IR Book | May. 2024

ST PHARM

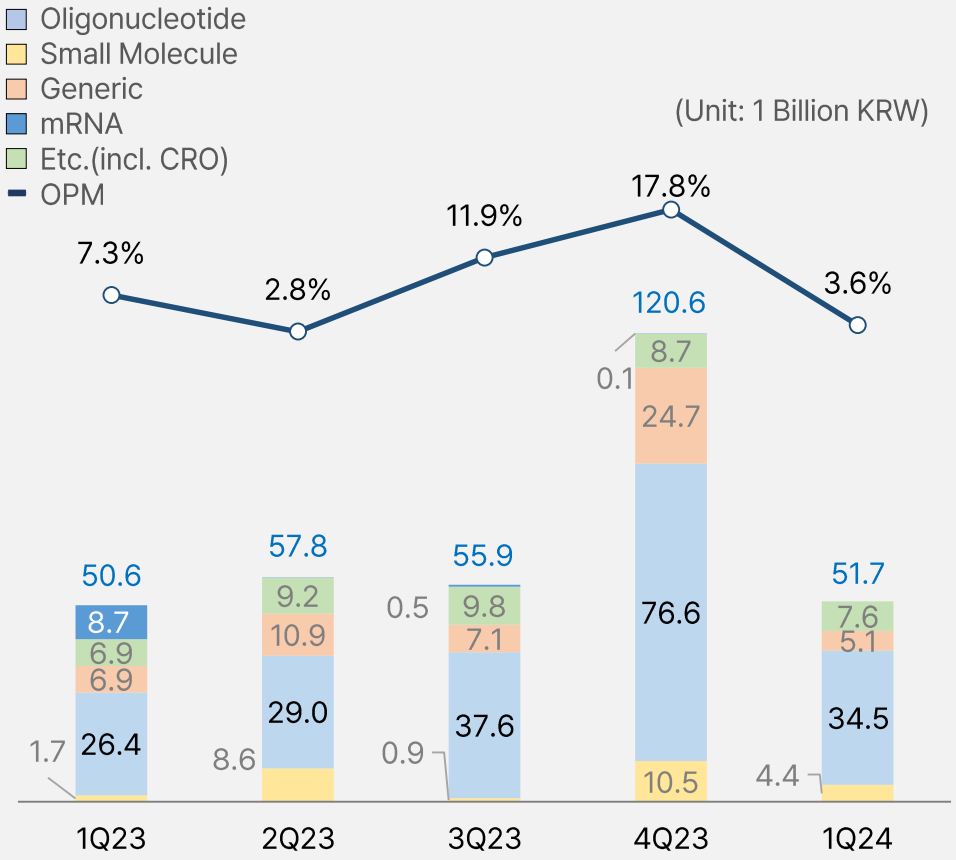
Technology Driven Gene therapy CDMO
From Oligonucleotide to xRNA

Earning Result

2024 1st Quarter Financial Results (Preliminary)

▪ Consolidated Financial Results

5-Quarterly Performance trend



▪ Financial Statement

2024.1Q Revenue
₩ 51.7 Billion, Operating Profit ₩ 1.9 Billion, Net Profit ₩ 5.4 Billion

Continued loss from subsidiaries and absence of mRNA Business sales compared to 2023.1Q were main causes of lower operating profit
Net profit improved as a result from stronger US dollar to Korean Won

Accounts (Unit: 1 Billion KRW)	2023	'23.1Q	'24.1Q	YoY
Revenue	**285.0**	**50.6**	**51.7**	+2.1%
Cost of Goods Sold	172.9	25.6	32.7	+27.8%
Gross Profit	112.1	25.0	19.0	-24.1%
SG & A Expenses	78.6	21.3	17.1	-19.8%
R&D Expenses	30.4	9.4	5.0	-47.4%
Operating Profit	**33.5**	**3.7**	**1.9**	-49.3%
Net Profit	**17.5**	**2.9**	**5.4**	+87.8%
Gross Profit Margin	*39.3%*	*49.5%*	*36.7%*	*-12.7%p*
Operating Profit Margin	*11.8%*	*7.3%*	*3.6%*	*-3.7%p*
EBITDA Margin	*16.3%*	*17.0%*	*22.2%*	*+5.3%p*

Earning Result

2024 1st Quarter Financial Results (Preliminary)

▪ Business Breakdown

(Unit: 1 Billion KRW)

Sector		'23.1Q	'23.2Q	'23.3Q	'23.4Q	'24.1Q	YoY
Oligo. CDMO	**Subtotal** (% of Total Revenue.)	**26.4** (52.0%)	**29.0** (50.3%)	**37.6** (67.2%)	**76.6** (63.5%)	**34.5** (66.8%)	+31.1% (+14.8p)
	Commercial	9.3	3.4	0.0	44.1	11.1	+20.2%
	Non-commercial	17.1	25.7	37.6	32.4	23.4	+30.7%
Small Molecule API (SMA)		1.7	8.6	0.9	10.5	4.4	+159.0%
mRNA		8.7	0.1	0.5	0.1	0.0	-99.5%
Generic API (GA)		6.9	10.9	7.1	24.7	5.1	-26.9%
Others		0.1	0.0	0.7	0.4	0.0	-75.5%
Total Separate Revenue		**43.8**	**48.7**	**46.7**	**112.3**	**44.1**	+0.7%
Subsidiaries (incl. CRO)		6.9	9.0	9.2	8.3	7.6	+11.3%
Total Consolidated Revenue		**50.6**	**57.8**	**55.9**	**120.6**	**51.7**	+2.1%

▪ Comments

Highlight: 31.1% revenue growth from Oligo. CDMO business compared to 2023.1Q, now accounting 66.8% of total revenue

- mRNA Business: sales dropped sharply due to canceled clinical trial from client.
- SMA Business: growth due to anticipation of new drug approval
- CRO: in process of recovery from losses in 2023, expected to return to profit on annual basis
- Events to watch:
  MDS treatment's new drug approval on June
  Progression of BIOSECURE Act

PART 01

Introduction

Introduction

HISTORY & SUPPLY RECORD

ST PHARM History

2010	Incorporation as Subsidiary of Dong-A Socio Group (comp. name to ST PHARM)
2011	HBV treatment selected as a world-class product (Ministry of Knowledge Economy)
2015	Construction of Banwol Plant 1, Acquisition of Banwol Plant 2 Acquired Certification: FDA (USA), PMDA (Japan) cGMP
2016	Establishment of ST America Research*(NJ, USA)* KOSDAQ(237690) IPO, Presidential Award for Innovative Enterprise
2018	Global Growth Excellence Leadership Award (Frost & Sullivan) Completion of Oligonucleotide Production Facility (Oligo Plant 1)
2019	Selected as Excellent Environmental Management Site (Banwol) Acquired AnaPath Services & Research (Non-Clinical CRO) STP1002 (Anti-cancer Drug) Phase 1 Clinical Trial (USA) IND
2020	Roche CDMO Award 2019 STP0404 (AIDS Treatment Drug) Phase 1 Clinical Trial (EU) IMPD
2021	Establishment of LEVATIO / VERNAGEN (mRNA & CAR-NKT) Construction of mRNA GMP (Mid-scale) Production Facility
2022	Best Asia-Pacific CDMO for Oligonucleotides CDMO, Corporate of the Year(CDMO) (Frost & Sullivan) Expansion of Oligo Plant 1 (Total Cap. of 6.4 Mole) Acquired Certification: FDA cGMP(NAI) – Banwol Campus
2023	Completion of of R&D Innovation Center (Banwol) FDA cGMP Regular Due Diligence (Banwol) Start construction of Oligo Plant 2 (Expected completion: H2 '25) Completion of mRNA GMP (Commercial scale) Production Facility

Supply Record

1988
Supplier of Thymidine (dT) (GSK, BMS)

"World's Largest Thymidine (dT) Supplier"

2000
Supplier of API for World's First HIV/AIDS Treatment (Zidovudine, GSK)

2002
World's Largest Monomer (Nucleoside) Supplier

2004
Supplier of API for Hepatitis B Treatment (Telbivudine, Novartis)

2007
Supplier of API for Hepatitis C Treatment Clinical Sample (Roche)

2012
Supplier of API for HIV/AIDS Treatment (Atazanavi, BMS)

2013
Supplier of API for World's First Hepatitis C Treatment (Gilead)

2015
Oligo API Supplier (Early Clinical Stage)

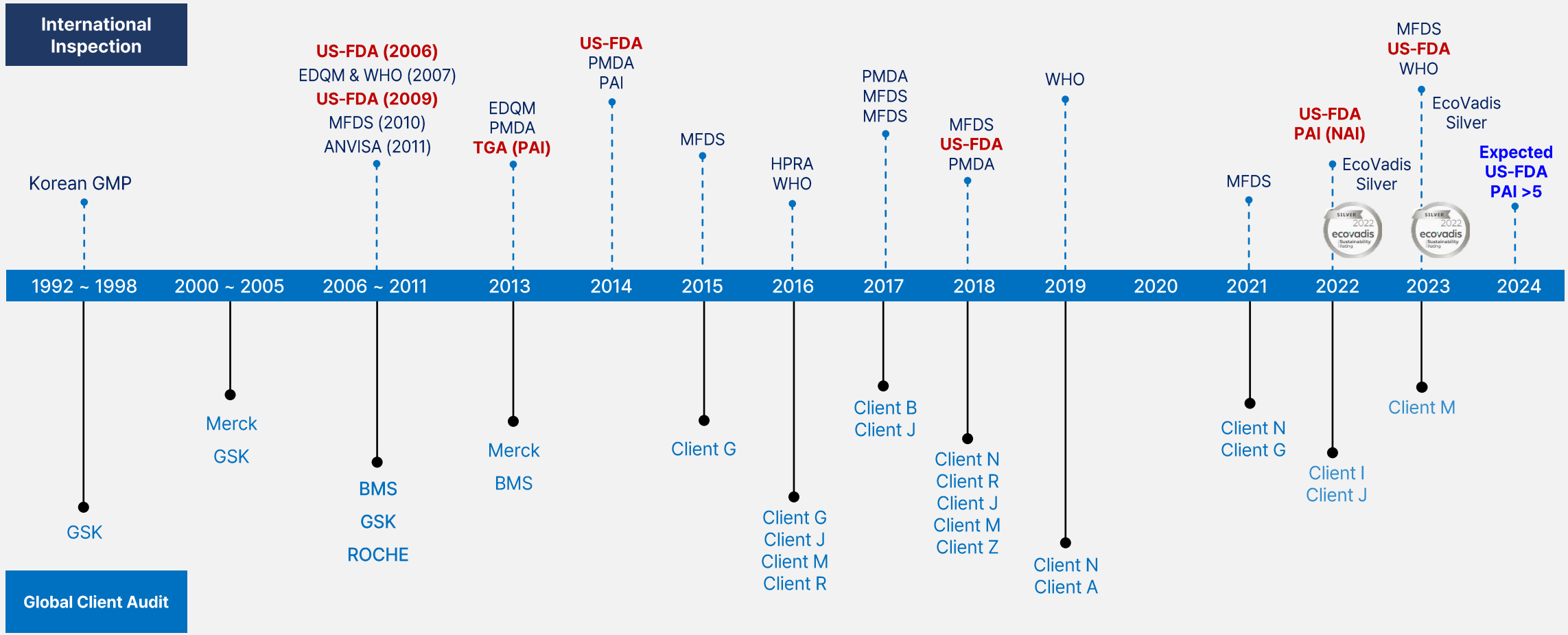
2020
Oligo API Supplier (Late Clinical Stage)

2021

2023
Oligo API Supplier (Commercial Scale)
mRNA LNP Lipid Supplier

Introduction

Global Inspection & Due Diligence Record



Successfully Inspected by

식품의약품안전처 Ministry of Food and Drug Safety · U.S. FOOD & DRUG ADMINISTRATION · World Health Organization · edqm European Directorate for the Quality of Medicines & HealthCare · ANVISA · Pmda · TGA Health Safety Regulation · HPRA Health Products Regulatory Authority

Introduction

ST PHARM GLOBAL FAMILY

CDMO Company Specializing from Oligonucleotide to xRNA Therapeutics

Incorporation of CDMO Value Chain from Non-clinical Animal Testing to Commercial Scale Production

AnaPath Research
Barcelona, Spain

AnaPath Services
Basel, Switzerland

ST PHARM
South Korea

LEVATIO
San Diego, USA

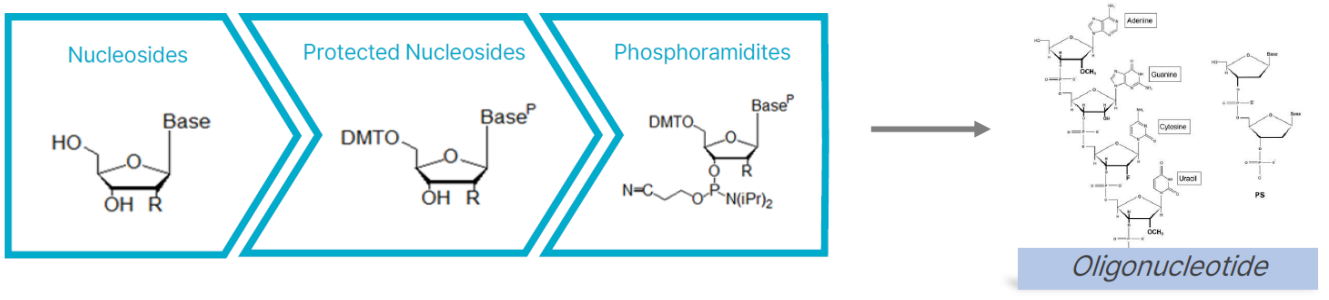
VERNAGEN
Atlanta, USA

STP America Research
Delaware, USA

Business

CDMO Business Overview

- ST PHARM CDMO Business Expansion

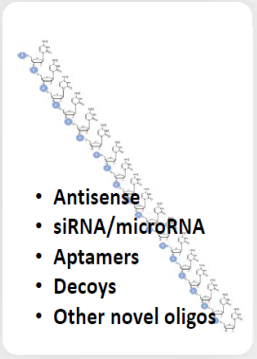


1983. Nucleoside/tide

- Monomer (PNS / PA)
- Zidovudine (HIV/AIDS)
- Sofosbuvir (Hepatitis C)

2008. Oligonucleotide

- Antisense (ASO)
- siRNA / miRNA
- Aptamer
- Decoys

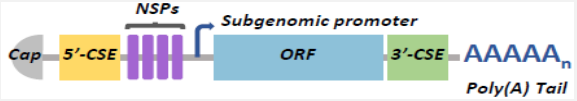


2018. Polynucleotide

- mRNA

- circRNA

- samRNA (self amplifying)



PART 02

Market Overview

Market

RNA-based Therapeutics Concept

▪ Overview

RNA Therapeutic is 3rd-Gen therapy that allows a more fundamental treatment by silencing or inhibiting expression of disease-inducing protein
Only 3% of all DNAs is transcribed to proteins via mRNA
The remaining 97% is transcribed to RNA
Most RNA functions unidentified ▶ Great potential RNA-related treatments

▪ RNA-based Therapeutics

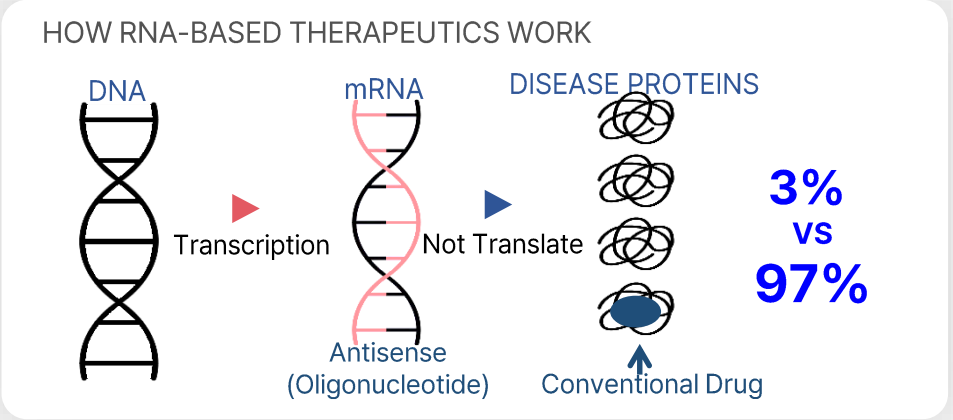
Mechanism: Inhibits expression of harmful proteins RNA
Types: Anti-sense (ASO), siRNA, miRNA etc.
Examples : Spinraza (Ionis / Biogen) Spinal Muscular Atrophy
Leqvio (Alnylam / Novartis) Hereditary Hyperlipidemia

▪ Characteristics of RNA-based Therapeutics

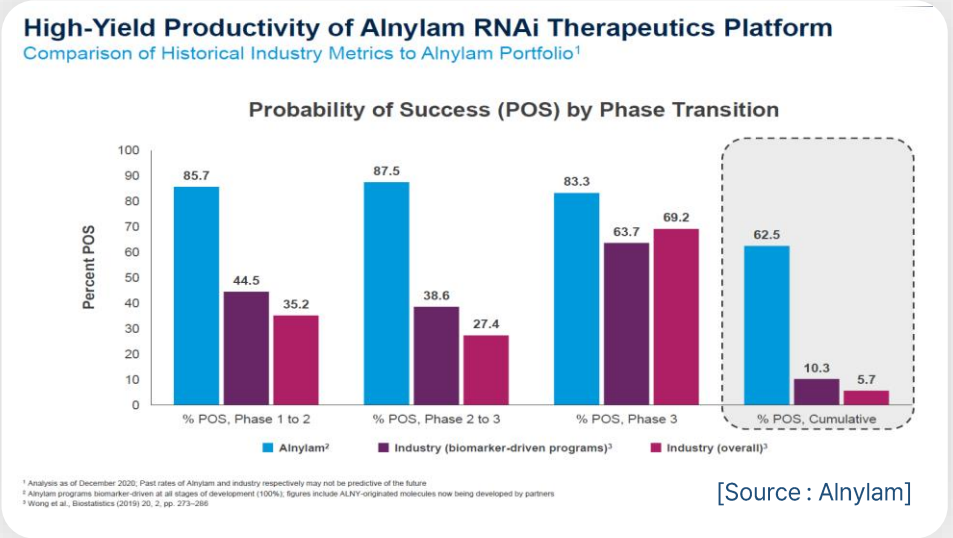
Strengths : High selectivity over target proteins
Quick & cost effective development ▶ ≥ 2yr of Pre-clinical phase
Very low tolerance
Excellent drug persistence ▶ Leqvio 6-months
Lower drug price ▶ Leqvio ≥ U$4,000 while Repatha = U$5,850

Weaknesses: Difficulty in delivery to organs/cells apart from liver or brain
Require delivery technology such as LNP etc.
▶ New methods: Avidity's Antibody oligonucleotide conjugates
Difficulty in mass production ⇒ Few capable CDMO companies

▪ Central Dogma & Non-coding DNA



▪ Alnylam's siRNA Clinical Trial Success Rate : 62.5%



[Source : Alnylam]

Market

RNA-based Therapeutics – Oligonucleotide

▪ Growth Potential of RNA-based Therapeutics

Liver delivery technology "Gal-Nac" developed in 2018

▶ Therapeutic areas extended to Auto-immune Diseases, Growing R&D investments in RNA-based therapy pipelines by major pharmaceuticals

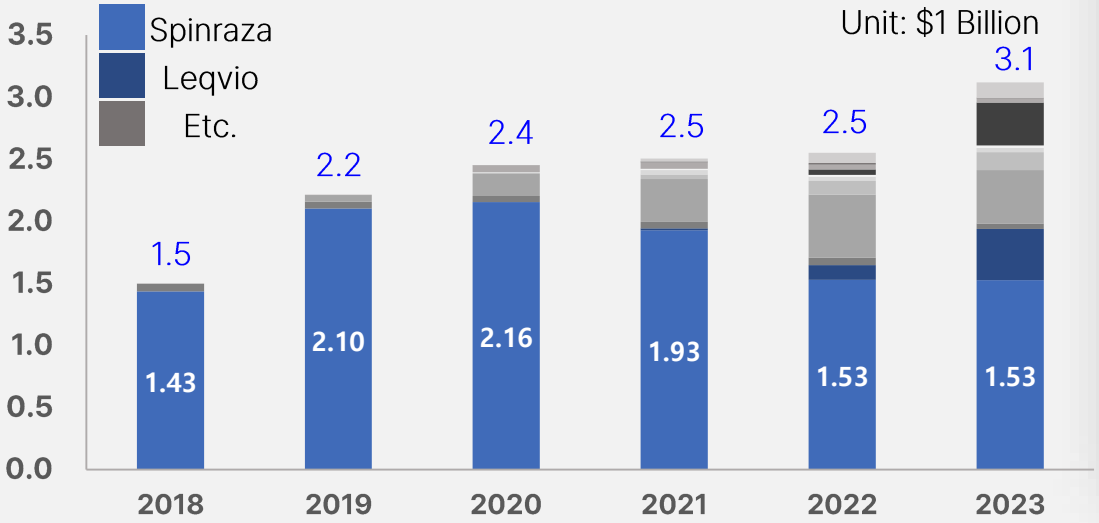
Blockbuster RNA-based treatments expected to commercialize starting in 2024 ▶ Surge in Oligonucleotide demand

▪ Market Outlook

Global RNA-based Therapeutics Global Market Size

: U$5 Bil. (6.5 Tril. KRW) (2021) ▶ U$25.7 Bil. (32.6 Tril KRW) (2030)

▪ Accumulated Sales of 14 FDA-approved RNA Treatments



[Source : IQVIA]

Demand for Oligonucleotides ▶ 12T/yr if all pipelines are commercialized

Oligonucleotide-based pipelines for Chronic Diseases: Overview & Demand Forecast

Company	Therapeutics	Therapeutic Areas	Target	Stage	Injection Guide (mg)	Dosing Interval	Target Patients (annu.)	Annu. Demand (kg)
Ionis	Pelacarsen	CVD	Apo(a)	P3	80	12/yr	1,000,000	960
	Olezarsen	CVD	ApoCIII	P3	50	12/yr	1,000,300	600
	IONIS-AGT-Lrx	Hypertension	AGT	P2	80	8/yr	540,675	346
	ION449 (AZD-8223)	Dyslipidemias	PCSK9	P2	120	2/yr	1,380,000	497
	ION224	NASH	DGAT2	P2	80	12/yr	640,000	614
	IONIS-MAPTrx	Alzheimer	TAU	P2	100	4/yr	1,500,000	600
	Bepirovirsen	Hepatitis B	HBV	P2	300	6/yr	1,000,000	1800
Alnylam	Leqvio(inclisiran)	Hyperlipidemia	PCSK9	Comm.	300	2/yr	1,380,000	828
	Zilebesiran	Hypertension	AGT	P2	600	2/yr	1,000,000	1200
	ALN-HBV02 (VIR-2218)	Hepatitis B	HBV	P2	600	2/yr	500,000	200
Dicerna	DCR-HBVS (RG-6346)	Hepatitis B	HBV	P2	360	4/yr	500,000	720
Arrow head	ARO-ANG3	Hyperlipidemia	ANGPTL3	P2	200	2/yr	1,380,000	552
	ARO-HSD	NASH	HSD17β13	P2	200	2/yr	1,000,000	400
	JNJ-3989	Hepatitis B	HBV	P2	400	3/yr	500,000	600
	AMG890 (olpasiran)	CVD	LP(a)	P2	200	4/yr	1,000,000	800

(Demand based on 10~20% of target patients in developed countries such as U.S., Europe, China, Japan, etc.)

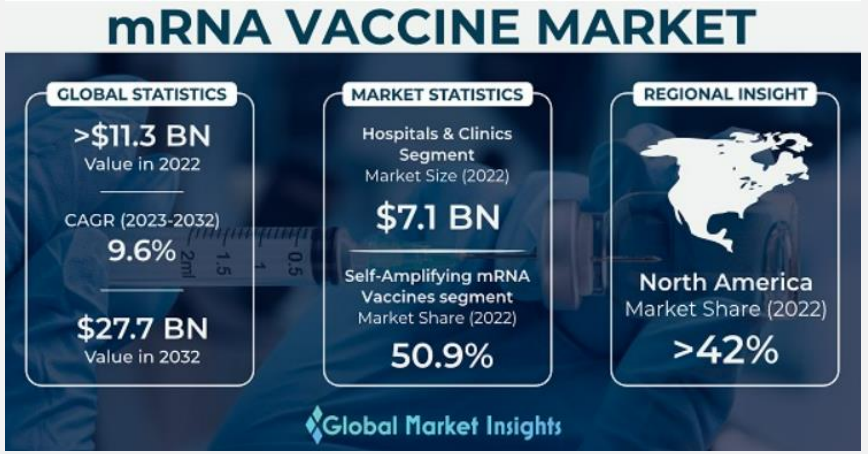
[Source : Samsung Securities]

▪ mRNA Vaccine Market Outlook & Potential

Global mRNA Vaccine Market Outlook:

U$11.3 Bil. (14 Tril. KRW) (2022) ▶ U$27.7 Bil. (36 Tril. KRW) (2032)

(Source: Global Market Insight)



▪ Characteristics of mRNA-based Therapeutics

Safety & Efficacy: High selectivity over target protein

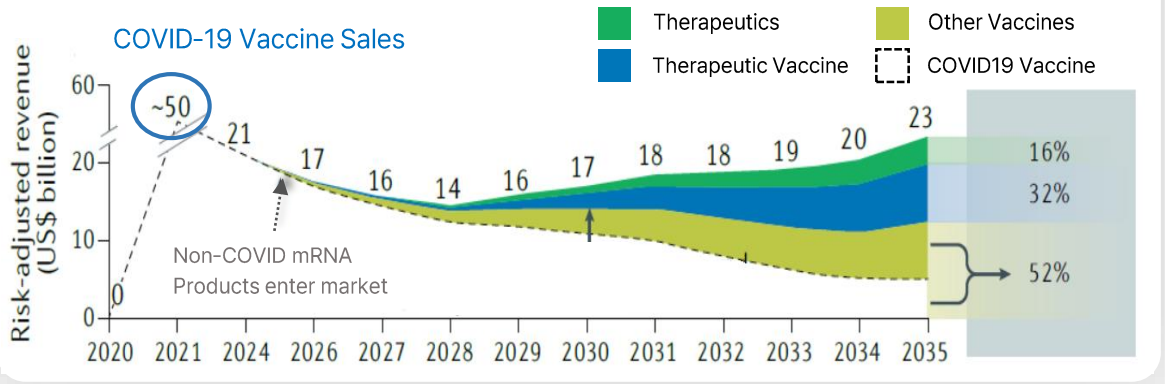
No need to penetrate nuclear membrane = lower risk

Productivity: Enables rapid scale-up and development

High potential for expanding therapeutic areas (Platform-like)

▶ potential to replace Antibody treatments

Global Revenue Outlook for mRNA Technology Market (risk-adjusted)



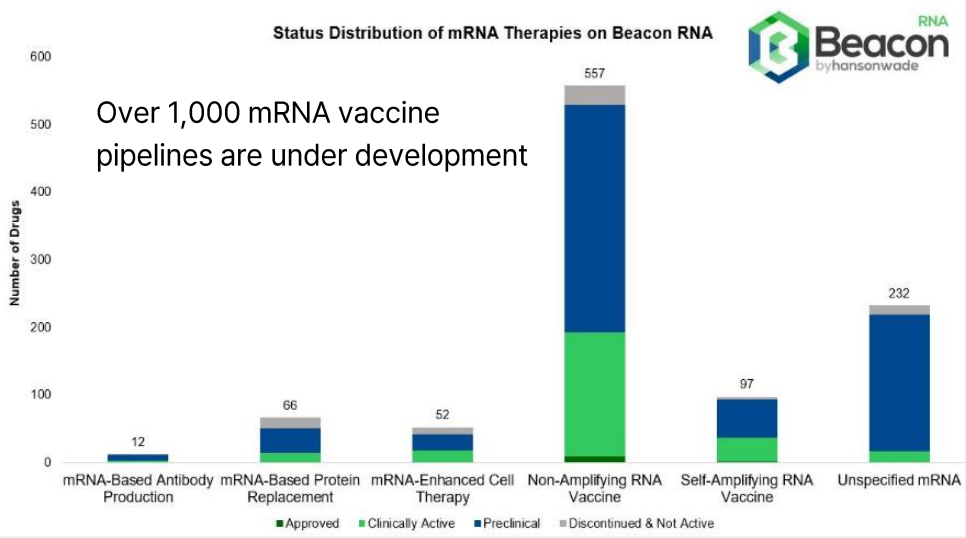
Market

RNA-based Therapeutics – Development Trends

- Convergence & Enhanced Delivery Technology ▶ Expansion of Targetable Area (from Rare to Chronic Diseases & Anticancer)

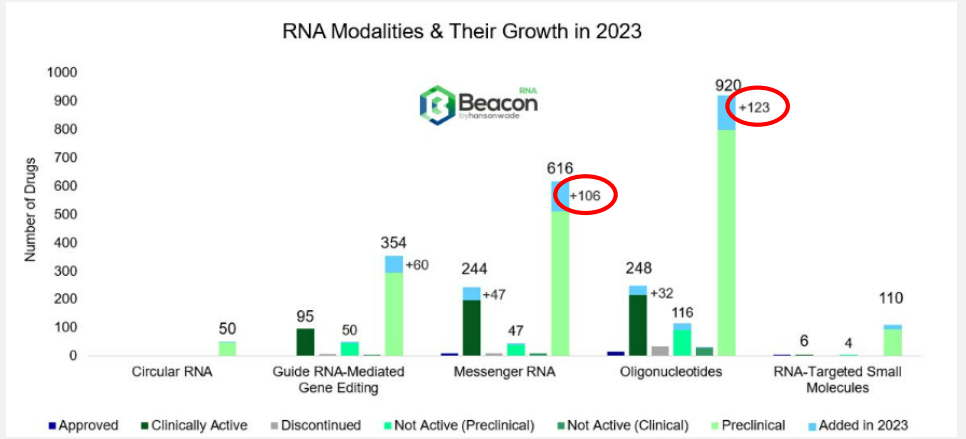
- R&D Trends of 2023

- 3,150 Pipelines throughout all stages of clinical trials
- 52% of Pipelines initiated in 2022. 229 new substances in 2023 alone (Oligo 123, mRNA 106)
- Over 1,000 mRNA vaccine pipelines under development
- Anticancer Oligo-based Therapeutics: 250 (incl. clinical & non-clinical)
- Anticancer mRNA Therapeutics : 193 (incl. clinical & non-clinical)

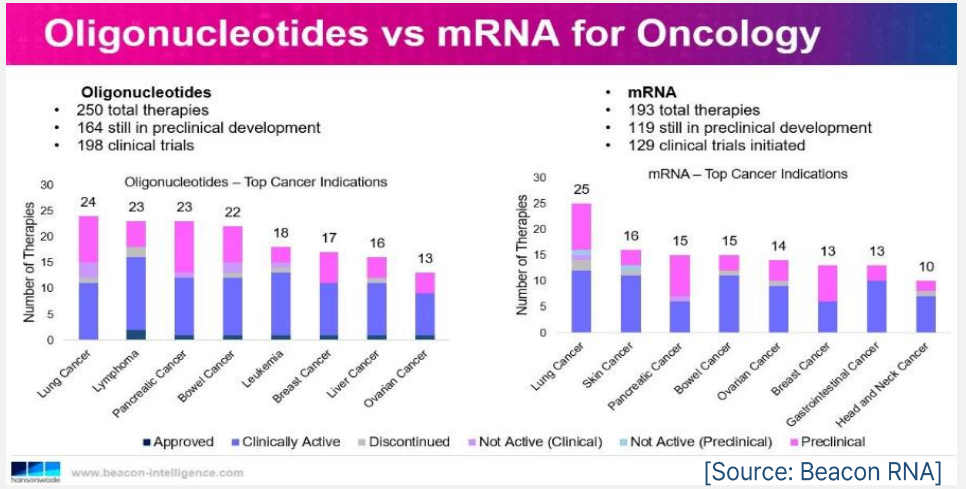


[Source: Beacon RNA]

Total of 229 **NEW** Candidate Substances Discovered in 2023



RNA-based Therapeutics are quickly entering Anti-cancer areas



[Source: Beacon RNA]

Market

RNA-based Therapeutics – Development Trends (Continued)

Novartis

- Expanded new drug development agreement with Ionis for ASO based CVD therapies beyond Pelacarsen
- Acquired Swiss DTx Pharma for its siRNA platform & delivery technology for U$1 Billion
- (Jan.24), joint new drug development agreement w/ Shanghai Argo Biopharma for CVD and metabolic disease therapies

Roche

- L/I Zilebesiran from Alnylam (Nasdaq: ALNY) for U$ 2.8 Billion
- (Oct.19), L/I HBV pipeline from Dicerna in 2019 for U$ 1.7 Billion
- (Sept.23), expanded joint development with Ionis for ASO-based Alzheimer & Huntington disease therapies
- (Jan. 24), RNA-targeting pill development w/ Remix Therapuetics

GSK

- (Feb.23) CEO announced "end investment in cell and gene therapy" and focus on "oligo strategy"
- (Dec. 22) collaboration w/ Wave Life Sciences + U$ 1,700 Mil. investment
- (Jul. 23) L/I nucleic acid encoding technology from Elsie Biotechnologies
- (Nov. 23) L/I HBV treatment pipeline JNJ-3989 from J&J

Novo Nordisk

- (Nov. 21) Acquired Dicerna Pharmaceuticals for U$3.3 Billion
- (21 Annual Report) to "apply RNAi tech across all therapy areas"
- (Jul. 23) Announced collaboration w/ Eleven Therapeutics
- (Oct. 23) FDA approved first siRNA treatment nedosiran
- (Mar. 24) Acquired Cardior Pharmaceuticals, developer of microRNA based CVD therapy, for €1 Billion

Lilly

- (Sept. 21) Invested U$ 1.25 Billion on RNA editing research collaboration w/ ProQR
- (Feb. 22) Invested U$700 Million on constructing "Institute for Genetic Medicine for study of RNA & DNA
- (24) Ongoing Phase 2 trial of lepodisiran (Lp(a) targeting siRNA)

Ionis

- (Nov. 23) EMA awarded PRIME Designation for elsunersen (w/ Praxis)
- (Feb. 24) FDA designated fast-track status for bepirovirsen(w/ GSK) & eplontersen(w/ AZ)
- (Feb. 24) FDA designated orphan drug status for olezarsen

Business Overview

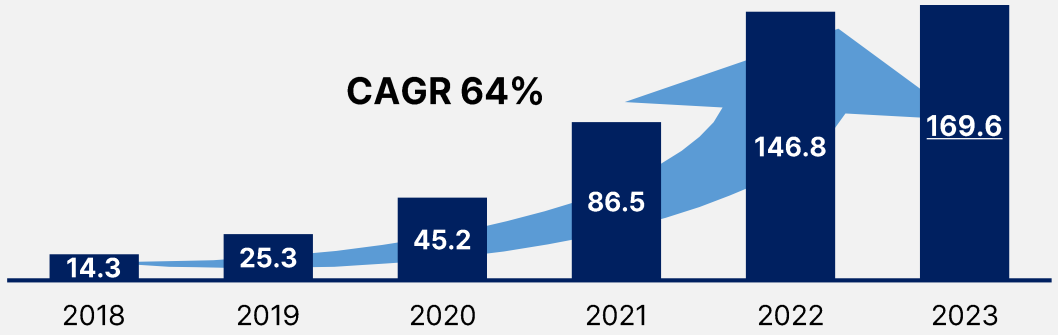
Business

Oligonucleotide CDMO

▪ Our Oligonucleotide CDMO **Edge**

- Positioned within Global Top-3 Oligo CDMO company
- Integrated supply-chain from Monomer to Oligonucleotide
  ▶ Cost-efficient, Consistent Quality, Sustainable Production
- Strong Track Record Since 1983 (≥ 15 years, incl. US & Eur.)

▪ ST PHARM Oligo CDMO Revenue [Unit: ₩ 1 Billion)



▪ ST PHARM Oligo Pipeline (Total ≥ 20 Pipelines)

Client	Indication	Stage			
		Phase1	Phase2	Phase3	Commercial
Client A	Hyperlipidemia				●
Client B	SMA				●
Client C	MDS/MF/AML			●	
Client D	CVD			●	
Client D	Hereditary Angioedema			●	
Client A	CVD			●	
Client E	Chronic Hepatitis B			●	
Client D	Thrombosis		●		
Client F	Chronic Hepatitis B		●		
Client G	AMD		●		
Client G	Chronic Hepatitis B		●		

▪ Planned New Pipelines for 2024

Client	Indication	Client	Indication	Client	Indication	Client	Indication
Client G	Hepatitis B	Client E	Antitrypsin Deficiency	Client H	Hemophilia	Client K	Unknown
Client G	Alzheimer's	Client A	Unknown	Client I	Parkinson's	Client L	Hyperlipidemia
Client G	Huntington's	Client A	Liver-target siRNA	Client J	Epilepsy	Client M	Skin Carcinoma

Business

Oligonucleotide CDMO – Production Facility

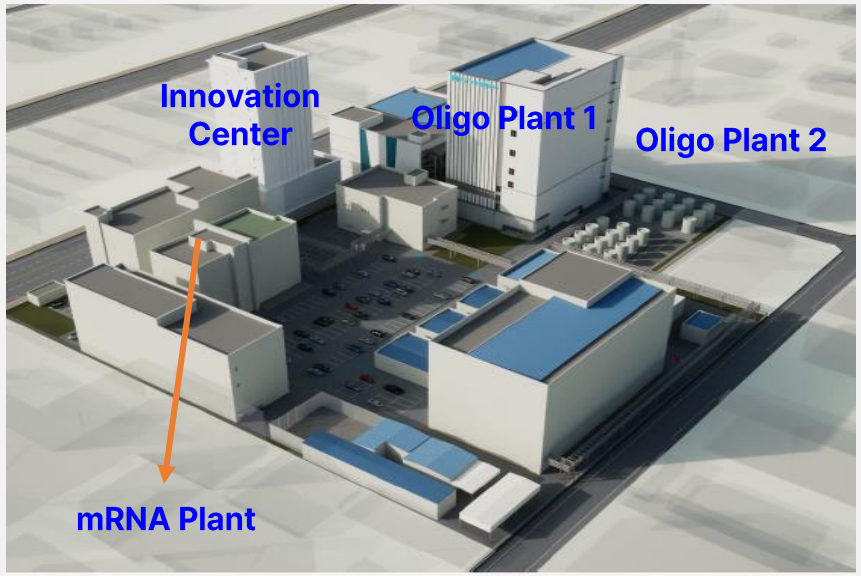
- Expansion projects to prepare for a **fast-growing market with strong future demand**

[1 mole ≈ 167kg ~ 500kg]

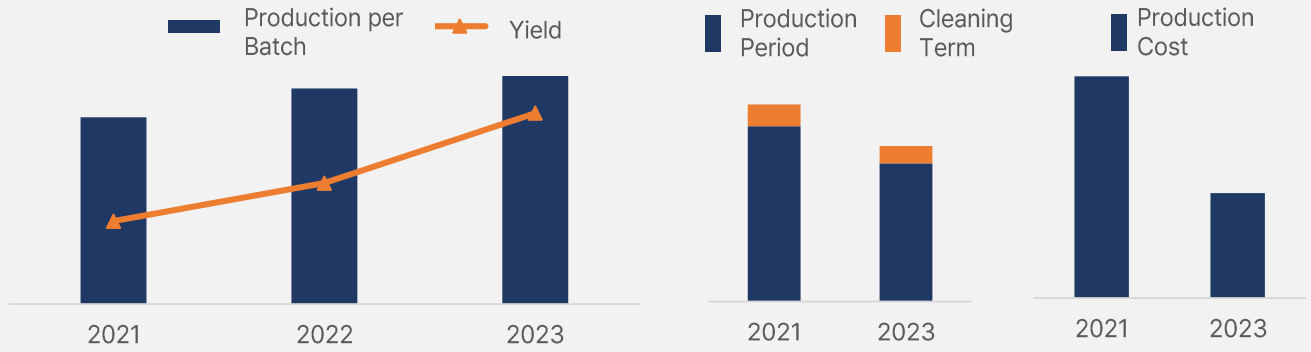
Oligonucleotide Facilities	2021	2022	Q2. 2025(Est.)	Q2. 2026(Est.)
	Plant 1	Plant 1 Phase 1 & 2 Expansion	Plant 2 Phase 1	Plant 2 Phase 2
No. of Line*	1	4	7	10
Total CAPA	2.0 mole (Approx. 330kg~1t)	6.4 mole (Approx. 1t-3.2t)	8~9 mole (Approx. 1.4t-4.6t)	12~14 mole (Approx. 2.3t-7t)

* No. of Line based on No. of Synthesizers

- View of Banwol Campus Facilities



- Yield (Production Efficiency) Improvements



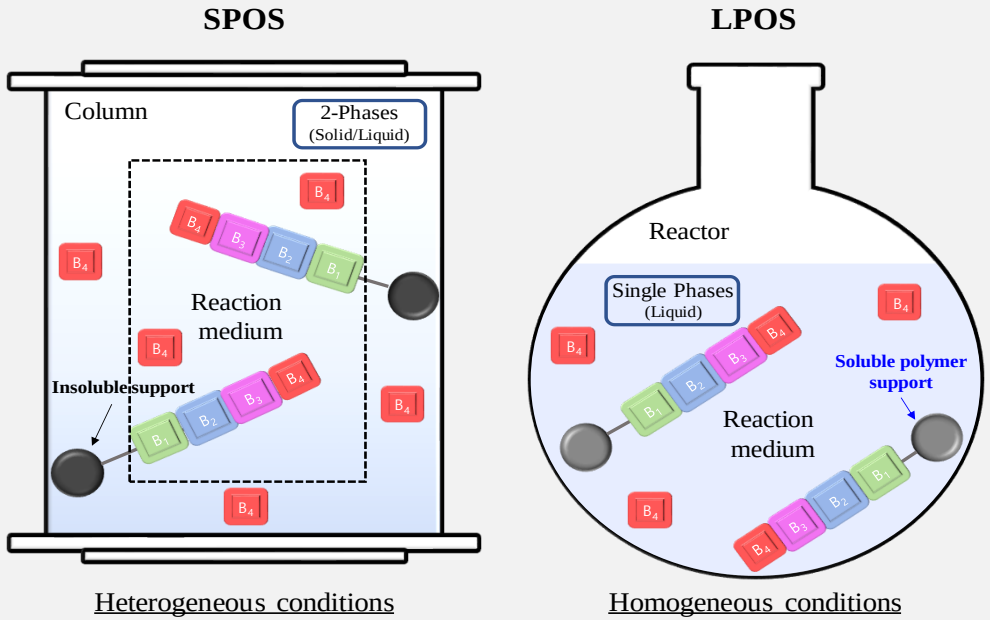
Production	2021	2023	
Productivity	n Batch 43kg	n Batch 54kg (25% ▲)	Synthesis Process & Outcome Purity Improvements
Production Period	n Batch Syn. & Pur. (27 Days)	n Batch Syn. & Pur. (19 Days, 29% ▼)	Skilled workers, Reduced cleaning term, etc.

Business

CDMO Technology Innovations

▪ LPOS (Liquid Phase Oligonucleotide Synthesis)

- Suitable for mass/commercial-scale production of Oligonucleotides (Max. batch size x10)
- License contracted with 1 Global company for technology's exploitation
- Currently research cooperation with 2 Global Pharmaceuticals
- More sustainable than Solid Phase OS



▪ CDMO Research Innovations

Oligo.
- PAT (Process Analytics Technology)
- sgRNA for DNA/RNA editing (CRISPR CasX)
- Protein Oligo Conjugation (similar concept to ADC)
- MsPA antisense (Novel PN chemistry)

Synthesis
- SmartCap® and Lipids for STLNP® and Genevant LNP
- LPOS (Liquid Phase Oligo Synthesis)
- SMB (Simulated Moving Bed)
- CFT (Continuous Flow Technology)

Biotech
- Plasmid DNA
- circ RNA
- Novel Drug Delivery System (DDS)
- Expedite-100 Days Strategy

Research Sup.
- Adopt novel software for efficient management
- DocuSign, LabManager Pro etc.
- Enhance in-house education system

Business

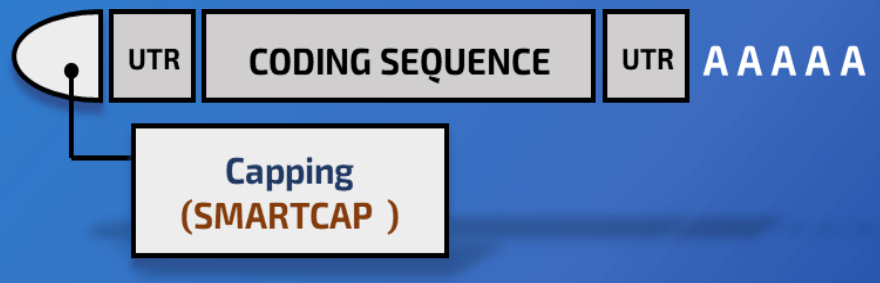
mRNA Platform Technologies

Core Technology

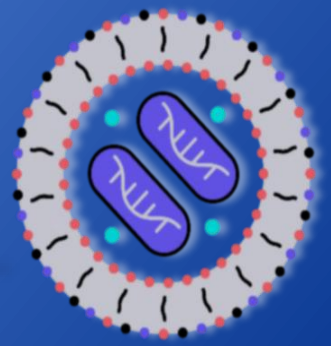
ST PHARM holds Two major mRNA synthesis technology

1) 5′capping 2) LNP Platform Technology

5′ Capping : SmartCap®
LNP Platform Technology : STLNP®



SmartCap®



STLNP®

SmartCap®

- Synthesis technology for mRNA stabilizer
- Registered S. Korea Patent (Oct. 2020)
  Ongoing registration for Global Patent
- +30 Capping Analogue
- Cost-efficient 5′ capping price

CAP Library Screening System

- Customizable based on Client's need
- Higher gene expression

LNP Platform Establishment Strategy

- 1. LNP L/I (Genevant LNP)
- 2. Independent LNP Development
  - Developed and applied for patent in 2020
  - Begin establishing platform for mRNA CDMO
- 3. Innovating Next Generation LNP (STLNP®)
  - Found 2 types of candidates in pre-clinical stage
  - Aim to improve LNP stability and immune response

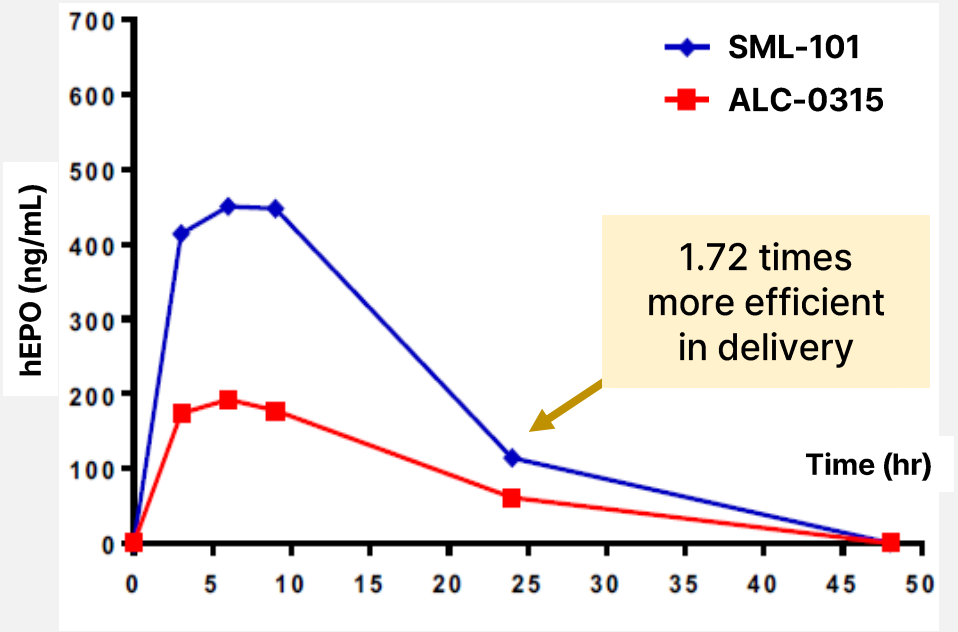
Business

Why STLNP?

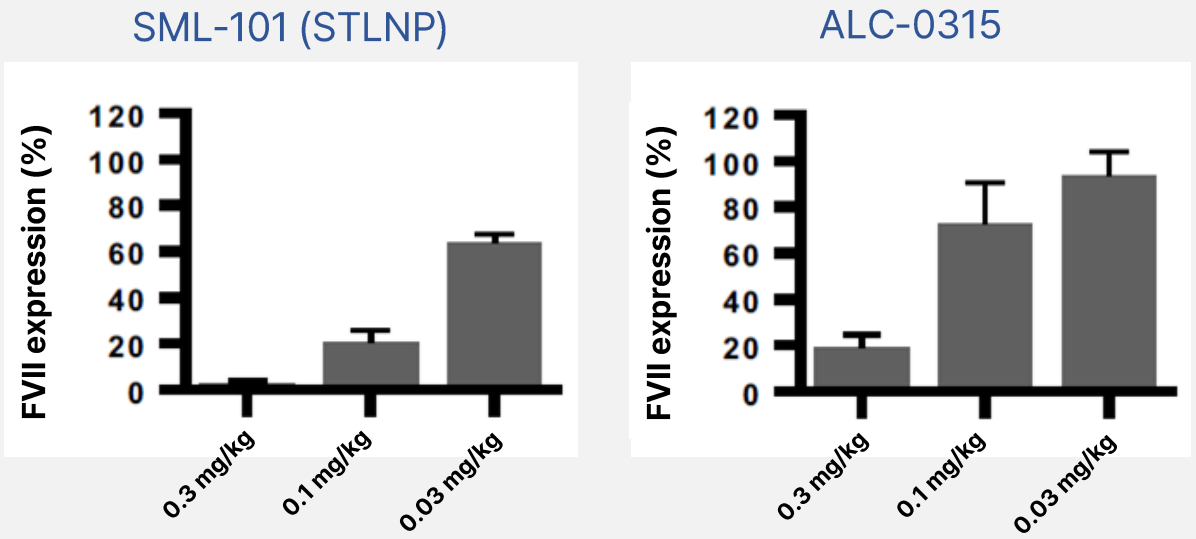
- STLNP Animal Testing Results

- Observed 1.7 times higher mRNA delivery efficiency than Pfizer-BioNTech's (based on blood drug concentration)
- Observed higher siRNA delivery efficiency for all dose types than Pfizer-BioNTech's LNP

- STLNP + mRNA Delivery Efficiency



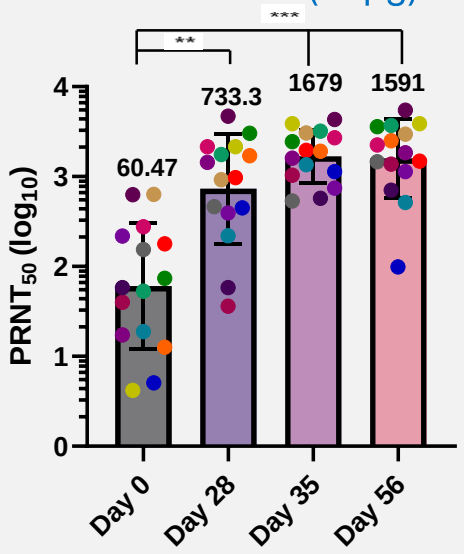
- STLNP + Delivery Efficiency



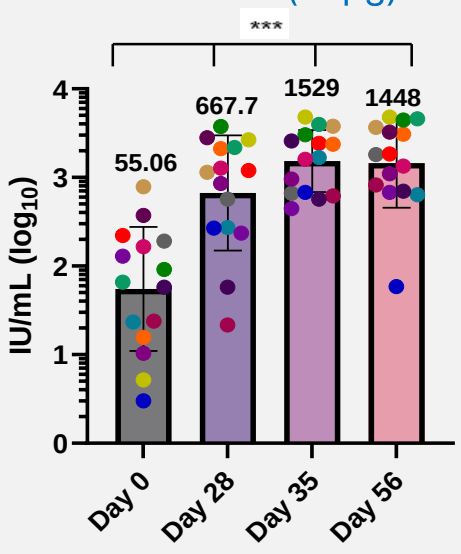
Business

ST2104 Phase 1 Results – High Level of Neutralizing Antibody

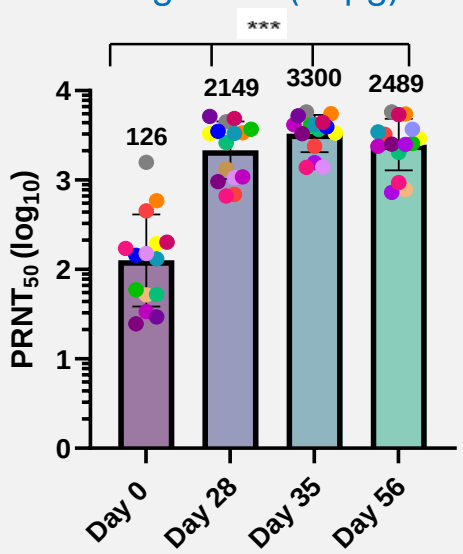
Low dose(25μg)



Low dose(25μg)



High dose(50μg)



High dose(50μg)

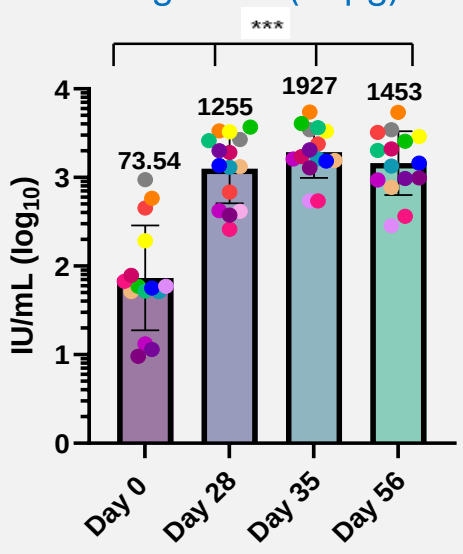
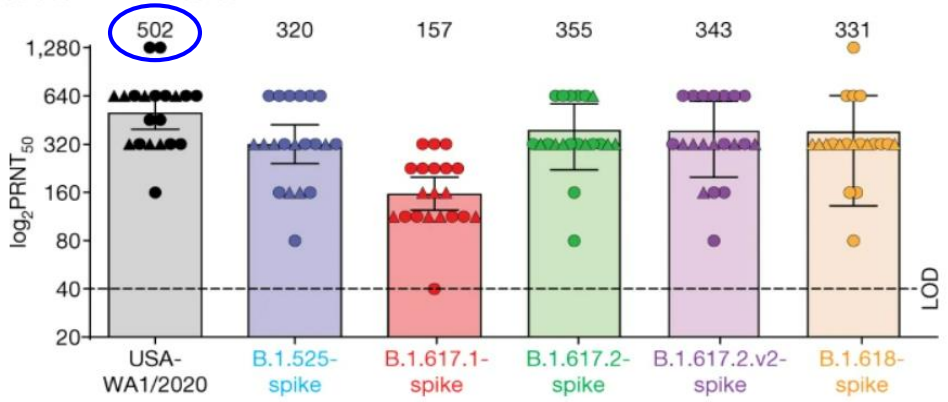


Fig. 1: Neutralization of USA-WA1/2020 and variant SARS-CoV-2 viruses by BNT162b2-induced immune sera.



[Source: Nature, 'BNT162b2-elicited neutralization of B.1.617 and other SARS-CoV-2 variants' ('21.06.10)]

- Day 0 (1st Vaccination), Day 28 (2nd Vacc.), Day 35 (+ 1 week), Day 56 (+ 4 weeks)
- Pfizer-BioNTech COVID-19 mRNA Vaccine: Day 56 Avg. $PRNT_{50}$ = 502
- STP2104: Day 56 $PRNT_{50}$ = 1,591 (Low Dose), 2,489 (High Dose)
  [Approx. 3 ~ 4 times higher]
- STP2104 Positive Rate* of Neutralizing Antibody
: Low Dose 100%, High Dose(50μg) 93%

* Achieved when level of neutralizing antibody increases x4 vs. before injection

Business

mRNA CDMO Production Facility

" From milligram to kilogram scale production"

Banwol Campus

1. R&D / Small scale production

Completion: Aug. 2020
Capacity : Pilot Scale

2. Mid-scale production (GMP)

Completion: May. 2021
Capacity: mg ~ g / month
(10 Mil. doses / year)

3. Large / Commercial scale production (GMP)

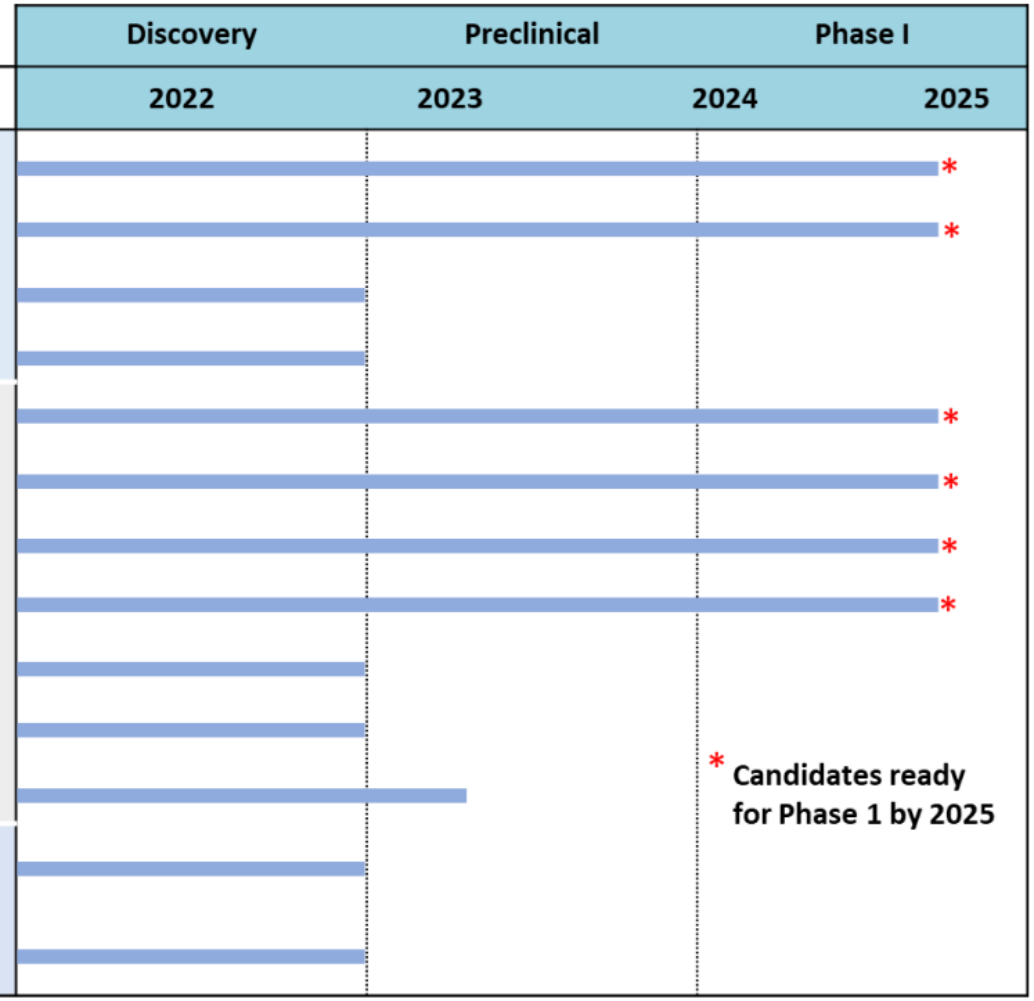
Completion: Aug. 2023
Capacity: 100 ~ 120 g / month
(35 Mil. ~ 100Mil. doses / year)

Business

Vernagen

- Vernagen's mRNA Vaccine Pipelines

Category	Pathogen	Collaborator
Global Market Vaccines *Targeting viral pathogens that infect the global populations*	**Shingles**	Emory University
	RSV A/B	Emory University
	Noro Virus	University of Michigan
	HMPV	*In-house*
Highly Pathogenic and Emerging Virus Vaccines *Targeting emerging, neglected, tropical and pandemic potential viral pathogens*	**Nipah Virus**	Duke-NUS
	YFV/ZKV/CHKV Combi	Simile Ltd.
	Heartland Virus	US-CDC
	SFTSV	Junbuk University
	Monkeypox Virus	*In-house*
	Sarbecovirus	CoVBIO
	Influenza A/B	*In-house*
Cancer Virus Vaccines *Targeting viral pathogens inducing cancer potential*	**Epstein-Bar V**	*In-house*
	HPV-9	*In-house*



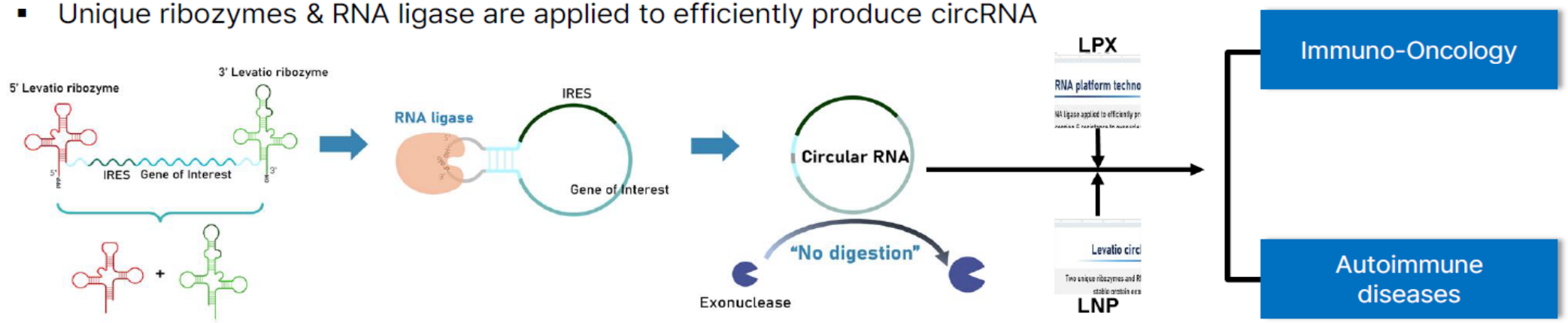
** WHO & CEPI Priority viruses*

Business

Levatio Therapeutics

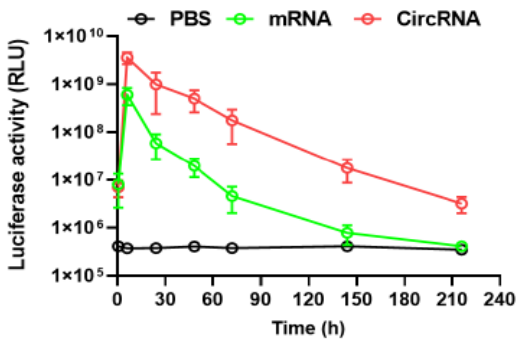
▪ Development of circRNA Platform

▪ Unique ribozymes & RNA ligase are applied to efficiently produce circRNA

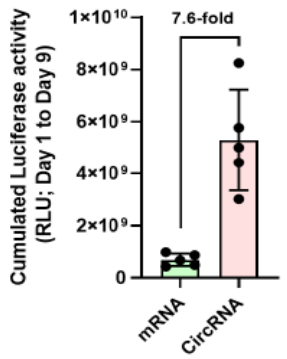


▪ Levatio's circRNA has a 7.6 folds higher cumulated Fluc activity (9days) than mRNA

➢ Luc activity kinetics



➢ Cumulated Luc activity



▪ Levatio's circRNA pipeline & milestones

	2021	2022	2023	2024
Platform	Platform Development	Engineering & Validation		
Autoantigen Vaccine	Candidate Optimization	MOA / POC	IND	
Neoantigen Vaccine	Candidate Optimization	MOA / POC	IND	
CAR-NKT (Cancers)	Candidate Optimization	MOA / POC		
CAR-NKT (Autoimmune)	Candidate Optimization	MOA / POC		

* MOA(활동 매카니즘 규명, Mechanism of Action), POC(개념 정립, Proof of Concept)

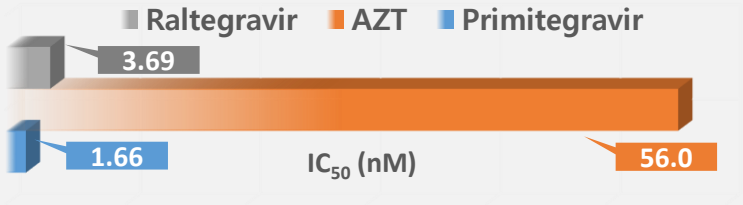
PART 04

Pipeline

Business

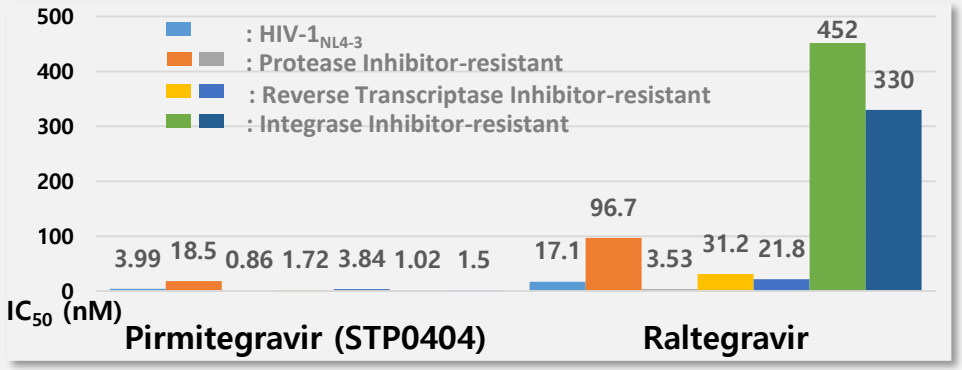
STP0404 - ALLINI Mechanism (New Mechanism)

- Anti-viral Efficacy (Cell Line MT-4)



❖ 2 ~ 33 times higher anti-viral efficacy than existing treatments
❖ High Safety Data results over HIV-1
Therapeutic Index(TI):
STP0404 > 6,020 wZhile Raltegravir > 2,710

- Anti-viral Efficacy against Inhibitor-resistant HIV



❖ Existing HIV/AIDS therapies are "inhibitors" of HIV activities
❖ This induces continuous drug usage & drug resistance
(+ no drug with new mechanism for over 10 years)
❖ STP0404 showed anti-viral efficacy even against inhibitor-resistant HIV (4 ~ 400 times efficient than Raltegravir)

Table 3. Antiviral activity in Raltegravir-resistant strains

Compounds	Average IC_{50} (range, nM)	
	PBMC	MT-4
STP0404	0.08 (0.02~0.22)	2.49 (0.95~3.48)
Zidovubine	7.96 (0.22~20.7)	37.94 (29.7~57.6)
Raltegravir	1,227.70 (12.5~3,036)	2525 (351~4,322)
Elvitegravir	-	2751.5 (276~10,000)
Dolutegravir	-	4.57 (3.07~8.54)

RAL-resistant strains: 4736_2, 4736_4, 6070_1, 6070_2, 1666_1

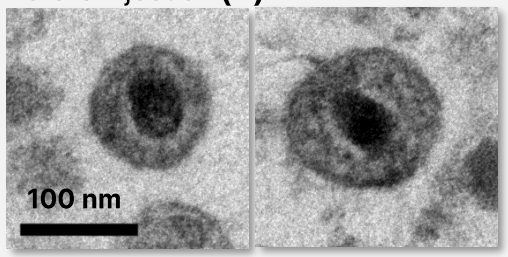
❖ Existing HIV/AIDS Drugs' Global Sales (as of 2022)
- Dolutegravir (GSK) Approx. U$1.8 Bil.
- Elvitegravir (Gilead) Approx. U$2.4 Bil.
- Raltegravir (MSD) Approx. U$633 Mil.

Business

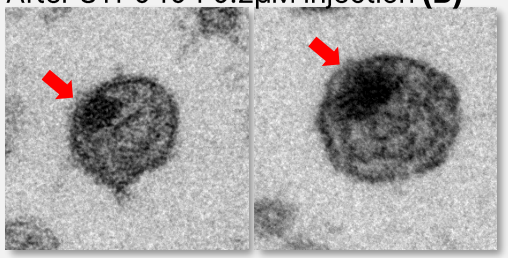
STP0404 - ALLINI Mechanism (New Mechanism)

▪ STP0404 Mechanism of Action

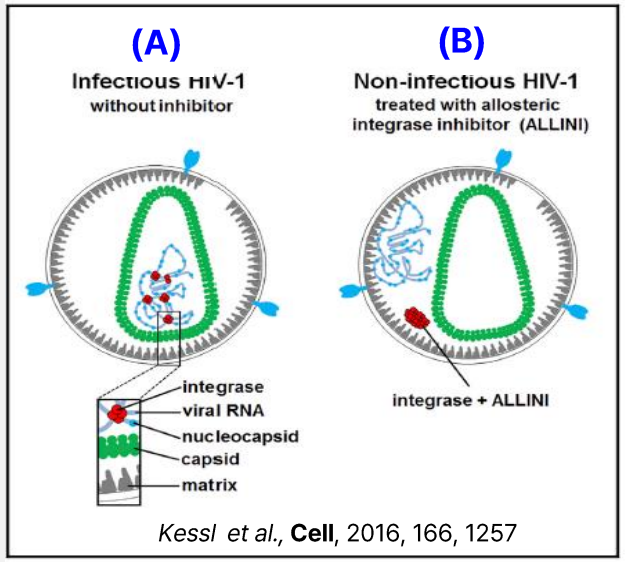
Before Injection **(A)**



After STP0404 0.2µM Injection **(B)**

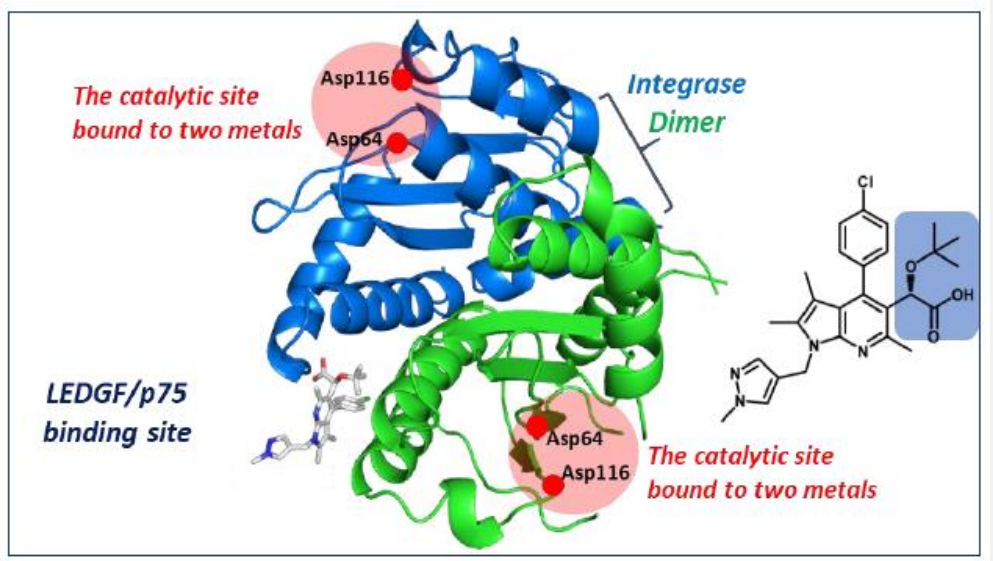


TEM study in Emory Univ.



Kessl et al., **Cell**, 2016, 166, 1257

▪ STP0404 X-ray Structure



- New mechanism ALLINI (Allosteric integrase inhibitor) founded by Prof. M. Kvaratskhelia (Univ. of Colorado) in 2016
- Integrase delivers HIV virus's RNA to host cell, inducing virion state (infection of host cell & capsid protection) **(A)**
- ALLINI inhibits delivery / merge of integrase with virus's RNA, causing mislocalization of HIV's RNA **(B)**
- STP0404 pulls the HIV virus's RNA outside the virus-protecting capsid, allowing the formation of non-infectious HIV-1 **(B)**
- New MOA for HIV-cure as "maturation inhibitor" - "Divide and Conquer", not 'Shock & Kill' or 'Block & Lock''
- Identification of ALLINI mechanism supported by US NIH grants in 2018. Collaboration with Emory University & University of Colorado Boulder

Business

STP0404 - ALLINI Mechanism (New Mechanism)

- Academic Publications and Media Features

Phase 2 Trial featured as one of "Three Trials to Watch in 2024" (Dec. 18)

PLOS PATHOGENS

July, 2021

RESEARCH ARTICLE

A highly potent and safe pyrrolopyridine-based allosteric HIV-1 integrase inhibitor targeting host LEDGF/p75-integrase interaction site

Tatsuya Maehigashi[1☯], Seohyun Ahn[2☯], Uk-Il Kim[2☯], Jared Lindenberger[3☯], Adrian Oo[1☯], Pratibha C. Koneru[3], Bijan Mahboubi[1], Alan N. Engelman[4,5], Mamuka Kvaratskhelia[3]*, Kyungjin Kim[2]*, Baek Kim[1,6]*

AMERICAN SOCIETY FOR MICROBIOLOGY | mBio®

The Drug-Induced Interface That Drives HIV-1 Integrase Hypermultimerization and Loss of Function

Matthew R. Singer,[a] Tung Dinh,[b] Lev Levintov,[c] Arun S. Annamalai,[b] Juan S. Rey,[c] Lorenzo Briganti,[b] Nicola J. Co
Ian A. Taylor,[d] Kyungjin Kim,[e] Alan N. Engelman,[f,g] Baek Kim,[h,i] Juan R. Perilla,[c] Mamuka Kvaratskhelia,[b] P

RETROINTEGRATION 2023

7th INTERNATIONAL CONFERENCE ON RETROVIRAL INTEGRATION

July 31 – August 4, 2023, Boulder, Colorado, USA

East End/West End Conference Room

SESSION 4: HIV-1 INTEGRASE INHIBITORS AND NOVEL ANTIRETROVIRAL COMPOUNDS

Chairperson: **Daniel Adu-Ampratwum**, *The Ohio State University*

8:00 AM – 10:00 AM

Kyungjin Peter Kim
ST PHARM, Seoul, Republic of Korea.
The Fellowship of the Ring: Quest to develop Pirmitegravir, a novel potent and safe HIV-1 allosteric integrase inhibitor (ALLINI).

38

Discovery and development of novel pyrrolopyridine derivatives as a highly potent and safe allosteric HIV-1 integrase inhibitor

Uk-Il Kim[1], Ill Young L

[1] ST PHARM, New Dr
Institute of Chemical
* Corresponding Auth

The Nonclinical & Clinical Development of a Novel Potent H Integrase Inhibitor, Pirmitegravir

Xue Meng[1], Uk-Il Kim[1], Baek Kim[2,3], Kyungjin Kim[1*]

[1] ST PHARM, New Drug Innovation, Seoul, Republic of K
University, School of Medicine, Department of Pediatrics, Atlanta,
Children's Healthcare of Atlanta, Center for Drug Discovery,
States
* Corresponding Author

Features

HIV: Three trials to watch in 2024

After a pivotal vaccine trial failed earlier this year, research into treatment and prevention of HIV continues to be vital.

Abigail Beaney | December 18, 2023

Share this article

Longer-acting, less resistant treatment is needed in HIV

ST Pharm's Pirmitegravir is a first-in-class potent HIV-1 allosteric integrase inhibitor (ALLINI) that targets the noncatalytic sites of the viral integrase and interferes with the integrase-viral RNA interaction during viral maturation.

The novel MoA could help in the fight against resistance and could be longer lasting than current therapies which would improve the quality of life for HIV patients.

The Phase IIa, randomised, double-blinded, placebo-controlled, study (NCT05869643) is investigating the antiviral effect, safety, tolerability, and pharmacokinetics of pirmitegravir in treatment-naïve adults.

"This was the first therapy with an ALLINI mechanism of action to reach clinical development," Chisholm says. "In Phase I, pirmitegravir was shown to be well tolerated with a consistent pharmacokinetic profile supporting once-daily dosing. With Phase II data eagerly anticipated, pirmitegravir will be one to watch in 2024."

Thank You

ST PHARM

Technology-Driven Gene therapy CDMO
From Oligonucleotide to xRNA