Financial Results
Q1 FY2022
(January to March 2022)

Carna Biosciences, Inc.

May 10, 2022

Stock Code: 4572

Q1 FY2022 Key Highlights

- Corporate
  - ✓ Upwardly revised FY2022 result forecast in May.

- Drug Discovery R&D
  - ✓ AS-1763: BioNova Pharmaceuticals Limited (BioNova), the licensee of AS-1763 in Greater China, submitted an Investigational New Drug (IND) application in China for AS-1763 (BN102) in January.
  - ✓ AS-1763: The patent was registered in Japan in January.
  - ✓ AS-1763: Carna received the first milestone payment from BioNova, triggered by an approval for the IND application in China in March.
  - ✓ AS-1763: Presented new preclinical and clinical data in two poster presentations at the American Association for Cancer Research (AACR) annual meeting in April.
  - ✓ STING antagonist: Entered into a licensed agreement with Brickell Biotech, Inc. (Brickell) in February.
  - ✓ DGKα inhibitor: Gilead Sciences, Inc. (Gilead) presented an investigational novel DGKα inhibitor GS-9911 discovered from the immuno-oncology program licensed from Carna at the company's "Oncology Deep Dive" in April.

Revision of FY2022 Business Plan

(JPY million)	FY2022 Plan as of Feb 10 (a)	FY2022 Plan as of May 10 (b)	(b)-(a)	Reason for changes
Total Sales	1,127	**1,186**	+58	
ddSP business	900	**900**	—	- Unchanged from the initial plan.
ddRD business	227	**286**	+58	- Upwardly revised to include a milestone payment from BioNova. - An upfront payment from Brickell is included in both previous and current plan.
Total Operating Loss	(1,730)	**(1,672)**	+58	
ddSP business	300	**300**	—	- Unchanged from the initial plan.
ddRD business	(2,031)	**(1,972)**	+58	- Upwardly revised to include the impact of a milestone payment from BioNova.
Ordinary Loss	(1,744)	**(1,685)**	+58	
Net Loss	(1,799)	**(1,740)**	+58	

(JPY million)	FY2022 Plan as of Feb 10 (a)	FY2022 Plan as of May 10 (b)	(b)-(a)	Reason for changes
R&D Cost	2,166	**2,166**	—	- Unchanged from the initial plan.
Capex	124	**124**	—	- Unchanged from the initial plan.

* Business plan for FY2022 as of May 10 includes an upfront payment from Brickell and a milestone payment from BioNova but does not include milestone payments and upfront payments related to other license agreements as the timing or the amounts are difficult to predict.

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

Q1 FY2022 Consolidated Financial Results

(JPY million)	Q1 FY2021 Actual	**Q1 FY2022 Actual**	YoY Change	FY2022 Plan as of May 10	
Sales	231	**554**	+323 +139.8%	1,186	- Sales at ddSP were strong in the U.S. and China. - Received an upfront payment from Brickell and a milestone payment from BioNova.
Operating Profit/Loss	(291)	**1**	+292	(1,672)	- Gross profit increased thanks to the upbeat sales at ddSP and sales recorded at ddRD. - Plan to invest in R&D as initially planned and full year operating loss of JPY1,672 mn is projected.
Ordinary Profit/Loss	(284)	**4**	+288	(1,685)	
Net Profit/ Loss	(286)	**(15)**	+271	(1,740)	- Impairment loss was recognized for lab equipment.
R&D Cost	357	**346**	(11) -3.1%	2,166	- Plan to invest in R&D as initially planned.

Note: Rounded down to the nearest million yen.

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

Q1 FY2022 Results by Business Segment

(JPY million)	Q1 FY2021 Actual	**Q1 FY2022 Actual**	YoY Change	FY2022 Plan as of May 10	Q1 FY2022/ FY2022 plan	
Total Sales	231	**554**	+323 +139.8%	1,186	46.8%	
ddSP business	231	**268**	+37 +16.1%	900	29.8%	- Sales of kinase proteins were strong in the U.S. and China.
ddRD business	—	**286**	+286	286	100%	- Received an upfront payment from Brickell Biotech. - Received a milestone payment from BioNova.
Total Operating Profit/Loss	(291)	**1**	+292	(1,672)	—	
ddSP business	88	**109**	+20 +23.6%	300	36.3%	- Gross profit increased as a result of an increase in sales.
ddRD business	(379)	**(107)**	+271	(1,972)	—	- Operating loss was smaller than the previous year thanks to an upfront payment and milestone payment.

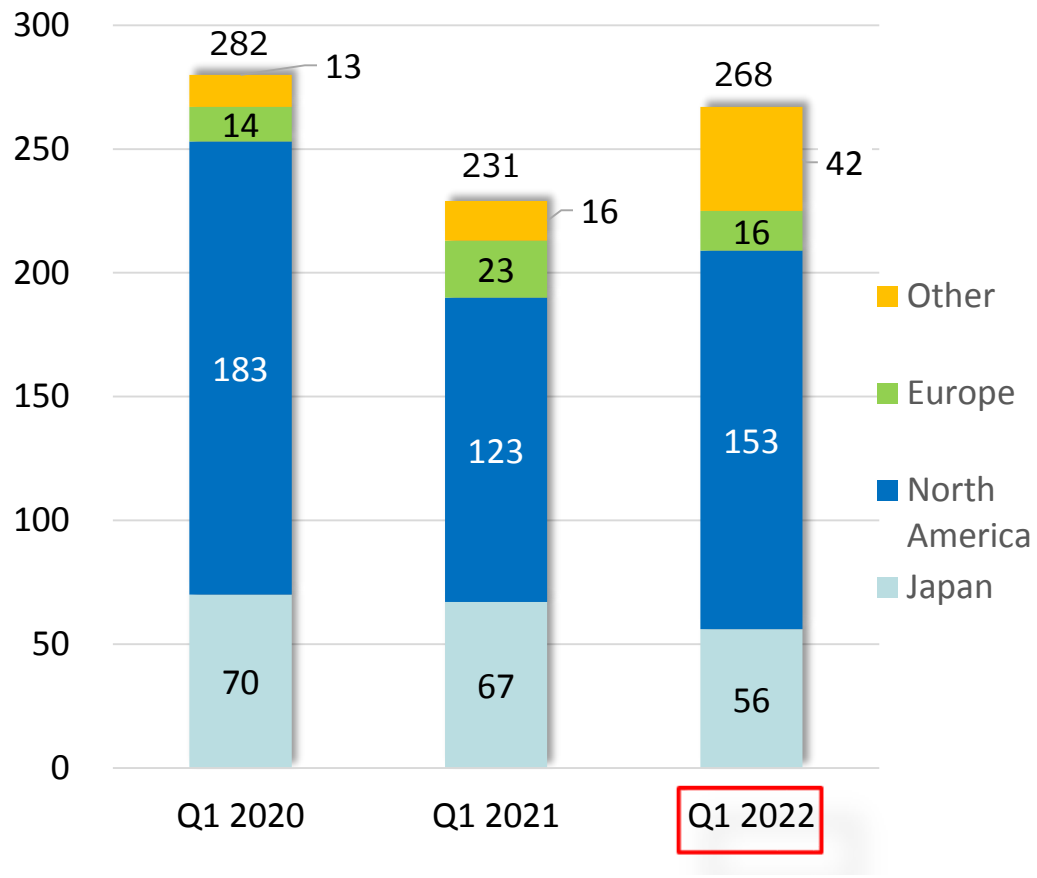
Note: Rounded down to the nearest million yen.

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

Q1 FY2022 Discovery Support (ddSP) Business Sales by Region

(JPY million)

ddSP Sales Trend by Region



- Japan: Decreased 16.3% YoY
  - Sales declined yoy due to weak demand in Japan. The decline was within the expectation.
- North America: Increased 23.6% YoY
  - Sales of kinase proteins were strong.
- Europe: Decreased 29.1% YoY
  - Sales declined as both kinase proteins and profiling service were weak.
- Other: Increased 153.8% YoY
  - Sales in China were strong.

Consolidated Balance Sheet

(JPY million)	As of Dec. 31, 2021	As of Mar. 31, 2022	Change	Reason for changes
Current assets	5,318	5,253	-65	Accounts receivable-trade -1,122 Cash and deposits +1,059
Cash and deposits	3,817	4,877	+1,059	+1,128 from a milestone payment recorded as sales in Dec. 2021
Non-current Assets	114	102	-12	
Total assets	5,432	5,355	-77	
Current liabilities	774	500	-274	Accounts payable -154
Non-current liabilities	342	313	-28	Long term loans payable -29 Bonds payable -14
Total liabilities	1,116	814	-302	
Total net assets	4,315	4,540	+225	Capital stock and capital surplus +194, Retained earnings -15
Total liabilities and net assets	5,432	5,355	-77	

Shareholders' equity ratio	79.3%	84.6%
BPS	323.5 yen	335.5 yen
PBR	3.4x	3.1x
Share price of Carna	1,102 yen	1,048 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 Brickell		BrickellBio

✓ As of May 2022

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

Deal with Brickell Biotech for STING Antagonist

In Feb. 2022, Carna and Brickell Biotech entered into a license agreement to grant Brickell the exclusive, worldwide rights to develop and commercialize Carna's portfolio of novel, potent, and orally available STING antagonists.

◆ Deal size	✓ Upfront payment of $2 million ✓ Success-based development, regulatory, and sales milestone payment of up to $258
◆ Royalty	✓ Tiered royalty payments ranging up to 10% of net sales

- Carna initiated the STING antagonist program in 2019 to create next wave of pipeline.
- The program was advanced to preclinical stage in Q4 2021.
- Carna can continue its own research on STING modulator (agonist/antagonist).
  (The antagonist research is limited to a new chemical scaffold in the filed of oncology.)

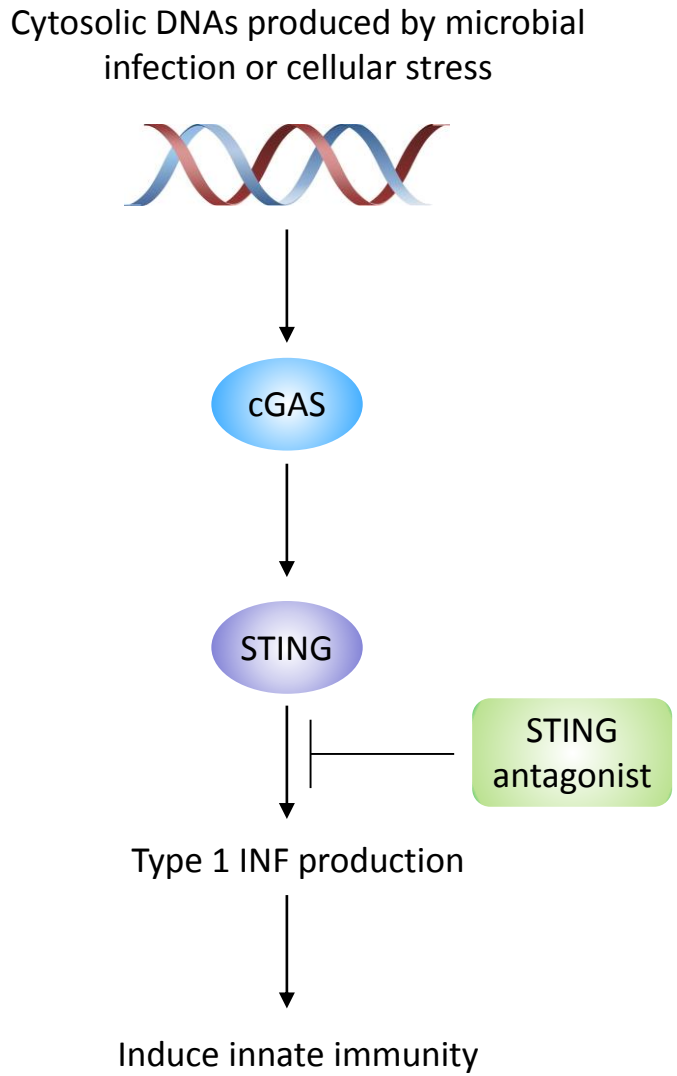
Successfully licensed non-kinase target project in a short period of time.

↓

Demonstrated Carna's high level of expertise in small molecule drug discovery.

About STING

- ✓ The cyclic GMP-AMP synthase (cGAS) - stimulator of interferon genes (STING) signaling pathway plays a central role in innate immunity.
- ✓ The cGAS-STING signaling is activated in response to the presence of cytosolic DNAs produced by microbial infection or cellular stress. The activated cGAS-STING signaling induces type I interferons (IFNs) production to trigger immune responses for host defense.
- ✓ It has been reported that aberrant cGAS-STING signaling is implicated in the pathogenesis of several diseases. Mutations in several genes have been identified that cause the constitutive activation of the cGAS-STING pathway, resulting in severe autoinflammation in lung, kidney, joint, etc.
- ✓ Moreover, numbers of non-genetic diseases are also suggested to be associated with the aberrant cGAS-STING signaling. These include a subset of systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and several cancers.
- ✓ There is a high unmet medical need to develop novel STING antagonists to treat these diseases. (ref.1)
- ✓ Recently, a research paper was published suggesting that STING antagonist has a potential to treat severe lung inflammation induced by SARS-Cov-2. (ref.2)



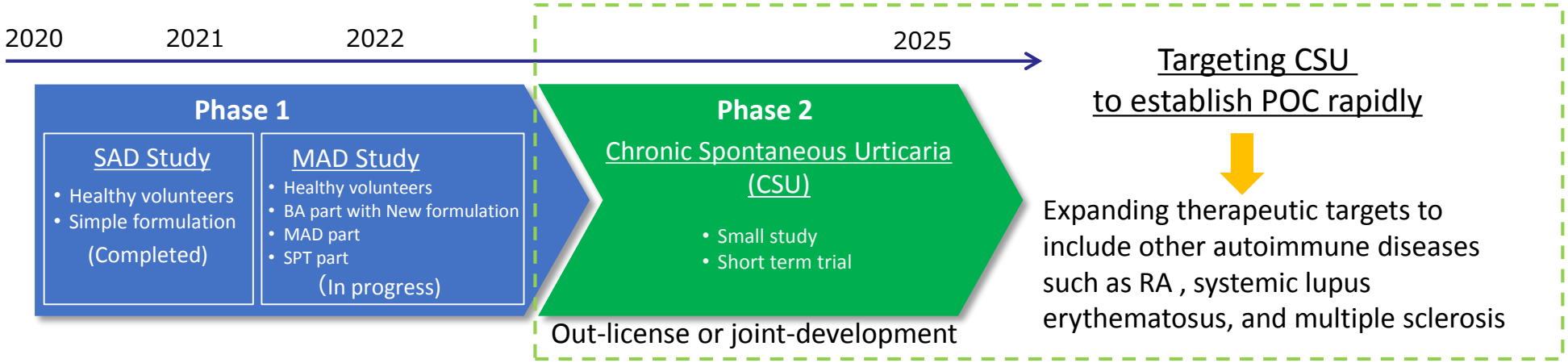
1) Decout A., et al. Nat Rev Immunol. 2021 Sep;21(9):548-569.
2) Di Domizio J., et al. Nature. 2022 Jan 19. doi: 10.1038/s41586-022-04421-w.

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
SPT: skin prick test
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 Profile
- ✓ Promising Pharmacodynamic 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 capsule and tablet formulations
MAD part	Evaluate the safety, tolerability, PK and PD in the 2-week multiple ascending dose of AS-0871
SPT part	Evaluate the effect on allergen-induced skin reaction in the skin prick test (SPT) to assess the potential of AS-0871 for the treatment of Chronic Spontaneous Urticaria (CSU), a disease with high unmet needs

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

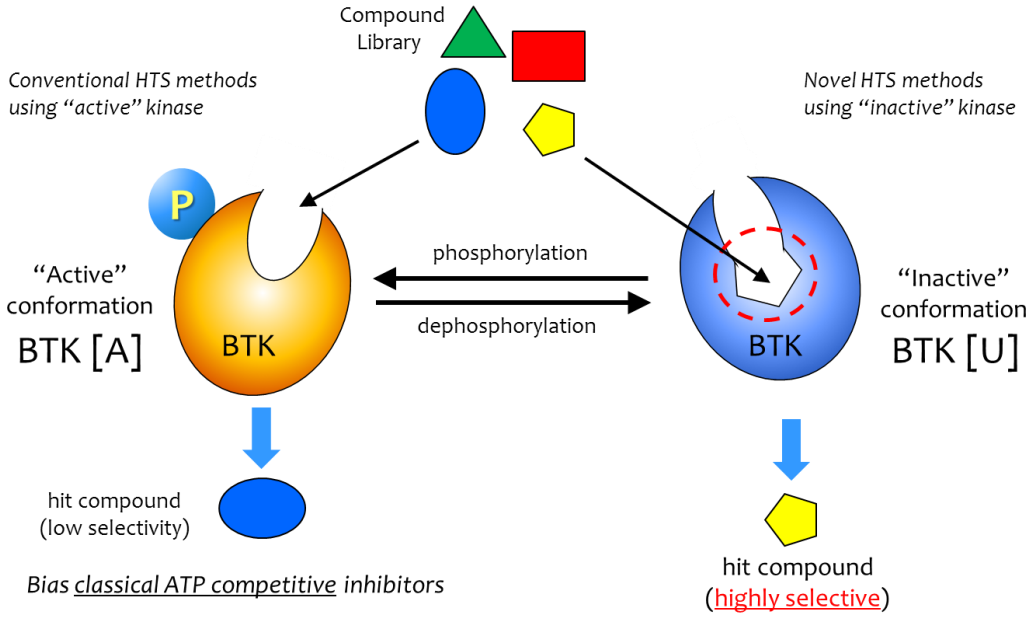
Article

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

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

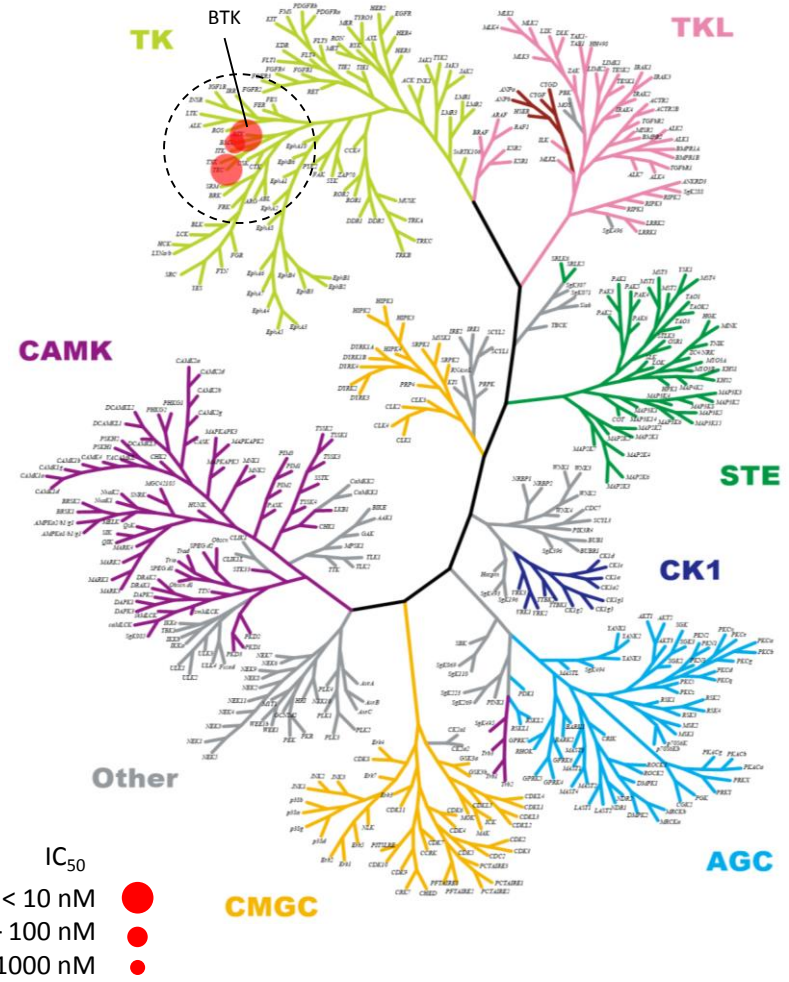


Bias classical ATP competitive inhibitors

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

◆ Kinase Selectivity Profiling

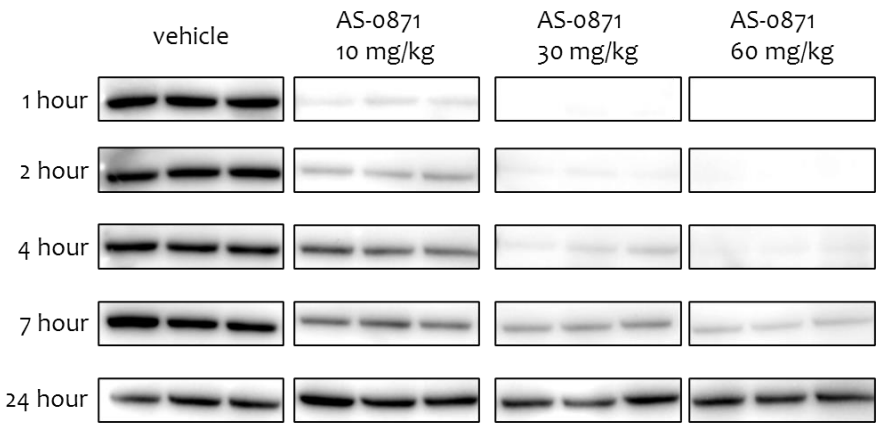
Only inhibited 2 other kinases in a total of 312 kinases tested at 0.3 μM concentration.

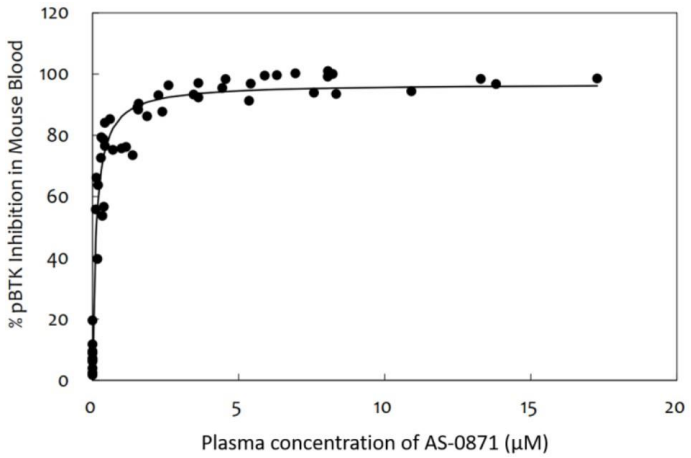


AS-0871: In Vivo Therapeutic Efficacy

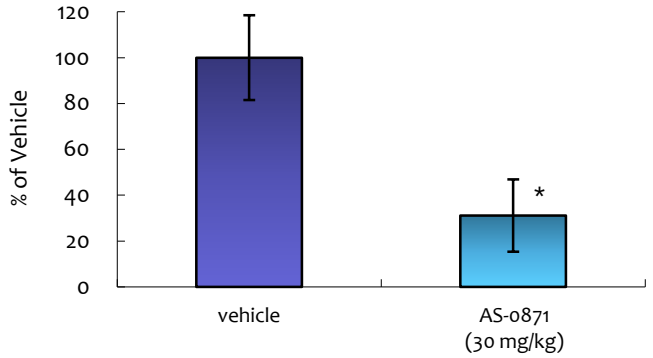
- PK/PD Study

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

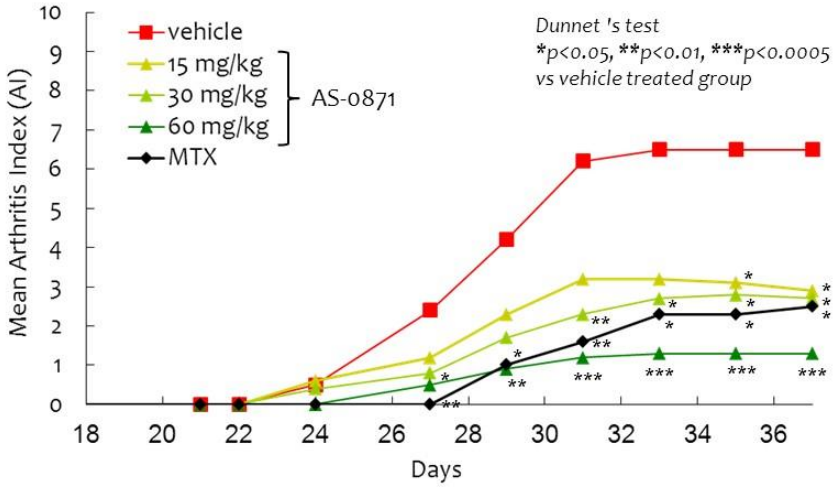




- Passive cutaneous anaphylaxis (PCA) mouse model (n=5)



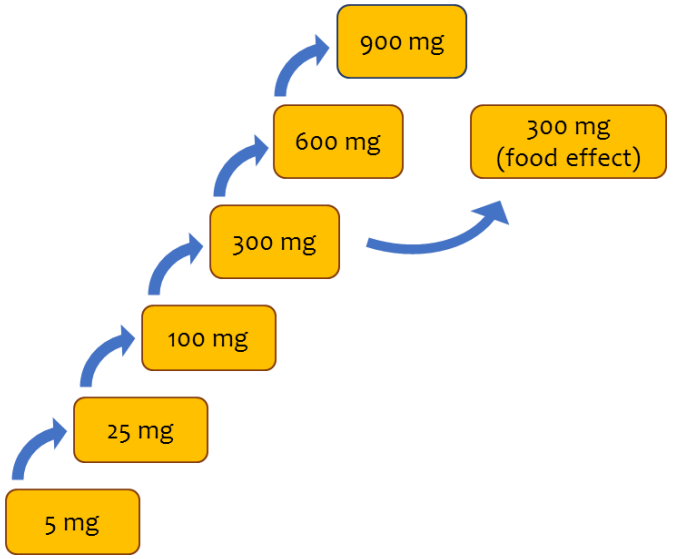
- Collagen-induced arthritis (CIA) mouse model (n=10)



AS-0871: FIH study

SAD Part (Completed)

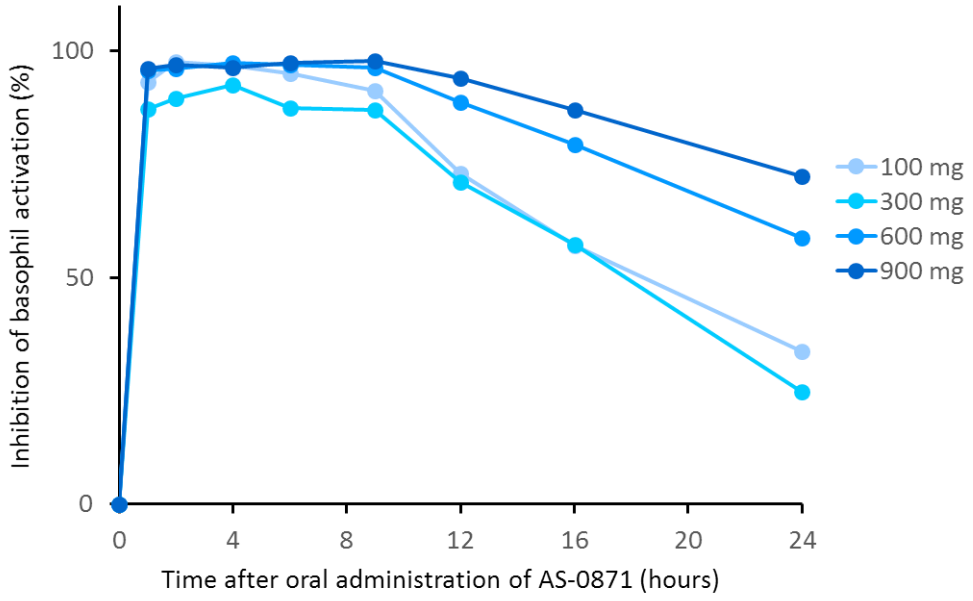
Step 1	Step 2
• 6 dose levels (8 subjects/cohort) • Placebo controlled (6 active / 2 placebo) • Safety and tolerability • Pharmacokinetics and pharmacodynamics	• Food effect

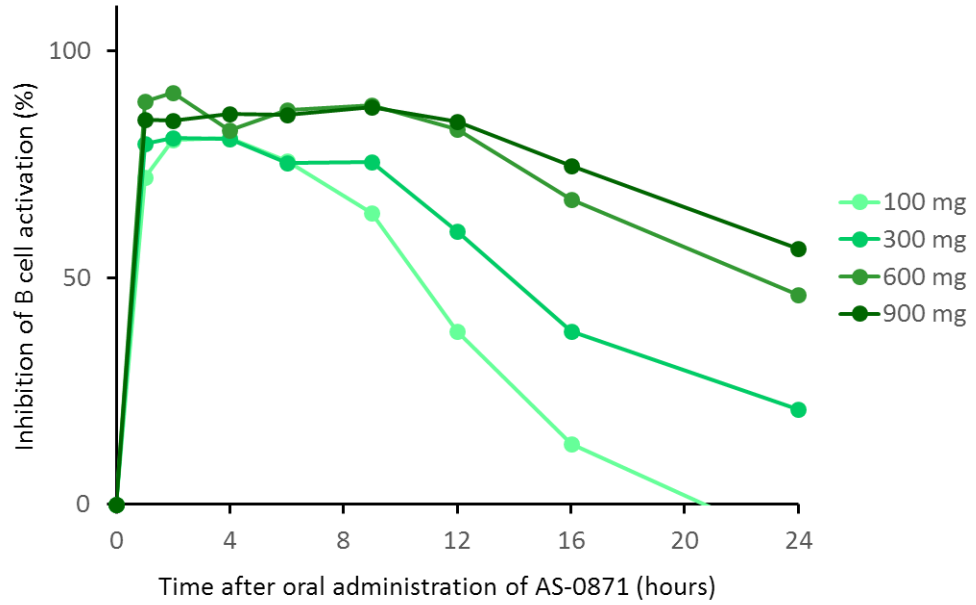


- ✓ AS-0871 is well-tolerated without any safety concerns.
- ✓ Favorable pharmacokinetic profile.
- ✓ Blood samples to assess PD effects were analyzed for evaluation of the B-cell and basophil responses. Administration of AS-0871 at 100mg or above resulted in strong inhibition of B-cell and basophil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



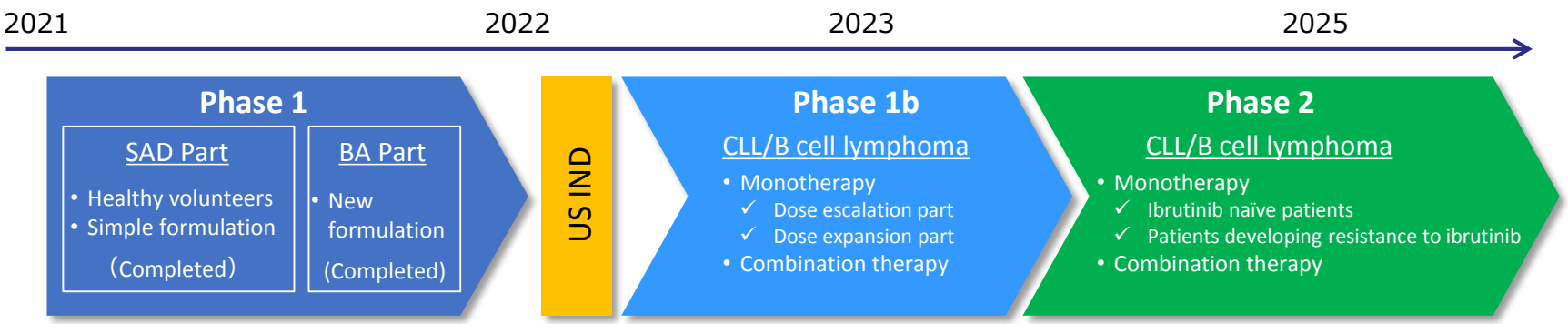


AS-1763: Next Generation BTK Inhibitor Targeting Blood Cancer

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
- Potential applications for autoimmune diseases
- Plan to accelerate the clinical studies utilizing the clinical data of BioNova, the licensee in Greater China



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

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

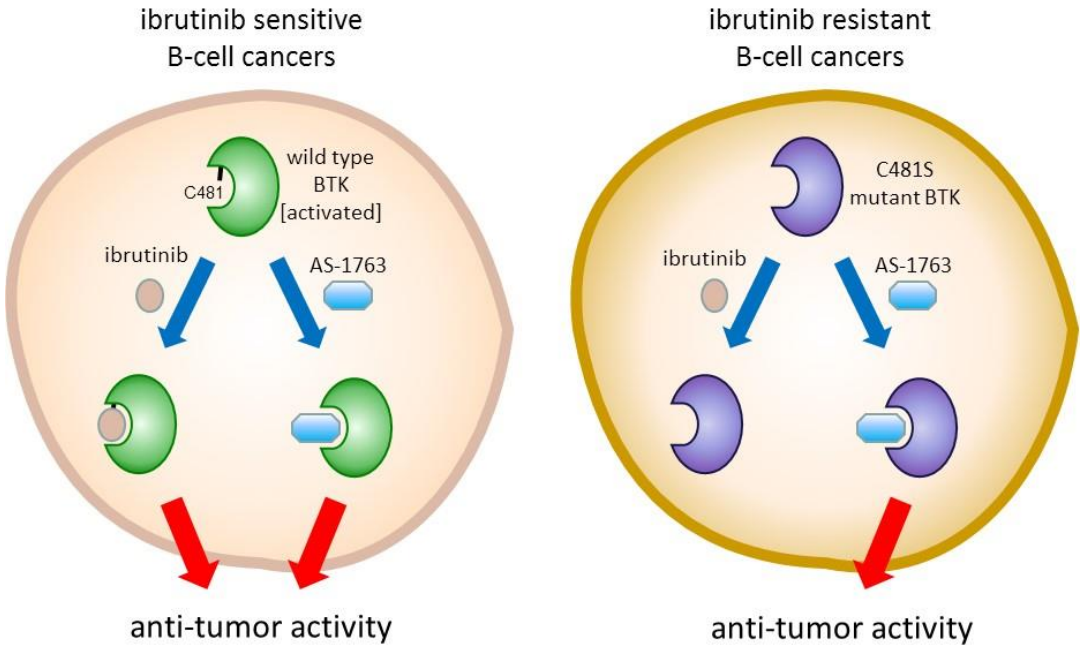
Completed

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

- ◆ Presented the Phase 1 data at AACR2022.
- ◆ In March, BioNova received an approval to initiate a clinical study in China.
- ◆ Submitted an IND in the end of April.

CLL: Chronic Lymphocytic Leukemia

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

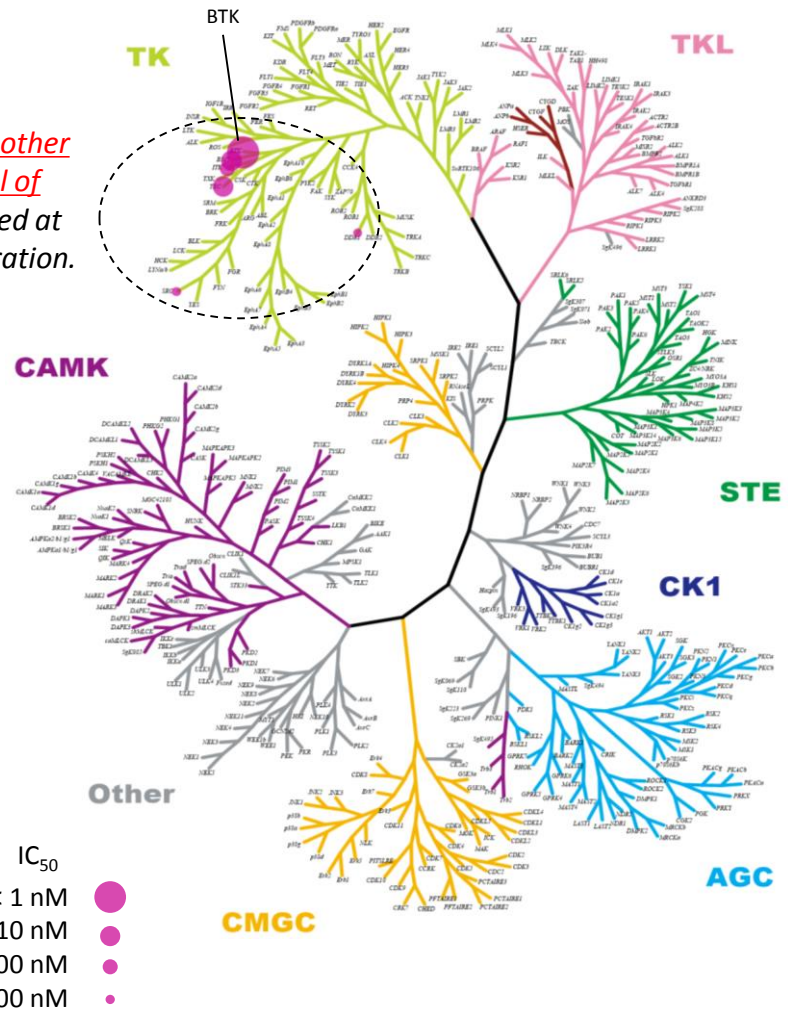
50-fold Stronger activity

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.

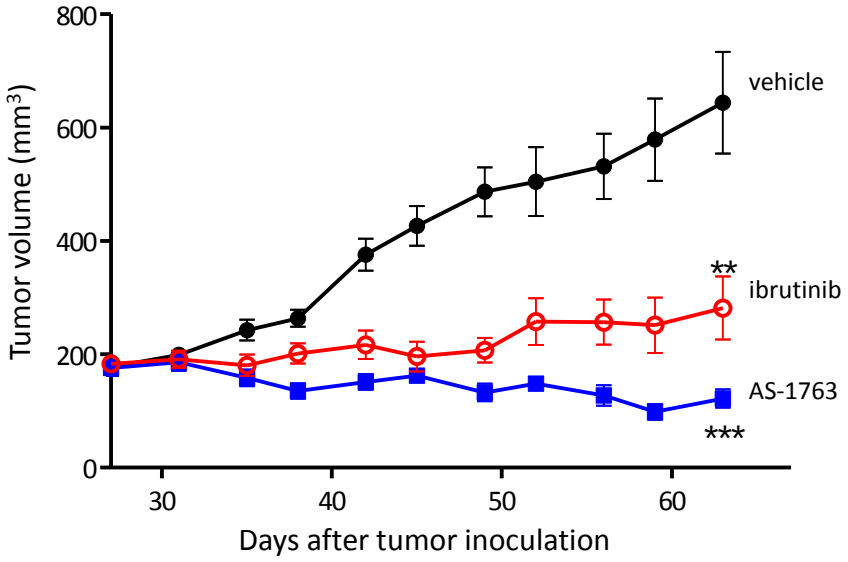
◆ Kinase selectivity profiling

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

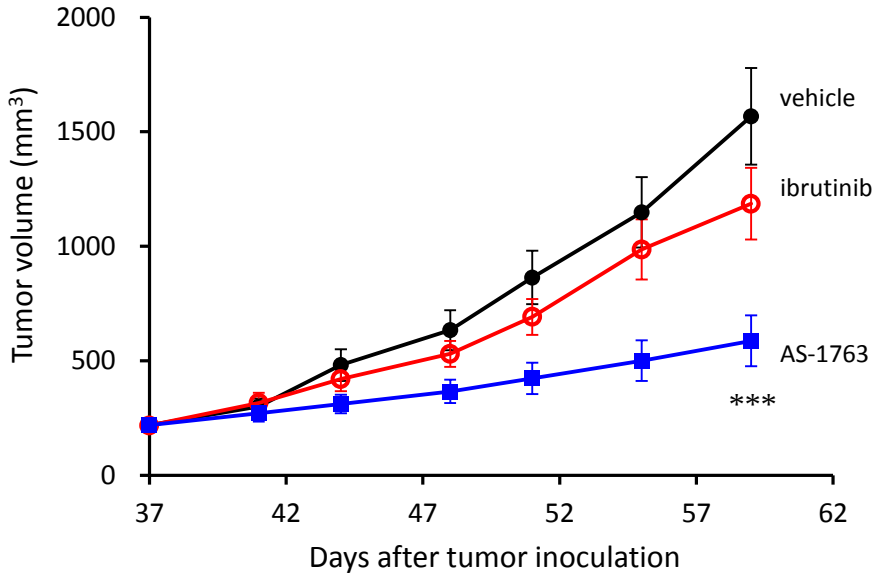
- In vivo antitumor effects of AS-1763 on human B-cell non-Hodgkin lymphoma cell line, OCI-LY10 tumor xenograft mouse model (n=8-10)



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

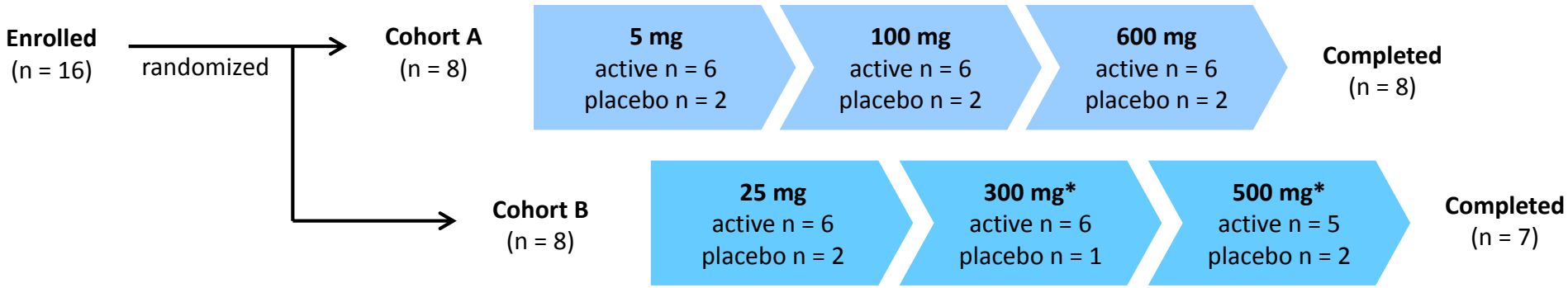
***: p<0.001

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

AS-1763: FIH Phase 1 Study 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

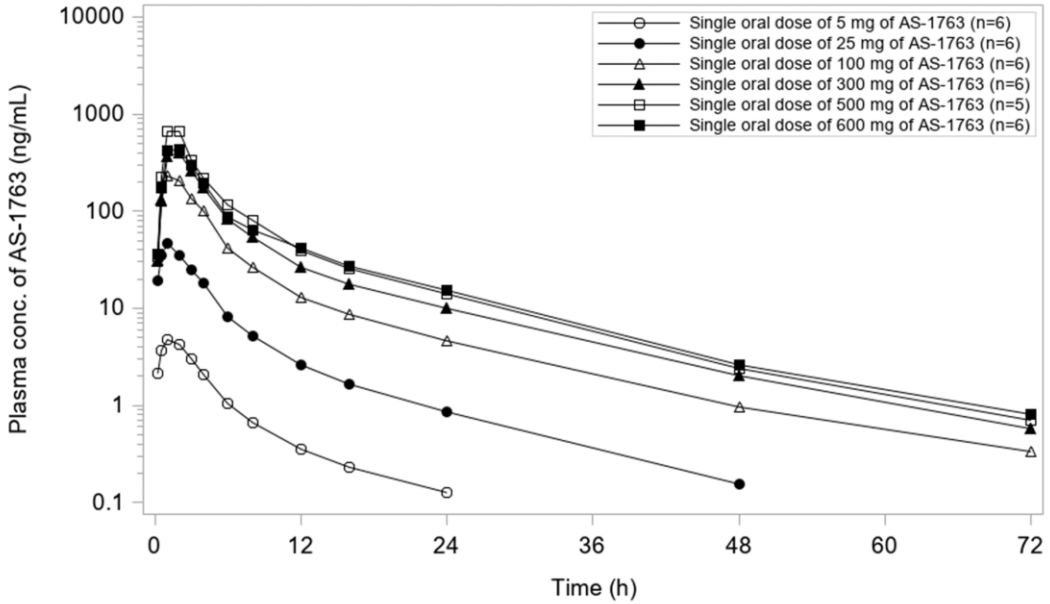
<Safety and tolerability>

- 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.

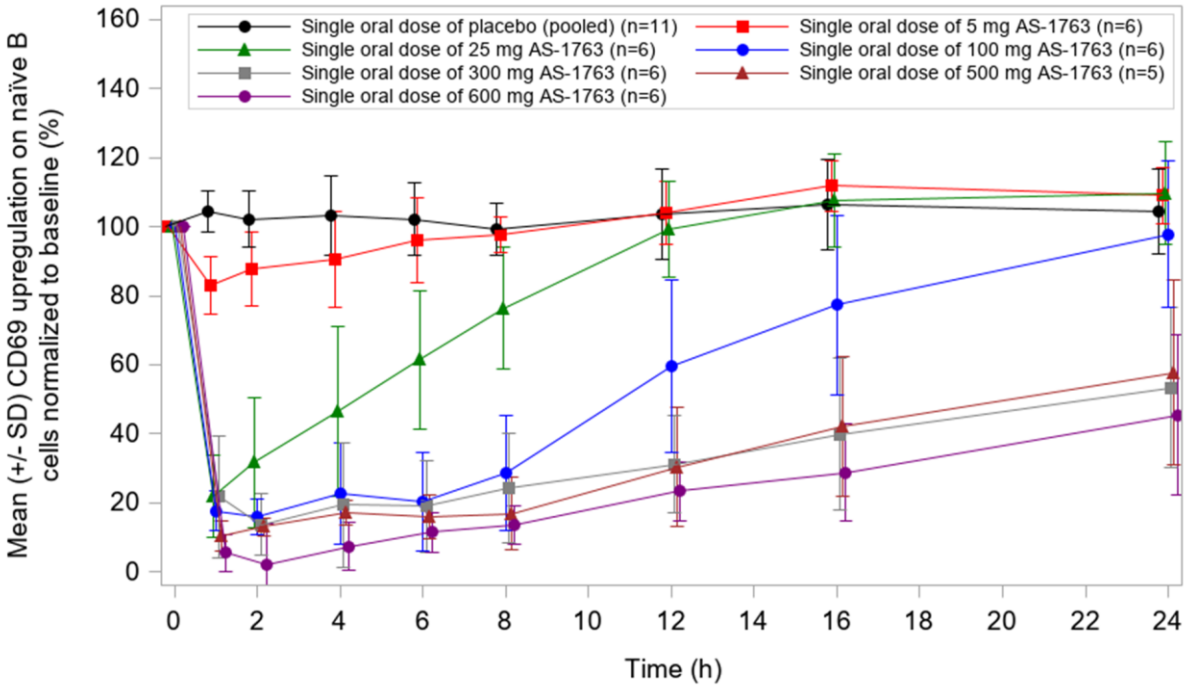
<Plasma concentration of a Single oral dose AS-1763>



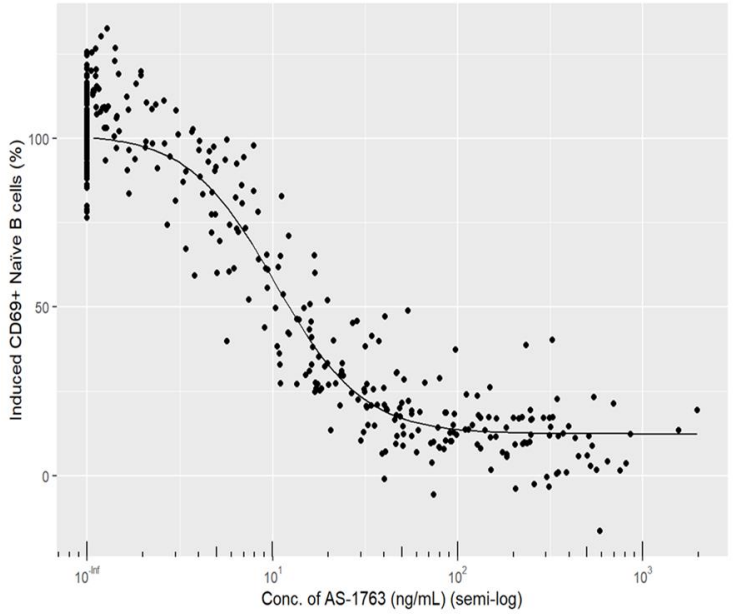
Pharmacodynamics of AS-1763

- 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>



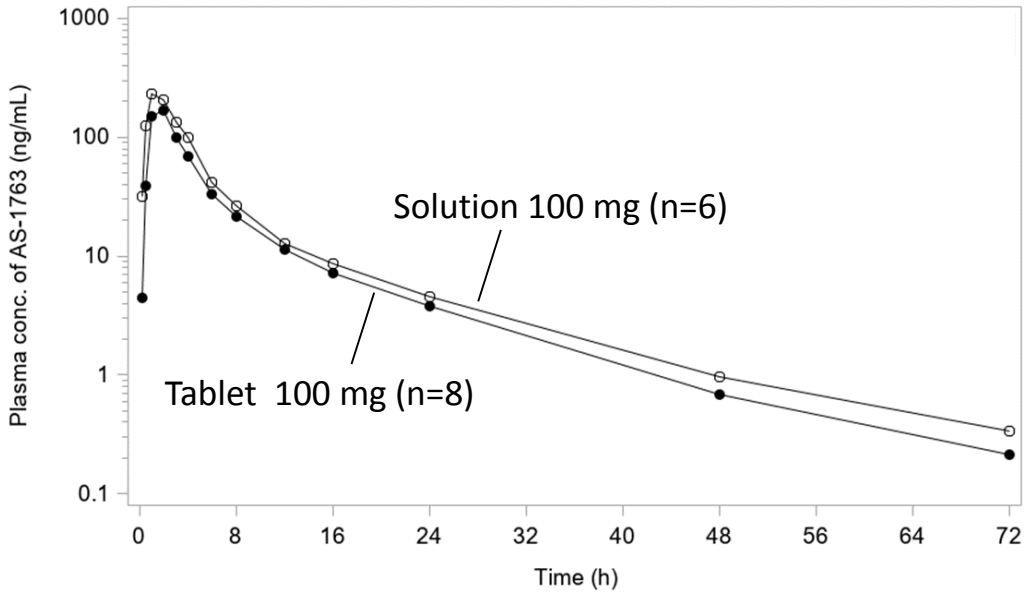
<PK/PD Correlation Analysis>



AS-1763: BA Part

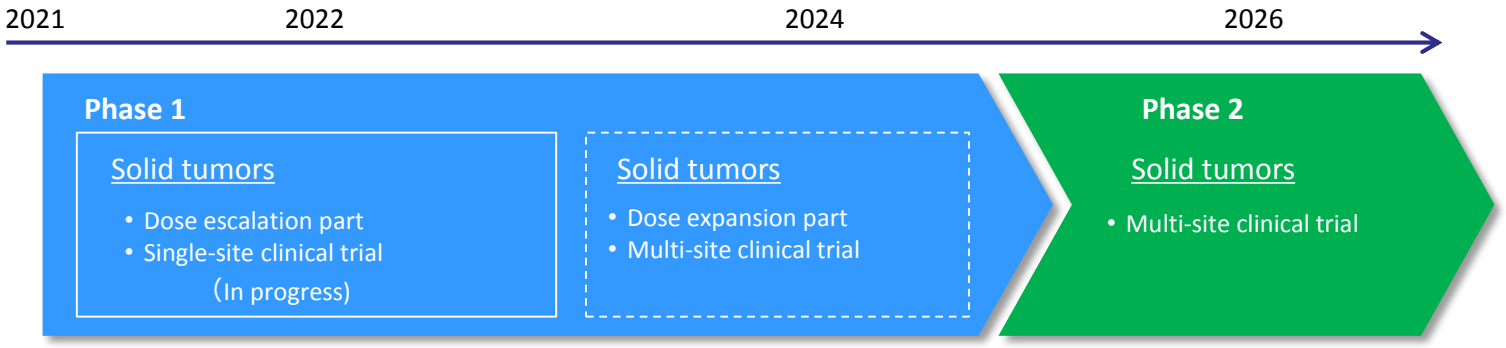
- In the BA part, 100 mg tablet and the solution showed almost the similar PK profile while the exposure of 100 mg tablet was slightly lower than the that of the solution.
- The PK/PD data and favorable safety profile in healthy volunteers support a planned Phase 1b clinical study with AS-1763 tablet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

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



AS-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 in Progress

Phase 1 Study in 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, preliminary anti-tumor activity, and pharmacokinetics (PK) / pharmacodynamics (PD) as well as to determine recommended Phase 2 dose.

● Ongoing Phase 1 Dose escalation part

Cohort	Dose level (5d on/2d off)	Status
1	20 mg BID	Completed
2	40 mg BID	Completed
3	80 mg BID	Completed
4	150 mg BID	Completed
5	250 mg BID	In progress
6	300 mg BID	Planning

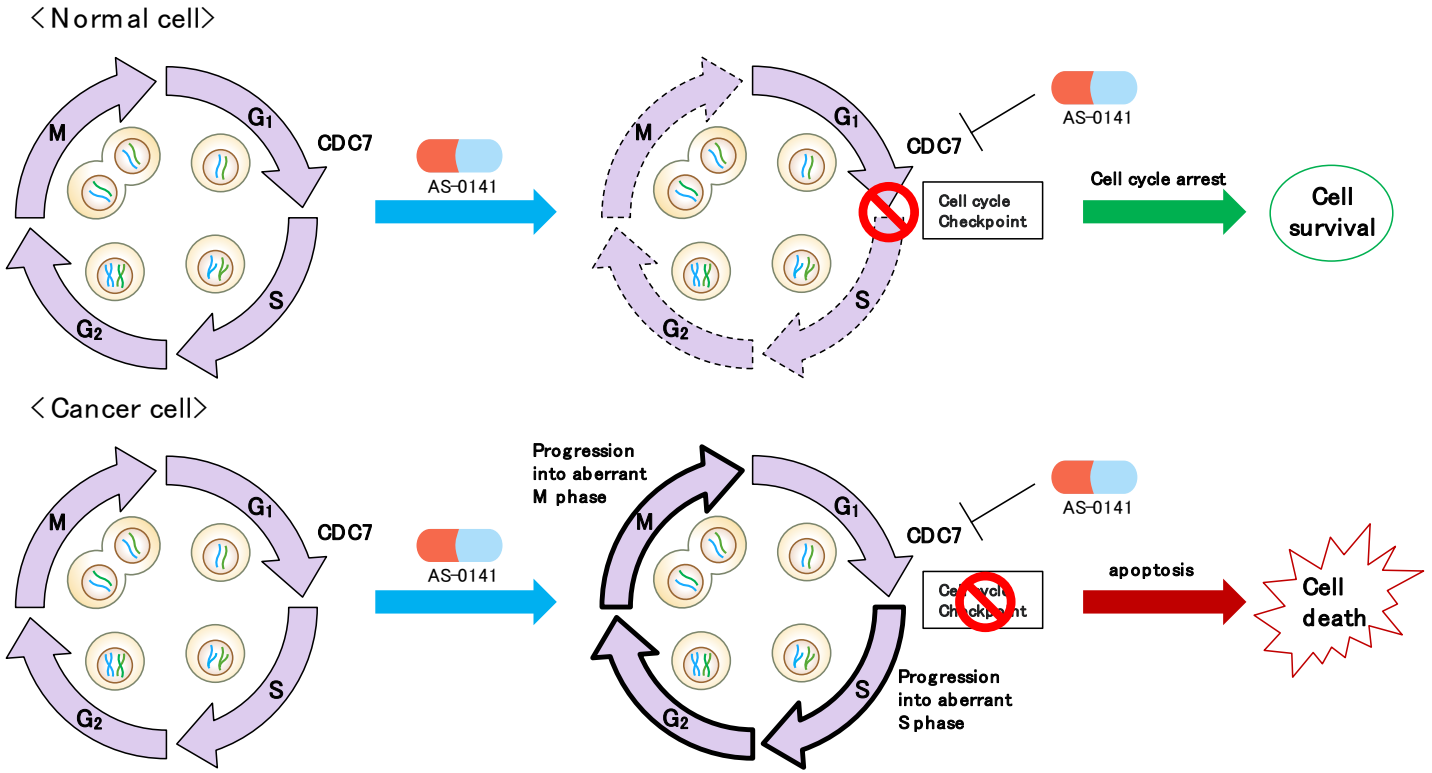
◆ No dose-limiting toxicity (DLT) has been observed and advanced to Cohort 5 (250 mg BID)

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

AS-0141: Highly Selective CDC7 Inhibitor

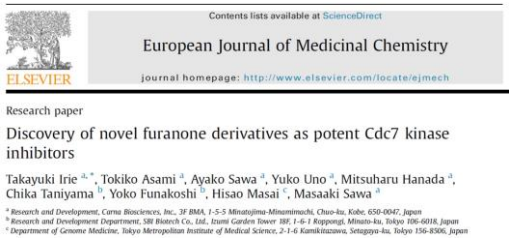
■ CDC7 kinase inhibitor

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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European Journal of Medicinal Chemistry

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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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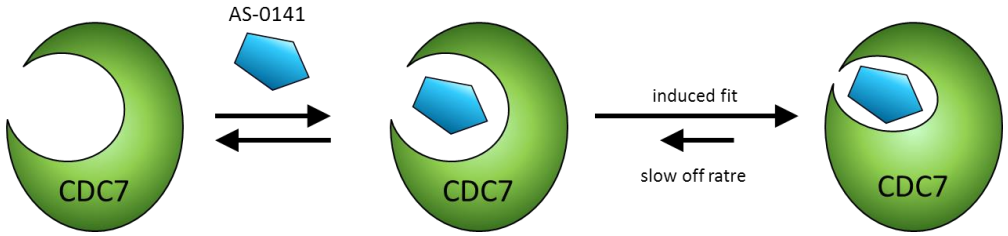


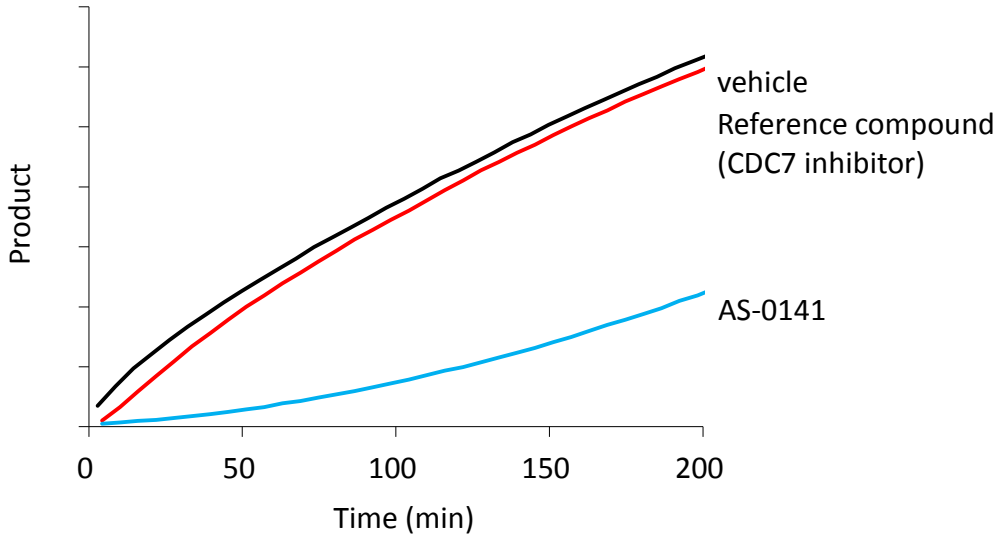
Inhibitory potency (IC_{50}) for CDC7 in the presence of 1 mM ATP

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

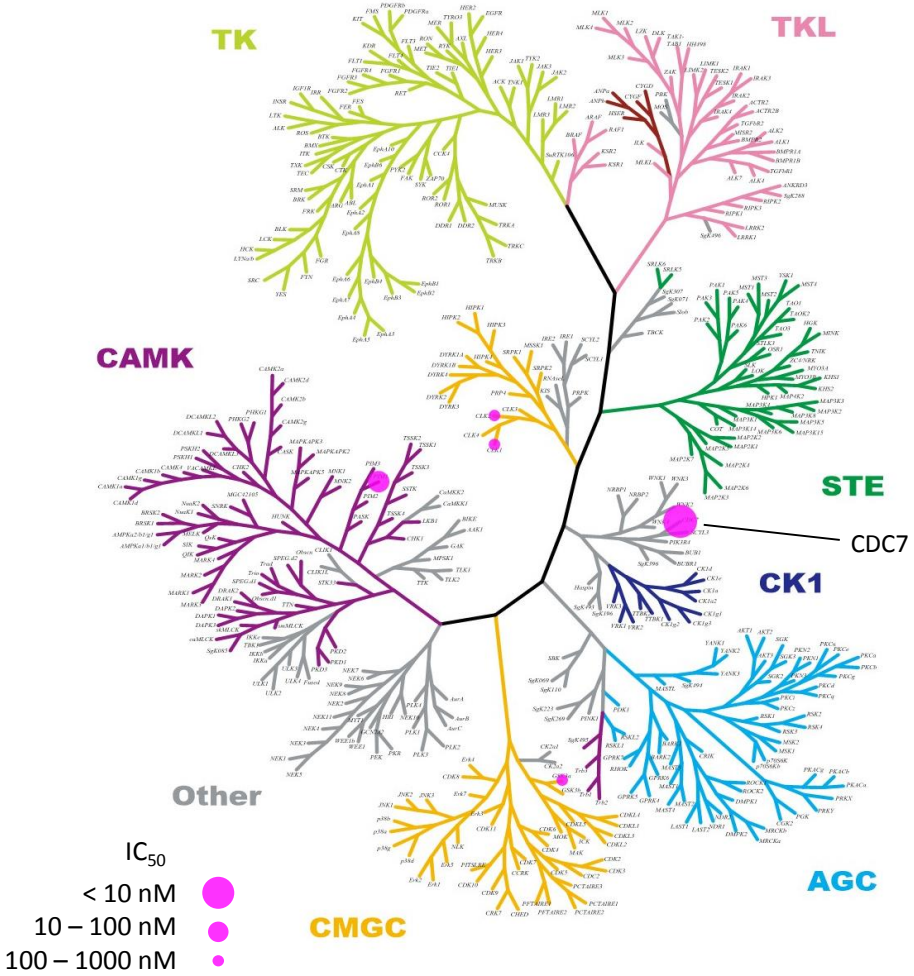
Rapid dilution assay for Cdc7 inhibitors. Recovery of enzymatic activity was monitored by formation of the phosphorylated product.



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
PIM1	30	34
CLK1	212	206
CLK2	270	227
GSK3α	189	251

210-fold

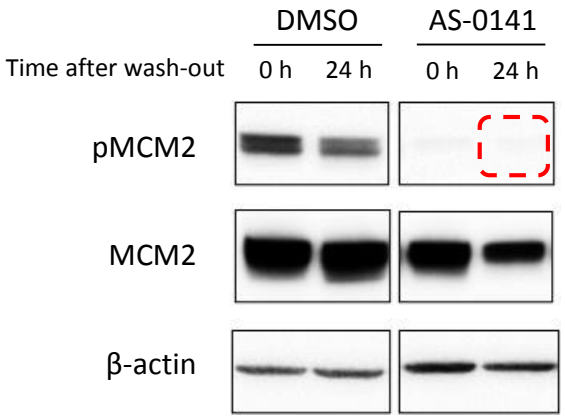
CDC7 is the only kinase that shows preincubation effect

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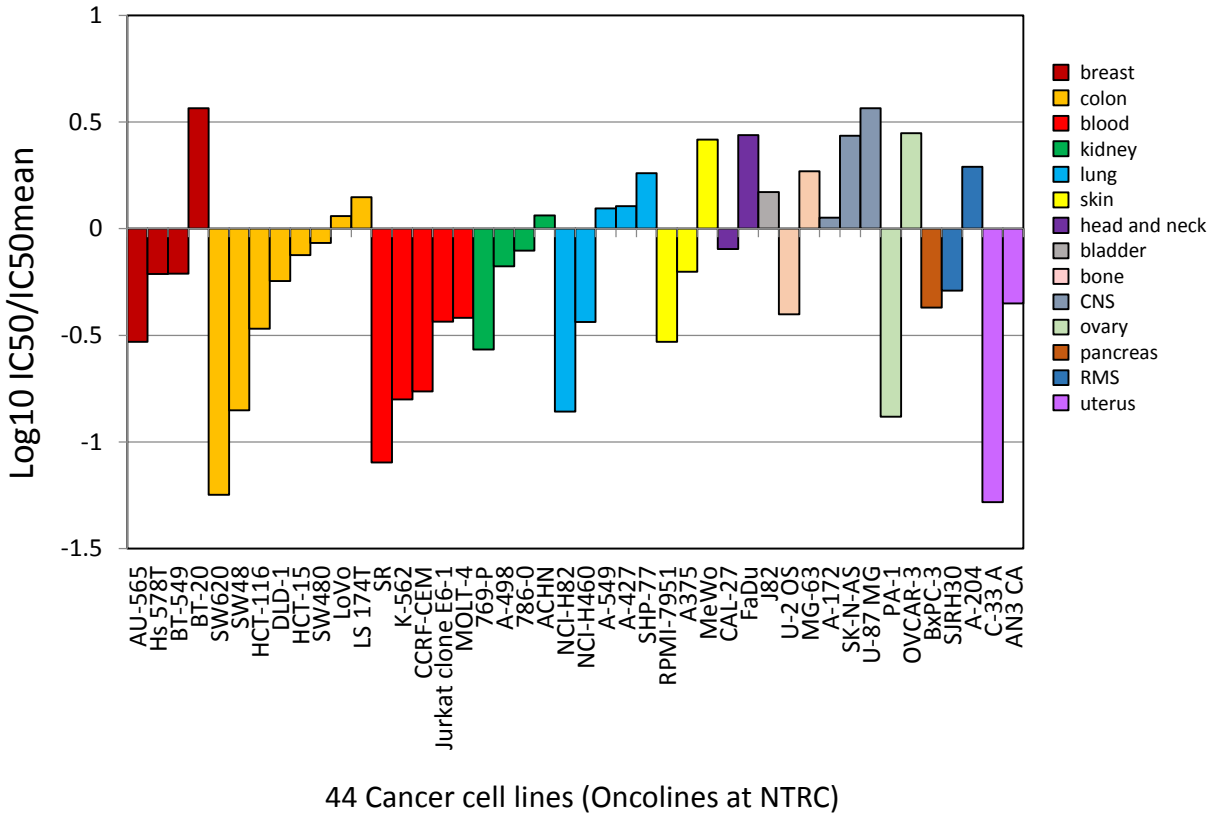
◆ AS-0141 potently inhibited growth in a wide range of tumor cell lines, including solid and hematological tumors

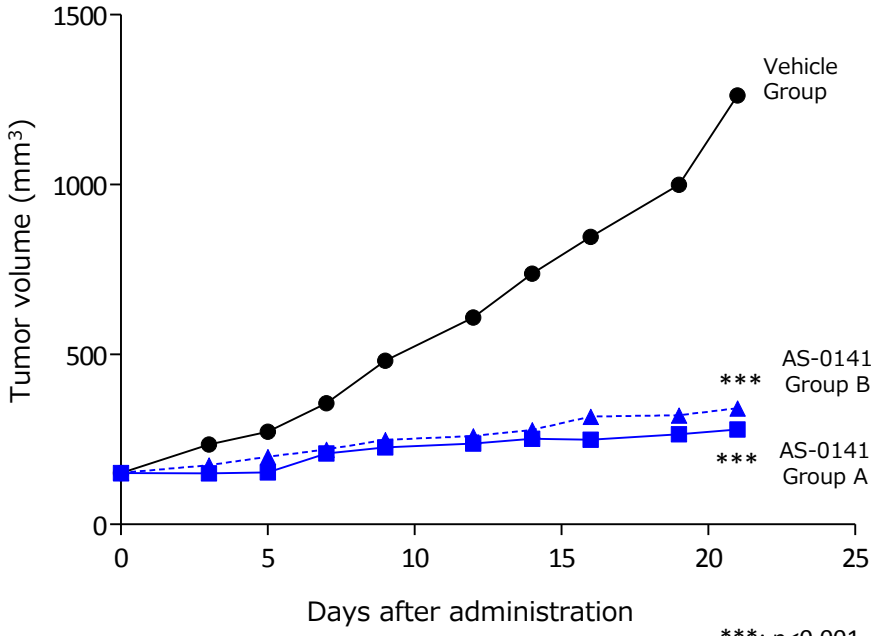


44 Cancer cell lines (Oncolines at NTRC)

AS-0141: Robust In Vivo Antitumor Efficacy

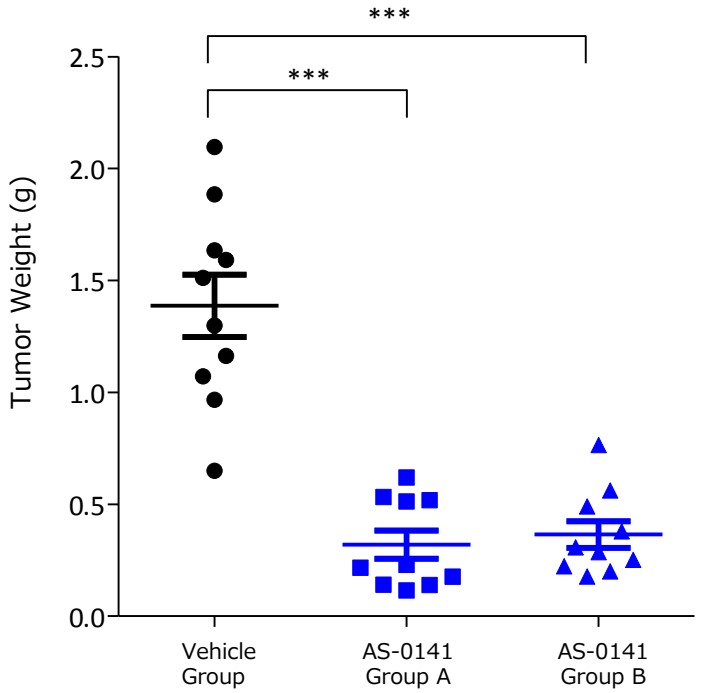
- In vivo antitumor efficacy of AS-0141 in a SW620 (human colon cancer) xenograft mouse model

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

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

Drug Discovery Support (ddSP) Business Key Highlights

- Q1 sales at ddSP were JPY268 mn, increased 16.1% yoy.
  - ✓ In North America, contribution from sales to Gilead continued and sales of kinase proteins, especially biotinylated proteins, were strong.
  - ✓ In Japan, sales decreased yoy, including kinase proteins and profiling service. Cell-based assay service (agent business) were robust.
  - ✓ In China, sales of kinase proteins were strong thanks to the continued expansion of the market.
- Expanding lineup of kinase proteins and profiling service
  - ✓ 6 kinase protein products, including high-demand mutant kinase biotinylated kinases, have been newly added to the line-up.
  - ✓ Launched a product and service website in Chinese for the convenience of users in China.
- Impact of China's Covid-19 lockdown
  - ✓ Export to China has been affected by the lockdown in Shanghai since April, although the demand from the agent has been strong. We are taking various measures to resume shipment in order to minimize the impact on 2Q sales.
- Impact of Russia's invasion of Ukraine on sales in Europe
  - ✓ Since the end of March, the export to Europe has been affected by the unstable logistics due to the war in Ukraine. We are taking various measures to resume shipment in order to minimize the impact on 2Q sales.

"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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