

Presentation Material

Expansion of DDS Business

November 20, 2024



My name is Yamamoto, and I am the General Manager of the Life Science Division.

Let me explain the expansion of our DDS business.

Contents

1. Market expansion of DDS materials	P4 - 6
2. Expansion of activated PEGs	P8 - 10
3. Expansion of functional lipids	P12 - 17
4. DDS business plan	P19 - 21

This slide shows you what I will explain today, which are these four items.

Contents

1. Market expansion of DDS materials	P4 - 6
2. Expansion of activated PEGs	P8 - 10
3. Expansion of functional lipids	P12 - 17
4. DDS business plan	P19 - 21

First, let me explain the market expansion of DDS materials.

Functions of DDS

To deliver
the required amount
of drugs
to where they are
needed
on a timely basis

- ◆ Improvement of therapeutic effects by efficient transport of drugs to affected areas
- ◆ Reduction in dosing frequency by improving drug retention in the body (Improved Quality of Life)
- ◆ Improvement of drug stability

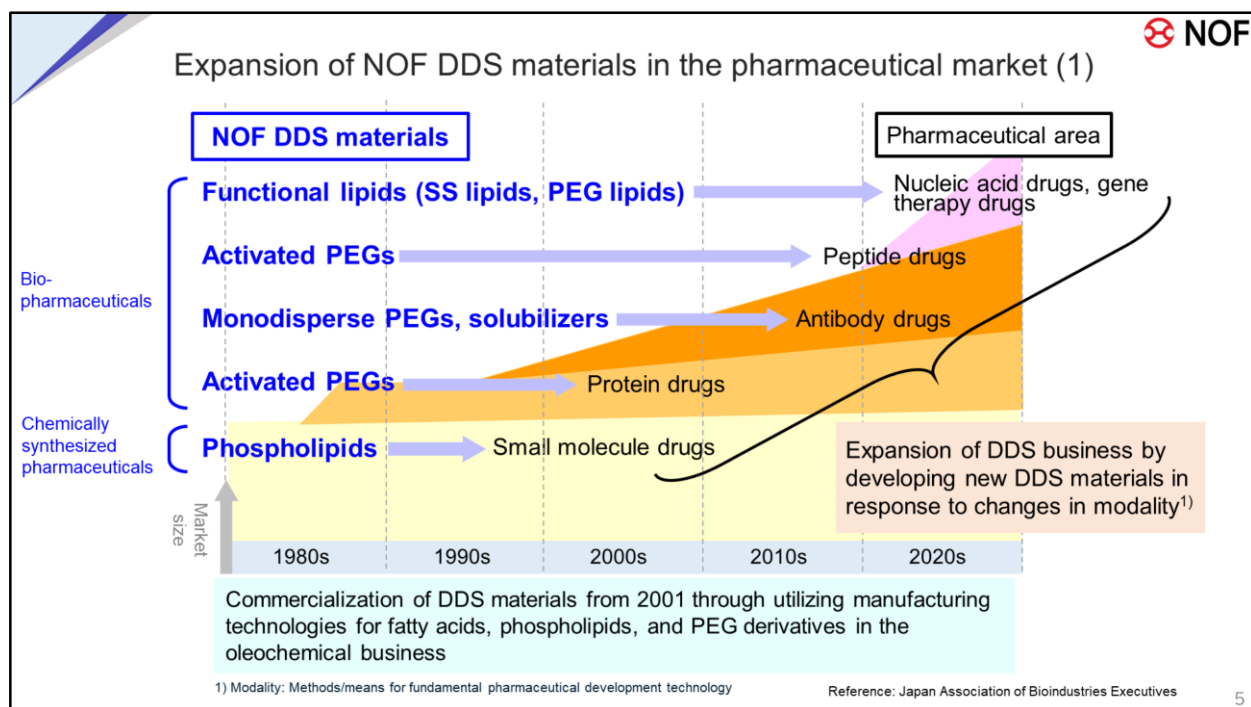
DDS : Drug Delivery System

These are the functions of DDS.

DDS is the abbreviation for Drug Delivery System, which is a system to deliver the necessary amount of drugs to where they are needed on a timely basis.

DDS enables the efficient transportation of drugs to affected areas, improves therapeutic effects, and reduces dosing frequency by improving drug retention in the body, thereby improving the quality of life of patients.

It also helps drug stability improvement.



Next, I show you the expansion of NOF DDS materials in the pharmaceutical market.

NOF commercialized DDS materials in 2001 by utilizing its manufacturing technologies for fatty acid, phospholipid, and PEG derivatives in the oleochemical business.

At the initial stage of commercialization, our business focused on phospholipids for small molecule drugs and activated PEGs for protein drugs. Later, NOF expanded its DDS business by developing new DDS materials in response to changes in modality, such as antibody drugs, peptide drugs, nucleic acid drugs, and gene therapy drugs.

Expansion of NOF DDS materials in the pharmaceutical market (2)



NOF DDS materials	Main pharmaceutical area		Market size		
			2023 (US dollars in millions)	2028 (US dollars in millions)	CAGR
Phospholipids	Chemically synthesized pharmaceuticals	Small molecule drugs	485,719	619,914	5%
Activated PEGs	Biopharmaceuticals	Protein drugs	124,959	192,265	9%
		Peptide drugs			
Monodisperse PEGs, solubilizers		Antibody drugs	230,375	354,460	9%
Functional lipids (SS lipids, PEG lipids)		Nucleic acid drugs, gene therapy drugs	6,383	36,852	42%

Prepared with reference to Arthur D Little document (2023) and Evaluate Pharma

6

The next slide shows the market size and growth rates of pharmaceuticals for which NOF DDS materials are used.

The size of the global market for small molecule drugs, which is the target of our efforts to expand phospholipids, was approximately USD 486.0 billion in 2023, and the CAGR for the period from 2023 to 2028 is estimated to be 5%. The market size for protein drugs and peptide drugs, which is the target of our efforts to expand activated PEGs, was approximately USD 125.0 billion, and the market size for antibody drugs, which is the target of our efforts to expand monodisperse PEGs and solubilizers, was approximately USD 230.0 billion. The CAGR for both of these markets is estimated to be 9%.

On the other hand, the market size for nucleic acid drugs and gene therapy drugs in 2023, which is the target of our efforts to expand functional lipids, such as SS lipids and PEG lipids, was only approximately USD 6.4 billion, but its CAGR is estimated to be 42%. NOF focuses on sales promotion and new product development targeting this market.

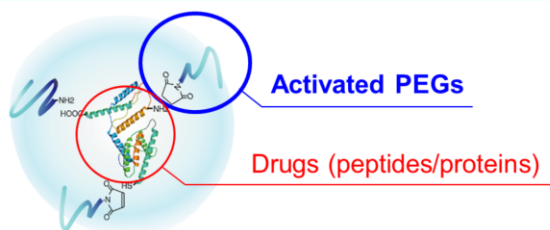
Contents

1. Market expansion of DDS materials	P4 - 6
2. Expansion of activated PEGs	P8 - 10
3. Expansion of functional lipids	P12 - 17
4. DDS business plan	P19 - 21

Next, let me explain the expansion of activated PEGs.

Activated PEGs for peptide/protein drugs

- **Activated PEGs are highly water soluble and can greatly enhance the water solubility of peptide/protein drugs by chemical modification.**
- **Peptide/protein drugs modified by activated PEGs have very high retention in the body.**
- **NOF has the largest share of the global market for activated PEGs, and the number of marketed drugs incorporating NOF's products has been increasing in recent years.**



I will start with activated PEGs for peptide and protein drugs.

Activated PEGs are highly water soluble and can add high water solubility to peptide and protein drugs by chemically modifying them.

In addition, peptide drugs and protein drugs modified by activated PEGs are known to have very high retention in the body.

NOF has the highest global market share in activated PEGs, and the number of launched drugs adopting NOF's products has been increasing in recent years.

- **The CAGR of the market for peptide and protein drugs, which is the target of our initiatives to expand activated PEGs, is 9%.**
- **Strengths of NOF**
 - **In-house manufacturing of high-quality PEG materials based on manufacturing technologies for PEG derivatives that have been developed over many years**
 - **Advanced manufacturing and quality control systems that are GMP¹⁾-conformant**
 - **An extensive track record of adoption by U.S. and European pharmaceutical manufacturers**
- **NOF focuses on customized responses to suit customer requirements and biosimilar²⁾ demand for PEGylated drugs.**

1) GMP (Good Manufacturing Practice)

Mandatory manufacturing/quality control standards to be followed by manufacturers and marketing authorization holders of pharmaceutical products, etc.

2) Biosimilar

A biologic drug that is almost identical to and has no clinically meaningful differences from an existing approved biologic drug that is already on the market (reference biologic product)

Next, I will move on to the business environment for activated PEGs and NOF's strengths.

The CAGR of the market for peptide and protein drugs, which is the target of our efforts to expand activated PEGs, is 9%.

The strengths of NOF are:

- In-house manufacturing of high-quality PEG materials based on manufacturing technologies for PEG derivatives that have been developed over many years
- Advanced manufacturing and quality control systems that are GMP-conformant
- An extensive track record of adoption by U.S. and European pharmaceutical manufacturers

In particular, NOF focuses on customized responses to suit customer requirements and biosimilar demand for PEGylated drugs.

New manufacturing facilities for raw materials* for DDS drug formulations

*Activated PEGs

Aichi Works

- **Start of operation: FY2025 (planned)**
- **Manufacturing capacity: about twice that of the DDS Plant at the Kawasaki Works (planned)**
- **Characteristics**
 - Able to manufacture on a larger batch scale than before with GMP-conformant facilities
 - Realize a smart factory through the digital transformation of manufacturing and quality control
 - Contribute to carbon neutrality by adopting solar panels and energy-saving design



Manufacturing Building (Under construction)



Quality Control Building
(Outdoor facility under construction)

These are our new manufacturing facilities for activated PEGs, which are raw materials for DDS drug formulations.

The manufacturing facilities for activated PEGs under construction at the Aichi Works are scheduled to start operation in FY2025 with a manufacturing capacity around twice that of the DDS Plant at the Kawasaki Works currently in operation.

They are state-of-the-art manufacturing facilities for raw materials for DDS drug formulations, and their characteristics are as follows:

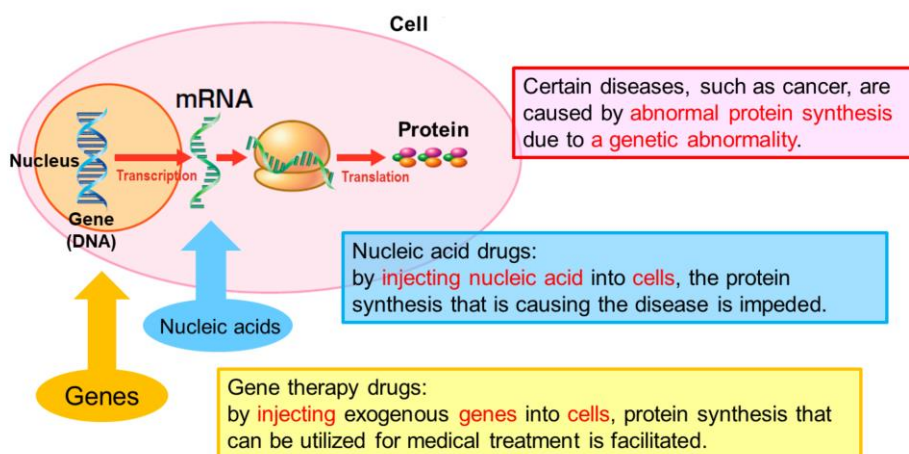
- Able to manufacture in a larger batch scale than before with GMP-conformant facilities
- Realize a smart factory through the digital transformation of manufacturing and quality control
- Contribute to carbon neutrality by adopting solar panels and energy-saving design

Contents

1. Market expansion of DDS materials	P4 - 6
2. Expansion of activated PEGs	P8 - 10
3. Expansion of functional lipids	P12 - 17
4. DDS business plan	P19 - 21

Next, let me explain the expansion of functional lipids.

Nucleic acid drugs and gene therapy drugs



- Nucleic acid- and gene therapy-based drugs can effectively treat genetic disorders and are also used in the manufacture of vaccines
- However, since nucleic acids and genes are unstable within the body, DDS technologies are essential to allow their utilization in medical treatment

Let me start with the explanation of nucleic acid drugs and gene therapy drugs.

Certain diseases, such as cancer, are caused by abnormal protein synthesis. Nucleic acid drugs elicit therapeutic effects by injecting nucleic acid in cells to impede the protein synthesis that is causing the disease.

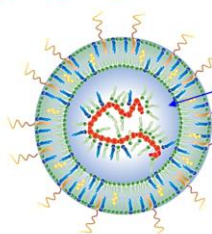
Gene therapy drugs elicit therapeutic effects by injecting exogenous genes in cells to facilitate protein synthesis that is useful for medical treatment.

While these nucleic acid drugs and gene therapy drugs are effective for treating genetic abnormality and for vaccine use, nucleic acid and genes are unstable within the body. Therefore, DDS technologies are essential for using them in medical treatment.

Functional lipids

- Lipid nanoparticles (LNPs) are used as part of DDS technologies for nucleic acid drugs and gene therapy drugs.
- LNPs consist of ionizable lipids, PEG lipids, etc.

Lipid NanoParticle (LNP)



	Constituent	Role
	Ionizable lipids (SS lipids)	Facilitates the inclusion and intracellular delivery of nucleic acids/genes
	PEG lipids	Improves drug retention in the body
	Phospholipids	Formation of lipid membrane
	Cholesterol	Stabilization of lipid membrane

- NOF has developed SS lipids as its proprietary ionizable lipids with enhanced bio-degradability in the body and is developing customers by proposing LNP prescriptions.
- NOF is promoting PEG lipids in the market by leveraging their track record of being adopted for COVID-19 vaccines.
- NOF is promoting phospholipids broadly in the market as generic materials.

Next, let me explain functional lipids.

As part of DDS technologies for nucleic acid drugs and gene therapy drugs, lipid nanoparticles (LNPs) are used.

As you can see from this diagram, LNPs consist of ionizable lipids, PEG lipids, etc.

NOF has developed SS lipids as its proprietary ionizable lipids with improved degradability in the body and is developing customers by proposing LNP prescriptions.

We are promoting PEG lipids in the market by leveraging their track record of being adopted for COVID-19 vaccines.

In addition, we are promoting phospholipids broadly in the market as generic materials.

- **The CAGR of the market for nucleic acid drugs and gene therapy drugs, which is the target of NOF's initiatives to expand functional lipids, is 42%.**
- **Strengths of NOF**
 - In-house manufacturing of ionizable lipids and PEG lipids by combining manufacturing technologies for fatty acids, phospholipids, and PEG derivatives, which are NOF's core technologies
 - Advanced manufacturing and quality control systems that are GMP-conformant
 - SS lipids, which are based on joint research with a university, and the capability to develop LNP formulations using these lipids

Next, I will move on to the business environment for functional lipids and NOF's strengths.

The CAGR of the market for nucleic acid drugs and gene therapy drugs, which is the target of our efforts to expand functional lipids, is 42%.

The strengths of NOF are:

- In-house manufacturing of ionizable lipids and PEG lipids by combining manufacturing technologies for fatty acids, phospholipids, and PEG derivatives, which are our core technologies
- Advanced manufacturing and quality control systems that are GMP-conformant
- SS lipids, which are based on a joint research with a university, and the capability to develop LNP prescriptions by using them

New manufacturing facilities for SS lipids

Aichi Works

➤ **Start of operation: FY2023**

➤ **Characteristics**

- Advanced manufacturing and quality control systems that are GMP-conformant
- Facilities to produce functional lipid products for LNPs



Desolvation facilities
(Rotary evaporator)



Solvent tanks



Production facilities

15

These are our new manufacturing facilities for SS lipids, which are functional lipids.

The manufacturing facilities for SS lipids at the Aichi Works started operation in FY2023.

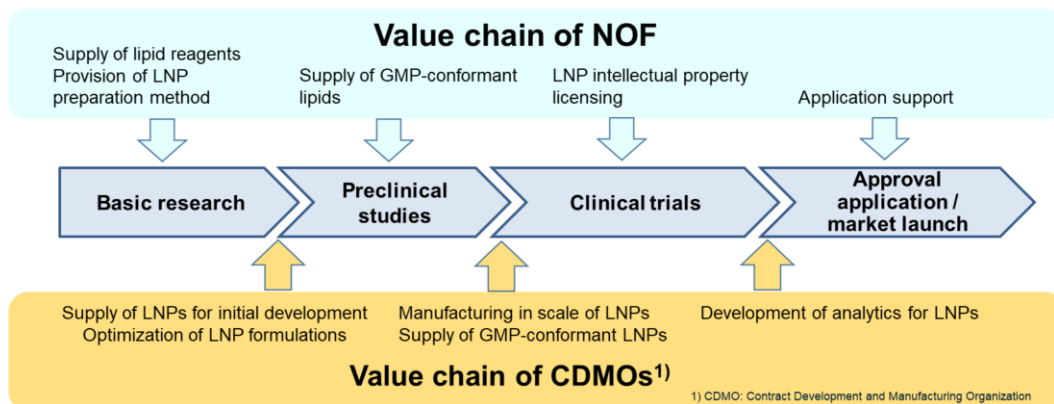
Their characteristics are as follows:

- Advanced manufacturing and quality control systems that are GMP-conformant
- Production facilities for functional lipid products for LNPs

Future sales strategies (1)

Issue

While customers demand LNPs optimized for each formulation, NOF's offerings have been limited to the provision of lipids and LNP prescription proposals.



NOF will expand a seamless solution business optimized for each development stage of its customers by combining NOF's lipid technologies and CDMOs' LNP technologies.

Now, let me show you our sales strategies going forward.

One of our issues is that while customers demand the provision of LNPs optimized for each formulation, our offerings have been limited to the provision of lipids and LNP prescription proposals.

In response to this issue, through the supply of LNPs for initial development, optimization of LNP prescriptions, manufacturing in scale of LNPs, supply of GMP-conformant LNPs, development of analytics for LNPs, etc., which are the value chain of CDMOs, we will expand a seamless solution business optimized for each development stage of customers by combining our lipid technologies and CDMOs' LNP technologies.

Future sales strategies (2)

- **NOF has chosen Phosphorex as its CDMO due to its advanced LNP technologies.**
- **NOF started collaborating with Phosphorex for development of LNP prescription and contract manufacturing in April 2024.**
- **NOF strengthened the partnership by making a capital contribution to the company in August 2024.**



- Phosphorex, LLC
Address: Hopkinton, Massachusetts, U.S.A.
- Located in the Boston area where nucleic acid and gene therapy drugs are actively being developed
- Founded in 2005, Phosphorex specializes in the development of particle-based drug delivery systems
- Phosphorex has a track record of contract development of LNP formulations for NOF customers



We have chosen Phosphorex as a CDMO that has such LNP technologies. We started collaborating with the company for LNP prescription development and contract manufacturing in April 2024, and have strengthened the partnership by making a capital contribution to the company in August 2024. Phosphorex is based in Hopkinton, Massachusetts, U.S.A. and is located near the Boston area where nucleic acid drugs and gene therapy drugs are actively developed.

Phosphorex is a company founded in 2005 and specializes in the development of particle-based drug delivery prescriptions. It has the technological strength required by NOF, with a track record of contract development of LNP prescriptions for NOF customers.

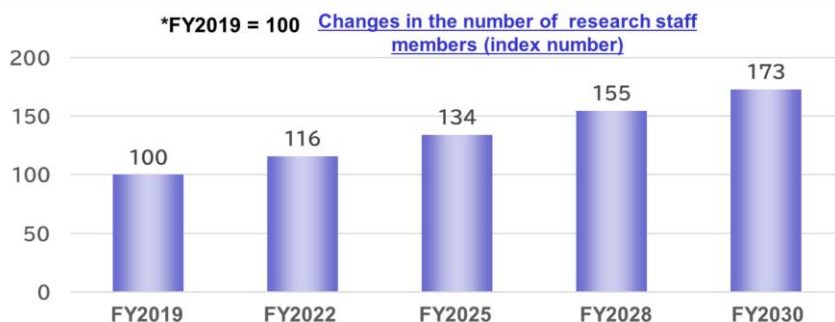
Contents

1. Market expansion of DDS materials	P4 - 6
2. Expansion of activated PEGs	P8 - 10
3. Expansion of functional lipids	P12 - 17
4. DDS business plan	P19 - 21

Next, let me explain our DDS business plan.

Research structure of DDS business

- Prompt implementation of customized responses to customer requirements for DDS materials
- Finding solutions for materials utilized in the production of nucleic acid drugs through MI¹⁾
- Development of new products, targeting modalities with high growth potential
- New technology development by expanding collaboration with external research institutes



1) MI: Materials Informatics

Let me explain the research structure of our DDS business.

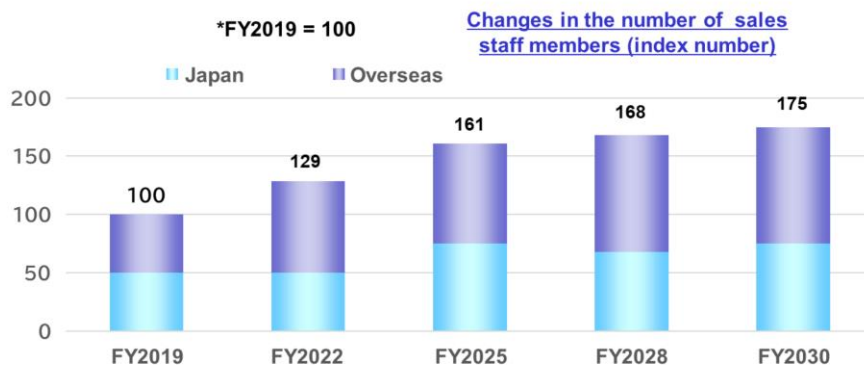
While promptly implementing customized responses to customer requirements for DDS materials, we will provide solutions for materials for nucleic acid drugs by utilizing MI.

We will develop new products on an ongoing basis, targeting modalities with high growth potential while actively engaging in new technology development by expanding collaboration with external research institutes.

In order to make rapid progress in such development, as you can see from this graph, we plan to systematically increase research staff by 70% by FY2030 compared to FY2019.

Sales structure of DDS business

- Assignment of sales staff to NOF offices in New York, San Francisco, Boston, Frankfurt, and Shanghai



Next, let me explain the sales structure of our DDS business.

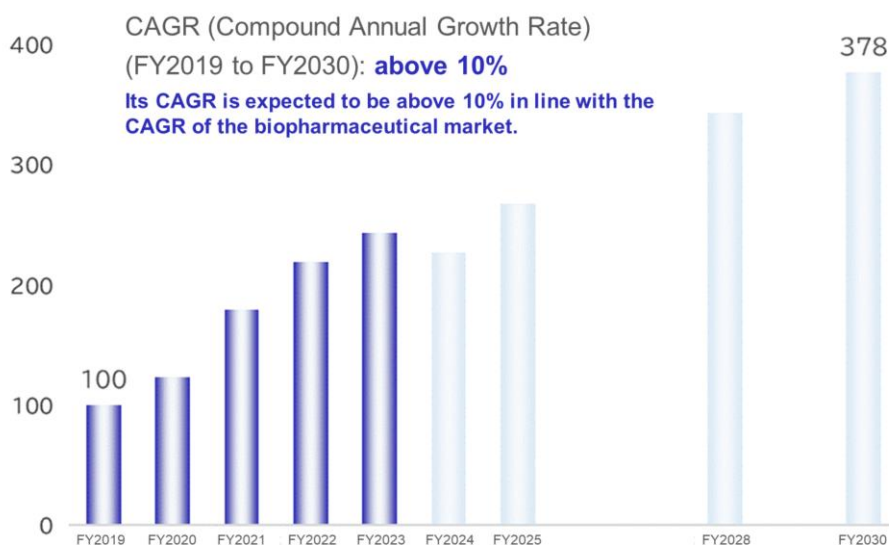
We have assigned sales staff to our offices in New York, San Francisco, Boston, Frankfurt, and Shanghai in order to accelerate market development in the U.S., Europe, and Asia.

As you can see from this graph, we will increase sales staff mainly at overseas locations to promote business expansion.

Sales plan for raw materials for DDS drug formulations (index number)



*Expressed in index number form based on FY2019 (set equal to 100)



21

Lastly, I will show you the sales plan for our DDS business in terms of index number.

Net sales for FY2024 are expected to decrease from the previous fiscal year mainly due to inventory adjustment at customers.

On the other hand, the CAGR of the biopharmaceutical market, which is the target market of the DDS business, is above 10%. Therefore, we expect our sales to grow at a pace that is nearly in line with the plan over the long term.

We have achieved a steady increase in the number of clinical trials and market launches for both functional lipids and activated PEGs by developing and proposing highly functional materials while providing generous customer support.

We will continue to expand our DDS business going forward by promoting the development of new products and technologies, the expansion of supply system, and the expansion of overseas network, while capitalizing on the growth of biopharmaceuticals.

- 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.
- Please be aware that decisions regarding investments are the responsibility of the users themselves.
- Please note that, in this material, amounts less than ¥100 million have been rounded off.
- In the event of any discrepancy between the Japanese original and this English translation, the original shall prevail.

Contact us : NOF CORPORATION
Investor Relations Office
Corporate Communications Dept.
Address : 20-3,EBISU 4-CHOME,SHIBUYA-KU,TOKYO 150-6012
E - mail : iroffice@nof.co.jp
Homepage : <https://www.nof.co.jp>

This concludes my presentation.
Thank you for your attention.