Carna Biosciences, Inc.

February 9, 2024

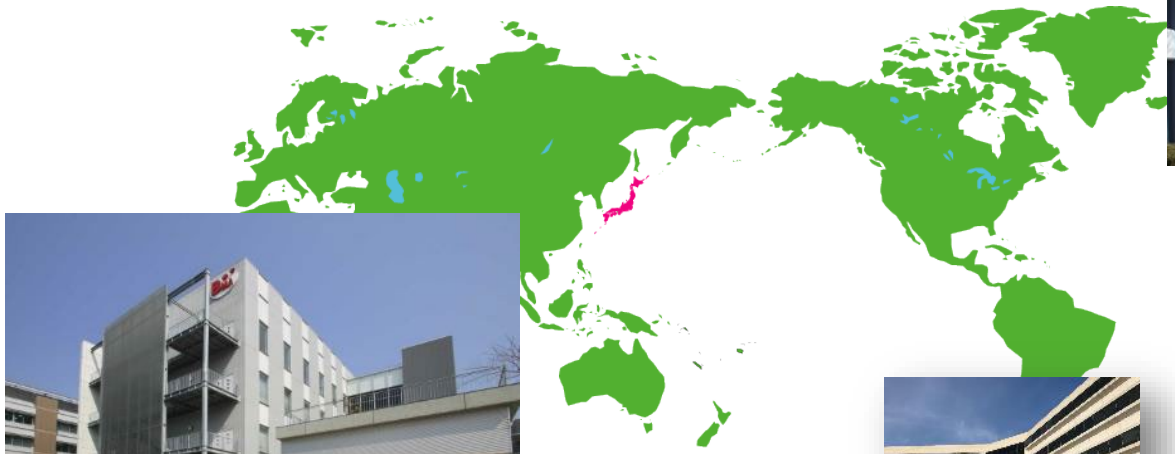
Stock Code: 4572

AGENDA

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, 2024)

Our Mission

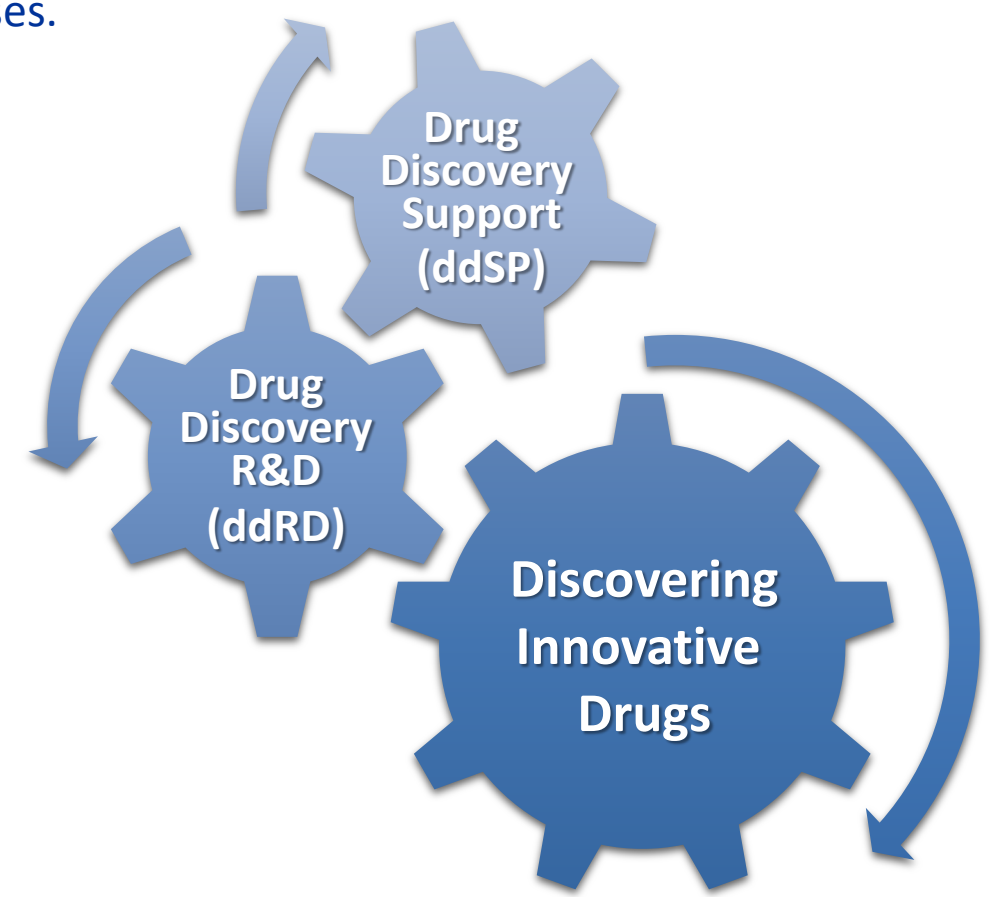
Discover and develop significant medical values that will provide therapeutic solutions for improving human health

Carna's powerful drug discovery engine invents a drug from scratch and drives our pipeline expansion

Continuously deliver innovative therapies for patients to treat serious unmet medical needs

Business Model to Drive Growth

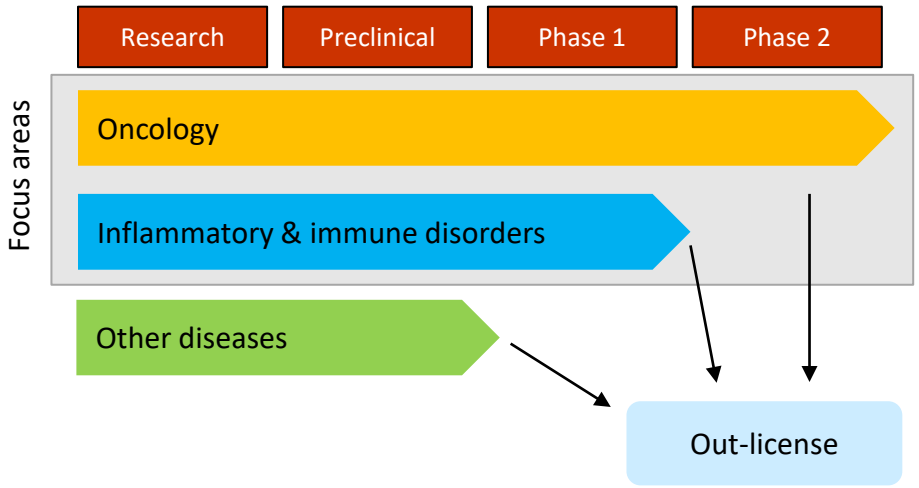
- Drug Discovery Support (ddSP) business provides pharmaceutical companies with the new tools to drive their kinase research. The stable income from the support business helps the drug discovery business to invest in R&D.
- Our small but powerful team with talented professionals at the Drug Discovery Research & Development (ddRD) business are focused on the research and development of innovative therapies targeting oncology and autoimmune diseases.



Business Model of Drug Discovery R&D (ddRD) Business

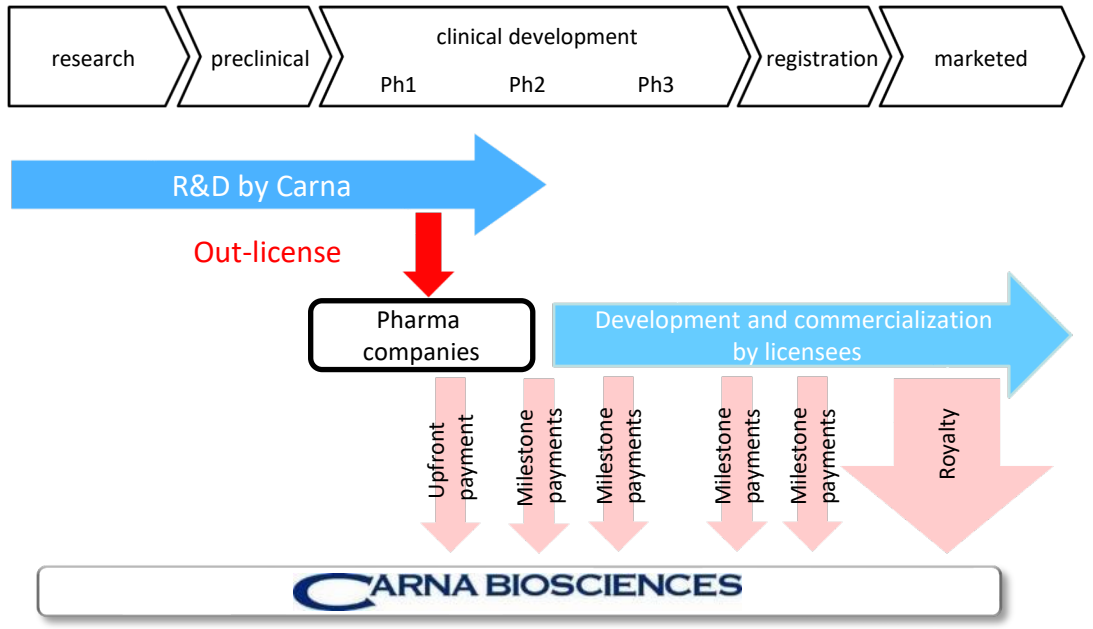
<R&D focus areas>

- ddRD business conducts research and development of innovative small molecule drugs including kinase inhibitors, focusing on oncology and inflammatory and immune disorders.
- We develop our oncology drug pipelines up to Phase 2 to maximize the potential values.
- For non-oncology pipelines, we basically license out at early stage before entering Phase 2 study to mitigate the development risk.



<Earnings model>

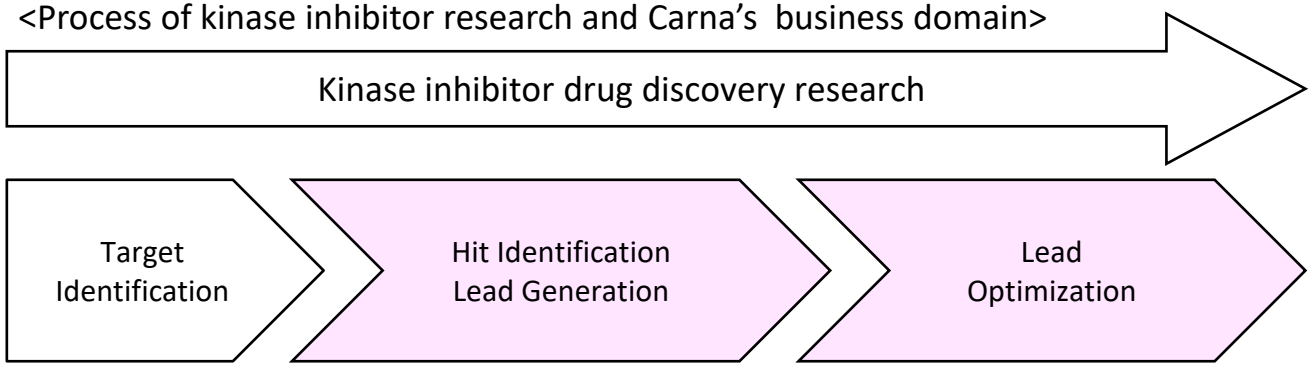
- We license our drug pipelines to pharma companies to generate revenue through upfront payments, milestone payments, and royalties on the resulting product sales.
- We intend to build long-term value by developing our own drug pipelines up to Phase 2 clinical trial on a fully burdened cost or in collaborations with development partners.



Business Model of Drug Discovery Support (ddSP) Business

- ddSP business develops and offers research tools for drug discovery, leveraging our proprietary kinase research technology, to generate stable cash flow. We apply the cash flows from ddSP business to ddRD business for the development of our own drug pipelines and the continued discovery of promising drug candidates in the future.

<Process of kinase inhibitor research and Carna's business domain>



Kinase proteins	Kinase proteins
Kinase Assay development Kinase Assay kits	Kinase Profiling service
Kinase Profiling service	Kinase Cell-based assay service
Kinase Screening service	X-Ray crystallography
Kinase Cell-based assay service	

Carna's products and services

Kinase proteins

Kinase Assay kits

Kinase Profiling and screening service

Drug Discovery R&D (ddRD) Business

Drug Discovery R&D: Pursuing Sustained Growth

Robust Drug Pipeline

Cancer

- AS-1763
- Monzosertib (AS-0141)
- GS-9911 (GILEAD)

Immune-inflammatory diseases

- Sofnobrutinib (AS-0871)
- STING antagonist*
- Joint Research (Sumitomo Pharma)
- Next Generation Pipeline

*Deleted compound code, FRTX-10 because Fresh Tracks Therapeutics, the licensee of the program, announced a plan of liquidation and dissolution in September 2023.

Extensive Expertise in Drug Discovery

Strong Science Background in both Biology and Medicinal Chemistry

Selected Publications


nature COMMUNICATIONS

ARTICLE

Received 28 Jan 2016 | Accepted 14 Jul 2016 | Published 26 Aug 2016 DOI: 10.1038/ncomms12586 OPEN

TNIK inhibition abrogates colorectal cancer stemness

Mari Masuda[1], Yuko Uno[2], Naomi Ohbayashi[3,*], Hirokazu Ohata[4,*], Ayako Mimata[1,*], Mutsuko Kukimoto-Niino[3], Hideki Moriyama[2], Shigeki Kashimoto[2], Tomoko Inoue[2], Naoko Goto[1], Koji Okamoto[4], Mikako Shirouzu[3], Masaaki Sawa[2,*] & Tesshi Yamada[1,*]


EXPERT OPINION

Review

Targeting the Wnt signaling pathway in colorectal cancer

Masaaki Sawa, Mari Masuda & Tesshi Yamada[†]


Journal of Medicinal Chemistry

Article

Cite This: J. Med. Chem. 2018, 61, 8917−8933 pubs.acs.org/jmc

Design and Synthesis of Novel Amino-triazine Analogues as Selective Bruton's Tyrosine Kinase Inhibitors for Treatment of Rheumatoid Arthritis

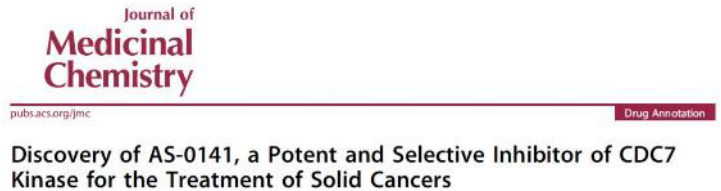
Wataru Kawahata,*[,†] Tokiko Asami, Takao Kiyoi, Takayuki Irie, Haruka Taniguchi, Yuko Asamitsu, Tomoko Inoue, Takahiro Miyake, and Masaaki Sawa[†]

Journal of Medicinal Chemistry

pubs.acs.org/jmc Drug Annotation

Discovery of AS-1763: A Potent, Selective, Noncovalent, and Orally Available Inhibitor of Bruton's Tyrosine Kinase

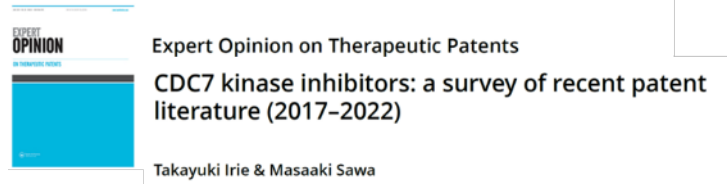
Wataru Kawahata,* Tokiko Asami, Takao Kiyoi, Takayuki Irie, Shigeki Kashimoto, Hatsuo Furuichi, and Masaaki Sawa


Journal of Medicinal Chemistry

pubs.acs.org/jmc Drug Annotation

Discovery of AS-0141, a Potent and Selective Inhibitor of CDC7 Kinase for the Treatment of Solid Cancers

Takayuki Irie,* Tokiko Asami, Ayako Sawa, Yuko Uno, Chika Taniyama, Yoko Funakoshi, Hisao Masai, and Masaaki Sawa


EXPERT OPINION

Expert Opinion on Therapeutic Patents

CDC7 kinase inhibitors: a survey of recent patent literature (2017–2022)

Takayuki Irie & Masaaki Sawa


SCIENTIFIC REPORTS

OPEN

Development of Highly Sensitive Biosensors of RAF Dimerization in Cells

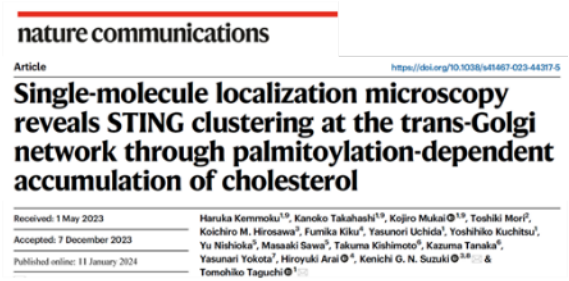
Kyoko Miyamoto[1] & Masaaki Sawa[1,2]


scientific reports

OPEN

A cell-free assay implicates a role of sphingomyelin and cholesterol in STING phosphorylation

Kanoko Takahashi[1], Takahiro Niki[1,^], Emari Ogawa[1], Kiku Fumika[1], Yu Nishioka[1], Masaaki Sawa[1], Hiroyuki Arai[2], Kojiro Mukai[1,2] & Tomohiko Taguchi[1,2]


nature communications

Article

Single-molecule localization microscopy reveals STING clustering at the trans-Golgi network through palmitoylation-dependent accumulation of cholesterol

Received: 1 May 2023

Accepted: 7 December 2023

Published online: 11 January 2024

Haruka Kemmoku[1,9], Kanoko Takahashi[1,9], Kojiro Mukai[1,9], Toshiki Mori[2], Koichiro M. Hirosawa[3], Fumika Kiku[4], Yasunori Uchida[1], Yoshihiko Kuchitsu[1], Yu Nishioka[3], Masaaki Sawa[3], Takuma Kishimoto[5], Kazuma Tanaka[6], Yasunari Yokota[7], Hiroyuki Arai[4], Kenichi G. N. Suzuki[3,8] & Tomohiko Taguchi[1]

over 40 publications (papers, reviews and books)

Updates on Pipelines in Clinical Development

1. **AS-1763**
2. **sofnobrutinib (AS-0871)**
3. **monzosertib (AS-0141)**

International Nonproprietary Name (INN) : sofnobrutinib, Code name : AS-0871
International Nonproprietary Name (INN) : monzosertib, Code name : AS-0141

Pipelines in Clinical Development

Compound	Target	Indication	Status
AS-1763	BTK	Blood Cancer	• Phase 1 SAD and BA part in healthy volunteers were completed in the Netherlands. • Phase 1b trial is ongoing in previously treated CLL/SLL and B-cell NHL patients in the U.S., and currently at third dose level (Jan, 2024). Multi-center clinical study Study Lead ：Dr. Nitin Jain, Department of Leukemia, University of Texas MD Anderson Cancer Center.
sofnobrutinib (AS-0871)	BTK	Immune-inflammatory diseases	• Completed Phase 1 clinical trials (SAD/MAD) in healthy volunteers. • Received the final Clinical Study Report (CSR) for the Phase 1 MAD study in November 2023. • Demonstrated a favorable safety and tolerability profile as well as a promising PK/PD profile in the MAD study.
monzosertib (AS-0141)	CDC7/ ASK	Cancer	• Phase 1 study in cancer patients is in progress in Japan. • Dose escalation part is ongoing. Clinical trial site : National Cancer Center Hospital and National Cancer Center Hospital East

SAD : Single Ascending Dose
MAD : Multiple Ascending Dose
BA : Bioavailability

AS-1763: Highlights

Refer to P.49-P.56 for more information

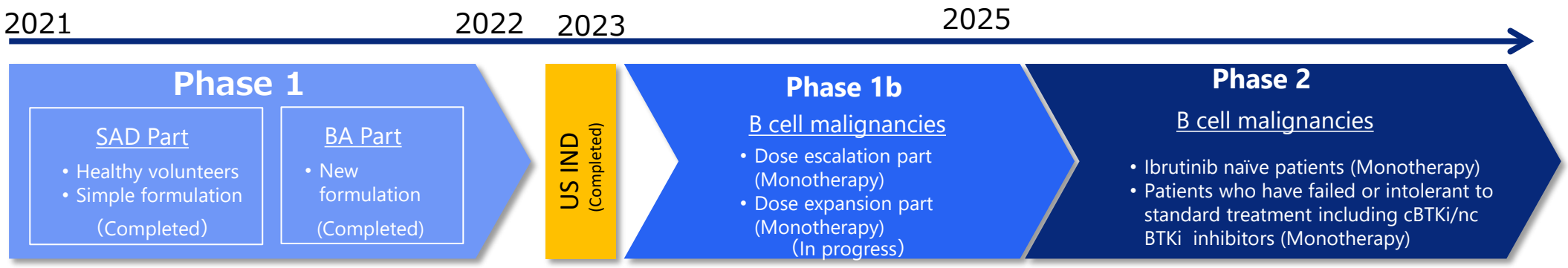
Mechanism/ Indication	**Orally available** small molecule inhibitor of Bruton's Tyrosine Kinase (BTK) targeting B cell malignancies
To overcome drug resistance	AS-1763 is a **non-covalent inhibitor** that reversibly inhibits BTK, **having a potential to be effective for patients who have developed resistance to the existing BTK inhibitors**.
To minimize a risk of side effects	AS-1763 is designed to selectively inhibit BTK **to reduce a risk of potential side effects.**

AS-1763: Next Generation BTK Inhibitor

AS-1763 : Targeting Blood Cancer

- Small molecule BTK inhibitor
- Non-covalent/reversible
- High kinase selectivity
- Pan-mutant BTK inhibitor
- Orally available

- Active against covalent/non-covalent BTK inhibitor-resistant mutations found in patients (C481x, T474x, T316A, L528x)
- The first patient was dosed in August 2023 in Ph 1b study in the U.S.



IND application: Investigational New Drug application
FPI: First Patient In
SAD: Single Ascending Dose
BA: Bioavailability
B-cell malignancies: Chronic Lymphocytic Leukemia (CLL), Small Lymphocytic Lymphoma (SLL), and B-cell non-Hodgkin Lymphoma (B-cell NHL), etc.
cBTKi: covalent BTK inhibitor
ncBTKi: noncovalent BTK inhibitor

AS-1763: Phase 1 Clinical Trial in Progress

Phase 1 in the Netherlands
(Healthy volunteers)

Completed

SAD Part

Evaluated the safety, tolerability and PK using simple formulation

- Completed dosing in SAD part
- Favorable Pharmacokinetic profile
- Safe and well-tolerated
- Promising Pharmacodynamic effects

BA Part

Evaluated relative bioavailability using new formulation

- Pre-IND meeting
- IND submission

Completed

On-going

Phase 1b in the U.S.
(Patients with CLL/SLL/B-cell NHL)

◆ The first patient was dosed in Phase 1b study in August 2023.

AS-1763: Ph I Clinical Trial in Healthy Volunteers

Ref. P.52-P.55

Objectives of the study

A single dose of AS-1763 was administered orally to healthy volunteers to evaluate:

- plasma concentration of AS-1763
- safety assessments (clinical laboratory, ECGs, or vital signs, etc.)
- inhibitory potency on B cell activation

Result of the study

After a single-dose administration of 5 mg, 25 mg, 100 mg, 300 mg, 500 mg, and 600 mg of AS-1763:

- plasma concentrations of AS-1763 were increased in a dose dependent manner
- no clinically meaningful issues were reported in all safety assessments
- dose-dependent inhibition in B cell activation assays was observed

New tablet formulation for Phase 1b study

Relative oral bioavailability was evaluated after administering newly developed tablet formulation containing 100 mg of AS-1763 to healthy volunteers.

- the new tablet formulation demonstrated good oral bioavailability, supporting that the tablet formulation can be used for Phase 1b study.

AS-1763: Phase 1b Clinical Trial

Ref. P.56

Multi-center clinical study
Study Lead：Dr. Nitin Jain, Department of Leukemia, University of Texas MD Anderson Cancer Center.

Clinical trails in progress	Phase 1b dose escalation part was initiated in the U.S.
Indication	Patients with CLL(Chronic Lymphocytic Leukemia), SLL(Small Lymphocytic Leukemia), and B-cell NHL(B-cell non-Hodgkin Lymphoma).
Status	• Opened 8 clinical sites. • Safe and well tolerated at the first two dose levels. • Treating patients at dose level 3 as of January 2024.

AS-1763: Potential Market Size (B-cell Malignancies)

Present

Covalent BTK inhibitors including ibrutinib, acalabrutinib, and zanubrutinib are key therapeutic options.

Est. market size

Estimated sales of covalent BTK inhibitors (ibrutinib, acalabrutinib, zanubrutinib)

Est. sales for 2021 $**9** billion

Est. sales for 2029 $**17** billion ※Expected CAGR is 8%

＊https://www.databridgemarketresearch.com/reports/global-bruton-tyrosine-kinase-btk-inhibitors-market

Opportunity

Patients treated with covalent BTK inhibitors are reported to develop resistance to the drugs

↓

High unmet needs for new therapeutic options to treat patients with B-cell malignancies who have developed resistance to covalent BTK inhibitors

↓

- Next generation **non-covalent BTK inhibitors** including AS-1763 are expected to be promising therapeutic options for the patients who have developed resistance to covalent BTK inhibitors. Our goal is to take a certain share of this potential large market, making AS-1763 a blockbuster drug.

BTK Inhibitors in clinical development

Competitors: other non-covalent BTK inhibitors in clinical development

Compound	Company	Development Phase
pirtobrutinib (LOXO-305)	Lilly (Loxo)	Approved/P3
nemtabrutinib (ARQ 531)	Merck (ArQule)	P3
TT-01488	TransThera	P1
HMPL-760	HutchMed	P1

- FDA granted an accelerated approval to pirtobrutinib, the most advanced competitor to AS-1763, in the U.S early 2023.
- Focused differentiation strategy from pirtobrutinib is the key to the success of AS-1763.
- In preclinical studies, AS-1763 demonstrated to be effective for mutant BTKs that confer resistance to pirtobrutinib in addition to ibrutinib.

*N. Engl. J. Med. 2022;386(8):735–743.

Sofnobrutinib (AS-0871): Highlights

Ref. P.57-P.62

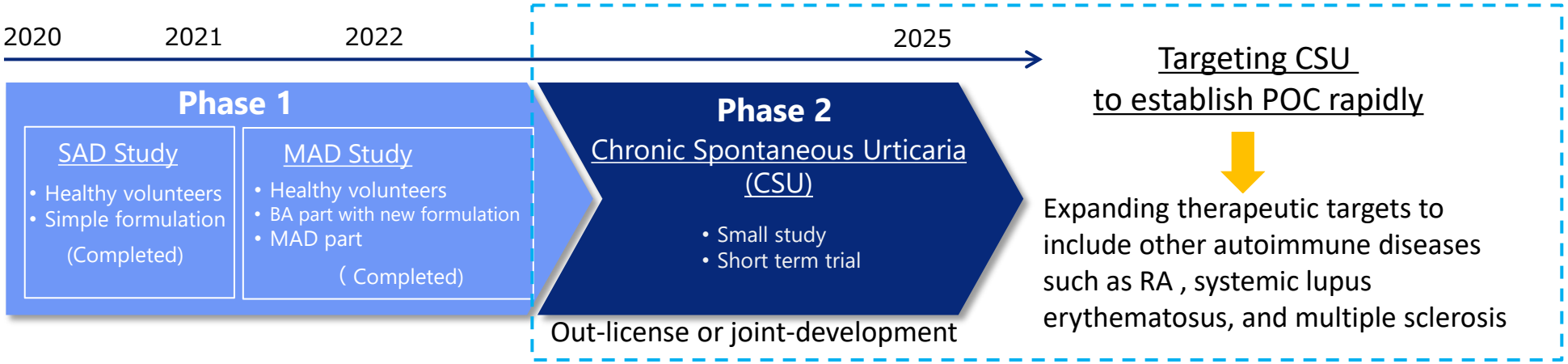
Mechanism/ Indication	Sofnobrutinib is an **orally available** Bruton's Tyrosine Kinase (BTK) inhibitor to treat autoimmune diseases by inhibiting activation of immune cells such as B cells, macrophages, and mast cells.
To minimize a risk of side effects	Sofnobrutinib is designed to selectively inhibit BTK **to reduce a risk of potential side effects**.
Characteristics	Sofnobrutinib is a **non-covalent BTK inhibitor** that reversibly inhibits BTKs to reduce safety concerns associated with covalent inhibitors.

Sofnobrutinib (AS-0871): Non-covalent BTK Inhibitor

Sofnobrutinib (AS-0871) : Targeting Immune-inflammatory diseases

- Small molecule BTK inhibitor
- Non-covalent/reversible
- High kinase selectivity
- Orally available

- Demonstrated significant efficacies in arthritis models
- Showed efficacy in systemic lupus erythematosus model
- Phase 1 MAD study was completed
- Find a partner to conduct further development



SAD: Single Ascending Dose
MAD: Multiple Ascending Dose
BA: Bioavailability
POC: Proof of Concept

Sofnobrutinib (AS-0871): Phase 1 Clinical Trial in Progress

CARNA BIOSCIENCES

Phase 1 in the Netherlands
SAD study (Healthy volunteers)

Completed

- Safe and well-tolerated at all dose levels
- Favorable Pharmacokinetic (PK) Profile
- Promising Pharmacodynamic(PD) effects
- Conducted using simple formulation

Developed multiple new formulations

Phase 1 in the Netherlands
MAD study (Healthy volunteers)

BA Part

Evaluate the relative bioavailability of multiple new formulations to select the best formulation

Completed

MAD Part

Evaluate the safety, tolerability, PK and PD in the 2-week multiple ascending dose of sofnobrutinib .

Completed

Sofnobrutinib (AS-0871): Results from the Phase I Clinical Trial (1)

CARNA BIOSCIENCES

Objectives of Single Ascending Dose (SAD) study

Ref. P.59-P.61

A single dose of Sofnobrutinib was administered orally to healthy volunteers to evaluate:

- plasma concentration of sofnobrutinib
- safety assessments (clinical laboratory, ECGs, or vital signs, etc.)
- inhibitory potency on B cell and basophil activation

Result of SAD study

After a single-dose administration of 5 mg, 25 mg, 100 mg, 300 mg, 600 mg, and 900 mg of sofnobrutinib:

- plasma concentration of AS-0871 were increased in a dose dependent manner.
- no clinically meaningful issues were reported in all safety assessments.
- sufficient inhibition of B cell and basophil activations was observed at 100 mg or above.

New formulations for Multiple Ascending Dose (MAD) study

Plasma concentration was evaluated after administering newly developed capsule formulation and tablet formulation containing 50 mg of sofnobrutinib to healthy volunteers:

- the new tablet formulation was shown to be safe and demonstrated good oral bioavailability, and the tablet formulation was selected for the MAD part.

Sofnobrutinib (AS-0871): Results from the Phase I Clinical Trial (2)

Ref. P.62

Multiple Ascending Dose (MAD) study MAD part design

- Double blinded, placebo-controlled, randomized multiple ascending dose study in healthy volunteers
- 14-day multiple oral doses of sofnobrutinib tablets in 3 cohorts (50, 150 or 300 mg twice daily)
- The safety, tolerability, PK and PD were evaluated.

Result of MAD study MAD part

- Well tolerated with no dose-limiting adverse events (AEs): AEs were mostly mild.
- Favorable safety profile up to 300 mg twice daily
- Favorable PK profile: approximately dose proportional with increasing doses
- Robust PD effect was observed: over 90% inhibition for basophils activation on Day 14 at 150 and 300 mg BID doses.

These results from the Phase 1 studies of sofnobrutinib support to advance sofnobrutinib into Phase 2 clinical development for further investigations.

Sofnobrutinib: CSU is a skin disease with unmet medical needs

Chronic Spontaneous Urticaria (CSU) is a distressing skin disorder that 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	P3

The Phase III trials met the primary endpoints and showed rapid symptom control in CSU, supporting the potential of BTK inhibitors as a new treatment option for those uncontrolled by first-line H1-antihistamines.*

＊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.

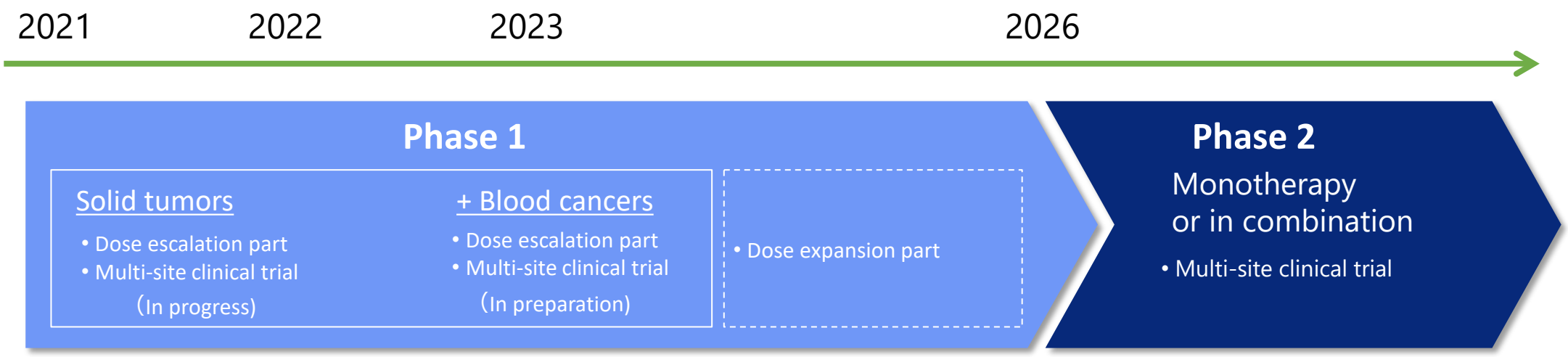
Monzosertib (AS-0141): Highlights

Ref. P.63-P.66

Mechanism/ Indication	Monzosertib is an **orally available** CDC7 kinase inhibitor targeting cancers.
To minimize a risk of side effects	Monzosertib is designed to selectively inhibit CDC7 kinase **to reduce a risk of potential side effects**.
Potentially effective for various cancers	Monzosertib exhibited **a potent anti-proliferative activity against a wide range of cancer cell lines in preclinical studies.**
Potential first-in-class molecule	Monzosertib has a potential to become a first-in-class drug as no CDC7 inhibitors have been approved.

Monzosertib (AS-0141): CDC7 Inhibitor

Monzosertib (AS-0141) : Targeting Cancer	
● Small molecule CDC7 inhibitor ● High kinase selectivity ● Potential First-in-class drug ● Orally available	● Potent anti-proliferative activity against various cancer cell lines ● Demonstrated strong anti-tumor activity in several human tumor xenograft models ● Conducting Phase 1 study in Japan targeting solid tumors ● Planning to expand to blood cancers as monotherapy or in combination with other drugs



Monzosertib (AS-0141): Phase 1 Clinical Trials

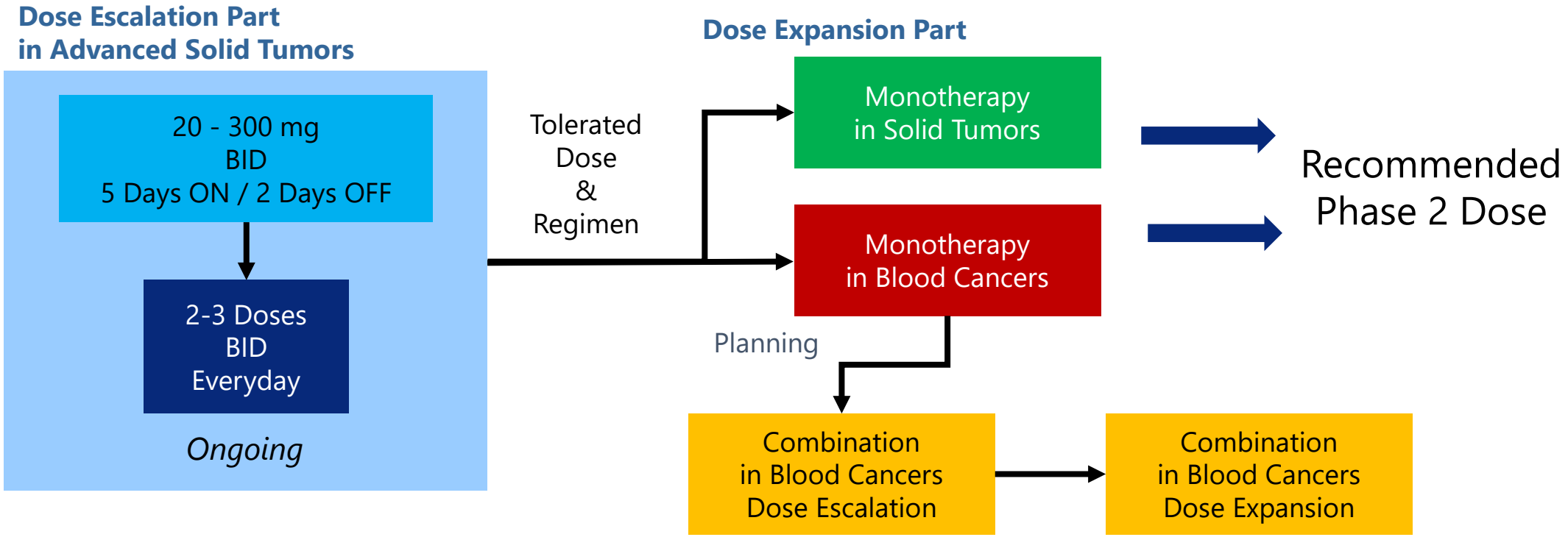
Clinical trial sites : National Cancer Center Hospital and National Cancer Center Hospital East

Clinical trails in progress	Phase 1 dose escalation study targeting cancer patients is ongoing.
Objectives of the study	The primary objectives of the dose escalation study is to assess safety, tolerability, maximum tolerated dose (MTD), preliminary anti-tumor activity, and pharmacokinetics (plasma concentration, duration) of monzosertib.
Dosage	Oral administration, twice a day
Status	• Treating patients at doses up to 300 mg BID (5d on/2d off or no drug holiday). • 80 mg BID (5d on/2d off) was well-tolerated and safe. • Switched to a continuous dosing schedule (without drug holiday) to maximize efficacy. • Planning to expand to blood cancers as monotherapy or in combination with other drugs.

Monzosertib (AS-0141): Phase 1 Clinical Trial

Phase 1 study targeting cancer patients

- The Phase 1 study in patients with advanced, metastatic, relapsed or refractory malignancies. The protocol has been changed to include patients with blood cancers.
- The study consists of two parts, a dose escalation and an expansion.
- The primary objective is to assess safety, tolerability, maximum tolerated dose (MTD), preliminary anti-tumor activity, and PK / PD as well as to determine RP2D.
- Pharmacodynamic effect of monzosertib was confirmed at 40 mg-80 mg BID and above.



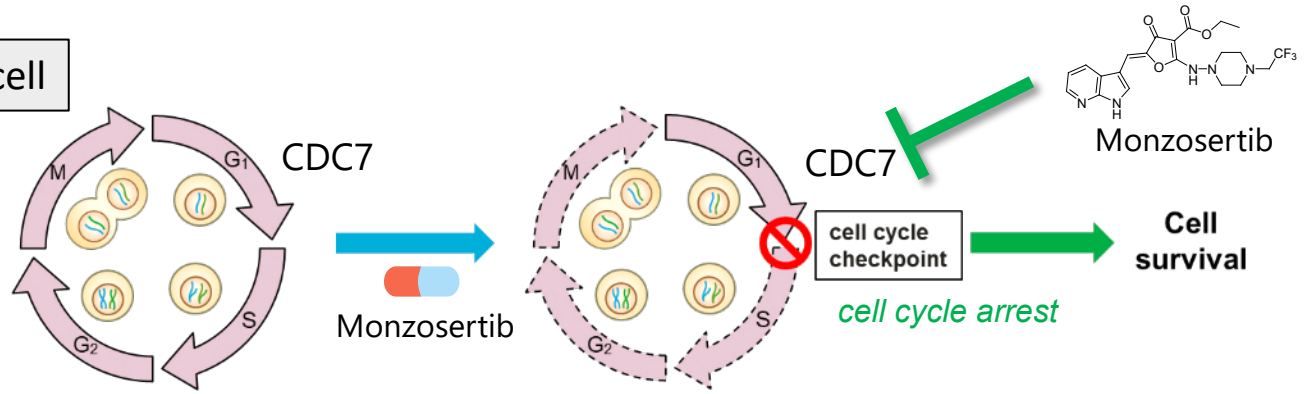
Monzosertib (AS-0141)

Potential Frist-in-class CDC7 Inhibitor Targeting Cancer

MoA of Monzosertib

◆ CDC7 (cell division cycle 7) is a serine/threonine kinase that facilitates DNA replication during DNA synthesis

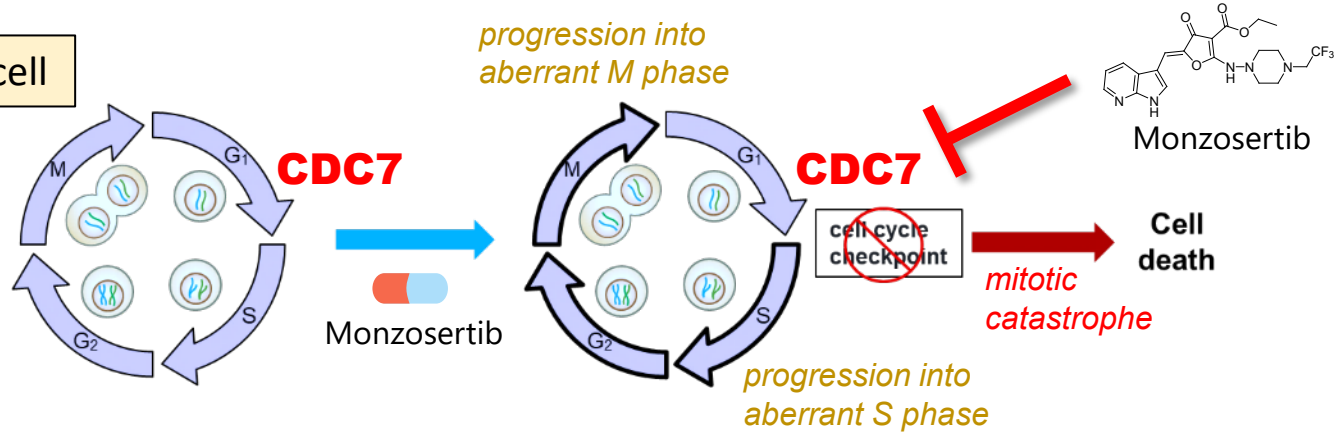
Normal cell



Inhibition of CDC7 in normal cells does not cause cell death, only leads to cell cycle arrest at the DNA replication checkpoint

◆ Over expression of CDC7 has been reported to cause uncontrolled proliferation of many cancer types

Cancer cell



Inhibition of CDC7 in cancer cells causes lethal S phase or M phase progression when the cancer cells have a defective cell cycle checkpoint

Updates on Licensed Pipelines

1. **DGKα Inhibitor** (Gilead Sciences, Inc.)
2. **Joint Research with Sumitomo Pharma**

Out-licensed Programs

Program/ Partner	Compound (Target)	Upfront payment	Total milestone payments expected	Royalty	Region	Contract date	Milestones received
DGKα inhibitor Gilead Sciences (Out-license)	GS-9911 (Immuno-oncology)	$20M	$450M	Undisclosed	Worldwide	Jun. 2019	Received milestones twice, totaling $15M
Joint Research with Sumitomo Pharma	Kinase inhibitor (Psychiatric and neurological disorders)	JPY80M (including research milestone)	JPY10.6B	Undisclosed	Worldwide	Mar. 2018	

※STING antagonist was removed from the list as Fresh Tracks Therapeutics, the licensee, announced in September 2023 its plant to liquidate and dissolve the company.

DGKα Inhibitor

Partner	Gilead Sciences, Inc. **Out-licensed in June 2019** (worldwide rights)
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

1. Investigational DGKα inhibitor: GS-9911

2. Indication: Cancer (immunotherapy)

- At JP Morgan Annual Healthcare Conference held in January 2024, Gilead introduced DGKα as next generation target in oncology and presented GS-9911 as the DGKα inhibitor in Phase 1 trials.

3. The Phase 1 study is ongoing targeting patients with solid tumors.

Refer Gilead's website for details of the study.
https://www.gileadclinicaltrials.com/study?nctid=NCT06082960

Joint Research with Sumitomo Pharma

Partner	Sumitomo Pharma Co., Ltd. Joint Research Agreement in March 2018 (worldwide rights)
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

1. **Joint research to discover novel kinase inhibitors to treat psychiatric and neurological disorders.**
2. **The term of the joint research was extended in December 2021.**
3. **Joint research is ongoing to identify preclinical candidates.**

Drug Discovery Support (ddSP) Business

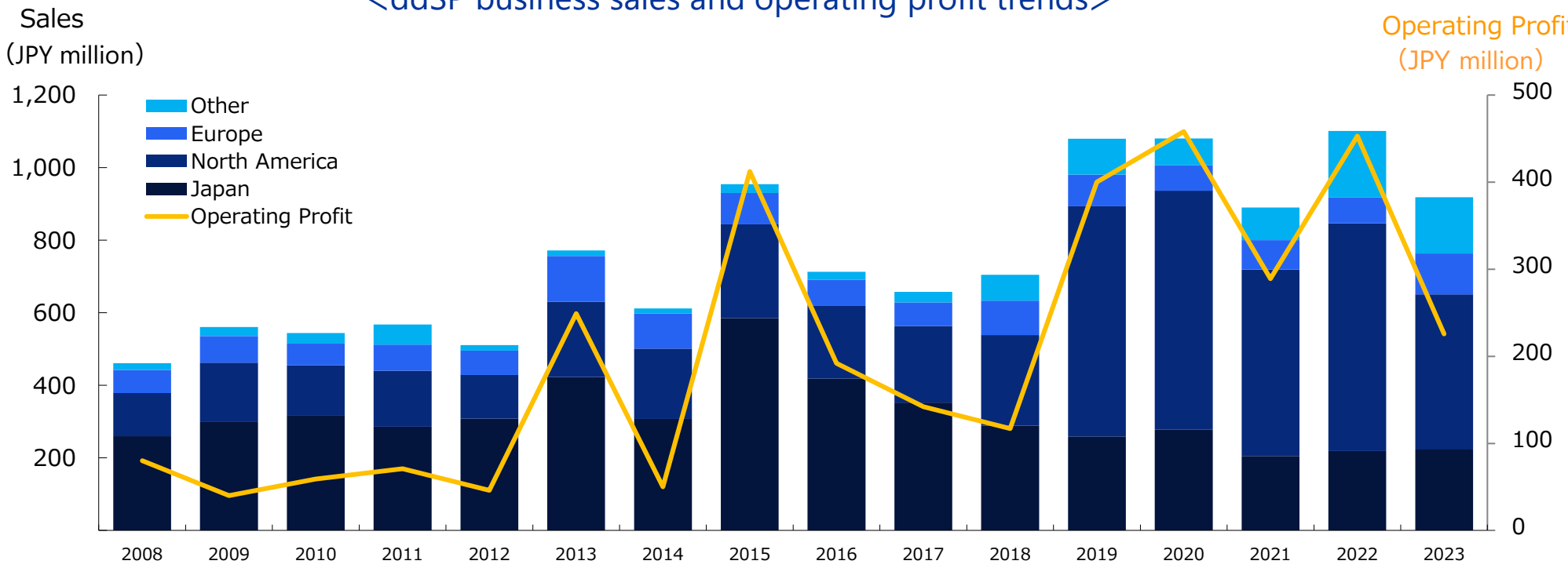
Drug Discovery Support Business：Strengths

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).**
- **These strengths enable our business to increase in sales continuously and significantly contribute to our performance with stable high profit margin.**

***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. Top sales company in immune-related reagents in China.

＜ddSP business sales and operating profit 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 a new innovative high throughput system, LSA^{XT}, which enabled small molecule screening and characterization in addition to antibody.
- Carna and Carterra collaborated to preliminary develop the assay with this new screening system in combination with Carna's single site biotinylated kinase proteins and Carterra's HT-SPR LSA^{XT} instrument.
- This collaboration successfully proved this new system screen about hundreds kinases and compound binding event just in 3 days.

Our biotinylated kinase protein sales is expected to be expand with the permeation of Carterra LSA^{XT}.

Profiling Services

- Conventionally, capillary electrophoresis has been known as highly reliable method for measuring kinase protein activity without using radioisotopes.
- Perkin Elmer (renamed Revvity in 2023)'s EZ Reader which equipped electrophoresis system on microchip with 12 capillaries has been a de facto standard for measuring kinase activity, was announced its discontinuation including supply of consumables and the support as of the end of this year. This boosts high demand for a substitute system with the same data quality.
- We have been providing high quality profiling services with EZ Reader.
- To continue offering profiling services, we challenged and succeeded in developing our original substitute 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.

Carna will continue reliable profiling services with this original system and aim to acquire even more customers.

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（Canada)、Reaction Biology（US)

- Carna is the only drug discovery support service provider specialized in kinase inhibitor drug discovery.

- Carna is the only major player who offers biotinylated kinases.

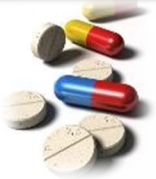
- Precise assays, appropriate product development and finely attentive technical support by scientists with drug discovery experiences and knowledges.

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	Continue delivering profits
2010-2015	2016-2020	2021-2025 (Plan)	2026-2030 (Plan)
• Established in-house research capability • Established pipeline	• Out-licensed multiple programs • Initiated clinical trials	• Advance clinical trials of 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	• 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



<ddRD>
- ✓ Advance clinical trials of 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)	FY2023 Actual	FY2024 Plan	Outlook for 2025 – 2028
Total Sales	1,625	**925**	
ddSP business	918	**925**	Maintain stable sales
ddRD business	707	**—**	Revenue from milestone payments and upfront payments
Total Operating Loss	(1,116)	**(2,201)**	
ddSP business	225	**229**	Maintain stable profit while investing in product developments
ddRD business	(1,342)	**(2,431)**	Continue to invest in R&D and deliver profits depending on the size of milestone payments and upfront payments
Ordinary Loss	(1,126)	**(2,208)**	
Net Loss	(1,152)	**(2,225)**	

(JPY million)	FY2023 Actual	FY2024 Plan	Outlook for 2025 – 2028
R&D Cost	1,903	**2,309**	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	11	**44**	Invest in equipment for R&D and IT system (JPY20 mn to 100 mn)

- Business plan for FY2024 dose not include potential milestone payments or upfront payments as the timing or the amounts are difficult to predict.
- Numerical targets for 2025-2028 are not disclosed for the same reason.

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

Key Milestones for 2024

Business		Key Milestones		
		Milestones for 2023	Achievement in 2023	Milestones for 2024
ddRD	AS-1763	☐ Ph1b FPI (US)	☑ Ph1b FPI (US) ・Dosing initiated in August 2023	☐ Present interim clinical data from ongoing Ph1b study
	Sofnobrutinib (AS-0871)	☐ Complete Ph1 MAD study ☐ Prepare a package for licensing	☑ Complete Ph1 MAD study ・Finalized the CSR in November 2023 ☑ Prepare a package for licensing	☐ Promote partnering activity to find a strategic partner
	Monzosertib (AS-0141)	☐ Initiate Ph1 expansion part	☐ Initiate Ph1 expansion part ・Changed to daily administration and dose escalation part is ongoing	☐ Enroll patients with blood cancers ☐ Initiate Ph1 dose expansion part
	Research program	☐ Bring one or more programs in preclinical stage or license a program	☑ Bring one or more programs in preclinical stage. ・Selected a development candidate for further evaluation	
ddSP		☐ Expand sales of in-house developed products and services in North America 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 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 and Asia ☐ Increase line-up of protein kinase products ☐ Expand sales of cell-based assay

*Starting 2024, ddRD business will only disclose the key milestones for the clinical development pipelines as priority objectives.

FPI: First Patient In
CSR：Clinical Study Report
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, 2022	As of Dec. 31, 2023	Change
Current assets	4,104	4,191	87
Cash and deposits	3,379	2,889※	-489
Non-current Assets	162	158	-3
Total assets	4,266	4,349	83
Current liabilities	436	375	-60
Non-current liabilities	188	96	-91
Total liabilities	624	472	-152
Total net assets	3,641	3,877	235
Total liabilities and net assets	4,266	4,349	83

※The milestone payment of $5 mn (JPY707 mn) from Gilead was recorded as sales in FY2023. However, it is not included in cash and deposit as of the end of FY2023 as the money was received in January 2024.

Financing

<Exercise of Subscription Rights to Shares in FY2023

	19th Subscription Rights to Shares	20th Subscription Rights to Shares	Total
Amount raised (JPY)	47mil.	1,302mil.	1,349mil.
No. of shares exercised (Shares)	50,000	2,836,500	2,886,500

<20th Subscription Rights to Shares >

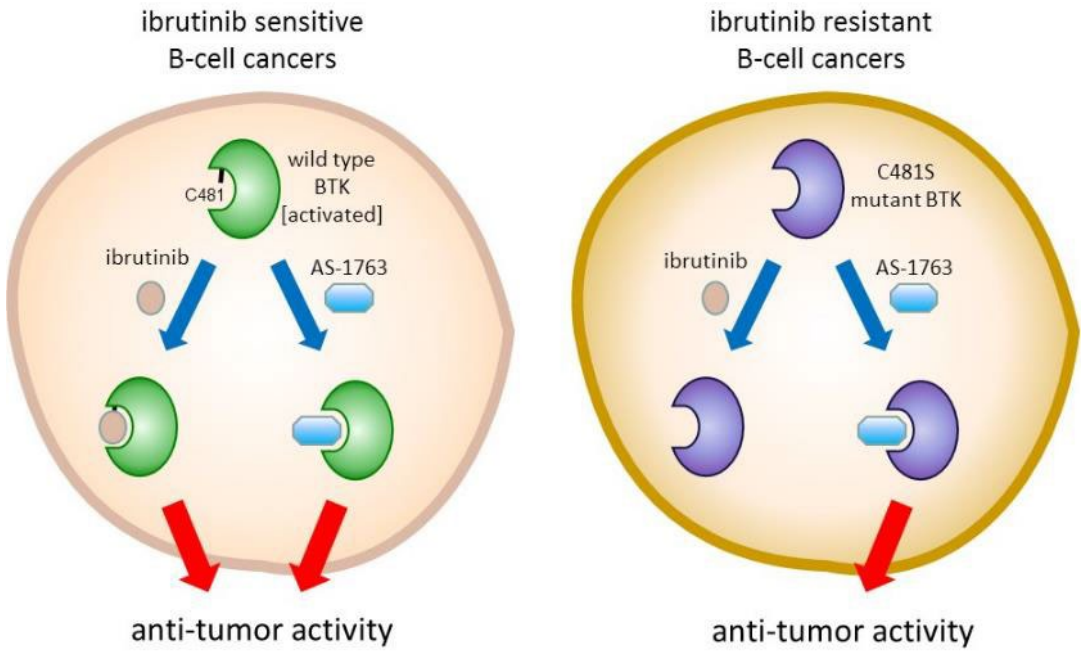
	DEC. 2022	JAN.-APR.2023	Total
Amount raised (JPY)	300 mil.	1,302mil.	1,602mil.
No. of shares exercised (Shares)	550,000	2,836,500	3,386,500
No. of Exercised rights / No. of total rights issued	16.2 %	83.8%	100%

Financing

Additional financing may be considered as necessary in order to accelerate the clinical trials of AS-1763, our most important asset.

Appendix 1

AS-1763: Potent Inhibitor of C481S mutant BTK



Journal of Medicinal Chemistry
pubs.acs.org/jmc
Drug Annotation

Discovery of AS-1763: A Potent, Selective, Noncovalent, and Orally Available Inhibitor of Bruton's Tyrosine Kinase

Wataru Kawahata,* Tokiko Asami, Takao Kiyoi, Takayuki Irie, Shigeki Kashimoto, Hatsuo Furuichi, and Masaaki Sawa

Cite This: *J. Med. Chem.* 2021, 64, 14129–14141 Read Online

- **IC_{50} values of AS-1763 against wild-type and C481S-mutant BTK**

	IC_{50} (nM)	
	BTK[A]	BTK^{C481S}
AS-1763	0.85	0.99

J Med Chem. 2021 Oct 14;64(19):14129-14141.

AS-1763: Strong Cellular Activity and High Kinase Selectivity

CARNA BIOSCIENCES

◆ In vitro pharmacological activities of AS-1763

	IC_{50} (nM)	
	AS-1763	Ibrutinib
Autophosphorylation BTK (Ramos)	1.4	1.1
CD69 activation (Human whole blood)	11	8.1
Cancer cell growth OCI-Ly10 cells	1.8	0.75
Cancer cell growth OCI-Ly10 [BTK C481S] cells	20	1030
Normal cell growth HEL299 cells	6370	6870

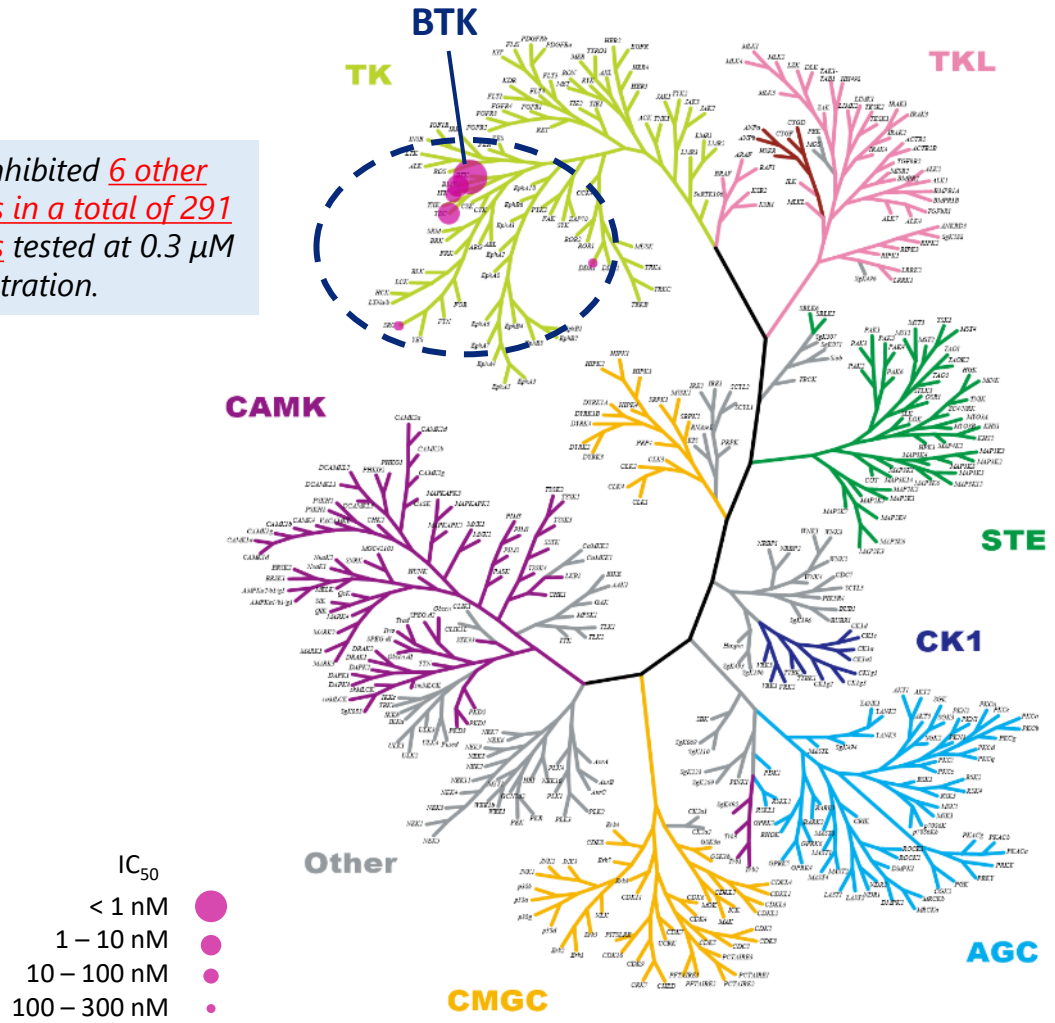
50-fold Stronger activity

Ramos: human Burkitt lymphoma cell line
OCI-Ly10: human B-cell non-Hodgkin lymphoma cell line
OCI-Ly10 [BTK C481S]: BTK[C481S] knock-in OCI-Ly10 cells
HEL299: human embryo lung cell line

J Med Chem. 2021 Oct 14;64(19):14129-14141.

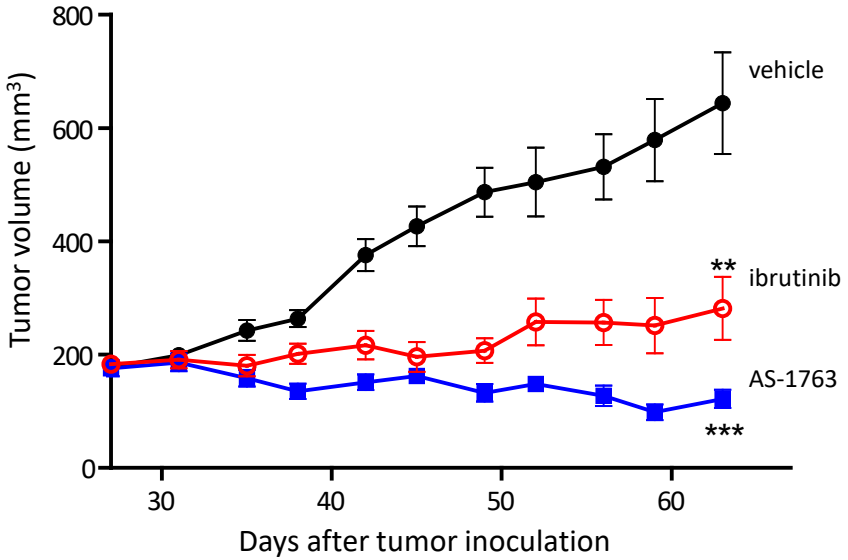
◆ Kinase selectivity profiling

Only inhibited 6 other kinases in a total of 291 kinases tested at 0.3 μM concentration.



AS-1763: In Vivo Antitumor Effect against BTK^{C481S} Mutant

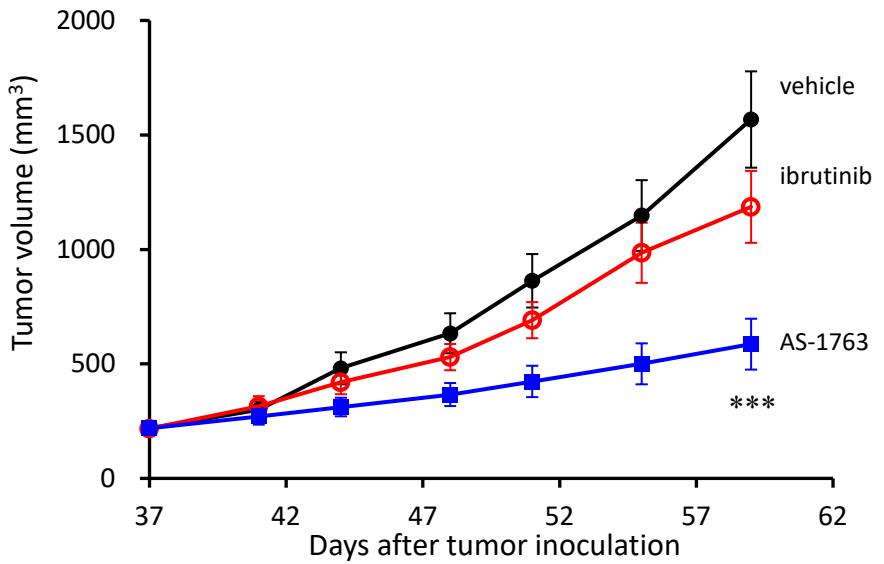
- **In vivo antitumor effects of AS-1763 on human B-cell non-Hodgkin lymphoma cell line, OCI-LY10 tumor xenograft mouse model (n=8-10)**



Ibrutinib: 25 mg/kg QD
AS-1763: 60 mg/kg BID

**: p<0.01
***: p<0.001

- **In vivo antitumor effects of AS-1763 on ibrutinib-resistant BTKC481S knock-in OCI-LY10 tumor xenograft mouse model (n=11)**



Ibrutinib: 25 mg/kg QD
AS-1763: 60 mg/kg BID

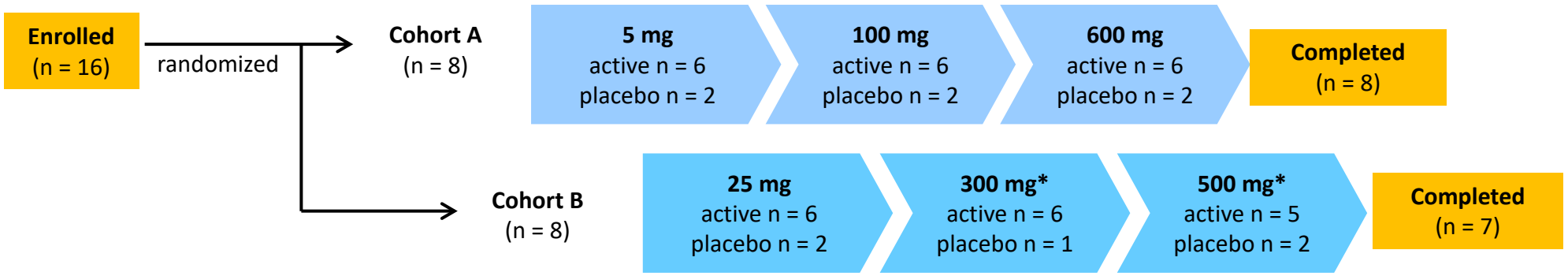
***: p<0.001

J Med Chem. 2021 Oct 14;64(19):14129-14141.

AS-1763: FIH Phase 1 Clinical Trial in Healthy Volunteers

Study Design

Step 1 Single Ascending Dose (SAD) Part	Step 2 Relative Bioavailability (BA) Part
• Double-blind, placebo-controlled, randomized FIH study • Simple formulation (solution) • 6 dose levels (8 subjects/cohort A, 8 subjects/cohort B) • 6 active / 2 placebo for each dose level • Safety and tolerability • Pharmacokinetics and pharmacodynamics (PD; CD69 upregulation on naïve B cells)	• Open label study • Another cohort of 8 subjects • The subjects were dosed with a single dose of AS-1763 100-mg tablet, and relative bioavailability with simple formulation was evaluated



*One subject was withdrawn from the study on Day 1 of 300-mg period before the intake of treatment medication (placebo) by physician's decision. This subject showed AEs (Grade 2 lymphocytosis and Grade 2 neutropenia) which were considered treatment-emergent but not trial medication-related. No replacement was done at 300-mg and the following 500-mg periods.

AS-1763: SAD Part

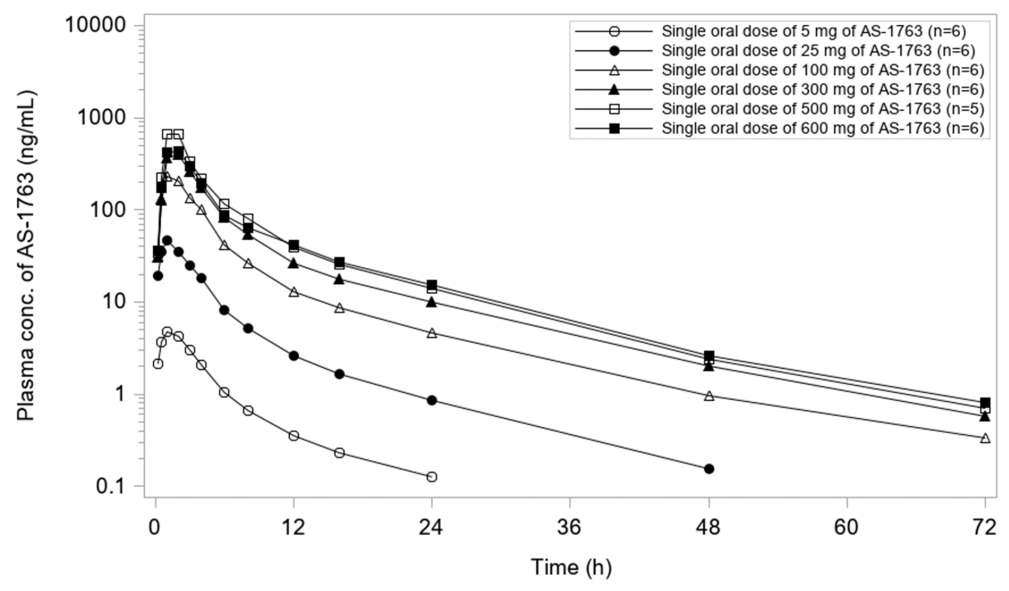
Safety and tolerability

- AS-1763 was well-tolerated after single dose administration up to the maximum dose level (600 mg).
- No serious adverse events (AEs) were reported during the trial.
- Two Grade 2 AEs were reported in one subject, which were considered not related to trial medication.
- Other AEs reported were of mild intensity and showed no apparent dose-relationship in frequency.
- No clinically relevant changes from baseline were observed in all other safety parameters assessed (clinical laboratory, 12-lead safety ECGs, vital signs, or physical examinations).

Pharmacokinetics

- After a single-dose oral administration, plasma concentration of AS-1763 rapidly reached the maximum and then declined in a biphasic manner across the dose range (median tmax between 0.5 and 1.5 hours; mean t1/2 between 8.4 and 12.1 hours).
- Mean AS-1763 exposures generally increased with dose up to 500 mg.

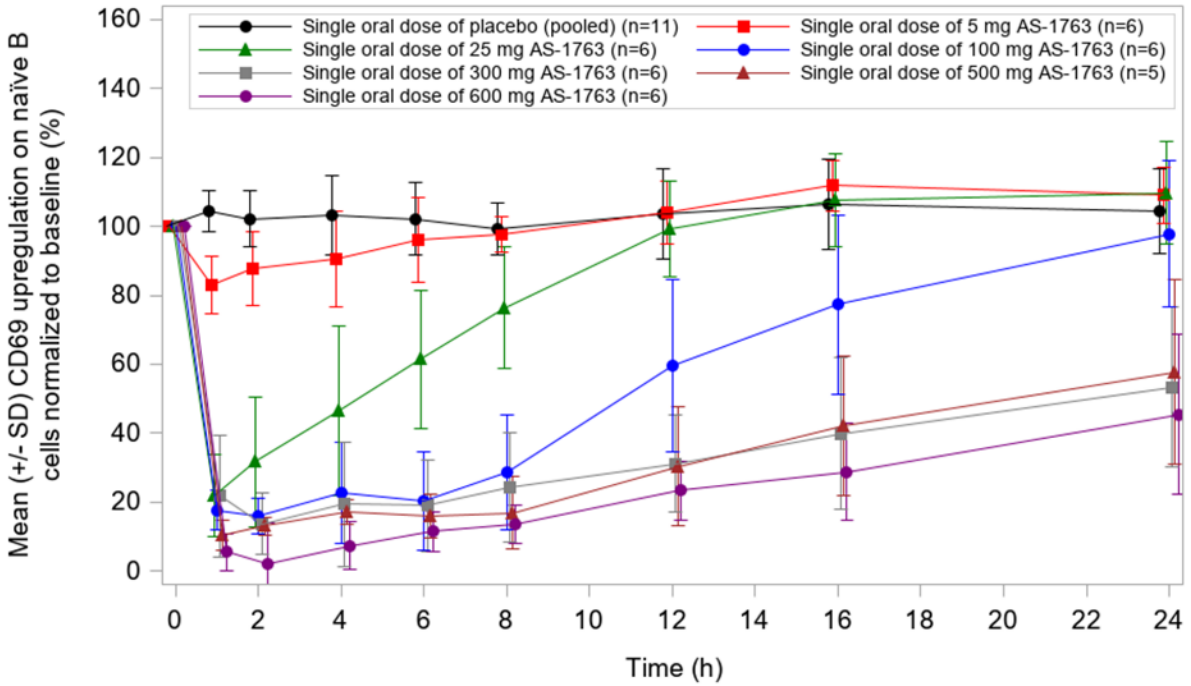
< Plasma concentration of a single oral dose of AS-1763 >



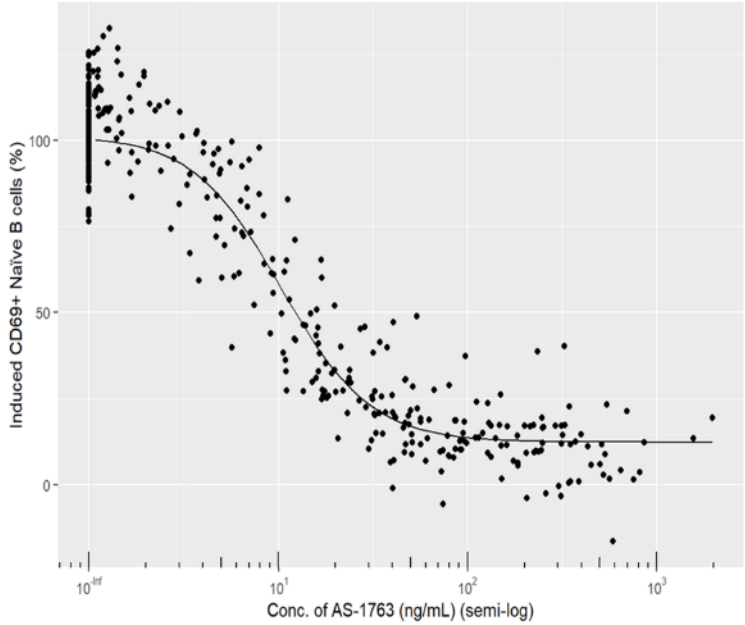
Pharmacodynamics of AS-1763

- Inhibition of B cell CD69 upregulation was observed for 5 mg onwards.
- Maximum inhibition (arbitrarily defined as ≥80%) was observed at 1-2 hours post-dose from 100 mg to 600 mg, and the duration of inhibition was dose-dependent with values of 2, 6, 8 and 8 hours for 100, 300, 500, and 600 mg, respectively.
- Based on a PK/PD correlation analysis, the IC50 value of AS-1763 on CD69 upregulation was calculated to be 10.5 ng/mL.

< B cell CD69 upregulation after a single oral dose of AS-1763 >



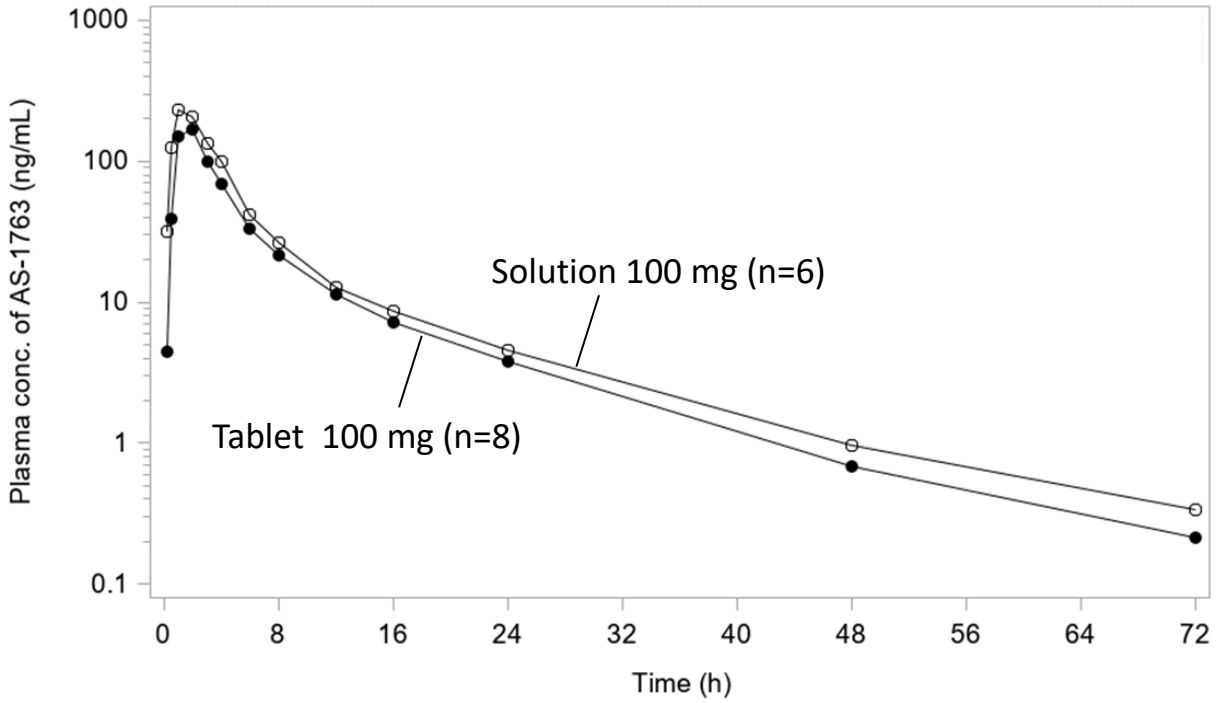
< PK/PD correlation analysis >



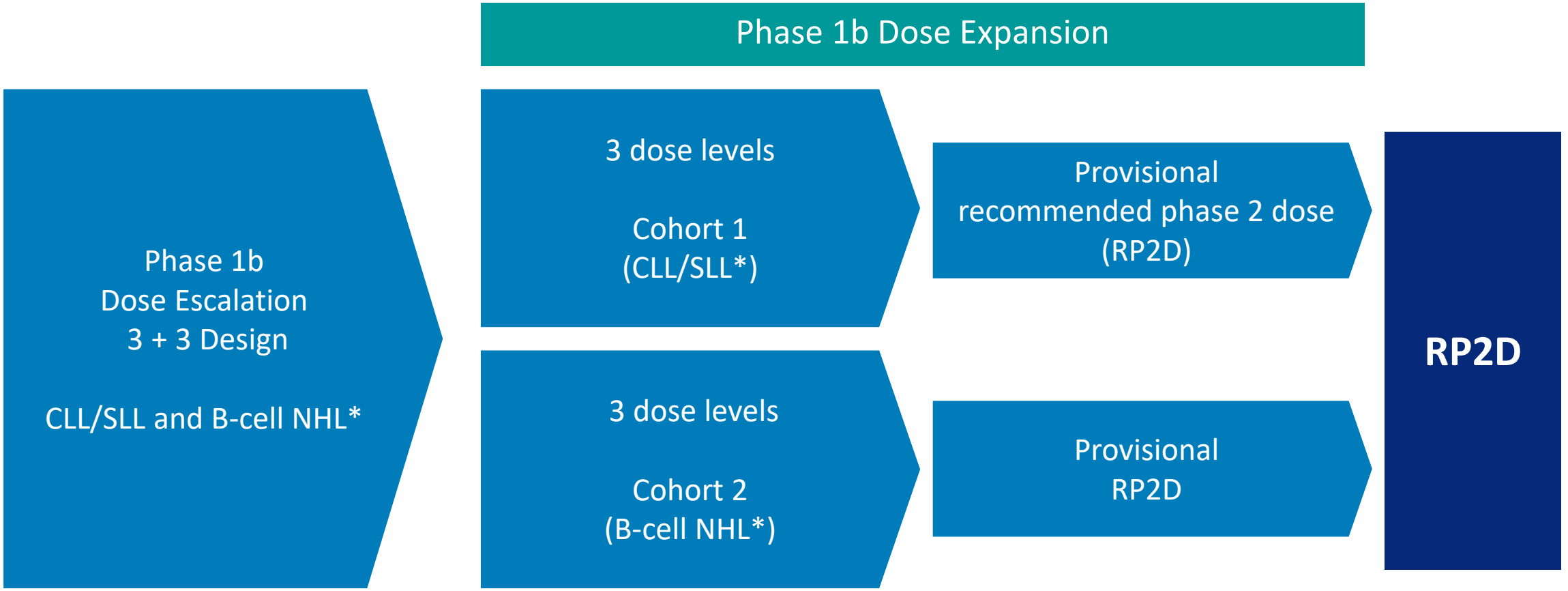
AS-1763: BA Part

- In the BA part, 100 mg tablet and the solution showed almost similar PK profile while the exposure of 100 mg tablet was slightly lower than the that of the solution.
- The PK/PD data and favorable safety profile in healthy volunteers support a planned Phase 1b clinical study with AS-1763 tablet twice daily dosing in relapsed/refractory CLL and B-cell NHL.

<PK of Tablet vs Solution after a Single oral dose AS-1763>



AS-1763: Phase 1b Schema (US)

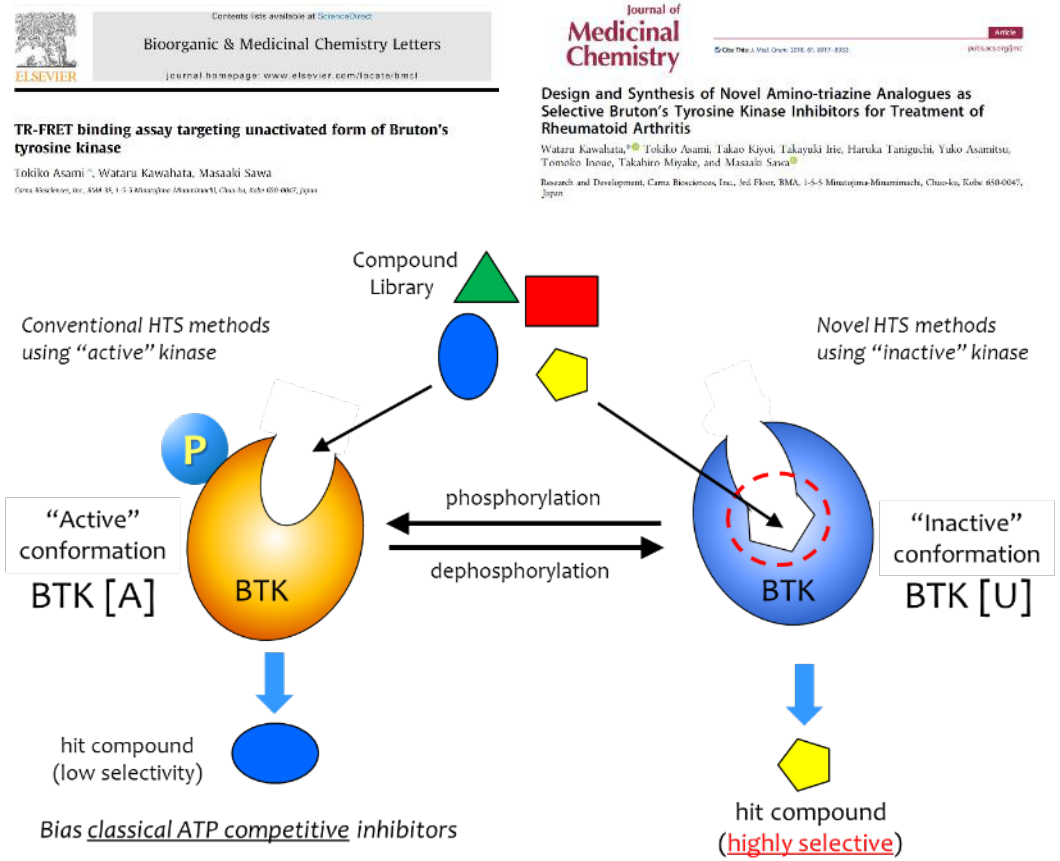


*Previously treated patients

◆ **The first patient was dosed in August 2023.**

Sofnobrutinib (AS-0871): Excellent Kinase Selectivity

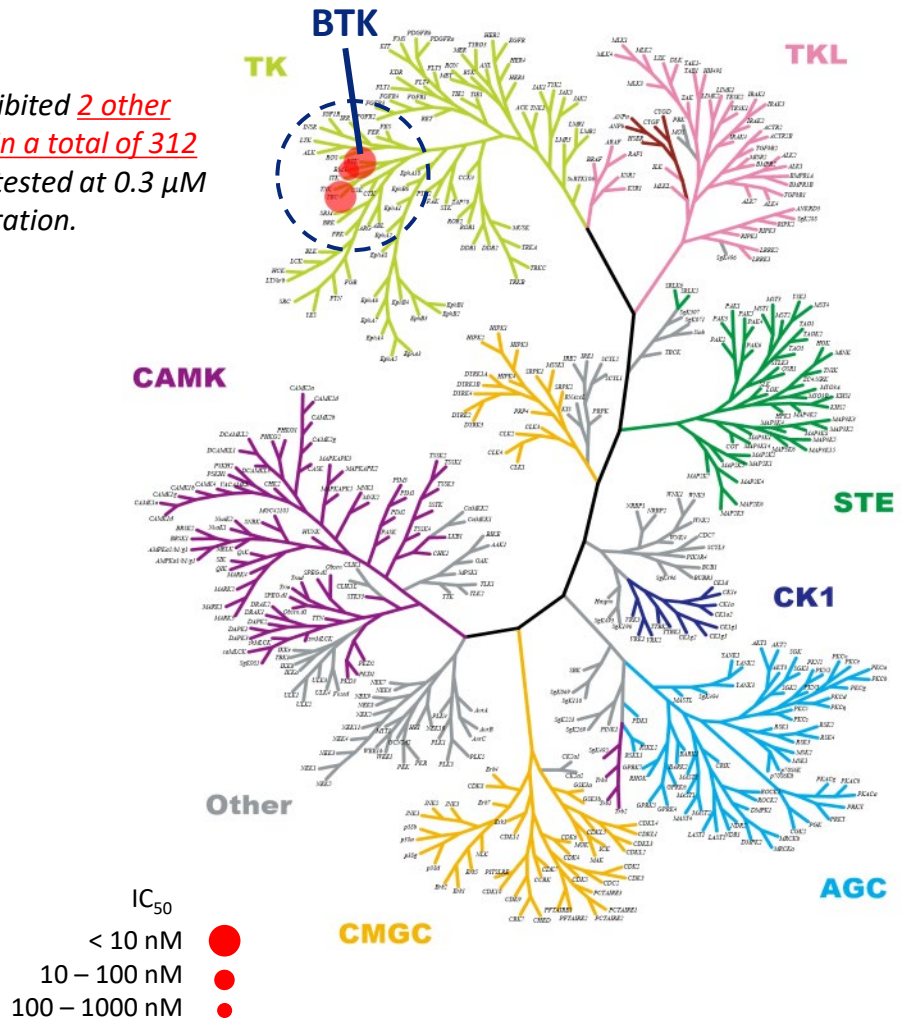
◆ Targeting Inactive Conformation of BTK



	BTK IC_{50} (nM)	
	BTK[A]	BTK[U]
sofnobrutinib	3.4	0.3

◆ Kinase Selectivity Profiling

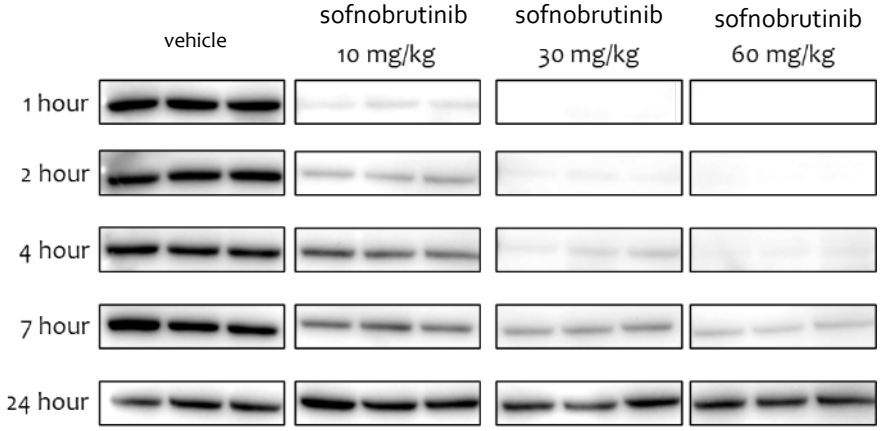
Only inhibited 2 other kinases in a total of 312 kinases tested at 0.3 μM concentration.

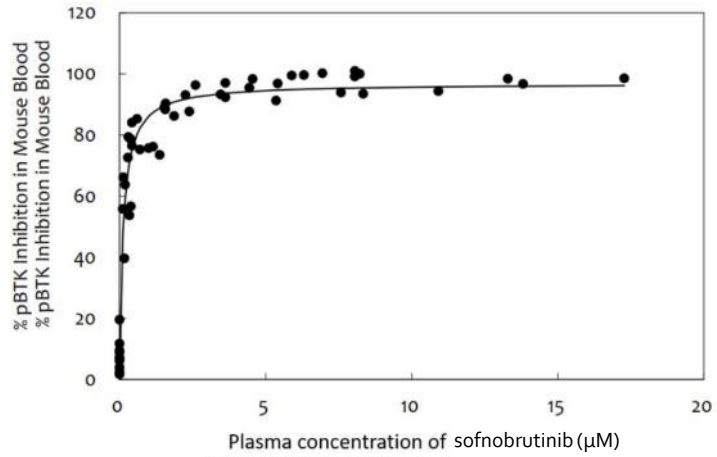


Sofnobrutinib (AS-0871): In Vivo Therapeutic Efficacy

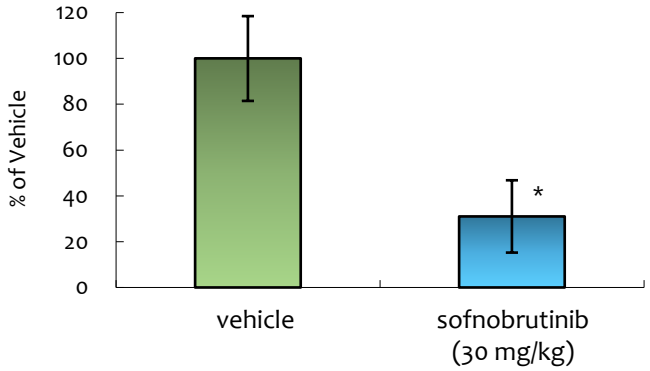
◆ PK/PD Study

Auto-phosphorylation status of BTK was measured following oral single administration of sofnobrutinib .

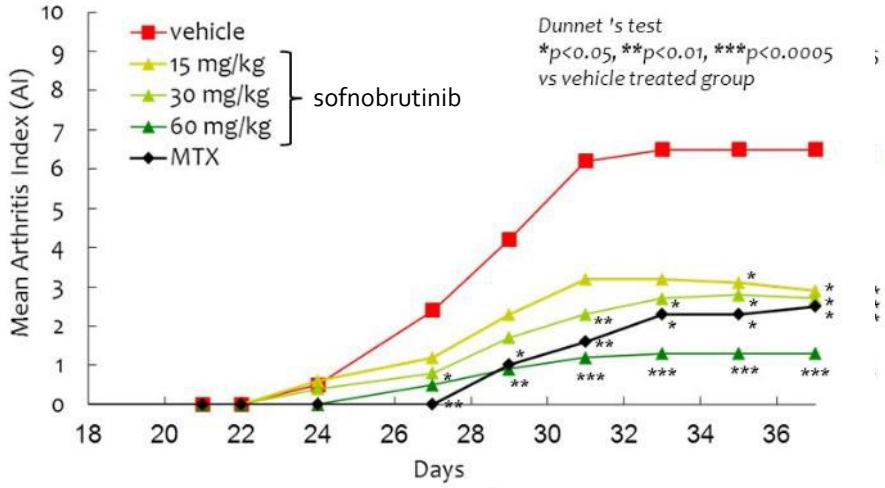




◆ Passive cutaneous anaphylaxis (PCA) mouse model (n=5)



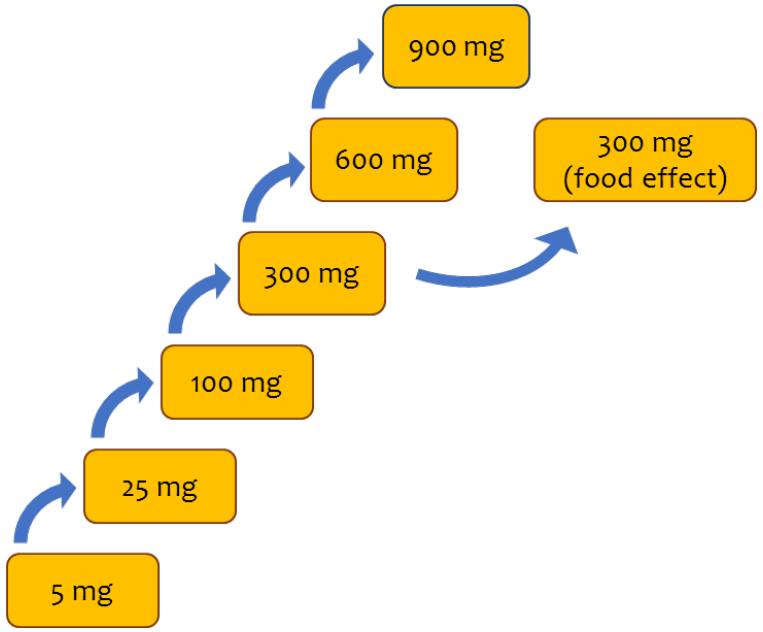
◆ Collagen-induced arthritis (CIA) mouse model (n=10)



Sofnobrutinib (AS-0871): FIH Study

SAD Part (Completed)

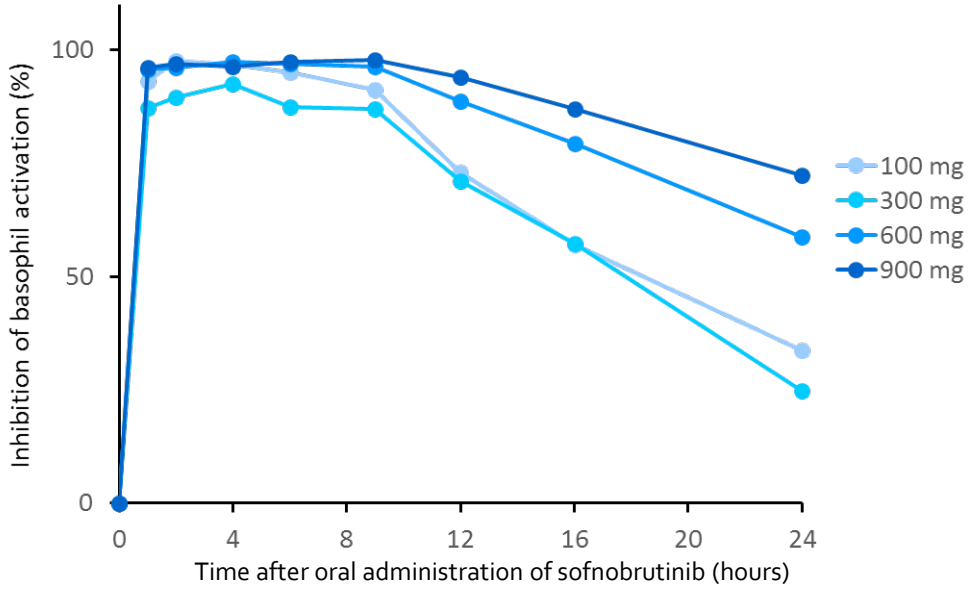
Step 1 Single Ascending Dose (SAD)	Step 2
• 6 dose levels (8 subjects/cohort) • Placebo controlled (6 active / 2 placebo) • Safety and tolerability • Pharmacokinetics and pharmacodynamics	• Food effect

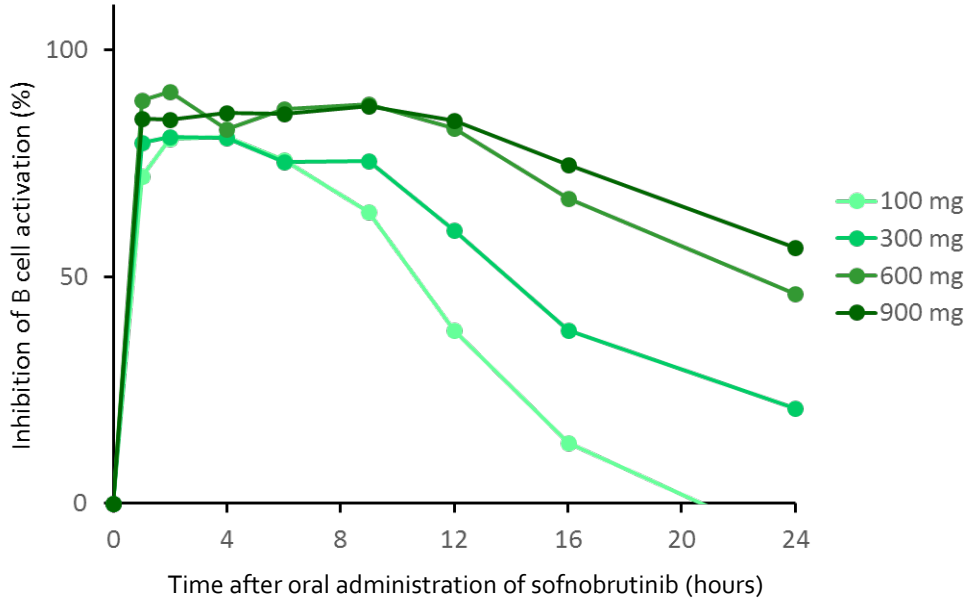


- Sofnobrutinib is well-tolerated without any safety concerns.
- Favorable pharmacokinetic profile.
- Blood samples to assess PD effects were analyzed for evaluation of the B-cell and basophil responses. Administration of sofnobrutinib at 100mg or above resulted in strong inhibition of B-cell and basophil activation.
- Switching to a new formulation in the MAD study.

Pharmacodynamics of sofnobrutinib (AS-0871)

- Pharmacodynamic study demonstrated that subjects who received sofnobrutinib showed dose proportional inhibitions in basophil and B-cell activations, and significant and sustained inhibitory effects were observed at 100 mg and above.
- Oral administration of sofnobrutinib achieved therapeutic plasma levels needed to inhibit B cells and basophils activation, suggesting that sofnobrutinib has a potential to become a new treatment option for inflammatory diseases.

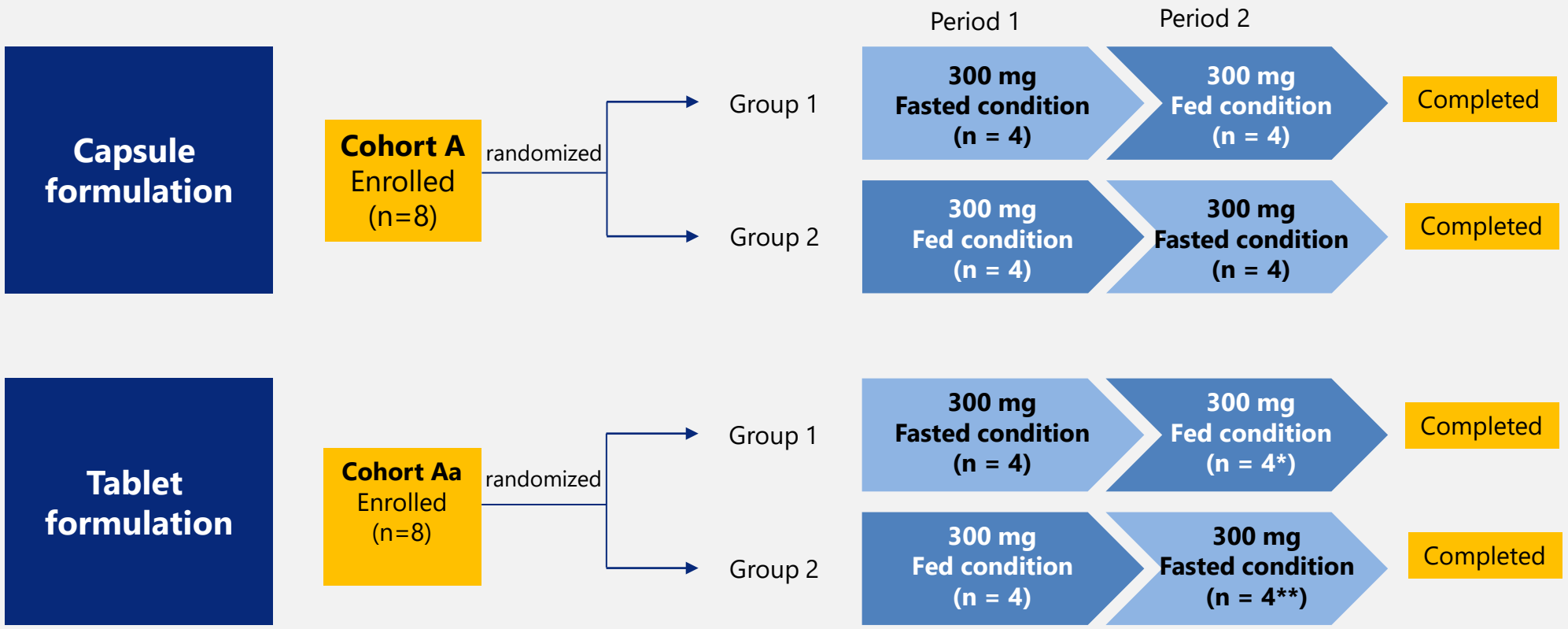




Sofnobrutinib (AS-0871): Phase 1 MAD Study BA part

Study Design of rBA/FE part

PK, safety, and tolerability after single-dose oral administration of sofnobrutinib, formulated as capsules or tablets, were evaluated under fasted and fed conditions in an open-label, randomized, 2-period crossover design. Eight healthy subjects (Cohort A or Cohort Aa) were randomized to either Group 1 or Group 2 (4 subjects per group).

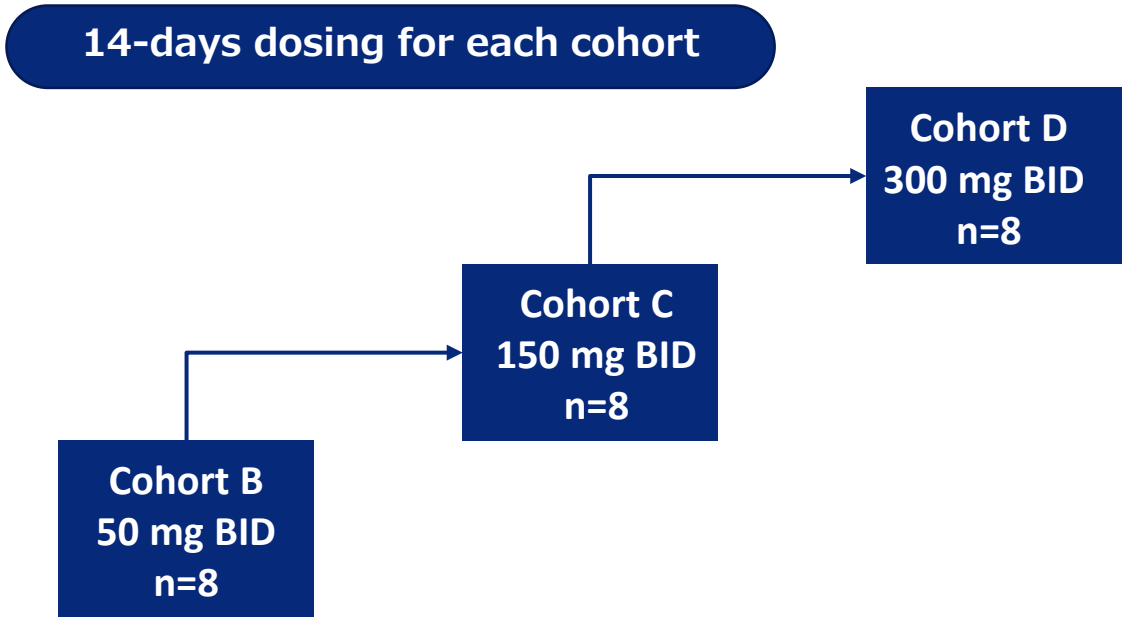


*One subject vomited after dosing (considered not related to study drug), excluded from the PK analysis.
**One subject withdrew from the study due to personal reasons before dosing.

Sofnobrutinib (AS-0871): Phase 1 MAD Study MAD part

Study Design of MAD part

- In the MAD part, safety, tolerability, PK, and PD of 3 multiple ascending doses of sofnobrutinib, following 14-day multiple dose oral administration of sofnobrutinib, will be investigated using a double blind, placebo-controlled, randomized design in 3 cohorts of 8 healthy subjects each.
- Dosing was completed as planned.
- The final Clinical Study Report (CSR) for the Phase 1 MAD study has been finalized in November 2023.



- Well tolerated with no dose-limiting AEs.
- Favorable safety profile up to 300 mg BID.
- The exposure levels increased dose-dependently, and favorable PK profile with tablet formulation was confirmed.
- Achieved almost complete inhibition of basophil activation (PD marker) at 150 mg and 300 mg BID at a steady state

Monzosertib (AS-0141): Time-Dependent Inhibitor of CDC7

◆ Monzosertib has a unique inhibitory mechanism for CDC7 kinase (time-dependent inhibition)


European Journal of Medicinal Chemistry

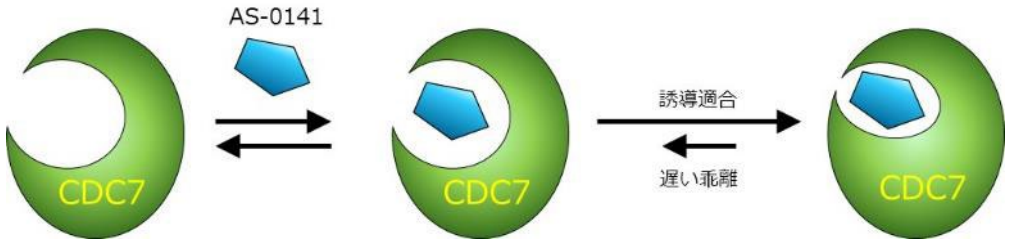
Research paper

Discovery of novel furanone derivatives as potent Cdc7 kinase inhibitors


Journal of Medicinal Chemistry

Discovery of AS-0141, a Potent and Selective Inhibitor of CDC7 Kinase for the Treatment of Solid Cancers

Takayuki Irie,* Tokiko Asami, Ayako Sawa, Yuko Uno, Chika Taniyama, Yoko Funakoshi, Hisao Masai, and Masaaki Sawa

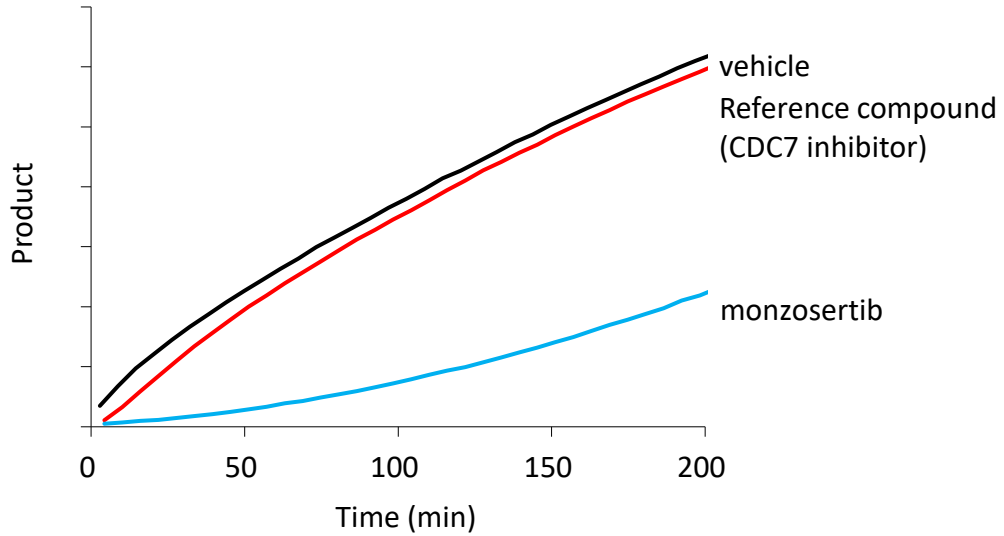


Inhibitory potency (IC50) for CDC7 in the presence of 1 mM ATP	
Without Preincubation	With Preincubation
503 nM	2.4 nM

J Med Chem. 2021 Oct 14;64(19):14153-14164.

◆ Monzosertib inhibits CDC7 in a reversible fashion but has a very slow off-rate

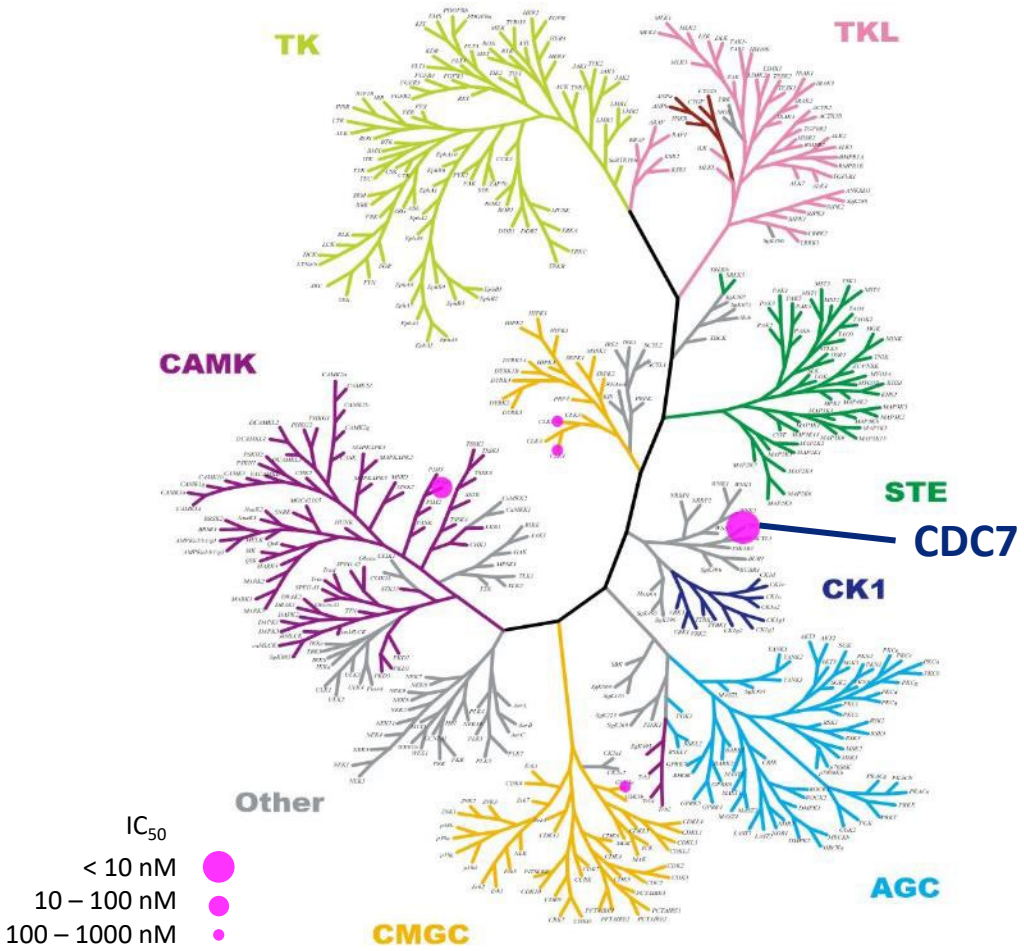
Rapid dilution assay for Cdc7 inhibitors. Recovery of enzymatic activity was monitored by formation of the phosphorylated product.



Monzosertib (AS-0141): High Kinase Selectivity

◆ Kinase Selectivity Profiling

In the presence of 1 mM ATP with preincubation



◆ IC50 values of hit kinases（at 1 mM ATP）

	IC_{50} (nM)	
	Preincubation	
	-	+
CDC7	503 (210-fold)	2.4
PIM1	30	34
CLK1	212	206
CLK2	270	227
GSK3α	189	251

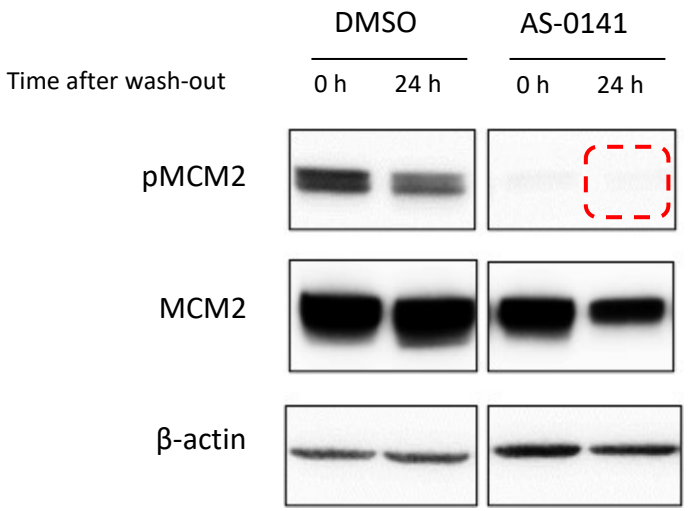
CDC7 is the only kinase that shows preincubation effect

J Med Chem. 2021 Oct 14;64(19):14153-14164.

Monzosertib (AS-0141): Strong Cellular Activity

◆ Prolonged inhibition in cells

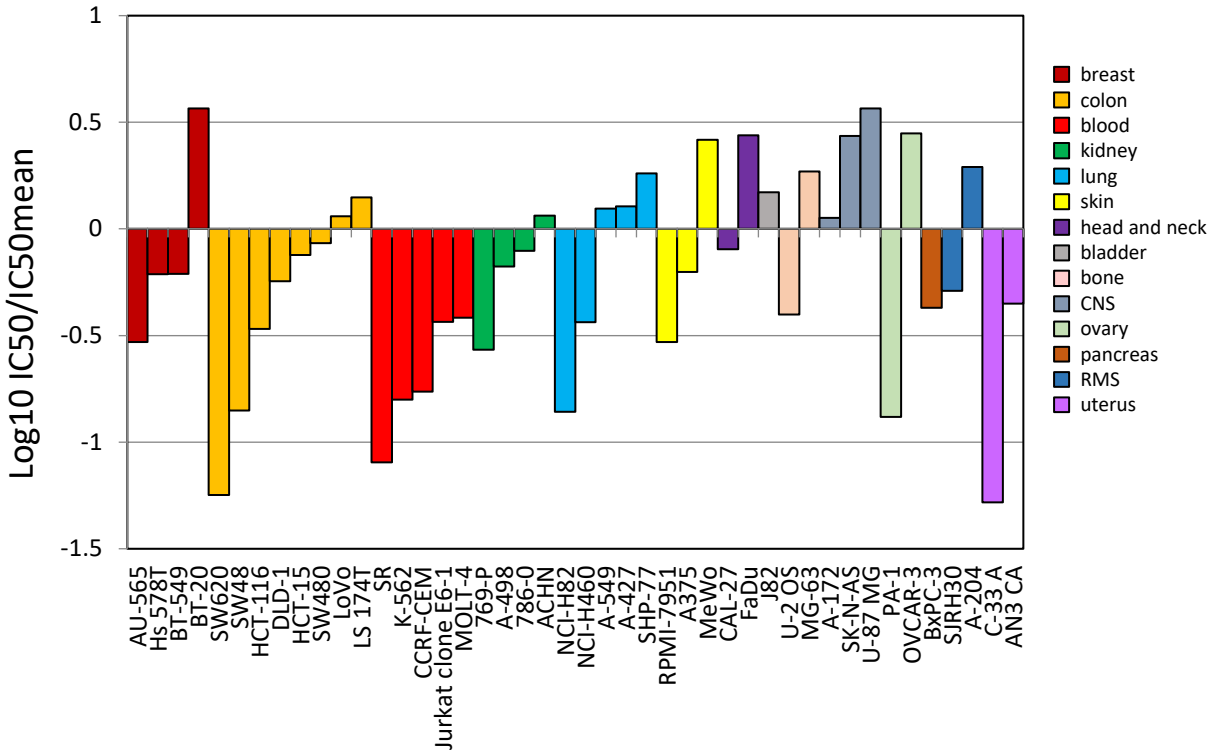
Human colon cancer cell line, Colo-205 cells were treated with DMSO control or monzosertib. After washout of the inhibitor, the cells were further incubated in the same media for 0 or 24 h and subjected to western blot analysis.



the inhibitory effect of monzosertib on the phosphorylation of MCM2 in cells continued up to 24 h after washing out

J Med Chem. 2021 Oct 14;64(19):14153-14164.

◆ Monzosertib potently inhibited growth in a wide range of tumor cell lines, including solid and hematological tumors

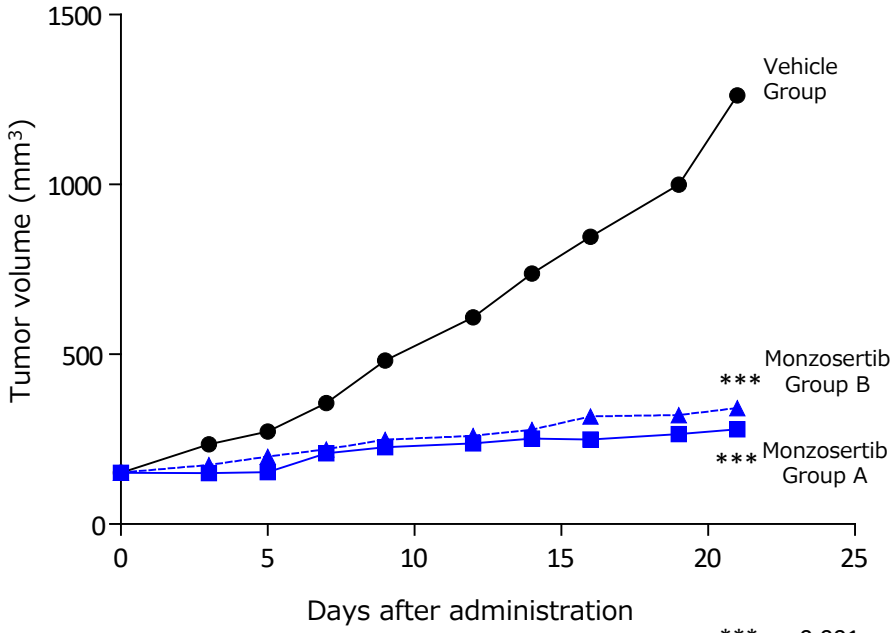


44 Cancer cell lines (Oncolines at NTRC)

Monzosertib (AS-0141): Robust In Vivo Antitumor

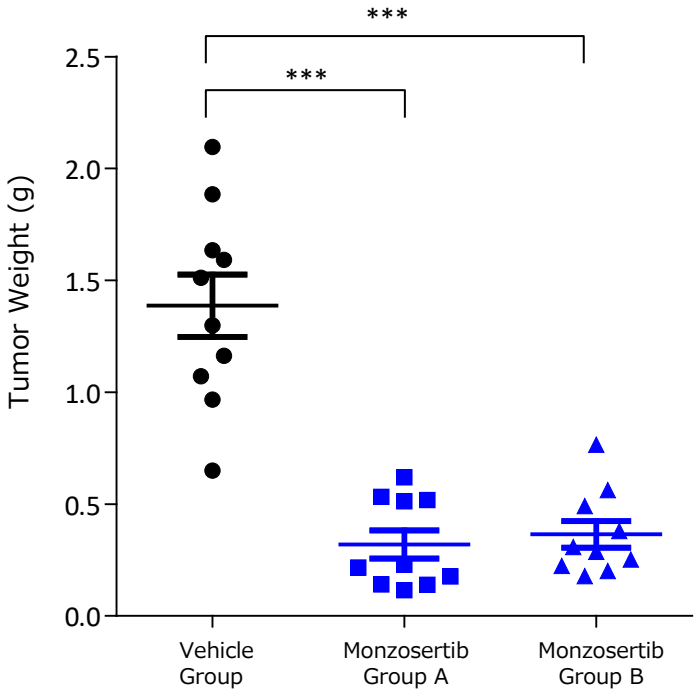
In vivo antitumor efficacy of monzosertib in a SW620 (human colon cancer) xenograft mouse model

Tumor Growth Curve (Mean, n = 10)



***: p<0.001

Final Tumor Weight of Each Mouse



***: p<0.001

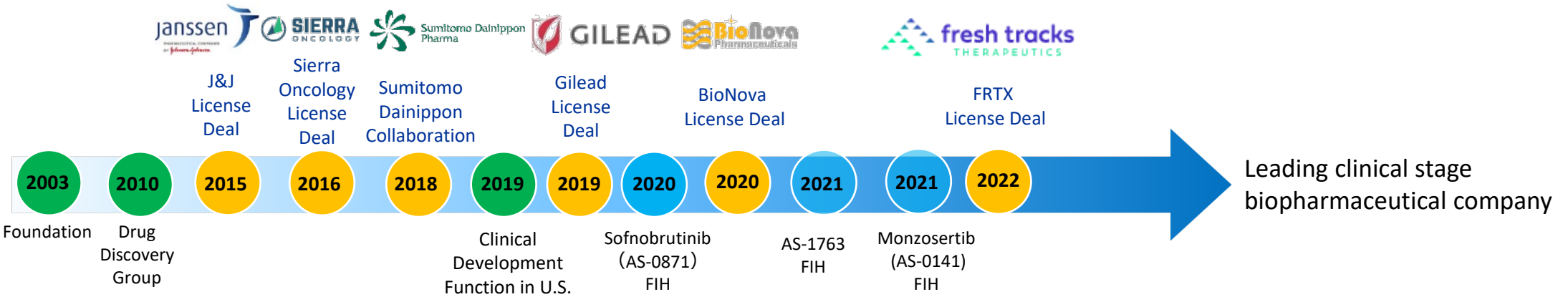
Monzosertib group A: 60 mg/kg TID, 4d ON/2d OFF
Monzosertib group B: 120 mg/kg QD

J Med Chem. 2021 Oct 14;64(19):14153-14164.

Appendix 2

Building Long-Term Value

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



2003 – 2023	2024 Plan	Long term plan
● Founding members who had expertise in kinase drug discovery technology spun out from Nippon Organon and established Carna. ● Started offering kinase proteins and screening services to pharmaceutical companies for kinase inhibitor drug discovery. ● In 2010, Drug Discovery Group was established to conduct internal drug discovery. ● Entered into five license agreements and one joint-development agreement with pharmaceutical companies. ● Initiated FIH study of BTK inhibitor AS-1763, sofnobrutinib (AS-0871) and CDC7 inhibitor monzosertib(AS-0141). ● Completed Phase 1 study of BTK inhibitor sofnobrutinib(AS-0871).	● Actively seek a strategic partner to bring sofnobrutinib into late clinical development stages. ● Advance Phase 1 studies of BTK inhibitor AS-1763 and CDC7 inhibitor monzosertib (AS-0141). ● Strengthen global clinical development capability. ● Create next wave of pipeline.	● Advance clinical studies of AS-1763 and monzosertib (AS-0141). ● Find strategic partners for late stage development and commercialization. ● Receive milestone payments and royalties from licensees and strengthen financial position. ● Create next wave of pipeline.

FIH: First in Human

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.

Norio Aikawa **Head of Drug Discovery and Support Business, Head of IP and Legal Department, Director**

Mr. Aikawa is one of the founding member of Carna Biosciences. Mr. Aikawa has a long and extensive experience in the area of intellectual property and has contributed to strengthening Carna's IP strategy. Before joining Carna in 2003, he was the head of Intellectual Property Department at Nippon Organon. Before that, he was the head of Intellectual Property Department at Kanebo Corporation.
He holds a bachelor's degree in Science from Hirosaki 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

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.

Teruo Takayanagi, Ph.D. **Outside Director**

Dr. Takayanagi joined the Board of Directors of Carna Biosciences in 2015. He was the Director of Daiichi Pharmaceutical Co., Ltd. from 2001 to 2006 where he engaged in the R&D management and led post-marketing surveillance to promote proper use of its pharmaceutical products. He also held a responsible role in business integration with Sankyo. He was a full-time Auditor of Daiichi Sankyo Company, Limited from 2007 to 2011. Dr. Takayanagi is an Auditor of Japanese Society of Drug Informatics.
Dr. Takayanagi received his Ph.D. from the University of Tokyo.

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