

# Life Science Business Briefing



**AGC Inc.**

**November 29, 2021**

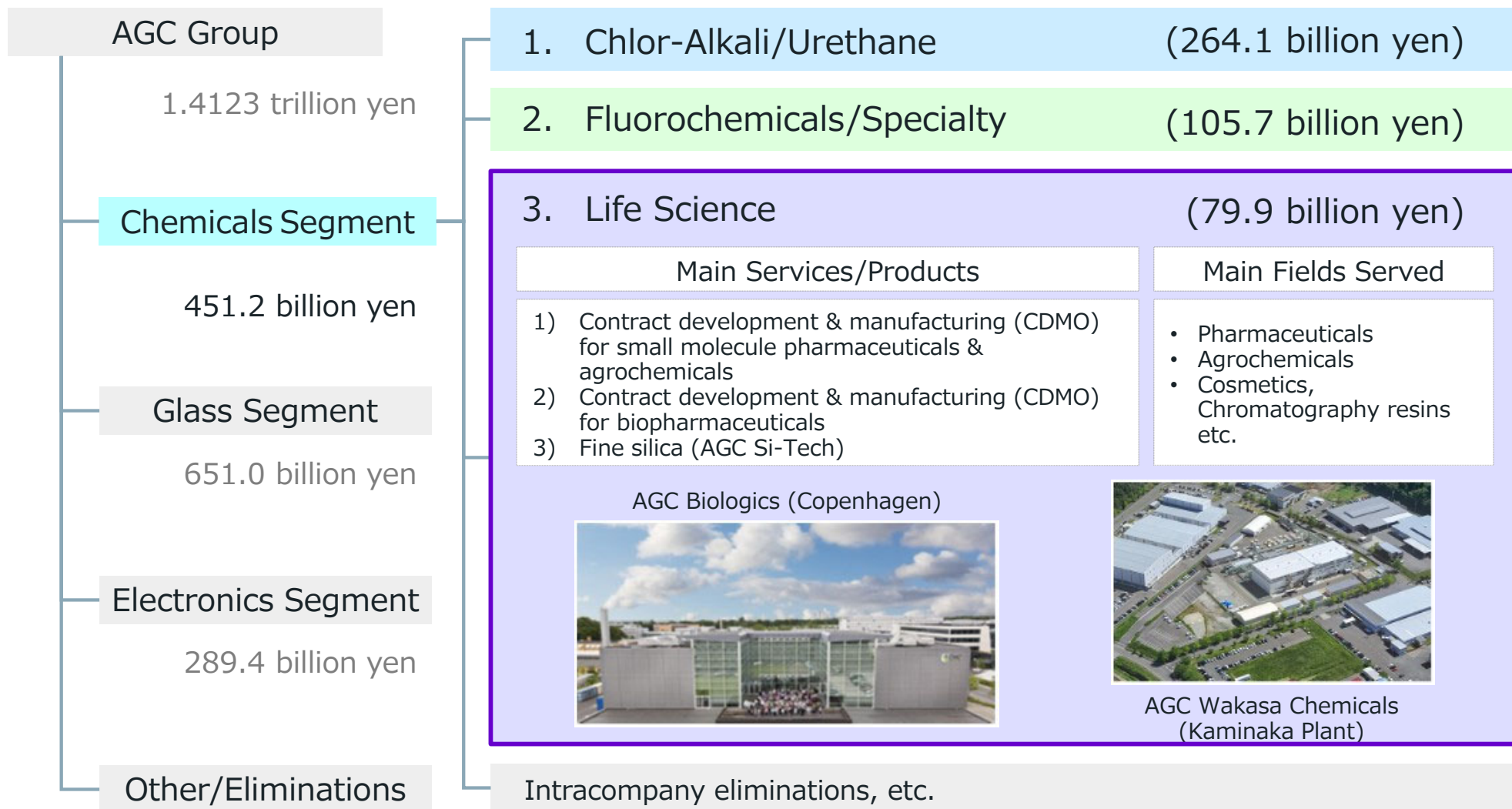
Your Dreams, Our Challenge

- **AGC's Life Science Business**
- **Industry Trends**
- **Our Strengths**
- **Our Growth**

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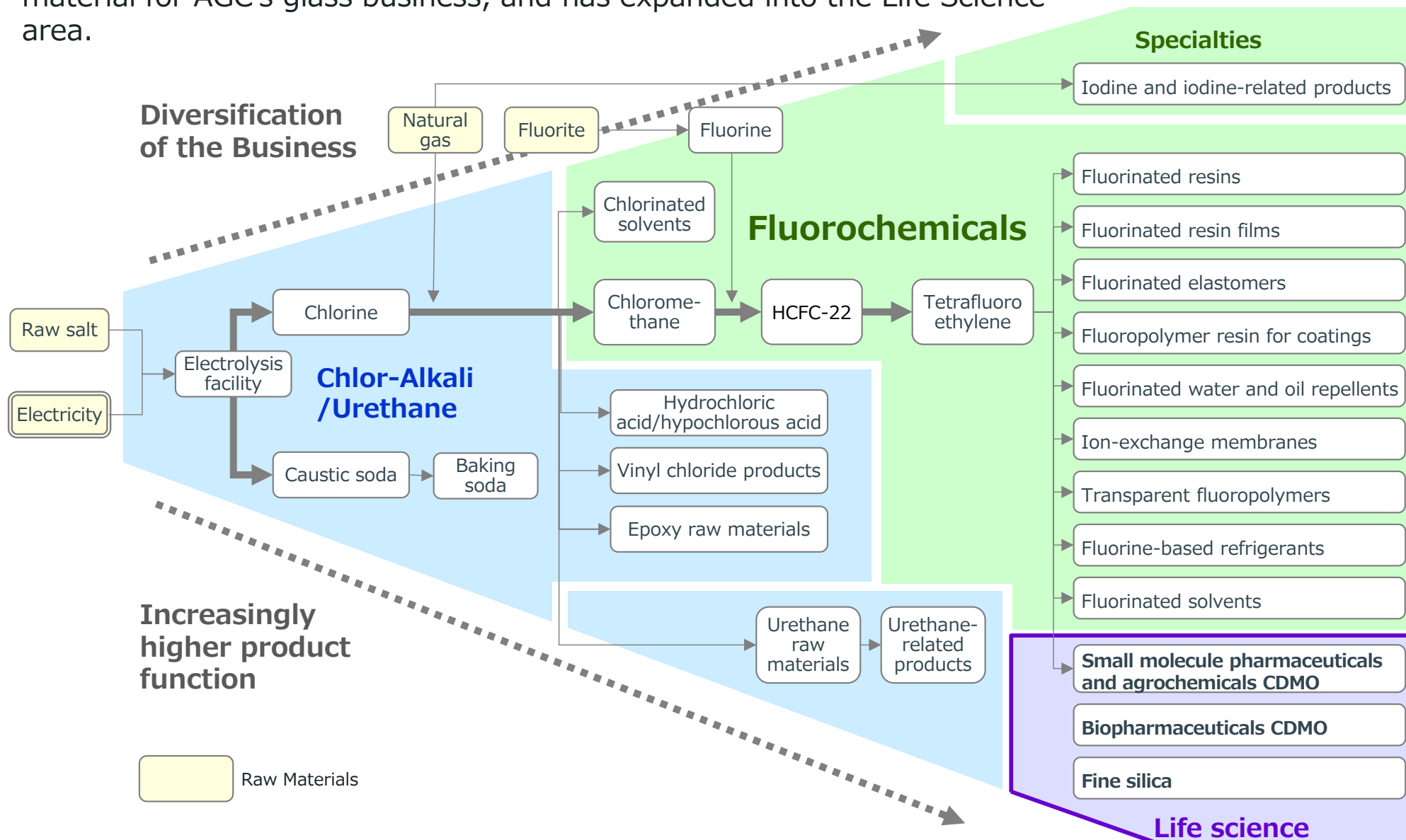
# Life Science as Part of the Chemicals Segment

(sales figures for the fiscal year ended December 2020)



# The Chemicals Business Domain – Historical Broadening - From Production of Glass Raw Materials to Life Science

- Our extensive chemical chain originated from producing soda ash, a raw material for AGC's glass business, and has expanded into the Life Science area.



# History of AGC's Life Science Business

➤ In 1973, the Life Science Team was launched as a research unit, and commercial operations begun in the 80s.

**1973** Launched The Life Science Team to investigate the applicability of AGC's fluorination technology to pharmaceutical & agrochemical production

## 1. Events related to contract development/manufacturing of **small molecule pharmaceuticals/agrochemicals**

**1985** Started contract manufacture/supply of fluorinated intermediates for use in antibiotics

**1997** Established AGC Wakasa Fine Chemicals.  
(currently AGC Wakasa Chemicals)

**2003** Established a GMP-compliant, multi-purpose facility for manufacturing clinical stage drug substances & intermediates at Chiba Plant

**2008** Obtained marketing approval for tafluprost, an anti-glaucoma drug substance

**2013** Established a new plant, Kaminaka Plant, in the Wakasa Techno-Valley (AGC Wakasa Chemicals)

**2019 Acquired** drug substance manufacturing plant in Spain (currently AGC Pharma Chemicals Europe)

**2019** Increased production capacity 10-fold at Chiba Plant

**2020** Decided to expand facilities at AGC Pharma Chemicals Europe

**2021** Decided to expand facilities at Kaminaka Plant of AGC Wakasa Chemicals

## 2. Events related to contract development/manufacturing of **biopharmaceuticals**

**1984** Formed the Biochemical Group focused on biopharmaceutical development

**2000** Formally launched the protein contract manufacturing business

**2008** Established a new facility at Chiba Plant with 10-fold higher capacity

**2016 Acquired** Biomeva, a major German biopharmaceutical contract manufacturing organization (currently AGC Biologics (Heidelberg))

**2017 Acquired** CMC Biologics, with several manufacturing bases in Europe and US (currently AGC Biologics)

**2020** Established new mammalian cell facility at Chiba Plant

**2020 Acquired** AstraZeneca's U.S. bio-pharma plant

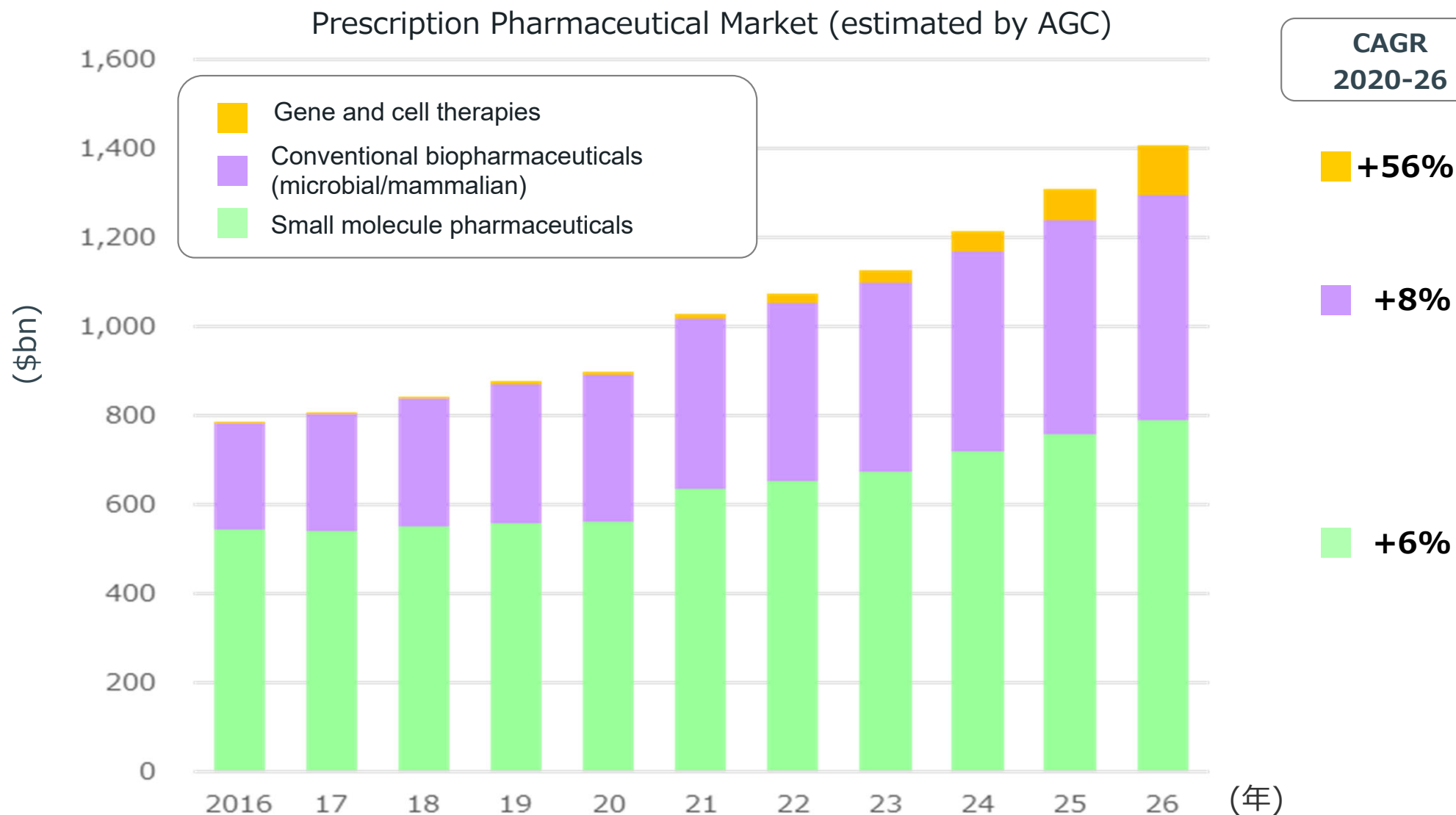
**2020 Acquired** Molmed in the gene/cell therapy area (currently AGC Biologics (Italy))

**2021 Acquired** U.S. gene therapy manufacturing plant

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# The Global Pharmaceutical Market

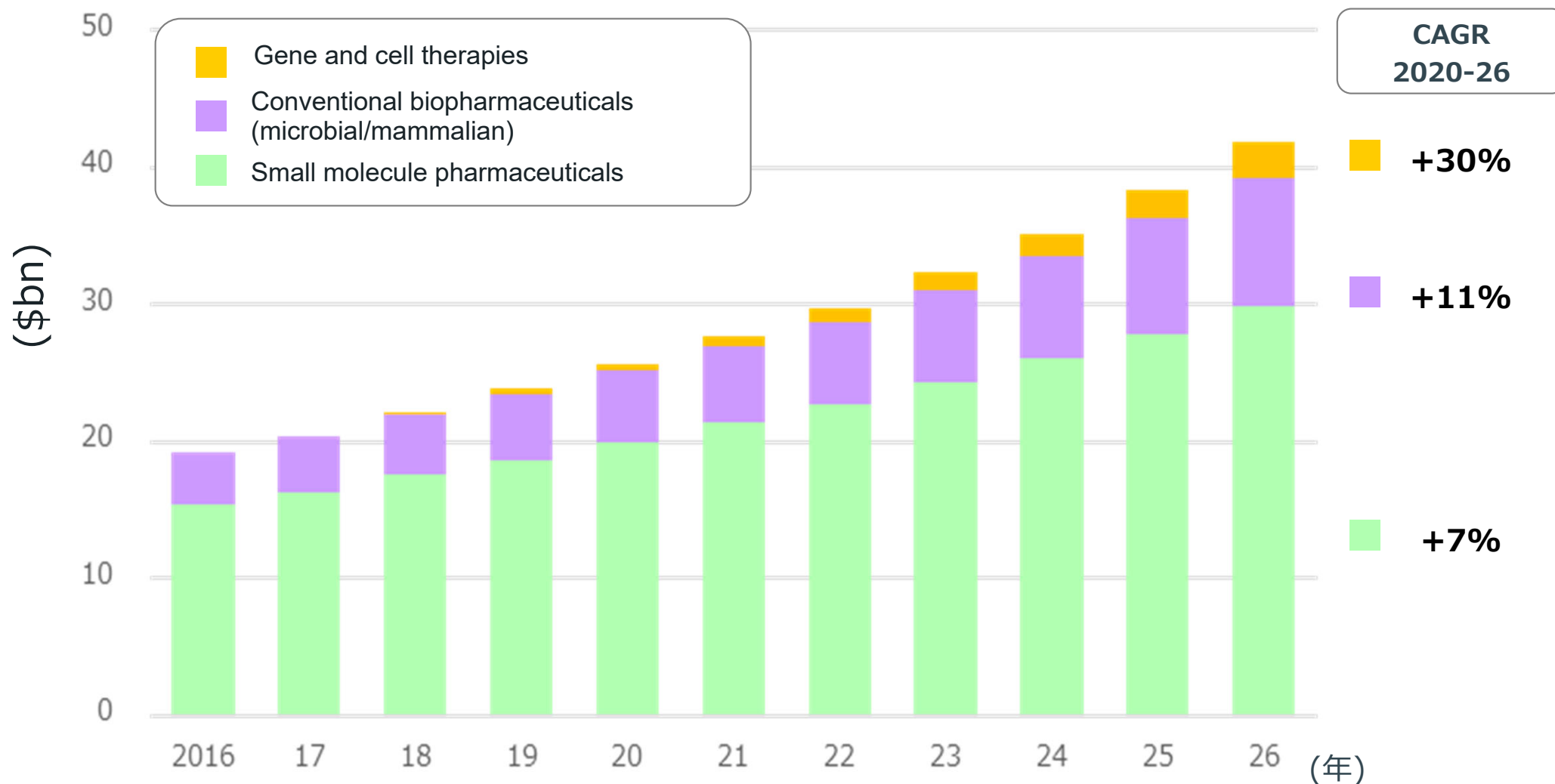
- With the increase of the elderly population, sophistication of healthcare and other factors, the global pharmaceutical market is expanding steadily





➤ With the trend towards increased outsourcing, the CDMO market is also expanding steadily.

Drug Substance CDMO Market (estimated by AGC)



- AGC's Life Science Business
- Industry Trends
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## **1. Production network catering to customer needs**

**Offering a wide range of services with high-level cGMP production network in three regions, Japan, the U.S., and Europe**

## **2. Track record in commercial phase manufacturing**

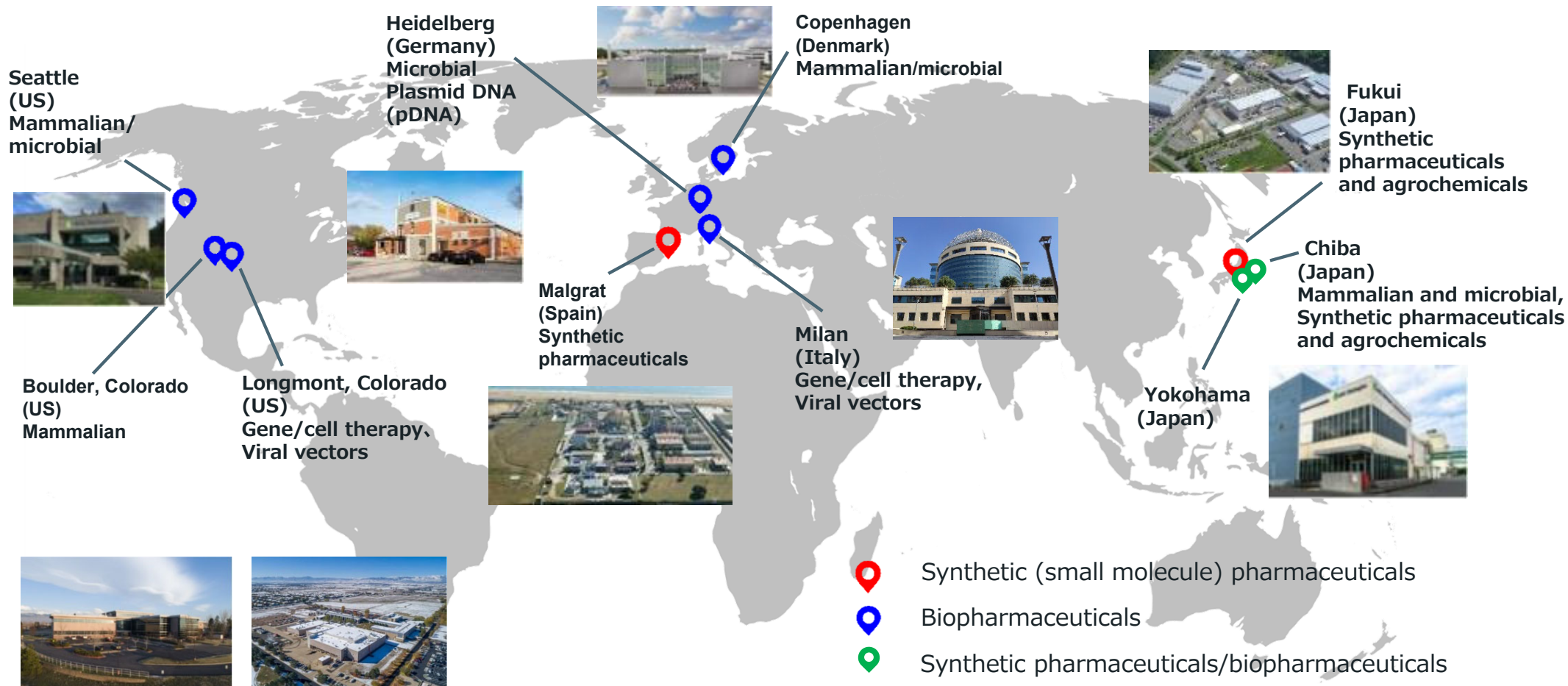
**With high-level quality and developmental capabilities, have undergone numerous inspections**

## **3. Technological competence**

**Use of cutting-edge technology to solve manufacturing and development challenges**

# 1. Production network catering to customer needs

- One of the few global CDMOs with major operations in Japan
- Offering a **wide range of services** with capabilities in synthetic/microbial/mammalian processes, pDNA, and cell & gene therapies, from clinical through commercial phase, based on high-level **cGMP production network in three regions, Japan, the U.S., and Europe**



# 1. Production network catering to customer needs

## Customer Centric Culture

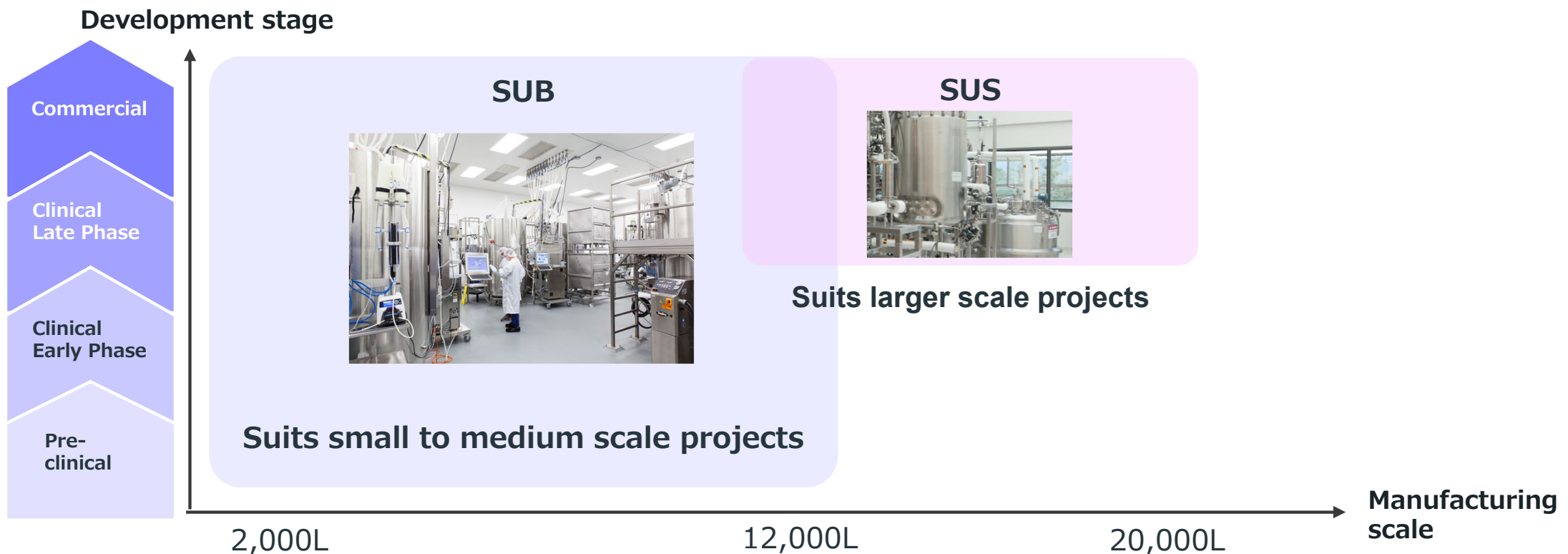
- AGC builds **close, long-term relationships** with customers, with management level members taking a hands-on approach.
- AGC **provides seamless services**, including tech-transfer between sites, made possible through our integrated operations among the three regions.
  - Optimal proposals including manufacturing location and timing according to needs
  - Reduction in communication hurdles, such as language and time differences

## We're the Proven Partner of Choice



# 1. Production network catering to customer needs

- We have established a well-balanced **flexible production network** with various scale bioreactors
  - Leveraging our extensive experience in single-use technology, **we serve small scale production needs** that is increasing with the development of orphan/niche pharmaceuticals.
  - We also provide flexible **services for medium to larger scale production needs**, with our SUBs operatable in a **6pack™** configuration, and with our **large-scale SUS bioreactors** located in Boulder, Colorado.
- As **production scale needs shift together with the progression of the development stage**, we provide **consistent services** from early developmental through commercial phase.



## 2. Track Record in Commercial Phase Manufacturing

- With high-level quality and developmental capabilities, we have successfully undergone numerous inspections.

### <Inspection Track Record at Our Sites> (\*Includes inspections for non-commercial products)

		FDA US Food and Drug Administration	EMA European Medicines Agency	PMDA Pharmaceuticals and Medical Devices Agency
Small Molecules	AGC Chiba Plant	●		●
	AGC Pharma Chemicals Europe (Catalonia)	●	●	●
Biopharmaceuticals	AGC Biologics (Seattle)	●	●	
	AGC Biologics (Copenhagen)	●	●	●
	AGC Biologics (Heidelberg)	●	●	
	AGC Biologics (Milan)		●	
	AGC Chiba Plant			●

## 2. Track Record in Commercial Phase Manufacturing

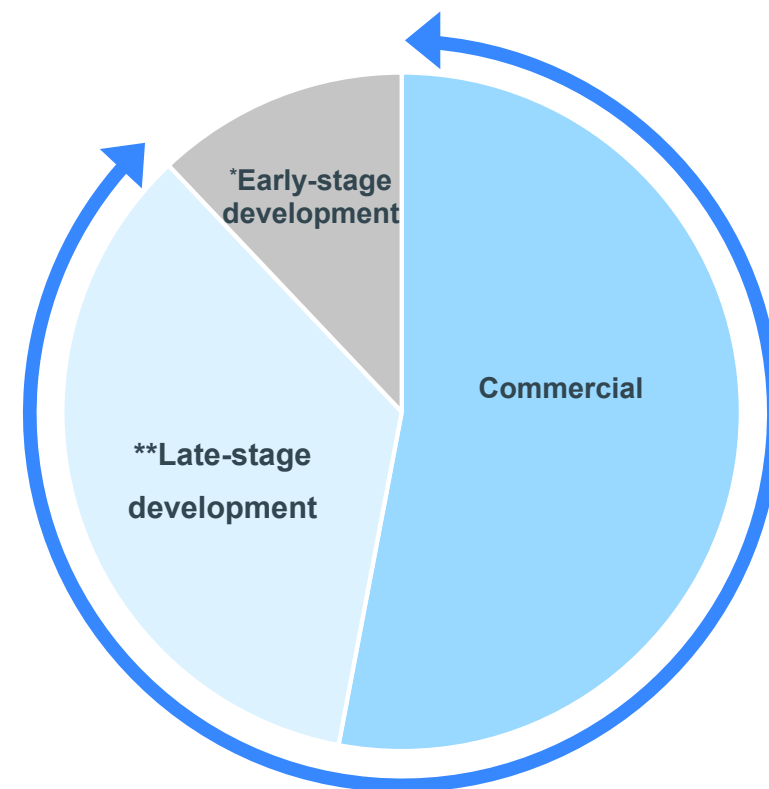
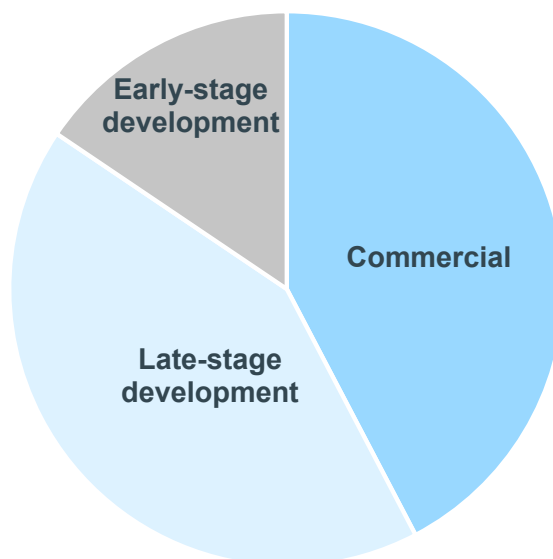
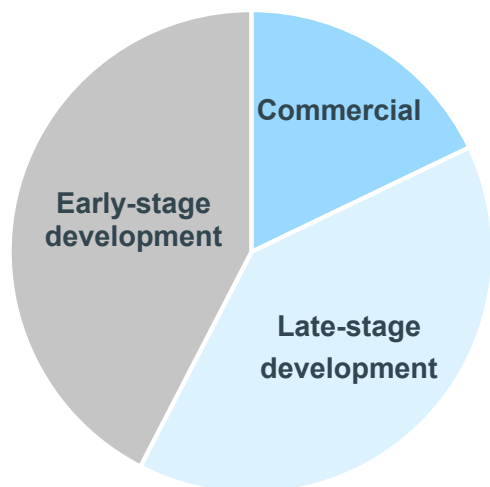
- Having built up an extensive track record, we have earned the **trust** from many pharmaceutical companies as a CDMO, and the proportion of commercial and late-stage development projects that **require high-level cGMP management** is increasing.
- Having both commercial projects that tend to stably continue, and early-stage projects that potentially grow larger as the developmental phase progresses, we are **well positioned for continued growth**.

Percentage of sales in terms of developmental phase (For Microbial & Mammalian Projects)

2019 results

2021 forecast

2022 forecast



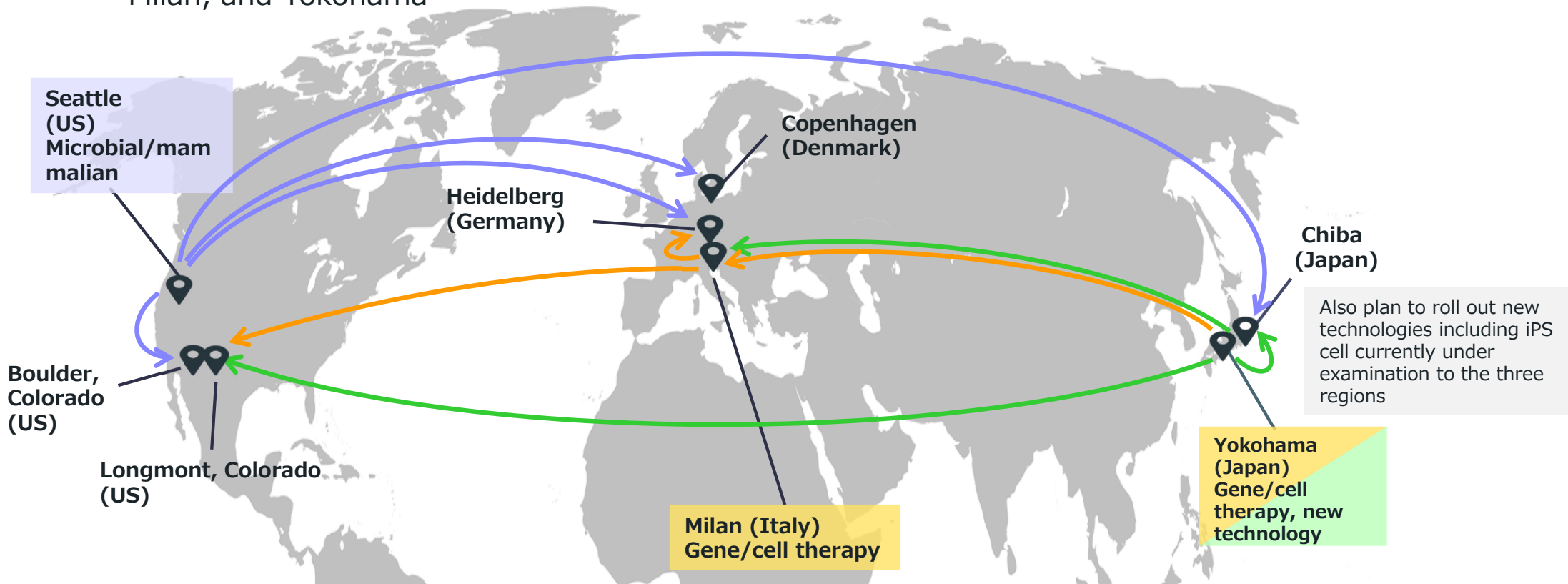
\* Early-stage development: Pre-clinical-Phase II

\*\* Late-stage development: Phase III



# 3. Technological Competence








- In addition to more than 25 years of experience as a CDMO, we **continually incorporate new technologies and work on new modalities to meet the ever evolving needs of customers**
  - Once of the first adopters of single-use technology since its naissance
  - Trial and incorporation of new manufacturing tools, not just those developed in-house
  - Contracted for various COVID-19 vaccine projects based on track record including pDNA; now expanding our services into mRNA
- **Roll out** of new technologies to **all three regions** from our **R&D Centers** located in Seattle, Milan, and Yokohama



# COVID-19-Related Projects

- We have been contracted for many COVID-19-related projects based on our high level of competence and track record.

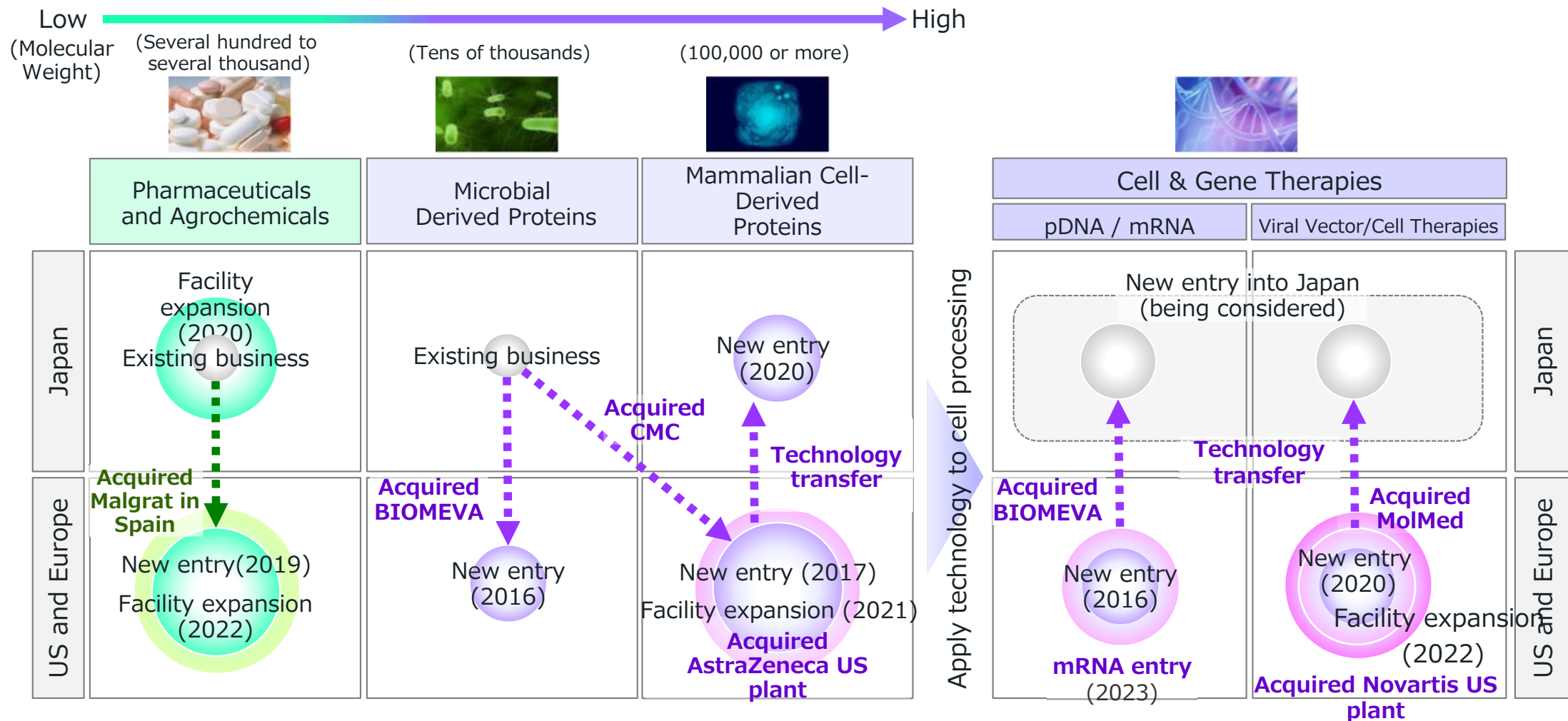
(As of November, 2021)

Announced Date	Contractor company	Announcement
05/14/20	AdaptVac (Denmark)	Manufacture of a vaccine candidate 
05/14/20	CytoDyn (US)	Leronlimab, a candidate for therapeutic drug, clinical trials underway in the US 
05/21/20	Takara Bio (Japan)	Manufacture of an intermediate for a DNA vaccine candidate 
06/04/20	Novavax (US)	Manufacture of an adjuvant of vaccine candidate NVX-CoV2373 
07/20/20	Molecular Partners AG (Switzerland)	Manufacture of MP0420, a therapeutic drug candidate 
08/18/20	Novavax (US)	Expanded the contract for the adjuvant of the vaccine candidate NVX-CoV2373 app. 1.5-fold 
06/08/21	BioNTech (Germany)	Manufacture of plasmid DNA, a raw material of the Pfizer-BioNTech COVID-19 vaccine 

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# Regional/Technological Broadening

- Since acquiring BIOMEVA in 2016, AGC has expanded its business regionally and technologically through substantial capital expenditures and M&As, forming a solid foundation as a pharmaceutical CDMO.
- Now, building on this foundation, further expanding in the cell & gene therapy area.



# Initiatives in the Cell & Gene Therapy Area (Acquisitions and Expansions)

## Milan, Italy

- 2020: Acquired (formerly MolMed)
- 2022: Adding suspension culture line for the manufacture of viral vectors, expanding analysis and development facilities



- Track record in commercial phase manufacturing while there are still not many commercial cell & gene therapy drugs in the world => **Outstanding track record and cutting edge technology**
- Over 250 experienced personnel. Reduced time to release product to customer, with in-house analytical capabilities for more than 160 tests.
- **Expanding production capacity** with suspension culture facility to respond to rapid market growth

## Longmont, Colorado, US

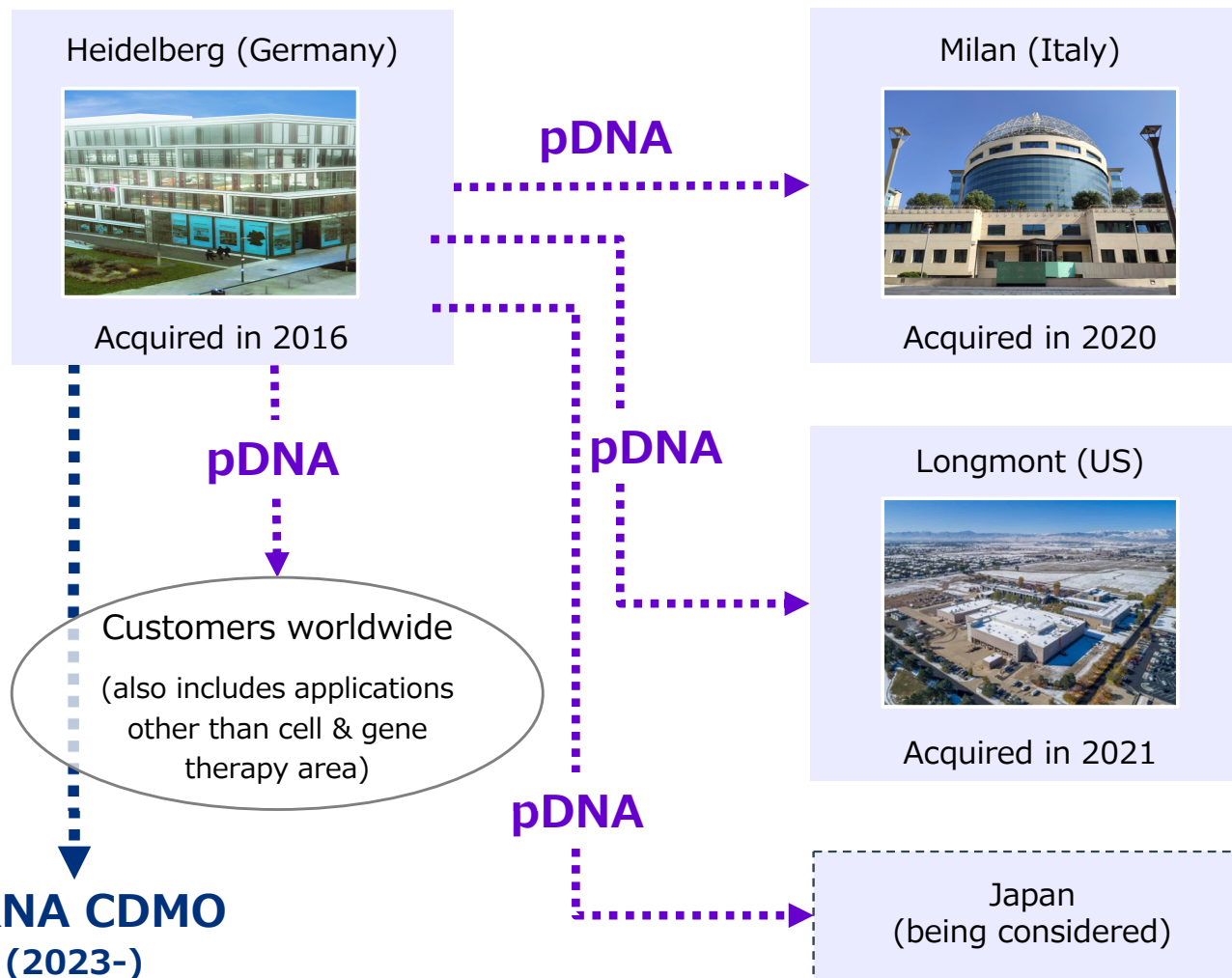
- 2021: Acquired (formerly a plant of Novartis Gene Therapies Inc.)
- 2022: Adding manufacturing facilities to cater to full-scale contract projects



- **Establishing production capacity in the US**, the world's biggest market
- Incorporating knowledge from Milan site to provide **high-level cGMP quality and services** for viral vectors and cell therapy drugs
- Vast floor area in excess of 60,000 m<sup>2</sup>, plenty of **potential for further expansion**

# Initiatives in the Cell & Gene Therapy Area

- AGC has expanded into a wide range of areas from the manufacture of plasmid DNA (pDNA), which is a raw material, to viral vectors (LVV/RVV/AAV) and cell therapies.



## Cell & Gene Therapy CDMO

- Viral vectors
  - Lentivirus (LVV)
  - Retrovirus (RVV)
  - Adeno-associated virus (AAV)
- Cell therapies

# Initiatives in the Small Molecule Pharmaceuticals and Agrochemicals Area

2020

AGC Chiba Plant  
(Chiba, Japan)



**Expansion:**  
**approx. 10-fold**

(from AGC GMP-compliant synthetic pharmaceutical manufacturing capacity)

2022

AGC Pharma Chemicals Europe  
(Malgrat, Spain)



**Expansion:**  
**approx. 1.3-fold**

Establishing a new R&D facility

2024

AGC Wakasa Chemicals  
(Fukui, Japan)



Announced  
in  
November  
2021



**Expansion: approx. 1.5-fold**

- Enhancing our one-stop service from raw material manufacture at Chiba Plant to pharmaceutical and agrochemical intermediates & active ingredients at AGC Wakasa Chemicals
- Catering to the needs of a wide range of Japanese and overseas pharmaceutical and agrochemical manufacturers

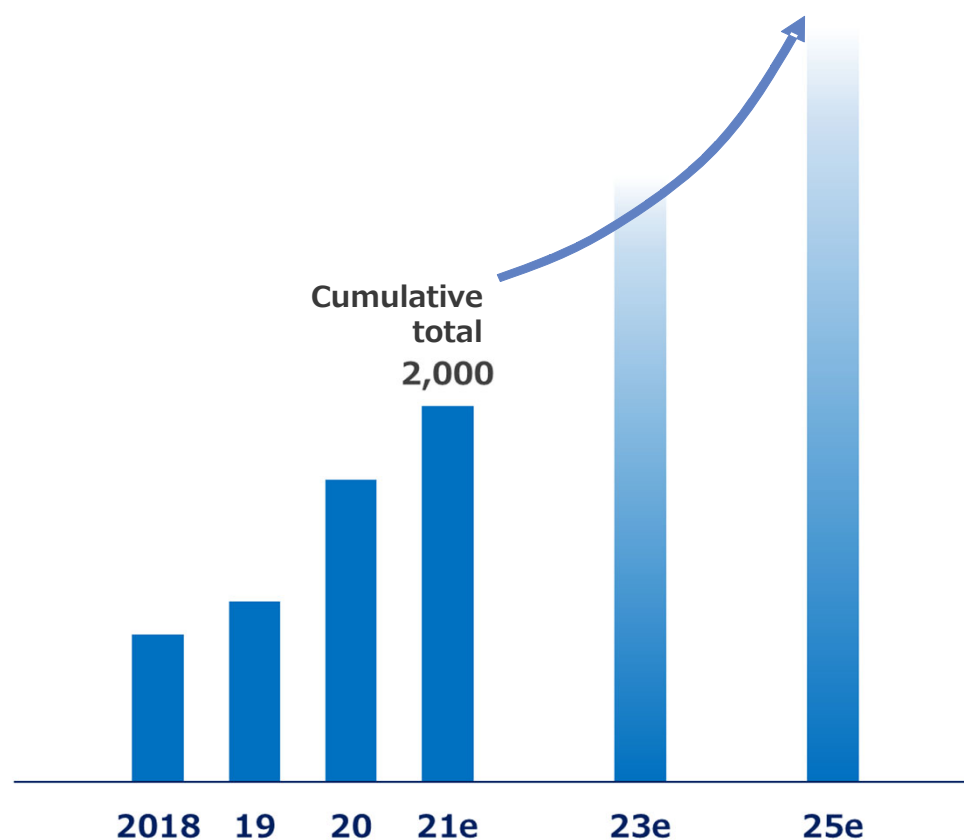
Based on the diverse and **advanced technical competence and quality systems**, which AGC has developed in fluorine synthesis and other areas, we are catering to customer needs by establishing a **wider range of services globally**, including capabilities to serve the needs for next-generation agrochemicals and high potency drugs. In general, such new areas demand even greater safety, and environmental considerations.

# Revenue Growth, Cumulative Investment

- AGC's cumulative investment will total (\*) approximately 200 billion yen in 2021, and the aim is to achieve our 2025 revenue goal of 200 billion yen or more, one year earlier.
- We plan to investment another 200 billion yen through 2022 to 2025, driving further business growth.

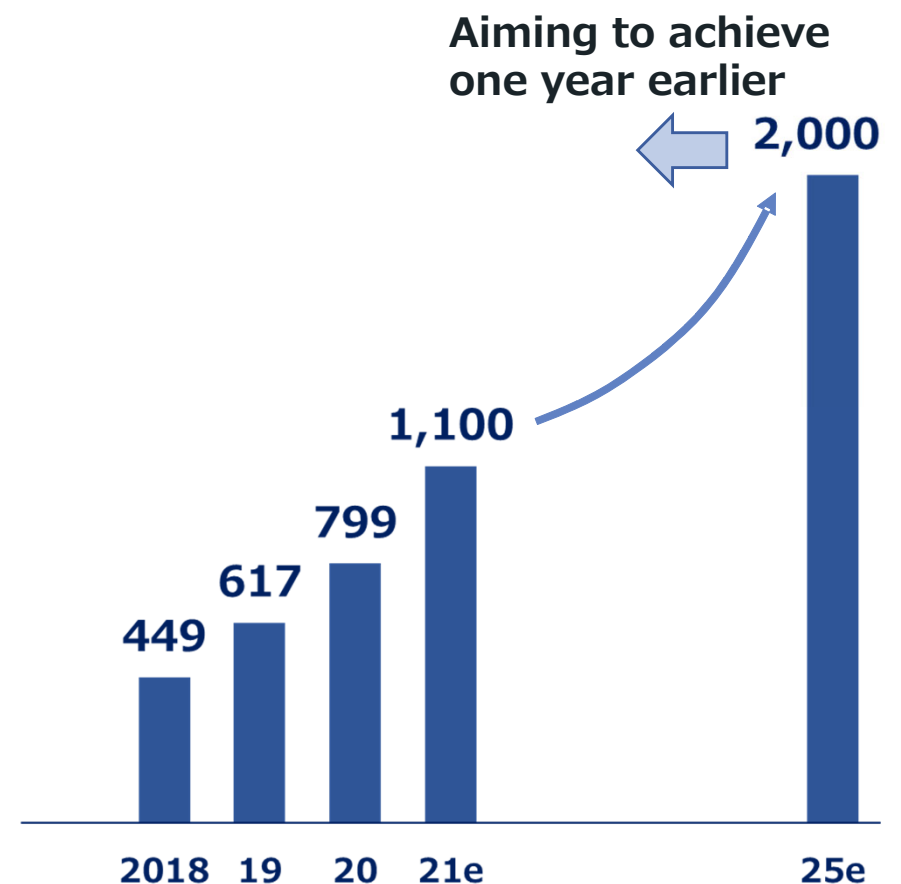
## Cumulative Investment in Life Science Business\*

(Unit: 100 million yen)



## Life Science Business Revenue Growth

(Unit: 100 million yen)



\*Cumulative total since 2015 (including M&A), including decided but not spent amounts in 2021.



# Capacity Expansion (Acquisitions and Facility Expansions)

- ① Active investments leading to achievement of initial revenue goal 4 years earlier than originally planned, with **2021 revenue estimate at 1,100 hundred million yen.**
- ② **Investments necessary to reach revenues of 2,000 hundred million yen already decided.** Investments carried out since 2020 coming online.
- ③ **Further M&As and Expansions** being considered for further growth.

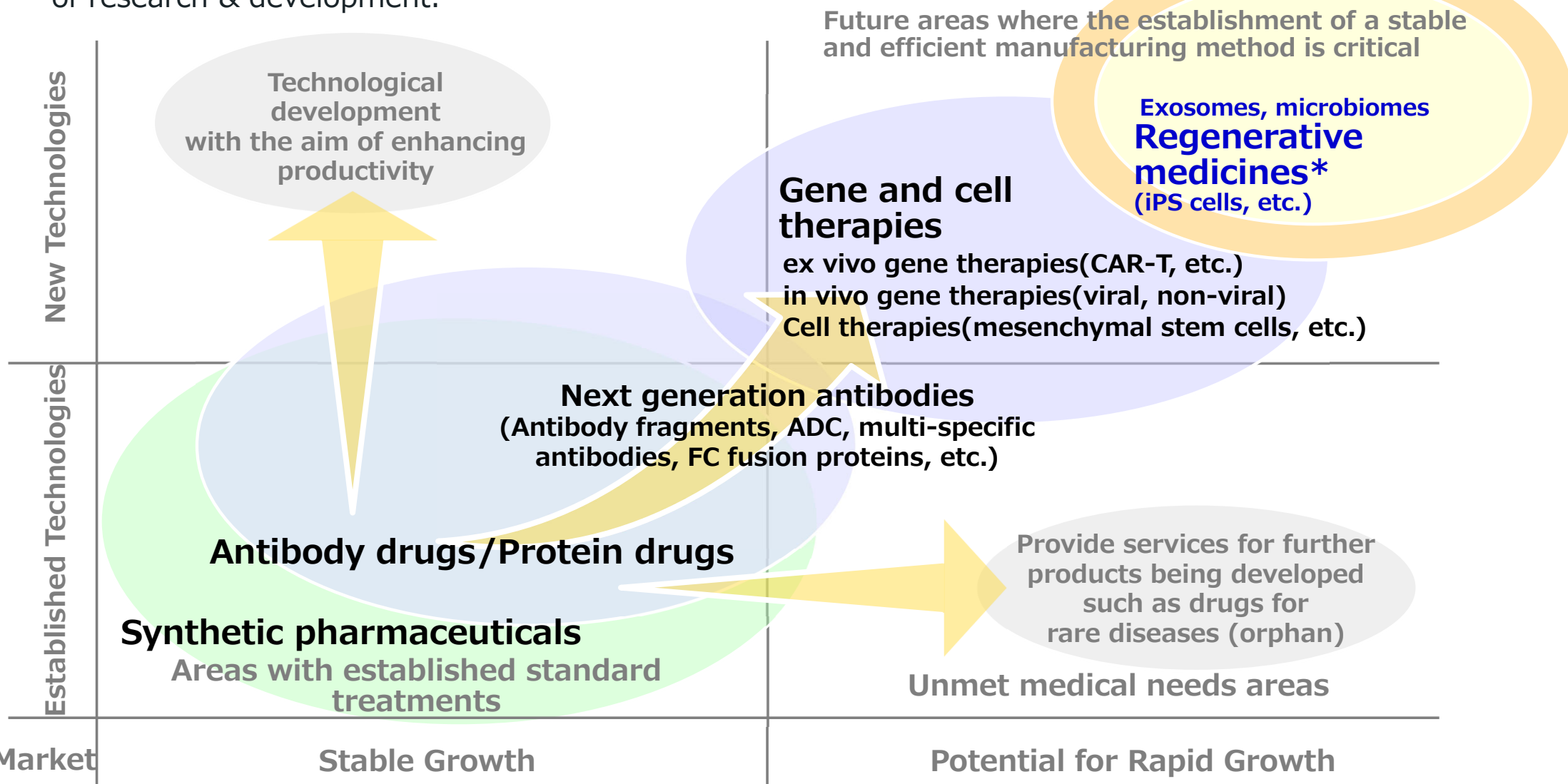
Considering Further Investments

		Location	2018	2019	2020	2021	2022	2023	2024	2025		
Small molecule	EU	Malgrat		Acquisition	Expansion(1.3 times)							
	JP	Chiba, Wakasa	Expansion(10 times)			Expansion						
Biopharmaceuticals	Microbial Mammalian Cell and gene	EU	pDNA Expansion + mRNA New Addition									
		EU	Copenhagen	Expansion(SUB 2,000Lx5)					Expansion(SUB)			
		US	Seattle	Expansion			Expansion(SUB 3 times)					
		US	Boulder	Acquisition								
		JP	Chiba	Expansion(Introduction of new culture equipment)								
		EU	Milan	Acquisition		Expansion(Introduction of new culture equipment)						
		US	Longmont	Acquisition								

\* Facility Expansions noted based on timing of start-up

# Future Technologies & Modalities

- We will be looking into timely entry into new fields, such as manufacturing services for regenerative medicines where extensive research is ongoing in the industry, and other new technologies and modalities that are in the early days of research & development.

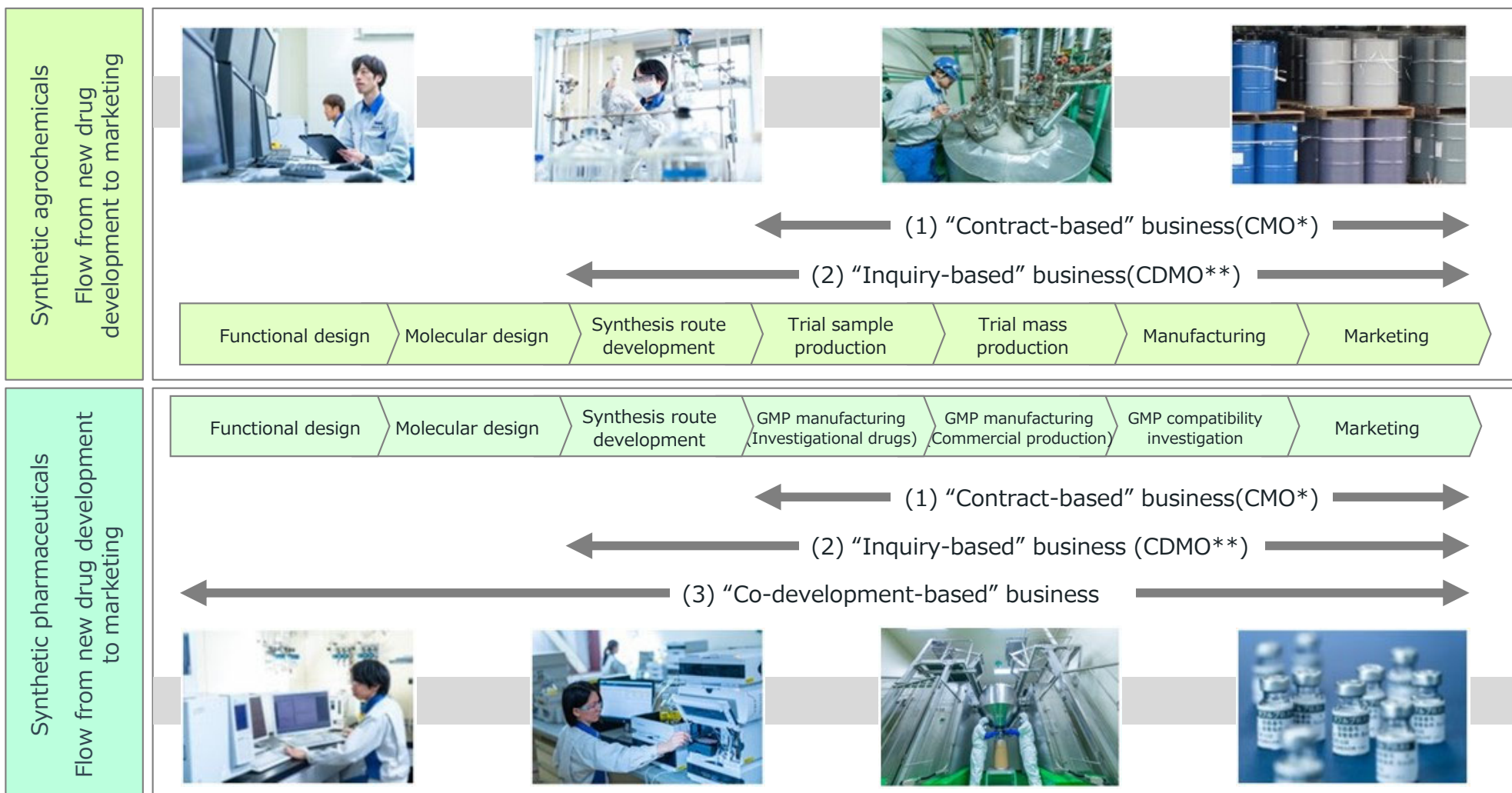


\*Black text (modalities that AGC has already entered), blue text (modalities the company will consider entering in the future)

# Appendix

# Life Science Business Scope (CDMO Services for Small Molecule Pharmaceuticals and Agrochemicals)

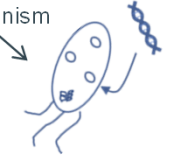

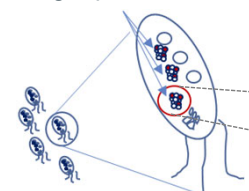



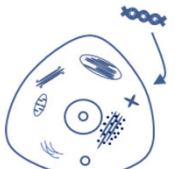

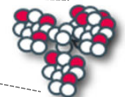
- Integrated production of raw materials, intermediates and APIs using fine organic chemistry technologies
- Efficient process development to enable low-cost, industrial-scale manufacturing of intermediates and APIs



\*CMO(Contract Manufacturing Organization)\*\*CDMO(Contract Development Manufacturing Organization)

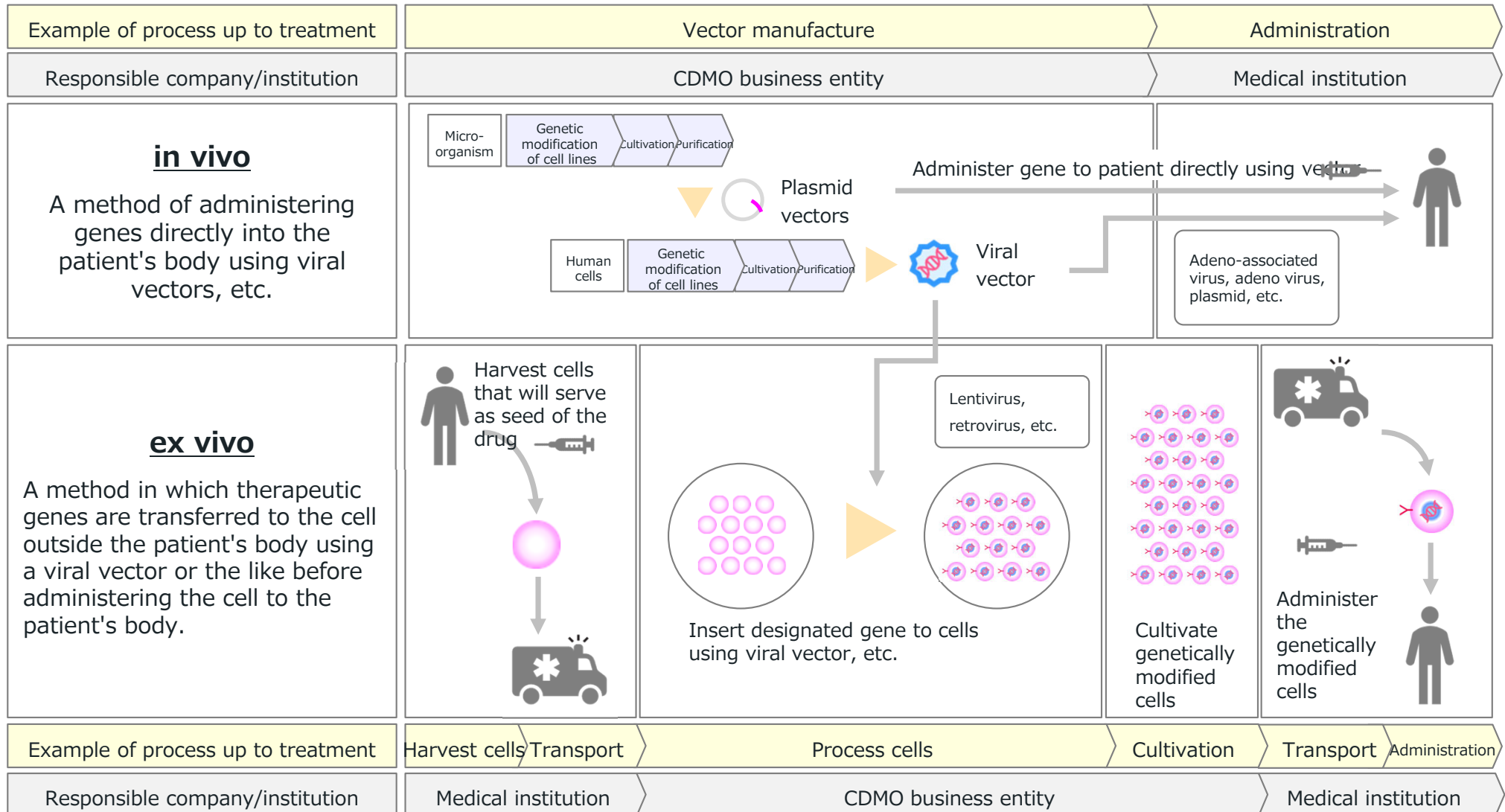
# Life Science Business Scope (CDMO Services for Conventional Biopharmaceuticals)

- AGC receives the “target gene” from the pharmaceutical company, and “cultures” the cell with the target gene, “harvests” and “purifies” to obtain the target protein, on a contract basis
- The manufacturing is for the “target protein (=biopharmaceutical)”. The general flow of the manufacturing process is the same in both microbial and mammalian cells.

Manufacturing process	Gene recombination	Culture	Harvest	Purification	Finishing into Product/Marketing
	Introduce a recombinant gene into microorganisms/cells.	Increase microorganisms/cells carrying the recombinant gene. At the same time, the target protein (drug) also increases.	Collect and purify the target protein (=drug substance)	-	-
Responsible manufacturer	Pharmaceutical company or contract manufacturer (e.g. AGC)				Pharmaceutical company
(1) Microbial	<p>Recombinant gene (=the seed of the target protein (=drug substance))</p> <p>Microorganism</p> <p>Size: several <math>\mu\text{m}</math></p> <p>Structure: simple</p>  	<p>Target protein</p>  	<p>Molecular weight: in the order of <math>10^4</math></p> <p>Structure: simple</p> <p>Drug examples: insulin (anti-diabetic), GCSF(anti-neutropenic)</p>  <p>Target protein (drug substance)</p> 	-	-
(2) Mammalian cell	<p>Recombinant gene (=the seed of the target protein (=drug substance))</p> <p>Size: <math>\geq 10 \mu\text{m}</math></p> <p>Structure: complicated</p> 	<p>Target protein</p> 	<p>Molecular weight: <math>\geq 10^5</math></p> <p>Structure: complicated</p> <p>Drug examples: antibodies (e.g. anti neoplastics, anti-rheumatics), EPO (anti-anemic)</p>  <p>Target protein (drug substance)</p>	-	-

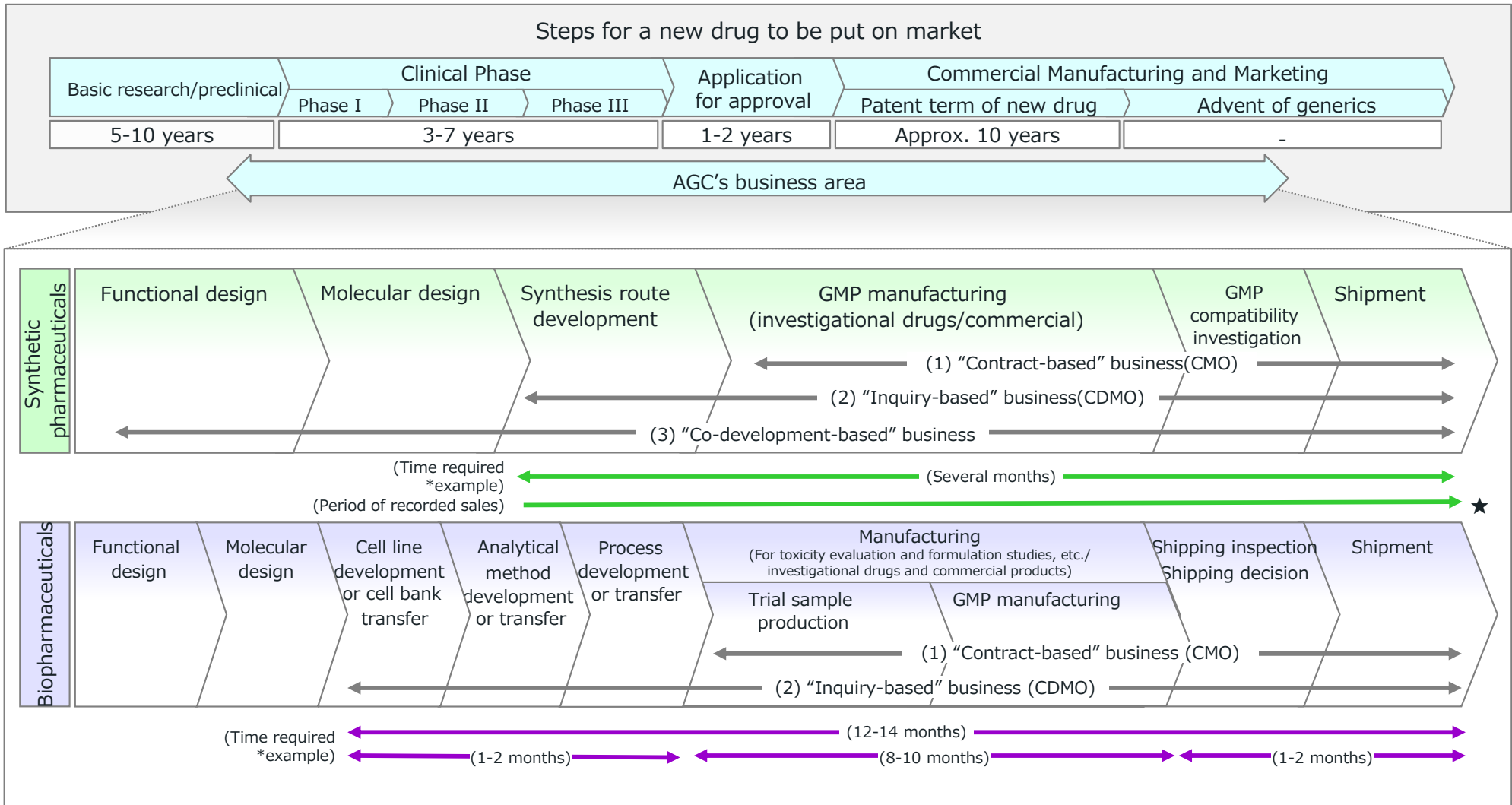
# Life Science Business Scope (CDMO Services for Cell & Gene Therapies)

- In gene/cell therapy, there are many common basic technologies where existing know-how is valuable.
- AGC has strengths in the manufacturing of viral vectors, cell processing technologies, handling of human-derived cells, and manufacturing/QC/QA.



# Drug Development and the CDMO Business Model

- Contract-periods for biopharmaceuticals tends to be longer with a contract period of two to three years compared to small molecules that could be as short as a few months. Revenue recognition is generally made at each stage and upfront payment is established in many regions, therefore the long contracts do not lead to income instability.
- There are short contracts for biopharmaceuticals as well, when for single stages such as “process development.”



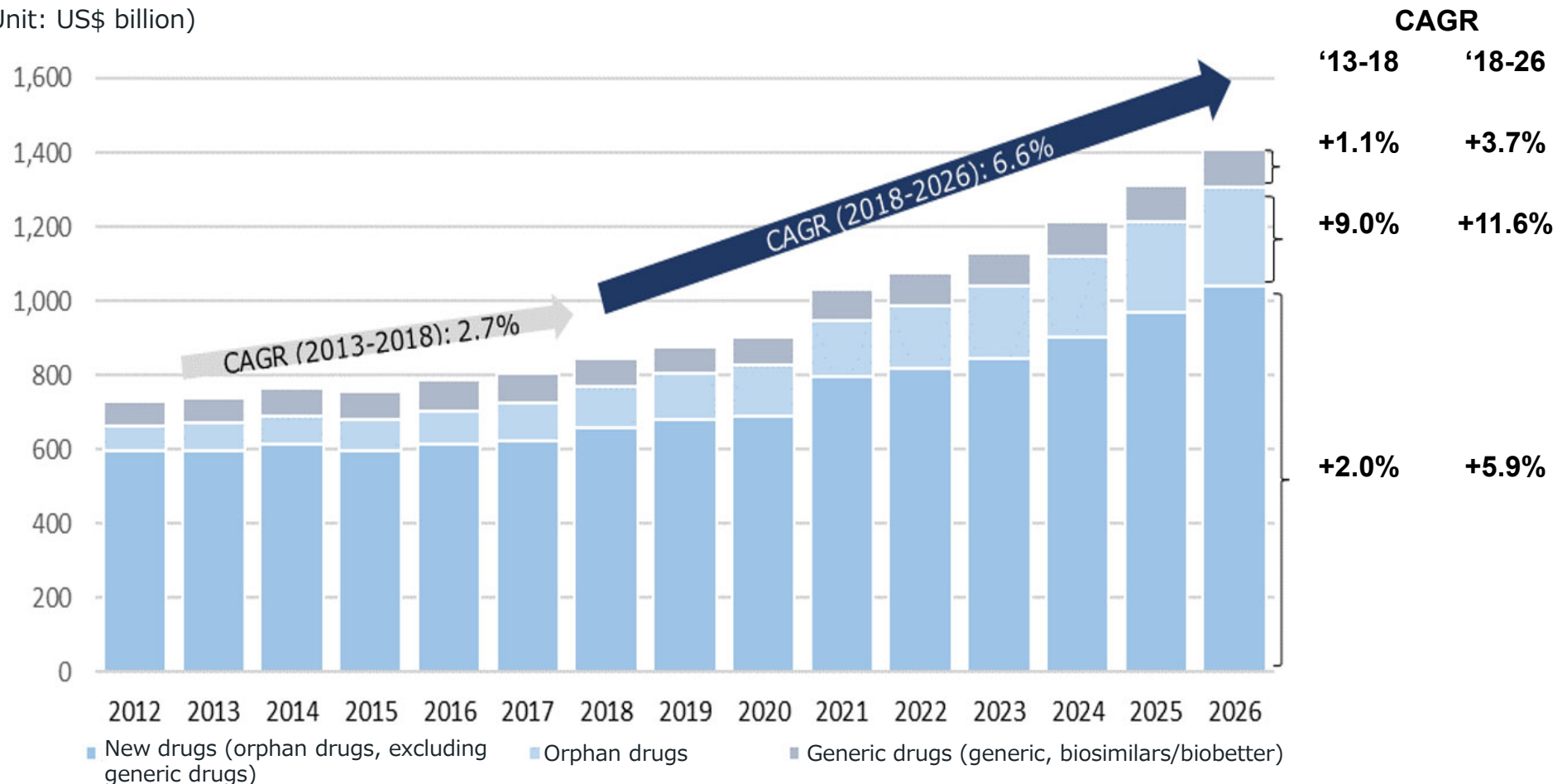
\*CMO(Contract Manufacturing Organization)\*\*CDMO(Contract Development Manufacturing Organization)

# Prescription Drug Market (For New Drugs, Orphan Drugs, and Generic Drugs)

- CAGR of prescription drug sales is 7.7% for 2020 – 2026 (2020 \$901bn→2026 \$1,407bn)
- Strong growth expected to continue for both new drugs and orphan drugs

## Breakdown of Sales Forecast for Prescription Drug Market (by drug class)

(Unit: US\$ billion)







Your Dreams, Our Challenge

**END**

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