Financial Results
FY2021
(January to December 2021)

Carna Biosciences, Inc.

February 10, 2022

Stock Code: 4572

FY2021 Key Highlights

- AS-0871 (BTK inhibitor) : Initiated Multiple Ascending Dose (MAD) study of Phase 1 study in Europe.
- AS-1763 (BTK inhibitor) : Completed dosing in Single Ascending Dose (SAD) part of Phase 1 study in Europe and initiated bioavailability (BA) part.
- AS-0141 (CDC7 inhibitor) : Initiated Phase 1 study in Japan.
- Received the first milestone payment from Gilead regarding novel immuno-oncology program licensed in 2019.
- STING antagonist: Advanced to preclinical stage.
- Issued Series 19th Subscription Rights Shares.

Key Milestones for 2021

Business		Milestones for 2021	Achievement in 2021
ddRD	AS-0871	☐ Initiate Ph1 MAD part (H2 2021)	☑ Initiated Ph1 MAD part in Dec. 2021
	AS-1763	☐ Initiate Ph1 (H1 2021)	☑ Initiated Ph1 in Apr. 2021
	AS-0141	☐ Initiate Ph1 (H1 2021)	☑ Initiated Ph1 in June 2021
	Research program	☐ Bring one or more programs in preclinical stage	☑ STING antagonist was advanced to preclinical stage
ddSP		☐ Achieve sales target of JPY920 mn ☐ Launch new products ☐ Expand NanoBRET service ☐ Propose project-based service to collaborate with clients, leveraging Carna's drug discovery technology	☐ Actual sales were JPY889 mn, 96% of initial target ☑ Launched 31 new kinase protein products and 4 new EGFR mutant targets to profiling service ☑ Expand NanoBRET service ☐ Propose project-based service to collaborate with clients, leveraging Carna's drug discovery technology

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

☑ Achieved
☐ Plan or to be achieved

Drug Discovery R&D (ddRD) Business

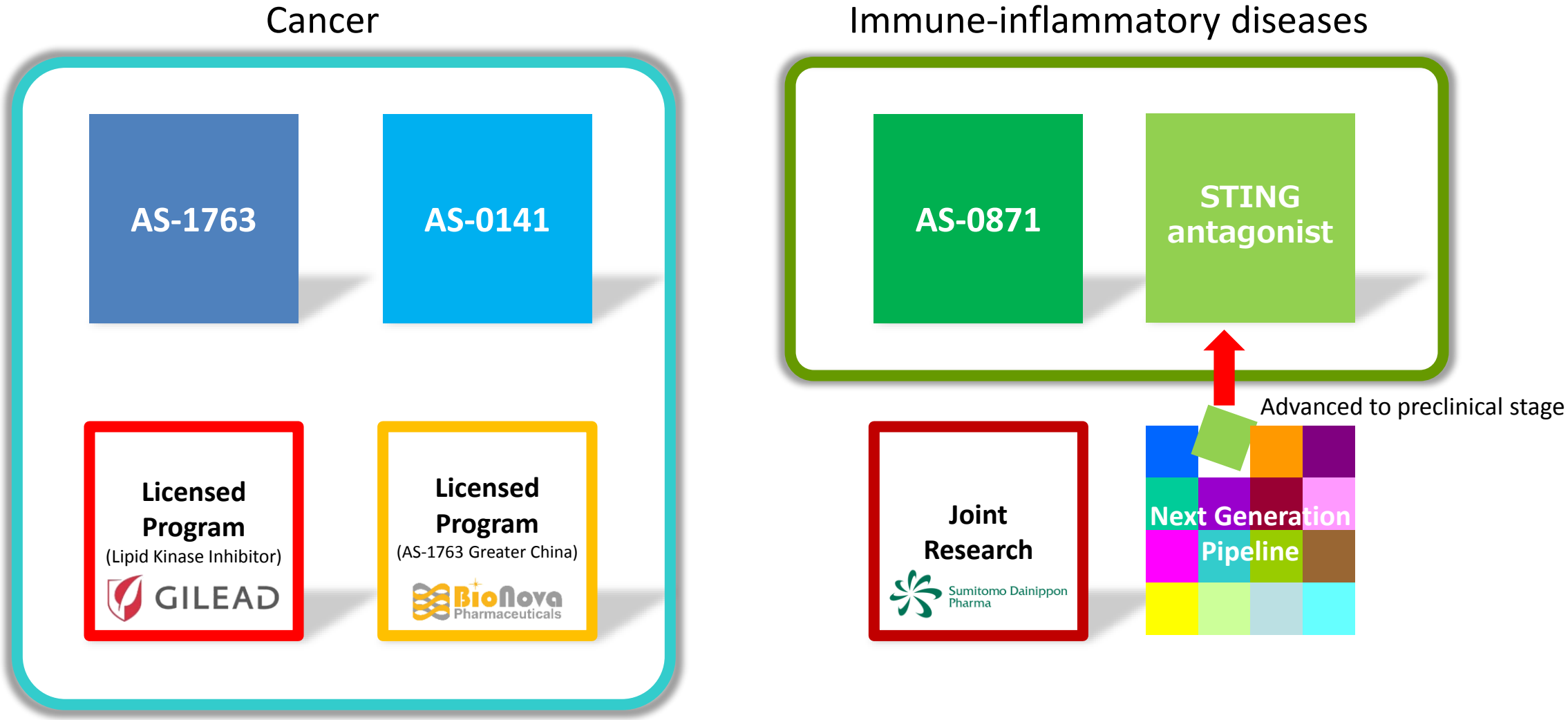
FY2021 Key Highlights for Drug Discovery R&D

- Clinical development
  - ✓ AS-0871: Completed Phase 1 SAD study and initiated MAD study in the Netherlands.
  - ✓ AS-1763: Completed dosing in Phase 1 SAD part and initiated BA part in the Netherlands.
  - ✓ AS-0141: Initiated Phase 1 study in Japan.
- Research
  - ✓ STING antagonist was advanced to preclinical stage.
  - ✓ Extended the term of joint research with Sumitomo Dainippon Pharma.
- Other highlights
  - ✓ Received the first milestone payment from Gilead under the agreement to develop and commercialize small molecule compounds in immuno-oncology.
  - ✓ BioNova Pharmaceuticals, the licensee of AS-1763 in Greater China, submitted an Initial New Drug(IND) application in China for AS-1763 (BN102) in January 2022.
  - ✓ The patents for AS-1763 were registered in Japan and China.
  - ✓ Published research papers in Journal of Medicinal Chemistry on the discovery of AS-1763 and AS-0141.

SAD: Single Ascending Dose
MAD: Multiple Ascending Dose

Drug Discovery R&D: Pursuing Sustained Growth

Robust Drug Pipeline (as of end of 2021)



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.

↓

Carna's expertise in small molecule drug discovery has been proven.

Drug Discovery R&D: Pursuing Sustained Growth

Robust Drug Pipeline (as of Q1 2022)

Cancer

AS-1763

AS-0141

Licensed Program
(Lipid Kinase Inhibitor)
GILEAD

Licensed Program
(AS-1763 Greater China)
BioNova Pharmaceuticals

Immune-inflammatory diseases

AS-0871

Licensed Program
(STING antagonist)
BrickellBio

Joint Research
Sumitomo Dainippon Pharma

Next Generation Pipeline

Robust Drug Pipeline

<Oncology>

Compound	Target	Indication	Discovery/Preclinical	Clinical	Partner
AS-0141	CDC7/ASK	Cancer			
Small Molecule	Kinase	Immuno-Oncology	Out-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 Dainippon Pharma		Sumitomo Dainippon Pharma
AS-0871	BTK	Immune-inflammatory diseases			
Small Molecule	N/A	Malaria			
Small Molecule	STING	Immune-inflammatory diseases	Out-licensed to Gilead		BrickellBio

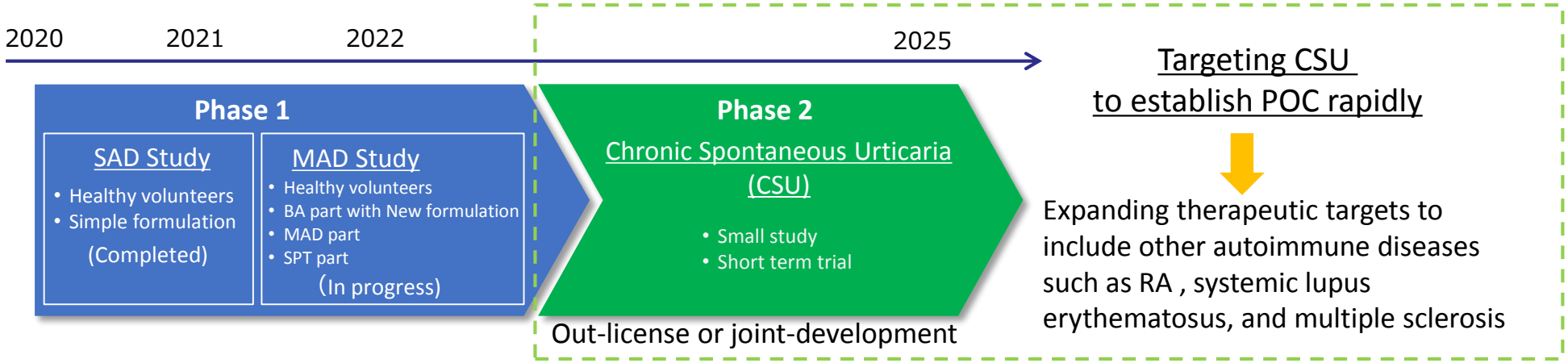
✓We are actively pursuing early discovery programs to create next wave of pipeline.

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



POC：Proof of Concept

AS-0871 : Phase 1 Clinical Trial in Progress

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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 several 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

SAD: Single Ascending Dose
MAD: Multiple Ascending Dose

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

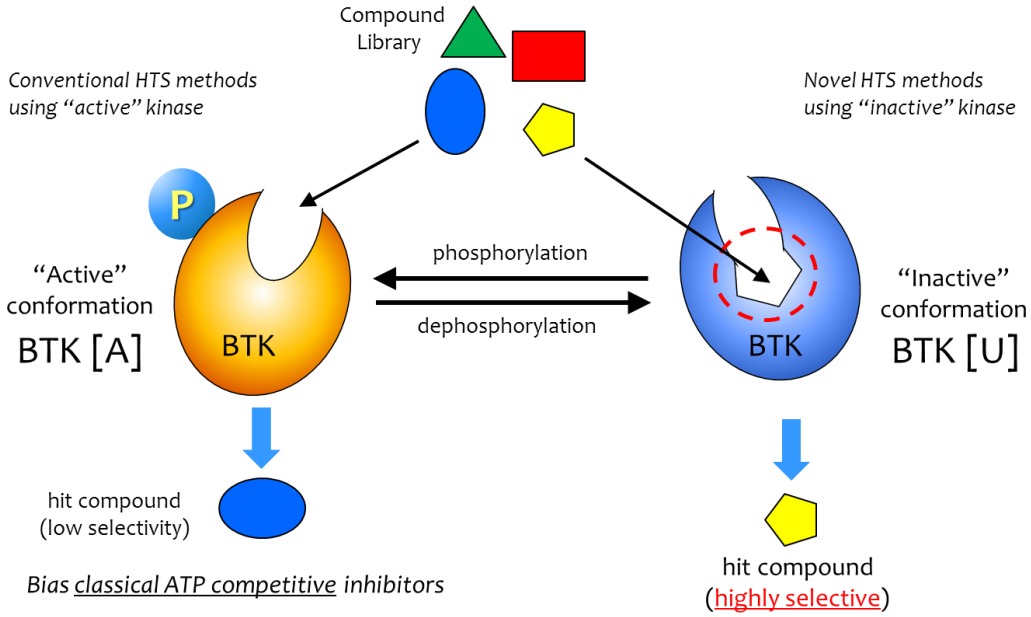
Article

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

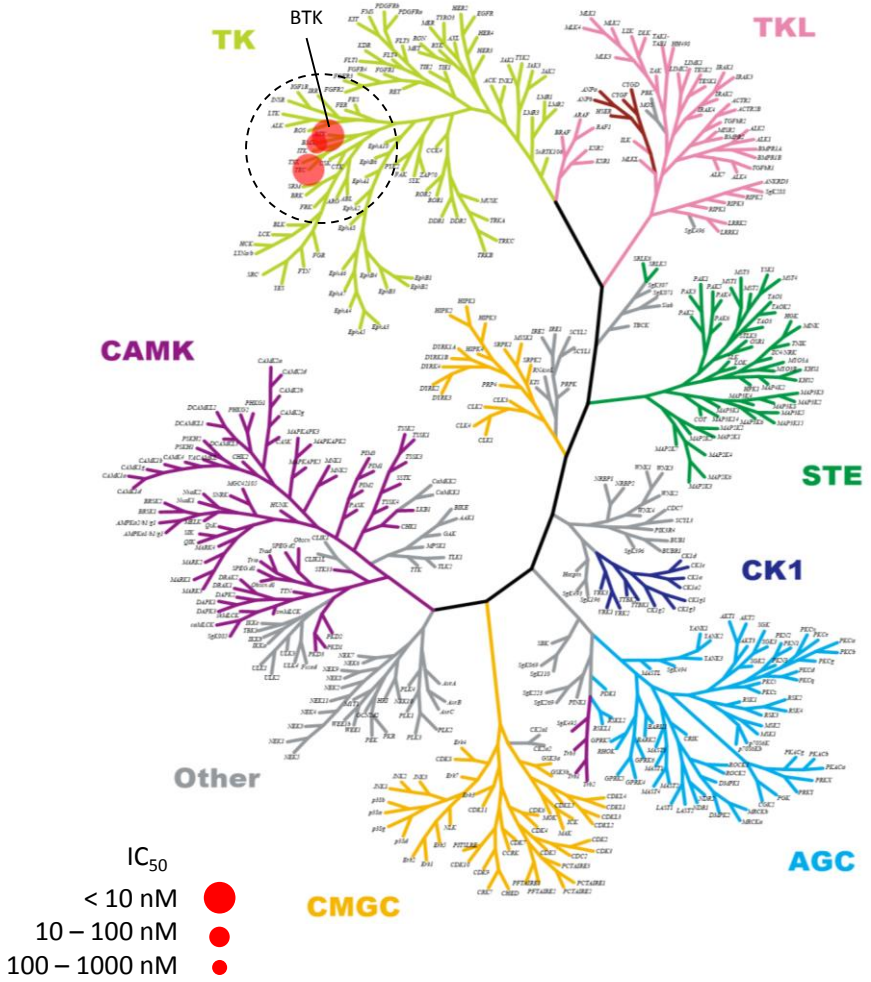


Bias classical ATP competitive inhibitors

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

◆ Kinase Selectivity Profiling

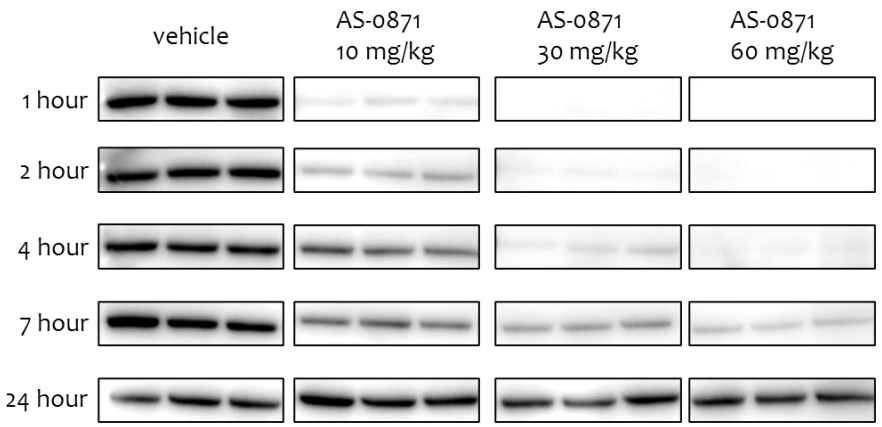
Only inhibited 2 other kinases in a total of 312 kinases tested at 0.3 μM concentration.

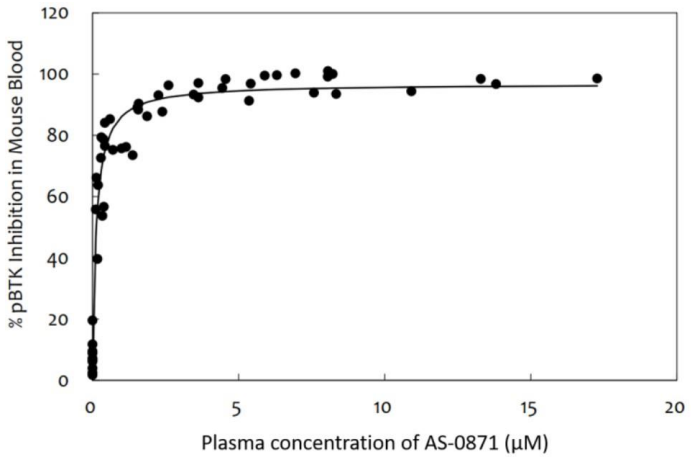


AS-0871: In Vivo Therapeutic Efficacy

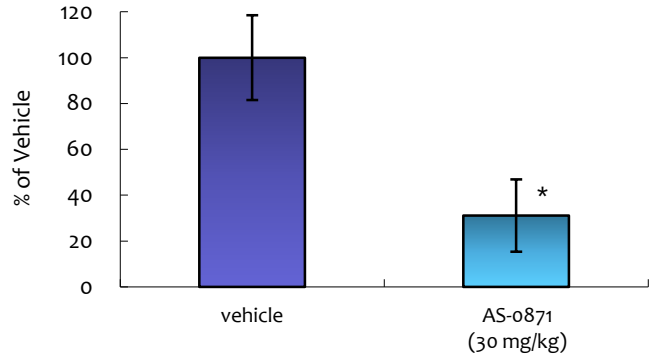
- PK/PD Study

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

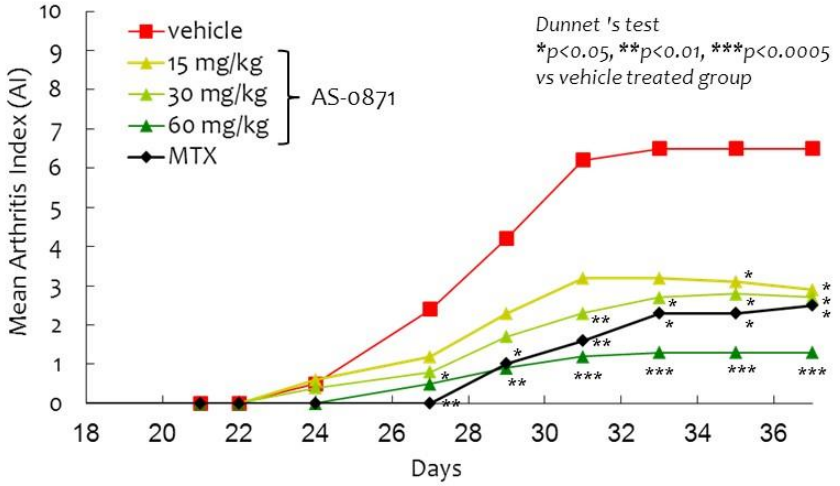




- Passive cutaneous anaphylaxis (PCA) mouse model (n=5)



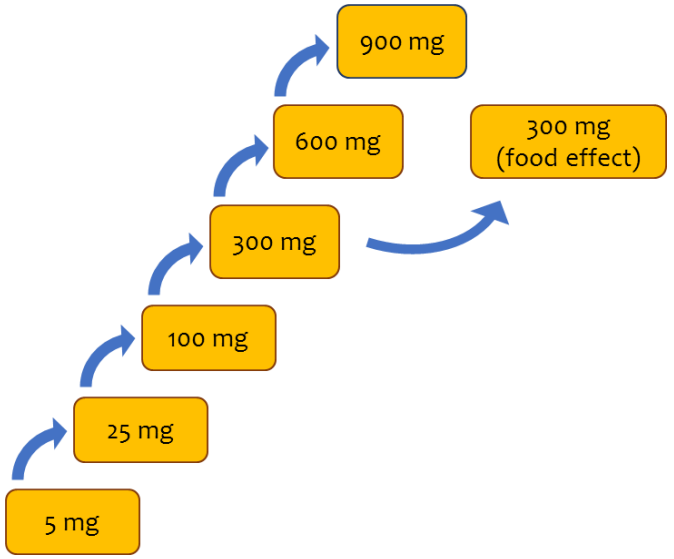
- Collagen-induced arthritis (CIA) mouse model (n=10)



AS-0871: FIH study

SAD Part (Completed)

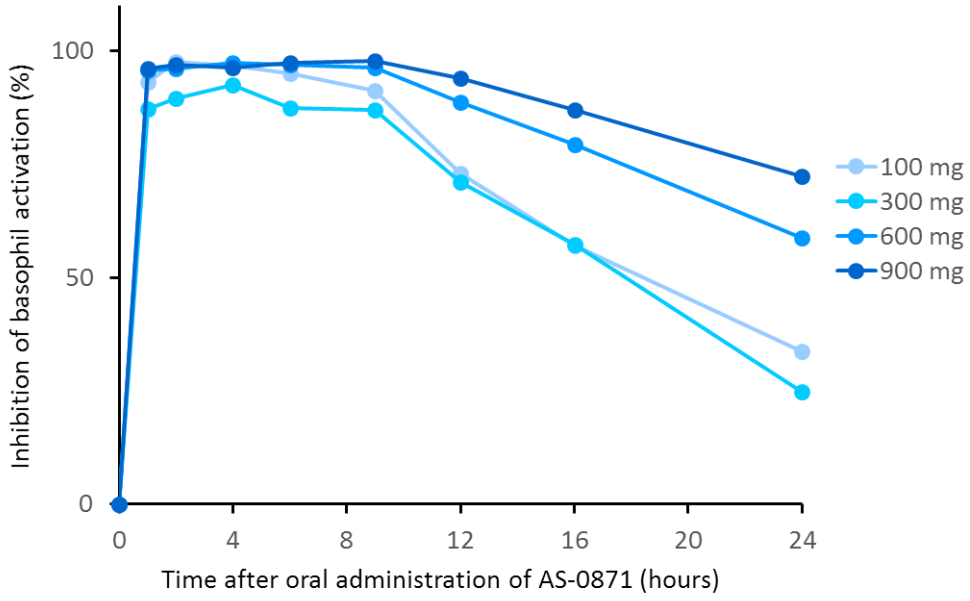
Step 1 Single Ascending Dose Study (SAD)	Step 2
• 6 dose levels (8 subjects/cohort) • Placebo controlled (6 active / 2 placebo) • Safety and tolerability • Pharmacokinetics and pharmacodynamics	• Food effect

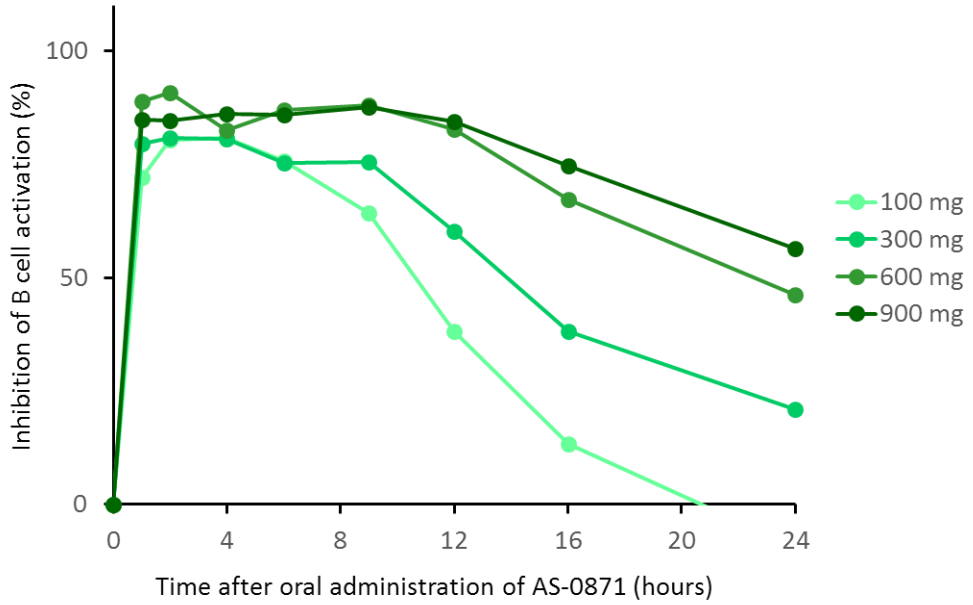


- ✓ AS-0871 is well-tolerated without any safety concerns.
- ✓ Favorable pharmacokinetic profile.
- ✓ Blood samples to assess PD effects were analyzed for evaluation of the B-cell and basophil responses. Administration of AS-0871 at 100mg or above resulted in strong inhibition of B-cell and basophil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



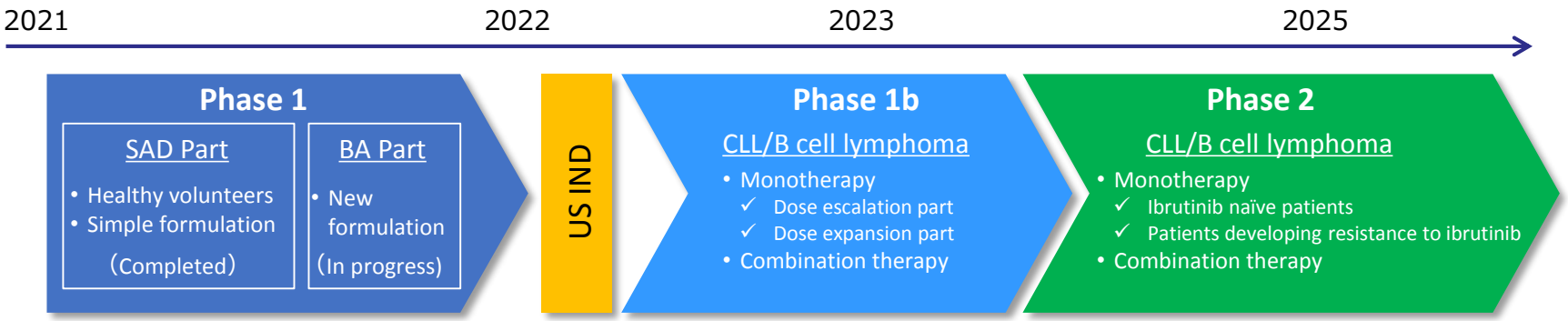


AS-1763：Next Generation BTK Inhibitor Targeting Blood Cancer

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



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

Completed

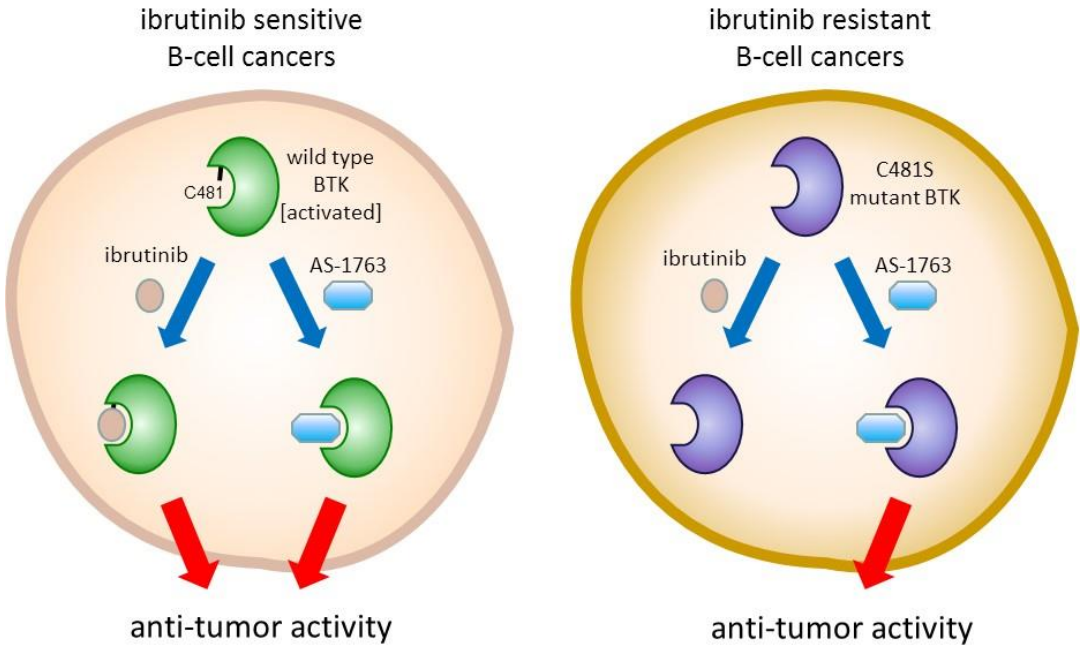
- ✓ Pre-IND meeting
- ✓ IND submission (in preparation)

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

- ◆ Plan to present the Phase 1 data at AACR2022
- ◆ Aim to conduct clinical studies efficiently, collaborating with BioNova

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

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◆ 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

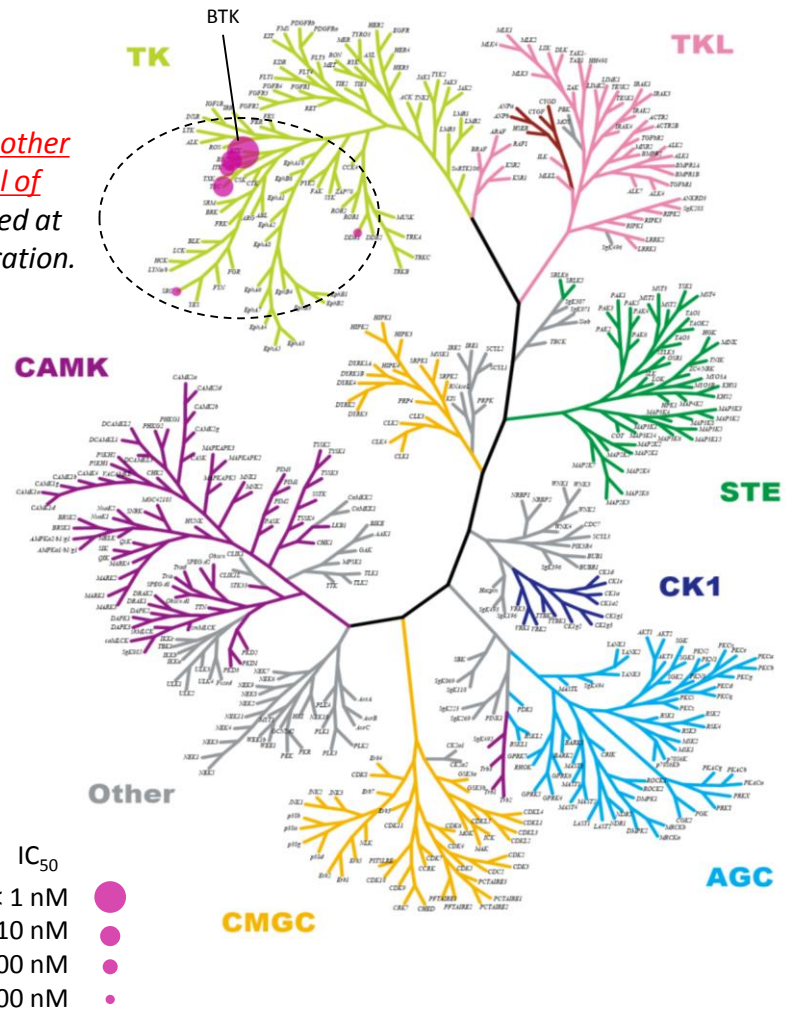
50-fold Stronger activity

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.

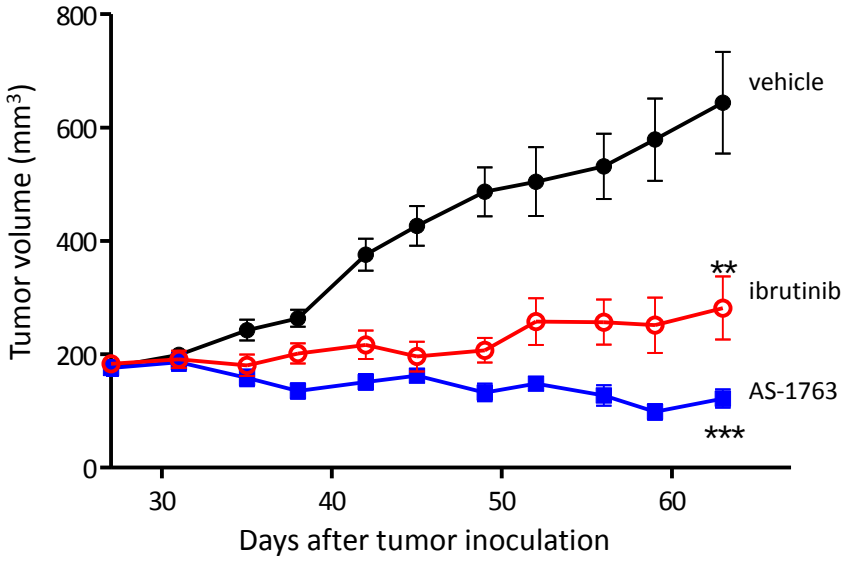
◆ Kinase selectivity profiling

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

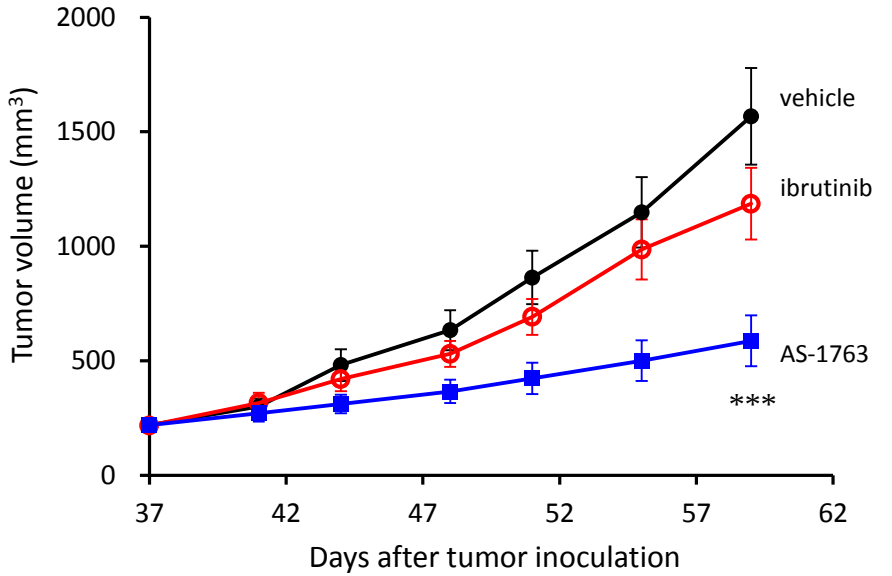
- In vivo antitumor effects of AS-1763 on human B-cell non-Hodgkin lymphoma cell line, OCI-LY10 tumor xenograft mouse model (n=8-10)



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)



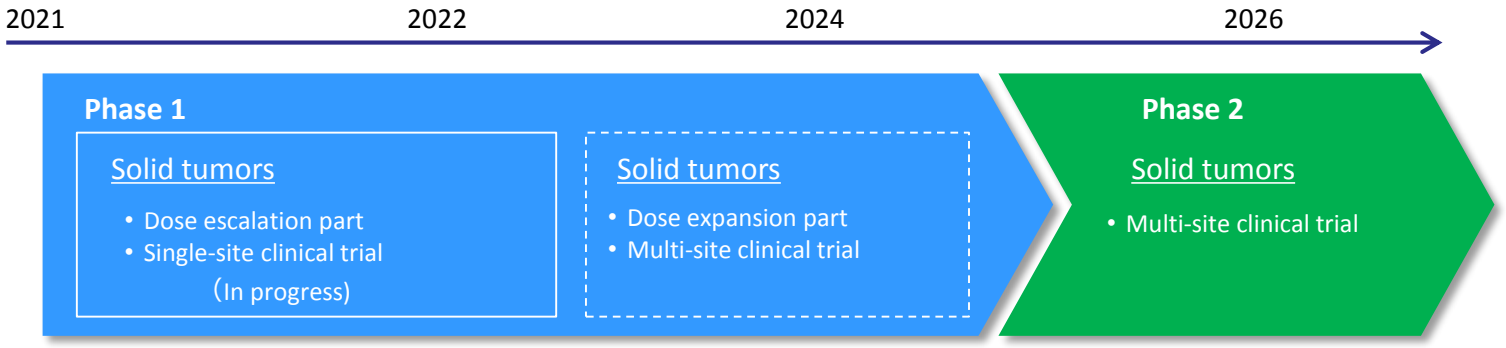
Ibrutinib: 25 mg/kg QD
AS-1763: 60 mg/kg BID

***: p<0.001

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

AS-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.
- ✓ The dose escalation part is ongoing.
- ✓ No dose-limiting toxicity (DLT) has been observed so far.
- ✓ Advanced to dose level 3 (Cohort 3) underway.

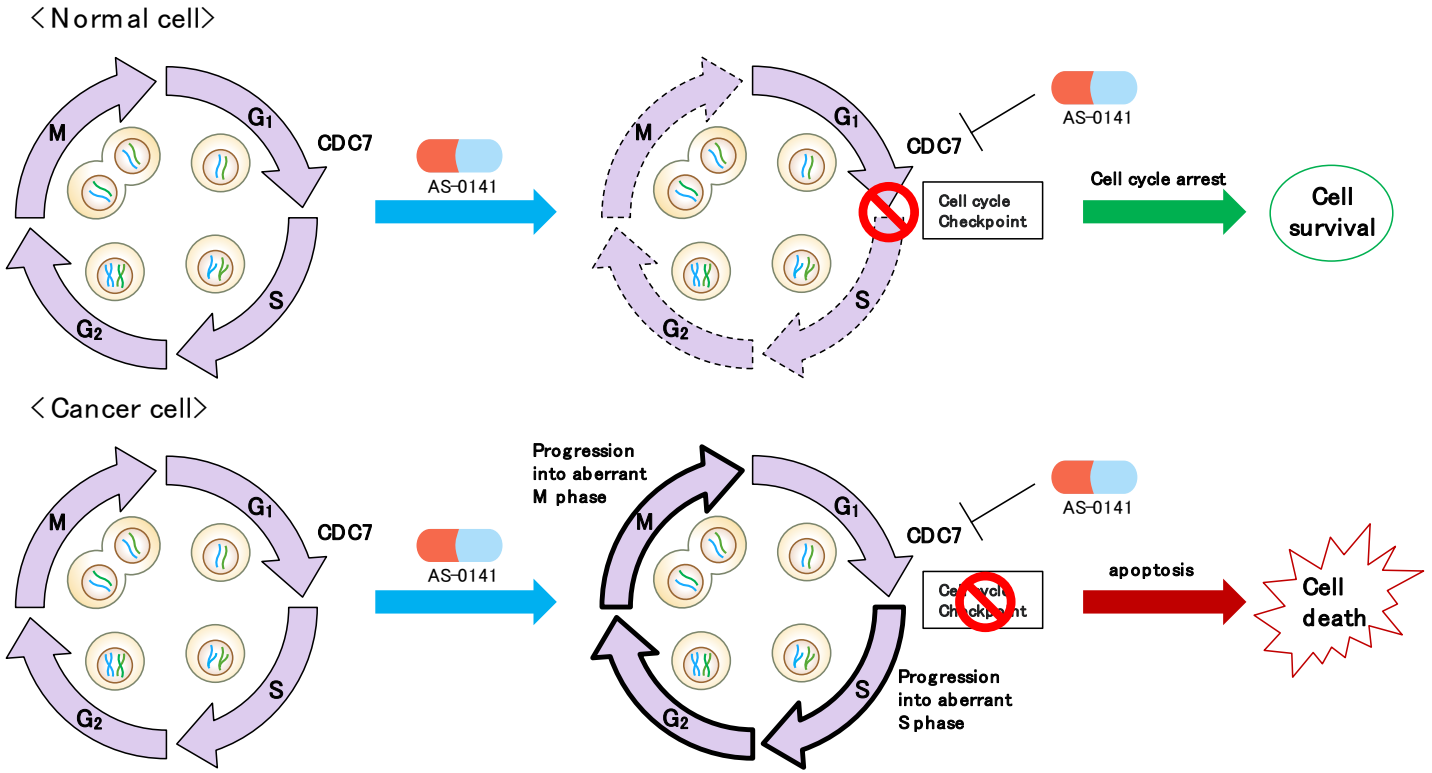
Clinical Development Plan

- ✓ Continuing dose escalation.
- ✓ Select dose level for expansion phase.
- ✓ Exploring multiple types of solid tumors.

AS-0141: Highly Selective CDC7 Inhibitor

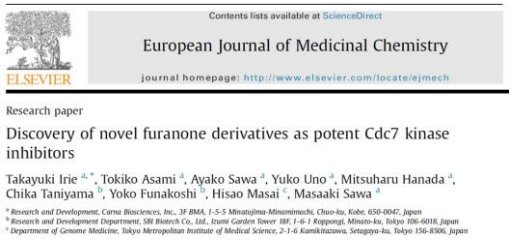
■ CDC7 kinase inhibitor

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)


Contents lists available at ScienceDirect

European Journal of Medicinal Chemistry

journal homepage: http://www.elsevier.com/locate/ejmech

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

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

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

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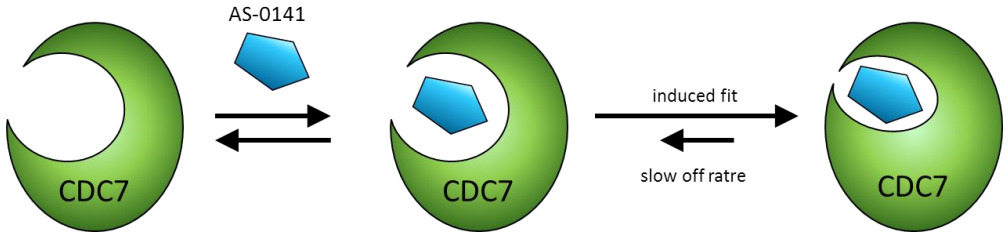


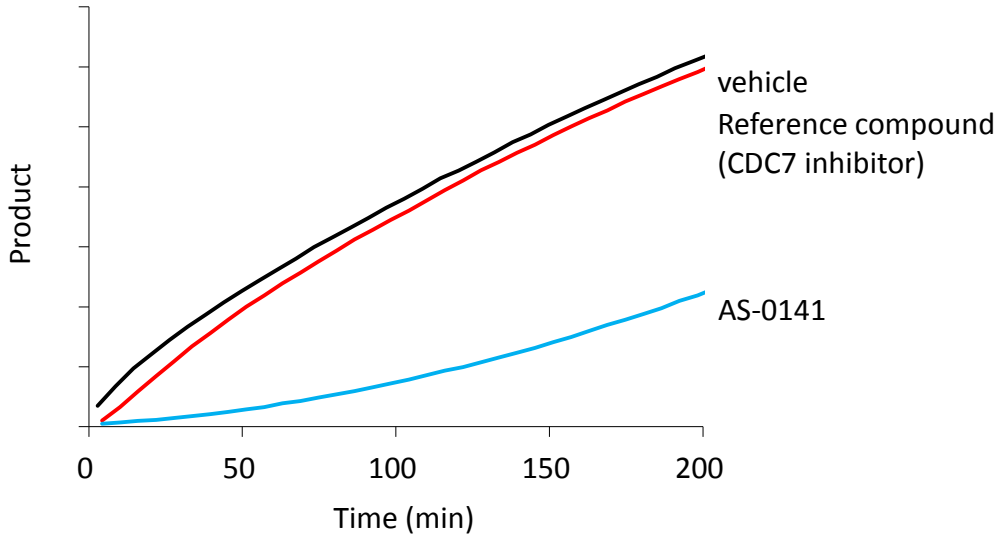
Inhibitory potency (IC_{50}) for CDC7 in the presence of 1 mM ATP

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

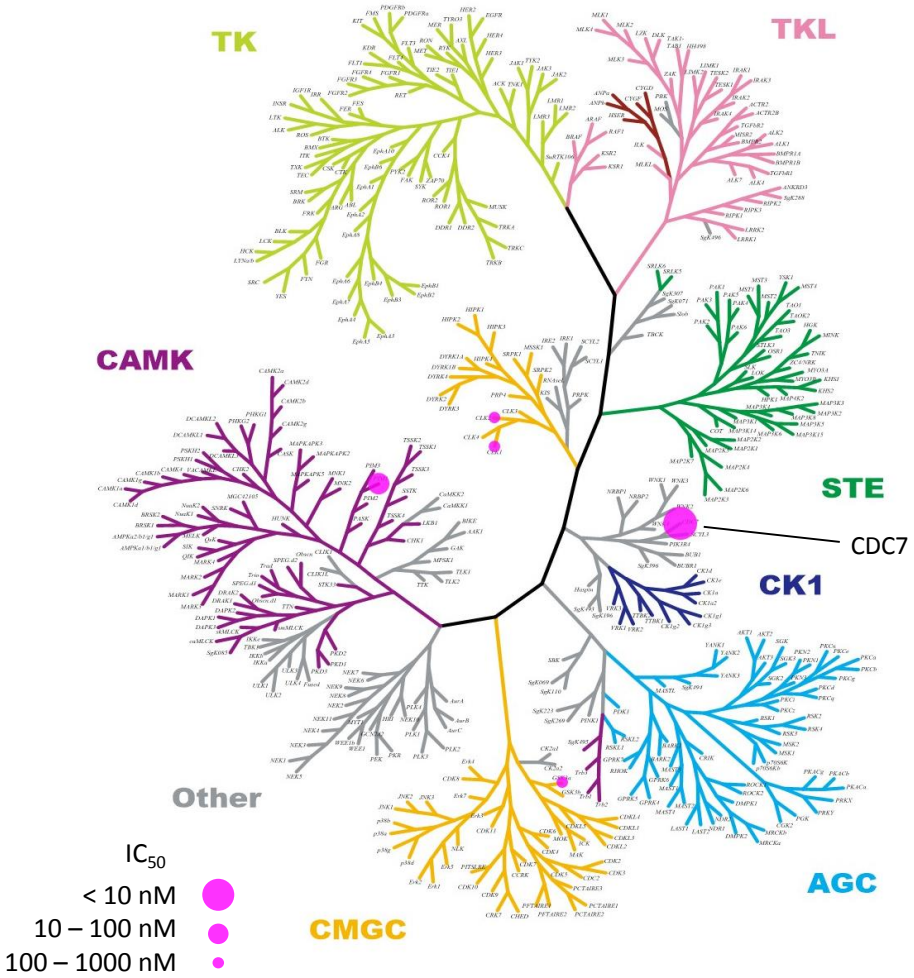
Rapid dilution assay for Cdc7 inhibitors. Recovery of enzymatic activity was monitored by formation of the phosphorylated product.



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)	
	Preincucabation	
	-	+
CDC7	503	2.4
PIM1	30	34
CLK1	212	206
CLK2	270	227
GSK3α	189	251

210-fold

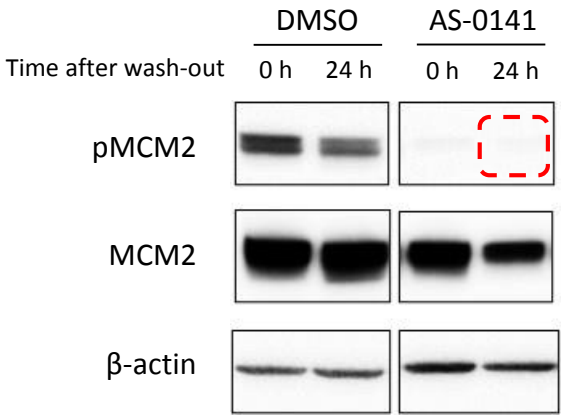
CDC7 is the only kinase that shows preincubation effect

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

AS-0141: Strong Cellular Activity

◆ Prolonged inhibition in cells

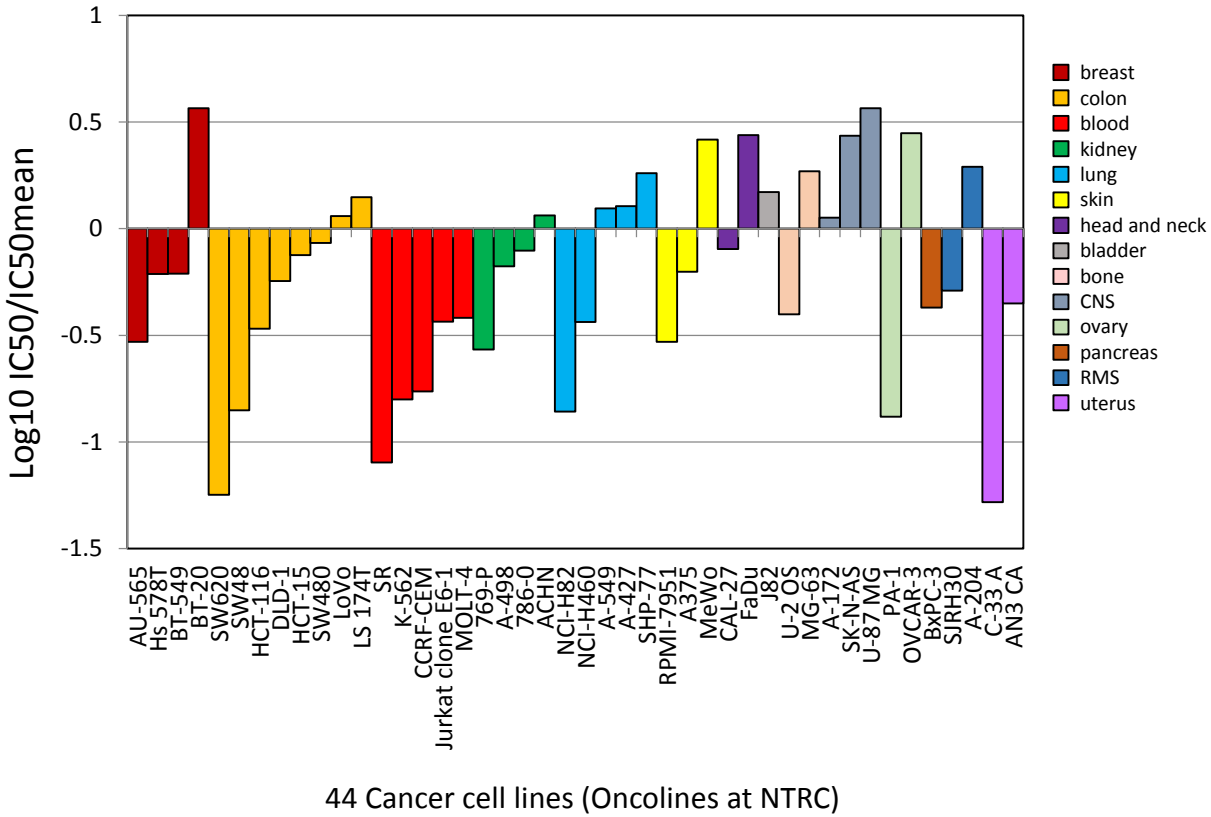
Human colon cancer cell line, Colo-205 cells were treated with DMSO control or AS-0141. After washout of the inhibitor, the cells were further incubated in the same media for 0 or 24 h and subjected to western blot analysis.



the inhibitory effect of AS-014 on the phosphorylation of MCM2 in cells continued up to 24 h after washing out

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

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

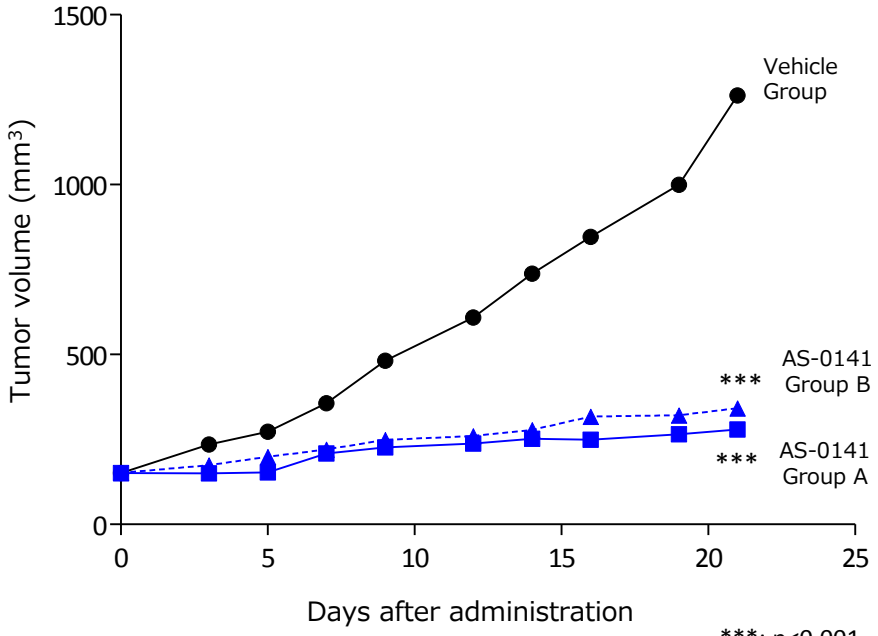


44 Cancer cell lines (Oncolines at NTRC)

AS-0141: Robust In Vivo Antitumor Efficacy

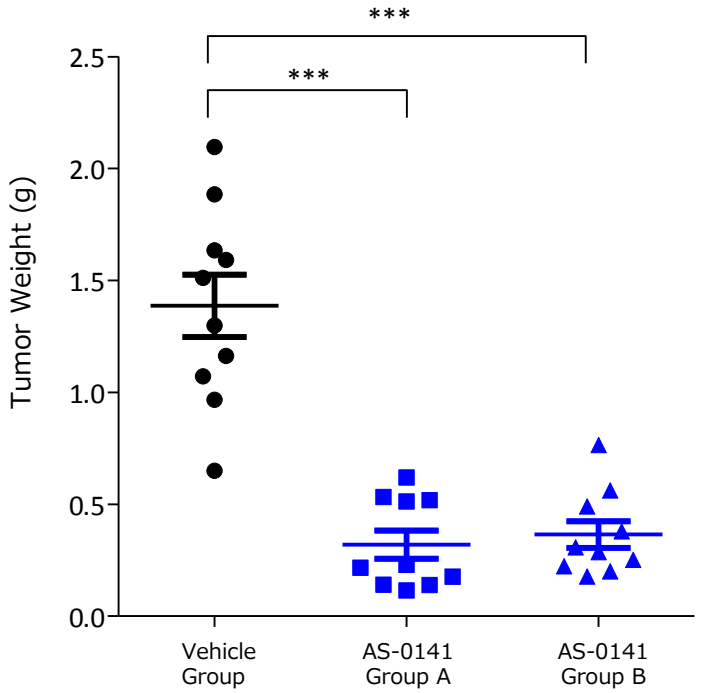
- In vivo antitumor efficacy of AS-0141 in a SW620 (human colon cancer) xenograft mouse model

Tumor Growth Curve (Mean, n = 10)



***: p<0.001

Final Tumor Weight of Each Mouse



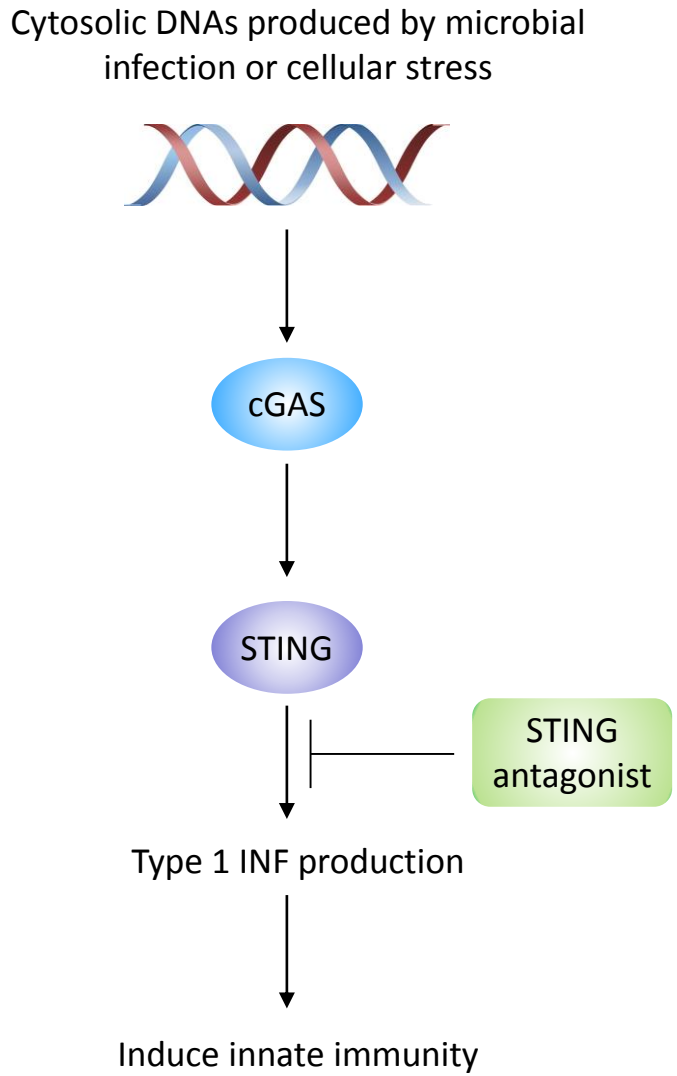
***: p<0.001

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.

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.

Discovery Support (ddSP) Business

Drug Discovery Support (ddSP) Business Key Highlights

- At ddSP, full year sales reached 96% of initial plan.
  - ✓ In North America, contribution from sales to Gilead continued.
  - ✓ In Japan, sales of kinase proteins were strong while profiling service and agent business (cell-based assay and X-ray crystallography) were weaker than expected. Weak agent business sales had limited impact on operating profit as the profitability of the agent business is relatively low.
  - ✓ In China, full year sales beat the initial plan although sales were temporarily affected in September and October by the delay in the import custom clearance due to COVID-19. Continue working closely with the agent to expand sales further.
- Robust start for the new service
  - ✓ Launched a full-panel assay service (192 kinds of kinases) for cell-based assay service using NanoBRET™ technology developed by Promega.
- Expanding lineup of kinase proteins and profiling service
  - ✓ 31 kinase protein products, including high-demand mutant kinase biotinylated kinases, have been newly added to the line-up.
  - ✓ 4 EGFR mutant targets were added to the profiling service.

FY2021 Financial Results

FY2021 Consolidated Financial Results

(JPY million)	FY2020 Actual	**FY2021 Actual**	YoY Change	FY2021 Initial Plan	FY2021 Dec. 23 Revised Plan	
Sales	1,133	**2,017**	+884 +78%	923	2,006	Sales were strong compared to the initial plan and the last year thanks to the first milestone from Gilead.
Operating Profit/Loss	(1,057)	**(531)**	+525	(1,811)	(548)	Operating loss was smaller compared to the initial plan and the last year thanks to milestone payment.
Ordinary Profit/Loss	(1,077)	**(522)**	+554	(1,816)	(552)	
Net Profit/ Loss	(1,111)	**(534)**	+576	(1,825)	(560)	
R&D Cost	1,474	**1,841**	+367 +24.9%	1,981	1,860	Investment in clinical studies.

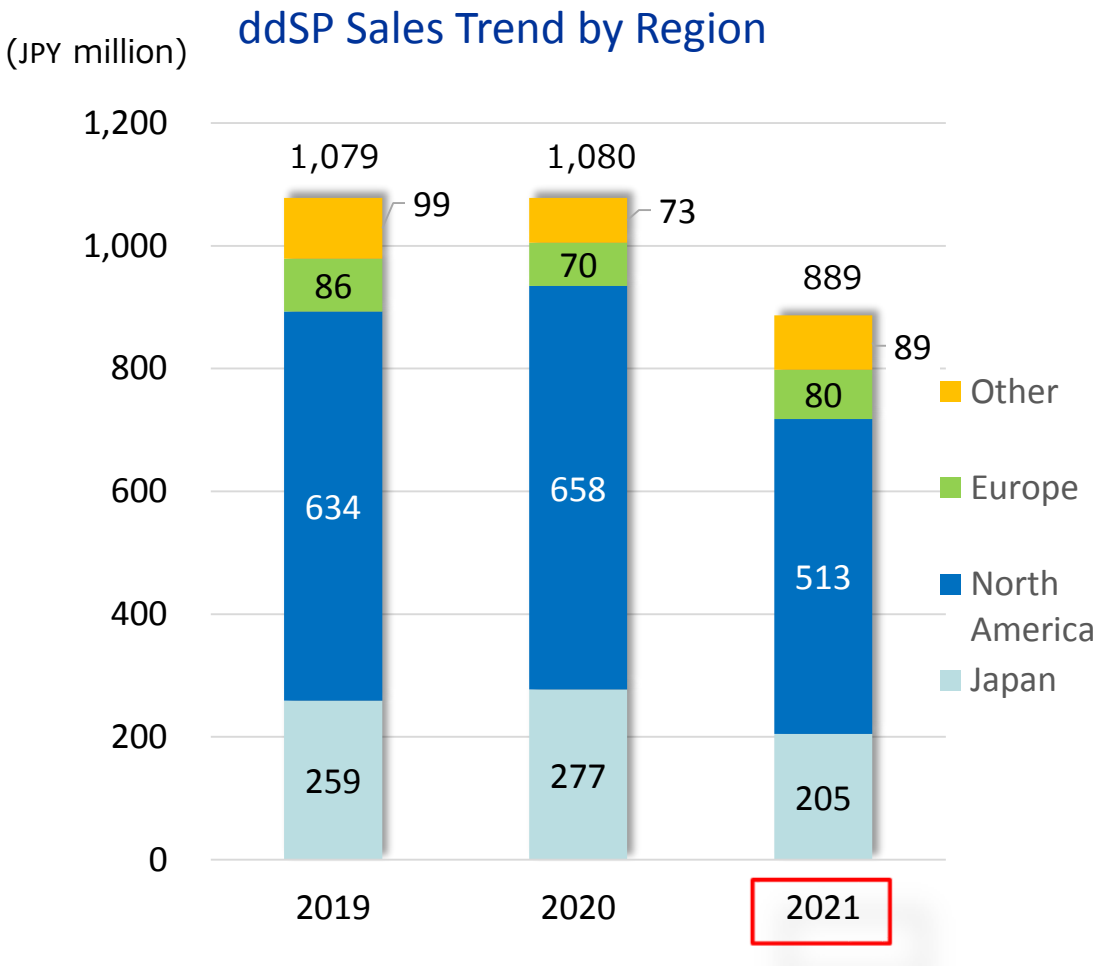
Note 1: Rounded down to the nearest million yen.
Note 2: YoY change % for Operating Profit/Loss, Ordinary Profit/Loss, and Net Profit/Loss are not presented since losses were recorded.
Note 3: FY2021 plan was disclosed on February 12, 2021. FY2021 plan was revised on Dec. 23, 2021.

FY2021 Results by Business Segment

(JPY million)	FY2020 Actual	**FY2021 Actual**	YoY Change	FY2021 Plan	FY2021 Dec. 23 Revised Plan	
Total Sales	1,133	**2,017**	+884 +78.0%	923	2,006	
ddSP business	1,080	**889**	(190) -17.7%	923	878	Slightly behind the FY sales plan due to weaker than expected sales in Japan.
ddRD business	53	**1,128**	+1,074 +2027%	—	1,128	Received milestone payment from Gilead.
Total Operating Profit/Loss	(1,057)	**(531)**	+525	(1,811)	(548)	
ddSP business	458	**289**	(169) -37.0%	207	288	Beat the initial plan thanks to robust sales of high-margin kinase proteins.
ddRD business	(1,515)	**(820)**	+695	(2,019)	(836)	Investment in clinical studies continued. Loss were smaller than the initial plan thanks to the milestone payment.

Note 1: Rounded down to the nearest million yen.
Note 2: YoY change % for consolidated operating profit/loss and ddRD operating profit/loss are not presented since since losses were recorded.
Note 3: FY2021 plan was disclosed on February 12, 2021. FY2021 plan was revised on Dec. 23, 2021.
Note 4: ddRD: Drug Discovery R&D business, ddSP: Drug Discovery Support Business

FY2021 Discovery Support (ddSP) Business Sales by Region



- Japan: Decreased 26.2% YoY
  - Sales of profitable kinase proteins were robust, offsetting weak profiling sales.
  - Agent business (cell-based assay service and X-ray crystallography) were weak but the impact on the operating profit was limited as its profitability is relatively low.
- North America: Decreased 21.9% YoY
  - Contribution from sales to Gilead continued.
  - NanoBRET assay service showed strong growth.
  - Agent business (cell-based assay service) were weak.
- Europe: Increased 14.3% YoY
  - Kinase proteins, profiling service and NanoBRET assay service were robust.
- Other: Increased 22.4% YoY
  - Full year sales were robust although sales in September and October were temporarily affected by the delay in the import custom clearance in China.

Consolidated Balance Sheet

(JPY million)	As of Dec. 31, 2020	As of Dec. 31, 2021	Change	Reason for changes
Current assets	4,708	5,318	+610	Accounts receivable-trade +1,114 Cash and deposits -481
Cash and deposits	4,299	3,817	-481	
Non-current Assets	127	114	-13	
Total assets	4,835	5,432	+597	
Current liabilities	727	774	+47	
Non-current liabilities	284	342	+58	Long term loans payable +88 Bonds payable -28
Total liabilities	1,011	1,116	+105	
Total net assets	3,824	4,315	+491	Capital stock and capital surplus +996, Retained earnings -534
Total liabilities and net assets	4,835	5,432	+597	

Shareholders' equity ratio	79.0%	79.3%
BPS	308.0 yen	323.5 yen
PBR	3.9x	3.4x
Share price of Carna	1,212 yen	1,102 yen

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

Business Plan for FY2022

Key Milestones for 2022

Business		Key Milestones		
		Milestones for 2021	Achievement in 2021	Next Milestones for 2022
ddRD	AS-0871	☐ Initiate Ph1 MAD part (H2 2021)	☑ Initiated Ph1 MAD part in Dec. 2021	☐ Start partnering activity
	AS-1763	☐ Initiate Ph1 (H1 2021)	☑ Initiated Ph1 in Apr. 2021	☐ Initiate Ph1b (US)
	AS-0141	☐ Initiate Ph1 (H1 2021)	☑ Initiated Ph1 in June 2021	☐ Initiate Ph1 expansion part
	Research program	☐ Bring one or more programs in preclinical stage	☑ STING antagonist was advanced to preclinical stage	☑ Bring one or more programs in preclinical stage or license a program.
ddSP		☐ Achieve sales target of JPY920 mn ☐ Launch new products ☐ Expand NanoBRET service ☐ Propose project-based service to collaborate with clients, leveraging Carna's drug discovery technology	☐ Actual sales were JPY889 mn, 96% of initial target ☑ Launched 31 new kinase protein products and 4 new EGFR mutant targets to profiling service ☑ Expand NanoBRET service ☐ Propose project-based service to collaborate with clients, leveraging Carna's drug discovery technology	☐ Expand sales of in-house developed products and services ☐ Expand line-up of protein kinase products ☐ Increase target kinases to expand profiling service ☐ Seek collaboration opportunities to boost Carna's business

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

☑ Achieved
☐ Plan or to be achieved

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-0871, AS-1763, and AS-0141 • 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-0871, AS-1763, and 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)	FY2021 Actual	**FY2022 Plan**	**Outlook for 2023 - 2026**
Total Sales	2,017	**1,127**	
ddSP business	889	**900**	Maintain stable sales
ddRD business	1,128	**227**	Revenue from milestone payments and upfront payments
Total Operating Loss	(531)	**(1,730)**	
ddSP business	289	**300**	Maintain stable profit while investing in product developments
ddRD business	(820)	**(2,031)**	Continue to invest in R&D and deliver profits depending on the size of milestone payments and upfront payments
Ordinary Loss	(522)	**(1,744)**	
Net Loss	(534)	**(1,799)**	

(JPY million)	FY2021 Actual	**FY2022 Plan**	**Outlook for 2023 – 2026**
R&D Cost	1,841	**2,166**	Invest in R&D (JPY1 bn to 2.5 bn) for the future growth.
Capex	41	**124**	Invest in equipment for R&D and IT system (JPY20 mn to 100 mn)

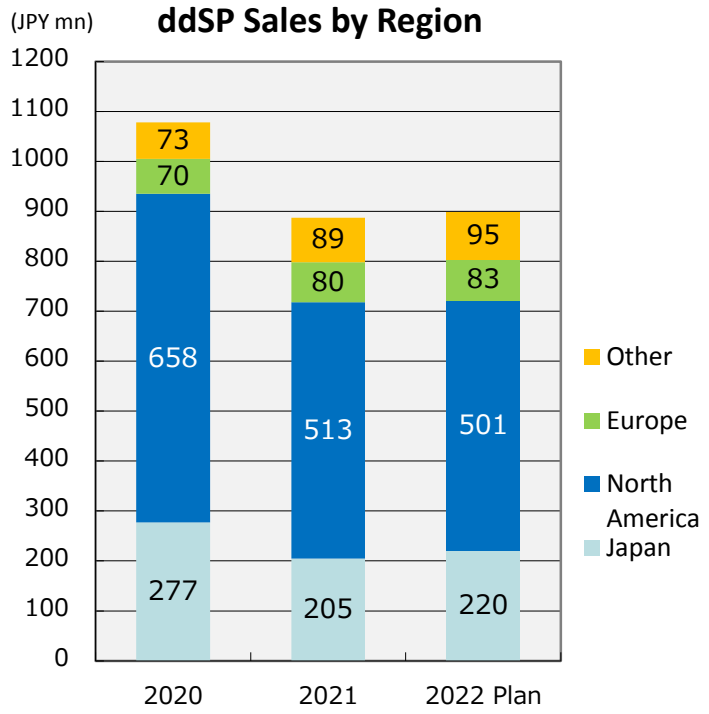
* Business plan for FY2022 includes an upfront payment from Brickell Biotech but does not include milestone payments and upfront payments related to other license agreements as the timing or the amounts are difficult to predict. Numerical targets for 2023-2026 are not disclosed for the same reason.

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

Drug Discovery Support (ddSP) Business: Sales by Region

(JPY mn)	FY2020 Actual	FY20201 Actual	FY2022 Plan
ddSP	1,080	889	**900**
Kinase Proteins	276	323	**372**
Assay Development	433	274	**184**
Profiling & Screening	230	203	**222**
Cell-based Assay	46	57	**96**
Cell-based Assay (agent business)	67	12	**10**
Others	23	17	**13**

Exchange rate(US$):	106.77 yen	109.90 yen	**110 yen**
% of Overseas sales:	74.3%	76.9%	**75.5%**



Note: Actual foreign exchange rate is average rate of the term

"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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