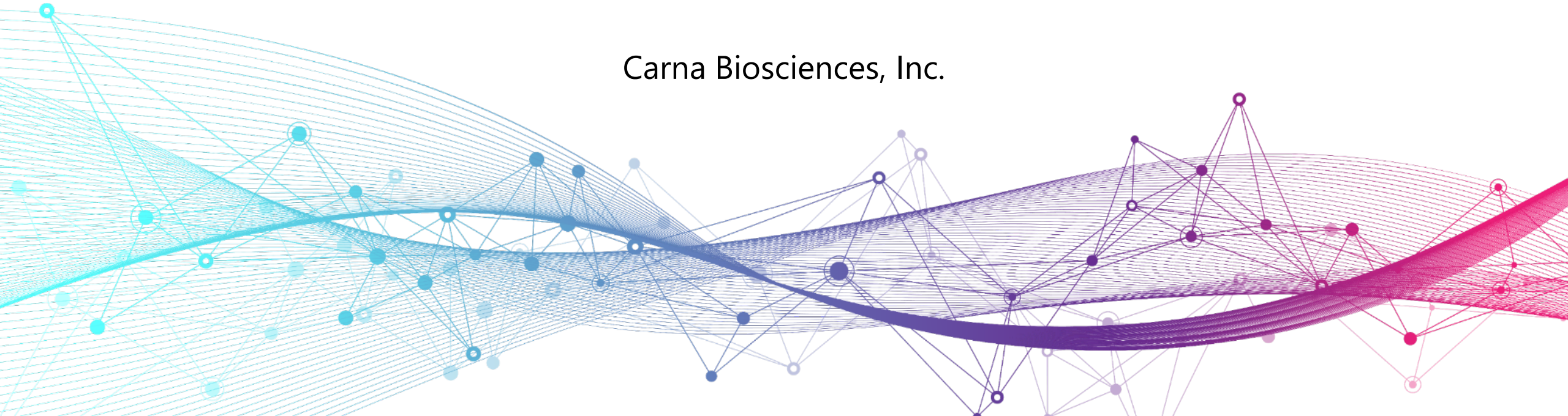
Financial Results
Q2 FY2026

（January to June 2026）

Carna Biosciences, Inc.



Executive Summary

Updates on the clinical stage pipeline

docirbrutinib (AS-1763)

Presented the latest clinical data from ongoing Phase 1b study at **EHA2026 (June)**

Docirbrutinib continued to demonstrate a favorable safety profile and promising efficacy as more patients enrolled

New preclinical findings were published in **Blood Cancer Journal (May 2026)**

monzosertib (AS-0141)

Preparations for the initiation of the **Phase 1b study (triplet combination therapy)** are underway.

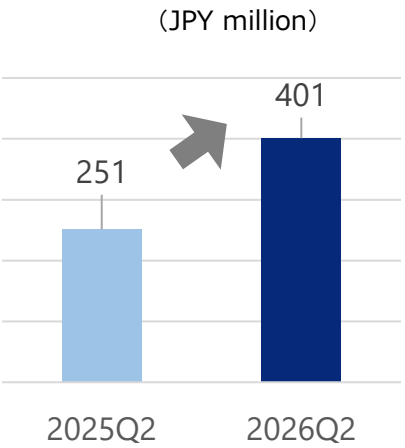
Received FDA Orphan Drug Designation for AML in July

New preclinical findings on monzosertib were presented at **AACR2026 (April)**

Drug Discovery Support business (ddSP) Sales

Sales increased 59% YoY

ddSP sales grew significantly



Financial results summary

(JPY million)	Q2 FY2026 Actual	FY2026 Plan	FY2026 Progress
Operating loss	954	2,028	47.0%
R&D expense	926	1,950	47.5%

Operating loss and R&D spending were in-line with the full year plan.

Executive Summary

Shinwa Kurihara Appointed Chief Business Development Officer (CBDO)

Effective July 27, Shinwa Kurihara, PhD, MBA has been appointed CBDO at Carna Biosciences. Before Carna, Dr. Kurihara served as Vice President of Business Development at Daiichi Sankyo Co., Ltd., where he was involved in the strategic partnership with AstraZeneca (UK) on the global co-development and commercialization of Enhertu (trastuzumab deruxtecan) and Datroway (datopotamab deruxtecan), and was further involved in the global development and commercialization partnerships for three antibody-drug conjugates (ADCs) with Merck & Co. (US), while also leading the out-licensing of numerous pipeline assets, making substantial contributions to phenomenal growth of Daiichi Sankyo.

Going forward, with Dr. Kurihara leading the effort, we will work to maximize the value of our pipelines.

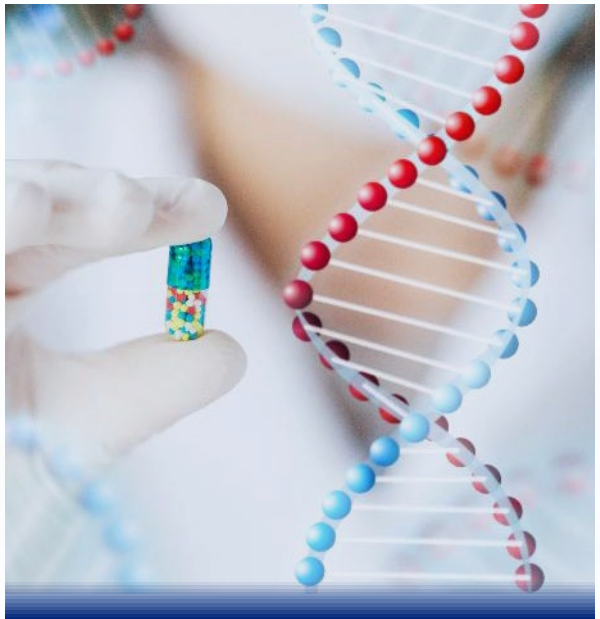
AGENDA

1. Company Overview
2. Updates on Pipelines
3. Financial Results
4. Appendix

Company Overview

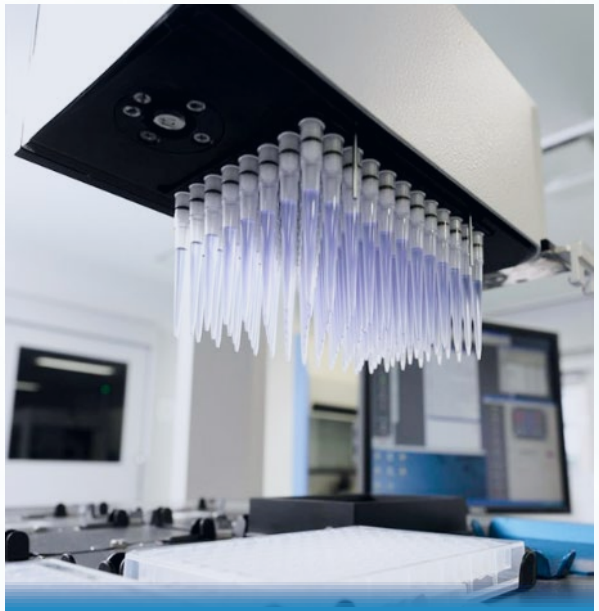
Our Business

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.30)
Ongoing joint research with Sumitomo Pharma (See P.31)

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.13)

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.

Discovery → **Preclinical** → **Clinical development** → **Registration Commercialization** → **Post-launch**

Costs related to scientists and experiments

Costs increase due to the studies and preparations required to initiate clinical trials

Substantial cost increases driven by clinical trials

Commercialization generate returns

Monetization

Revenue

Investment

Time

Developing and commercializing a new drug takes over a decade and demands major R&D investment

Over 10 years from discovery phase to monetization

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)

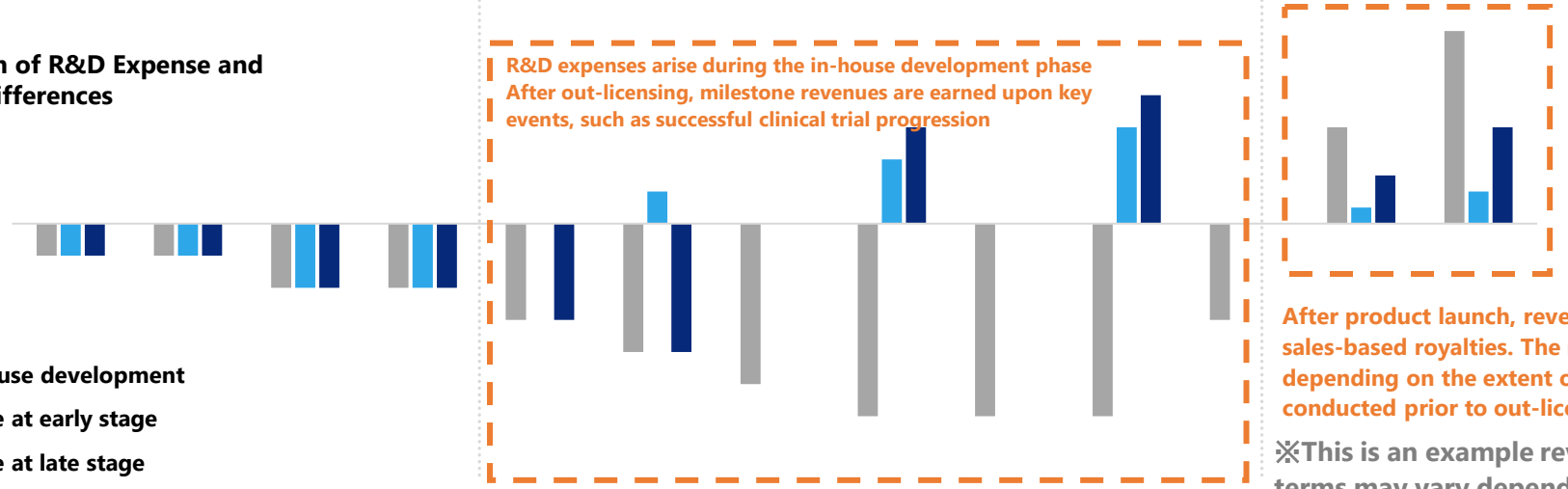
Commercially launched and prescribed to patients for treatment

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.

	Discovery/Preclinical	Clinical development	Post-launch	R&D costs	Revenue
Fully in-house development	In-house development		Sales revenue ¥, Sales revenue ¥	Large	Large
Out-license at early stage	In-house development	Out-license, Milestone ¥, Milestone ¥, Milestone ¥	Royalty ¥, Royalty ¥	Small	Small
Out-license at late stage	In-house development	Out-license, Milestone ¥, Milestone ¥	Royalty ¥, Royalty ¥	Medium	Medium

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

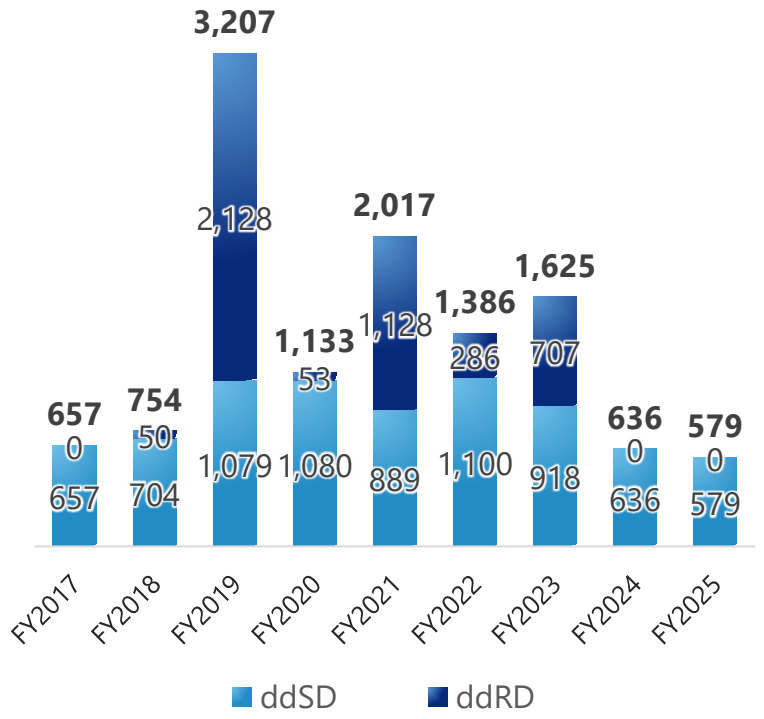
- ✓ ddRD business conducts research and development of innovative small molecule drugs including kinase inhibitors
- ✓ We focus on oncology and inflammatory/immune disorders
- ✓ We develop our oncology pipelines up to Phase 2 to maximize their potential value, while for other therapeutic areas, we typically 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

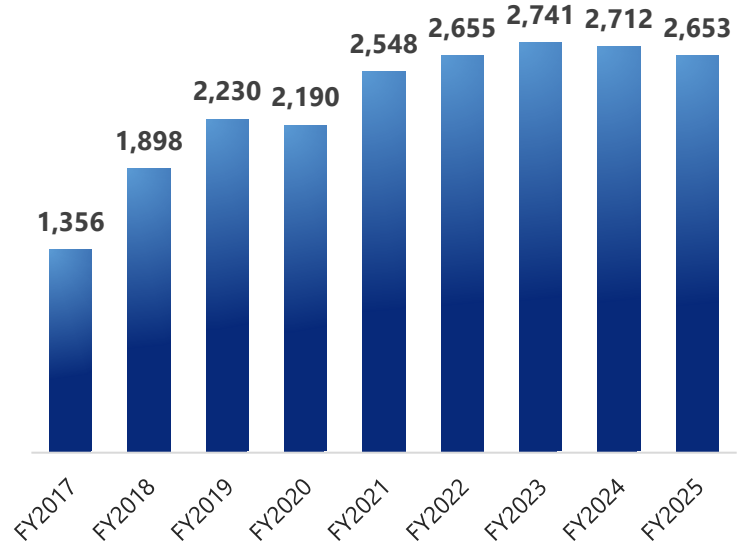
(JPY mn)



- ✓ 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)	Preparing for a Phase 1b clinical study (Cancer patients, US) → Target: Complete Phase 1 study Support the initiation of Phase 1b study (Investigator-Initiated Trial) 2026

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

Updates on Clinical Studies

- **docirbrutinib : Phase 1b clinical study is ongoing**
- **monzosertib: Preparing for a Phase 1b clinical study (Investigator-Initiated Trial)**
- **sofnobrutinib: Phase 1 clinical study is completed. Seeking a partner to conduct Phase 2 study**

docirbrutinib

Indication: Blood cancers

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

Key points

- ✓ **Dr. Nitin Jain, Professor of Leukemia, UT 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 promising clinical data at EHA2026 in June**
- ✓ **New preclinical findings were published in Blood Cancer Journal in May**

sofnobrutinib

Indication: Immune-inflammatory diseases

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

Indication: Solid tumors and blood cancers

Phase 1b Preparation Ongoing
(the U.S. , Investigator-Initiated Trial)

Update

- ✓ **Phase 1 study completed**
- ✓ **Preparing for a Phase 1b study (Investigator-Initiated Trial) in patients with blood cancers**

  Principle Investigator
  Dr. Abhishek Maiti, Department of Leukemia, UT MD Anderson Cancer Center

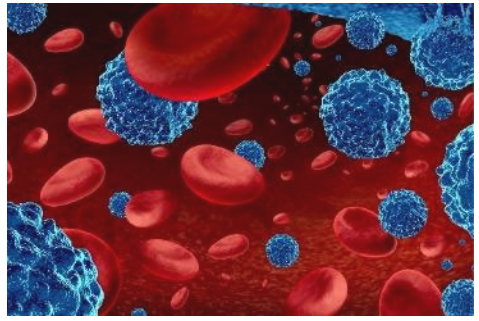
- ✓ **Received FDA Orphan Drug Designation for AML in July**
- ✓ **Presented new preclinical findings at AACR2026 in April**

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.

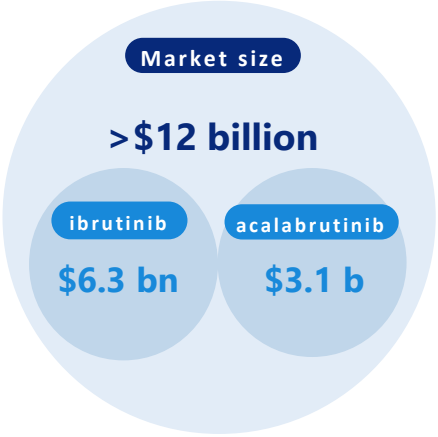


Target Product Profile

- 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

2026 — **Poster presentation at EHA2026**
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.

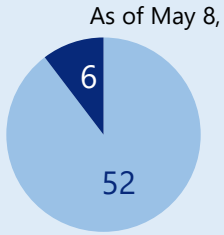
Profile 01 Favorable safety profile

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

docirbrutinib

Grade ≥3 TEAEs※1

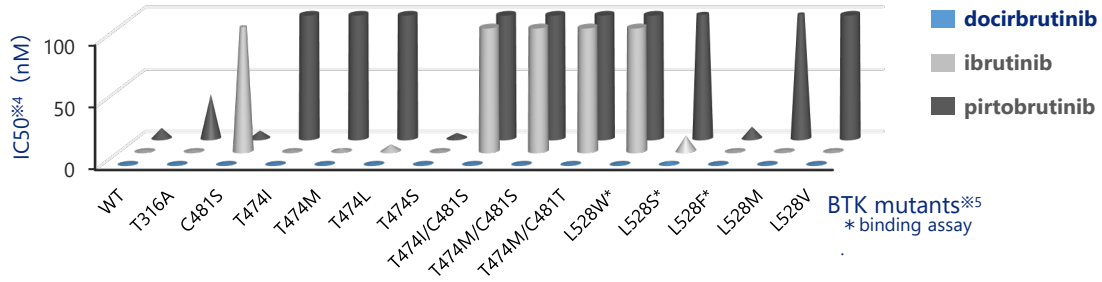
10%



- No drug-related atrial fibrillation or hypertension was reported, even with additional patients enrolled since the previous presentation. Grade ≥3 Treatment-related AEs (TRAEs) were reported in 10% of patients, suggesting favorable safety profile.
- Many patients have remained on treatment, with several receiving docirbrutinib for more than two years, consistent with its 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 (MK-1026, ARQ-531)	Non-covalent BTK inhibitor	Effective against several mutants	Reported	Merck (ArQule)	P3
bexobrutideg (NX-5948)	BTK degrader	Effective against various mutants	Reported (low frequency)	Roche (Nurix)	P3
catadegbrutinib (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.16**	**Carna**	**P1**

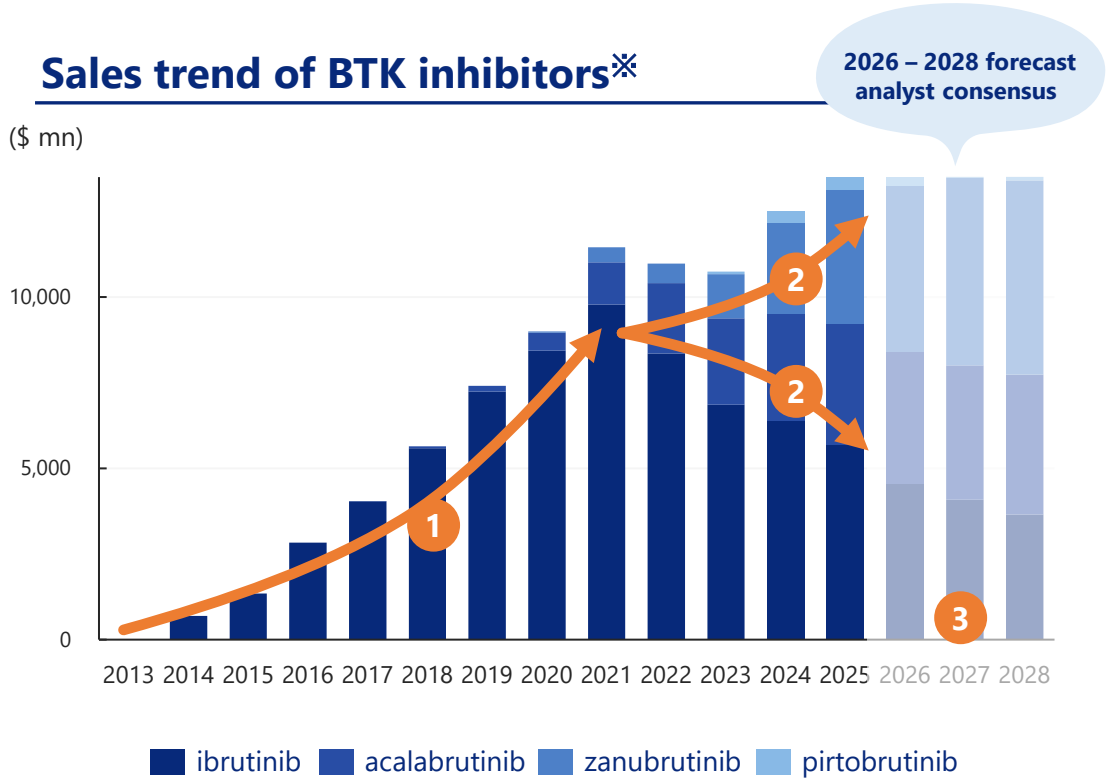
Drug resistance: the reduction in effectiveness of a drug during targeted therapies due to alterations of drug targets including the mutation of the target proteins.

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

docirbrutinib (AS-1763)

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 | New Development | Application to Kidney Disease | Differentiation Competition

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 target diseases

- Chronic Spontaneous Urticaria※1 (CSU), is one of the most promising indications, potential market size is estimated to be $2.2 billion across the major seven markets, with significant growth expected. (See P.51)
- BTK inhibitors' application to chronic kidney disease has recently drawn attention, with several BTK inhibitors advancing clinical trials targeting membranous nephropathy (see p.24, 52)

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 2: sofnobrutinib (AS-0871)

sofnobrutinib (AS-0871)

Highlights | New Development | Application to Kidney Disease | Differentiation Competition

A major BTK inhibitor licensing agreement was announced in June 2026

Everest Medicines Out-Licenses Kidney-Disease BTK Inhibitor Civorebrutinib to Travere Therapeutics

Everest Medicines
China-based / Hong Kong-listed

→ Grant exclusive global rights →

Travere Therapeutics
US-based, strong in kidney disease

Upfront Payment	Milestone Payments	Tiered Royalties
$112M	up to $1.03B	high-single to low-double-digit %

Civorbrutinib (EVER001): An orally administered, covalently reversible BTK inhibitor. Everest is conducting clinical trials in China across multiple immune-mediated kidney diseases — primary membranous nephropathy (pMN), immune-mediated FSGS, minimal change disease (MCD), and IgA nephropathy.

In addition to focusing on dermatological diseases as a key therapeutic area, we have also recognized the potential of sofnobrutinib in kidney diseases and established a strategic development plan based on our assessment of the scientific and clinical rationale. As a result, several companies have expressed interest in the development of sofnobrutinib for kidney disease indications. Following the announcement above, we were able to further expand our outreach and held meetings with numerous companies focused on kidney diseases at BIO 2026. Going forward, we plan to move quickly on discussions with these companies, in addition to those we had already been negotiating with, to maximize the value of sofnobrutinib through out-licensing to the most suitable partner.

sofnobrutinib (AS-0871)

Why Sofnobrutinib for pMN?

Strong Biological Rationale for MN (Membranous Nephropathy)

- BTK plays a central role in B-cell activation and autoantibody production, which drive the pathophysiology of pMN
- Selective, non-covalent BTK inhibition offers a rational approach to modulating disease-driving immune pathways while limiting systemic toxicity

Compelling Nonclinical Data

- Suppressed autoantibody-mediated renal injury in a lupus nephritis model

Differentiated Profile with High Safety Potential

- An oral, non-covalent BTK inhibitor suited for chronic kidney disease and long-term administration
- Designed for high selectivity and a favorable safety profile for chronic therapy

Sofnobrutinib has the potential to become a best-in-class treatment option for pMN

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

sofnobrutinib (AS-0871)

Highlights | New Development | Application to Kidney Disease | Differentiation Competition

Interim Results for BTK Inhibitors in Clinical Trials for Membranous Nephropathy (pMN): Substantial Adverse Events Observed

Drug	Zanubrutinib *1	Civorebrutinib (EVER001) *2
Developer	BeOne	Everest
Inhibitor Type	Covalent	Covalent
Clinical Stage	P2/3	P1b/2a
Efficacy	PLA2R antibody: decreased Proteinuria: decreased	PLA2R antibody: decreased Proteinuria: decreased
Safety	Treatment-emergent AEs (TEAEs): 87% (26/30 pts) Severe TEAEs: 13% (4/30 pts), of which 3% (1/30 pts) was treatment-related.	Treatment-related AEs (TRAEs): 58% (18/31) Serious TRAEs: 13% (4/31)

Sofnobrutinib's favorable safety profile positions it as a potential best-in-class oral therapy for pMN

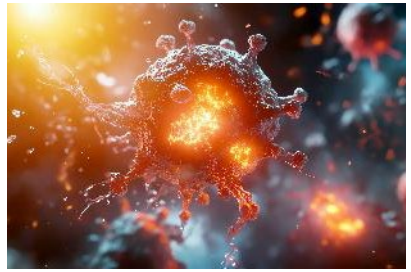
*1 Source: American Society of Nephrology Kidney Week 2024
*2 Source: 62nd Congress of the European Renal Association (June 2025)

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

monzosertib (AS-0141)

Highlights | Profile | Update

Despite the availability of standard therapies including AZA/VEN for AML in elderly and unfit patients, significant unmet medical needs remain. Monzosertib is being developed to provide a novel treatment option for this patient population.



Target Product Profile

- **An orally available small-molecule therapy under development primarily for AML**
  (A CDC7 inhibitor with potential future expansion into solid tumors and hematologic malignancies)

Market Opportunity and Competitive Landscape

- No CDC7 inhibitor has been approved to date. Having completed a Phase 1 study in Japan, monzosertib aims to become **a first-in-class CDC7 inhibitor**.
- The AML therapeutics market is valued at US$3.8 billion and continues to grow.
- Elderly and unfit patients represent a major segment of the AML population. Development is initially focused on this group, with future expansion to broader AML populations.

Market size for AML therapies

$3.8billion※

Development timeline and key events

- 2021 ✓ Initiation of Phase 1 Study in Japan
- 2025 ✓ Favorable preclinical triple-combination efficacy presented at AACR
- ✓ MOU with MD Anderson for AML triplet-combination IIT
- 2026 ✓ Completion of Phase 1 Study in Japan
- ✓ FDA Orphan Drug Designation for AML

Next milestone

- 2026 CTA execution with MD Anderson
- Start of AML IIT enrollment
- 2027 Start of AML IIT combination cohort

AML: acute myeloid leukemia　AZA/VEN: azacitidine (AZA; a DNMT inhibitor) plus venetoclax (VEN; a BCL-2 inhibitor)　IIT: Investigator-Initiated Trial.

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

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

monzosertib (AS-0141)

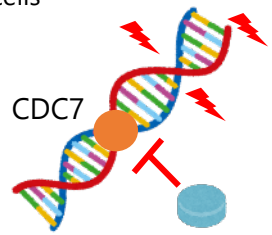
Highlights | **Profile** | Update

Monzosertib is an orally available small-molecule CDC7 inhibitor that induces replication stress and DNA damage, leading to cancer cell apoptosis. Triple-combination therapy with DNMT and BCL-2 inhibitors demonstrated enhanced anti-tumor efficacy (AACR 2025).

Profile **A novel therapeutic approach through CDC7 inhibition with the potential to overcome AZA/VEN resistance and improve treatment outcomes in AML**

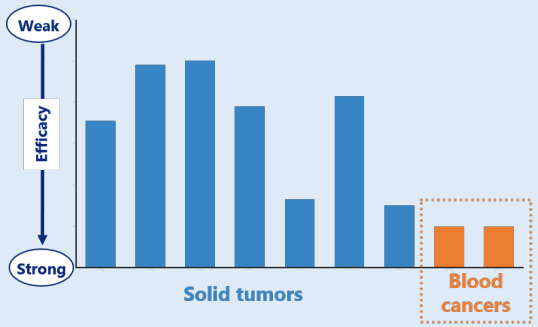
Anti-tumor Mechanism

- CDC7 is a key kinase required for initiation of DNA replication
- Monzosertib selectively inhibits CDC7
- Induces DNA replication stress
- Promotes accumulation of DNA damage
- Triggers apoptosis of cancer cells



Research Finding 1

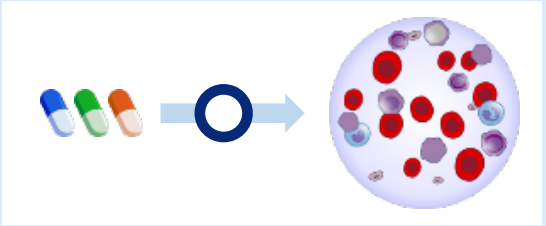
Preclinical studies demonstrated potent **anti-tumor activity in hematologic malignancies**



Growth inhibitory activity of monzosertib (AS-0141) in 35 cancer cell lines

(Each bar represents the mean of 1–7 cell lines)

Research Finding 2



Triple-Combination Therapy

monzosertib + DNMT inhibitor + BCL-2 inhibitor

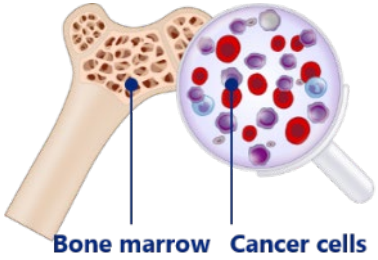
Triple-combination therapy including monzosertib (AS-0141) induced cancer cell apoptosis and demonstrated enhanced anti-tumor efficacy*

* In human AML cell lines and AML xenograft mouse models

(Presented at AACR 2025)

Acute Myeloid Leukemia (AML)

- ✓ An aggressive hematologic malignancy with poor clinical outcomes.
- ✓ The most prevalent form of acute leukemia. The market for AML treatment exceeds $3.8 billion.※2



DNMT: DNA methyltransferase AML: acute myeloid leukemia AZA/VEN: azacitidine (AZA; a DNMT inhibitor) plus venetoclax (VEN; a BCL-2 inhibitor)

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

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

monzosertib (AS-0141)

Highlights | Profile | **Update**

Monzosertib has been evaluated in a Phase 1 study in Japan since 2021 to assess its safety and efficacy. Following the presentation of preclinical AML data at AACR 2025, MD Anderson Cancer Center proposed an investigator-initiated trial. Preparations are currently underway to initiate the study in AML patients.

AML Phase 1b triplet therapy IIT* advancing with MD Anderson

Dose escalation starting from a small number of patients to evaluate safety, tolerability, and determine the maximum tolerated dose (MTD) and recommended dose.

Investigator-initiated Phase 1b study in AML patients at MD Anderson Cancer Center evaluating monotherapy and triplet therapy.

Phase 2 AML triplet therapy study aimed at accelerated approval.

AML: acute myeloid leukemia AZA/VEN: azacitidine (AZA; a DNMT inhibitor) plus venetoclax (VEN; a BCL-2 inhibitor) IIT: Investigator-Initiated Trial.

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.30	● 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

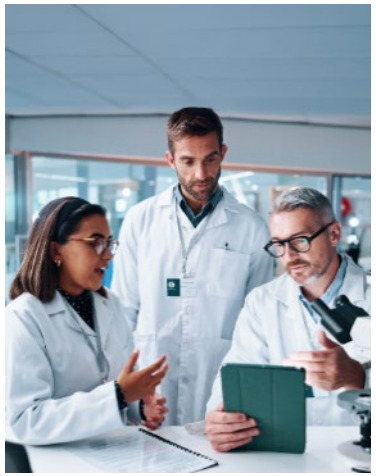
- Upfront payment + Research milestone JPY80 million
- Maximum of JPY10.6 billion potential milestone payments upon achievement of certain development and commercial milestones

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

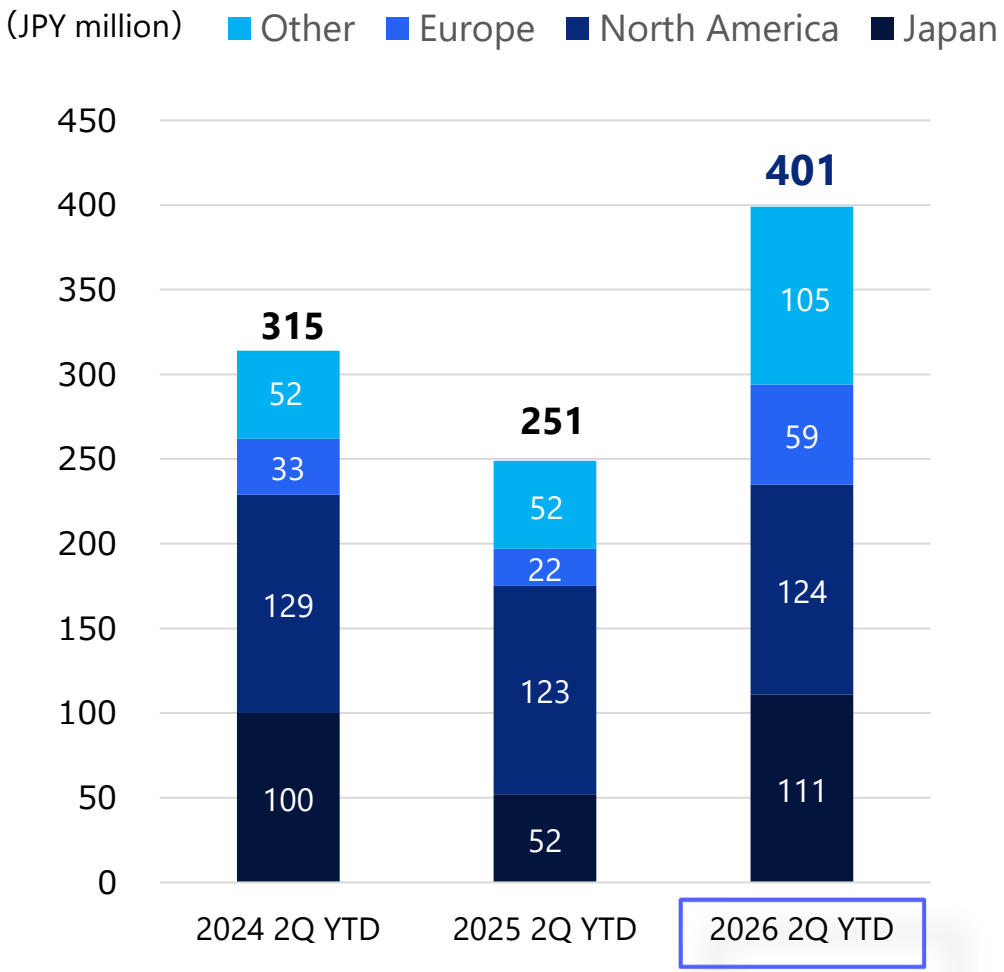
- **Mar. 2018** Entered into a joint research agreement with Sumitomo Pharma
- **Dec. 2021** The term of the joint research was extended until March 27, 2025
- **Mar. 2025** The term of the joint research was extended further until March 27, 2027 to evaluate a potential development candidate
- **Current**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

FY2026 Q2 Results

FY2026 Q2 YTD Drug Discovery Support Business Sales Trend

Drug Discovery Support Business Sales Trend by Region (Consolidated)



Japan

Increased 111.0% YoY

- Sales of proteins remained robust.
- Orders for profiling services from major customers remained strong.
- Multiple mid-sized orders for custom-proteins, custom assays services and NanoBRET™ services from biotech startups contributed to sales.

North America

Increased 1.2% YoY

- Sales of proteins and profiling services were soft in the first quarter but recovered in the second quarter.
- Sales of NanoBRET™ services remained strong.

Europe

Increased 163.0% YoY

- Large-scale orders for profiling services from drug discovery biotech startups continued to contribute significantly to overall sales.
- Sales of proteins also remained strong.

Other

Increased 100.7% YoY

- Sales of proteins to Chinese CROs, our major customers, remained at a high level.

FY2026 Q2 Results by Business Segment

(JPY million)	Q2FY2025 Actual	**Q2FY2026 Actual**	YoY Change	FY2026 Plan	
Total Sales	251	**401**	+150 +59.8%	720	
ddSP business	251	**401**	+150 +59.8%	720	・Sales in Japan, Europe and China reached more than doubled YoY. ・Sales in the U.S. remained stable YoY.
ddRD business	—	**—**	—	—	
Total Operating Loss	(1,052)	**(954)**	+98	(2,028)	
ddSP business	(51)	**66**	+118	108	
ddRD business	(1,001)	**(1,020)**	-19	(2,137)	• Continued investment in the clinical-stage programs.
Ordinary Loss	(1,055)	**(1,005)**	+49	(2,053)	
Net Loss	(1,056)	**(1,039)**	+16	(2,090)	
R&D cost	903	**926**	+23	1,950	• Phase 1b study of docirbrutinib (AS-1763) is on track. • Continued investment in the clinical-stage programs including costs related to clinical studies and manufacturing of investigational new drugs for docirbrutinib (AS-1763).

Business plan for FY2026 dose not include potential milestone payments or upfront payments as the timing or the amounts are difficult to predict.

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

Note : Rounded down to the nearest million yen

Consolidated Balance Sheet

(JPN million)	As of Dec. 31,2025	As of June. 30,2026	Change	Reason for changes
Current assets	1,175	1,700	+524	Cash and deposits +583
Cash and deposits	516	1,100	+583	
Non-current Assets	54	65	+10	
Total assets	1,229	1,765	+535	
Current liabilities	168	140	-27	
Non-current liabilities	752	2,032	+1,280	Issuance of Second Series Unsecured Bonds +1,734 Conversion and Redemption of Convertible Bonds with Stock Acquisition Rights -450
Total liabilities	920	2,173	+1,252	
Total net assets	309	-407	-717	Net loss -1,039 Increase in capital stock and capital surplus through share issuance +294
Total liabilities and net assets	1,229	1,765	+535	

Shareholders' equity ratio	25.1%	-23.9%
BPS	16.16yen	-20.48yen
PBR	22.0x	–
Share price of Carna	356yen	340yen

Note: BPS is not presented as net assets are negative. Share price is the closing price at the end of the period.

Status of Warrant Exercises and Convertible Bond Conversions

Third Series Unsecured Convertible Bonds

100% converted by the end of June
# of shares issued : 1,335,469 shares
Total conversion amount : JPY 228 million

Second Series Unsecured Convertible Bonds

37.5% converted in July
# of shares issued : 471,342 shares
Total conversion amount : JPY 86 million

docirbrutinib (AS-1763) development-accelerating Stock Acquisition Rights (Issued on February 17, 2026)

Exercised by the end of June :
# of shares issued : 88,000 shares
Funds raised : JPY 32 million
Exercised in July :
# of shares issued : 40,000 shares
Funds raised : JPY 11 million

Financing
As of June 30, the Company held cash and cash equivalents of JPY 1.1 billion. In contrast, the full-year forecast for the fiscal year ending December 31, 2026, projects a net loss of JPY 2.0 billion. Given the net loss of JPY 1.0 billion recorded in the first half of 2026, the expected net loss for the second half is approximately JPY 1.0 billion.The Company aims to secure cash inflows through the timely out-licensing of its development pipeline. However, out-licensing activities are inherently subject to uncertainty. In addition, proceeds from the exercise of the AS-1763 (docirbrutinib) Development Acceleration Stock Acquisition Rights will be used primarily for the redemption of the Second Unsecured Straight Bond. Accordingly, until such redemption has been completed, the portion of these proceeds available for funding the Company's operations will be limited.Therefore, the Company will also consider raising additional capital to secure the funds necessary for its future business operations.

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

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

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

Phase 2 study

*** Cohort 1: Updated enrollment strategy**
10 patients were enrolled at 300 mg BID and 400 mg BID as planned.
Additional patients will be enrolled at 400 mg BID, the provisional RP2D, to enhance data robustness.

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 June 30, 2026）

- 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.**

EHA2026 Poster Presentation Executive Summary

- **Presented the latest clinical data from ongoing Phase 1b study at EHA2026**
- **Docirbrutinib continued to demonstrate a favorable safety profile and promising efficacy as more patients enrolled**

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 (TRAEs) reported in 10% of patients

Efficacy

- ✓ Robust response was observed in patients with CLL/SLL, MCL, and WM※
- ✓ 400 mg BID was selected as the provisional RP2D (recommended Phase 2 dose)
- ✓ Additional patients will be enrolled to verify the efficacy

※ 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 previousely 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

EHA2026: Safety in the Ongoing Phase 1b Trial

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

May 8, 2026

Grade ≥3 Treatment-Emergent Adverse Events (TRAEs)

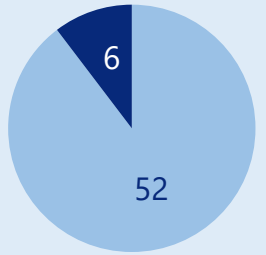
- ✓ **58 patients have been enrolled, including 20 additional patients** since the previous presentation at ASH2025
- ✓ In dose escalation, **docirbrutinib was well tolerated at doses up to 500 mg BID, and the maximum tolerated dose was not reached**
- ✓ No drug-related atrial fibrillation or hypertension was reported, even with additional patients enrolled since the previous presentation. **Grade ≥3 Treatment-related AEs (TRAEs) were reported in 10% of patients**, suggesting favorable safety profile
- ✓ Many patients have remained on treatment, with several receiving docirbrutinib for more than two years, consistent with its 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

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

docirbrutinib

Grade ≥3 TRAEs※

10%



	TEAEs N (%)	TRAEs N (%)
Any TEAEs	51 (88)	37 (64)
Grade ≥3	25 (43)	6 (10)
Serious	14 (24)	2 (3)
Led to dose interruption/reduction	21 (36)	3 (5)
Led to dose discontinuation	1 (2)	1 (2)
Led to death	2 (3)	0 (0)

※ Preliminary data from Phase 1b study of docirbrutinib (EHA 2026 presentation)

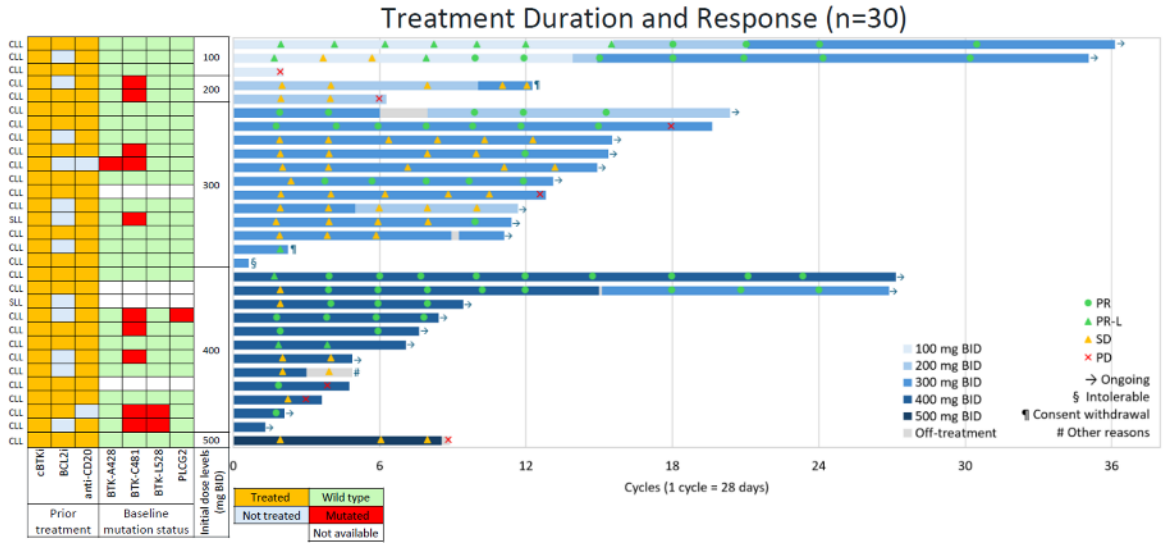
Glossary

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

EHA2026: Efficacy in the Ongoing Phase 1b Trial: CLL/SLL

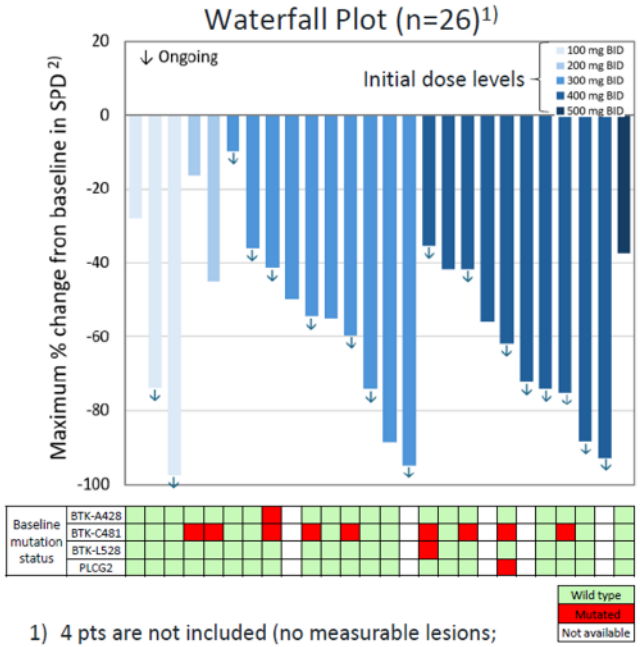
Robust responses were observed in patients with CLL/SLL

- **Robust efficacy was observed in heavily-treated patients**
  - ✓ At the 400 mg BID, an ORR of 86% was achieved even among patients double-exposed to cBTKi and BCL2i. Among 4 patients harboring BTK mutation, 3 patients achieved PR, including 1 patient with both BTK C481S and L528W and 1 patient with both BTK C481S and phospholipase C gamma 2 (PLCG2) mutations.
  - ✓ Among 28 efficacy-evaluable patients with CLL/SLL, including 8 additional patients enrolled since ASH2025, the ORR was 57% across all dose levels, compared with 40% reported at ASH2025. At the 400 mg BID dose, the ORR was 73% (8/11).
- **400 mg BID was selected as provisional RP2D, recommended Phase 2 dose, and additional patients will be enrolled for further evaluation.**
- **Pirtobrutinib-pretreated patients (Cohort 3)**
  - ✓ 3 patients have been enrolled; all remain on treatment. 1 patient achieved SD and 2 patients were not evaluable for efficacy. Furter investigation is needed to adequately evaluate efficacy.



May 8, 2026

Tumor Response
CLL/SLL patients enrolled in dose escalation and Cohort 1



1) 4 pts are not included (no measurable lesions; early terminated before response assessment; not yet reached the first post-dose assessment point; data not yet available)
2) SPD: Sum of products of diameters

Tumor response was assessed per iwCLL for CLL and Lugano for SLL

cBTKi: Covalent BTK inhibitor **BCL2i : BCL2 inhibitor**

Efficacy-evaluable patients: Patients who have been evaluated for tumor response more than once and whose data is available

ORR (Overall Response Rate): Proportion of patients who achieved PR, PR-L or CR among all patients who received treatment

CR (Complete Response) : Indicates that all signs of cancer, including lymph nodes, has disappeared

PR (Partial Response): Indicates that the size of lymph nodes has decreased ≥50%, and other parameters for PR, such as reduction in the number of lymphocytes, have been met

PR-L (PR-Lymphocytosis): Indicates that the size of lymph nodes has decreased ≥50% but the reduction in the number of lymphocytes has not met the criteria for PR

SD (Stable Disease): Indicates that the disease remains stable

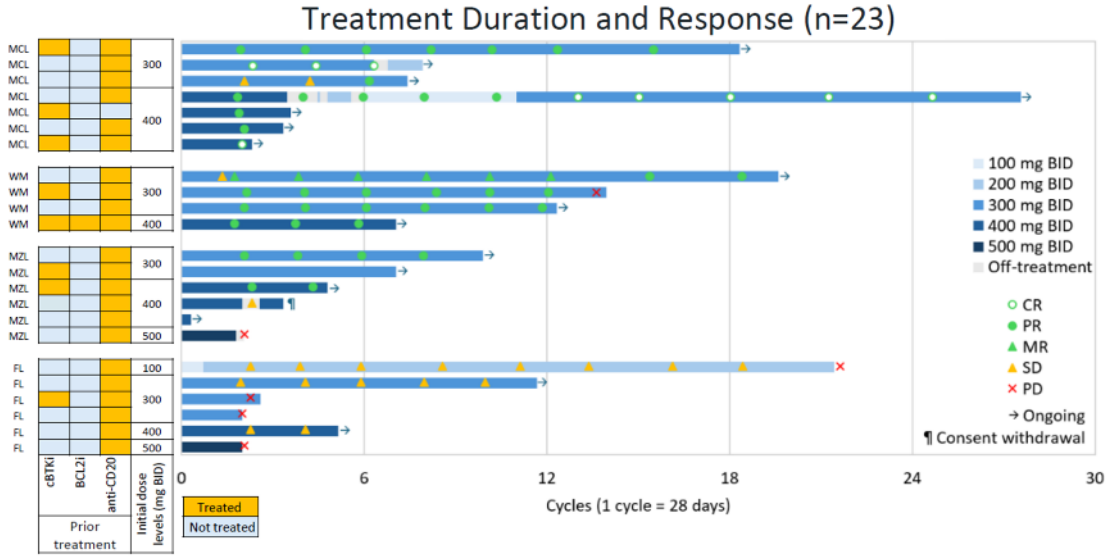
PD (Progressive Disease): Indicates that the diseases has progressed

EHA2026: Efficacy in the Ongoing Phase 1b Trial: NHL

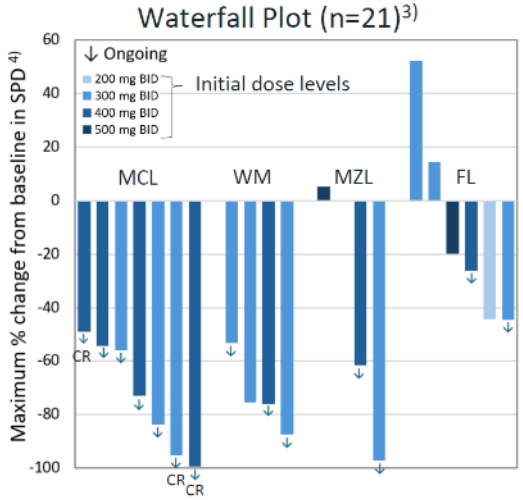
Robust efficacy was observed in patients with MCL and WM

May 8, 2026

- **ORR and major response in MCL and WM**
  - ✓ In MCL, the ORR was 100% (7/7), including 3 CRs. In WM, both the ORR and major response rates were 100% (4/4). Responses were also observed in both MCL and WM patients with prior cBTKi treatment.
- **Overall NHL patients**
  - ✓ 25 NHL patients (9 MCL, 4 WM, 6 MZL, 6 FL) have been enrolled, of which 36% were previously treated with cBTKi. Efficacy-evaluable patients were 23. The ORR was 50% for MZL and 0% for FL.
- **Pirtobrutinib-pretreated patients (Cohort 3)**
  - ✓ 2 MCL patients have been enrolled; one achieved SD and one had PD. Furter investigation is needed to adequately evaluate efficacy.



Tumor Response
NHL patients enrolled in dose escalation and Cohort 2



3) 2 pts are not included (not yet reached the first post-dose assessment point; data not yet available)
4) SPD: sum of products of diameters for MCL, MZL, and FL, serum IgM levels for WM

Tumor response was assessed per Lugano for MCL, MZL and FL and IWWM6 for WM.

Glossary

Major Response Rate (assessment for WM)
ORR is the proportion of patients who achieved Minor Response (≥25% serum IgM level reduction) or higher, whereas Major Response is the proportion of patients who achieved PR (≥50% serum IgM level reduction) or higher.

MCL	Mantle cell lymphoma
WM	Waldenström macroglobulinemia
MZL	Marginal zone lymphoma
FL	Follicular Lymphoma

New Publication in Blood Cancer Journal

New preclinical findings on docirbrutinib were published in Blood Cancer Journal (BCJ), based on collaborative research with Prof. Varsha Gandhi, Ph.D. and Prof. Nitin Jain, M.D. of The University of Texas MD Anderson Cancer Center, highlighting its therapeutic potential for the treatment of hematologic malignancies.

Title

Docirbrutinib is a pan-mutant BTK inhibitor and inhibits B-cell receptor signaling in chronic lymphocytic leukemia cells in preclinical and early clinical investigations

Authors

Natalia Timofeeva,[1] Breana Herrera,[1] Hitomi Fujiwara[2], Tokiko Asami[2], Hiroko Endo[2], Mariko Hatakeyama[2], Fumio Nakajima[2], Hiroshi Ohmoto[2], Yu Nishioka[2], Kyoko Miyamoto[3], Akinori Arimura[2,3], Shady I. Tantawy[1,4], Javier Pinilla-Ibarz[5], Catherine C. Coombs[6], Nitin Jain[7]*, Masaaki Sawa[2]*, and Varsha Gandhi[1,7]*

[1]Department of Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center, Houston, Texas; [2]Carna Biosciences, Inc., Kobe, Japan; [3]CarnaBio USA, Inc., South San Francisco, CA; [4]Internal Medicine and Clinical Hematology Department, Suez Canal University, Egypt; [5]Moffitt Cancer Center, Tampa; [6]University of California, Irvine;[7]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, Texas

*These authors contributed equally

Bruton's tyrosine kinase (BTK) inhibitors are a standard therapy for chronic lymphocytic leukemia (CLL). However, drug resistance frequently emerges through BTK mutations. In this newly published study, docirbrutinib demonstrated pan-mutant activity across 14 BTK mutants in a preclinical setting, supporting its potential as a therapeutic option for hematologic malignancies.

BCJ is an international, open access journal published by Springer Nature focusing on hematologic malignancies and is ranked in the highest quartile (Q1) in Hematology/Oncology

Study Background (BCJ Publication)

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, T474I, 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

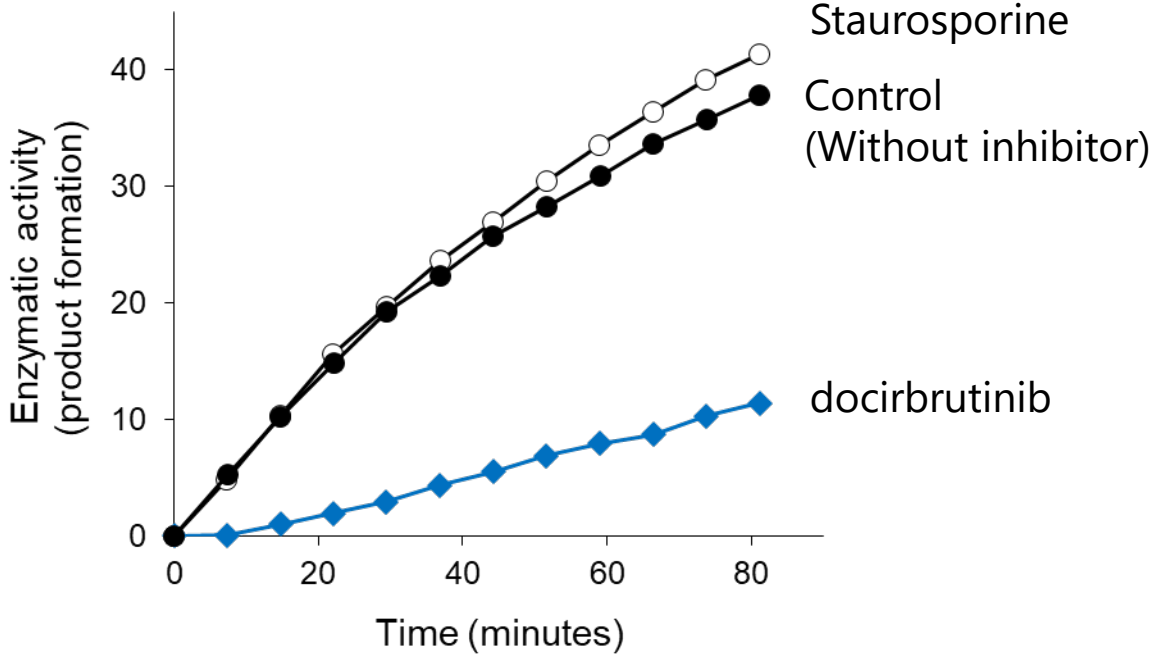
Key Findings from the BCJ Publication (1)

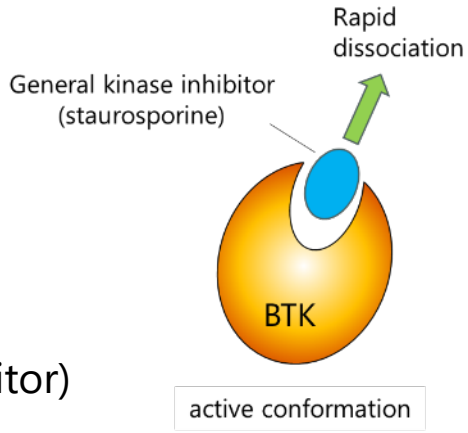
Docirbrutinib is expected to provide prolonged therapeutic effects through sustained BTK inhibition

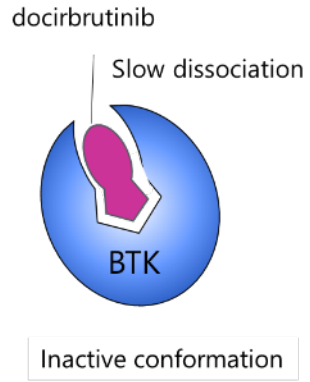
Unique inhibitory profile

- ✓ Biochemical analyses suggest that docirbrutinib binds to an inactive conformation of BTK and exhibits a slow off-rate profile

Rapid dilution assay







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

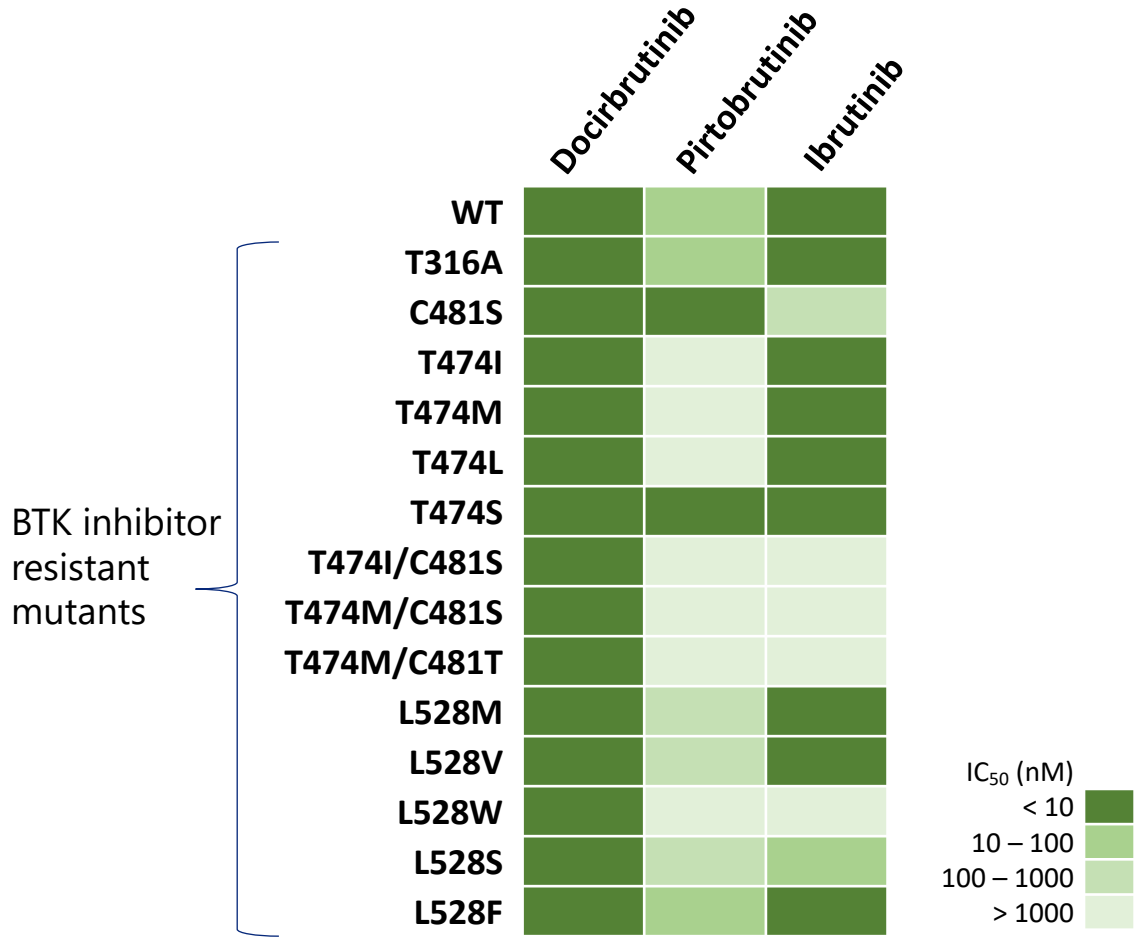
Rapid dilution assay
In this assay, an enzyme–inhibitor complex is rapidly diluted, and the recovery of enzyme activity is monitored to assess how quickly the inhibitor dissociates (off-rate). This assay is used to evaluate strength of binding and duration of action.

Key Findings from the BCJ Publication (2)

Docirbrutinib has the potential to benefit patients with resistance to existing BTK inhibitors

Efficacy against resistant BTK-mutants

- ✓ Docirbrutinib demonstrated broad inhibitory activity across all 14 BTK mutants examined in this study
- ✓ Cellular potency of docirbrutinib was also confirmed in DLBCL cell lines harboring BTK resistance mutations



Glossary

IC50
Refers to the concentration required to inhibit 50% of a specific target. A lower IC50 value indicates higher potency.

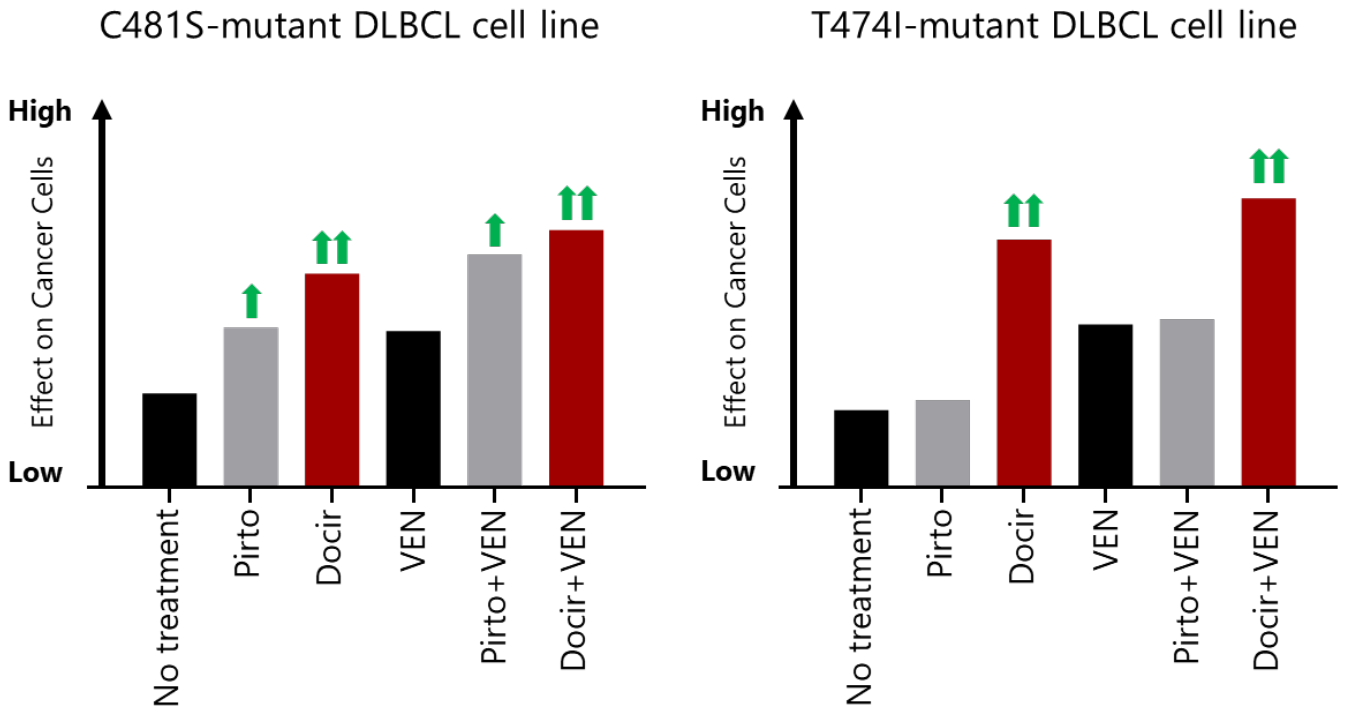
DLBCL cell line
A cell line established from diffuse large B-cell lymphoma (DLBCL) for research use

Key Findings from the BCJ Publication (3)

Combination therapy with docirbrutinib and venetoclax may provide additional therapeutic benefit

Combination effects with venetoclax

- ✓ In combination with venetoclax, docirbrutinib induced significant cell death in DLBCL cell lines harboring BTK resistance mutations as well as in primary CLL samples
- ✓ Docirbrutinib also exhibited enhanced activity when combined with the MCL-1 inhibitor AZD5991.



Pirto: Pirtobrutinib
Docir: Docirbrutinib
VEN; Venetoclax

Glossary

MCL-1 inhibitor

AZD5991 is an investigational compound under development to inhibit MCL 1, an anti apoptotic protein that supports the survival of certain cancer cells, including leukemia cells, with the aim of inducing apoptosis.

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

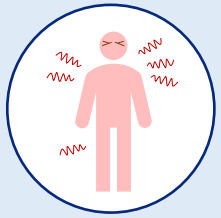
- Approval of new treatment options may trigger the expansion of CSU market.
- We plan to pursue the clinical implications of sofnobrutinib (non-covalent BTK inhibitor) to provide clinical benefits by minimizing potential adverse events associated with covalent BTK inhibitors including remibrutinib.

Chronic Spontaneous Urticaria (CSU)

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

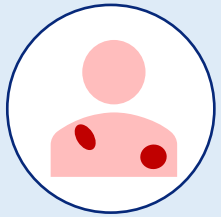
Symptoms

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

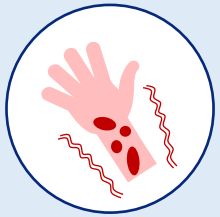


Spontaneously present & re-occur

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



Red swollen hives



Itch

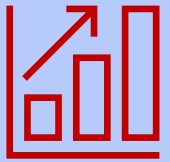
Number of Patients

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

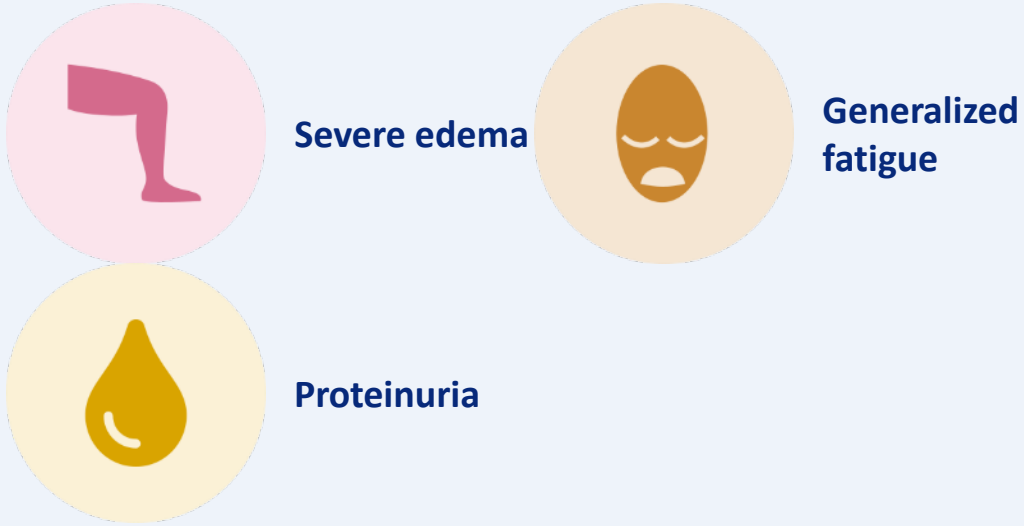
- ✓ The market size of CSU in major seven countries is expected to reach $5.4 bn by 2032 growing at a CAGR of 11.7% from 2024.

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

Primary membranous nephropathy (pMN)

Membranous nephropathy (pMN) is a disease in which immune deposits accumulate on the walls of the glomeruli — the kidney's filtering units — causing the walls to thicken and allowing large amounts of protein to leak into the urine. It is one of the most common causes of nephrotic syndrome in adults (edema and heavy proteinuria), and is especially prevalent among middle-aged and older adults from their 40s onward.

Symptoms



Region	Est. Patients
United States	Approx. 30,000[1]
Europe (Germany, France, Italy, Spain, UK)	Approx. 25,000[1]
Japan	Approx. 18,000[1]
China	Approx. 1.4 million[2]

[1] Data source: Company estimates based on DelveInsight, Idiopathic Membranous Nephropathy - Epidemiology Forecast - 2034. The estimate for the United States is based on antigen-specific IMN patient populations, while the estimates for Europe and Japan are derived from regional patient share data within the seven major markets (United States, EU4, the United Kingdom, and Japan).
[2] Data source: Tianguangshi Prospectus (Draft Registration Statement). Represents the number of patients with moderate-to-severe PMN in China in 2023.

Treatment and Challenges

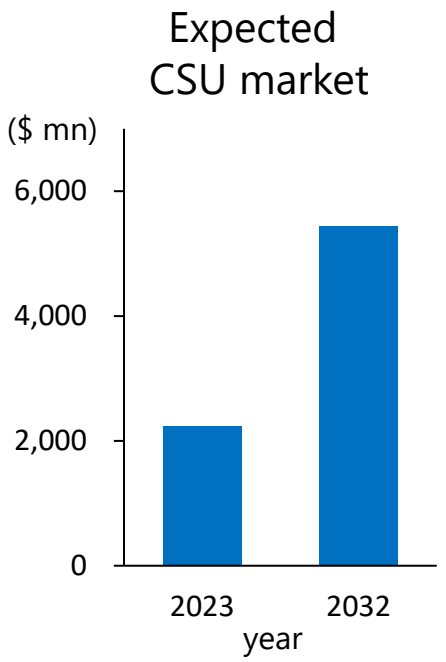
Corticosteroids and immunosuppressants are the main treatments, but efficacy is not always sufficient.
As pMN worsens, it can progress to massive proteinuria and severe systemic edema (nephrotic syndrome), along with thrombosis from the resulting hypercoagulable state. If the disease advances further, it can lead to end-stage renal failure with complete loss of kidney function, requiring dialysis or kidney transplantation. **There is an unmet need for more effective therapies.**

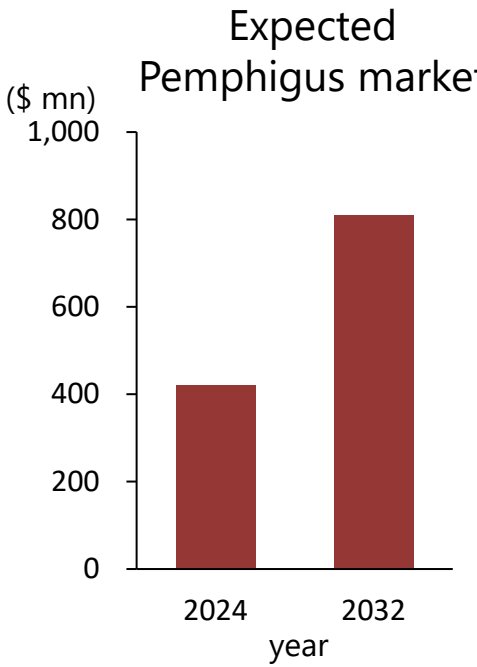
Potential Market Size for Sofnobrutinib (AS-0871)

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

"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