| **MAKE** | Efficiently produce a library of novel formulations | Systematically explore process parameters and compositions | Fine-tune critical process parameters (CPPs) including FRR, TFR and dilution | Establish CPP ranges of large-scale systems and initiate downstream process development steps including TFF |
| **TEST** | Perform *in vitro* or *in vivo* screens and proof of concept<br>Determine potency and toxicity of excipients | Characterize physico-chemical properties<br>Test in relevant biological models | Profile PK, biodynamics, efficacy and toxicity in disease model<br>Develop analytical methods | Confirm CQAs<br>Determine and optimize the lead candidate(s) tolerance for TFF |
| **SELECT** | Select excipients for formulation development | Select lead formulations for further optimization<br>Establish target performance specifications | Select lead candidate(s) for scale-up process development | Select lead candidate(s) for process scale-up |

## Summary of Features

### REPRODUCIBLE
Reduce batch-to-batch and user variability with automated, advanced microfluidics

### EASY-TO-USE
Formulate nanoparticles using a simple workflow with minimal setup and training

### SCALABLE
Predictably scale optimized formulations across the NanoAssemblr platform

### CONTROLLED ASSEMBLY
Tune critical quality attributes (CQAs) including particle size with precise control over fluid flow rates and ratios

### MINIMIZED RISK
Model clinically relevant parameters and processes at small volumes

### ACCELERATED TIMELINES
Single-use technology, simple workflows and comprehensive support accelerate drug development

# NxGen Microfluidics

## A Disruptive Technology Accelerating Transformative Medicine Development

NxGen technology enables flow rates thousands of times higher than conventional microfluidic designs while maintaining controlled mixing conditions for precise nanoparticle assembly.

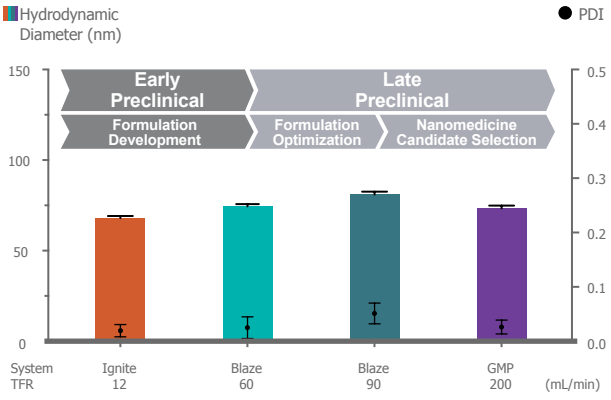
**Precise** - Non-turbulent particle formation ensures the most reproducible results for a wide range of nanoparticle types

**Scalable** - More than 25X throughput in a single mixer reduces risk during scale-up while maintaining particle quality and reproducibility compared to a classic mixer

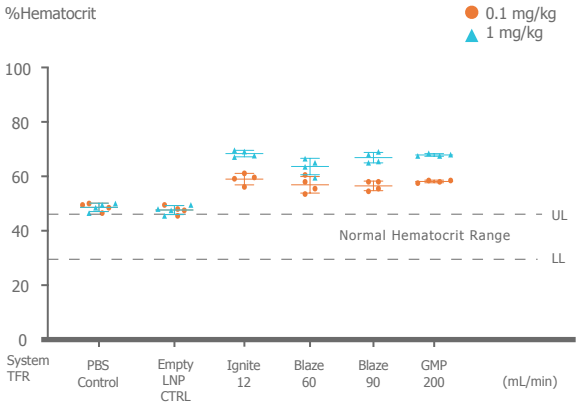
**Innovative** - NxGen redefines the limits of scaling with microfluidics

## NanoAssemblr Ignite: Bring the Scalable Power of NxGen to the Earliest Stages of Development

**mRNA Encoding Erythropoietin Was Formulated into LNPs with Equivalent Size and PDI Across Stages of Development**




**Erythrocyte Production Was Elevated Equivalently in Mice Treated with Erythropoietin mRNA-LNPs Produced Across Stages of Development**




**Background:** Recombinant Erythropoietin (EPO) is an approved therapy for anemia caused by cancer chemotherapy. Instead of delivering a protein, we encoded EPO in a messenger RNA (mRNA) where the patient's own cells can translate it into protein. This approach is modular: the same formulations, equipment and analytical methods can be leveraged to make mRNA-based treatments for a variety of indications.

Human EPO was encoded in mRNA with cap1 structure and 5 moU modifications. mRNA was combined with GenVoy-ILM™ ionizable lipid mix in a NxGen micromixer using Ignite to formulate mRNA-loaded LNPs. C57BL mice were treated with a single i.v. injection of LNPs and blood hematocrit levels (red blood cell production) were assessed 7 days later using microhematocrit tubes.

To learn more, visit precisionnanosystems.com/mRNA-case-study

# NanoAssemblr Ignite+

## Expand Preclinical Capabilities and Simplify Scale-Up

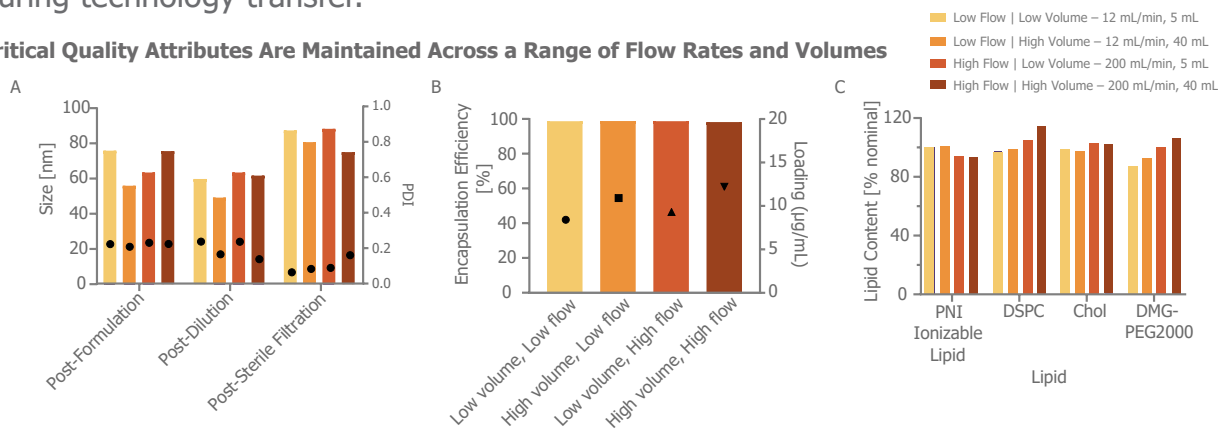
Ignite+ expands the capabilities of Ignite with increased flow rates of up to 200 mL/min pre-dilution and volumes of up to 60 mL, enabling larger preclinical and early process development studies. It also simplifies scale-up by maintaining the same CPPs as the NanoAssemblr Blaze and GMP System. Using the NxGen 500 microfluidic mixer which is also used in larger systems ensures consistent CQAs as you transition to clinical development and manufacturing while maintaining the familiar workflow of Ignite.

Larger volumes enable the incorporation of downstream process development including tangential flow filtration (TFF) at the earliest stages of preclinical development and expand efficacy and toxicity testing for large-cohort small-animal and larger animal studies including non-human primates (NHPs).

## Seamless Transfer of Manufacturing Processes

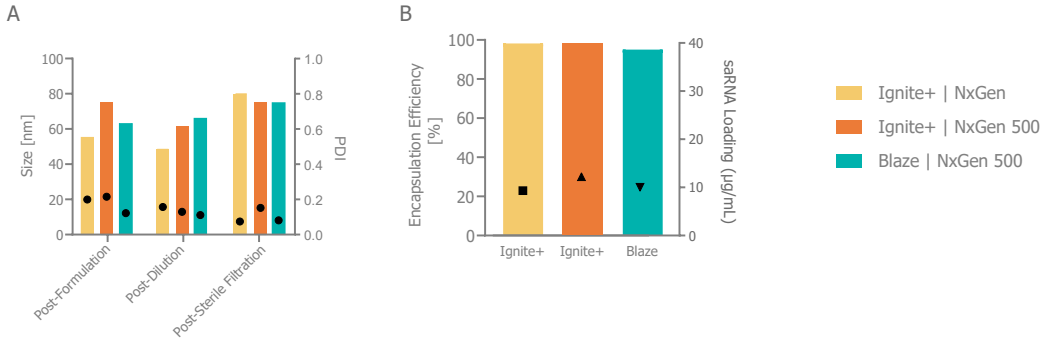
Establishing new specifications for CPPs including total flow rate (TFR) for large-scale preclinical and clinical systems is critical for successful scale-up. Perform these studies at the bench scale, enabling the direct protocol transfer of formulation and process parameters to larger systems, new teams or manufacturing facilities. This ensures CQAs are maintained across scales, saving time and resources while reducing risk during technology transfer.

**Critical Quality Attributes Are Maintained Across a Range of Flow Rates and Volumes**




Using SARS-CoV-2 self-amplifying RNA (saRNA)-LNPs as a model system, volumes were scaled from 5 mL to 40 mL on Ignite+ while changing CPPs from the bench scale (12 mL/min, 5 mL) to clinical scale (200 mL/min, 40 mL). CQAs of in-process and finished SARS-CoV-2 saRNA-LNPs including **A)** size and polydispersity index (PDI) following formulation, in-line dilution and sterile filtration and **B)** encapsulation efficiency are similar across a range of flow rates and volumes when prepared on Ignite+. **C)** Lipid content is also similar across flow rates and volumes.

**saRNA-LNPs Have Consistent Physicochemical Characteristics Using the NanoAssemblr Ignite+ and Blaze**




Physicochemical characteristics including the **A)** size, PDI and **B)** encapsulation efficiency of an saRNA-LNP vaccine candidate for SARS-CoV-2 were consistent when prepared on Ignite+ and Blaze using NxGen Dilution or NxGen 500D cartridges following formulation, in-line dilution and sterile filtration.

# Ordering Information

| INSTRUMENTS AND CARTRIDGES | | PRODUCT CODE | DESCRIPTION |
|---|---|---|---|
|  | **NanoAssemblr Ignite Instrument** | NIN0001 | The NanoAssemblr Ignite is a scalable, reproducible and easy-to-use system for preclinical genomic medicine development. It formulates at the bench scale with volumes of up to 20 mL and flow rates of up to 20 mL/min. |
|  | **NanoAssemblr Ignite+ Instrument** | 1001413 | The NanoAssemblr Ignite+ builds on the features of Ignite with additional capabilities. It formulates up to 60 mL at up to 200 mL/min, enabling small-scale de-risking of large-scale systems and initiating process development activities using simple, low-volume workflows. |
|  | **NanoAssemblr Ignite Upgrade Kit** | 1001409 | All components and installation required to upgrade an Ignite to an Ignite+. |
|  | **NxGen Cartridges - 100 and 200 Pack** | NIN0061<br>NIN0062 | Single-use microfluidic cartridges optimized for flow rates of up to 20 mL/min. Two reagents from 2 inlets flow through a NxGen mixer. Optionally, dilution buffer from a third inlet may be introduced at the end of the mixer to enable in-line dilution. |
|  | **NxGen Dilution Cartridges - 50 and 100 pack** | NIN0063<br>NIN0064 | |
|  | **NxGen 500 Cartridges - 50 and 100 pack** | 1001397<br>1001398 | Single-use microfluidic cartridges optimized for flow rates of up to 200 mL/min. Two reagents from 2 inlets flow through a NxGen 500 mixer. Optionally, dilution buffer from a third inlet may be introduced at the end of the mixer to enable in-line dilution. |
|  | **NxGen 500D Cartridges - 25 and 50 pack** | 1001399<br>1001400 | |
| **REAGENTS** | | **PRODUCT CODE** | **DESCRIPTION** |
|  | **GenVoy-ILM** | NWW0041<br>NWW0042 | GenVoy-ILM is an off-the-shelf, research-use-only LNP reagent that lowers the barriers of genomic medicine development using Ignite. |
|  | **GenVoy-ILM T Cell Kit for mRNA, Ignite** | 1001144<br>1001161 | GenVoy-ILM T Cell Kit for mRNA, Ignite is an off-the-shelf LNP reagent mix optimized for the delivery of mRNA or Cas9 mRNA/sgRNA into activated human primary T cells. |
|  | **Formulation Buffer** | NWW0043 | 20 mL Formulation Buffer |
| **ACCESSORIES** | | **PRODUCT CODE** | **DESCRIPTION** |
| **Ignite Heating Package** | | NIN0067 | One Ignite heating module to individually heat reagent syringes up to 75°C. Five syringe inserts for use with various syringes. |
| **Ignite+ Heating Package** | | 1001403 | One Ignite+ heating module to individually heat reagent syringes up to 65°C. Six syringe inserts for use with various syringes. |

## 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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