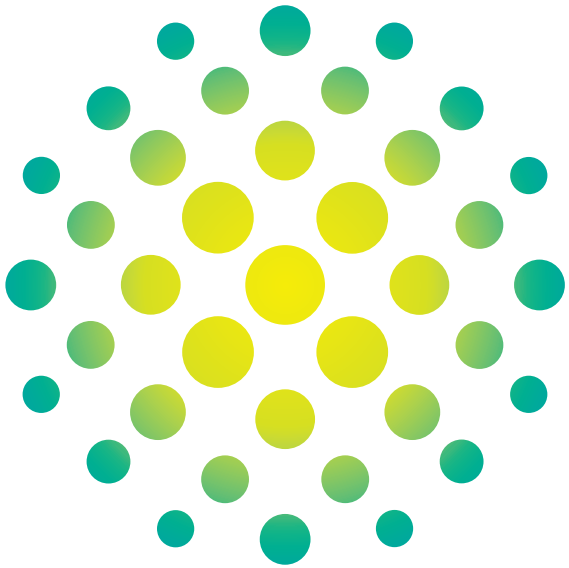


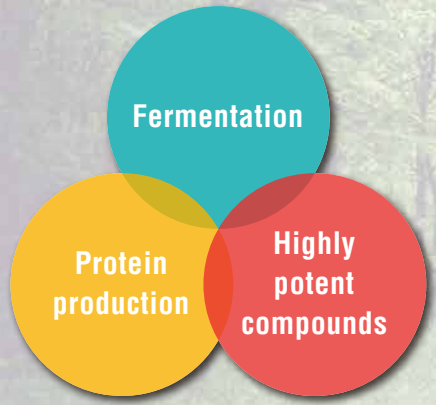
MicroBiopharm Japan

Company Profile

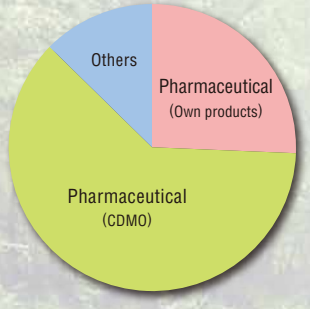
MicroBiopharm Japan (MBJ) specializes in comprehensive microbial technologies and has 80 years of experience.

We utilize microorganisms to support our partners in various stages of research, development, and commercial production.

■Core Technologies



■Product Categories



■Major Markets and Partners

■Corporate Profile

Establishment July 1st, 2011 (Formerly the Pharmaceutical Chemical Division of Mercian Corp.)

Total employees Business 344 (PhD: 31, Master's: 71; as of April 1st, 2022)

- CDMO services by applying the natural power of microorganisms
- Pharmaceuticals and chemicals provision

History/Our Sites

History

1941 Started the production of Acetone and Butanol by fermentation at Showa Nosan Kako Co., Ltd. (currently Mercian Corporation) Yatsushiro plant (Business started)

1981 Started the production of the injectable Aclarubicin

1988 Started the production of Daunorubicin
Started the production of injectable Pirarubicin

1989 Started the production of Doxorubicin

1994 Started the production of Calcitriol

2007 Started the production of Epirubicin

2010 Started the production of 25-Hydroxyvitamin D_3

2011 MBJ was founded and we started the business by the succession of the Pharmaceuticals & Chemicals Division of Mercian Corporation.

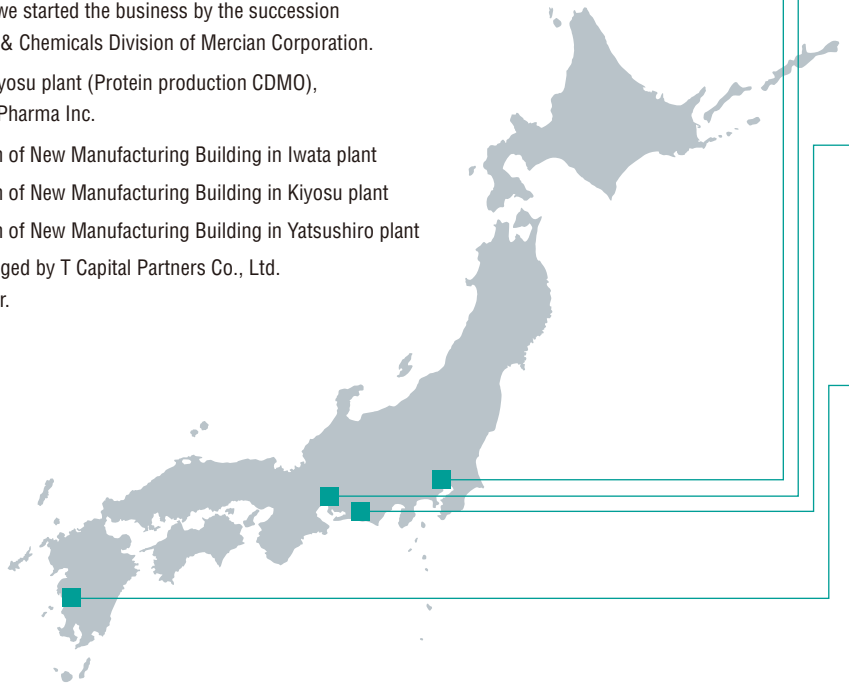
2016 Operation start up at Kiyosu plant (Protein production CDMO), acquired from Astellas Pharma Inc.

2018 Completed construction of New Manufacturing Building in Iwata plant

2019 Completed construction of New Manufacturing Building in Kiyosu plant

2020 Completed construction of New Manufacturing Building in Yatsushiro plant

2021 Investment funds managed by T Capital Partners Co., Ltd. became our shareholder.



Sites and Facilities

Head Office (Tokyo)

Kiyosu Plant

Plant
・Protein production

R & D
・Basic research
・Fermentation and synthesis

Audit experience
・Local authority (PMDA)

Iwata Plant

Plant
・Mid scale fermentation (Up to 30 kL)

R & D
・Pilot plant
・Fermentation and synthesis

Audit experience
・Local authority / FDA etc.

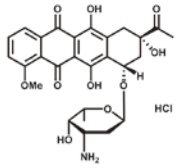
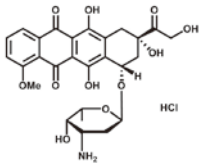
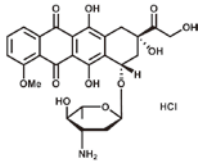
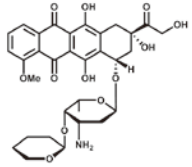
Yatsushiro Plant

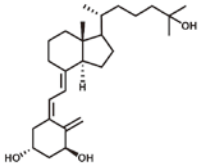
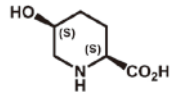
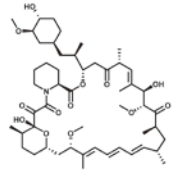
Plant
・Large scale fermentation (Up to 100 kL)
・Chemical synthesis and purification facility

Audit experience
・Local authority / FDA etc.

Our Products/Service

Commercial

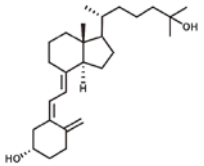
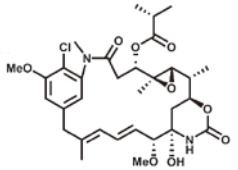
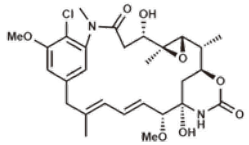
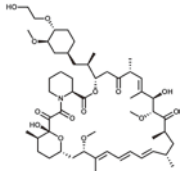
Category	Compound name	Specification	Structure
Anti cancer drug Anthracycline	**Daunorubicin Hydrochloride**	In-house	
	Doxorubicin Hydrochloride	USP, JP, EP	
	Epirubicin Hydrochloride	JP, EP	
	Pirarubicin*	JP	

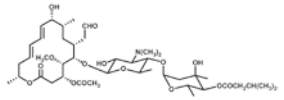
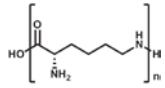
Category	Compound name	Specification	Structure
Osteoporosis	**Calcitriol**	USP, JP, In-house	
Rare Amino acid	***cis*-5-Hydroxy-L-Pipecolinic acid**	In-house	
Immuno suppressant	**Rapamycin (Sirolimus) Crude**	In-house	

* API production and formulation

Fermentation products
Fermentation + Synthesis products
Bioconversion products

Under Development & CDMO

Category	Compound name	Specification	Structure
Under Development	**25-Hydroxy-Vitamin D_3**	Pharmaceutical	
	Ansamitocin P-3	Payload for ADC etc.	
	Maytansinol	Payload for ADC etc.	
	Everolimus	Pharmaceutical	

Category	Compound name	Specification	Structure
CDMO	**Josamycin**	Antibiotics	
	E-poly-L-Lysine	Food additive	

* There are several other CDMO projects

* Under development of ADC site-specific conjugation technology

Service

Item	Overview
Plasmid	• Established plasmid manufacturing processes using recombinant microorganisms • Expanding single-use fermentation and purification facilities, and starting operation of workshop for manufacturing and development in 2022

Fermentation products
Fermentation + Synthesis products
Bioconversion products

Our Collaboration Scheme

MBJ provides collaboration services at each stage.

1 Drug Discovery Support

- Explore lead compounds
- Diversify compound properties
- Improve compound properties

2 Process Development

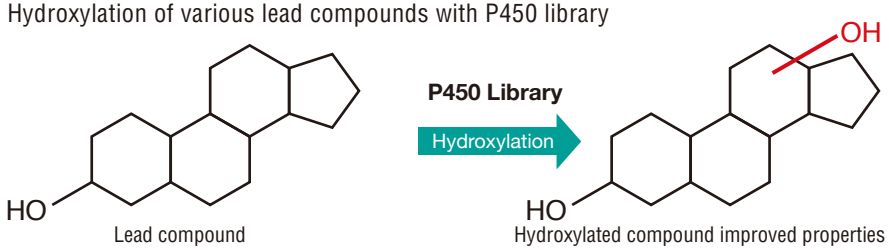
- Optimize processes
- Streamline processes
- Maximize productivity

3 Commercial Manufacturing

- GMP compliant
- Multi-item manufacturing
- Fermentation + chemical synthesis

1 Drug Discovery Support

Hydroxylation of various lead compounds with P450 library

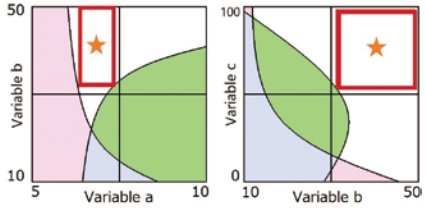


Production of new derivatives difficult by chemical synthesis

Improvement of physical properties

2 Process Optimization・Process Development

2-1. Process optimization and robustness improvement based on QbD (Quality by Design)



Assemble design space by multivariate analysis

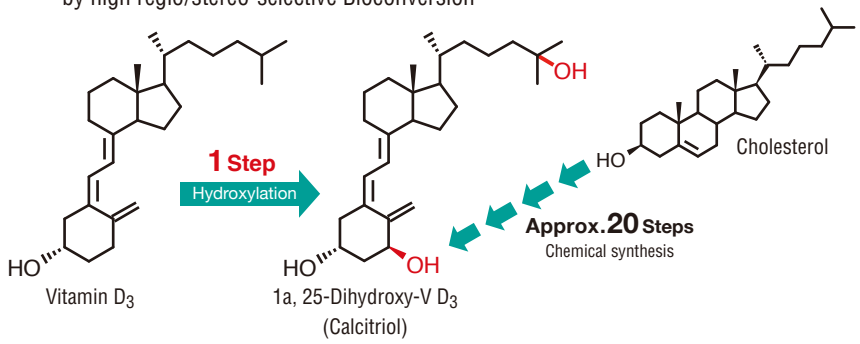
Process development for commercial use

Development of recombinant protein manufacturing processes

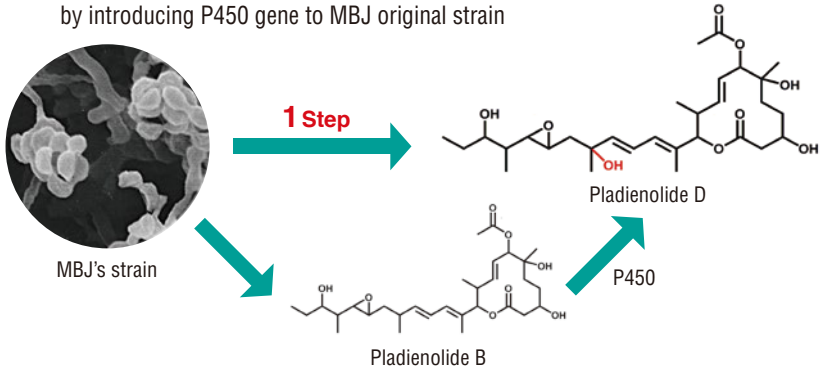
Scalable processes for plasmid DNA manufacturing

Efficient production of compounds which are difficult to synthesis chemically

2-2. Optimization of manufacturing processes by high regio/stereo-selective Bioconversion



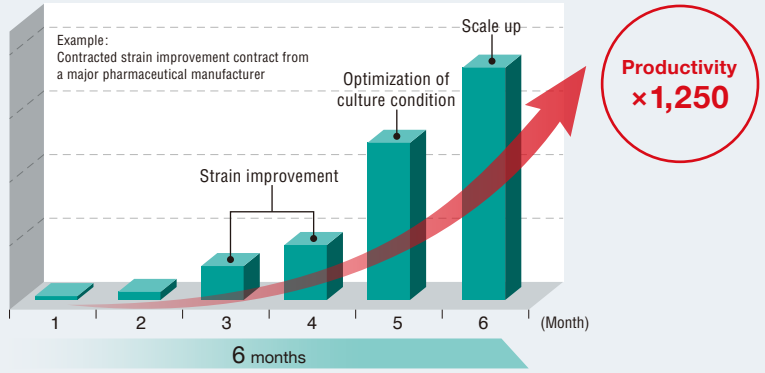
2-3. Development of one step bioconversion for obtaining hydroxylated compound by introducing P450 gene to MBJ original strain



3 Commercial Manufacturing

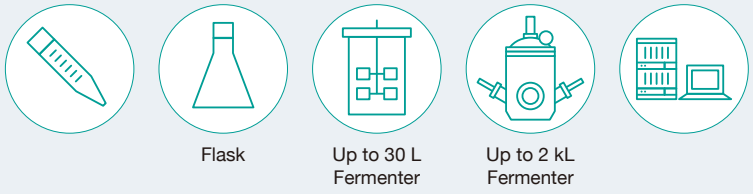
Low molecular compound

CDMO for Low Molecular Compound using Microorganisms from Lab to Commercial



Biopharm-aceutical

CDMO for Biopharmaceutical etc. using Microorganisms from Lab to Commercial



Cell Banking and Storage → **Manufacturing** Scale up and Manufacturing → **Quality Control**

- Cell bank preparation and storage (WCB/MCB)
- GILSP compliance
- Sample and clinical batch production
- GMP manufacturing
- Quality & cost improvement by improving the existing process
- Manufacturing process design for commercial scale

Commercial production under optimized conditions

There are multiple commercial and development projects

Low molecular compound
(Fermentation / Bioconversion + Synthesis),
protein, plasmid and peptide etc.

Equipment List

Research & Development

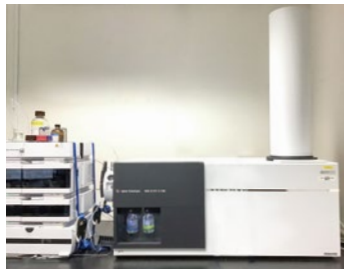
Basic research/ Pilot production

Equipment list of R&D
(Investigational drug GMP/GILSP)

	R&D in Kiyosu	R&D in Iwata
For	Basic research ・Explore microorganism ・Seed culture ・Develop manufacturing process	Optimization ・Pilot manufacturing ・Establishment of product specification
Fermentation tank	Lab testing Up to 30 L	From lab testing to pilot production Up to 5 kL
Equipment	Centrifuge TFF membrane Homogenizer Up to 45 L column Isolator (0.1 μg/m^3) Freeze dryer Droplet generator Cell sorter	Centrifuge Filter press TFF membrane Up to 1,000 L column Thin film evaporator Reactors







Plants

Manufacturing of low molecular compound

Fermentation & Bioconversion (GMP/GILSP)



	Iwata Plant	Yatsushiro Plant
For	Mid scale fermentation (Pilot scale production, manufacturing small scale high value-added products)	Large scale fermentation (Synthesis, purification, bioconversion of highly potent compounds)
Fermentation tank	Up to 30 kL	Up to 100 kL
Equipment	Filter press TFF membrane Reactors Isolator (handle highly potent) Balance enclosure	TFF membrane Up to 40 kL column Thin film evaporator Spray dryer Reactors Shelf dryer Handle highly potent (0.2 μg/m^3)

Manufacturing of biopharmaceutical

Protein, Peptide & Plasmid etc. (GMP/GILSP)

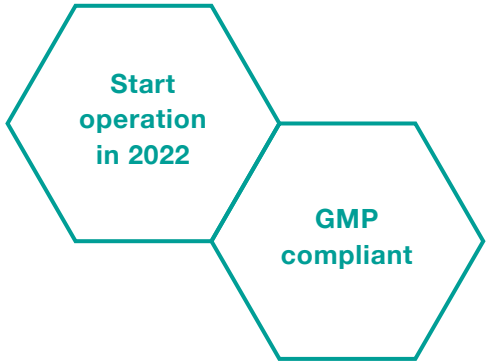


	Kiyosu Plant
For	Production of recombinant protein API, intermediate and peptide (Enzyme, hormone, cytokine, small molecule antibody etc.)
Fermentation tank	Stainless up to 2 kL
Equipment	Centrifuge TFF membrane Homogenizer Up to 45 L column Freeze dryer

Bio Pilot at Kiyosu

- **Workshop for manufacturing and development of plasmid DNA using recombinant microorganisms**
- **GMP/Non-GMP**

	Bio Pilot
Objective	Plasmid DNA for gene therapy and API
Main equipment	•Single-use fermentation tank (300 L) •Single-use chromatography •TFF membrane



Containment Workshops at Yatsushiro

- **40 + years of experience in the production of highly potent APIs**
- **Inspected by the FDA**
- **Capable of handling highly potent compounds (Reactors up to 200 L/Category 4, 5)**

Category	4 5 (OEL 0.1 μg/m^3)
Cleanness (USA Fed.Std.209E)	100,000
Main equipment	•Reactor: 200 L (GL) •Crystallization tank: up to 320 L (SUS) •Purification column •Filter, Concentrator (EVAPOR), Dryer (Shelf type and Hastelloy filter type)

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