# Bio CDMO Div. & Life Sciences Business Div. Business Briefing

December 15, 2022 FUJIFILM Holdings Corporation

Forward-looking statements, such as those relating to earnings forecasts and other projections contained in this material, are management's current assumptions and beliefs based on currently available information. Such forward-looking statements are subject to a number of risks, uncertainties, and other factors. Accordingly, actual results may differ materially from those projected due to various factors.





# **Life Sciences Business Group**

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**FUJIFILM Corporation** 

Director, Senior Executive Vice President, CLSO

General Manager, Life Sciences Strategy Headquarters

## **Bio CDMO Division**

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## **Life Sciences Business Division**

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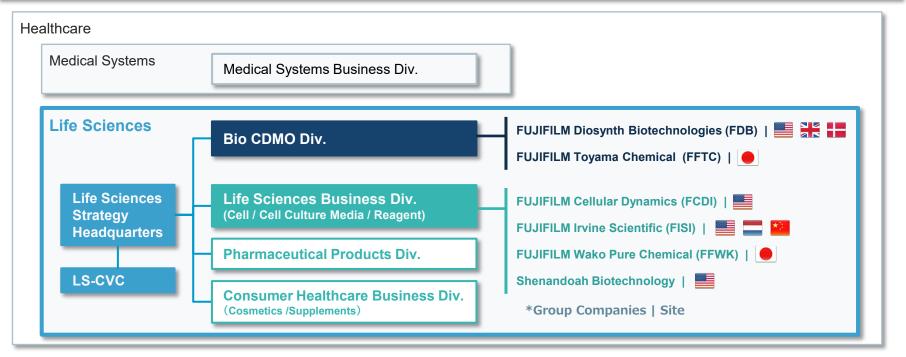
Corporate Vice President,

General Manager, Life Sciences Business Division

1 | Life Sciences Business Group

#### 1-1 | Life Sciences Business Group : Organization

- "Healthcare" segment has two business groups; "Medical Systems" and "Life Sciences".
- "Life Sciences" business group to strengthen and prioritize Bio CDMO and drug development support businesses.
- **⇒** Become a leader within the life science industry, by offering value of end-to-end solutions as a company strongly supporting the creation of cutting-edge medicine.



#### 1-2 | Life Sciences Business Group : Financial Target toward FY30

Toward FY30, Life Sciences Business Group will achieve strong business growth; i) Revenue: ¥750B+, ii) FY18-30 CAGR: 15%+, iii) Operating Profit Margin: 25%+. 25%+ **Operating** Profit% **Upside Potential** (Forex etc.) ¥750B+ Life Sciences Gr. FY18-30: 15%+ ¥250B+ LS Solutions \* Revenue **Bio CDMO** ¥500B+ \* Total of 3 Business Div.; - Life Sciences - Pharmaceutical - Consumer Healthcare FY18 FY19 FY20 FY21 FY22 FY25 FY30

#### 1-3 | Life Sciences Business Group : LS-CVC (Life Sciences Corporate Venture Capital)

- In Feb. 2022, launched LS-CVC.
- In Dec. 2022, invested in PhenoVista Biosciences, a leading CRO of providing the imaging-based assay services.

#### **Goals and Objectives**

- Access cutting-edge and innovative biotechnologies and know-how outside of Fujifilm group.
- Through strategic alliance with early-stage companies / biotech startups,
- 1 create synergy, 2 enhance current businesses and expand product/service portfolio, 3 enter new business.
- Accelerate business overall growth of Life Sciences Business Group overall.

#### **Target**

- **Bioprocess technologies for novel biopharmaceutical**: Cell and gene therapy, mRNA, Novel antibodies
- **Innovative cell technologies**: Editing, Analysis
- Innovative biomanufacturing technologies

2 | Bio CDMO Division

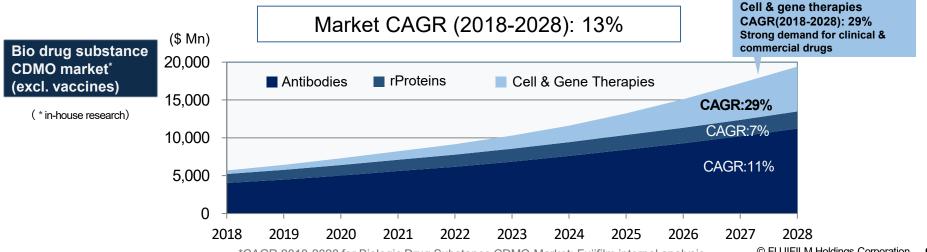
- 1. Overview of Bio CDMO Business
- Outlook of Bio CDMO Business
- 3. Technological Advantage
- 4. Environmental Approach
- 5. Wrap-up

#### 1-1 | Bio CDMO Market Trend

#### In addition to conventional modalities such as antibodies, technological developments within next gen biopharmaceuticals further increase the demand for CDMOs

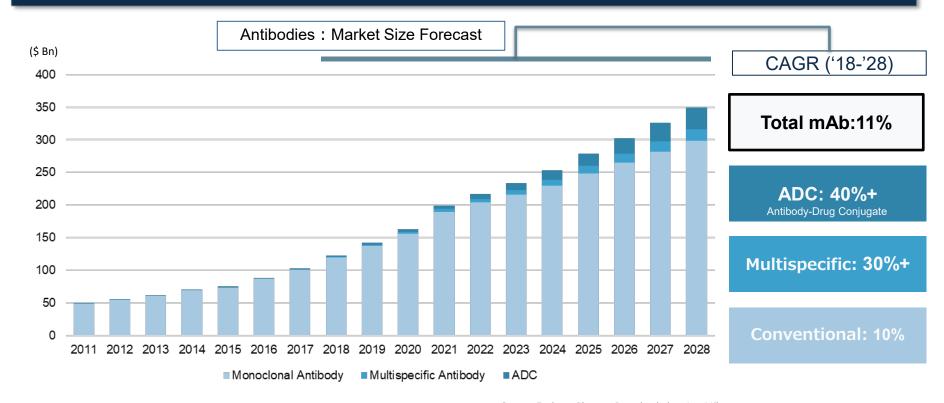
The growth of the Bio CDMO drug substance market further accelerates. Recent topics:

- 1) Accelerated development of cell and gene therapies: CAGR to increase to 29% No. of drugs approved and under development continues to increase and advancements in development is expected to lead to further market expansion beyond 2025
- 2) Increase in demand for next gen biopharmaceuticals: The antibody segment is expected to maintain a high CAGR of 11%. In addition to steady growth of conventional antibodies, next gen antibody drugs with high therapeutic effect such as ADCs\* and bispecifics contribute to the growth \*ADC: Antibody-Drug Conjugate



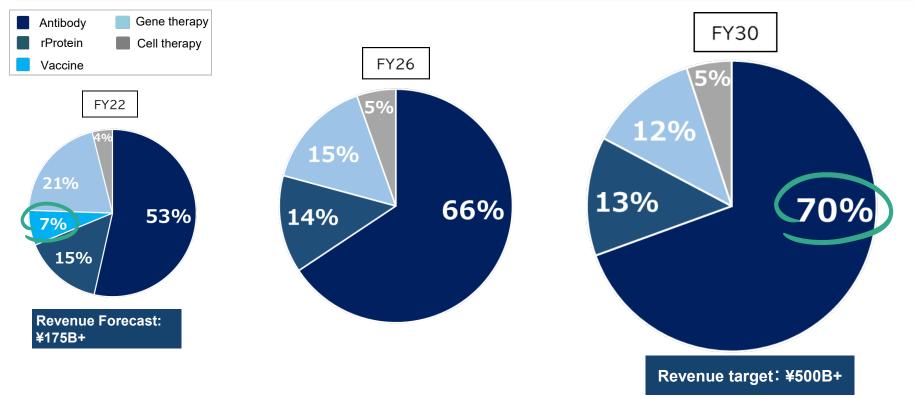
#### 1-2 | Antibody Drug Global Market Trend

The market for antibody drugs is being driven by next gen antibody drugs such as ADCs and bispecifics and the current outlook is for an annual demand growth of more than 10%



#### 1-3 | Fujifilm's CDMO Business: Revenue Ratio (%) by Modality

- Capacity increases from facility investments mean the ratio of antibodies will increase.
- Since vaccine demand is uncertain it has not been included in the future business plan.



#### 1-4 | Global Footprint

### Offering end-to-end solutions from small-to-large scale bulk drug substance production to formulation and packaging

As of Dec,2022	North America New New					Europe		Asia
(w/o Small molecules) RTP NC, US Co		College Station TX, US	Thousand Oaks CA, US	Boston MA, US	Holly Springs NC, US	Billingham UK	Hillerød Denmark	Toyama Japan
		2	3	4	(5) 	6	7	8
(Services since)	(2011)	(2014)	(2022)	(2022)	(TBO 2025)	(2011)	(2019)	(TBO 2026)
Antibodies	•	•			•	•	•	•
Recombinant proteins	•					•		
Cell/Gene therapies		•	•	•		•		
Vaccines	•	•				•		•
Formulation			•		• -		•	•
Assembly, Labeling & Packaging						12	•	

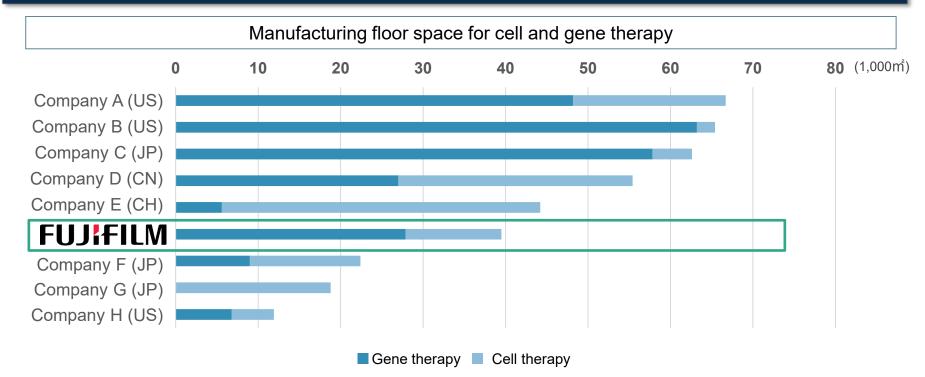






#### 1-5 | CDMO Business Expansion: Cell Therapy CDMO Full-Blown Market Entry

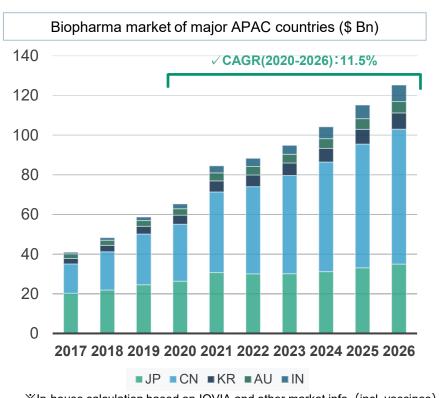
Made a full-blown entry into the cell therapy CDMO business in April 2022 through the acquisition of the cell therapy manufacturing site (currently Fujifilm Diosynth Biotechnologies California) of Atara Biotherapeutics, inc. located in California, US

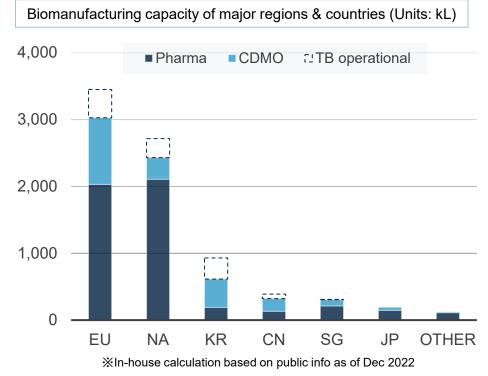


<sup>\*\*</sup>Calculated floor space based on public information from each company on operational mfg. facilities (and partly from conjecture) Abbreviations of country names indicate the location of company headquarters.

#### 1-6 | CDMO Business Expansion: APAC Biopharma Market vs. Manufacturing Capacity

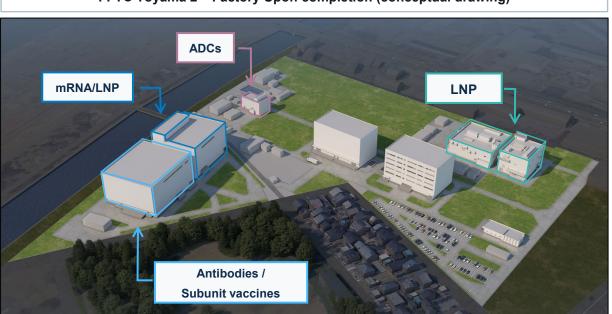
The APAC biopharmaceutical market is expected to expand. However, Japan is lagging behind other major APAC countries in terms of biomanufacturing capacity and there are calls for expansion.





#### 1-7 | CDMO Business Expansion: Establishing a Bio CDMO site for Japan & Asia

- Promote a bio CDMO "local production, local consumption model" to respond to the increase in market size and demand in Japan & the APAC region
- Build a bio CDMO site within Fujifilm Toyama Chemical's 2<sup>nd</sup> factory
- Wide variety of modalities within new areas such as ADC and mRNA in addition to LNP and antibodies
- Chosen for a subsidy from the Japanese government under the premise of dual use in the event of a pandemic

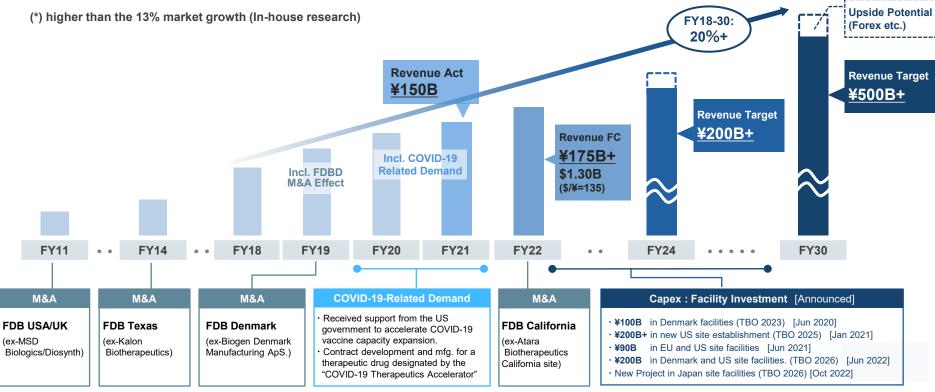


FFTC Toyama 2<sup>nd</sup> Factory Upon completion (conceptual drawing)

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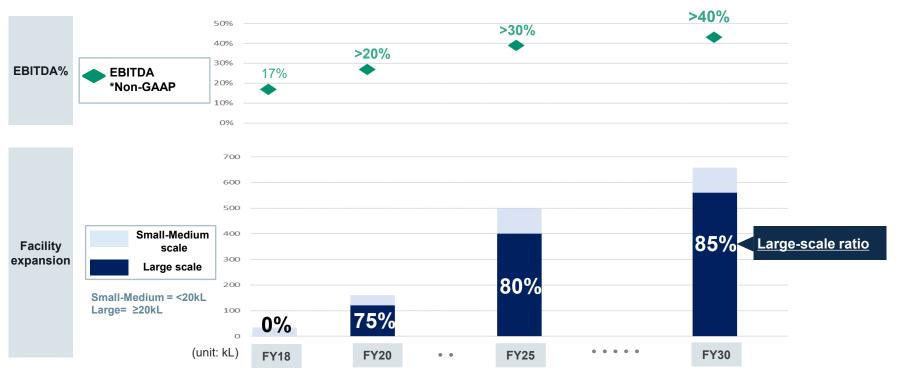
#### 2-1 | Revenue: CAGR exceeding that of the Market

The Bio-CDMO Division will expand business through facility investments and M&A, and expects revenue growth of i) \(\frac{4}{200}\)B+ in FY24 and \(\frac{4}{500}\)B+ in FY30, ii) FY18-30 CAGR 20%+ (\*)



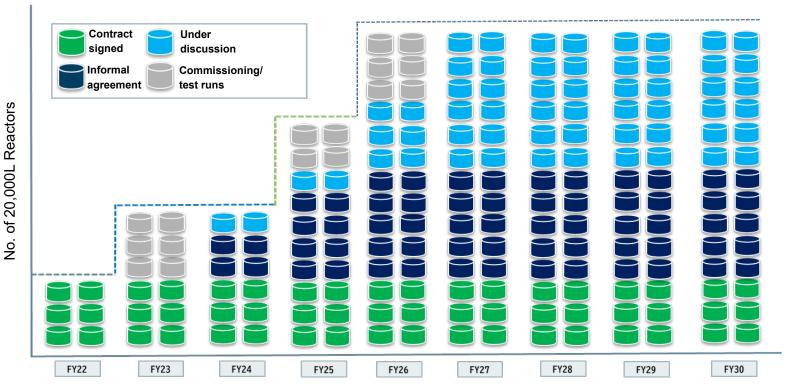
#### 2-2 | Facility Investments: Manufacturing Capacity Expansion Plan

Increase ratio of high profit margin large scale facility through large scale investments in US and EU sites, and aim for EBITDA of over 40% in FY30



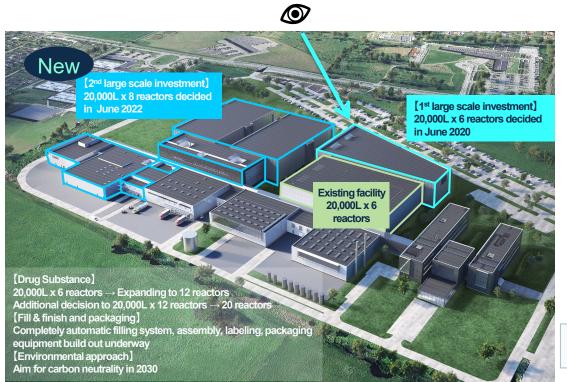
#### 2-3 | Facility Investment: Capacity Expansion and Commercial Activity

Carrying out commercial negotiations at a steady pace aimed at the operation start of large-scale facilities. Will ensure that market demand is captured to generate business growth



#### 2-4 | Denmark Site: 2<sup>nd</sup> Facility Investment/Capacity Increase (June 2022 announcement)

Denmark site additional expansion decided and began construction Sep 2022. Set to become the largest pharma/CDMO manufacturing site in the EU (25,000m floor space)







Steady progress on 1st investment (Picture taken on October 2022)

#### 2-5 | North Carolina, US: New Site Construction (Jan 2021 announcement)

Currently constructing a new site with 20,000L x 8 bioreactors, fill & finish and packaging in North Carolina, US. The site is set to become the largest bio CDMO manufacturing site in North America.

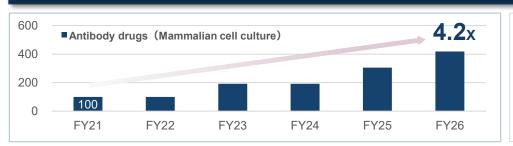
- 20kl Bio reactors  $8 \stackrel{\text{Under}}{\longrightarrow} \text{Maximum} \ 32 \stackrel{\text{Can be}}{=} \text{expanded}$  All-Automated fill & finish system Assembly, labelling, packaging
- \*New NC, US Site:
- Site area 610km² (x85 soccer fields) → largest in North America
- Plan to use 100% electricity from renewable sources
- Aim for carbon neutrality in 2030





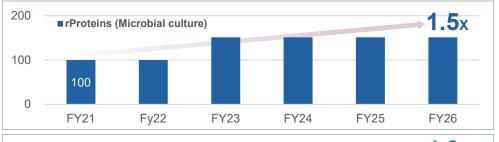
#### 2-6 | Manufacturing Capacity Expansion Plan

#### Large scale investments for each modality to achieve ¥500B revenue by FY2023



### Antibody drug (mammalian culture):

- Facility expansion in the EU and US underway
- Strengthening both continuous and conventional batch manufacturing capacity





#### rProtein (microbial culture)

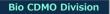
Continue investments in line with market demand

#### **Gene therapy:**

- Expand capacity faster than market growth rate
- Establish high productivity manufacturing technology and solve current issues (complex manufacturing process, hard to mass produce, high cost)

#### **Cell therapy:**

Focus on allogeneic cells and aim to establish high productivity manufacturing technology



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(In-house research)

#### Industry top-level productivity for each modality

				(III-House researon)		
			Fujifilm	Competitors		
		mAb	>10g/L	3∼8g/L		
Antibody drug	Productivity	BiAb*1	~5g/L Apollo <sup>™</sup> X	1∼2g/L		
(Mammalian culture)	New	Fc fusion Protein	1-2g/L (*pool) several cases	1g/L (*pool)		
	Cell line development (Process development)		10 weeks (34 weeks)	12∼18 weeks (40∼48 weeks)		
rProtein	Productivity		>15g/L paveway _	>15g/L		
(Microbial culture)	Cell line development		4 weeks	6∼8 weeks		
Gene therapy	Prod	New uctivity	3 x past results ⇒ 100 x <sup>2</sup> (Conventional: 1.0×10 <sup>11</sup> vg/mL)	-		

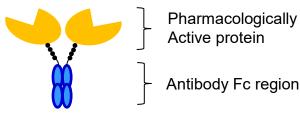
<sup>\*1</sup> BiAb: bispecific antibodies

#### 3-2 | Next Generation Antibodies

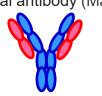
Adapted our proprietary production platform (ApolloX) to Fc fusion proteins, one of the next gen categories of antibodies, and obtained data demonstrating higher productivity than our competitors for several model molecules. Will continue to approach the next gen market.

#### What is Fc fusion proteins?

- Fc fusion proteins
- Artificial protein made by fusing Fc region of an antibody and a pharmacologically active protein (molecular size 50-150kDa)
- ⇒Longer half-life than non-fusion proteins



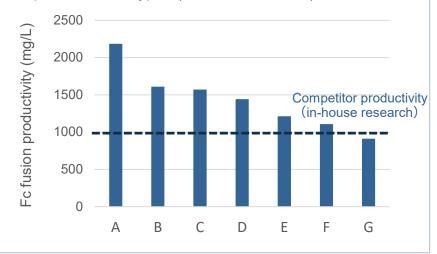
Normal antibody (Made up of Fc and Fab region)



Fab region (binds to specific antigen)

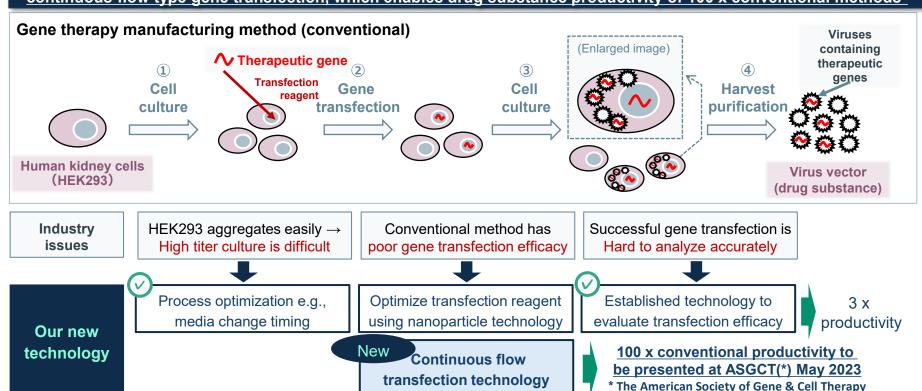
#### Fc fusion protein productivity track record

- Have verified the productivity of ApolloX using 7 different types of Fc fusion proteins
- Were able to confirm productivity equal or higher than competitors for all types (in-house research).



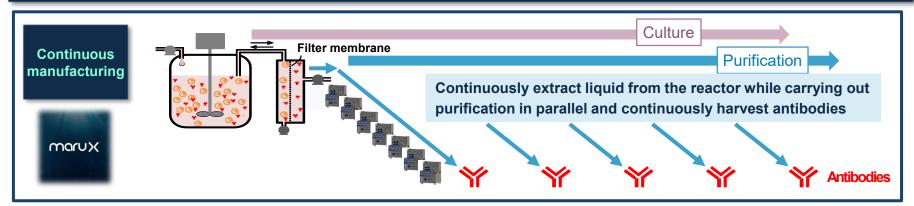
(\*In-house research)

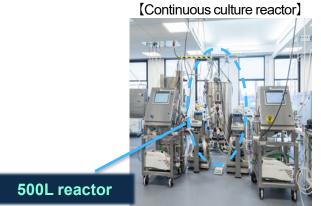
Realized 3 x productivity through process technology, nanoparticle control technology, Al analysis and developing fundamental AAV high productivity technology using continuous flow type gene transfection, which enables drug substance productivity of 100 x conventional methods\*



#### 3-4-1 | Industry-First Culture to Purification Continuous Manufacturing System

#### World's first "integrated culture to purification 500L scale facility" for continuous manufacturing GMP manufacturing facilities under construction in the UK and US





[Automatic continuous purification device: Symphon X]



**Purification device** (7 units connected)

#### 3-4-2 | Comparison of Continuous Manufacturing Systems

Industry leader with integrated culture and purification for commercial scale (500L) high titer culture. Carrying out scale-up development for 2,000L scale (output equivalent to 20,000L batch manufacturing).

Comparison of continuous manufacturing across different companies

\*No available information found for Samsung Biologics

		CDMO · Equipment Company				Pharma companies				
		FUJIFILM	Lonza	WuXi Biologics Global Solution Provider	ThermoFisher SCIENTIFIC	AstraZeneca	<sup>®</sup> Biogen.	AMGEN	<b>♦</b> MERCK	sanofi
Continuous culture	Cell titer	120Mcells/ml	Started R&D for small scale	40~100M cells/ml	120M cells/ml	90M cells/ml ※	120M cells/ml	80M cells/ml ※	Undisclosed	120M cells/ml
	Scale	500L ⇒2,000L Under development		150L	500L	500L:: (3000L under development)	500L:: (2000L under development)	Implemented cGMP equipment	500L (3000L Under development)	500L (no mention of scale up)
	ontinuous Irification	Proprietary equipment enables full integration ⇒2,000L scale (already applied)	_	Only partly continuous, some steps are done in batches	_	_	Only partly continuous, some steps are done in batches	Only partly continuous, some steps are done in batches	_	Only partly continuous, some steps are done in batches



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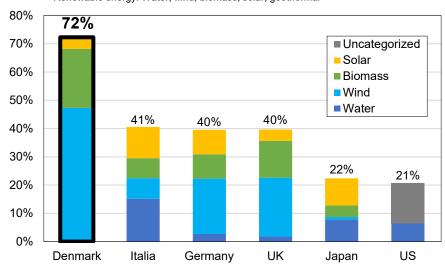
#### 4-1 | Environmental Approach

Promoting "Reduction of CO2 emissions" and "Reduction of water consumption" to achieve SVP2030.

- Denmark: Promote switch to electricity derived power boiler energy and recycling wastewater into cooling water.
  - \* Denmark has high affinity with our policy in that it is taking a proactive approach to the environment and its ratio of renewable energy is over 70%.
- US (North Carolina): Include 100% renewable energy derived from electricity in large scale facility investment.

#### Ratio\* of renewable energy for electricity generation in 2021

\*Renewable energy: Water, wind, biomass, solar, geothermal



Source: ISEP, EIA

### 1) Reduction of CO<sub>2</sub> emissions



- Switching from gas to electricity powered boiler to reduce CO<sub>2</sub> emissions (Denmark 2<sup>nd</sup> facility investment)
- Plan to use electricity from 100% renewable energy (US large scale investment)

### 2) Reduction of water consumption



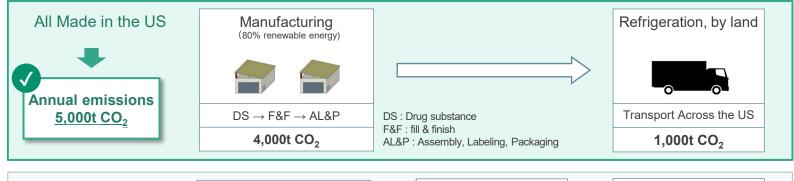
By recycling waste water (drainage etc.) into cooling water

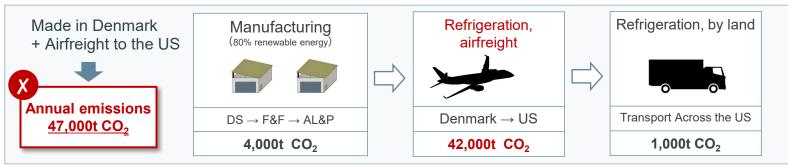
#### 4-2 | CO<sub>2</sub> emissions from shipment of Biopharmaceuticals

#### Reduce the environmental burden of the pharmaceutical supply chain by promoting "local production for local consumption".

#### CO<sub>2</sub> emissions from supplying products to the US (in-house simulation\*)

(\* Premise: Comparison of CO<sub>2</sub> emission for the same amount of the same drug manufactured for the US until reaching the patients





→ Significant amount of CO₂ emissions when manufacturing products for the US within the EU due to the need for Refrigeration and airfreight



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Strengthen offering for various modalities

→ Strengthen especially cutting-edge modalities (e.g. ADCs, advanced vaccine, cell and gene therapy)

Pursue highest level of productivity for each modality

→ Strive to become the industry leader not only within antibody drugs and recombinant protein drugs, but also cell and gene therapy

Offer services globally incl. APAC

→ Expand into the APAC market from the new Japan site in addition to the existing EU and US sites

# Reinforce the "End-to-End Service" offering → Strengthen end-to-end solutions at each site, including formulation and packaging

Environmental awareness
 → Promote "local production for local consumption model" at US site and use of renewable energy to reduce environmental burden

2 | Life Sciences Business Division

## Overview /Outlook of Life Sciences Business

- Cell Therapy Process Development & Manufacturing Service
- Drug Discovery & Manufacturing Support 1 iPS Cell: Drug discovery R&D support business 2 Cell culture media business
- Wrap-up

#### 1-1 | Business Area of Life Science Business Division

#### Handling R&D and production of innovative drugs and offering solutions in the field of cell therapy to contribute to addressing unmet medical needs

#### **Cell Therapy Process Development** & Manufacturing Service

- We will create synergy, with a focus on FCDI's iPS Cell, that makes use of FUJIFILM group-wide unique engineering technologies, resources, and facilities. \*FCDI:FUJIFILM Cellular Dynamics, Inc.
- Utilizing synergy as a platform, we will **promote** in alliance with partners efficient R&D and promote business developing and manufacturing cell therapy products.



**GMP facility: i-FACT** (Madison, Wisconsin, US)



#### **Drug Discovery & Manufacturing Support**

- Supplying cells (e.g. human iPS Cell for drug discovery), cell culture media, cytokine, reagents and related products to contribute to discovery research and production of new innovative drugs. |COVID-19|
- Cell culture media has grown rapidly due to increased demand for use in the manufacturing biopharmaceutical.









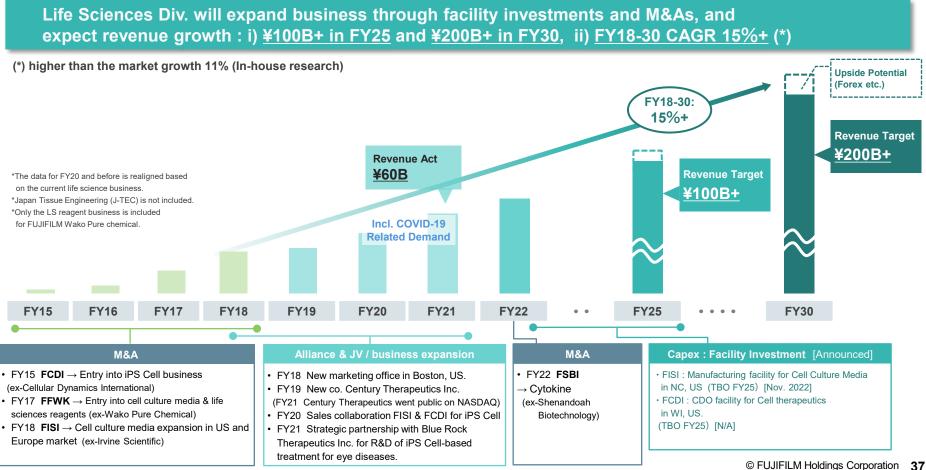
iPS Cell

Cell culture media

Reagents

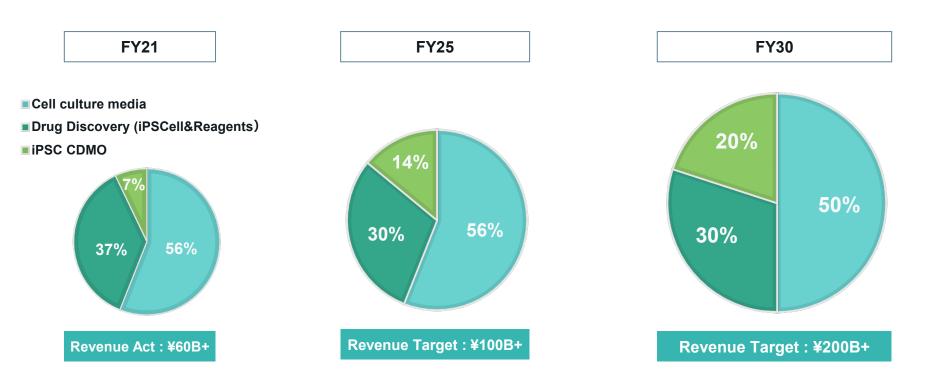
Cytokine

## 1-2 | Revenue : CAGR exceeding that of the Market



## 1-3 | Revenue Ratio (%) by Business Unit

The cell culture media business will grow due to high demand for antibody drugs. In addition, we will expand drug discovery support and CDMO businesses, with leveraging iPS cell



## 1-4 | Cell Culture Media : New Facility Investment

## FUJIFILM Irvine Scientific (FISI) Invests \$188 million in a second manufacturing facility in the US. to supply products to customers on the East Coast

#### **Upon completion (conceptual drawing)**



FISI purchased 259,000m2 land including a further room for expansion, in the Research Triangle Park(RTP) in NC state of US.

- **Reduce transit time and cost** from NC site beyond that from CA site, and ensure business continuity.
- Ensure a steady supply of cell culture media for biologics, cell and gene therapies, and other key medicines that are essential for human health. Customized cell culture media appropriately meeting customer needs can be provided.
- Realize **more efficient production** with improvied workflow.
- RTP in NC state is a leading life sciences cluster. This location makes easier to secure biotechnology resources required for manufacturing operations.

## 1-5 | iPS Cell Products & iPS Cell Therapy : New Facility Investment

## Fujifilm Cellular Dynamics (FCDI) decided to establish a new GMP facility to expand development and production capacity

#### **New Facility (Madison, WI, US)**



(48,000m includes further room for expansion)



HQ Office



- Production facility for DR cell products
- Quality Control(QC) Div.



- Production facility for clinical trial products
- Warehouse
- · Logistic Div.



Overview /Outlook of Life Sciences Business

# **Cell Therapy Process Development & Manufacturing Service**

- **Drug Discovery & Manufacturing Support** 1 iPS Cell: Drug discovery R&D support business 2 Cell culture media business
- Wrap-up

Therapeutics

## iPS cell have self-propagating ability and pluripotency, which can be used for various types of therapies.

**iPSCs** 

Differentiation.

iPS cell (iPS=induced pluripotent stem)

**Human body** 

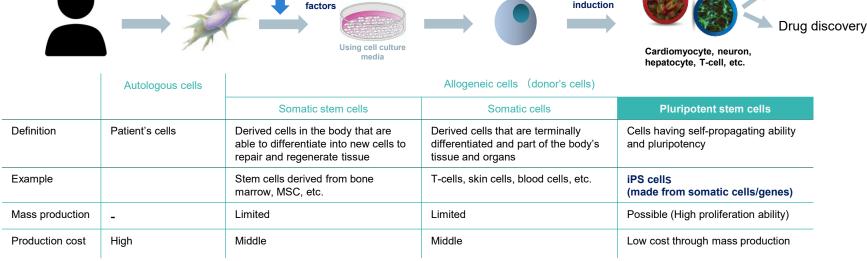
Somatic cells

iPS cells are produced by introducing a small number of genes known as reprogramming factors into human skin tissue and blood-derived somatic cells to enable differentiation into various tissues and organ cells as well as enable almost indefinite propagation.

Culture

Inserting

reprogramming



Differentiated cells

## 2-2 | iPS Cell : Challenges and Solutions

By using our proprietary technology for mass production, iPS cells can be stably supplied at a lower cost. iPS cells will be a key material in the next generation of therapeutic modalities and drug discovery support.

#### 1) Cell Therapy

#### Challenges

Stable Supply and Stable Quality

- 1. Shortage of cell donors for rare disease
- 2. Unstable cell quality due to individual difference

#### **Solutions**

Modality using iPS cells

- 1. Stable supply of iPS cells because of their selfproliferation ability.
- 2. Stable cell quality as they are derived from the same cell line.

## 2) New drug development support:

#### Challenges

**Improving efficiency** and **Reducing cost** of new drug development

- 1. No new drug evaluation method due to complicated disease mechanisms.
- 2. In some cases, animal tests are OK, but clinical tests are not because of the difference between humans and animals.

#### **Solutions**

New drug screening with iPS cells

- 1. Disease analysis with iPS cells derived from patients with intractable diseases.
- 2. Toxicity/drug efficiency/safety tests using iPS cellderived disease model before clinical trial.

## 2-3 | Cell Therapy : CDMO Market

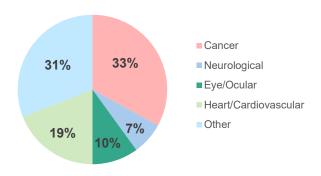
## Number of clinical trials involving iPS cells: Approximately 100 (7% of total cell therapies) Increasing trend of allogenic cells, CY20-CY30:CAGR15%+

#### iPS Cell derived cell therapy products – clinical trial

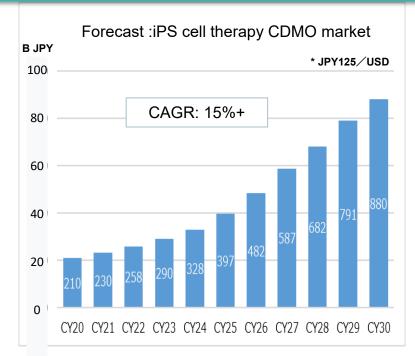
Area			*)	Other
Number	51	18	24	5

Target disease of iPS Cell derived cell therapy clinical trials

#### **FUJIFILM** covers major disease with partners



Source: Locust Walk; iPSC Market Overview, Sep. 30th, 2021



Based source: Cell Therapy Manufacturing Market (3rd Edition), 2020-2030 (Roots Analysis)

\*Estimated ratio: 10% iPSC out of Cell therapy

## 2-4 | iPS Cell Therapy : Process Development/Manufacturing(CDMO) Business

## Establish recurring revenue business enabling sustainable growth through a combination of grant of iPS cell-related IP licenses and process development & manufacturing services

Investment into cell therapeutic firms

Grant of IP license for iPS Cell related

- Strategic alliance
- Contract development and manufacturing
- Reprogramming
- Differentiation

**Expansion of** target diseases

Establishment of technologies involved **Business expansion though CDMO service** 

2. Cell Therapy **Development**   Promote cell therapy development through alliances with partners

Recurring revenue from up-front, milestones, and royalties from licensees

3. **Providing Cell Lines** 

- Providing materials for R&D
- Developing new customers.

Increase customer satisfaction with support for their R&D

**Acquisition of future CDMO clients** 

## 2-5 | iPS Cell Therapy : CDMO business update and GMP facility expansion

#### 1. CDMO business from investee firms

Indication	Partner	Update	
Cancer Immunotherapy	CENTURY THERAPEUTICS	Century Therapeutics received <b>IND clearance from the FDA.</b> FCDI is contracted with Century for <b>manufacturin</b> g and clinical supply.	
<ul><li> GvHD</li><li> Knee osteoarthritis</li></ul>	CUNDTO therapeutics	NDA approved by FDA (Using FCDI iPS Cell line ) CMO potential customer: Clinical supply and commercial manufacturing	
New Parkinson's disease	Ryne Bio:	In Aug. 2022 FCDI <b>licensed program of a next-generation Parkinson's treatment derived from iPS cells</b> to Ryne Biotechnology Inc, the licensee and manufacturing partner of FCDI. FCI Contracted <b>CDMO services</b> with Ryne to manufacture dopaminergic progenitor cells.	

#### 2. Cell therapy development

Indication	Partner		Update	
<ul><li>Retinitis pigmentosa</li><li>Age-rerated macular degeneration</li></ul>	BlueRock	Autologous cell derived iPS cell thera Under development	py PJT	

#### 3. Providing iPS cell lines

Licensing out for several pharmaceutical companies aiming future CDMO business

**Increasing CDMO business** 

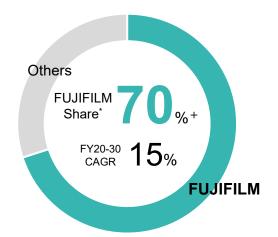
Facility expansion planned in 2025 and beyond to prepare for future demand increase.

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- **Drug Discovery & Manufacturing Support** 1 iPS Cell: Drug discovery R&D support business 2 Cell culture media business
- Wrap-up

## 3-1-1 | iPS Cell Products : Drug Discovery R&D Support Business

## Over 400 Customers: Top 10 big pharma in Japan, Europe, US, etc.

\*Share against the demand for iPS Cell derived cells purchased from 3<sup>rd</sup> party (Our research)



#### [Drug Discovery Process]



Pre-

Clinical

Clinical Trial

## Medicinal effect test | Pharmacological test

1. Microglia (Launched in Jan, 2019) Good reputation as a pharmacological test tool (FY22 1st half: YoY+76%)

Safety - Pharmacokinetic test

#### Safety - Toxicity test

2. Cardiomyocyte on new cell line (Launched in Sep. 2020) Good reputation as a cardiotoxicity test tool

#### 3. LS - CVC

The 1st case (PhenoVista)

Optimize drug discovery process by combining with cell image analyzing technology

## iPS cell-derived cell products



Cardiomyocyte

Mvocardial progenitor cells



Microglia



**Astrocytes** 



**DopaNeurons** 





GABANeurons Endothelial cells



MSC



Liver cells



Retinal cells

## 3-1-2 | iPS Cell Products : Microglia

#### What is Microglia?

- Microglia are a type of glial cells located throughout the brain. It's the only cell in the brain that has a very critical function for a normal brain's working immune system defending the body against infection.
- Although the mechanism has yet to be fully elucidated, it is known to be involved in the development of neurological disorders, such as Alzheimer's dementia and Parkinson's disease for which radical therapies have yet to be established.

[Challenge of new drug discovery for neurological diseases] The success rate has been low due to difficulty of obtaining appropriate preclinical evaluation tests for effectiveness/toxicity.

- Launched iPS cell-derived human **microglia** in January 2019.
- Utilization of microglia constructs a new evaluation method that recreates an environment similar to the human central nervous system. It is expected to contribute to enhancing trial effectiveness as well as speed up and reduce cost of new drug R&D.

## Center nervous system



#### Nerve cells (>100 billion)

Information processing&Communication

#### Glia cells (>1 trillion)

Support nerve cells

#### **Astrocytes**

- Transport nutrition to nerve
- Support communication
- Power up of brain barrier

#### Oligodendrocytes

Control order communication speed

#### Microglia(10% of glia cells)

Only one immune cells in brain

- 1 Fix brain damage
- ② Foreign matter removal (Pathogen, dead cells)



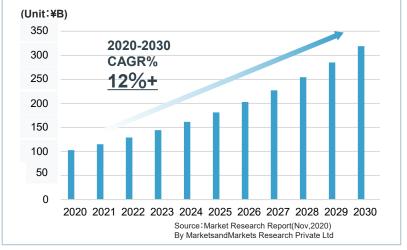
## 3-2-1 | Cell Culture Media : Global Market of BP Media

Bioproduction media Fujifilm is focusing on is the growing market with CAGR +12%. Fujifilm will be a market leader for BP Media holding >30% market share with ¥100B sales by 2030.

#### **BP Media: Global Market Outlook**

- Total demand of serum-free culture media<sup>\*</sup> for bioproduction (BP), a focus area for Fujifilm, is expected to grow at the rate of CAGR+12%.
- \*Serum-free culture media:

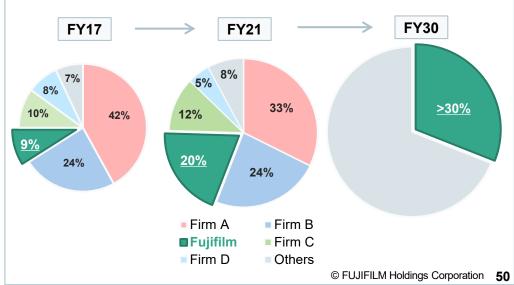
  Serum-free culture media is formulated to mitigate risks from the use of undefined and highly-variable serum products. For this reason, serum-free culture media are widely used for commercial production for biomedicine."



#### **BP Media : Market Share Outlook**

(In-house research)

- Following the acquisition of FISI in 2018, Fujifilm has doubled its market share and increased sales by 4 times (over CAGR+50%).
- The goal is to hit ¥100B in revenue by FY2030.



## Coordinating departments to provide powerful customer support to trade with 15 out of the world's top 20 pharmaceutical companies

#### R&D

- More than 50 years of cell culture media expertise and an advanced media portfolio.
- Ability to provide solutions by conducting quick testing at FCDI·FDB and optimizing through "cells / cell culture media / culture processes".
- Applying the state-of-the-art technology in powder and liquid process, developed through the photo film business.

## **Manufacturing**

- Using GMP-compliant manufacturing facilities to produce high-quality cell culture media.
- Products-supply from a global production framework consisting of sites in Japan, EU and US.
- Using advanced analysis technology, etc. for Quality Control & Quality Assurance.

## Sales & Operation

- Deploying an enhanced product line-up including cell culture media for broadbased applications, buffers, sterile water for injection, and cytokines.
- · Robust global sales networks, combined with sales teams with outstanding expertise.
- · We built up new customized service center in China where the market Is growing very rapidly.

Handling processes from development to manufacturing and quality assurance swiftly to supply high-quality products in a timely fashion

Identifying customer needs accurately and providing it to R&D as feedback

## 3-2-3 | Cell Culture Media : Global Footprint

## **Manufacturing & Customized service center**

As of Dec,2022	North America New		Europe	China New	Jap	oan
	Santa Ana CA, US	RTP NC, US	Tirburg Netherlands	New District Suzhou	Saitama	Aichi
		2	3	4	5	6
(Services since)	(2018)	(2025)	(2021)	(2022)	(2018)	(2017)
Main market	West coast US.	East coast US	Europe	_	Japan & Korea	Japan & Korea
Factory: Powder (Maximum Capacity)	(1,200t / FY23)	(800t / FY30)	(320t / FY23)	_	(90t / FY23)	(100t / FY24)
Factory: Liquid (Maximum Capacity)	(1,200kL / FY23)	(3,300kL / FY30)	• (470kL / FY23)	_	_	• (720kL / FY23)
Customized Service		-			•	_

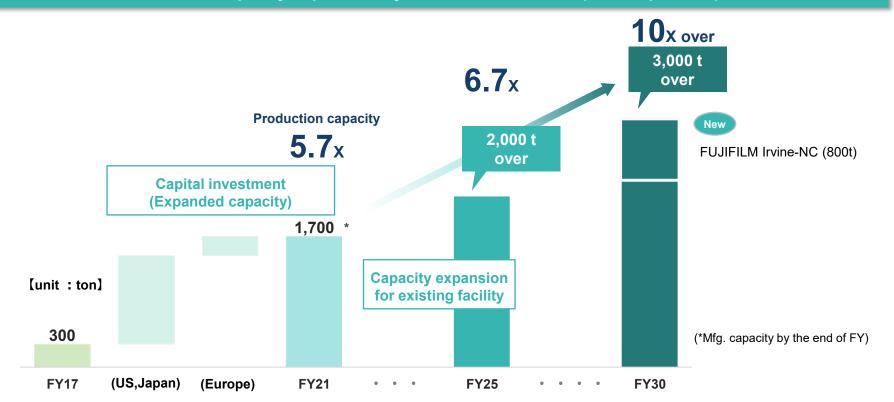






## 3-2-4 | Cell Culture Media: Production Capacity Expansion Plan (Powder)

## Continuous capital investment in US, Europe and Japan Tenfold capacity expansion by 2030 over 2017 level (FISI acquisition)



## 3-2-5 | Cell Culture Media: Acquisition of Shenandoah Biotechnology

High quality "cytokines" joined to our product portfolio → Power up of our comprehensive proposal to meet wide customers needs

#### **Feature**

- 300 high quality protein
- **Animal free products lineup**
- cGMP level QC system
- Human resorces with unique knowhow

## **Effect**

Among FUJIFILM group companies,

- 1) Synergy creation by fusing with existing technologies and products for new product & service proposals Next page
- 2) Power up of comprehensive proposal and sales revenue increase by utilizing current product sales channels

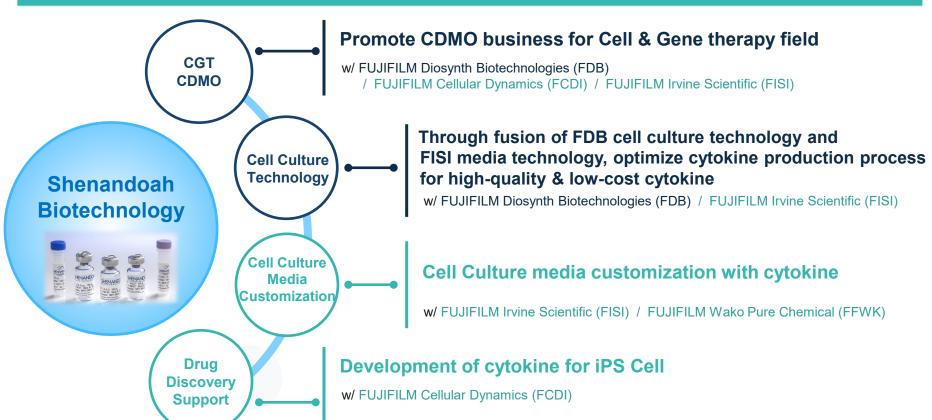






## 3-2-5 | Cell Culture Media: Synergy Creation w/ Shenandoah Biotechnology

## Cytokine of Shenandoah Biotechnology enable Life Sciences Business Group to create synergy



- Overview /Outlook of Life Sciences Business
- Cell Therapy Process Development & Manufacturing Service
- Drug Discovery & Manufacturing Support 1 iPS Cell: Drug discovery R&D support business 2 Cell culture media business
- Wrap-up

# Strengthen drug discovery & manufacturing support

→ Provide pharma companies and academia with "solutions combining cells, cell culture media, cytokines and reagents" by leveraging expanded utilization of drug discovery screening and pharmacological testing with human iPS cells.

## Significant growth of cell culture media business

- → Expand global footprint in US. (incl. new FISI NC factory), Japan and Europe though continuous Capex.
- → Aim to be market leader in serum-free culture media for bioproduction (BP) holding **30% share by FY30** by developing customized cell culture media to meet customers' diverse needs.

# **Expand cell therapy PD & Mfg service business**

→ Establish recurring revenue business model, enabling achievement of sustainable growth by granting IP licenses for iPS cell and related technology as well as process development & manufacturing services utilizing **GMP facilities** (i-FACT)."

## **Environmental awareness**

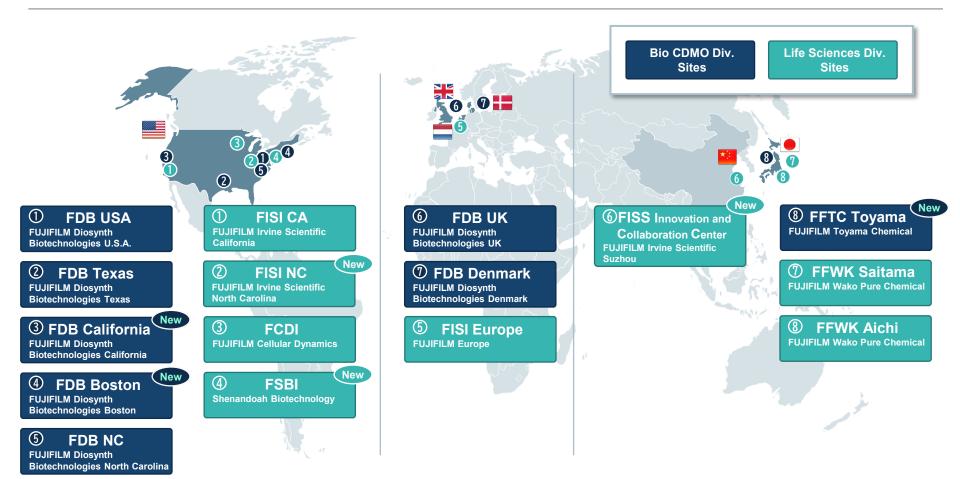
→ Localization of production with 3 sites (US, Japan and Europe) and use renewable energy to reduce environmental footprint.



# Appendix

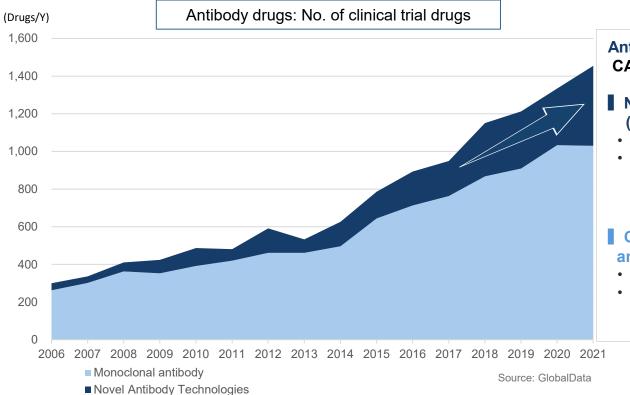
- 1 | Life Sciences Business Group
- 2 | Bio CDMO Division
- 3 | Life Sciences Business Division

## Appendix 1-1 | Life Sciences Business Group: Global Footprint



## **Appendix 2-1 | Global Trend for Antibody Clinical Trials**

As for development, the number drugs for which clinical trials being carried out is also increasing due to next gen antibody drugs such as ADCs and bispecifics



Antibody clinical drug growth rate CAGR (2006-2021): 11.1%

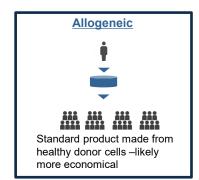
- Next gen antibody technology (ADC, multispecific, FC fusion):
  - CAGR (2006-2021): 17.7%
  - Over 400 drugs entered clinical trial in 2021
- Conventional monoclonal antibodies:
- CAGR (2006-2021): 9.5%
- More than a 1000 per year entered clinical trials in the recent years

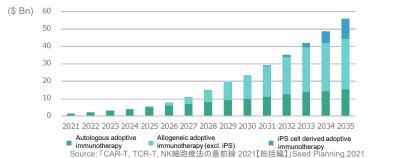
## **Appendix 2-2 | Cell Therapy CDMO Full-Blown Market Entry**

The site is strong when it comes to development and manufacturing of immune cell therapies (e.g. CAR-T cell therapy), especially allogeneic cell therapies, which are expected to see strong growth going forward.

Allogeneic cell therapy is more economical than autologous, and development is picking up speed in anticipation of future market growth

# Autologous Individualized production for each patient using patient's own cell – high production cost





Atara Biotherapeutics is a pioneer within allogeneic immune cell therapy and is expected to receive commercial approval in the EU within 2022

October 14, 2022 ATARA BIO\*

CHMP Recommends Approval of Atara Biotherapeutics' Ebvallo™ (tabelecleucel) for the Treatment of Epstein-Barr Virus-Positive Post-Transplant Lymphoproliferative Disease

Ebvallo<sup>TM</sup> on Track to be the First Ever Allogeneic T-Cell Therapy Approved

Positive Opinion Based on Pivotal Phase 3 ALLELE Study Demonstrating a Favorable Risk-Benefit Profile

European Commission Approval Evanturia Commission

CAR-targeted activity and durability

· Can be modified to express



EBV-driven diseases\*

Potential to minimize toxicity

Robust manufacturing process

[Characteristic of Atara's product]
Give EBV (Epstein-Barr virus) specificity
to allogeneic T cells from a donor.
Developing technology unique to
allogeneic cell therapy such as immune
evasion and develops CAR-T

\*\*Source: Atara Biotherapeutics HP, viewed on Dec 12th, 2022

Fujifilm will push for market expansion of allogeneic cell therapies through continued development and manufacturing for our costumers

## **Appendix 2-3 | Fujifilm's Continuous Manufacturing System**

## Set to begin GMP operation from 2023 and are currently having discussions with several clients

	Features of Fujifilm's Continuous Manufacturing	Batch Production
Quality	<ul> <li>Ability to achieve high purity compared to batch production</li> <li>Enables manufacturing of unstable antibodies that are difficult to produce with batch production.</li> </ul>	Unstable antibodies are hard to manufacture
Production capacity	By adjusting the production time small to large scale lots can be made at the same facility	Different facilities needed for different lot sizes
Facility investment Mfg. cost	<ul> <li>Takes up 25-75% less space compared to batch production</li> <li>Facility investment amount is likewise reduced by 25-75%</li> <li>25% reduction in manufacturing costs(In-house research)</li> </ul>	Need to invest in bio reactors depending on the amount to be manufactured
Technology	<ul> <li>Systems for automatic titer control and continuous monitoring of culture conditions are necessary (development complete)</li> <li>The automatic continuous manufacturing device also needs an automatic control system (development complete)</li> </ul>	-
Culture media	<ul> <li>Media optimized for continuous manufacturing is necessary and Fujifilm has developed a high-quality media for this purpose.</li> </ul>	-

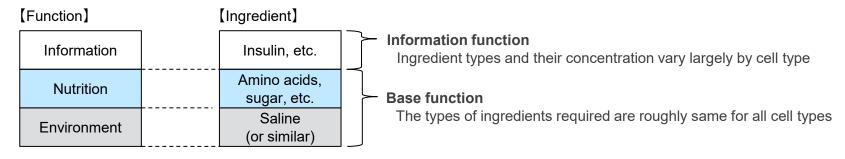
(\*Automatic continuous purification device and monitoring technology can also be used for batch production.)

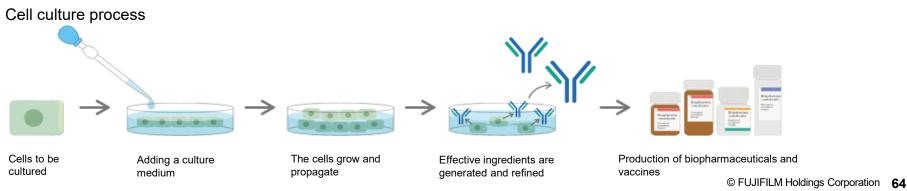
## **Appendix 3-1 | What are Cell Culture Media?**

#### What are Cell culture media?

Cell culture media are important materials, essential for facilitating cell growth and production of end objects generated from cells. It has the function of providing "environment, nutrients and information" to cells.

Just as people have personal preferences, cells and cell products have individual preference in optimum composition of culture media.





## Appendix 3-2 | What are Cytokines?

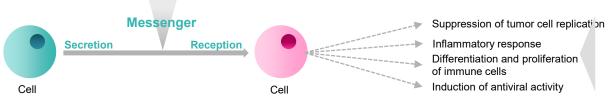
#### **■** Cytokines are:

- A category of proteins produced and secreted by certain cells of the immune system (cells that are present inside white blood cells and protect the body from infection by pathogens) in response to an invasive pathogen.
- Cytokines are the mechanism by which cells "talk" to each other. They activate and control immune system cells, and play an important role in balancing immune function.

#### ■ Types and functions of cytokines

- It is not just immune system cells that produce cytokines. They are also secreted from hundreds of types of cells. Even today, more types of cytokines are being discovered.
- Progress is being made on developing drugs that target cytokines with the hope they will be effective in controlling tumors and other proliferative diseases as well as suppressing rejection when transplants are performed.

	Types (main categories)	Function
1	Interleukins	Mainly secreted by leukocytes, interleukins modulate growth, differentiation, activation, death, etc. of immune cells.
2	Chemokines	Chemokines play a control function guiding leukocytes to sites of inflammation (chemotaxis).
3	Interferons	Interferons are secreted in response to the presence of a virus or tumor cells and suppress viral and tumor cell replication.
4	Growth factors	Growth factors stimulate the proliferation of specific cells other than hemocytes.
5	Hematopoietic factors (colony-stimulating factors)	Hematopoietic factors promote differentiation and proliferation of immune cells and hemocytes (erythrocytes, leukocytes and thrombocytes)
6	Tumor necrosis factors	Tumor necrosis factors induce necrosis and apoptosis in tumor cells. They also involved in inflammatory response.



#### ■ Examples of the use of cytokines

Cytokines are often used as a culture medium additive mainly when culturing cells.

- Stem cell culture: Maintain undifferentiated stem cells and promote differentiation into specific cells
- Field of cell therapy: Used for cell proliferation and to activate t-cells

**Maintenance** 

of immune

**function** 

balance

