ST PHARM

What's the next round of mRNA platform technology after COVID-19 pandemic world?

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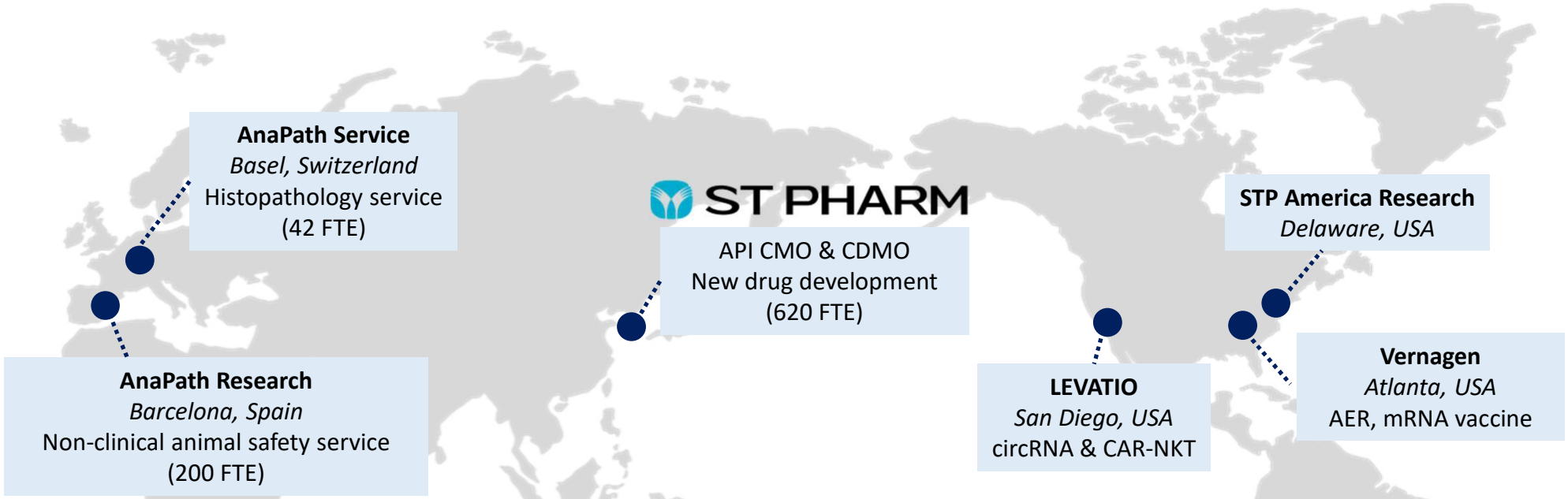
Share holder of ST PHARM. Co., Ltd.

ST PHARM Family



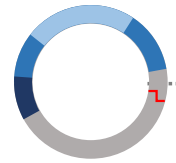
Total > 850 FTE

Gene therapy CDMO business from oligonucleotide to xRNA
Seamless development from manufacturing to non-clinical CRO service

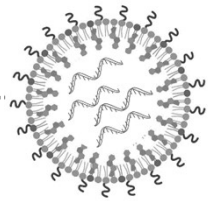
Evolution of STP's mRNA Platform Technology

Stage 1	Stage 2	Stage 3
Developing core mRNA technology and COVID-19 mRNA vaccine	**Establishing mRNA GMP manufacturing and One-stop CDMO service**	**Preparing the emerging infectious disease and Expanding to the next round**
▪ **Initiated mRNA platform in 2018** ▪ **5' Cap analog** - SmartCap® - Capping Library Screening (>30) ▪ **Lipid nanoparticle (LNP) DDS** - SMARTLNP®, STLNP® - Genevant LNP ▪ **In-house COVID-19 mRNA vaccine** - STP2104: Ancestral strain vaccine - STP2152: Omicron strain vaccine - STP2250 & 2260: Pan-coronavirus vaccine	▪ **mRNA GMP manufacturing facility** - Completed mid-scale (May 2021) - Large-scale under construction (1Q 2023) ▪ **GMP production of key raw materials** - 5' Caps (kg/yr) - Ionizable & PEG-lipids in LNP (MT/yr) ▪ **One-stop mRNA CDMO service** - From R&D: Asset development - To IND-enabling package: AMD, CMC, etc.	▪ **Expedite-100 Days Strategy** - Rapid development of mRNA vaccine against diverse infectious disease within 100 days - Collaborations with Vernagen ▪ **Beyond COVID-19 pandemic world** - Expanding to new indications (cancer, autoimmune disease) - Planting new modality (circRNA, CAR-NKT) - Collaborations with Levatio Therapeutics

ST PHARM's mRNA Platform Technology



Plasmid DNA



LNP-mRNA

IVT Synthesis

- In-house codon optimization
- **Ample experience in IVT optimization**

SmartCap®

- Novel 5'-capping reagent, **SmartCap®**
- **Capping library screening** to select the best capping analog

DDS

- LNP-encapsulated mRNA
- **LNP screening - SmartLNP®, STLNP®**
- Lipoplex, polyplex, etc.

Downstream

- Leveraging oligo-purification know-hows to LNP-mRNA

CMC & Regulatory	▪ Analytical and biophysical characterization & analytical method development ▪ Regulatory SOP & guideline preparation
GMP Manufacturing	▪ Strong track record of nucleotide /oligonucleotide GMP manufacturer ▪ All steps controlled under GMP conditions

SmartCap® & Capping Library Screening

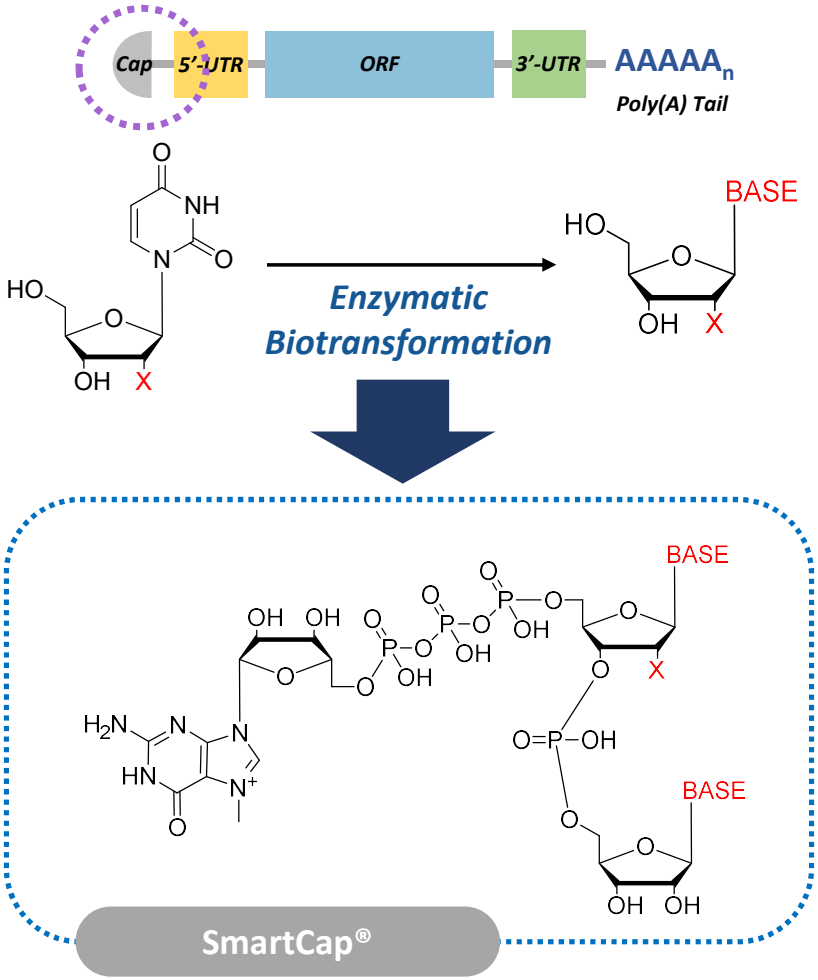
From Nucleoside to 5'-Capping Reagent

SmartCap®

- In-house 5'-capping analogs (ca. 30) with different ribose and base combination
- Utilizing the know-hows & experience from oligonucleotide RSM synthesis
- Strong IP position
- **Updating stability data**
  → Both powder and solution form are stable at room temperature (> 12 months)

Capping Library Screening (CLS)

- Screening capping library to identify the most suitable 5'-cap analog with highest efficiency
- **ORF and/or target-specific screening and selection**



STLNP® & SmartLNP®

From conventional to next generation LNP

- **ST PHARM is running three different LNP platform strategies**

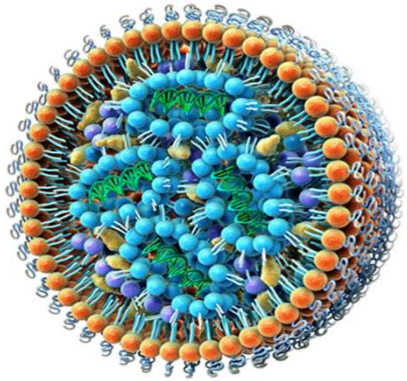


Image Source from *Precision Nanosystems*

In-licensing LNP

- Genevant LNP technology
- Proven, unsurpassed and best LNP technology
- Applied to COVID-19 mRNA vaccine development

STLNP®

- ST PHARM's first generation LNP
- Used for mRNA CDMO business
- Further application to cancer and autoimmune disease vaccines

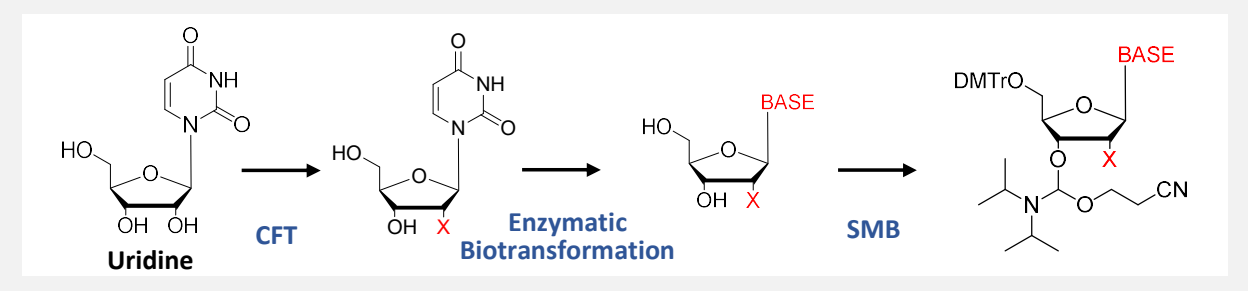
SmartLNP®

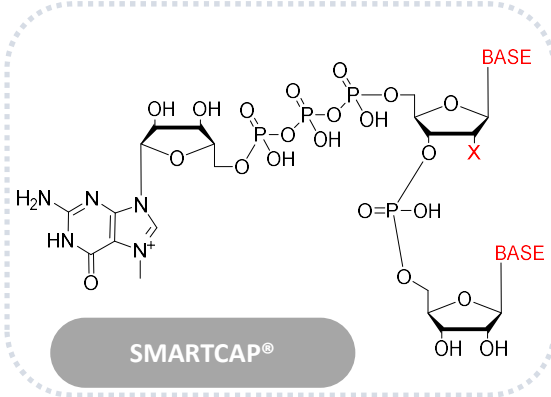
- ST PHARM's next generation LNP
- Developed in collaborations with Ewha U. in KOREA
- Focused in improving immune response

5’ Cap Mass Production

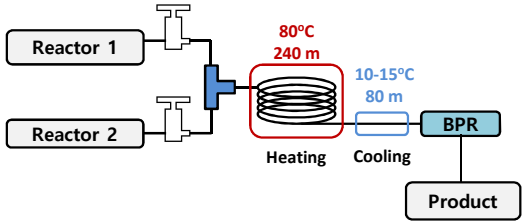
- **Incorporating CFT and SMB technology for capping mass production**: SmartCap® from key raw materials (multi-kgs/yr)
- Mass production available for diverse capping reagents including the key companies’: BioNTech-Pfizer & Moderna
- ***Both non-GMP and GMP-grade intermediate and product available***

- **5’-capping reagent mass production scheme**

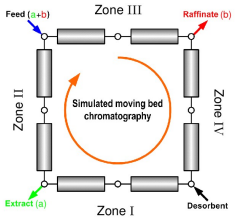




Continuous Flow Technology (CFT)



Simulated Moving Bed (SMB) Technology



Lipids Mass Production

GMP or GMP-like LNP Manufacturing Service

❖ Mass production of lipids in LNP

- RMs are supplied by strategic domestic partners that are reliable, qualified and cost-effective
- ST PHARM is manufacturing both ionizable and PEG-lipid, required for LNP formulation
- Production of key lipids will be available upon client's request (Pfizer, Moderna, Genevant, and etc.)

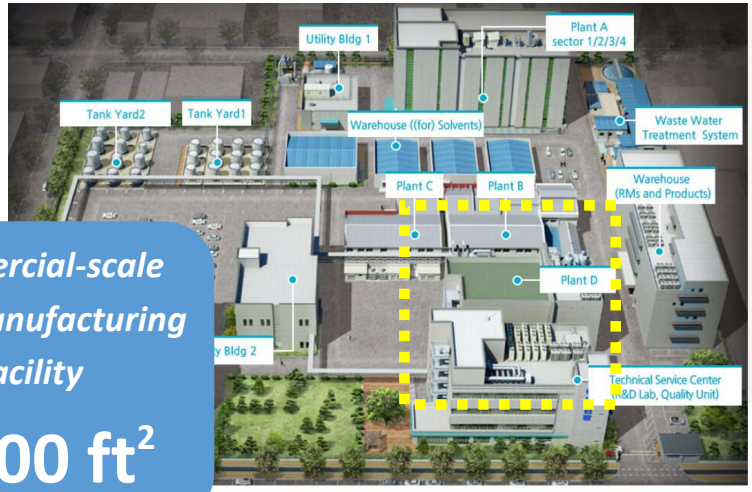
		BioNTech-Pfizer		Moderna	
LNP components	**Ionizable lipid**	ALC-0315	>3 MT/yr*	SM-102	>3 MT/yr*
	PEG lipid	ALC-0159	>1 MT/yr*	PEG2000-DMG	>1 MT/yr*

** ST Pharm's manufacturing capacity in Sihwa campus*

ST PHARM mRNA GMP Facility

mRNA synthesis from milligram to kilogram scale production

1. **R&D and small-scale production (non-GMP)**
   - mRNA Plant (3F): Established in August 2020
   - mRNA R&D and small-scale production for non-clinical animal study
2. **Mid-scale production (GMP)**
   - mRNA Plant (1F & 4F): Expansion for ST PHARM's COVID mRNA vaccine manufacturing in May 2021
   - Production Capacity: Multi-gram/month
3. **Commercial-scale production (GMP)**
   - mRNA Plant (3F-6F): Further expansion of mRNA manufacturing facility equipped with MF system
   - Expected expansion capacity: Multi-kgs/year
   - *Customized or dedicated facility available as per client's request*



Commercial-scale GMP Manufacturing Facility

7,000 ft²

Mid-scale GMP Manufacturing Facility

2,237 ft²

ST PHARM COVID-19 mRNA Vaccines

ST PHARM COVID-19 mRNA vaccine programs

1) **STP2104:** Ancestral strain vaccine*
2) **STP2152:** Omicron strain vaccine
3) **STP2250 & STP2260:** Pan-coronavirus vaccine**

**Supported by Kore Drug Development Fund*

Monovalent COVID-19 vaccines

Moderna vaccine
50ug of S-protein from
"ancestral" (S-type) SARS-CoV-2

Pfizer-BioNTech vaccine
30ug of S-protein from
"ancestral" (S-type) SARS-CoV-2

Bivalent COVID-19 vaccines

Moderna vaccine
25ug of Ancestral (S-type)
25ug of Omicron SARS-CoV-2

Pfizer-BioNTech vaccine
15ug of Ancestral (S-type)
15ug of Omicron SARS-CoV-2

STP pan-coronavirus vaccines**

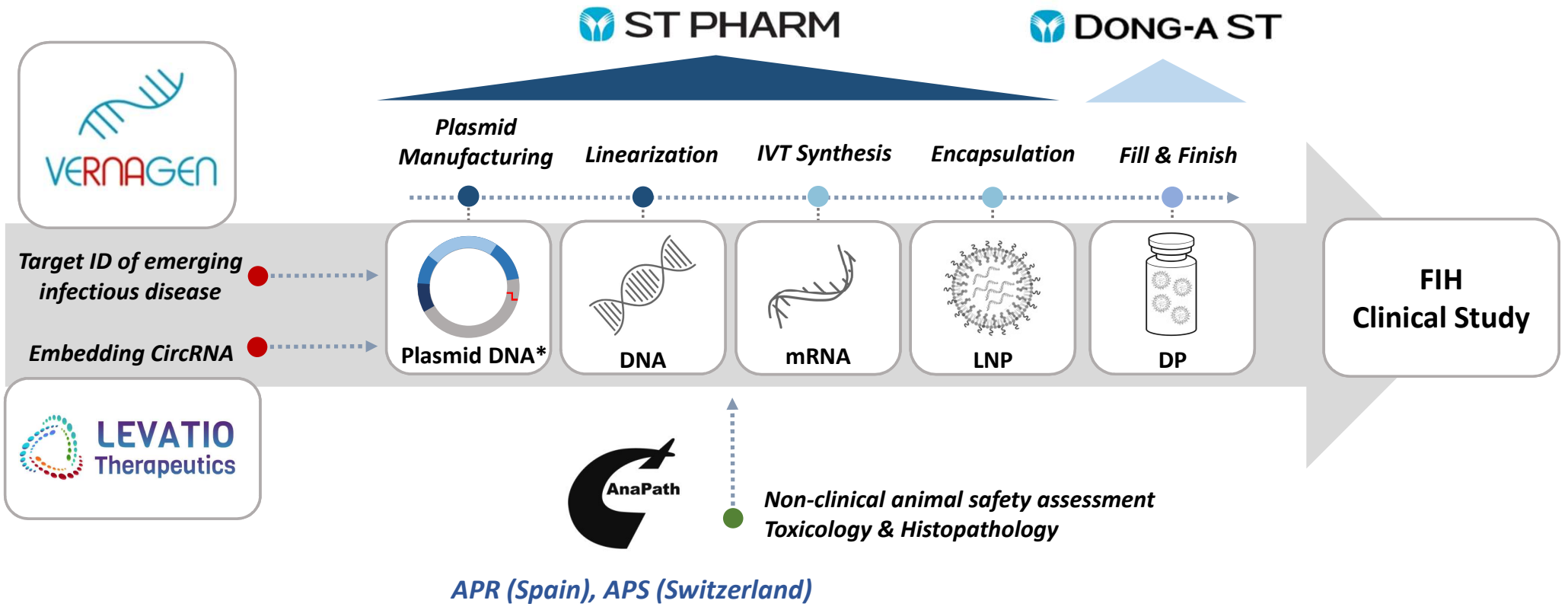
STP2250 vaccine
STP2152 Omicron SARS-CoV-2
STP22137 2nd Ag from SARS-CoV-1 & -2

STP2260 vaccine
STP2104 Ancestral (S-type)
STP2152 Omicron SARS-CoV-2

***Supported by Ministry of Health and Welfare New Infectious Diseases mRNA Project Department*

Pandemic Response: Expedite-100 Days Strategy

Developing xRNA vaccine against emerging infectious disease within 100 days



Pandemic Response: Collaborations with Vernagen

- Located in Atlanta, GA, USA
- Antibody Encoding mRNA (AER) strategy: mRNA-based vaccines for infectious diseases
- Applied ST PHARM mRNA platform technology & LNP-mRNA GMP manufacturing

Target	Collaboration & Co-Development
Varicella Zoster Virus	Emory University, USA
Respiratory Syncytial Virus	Emory University, USA
SFTS Virus	Jeonbuk University, Korea
Nipah Virus	Duke-NUS University (Singapore)
Langya Virus	Duke-NUS University (Singapore)
Heartland Virus	US-Centers for Disease Control and Prevention

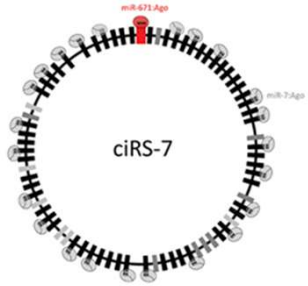
Beyond COVID-19: Collaborations with Levatio

LEVATIO Therapeutics

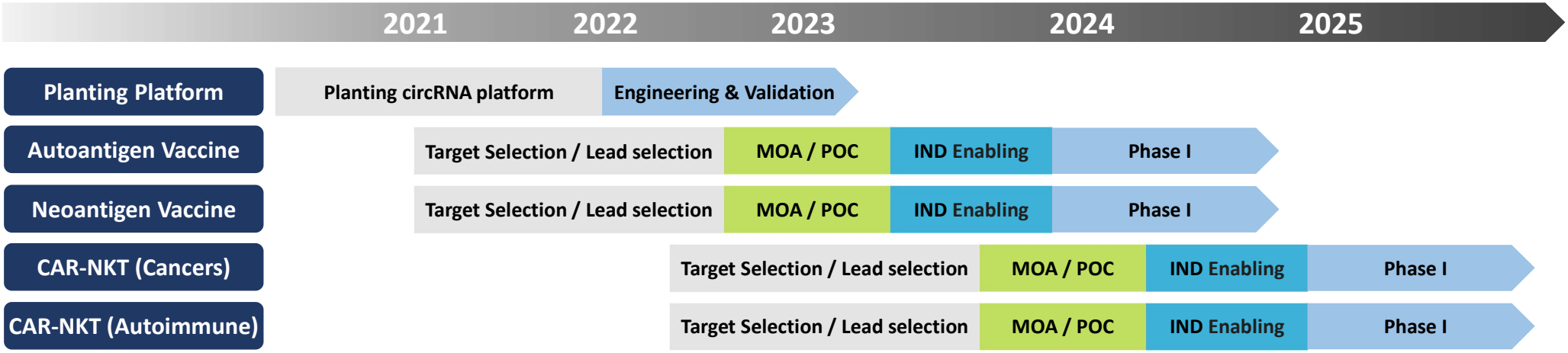
- Located in San Diego, CA, USA
- Building-up circRNA platform technology in Levatio & planting circRNA GMP manufacturing in ST PHARM

RNAbiology

The emerging landscape of circular RNA in life processes, S. Qu and et al, 2016, 992-999



RNAs	Stability	Storage	Purification	Expression	Size
mRNA	X	X	X	X	O
Self-replicating RNA	X	X	X	O	△
CircRNA	O	O	O	O	△



Summary

mRNA CDMO Business

- Manufacturer of key raw materials in GMP or non-GMP standard
- Providing one-stop service from CDMO to non-clinical GLP studies

LNP Technology and Lipid Mass Production

- Genevant LNP
- In-house STLNP®, SmartLNP®
- Mass production of key lipids for LNP formulation – ionizable and PEG-lipids

5’ Cap Technology and Mass Production

- In-house 5’-capping analog, SmartCap®
- Total 30 capping analogs for capping library screening
- Cost effective large-scale production of diverse 5’-capping reagents

Post-COVID Strategy

- Expanding CDMO business of RNA therapeutics through strategic partnerships with various RNA companies
- Building up of xRNA projects through Levatio (circRNA) and Vernagen (mRNA)

Acknowledgements

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- Ewha Women University
- Sogang University
- Catholic University of Korea
- Korea University
- Chungbuk University

ST PHARM family members

:D
WE BELIEVE VISION 2025

감사합니다 Natick Dankon Taing
Grazie Danke Ευχαριστώ Dalu 唔該
Obrigado Thank You köszönöm شكرا
Tack Takk
Спасибо Dank Gracias धन्यवाद
Tak
谢谢 Merci ありがとう Toda
Tesekkür ederim Дякую khop kun
Asante Gratias Shokran cám ơn

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