

Presentation Material

Expansion of DDS Business

November 17, 2021

 **NOF CORPORATION**

Table of Contents

- 1. Market Expansion of DDS Materials**
- 2. Expansion to Peptide/Protein Drugs and Antibody Drugs**
- 3. Expansion to Nucleic Acid Drugs**
- 4. DDS Business Plan**

DDS: **D**rug **D**elivery **S**ystem

1. Market Expansion of DDS Materials

Functions of DDS

Provide Drugs

Where needed

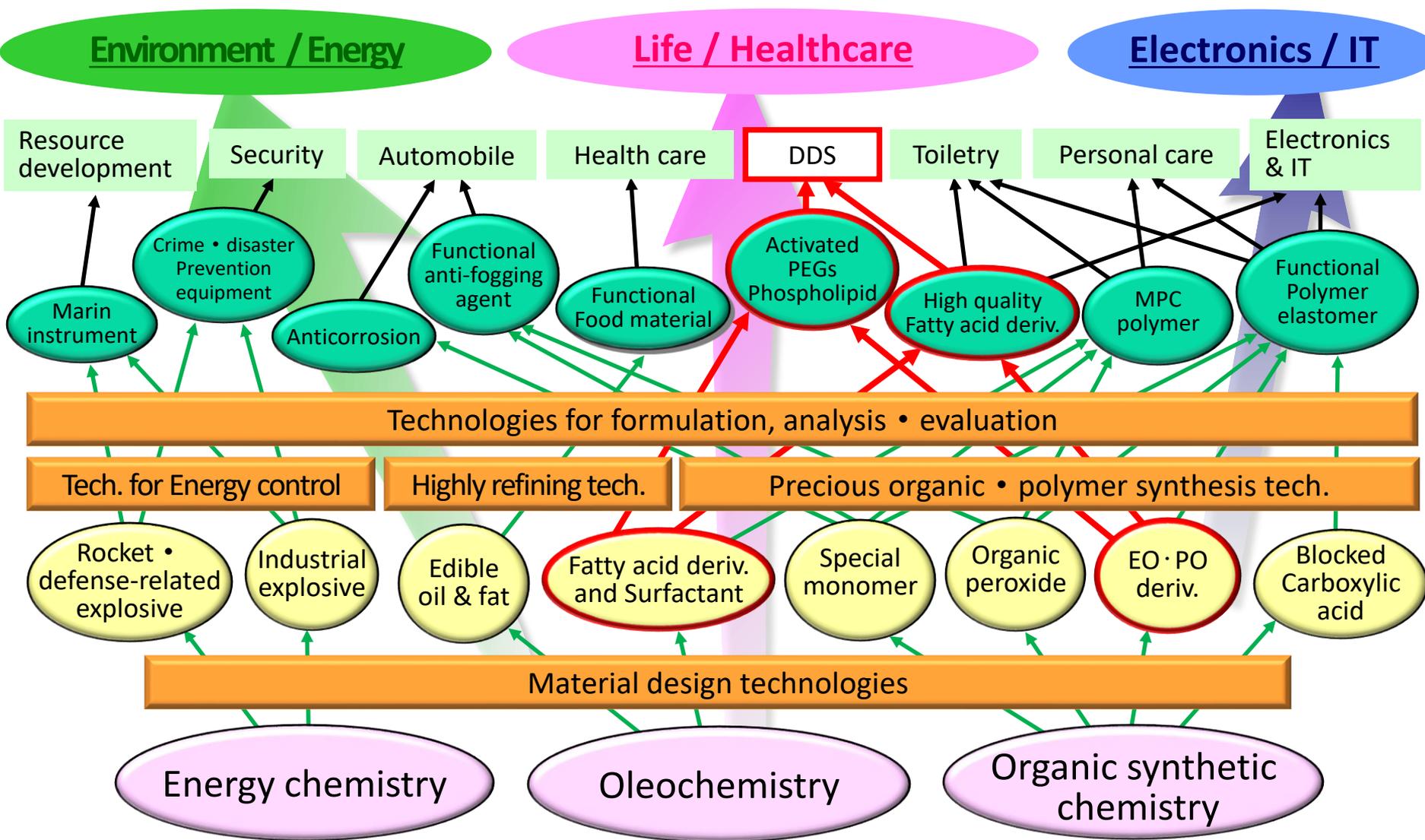
When needed

Necessary amount

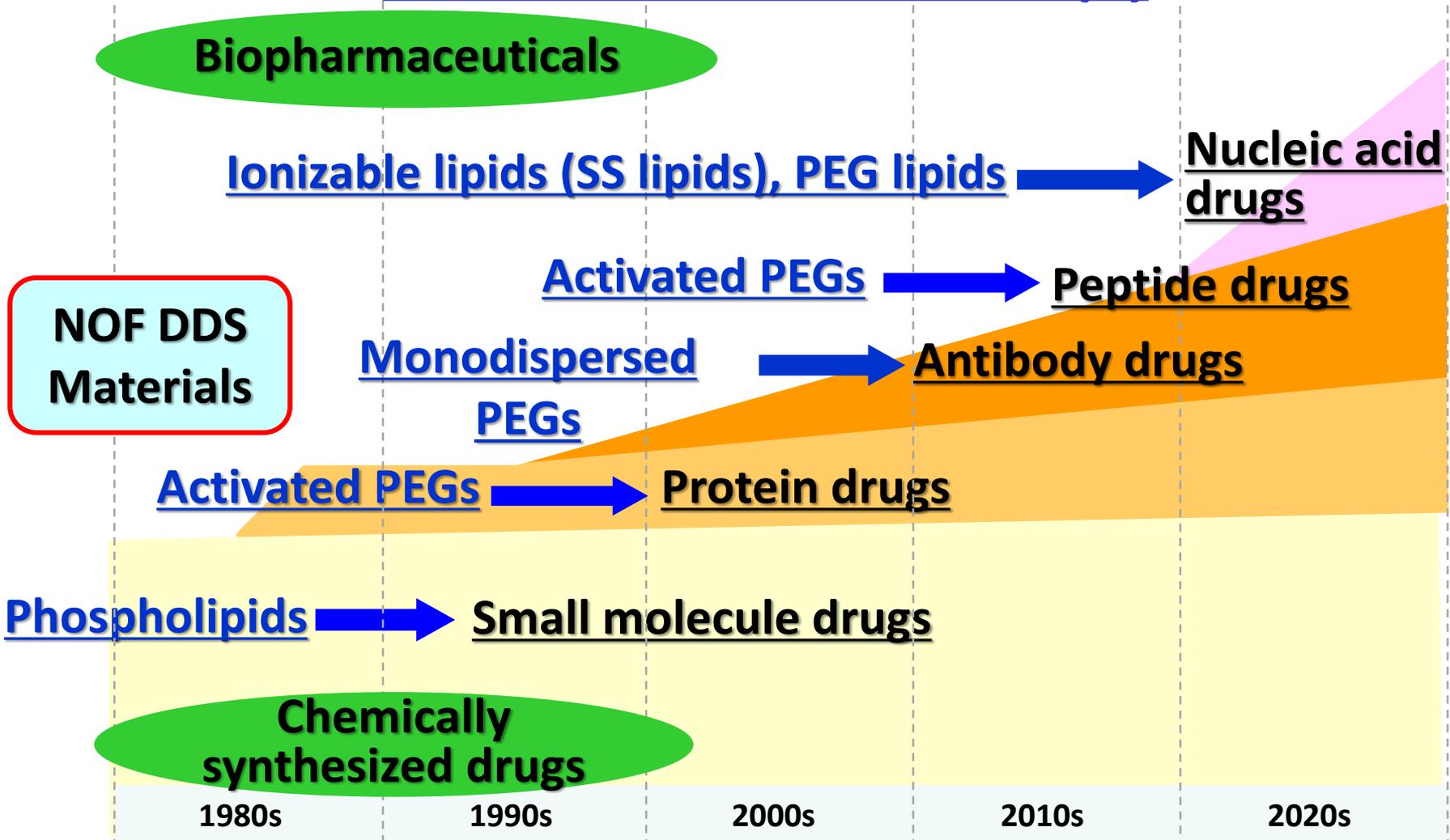
- ◆ Improved effect by efficient transportation to the affected area
- ◆ Reduced dosing frequency by improving retention in the body (Improved QOL)
- ◆ Improved stability

DDS: **D**rug **D**elivery **S**ystem

Technologies and materials of the NOF Group



Expansion of NOF DDS Materials on the Pharmaceutical Market (1)



Reference material: Japan Association of Bioindustries Executives (March 2016)

Expansion of NOF DDS Materials on the Pharmaceutical Market (2)

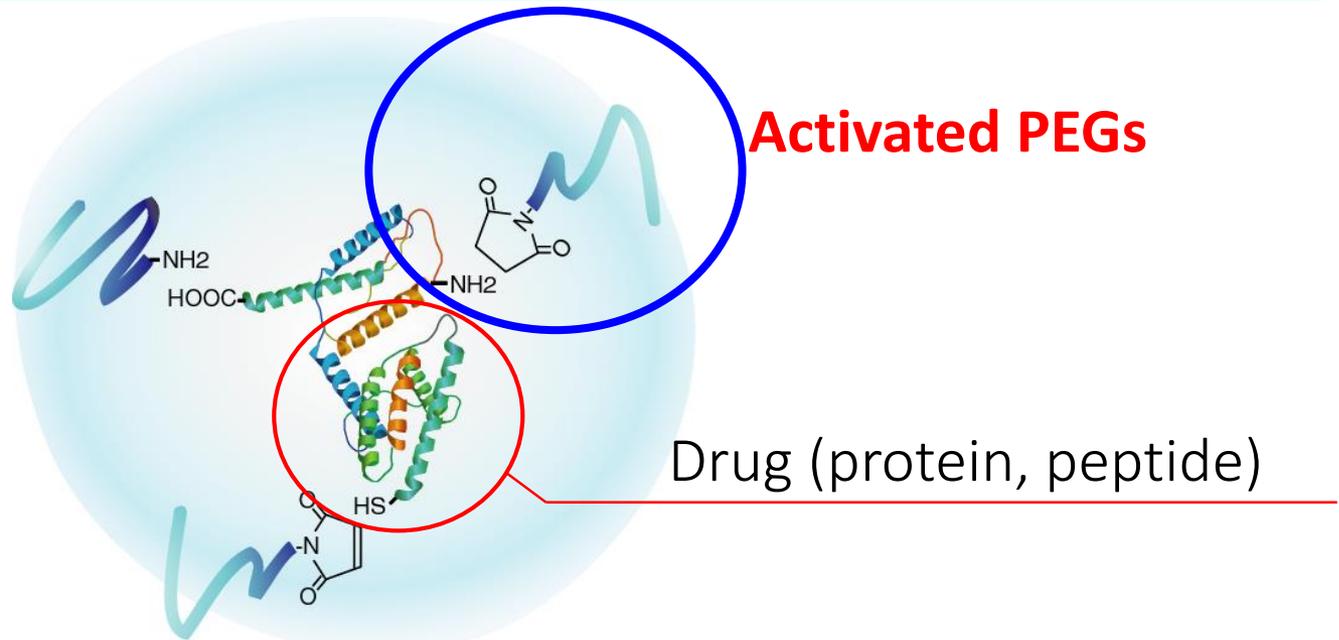
NOF DDS Materials	Pharmaceutical field	Market size (2020)	Compound average growth rate (2020 - 2030)
Ionizable lipids (SS lipids) PEG lipids	Nucleic acid drugs	Regenerative therapy	High (27%)
		Gene therapy	High (32%)
		RNA drugs	High (24%)
Activated PEGs	Peptide drugs	3.2 trillion yen	Medium (8%)
Monodispersed PEGs	Antibody drugs	16 trillion yen	Medium (8%)
Activated PEGs	Protein drugs	6.4 trillion yen	Low (4%)
Phospholipids	Small molecule drugs	48 trillion yen	Low (Slight increase)

Prepared using the material of Arthur D Little (2021) and Nature review; Evolution of the market for mRNA technology (September 02, 2021) as references

2. Expansion to Peptide/Protein Drugs and Antibody Drugs

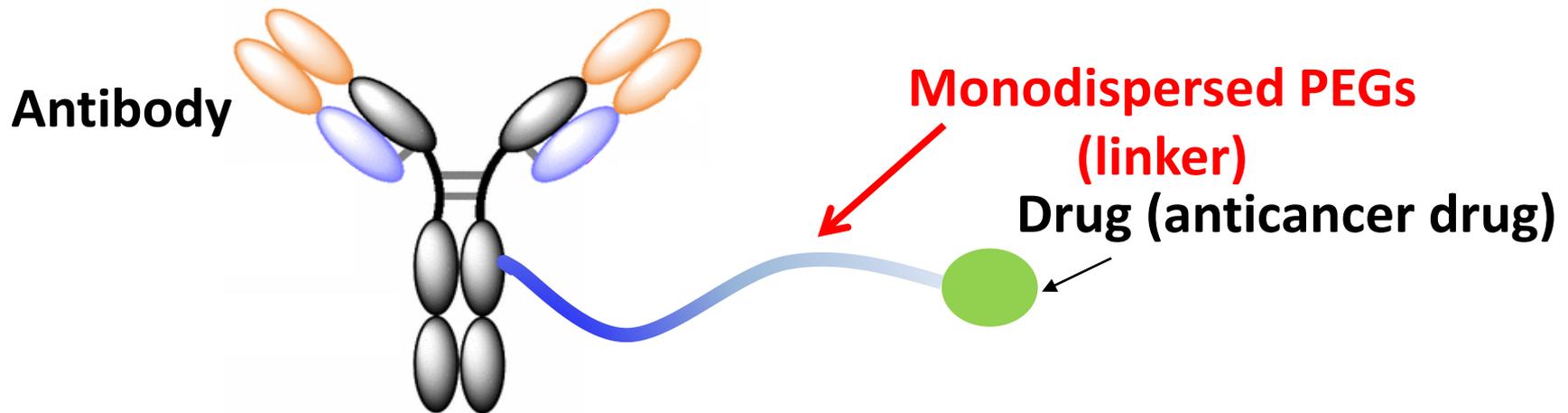
Activated PEGs for Peptide/Protein Drugs

- Used as a raw material for PEGylated drugs that modify peptides and proteins, contributing to improved retention of peptide and protein drugs in the body
- The largest global market share of activated PEGs. The number of launched drugs adopting NOF's products has been increasing in recent years.



Monodispersed PEGs for Antibody Drugs

- Used as the linker¹⁾ for antibody-drug conjugates, a type of antibody drug
- Aggregation can be suppressed even when hydrophobic drugs (anticancer drugs) bind to antibodies
- Multiple drugs can bind to antibodies



1) Linker: A substance that connects the drug and antibody

3. Expansion to Nucleic Acid Drugs

What are Nucleic Acid Drugs?

- **Drugs with “nucleic acids” such as DNA¹⁾ and RNA²⁾ as the basic structure**
- **Nucleic acid drugs include mRNA,³⁾ antisense , siRNA⁴⁾ aptamer, etc.**
- **Applied to regenerative therapy, gene therapy, and RNA drugs**
- **Controls the functions of genes and proteins that cause diseases**
- **Actively developed for cancer treatment and as vaccines**

1) DNA: Deoxyribonucleic acid

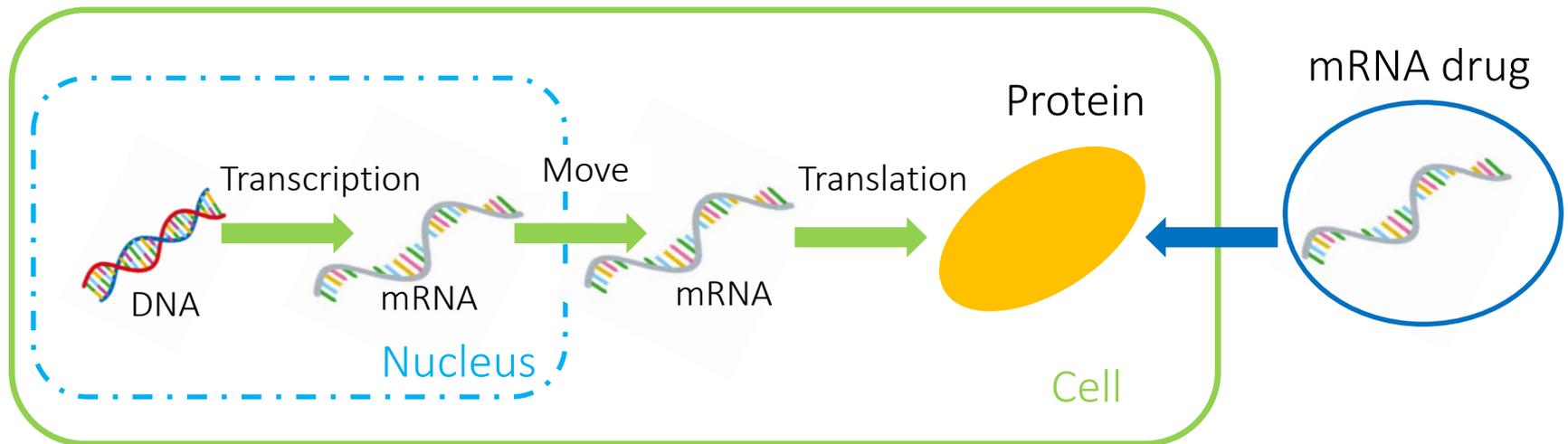
2) RNA: Ribonucleic acid

3) mRNA: Messenger ribonucleic acid

4) siRNA: Small interfering ribonucleic acid

mRNA Drugs

- Insert mRNA, a protein blueprint, into a cell to synthesize an effective protein for treatment
- Effective for rare diseases in which normal proteins cannot be synthesized due to genetic abnormalities
- Active application development of anticancer drugs and infectious disease vaccines because antigen proteins (part of virus) can be synthesized

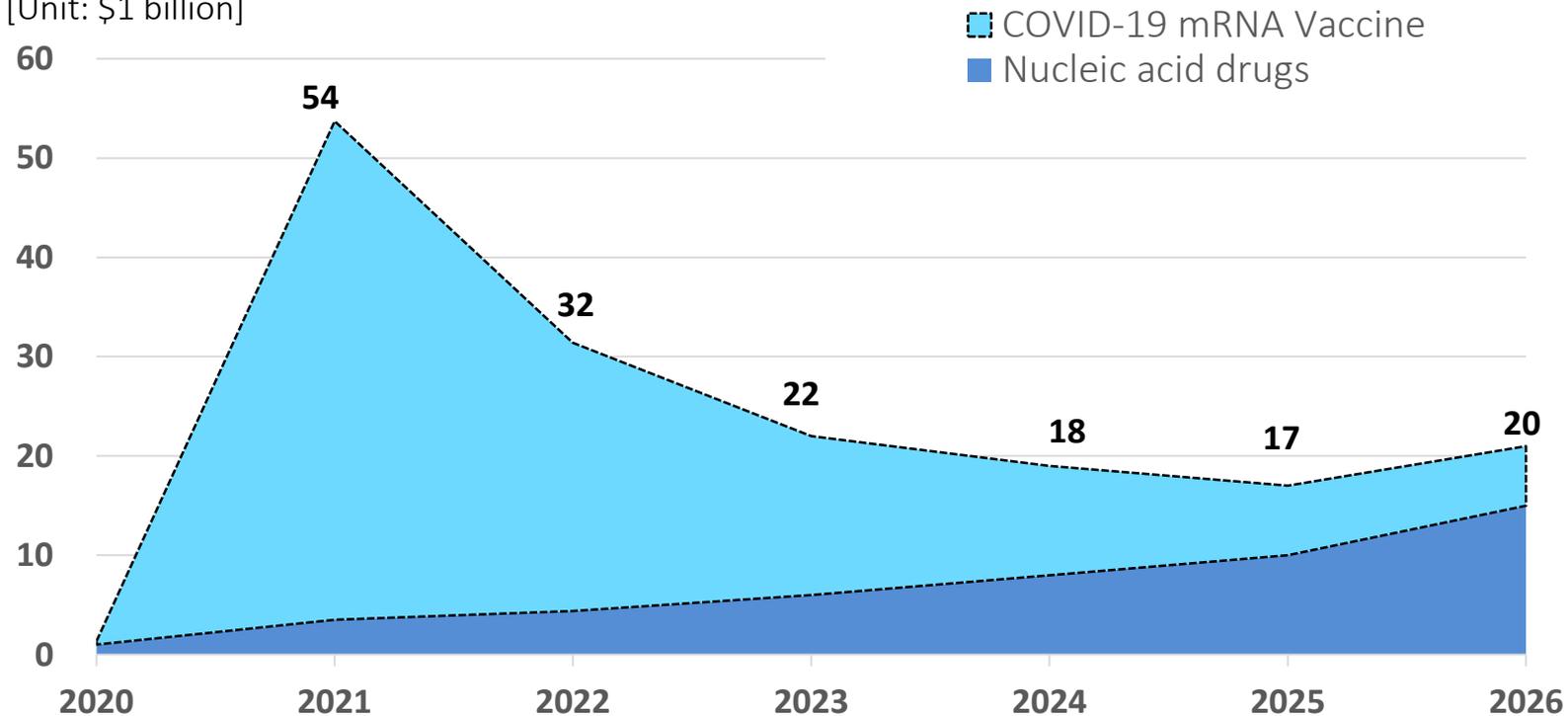


Market Trend of Nucleic Acid Drugs (including COVID-19 mRNA vaccines)

Two COVID-19 vaccines using mRNA technology were approved in 2020

- **The COVID-19 vaccine market peaks in 2021 and will shrink**
- **Nucleic acid drug market will show high growth**

[Unit: \$1 billion]

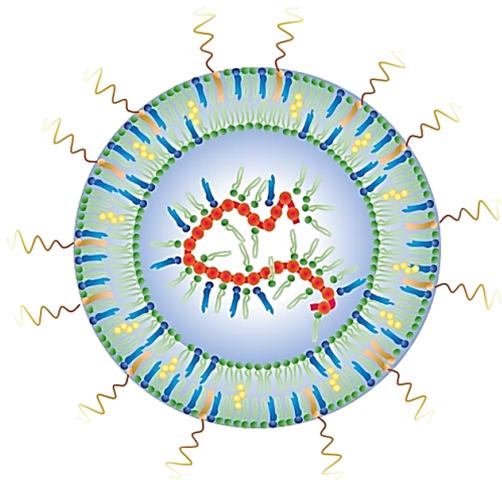


Estimation by NOF based on Evaluate Pharma

DDS Materials for Nucleic Acid Drugs (mRNA drugs)

- Lipid nanoparticles (LNP) are used as the DDS material because nucleic acid is unstable in the body
- Lipid nanoparticles consist of ionizable lipids, PEG lipids, etc.

Lipid NanoParticle: LNP



Constituent	Role
Ionizable lipids (SS lipids)	Contribute to the encapsulation and intracellular delivery of nucleic acids and genes
PEG lipids	Improve retention in the body
Phospholipids	Lipid membrane formation
Cholesterol	Stabilization of lipid membranes

Ionizable Lipid and PEG Lipid Products

◆ COATSOME® SS-series (ionizable lipids)

Product No.	Effect
SS-E	Stable release of nucleic acids in cells
SS-EC	
SS-OP	

◆ SUNBRIGHT® G-series (PEG lipids)

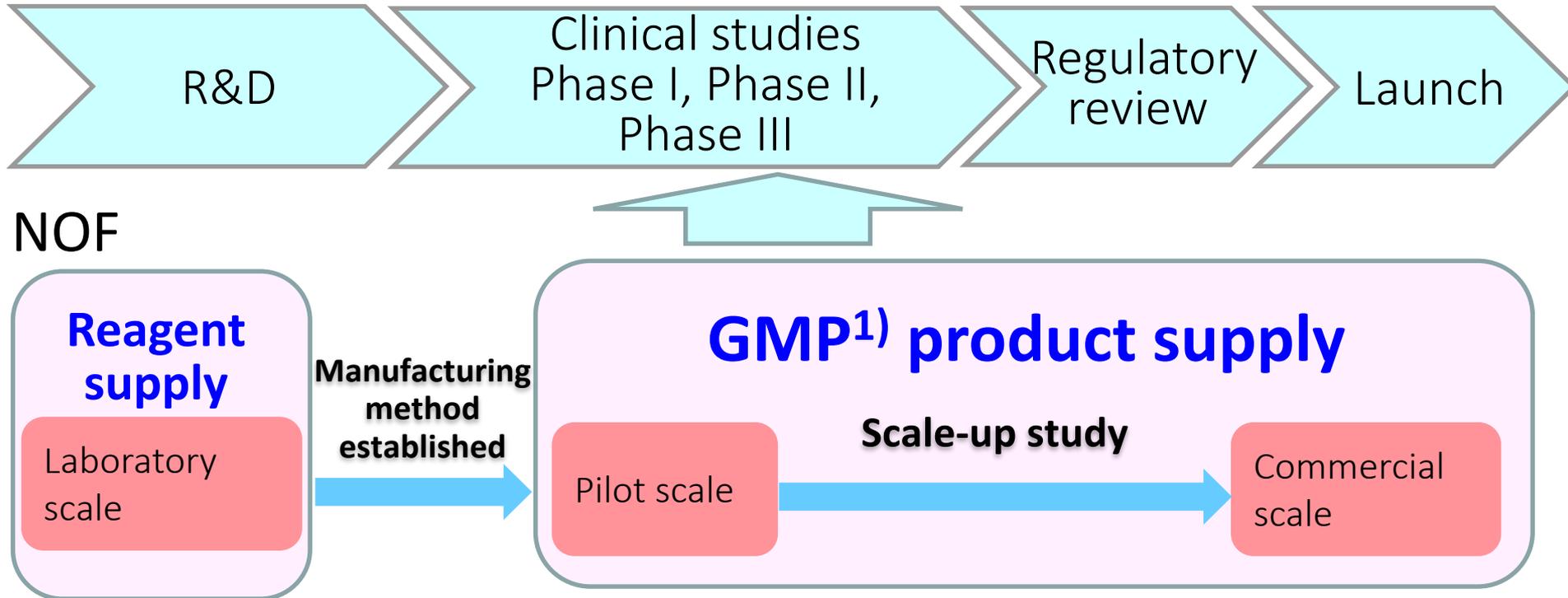
Product No.	Effect
GM-020	Improved retention in the body and efficient delivery of LNP to cells
GP-020	
GS-020	

* Select the product number according to the intended use of the vaccine, therapeutic drug, etc.

4. DDS Business Plan

Business Model of DDS Products

Development Stage of Customer (Pharmaceutical Manufacturer)

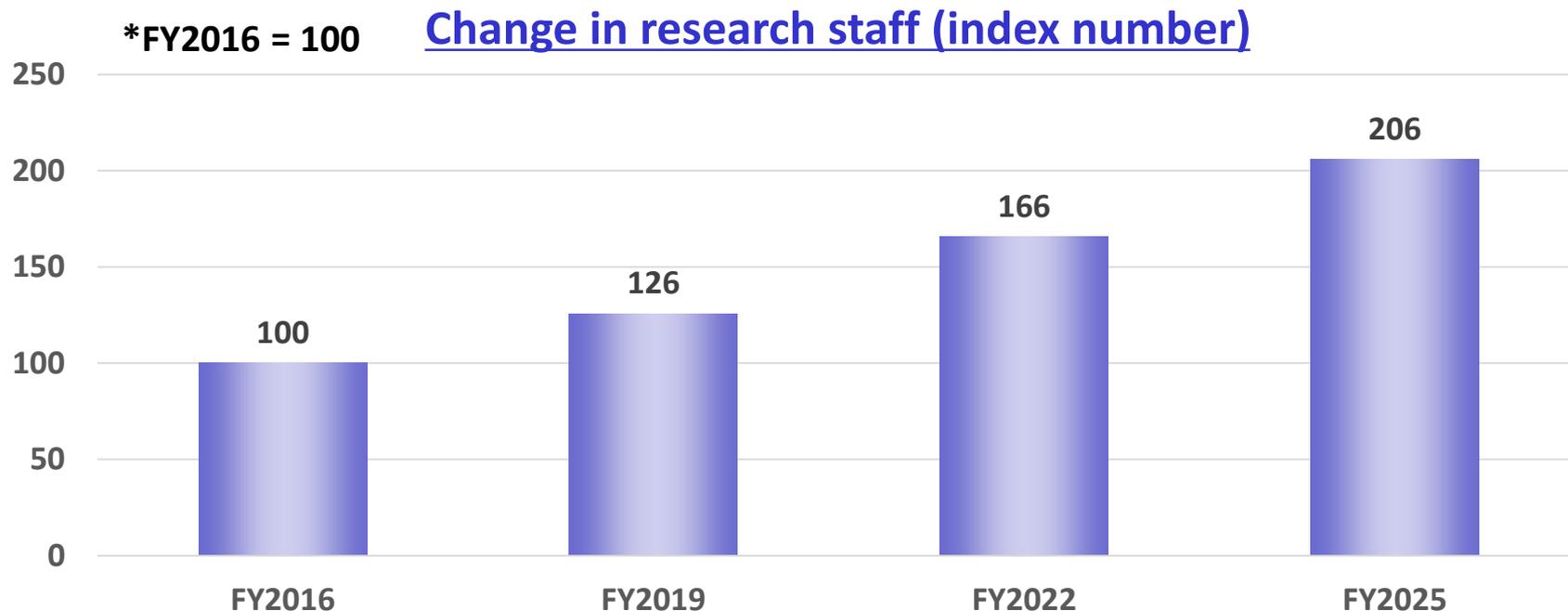


1) GMP (Good Manufacturing Practice):

Manufacturing control/quality control standard requirements for manufacturers and marketing authorization holders of drugs, etc.

Research Structure of DDS Business

- Development of materials for nucleic acid drugs using MI¹⁾
- Customization of activated PEGs, etc.
- Cooperation with external research institutions



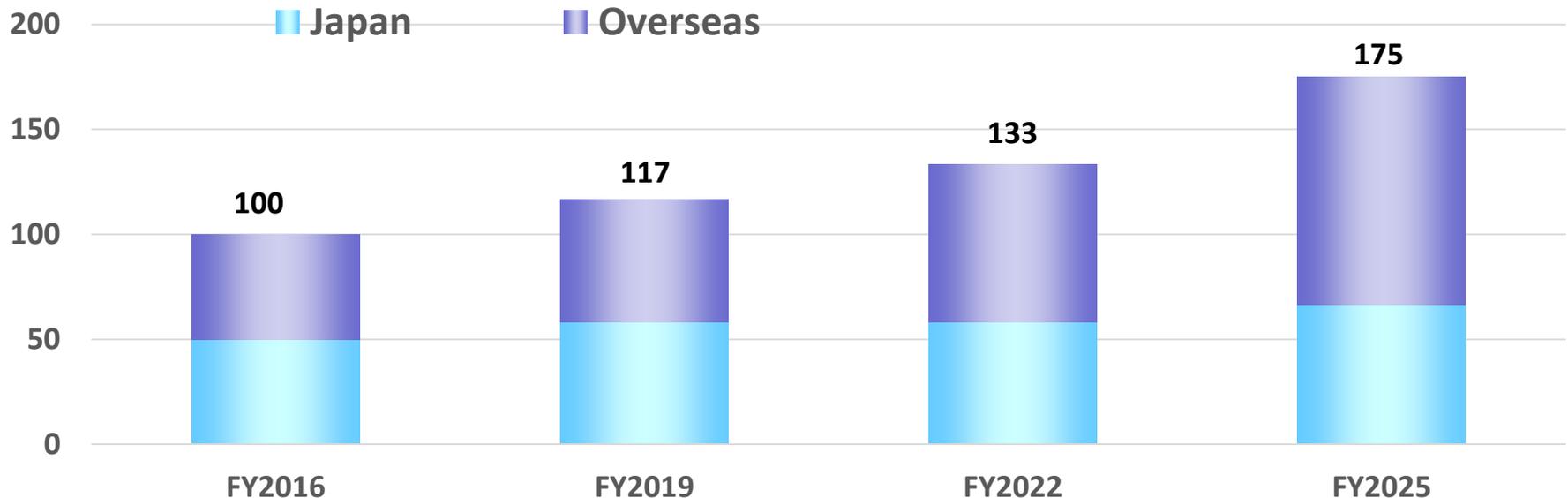
1) MI: Materials Informatics

Sales Structure of DDS Business

- In addition to those in Frankfurt, New York, San Francisco, and Shanghai, opened a satellite office in Boston
- Sales activities by consultants

*FY2016 = 100

Changes in sales staff (index number)



Product Supply System of DDS Business

(1) Manufacturing system

- Much experience with GMP manufacturing
- Product supply at a laboratory, pilot and commercial scale, depending on the development stage of the customer
- Advanced manufacturing technology (synthesis/high-purity purification technology)

(2) Quality control system

- GMP-compliant quality control system
- Prevention of analytical data alteration by DI¹⁾ system
- Reinforced control by introduction of LIMS²⁾ and QMS³⁾

1) DI: **D**ata **I**ntegrity - the completeness, consistency, and accuracy of data

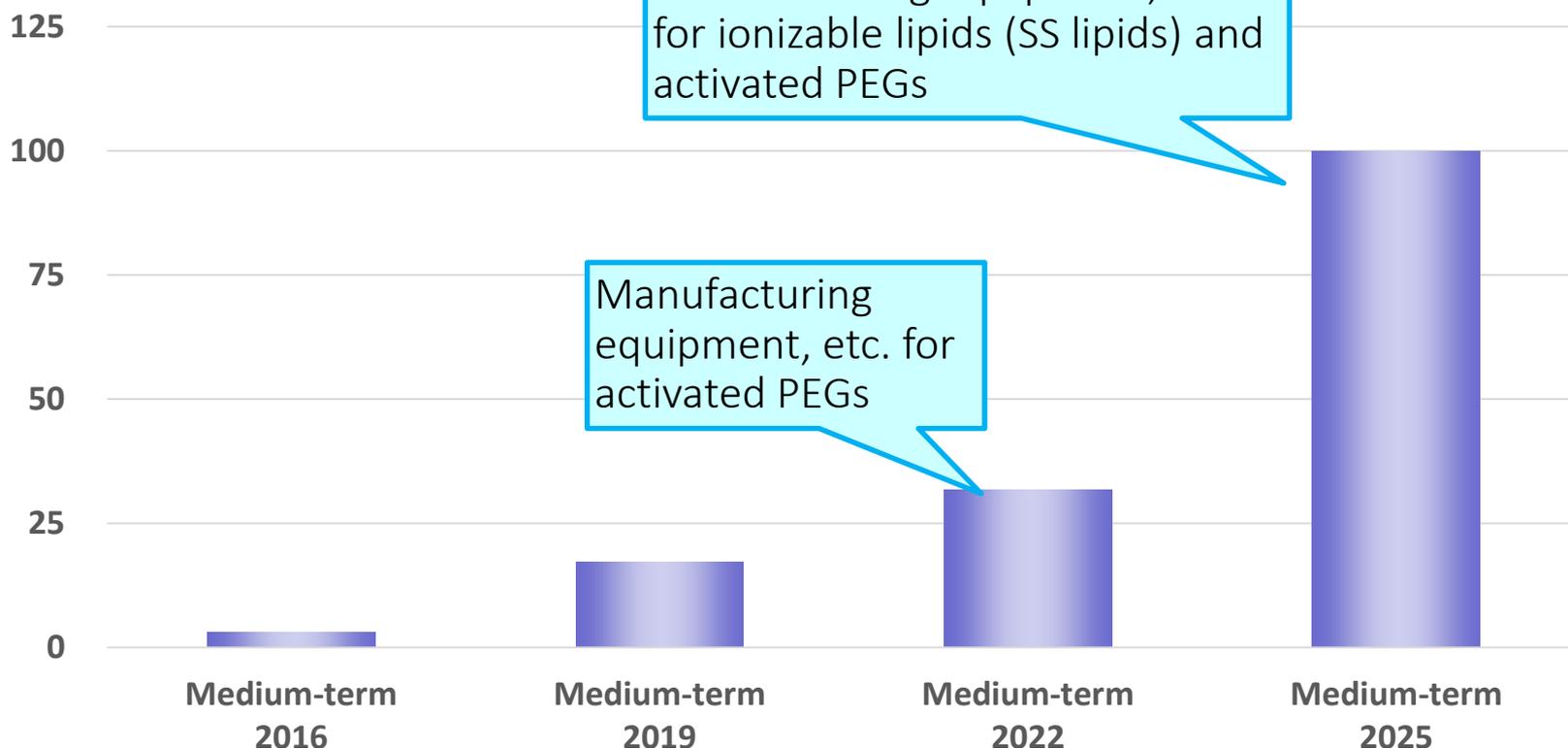
2) LIMS: **L**aboratory **I**nformation **M**anagement **S**ystem

3) QMS: **Q**uality **M**anagement **S**ystem

Capital Investment Plan for DDS Business

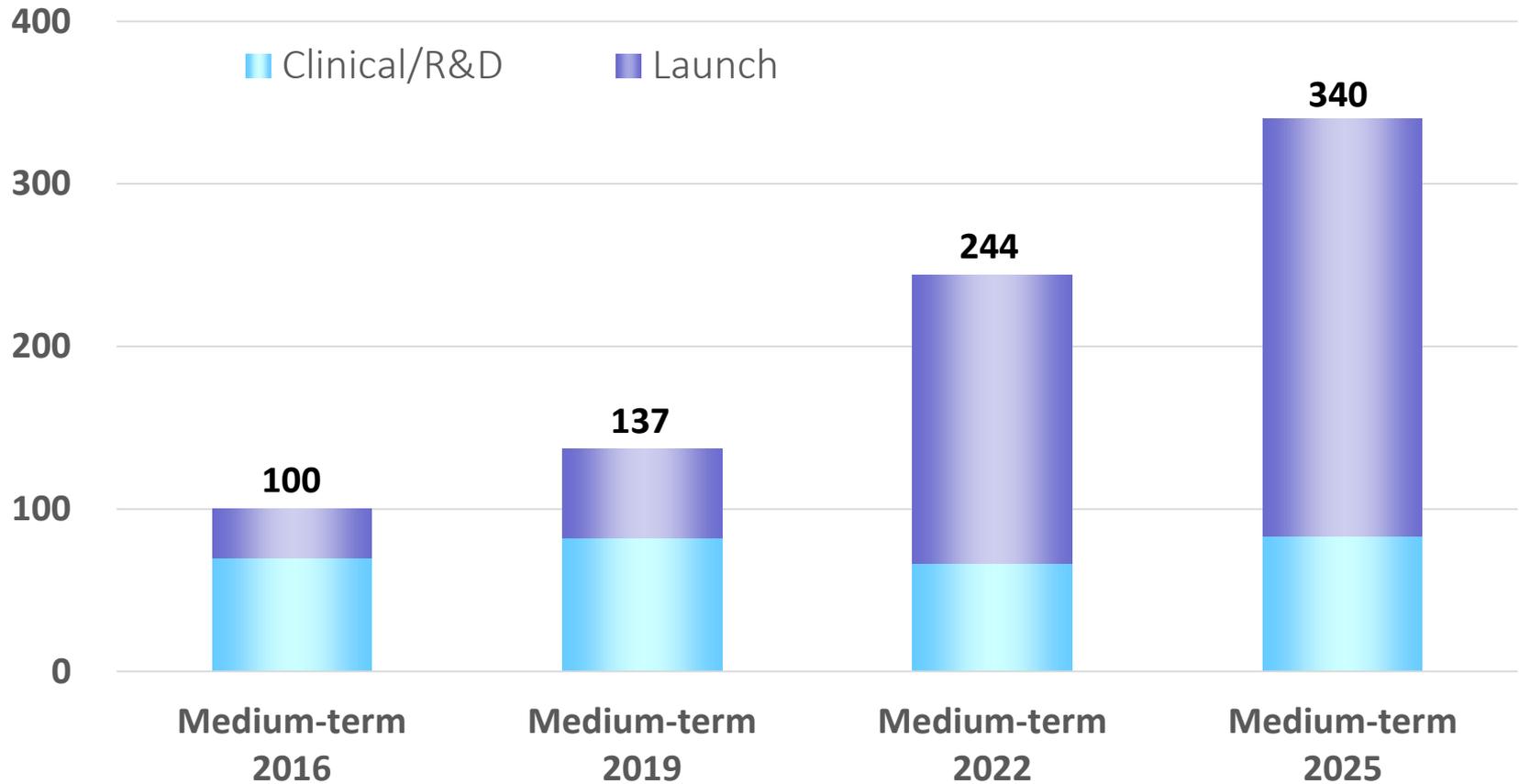
- Enhancement of production capacity associated with an increase in marketed products
- Invest more than 10 billion yen by FY2025

[Unit: 100 million yen]



Sales Plan for DDS Business (index number)

* Expressed as index numbers using the 2016 medium-term business plan as 100



- This material is intended to provide an explanation of the company and its business, not to induce investment or any other action.
- The results forecasts presented in this document are based upon currently available information and assumptions deemed rational. A variety of factors could cause actual results to differ materially from forecasts.
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