



TOP INNOVATOR
TOP i 2030

Chugai Company Information Meeting

Chugai Pharmaceutical Co., Ltd.

June 30, 2023



創造で、想像を超える。



Important Reminders

This presentation may include forward-looking statements pertaining to the business and prospects of Chugai Pharmaceutical Co., Ltd. (the “Company”). These statements reflect the Company’s current analysis of existing information and trends. Actual results may differ from expectations based on risks and uncertainties that may affect the Company’s businesses.

Information regarding pharmaceuticals (including products under development) is included in this presentation, but is not intended as advertising or medical advice.

Agenda



01

A Brief Overview of Chugai

Dr. Osamu Okuda

Representative Director, President & CEO

02

Proprietary Innovative Antibody Engineering Technologies

Dr. Tomoyuki Igawa

Associate Vice President,
Head of Translational Research Div.



A Brief Overview of Chugai

Representative Director, President & CEO

Dr. Osamu Okuda

Company Overview

An R&D-Driven Pharma Company with Expertise in Oncology and Biologics

A Leading Japanese Drug Manufacturer (FY2022 IFRS on a Core basis)

Revenue 1,168.0 billions of yen, operating profit 451.7 billions of yen, 7,771 employees

No. 1* share of Japanese oncology market

No. 1* share of Japanese antibody drug market

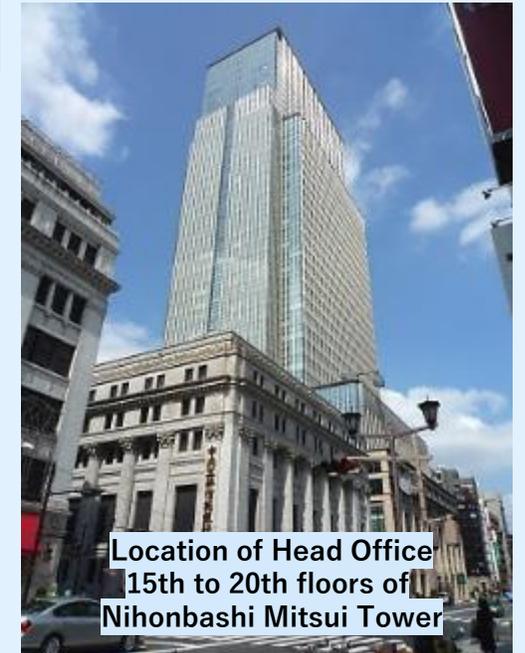
A Unique Business Model

Chugai's strategic partner Roche holds 59.89% of Chugai's shares

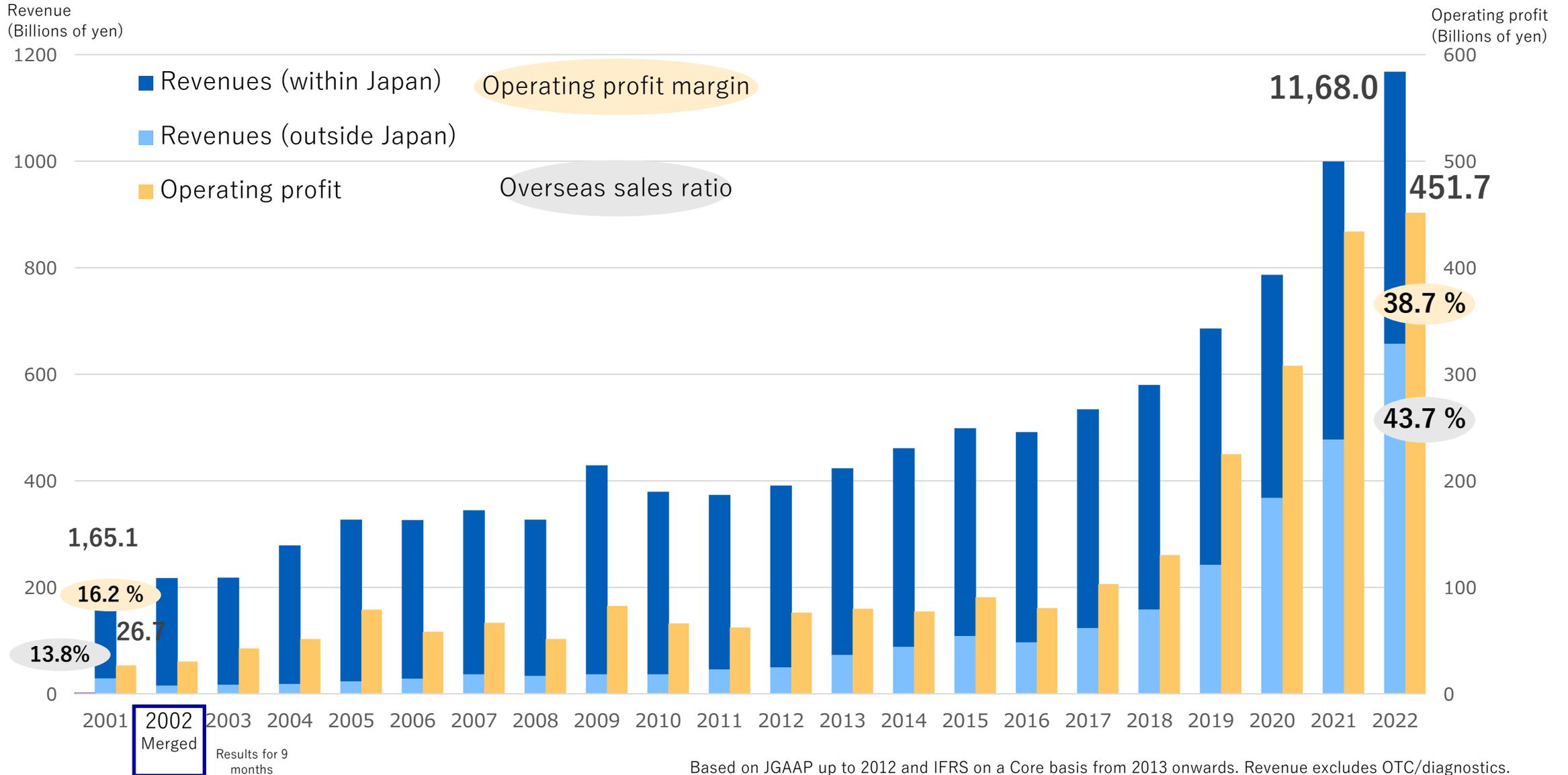
Chugai autonomously operates as an independent listed company

Unique Science and Drug-Discovery Technologies

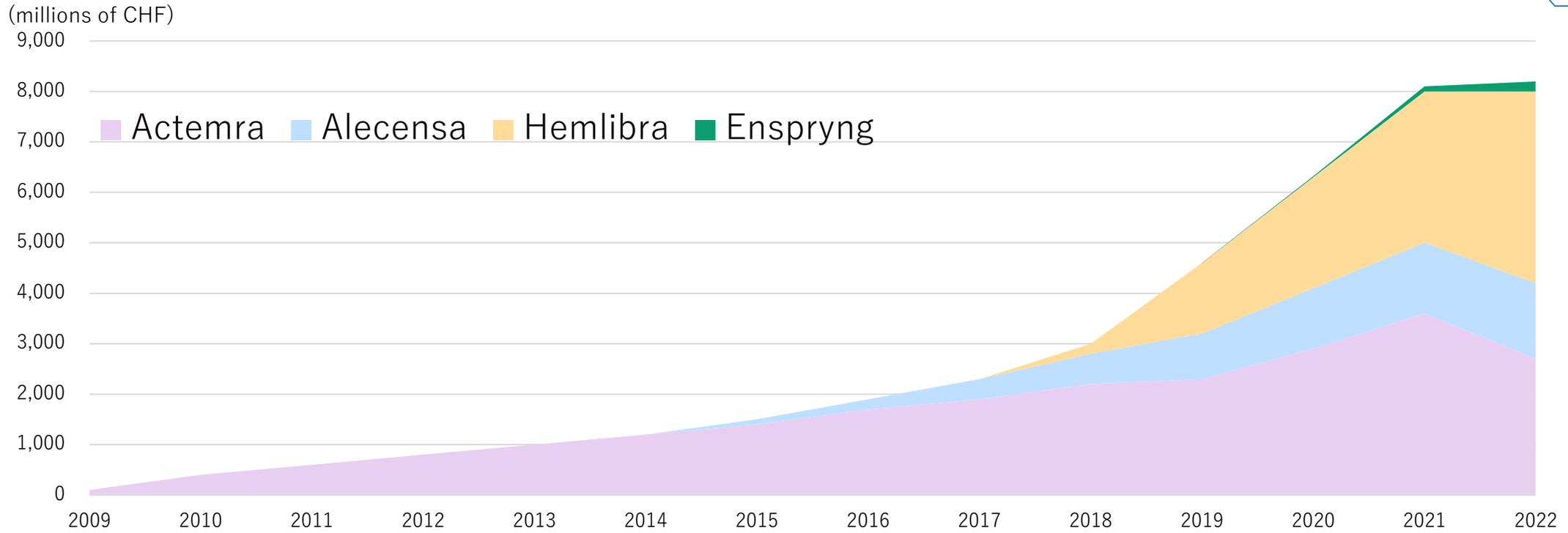
Chugai launched the first Japanese therapeutic antibody and has world-leading drug discovery technologies in antibodies, mid-size molecules, etc.



Trajectory of 20 Years



Global Sales of Chugai Originated Products



Actemra®



- First Japanese antibody drug
- Indications: Rheumatoid arthritis, etc.
- Global sales exceed 300.0 billions of yen

Alecensa®



- Representative of personalized health care promoted by Chugai
- Indication: ALK-positive lung cancer
- Approved as first-line treatment (JP/US/EU)
- Global sales exceed 150.0 billions of yen

Hemlibra®



- Uses proprietary antibody technology
- Indication: Hemophilia A
- Global sales exceed 500.0 billion yen

Enspryng®



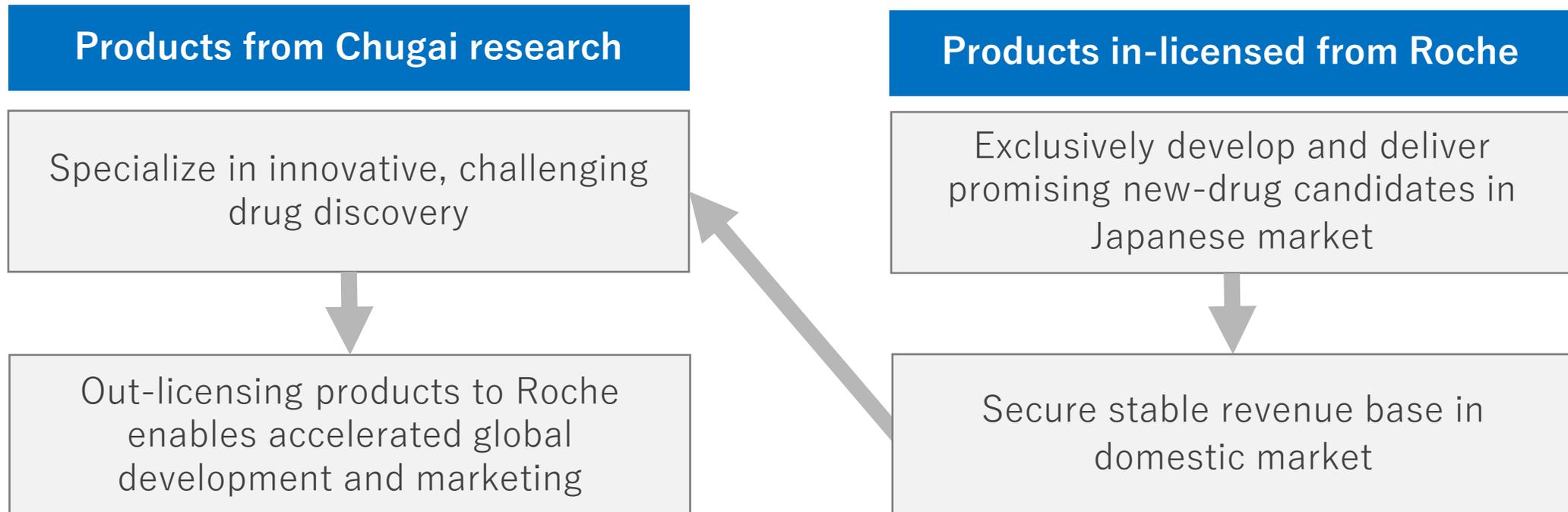
- Uses proprietary antibody technology
- Indication: Neuromyelitis optica spectrum disorders

Business Model That Implements Managerial Autonomy Based on a Strategic Alliance with Roche



- Chugai products are maximized in the global market
- Abundant Roche products are marketed in Japan

- Roche products are maximized in the Japanese market
- Innovative Chugai originated products are marketed globally



Features of the Earnings Structure Apparent in Our Unique Business Model

■ Chugai achieves a high operating profit margin of approx. 40%

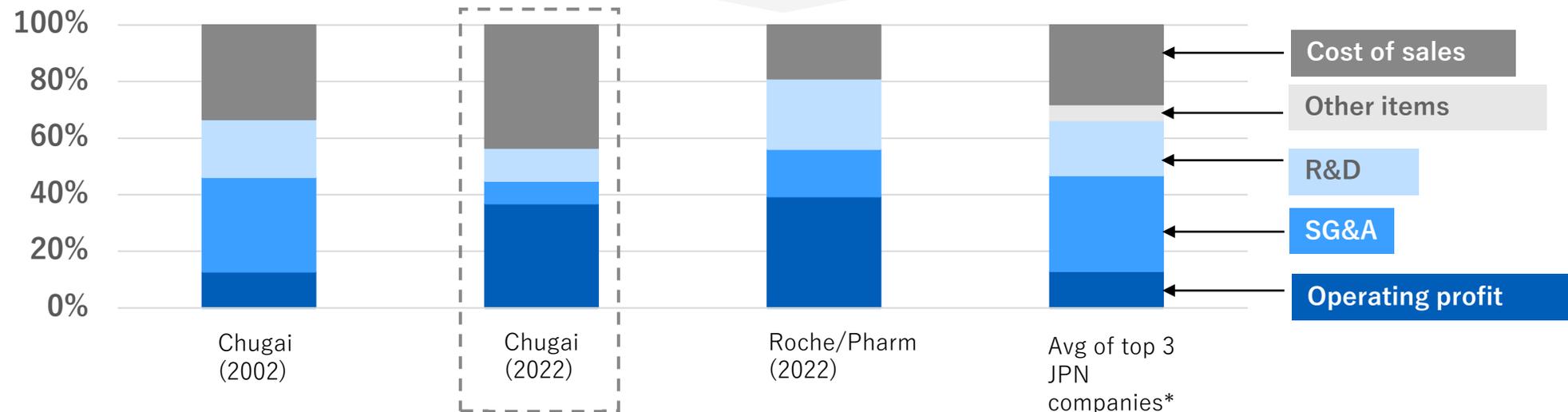
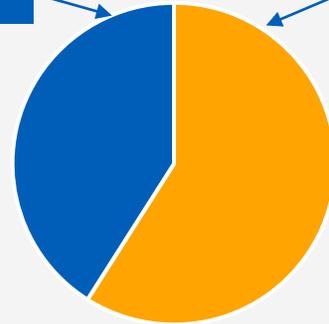
Share of revenue (2022)

Products in-licensed from Roche (41%)

Products from Chugai research (59%)

Research: —
 Development: ★ Early development by Roche
 M&D: ★ Japan only
 Costs: ★★ Import from Roche

Research: ★★★ Concentrated investment
 Development: ★ Overseas late-stage development out-licensed
 M&D: ★ Japan and certain other countries
 Costs: ★ Certain level



*Average of the top three listed pharmaceutical companies in Japan for ethical drugs (Takeda Pharmaceutical Company Limited, Astellas Pharma Inc., and Daiichi Sankyo Co., Ltd.); from each company's financial results materials for the fiscal year ended March 31, 2022

Growth Strategy for 2030, “TOP I 2030”

“Double R&D output” & “Launch global in-house products every year”

Global First-class Drug Discovery

- ▶ Expansion of existing technological bases and building a new technological foundation to materialize unique drug discovery ideas
- ▶ Launch in-house global products every year by doubling R&D output
- ▶ Accelerating innovation opportunities by strengthening collaboration with leading global players and leveraging digital technologies

Futuristic Business Model

- ▶ Dramatic improvement in product / patient value by restructuring business model, having digital utilization as a core
- ▶ Improve productivity of entire value chain by leveraging digital technologies.
- ▶ Commercialization of insight business with the aim of maximizing the value of pharmaceuticals and having a new business pillar

Key Drivers

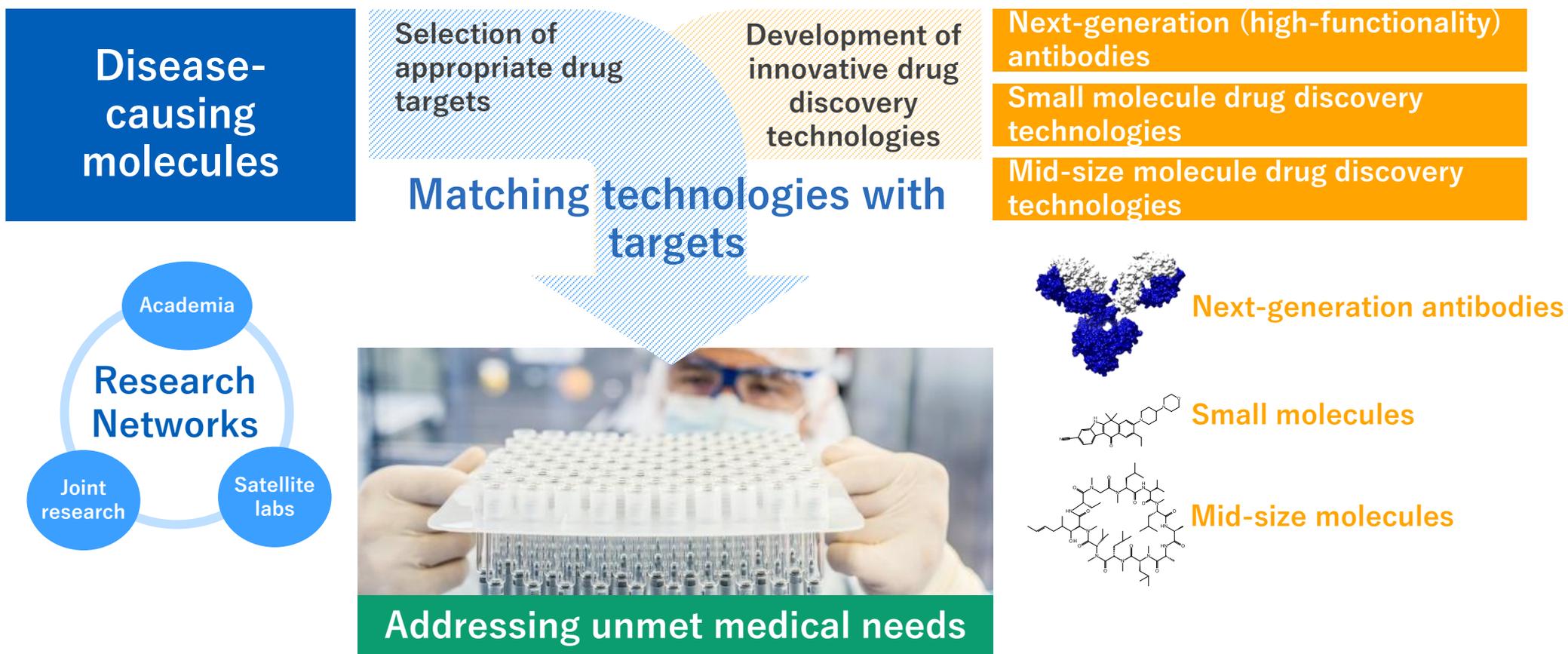
▶ **DX**

▶ **RED SHIFT**

▶ **Open Innovation**

Chugai Research Strategy: A technology-driven approach

- Enabling an optimal approach for disease targets by developing mid-size molecule drug discovery technologies in addition to antibody engineering technologies and small molecule drug discovery technologies
- Acquiring innovative “seeds” by enhancing oncology and immunology research infrastructure



Proprietary Innovative Antibody Technologies

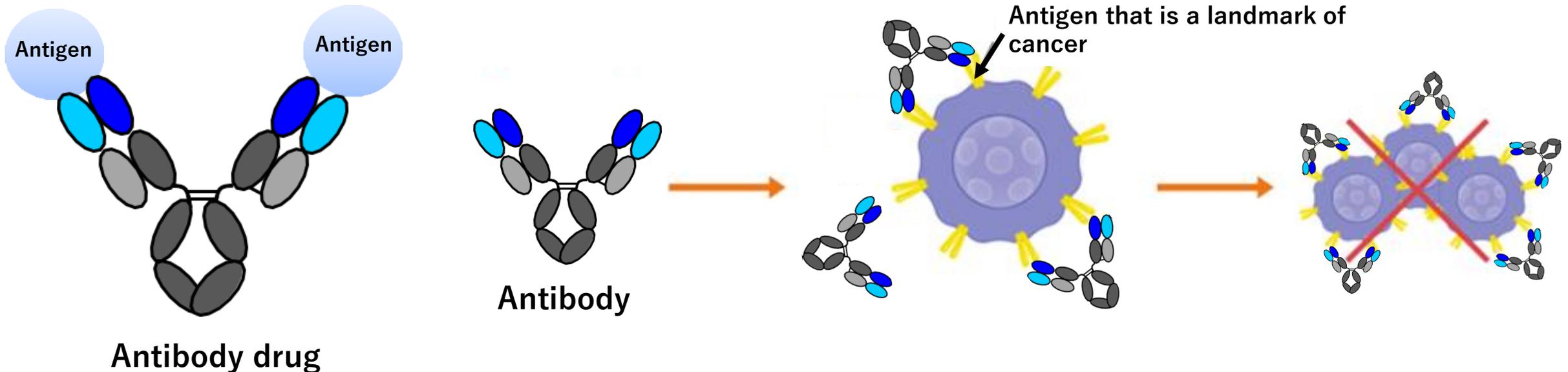
Associate Vice President, Head of Translational Research Div.

Dr. Tomoyuki Igawa

What is an Antibody Drug?

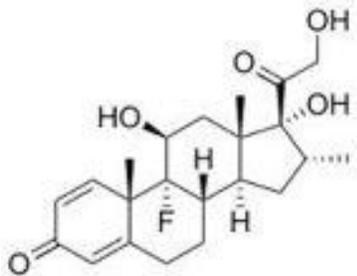
When a pathogen or other **foreign substance (antigen)** enters the body, **antibodies** exhibit an **antigen-antibody reaction** that binds to the foreign substance and detoxifies it as an immune reaction.

Antibody drugs are **drugs that artificially use this antigen-antibody reaction**. Uniform antibodies are mass produced using biotechnology and used as drugs.

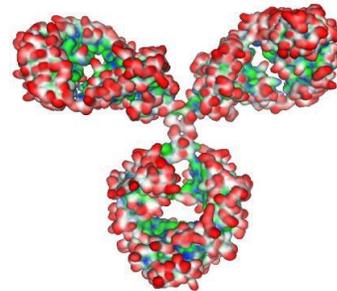


From Small Molecules to Antibodies and then Next-generation Antibodies

Small molecule drugs



Antibody drugs

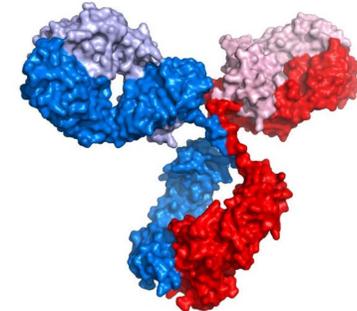


Antibody binds to target, inhibiting its activity.

Actemra®

Mitchga®

Next-generation antibody drugs

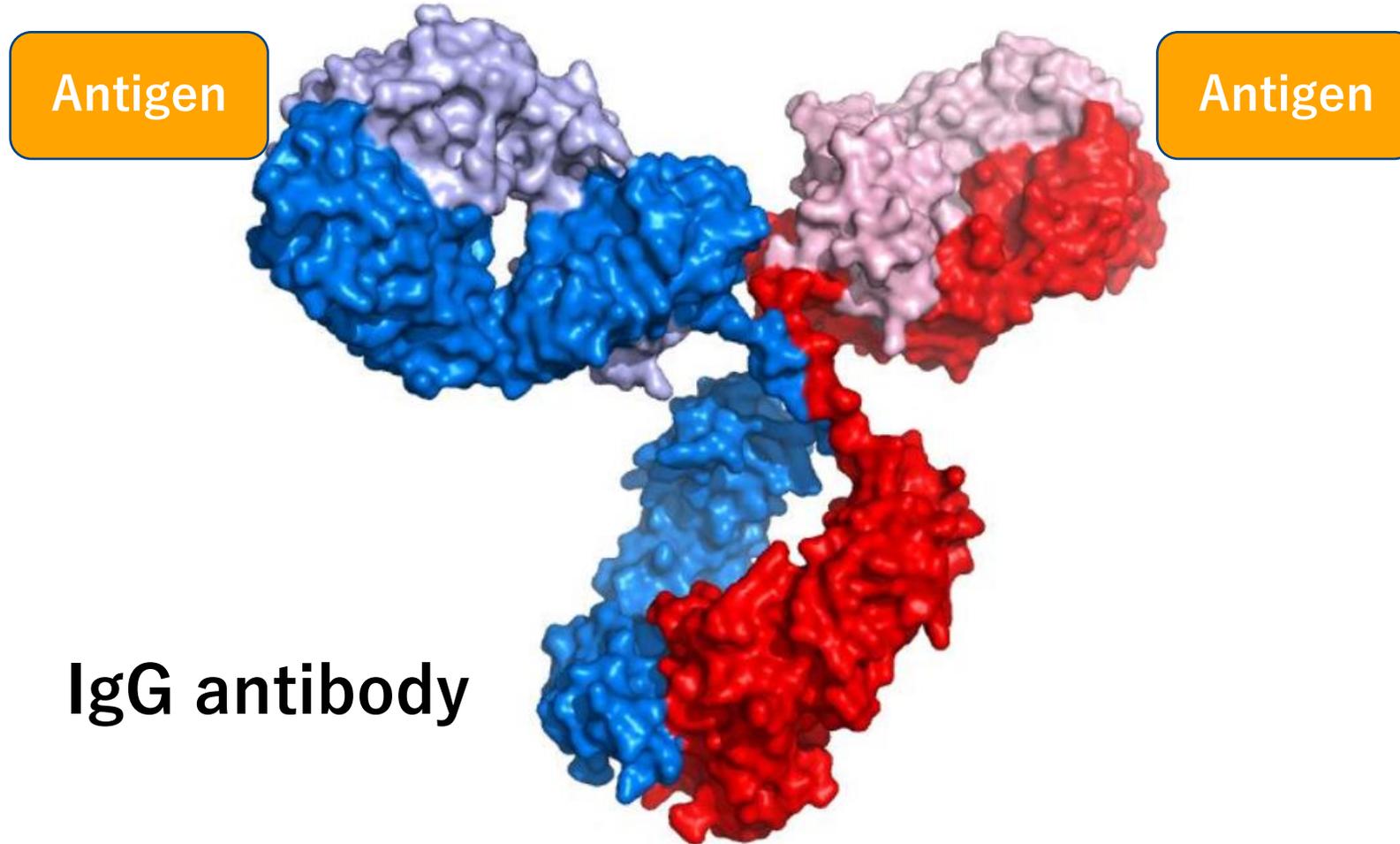


Antibody engineering technologies are used to make next-generation antibodies capable of actions not possible with conventional antibodies

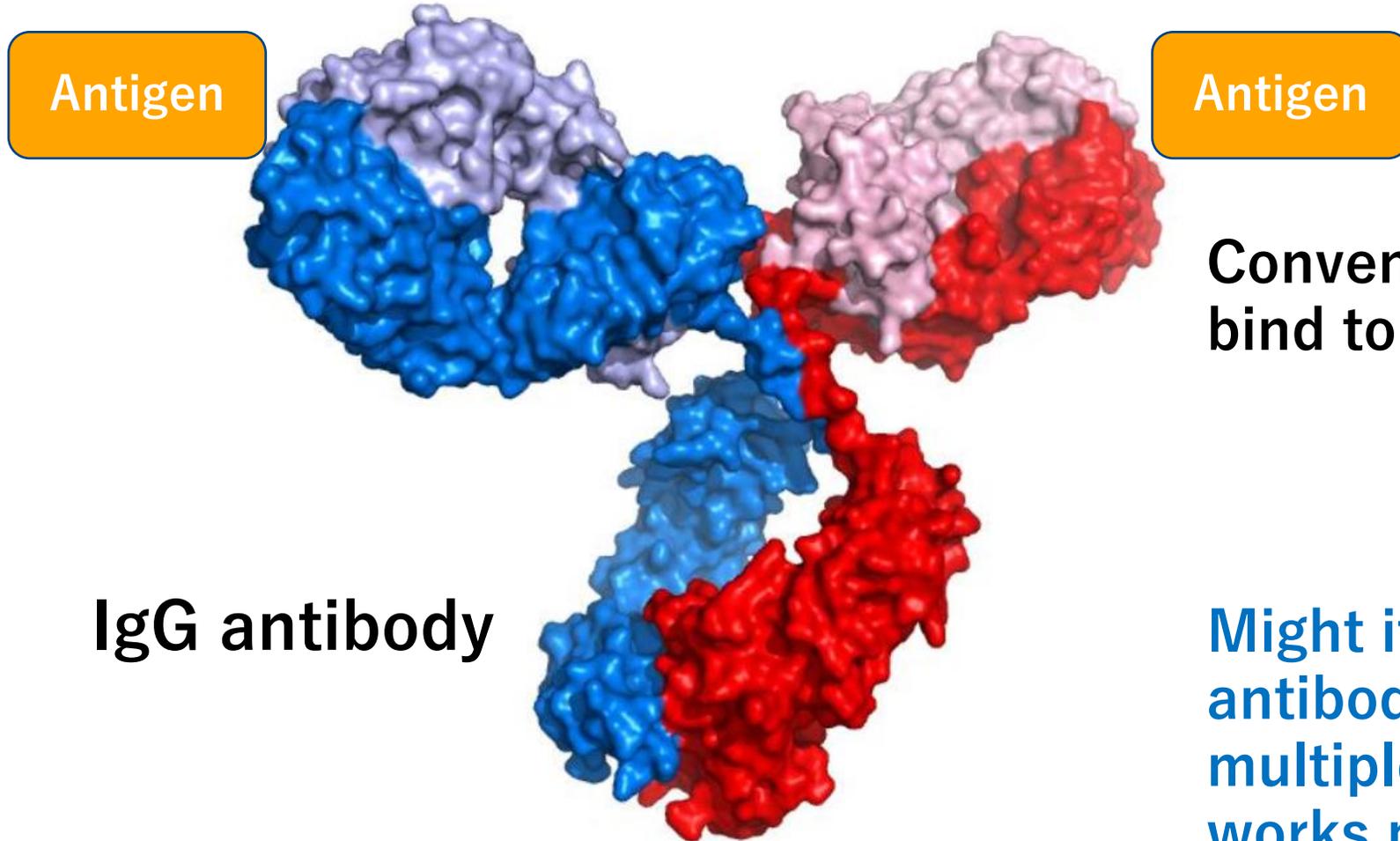
Hemlibra®

Enspryng®

Looking Deep into Antibodies to Make the Impossible Possible



What Antibody Drugs Cannot Do (1)



Conventional antibodies can bind to an antigen only once.

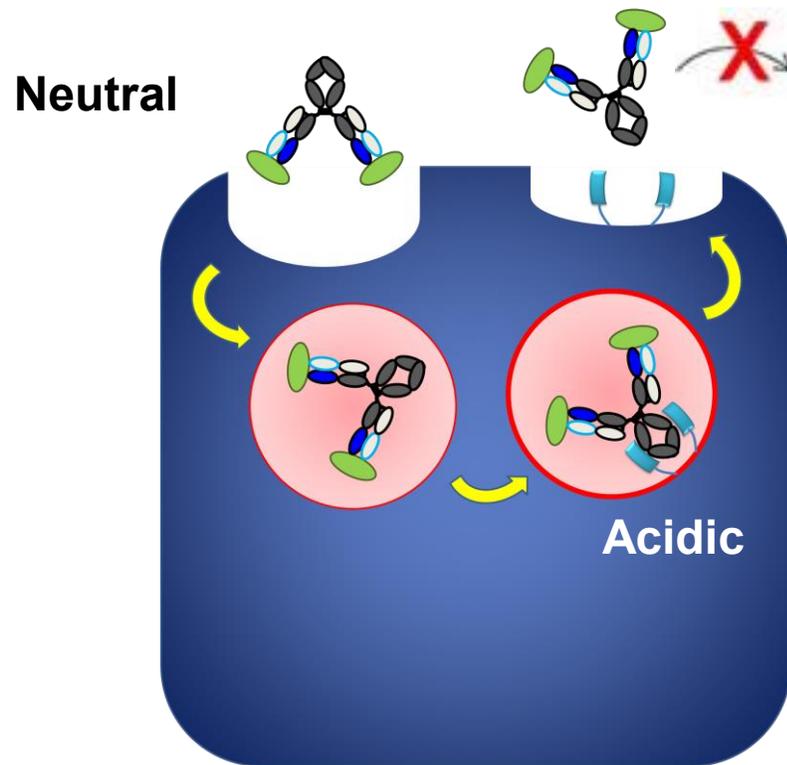


Might it be possible to make an antibody that binds to antigens multiple times and thereby works more efficiently?

Recycling Antibody[®]

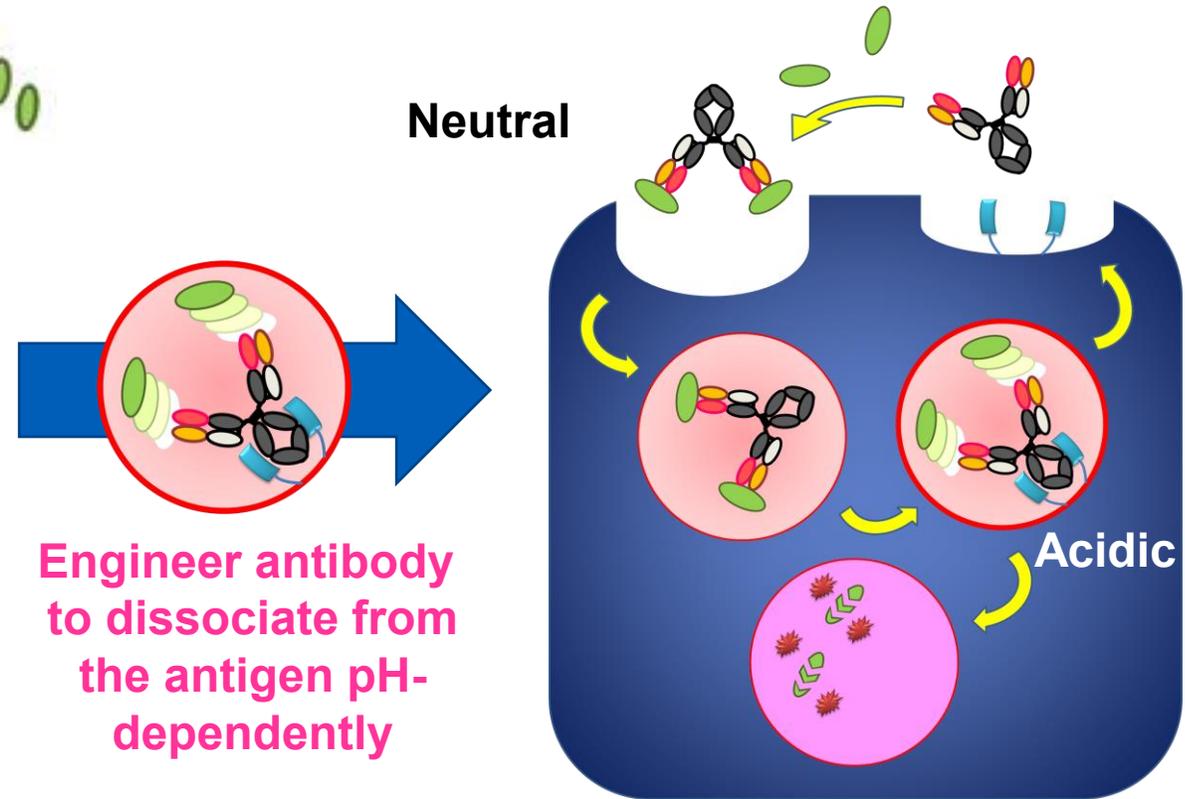
Antibody that binds to antigens many times, maintaining long-term efficacy

Conventional Antibody



Antibody binds to the antigen only once

Recycling Antibody[®]



Antibody can bind to antigens multiple times

Advantages of Recycling Antibody®

Inconvenient intravenous administration



The antibody is repeatedly used in the body

**Prolonged dosing interval
Reduced administration volume
allows subcutaneous administration**



Photo: Pixabay

**Administration
in a hospital**

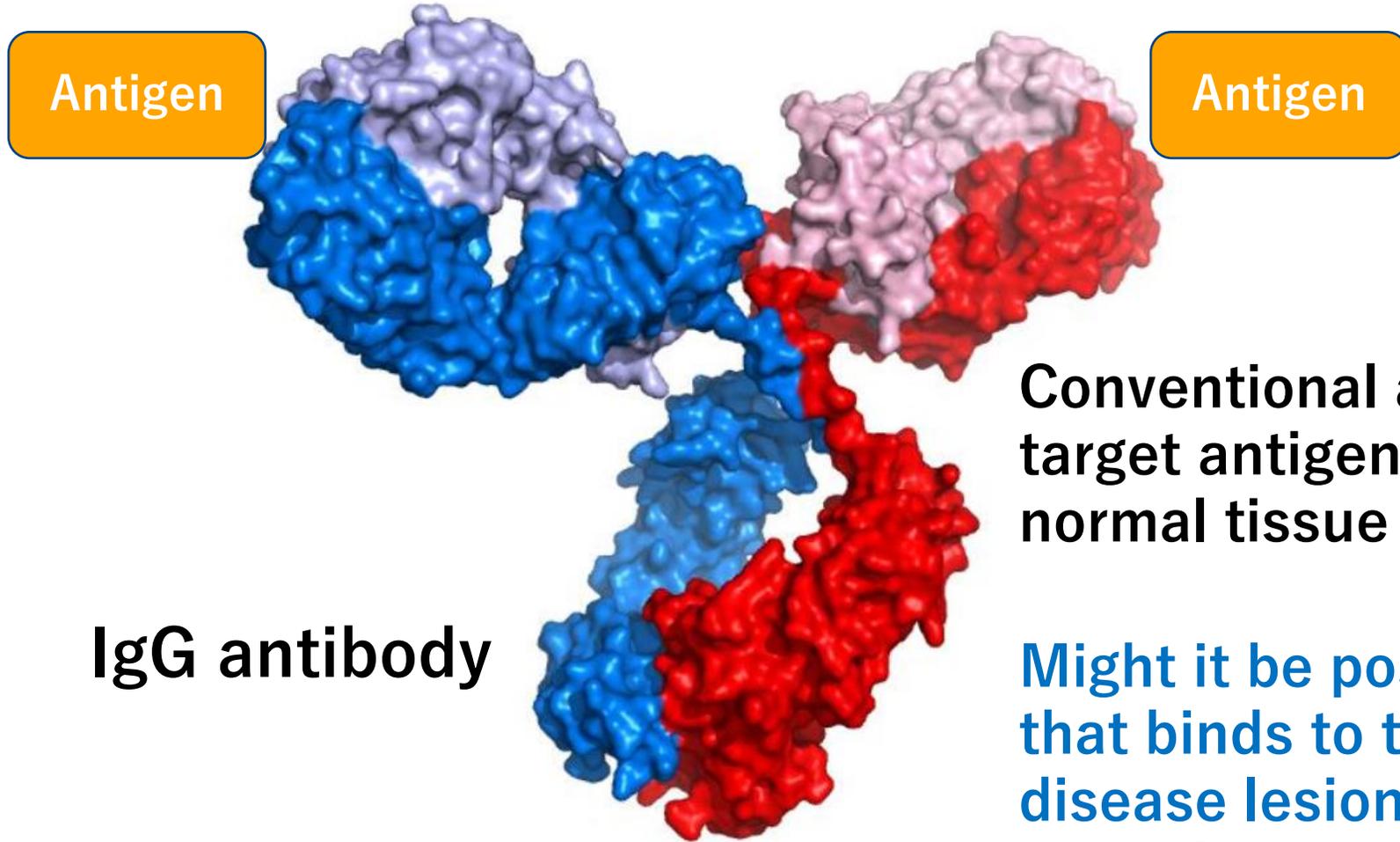
**Burden of
administration
time**



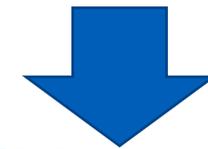
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**Patients can
self-administer
at home without
visiting the
hospital**

What Antibody Drugs Cannot Do (2)



Conventional antibody binds to the target antigen in both disease lesion and normal tissue



Might it be possible to make an antibody that binds to the target antigen only in disease lesion to reduce side effect in normal tissue?

Features Targeted with Switch Antibody™

Antibody drug is unusable because it causes systemic side effect

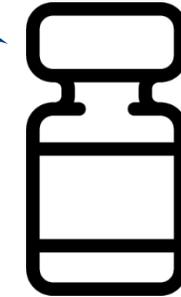


Specifically acts in disease lesion, reducing side effect

Liver toxicity

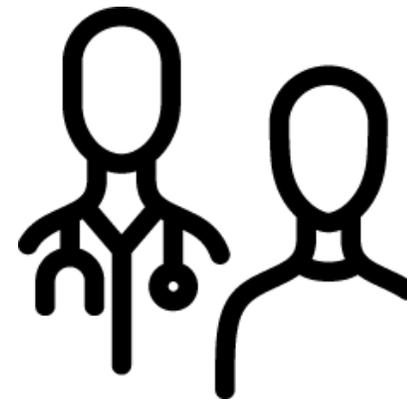
Immune system attacks normal tissue

Skin toxicity



Targets not druggable due to side effects can be targeted

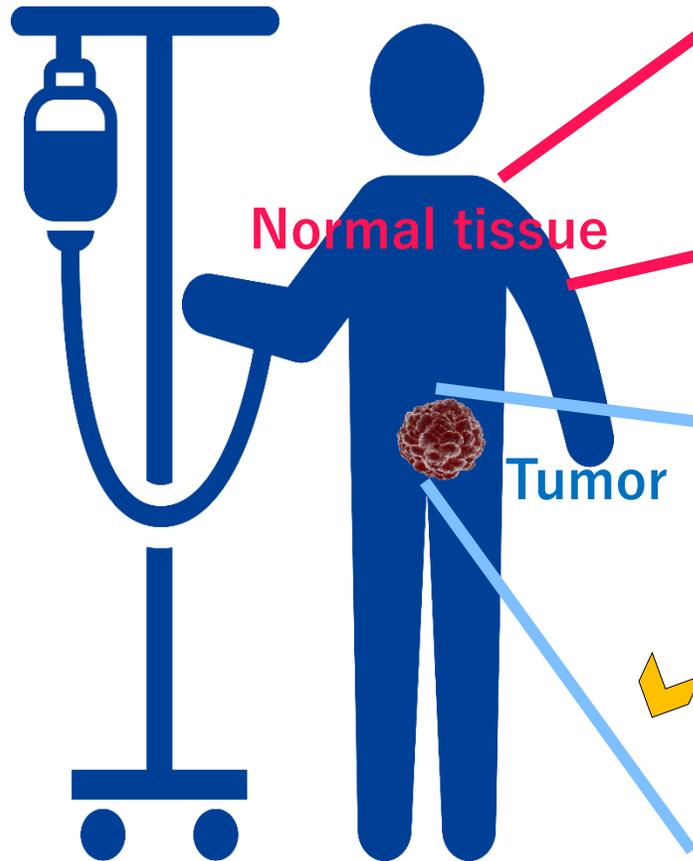
Patients can stay on treatment



Switch Antibody™ Technology

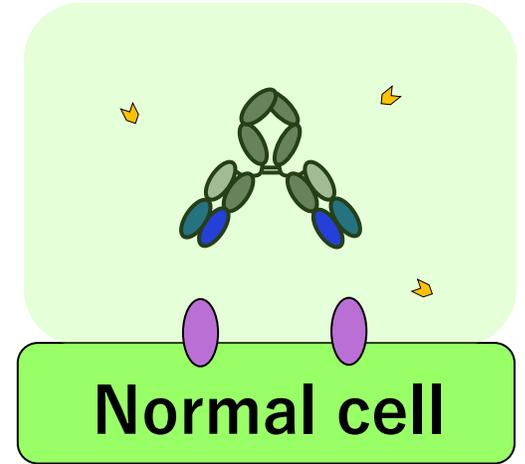
Antibody that specifically acts in disease lesion

Switch Antibody™



Switch OFF

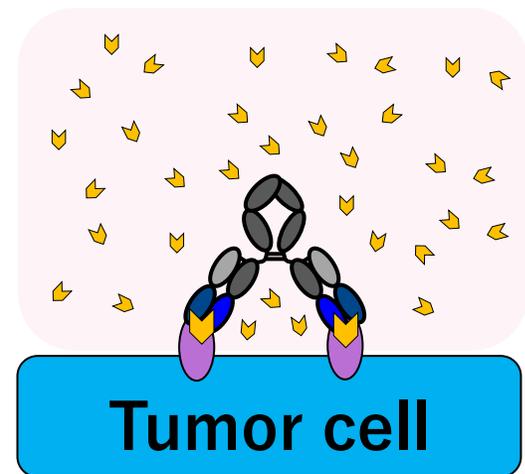
Does not bind to the target antigen in normal tissue because there are few switch molecules



Normal cell

Switch ON

Binds to the target antigen in tumors because there are many switch molecules



Tumor cell

Creating a Proprietary Pipeline with Recycling Antibody[®] and Switch Antibody[™]

*Chugai's first Recycling Antibody[®]
Approved/marketed*

✓ Marketed
✓ Filed

Enspryng[®]

ENSPRYNG ✓
IL6R
Recycling

Crovalimab ✓
C5
Recycling

GYM329
Myostatin
Sweeping*

AMY109
IL8
Recycling

RAY121
-
Recycling

STA551
CD137
Switch



↑
**Recycling Antibody[®]
technology
established**

↑
**Switch Antibody[™]
technology
established**

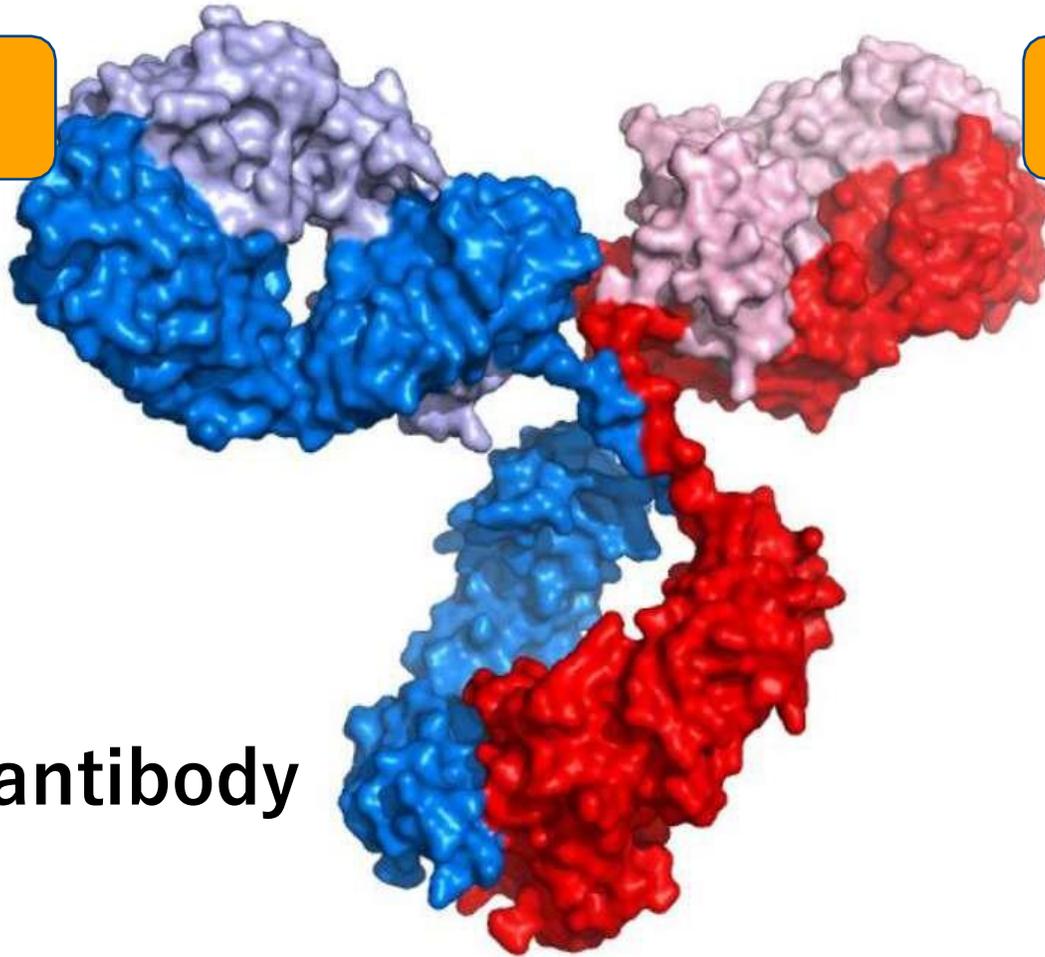
* Sweeping Antibody[®] is a further improved version of Recycling Antibody[®]

What Antibody Drugs Cannot Do (3)

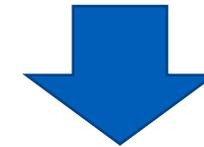
Antigen

Antigen

IgG antibody



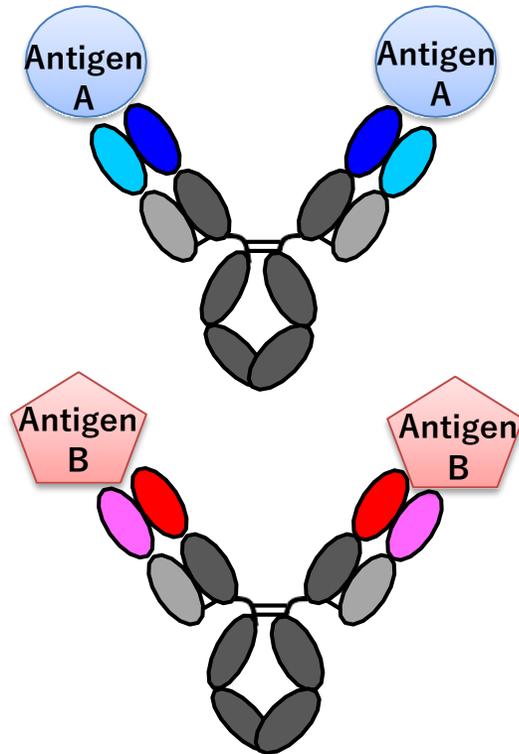
Conventional antibody binds to only one type of antigen and the function is limited to inhibition.



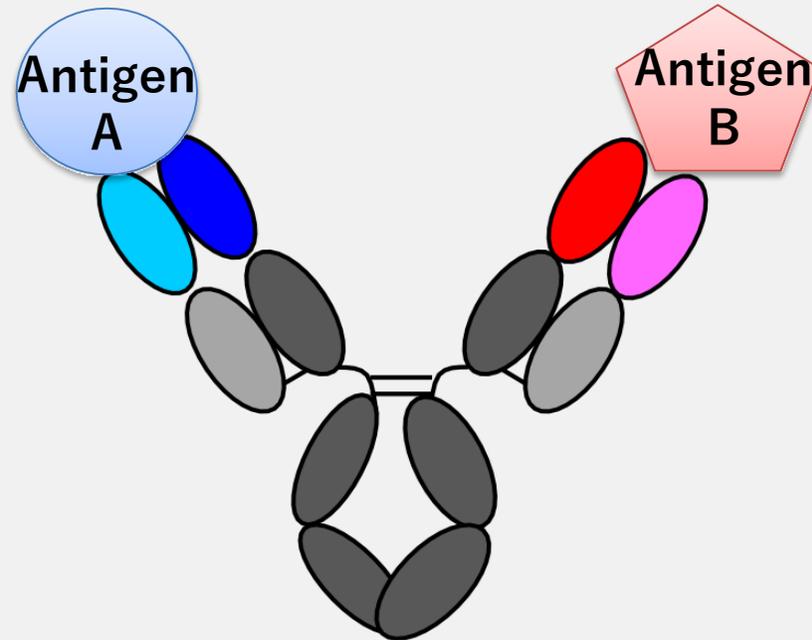
Might it be possible to make an antibody whose arms bind to different antigens to bring those antigens into proximity, and exhibit a new action not previously seen?

Bispecific Antibodies Capable of Binding to Two Different Antigens

Conventional antibody



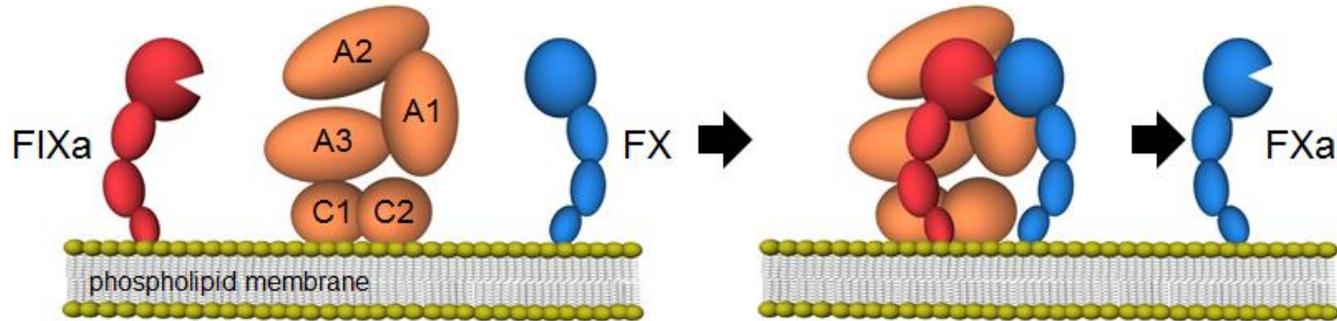
Bispecific antibody



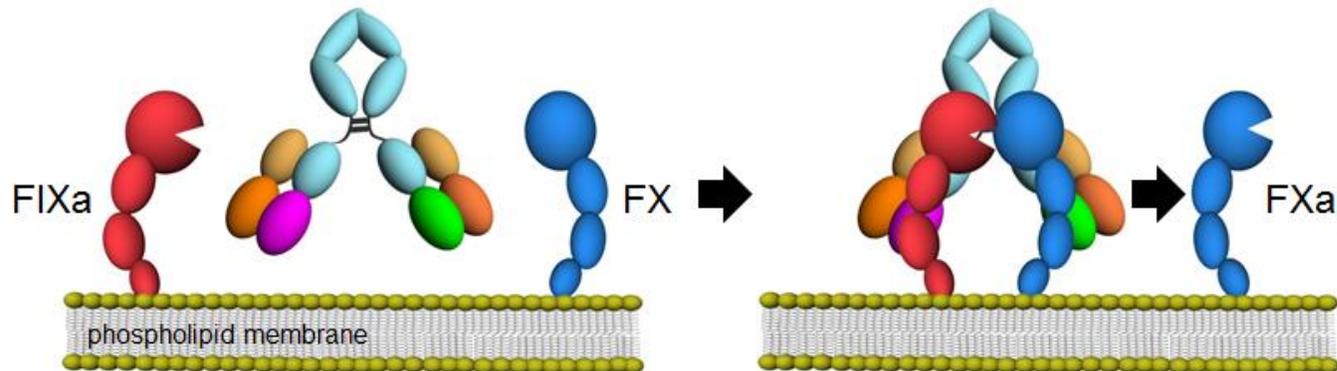
Treatment of Hemophilia A with Bispecific Antibody

Convenient subcutaneous formulation that can be self-injected at home

Coagulation factor
VIII



Bispecific antibody



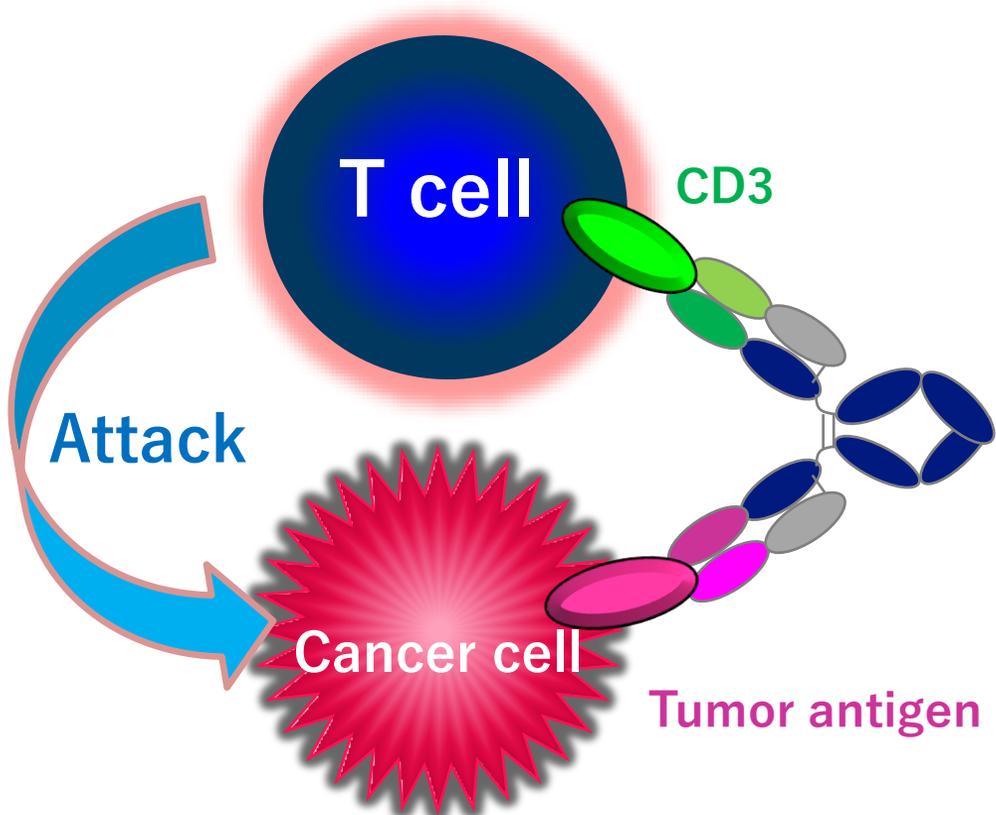
Hemlibra[®]

Kitazawa et al, Nature Medicine, 2012.

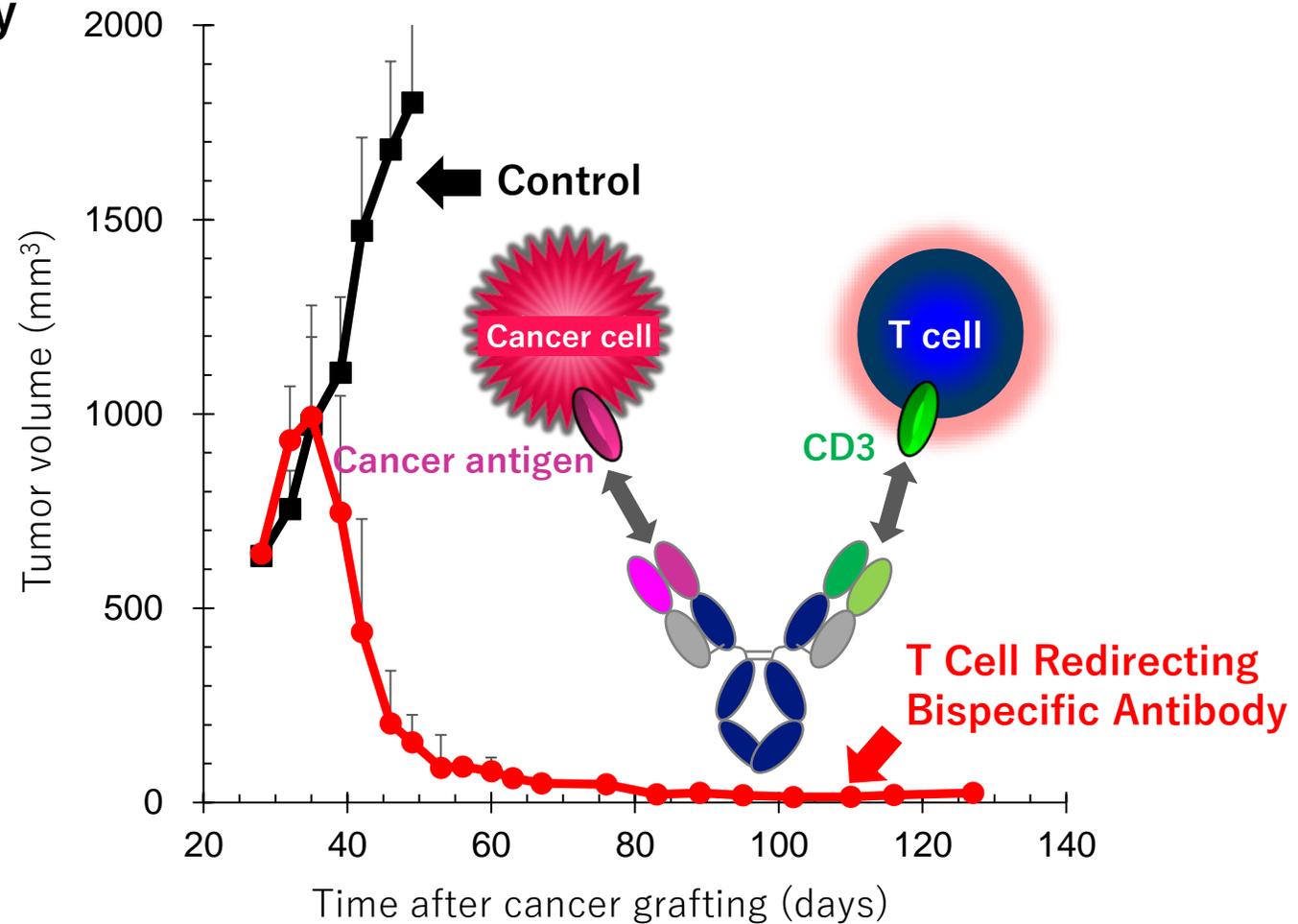
Oldenburg J, et al, N Engl J Med. 2017.

T Cell Redirecting Bispecific Antibody to Attack Tumor Cell

T Cell Redirecting Bispecific Antibody



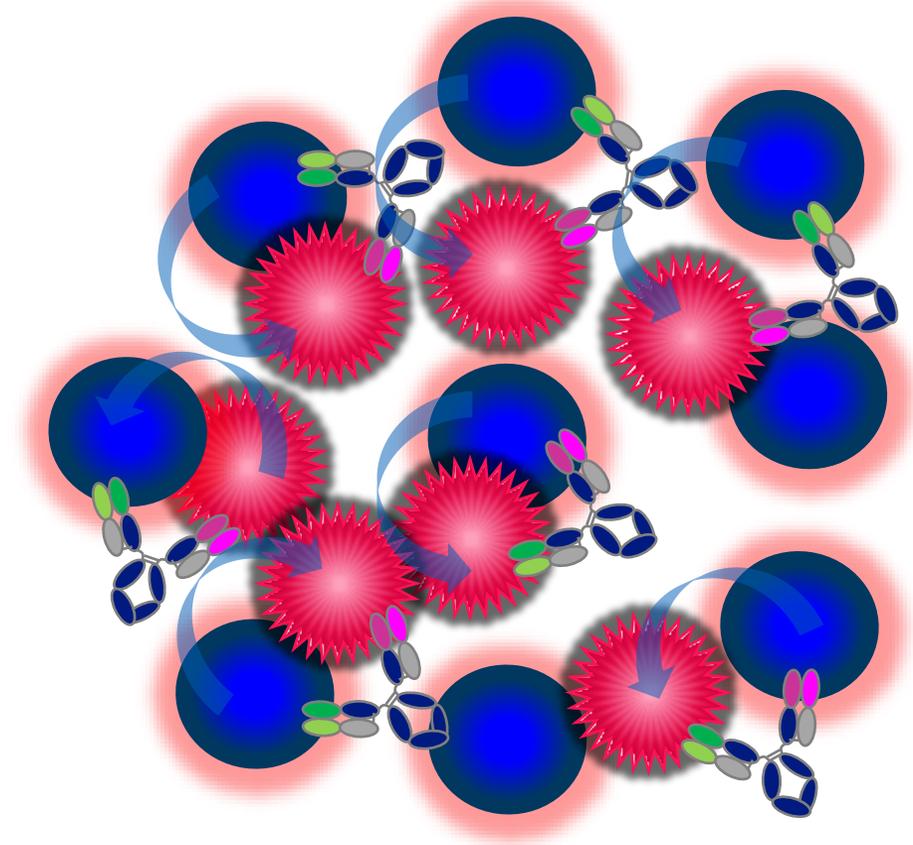
Anti-tumor activity in mice



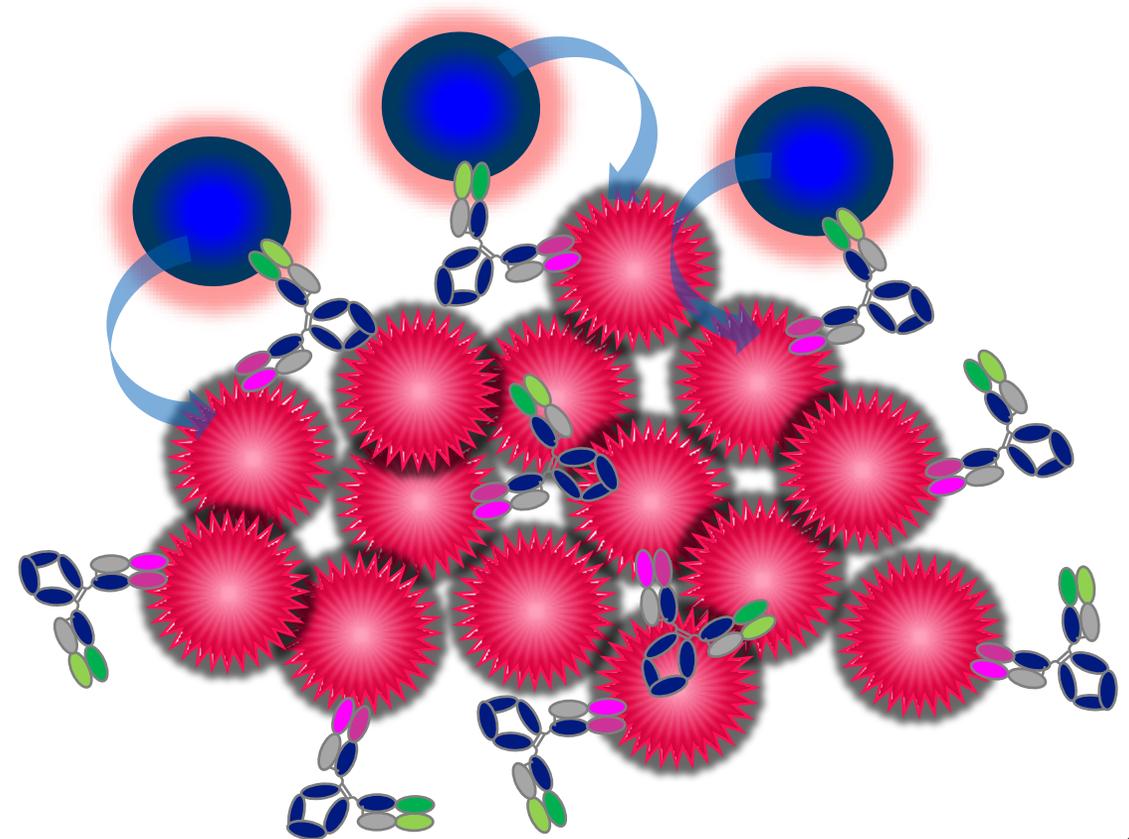
Ishiguro T. et al. Sci Trans Med 2017.

When Few T Cells are Present in Tumor site, the Effects of T Cell Redirecting Bispecific Antibody are Limited

High anti-tumor activity is achieved when sufficient T cells are present

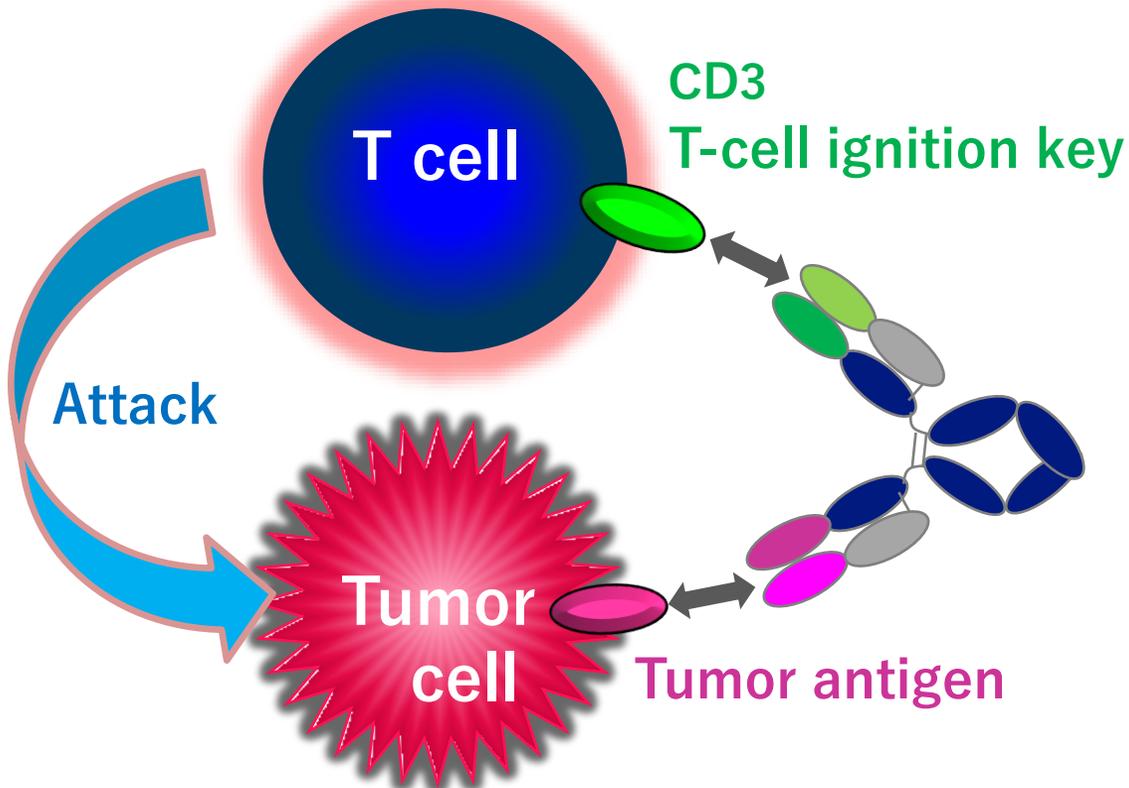


Anti-tumor activity is limited when few T cells are present

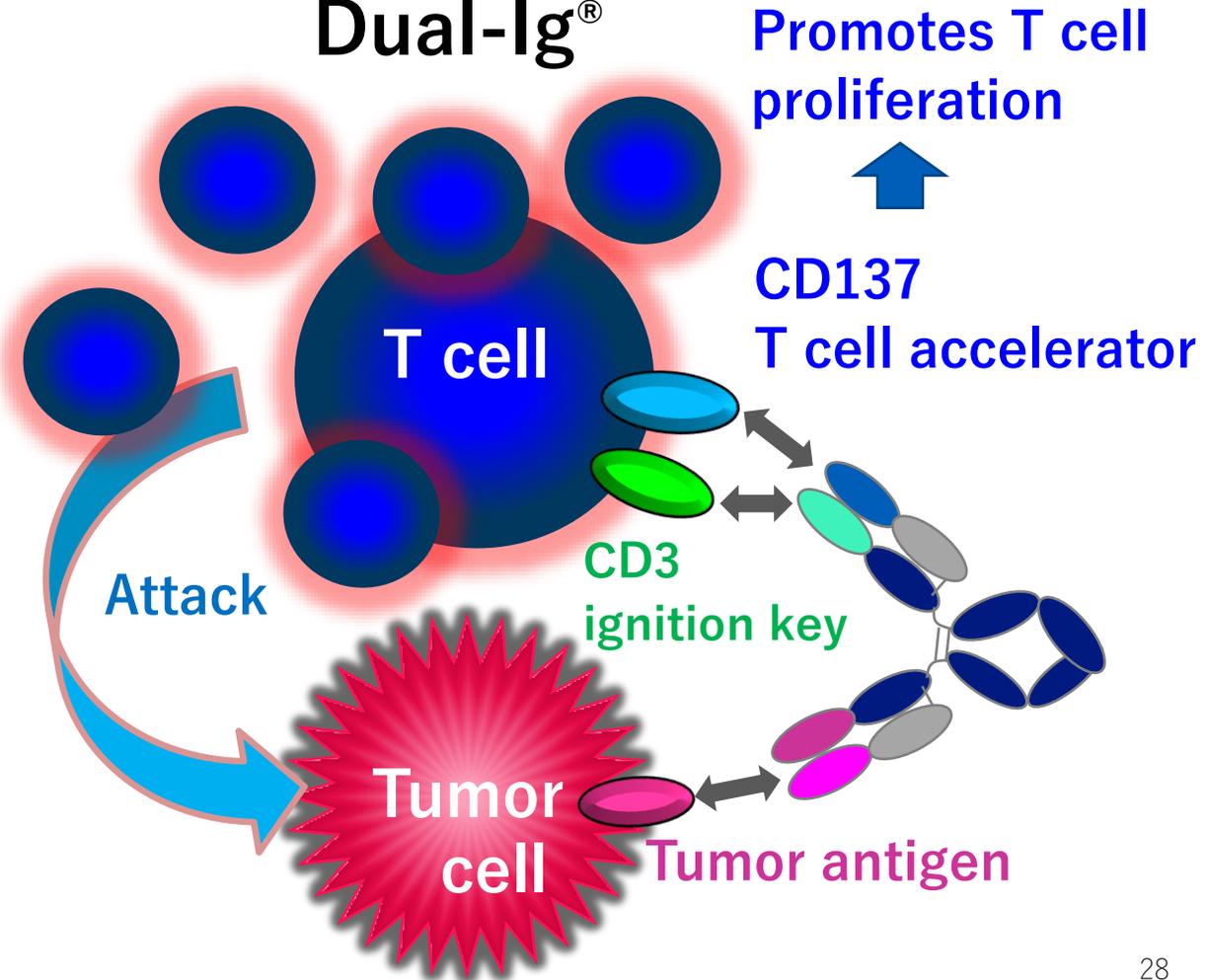


Designing a Second-generation T Cell Redirecting Bispecific Antibody

1st generation TRAB™

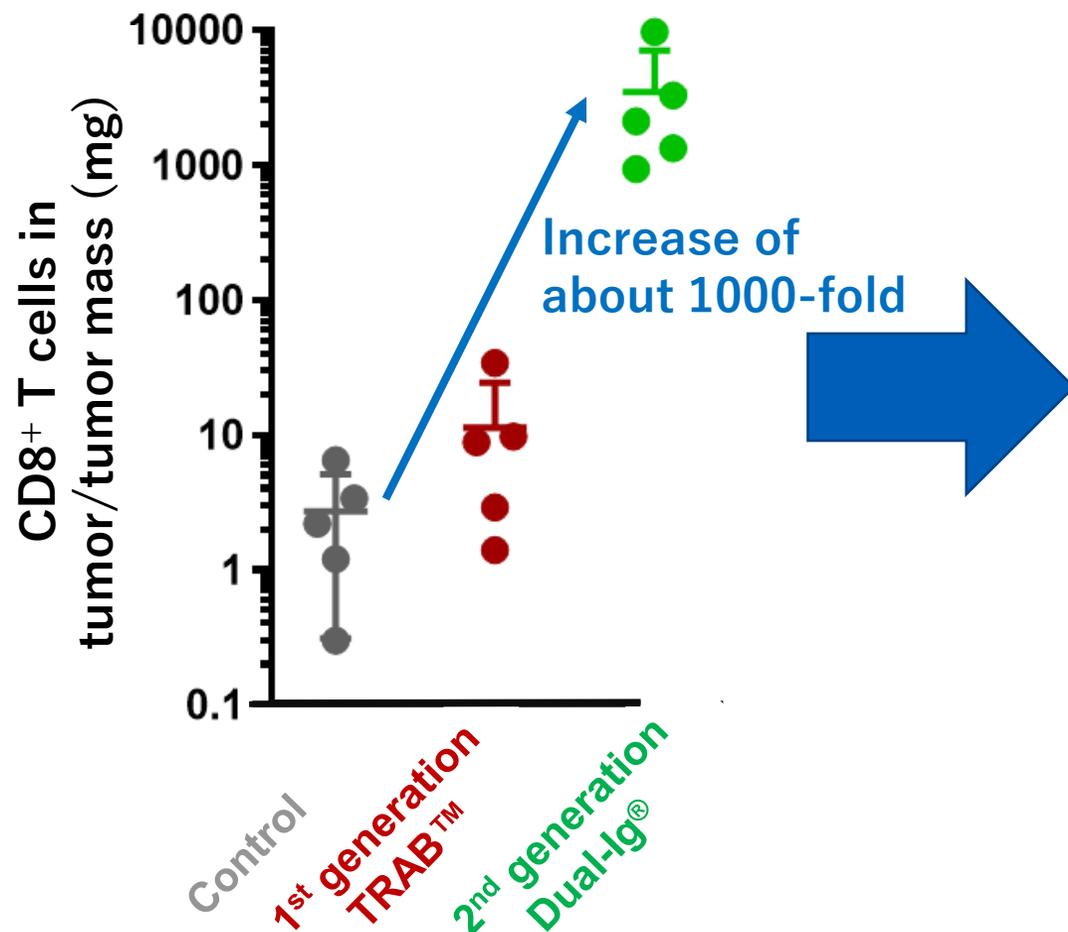


2nd generation Dual-Ig[®]

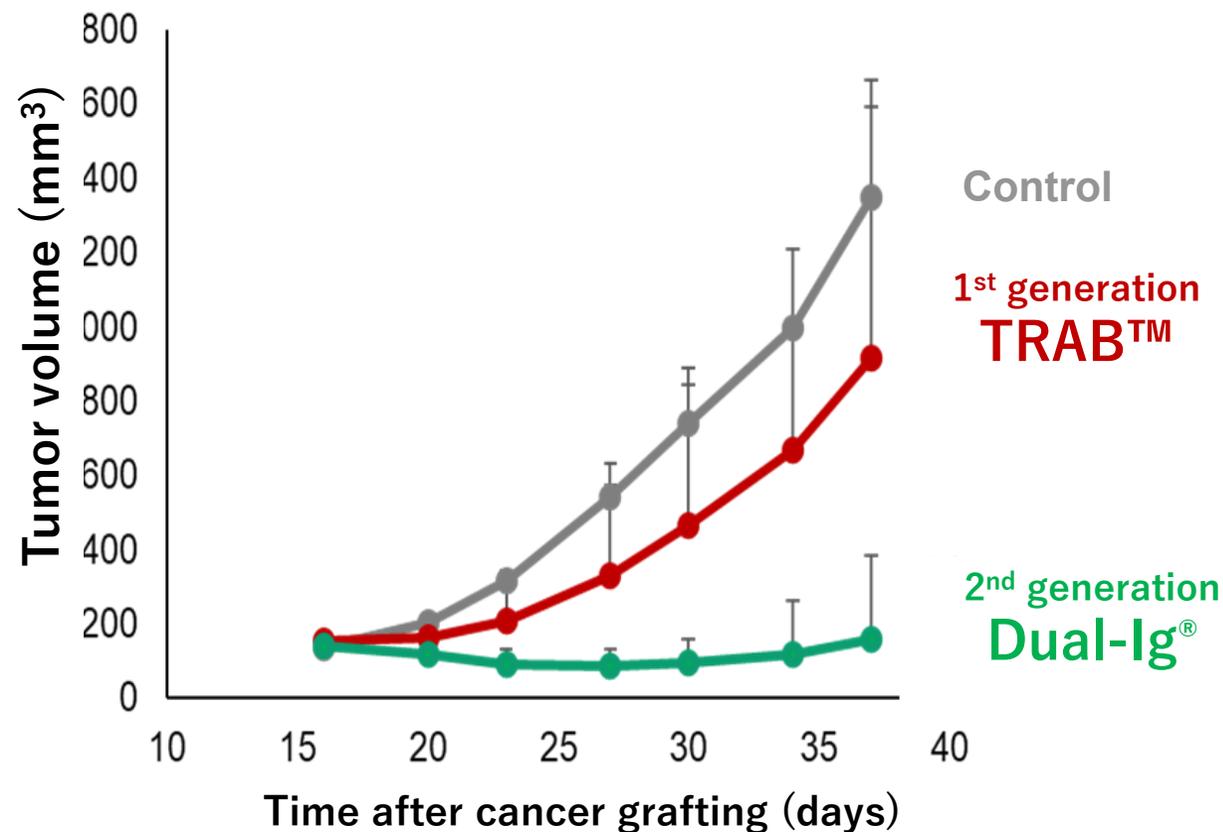


2nd Generation T cell Redirecting Bispecific Antibody, Dual-Ig[®] Greatly Increases the Level of T Cells Capable of Attacking Tumors

Number of T cells in mouse tumor



Anti-tumor activity in mice



Creating a Proprietary Pipeline with Bispecific Antibody Technology

✓ Marketed

The world's first human IgG bispecific antibody: Approved and marketed

Hemlibra
FIXa/FX
bispecific ✓

NXT007
FIXa/FX
bispecific

ERY974
GPC3/CD3
bispecific

DONQ52
DQ2.5/gluten
bispecific

ALPS12
DLL3/CD3/CD137
Dual-Ig®



↑
Bispecific antibody
technology established

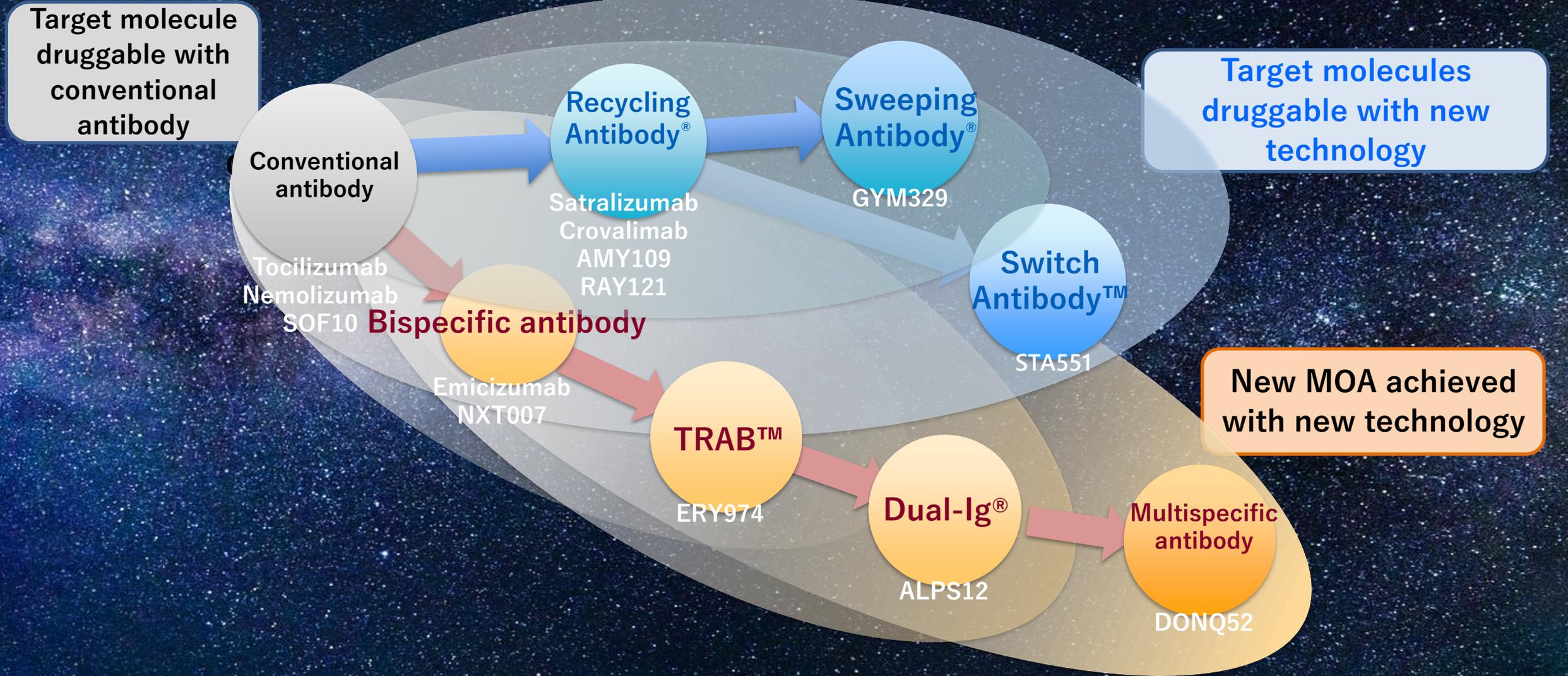
→
Evolution of
technology

↑
Establishment of
technology for 1st T cell
redirecting bispecific
antibody (TRAB™)

→
Evolution of
technology

↑
Establishment of
technology for 2nd T-cell
redirecting bispecific
antibody (Dual-Ig®)

Expanding Drug Space with Proprietary Innovative Antibody Technologies



Contact Information

Investor Relations Group, Corporate Communications Dept.

Phone: +81-3-3273-0554

Email: ir@chugai-pharm.co.jp

Personnel: Takayuki Sakurai, Hideki Sato,
Tomoyuki Shimamura, Sachiyo
Yoshimura, Yayoi Yamada

INNOVATION BEYOND IMAGINATION