IR Book | Jul. 2024

ST PHARM

Technology Driven Gene Therapy CDMO
From Oligonucleotide to xRNA

PART 01

Introduction

Overview

Introduction

▪ Summary

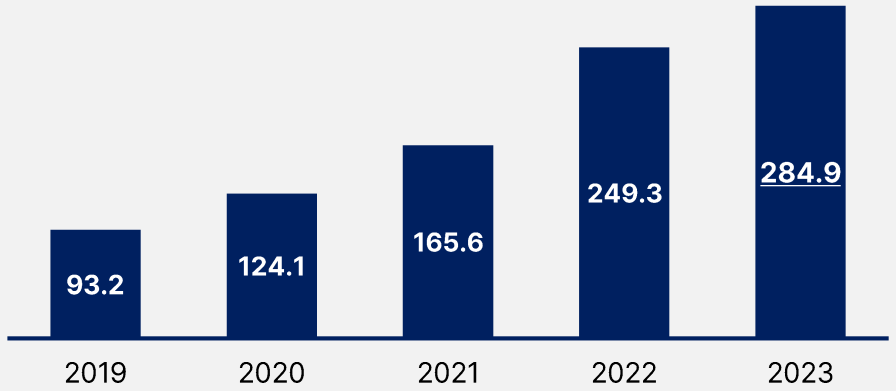
(By end of 2023)

Establishment	1983
Equity	386.9 Billion KRW
Employees	669
Revenue	285 Billion KRW (Overseas 82%, Domestic 18%)
Shareholders	Affiliated / Affiliated Persons hold 45.6%

- CDMO Specializing from Oligonucleotide to xRNA Therapeutics
- Incorporated CDMO Value Chain from Non-clinical Animal Testing to Commercial Scale Production

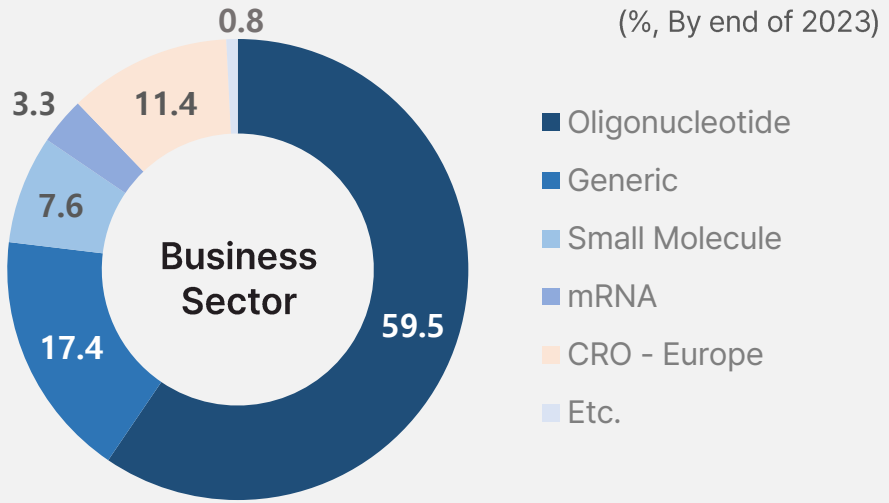
▪ Consolidated Revenue Change

(Unit: ₩ 1 Billion)



▪ Revenue Breakdown

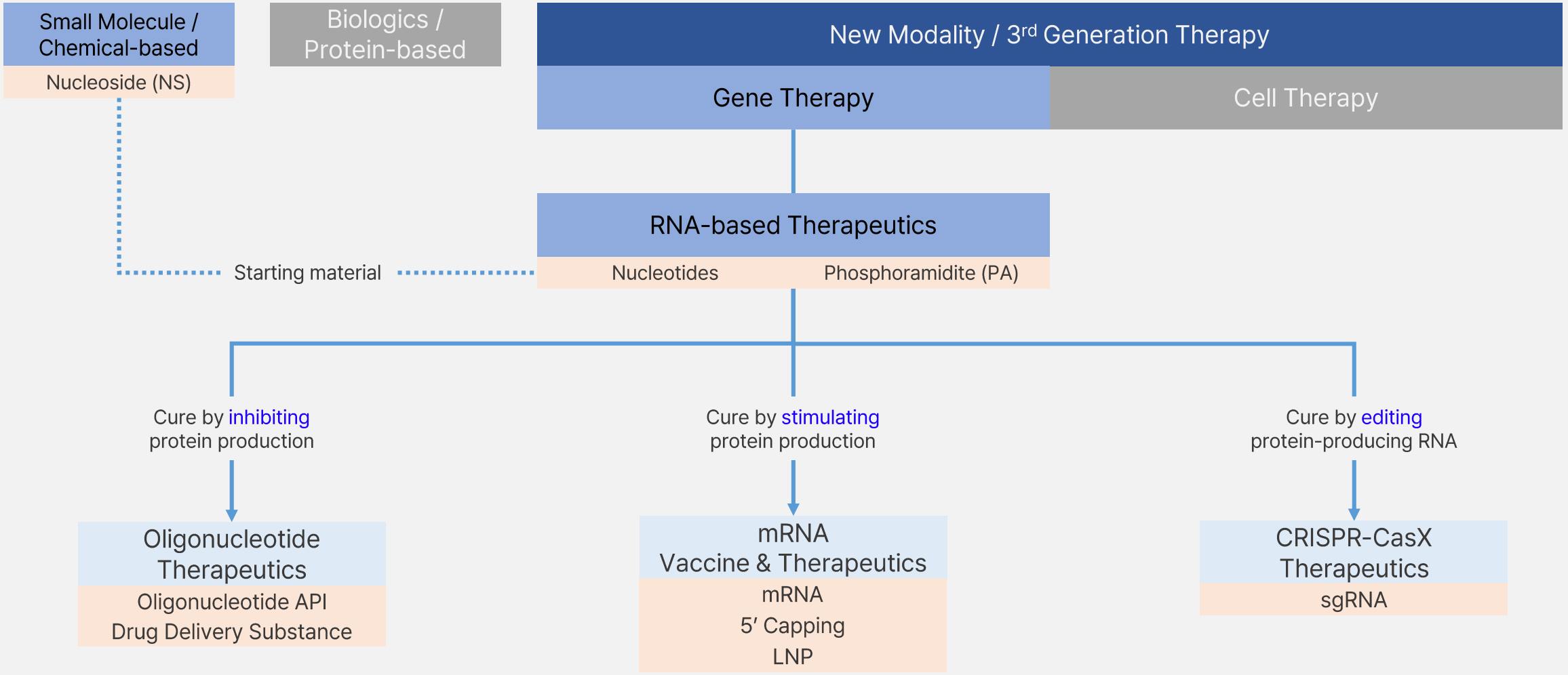
(%, By end of 2023)



Overview

Landscape of Therapeutics based on Modality

- Therapeutics Landscape

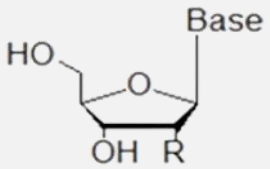


Overview

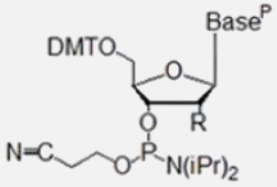
History & CDMO Records

Nucleosides API

Nucleoside



Phosphoramidite



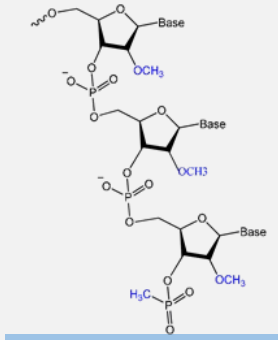
CDMO specializing in small-molecule nucleoside APIs for anti-viral medications

API Supplier of

GSK Thymidine
GSK Zidovudine
Novartis Telbivudine
Gilead Sofosbuvir

Integrated supply chain from nucleosides to phosphoramidites

Oligonucleotide API



Small-interfering

Anti-Sense

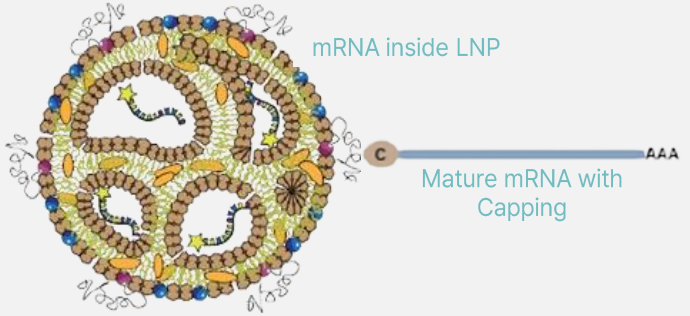
2018
- First commercial-scale Oligo. production facility

2022
- NAI grade from US FDA PAI Inspection

2023
- US FDA Inspection for Banwol Site
- 2nd commercial-scale plant (under construction)

2024
- 3rd Commercial-scale project with US FDA's approval of MDS medication

xRNA CDMO Platform



2021
- Clinical trial of mRNA vaccine with in-house developed SmartCap®

2022
- First delivery of LNP lipid

2023
- Commercial-scale mRNA production facility

2024
- Application of STLNP® Patent(PCT)

PART 02

Business Overview

Market

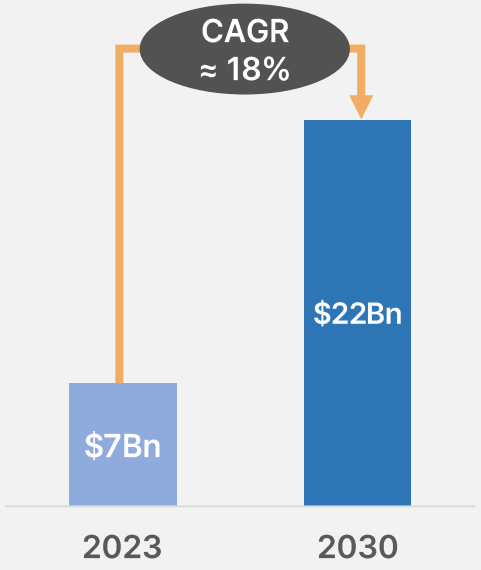
Oligonucleotide Therapeutics & CDMO Market

▪ Oligonucleotide Market Growth Forecast

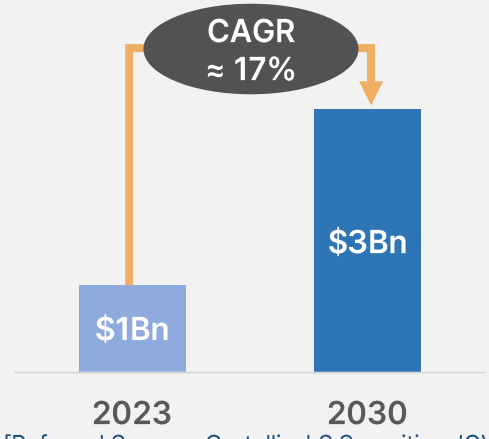
Global Market size to achieve **double-digit growth** through 2030

R&D landscape expanding to target diseases with larger population:
→ **from rare & hereditary to chronic diseases (CVD, metabolic, etc.)**

Global Oligo Therapeutics Market

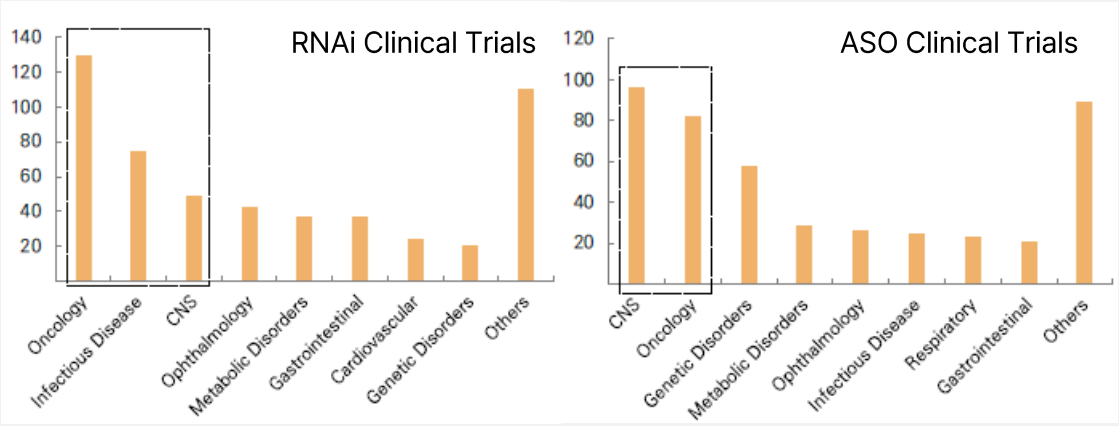


Global Oligo CDMO Market



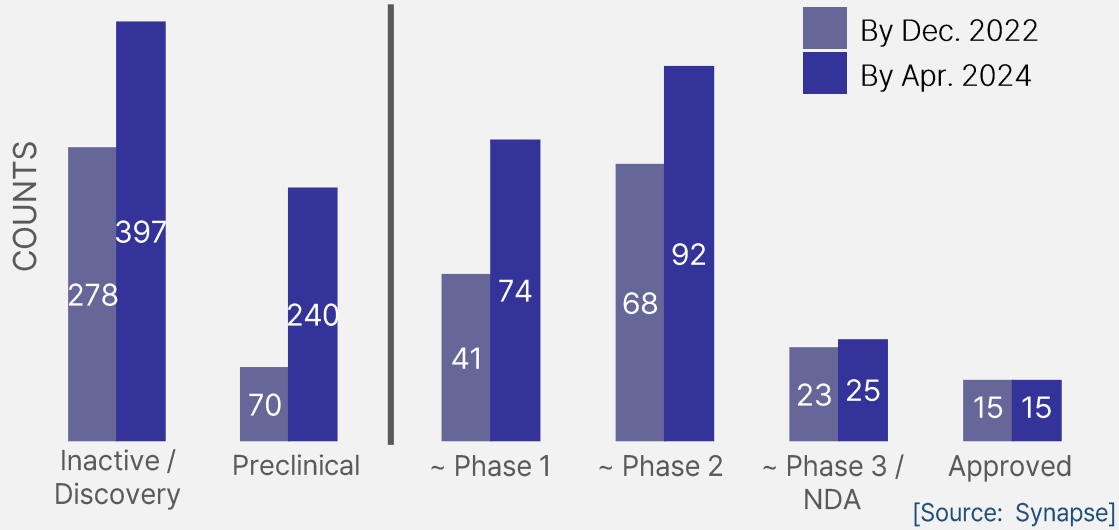
[Referred Source: Cortellis, LS Securities, IQVIA]

▪ Therapies targeting Diseases with Larger Patients Population



[Source: Mirae Asset Securities, Globaldata(2022)]

▪ Pipeline Development Landscape (ASO + RNAi)



[Source: Synapse]

Market

Oligonucleotide Therapeutics & CDMO Market

- Industry Tailwinds from Global Pharmaceuticals

GSK

To "end our investment in (new) cell and gene therapy" after exiting 2 cell therapy deals. And "oligonucleotides to take its place" (Feb. '23)

[Source: Fierce Pharma]

NOVARTIS

2 of 4 key CRM (Cardiovascular, Renal, Metabolic) assets through 2027 are oligonucleotide-based therapies

[Source: Novartis]

novo nordisk®

Approval of first siRNA medication Rivfloza (acquired from Dicerna Pharm. in Nov., '21) for primary hyperoxaluria in Sept., '23

- Recent Deals & Partnerships

Date	Target	Pharmaceutical	Size($)	Details
Jul. 24, '23	Alnylam Pharmaceutical	Roche	~2.8 B	Zilebesiran
Oct. 31, '23	Arrowhead (Janssen)	GSK	~1 B	JNJ-3989
Jan. 3, '24	Ribo Life Science	Boehringer Ingelheim	~2 B	Dev. Of MASH treatment
Jan. 4, '24	Remix Therapeutics	Roche	~1 B	Dev. Of RNA Processing
Jan. 7, '24	Shanghai Argo Biopharma	Novartis	~4.2 B	Dev. Of CVD treatment
Mar. 25, '24	Cardior Pharma	Novo Nordisk	~1.1 B	Acquisition
Apr. 22, '24	Ochre Bio	Boehringer Ingelheim	~1.3 B	Dev. Of MASH treatment
Jun. 3, '24	QurAlis	Eli Lilly	45 M	Dev. Of ALS treatment
Jun. 6, '24	Elsie Biotechnologies	GSK	50 M	Acquisition
Jun. 18. '24	Ascidian Therapeutics	Roche	~1.8 B	RNA editing partnership

Market

Oligonucleotide Therapeutics & CDMO Market

▪ Demand Forecast of Major Chronic Disease-targeting Pipelines

Required production based on 10~20% of total target patients in developed/large-size economics such as U.S., Europe, China, Japan

Company	Pipeline	Indication	Trial Phase	Dosage Guide (mg)	Dosing Interval	Target Patients (Annually)	Annual Required Production (kg)	Expected Approval
Ionis	**Pelacarsen**	**AS CVD**	**P3**	**80**	**12/yr**	**1,000,000**	**960**	2025 ~
	Olezarsen	**CVD (sHTG)**	**P3**	**50**	**12/yr**	**1,000,300**	**600**	2026 ~
	Bepirovirsen	**Hepatitis B**	**P3**	**300**	**6/yr**	**1,000,000**	**1,800**	2026 ~
	IONIS-AGT-Lrx	Hypertension	P2	80	8/yr	540,675	346	-
	ION449 (AZD-8223)	Dyslipidemias	P2	120	2/yr	1,380,000	497	-
	ION224	NASH	P2	80	12/yr	640,000	614	-
	IONIS-MAPTrx	Alzheimer's	P2	100	4/yr	1,500,000	600	-
Alnylam	**Inclisiran**	**Hyperlipidemia + AS CVD**	**Approved**	**300**	**2/yr**	**1,380,000**	**828**	AS CVD 2027 ~
	Zilebesiran	**Hypertension**	**P2**	**600**	**2/yr**	**1,000,000**	**1,200**	2027 ~
	ALN-HBV02	Hepatitis B	P2	600	2/yr	500,000	200	-
Dicerna	DCR-HBVS (RG-6346)	Hepatitis B	P2	360	4/yr	500,000	720	-
Arrow-head	ARO-ANG3	Hyperlipidemia	P2	200	2/yr	1,380,000	552	-
	ARO-HSD	NASH	P2	200	2/yr	1,000,000	400	-
	JNJ-3989	Hepatitis B	P2	400	3/yr	500,000	600	-
	Olpasiran	CVD	P2	200	4/yr	1,000,000	800	-

5 tons/yr

APIs required by 2027 ~

(highlighted late P2 ~ P3 pipelines only)

[Source : Samsung Securities, 2021 / Company websites / NIH-ClinicalTrials]

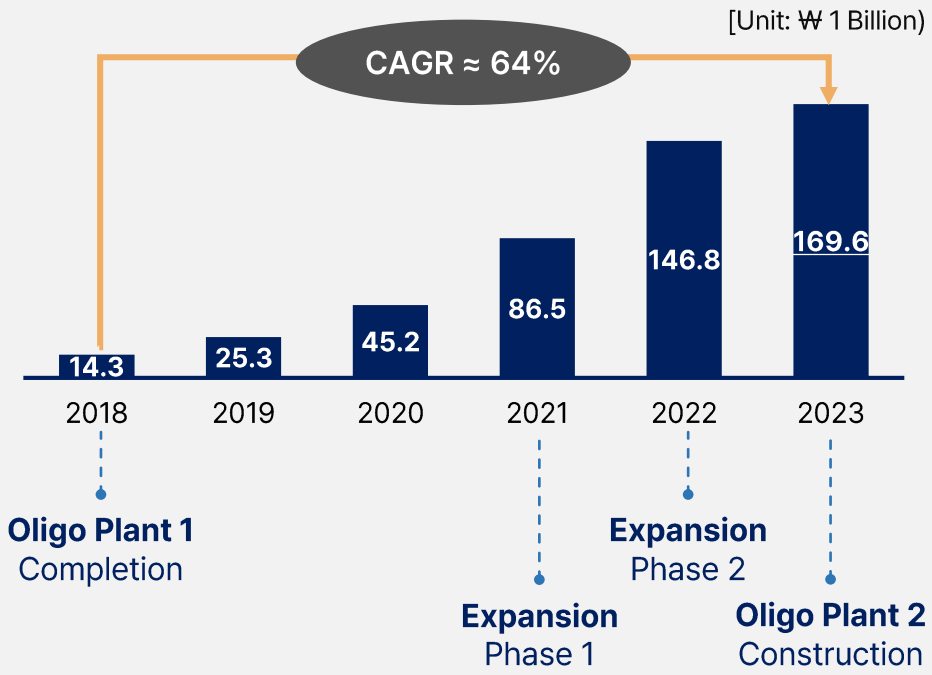
▪ Global Oligonucleotide CDMO Player

Rapid growth in becoming global major player in Oligo. CDMO

Growth driven by:

- Late-stage **Projects with larger API demand**
- Steady per-batch **yield improvements**

▪ Sales driven by Capacity Increase



▪ Major Oligo. CDMO Projects (Total of 20+ Pipelines)

#	Client	Indication	Stage			
			P1	P2	P3	NDA
1	Client A	Hyperlipidemia				
2	Client B	Spinal Muscular Atrophy				
3	Client C	Myelodysplastic Syndrome				
		Myelofibrosis (MF)	↳ Indication expansion			
4	Client D	FCS* (CVD)				
		Severe Hypertriglyceridema	↳ Indication expansion			
5	Client D	Hereditary Angioedema				
6	Client A	Atherosclerosis (CVD)				
7	Client E	Chronic Hepatitis B				
8	Client G	IgA Nephropathy				
9	Client G	Chronic Hepatitis B				

* FCS: Familial chylomicronaemia syndrome

▪ Improvements in Efficiency through **Dimer Block**

Production	2021	2023
Batch Yield	Total "N" Batches = 43kg	Total "N" Batches = 54kg **(25% ▲)**
Production Period (Interval)	N Batches S. & P.* = 27 Days	N Batches S. & P. = 19 Days **(29% ▼)**

* S. = Synthesis / P. = Purification

Business

Oligonucleotide CDMO – Production Facility (GMP)

- Capacity expansions to prepare for a **fast-growing market with strong future demand**

[1 mole ≈ 167kg ~ 500kg]

Facility	2021	2022	2025.Q2 ~ Q3	2026
	Plant 1	**Plant 1** (P1 & P2 Expansion)	**Plant 2**	**Plant 2** (P1 Expansion)
Total No. of Lines*	1	4	7	10
Total Capacity	2.0 mole (≈ 330kg~1t)	6.4 mole (≈ 1t-3.2t)	8~9 mole (≈ 1.4t-4.6t)	12~14 mole (≈ 2.3t-7t)
Total CAPEX	100 Billion KRW **		150 Billion KRW	

* No. of Line based on Installed Synthesizers
** incl. Client's investment for line dedication

- View of Banwol Campus Facilities

- Potential New Projects Under Negotiation

Client	Indication	Client	Indication
Client G	Hepatitis B	Client G	Hypertension
Client G	Alzheimer's	Client E	Antitrypsin Deficiency
Client G	Huntington's	Client A	Not disclosed
Client H	Hemophilia	Client A	Liver-target siRNA
Client I	Parkinson's	Client L	Hyperlipidemia
Client J	Epilepsy	Client M	Skin Carcinoma

Extending portfolio by adding more early ~ mid-phase pipelines

Market

mRNA Therapeutics & Vaccine Market

▪ mRNA Therapy Market Outlook & Potential

mRNA vaccines stimulate adaptive immune system to create pathogen(antigen)-targeting antibodies

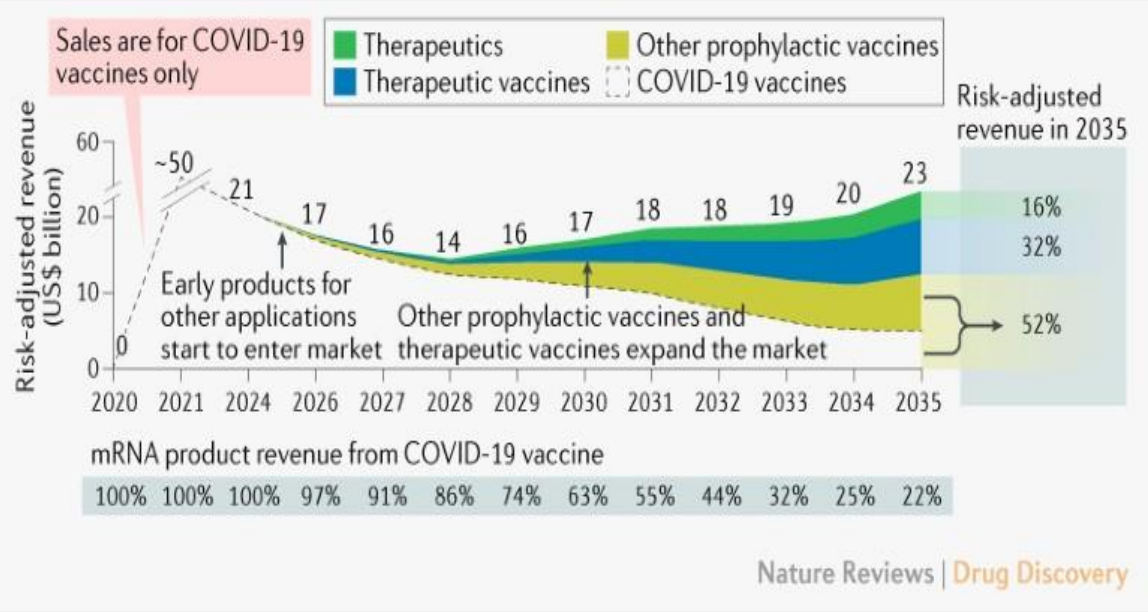
⇒ mRNA Market potentially larger than mAb Market

▪ Growing Value of mRNA-based Pipelines

mRNA pipeline landscape has grown rapidly thanks to increase in number of experiment programs and value of progressing pipelines

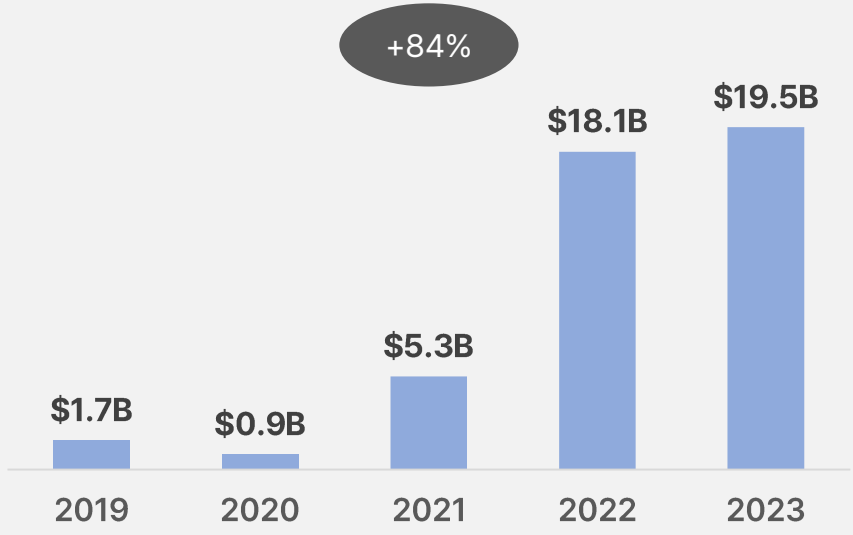
Recent tailwinds from major players expected to boost growth

[Risk-adjusted mRNA Therapy Revenue Forecast]



[Source : Nature Reviews, 2021]

[Projected Growth in mRNA-based Pipeline Value]



[Source : BCG "New Drug Modalities", 2023]

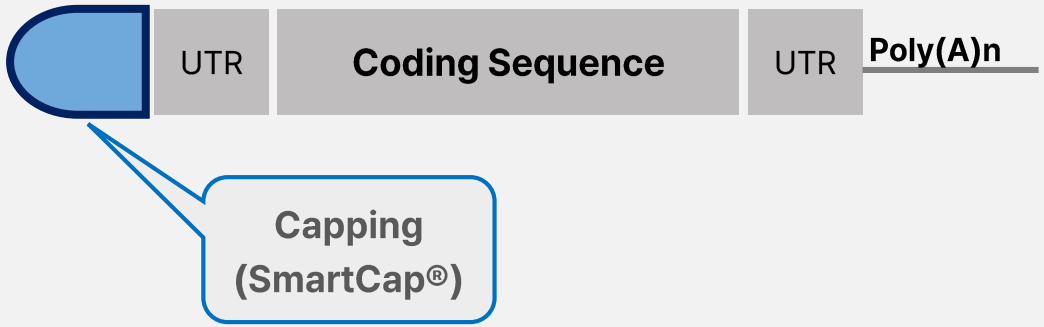
Business

mRNA Platform Technologies

▪ ST Pharm's In-house Platform Technologies

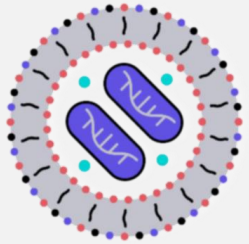
SmartCap® (Stability)

- Registered patent in Korea
- Ongoing PCT International Patent Publication
- Over 30 capping analogues → highly customizable
- Efficacy & Safety data through STP-2104 clinical trial



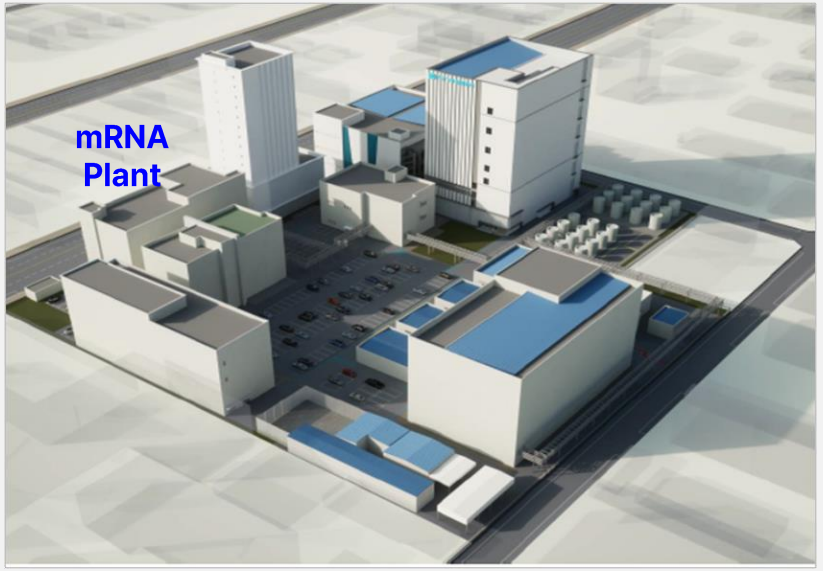
STLNP® (Delivery)

- Ongoing PCT International Patent Publication



▪ Production Facility

Comprehensive plant accommodating pilot/small-scale to **commercial-scale facilities under GMP standards**



Commercial Scale Facility:
100 ~ 120 g / month
(35 Mil. ~ 100 Mil. doses / year)

PART 03

Technology & Pipeline

Technology

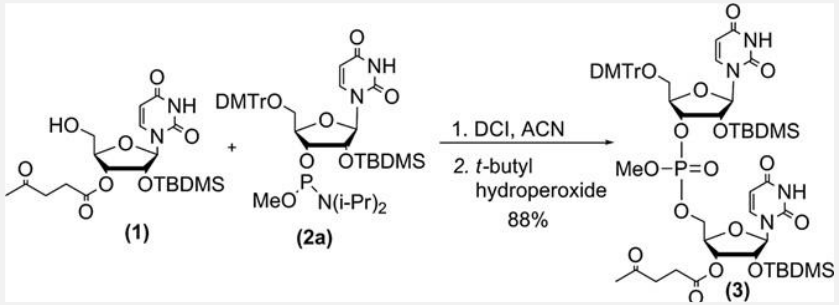
Dimer Block RNA Synthesis for Oligonucleotide CDMO

- Synthesis of siRNA Using Dimer Blocks

  Synthesis of block-PA(condensed di-nucleotide PA) on solid support, instead of single-monomer PA

  Allow faster reactions & higher yield, skipping several synthesis steps

  ↳ suitable for **large scale API production** with established production protocol



Example of Dimer Block Synthesis

- Comparison between Monomeric Synthesis with Block Synthesis

Synthesis of oligonucleotides via monomer and block coupling

Entry	Oligomer 5′-to-3′	Amidite	Concd (M)	# of couplings	Time (min)	Coupling efficiency (%)	Yield[a] (%)	
I	$(rU)_{18}dT$	rU (**2a**)	0.10	18	10	98.5	76.5	→ Monomer
II	$(rU)_{18}dT$	rU (**2a**)	0.15	18	20	98.7	80.1	
III	$(rU)_{18}dT$	rUU (**9a**)	0.10	9	10	97.2	77.8	→ Dimer Block
IV	$(rU)_{18}dT$	rUU (**9a**)	0.15	9	20	98.3	85.9	
V	$(rU)_{18}dT$	rUUU (**14a**)	0.10	6	10	86.5	41.8	→ Trimer Block
VI	$(rAAUU)_4dTdT$	rUUU (**14a**)	0.15	6	20	97.2	84.7	
VII	$(rAAUU)_4dTdT$	rU (**2a**), rA (**2b**)	0.15	16	20	98.0	72.5	
VIII	$(rAAUU)_4dTdT$	rUU (**9a**), rAA (**9b**)	0.15	8	20	98.5	88.8	

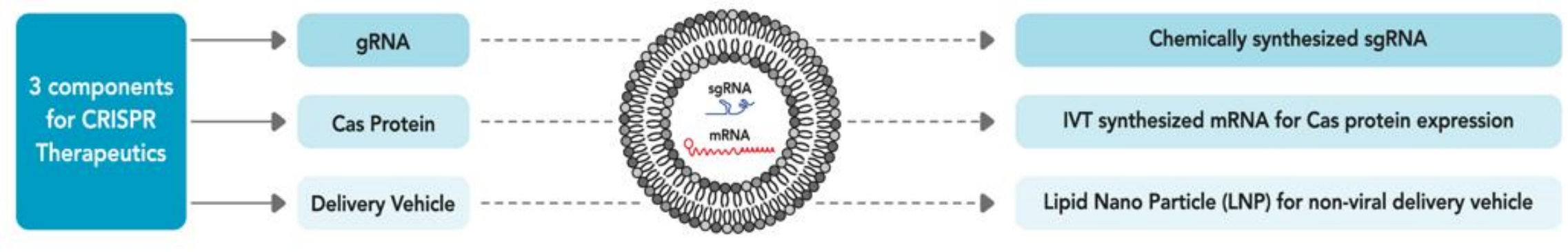
Overall, block synthesis yielded 4~5% more products with similar efficiency compared to monomeric synthesis

[Source : "RNA synthesis via dimer and trimer phosphoramidite block coupling", Tetrahedron Letters]

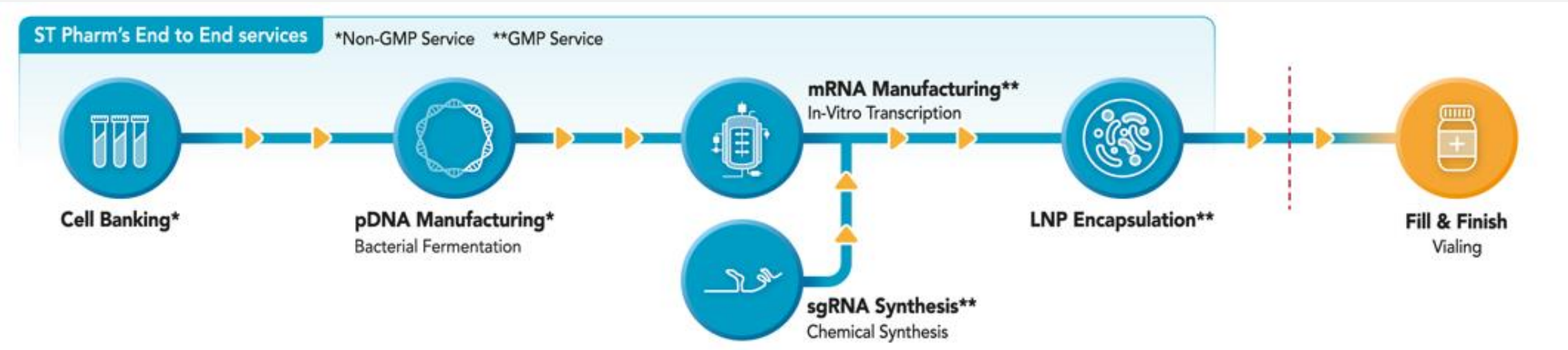
Technology

sgRNA Platform for CRISPR Solution

- CRISPR Therapeutics Structure



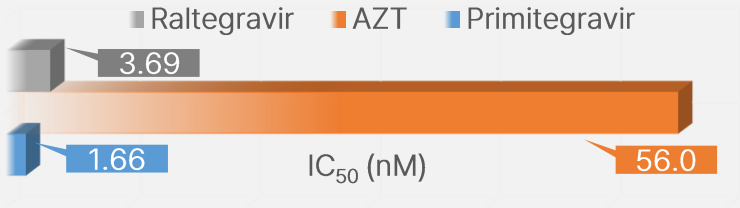
- ST Pharm's sgRNA(single guide RNA) Platform



Pipeline

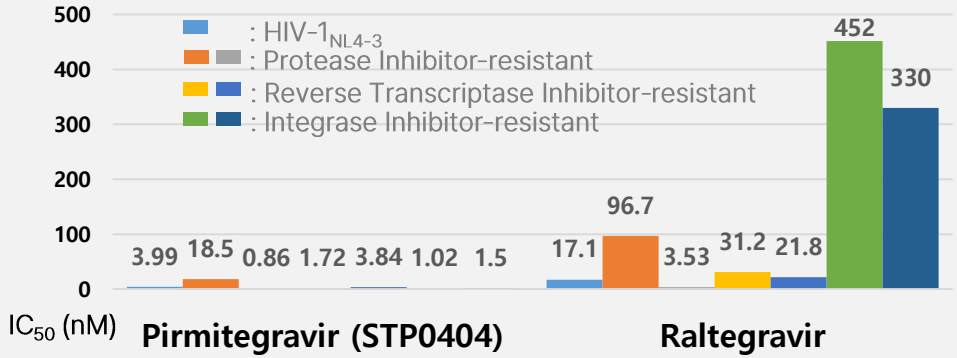
STP0404 - ALLINI Mechanism (New Mechanism)

- 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 while 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, 5070_1, 5070_2, 1566_1

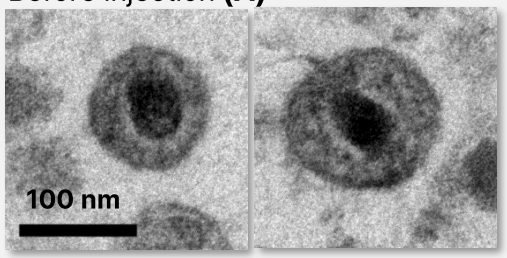
Existing HIV/AIDS Drugs' Global Sales (as of 2022)
- Dolutegravir (GSK) Approx. U$1.8 Bil.
- Elvitegravir (Gilead) Approx. U$2.4 Bil.
- Raltegravir (MSD) Approx. U$633 Mil.

Pipeline

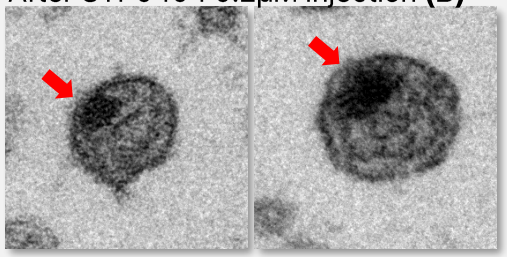
STP0404 - ALLINI Mechanism (New Mechanism)

▪ STP0404 Mechanism of Action

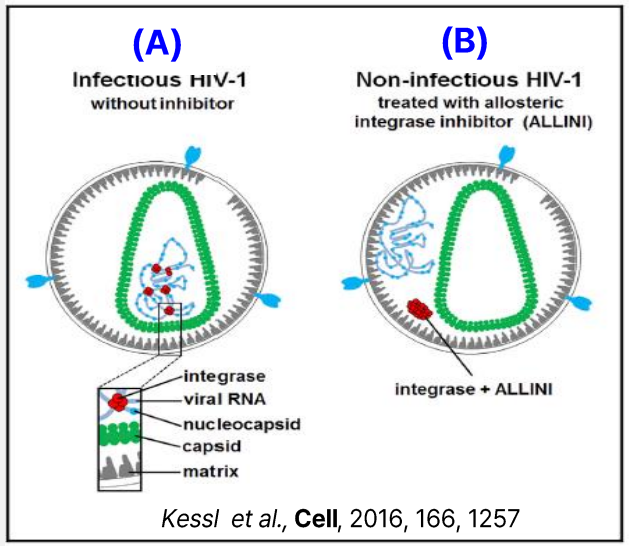
Before Injection **(A)**



After STP0404 0.2µM Injection **(B)**

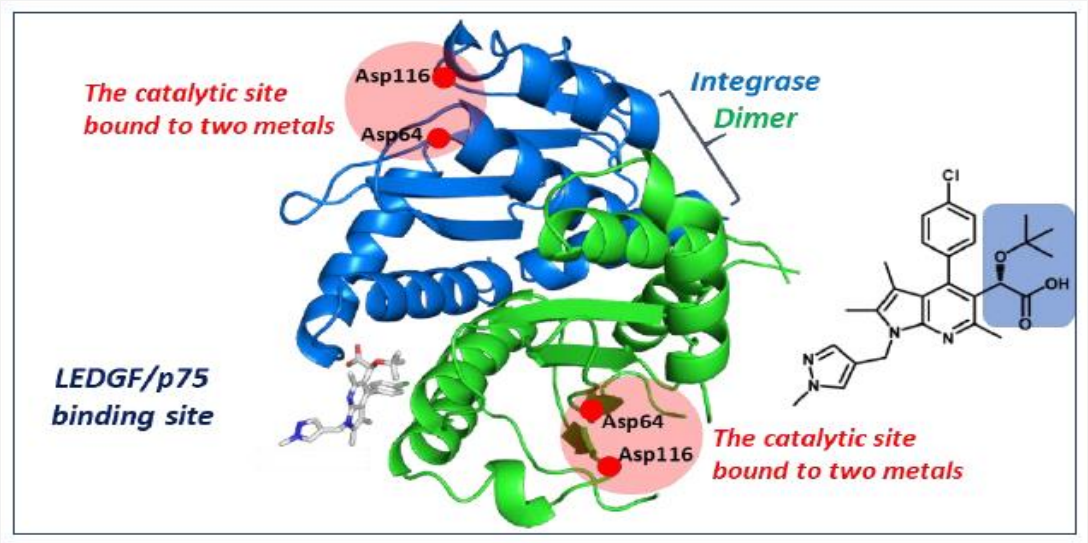


TEM study in Emory Univ.



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

Thank You

ST PHARM

Technology-Driven Gene therapy CDMO
From Oligonucleotide to xRNA

PART 04

Appendix

Appendix

Summarized Consolidated Balance Sheet

[Unit : 1 Billion KRW]

	2Q23	3Q23	4Q23	1Q24	2Q24
Asset	556.0	644.4	675.4	675.8	**666.2**
Current Asset	232.2	320.4	348.4	341.4	**324.4**
Cash and Cash Equivalent	34.4	21.5	50.1	71.1	**29.5**
Account Receivables	46.3	57.6	120.6	72.8	**44.6**
Inventory	134.3	149.2	120.7	133.8	**154.7**
Non-current Asset	323.8	324.1	327.1	334.4	**341.8**
Liabilities	215.4	265.5	288.5	284.4	**238.0**
Current Liabilities	169.7	155.0	83.7	88.5	**76.3**
Non-current Liabilities	45.7	110.4	204.8	195.9	**161.7**
Short & Long-term Borrowings	139.0	198.0	188.9	180.8	**156.1**
Equity	340.6	379.0	386.9	391.4	**428.2**
Current Ratio	*136.8%*	*206.7%*	*416.2%*	*385.8%*	***425.1%***
Debt-to-Equity Ratio	*63.2%*	*70.1%*	*74.6%*	*72.7%*	***55.6%***
Borrowings / Equity	*40.8%*	*52.2%*	*48.8%*	*46.2%*	***36.5%***
Net Borrowings / Equity	*30.7%*	*46.6%*	*35.9%*	*28.0%*	***29.6%***

Appendix

Summarized Consolidated Income Statement

[Unit : 1 Billion KRW]

	1Q23	2Q23	3Q23	4Q23	2023	2Q24
Revenue	50.6	57.8	55.9	120.6	285.0	**44.6**
Cost of Goods Sold	25.6	35.5	31.6	80.2	172.9	**29.3**
Gross Profit	25.0	22.3	24.3	40.4	112.1	**15.3**
SG & A Expenses	21.3	20.7	17.7	18.9	78.6	**18.3**
R&D Expenses	9.4	8.0	6.6	6.4	30.4	**6.1**
Operating Profit	3.7	1.6	6.7	21.5	33.5	**-3.1**
Non-operating Income	0.1	0.0	0.0	0.5	0.6	**0.0**
Non-operating Cost	0.1	0.1	0.1	0.1	0.4	**0.2**
Financial Income	4.1	2.0	1.9	1.4	9.4	**7.3**
Financial Cost	3.9	2.5	3.4	9.9	19.7	**3.2**
EBT	3.9	1.0	5.1	13.4	23.4	**0.9**
Net Profit	2.9	1.2	3.4	10.1	17.5	**0.9**
Gross Profit Margin	*49.5%*	*38.6%*	*43.5%*	*33.5%*	*39.3%*	***34.3%***
Operating Profit Margin	*7.3%*	*2.8%*	*11.9%*	*17.8%*	*11.8%*	***-6.9%***
EBT Margin	*7.6%*	*1.7%*	*9.1%*	*11.1%*	*8.2%*	***2.0%***
Net Profit Margin	*5.7%*	*2.1%*	*6.0%*	*8.3%*	*6.1%*	***2.0%***