



## **NANO REVOLUTION**

**The ultimate  
nanoformulation  
manufacturing platform**



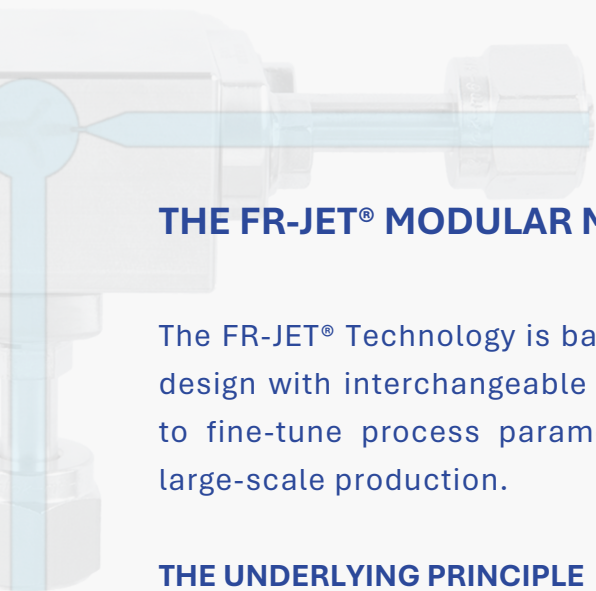


## REVOLUTIONIZING NANOENCAPSULATION

Our proprietary FR-JET® technology and comprehensive product suite are redefining the future of lipid and polymer nanoparticle manufacturing.

With its scalable, clog-free, single-use, robust, versatile and precision-controlled technology, FR-JET® sets new standards in nanoencapsulation - empowering the next generation of nanoparticle-based advanced therapy medicinal products (ATPMs) and vaccines.

We deliver cost-effective, GMP-ready equipment that eliminates complexity while ensuring operational efficiency. Whether in early-stage research or large-scale production, our solutions enable a smooth transition without the need for reformulation or system changes - bringing your therapeutic innovations to market faster and more efficiently.



### THE FR-JET® MODULAR MIXER

The FR-JET® Technology is based on jet-impinging principles and features a modular design with interchangeable parts. This innovative approach provides the flexibility to fine-tune process parameters from the early development stages through to large-scale production.

#### THE UNDERLYING PRINCIPLE

Two liquids are injected into the mixing chamber under pressure through two nozzles. This process establishes a highly turbulent yet stable mixing process, in which the liquids mix in a very short period of time within the mixing chamber.

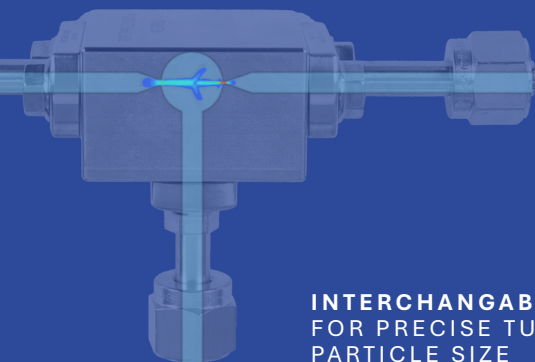
The unique internal geometry of our mixer core maximizes turbulent mixing efficiency by minimizing the surface area-to-volume ratio and reduces deviations from ideal reactors by eliminating stagnant or dead volumes.



## UNIQUE PROPRIETARY MIXER GEOMETRY, NOT JUST ANOTHER T-MIXER

# FR-JET

technology



**UNIQUE MODULAR CONCEPT**  
FOR SEAMLESS SCALE-UP

**INTERCHANGABLE CORE**  
FOR PRECISE TUNING OF  
PARTICLE SIZE

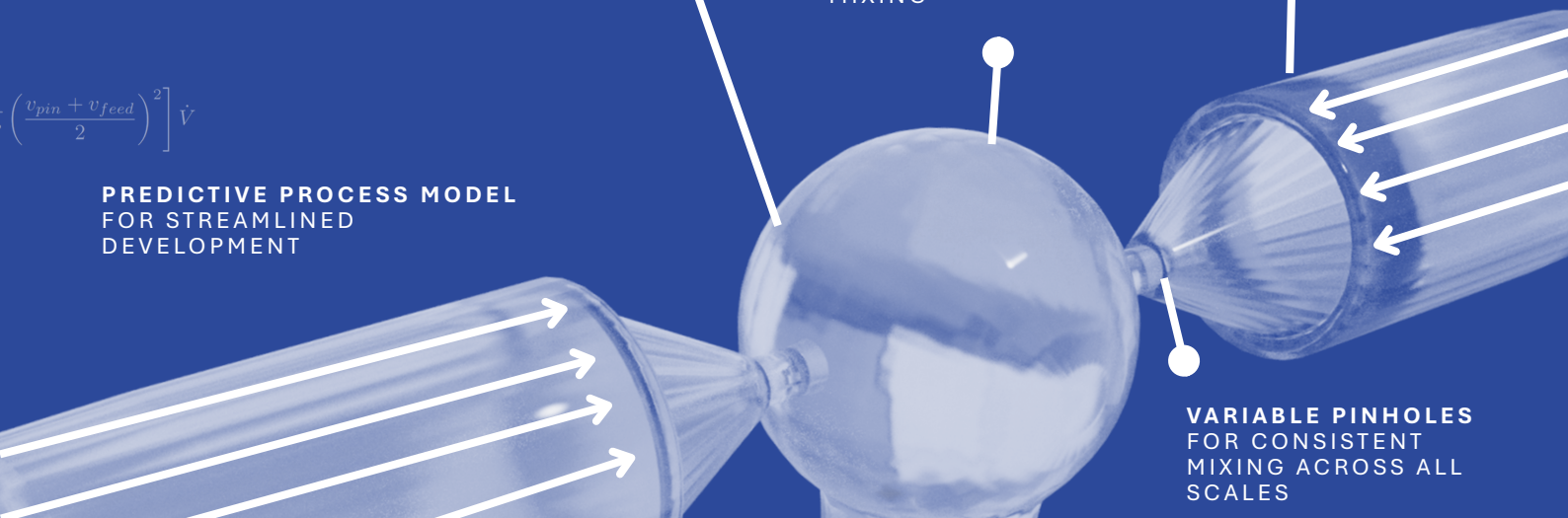
**INTERCHANGABLE PINHOLES**  
FOR FULL FORMULATION  
FLEXIBILITY

**IDEAL GEOMETRY**  
FOR HIGHLY EFFICIENT  
MIXING

$$\left( \frac{v_{pin} + v_{feed}}{2} \right)^2 \dot{V}$$

**PREDICTIVE PROCESS MODEL**  
FOR STREAMLINED  
DEVELOPMENT

**VARIABLE PINHOLES**  
FOR CONSISTENT  
MIXING ACROSS ALL  
SCALES



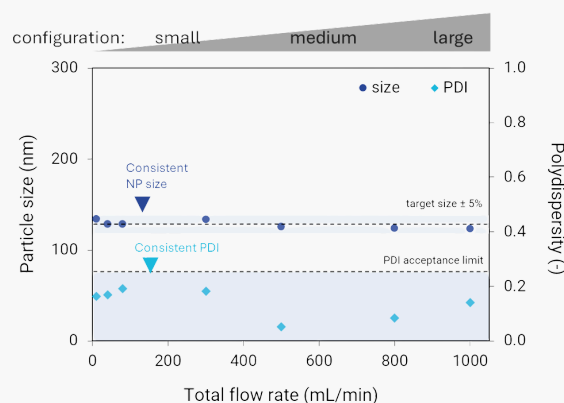
Conventional GMP-compliant manufacturing methods of nanoparticle-based products like microfluidics and T-mixing struggle with mitigating the risk of aseptic manufacturing, suboptimal product CQAs, high batch-to-batch variability, limited robustness/versatility, and steep production costs.

Recognizing the complexity of the emerging drug modalities, LEON has introduced the FR-JET® modular mixer with following features addressing the challenges of conventional methods:



## EASY SCALE UP

- Robust and simple scale-up with predictive mathematical tools
- Simple 1-step process transfer to GMP systems

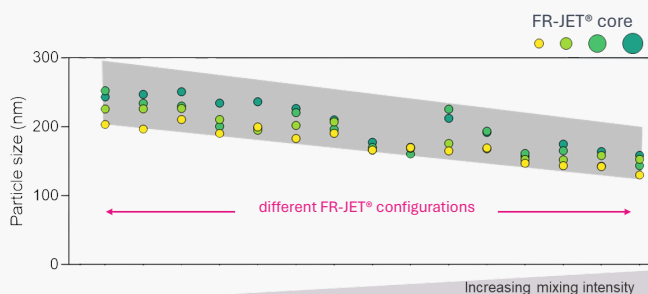


FR-JET® enables consistent particle CQAs during scale-up. Precise particle size control was achieved using the modular FR-JET® system over a 100-fold scale-up, consistently maintaining particle size within  $\pm 5\%$  as flow rates increased from 10 to 1000 mL/min.



## BROAD DESIGN SPACE

- Performs at both very low and very high flow rates
- Operates across a wide range of flow rate ratios



Effects of specific changes in reactor configuration can be predicted and used to design the process, enabling full exploitation of a broader nanoparticle design space. FR-JET® process design parameters correlate with the calculated mixing energies



## SAME FORMULATION - BETTER PARTICLES

- FR-JET<sup>®</sup> mixer produces a higher percentage of uniform solid-core nanoparticles
- Same formulation manufactured with FR-JET<sup>®</sup> mixer shows enhanced biological activity



## VERSATILE

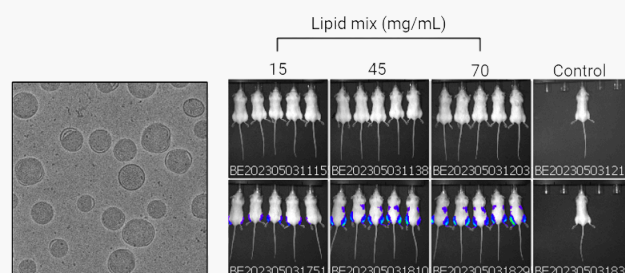
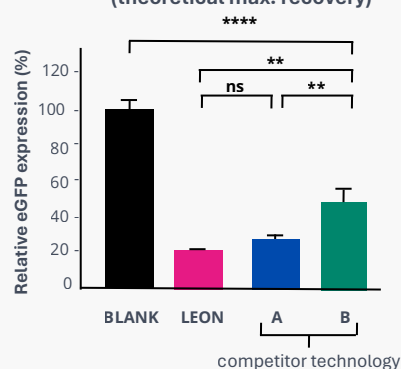
- Wide variety of nanoparticles (lipid nanoparticles, liposomes, polymeric nanoparticles, nanocrystals, etc)
- Enables encapsulation of diverse payloads (mRNA, siRNA, saRNA, circRNA, pDNA, small molecules...)
- Allows processing at high starting materials concentrations (lipids and RNA)



## RELIABLE & ROBUST

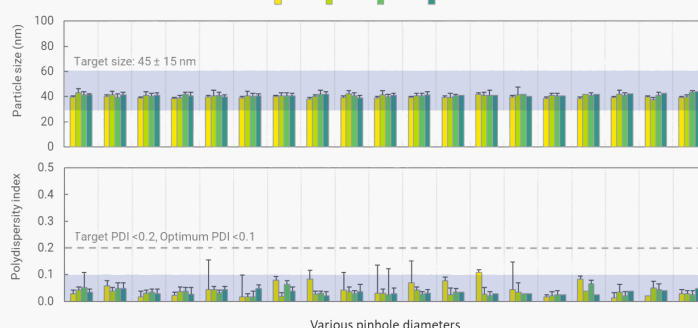
- Broad chemical compatibility of the FR-JET<sup>®</sup> stainless steel and polymer mixer
- Handles high-viscosity starting materials
- Minimizes material build-up and reduces risk of clogging

Relative eGFP expression in H1299-eGFP cells transfected dose: 2  $\mu$ mol (theoretical max. recovery)



(Flow rates in L/min)

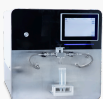
Various reactor chamber dimensions



The FR-JET<sup>®</sup> modular mixer robustly produced liposomes with consistent particle properties at a high TFR (total flow rates) in all reactor configurations .

## MANUFACTURING SYSTEMS AT ALL SCALES

Our systems have been developed keeping GMP-compliant design in mind. This is why they can meet the demanding need for a cost-effective, aseptic manufacturing process while ensuring batch-to-batch reproducibility at the same time, whether producing low or high product volumes.



NANO **screen**

User-friendly platform designed to screen formulations for research and early-stage projects.



NANO **lab**

Benchtop device for simplified formulation process development and preclinical studies.



NANO **me**

Efficient system for GMP back-to-back aseptic manufacturing of small-/mid-sized batches.



NANO **js**

Fully-automated aseptic system for large scale, high-speed nanoencapsulation under GMP.



## NANOscreen

### **EARLY DEVELOPMENT AND FORMULATION SCREENING**

The NANOscreen® is optimized for early-stage research and screening of formulations.

### **STRAIGHT-FORWARD R&D PLATFORM**

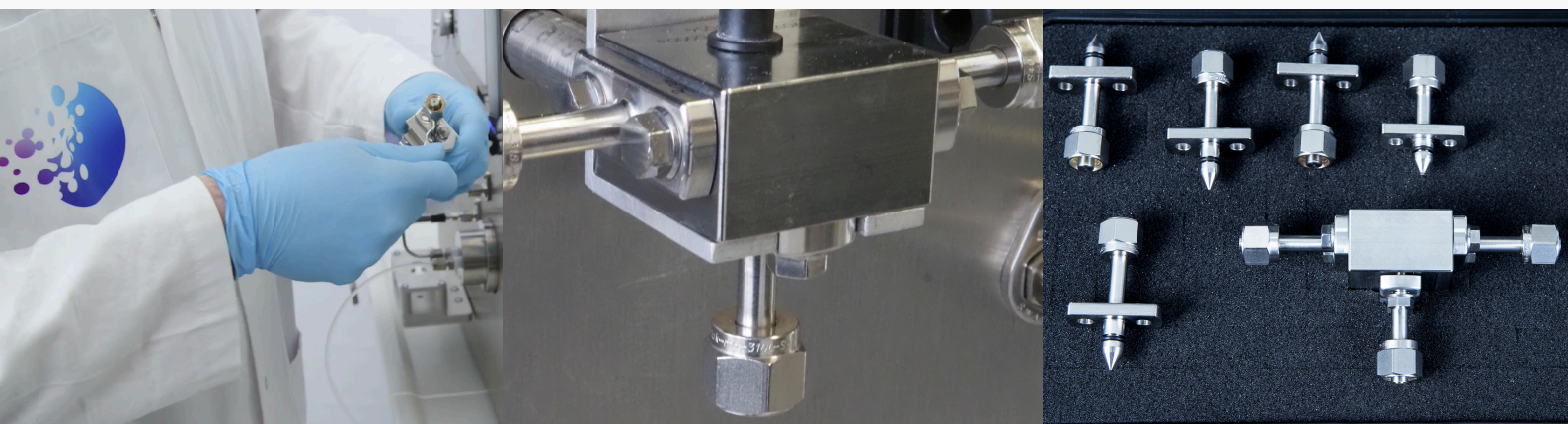
Easy-to-use user interface & monitoring of all relevant process parameters.

### **MINIMAL MATERIAL LOSS**

Reduced hold-up volume to reduce material loss - optimizing efficiency during R&D.

### **TIGHTLY CONTROLLED MIXING PROCESS**

The FR-JET® modular mixer enables precise control of process parameters and nanoparticle properties.





### **SIMPLIFIED PROCESS DEVELOPMENT**

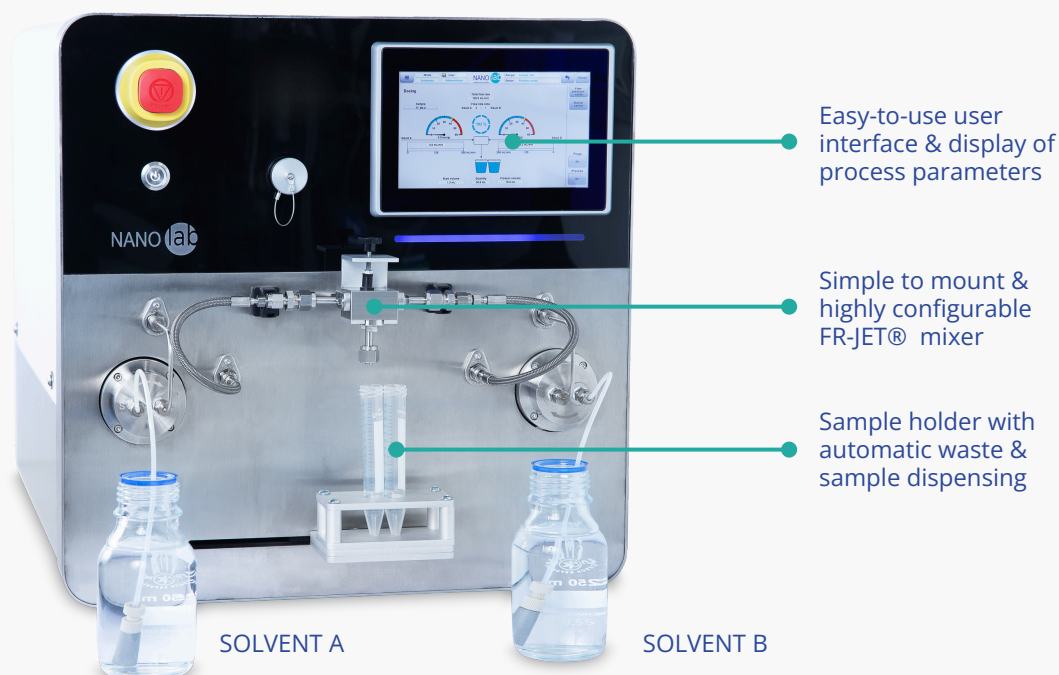
The NANOlaboratory® features a broad operational window (e.g. flow rate) combined with the modular design of our proprietary FR-JET® system, enabling precise control over nanoparticle properties.

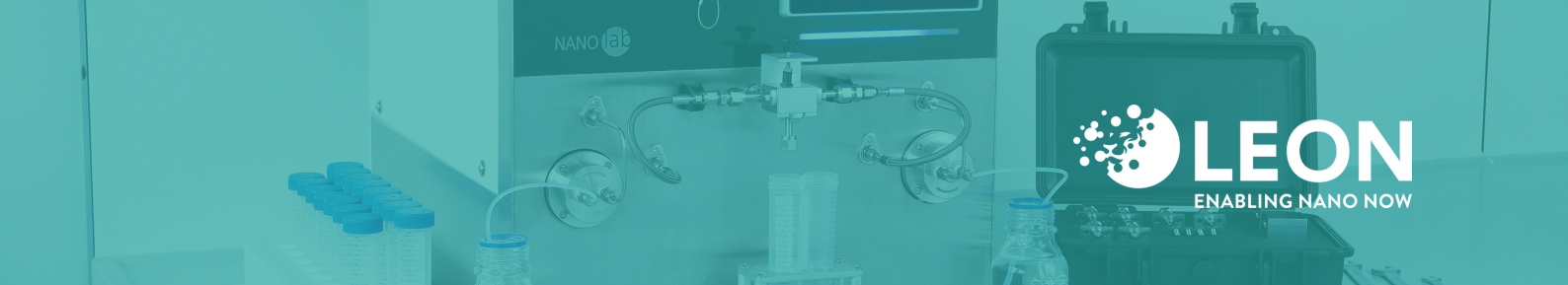
### **DELIVER YOUR TARGET SPECIFICATIONS**

A highly configurable system makes it easy to screen and identify the right process parameters to achieve particle properties that meet your needs.

### **DIRECT ONE-STEP PROCESS TRANSFER TO GMP**

The process parameters can be scaled up directly to our GMP NANOme® or NANOus® devices without the need for intermediate steps or additional equipment.





## TECHNICAL DETAILS

### Description

NANOlab® bench-top system for nanoparticle formulation process development

### Scope

Non-clinical pharmaceutical nanoparticle formulations

### Dimensions

45 cm × 45 cm × 60 cm (approximate)

### Weight

25 kg

### Features

- FR-JET® mixer (included) for mixing two solutions
- FR-JET® mixer offers combination of pinholes, cores and outlets to tune process
- Flow-controlled feed of educt streams using micro-gear pumps with a low internal volume
- Manual operation mode for protocol development
- Customizable protocols for automated process runs
- Export function for process parameter logs (flow rates, total flow rates or TFR, pressure)

### Operation parameters

- Flow rate of single pump: 3-250 mL/min
- Total flow rate: 6-500 mL/min (FRR 1:1)
- Pressure rating ≤ 40 bar
- Samples can be dispensed automatically (≤1 mL applicable at low TFRs only)

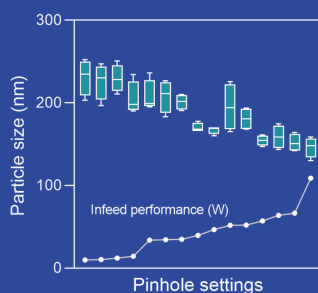
### Output

- Minimum product volume: starting at 1 mL (for 10 second run at lowest TFR, FRR 1:1)
- Maximum product volume: N/A (continuous operation mode)

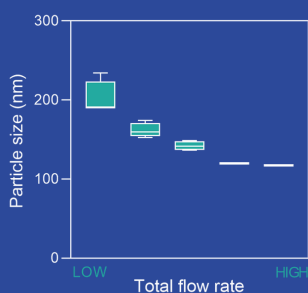
### EXAMPLE WORKFLOW TO OPTIMIZE PROCESS

Representative data shown with model PLGA nanoparticles. Data for other nanoparticles, including lipid nanoparticles, available.

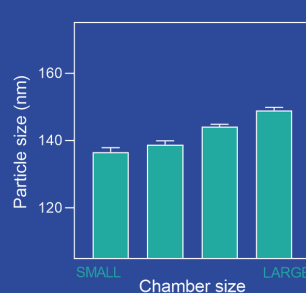
#### 1. SCREEN SIZE RANGE



#### 2. MODULATE



#### 3. FINE TUNE







### **PUMPLESS GMP SYSTEM FOR SMALL TO MID-SIZED BATCHES**

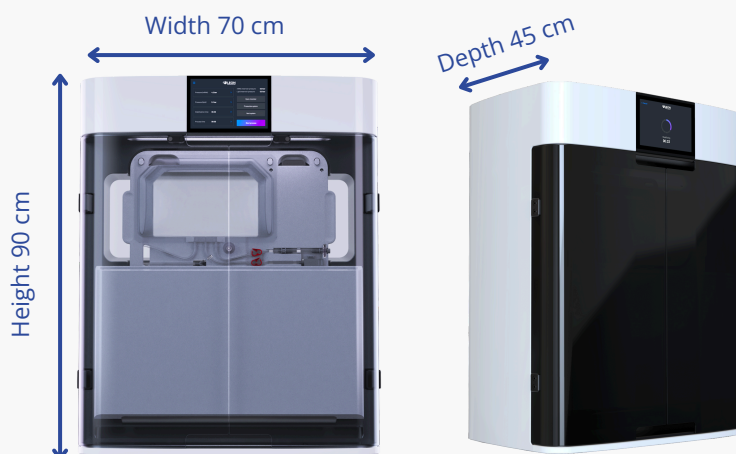
Our benchtop NANOme® GMP equipment redefines back-to-back aseptic manufacturing intended for clinical batches and small- to mid-sized commercial batches.

### **FULLY CLOSED AUTOMATED SYSTEM**

The only system offering a fully closed single-use sterile fluid path with zero contact between product and reusable parts for high sterility assurance.

### **DIRECT PROCESS TRANSFER FROM THE NANOLab®**

The process established on the NANOLab® can be transferred directly to the GMP NANOme® system without the need for intermediate scale up steps.





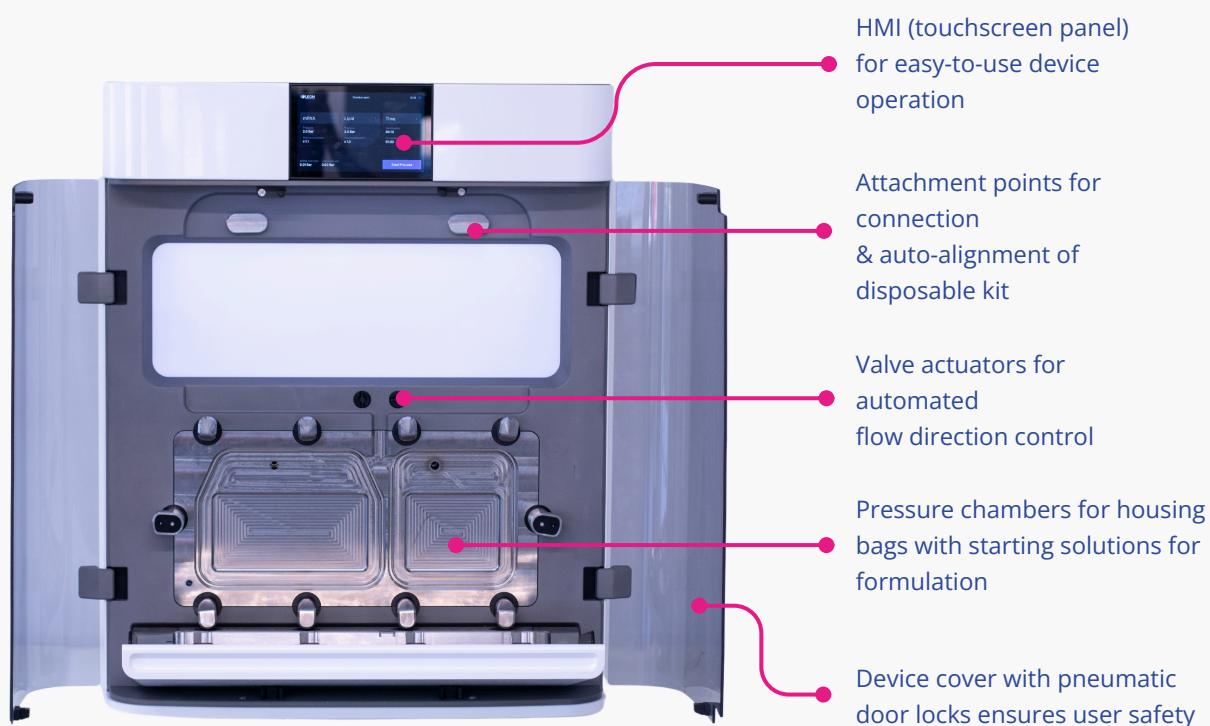
## TECHNICAL DETAILS

### System: NANOme® benchtop system for GMP nanoparticle production

APPARATUS	<b>Description</b>	Pumpless apparatus for processing fluids in disposable kits for aseptic nanoparticle manufacturing under GMP.
	<b>Scope</b>	Aseptic manufacturing of pharmaceutical nanoparticle formulations intended for clinical batches and small- to mid-sized commercial batches
	<b>Dimensions</b>	45 cm × 70 cm × 90 cm (145 kg)
	<b>Features</b>	<ul style="list-style-type: none"> <li>• Automated system with touchscreen operation</li> <li>• Export function via USB outlet for process parameter logs</li> <li>• Storage of pre-written formulation protocols and process data tables</li> <li>• 21 CFR Part 11-compliant software (option for remote software updates)</li> <li>• Designed for aseptic production in Grade C clean rooms</li> <li>• No need for system cleaning between batches (including product changeover)</li> </ul>
	<b>Operation parameters</b>	<ul style="list-style-type: none"> <li>• Flow rates - inlet A: 10 - 160 mL/min, inlet B: 5 - 80 mL/min (flow stabilizes in &lt;4 seconds)</li> <li>• Mixer configuration adapted for seamless process transfer from NANOlabor®</li> </ul>
	<b>Output</b>	<ul style="list-style-type: none"> <li>• Pressure rating ≤ 16 bar</li> <li>• Maximum total flow rate: 200 mL/min (assuming typical FRR 3:1 for LNPs)</li> <li>• Maximum product volume: approx. 1.5 L</li> </ul>

DISPOSABLE KIT	<b>Description</b>	Disposable kit to be used with the NANOme® apparatus
	<b>Features</b>	<ul style="list-style-type: none"> <li>• Sterile fluid path with closed design for GMP aseptic manufacturing</li> <li>• Ready-to-go kit: pre-assembled, triple-packaged &amp; gamma-sterilized</li> <li>• Kit includes bioprocessing bags, with detachable product bag for downstream processing</li> <li>• Built-in aseptic connectors &amp; disconnectors for maintaining a closed-loop workflow</li> <li>• Built-in sterile sampling feature for Quality Control</li> <li>• Easy handling, secure transport, and risk-free mounting and unmounting within seconds</li> <li>• Minimal internal hold-up volume to minimize material loss (&lt;15mL)</li> <li>• Option to select between in-line or pre-filled in-bag dilution</li> <li>• Filling aid prop for easy handling during the filling operation (included)</li> </ul>

Note: Filling of single-use bags requires external pump, syringes, or similar equipment and in-line dilution requires an external pump (not included)



## HOW IT WORKS

### SIMPLE PLUG & PLAY APPROACH FOR BACK-TO-BACK NANOPARTICLE MANUFACTURE

- 1 Place the filled NANOme® disposable kit into the NANOme® apparatus.
- 2 Select process parameters and run the process.
- 3 Remove the filled product bag for downstream processing.

Repeat steps 1-3 for next batch. Typical cycle time is 20 minutes.

Disposable kit with a closed design for aseptic processing

Product bag with an attached aseptic connector and disconnector for collecting nanoparticle suspension

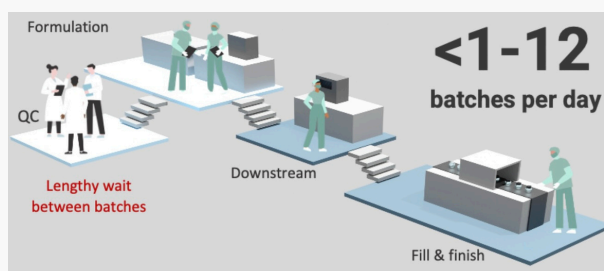
Starting material bags with attached sterile filters



## BATCH OR PRODUCT CHANGEOVER IN AS LITTLE AS 5 MINUTES!

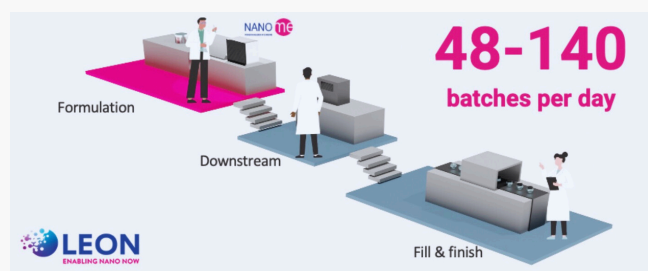
A user-friendly system which eliminates the need for cleaning between batches, minimizes facility requirements, saves time, and lowers manufacturing costs.

### Conventional systems



Conventional 'use and reuse' systems require cleaning and cleaning validation between batches

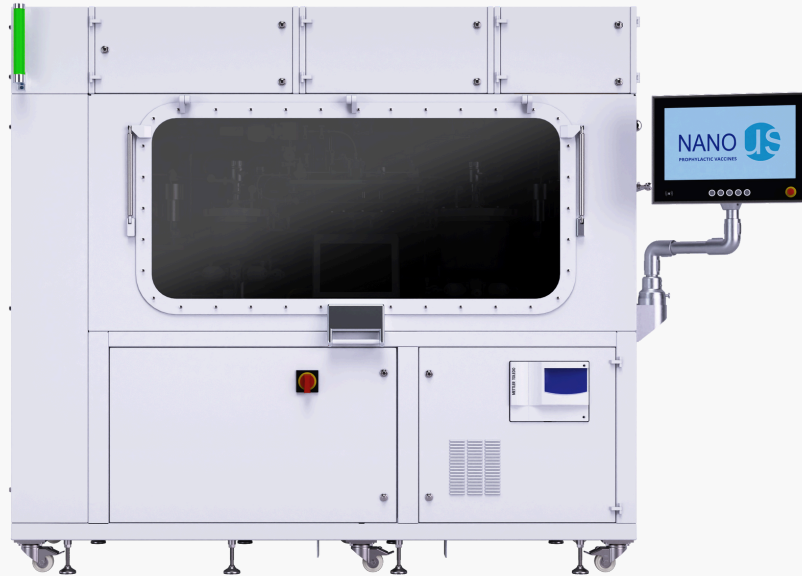
### LEON: GMP batch of 1 – 100.000 doses\*



No cleaning or cleaning validation steps necessary between formulation batches with the NANOme®

Note: Number of batches estimated assuming 24-hour operations.

\*from individual doses with bag fills of 30ml (sufficient for QC & therapeutic dose), to 100.000 batch size in saRNA approaches with fully filled bag and payload of up to 600mg RNA



### **EFFORTLESS LARGE-SCALE GMP STERILE BATCHES**

Our fully automated large scale NANOUs® system for continuous aseptic manufacturing takes GMP production to a new level

### **FULLY CLOSED AUTOMATED SYSTEM FOR LARGE BATCHES**

Integrated in-process controls and built-in aseptic process conditions enable time savings and ensure high product quality even at multi-liter volumes (throughput up to 1200 mL/min).

### **CUSTOMIZABLE TO YOUR MANUFACTURING NEEDS**

NANOUs® system features such as CIP/SIP, PAT and temperature control can be fully customized to serve your manufacturing process requirements.



## LEON SERVICES

### Process development and optimisation

Our experienced team of scientists can support you with your process development needs using the FR-JET® modular mixer and LEON systems.

### Equipment demo and training

Experience our technology firsthand with a personalized equipment demo. See how our solutions can integrate seamlessly into your processes and drive tangible results.

### Technical support

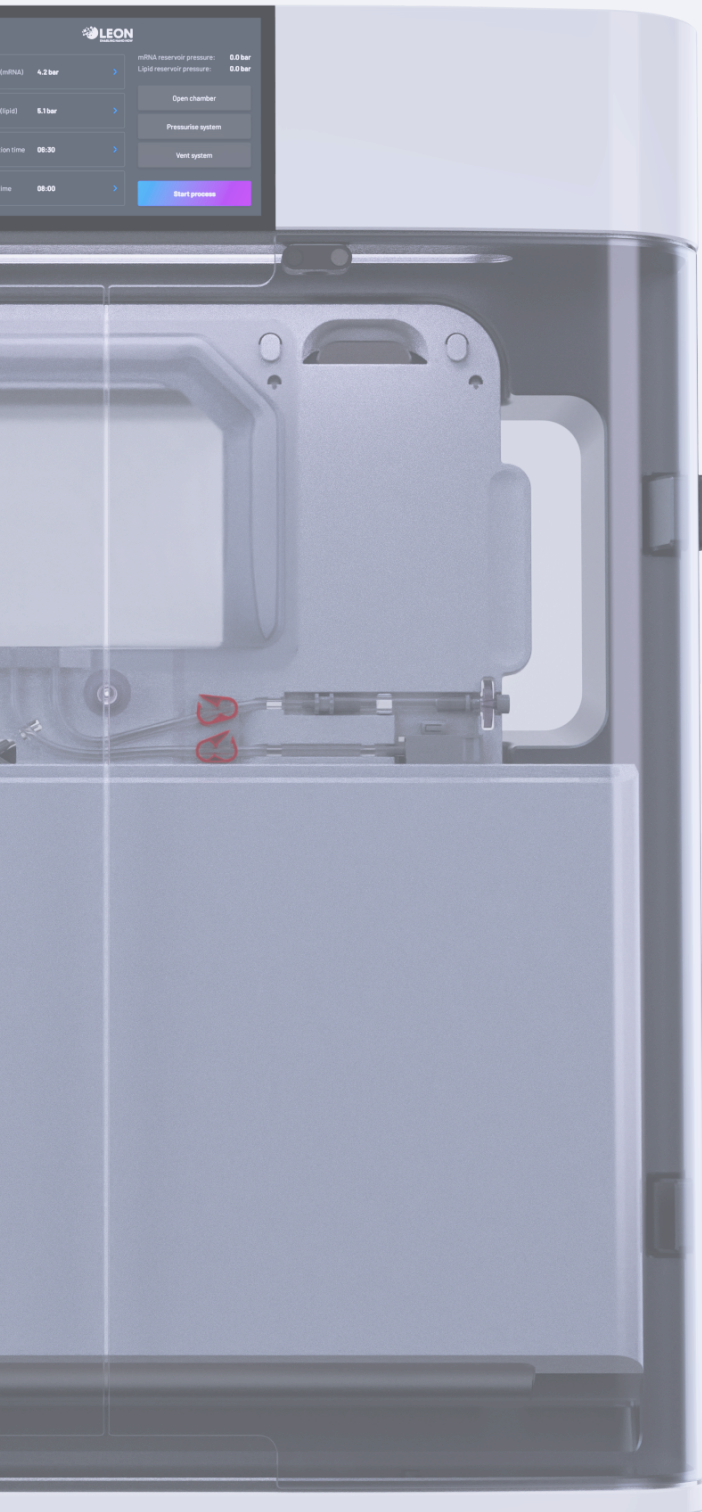
Our team of experts is here to provide comprehensive technical support throughout the collaboration process, ensuring a smooth integration of our technology into your operations.

## COMMERCIAL OPTIONS

Looking to test, evaluate, rent, or buy? LEON offers agile & scalable solutions that align with your goals in advanced nanoparticle manufacturing.



We're open to all types of collaborations with pharma and biotech partners who want to integrate our advanced technology into their processes.



**The complete solution to  
high-quality GMP  
nanoparticle manufacturing**

## **CONTACT US**

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### **FOR GENERAL ENQUIRIES**

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### **VISIT OUR WEBSITE**

[www.leon-nanodrugs.com](http://www.leon-nanodrugs.com)

### **FOR COLLABORATION OPPORTUNITES**

We are inviting industry partners to explore our devices. If you are Interested or would like a demo, please contact:

[request@leon-nanodrugs.com](mailto:request@leon-nanodrugs.com)