



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

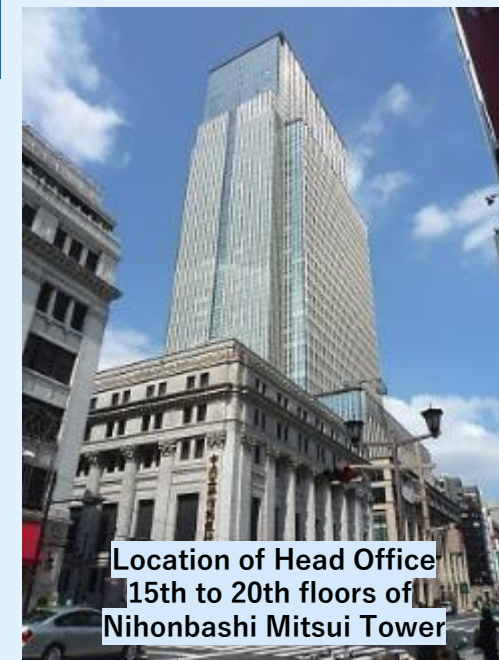
### A Unique Business Model

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

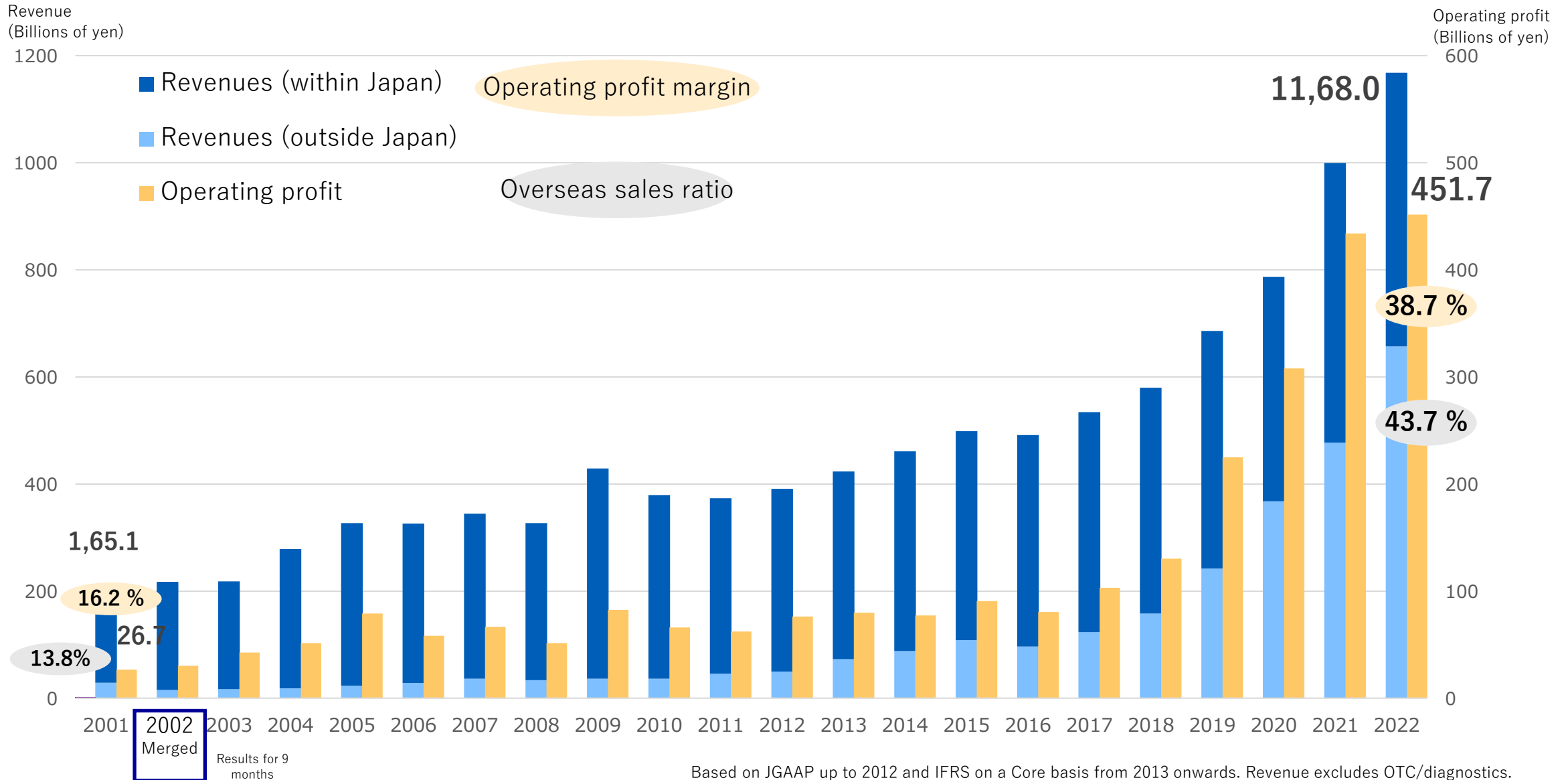
Chugai autonomously operates as an independent listed company

### 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.

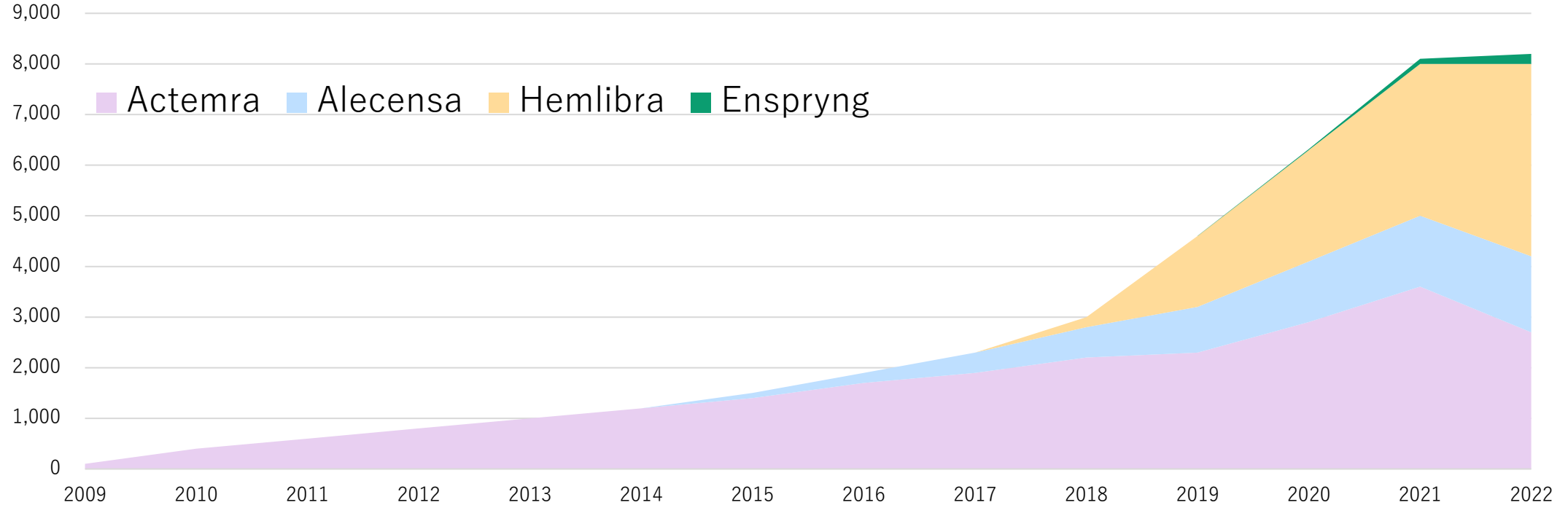


# Trajectory of 20 Years



# Global Sales of Chugai Originated Products

(millions of CHF)



## 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

## Products from Chugai research

Specialize in innovative, challenging drug discovery



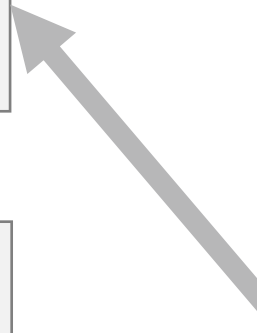
Out-licensing products to Roche enables accelerated global development and marketing

## Products in-licensed from Roche

Exclusively develop and deliver promising new-drug candidates in Japanese market



Secure stable revenue base in domestic market



# Features of the Earnings Structure Apparent in Our Unique Business Model

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

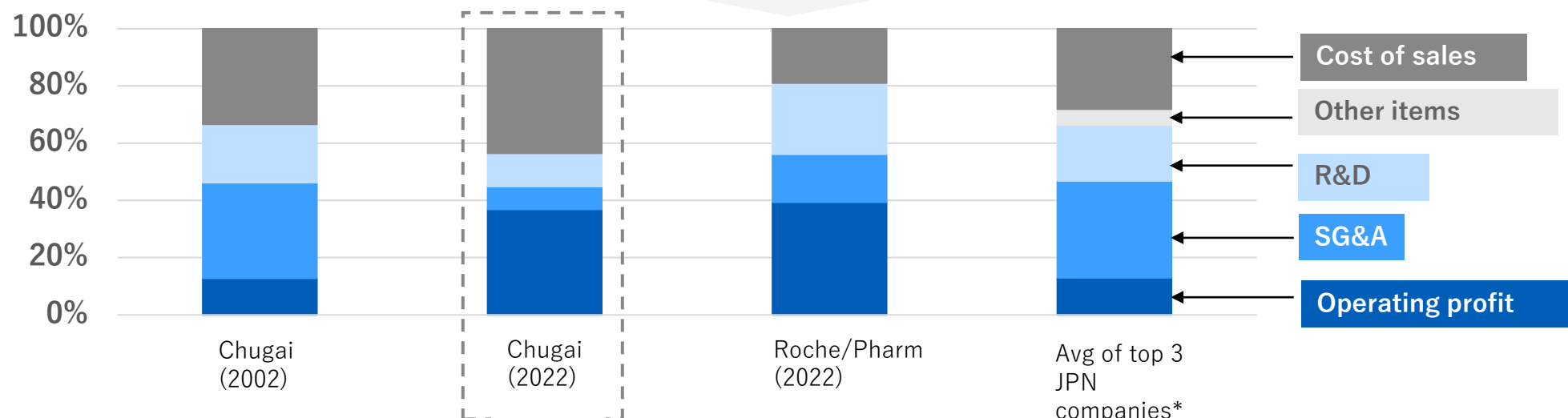
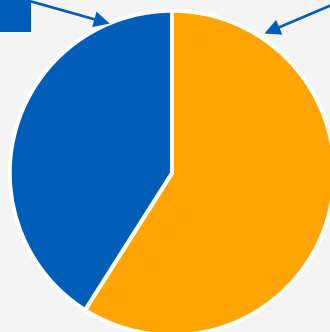
### Share of revenue (2022)

**Products in-licensed from Roche (41%)**

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

**Products from Chugai research (59%)**

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



# 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

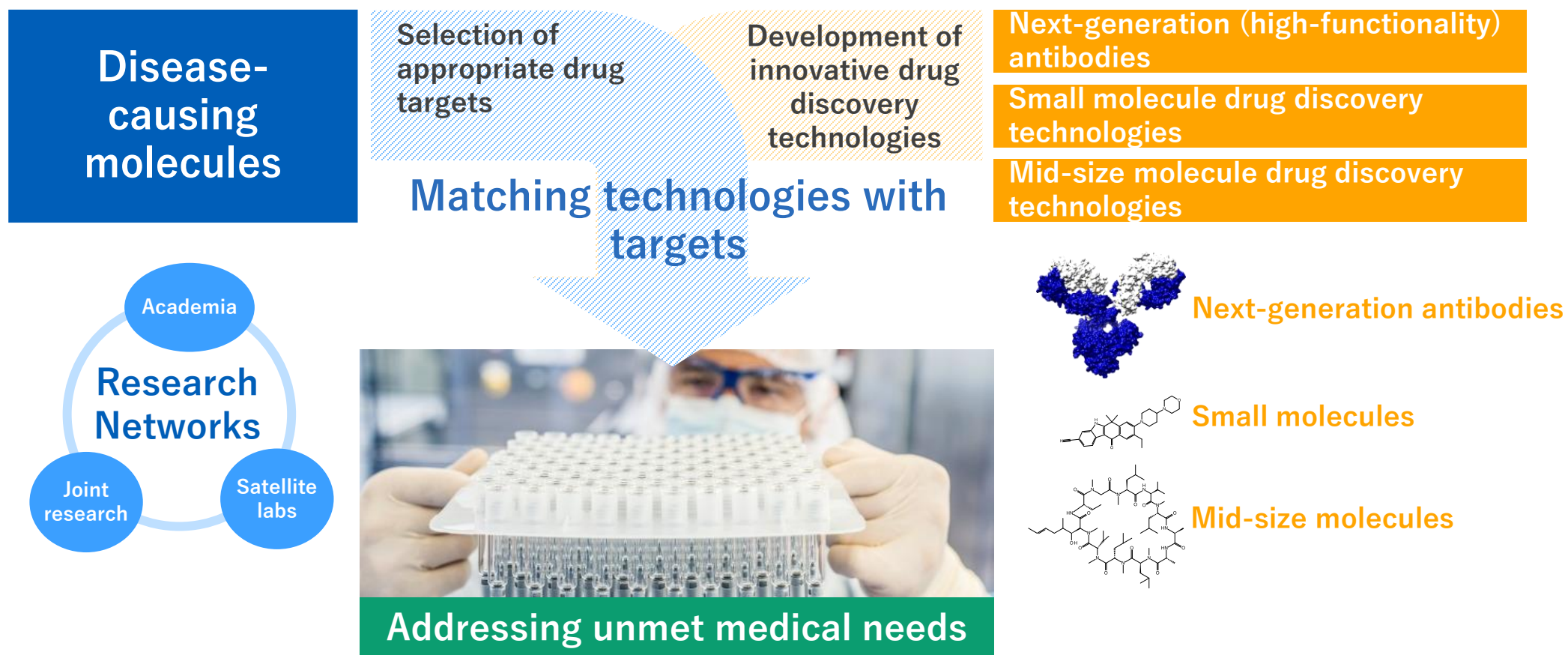
▶ DX

▶ 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

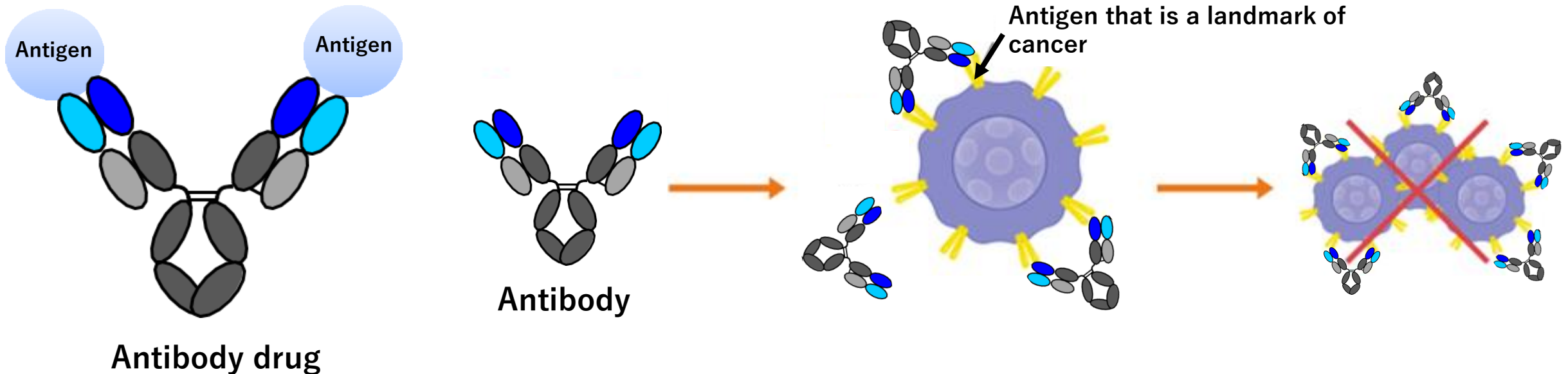
Associate Vice President, Head of Translational Research Div.

**Dr. Tomoyuki Igawa**

# What is an Antibody Drug?

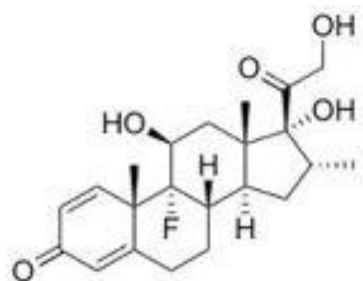
When a pathogen or other **foreign substance (antigen)** enters the body, **antibodies** exhibit **an antigen-antibody reaction** that binds to the foreign substance and detoxifies it as an immune reaction.

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

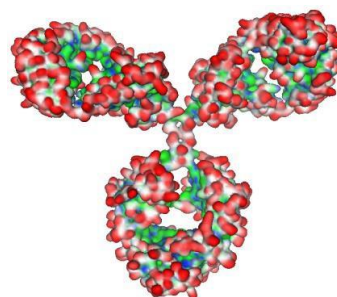


# From Small Molecules to Antibodies and then Next-generation Antibodies

Small molecule  
drugs



Antibody  
drugs

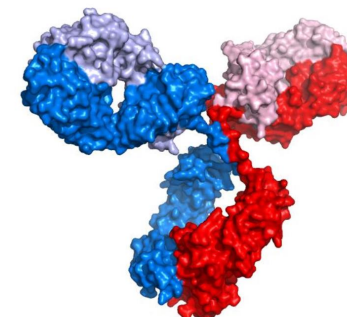


Antibody binds to target,  
inhibiting its activity.

Actemra®

Mitchga®

Next-generation  
antibody drugs

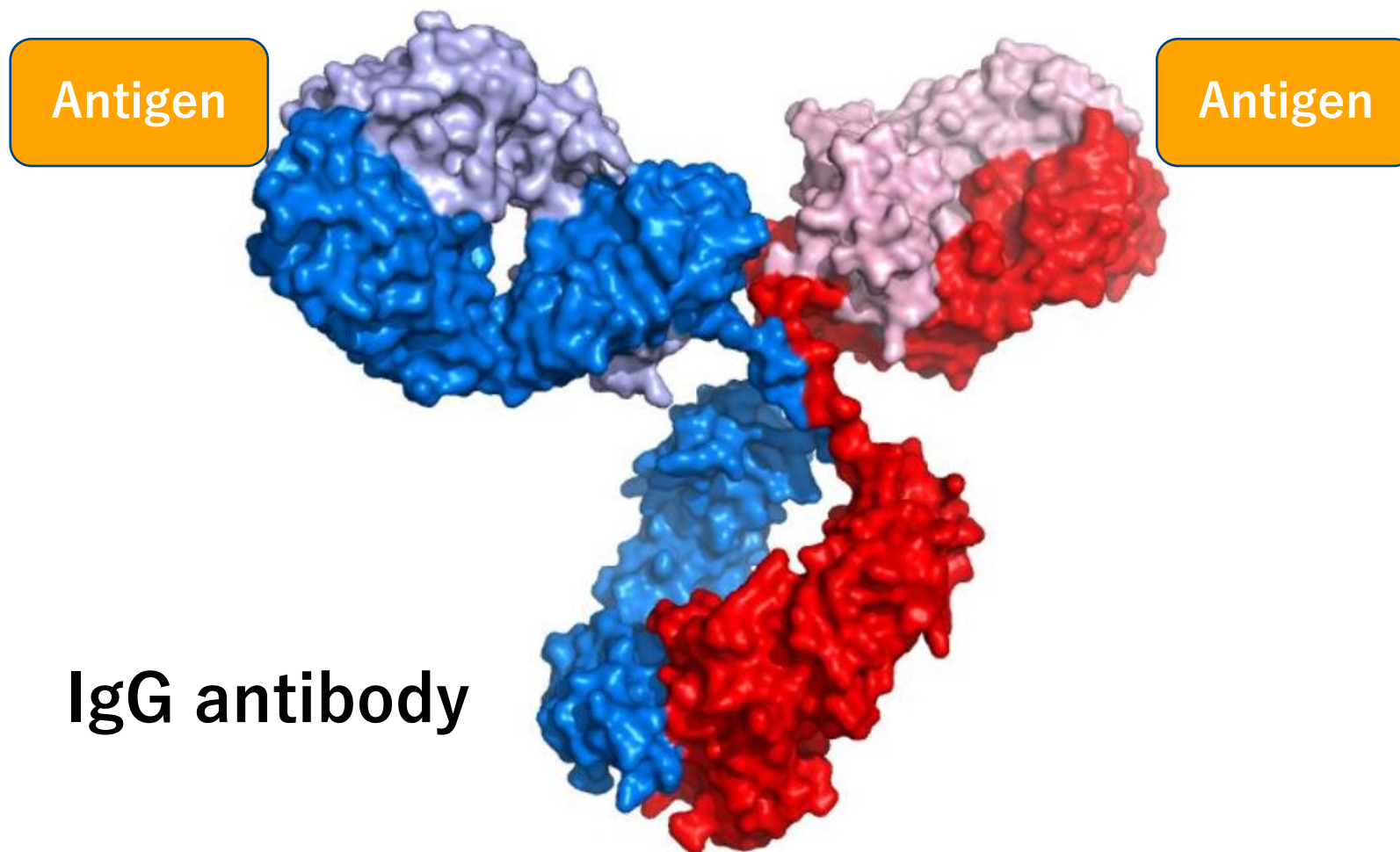


Antibody engineering  
technologies are used to make  
next-generation antibodies  
capable of actions not possible  
with conventional antibodies

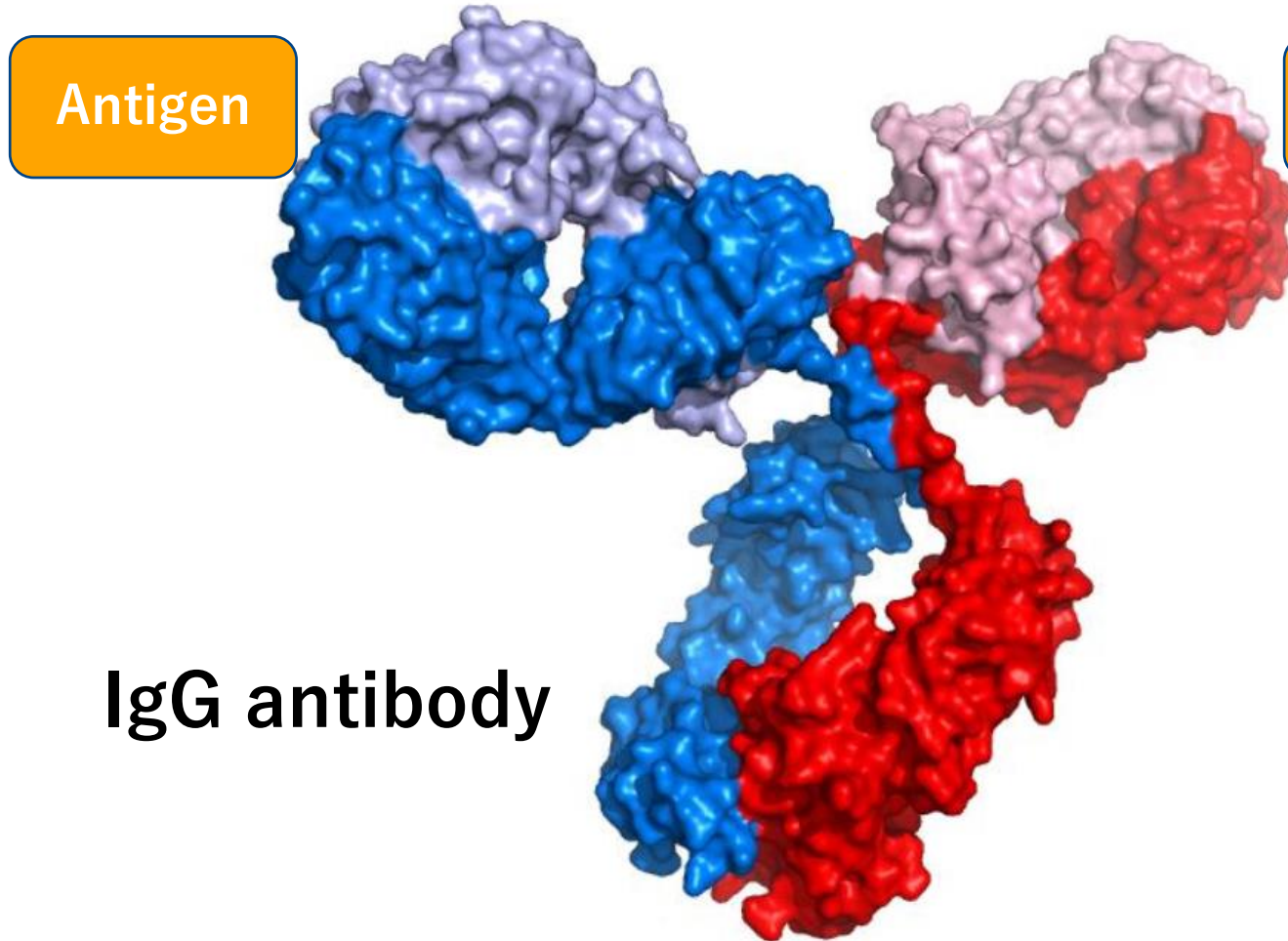
Hemlibra®

Enspryng®

# Looking Deep into Antibodies to Make the Impossible Possible



# What Antibody Drugs Cannot Do (1)



Antigen

Conventional antibodies can bind to an antigen only once.

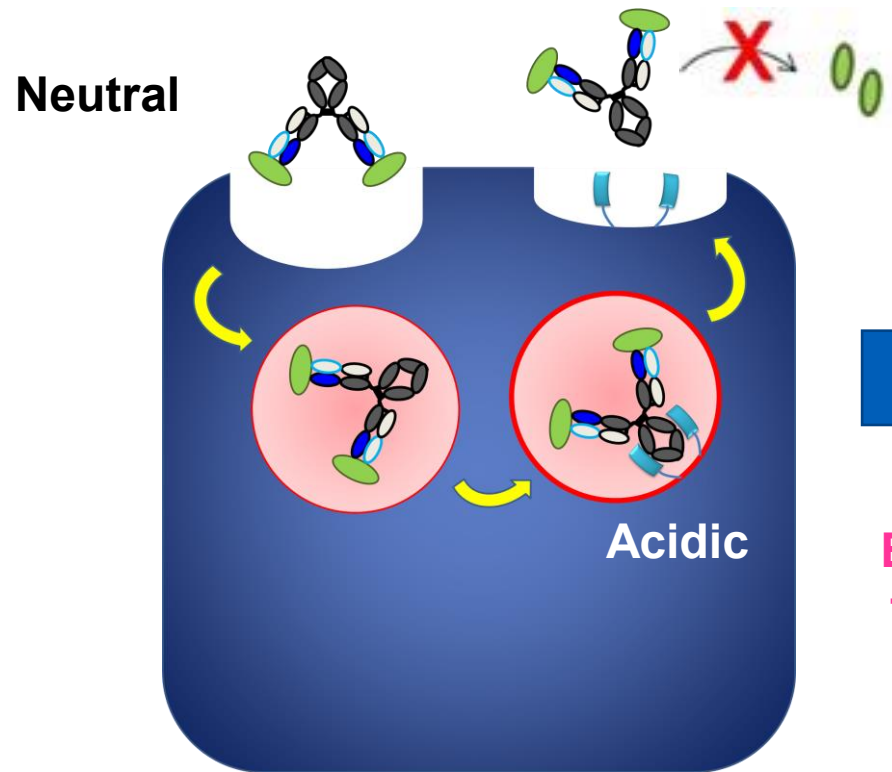


Might it be possible to make an antibody that binds to antigens multiple times and thereby works more efficiently?

# Recycling Antibody<sup>®</sup>

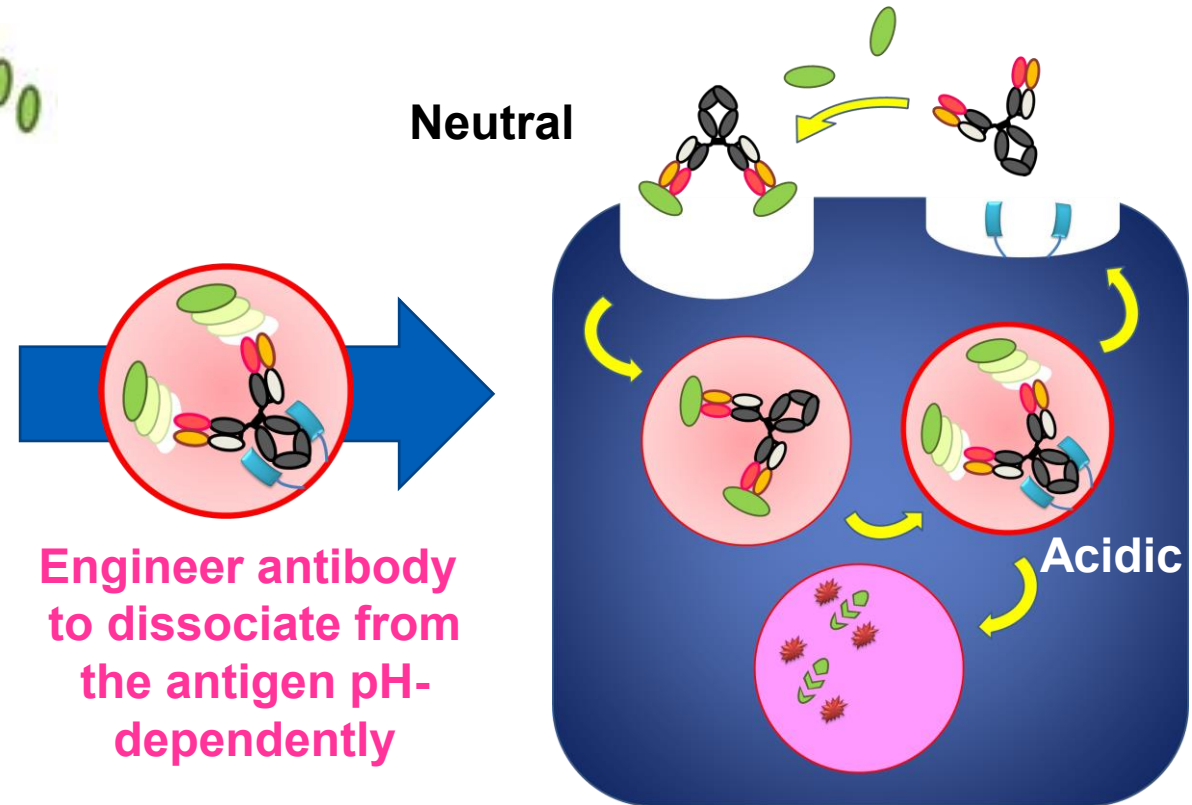
Antibody that binds to antigens many times, maintaining long-term efficacy

## Conventional Antibody



Antibody binds to the antigen  
only once

## Recycling Antibody<sup>®</sup>



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**

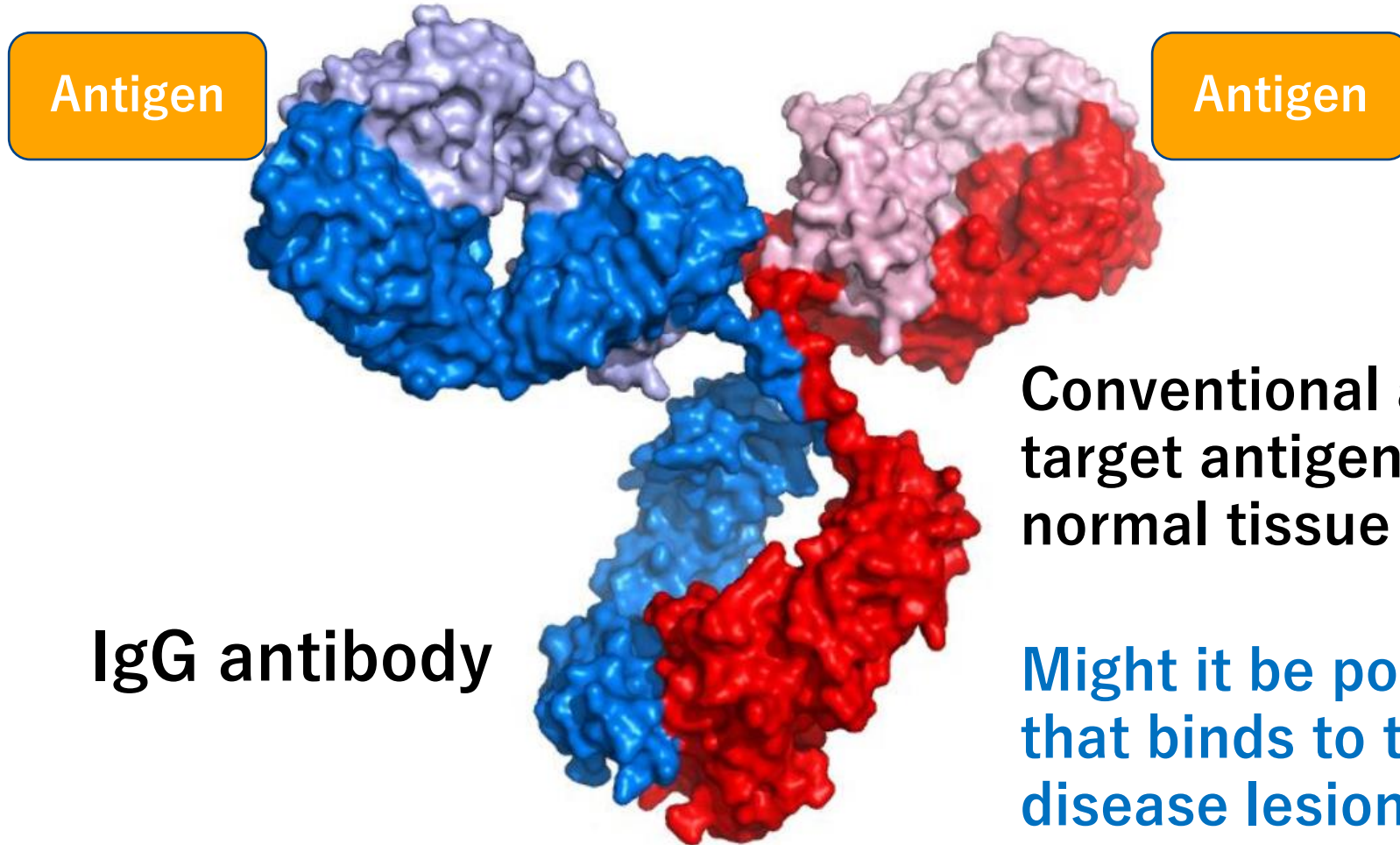
**Burden of  
administration  
time**



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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**

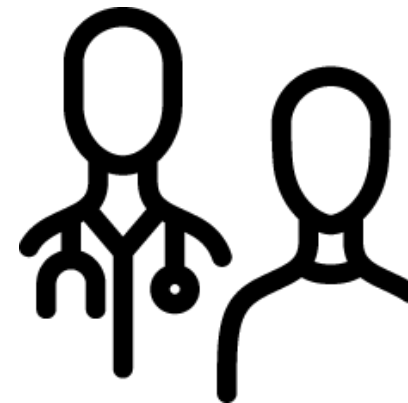
**Immune  
system attacks  
normal tissue**

**Skin toxicity**



**Targets not  
druggable due to  
side effects can be  
targeted**

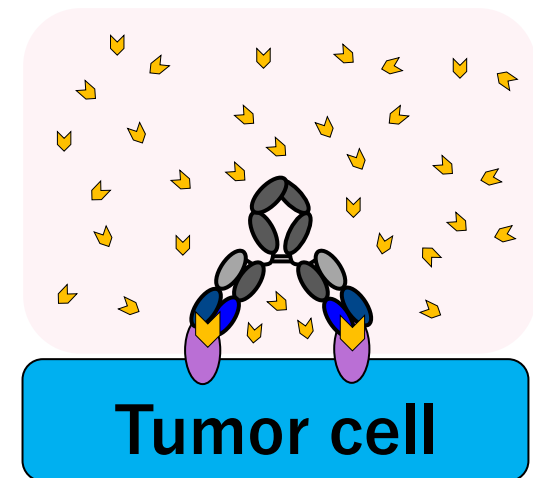
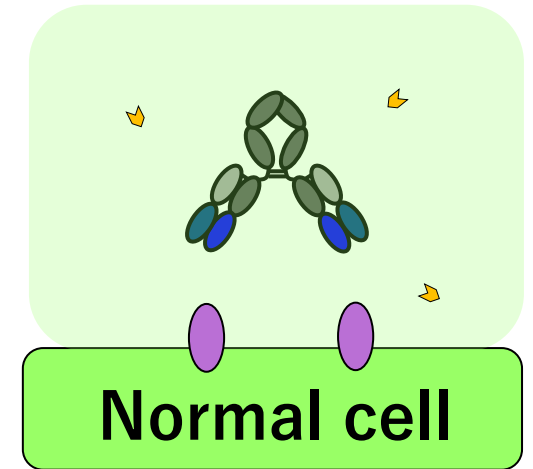
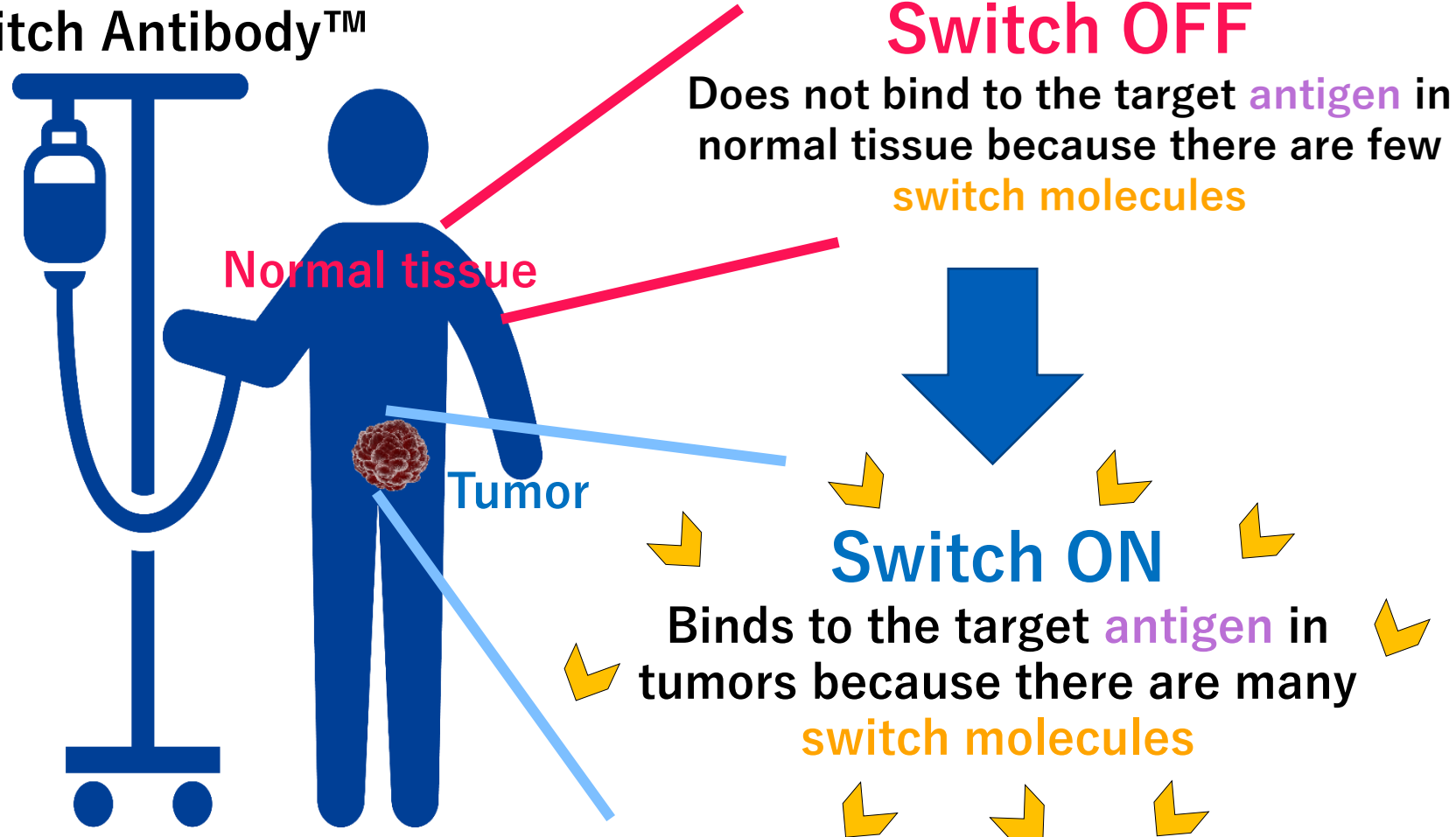
**Patients can stay on  
treatment**



# Switch Antibody™ Technology

Antibody that specifically acts in disease lesion

Switch Antibody™



# Creating a Proprietary Pipeline with Recycling Antibody<sup>®</sup> and Switch Antibody<sup>™</sup>

*Chugai's first Recycling Antibody<sup>®</sup>  
Approved/ marketed*

✓ Marketed  
✓ Filed

**Enspryng<sup>®</sup>**

**ENSPRYNG** ✓  
IL6R  
Recycling

**Crovalimab** ✓  
C5  
Recycling

**GYM329**  
Myostatin  
Sweeping\*

**AMY109**  
IL8  
Recycling

**RAY121**  
-  
Recycling

**STA551**  
CD137  
Switch

2008-2013

2014-2017

2018-2021

↑  
**Recycling Antibody<sup>®</sup>  
technology  
established**

↑  
**Switch Antibody<sup>™</sup>  
technology  
established**

\* Sweeping Antibody<sup>®</sup> is a further improved version of Recycling Antibody<sup>®</sup>

# What Antibody Drugs Cannot Do (3)

Antigen

Antigen

IgG antibody

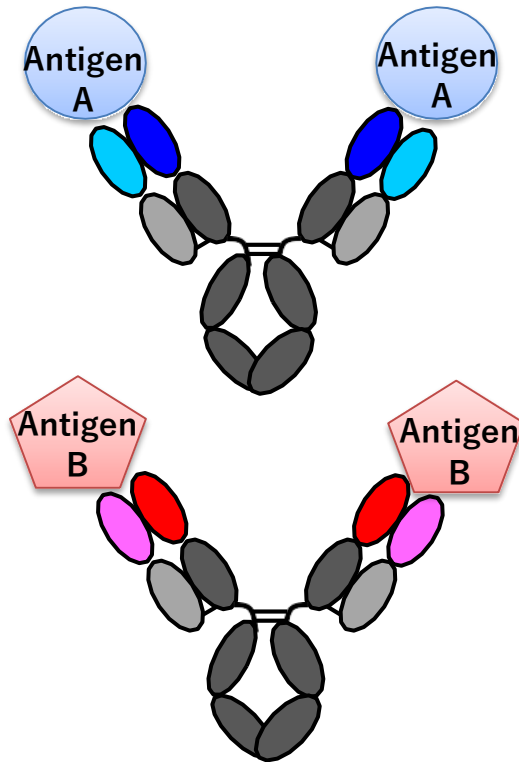
Conventional antibody binds to only one type of antigen and the function is limited to inhibition.



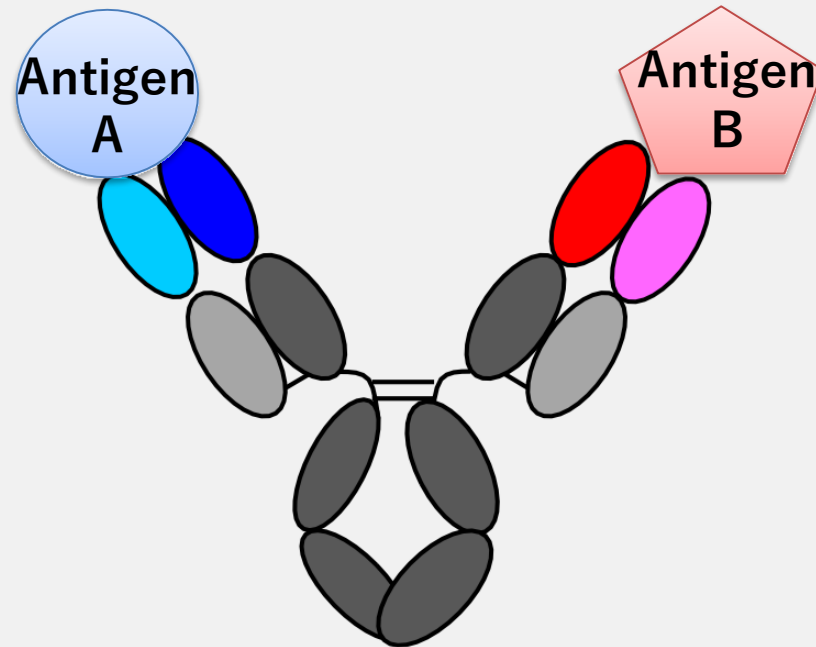
Might it be possible to make an antibody whose arms bind to different antigens to bring those antigens into proximity, and exhibit a new action not previously seen?

# Bispecific Antibodies Capable of Binding to Two Different Antigens

Conventional antibody



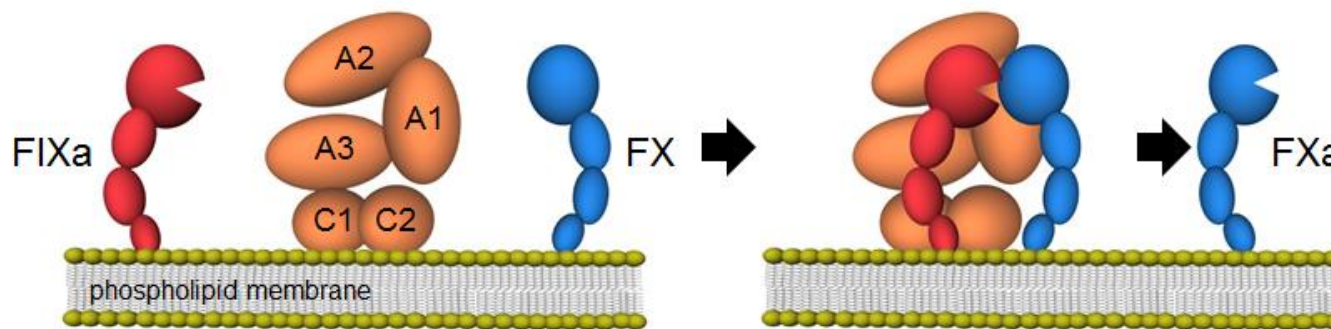
Bispecific antibody



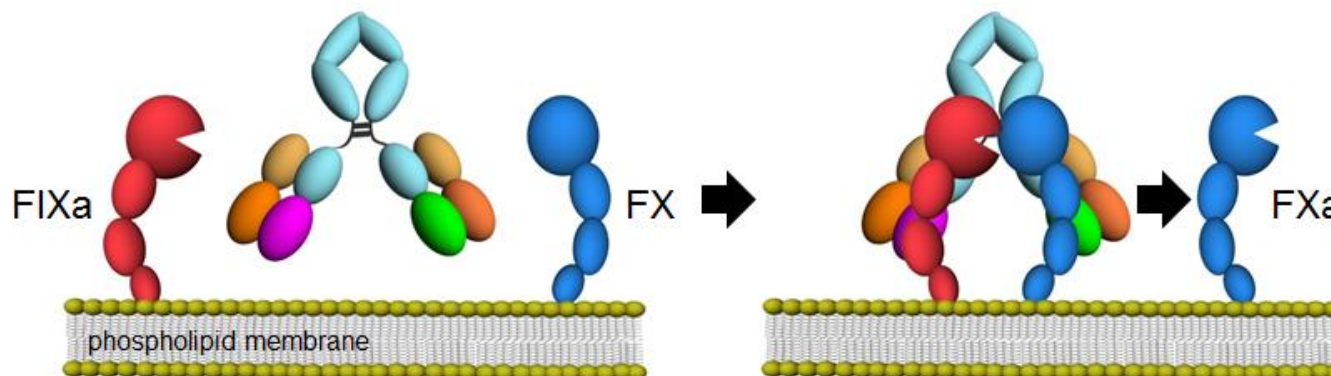
# Treatment of Hemophilia A with Bispecific Antibody

Convenient subcutaneous formulation that can be self-injected at home

Coagulation factor  
VIII



Bispecific antibody

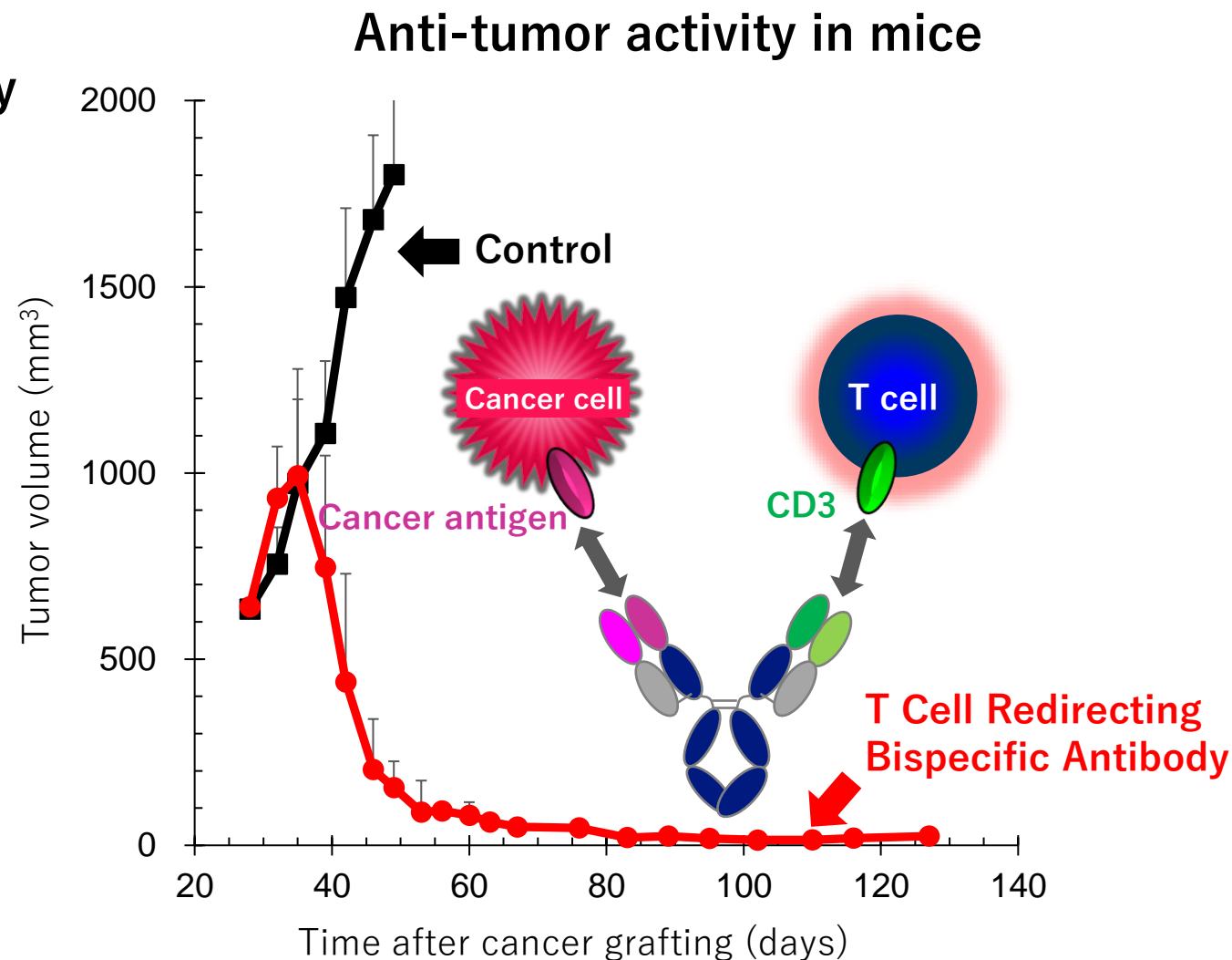
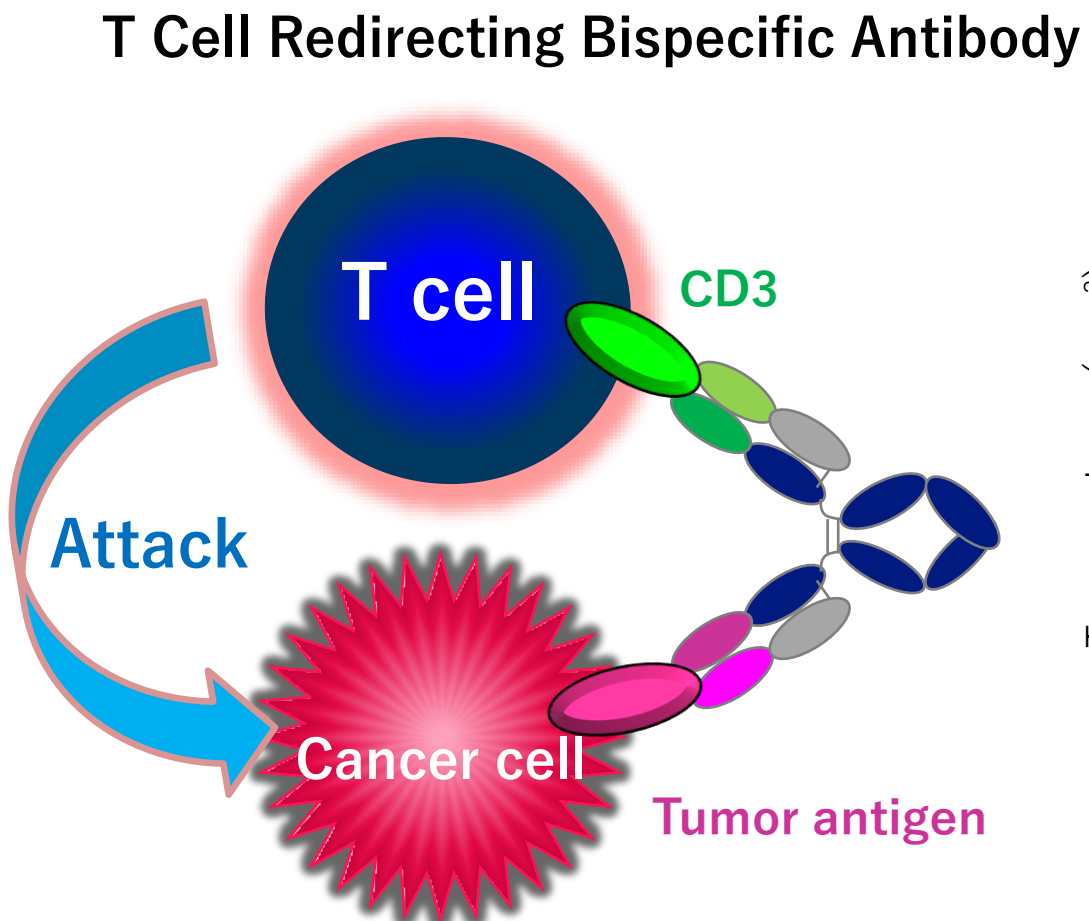


**Hemlibra®**

Kitazawa et al, Nature Medicine, 2012.

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

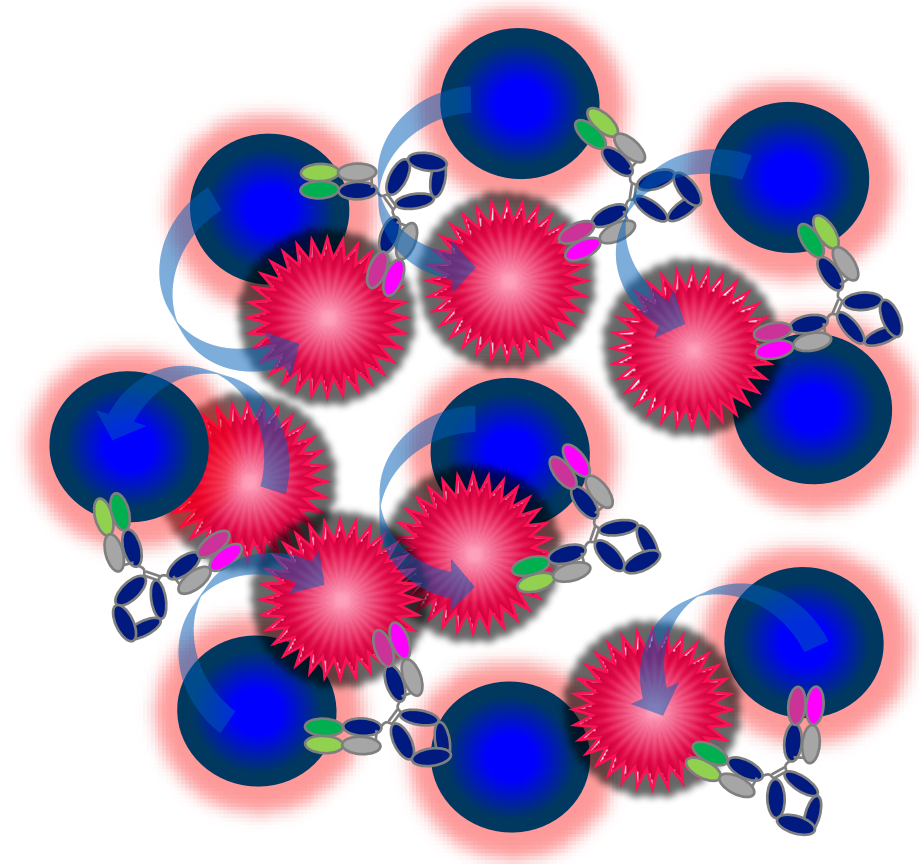
# T Cell Redirecting Bispecific Antibody to Attack Tumor Cell



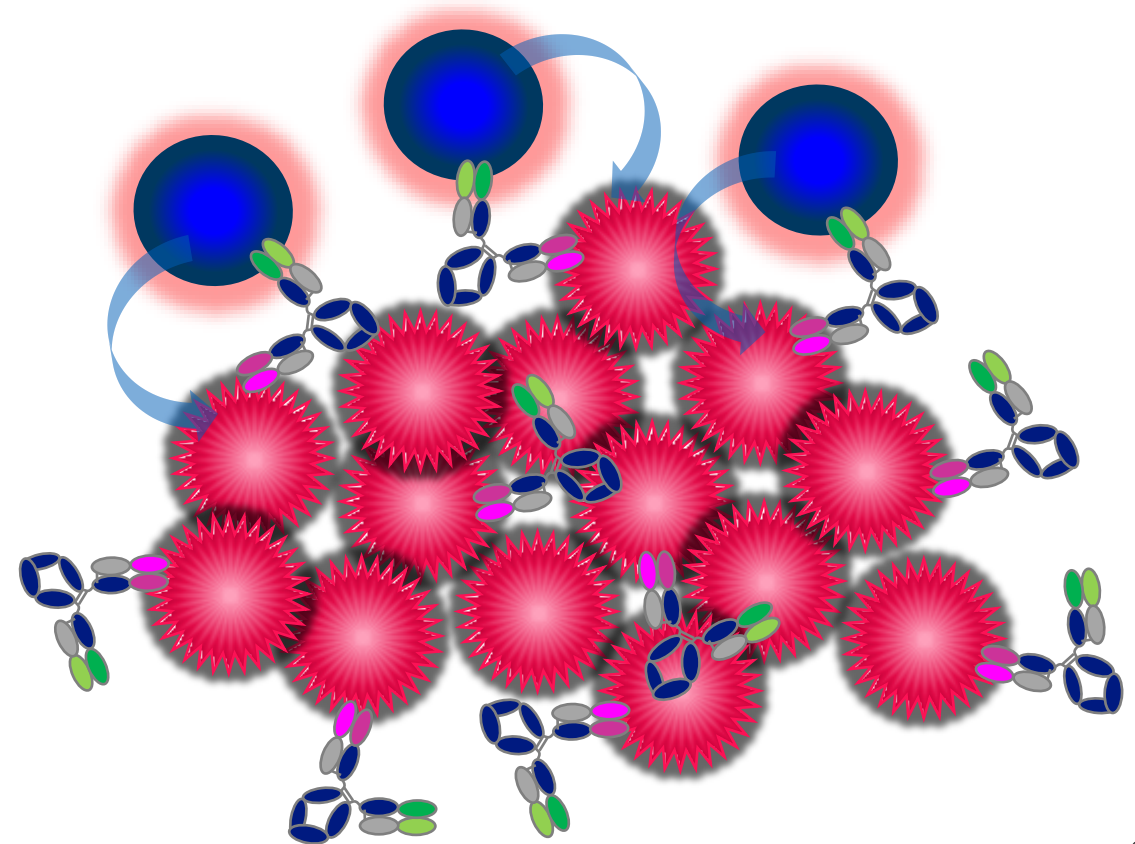
Ishiguro T. et al. Sci Trans Med 2017.

# 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

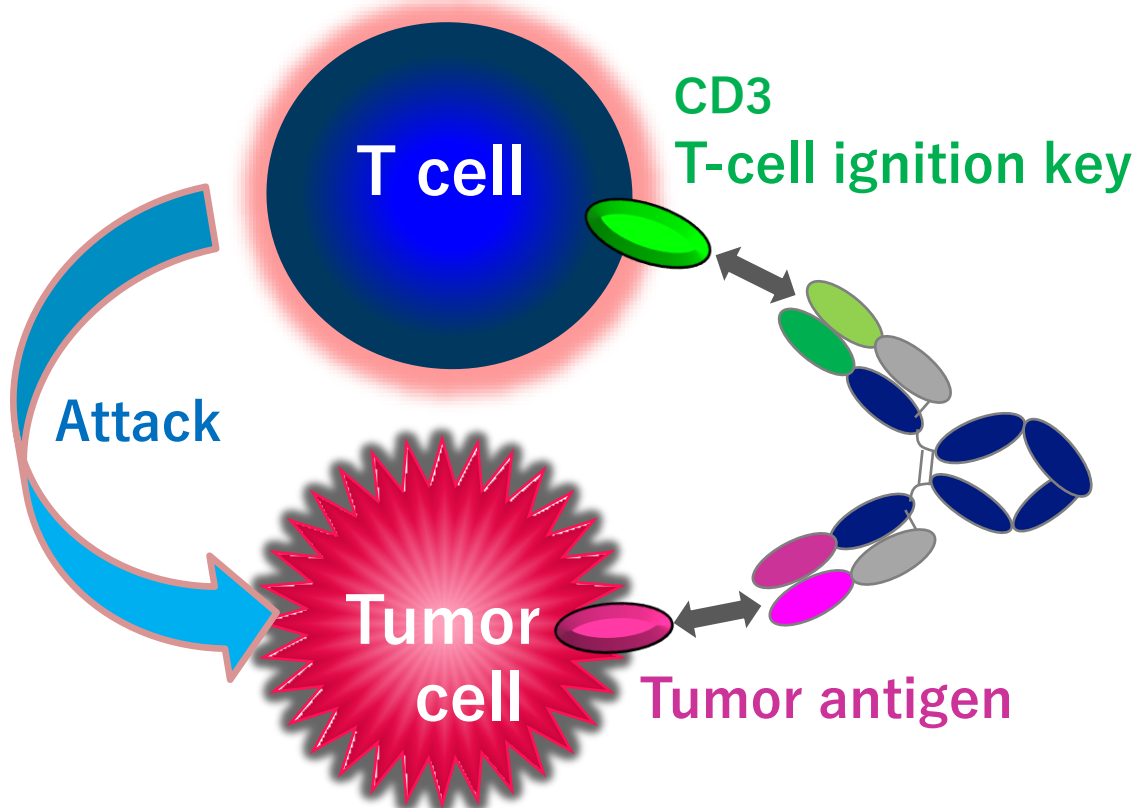


Anti-tumor activity is limited when few T cells are present

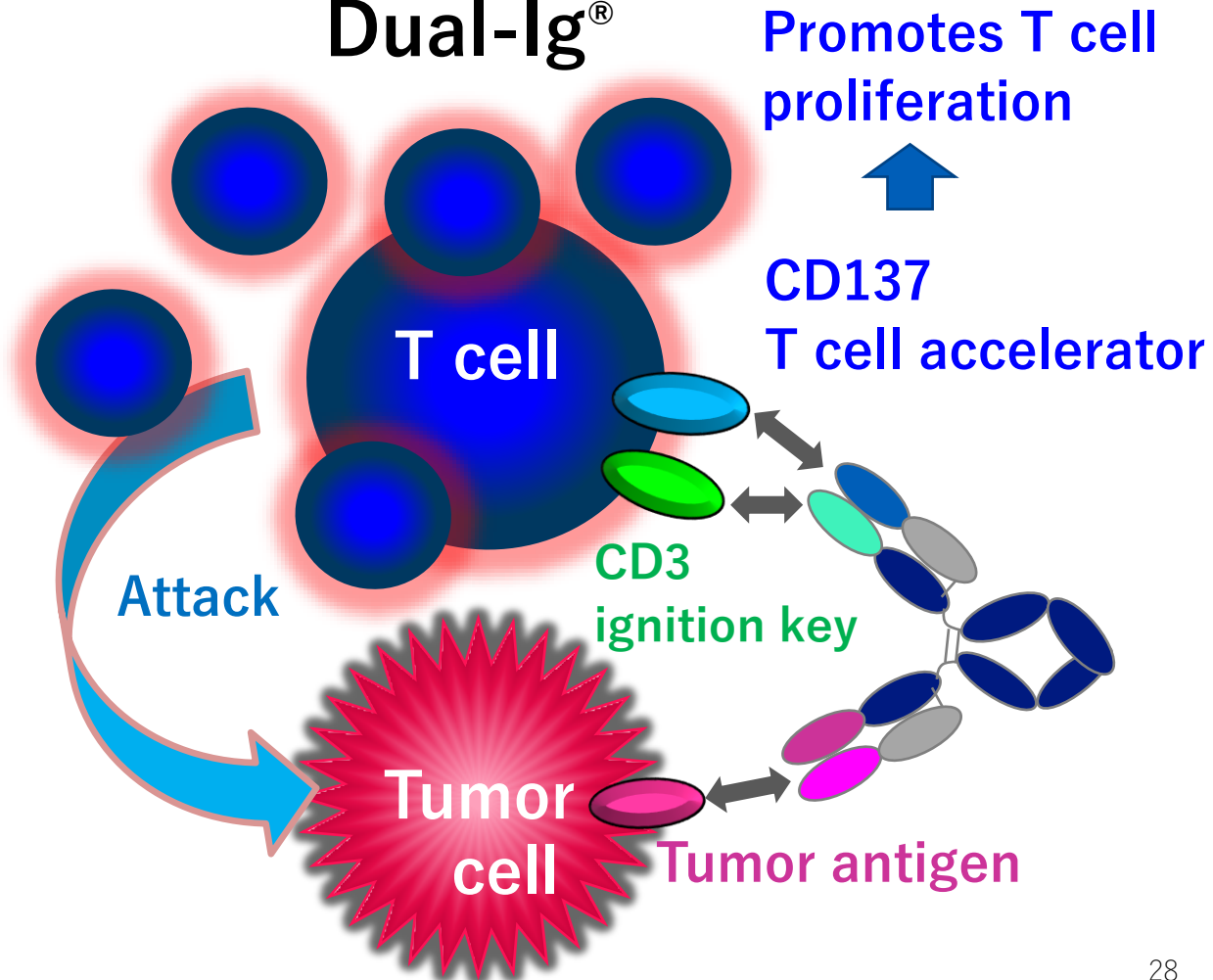


# Designing a Second-generation T Cell Redirecting Bispecific Antibody

## 1<sup>st</sup> generation TRAB™

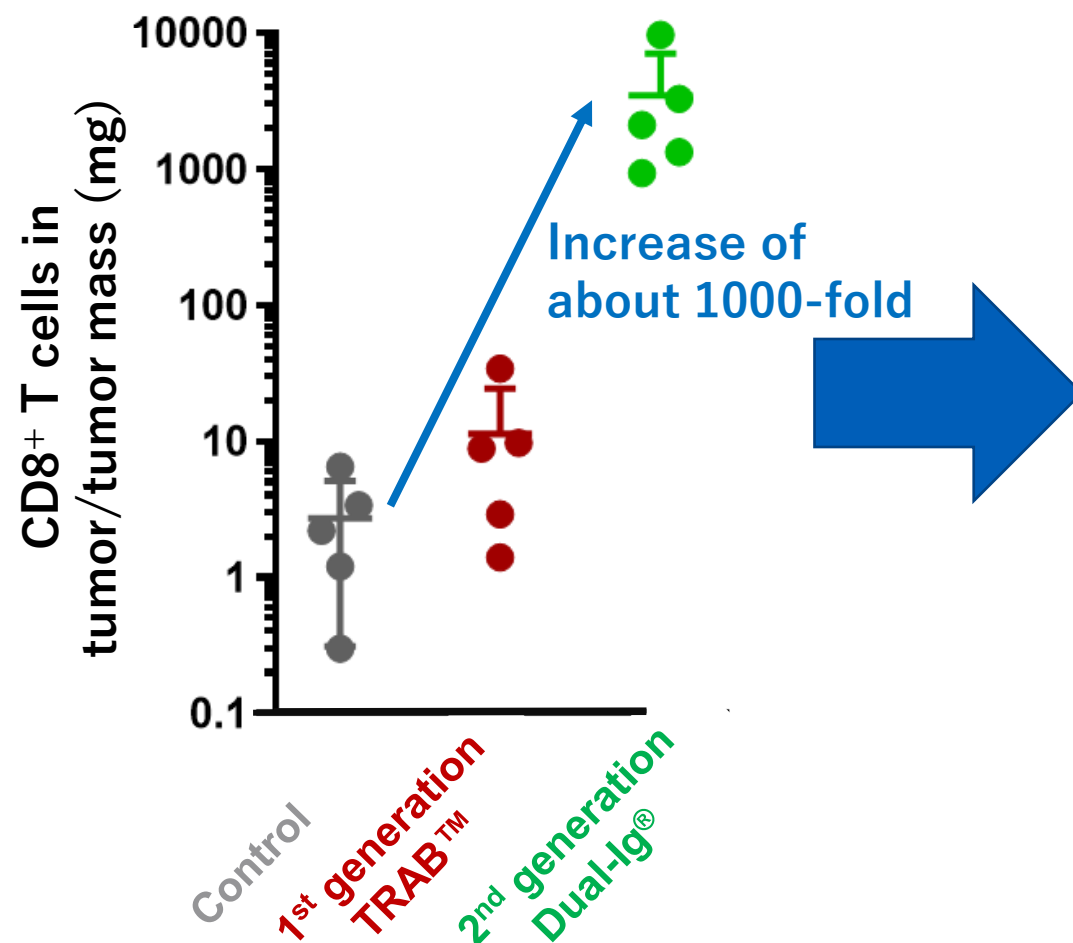


## 2<sup>nd</sup> generation Dual-Ig®

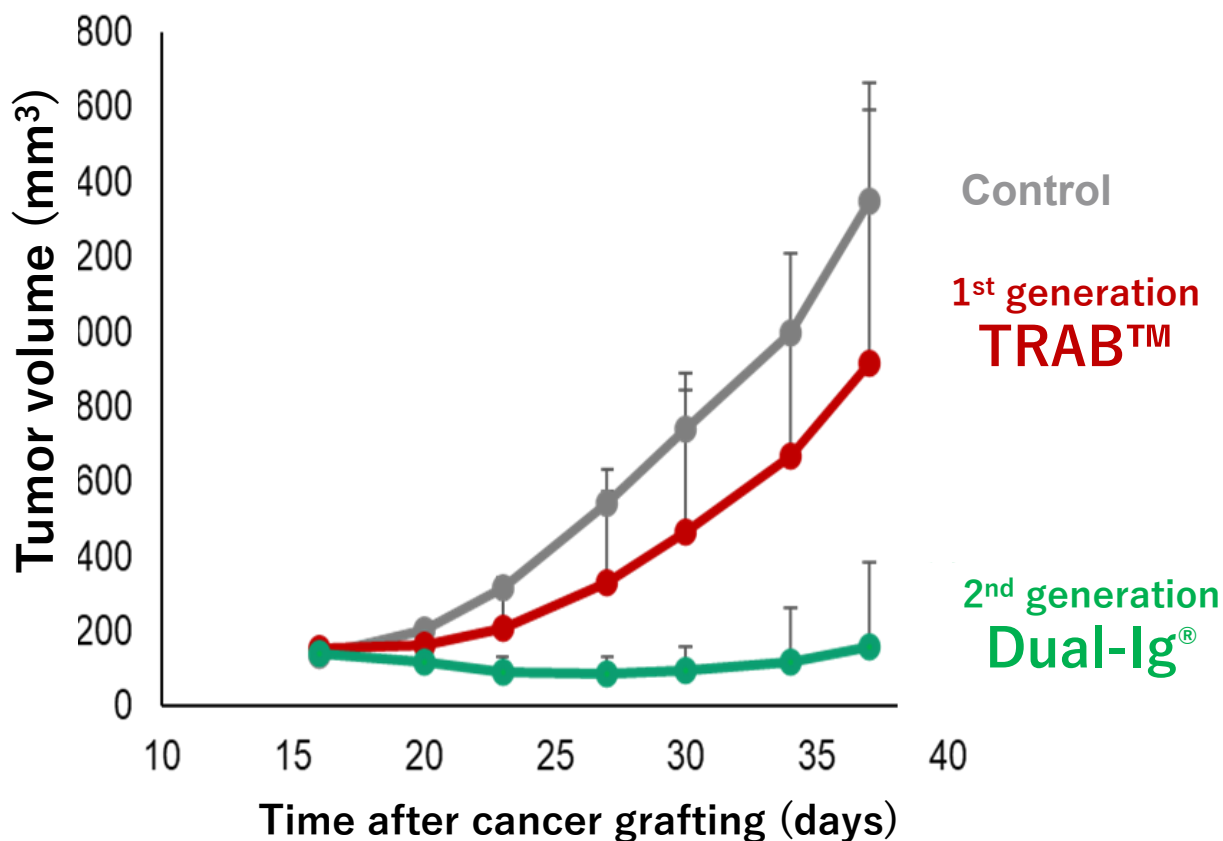


# 2<sup>nd</sup> Generation T cell Redirecting Bispecific Antibody, Dual-Ig<sup>®</sup> Greatly Increases the Level of T Cells Capable of Attacking Tumors

## 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®

2008-2013

2014-2017

2018-2021

↑  
Bispecific antibody  
technology established

→  
Evolution of  
technology

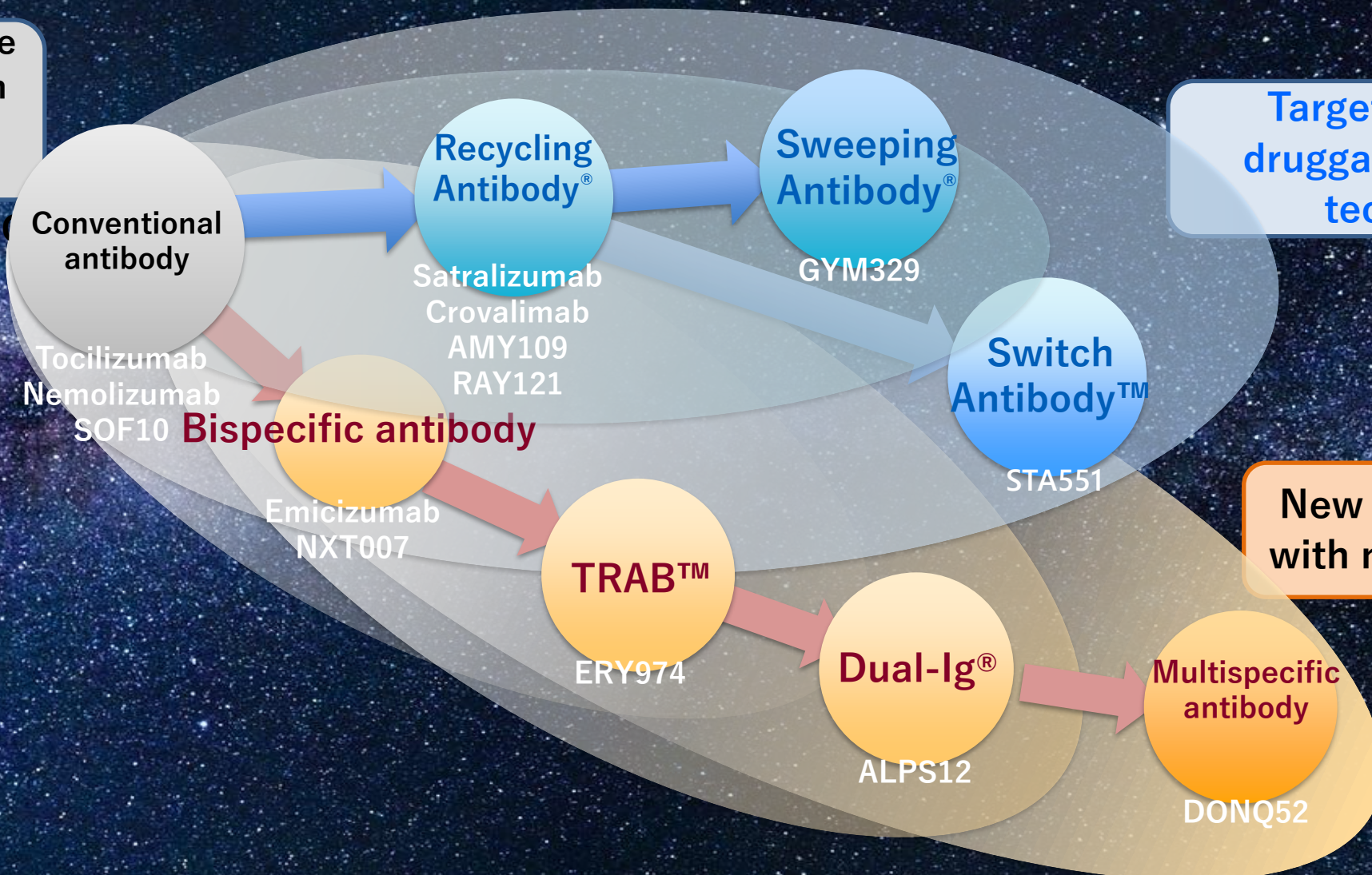
↑  
Establishment of  
technology for 1<sup>st</sup> T cell  
redirecting bispecific  
antibody (TRAB™)

→  
Evolution of  
technology

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

# Expanding Drug Space with Proprietary Innovative Antibody Technologies

Target molecule  
druggable with  
conventional  
antibody



Target molecules  
druggable with new  
technology

New MOA achieved  
with new technology

# Contact Information

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# INNOVATION BEYOND IMAGINATION