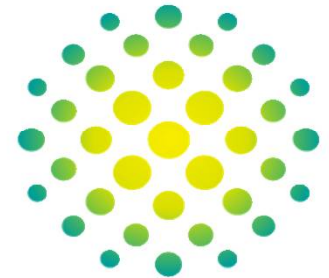


MicroBiopharm Japan Co., Ltd. (MBJ)



MicroBiopharm Japan

WHO WE ARE

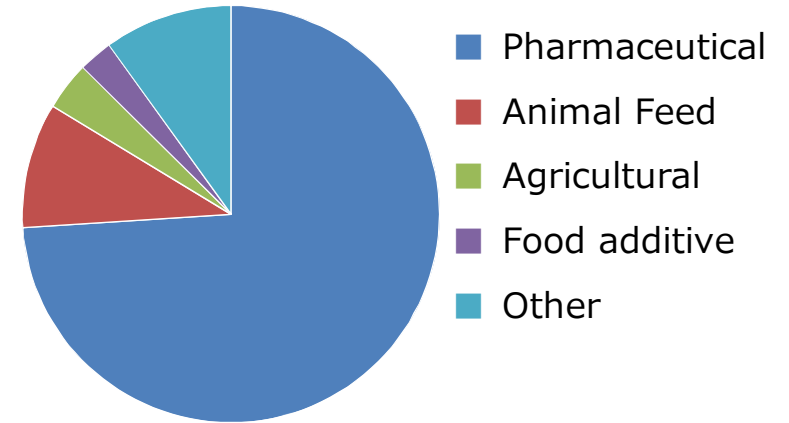
MicroBiopharm Japan (MBJ)

is a specialist in fermentation with 70 years of experience.
 We utilize microorganisms to support our partners in various stages of research, development and commercial production.

Core technologies



Product category



Major Markets and Partners



Founded	July 1st, 2011 (Former; Pharmaceutical Chemical Division of Mercian Corp.)
Total Employee	383 (PhD 37) as is 1 April 2021
Business	- CDMO services by microbial fermentation etc. - Pharmaceuticals and Chemicals provision
Net Sales	84 million USD (as is 31st Mar, 2019)

Company History

1941	Start of business (as Mercian)
1981	Launch of Aclarubicin Injection
1988	Start the production of Daunorubicin
	Launch of Pirarubicin Injection
1989	Start the production of Doxorubicin
1990	Established Shenzhen Main Luck Pharmacuetical Inc.
1994	Start the production of Calcitriol
2007	Start the production of Epirubicin
2010	25-Hydroxyvitamin D3
2011	MBJ established by the succession of Pharmaceuticals & Chemicals division of Mercian Corp.
2016	Acquisition of Kiyosu Plant from Astellas Protein production CMO
2018	Completion of new building at Iwata site
2019	Completion of new building at Kiyosu site
2020	Completion of new building at Yatsushiro site



Aclarubicin Injection



Pirarubicin Injection



Main Luck Pharmaceutical Inc.



MicroBiopharm Japan



Our Sites



Yatsushiro site

Factory

- Large scale fermentation
~100kL
- Chemical synthesis and purification facility
- *Highly potent compound
(OEL > 0.2µg/m³)



Iwata site

Factory

- Mid scale fermentation
~30kL

R & D dept.

- Pilot plant
Fermentation, Synthesis



Kiyosu site

Factory

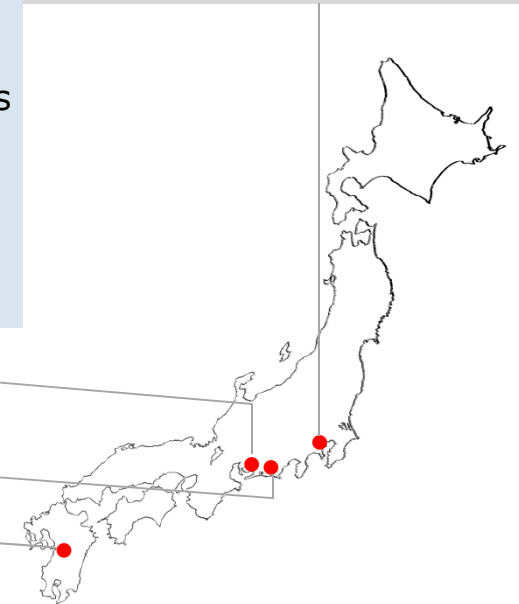
- Protein production with recombinant microorganisms

R & D dept.

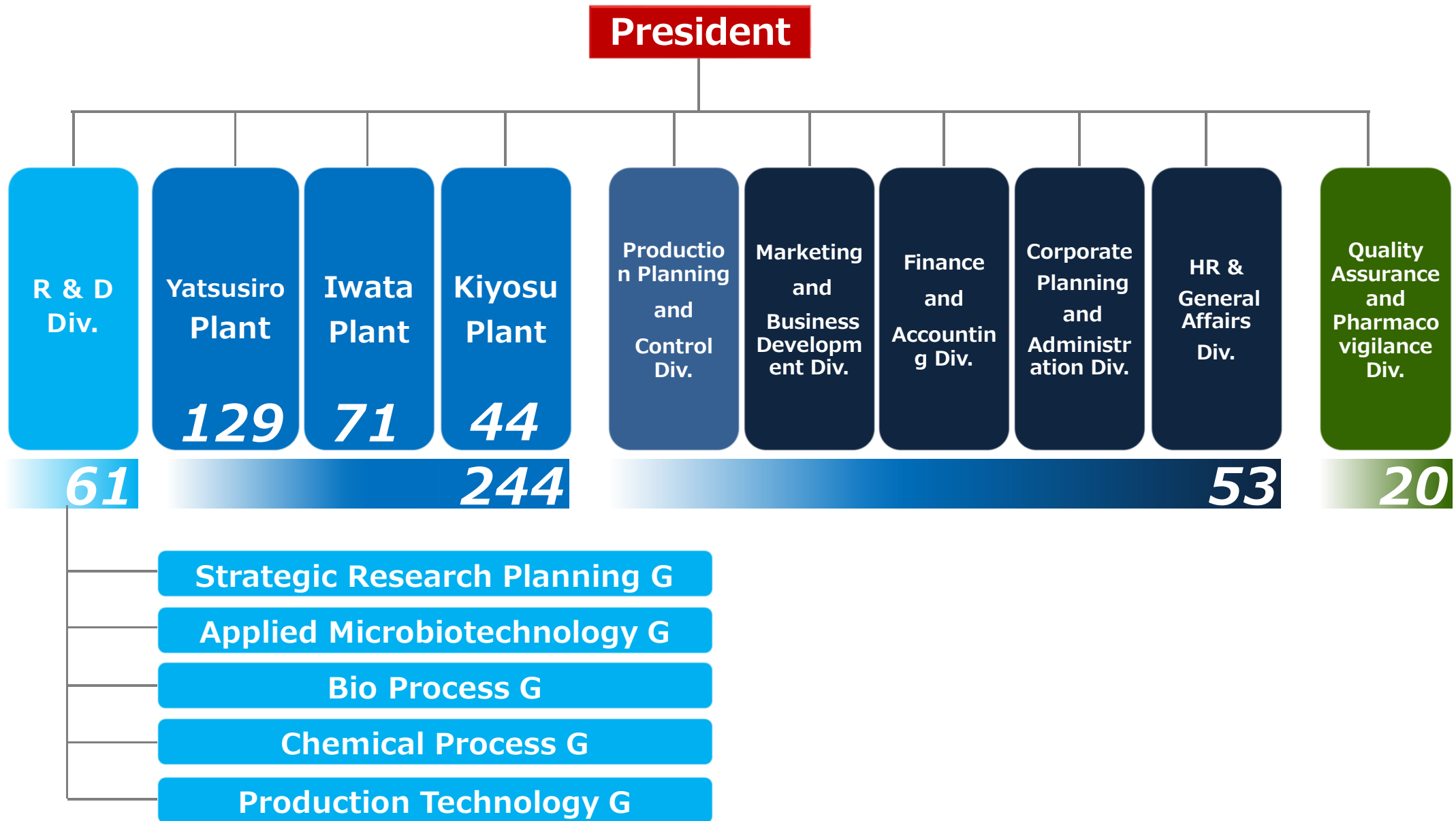
- Basic research
Fermentation, Synthesis



Headquarter



Organization



Inspection history

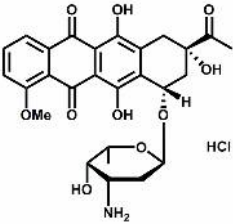
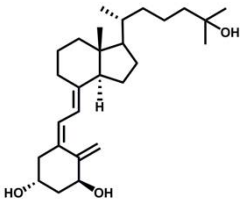
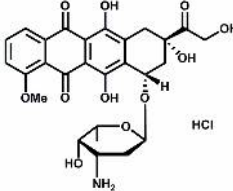
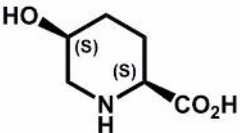
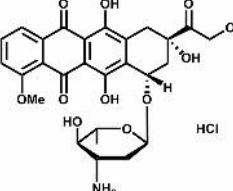
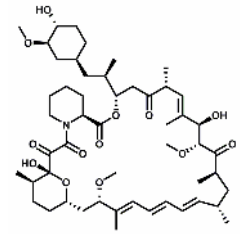
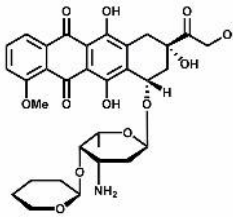
As a Pharmaceutical Manufacturer, we have received Audit by Domestic and Overseas authorities.



Site	Domestic	Overseas
Iwata Site	Local Authority (Shizuoka Prefecture Government office)	FDA etc
Yatsushiro Site	Local Authority (Kumamoto Prefecture Government office)	FDA etc
Kiyosu Site	Local Authority (PMDA)	—

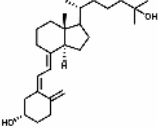
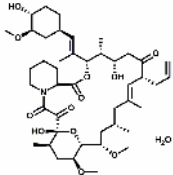
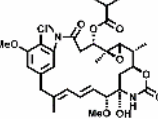
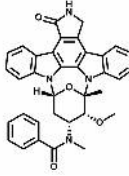
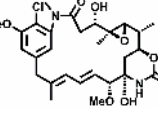
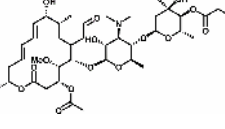
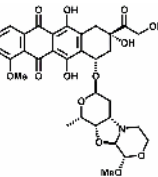
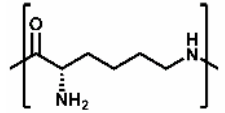
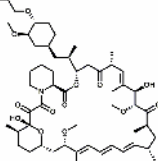
* In addition to the above experience, we receive more than 10 customer audits per year in average.

Our Product List (Commercial)

Category		Name	Spec	Structure	Category		Name	Spec	Structure
Anti cancer drug Anthra cycline	■	Daunorubicin Hydrochloride	In-house		Osteoporosis	■	Calcitriol	USP, JP, In-house	
	■	Doxorubicin Hydrochloride	USP, JP, EP		Rare Amino acid	■	<i>cis-5-OH-L-Pipecolic acid</i>	In-house	
	■	Epirubicin Hydrochloride	USP, JP, EP		Immuno suppressant	■	Rapamycin (Sirolimus) Crude	In-house	
	■	Pirarubicin *	JP						

- ; Fermentation Products
 - ; Fermentation + Synthesis products
 - ; Bio-conversion Products
- * API production and formulation

Our Product List (Under Development & CMO)

Category	Name	Application	Structure	Category	Name	Spec	Structure
Under Development	■ 25-OH-VitaminD3	Pharmaceutical		Under Development	■ Tacrolimus	Pharmaceutical	
	■ Ansamitocin P-3	Intermediate			■ Midostaurin	Pharmaceutical	
	■ Maytansinol	Intermediate		CMO	■ Josamycin	Antibiotics	
	■ PNU-159682	Payload for ADC			■ E-poly-L-Lysine	Food Additive	
	■ Everolimus	Pharmaceutical					

- ; Fermentation Products
 - ; Fermentation + Synthesis products
 - ; Bio-conversion Products
- * API production and formulation

Collaboration scheme with MBJ

MBJ provides collaboration service each stage.

1. Drug Discovery Support

- Explorer of lead compounds
- Diversity properties of compound
- Improve property of compound



2. Process Development

- Optimize Process
- Simplify Process
- Maximize productivity



3. Commercial Manufacturing

- GMP compliant
- Multi-item Manufacturing
- Variation of Facility



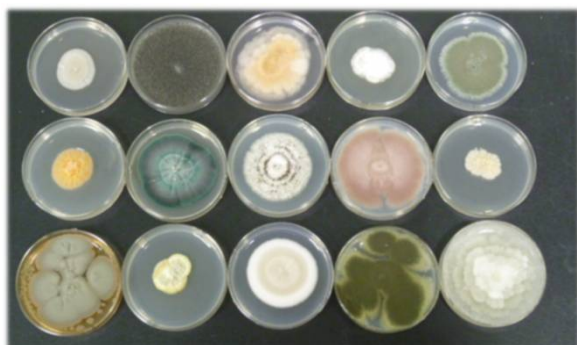
1. Drug Discovery Support



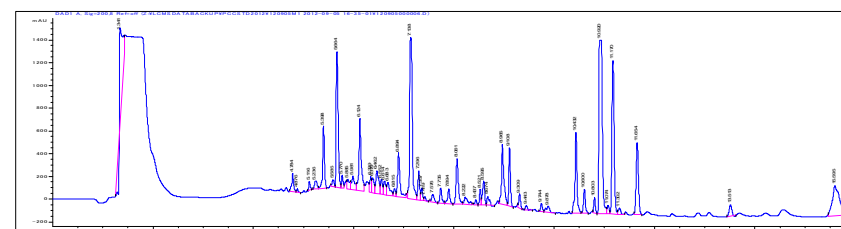
Extractions from microbial culture broth

MBJ's Microbe resources

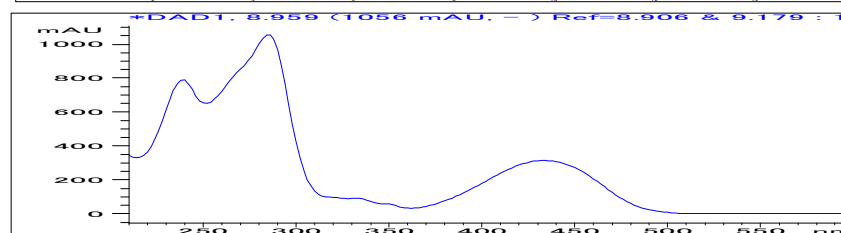
Strains	Actinomycetes	25,000
	Fungi	25,000
Extracts		70,000
Compounds		Contact us



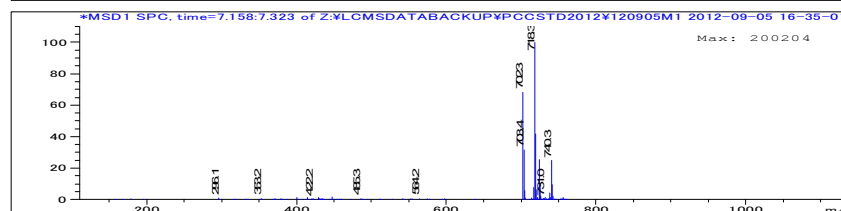
- ★ Extractions including large variety of compounds
- ★ Extractions including known compounds
- ★ Series of compounds



HPLC



UV

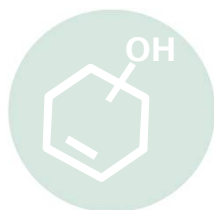


MS

Other information

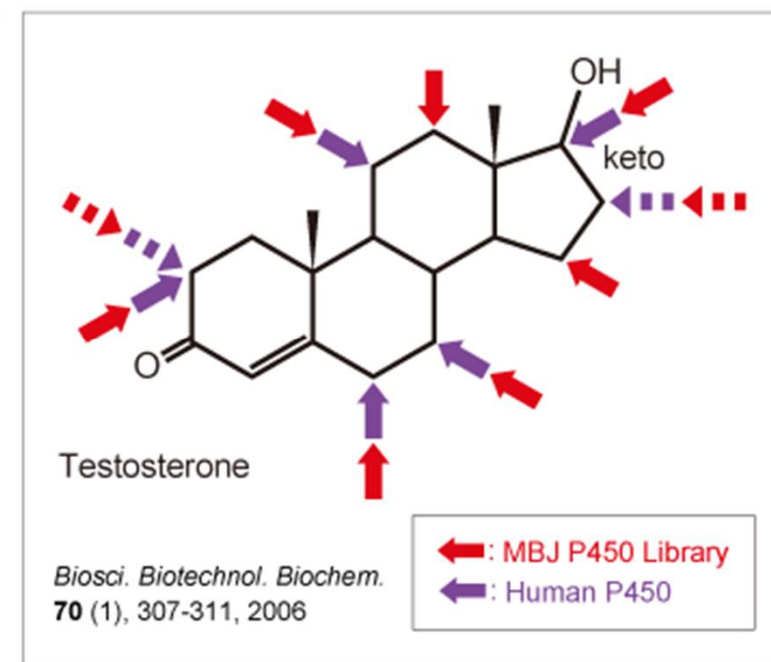
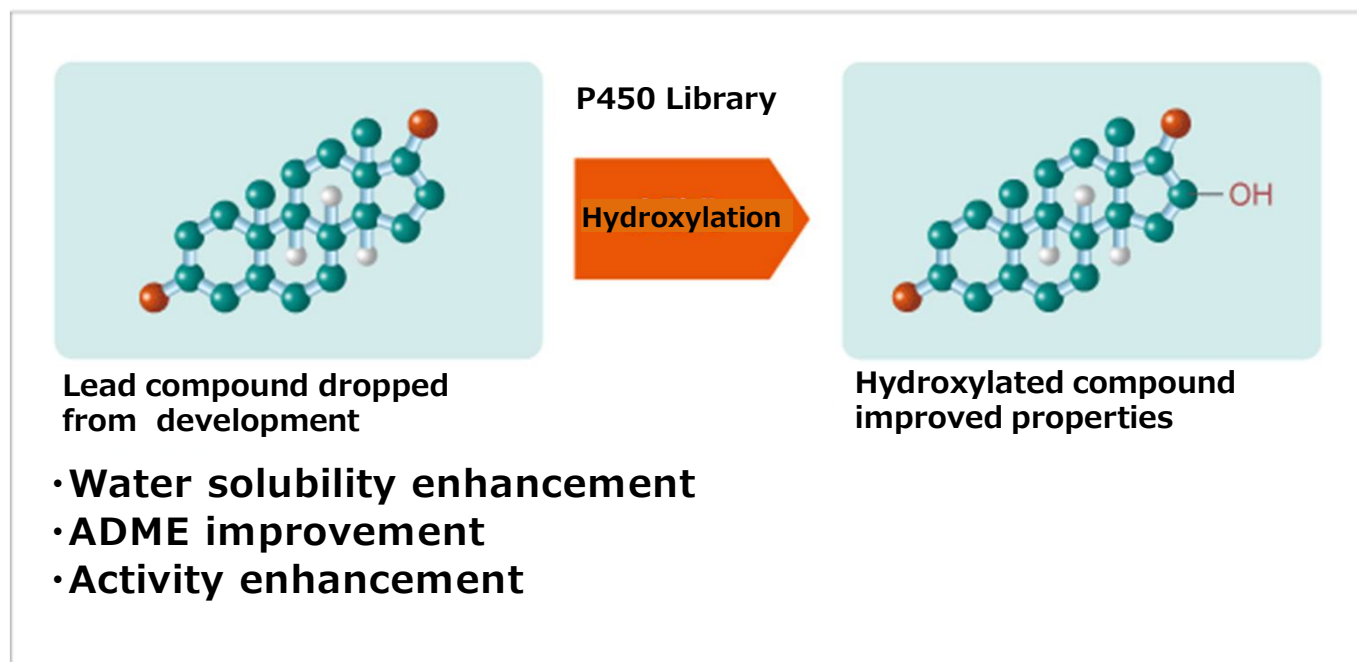
- Sequence info. of 16s rDNA
- Taxonomy info.
- Chemical Info.

1. Drug Discovery Support



Diversify or improve properties of compound

MBJ has novel P450 libraries as tool to add hydroxyl group(s) to compound regioselectively and stereoselectively.

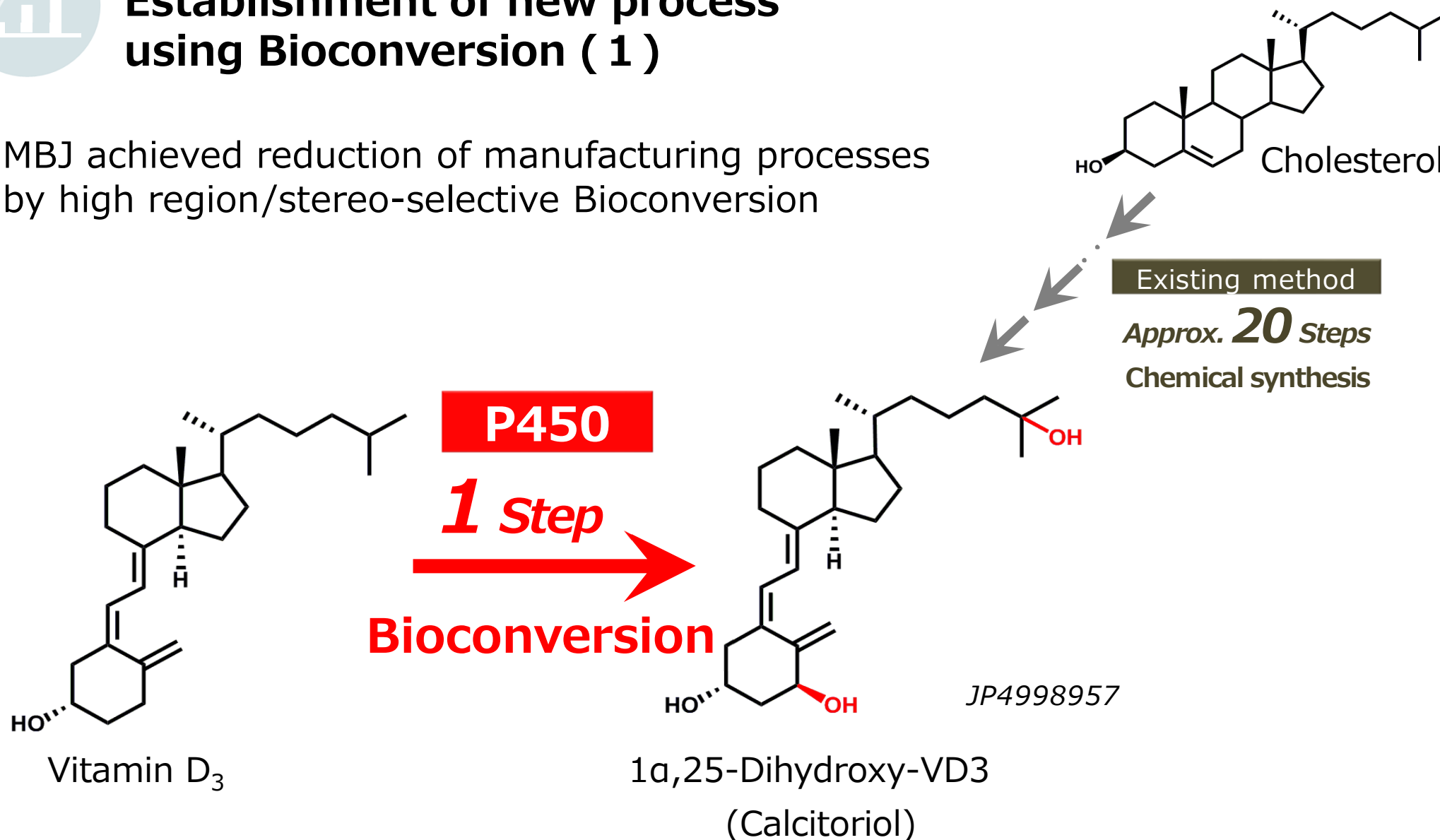


2. Process Development



Establishment of new process using Bioconversion (1)

MBJ achieved reduction of manufacturing processes by high region/stereo-selective Bioconversion

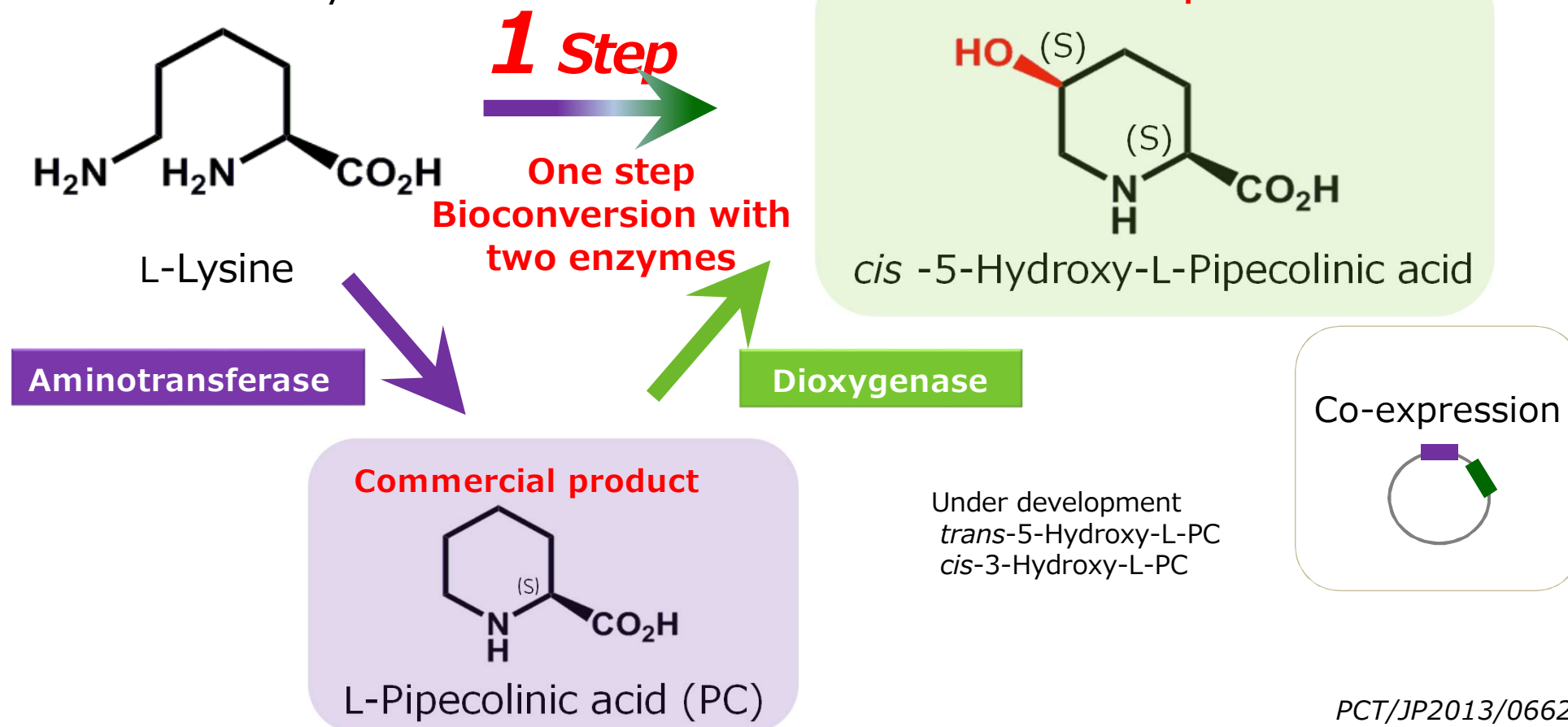


2. Process Development



Establishment of new process using Bioconversion (2)

We achieved to make one step bioconversion for obtaining compound with functional group by express of two enzymes at same time.

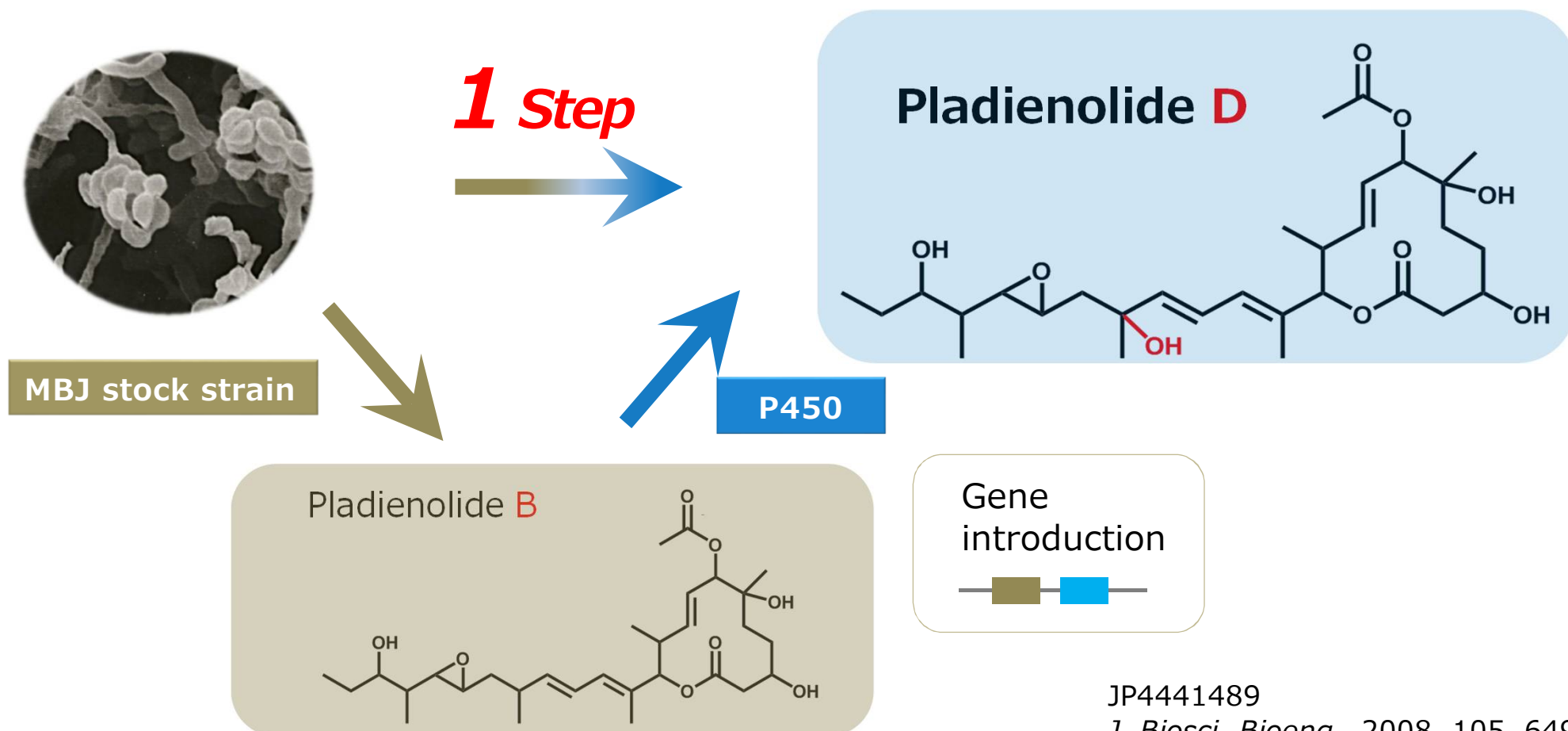


2. Process Development



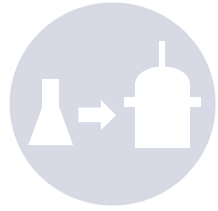
Fermentation & Bioconversion (Collaboration case)

We achieved to make one step bioconversion for obtaining hydroxylated compound by gene introduction of P450 to MBJ original strain.



JP4441489
J. Biosci. Bioeng., 2008, 105, 649

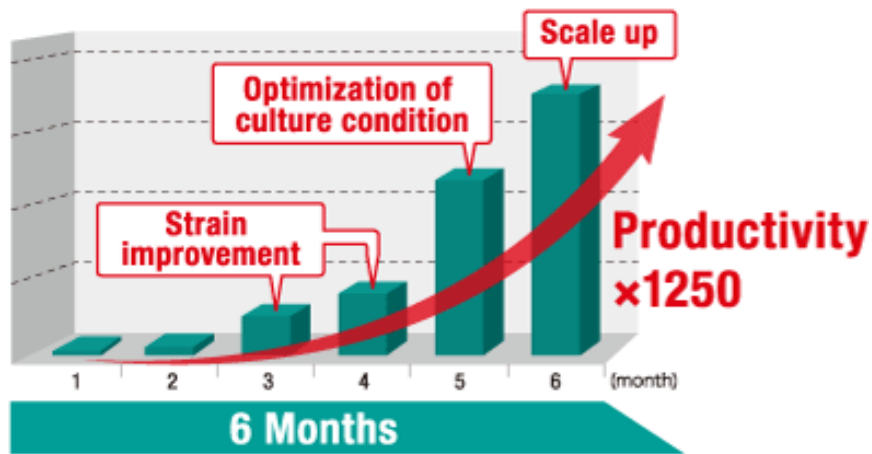
2. Process Development



Scale-up Process improvement

We met customers' needs of scale-up from lab to commercial with our expertise. We will continue working on reducing manufacturing cost for our clients by process optimization of fermentation and purification step.

MBJ can maximize potency of strain and improve process of manufacturing.



Our Technology

Strain Improvement

- Introduction of mutation
- Genetic Recombination

Process Improvement

- Optimization of culture condition
- Establishment of efficient purification process

2. Process Development ~ Labo to Pilot ~



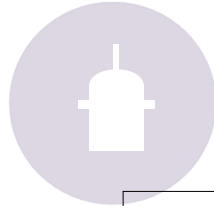
Equipment list of R&D (investigational drug GMP ·GILSP)

	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 3L, 30L	Lab Testing~Pilot Production 3L, 30L, 200L, 2kL, 5kL
Equipment	Centrifuge TFF membrane Homogenizer 4~45L Column Isolator (0.1 μ g/m ³) Freeze dryer	Centrifuge Filter press TFF membrane (MF, UF, NF, RO) 5~1000L Colomn Thin film evaporator Reactors



3. Commercial Production

~ Fermentation & Bioconversion ~



List of Equipment (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	30kL	1.8kL, 75kL, 100kL
Equipment	Filter press TFF membrane (MF,UF, NF) Reactors Spray dryer	TFF membrane(MF, UF, NF, RO) 10-40kL Column Thin film evaporator Spray dryer Reactors Shelf dryer Handle highly potent (0.2µg/m ³)



3. Commercial Production

~ Protein & peptides ~



List of Equipment (GMP·GILSP)

	Kiyosu Plant
For	Recombinant Protein/production of intermediate·peptide (production of enzyme·hormone·cytokine·small molecule antibody etc.)
Fermentation Tank	3、30、90、300、3000L
Equipment	Centrifuge TFF membrane (MF、UF) Homogenizer Cyanide equipment 4~45L Column Freeze dryer



New Containment Workshops

- **Handling highly potent compounds**
 - Reactor 200L
 - Up to **Category 5 (OEL 0.2 μ g/m³)**
- Four Workshops & one Free space
- 30+ years experience in production of highly potent APIs
- Inspected by FDA many times



Yatsushiro site

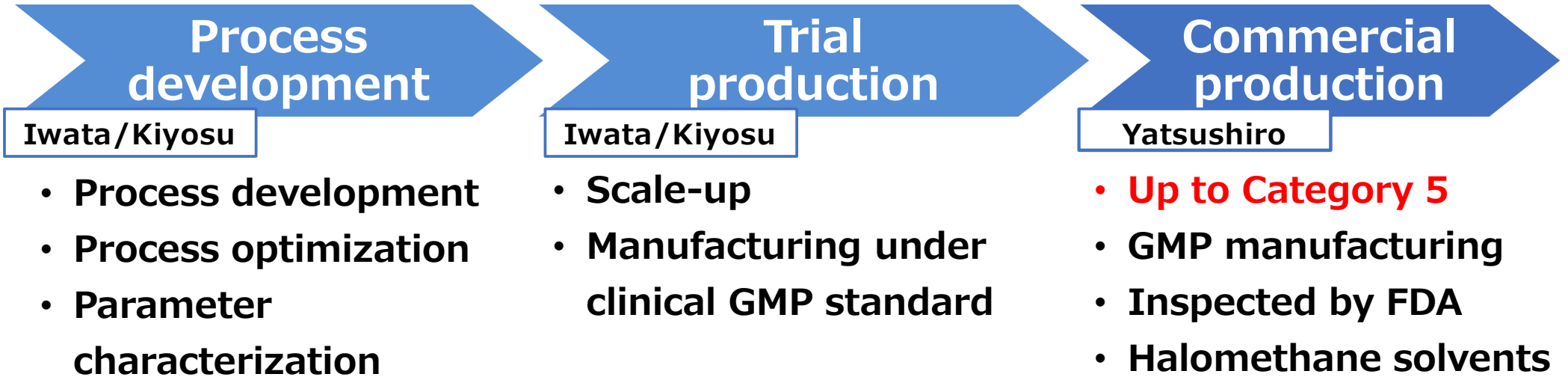


Workshops & Equipment

Facility	Category	Cleanness (Class)	Area (Sqm)	Main equipment		Available from
New Facility	5 OEL 0.2 µg/m ³	100,000	13,200	Line A	<ul style="list-style-type: none"> Reactor(GL;900L, 2.8kL, SUS; 600L,4.4kL) Purification column (1,500L, 3,000L) Dryer(Hastelloy filter type), Isolator 	2022
				Line B	<ul style="list-style-type: none"> Reactor(GL;220L, 920L, 1.23kL, SUS ; 55L, 200L, 500L, 1.56kL, 1.9kL) Concentrator, Purification column (75L) Dryer(Hastelloy, SUS filter type), Isolator 	
				Line C	<ul style="list-style-type: none"> Reactor(SUS; 85L, 320L, 650L, 1.7kL) Concentrator, Purification column (80L,120L) Dryer(SUS filter type, Shelf type), Isolator 	
	Free Space	TBD	1,300	NA		2021
Workshop 1	4 (Under renovation)	100,000	3,300	<ul style="list-style-type: none"> Reactor (GL ; 300L, SUS ; 75L, 150L, 900L) Purification column (150, 270L) Filter, Concentrator, Reflux, Dryer, Isolator 		2025
Workshop 2	5 (Under renovation)	100,000	2,050	<ul style="list-style-type: none"> Reactor (SUS ; 5L, Teflon;7L) Photoreactor, Preparative HPLC Concentrator, Isolator 		2025
Workshop 3	4	100,000	4,500	<ul style="list-style-type: none"> Reactor (GL ; 300× 2、1kL, SUS ; 2.2kL×2) Filter, Concentrator, Dryer(Shelf type) 		2022

Collaboration Scheme with MBJ

MBJ provides collaboration service at each stage;



Scale : up to 100g/batch



Thank you !