

## Online Meeting with Investors: Life Science Business

TOYOBO CO., LTD.

Director & Managing Executive Officer Head, Life Science Solutions Division Yutaka Ouchi



- I . Positioning of the Life Science Business
- **II. Biotechnology Business**
- **III. Medical Materials Business**
- **IV. Future Development**
- **V. Terms**

Corporate Philosophy System TOYOBO PVVs

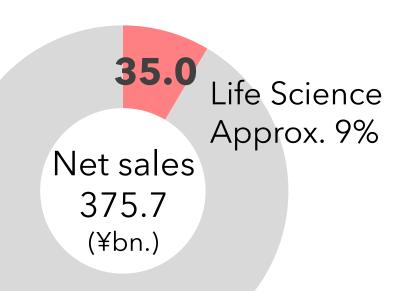


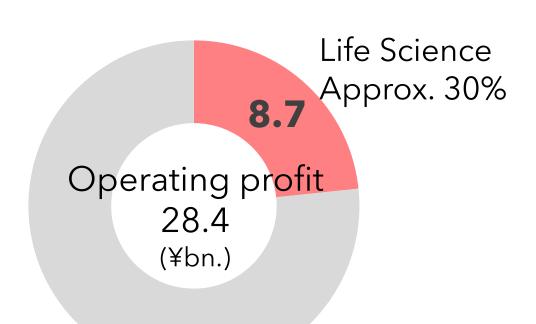
### **TOYOBO**

## I . Positioning of the Life Science Business



FY 3/22 Results





#### Biotechnology







#### Medical materials





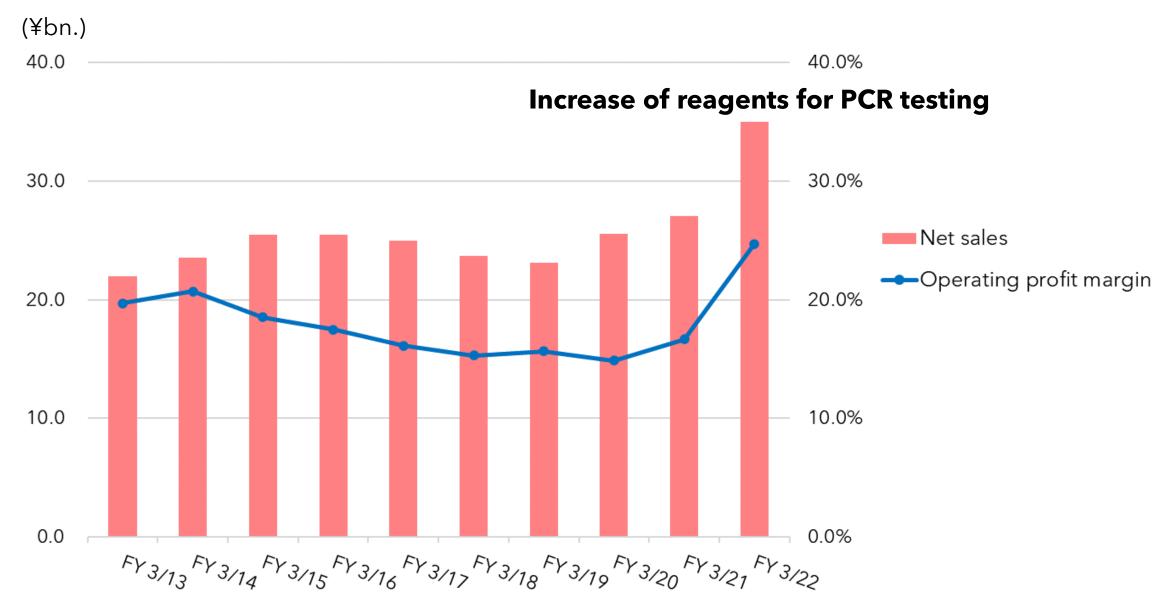


Contract manufacturing of pharmaceuticals



## Change in Net Sales and Operating Profit Margin of the Life Science Business





### Life Science Business Bases

#### **TOYOBO**

## Bases in Japan



Tsuruga Research and Production Center (Biotechnology)



Research Center (Biotechnology, Medical materials)



Otsu Pharmaceuticals Plant



## Production, R&D

Sales

#### Overseas Bases

- TOYOBO (SHANGHAI) BIOTECH CO., LTD.
- TOYOBO (TAIWAN) CO., LTD.
- TOYOBO Korea Co., Ltd.
- TOYOBO U.S.A., INC.
- TOYOBO DO BRASIL PARTICIPACOES LTDA.
- TOYOBO Chemicals Europe GmbH
- Spinreact, S.A.U.



Iwakuni Production Center (Medical materials)



Head office (Osaka)

### Contributing to Solving Social Issues through the Life Science Business

(from Sustainable Vision 2030)

**TOYOBO** 

#### Vision: We will continue to create the solutions needed by people and the earth with our materials and science

#### Relations between five social issues and SDGs



Employees' well-being and human rights in the supply chains







- People First: employees' safety, pride, rewarding work
- Respecting human rights in the entire supply chain

**People** 



Healthy lifestyle and health care



- Contributing to the field of infectious diseases
- Improving QOL with medical membranes, etc.





Smart community and comfortable space



- Creating a humancentric, digital society with highly functional films and advanced materials
- Dealing with new technologies such as CASE and MaaS and creating safe and comfortable mobility space

**Planet** 



Decarbonized society and circulating society







- Achieving carbon neutrality in Scope 1,2 by FY 3/51
- Establishing and joining an ecosystem for circulating resources used in products



Good condition of water 6 CLEAN WAITER AND SANITATION area, atmosphere and soils, and biodiversity







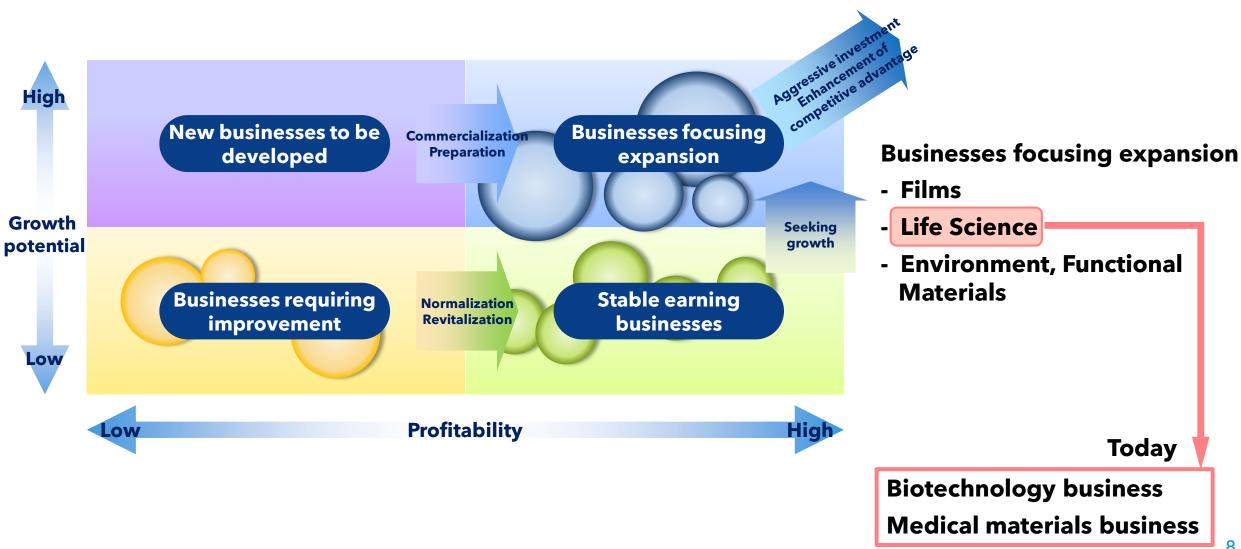
- Reducing the impact on and bettering the environment with functional membranes and equipment to recover solvents
- Reducing food loss with highly functional packaging films
- Sustainable food

## Reorganization of the Business Portfolio

(from 2025 Medium-Term Management Plan)

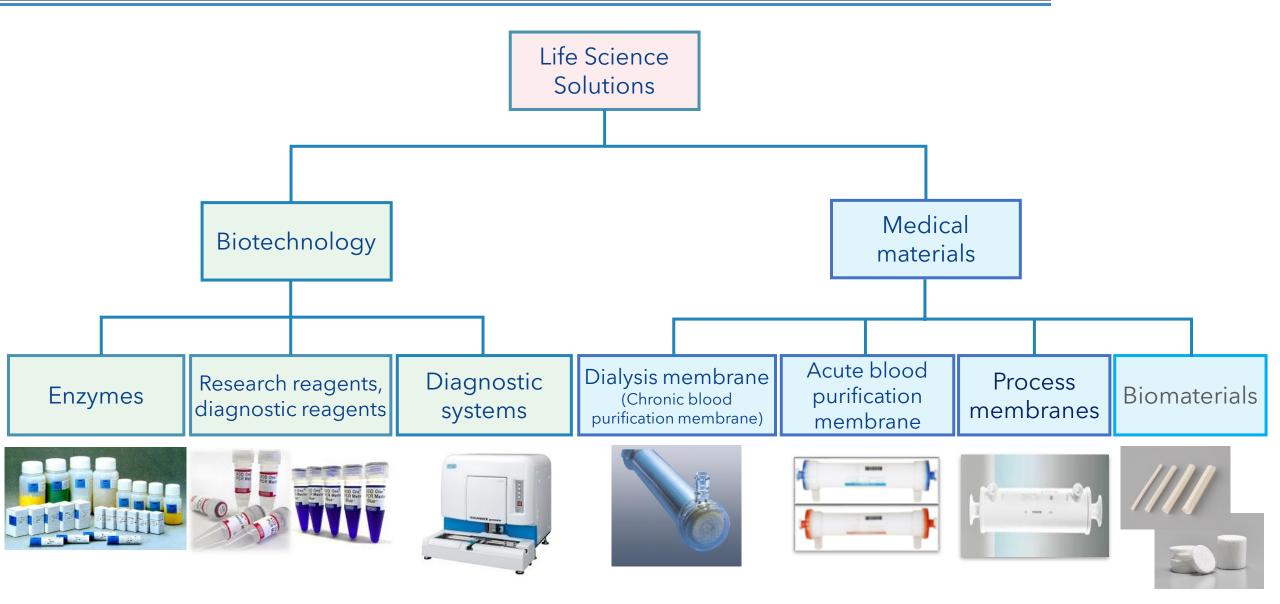


Assess and stratify each business into 4 quadrants with 2 axes: "Profitability" and "Growth potential"



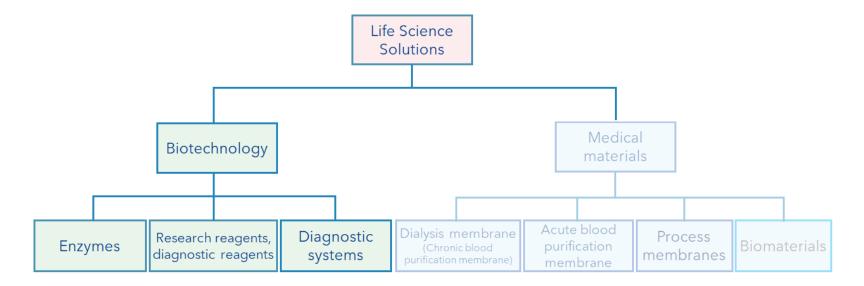
## Key Products of the Life Science Business





## **TOYOBO**

## **II. Biotechnology Business**



## History of the Biotechnology Business



- 1948 Biotechnology business derived from pulp business
  - Began research on yeast cultivation for **the treatment of pulp effluent**, the raw material for rayon fiber
- 1972 Entered the enzymes & diagnostic reagent market as a biochemistry business (current biotechnology business)
  - Launched uric acid measurement testing chemical
- 1982 Entered the life science reagent field as a biochemistry business
  - Began sales of reagents for genetic engineering
- 1986 Completed construction of a new research building at the Tsuruga Enzyme Plant, and further enhanced the R&D system
- 1990 Launched enzymes for blood glucose monitoring
- 1995 Began sales of PCR enzymes "KOD" DNA polymerase
- 2003 Established TOYOBO (SHANGHAI) BIOTECH CO., LTD. as a Chinese base for the biotechnology business
- 2013 Acquired Spain's Spinreact, S.A.U., a global manufacturer and marketer of diagnostic reagents and instruments
- 2015 Constructed a new facility for enzyme purification in Tsuruga Research and Production Center to increase refining capacity by 50%

## Outline of the Biotechnology Business

#### **TOYOBO**

#### **Enzymes**

Developed enzymes with superior functionality and stability through gene modification





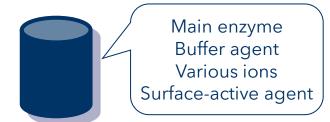
(Image of enzymes)



## Research reagents, diagnostic reagents

Developing enzymes and substances that assist enzyme function to make reagents and diagnostic reagents





(Image of reagents)



#### **Diagnostic systems**

Devices and systems that use specimens (urine, saliva, etc.) to examine abnormalities in the human body



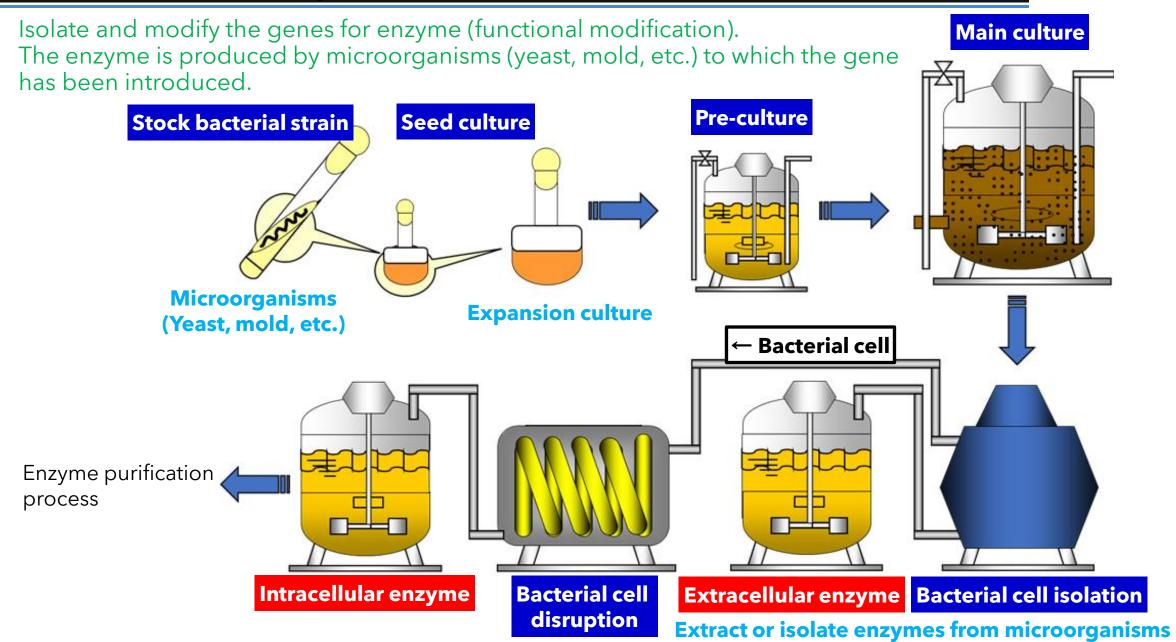
#### [Our strengths] Technology for making high-functionality proteins

Enzymes and substances that assist enzyme function are both proteins

Several to dozens of types

## Process of Enzyme Production | Cultivation





## Products | Enzymes for Biochemical Diagnosis



- Microorganism culture → Enzyme purification → Pulverization to produce enzymes for biochemical diagnostic reagents
  - Blood glucose (Diabetes)
  - Cholesterol (Arteriosclerosis)
  - Creatinine (Renal function)
  - GOT / GPT (Liver function) etc.
- Market: Enzyme market ¥20.0 bn. (Chinese market ¥6.0 bn.)
   Growth rate 1~3% / year (Chinese market 5% /year)
- Share: Approx. 25% (TOYOBO's estimate) (2nd in the world)
- Overseas sales ratio: Approx. 70%
- Future: Expand sales to emerging countries

#### [Our strengths]

- Genetic recombination technology for microorganisms
  - → Realization of functional modification and mass production of enzymes
- Large product lineup





#### Products | Enzymes, Research Reagents, Diagnostic Systems for Genetic Testina

#### **Enzymes for genetic testing (PCR enzymes)**

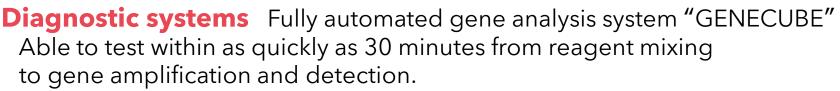
- "KOD" DNA polymerase: amplify rapidly, copy accurately
- "TTx" DNA polymerase: highly resistant to contaminants
- Share of PCR enzymes: **Domestic approx. 15%** ← Pre-Corona approx. 5% (TOYOBO's estimate) Top 3 in Japan

#### Research reagents (Reagents for PCR testing) (e.g.) Detection kit for COVID-19

Eliminates work to remove impurities in samples (throat swab, saliva) with unique enzymes, etc., and reduces the processes for gene extraction.

#### Able to test for COVID-19 within a minimum of 60 minutes.

◆Also possess reagents for norovirus testing.



**♦ Multiple items can be measured simultaneously** 

(4 items×6 specimens maximum)

(e.g.) - COVID-19 & Influenza virus - COVID-19 & RS virus

- Whooping cough & Mycoplasma pneumoniae - Whooping cough & Para-pertussis





"GENECUBE" (model C) Diagnostic reagents

[Our strengths] Possess enzymes, reagents, diagnostic reagents and diagnostic devices for genetic testing

## Detection Kit for COVID-19 | Points

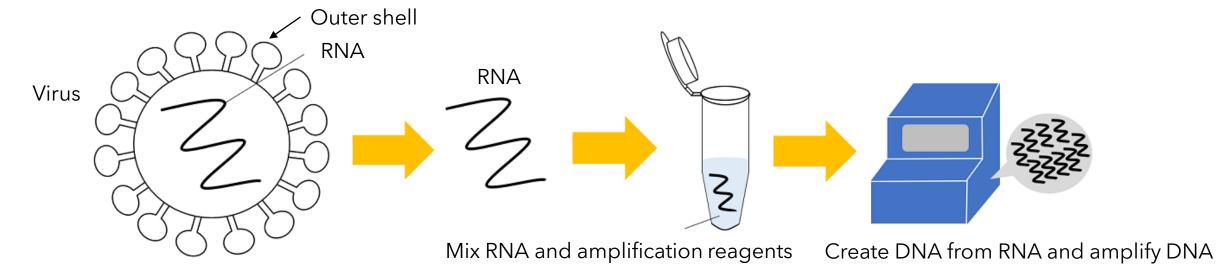


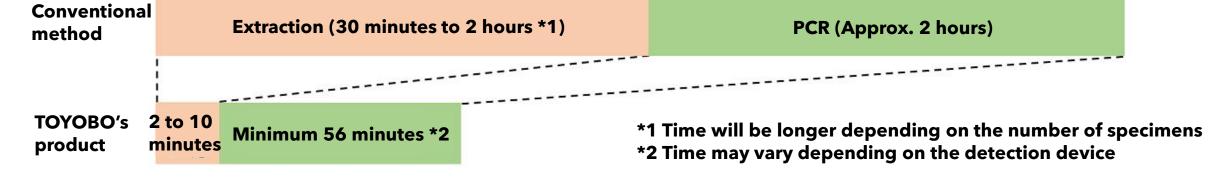
## RNA extraction by crushing the outer shell of the virus

Highly efficient reagent that destroys the structure of viral particles and exposes RNA

RNA extraction process and time reduction

**\*Deployment of know-how concerning norovirus test reagents** 

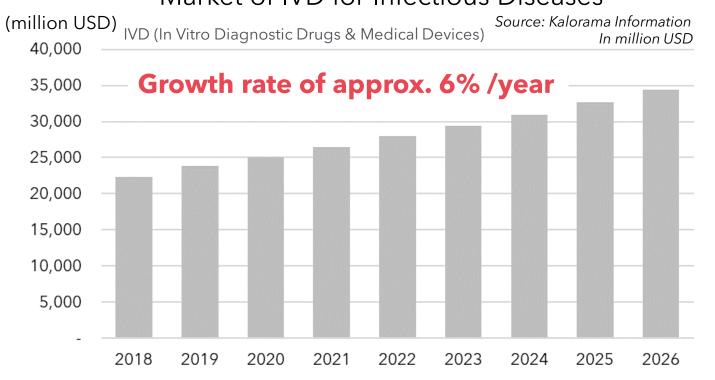






Focus on the area of infectious diseases, which is a growing market and an area in which pandemics are expected to return





#### **Genetic testing**

- COVID-19
- Influenza virus
- RS virus
- Whooping cough
- Para-pertussis
- Tuberculosis

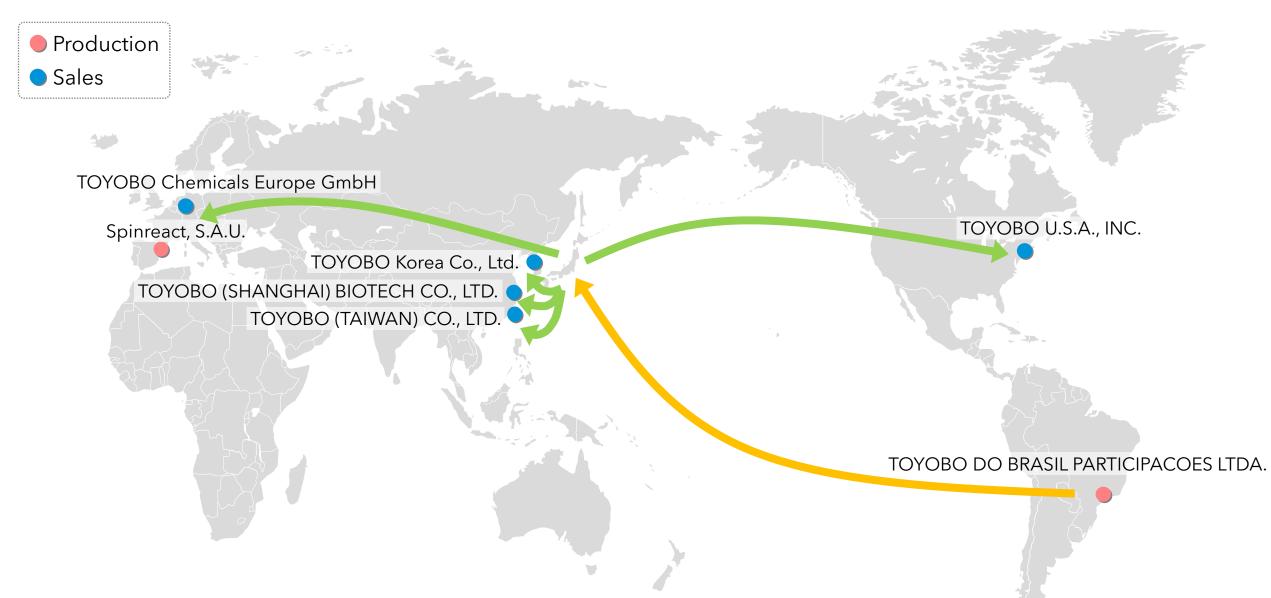
#### **Antigen testing**

- COVID-19

Aiming to be the industry's number one player in the growing market of infectious diseases, providing integrated solutions from raw materials to testing and diagnosis

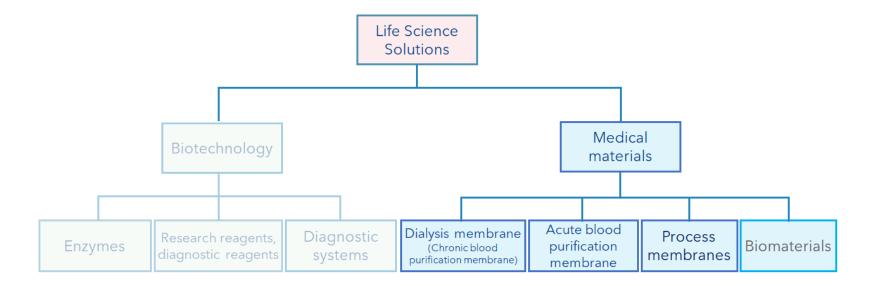
# Future Development | Global Expansion of the Biotechnology Business





### **TOYOBO**

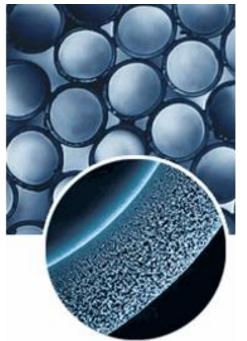
### **III. Medical Materials Business**



## History and Outline of the Medical Materials Business



- 1980 Began production of reverse osmosis membranes for seawater desalination "HOLLOSEP"
- 1984 Began full-scale production of artificial kidney hollow fiber
- 2012 Began production of virus removing membrane Entered the biomaterials market
- 2020 Entered the acute blood purification market



Enlarged cross-sectional view of hollow fiber membranes

#### **Hollow-type separation membranes**

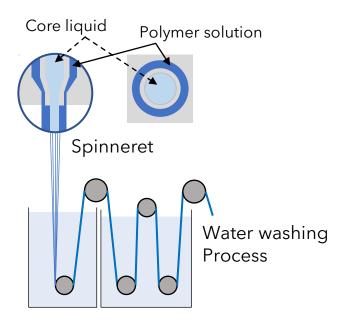
Separation membranes with microscopic pores in the cross section of the hollow fiber

- Blood purification membrane (removes toxic substances from the blood)
- Separation membranes for the antibody drug manufacturing process

#### [Our strengths]

#### Membrane production technology

- Technology that controls pore size
- Technology that designs the cross-sectional structure of hollow fibers



Coagulation process

## Outline of Artificial Kidney Hollow Fiber (Chronic Blood Purification Membrane)



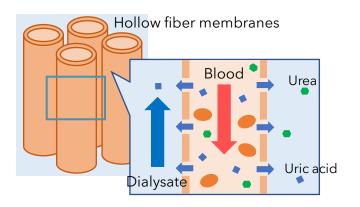
Dialysis: Prevents renal failure patients from becoming uremic by "removing waste products," "maintaining electrolytes," and "maintaining fluid volume" in the blood

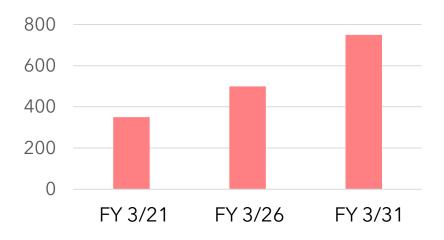
- Composition/Function: Hollow fiber membranes made up of micropores. Filters blood and removes waste products (urea, uric acid, etc.)
  - Hemodialysis:
    - Utilizes the principle of diffusion.

      Moves waste products from highly dense blood to the dialysate side.
    - Removes small toxins (urea, creatinine, etc.)
  - Hemodiafiltration:
    - The dialysate side is depressurized, and the pressure difference causes waste products to move to the dialysate side.
    - Removes large toxins (proteins with low to medium molecular weight).
    - Improved quality of life for long-term dialysis patients
- The number of dialysis patients: 7% increase per year
   (Rate of increase: Domestic 2% /year, China 15% /year)



Dialyzer





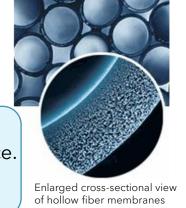
Forecast of number of dialysis patients (tens of thousands)

## Products | Artificial Kidney Hollow Fiber (Chronic Blood Purification Membrane)

#### **TOYOBO**

#### [Our strengths]

- Excellent biocompatibility due to cellulose triacetate membranes (PVP free)
- Possible up to filtration with cellulose triacetate membranes
- Share: Global 6% (domestic approx. 20%, China 13%, other countries 1-2%)
- $\rightarrow$  Extremely low incidence of allergy.
- → Less clogging and stable performance. Less blood pressure fluctuation and improved QOL.



#### Plan to build an integrated production plant jointly with Nipro Corporation (FY 3/25)

- Objective: To strengthen the production system and meet growing global demand
- Integrated production system from hollow fiber production to processing and commercialization of dialyzers

Front-end process: Make hollow fibers from raw materials (TOYOBO) Back-end process: Make finished products (Nipro)

- Commercial distribution: TOYOBO (Membrane production)
  - ⇒ Nipro (Modularization and commercialization)
  - ⇒ Hospitals in Japan and overseas



#### Integrated production plant for CTA dialyzer

- Inside Nipro's Odate factory site (Odate City, Akita Prefecture)
- Capital investment: About ¥5.0 billion (equipment for making hollow fiber membranes)

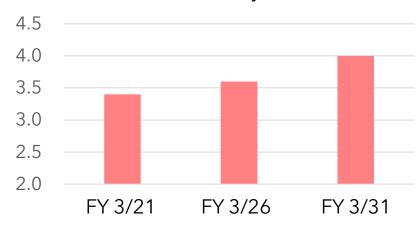
## Products | Acute Blood Purification Membrane



#### **Ascites filtration and concentration membrane (CART)**

On sale since 2020

Treatment of ascitic fluid that has accumulated due to cancer or cirrhosis, using a filter and concentrator to concentrate useful protein components (e.g. albumin) and return them to the body via intravenous infusion.

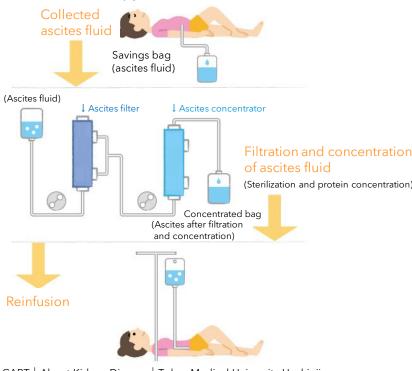


Market of blood purification membrane (number) (ten thousand)

#### **♦** Potential for expansion in the field of blood purification

- Septicemia treatment membranes (cytokine adsorption membranes), etc. When the immune system goes haywire due to infection and cytokine levels become uncontrollable, symptoms are alleviated through the adsorption of cytokines
- > Hollow-type separation membrane technology is applied to niche, high value-added fields
- > From sales of hollow fibers to adding sales of modules into the scope

Image of Cell-free and Concentrated Ascites Reinfusion Therapy (CART) treatment



CART | About Kidney Disease | Tokyo Medical University Hachioji Medical Center - Kidney Disease Center (hachioji-kidney.jp) \* Translate Japanese website into English

#### Products | Separation Membranes for the Antibody Drug Manufacturing Process

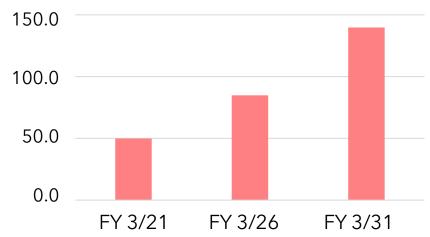


#### Virus removing membranes

- Membrane that separates antibodies and viruses for use in the final manufacturing process for antibody drugs
- Antibody drugs bind to disease-causing antigens and target them with pinpoint accuracy, resulting in high therapeutic efficacy and reduced side effects
- Market: Growing market tripling in size over the ten year period

#### Filtration membrane for culture media

- The virus is filtered out of the culture medium at the beginning of the antibody drug production process
- ◆ Potential in the field of the antibody drug manufacturing process
  - Impurity removal membranes that utilize new removal mechanisms



Market of separation membranes for the antibody drug process (module) (¥bn.)

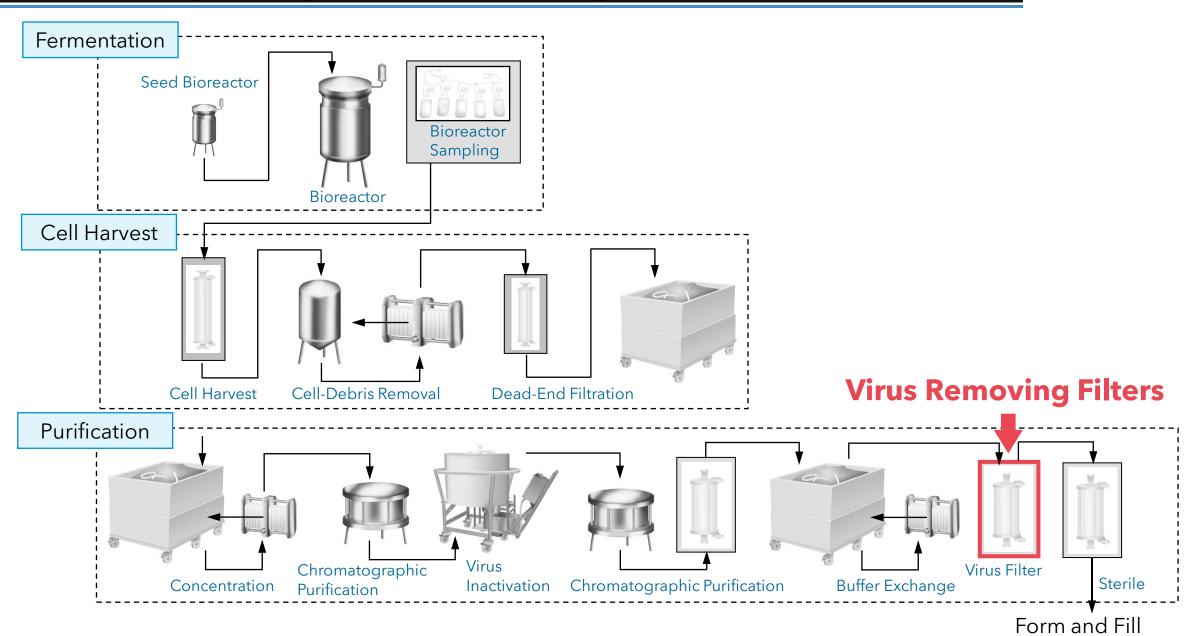
[Our strengths]

Combines reliable virus blocking performance with high-speed processing capabilities (Membrane production technology)

Hollow-fiber structure allows for a large treatment area and large treatment volume

## Antibody Drug Manufacturing Process





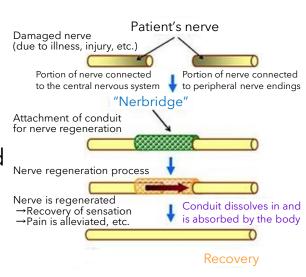
## Products | Biomaterials

### **TOYOBO**

#### Nerve regeneration conduit "Nerbridge"

- Function: Promotes regeneration of peripheral nerves that are torn or missing due to trauma etc. Absorbed into the body in about three months
- Our strengths: Nerve regeneration devices that reduce the burden on patients for autogenous nerve grafts
- Composition: PGA (polyglycolic acid) tubes are filled with collagen. Tubes are knitted (Japan) length 55mm, inner diameter 7types (U.S.) length 1inch (25mm), inner diameter 4types
- Market: 23,000 nerve regeneration tubes/year
- Full-scale sales promotion in the United States starting from FY 3/22. The United States is the world's largest market





#### Bone regeneration inducing materials "Bonarc"

- Function: Used for bone regeneration therapy by filling bone defects or cavities in the upper and lower jaw and alveolar bone
- Composition: Octacalcium phosphate (OCP) in powder form and collagen as raw materials, processed **into sponge-like discs and rods**
- (Size) disc: diameter 9mm x thickness 1.5mm, rods: diameter 9mm x thickness 10mm
- Market: Artificial bone ¥1.7 bn. (domestic), ¥60.0 bn. (overseas)
- Applications: Implant placement, bone regeneration in cleft jaws and cyst cavities

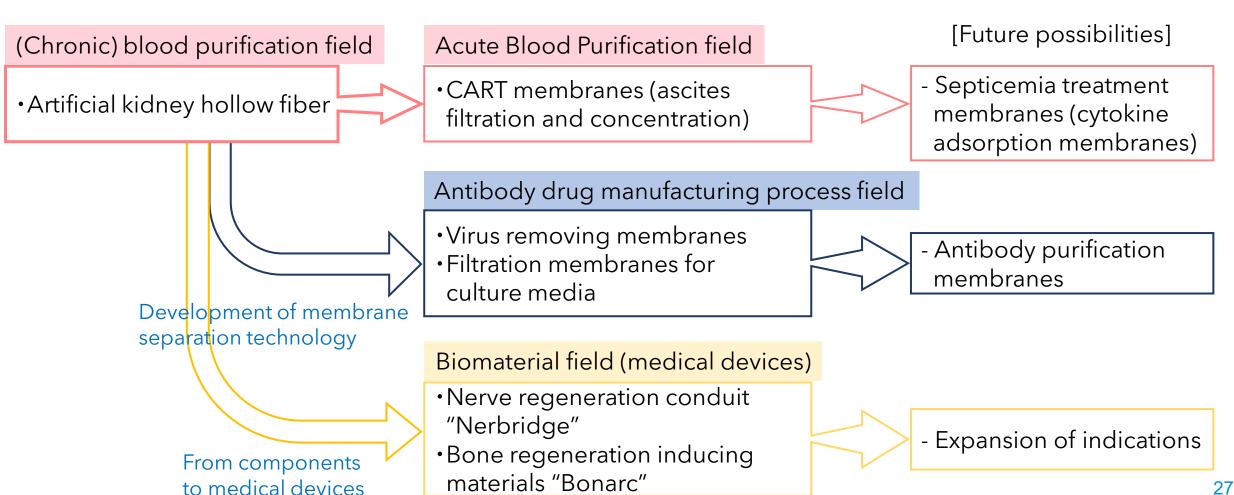


#### Future Development | Expansion of Applications and Technological Evolution of the Medical Materials Business



> Development of hollow-type separation membranes

Expansion of value chain for blood purification by entering into module manufacturing and medical device sales



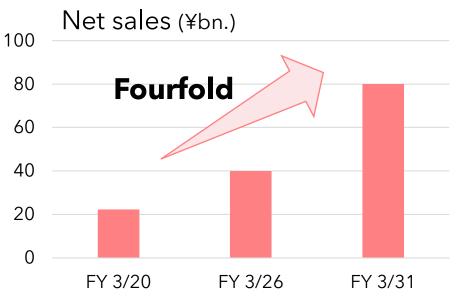
## **TOYOBO**

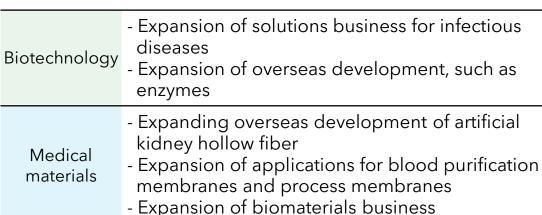
## IV. Future Development

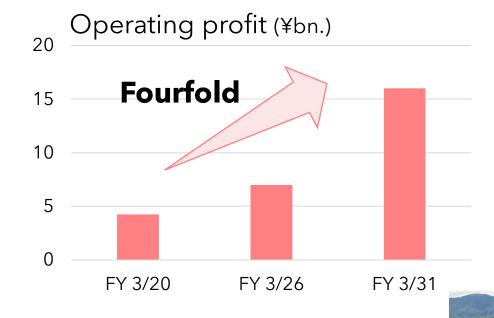


### ~ Global Niche Category Leader Strategy ~

#### Aiming to be the top global niche company!







#### CAPEX approx. ¥20.0 bn. in 4 years

- New biotechnology building (2024)
- Medical Research Laboratory (2024)
- Construction of a plant for dialysis membranes for artificial kidneys (2024)

## **TOYOBO**

## **V. Terms**

#### Terms



#### - Enzymes

Substances (biocatalysts) that speed up chemical reactions (protein breakdown, fat breakdown, etc.) that occur inside and outside the body. A type of protein. The property of selectively allowing only the desired reaction to proceed

#### - Test reagents

Reagents used to diagnose diseases and examine abnormalities or changes in the body by mixing it with a specimen (blood, urine, etc.) collected from a human being

#### - Diagnostic reagents

Drugs intended to be used exclusively for the diagnosis of diseases

#### - Dialysis

Moves waste products from highly dense blood to the dialysate side (diffusion). Mainly removes small toxins (urea, creatinine).

#### - Filtration

The dialysate side is depressurized, and the pressure difference causes waste products to move to the dialysate side. Highly efficient removes large toxins (proteins with low to medium molecular weight).



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