

IR Book | Jul. 2024

ST PHARM

Technology Driven Gene Therapy CDMO
From Oligonucleotide to xRNA





PART 01

Introduction



Summary

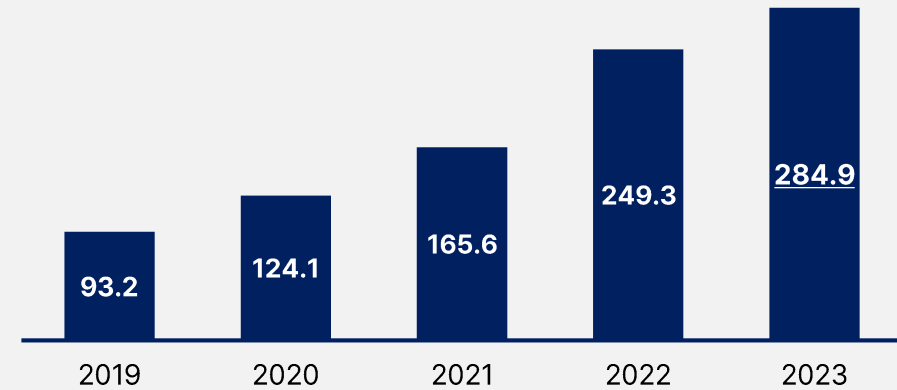
(By end of 2023)

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

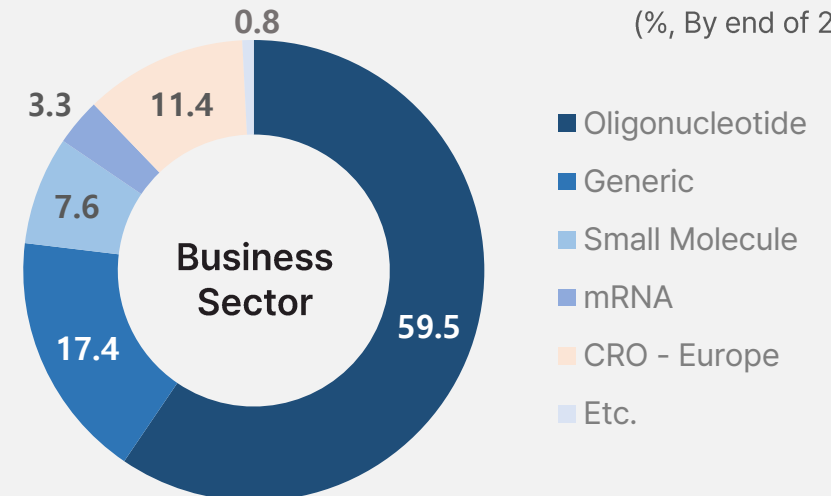
Consolidated Revenue Change

(Unit: ₩ 1 Billion)



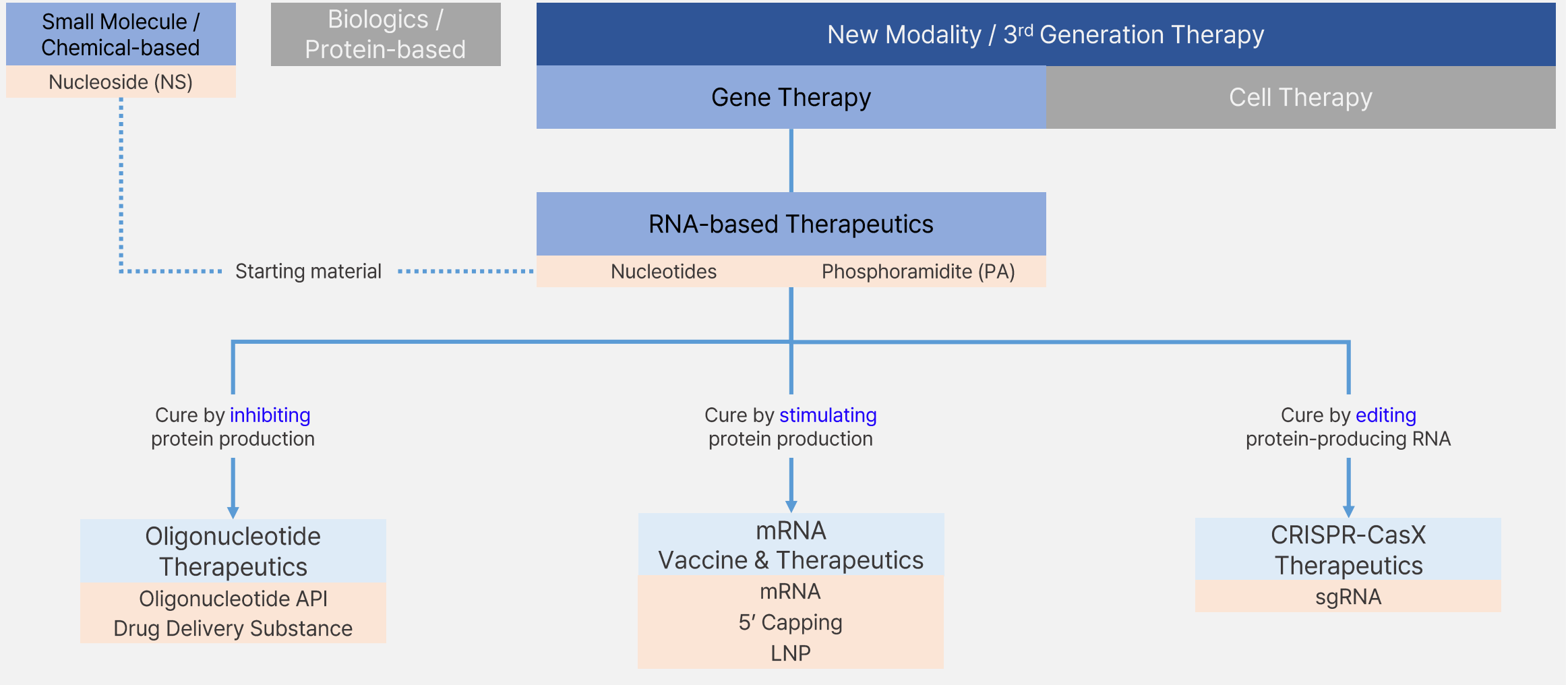
Revenue Breakdown

(%, By end of 2023)





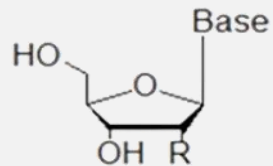
Therapeutics Landscape



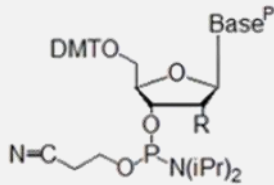


Nucleosides API

Nucleoside



Phosphoramidite



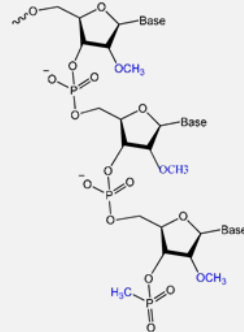
CDMO specializing in small-molecule nucleoside APIs for anti-viral medications

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

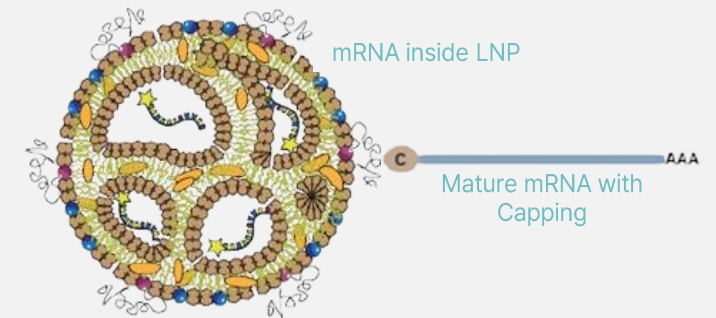
2023

- 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



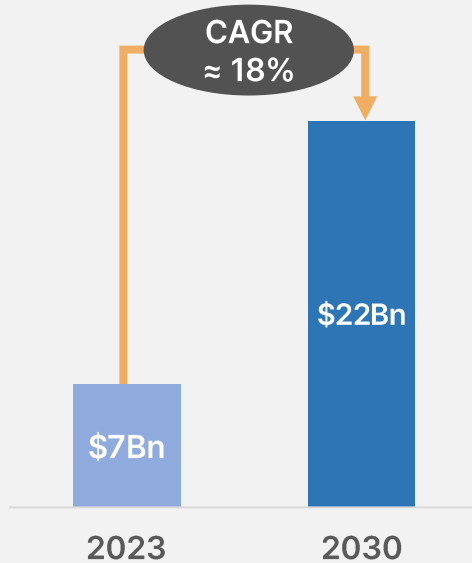
Oligonucleotide Therapeutics & CDMO Market

■ Oligonucleotide Market Growth Forecast

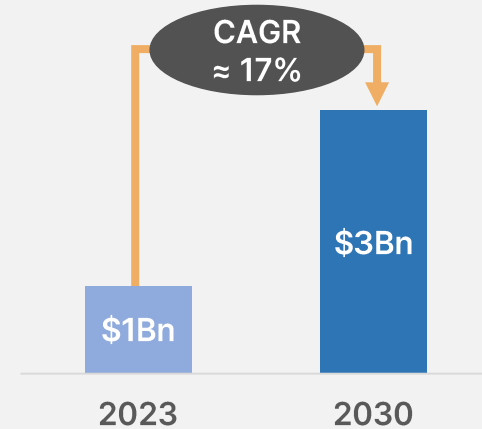
Global Market size to achieve **double-digit growth** through 2030

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

Global Oligo Therapeutics Market

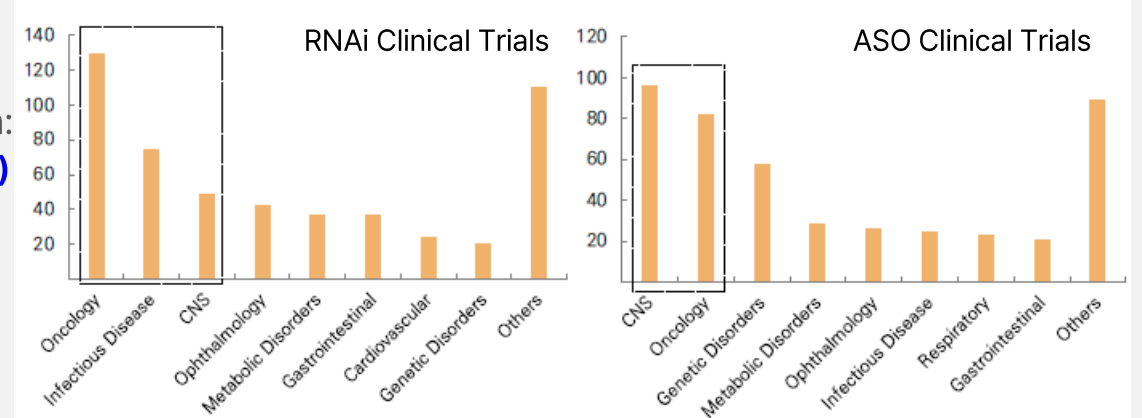


Global Oligo CDMO Market



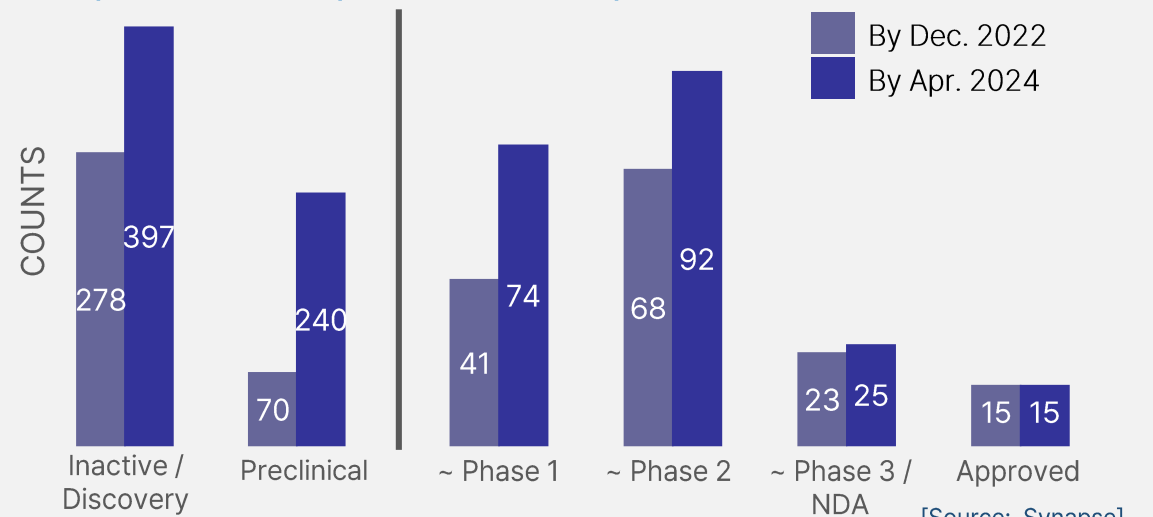
[Referred Source: Cortellis, LS Securities, IQVIA]

■ Therapies targeting Diseases with Larger Patients Population



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

■ Pipeline Development Landscape (ASO + RNAi)



[Source: Synapse]



Industry Tailwinds from Global Pharmaceuticals



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]



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

[Source: Novartis]



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	Alnyam 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



▪ 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]



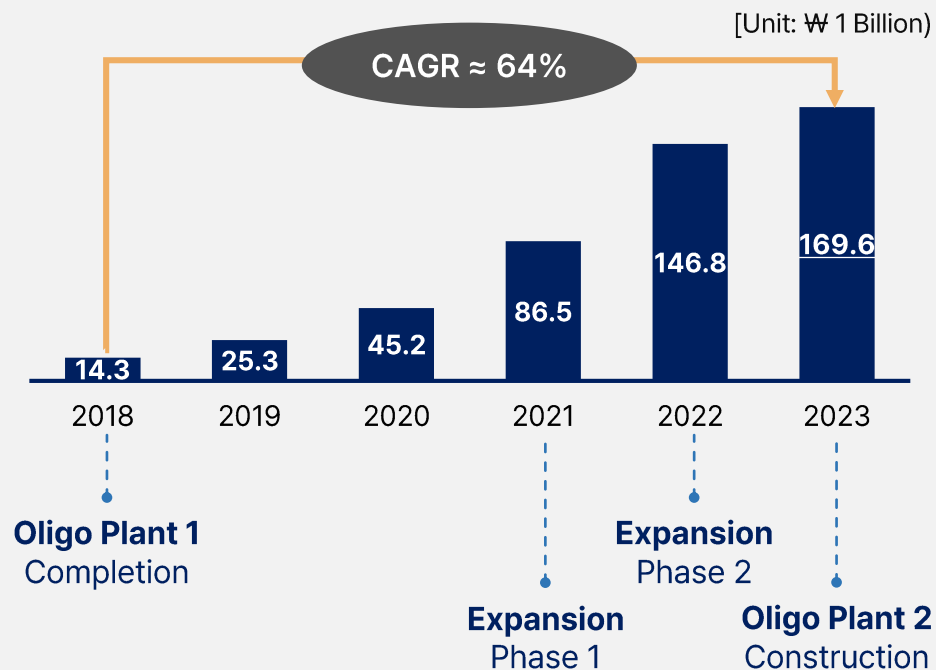
Global Oligonucleotide CDMO Player

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



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



▪ mRNA Therapy Market Outlook & Potential

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

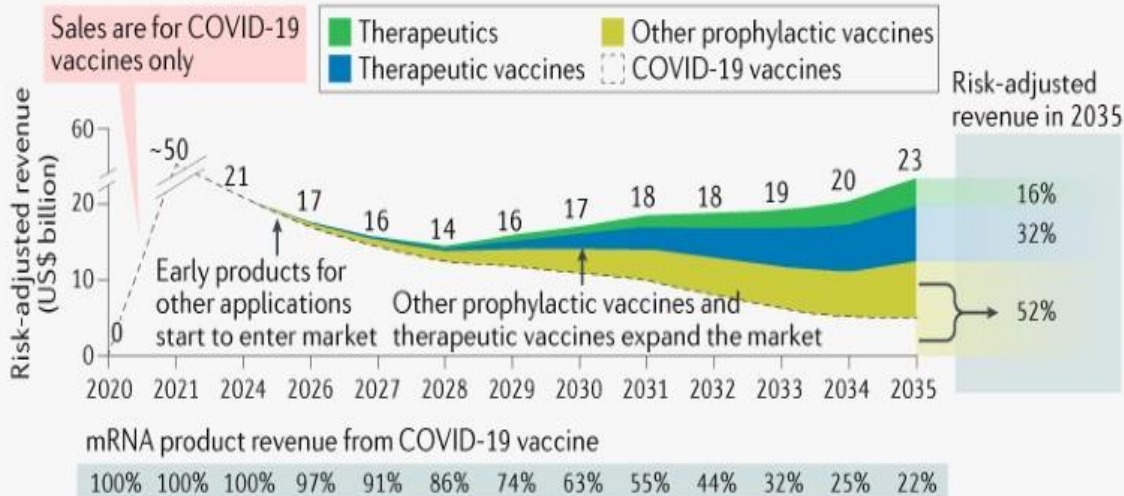
⇒ mRNA Market potentially larger than mAb Market

▪ 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

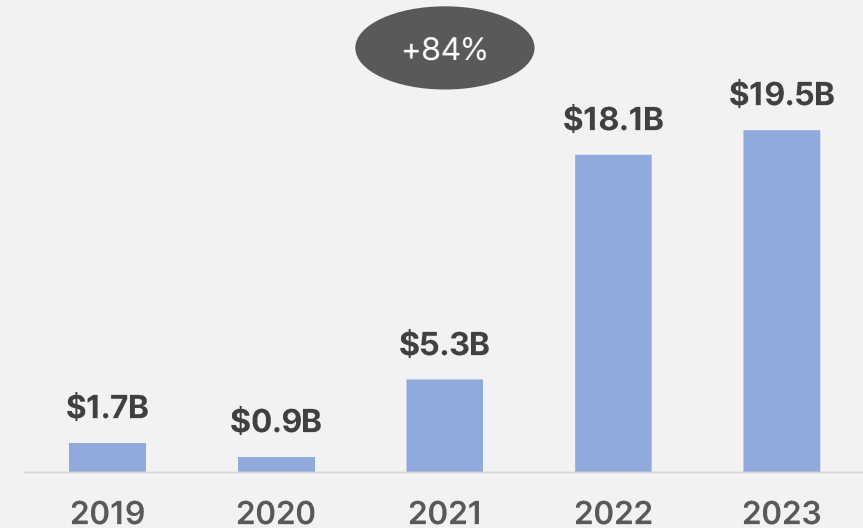
[Risk-adjusted mRNA Therapy Revenue Forecast]



Nature Reviews | Drug Discovery

[Source : Nature Reviews, 2021]

[Projected Growth in mRNA-based Pipeline Value]



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



ST Pharm's In-house Platform Technologies

SmartCap® (Stability)

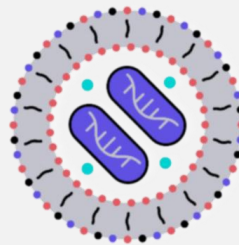
- Registered patent in Korea
- Ongoing PCT International Patent Publication
- Over 30 capping analogues → highly customizable
- Efficacy & Safety data through STP-2104 clinical trial



Capping
(SmartCap®)

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

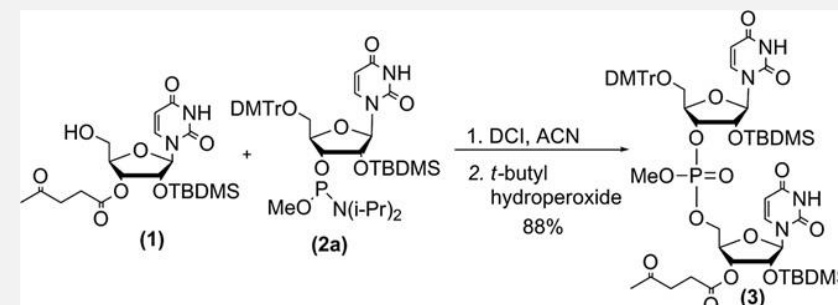
Technology & Pipeline

■ 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
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
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
VI	(rAAUU) ₄ dTdT	rUUU (14a)	0.15	6	20	97.2	84.7
VII	(rAAUU) ₄ dTdT	rU (2a), rA (2b)	0.15	16	20	98.0	72.5
VIII	(rAAUU) ₄ dTdT	rUU (9a), rAA (9b)	0.15	8	20	98.5	88.8

→ Monomer
→ Dimer Block
→ Trimer Block

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

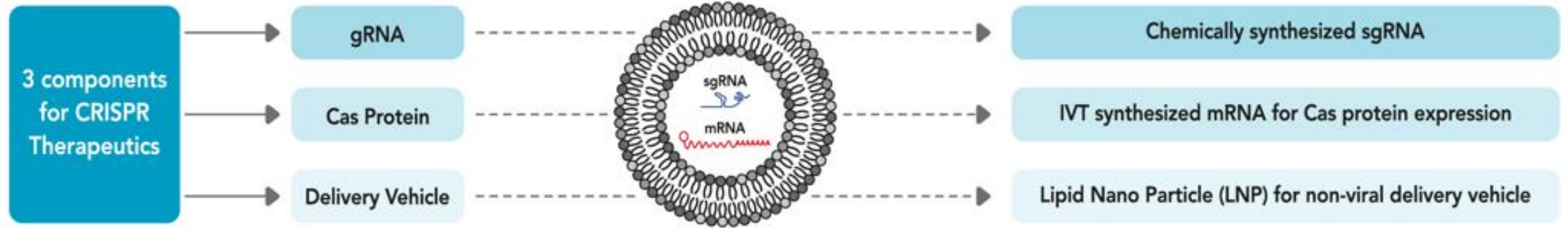
[Source: "RNA synthesis via dimer and trimer phosphoramidite block coupling", Tetrahedron Letters]

Technology

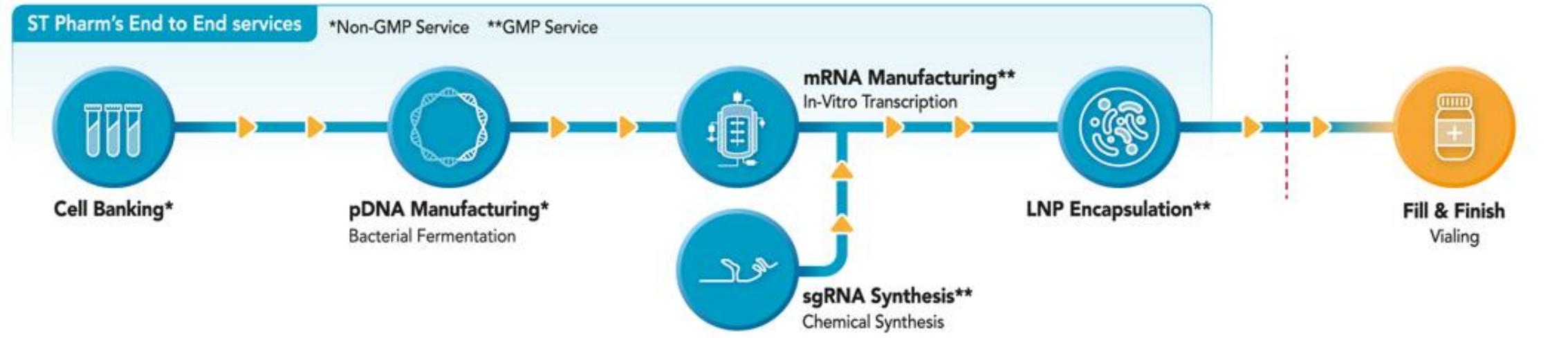


sgRNA Platform for CRISPR Solution

CRISPR Therapeutics Structure

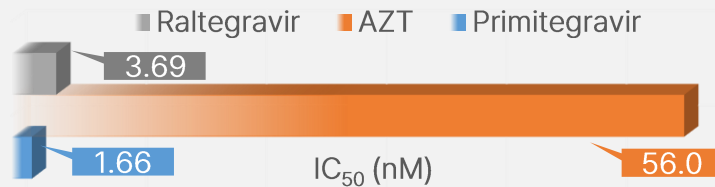


ST Pharm's sgRNA(single guide RNA) Platform





Anti-viral Efficacy (Cell Line MT-4)



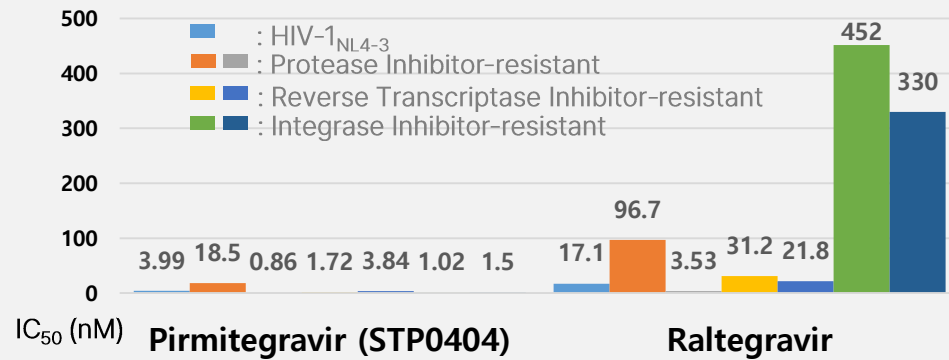
2 ~ 33 times higher anti-viral efficacy than existing treatments

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 (29.7~57.8)
Raltegravir	1,227.70 (12.5~3,038)	2525 (351~4,322)
Elvitegravir	-	2751.5 (276~10,000)
Dolutegravir	-	4.57 (3.07~8.54)

RAL-resistant strains: 4736_2, 4736_4, 8070_1, 8070_2, 1666_1

Existing HIV/AIDS Drugs' Global Sales (as of 2022)

- Dolutegravir (GSK) Approx. U\$1.8 Bil.

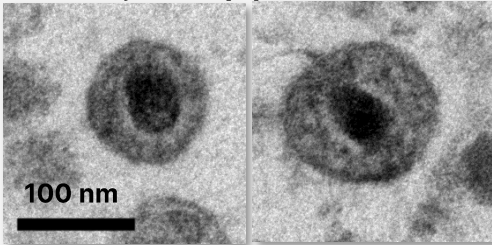
- Elvitegravir (Gilead) Approx. U\$2.4 Bil.

- Raltegravir (MSD) Approx. U\$633 Mil.

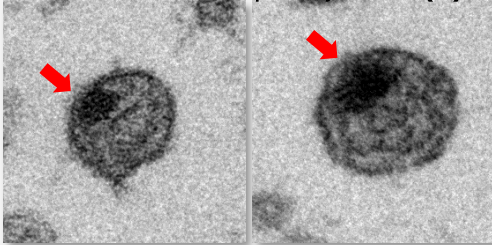


STP0404 Mechanism of Action

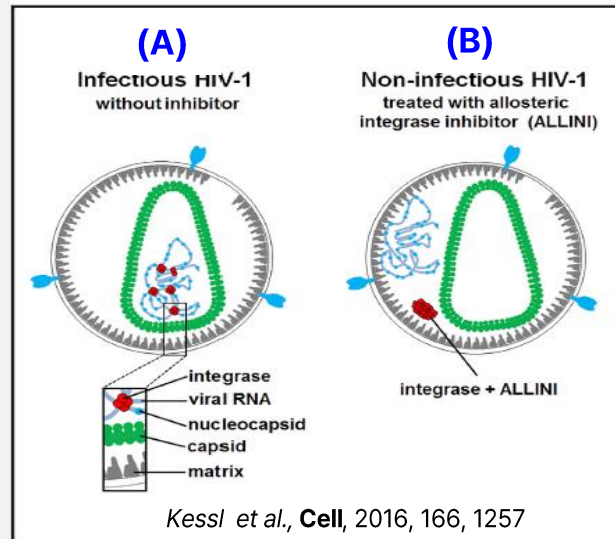
Before Injection (A)



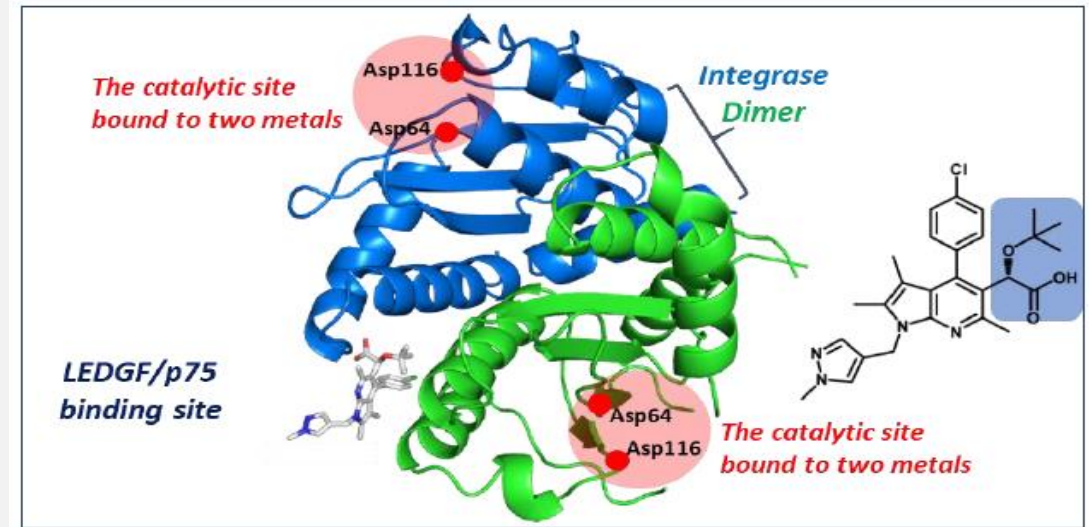
After STP0404 0.2µM Injection (B)



TEM study in Emory Univ.



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



PART 04

Appendix



	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%

Thank You

ST PHARM

Technology-Driven Gene therapy CDMO
From Oligonucleotide to xRNA

