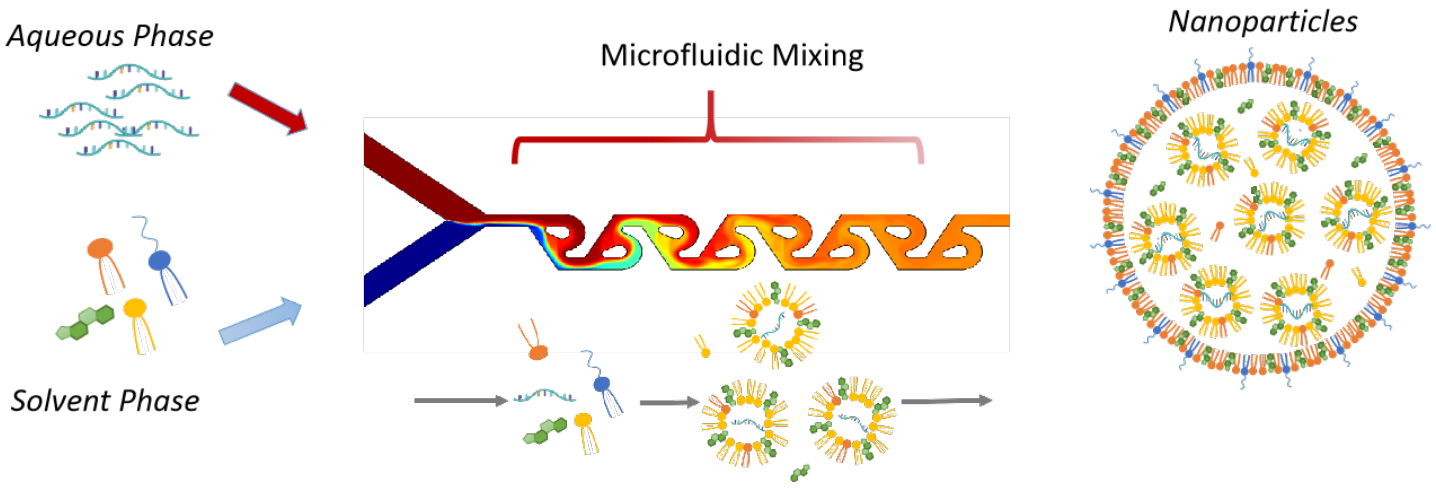
NanoGenerator® cGMP Nanoparticle Synthesis System

PreciGenome

AUG 2025

What are Lipid Nanoparticles?

Lipid nanoparticles (LNPs) are self-assembling structures of natural or synthetic lipids in an aqueous environment.



Cationic/ionizable lipid

Structural lipid

Cholesterol

PEGylated lipid

Nucleic acid payload

RNA-LNP Therapeutics and Vaccines

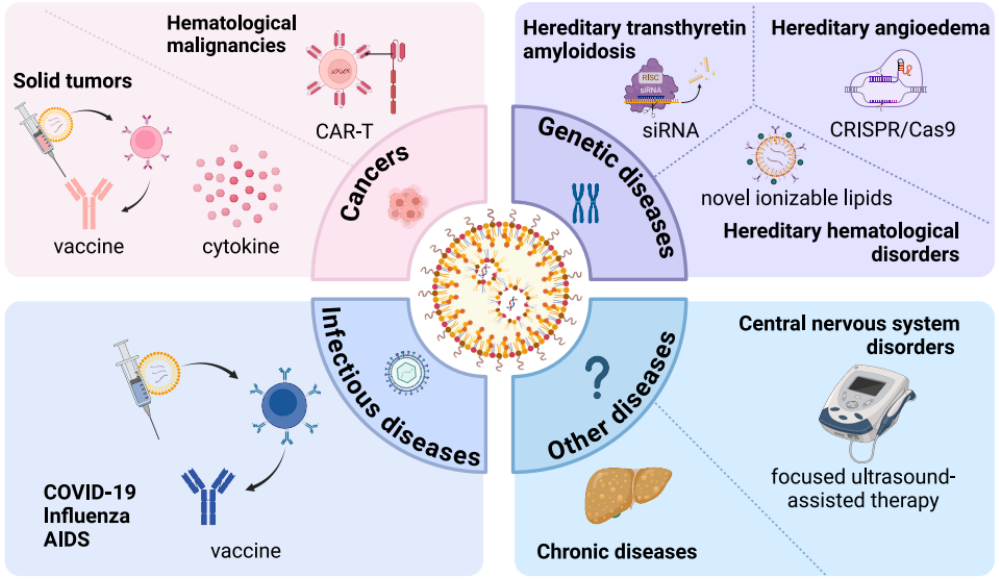


Table 1. Representative mRNA-LNP cancer vaccines in clinical trials

Name	Encoded antigen	Administration route	Condition	Stage	NCT number
BNT112	kallikrein-2, kallikrein-3, acid phosphatase prostate, homeobox B13, and NK3 homeobox 1	i.v.	prostate cancer	phase 1/2 study	NCT04382898[127]
BNT113	HPV-16 oncoproteins E6 and E7	i.v.	head and neck cancer	phase 2 study	NCT04534205[128]
BNT122	up to 20 neoantigens	i.v.	pancreatic cancer	phase 1 study	NCT04161755[125]
mRNA-4157	up to 34 neoantigens	i.m.	non-small cell lung cancer	phase 3 study	NCT06077760[129]
	up to 34 neoantigens	i.m.	melanoma	phase 3 study	NCT05933577[130]
mRNA-5671	4 prevalent *KRAS* mutant antigens	i.m.	tumors with *KRAS* mutation	phase 1 study	NCT03948763[131]

Table 2. Representative mRNA-LNP clinical development for infectious diseases

Drug name	Administration route	Target virus	Stage
mRNA-1273	i.m.	COVID-19	approved
BNT162b2	i.m.		approved
ARCT-154	i.m.		approved
DCVC H1 HA mRNA vaccine	i.m.	H1N1	phase 1 study
H3 mRNA/LNP vaccine	i.m.	H3N2	phase 1 study
mRNA-1769	i.m.	MPXV	phase 1/2 study

Table 3. Representative mRNA-LNP clinical development for gene editing

Name	Gene-editing technology	Administration route	Condition	Stage
NTLA-2001	CRISPR-Cas9	i.v.	hATTR	phase 3 study
NTLA-2002	CRISPR-Cas9	i.v.	HAE	phase 3 study
VERVE-101	base editing	i.v.	HeFH	phase 1 study

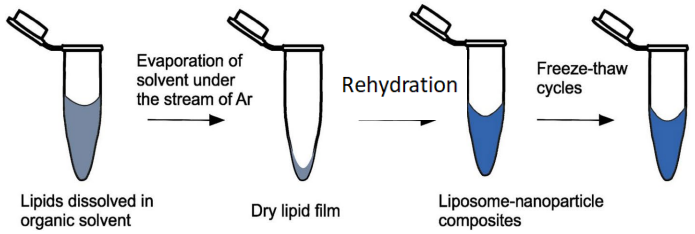
HeFH, heterozygous familial hypercholesterolemia.

Molecular Therapy Methods & Clinical Development. 2025, Volume 33, Issue 2, 101463

Lipid Nanoparticle Synthesis Methods

Conventional Methods

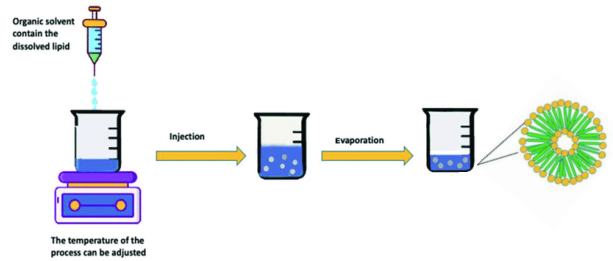
A Film hydration



- Established method
- Versatile method

- High consumption of the organic solvent
- High PDI
- Lack of reproducibility
- Need for additional downsizing step
- Difficulties in scaling-up

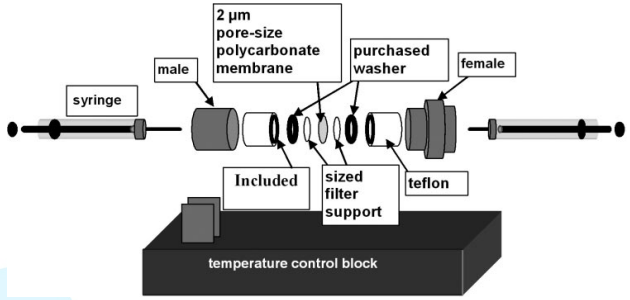
B Solvent injection



- Simple and fast
- Scaling-up possibility
- Controllable

- Exposing to organic solvent
- High PDI
- Stability problem

C Extrusion



- Established method
- Uniform and homogenous formulation

- Possible clogging of the membrane pores
- Difficulties in scaling up

Nanomaterials, Volume 11, 2021, 3440

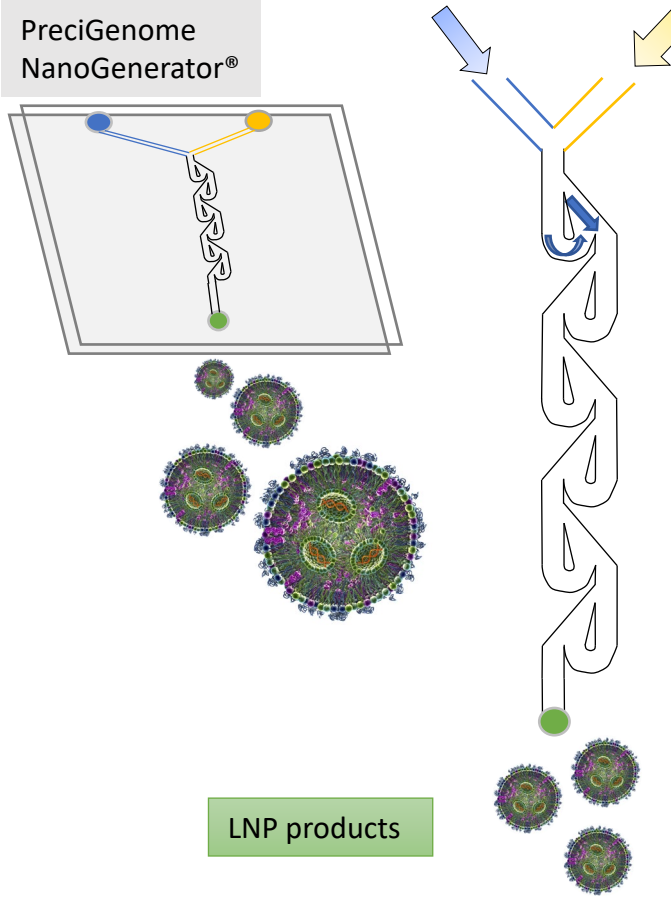
VS.

Microfluidic Mixing

Aqueous phase: DNA, mRNA, protein

Organic Phase: Lipids

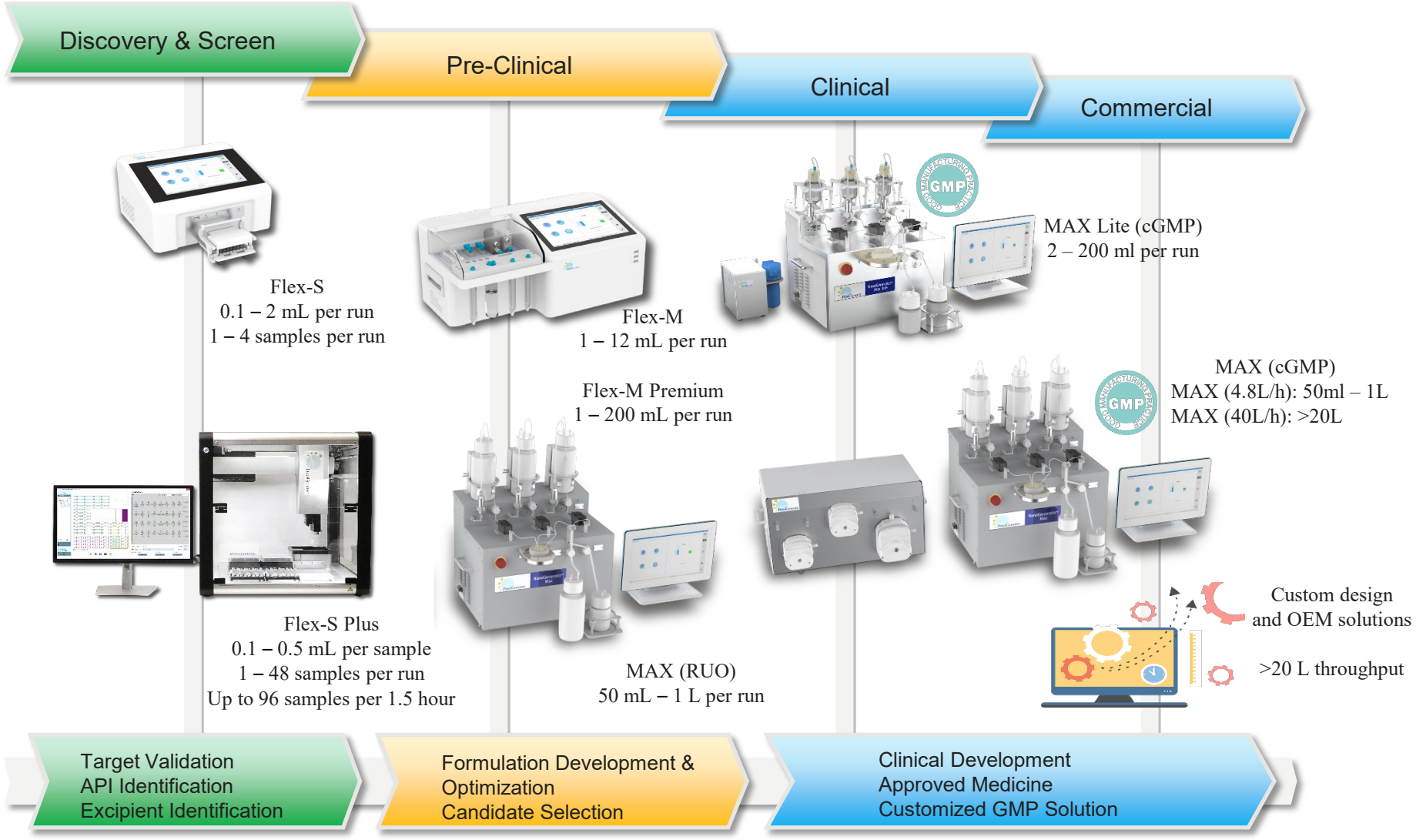
PreciGenome NanoGenerator®



- Low PDI
- Fast & Scalable
- Reproducibility
- Controllable
- Low cost

- Complex fabrication
- Potential clogging

NanoGenerator® - Nanoparticle Synthesis System



Scalable LNP Production

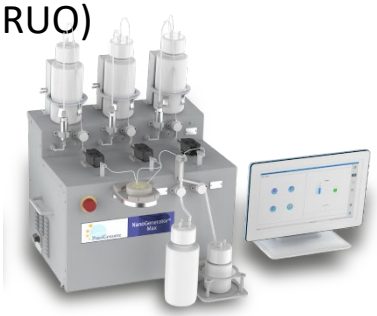
NanoGenerator® Flex-S/Flex-S Plus

Early Screening
0.1 – 2 mL (Flex-S)
0.1 – 0.5 mL (Flex-S Plus)

NanoGenerator® Flex-M/Flex-M Premium

Small/Medium Production
1 – 12 mL (Flex-M)
1 – 200 mL (Flex-M Premium)

NanoGenerator® MAX (RUO)



Large production
50 mL – 1 L
Custom design for larger volume

cGMP solutions

NanoGenerator® MAX Lite (cGMP)

Small/Medium Production
2 – 200 mL

NanoGenerator® Max (cGMP)

Commercial Production
50 mL – 1 L (MAX 4.8L/h);
> 20 L (MAX 40L/h)

OEM

Custom design and OEM solutions
cGMP certified manufacturing
>200 L throughput

NanoGenerator® MAX — Spec

Model	NanoGenerator® MAX Lite	NanoGenerator® MAX			
		RUO flow kit 4.8 L/h	GMP flow kit 4.8 L/h	RUO flow kit 40 L/h	GMP flow kit 40 L/h
cGMP compliance	Yes	N/A	Yes	N/A	Yes
Software (21 CFR Part 11 compliant)	Yes	Optional	Yes	Optional	Yes
Throughput	2 – 200 ml	50 ml – 1 L		> 20 L	
Total flow rate	10 – 24 ml/min	1.2 – 4.8 L/h		Up to 40 L/h	
Flow rate ratio	1:1 – 9:1	1:1 – 9:1		1:1 – 5:1	
Inline dilution	1:1 – 5:1				
Size range	40 – 200 nm				
PDI	0.05 – 0.2				
Encapsulation efficiency	Up to 99%				
Payload	DNA, mRNA, siRNA, protein, small molecules, etc.				
Dimension (L × W × H)	420 × 300 × 300 mm	620 × 380 × 430 mm			
Weight	35 Kg	50 Kg		65 Kg	

NanoGenerator® Max Lite — Intro

- The NanoGenerator® Max Lite (cGMP) is designed for clinical and commercial production, especially for early phase clinical study and personalized medicine study.
- Disposable consumables: all wet materials are disposable (but can be reused if needed)
- Synthesizing volume: 2 – 200 ml
- Total flow rate up to 24 ml/min
- Flow rate ratio: 1:1 – 9:1
- Inline dilution ratio: 1:1 – 5:1

NanoGenerator® MAX — Intro

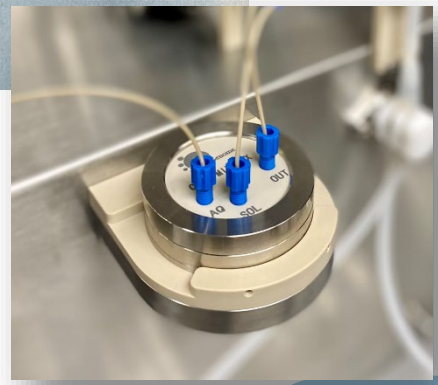
- The NanoGenerator® Max is designed for clinical and commercial production.
  - RUO: Preclinical applications
  - cGMP: Clinical and commercial production
- Two flow kits are available with different supported throughput:
  - 4.8 L/h flow kit: 50 mL – 1 L
  - 40 L/h flow kit: >20 L (cGMP version only)
- 40L/h flow kit allows continuous synthesis mode.
- With the accessory (pump system), pump system can fill raw materials to the sample bottles to prevent the raw material run out

NanoGenerator® MAX — Contents

Instrument:

- Pneumatic system
- Valves
- Flow rate sensors
- Consumable kit
- Monitor (optional)
- Pumps (optional)

Consumable Kit:
(Sterilized, Nuclease free, pre-assembled)

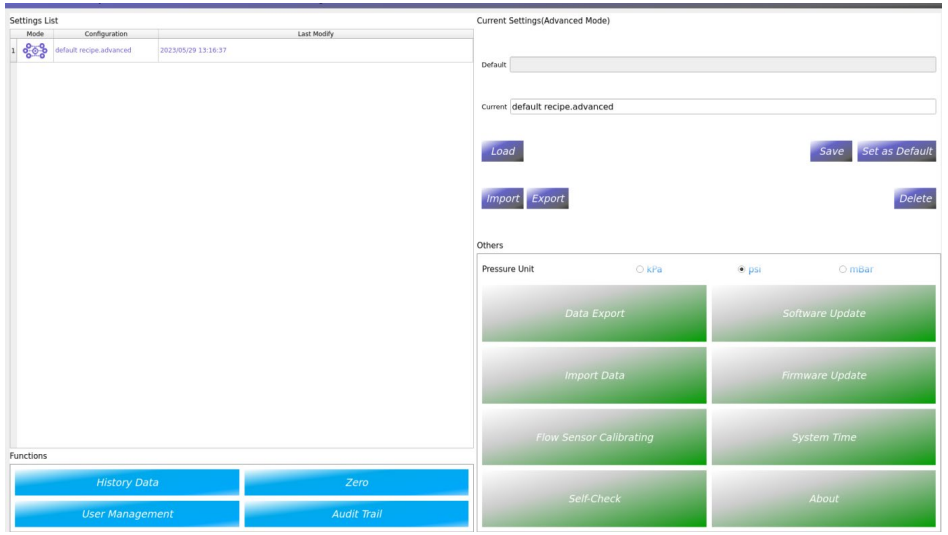


- Sample bottle (aqueous)
- Sample bottle (solvent)
- Sample bottle (dilution)
- Waste bottle
- Bioprocessing bag (collection)
- Tubing & connectors
- Mixing chip

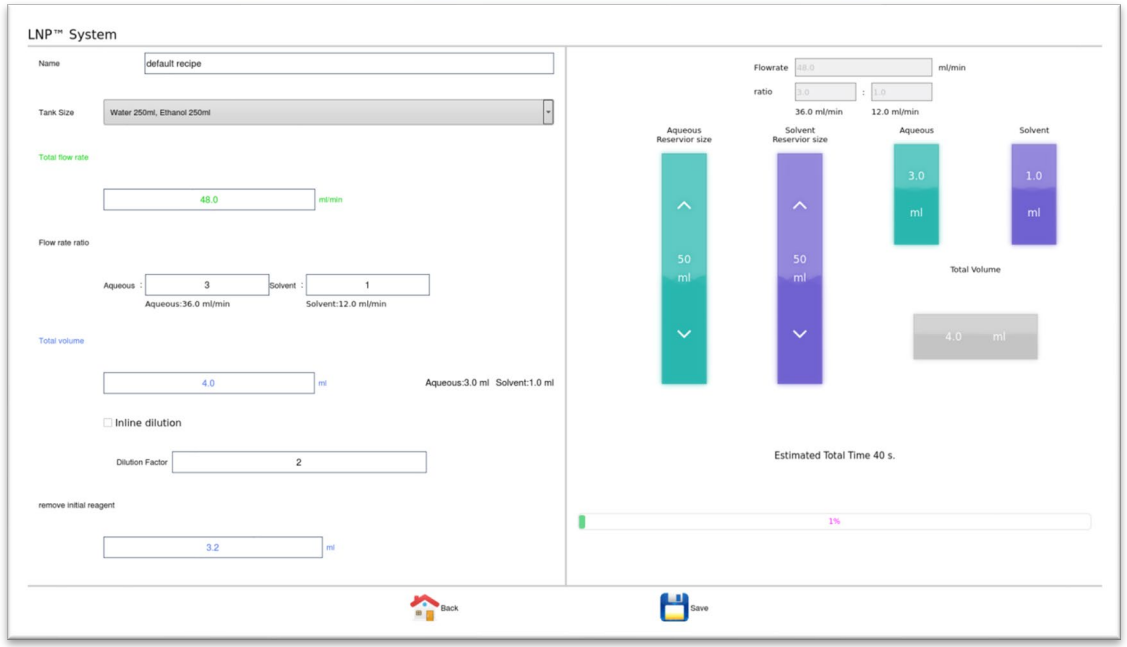
NanoGenerator® MAX — Software

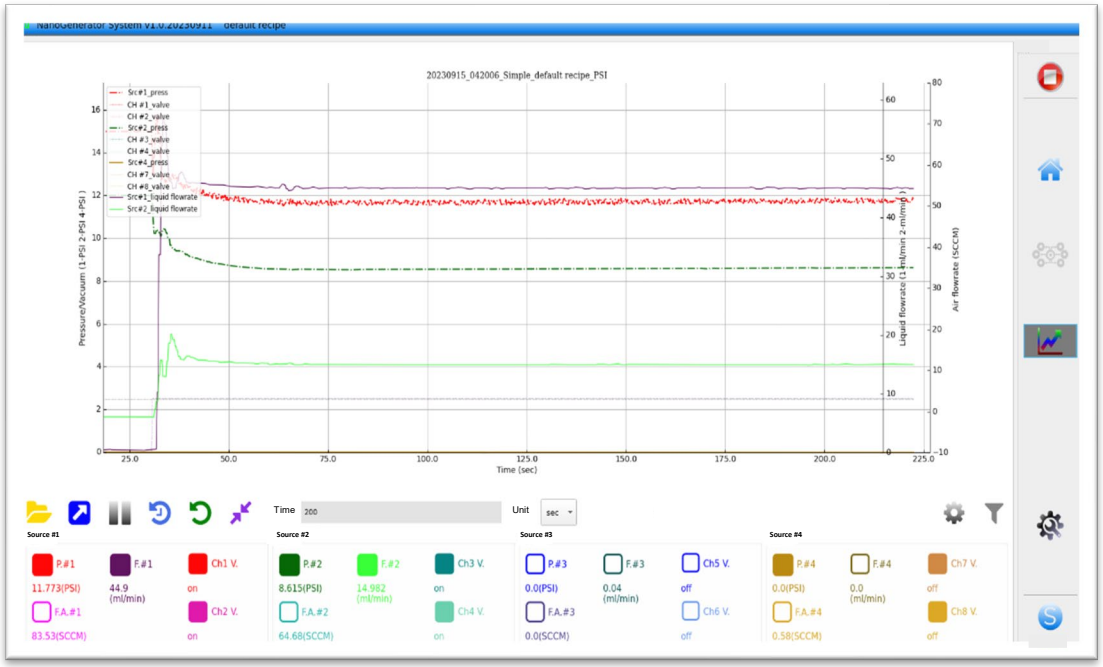
Software (21 CFR Part 11) Features:

- Experimental parameter setting
- Experimental recipe save/load
- Real-time pressure/flow rate chart
- Historic experimental parameter tracking
- Historic pressure/flow rate tracking
- System self-diagnostic system
- Real-time flow rate diagnostic system
- Warning system
- Manual & automatic emergency stop system
- User management
- Audit trail
- Zero flow calibration
- Flow sensor maintenance & re-calibration (Service)



NanoGenerator® MAX — Software





Easy-to-use UI to set parameters including:

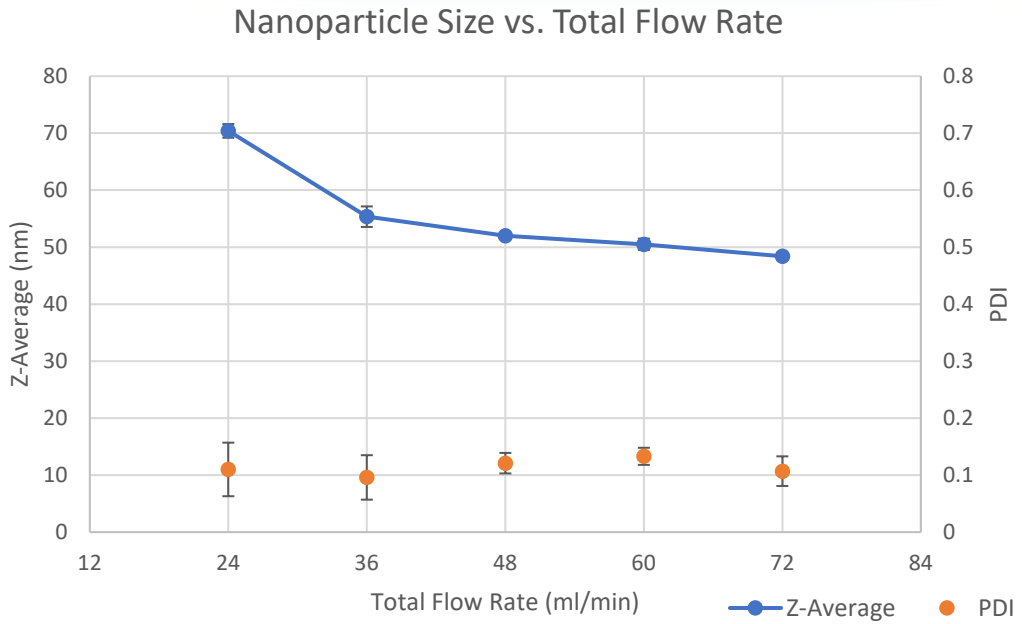
- Total flow rate
- Flow rate ratio
- Production volume
- Inline dilution factor
- Waste volume

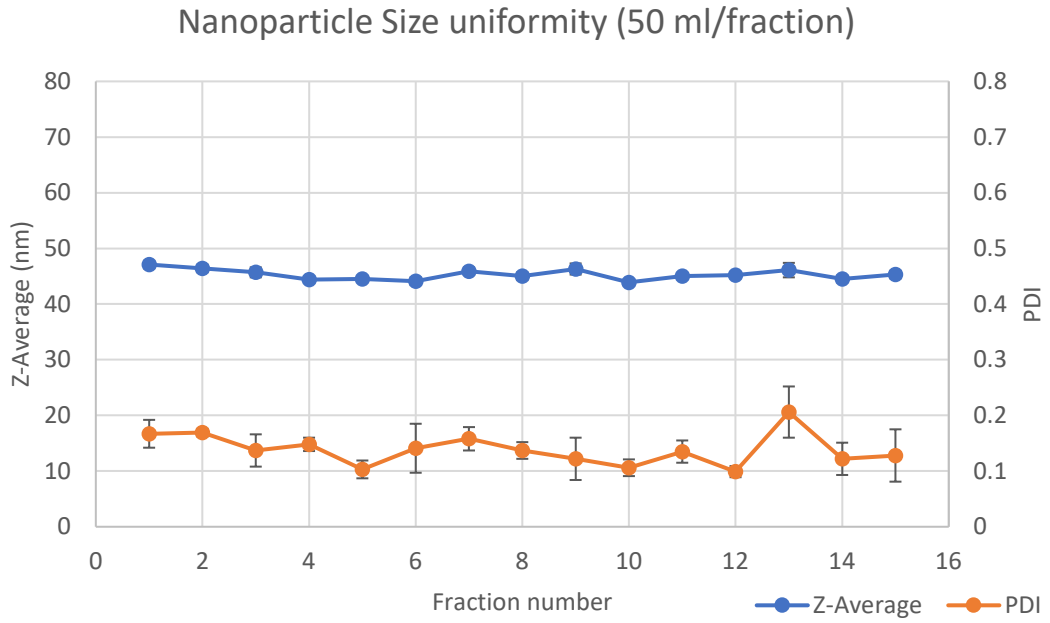
Easy-to-use real-time flow rate /pressure chart including:

- Flow rate
- Pressure
- Air flow rate

All parameters are tracked for aqueous, solvent, and inline dilution lines

NanoGenerator® MAX — Performance





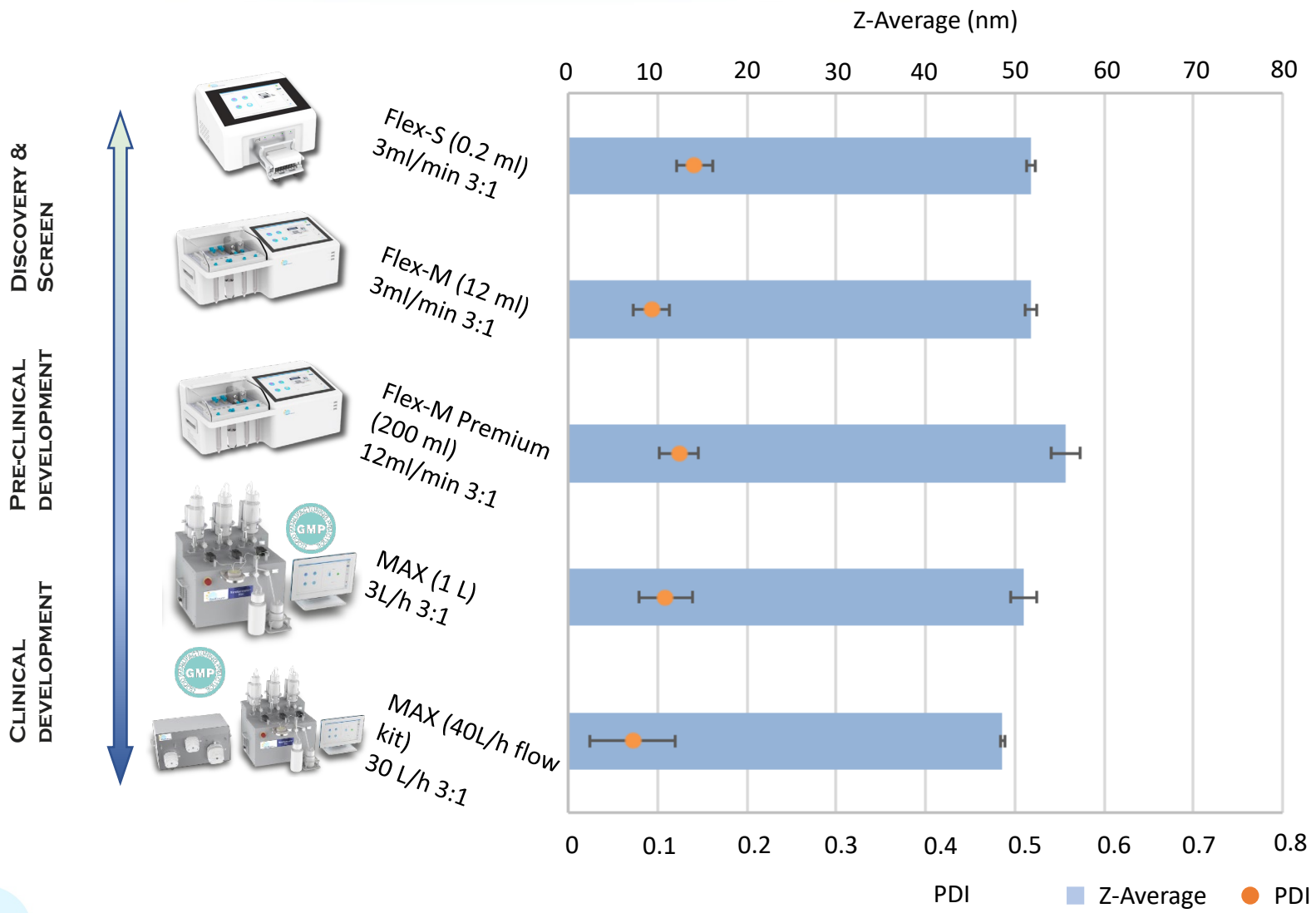
- Nanoparticle size decreases as total flow rate increases
- Size decrease experiences diminishing returns when the flow rate reaches 48 ml/min

	Reagents
Aqueous phase	Sodium acetate buffer (100mM, pH5.2)
Solvent phase	LipidFlex, 15mM in ethanol

- Throughout the entire production run, there is no significant difference in the nanoparticle size and PDI

	Reagents
Aqueous phase	Phosphate-Buffered Saline (1X, pH7.4)
Solvent phase	LipidDemo, 15mM in ethanol

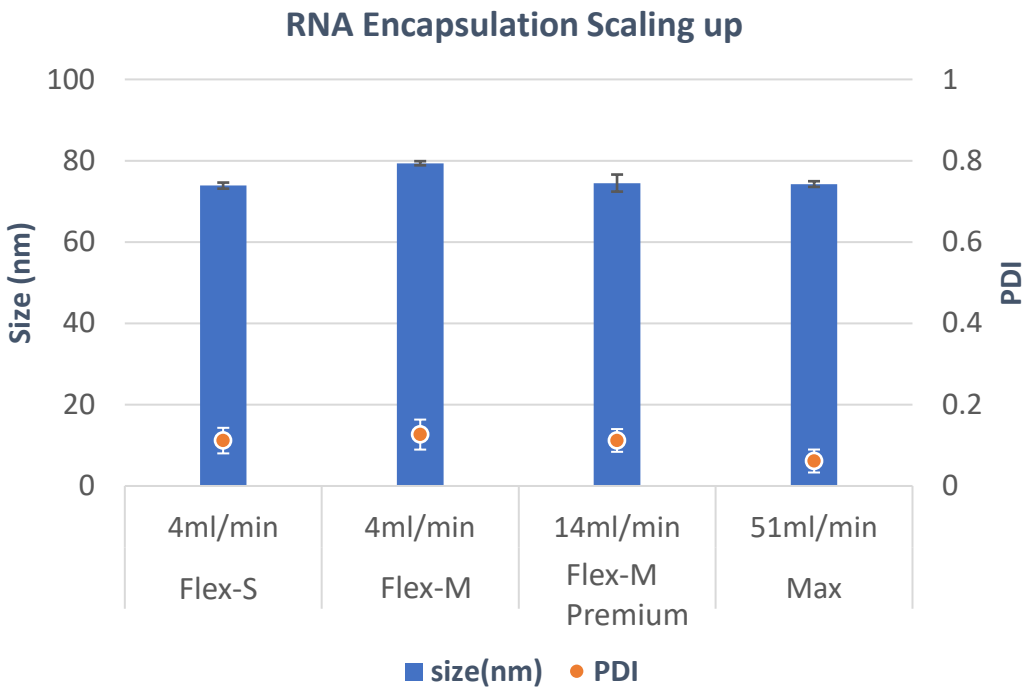
NanoGenerator® — Scale Up

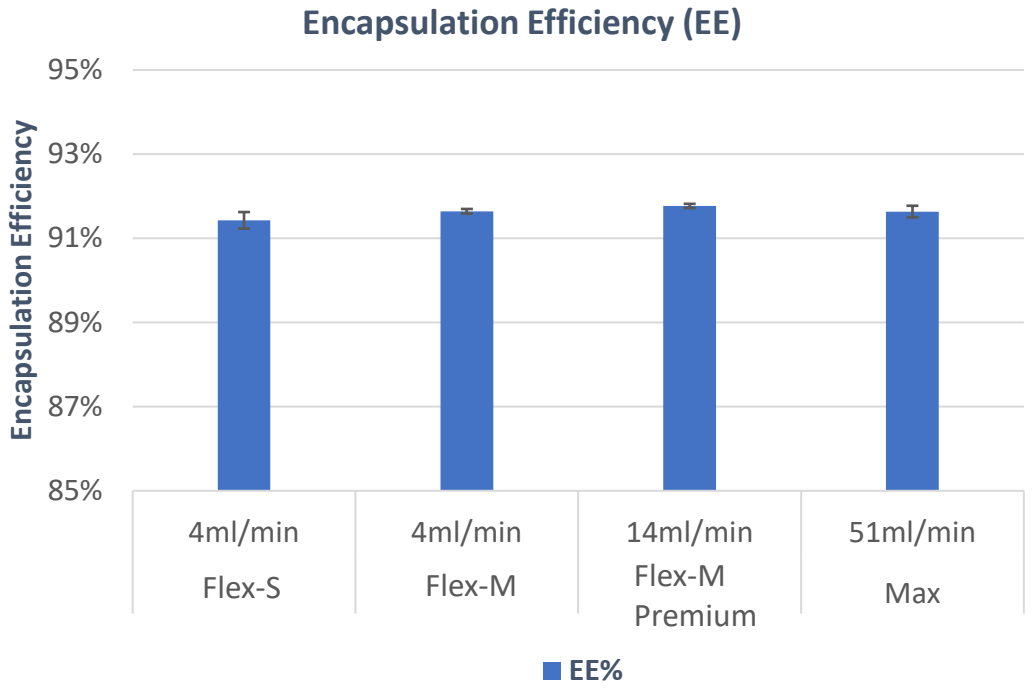


- Nanoparticle size is consistent across different production volumes if using optimal flow rates
- Mixing mechanism is the same for all PreciGenome instruments
- Production can be scaled up from discovery & screening to preclinical & clinical trial production

	Reagents
Aqueous phase	Sodium acetate buffer (100mM, pH5.2)
Solvent phase	LipidFlex, 15mM in ethanol

NanoGenerator® — Scale Up





	Reagents
Aqueous phase	Sodium acetate buffer (100mM, pH5.2)
Payload	RNA (~600 nt)
Solvent phase	LipidFlex RNA-LNP kit

Case Study I: mRNA LNPs for T cell Transfection

eGFP mRNA Lipid Nanoparticles

Z-Average Diameter: 67.3 nm

PDI: 0.106

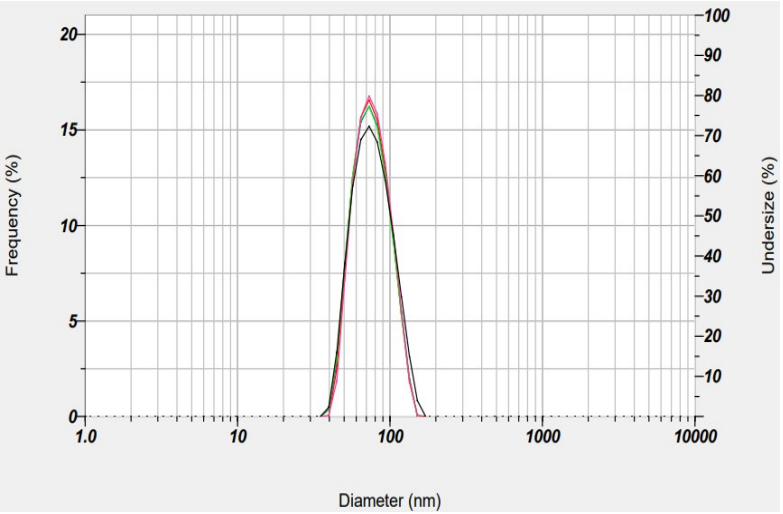


Figure 1. mRNA(eGFP)-LNP Synthesized by NanoGenerator. Average diameter is 67.3 nm. PDI is 0.106. Encapsulation efficiency is 94.5% (Ribo Green RNA Quantification Kit).

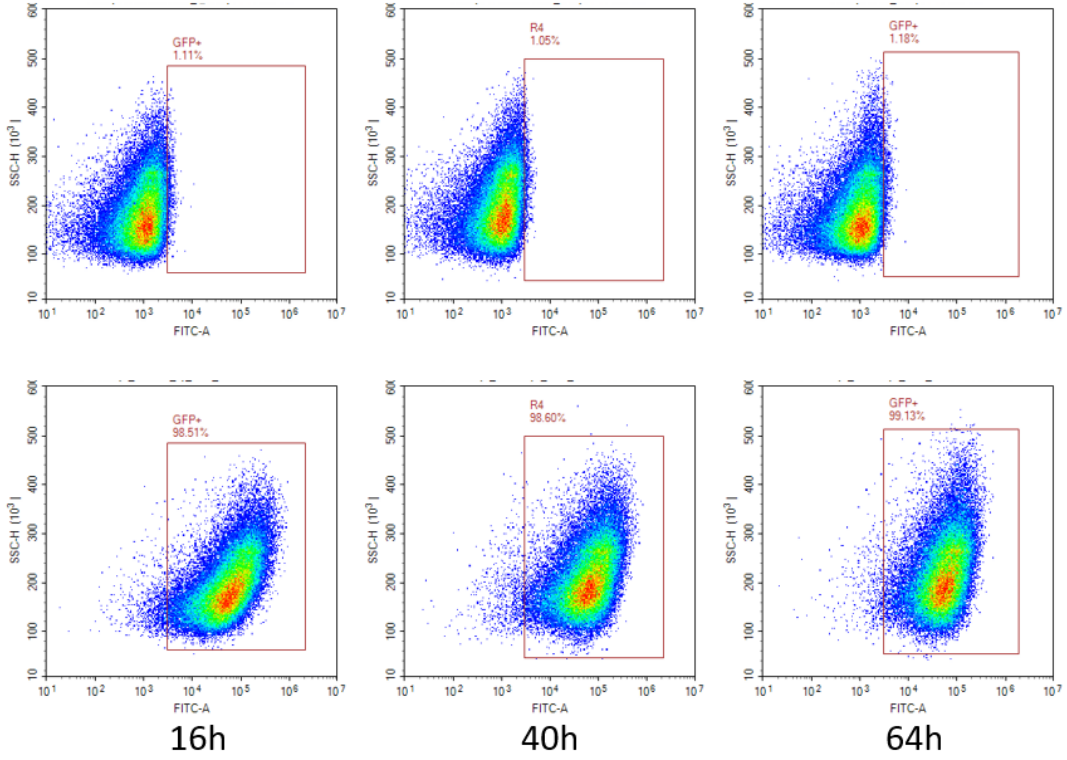
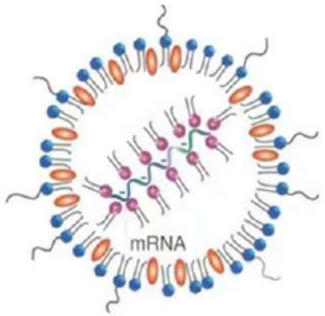


Figure 2. GFP(+) positive population of control (non-treat) and EGFP mRNA LNP treated primary T cells at 16, 40 and 64 hours. Cells were stained (1:50) using Biolegend 7-AAD Viability Staining for 10 minutes. Gating: First select for individual cells (excluding doublets). Then select for the healthy cell population. Then select for viable cells by excluding cells which are positive for 7-AAD. Gate for FitC-A channel (GFP)

Case Study II: Bi-specific Antibody Delivered by mRNA-LNP

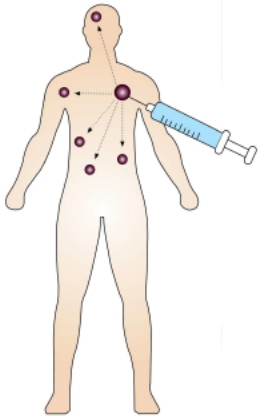


mRNA Encapsulation

In Vitro Transcription of mRNA encoding bispecific antibody & others.

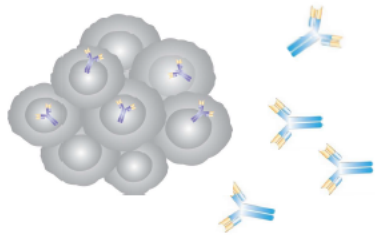
Co-encapsulation or Co-injection with:

Checkpoint Inhibitor: PD-1 ab, PD-L1 ab...
Immunomodulator: CD40, OX40L, CD70...
Chemokine: CXCL2, CXCR1, CXCL9...



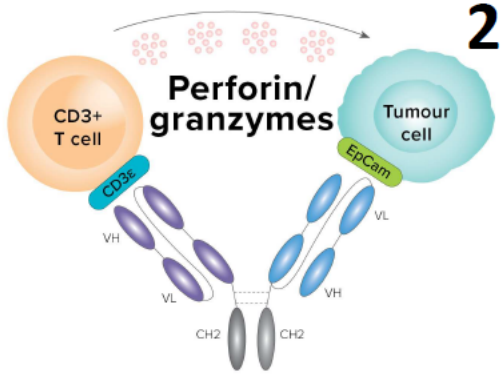
Intra-tumoral injection

What happens post-injection?



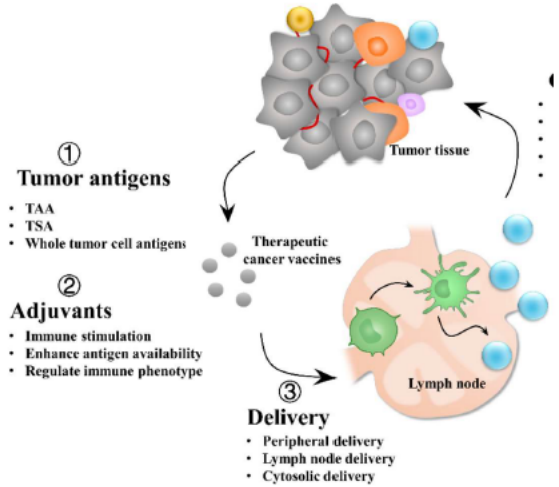
1

Tumor cells translate mRNAs into bispecific antibody and Immuno-mediator (Tumor factory)



2

Antibody + T cell infiltration = Tumor cell lysis (T cell Therapy)

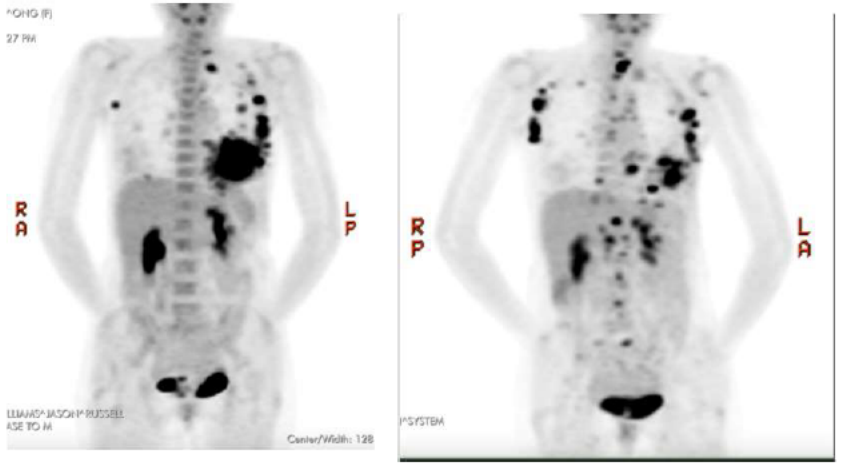


3

Released TAA & Neoantigen from lysate + Immuno-mediator (adjuvant)
= Innate Immune system activation (Tumor vaccine)

Case Study II: Bi-specific Antibody Delivered by mRNA-LNP

Treatment of Two Late-Stage Breast Cancer Cases



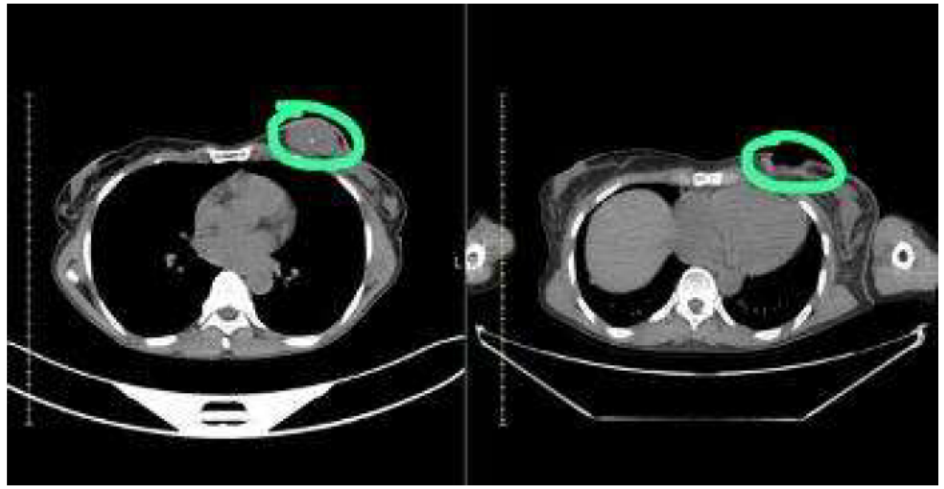
PET-CT 12/14/2023
Pre-treatment

PET-CT 6/18/2024
Post-treatment

Unresectable breast cancer with skin lesion

Case 1 Three photos

1. Appearance before treatment
2. Considerable change in appearance on skin lesions after first treatment
3. Continued improvement on skin lesions after two treatments



4/1/2024 Baseline

4/22/2024 After one Injection

Triple negative breast cancer

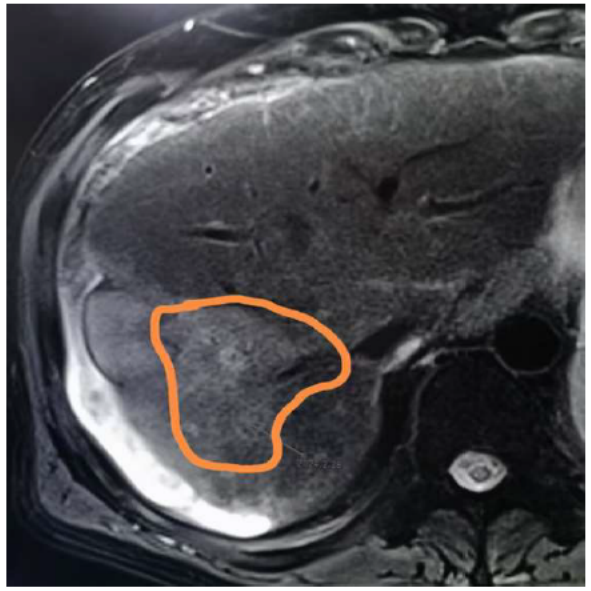
Case 2

Left: CT scan showing a stage 3 invasive ductal carcinoma that did not respond to prior immunotherapy

Right: After one treatment, the tumor has dramatically resolved.

Case Study II: Bi-specific Antibody Delivered by mRNA-LNP

Cholangiocarcinoma with Liver Metastasis



02/28/2024 after one injection

07/24/2024, after four injections

Case Information: A 45-year-old male patient, HBsAg positive for over 2 years, presented with intrahepatic lesions and abdominal distension. A recent CT scan revealed a large abnormal density in the liver's right lobe, enlarged abdominal lymph nodes, and a portal vein defect, indicating hepatocellular carcinoma with lymph node metastasis and portal vein cancer thrombosis. The patient's liver function was Child-Pugh grade A with some blood count abnormalities.

The posttreatment CT scan showed dramatic shrink of the intrahepatic cholangiocarcinoma after four intratumoral injections of the EpCAM-CD3-Fc+IM-1+IM-2 cocktail mRNA-LNP. The Patient requested more injections on 9/12/2024

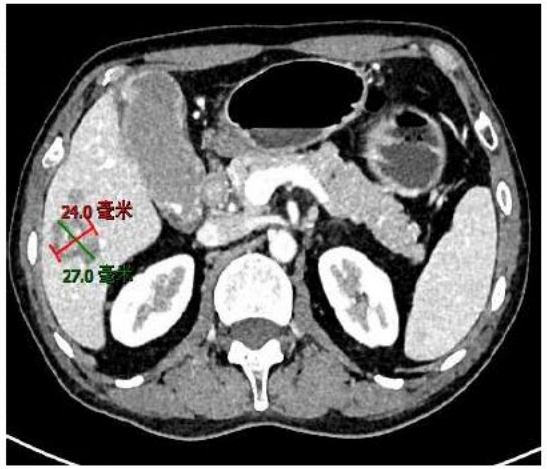
Case Study II: Bi-specific Antibody Delivered by mRNA-LNP

Liver Metastases from Colorectal Cancer

Lesion 1

37.0 x 28.0 mm

3/25/2024



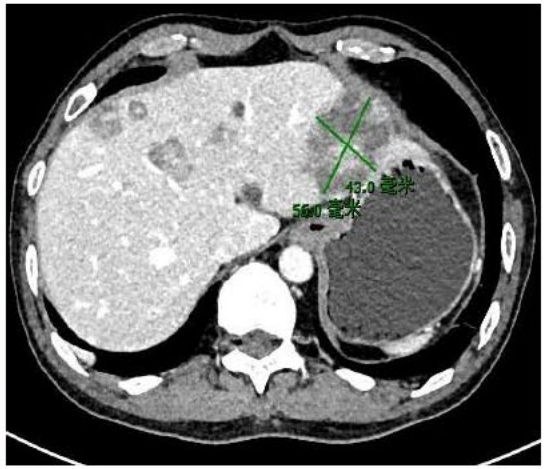
27.0 x 24.0 mm

4/27/2024

Lesion 2

70.0 x 60.0 mm

3/25/2024



56.0 x 43.0 mm

4/27/2024

The enhanced CT scan of the upper abdomen showed that the intrahepatic tumor had shrunk

Why PreciGenome?

High Performance & Efficiency

- Tunable size (40-200 nm)
- Low PDI (0.05-0.2)
- High encapsulation efficiency

Open Platform

- Upgradable system
- Transferable microfluidic chips

Scalable Throughput

- Low volume for screening (Flex-S)
- Medium volume production (Flex-M)
- High volume production (Pro, MAX-GMP)

Simple Operation

- Simple setup
- Compact size
- Intuitive UI w/ touchscreen

Cost Effective

- Affordable configuration
- Lower cost per run

Custom Support

- Demo, Training and Support
- Extended Warranty
- Hot swap option
- Local US company

Appendix I

- **Manual**
- **Standard Operation Procedure (SOP)**
- **Warranty (1 year)**
- **Documentation related to cGMP compliance (cGMP version)**
  - ✓ Installation qualification, operational qualification, performance qualification
  - ✓ Report of consumable items
  - ✓ Chemical compatibility report of consumable items
  - ✓ Report of endotoxin test
  - ✓ Report of RNase/DNase free test
  - ✓ Report of sterilization test
  - ✓ Report of ethylene oxide residue test
  - ✓ 21 CFR Part 11 report
  - ✓ Electromagnetic compatibility report
  - ✓ Report of safety regulations
  - ✓ Other reports by requesting

Appendix II

PurePower Medical — Suzhou Purepower Medical Technology Co.,Ltd

Sterility Test Report

No.: QT/QG/Q01-01

Product Name	GMP Consumable Bag	Type	Sample	Lot No.	Sample
Sample ID.	1. 2. 3. 4	Sterilization Lot No.	2023.07.22.01	Test Date	2023.07.24
Inoculation Method	☐Membra ☑Direct In				
FTM Lot No.	FTM-2307.24				
TSB Lot No.	TSB-2307.24				
Positive Strain	Staphylococcus aureus				

Test Result:

Culture Medium	Sample ID.	1	2
FTM 30～35℃	1	–	–
	2	–	–
	3	–	–
	Positive: 4	+	+
	Negative	–	–
TSB 20～25℃	1	–	–
	2	–	–
	3	–	–
	Negative	–	–

Incubation Temperature (℃)	33
Dish No. / Incubation Time	1
24h	
48h	
Average	

Conclusion: ☑Con

Remark: /

Notice:Put the "√" in the "□", in the "Re

Tested by/Date: Y. Yuwen 2023

PurePower Medical — Suzhou Purepower Medical Technology Co.,Ltd

EO Residual Test Report

No.: QT/QG/Q04-02 No.: 8.2023.0731-01

Sample Name	GM
Lot No.	
Sample No.	
Test Date	2

Test Reference :

JL-QG/Q04 EO Residual T

Item	
Sample1	
Sample2	
Sample3	
Conclusion	
Remark	/

Tested by/Date: Yu Yu

CTI PHARMA

Extractables Test Report

Report title	The Extractables Study Report of Nanoparticle Synthesis System Consumables Kit
Report number	EL-REP-23-019.01-E
Project No.	N/A
Customer	PreciGenome LLC
Address	2176 Ringwood Ave. San Jose, CA, 95131, USA
Testing laboratory	Centre Testing International Pinchuang (Shanghai) Co., Ltd.
Testing laboratory address	1351 Wanfang Road, Minhang District, Shanghai

Underwriters Laboratories (UL LLC)
IEC/EN Safety Report

UL Solutions

Model:
Device Description:
Applicant:
Manufacturer:
Manufacturing Facility(ies):
Report No.:
Report (Re)Issue Date:
Base Standard(s):
Additional Standards:
Report Types:

This report covers the Sa
above.

Test Report issued under the responsibility of:

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Report Number .....:
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Test specification:
Standard.....:
Test procedure .....:
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No: 4790895205-2.1-S1
Issue Date:2023-08-26

Statement of Compliance

Project No.:	4790895205-2.1
Applicant:	PreciGenome LLC
Address of Applicant:	2176 Ringwood Ave, San Jose, CA, 95131, USA
Product Description:	NanoGenerator™ Max Nanoparticle Synthesis System
Model No.:	PG-SYN-G
Test Standard:	EN IEC 61326-1:2021
Test Report Number(s):	4790895205-2.1-1

This verification of EMC Compliance has been granted to the applicant based on the results of the tests, performed by laboratory of UL-CCIC Company Ltd. on the sample of the above-mentioned product in accordance with the provisions of the relevant specific standards and Directive 2014/30/EU. The CE mark as shown below can be used, under the responsibility of the manufacturer, after completion of an EC Declaration of Conformity and compliance with all relevant EC Directives.

CE

Leon Wu

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