PRECISION NANOSYSTEMS

Create Transformative Medicines™

# NanoAssemblr® Blaze™

NXGen™ Technology

## Power to Scale

# Scale Up Your Genetic Medicines

## Select a Lead Candidate

A candidate drug must be shown to be both potent and non-toxic in relevant models. While early screening in murine models is enough to begin a program, the **demands for data from larger models will increase**.

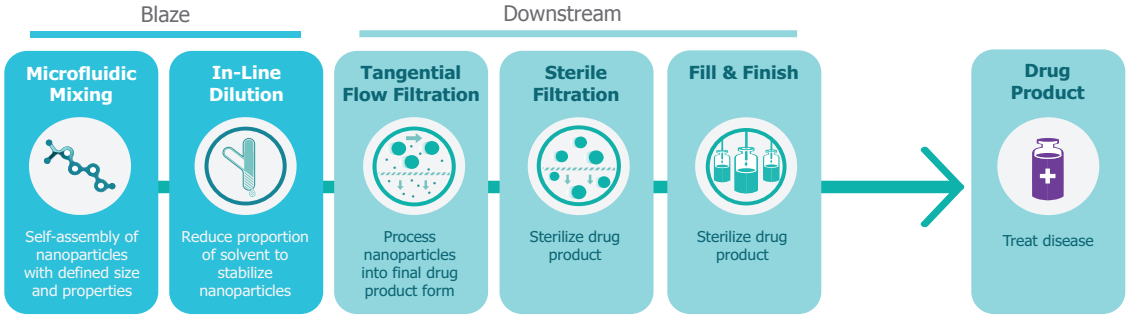
Traditionally, process development for nanomedicine production at an intermediate scale is a barrier to this work. With NxGen™ technology on the NanoAssemblr® Blaze™, these important studies can be conducted efficiently with a process that **mirrors a clinical scale implementation**. In addition, the Blaze+ Upgrade allows the formulation of volumes from 1 L to 10 L to enable late preclinical experiments and process development activities to be performed in house at lower cost.

| | Mouse | Rat | Macaque | Dog |
|---|---|---|---|---|
| **MASS** (Typ.) | 20 g | 300 g | 6000 g | 10,000 g |
| **DOSE** (rel. to mouse) | 1 unit* | 15 units | 300 units | 500 units |

# A Direct Path to the Clinic

## An End-to-End Process

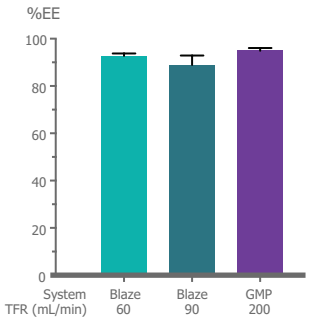
The success of a new drug program requires a scalable process. NxGen technology delivers a scalable means to perform the critical particle formation step in the nanomedicine development process. Using the NanoAssemblr Blaze with NxGen technology, process development can be conducted on both the upstream and downstream portions—from material preparation to buffer exchange, filtering and analytics—to ensure that **a program is ready to quickly accelerate to the clinic**.



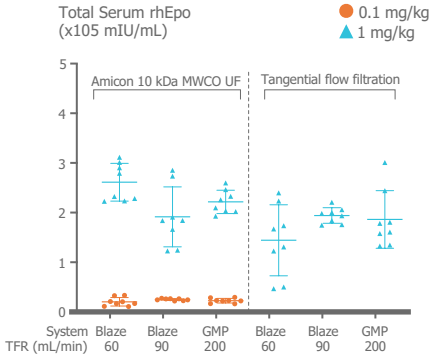

## Seamless Transfer of Manufacturing Processes

The NanoAssemblr Blaze uses the **same microfluidic architecture** as the NanoAssemblr GMP System, allowing for formulation optimization to be performed on Blaze while **minimizing risk during scale-up to clinical manufacturing**. With the optimized formulation, Precision Nanosystems' Clinical Solutions team can help you build your custom GMP system to match your specifications and then transfer your formulations **from the Blaze to the GMP system**.

**>90% encapsulation efficiency of mRNA in LNPs was achieved**




**Epo mRNA-LNP mediated comparable serum Epo levels in mouse study**

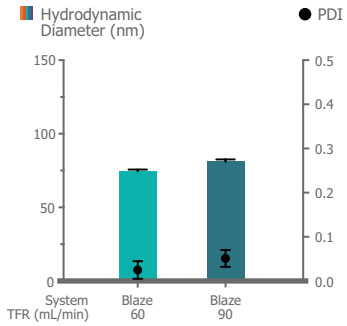


# Simple and Reproducible Nanomedicine Development

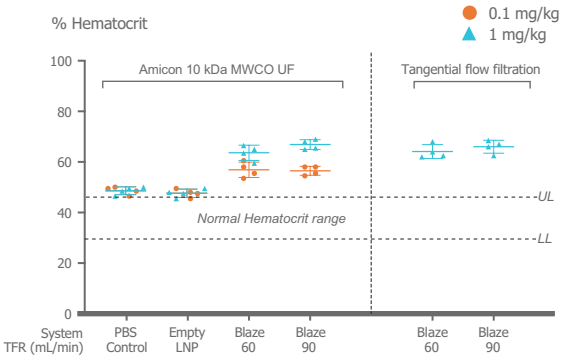
## Accelerate the Developement of Gene Therapies

Background: Recombinant Erythropoietin (Epo) is an approved therapy for anemia caused by cancer chemotherapy. Instead of delivering a protein, we encoded Epo in an 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.

**mRNA-LNPs were produced with ideal size for targeting liver *in vivo***




**Intended physiological response confirmed in mice treated with mRNA-LNPs**

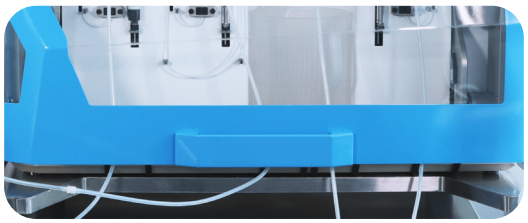



Human Epo was encoded in mRNA with cap1 structure and 5 moU modifications. mRNA was combined with GenVoy-ILM™ ionizable lipid mix in a NxGen micromixer using Blaze to formulate mRNA-loaded LNPs. Tangential flow filtration was then performed. C57BL mice were treated with a single i.v. injection of LNPs,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

# Designed for a Scalable Process

## Larger Formulation Volumes with the Blaze+ System Upgrade

The Blaze+ System Upgrade unlocks the ability of Blaze to r**un volumes of up to 10L**. Using Blaze+ reduces cost of process development and accelerates timelines by allowing users to **perform more large scale formulations on a lower cost system in less time**.

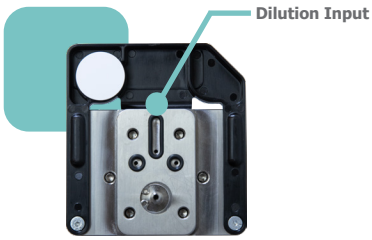


*Formulation run with adjustment plate installed.*

## Same Geometry, Different Flow Rates

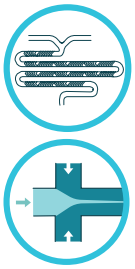
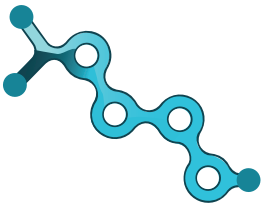
Two different cartridge variations, the **NxGen 400 and NxGen 500**, are available. Both use the same mixer in different dimensions, offering different flow and shear rates to better suit the formulation design space.

**Dilution cartridges** mix the reagents in the same manner as non-dilution cartridges to allow modelling of the processes that will be required for the future GMP production.



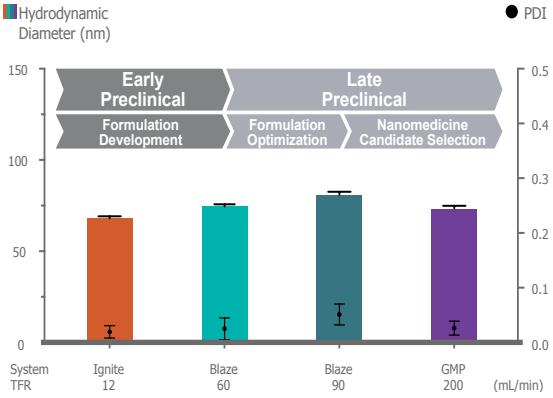
# NXGen™ Technology: A new paradigm in scalable manufacture of Nanomedicines

NxGen Microfluidics

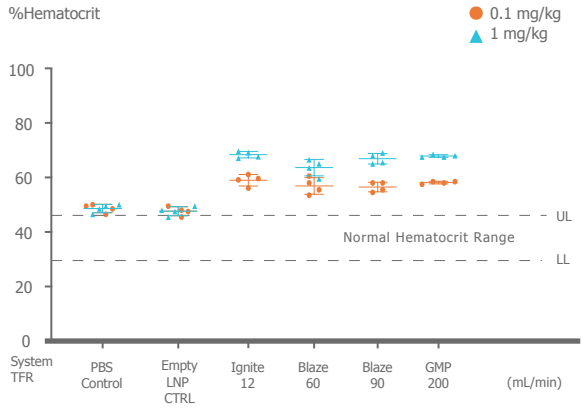
| High Energy Techniques | In-Line Macromixing | Microfluidic Approaches | NxGen Microfluidics |
|---|---|---|---|
|  |  |  |  |
| | | - Some scaling challenges remain | + Easy to Scale |
| | | - Mixers are difficult to make | + Mixers are Easy to make |
| - Limited applications | - Limited applications | + Expanded Applications | + Potential multi-mixer integration opens possibilities |
| - Difficult to reproduce | - Difficult to reproduce | + Reproducible | + Reproducible |
| - Harsh process conditions | + Gentler process conditions | + Non-turbulent process conditions | + Non-turbulent process conditions |
| - Difficult to scale | + Improved Scalability | | |

## Blaze brings the highly scalable power of NxGen microfluidic technology to the late preclinical 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**




# NanoAssemblr® Users are Transforming Medicine

To view over 200 publications, visit precisionnanosystems.com/resource-center

## Rapid Process Development to Accelerate Product Scale-up

Researchers at the University of Strathclyde developed a platform for de-risking the scale-up of liposome formulations entrapping proteins and demonstrated the scale-independent production of their lead formulation. This is in contrast to traditional methods requiring process redevelopment at each scale.

Forbes, N. et al. International Journal Of Pharmaceutics 556, 68-81 (2019).

## Efficient & Scalable Protein Encapsulation

A protein encapsulating liposome was developed and characterized for size, encapsulation and release from bench scale through to a NanoAssemblr GMP System, demonstrating the power to quickly develop and advance nanomedicine programs.

Webb, C. et al. International Journal of Pharmaceutics 582, 1-12 (2020).

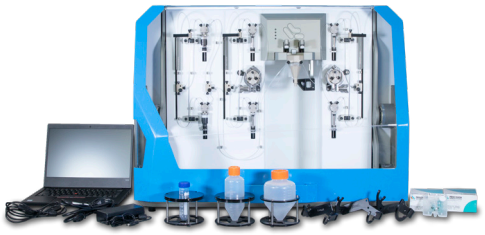
## Gene Therapy

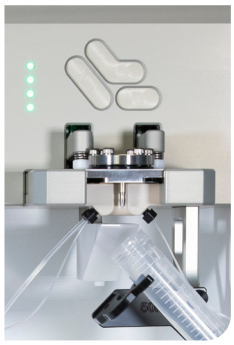
Scientists from M.D. Anderson Cancer Center and Arcturus Therapeutics have developed and scaled up miRNA lipid nanoparticles for the treatment of gliomas. By targeting intracellular immune pathways, the authors have demonstrated a median survival exceeding 70 days, with an associated reversal of tumor-mediated immunosuppression and induction of immune memory and a favorable toxicity profile in canine and murine models

Yaghi, N.K. et al. Neuro-Oncology 19, 372-382 (2017).

# Scale Nanomedicines


| | Formulation Optimization | Nanomedicine Candidate Selection |
|---|---|---|
| MAKE | Efficiently produces batches for large scale *in vivo* studies using high capacity NxGen microfluidics | Scale-up end-to-end processes, including upstream and downstream steps, for lead candidate manufacturing |
| TEST | Determine efficacy and toxicity in relevant disease models and second species | Conduct CMC studies encompassing all manufacturing steps |
| SELECT | Select lead candidate(s) for process scale-up | Lead candidate ready for technology transfer to GMP manufacturing |





# Summary of Features

### THE SCALABLE POWER OF NXGEN™

Advance candidates developed at bench scale by scaling up to the NxGen 400 and NxGen 500 cartridges—the same ones on the GMP System.

### EXPANDED PROCESS DEVELOPMENT CAPABILITIES

Continuous flow pumping and in-line pressure monitoring provide an efficient platform for process development.

### OUTSTANDING REPRODUCIBILITY

Exquisite batch-to-batch reproducibility enables the identification of critical process attributes from raw material supply to the final manufacturing steps.

### INTUITIVE WORKFLOW

Familiar interface, built-in checklists, saved recipes and complete run history ensures new users are quickly able to perform the studies they need.

# Product Specifications, Access and About PNI

| | Blaze | Blaze+ |
|---|---|---|
| **Cartridges** | **Classic**<br>*Dilution:*<br>**NxGen 400D, 500D**<br>*No Dilution:*<br>**NxGen 400, 500** | *Dilution:*<br>**NxGen 400D, 500D**<br>*No Dilution:*<br>**NxGen 400, 500** |
| **Maximum Volume** | 1 L | 10 L |
| **Maximum Flow Rate** | 18 mL/min - Classic<br>115 mL/min - NxGen | 115 mL/min - NxGen |
| **Inline Monitoring** | Onboard pressure | |

## Ordering Information for NanoAssemblr Blaze

| INSTRUMENT | | PRODUCT CODE |
|---|---|---|
|  | NanoAssemblr® Blaze™ | NIB0055 |

| CARTRIDGES | | PRODUCT CODE |
|---|---|---|
|  | **NxGen Cartridges** | |
| | NxGen 400<br>NxGen 500 | 1000458<br>1000460 |
|  | **NxGen Cartridges With Dilution** | |
| | NxGen 400D<br>NxGen 500D | 1000459<br>1000461 |
|  | **Classic Blaze Cartridges** | |
| | Classic<br>Classic with Dilution | NIB0002<br>NIB0003 |

| BLAZE+, VOLUMES UP TO 10 L | | PRODUCT CODE |
|---|---|---|
|  | NanoAssemblr Blaze+ System Upgrade | NIB0061 |
|  | NanoAssemblr Blaze+ Tubing Kit | 1000535 |

## About Precision NanoSystems

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