Carna Biosciences, Inc.

February 10, 2026

Stock Code: 4572

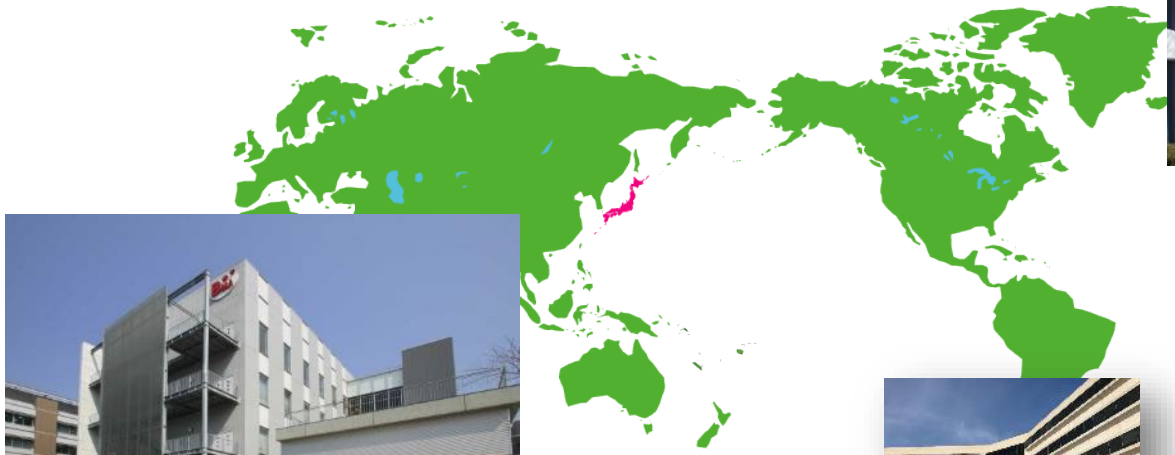
AGENDA

1. Company Overview
2. Updates on Pipelines in Clinical Development
3. Updates on Licensed Pipelines
4. Drug Discovery Support (ddSP) Business
5. Business Plan
6. Appendix

Company Overview

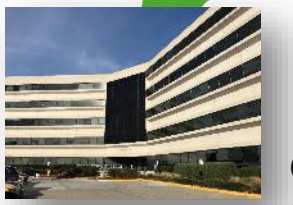
Company Overview

- Founded in April 2003 (spin-out company from N.V. Organon [MSD])
- Initial Public Offering (JASDAQ 4572) in March 2008
- 83 people
- Offices:
  - Carna Biosciences, Inc. - Kobe, Japan;
  - CarnaBio USA, Inc. - Natick, MA
  - Clinical Development Office – South San Francisco, CA



Carna Biosciences, Inc.
(Kobe, Japan)

CarnaBio USA
(Natick, MA)

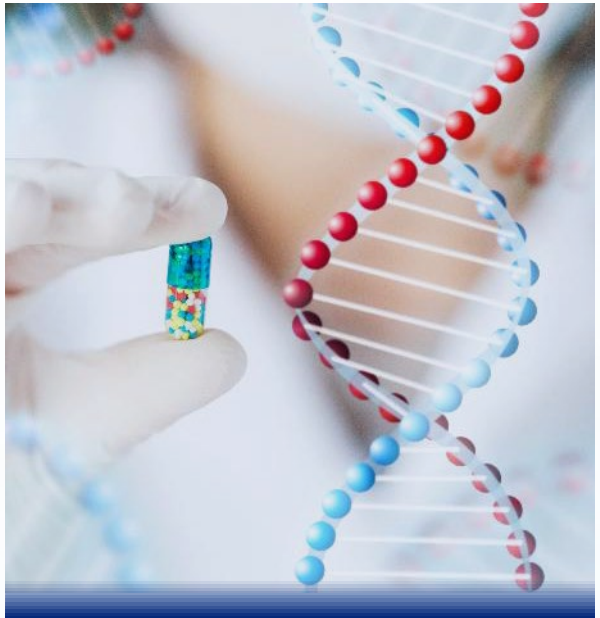


Clinical Development Office
(SSF, CA)

(As of January 31, 2026)

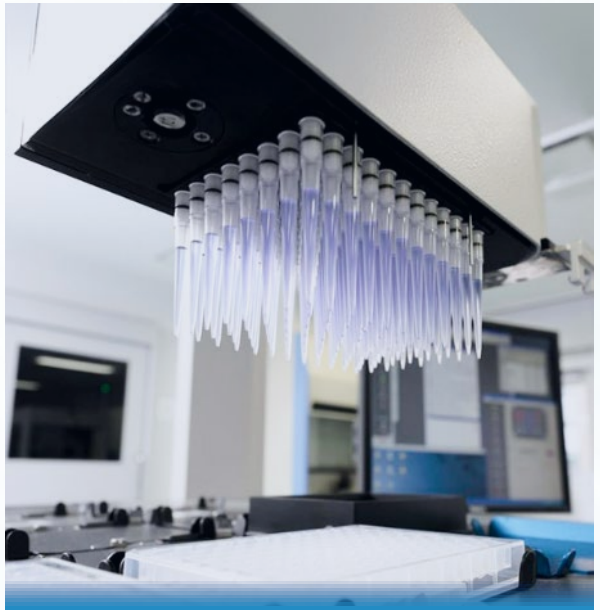
Our Business

Carna leverages its proprietary kinase drug discovery technology across two business areas: Drug Discovery R&D (ddRD) and Drug Discovery Support (ddSP)



Drug Discovery R&D

Aiming to discover and develop innovative drugs



Drug Discovery Support

Providing pharmaceutical companies with new tools to support their kinase inhibitor research

*Kinases are important enzymes that play a crucial role in various cellular signaling pathways, and their dysregulation is associated with numerous diseases

Specializing in small molecule drugs including kinase inhibitors

Proprietary compound library and expertise in drug discovery technologies

Founded as a spin-out from a major pharmaceutical company

Highly experienced team with strong scientific background

Proven track record of partnerships with global pharmaceutical companies

Out-licensed a proprietary program to Gilead Sciences (see P.27)
Ongoing joint research with Sumitomo Pharma (See P.28)

Multiple drug candidates discovered by Carna are in clinical development

Carna is advancing clinical development of three investigational drugs targeting cancer, autoimmune, and inflammatory diseases (See P.12)

Building Long-Term Value

Our goal is to deliver innovative therapies for patients suffering from serious diseases.

2003
A spin-out from Nippon Organon, founded by experts in kinase drug discovery

Started providing kinase proteins and screening services to pharmaceutical companies for kinase inhibitor drug discovery

2010
Drug Discovery Group was established to initiate in-house kinase drug discovery research, focusing on cancer, immune, and inflammatory diseases

2019
Established a clinical development office in South San Francisco, CA

2003 2010 2019 2026

Leading clinical stage biopharmaceutical company

Out-licensing deals

2015	J&J License Deal
2016	Sierra Oncology License Deal
2018	Sumitomo Pharma Collaboration
2019	Gilead License Deal
2020	BioNova License Deal
2022	FRTX License Deal

Pipelines

2020	Initiated FIH study of BTK inhibitor sofnobrutinib (AS-0871)
2021	Initiated FIH study of BTK inhibitor docirbrutinib (AS1763)
	Initiated FIH study of CDC7 inhibitor monzosertib(AS-0141)

2026 Plan

- Actively seek a strategic partner to bring sofnobrutinib (AS-0871) into late clinical development stages
- Advance Phase 1 studies of BTK inhibitor docirbrutinib (AS-1763) and CDC7 inhibitor monzosertib (AS-0141)
- Strengthen clinical development capability
- Create next wave of pipeline

Mid- to Long- term strategy

- Advance our clinical development programs
- Find strategic partners for late-stage development and commercialization
- Strengthen financial position through revenue from milestone payments and royalties generated by licensees
- Create next wave of pipeline

From Drug Discovery to Monetization

Bringing a drug candidate from discovery phase to commercialization typically takes 10 to 15 years and requires a substantial investment in research and development.

Generating drug candidates by optimizing lead compounds
.

Evaluating drug candidates for efficacy, ADME, safety, and toxicity, as well as manufacturing processes and formulation stability

Evaluating safety and efficacy in patients to obtain regulatory approval

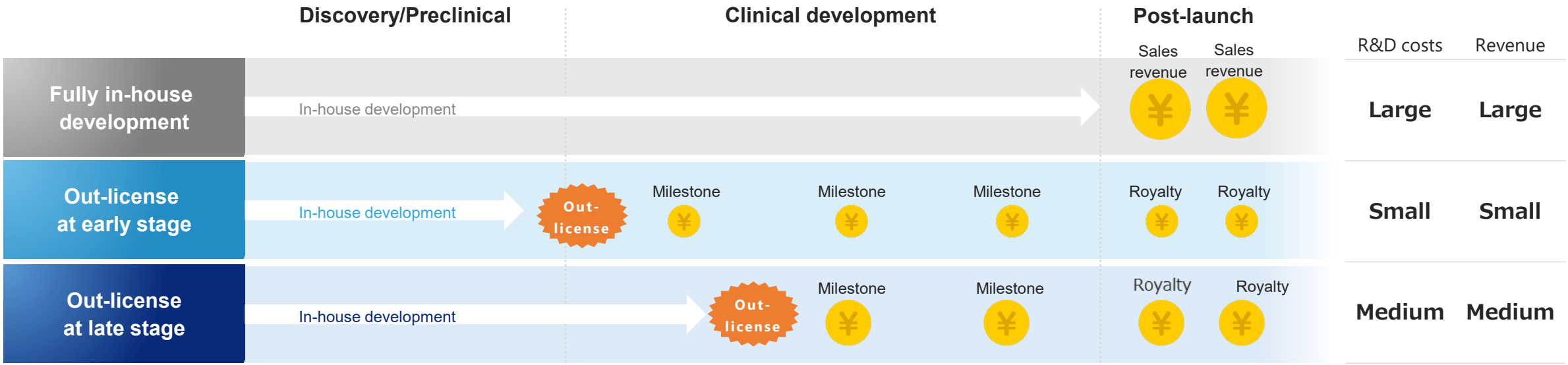
General process of clinical trials

Phase 1	Phase 2	Phase 3
Safety evaluation	Efficacy evaluation (small cohort)	Efficacy evaluation (large cohort)

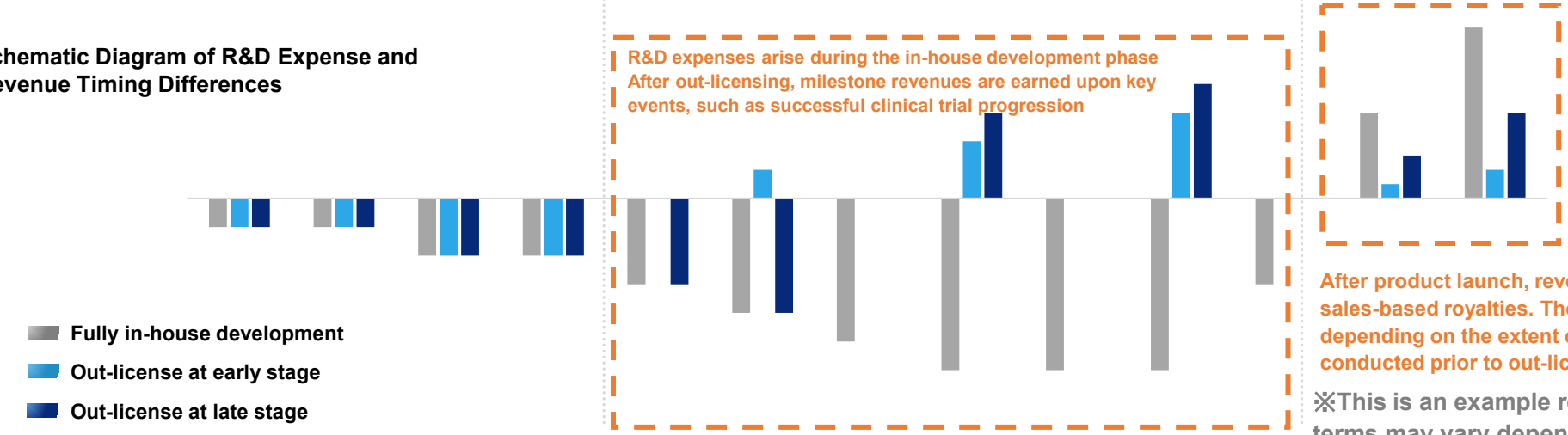
Commercially launched and prescribed to patients for treatment

Business Model of Biotech Startups

Due to the heavy burden of R&D costs, biotech startups may choose to out-license their drug candidates at an early stage to pharmaceutical/biotech companies in return for milestone payments and sales royalties.



Schematic Diagram of R&D Expense and Revenue Timing Differences



After product launch, revenue is generated through sales-based royalties. The royalty rate may vary depending on the extent of in-house development conducted prior to out-licensing

※This is an example revenue structure, and actual terms may vary depending on each drug candidate

Pipeline Development for Corporate Growth

Biotech Startups aim to maximize their corporate value by developing innovative pipelines and enhancing the medium to long term value of each pipeline.

Building a high-value pipeline portfolio

Market size
- ✓ Target indications
- ✓ Potential to expand indications
- ✓ Target product profile

Projected market share
- ✓ Advantages and differentiation over existing drugs

Deal structure
- ✓ Timing of out-license
- ✓ Milestones and royalty rate

Probability of success
- ✓ Reviewing results and progress of clinical Trials

Sustained expansion of the pipeline portfolio

Maximize corporate value

Our Business and Performance Overview

- **We operate two core segments: Drug Discovery R&D (ddRD) and Drug Discovery Support (ddSP)**
- **We have been advancing clinical trials for our proprietary pipelines, which has led to increased costs associated with these trials.**

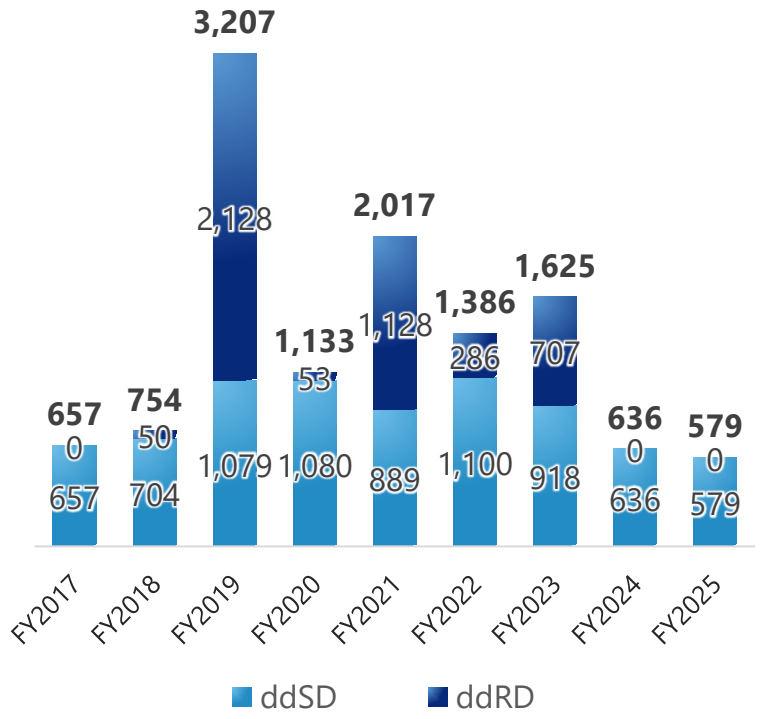
ddRD

- ✓ ddRD business conducts research and development of innovative small molecule drugs including kinase inhibitors
- ✓ We focus on oncology and inflammatory/immune disorders
- ✓ We develop our oncology pipelines up to Phase 2 to maximize their potential value, while for other therapeutic areas, we typically out-license at an early stage, before entering Phase 2 study, to mitigate development risk

ddSP

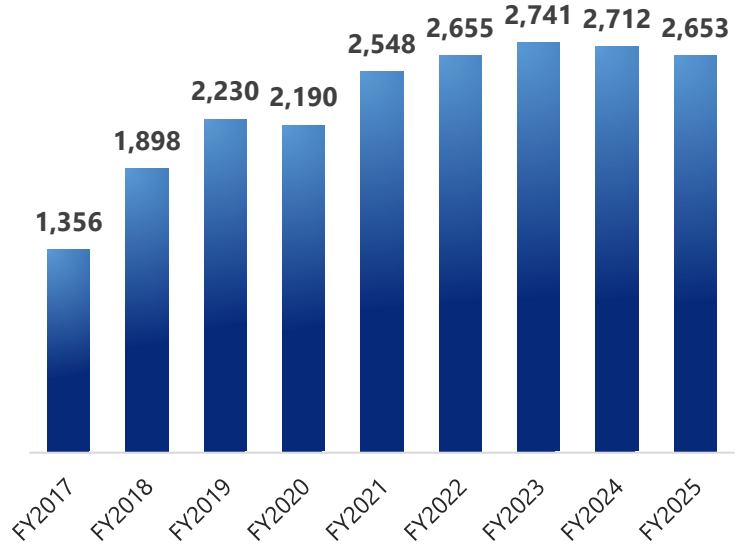
- ✓ ddSP business offers research tools for drug discovery, leveraging our proprietary kinase research technology for lead identification and optimization

Sales trend (JPY mn)



- ✓ Sales of ddSP segment declined YoY in FY2025, as our major customers scaled down their R&D budgets

Operating costs trend (JPY mn)



- ✓ Operating costs have been trending upward since the initiation of clinical trials of our pipelines, including docirbrutinib

Updates on Pipelines in Clinical Development

Clinical Development Pipeline

We are currently advancing the development of three drug candidates: docirbrutinib, sofnobrutinib, and monzosertib.

	Compound	Indication	Next milestone	Development status and outlook
1	docirbrutinib (AS-1763)	Blood cancers	Finding a partner and the initiation of Phase 2 study	Phase 1b study is ongoing (Cancer patients, US) → Target: Finding a partner and the initiation of Phase 2 study 2026
2	sofnobrutinib (AS-0871)	Immune-inflammatory diseases	Finding a partner and the initiation of Phase 2 study	Phase 1 study is completed (Health volunteers, the Netherlands) → Target: Finding a partner and the initiation of Phase 2 study 2026
3	monzosertib (AS-0141)	Solid tumors and blood cancers	Complete Phase 1 study Support the initiation of Phase 1b study (Investigator-Initiated Trial)	Phase 1 study is ongoing (Cancer patients, Japan) → Target: Complete Phase 1 study Support the initiation of Phase 1b study (Investigator-Initiated Trial) 2026

Preclinical | Phase 1 | Phase 2 | Phase 3 | Launch

Status of Clinical Development Pipeline

- Docirbrutinib and monzosertib: Phase 1 clinical studies are ongoing
- Sofnobrutinib: Phase 1 clinical study is completed. Seeking a partner to conduct Phase 2 study

docirbrutinib

Phase 1b Ongoing
(the U.S. since August 2023)

Key points

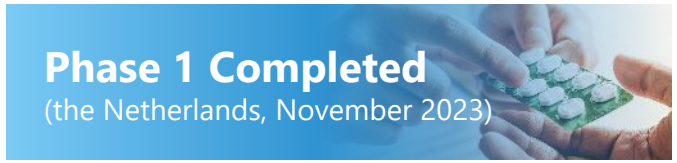
- ✓ **Dr. Nitin Jain, Professor of Leukemia, University of Texas MD Anderson Cancer Center is leading the multi-site clinical study**
- ✓ Initiated the dose expansion part in October 2024

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Update

Presented the latest clinical data and preclinical results at ASH2025, held in December 2025.

sofnobrutinib



Phase 1 Completed
(the Netherlands, November 2023)

Key points

- ✓ Favorable safety and tolerability profile
- ✓ Promising PK/PD profile were confirmed
- ✓ Negative in the EFD study
- ✓ Seeking a strategic partner for further development

Update

–

monzosertib

Phase 1 Ongoing
(Japan, since June 2021)

Key points

- ✓ **Phase 1 study is on going at National Cancer Center Hospital, National Cancer Center Hospital East and The Cancer Institute Hospital of JFCR**

Update

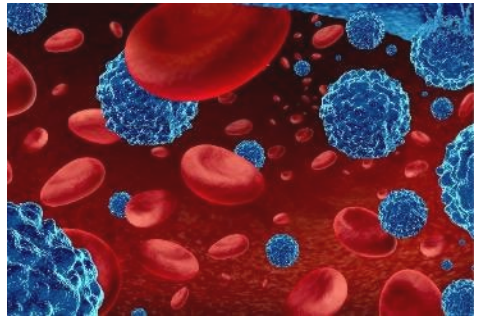
- **Phase 1 study for solid tumors and blood cancers in Japan**
  - **The last patient has completed the study, and data analysis is underway**
- **Phase 1b study (Investigator-Initiated Trial for blood cancers)**
  - **Memorandum of Understanding (MOU) signed with MD Anderson Cancer Center to support the Phase 1b study**

Clinical-Stage Pipeline 1 : docirbrutinib (AS-1763)

docirbrutinib (AS-1763)

Highlights | Profile | Differentiation | Market

Early clinical data suggest that docirbrutinib has the potential to address unmet medical needs in patients who have developed resistance to existing BTK inhibitors. Carna is actively advancing the Phase 1b study and aims to initiate a Phase 2 study as early as possible.

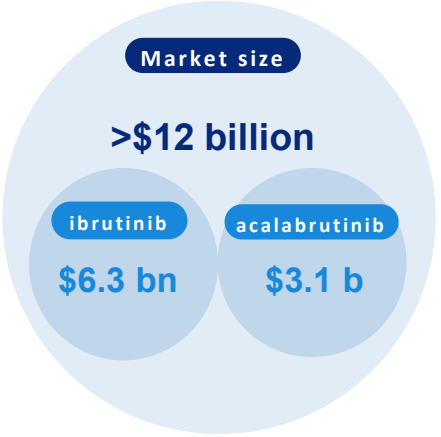


Target Product Profile

- Orally available, small molecule non-covalent inhibitor of Bruton's Tyrosine Kinase (BTK) targeting B-cell malignancies
- Potentially effective in patients who have developed resistance to existing BTK inhibitors
- Potentially effective in patients who are intolerant to existing BTK inhibitors

Potential market size and competitors

- The combined sales of existing BTK inhibitors exceed $12 billion, and the market is expected to expand further.
- Sales of ibrutinib, a BTK inhibitor (AbbVie / Johnson & Johnson), reached $6.3 billion in 2024.
- Sales of acalabrutinib (AstraZeneca) reached $3.1 billion in 2024.



Development timeline and Key Events

2021 — **Phase 1 study in healthy volunteers was conducted in the Netherlands (completed)**
Confirmed safety, tolerability, and favorable pharmacokinetic and pharmacodynamic profile at all dose levels

2023 — **Phase 1b study was initiated in patients in the U.S. (ongoing)**
Primary objective is to determine recommended phase 2 dose and maximum tolerated dose

2025 — **Poster presentation at EHA2025 and ASH2025**
Presented promising tumor responses observed in Phase 1b study

Next milestone

2026 — **Finding a partner and the initiation of Phase 2 study**

Clinical-Stage Pipeline 1 : docirbrutinib (AS-1763)

docirbrutinib (AS-1763)

Highlight | **Profile** | Differentiation | Market

Preliminary data from the ongoing clinical study suggest that docirbrutinib may offer a safer profile, with fewer serious adverse events compared to other BTK inhibitors. Non-clinical studies have demonstrated its strong efficacy against BTK mutants that are resistant to existing BTK inhibitors.

Profile 01 Favorable safety profile

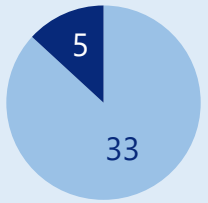
▼ Incidence of severe adverse events (SAEs, Grade≥3)

docirbrutinib

Grade ≥3 TEAEs※1

13%

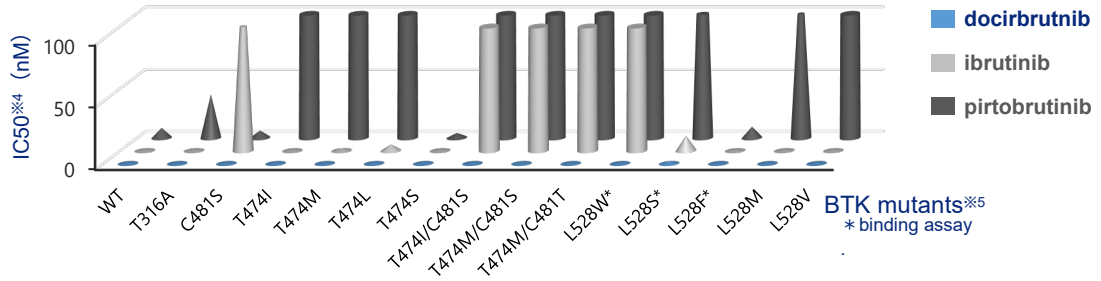
As of October 17, 2025



- No drug-related atrial fibrillation or hypertension was reported. Grade ≥3 TEAEs were reported in 13% of patients, suggesting favorable safety profile
- Many patients have been on long-term treatment due to the low incidents of adverse events, with several receiving docirbrutinib for over a year, indicating an excellent safety profile. (41% of patients treated with ibrutinib were reported to have discontinued the treatment, with half of those discontinuations attributed to intolerance ※2)
- Additional patient enrollment is planned to establish the safety profile of docirbrutinib

Profile 02 Potential to address various BTK mutations※3

Inhibitory potency of BTK inhibitors against BTK mutants (IC50)



- In preclinical study, docirbrutinib showed strong inhibitory potency against all resistant BTK mutations, whereas ibrutinib and pirtobrutinib showed only weak inhibitory activity against theses mutations.
- Docirbrutinib is expected to be effective against patients who have developed resistance to the existing BTK inhibitors.

※1 The preliminary data from Phase 1b study of Docirbrutinib
※2 Mato AR, et al., Haematologica. 2018;103(5):874-879

※3 Data from ASH2024 poster presentation ※4 IC50: Refers to the concentration required to inhibit 50% of the activity of a specific enzyme, cell, or receptor; A lower IC50 value indicates higher potency. ※5 BTK mutants :T316A, C481S etc. : Resistant mutations in BTK, each indicats the types of amino acid and the position of mutations.

Clinical-Stage Pipeline 1 : docirbrutinib (AS-1763)

docirbrutinib (AS-1763)

Highlight | **Profile** | Differentiation | Market

Limitations of Current CLL Treatments & Unmet Medical Needs

Resistance to Existing Therapies

- No effective treatment options are available after current BTK inhibitors.
- Particularly after pirtobrutinib, representing the largest remaining unmet need.

Maintaining Deep Responses*

- Treatment is often interrupted by adverse events before reaching a deep response*.
- This prevents patients from maximizing the full therapeutic benefit.

Safety

- Atrial fibrillation, hypertension and bleeding are key barriers to maintaining treatment.
- Discontinuation prevents patients from achieving deep responses (uMRD)*.

Economic Burden

- Long-term therapy increases costs and the burden on healthcare resources.
- Treatment options must be designed to remain effective even upon relapse.

Potential of docirbrutinib

- Demonstrates durable efficacy in patients who have become resistant to existing therapies.
- Potential to achieve and sustain deep responses* using combinations with existing oral agents.
- Highly favorable safety profile that does not hinder treatment continuation even in elderly patients.
- Enables a long-term, low-burden treatment model centered on outpatient oral therapy.

The Next-Generation CLL Therapy Enabled by docirbrutinib

Unmet Need Segments
Second-line / Post-pirtobrutinib
A next-generation BTK inhibitor capable of delivering durable responses even after resistance to current BTK inhibitors and pirtobrutinib.

Mid-term / Expanding Market
First-line / Second-line
A best-in-class oral combination therapy that achieves both deep responses and high treatment continuity.

Long-term / Largest Market
First-line
A next-generation BTK inhibitor that is effective and safe even in the major patient population of elderly CLL patients.

*A description of “deep response” is provided on the next page.

docirbrutinib (AS-1763)

Deep Response: Definitions and Importance

Deep Response

A “deep response” is achieved when the following conditions are met:

- **Complete Response (CR) / Complete Remission**: No detectable disease activity based on blood tests, CT imaging, or clinical symptoms.
- **uMRD (undetectable Minimal Residual Disease)**: Even with highly sensitive detection technologies (flow cytometry or PCR),≤1 cancer cell per 10,000–100,000 normal leukocytes is found.

Importance of Achieving a Deep Response

Achieving a deep response (especially uMRD) is associated with:

- **Prolonged Progression-Free Survival (PFS)**: A significantly longer period before relapse.
- **Extended Treatment-Free Remission**: Patients can discontinue therapy while maintaining disease stability without progression.

Therapies That Induce Deep Response

- Achieving uMRD with BTK inhibitor monotherapy is rare.
- Combining BTK inhibitors with other agents such as BCL2 inhibitors (e.g., venetoclax)enhances cancer cell clearance and frequently leads to uMRD.
- However, the limitations of existing BTK inhibitors—adverse events and resistance—restrict the use of such combination regimens.

docirbrutinib has the potential to overcome these limitations.

Clinical-Stage Pipeline 1 : docirbrutinib (AS-1763)

docirbrutinib (AS-1763)

Highlight | Market | **Differentiation** | Profile

Docirbrutinib demonstrates strong inhibitory potency against various BTK mutants and exhibits a favorable safety profile, positioning it as a potential best-in-class candidate among BTK inhibitors and degraders currently in development.

Comparative overview of non-covalent BTK Inhibitors and BTK degraders (approved and in clinical development)

Compound	MoA	Effectiveness against resistant mutants	Adverse Event Grade ≥3	Company	Phase
pirtobrutinib (LOXO-305)	Non-covalent BTK inhibitor	Not effective against T474I, L528w, etc.	Reported (low frequency)	Lilly (Loxo)	Approved/P3
nemtabrutinib (ARQ 531)	Non-covalent BTK inhibitor	Effective against several mutants	Reported	Merck (ArQule)	P3
NX-5948	BTK degrader	Effective against various mutants	Reported (low frequency)	Nurix	P2
BGB-16673	BTK degrader	Effective against various mutants	Reported	BeOne	P3
docirbrutinib (AS-1763)	**Non-covalent BTK inhibitor**	**Effective against various mutants, including T474I and L528W**	**Refer to P.15**	**Carna**	**P1**

Drug resistance: the reduction in effectiveness of a drug during targeted therapies due to alterations of drug targets including the mutation of the target proteins.

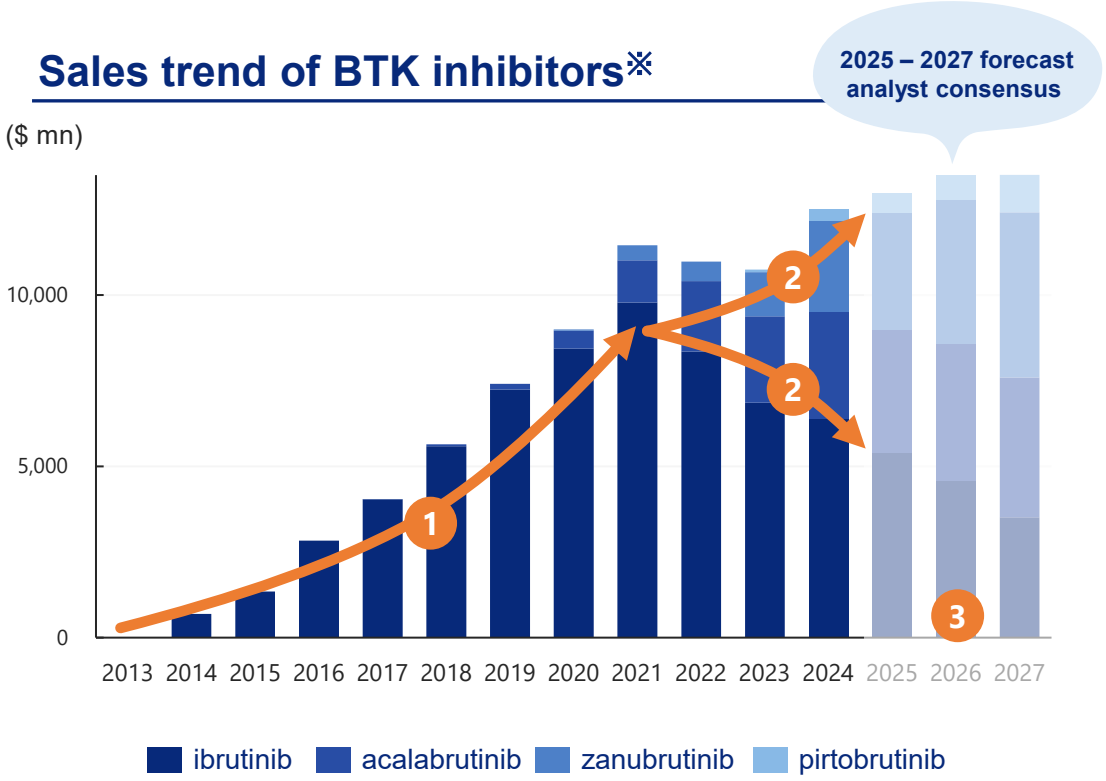
Clinical-Stage Pipeline 1 : docirbrutinib (AS-1763)

docirbrutinib (AS-1763)

Highlight | Profile | Differentiation | **Market**

Combined sales of BTK inhibitors exceed $12 billion and are expected to expand continue growing. Significant unmet medical needs remain due to tolerability issues and acquired resistance to existing BTK inhibitors.

Sales trend of BTK inhibitors※



1. Ibrutinib (Imbruvica) was launched in 2013 and created the market as it expanded sales until 2021
2. Recently, acalabrutinib, zanubrutinib, and pirtobrutinib have begun capturing market share from ibrutinib, due to their improved safety profiles.
3. However, the emergence of mutant BTKs that are resistant to ibrutinib, acalabrutinib, zanubrutinib and pirtobrutinib underscore the urgent need for a new treatment option.

BTK inhibitors

BTK inhibitors inhibit the activation of Bruton's tyrosine kinase, an enzyme that plays a crucial role in B cell development. By inhibiting BTK, these drugs prevent the proliferation of cancer cells and treat blood cancers.

※Source: Clarivate

Clinical-Stage Pipeline 2: sofnobrutinib (AS-0871)

sofnobrutinib (AS-0871)

Highlights

Following the completion of the Phase 1 study of sofnobrutinib in 2023, we are currently actively seeking a partner for out-licensing or co-development.
We are conducting additional preclinical studies to highlight advantages of sofnobrutinib over other BTK inhibitors.

Target Product Profile

- **Orally available, small molecule non-covalent inhibitor of Bruton's Tyrosine Kinase (BTK) targeting immune-inflammatory diseases**

Potential market size and competitors

- The market for Chronic Spontaneous Urticaria※1 (CSU), one of the most promising indications, is estimated to be $2.2 billion across the major seven markets, with significant growth expected. (See P.56)
- Remibrutinib, a covalent BTK inhibitor (FDA approved in September 2025), is one of the major competitors
- Many other potential indications including Pemphigus

Development timeline and key events

2023
Phase 1 study in healthy volunteers was conducted in the Netherlands (completed)

2024
Key nonclinical studies were conducted
The key nonclinical studies provided evidence of a potential advantage of sofnobrutinib over other BTK inhibitors

Partnering activity is ongoing
Find a partner for out-licensing or co-development to enable the initiation of the Phase 2 study

Next milestone

2026
Find a partner for out-license or co-development
Initiate Phase 2 study

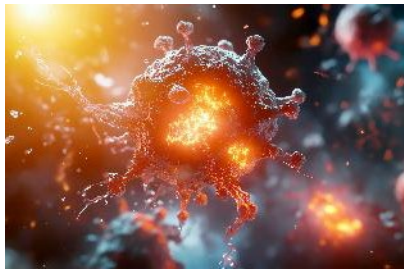
※1 CSU is a debilitating skin disease of chronic itch, hives and angioedema, lasting six weeks or more.

Clinical-Stage Pipeline 3: monzosertib (AS-0141)

monzosertib (AS-0141)

Highlights | Profile | Update 1 | Update 2

Monzosertib is currently being investigated for its efficacy across various cancer types in a Phase 1 study as monotherapy.
In nonclinical study using AML cell lines, monzosertib demonstrated significant antitumor activity in combination with standard therapy.
We signed an MOU with MD Anderson Cancer Center to support an investigator-initiated Phase 1b trial of triplet therapy in patients with AML.



Target Product Profile

- **Orally available, small molecule inhibitor of Cell Division Cycle 7 (CDC7) Kinase targeting solid tumors and blood cancers**

Potential market size and competitors

- The market size for AML therapies has reached USD 3.8 billion and is expected to continue growing. We will support the investigator-initiated Phase 1b study currently in preparation to evaluate the potential of monzosertib in AML.
- Monzosertib is a potential first-in-class CDC7 inhibitor, as no drugs targeting CDC7 kinase have been approved to date.

Market size for AML therapies

$3.8billion

Development timeline and key events

2021
- **Phase 1 study was initiated in Japan targeting solid tumors**
- **Protocol was amended to include patients with blood cancers**

2024
- **Dose escalation part was initiated targeting blood cancers**
  Primary objective is to assess safety and to determine recommended Phase 2 dose.

2025
- **New preclinical data presented at AACR, demonstrating the synergistic antitumor efficacy of monzosertib in triplet combination therapy**

Next milestone

2026
- **Complete Phase 1 study**
- **Support the investigator-initiated Phase 1b trial**

Clinical-Stage Pipeline 3: monzosertib (AS-0141)

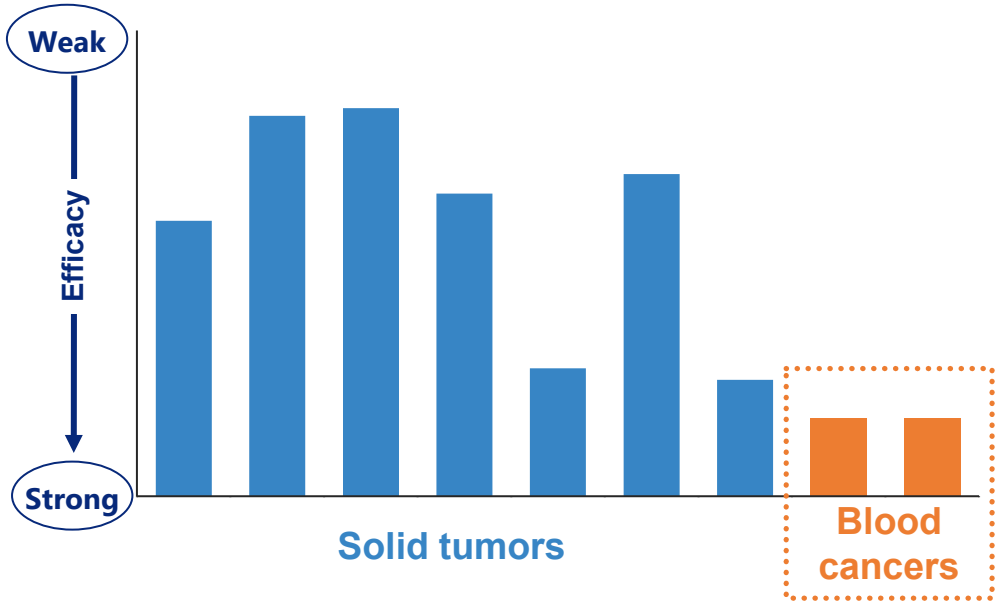
monzosertib (AS-0141)

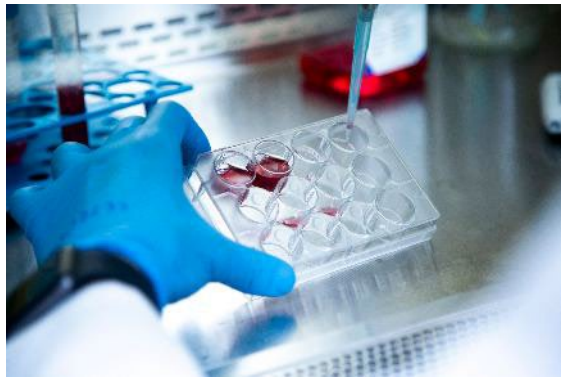
Highlights | Profile | Update 1 | Update 2

In nonclinical studies, monzosertib demonstrated potent anti-proliferative activity across various cancer cell-lines and exhibited robust antitumor efficacy against blood cancers.

Profile Robust antitumor efficacy against blood cancers

Antiproliferative effects of monzosertib on 35 human cancer cell lines
Each bar is presented as mean of different cell lines (N = 1 – 7)





Monzosertib demonstrated significant antitumor activity in a human AML xenograft mouse model.

Clinical-Stage Pipeline 3: monzosertib (AS-0141)

monzosertib (AS-0141)

Highlights | Profile | **Update 1** | Update 2

Last patient treated with monzosertib monotherapy (solid tumors or blood cancers) has completed the study, and data analysis is underway
Entered into an MOU with MD Anderson Cancer Center to support an investigator-initiated Phase 1b trial evaluating the potential of monzosertib in patients with AML.

Solid tumors — Monotherapy

Blood cancers — Monotherapy

Combination

MOU signed with MD Anderson Cancer Center to support initiation of an investigator-initiated Phase 1b triplet-therapy trial in AML.

Dose escalation part

The last patient has completed the study, and data analysis is underway

A small number of patients are administered monzosertib with gradually increasing doses to assess safety and tolerability. The maximum tolerated dose and recommended dose is determined.

Dose expansion part

Last-patient out achieved Data evaluation is ongoing

More patients are administered monzosertib at the dose level selected during dose escalation to determine the recommended Phase 2 dose (RP2D).

Phase 2 study

Patients receive monzosertib at the RP2D to evaluate efficacy and safety.

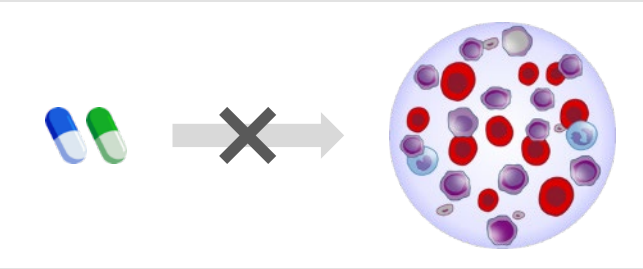
Clinical-Stage Pipeline 3: monzosertib (AS-0141)

monzosertib (AS-0141)

Highlights | Profile | Update 1 | Update 2

Nonclinical data presented at AACR Annual Meeting in April 2025 demonstrated significant antitumor effects of monzosertib in combination with DNMT inhibitors and BCL-2 inhibitors in AML models.

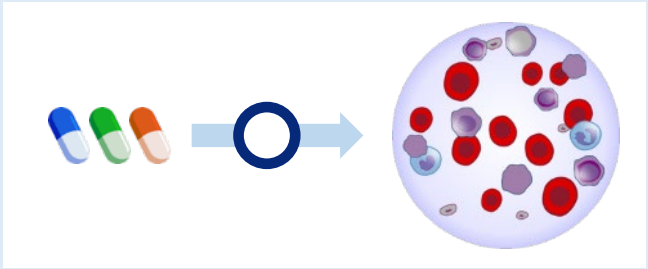
Current Therapy



DNMT inhibitor + BCL-2 inhibitor
Combination therapy

Standard treatment for AML patients who are unfit for intensive chemotherapy. However, **resistance to this regimen has become a major concern**.

Our Findings



Monzosertib + DNMT inhibitor + BCL-2 inhibitor
Triplet therapy

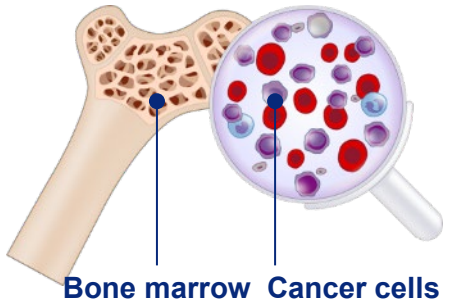
The triplet combination enhanced apoptosis and demonstrated significant antitumor effects ※1

※1 Human AML cell lines and human AML xenograft mouse models

Triplet therapy may offer a new treatment option for patients with AML

Acute Myeloid Leukemia (AML)

- ✓ A type of blood cancer that is highly malignant and difficult to treat.
- ✓ The most prevalent form of acute leukemia. The market for AML treatment exceeds $3.8 billion.※2



※2 Source: BCC Research「Global Acute Myeloid Leukemia (AML) Treatment Market」https://www.bccresearch.com/market-research/pharmaceuticals/acute-myeloid-leukemia-market.html

Updates on Licensed Pipelines

Out-licensed Pipeline

License agreement with Gilead: out-licensed DGKα inhibitors for immuno-oncology
Joint research with Sumitomo Pharma: currently evaluating a potential development candidate

	Partner／Target	Status	Deal Summary	Upfront payment	Milestones
1	 DGKα inhibitor (Immuno-oncology therapy) GILEAD	Refer to P.27	● Out-licensed in June 2019 ● Worldwide rights ● Royalties on future net sales	$20M	Total milestone payments expected $450M Milestone payments received Received twice, totaling $15M
2	 Joint Research with Sumitomo Pharma (Psychiatric and neurological disorders) Sumitomo Pharma	Late discovery	● Joint Research Agreement in March 2018 ● Worldwide rights ● Royalties on future net sales	JPY80M Upfront payment + Research milestone	Total milestone payments expected JPY10.6B

Out-licensed Pipeline 1: DGKα Inhibitor

DGKα Inhibitor

Partner Gilead Sciences, Inc.

Carna out-licensed its DGKα inhibitor program in June 2019 and has so far received upfront and milestone payments totaling $35M

About Gilead Sciences

- ✓ Gilead Sciences, Inc. is one of the leading research-based biopharmaceutical companies, operating in more than 35 countries worldwide, with headquarters in Foster City, California.
- ✓ Gilead is a pioneer in the development of antiviral drugs, including viral hepatitis, AIDS and influenza.
- ✓ In recent years, Gilead has committed to advancing its innovations in oncology.

Deal size

- **Upfront payment $20 million**
- **Maximum of $450 million** potential milestone payments upon achievement of certain development and commercial milestones

Royalties

- Royalties on future net sales

Summary of the license agreement

Compound	All compounds identified from the program
Indication	Cancer (immuno-therapy)
Region	Worldwide

Development timeline and key events

Jun. 2019 — **Out-lisenced to Gilead**
Worldwide development and commercialization rights

Dec. 2024 — **Initiated a Phase 1b study of GS-9911 in patients with solid tumors.**

(Current status)

In August 2025, GS-9911 was removed from the pipeline based on Gilead's internal portfolio prioritization. Gilead's project team stopped enrollment in the Phase 1 study but is continuing to oversee the research and development of the DGKα inhibitor program. At the same time, we have been informed that the license agreement remains fully in effect. We will promptly provide an update should any new information arise regarding the future direction of this drug discovery program.

Out-licensed Pipeline 2: Joint Research with Sumitomo Pharma

Joint Research with Sumitomo Pharma

Partner Sumitomo Pharma Co., Ltd.

Carna entered into a joint research agreement with Sumitomo Pharma to develop novel kinase inhibitors for the treatment of psychiatric and neurological disorders in March 2018. A potential development candidate is currently being evaluated.

Deal size

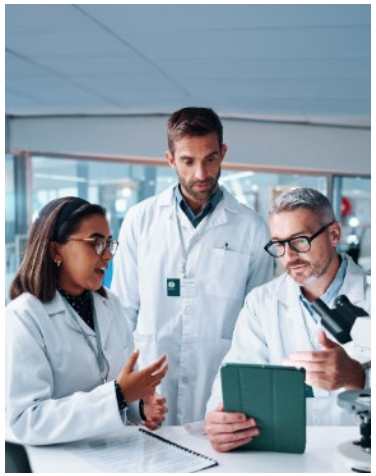
- Upfront payment + Research milestone JPY80 million
- Maximum of JPY10.6 billion potential milestone payments upon achievement of certain development and commercial milestones

Royalties

- Royalties on future net sales

Joint research overview

Modality※1	Orally available small molecule
Indication	Psychiatric and neurological disorders
Region	Worldwide



Development timeline and key events

- **Mar. 2018** — Entered into a joint research agreement with Sumitomo Pharma
- **Dec. 2021** — The term of the joint research was extended until March 27, 2025
- **Mar. 2025** — The term of the joint research was extended further until March 27, 2027 to evaluate a potential development candidate
- **Current** — Evaluation of a development candidate is ongoing

※1 "Modality refers to the classification of therapeutic approaches, such as small molecule drugs, antibody drugs, and nucleic acid drugs.

Drug Discovery Support (ddSP) Business

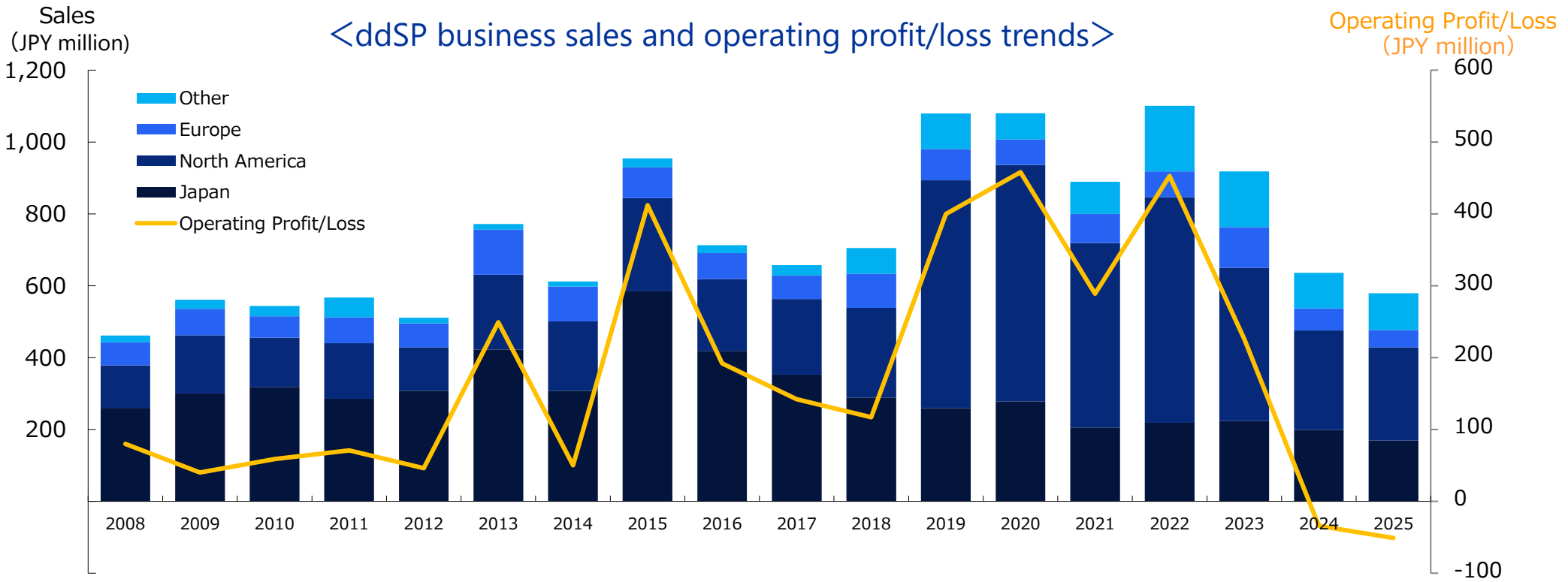
Drug Discovery Support Business : Strengths

Carna's kinase proteins and services have grown as one of the world's top brands.

- ✓ **Established the direct sales channels in Japan and the U.S.**
- ✓ **Our products and services are distributed through our exclusive agent in Europe.**
- ✓ **In China, SUBC*, one of the leading research tool provider in China distributes our kinase proteins (exclusive for us in kinase related products).**
- ✓ **While sales of proteins were robust in China and Japan, overall sales remained weak due to the lack of orders of profiling services in Japan and kinase proteins in Europe. Accompanied with our major customers' projects progress, the needs of kinase proteins and profiling services declined.**

*Shanghai Universal Biotech Co.(SUBC)
SUBC is one of the leading reagents suppliers in China, headquartered in Shanghai, has 36 branches with over 700 employees.

<ddSP business sales and operating profit/loss trends>



Kinase Proteins

- World-class product lineup：over 500 products including mutants
- Built a mass-production system：provide custom made kinase proteins of several dozen mg.
- High quality：highly active, high purity and stable quality（less variations among batches）

Biotinylated Protein Kinases

- Established our own technology of manufacturing biotinylated protein kinases: biotinylated protein kinases are suitable for the drug discovery research of next generation kinase inhibitors.
- Biotinylated protein kinases of over 200 kinds are available and product lineup is expanding.

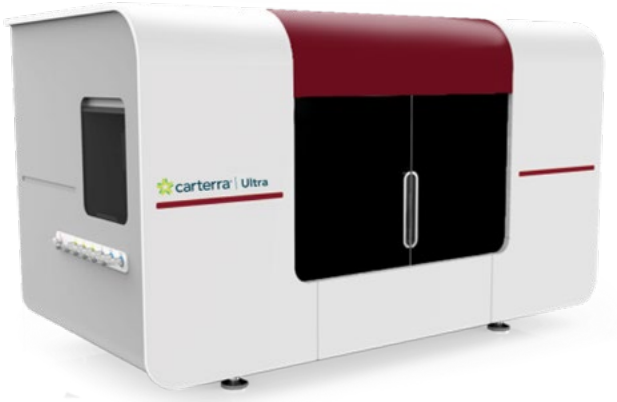
Profiling Services

- Data accuracy is the most important factor in kinase inhibitor selectivity profiling.
- Our customers, including both domestic and international pharmaceutical companies, highly evaluate Carna's profiling services for its data accuracy.

Our customers, the world's major pharmaceutical companies and promising bio-ventures, who use our kinase proteins and profiling services, launched many molecular target drugs. Some of the approved drugs became blockbusters.

Biotinylated Protein Kinases

- The demand for high throughput screening systems for small molecule compounds which bind to kinase proteins is increasing.
- Carterra (U.S) developed new innovative high throughput systems, LSA^{XT} and Ultra, which enabled small molecule screening and characterization in addition to antibody.
- Carna and Carterra collaborated to preliminary develop the assay with these new screening systems in combination with Carna's single site biotinylated kinase proteins and Carterra's HT-SPR LSA^{XT} or Ultra.
- This collaboration successfully proved these new systems screen about hundreds kinases and compound binding event just in 3 days.



With the continued adoption of Carterra LSA^{XT} and Ultra, we expect ongoing growth in sales of our biotinylated kinase proteins.

Profiling Services

- We challenged and succeeded in developing our original profiling system. The new system consists of combination with Sciex BioPhase8800 of 8 capillary electrophoresis, and the robot arm with stacker which we originally installed by combining stand alone machines.
- With this original system, we became the sole provider of profiling services utilizing highly reliable Mobility Shift Assay (MSA) System.
- In addition to MSA, we are also pursuing the development of additional profiling assay platform to meet broader customer needs.
- We share the expertise obtained through the kinase assay development process in our web pages titled “Kinase Assay Support Portal” to enhance convenience for individual customers and our brand recognition.
- Highly accurate profiling data is essential for AI-driven drug discovery. Our data accuracy is expected to be fully compatible with these requirements, positioning us to secure large-scale orders from companies engaged in AI-driven drug discovery.

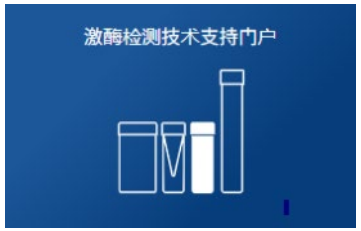
By consistently providing high-quality profiling data with high reproducibility and accuracy, we have established strong and lasting trust with our customers.

Updates on Drug Discovery Support Business

Launched newly categorized web pages titled “Kinase Assay Support Portal”

Kinase Assay Support Portal provides comprehensive expertise to develop various kinase assays.

Launched in Japanese, English and Chinese



Essential assay reagents (substrates and assay buffer) are now available.

Offering comprehensive list of platform-specific support information for developing kinase assays.

Our expertise in these web pages enables our customers to develop highly reliable kinase assays easily and quickly.
The launch of this portal is expected to promote the adoption of our products.

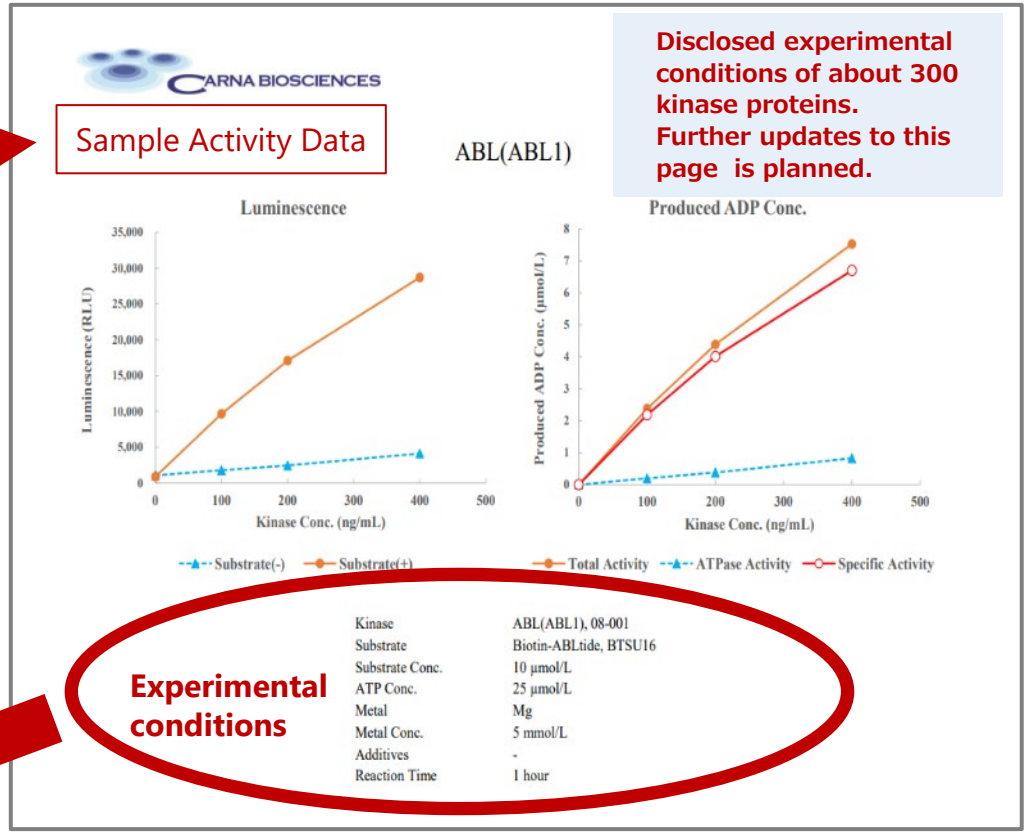
Updates on Drug Discovery Support Business

Kinase Assay Support Portal ：Disclosure of experimental conditions of kinase products

Kinase Assay experimental conditions and data through the use of our kinase products are disclosed.

ADP-Glo™ Kinase Assay　反応条件一覧表

Kinase Name	Protein Kinase			Substrate			Assay Buffer	ATPase Activity	Sample Activity Data
	Tag	Carna Product Name	Cat. No.	Carna Substrate Name	Cat. No.	Conc. (uM)	Cat. No.	H:High M:Moderate L:Low	
ABL(ABL1)	HIS	ABL(ABL1)	08-001	Biotin-ABLtide	BTSU16	10	ASBF01	L	
ABL(ABL1)[E255K]	HIS	ABL(ABL1)[E255K]	08-094	Biotin-ABLtide	BTSU16	10	ASBF01	L	
ABL(ABL1)[T315I]	HIS	ABL(ABL1)[T315I]	08-093	Biotin-ABLtide	BTSU16	10	ASBF01	L	
ACK(TNK2)	GST	ACK(TNK2)	08-196	Biotin-WASP peptide	BTSU39	50	ASBF01	L	
AKT1	GST	AKT1	01-101	Biotin-Crosstide	BTSU19	10	ASBF01	L	
AKT2	GST	AKT2	01-102	Biotin-Crosstide	BTSU19	10	ASBF01	L	
AKT3	GST	AKT3	01-103	Biotin-Crosstide	BTSU19	10	ASBF01	L	
ALK	GST	ALK	08-518	Biotin-Srctide	BTSU01	10	ASBF01	L	
ALK[C1156Y]	GST	ALK[C1156Y]	08-530	Biotin-Srctide	BTSU01	10	ASBF01	L	
ALK[F1174L]	GST	ALK[F1174L]	08-519	Biotin-Srctide	BTSU01	10	ASBF01	L	



Disclosed experimental conditions of about 300 kinase proteins. Further updates to this page is planned.

Adopting our protein products under clearly defined experimental conditions enables customers to :

- **Reproduce highly reliable assays**
- **Conduct assays without prior optimization of the experimental conditions**

Providing customers with access to our reliable information for experimental conditions will help to lower psychological barriers that prevent customers from taking up our products.

Market environment for Drug Discovery Support Business

Market environment

- The demand for kinase inhibitor drug discovery research services is strong in North America and China. More stable in Japan.

Competitors・Our advantage

- Major competitors:
  Thermo Fisher Scientific (US), Eurofins（EU）
  SignalChem (Sino Biological, China), Reaction Biology (US)
- Carna is the only drug discovery support service provider specialized in kinase inhibitor drug discovery.
- Carna's proprietary manufacturing technologies contribute to establish the uniqueness and predominance of biotinylated kinases with an abundant product lineup and quality in the global market.
- Precise assays, appropriate product development and finely attentive technical support by scientists with drug discovery experiences and knowledges.

Business Plan

Growth Strategy

➢ Advance clinical trials of our innovative pipelines to maximize corporate value

	Started internal drug discovery activity	Demonstrated strong capabilities in drug discovery	Maximize the value of pipelines	Maximize the value of pipelines and continue delivering profits
	2010-2015	2016-2020	2021-2025	2026-2030 (Plan)
PLAN	• Established in-house research capability • Established pipeline	• Out-licensed multiple programs • Initiated clinical trials	• Advance clinical trials of docirbrutinib (AS-1763), sofnobrutinib (AS-0871) and monzosertib (AS-0141) • Earn revenue from new license deals • Receive milestone payments from the out-licensed programs and deliver profits • Initiate pre-clinical and clinical studies of new pipelines	• Advance clinical trials of docirbrutinib (AS-1763) and monzosertib (AS-0141) • Receive milestone payments and royalty income from the out-licensed programs and expand profits • Earn revenue from new license deals • Initiate pre-clinical and clinical studies of new pipelines
ACTUAL	✓ Out-licensed : J&J (2015)	✓ Out-licensed : Sierra Oncology (2016) ✓ Joint research : Sumitomo Pharma (2018) ✓ Out-licensed : Gilead (2019) ✓ Out-licensed : BioNova (2020) ✓ Initiated clinical trials of sofnobrutinib (2020)	✓ Out-licensed : Fresh Tracks Therapeutics (2022) ✓ 1st Milestone : BioNova (2022) ✓ 1st Milestone : Gilead (2021) ✓ 2nd Milestone : Gilead (2023) ✓ Initiated clinical trials of docirbrutinib (2021) ✓ Initiated clinical trials of monzosertib (2021)	

<ddRD>

- ✓ Advance clinical trials of docirbrutinib (AS-1763) and monzosertib(AS-0141)
- ✓ Create next wave of pipeline
- ✓ Receive milestone payments and royalty income from out-licensed programs

<ddSP>

- Expand sales of in-house developed products and services in North America and Asia
- Secure sustainable sales growth by launching new products and services and reaching out to new customers
- Generate cash to invest in ddRD

ddRD: Drug Discovery R&D business
ddSP: Drug Discovery Support Business

Business Plan

(JPY million)	FY2025 Actual	**FY2026 Plan**	**Outlook for 2027 – 2030**
Total Sales	579	**720**	
ddSP business	579	**720**	Maintain stable sales
ddRD business	—	—	Revenue from milestone payments and upfront payments
Total Operating Loss	(2,074)	**(2,028)**	
ddSP business	(50)	**108**	Maintain stable profit while investing in product developments
ddRD business	(2,024)	**(2,137)**	Continue to invest in R&D and deliver profits depending on the size of milestone payments and upfront payments
Ordinary Loss	(2,144)	**(2,053)**	
Net Loss	(2,171)	**(2,090)**	

(JPY million)	FY2025 Actual	**FY2026 Plan**	**Outlook for 2027 – 2030**
R&D Cost	1,851	**1,950**	Continue to invest in R&D for the future growth. The R&D cost may vary from JPY 1 bn to 2.5 bn, depending on the size of clinical studies.
Capex	9	**35**	Invest in equipment for R&D and IT system (JPY20 mn to 100 mn)

- Business plan for FY2026 dose not include potential milestone payments or upfront payments as the timing or the amounts are difficult to predict.
- Numerical targets for 2027-2030 are not disclosed for the same reason.

ddRD: Drug Discovery R&D business
ddSP: Drug Discovery Support Business

Key Milestones for 2026

Business		Key Milestones		
		Milestones for 2025	Achievement in 2025	Milestones for 2026
ddRD	Docirbrutinib (AS-1763)	☐ Promote Ph1b dose expansion part and present interim clinical data from the study	☑ Promote Ph1b dose expansion part and present interim clinical data from the study	☐ Promote Ph1b study ☐ Out-license or initiate Ph2 by joint-development
	Sofnobrutinib (AS-0871)	☐ Out-license or initiate Ph2 by joint-development	☐ Out-license or initiate Ph2 by joint-development	☐ Out-license or initiate Ph2 by joint-development
	Monzosertib (AS-0141)	☐ Promote Ph1 study and choose cancer types for the clinical development	☑ Promote Ph1 study ☐ choose cancer types for the clinical development	☐ Complete Phase 1 study ☐ Support the initiation of Phase 1b study (Investigator-Initiated Trial)
ddSP		☐ Expand sales of in-house developed products and services in North America, Europe and Asia ☐ Increase line-up of protein kinase products ☐ Expand sales of cell-based assay	☐ Expand sales of in-house developed products and services in North America, Europe and Asia ☑ Increase line-up of protein kinase products ☐ Expand sales of cell-based assay	☐ Expand sales of in-house developed products and services in North America, Europe and Asia ☐ Increase sales of protein kinase products ☐ Expand sales of profiling services

ddRD: Drug Discovery R&D business
ddSP: Drug Discovery Support Business

☑ Achieved
☐ Plan or to be achieved

Balance Sheet

- In order to advance clinical trials, we aim to maintain adequate cash position by generating cash from Drug Discovery Support(ddSP) business and licensing, as well as by raising funds from capital markets.

(JPY million)	As of Dec. 31, 2024	As of Dec. 31, 2025	Change
Current assets	2,737	1,175	-1,562
Cash and deposits	2,108	516	-1,591
Non-current Assets	34	54	19
Total assets	2,772	1,229	-1,542
Current liabilities	222	168	-54
Non-current liabilities	73	752	678
Total liabilities	296	920	623
Total net assets	2,475	309	-2,166
Total liabilities and net assets	2,772	1,229	-1,542

Financing Overview

We have implemented a comprehensive convertible bonds issuance program totaling JPY675 million.
As planned, we have successfully completed the issuances of all three series of unsecured convertible bonds.

Allotment Resolution Date	July 11th, 2025	September 12th, 2025	November 11th, 2025
Bond Name	Carna Biosciences, Inc. First Series Unsecured Convertible Bonds	Carna Biosciences, Inc. Second Series Unsecured Convertible Bonds	Carna Biosciences, Inc. Third Series Unsecured Convertible Bonds
Issue Price of Bonds and Stock Acquisition Rights	Bonds: JPY225,000,000 Stock Acquisition Rights: No cash payment required	Bonds: JPY225,000,000 Stock Acquisition Rights: No cash payment required	Bonds: JPY225,000,000 Stock Acquisition Rights: No cash payment required
Total Proceeds	Total JPY225,000,000	Total JPY225,000,000	Total JPY225,000,000
Payment Date	July 28th, 2025	September 29th, 2025	November 27th, 2025
# of Underlying Shares	791,389 shares	1,256,913 shares	1,335,470 shares
Conversion Price	JPY315.9 (90% of the closing price on July 10th; no reset of Conversion Price)	JPY198.9 (90% of the closing price on September 11th; no reset of Conversion Price)	JPY187.2 (90% of the closing price on November 10th; no reset of Conversion Price)
Interest Rate	1.0% per annum	Same as on the left	Same as on the left
Maturity Date	July 28th, 2028	September 29th, 2028	November 27th, 2028
Method of Offering	Third-party Allotment	Same as on the left	Same as on the left
Designated Allottee	Cantor Fitzgerald Europe	Same as on the left	Same as on the left

(Announced on Jan. 29th, 2026) Fundraising - Overview

We have decided to implement this fundraising to strengthen our financial base, which is necessary to steadily advance our drug discovery business centered on the clinical development of docirbrutinib (AS-1763) and monzosertib (AS-0141). In addition to the issuance of unsecured straight bonds, we will carry out an allotment of new shares to our Representative Director and the issuance of stock acquisition rights.

Second Series Unsecured Bonds ("the Bonds")

Total Issue Price	JPY1,711 mm
	(JPY92.5 per Face Value of JPY100)
Payment Date	Feb. 17th, 2026
Redemption Date	Feb. 17th, 2028
Interest	0%
Allottee	Cantor Fitzgerald Europe

Total face value

JPY1,850 mm

✓ Redeem sequentially with the progress of exercise of the SARs to reduce debt risk

Allotment of New Shares to Representative Director

Total Issue Price	JPY20 mm
	(JPY433 per share)
Allottee	**Representative Director Kohichiro Yoshino**

# of new shares to be issued

46,200 shares

✓ The allotment was resolved following the intention of our Representative Director, Kohichiro Yoshino, to subscribe for new shares at market price

✓ The Representative Director demonstrates a strong commitment to the Company's medium- to long-term business growth through his own investment.

docirbrutinib (AS-1763) development-accelerating Stock Acquisition Rights ("the SARs")

# of Units	76,983 units
# of Underlying Shares	7,698,300 shares
Initial Strike Price※1	JPY389.7
Allottee	Cantor Fitzgerald Europe

Total raising amount ※2

JPY3,015 mm

(Net raising amount of JPY2,995 mm after issuing costs, etc.)

※1 Strike price will be adjusted to 90% of the closing price on the last trading day of the week preceding the week in which the exercise notice date falls

※2 Amount to be raised if all the SARs are exercised based on the initial strike price (including the total issuance price of the SARs of JPY15 mm)

✓ After redeeming the Bonds with the exercise proceeds, enable the procurement of additional business funds during future periods of share price appreciation

Repurchase and Cancel of First Series Convertible Bonds

Issue Date	Jul. 28th, 2025
Repurchase and Cancel Date	Feb. 17th, 2026
Funds for Repurchase	Funds from the Bonds
Coupon	1% per year
Decrease in # of dilutive shares	791,389 shares

Total repurchasing amount

JPY250 mm

✓ Repurchase and cancel using the funds raised through the Bonds

✓ Reduce interest costs and the number of dilutive shares

（Announced on Jan. 29th, 2026）Fundraising - Use of proceeds

Breakdown of the fundraising structure and details of the use of proceeds are as follow.

Total amount of fundraising and costs for redeeming the Bonds and repurchasing the convertible bonds		
The Bonds	※Estimated net proceeds after deducting issuance-related expenses from the total amount to be raised assuming all the SARs are exercised based on the initial strike price (including the total issuance price of the SARs of JPY15 mm)	JPY1,711 mm
The SARs		※JPY2,995 mm
Allotment of the New Shares		JPY20 mm
	Fundraising	**Total JPY4,726 mm**
Repurchase of the First Series Convertible Bonds		JPY250 mm
Early Redemption of the Bonds		JPY1,850 mm
	Repurchase of Convertible Bonds and Redemption of the Bonds	**Total JPY2,100 mm**
	Net Fundraising after the Repurchase and Redemption	**Total JPY2,626 mm**

Use of Proceeds	
Costs for the clinical development of docirbrutinib（AS-1763）and monzosertib（AS-0141）	JPY1,335 mm
Costs for the creation of development compounds and research expenses, etc. *Including non-clinical research expenses for docirbrutinib (AS-1763) and monzosertib (AS-0141)*	JPY762 mm
Working Capital	JPY529 mm
	Total JPY2,626 mm

Appendix

docirbrutinib（AS-1763）

docirbrutinib (AS-1763): Phase 1b Study

Primary objective of the Phase 1b study is to determine the recommended phase 2 dose (RP2D) and to exploratorily evaluate the efficacy of docirbrutinib

Objective	Determine the RP2D and exploratorily evaluate the efficacy
Eligible patients	Patients with CLL/SLL and B-cell NHL who have received at least two prior lines of systemic therapy

Phase 2 study

Dose escalation part

- **3+3 design**
- **Twice daily administration (BID)**
- **Completed enrollment at 100–500mg BID dose levels**

Dose expansion part

- **3 cohorts**
- **Cohort 1: CLL/SLL**
- **Cohort 2: B-cell NHL**
  Cohort 3: pirtobrutinib-pretreated patients
- **Each cohort has two or three dose levels**

Cohort 1	Cohort 2	Cohort 3
Dose levels and current enrollment status		
300mg BID (Completed enrollment)	300mg BID (Completed enrollment)	**400mg BID (Enrolling)**
400mg BID (Enrolling)	**400mg BID (Enrolling)**	500mg BID
500mg BID	500mg BID	

Glossary

Patients who have received at least two prior lines of systemic therapy
Patients who have developed resistance or are intolerant to at least two types of systemic treatment

CLL/SLL
CLL: Chronic Lymphocytic Leukemia
SLL: Small Lymphocytic Lymphoma

B-cell NHL
B-cell non-Hodgkin Lymphoma

Dose escalation part
This part starts at a low dose and gradually increases the dose to assess safety and tolerability and to identify the maximum tolerated (Maximum Tolerated Dose) or recommended dose

3+3 design
In this design, three patients are treated at each dose level, and decisions to escalate to the next dose are made based on the adverse events observed

Dose expansion part
In this part, doses selected in the dose escalation phase are further evaluated in more patients

Cohort
A group of people in a clinical trial who receive the same treatment or dose level

pirtobrutinib
Non-covalent BTK inhibitor developed by Eli Lilly

Docirbrutinib Ph 1b study: Clinical sites

Clinical sites（As of December 31, 2025）

- UC Irvine Health
- Mount Sinai Comprehensive Cancer Center
- Moffitt Cancer Center
- Northwestern Memorial Hospital
- American Oncology Partners
- University of Maryland Medical Center-Greenebaum Comprehensive Cancer Center
- University of Massachusetts Memorial Medical Center
- Optum Medical Care PC
- Duke University
- Taylor Cancer Research Center
- Oncology Consultants
- University of Texas MD Anderson Cancer Center
- The Medical College of Wisconsin

✓ **Phase 1b study is ongoing at thirteen clinical sites in the US.**

ASH2025 Poster Presentation Executive Summary

- **Presented updates from ongoing Phase 1b study and new preclinical findings of docirbrutinib at ASH2025**
- **In the Phase 1 study, docirbrutinib demonstrated a favorable safety profile and promising efficacy**
- **Preclinical study indicates that docirbrutinib may offer effective solution to challenges observed with existing BTK inhibitors**

*ASH2025: the 67th American Society of Hematology Annual Meeting & Exposition held in December 2025

Updates from ongoing Phase 1b study

Safety

- ✓ In dose escalation, docirbrutinib was well tolerated
- ✓ In general, docirbrutinib demonstrated a favorable safety profile with Grade ≥3 treatment-related adverse events (TEAEs) reported in 13% of patients

Efficacy

- ✓ All patients with CLL/SLL, MCL and WM experienced reduction in tumor size ※ Serum IgM levels for WM

Docirbrutinib demonstrated a favorable safety profile and showed promising and durable responses in patients with CLL/SLL, MCL and WM who had recevied at least two prior lines of systemic therapy. Theses findings suggest that docirbrutinib has the potential to become a new therapeutic option for theses indications

Preclinical study

Unique inhibitory profile

- ✓ Docirbrutinib has a unique inhibitory activity profile that enables sustained BTK inhibition and may provide prolonged therapeutic effects

Implication for efficacy in drug-resistant patients

- ✓ Docirbrutinib is effective against human DLBCL cell lines harboring BTK resistance mutations

Combination therapy with venetoclax

- ✓ In combination with venetoclax, docirbrutinib induced marked cell death

Docirbrutinib has the potential to overcome the challenges associated with currently approved BTK inhibitors

ASH2025: Encouraging Safety Findings from the Ongoing Phase 1b Trial

Docirbrutinib has demonstrated favorable safety and tolerability profile in ongoing Phase 1b study

October 17, 2025

Low incidence of Grade ≥3 Treatment-related Adverse Events (TEAEs)

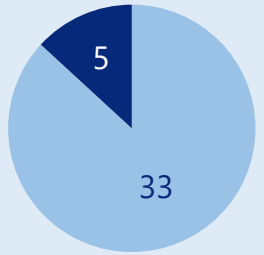
- ✓ **38 patients were enrolled, including 23 additional patients** since the previous presentation at ASH2024
- ✓ In dose escalation, **docirbrutinib was well tolerated at doses up to 500 mg BID, and the maximum tolerated dose was not reached**
- ✓ No drug-related atrial fibrillation or hypertension was reported, even with additional patients enrolled since the previous presentation. **Grade ≥3 TEAEs were reported in 13% of patients**, suggesting favorable safety profile
- ✓ Many patients have been on long-term treatment due to the low incidents of adverse events, with several receiving docirbrutinib for over a year, indicating an excellent safety profile. (41% of patients treated with ibrutinib were reported to have discontinued the treatment, with half of those discontinuations attributed to intolerance ※)
- ✓ Additional patient enrollment is planned to establish the safety profile of docirbrutinib

※ Mato AR, et al., Haematologica. 2018;103(5):874-879

docirbrutinib

Grade ≥3 TEAEs※

13%



Diseases			Pts
CLL/SLL	CLL	Chronic Lymphocytic Leukemia	21
	SLL	Small Lymphocytic Lymphoma	2
B-cell NHL	FL	Follicular Lymphoma	5
	MCL	Mantle cell lymphoma	5
	WM	Waldenström macroglobulinemia	3
	MZL	Marginal zone lymphoma	2
		Total	38

Dose levels	Pts
100 mg BID	3
200 mg BID	3
300 mg BID	22
400 mg BID	7
500 mg BID	3
Total	38

※ Preliminary data from Phase 1b study of docirbrutinib (ASH2025 presentation)

Glossary

Grade 3 Adverse Events
Adverse events that are severe or medically significant but not immediately life-threatening

ASH2025: Emerging Evidence of Efficacy in the Phase 1b Study

All CLL/SLL, MCL, and WM patients experienced reduction in tumor size

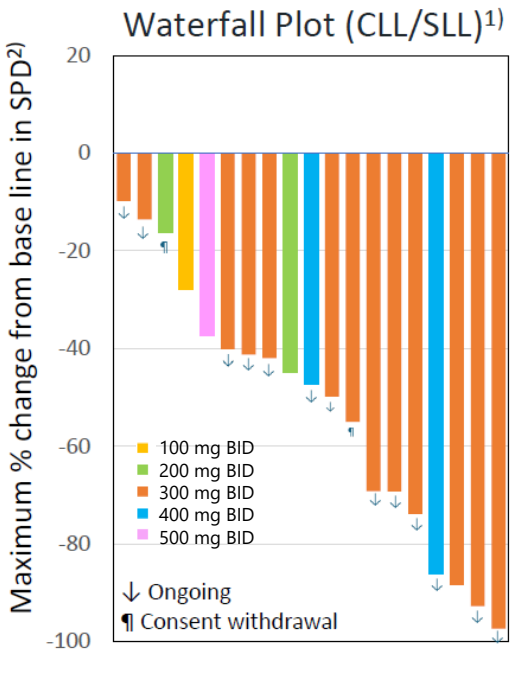
CLL/SLL patients

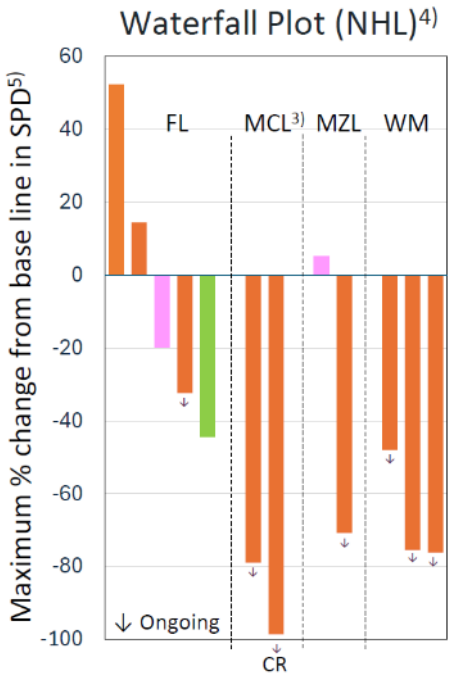
- ✓ **20 efficacy-evaluable patients**, representing an **addition of 11 patients** since the previous presentation at ASH2024
- ✓ **Overall response rate (ORR) was 40%**, compared to 67% as of ASH2024, with more patients who recently entered the trial included in the evaluation
- ✓ 5 patients who evaluated as stable disease showed ≥40% tumor reduction (40.1–49.9%), and further improvement in ORR is projected as treatment continues
- ✓ 400 mg cohort now enrolling, and further improvement in ORR is anticipated

NHL patients

- ✓ **12 efficacy-evaluable patients**, representing an **addition of 7 patients** since the previous presentation at ASH2024
- ✓ Among NHL patients, **ORR was 100% for MCL (2 patients) and WM (3 patients)**
- ✓ All MCL and WM patients remain on treatment
- ✓ 1 MCL patients achieved complete response (CR)

As of October 17, 2025





1) Dose levels at best tumor response are shown. One patient is not included due to no target lesion.
2) SPD: Sum of products of diameters
3) A pirtobrutinib-pretreated pt enrolled in Cohort 3 is not included.
4) Dose levels at best tumor response are shown
5) Serum IgM levels for WM

Glossary

Response
Evaluated as Response when tumor size decreases ≥50% or disappers. For WM, Serum IgM levels is a primary criterion and includes minor response with ≥25% reduction

Overall Response Rate (ORR)
Proportion of patients who achieved Response among all patients who received treatment

Unmet medical need for next generation BTK inhibitors due to resistance to approved agents

Role of BTK inhibitors	• BTK inhibitors are a standard of care for chronic lymphocytic leukemia (CLL)
Drug resistance	• Covalent BTK inhibitors suffer from drug resistance driven by mutation at C481 in BTK • Drug resistance associated with mutations such as T474I and L528W has been reported for non-covalent inhibitors
Need for novel inhibitors	• Novel inhibitors that can target multiple resistance mutations in BTK are urgently needed.
Inhibitory potency of docirbrutinib against resistance mutations in BTK	• Docirbrutinib is an orally available, potent and highly selective BTK inhibitor, effective against multiple BTK resistant mutations

In this study, efficacy of docirbrutinib was examined in human diffuse large B-cell lymphoma (DLBCL) harboring multiple BTK resistance mutations, both alone and in combination with venetoclax. Activity of docirbrutinib in primary CLL cells was also assessed.

Glossary

BTK inhibitor
Drugs for hematologic cancers that block Bruton's tyrosine kinase (BTK), an enzyme essential for B-cell function, thereby suppressing the proliferation of malignant B cells

Drug resistance
For molecular targeted drugs, therapy can become ineffective during treatment due to the emergence of mutations in the drug's target protein (drug resistance mutations)

Covalent BTK inhibitor
Covalent BTK inhibitors irreversibly bind to BTK at the 481 cysteine residue. Patients are reported to develop resistance during the treatment due to C481S mutation.

C481, T373I, L528W
The specific residue position within the BTK amino acid sequence at which the mutation occurs

Non-covalent BTK inhibitor
Inhibitors designed to block BTK without forming a covalent bond with the C481S mutant residue in BTK, and therefore effective against the C481S resistance mutation

DLBCL cell line
A cell line established from diffuse large B-cell lymphoma (DLBCL) for research use

Venetoclax
A drug that reduces cancer cells by blocking a protein called BCL-2

ASH2025: Preclinical Study – Poster Summary

The study indicates that docirbrutinib has the potential to overcome the challenges associated with currently approved BTK inhibitors

Unique inhibitory profile

- ✓ The study indicated that docirbrutinib binds to an inactive conformation of BTK and has a slow off-rate profile
- ✓ **Docirbrutinib is expected to provide robust efficacy through sustained BTK inhibition**

Efficacy against BTK-mutant cancer cell lines

- ✓ We generated DLBCL cell lines harboring BTK mutations and demonstrated that docirbrutinib is effective at the cellular level as well
- ✓ **Docirbrutinib is expected to be effective for patients who have developed resistance to the currently approved BTK inhibitors**

Synergy with venetoclax

- ✓ In combination with venetoclax, docirbrutinib induced significant cell death in OCI-Ly10 cells harboring BTK resistance mutations and in primary CLL samples
- ✓ **Combination therapy with docirbrutinib and venetoclax is anticipated to further enhance therapeutic efficacy**

Glossary

Slow off-rate
Indicator used in pharmacology and biochemistry to describe the slow dissociation (prolonged binding) of a drug from its target after binding. Drugs with a slow off-rate are generally expected to exhibit higher efficacy.

Cell death
The process in which a cell stops functioning and dies. Many cancer drugs eliminate cancer cells by inducing apoptosis, one of the major cell death processes.

Appendix

sofnobrutinib（AS-0871）

Sofnobrutinib (AS-0871) : Potential best-in-class

Embryo-Fetal Development (EFD) toxicity study was performed to prove potential advantages of sofnobrutinib over other BTK inhibitors.

Sofnobrutinib showed "No Teratogenic Effect“ in the EFD study, suggesting it is suitable for the treatment of dermatologic diseases including CSU.

As most BTK inhibitors approved are teratogenic, their use should be limited especially for women.
Sofnobrutinib is confirmed to be non-teratogenic in the EFD toxicity study, providing a treatment option for a wider range of patients.

Sofnobrutinib is the only BTK inhibitor having a non-covalent inhibitory mechanism of action with no teratogenic effect.

Sofnobrutinib (AS-0871) : CSU is a skin disease with unmet medical needs

Chronic Spontaneous Urticaria (CSU) is a distressing skin disorder that is characterized by itching and hives lasting for more than 4 weeks with unknown causes. The symptoms can last months or years, affecting QoL of patients.

Challenges of CSU

- A significant number of patients having uncontrolled CSU by existing drugs.
- High socio-economic costs for patients with high disease activity*
- Large number of patients; approximately 1% of the global population is affected*

High unmet medical needs with potential large market

＊Br J Dermatol 2021;184:226-36.

Competitors

Compound	Company	Development Phase
Remibrutinib (LOU064)	Novartis	FDA approved

Remibrutinib was approved by FDA in September 2025 as the first BTK inhibitor for the treatment of CSU.
It is also being investigated in ongoing clinical trials across a variety of immune-related conditions.*

＊https://www.novartis.com/news

Opportunity

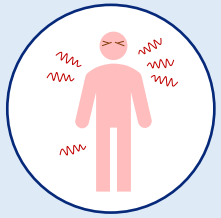
- Approval of new treatment options may trigger the expansion of CSU market.
- We plan to pursue the clinical implications of sofnobrutinib (non-covalent BTK inhibitor) to provide clinical benefits by minimizing potential adverse events associated with covalent BTK inhibitors including remibrutinib.

Chronic Spontaneous Urticaria (CSU)

CSU is a debilitating disease of chronic itch, hives and angioedema, lasting six weeks or more.

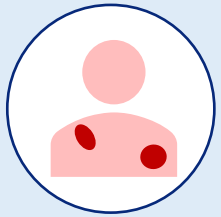
Symptoms

There is no specific external trigger for CSU, but the autoimmune system may play a role

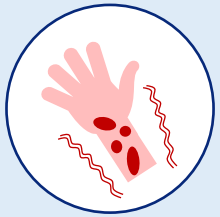


Spontaneously present & re-occur

Lack of Energy
Depression/Anxiety
Chronic (Lasting for at least six weeks)



Red swollen hives



Itch

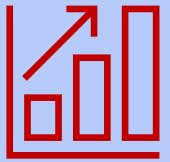
Number of Patients

2.8 million

diagnosed prevalent cases in major seven markets

- ✓ Approximately 1% of the population worldwide is affected.
- ✓ Approximately 50% of CSU patients don't respond to H1-antihistamine.
- ✓ Curative treatment is not available.
- ✓ High socio-economic costs for patients with high disease activity.

Market Size



$2,240 million

in 2023

- ✓ The market size of CSU in major seven countries is expected to reach $5.4 bn by 2032 growing at a CAGR of 11.7% from 2024.

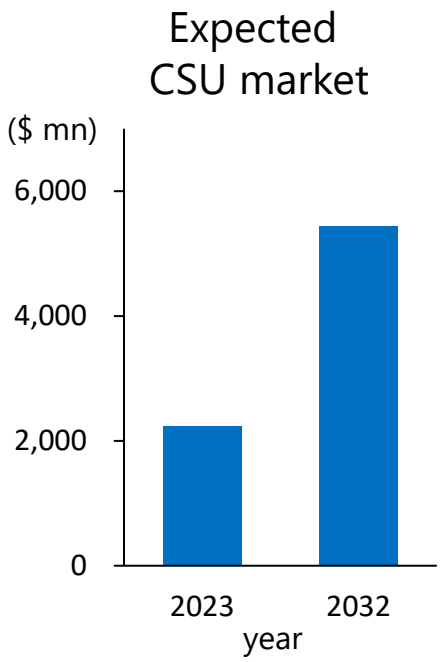
https://www.credenceresearch.com/report/chronic-spontaneous-urticaria-market
Maurer M, et al. Allergy. 2011;66:317–330.

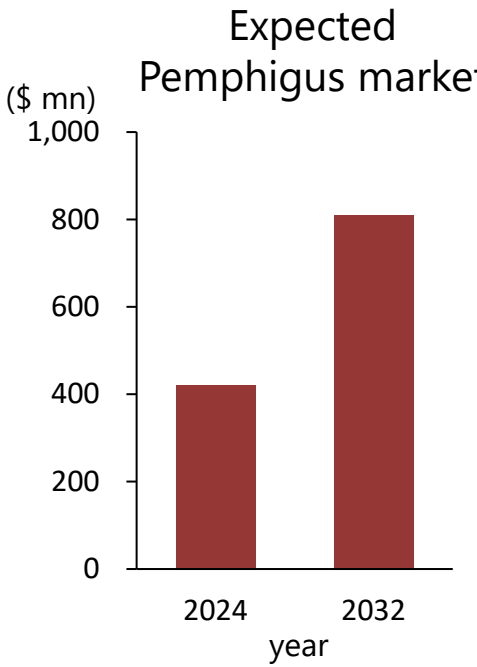
Potential Market Size for Sofnobrutinib (AS-0871)

Initial focus

Diseases	Number of patients
CSU	• Diagnosed prevalent cases : 2.8 mn* • WW population affected: 76 mn
Pemphigus	• Diagnosed prevalent cases : 40,000*

*in major 7 markets





Other potential therapeutic area

Diseases	Number of patients	Market size in value
Systemic lupus erythematosus (SLE)	Global SLE prevalence is estimated to be 15.87 to 108.92 per 100,000 people	expected to reach $3,517 mn by 2030
Multiple sclerosis (MS)	In 2016, an estimated 2.2 million people worldwide had MS, corresponding to a prevalence of 30.1 cases per 100,000 population	expected to reach $34 bn by 2031
Rheumatoid arthritis (RA)	18 million people worldwide were living with RA	expected to reach $70 bn by 2030

https://www.delveinsight.com/
https://www.databridgemarketresearch.com/
https://ard.bmj.com/
https://straitsresearch.com/
https://www.skyquestt.com/
https://www.who.int/
Ann Rheum Dis 2023;82:351–356
Lancet Neurol 2019 ; 18: 269–85
Source : Clarivate

Appendix (others)

Management Team

Directors

Kohichiro Yoshino, Ph.D. **President & Chief Executive Officer, Representative Director**

Dr. Yoshino founded Carna Biosciences in 2003 as a spin-out venture from Nippon Organon, a subsidiary of N.V. Organon where he was the head of the Osaka Research Center. As a member of Organon Research Committee, Dr. Yoshino contributed to research and development of NV Organon. Before joining Nippon Organon, he engaged in the research and development of small molecule drugs at Kanebo Corporation Inc.
From 2004 to 2008, he was a Visiting Professor at Center for Advanced Science and Innovation, Osaka University.
He earned M.S. in Chemistry from the Graduate School of Tokyo Institute of Technology and Ph.D. from Kyoto University

Masaaki Sawa, Ph.D. **Chief Scientific Officer, Director**

Dr. Sawa built the current drug discovery group at Carna. Before joining Carna, he held positions at Sumitomo Dainippon Pharma.
Prior to that, he was a medicinal chemist at Nippon Organon, a subsidiary of N.V. Organon.
From 2004 to 2006, he was a visiting scientist at the Scripps Research Institute in San Diego.
Dr. Sawa was a Visiting Professor at Graduate School of Medicine, Kobe University from 2013 to 2015.
He received his Ph.D. from Kyoto University.

Emi Yamamoto **Chief Financial Officer, Director, President of CarnaBio USA, Inc.**

Ms. Yamamoto joined Carna Biosciences in 2004 after engaged in fund administration at CSK Venture Capital. She built Carna's accounting and business management group and held a responsible role in Carna's IPO. Since 2017, she leads administration group, in charge of accounting, finance, human resources, and corporate planning.
Ms. Yamamoto holds a bachelor's degree in Business Administration from Aoyama Gakuin University, and a Certified Public Accountant.

Akinori Arimura, Ph.D. **Chief Development Officer, Director**

Dr. Arimura joined Carna Biosciences in 2018 as head of newly established clinical development department and has since established Carna's clinical development capability both in Japan and in the U.S. Prior to joining Carna, Dr. Arimura led the global development of anticancer drugs at Shionogi & Co., Ltd, with responsibility for planning and implementing the clinical studies as well as for collaboration with biotech companies. Prior to that, he engaged in the drug discovery research at Shionogi as head of allergy, immunology and oncology areas.
He was a visiting scientist at Columbia University, where he was recognized for his achievement in Molecular Immunology research.
Dr. Arimura received his Ph.D. from Gifu Pharmaceutical University.

Management Team

Directors

Kaoru Suzuki, Ph.D. **Outside Director**

Dr. Suzuki joined the Board of Directors of Carna Biosciences in 2024. Before joining Carna, Dr. Suzuki held key senior positions in business development and partnering at Roche Pharma Japan, Roche Partnering. He was the representative of Roche Pharma Japan, Roche Partnering and the Japan/Korea Business Development Head from 2010 to 2022 and has been serving as a Senior Advisor since 2022. Prior to that, he engaged in research & development, business development and licensing activities at Daiichi Pharmaceutical Co., Ltd. Dr. Suzuki earned a M.S. in Pharmacy from the Graduate School of Tokyo University of Science and his Ph.D. in Medicine from the Jikei University School of Medicine.

Atsuo Arita **Outside Director**

Before joining the Board of Directors in 2020, Mr. Arita served as External Auditor of Carna Biosciences from 2004 to 2020, overseeing its management as a full-time company auditor. He held various responsible roles in accounting, finance, and sales management at Kanebo Corporation Ltd. and was the head of business management at Kanebo.
He holds a bachelor's degree in Business and Commerce from Keio University.

Tsuguo Ogasawara **Outside Director**

Mr. Ogasawara served as External Auditor of Carna Biosciences from 2005 to 2020 before joining the Board of Directors in 2020. He has brought Carna his extensive experience in international business. He was a Director at Chugai Pharmaceutical Co. Ltd., in charge of international business. Prior to that, he was engaged in business management, finance, and international business at Toray Industries, Inc.
He holds a bachelor's degree in Economics from Keio University.

Takao Matsui **Outside Director**

Mr. Matsui served as External Auditor of Carna Biosciences since 2019 to 2020 before joining the Board of Directors in 2020. He has over 35 years of experience in financial audit and related advisory business. He served as Certified Public Accountant at KPMG AZSA LLC. from 1982 to 2018. Mr. Matsui also currently serves as Outside Director of AIR WATER, INC. He was a Specially Appointed Professor at School of Accountancy, Kansai University since April 2018 to March 2020. He is a part-time lecturer at Kansai University and School of Accountancy, Kansai University since April 2020.
Mr. Matsui holds a bachelor's degree in School of Business Administration from Kwansei Gakuin University, and a Certified Public Accountant.

"Carna" is a goddess of Roman mythology who takes care of human health, protecting the human heart and other organs as well as everyday life, and is said to be the root for the word "cardiac."

The word "biosciences" is derived from the words 'biology' and 'life sciences.'

Carna Biosciences has created contemporary Carna goddess with protein kinase.

Carna Biosciences, Inc.

Corporate Planning

BMA3F 1-5-5 Minatojia-Minaimachi,

Chuo-ku, Kobe 650-0047

https://www.carnabio.com/

ir-team@carnabio.com