Financial Results
Q3 FY2022
(January to September 2022)

Carna Biosciences, Inc.

Nov. 7, 2022

Stock Code: 4572

Q3 (Jul.- Sep.) FY2022 Key Highlights

- Drug Discovery R&D
  - ✓ AS-0871: Conducting the Phase 1 Multiple Ascending Dose (MAD) study in healthy volunteers. Evaluating multiple new formulations in the Bioavailability (BA) part before moving to the MAD part.
  - ✓ AS-1763: Assessing and selecting clinical sites to conclude contracts.
  - ✓ AS-0141: Conducting the dose escalation part of the Phase 1 study in patients.
- Drug Discovery Support
  - ✓ Q3 (Jul.- Sep.) sales were JPY256 million, up 24.0% yoy, thanks to robust kinase protein sales in the U.S. and China.
  - ✓ Sales of kinase proteins in the U.S. and China increased strongly in local currency and in yen terms.
- Impact of weak yen
  - ✓ Weak yen boosts U.S. and EU sales in yen terms.
  - ✓ Weak yen normally puts upward pressure on the cost of clinical trials as the most of the payment to third party contractors are in US dollar or Euro. However, the impact of weak yen on FY2022 earnings is expected to be limited thanks to the measures to mitigate the impact of currency fluctuations.

<JPY/USD>

2021 Actual	2022 Forecast	2022Q3 Actual
109.9	110	128.3

Q3 FY2022 Consolidated Financial Results

(JPY million)	Q3 FY2021 Actual	**Q3 FY2022 Actual**	YoY Change	FY2022 Plan as of May 10	
Sales	636	**1,095**	+459 +72.1%	1,186	- Sales at ddSP were strong in the U.S. and China. - Received an upfront payment from FRTX (Brickell) and a milestone payment from BioNova.
Operating Profit/Loss	(1,169)	**(753)**	+415	(1,672)	- Gross profit increased thanks to the upbeat sales at ddSP and sales recorded at ddRD.
Ordinary Profit/Loss	(1,171)	**(735)**	+436	(1,685)	
Net Profit/ Loss	(1,178)	**(795)**	+382	(1,740)	- Impairment loss of JPY43 million was recognized for lab equipment.
R&D Cost	1,310	**1,267**	-42 -3.3%	2,166	- Plan to invest in R&D as initially planned.

Note 1: Rounded down to the nearest million yen.
Note 2: Brickell Biotech was renamed to Fresh Tracks Therapeutics (FRTX).

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

Q3 FY2022 Results by Business Segment

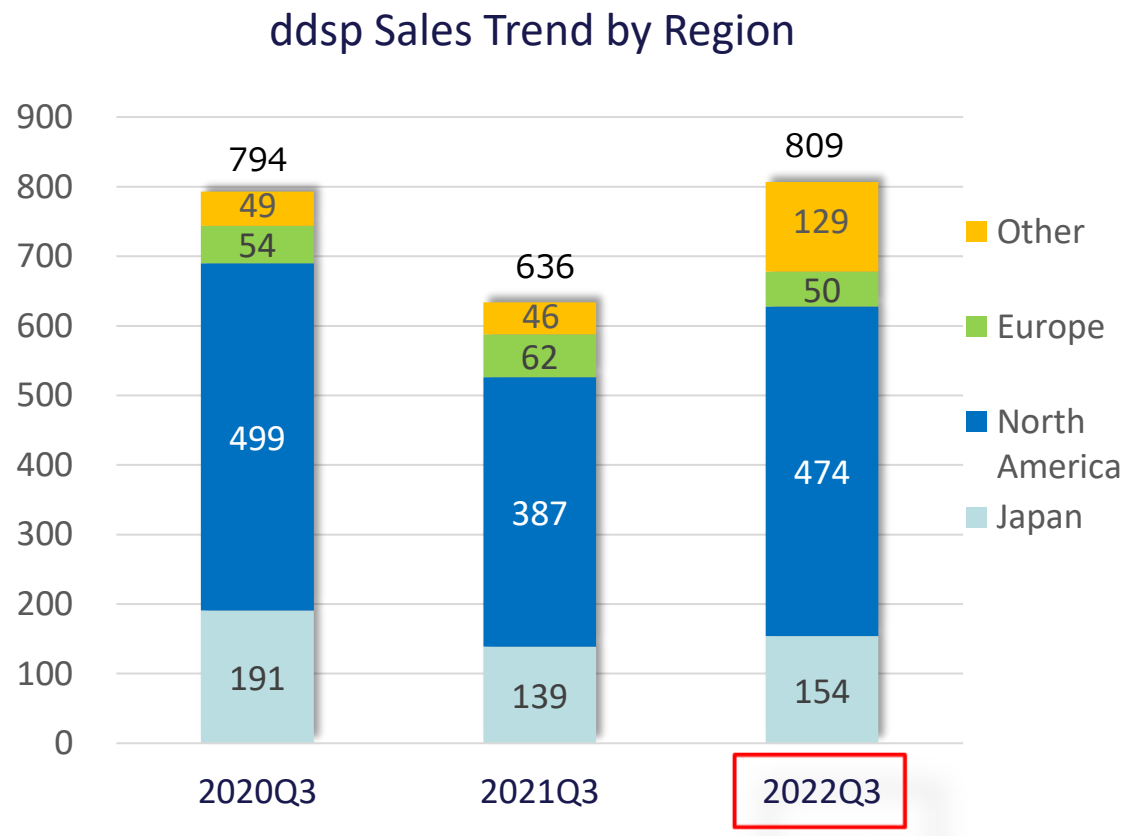
(JPY million)	Q3 FY2021 Actual	**Q3 FY2022 Actual**	YoY Change	FY2022 Plan as of May 10	Q3 FY2022/ FY2022 plan	
Total Sales	636	**1,095**	+459 +72.1%	1,186	92.4%	
ddSP business	636	**809**	+173 +27.2%	900	89.9%	- Sales of kinase proteins were strong in the U.S. and China.
ddRD business	—	**286**	+286	286	100%	- Received an upfront payment from FRTX in Q1. - Received a milestone payment from BioNova in Q1.
Total Operating Profit/Loss	(1,169)	(753)	+415	(1,672)	—	
ddSP business	199	**335**	+136 +68.4%	300	111.6%	- Gross profit increased as a result of an increase in sales.
ddRD business	(1,368)	(1,089)	+279	(1,972)	—	- Operating loss was smaller than the previous year thanks to an upfront payment and a milestone payment.

Note 1: Rounded down to the nearest million yen.
Note 2: Brickell Biotech was renamed to Fresh Tracks Therapeutics (FRTX).

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

Q3 FY2022 Discovery Support (ddSP) Business Sales by Region

(JPY million)



- Japan: Increased 10.7% YoY
  Sales increased 10.7% yoy thanks to robust sales of kinase proteins, cell-based assay service and crystallography while profiling service sales were weak.
- North America: Increased 22.4% YoY
  Sales of kinase proteins were strong.
- Europe: Decreased 18.1% YoY
  Sales declined as both kinase proteins and profiling service were weak.
- Other: Increased 176.3% YoY
  Sales of kinase proteins were strong in China.
  Profiling service increased as well.

Consolidated Balance Sheet

(JPY million)	As of Dec. 31, 2021	As of Sep. 30, 2022	Change	Reason for changes
Current assets	5,318	4,367	-951	Accounts receivable-trade -1,135 Cash and deposits -90
Cash and deposits	3,817	3,727	-90	
Non-current Assets	114	180	+66	
Total assets	5,432	4,547	-884	
Current liabilities	774	370	-404	Accounts payable -127
Non-current liabilities	342	234	-108	Long term loans payable -89 Bonds payable -32
Total liabilities	1,116	604	-512	
Total net assets	4,315	3,943	-372	Capital stock and capital surplus +348, Retained earnings -795
Total liabilities and net assets	5,432	4,547	-884	

Shareholders' equity ratio	79.3%	86.5%
BPS	323.5 yen	288.1 yen
PBR	3.4 x	3.0 x
Share price of Carna	1,102 yen	855 yen

Note: Share price is the closing price of the term end.

Robust Drug Pipeline

<Oncology>

Compound	Target	Indication	Discovery/Preclinical	Clinical	Partner
AS-0141	CDC7/ASK	Cancer			
Small Molecule	DGKα	Immuno-Oncology	Licensed to Gilead		GILEAD
AS-1763	BTK	Blood Cancer			BioNova Pharmaceuticals *
Small Molecule	ALK5	Immuno-Oncology			
Small Molecule	CDK1	Cancer			

*Greater China only

<Other Therapeutic Areas>

Compound	Target	Indication	Discovery/Preclinical	Clinical	Partner
Small Molecule	Kinase	Psychiatry & neurology	Joint research with Sumitomo Pharma		Sumitomo Pharma
AS-0871	BTK	Immune-inflammatory diseases			
Small Molecule	N/A	Malaria			
Small Molecule	STING (antagonist)	Immune-inflammatory diseases	Licensed to Fresh Tracks Therapeutics (Rebranded from Brickell Biotech)		fresh tracks THERAPEUTICS

✓ As of November 2022

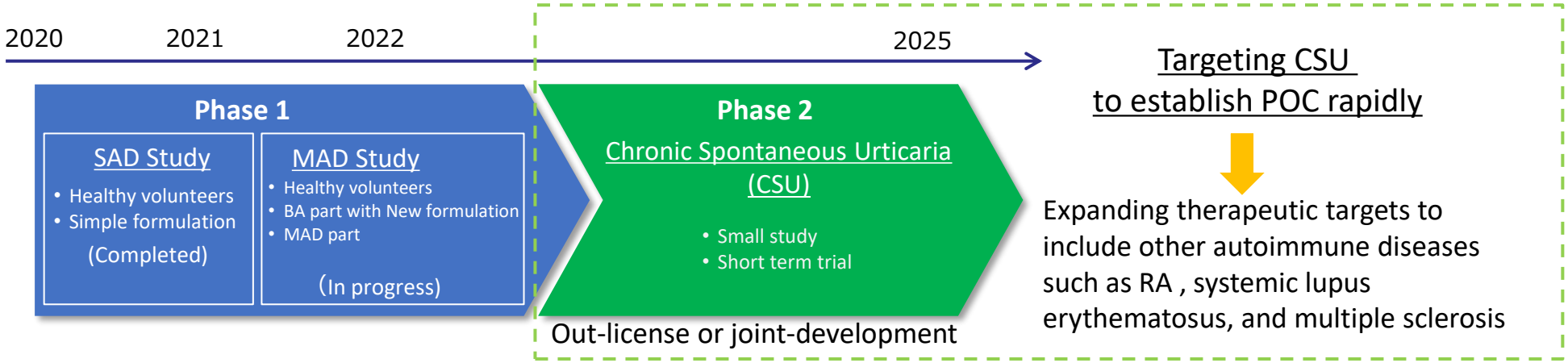
✓ We are actively pursuing early discovery programs to create next wave of pipeline.

AS-0871: Non-covalent BTK Inhibitor Targeting Immune-inflammatory diseases

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
- Find a partner to conduct further development after completing Phase 1 study



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

AS-0871: Phase 1 Clinical Trial in Progress

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

Developing multiple new formulations

Phase 1 in the Netherlands MAD study (Healthy volunteers)

Ongoing

BA part	Evaluate the relative bioavailability of multiple new formulations to select the best formulation
MAD part	Evaluate the safety, tolerability, PK and PD in the 2-week multiple ascending dose of AS-0871

*The protocol has been amended to skip the SPT (Skin Prick test) part based on the recent clinical outcomes of competing BTK inhibitor drug candidates, which enable us to predict the efficacy from the PD effects.

AS-0871: Excellent Kinase Selectivity

◆ Targeting Inactive Conformation of BTK


Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry Letters

journal homepage: www.elsevier.com/locate/bmcl

TR-FRET binding assay targeting unactivated form of Bruton's tyrosine kinase

Tokiko Asami *, Wataru Kawahata, Masaaki Sawa

Carna Biosciences, Inc., BMA 3F, 1-5-5 Minatojima-Minamimachi, Chuo-ku, Kobe 650-0047, Japan

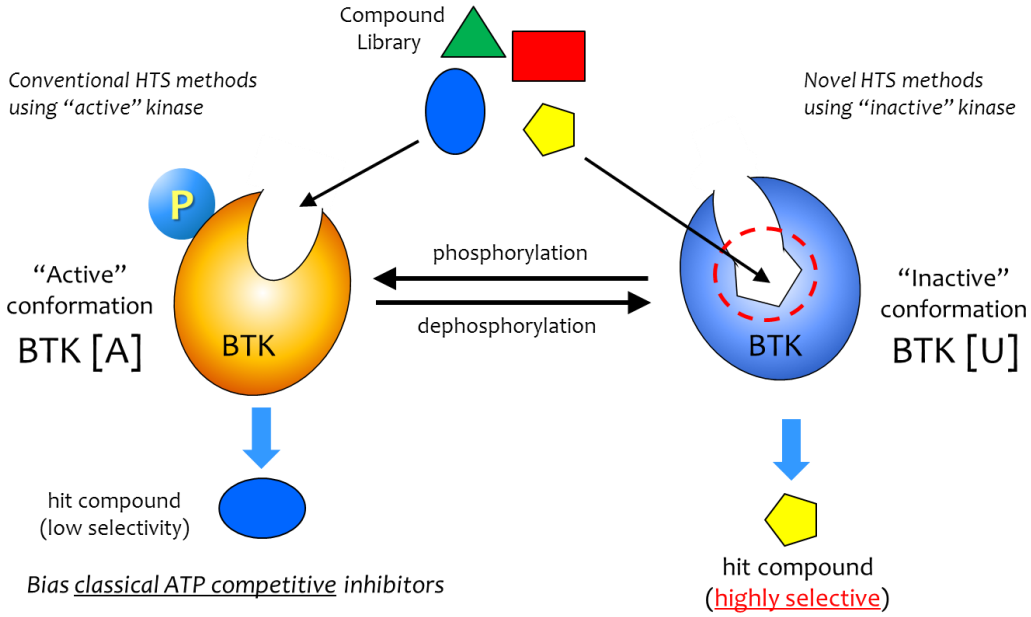

Journal of Medicinal Chemistry

Article

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

Research and Development, Carna Biosciences, Inc., 3rd Floor, BMA, 1-5-5 Minatojima-Minamimachi, Chuo-ku, Kobe 650-0047, Japan

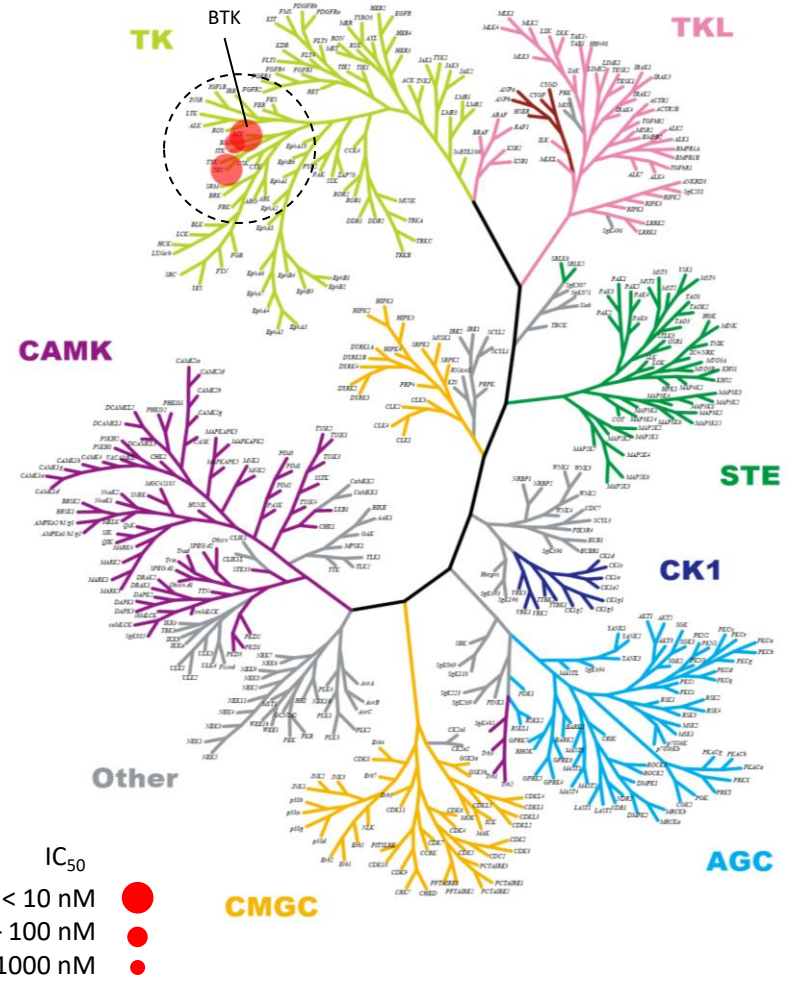


Bias classical ATP competitive inhibitors

	BTK IC_{50} (nM)	
	BTK [A]	BTK [U]
AS-0871	3.4	0.3

◆ Kinase Selectivity Profiling

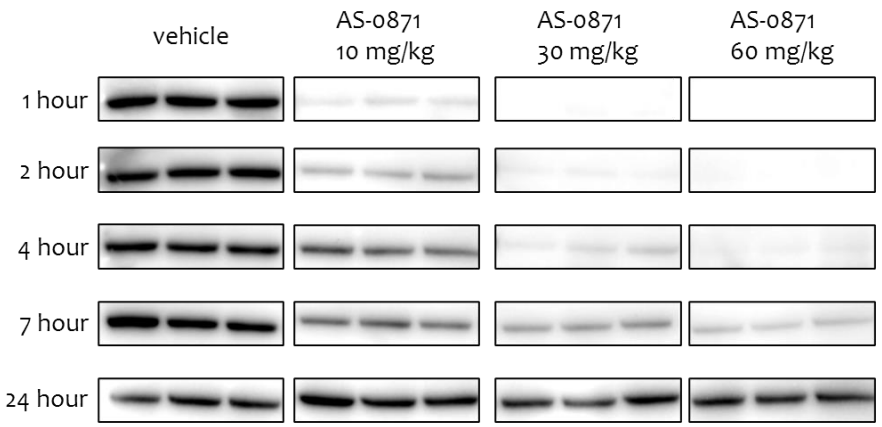
Only inhibited 2 other kinases in a total of 312 kinases tested at 0.3 μM concentration.

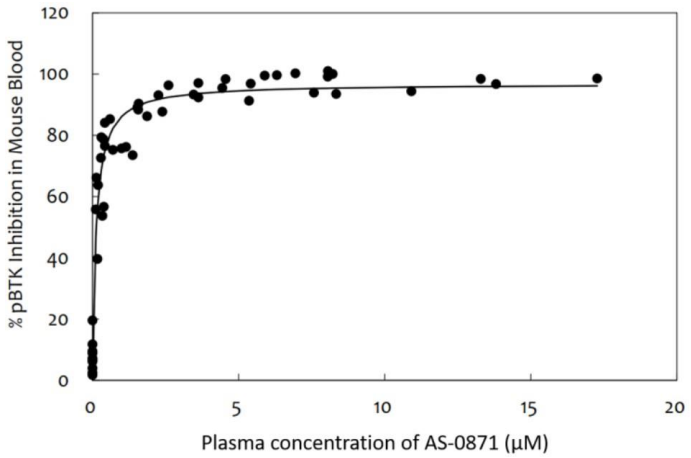


AS-0871: In Vivo Therapeutic Efficacy

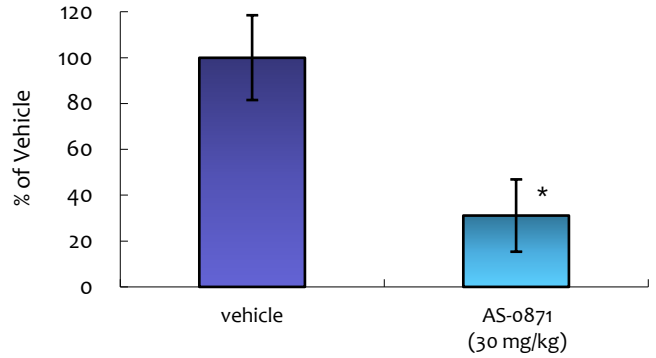
- PK/PD Study

Auto-phosphorylation status of BTK was measured following oral single administration of AS-0871

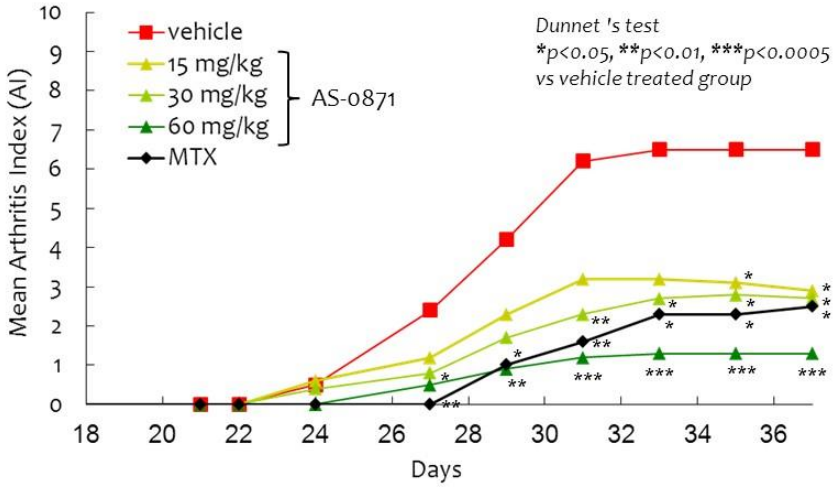




- Passive cutaneous anaphylaxis (PCA) mouse model (n=5)



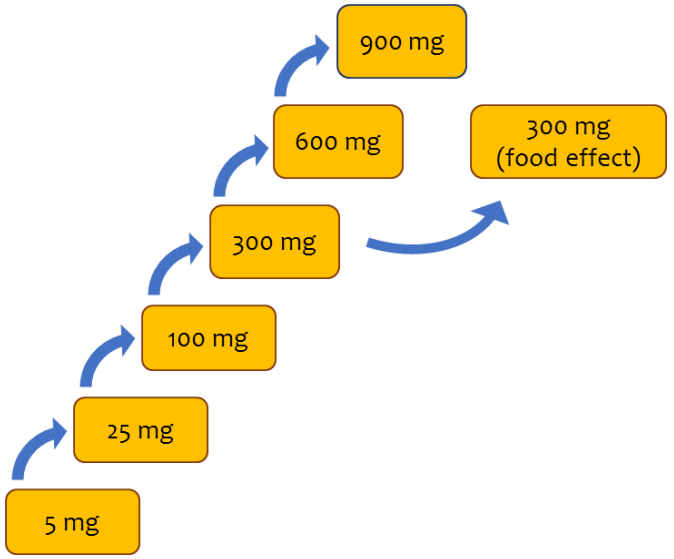
- Collagen-induced arthritis (CIA) mouse model (n=10)



AS-0871: FIH study

SAD Part (Completed)

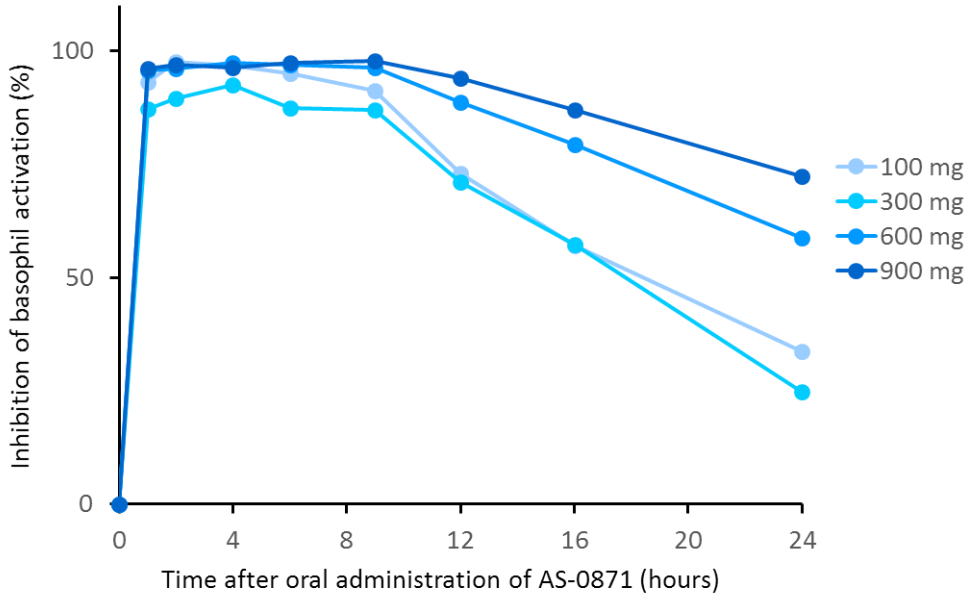
Step 1	Step 2
• 6 dose levels (8 subjects/cohort) • Placebo controlled (6 active / 2 placebo) • Safety and tolerability • Pharmacokinetics and pharmacodynamics	• Food effect

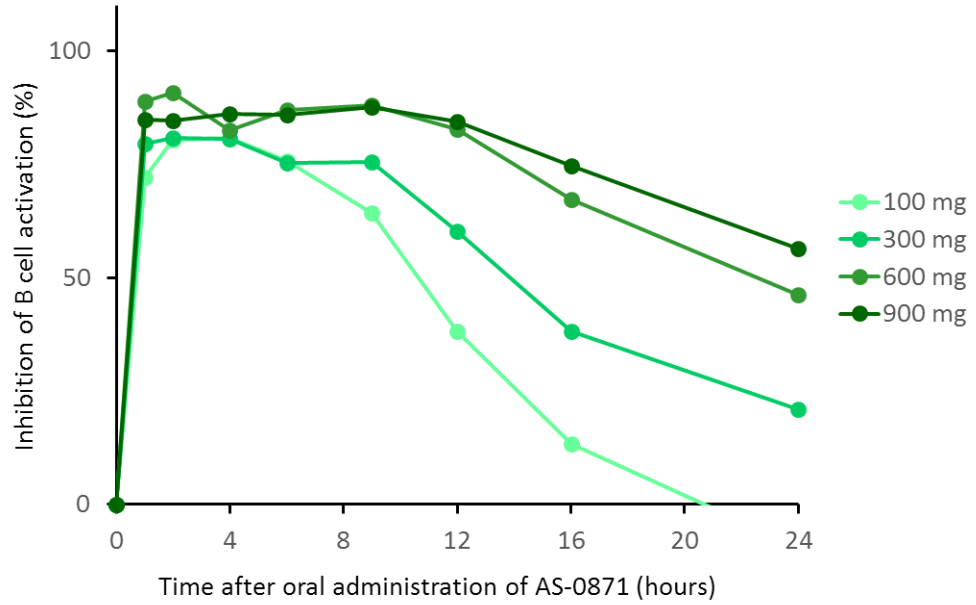


- ✓ AS-0871 is well-tolerated without any safety concerns.
- ✓ Favorable pharmacokinetic profile.
- ✓ Blood samples to assess PD effects were analyzed for evaluation of the B-cell and basophil responses. Administration of AS-0871 at 100mg or above resulted in strong inhibition of B-cell and basophil activation.
- ✓ Switching to a new formulation in the MAD study.

Pharmacodynamics of AS-0871

- ✓ Pharmacodynamic study demonstrated that subjects who received AS-0871 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 AS-0871 achieved therapeutic plasma levels needed to inhibit B cells and basophils activation, suggesting that AS-0871 has a potential to become a new treatment option for inflammatory diseases.



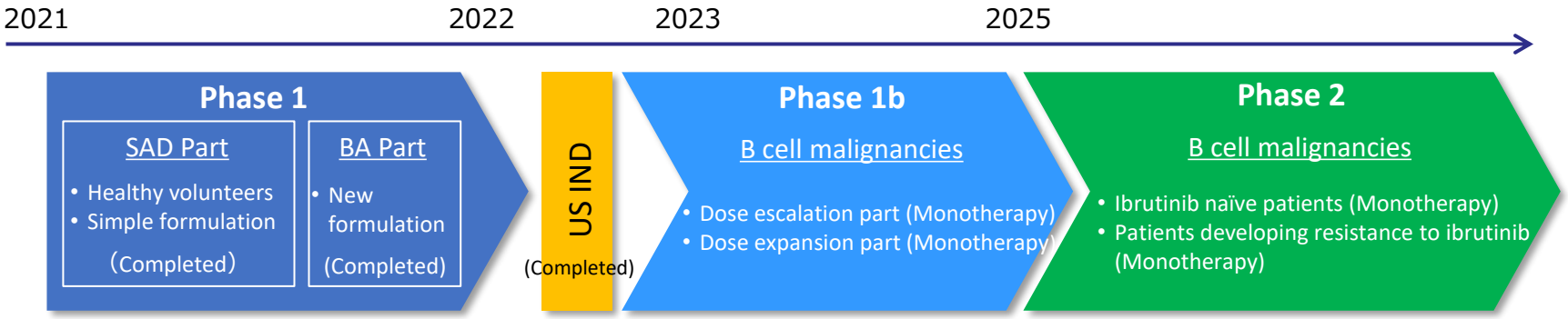


AS-1763: Next Generation BTK Inhibitor Targeting Blood Cancer

AS-1763：Targeting Blood Cancer

- Small molecule BTK inhibitor
- Non-covalent/reversible
- High kinase selectivity
- Inhibits both BTK wild type and ibrutinib resistant BTK C481S mutants
- Orally available

- Displayed strong anti-tumor effects in lymphoma model with both wild type and C481S mutant BTK
- Displayed efficacy in immuno-oncology model
- Completed an IND application process in the U.S.
- Plan to accelerate the clinical studies utilizing the clinical data of BioNova, the licensee in Greater China



IND application: Investigational New Drug application
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.

AS-1763: Phase 1 Clinical Trial in Progress

Phase 1 in the Netherlands (Healthy volunteers)

Completed

SAD part Evaluate the safety, tolerability and PK using simple formulation

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

BA part Evaluate comparative bioavailability using new formulation

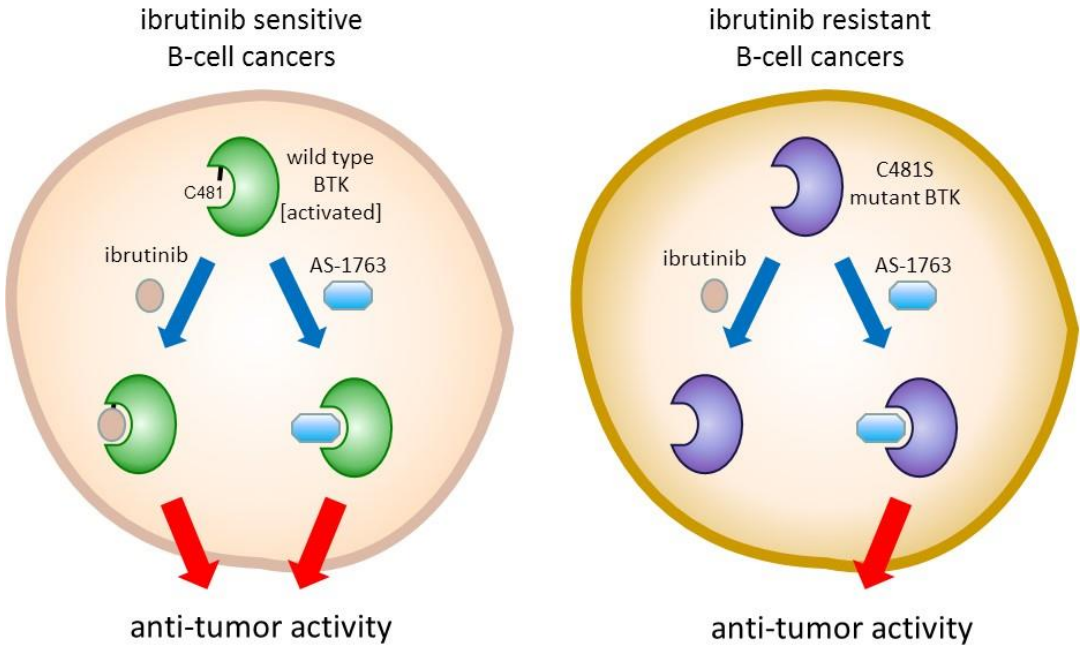
- ✓ Pre-IND meeting
- ✓ IND submission

Completed

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

- In May, Carna received an approval for an IND to initiate Phase 1 study in the U.S.
- Site selection of the clinical trial is ongoing to identify the best performing sites, maximizing the chance of success.

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

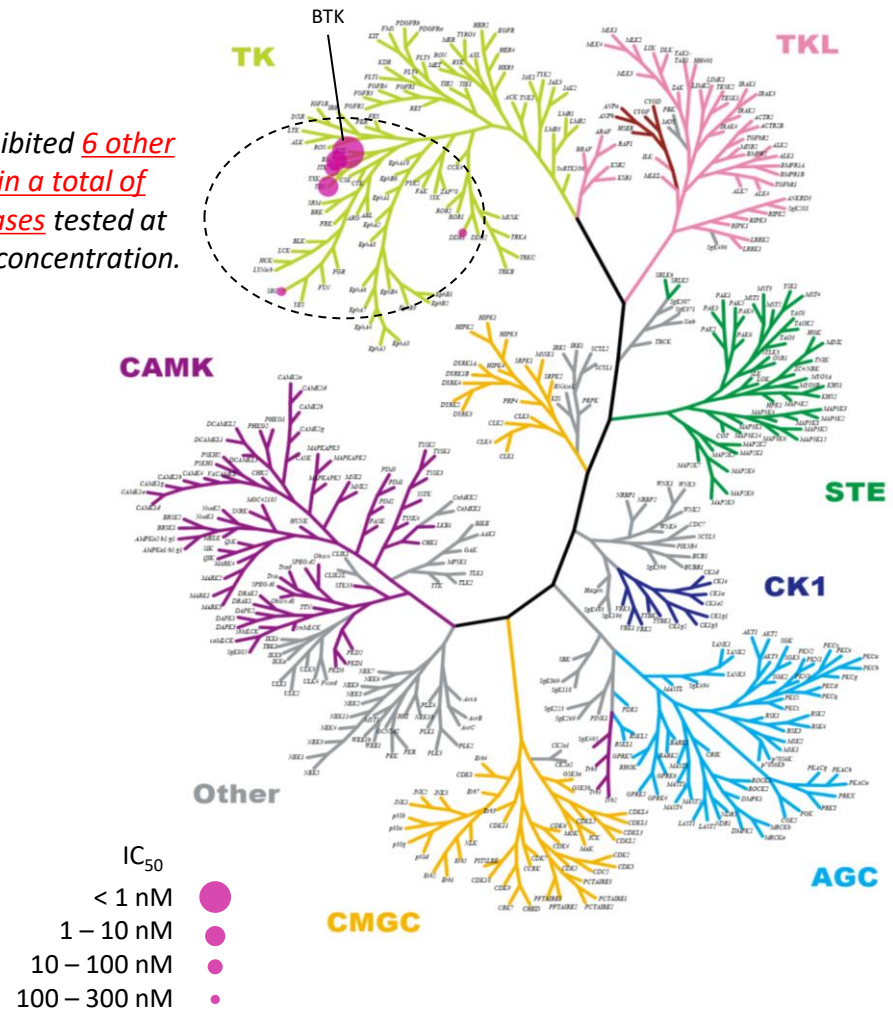
50-fold Stronger activity

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.

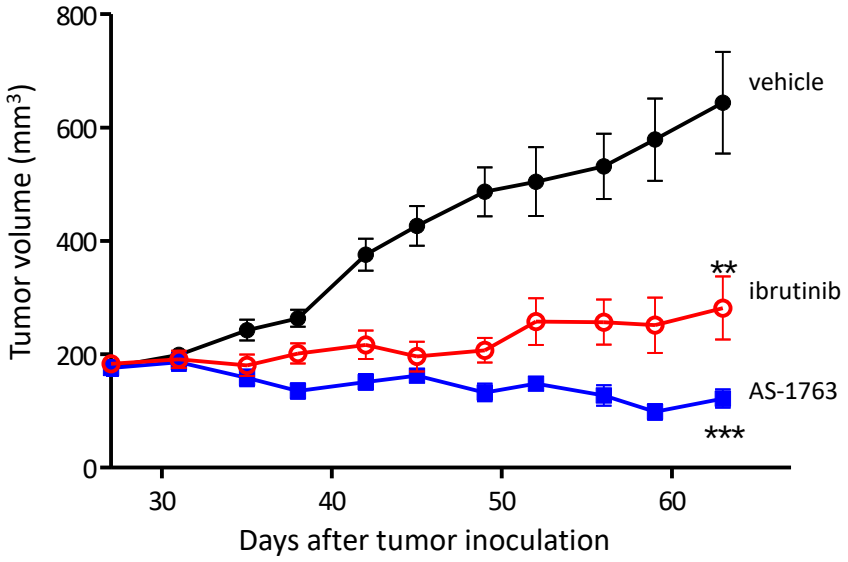
◆ Kinase selectivity profiling

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

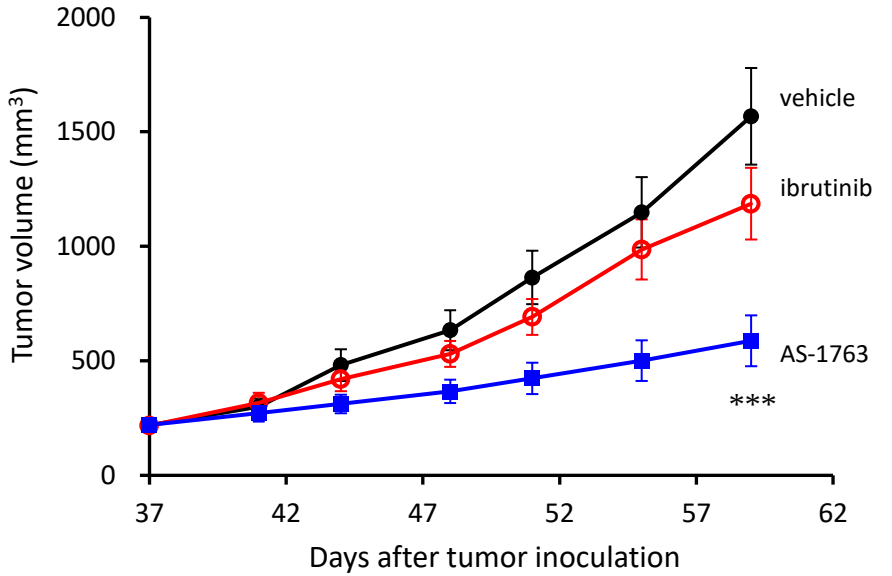
- In vivo antitumor effects of AS-1763 on human B-cell non-Hodgkin lymphoma cell line, OCI-LY10 tumor xenograft mouse model (n=8-10)



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 BTK^{C481S} knock-in OCI-LY10 tumor xenograft mouse model (n=11)



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

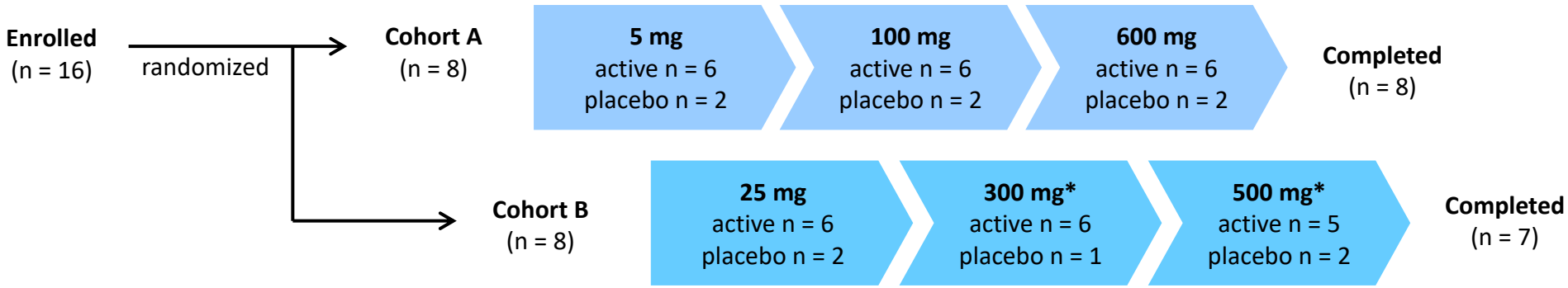
***: p<0.001

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

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

Study Design

Step 1 SAD Part	Step 2 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

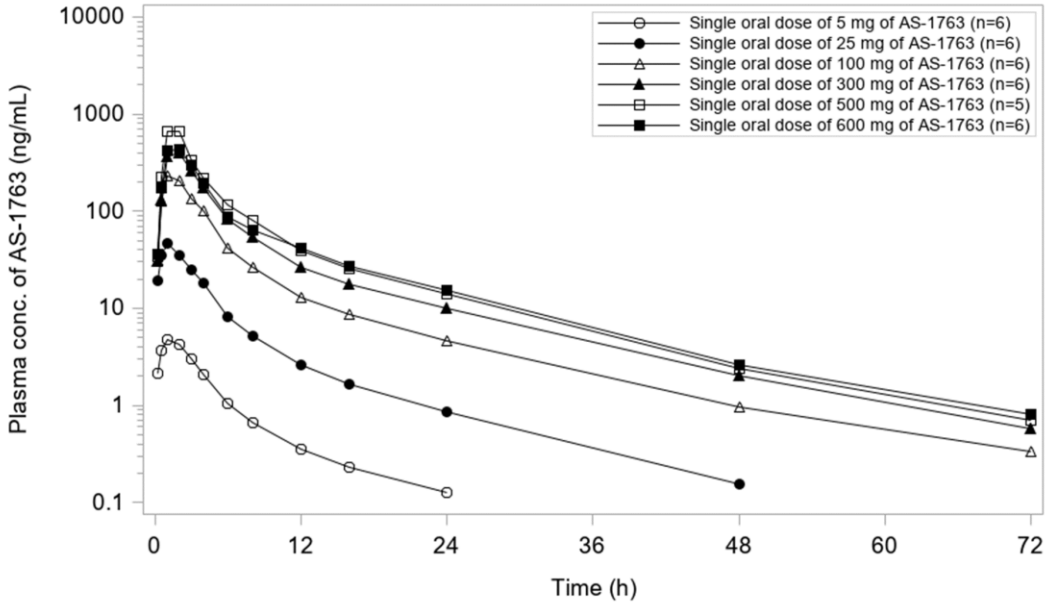
<Safety and tolerability>

- 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 t_{max} between 0.5 and 1.5 hours; mean $t_{1/2}$ between 8.4 and 12.1 hours).
- Mean AS-1763 exposures generally increased with dose up to 500 mg.

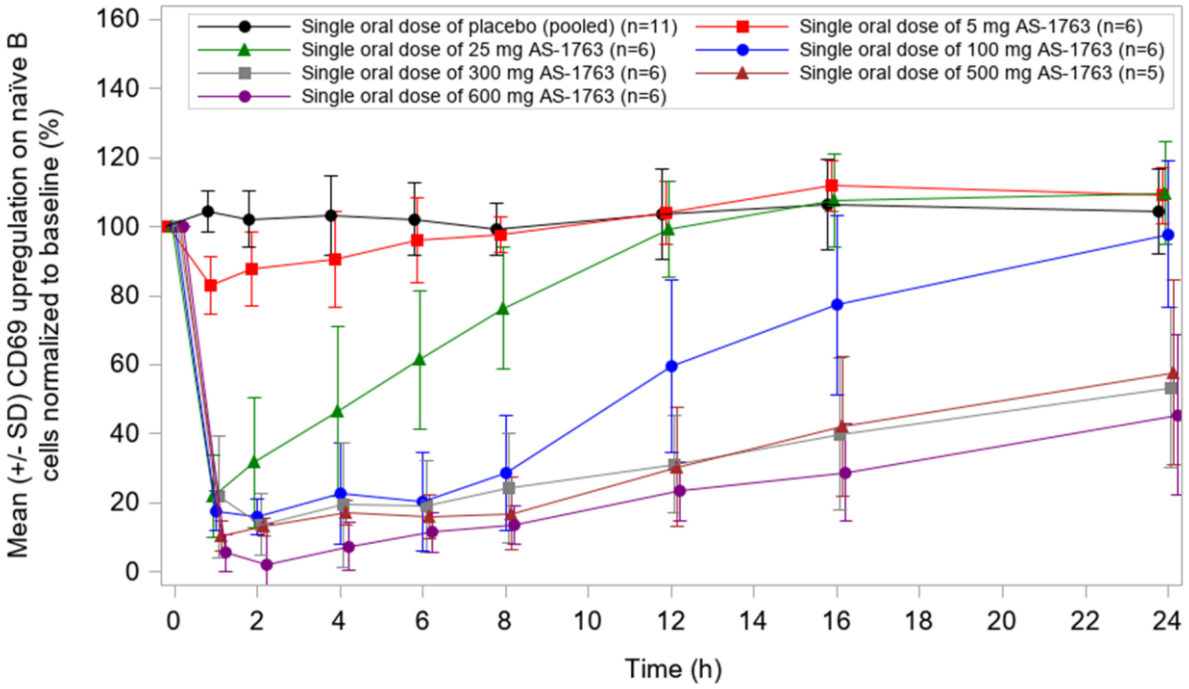
<Plasma concentration of a Single oral dose AS-1763>



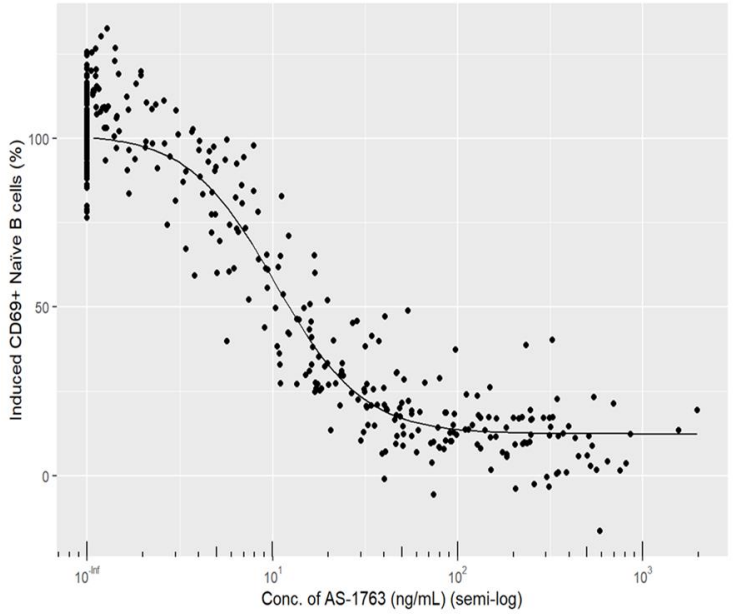
Pharmacodynamics of AS-1763

- 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 AS-1763>



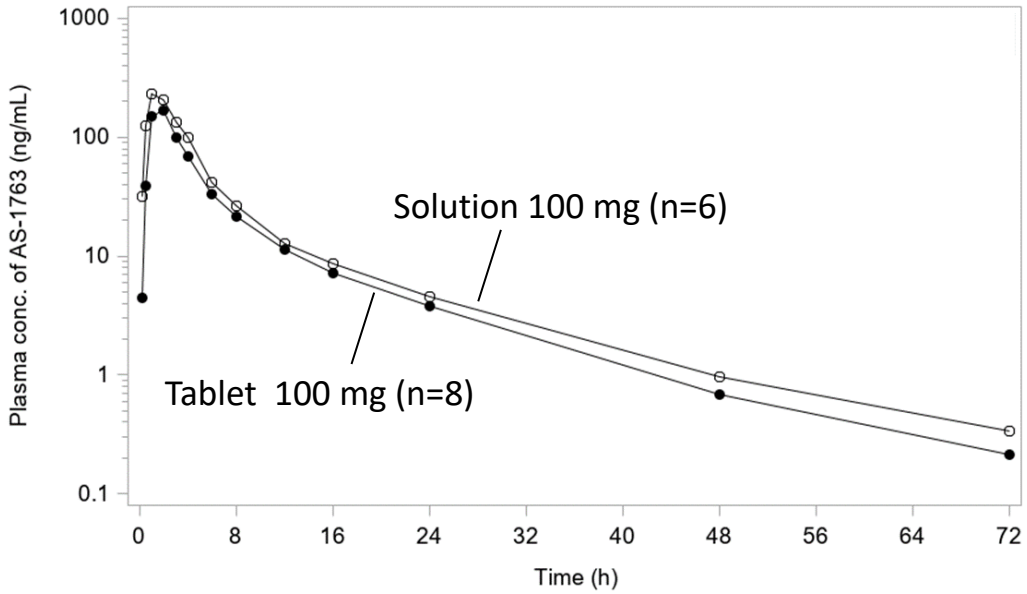
<PK/PD Correlation Analysis>



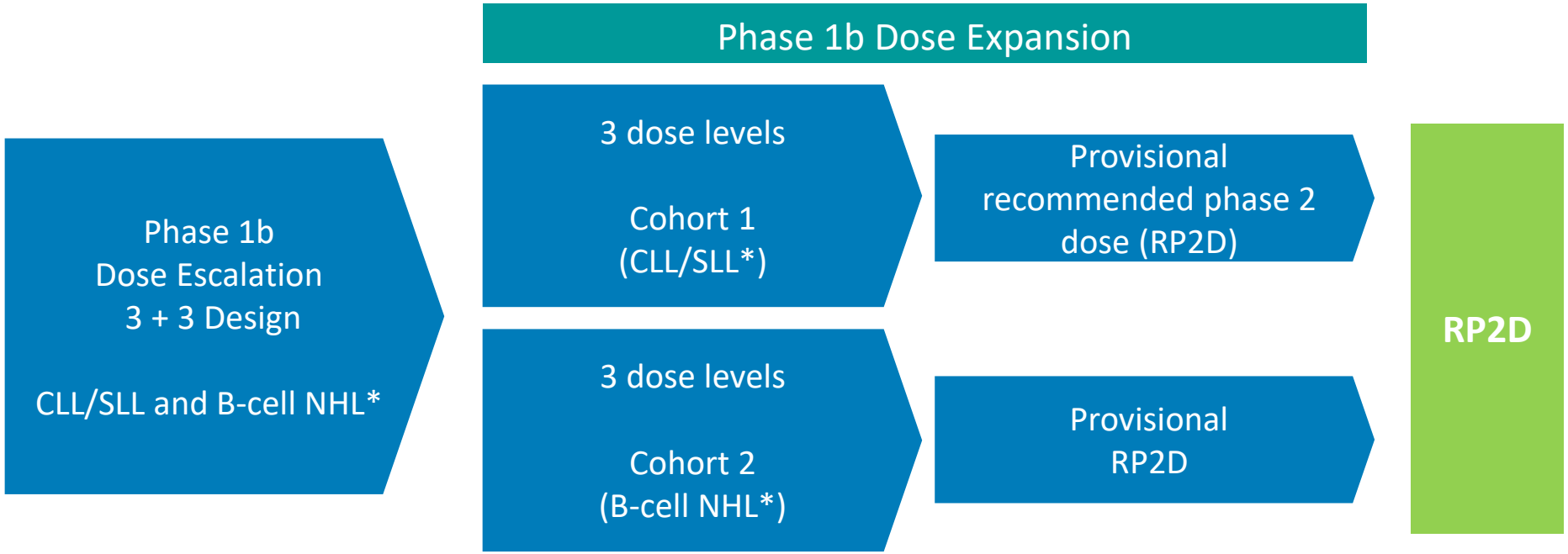
AS-1763: BA Part

- In the BA part, 100 mg tablet and the solution showed almost the 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)

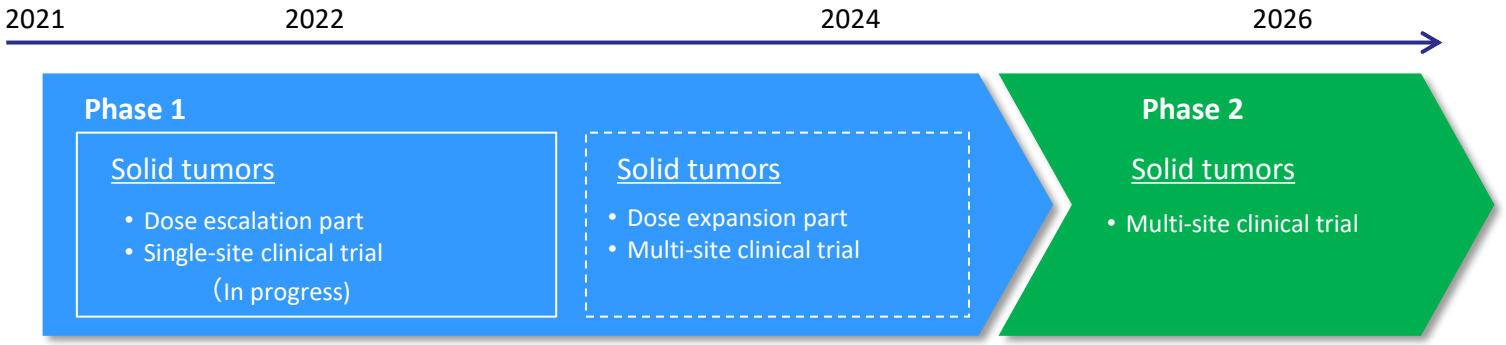


*Previously treated patients

- In process of making contracts with clinical sties.
- Initiating the patient recruitment upon the approval by the ethic committees of the clinical sites. The first patient is expected to be dosed with AS-1763 by Q1 2023.

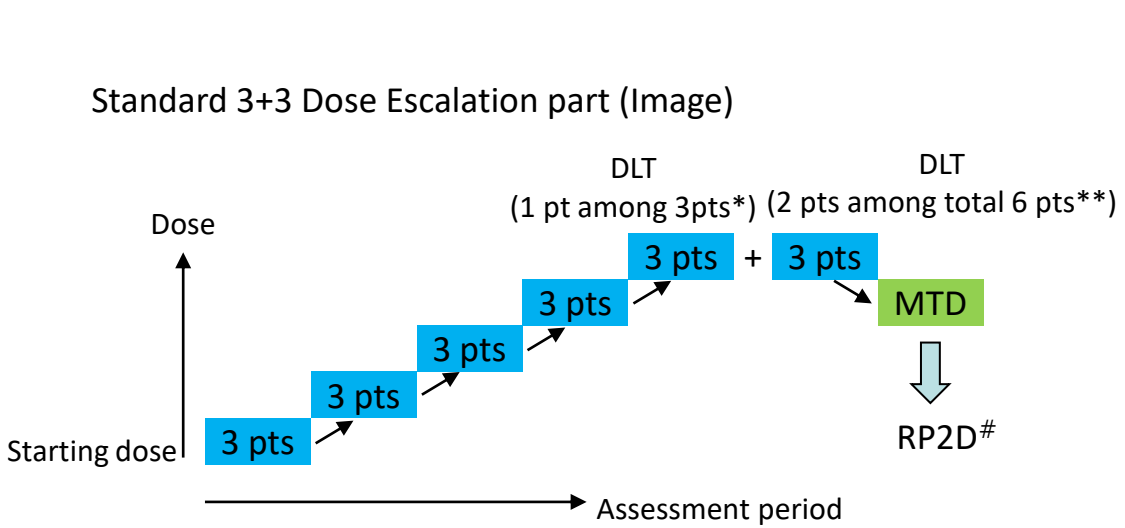
AS-0141: CDC7 Inhibitor

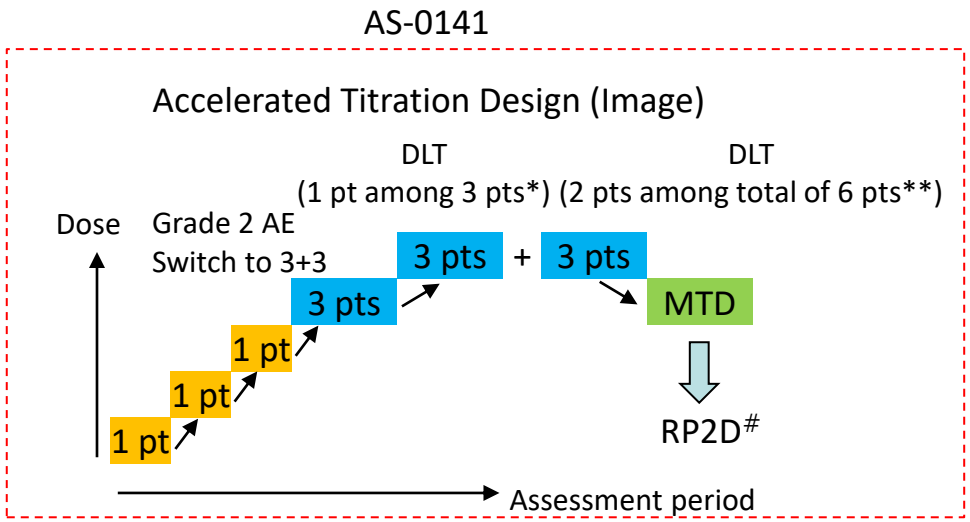
AS-0141：Targeting Cancer	
● Small molecule CDC7 inhibitor ● High kinase selectivity ● Potential First-in-class drug ● Orally available	● Potent anti-proliferative activity against various cancer cell lines ● Demonstrated strong anti-tumor activity in several human tumor xenograft models ● Conducting Phase 1 study in Japan targeting solid tumors



AS-0141: Phase 1 Clinical Trial

- Phase 1 study targeting cancer patients
  - ✓ The Phase 1 study in patients with unresectable, advanced, recurrent, or metastatic solid tumors was initiated in Japan in H1 2021.
  - ✓ 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.
  - ✓ The dose escalation part employs accelerated titration design.
    - One patient is treated per cohort unless a Grade ≥ 2 AE occurs during dose limiting toxicity (DLT) assessment period.
    - Switch to 3+3 dose escalation design when any Grade ≥ 2 AEs are observed during DLT assessment period.





* No more patients will be added to this cohort if 2 pts among 3 pts experience DLT.
** If only 1 pt experiences a DLT among 6 pts, 3+3 design will be continued with higher dose levels.
# Recommended dose level will be determined at MTD or lower dose level.

pt/pts: patient(s)

AS-0141: Phase 1 Clinical Trial in Progress

- ✓ Favorable pharmacokinetic profile at dosage of 20 mg BID to 300 mg BID.
- ✓ The study was switched to 3+3 design as one Grade 2 AE was observed in Cohort 6 (300 mg BID).
- ✓ After switching to 3+3 design, 2 patients among 3 patients experienced dose-limiting toxicities (DLTs). The MTD is considered at the dose lower than 300 mg BID as 2/3 patients experienced DLTs.
- ✓ Additional patients will be enrolled at lower dose levels to determine MTD and recommended dose level.

- Ongoing Phase 1 Dose escalation part

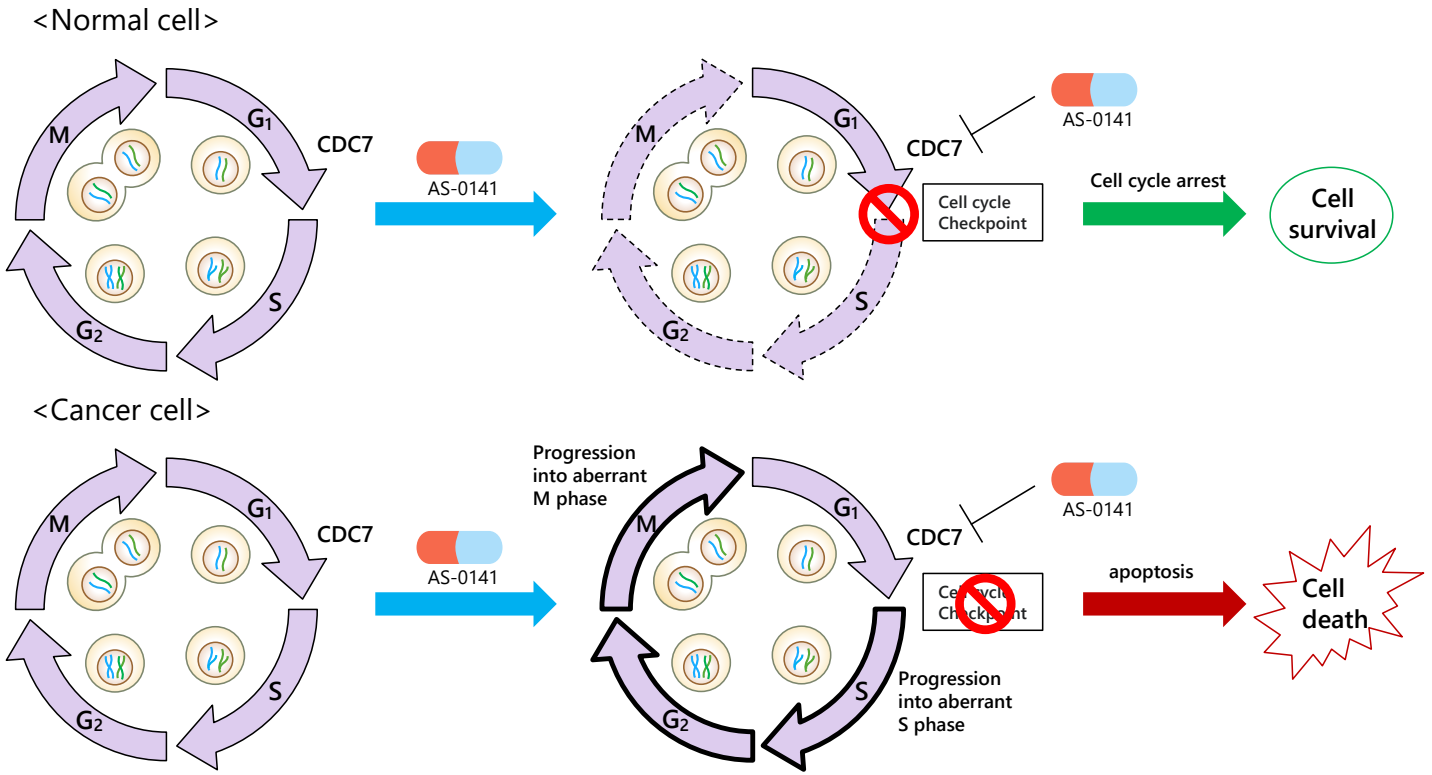
Cohort	Dose level (5d on/2d off)		Status
1	20 mg BID	N=1	No G2 AE/No DLT
2	40 mg BID	N=1	No G2 AE/No DLT
3	80 mg BID	N=1	No G2 AE/No DLT
4	150 mg BID	N=1	No G2 AE/No DLT
5	250 mg BID	N=1	No G2 AE/No DLT
6	300 mg BID (switched to 3+3 design)	N=3	DLT（2/3 pts）
	< 300 mg BID (3+3 design)		

*BID: Twice a day, 5d on/2d off: 5 days medication followed by 2 days drug holiday

AS-0141: Highly Selective CDC7 Inhibitor

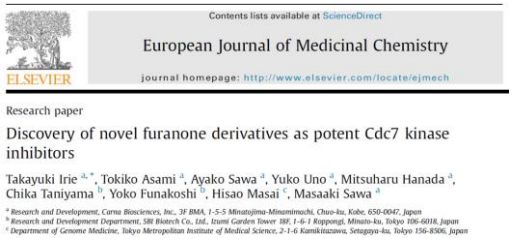
■ CDC7 kinase inhibitor

CDC7 (cell division cycle 7) is a serine-threonine kinase that plays a critical role in DNA synthesis and is required for the activation of DNA replication origins throughout the S phase of the cell cycle. Inhibition of CDC7 in cancer cells causes lethal S phase or M phase progression, whereas normal cells survive, most likely through induction of cell cycle arrest at the DNA replication checkpoint. It has been reported in the literature that CDC7 is overexpressed in many cancers. Therefore, CDC7 is an attractive target for cancer drug development.



AS-0141: Time-Dependent Inhibitor of CDC7

- AS-0141 has a unique inhibitory mechanism for CDC7 kinase (time-dependent inhibition)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Research paper

Discovery of novel furanone derivatives as potent Cdc7 kinase inhibitors

Takayuki Irie [a, *], Tokiko Asami [a], Ayako Sawa [a], Yuko Uno [a], Mitsuharu Hanada [a], Chika Taniyama [b], Yoko Funakoshi [b], Hisao Masai [c], Masaaki Sawa [a]


Journal of Medicinal Chemistry

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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

Cite This: J. Med. Chem. 2021, 64, 14153−14164

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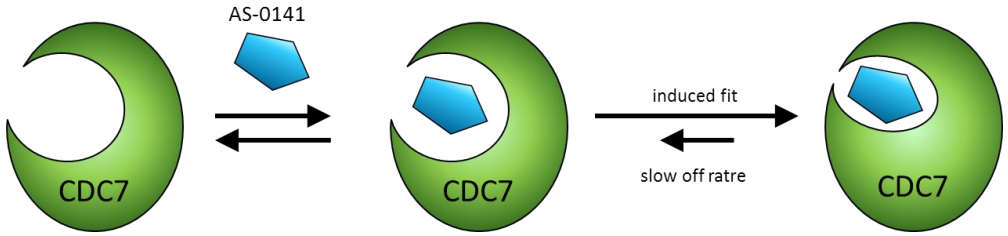


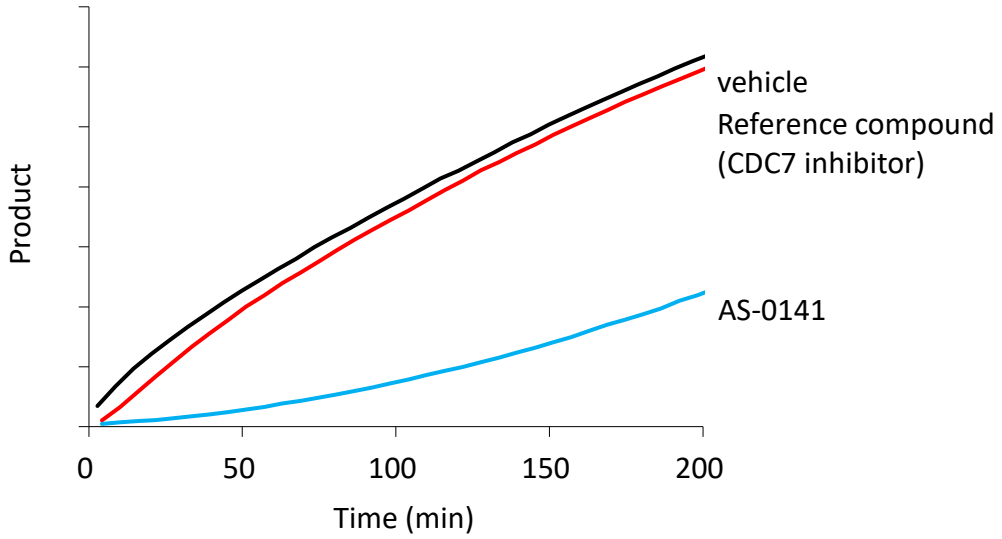
Inhibitory potency (IC_{50}) for CDC7 in the presence of 1 mM ATP

Without Preincubation	With Preincubation
503 nM	2.4 nM

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

- AS-0141 inhibits CDC7 in a reversible fashion but has a very slow off-rate

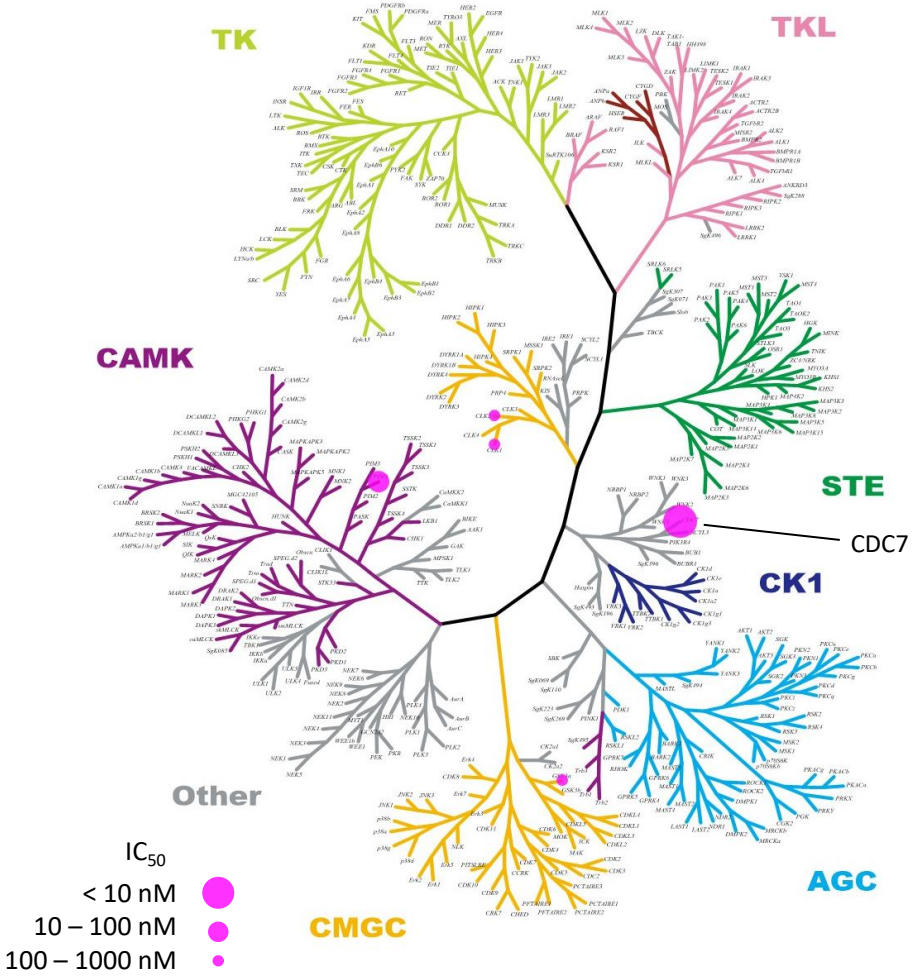
Rapid dilution assay for Cdc7 inhibitors. Recovery of enzymatic activity was monitored by formation of the phosphorylated product.



AS-0141: High Kinase Selectivity

◆ Kinase Selectivity Profiling

In the presence of 1 mM ATP with preincubation



◆ IC_{50} values of hit kinases （at 1 mM ATP）

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

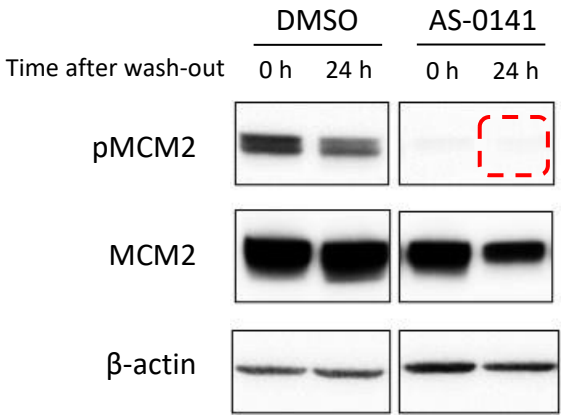
CDC7 is the only kinase that shows preincubation effect

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

AS-0141: Strong Cellular Activity

◆ Prolonged inhibition in cells

Human colon cancer cell line, Colo-205 cells were treated with DMSO control or AS-0141. 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 AS-014 on the phosphorylation of MCM2 in cells continued up to 24 h after washing out

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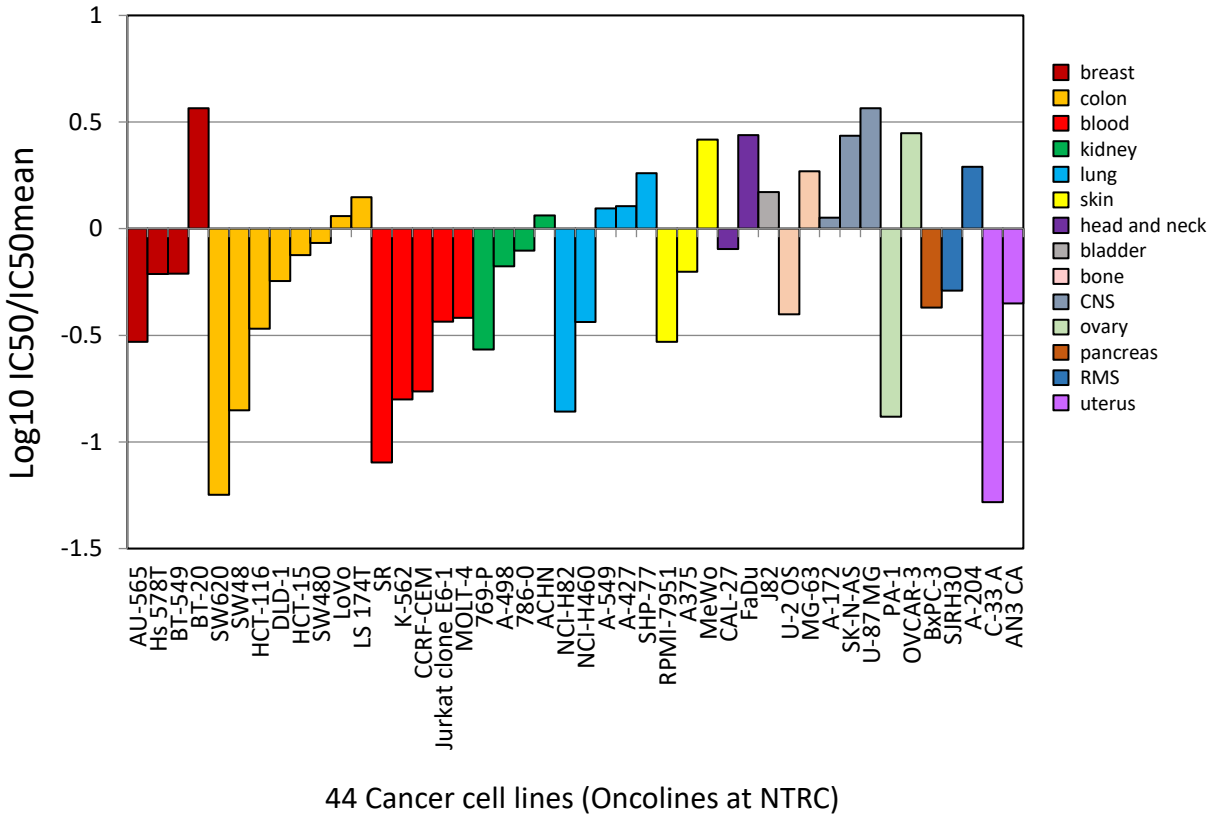
◆ AS-0141 potently inhibited growth in a wide range of tumor cell lines, including solid and hematological tumors

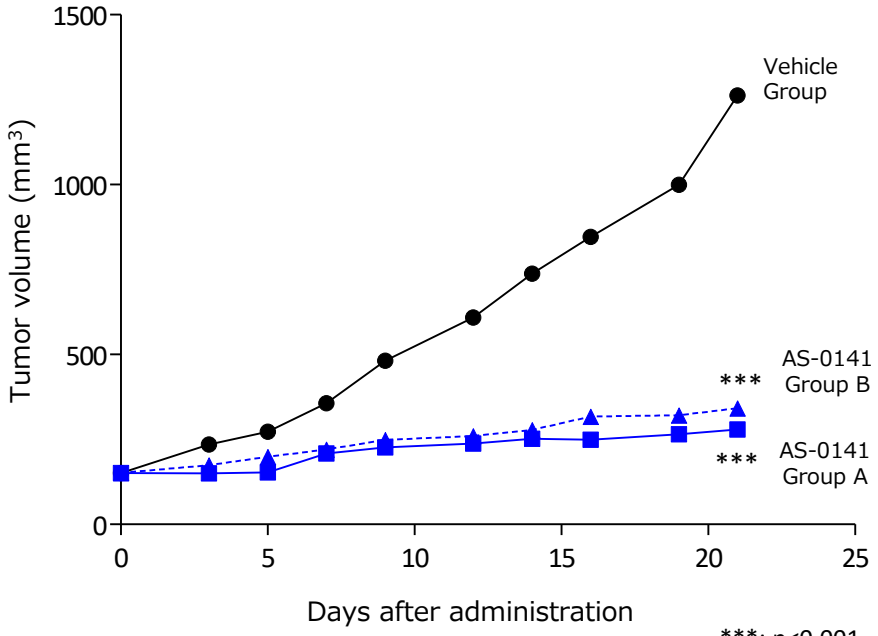


44 Cancer cell lines (Oncolines at NTRC)

AS-0141: Robust In Vivo Antitumor Efficacy

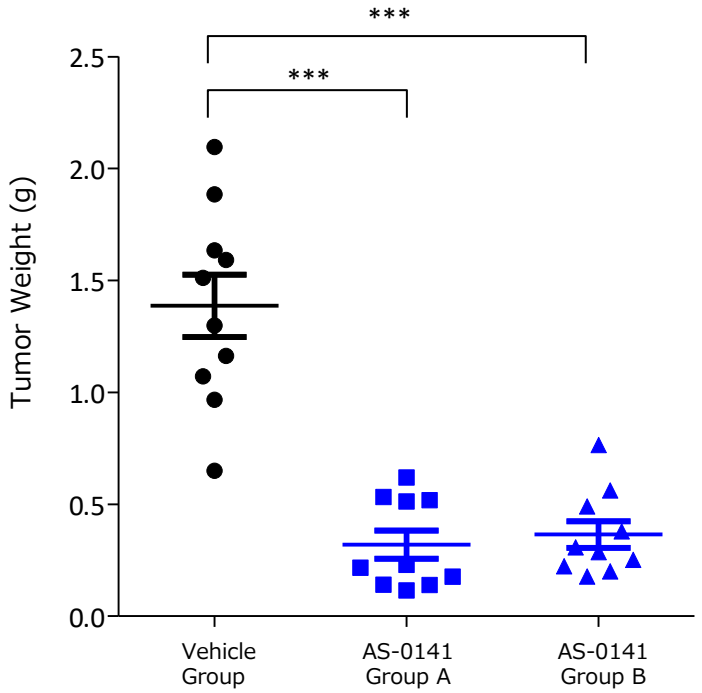
- In vivo antitumor efficacy of AS-0141 in a SW620 (human colon cancer) xenograft mouse model

Tumor Growth Curve (Mean, n = 10)



***: p<0.001

Final Tumor Weight of Each Mouse



***: p<0.001

AS-0141 group A: 60 mg/kg TID, 4d ON/2d OFF
AS-0141 group B: 120 mg/kg QD

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Drug Discovery R&D: Pursuing Sustained Growth

Robust Drug Pipeline

Cancer

- **AS-1763**
- **AS-0141**
- **GS-9911** — GILEAD
- **BN102** (AS-1763 Greater China) — BioNova Pharmaceuticals

Immune-inflammatory diseases

- **AS-0871**
- **FRTX-10** — fresh tracks THERAPEUTICS
- **Joint Research** — Sumitomo Dainippon Pharma
- **Next Generation Pipeline**

Potential Revenue from Out-licensed Programs

- Carna is in license agreements with the pharmaceutical companies listed below and eligible to receive milestone payments upon achievement of certain development and commercial milestones. Carna will also receive royalties on future net sales.

< License/joint research agreements with pharmaceutical companies >

Partner	Compound (Target)	Upfront payment	Total milestone payments expected	Royalty	Region	Contract date	Milestones received
Sumitomo Pharma (Joint research)	Kinase inhibitor (Psychiatric and neurological disorders)	JPY80M (including research milestone)	JPY10.6B	Undisclosed	Worldwide	Mar. 2018	
Gilead Sciences (Out-license)	GS-9911	$20M	$450M	Undisclosed	Worldwide	Jun. 2019	$10M (Dec. 2021)
BioNova Pharmaceuticals (Out-license)	AS-1763 (BN102)	Undisclosed	$205M	Up to two digits %	Greater China	Mar. 2020	$0.5M (Mar. 2022)
Fresh Tracks Therapeutics (Out-license)	FRTX-10	$2M	$258M	Up to 10%	Worldwide	Feb. 2022	

* The amount and timing of milestone payments as well as royalty rates are not disclosed due to the agreements with the partners.

Drug Discovery Support (ddSP) Business Key Highlights

- Q3 sales at ddSP were JPY809 mn, increased 27.2% yoy.
  - ✓ In North America, sales increased 22.4% yoy. Sales of kinase proteins, especially biotinylated proteins, were strong. Demand from biotech companies has been strong and we have acquired new clients including AI-driven drug discovery companies. Sales to Gilead also contributed.
  - ✓ In Japan, sales increased 10.7% yoy. While overall demand has been weak, cell-based assay service (agent business) and kinase proteins were robust as well.
  - ✓ In other area including China, sales increased 176.3% yoy. Sales of kinase proteins were strong thanks to the continued expansion of the market in China. Although the export to China was temporarily affected in Q2 by China's strict coronavirus restrictions, the issues with the logistics have been resolved.
  - ✓ In Europe, sales decreased 18.1% yoy. The demand was weak and the logistics was unstable due to the war in Ukraine. The shipment has stabilized after changing our logistic company.
- Expanding lineup of kinase proteins and profiling service
  - ✓ 29 kinase protein products, including high-demand mutant kinase biotinylated kinases, have been newly added to the line-up by September.
- Resumed sales of DGK products and services
  - ✓ All 10 Diacylglycerol kinase (DGK) isozyme products and services are now available, after a strategic pause from their initial release in 2016.

"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

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