Financial Results
FY2022
(January to December 2022)

Carna Biosciences, Inc.

February 10, 2023

Stock Code: 4572

FY2022 Key Highlights

Drug Discovery

- AS-1763
  - ✓ Completed an IND process to initiate the Phase 1b study in the U.S.
  - ✓ BioNova completed an IND process in China and Carna received the first milestone payment.
- AS-0871
  - ✓ Successfully developed a new tablet formulation and initiated the BA part of the Phase 1 MAD study using the new tablet formulation.
- New pipeline
  - ✓ Licensed the STING antagonist program to Fresh Tracks Therapeutics (FRTX).

Drug Discovery Support

- ✓ Achieved record-high sales of JPY1,100 mn.

Corporate

- ✓ Issued Series 20th Subscription Rights Shares.

IND : nvestigational New Drug Application
MAD : Multiple Ascending Dose
BA : Bbioavailability

Key Milestones for 2022

Business		Milestones for 2022	Achievement in 2022
ddRD	AS-0871	☐ Start partnering activity	☑ Started partnering activity
	AS-1763	☐ Initiate Ph1b (US)	☑ Completed IND (US) ☐ FPI is expected in Q1 2023
	AS-0141	☐ Initiate Ph1 expansion part	☑ Switched to 3+3 design in Ph1 dose escalation part ☐ Plan to initiate Ph1 expansion part in H2 2023
	Research program	☐ Bring one or more programs in preclinical stage or license a program.	☑ STING antagonist was licensed to FRTX
ddSP		☐ 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	☑ Strong sales in North America and Asia. ☑ Launched 36 new kinase protein products ☑ Added 5 new PIK3 mutant targets to profiling service and 12 new targets to 1 mM assay ☑ Started discussion with potential collaboration partners

ddRD: Drug Discovery R&D business
ddSP: Drug Discovery Support Business
FPI: First Patient In

☑ Achieved
☐ Plan or to be achieved

Drug Discovery R&D (ddRD) Business

FY2022 Key Highlights for Drug Discovery R&D

◆ AS-1763

- ✓ IND was approved in the U.S. to initiate the Phase 1b study.
- ✓ FPI is expected in Q1 2023 in the U.S.
- ✓ The patent was registered in Japan.
- ✓ Presented new preclinical and clinical data in two poster presentations at American Association for Cancer Research (AACR) annual meeting 2022.
- ✓ IND was approved in China and received the first milestone payment from BioNova.

◆ AS-0871

- ✓ Successfully developed a new tablet formulation and initiated the BA part of the Phase 1 MAD study using the new tablet formulation.

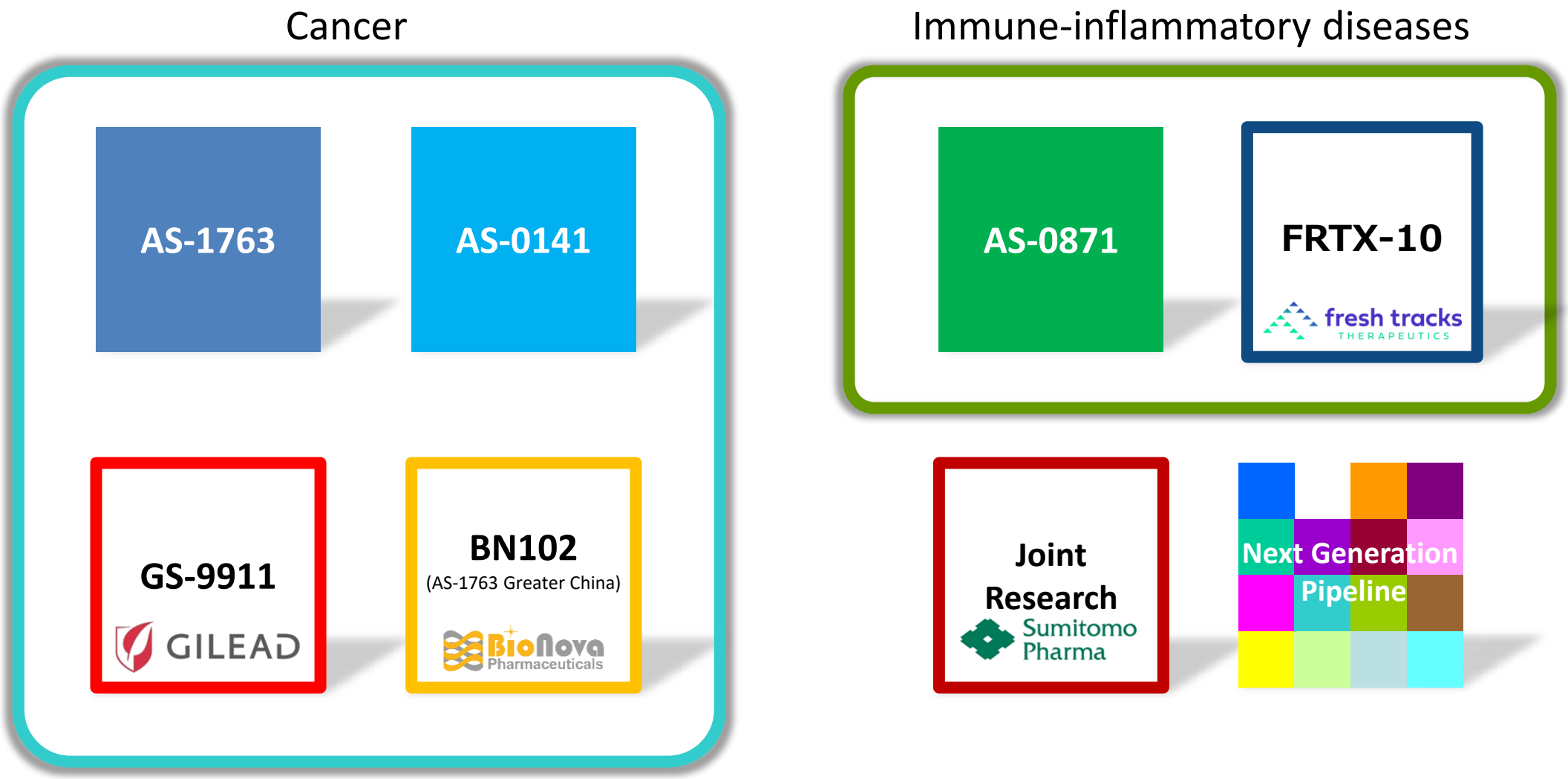
◆ AS-0141

- ✓ Ongoing Phase 1 dose escalation in solid tumors.
- ✓ The dose escalation was initiated with an accelerated titration design, and currently switched to a standard 3+3 design.

◆ New pipeline

- ✓ 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.
- ✓ STING antagonist: Licensed to FRTX.

Drug Discovery R&D: Pursuing Sustained Growth



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 February 2023

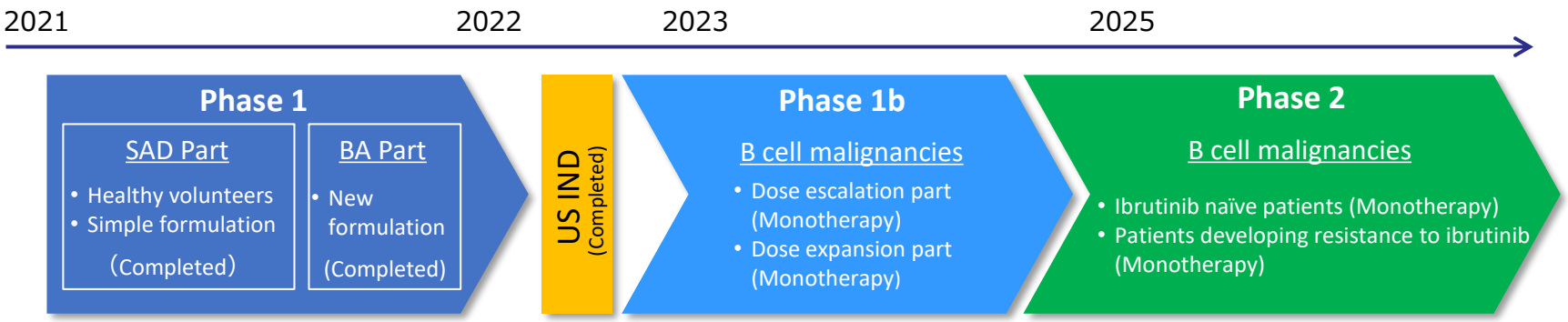
✓ We are actively pursuing early discovery programs to create next wave of pipeline.

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.
- FPI in the U.S. is expected in Q1 2023.
- Plan to accelerate the clinical studies utilizing the clinical data of BioNova, the licensee in Greater China



IND application: Investigational New Drug application
FPI: First Patient In
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 Evaluated comparative bioavailability using new formulation

- ✓ Pre-IND meeting
- ✓ IND submission

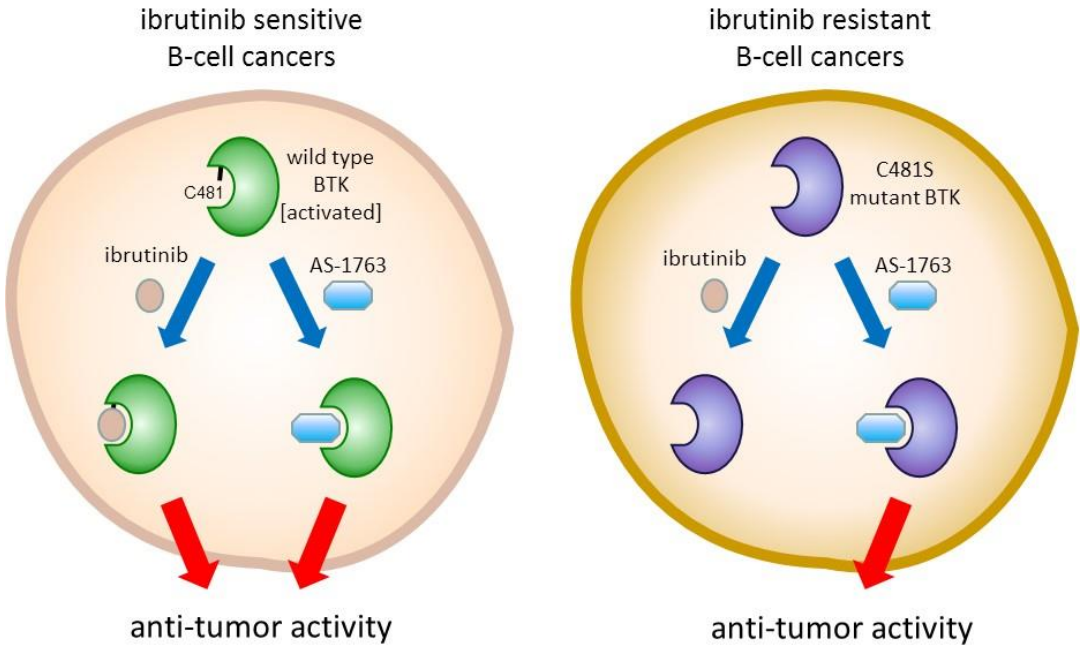
Completed

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

In preparation

- In May, Carna received an approval for an IND to initiate Phase 1 study in the U.S.
- FPI in the U.S. is expected in Q1 2023.

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

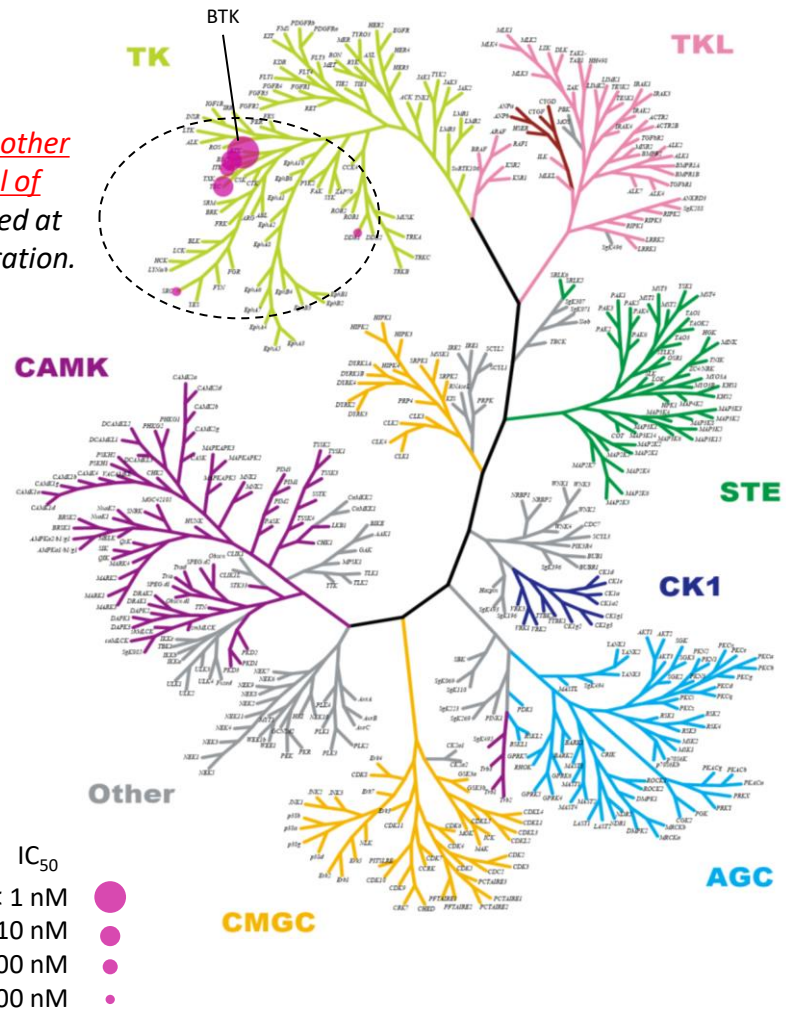
50-fold Stronger activity

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.

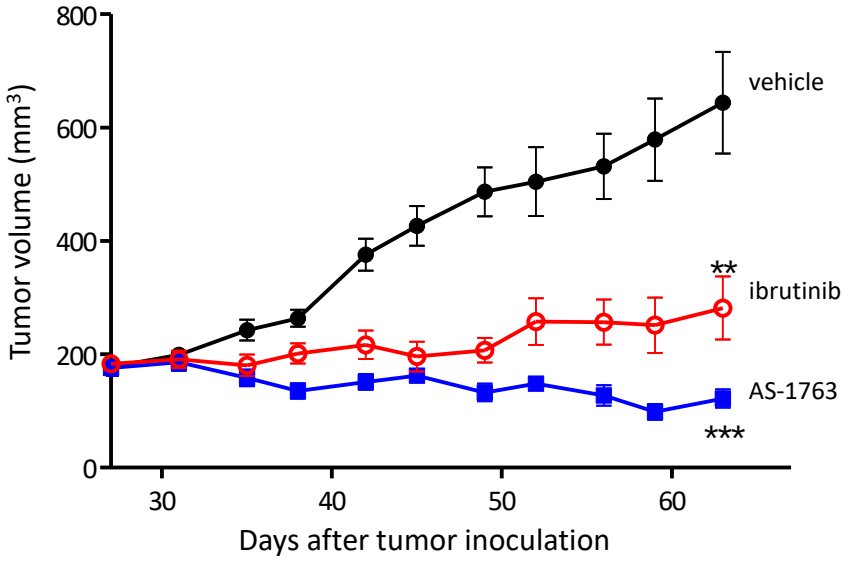
◆ Kinase selectivity profiling

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

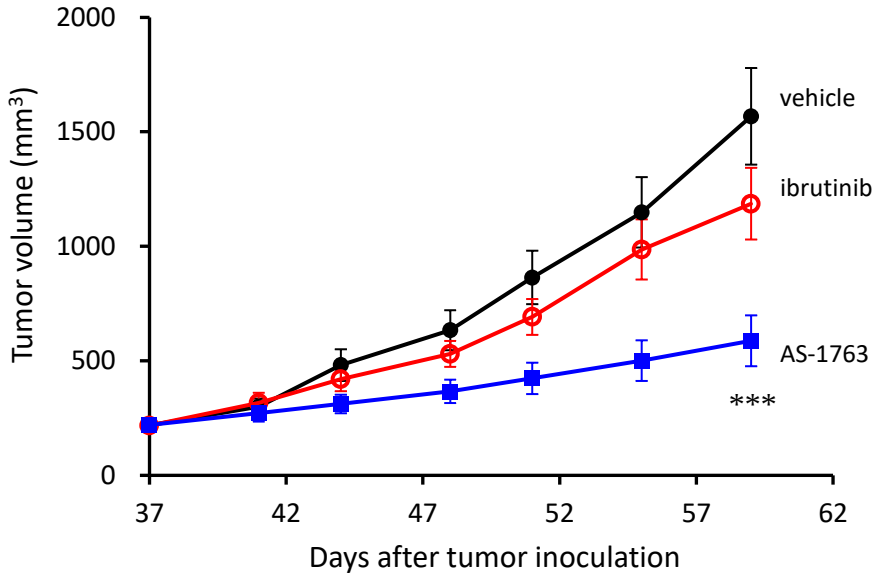
- In vivo antitumor effects of AS-1763 on human B-cell non-Hodgkin lymphoma cell line, OCI-LY10 tumor xenograft mouse model (n=8-10)



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

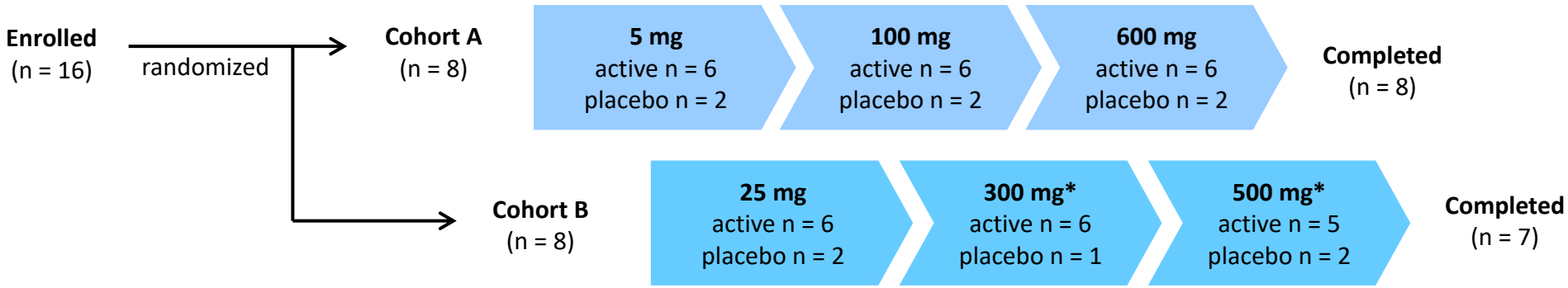
***: p<0.001

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

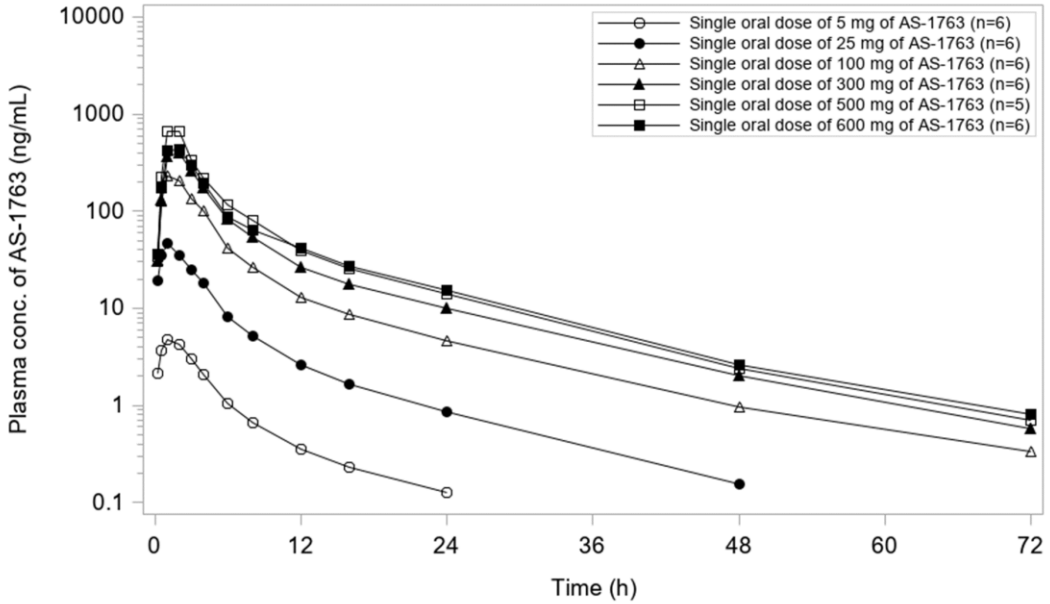
<Safety and tolerability>

- 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.

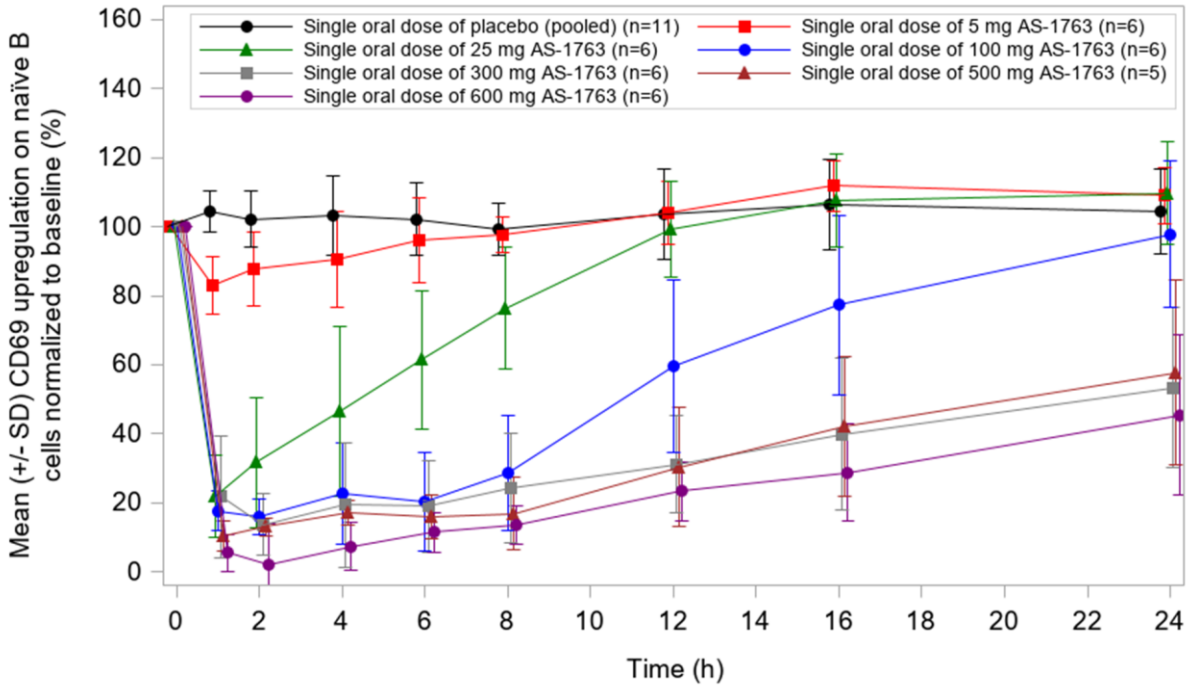
<Plasma concentration of a Single oral dose AS-1763>



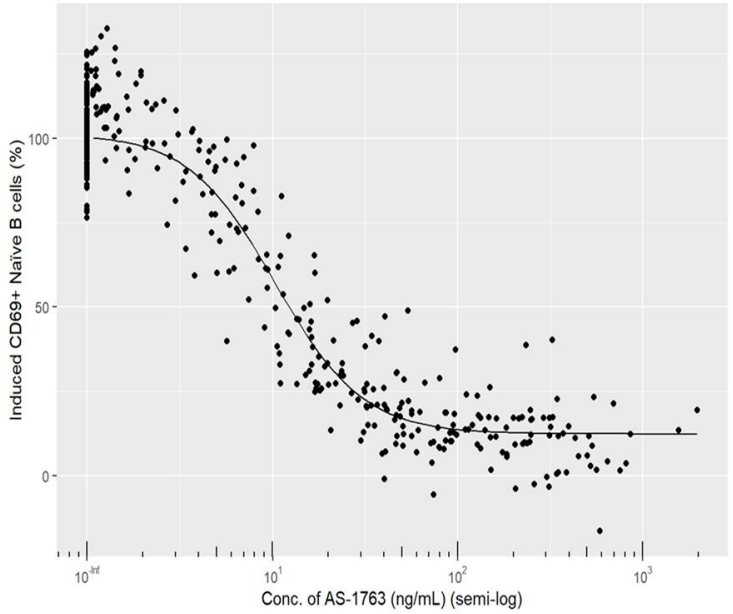
Pharmacodynamics of AS-1763

- 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>



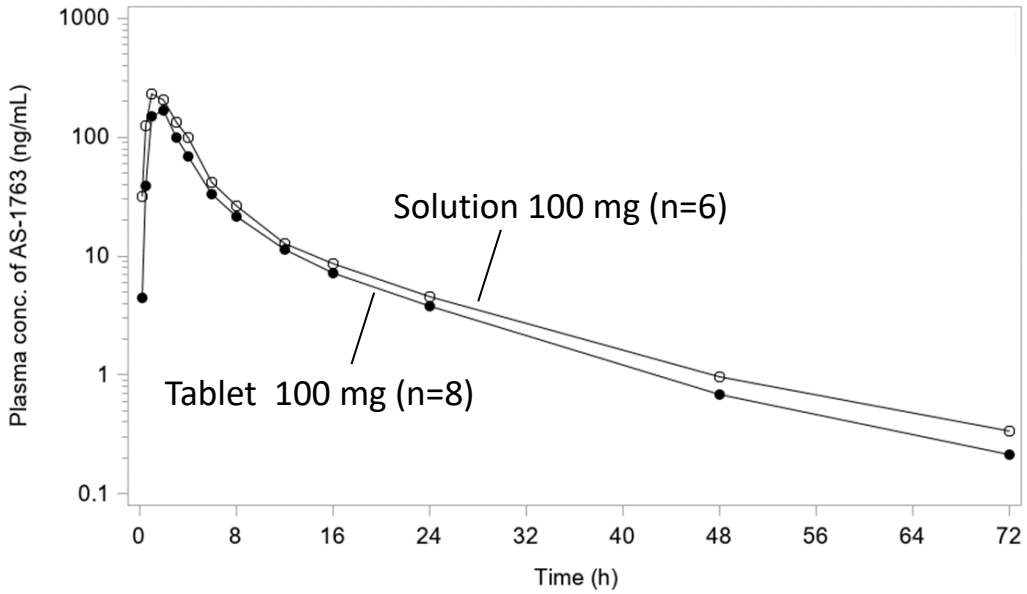
<PK/PD Correlation Analysis>



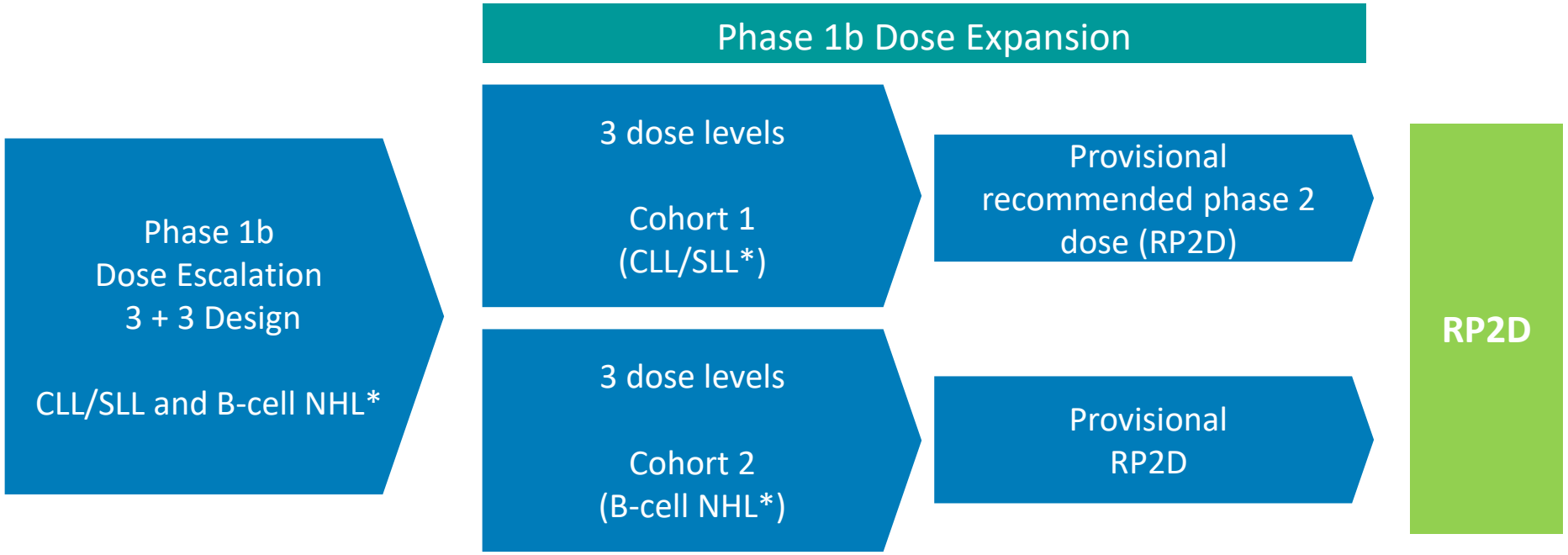
AS-1763: BA Part

- 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

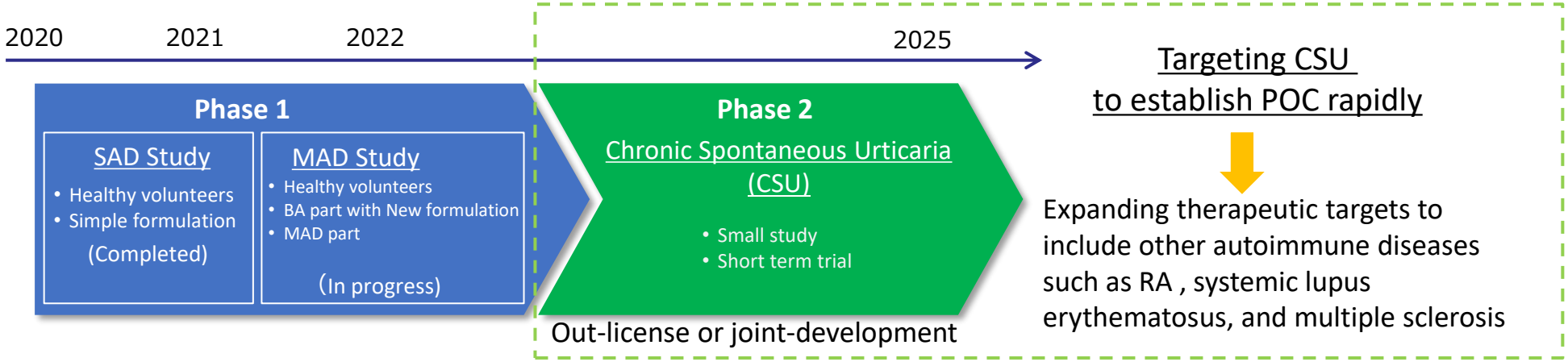
- FPI in the U.S. is expected in Q1 2023.

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
- Phase 1 MAD study is in progress
- 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)

Completed

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

Ongoing

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

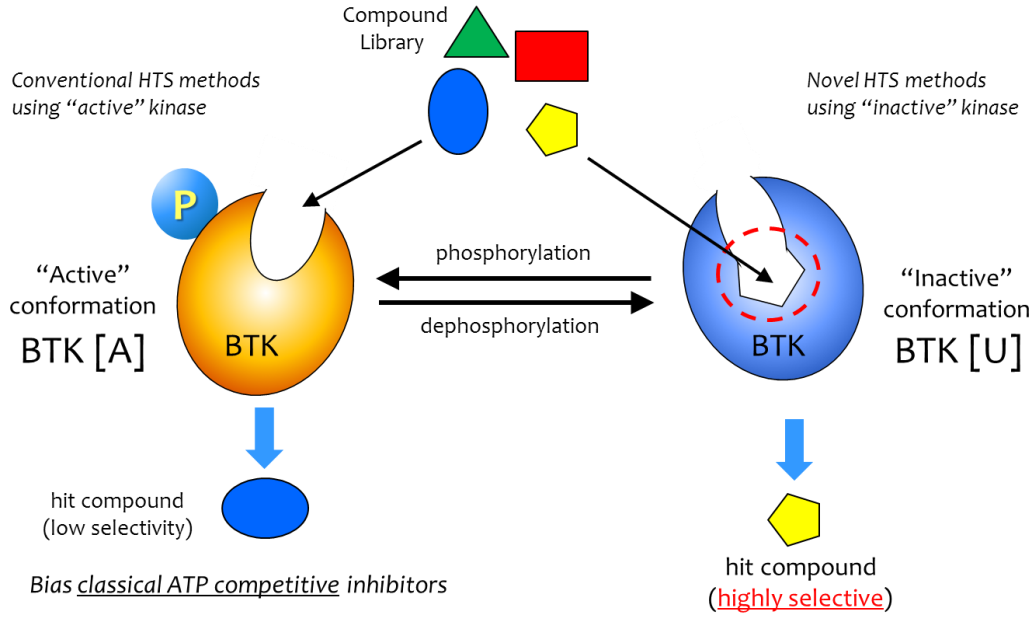
Article

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

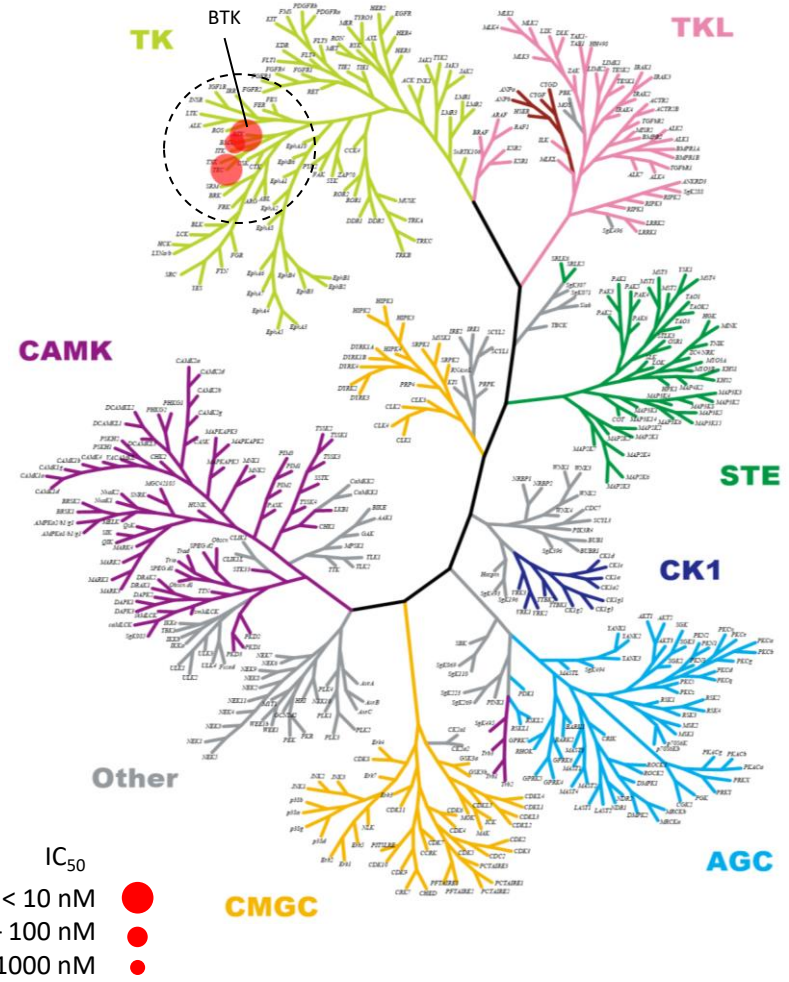


Bias classical ATP competitive inhibitors

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

◆ Kinase Selectivity Profiling

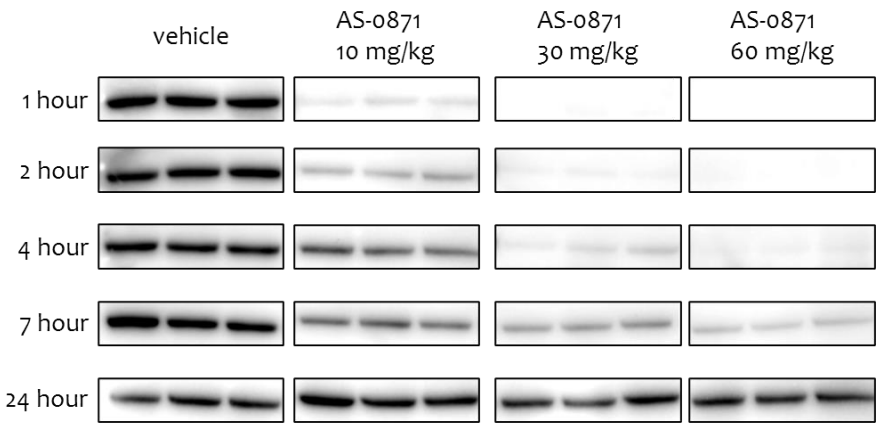
Only inhibited 2 other kinases in a total of 312 kinases tested at 0.3 μM concentration.

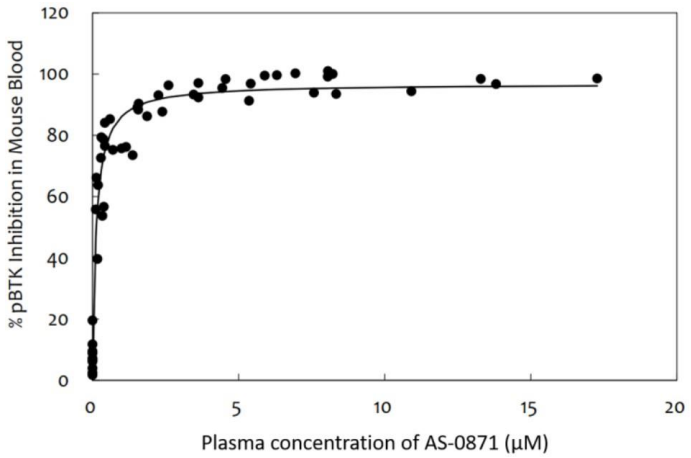


AS-0871: In Vivo Therapeutic Efficacy

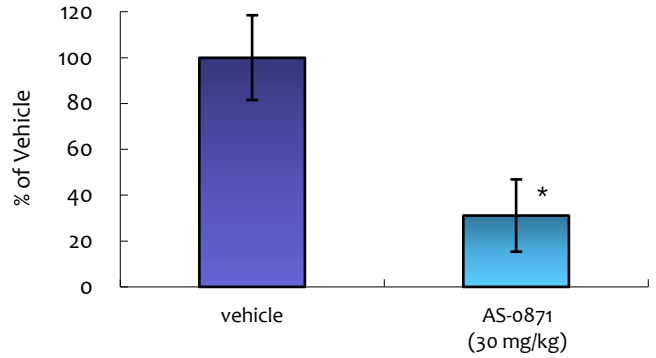
- PK/PD Study

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

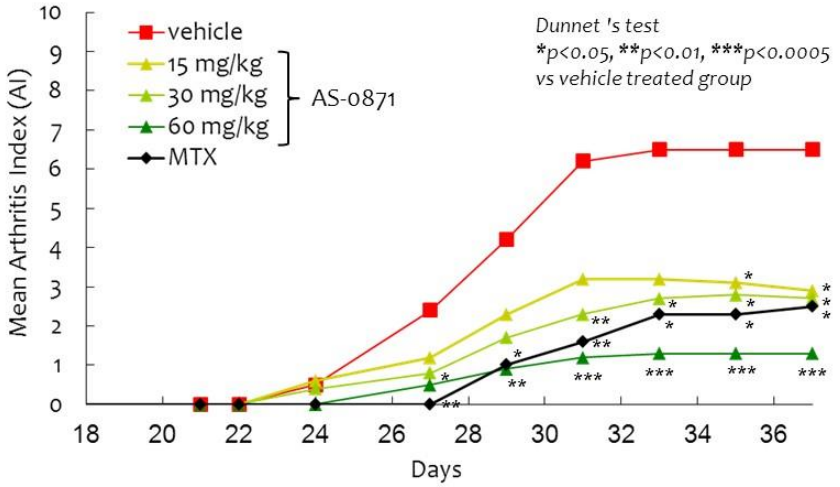




- Passive cutaneous anaphylaxis (PCA) mouse model (n=5)



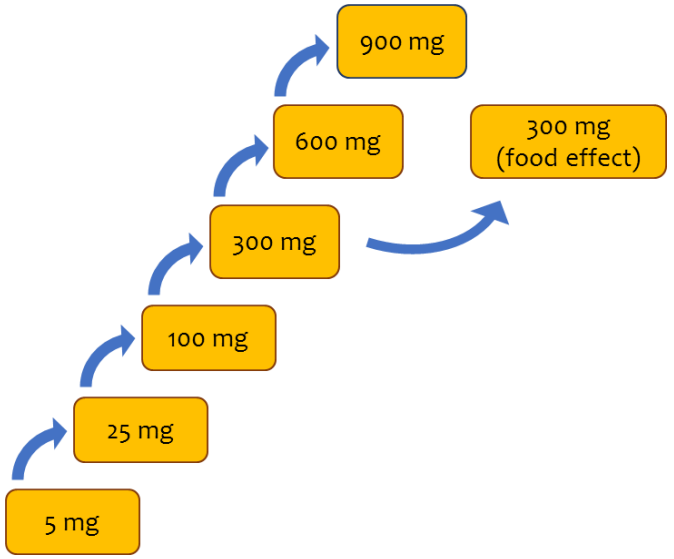
- Collagen-induced arthritis (CIA) mouse model (n=10)



AS-0871: FIH study

SAD Part (Completed)

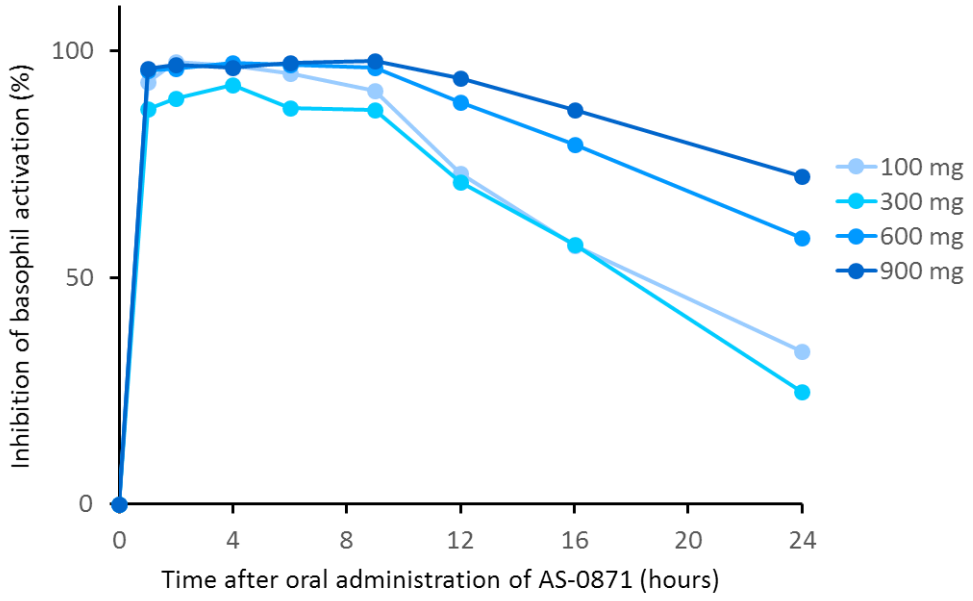
Step 1	Step 2
• 6 dose levels (8 subjects/cohort) • Placebo controlled (6 active / 2 placebo) • Safety and tolerability • Pharmacokinetics and pharmacodynamics	• Food effect

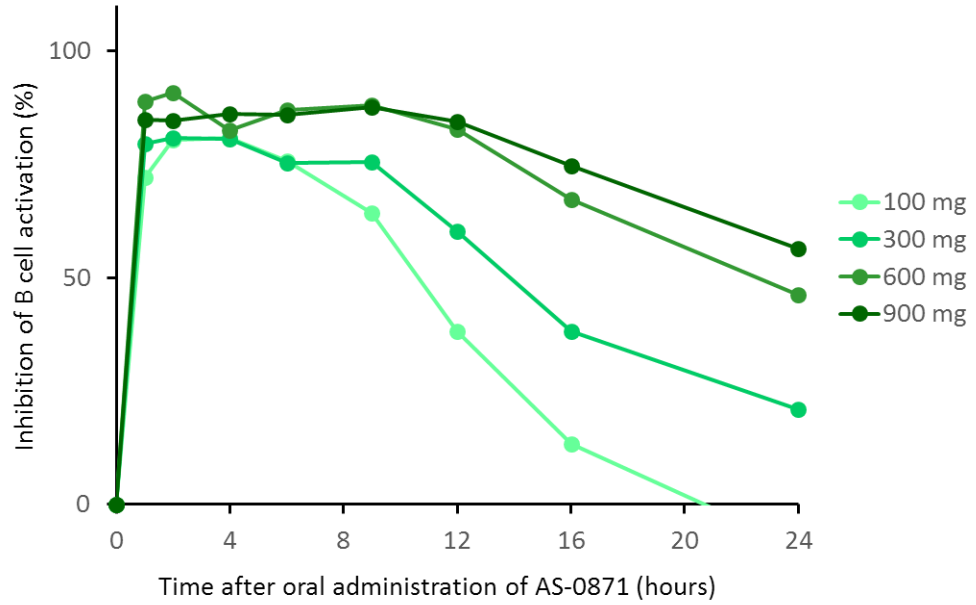


- ✓ AS-0871 is well-tolerated without any safety concerns.
- ✓ Favorable pharmacokinetic profile.
- ✓ Blood samples to assess PD effects were analyzed for evaluation of the B-cell and basophil responses. Administration of AS-0871 at 100mg or above resulted in strong inhibition of B-cell and basophil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

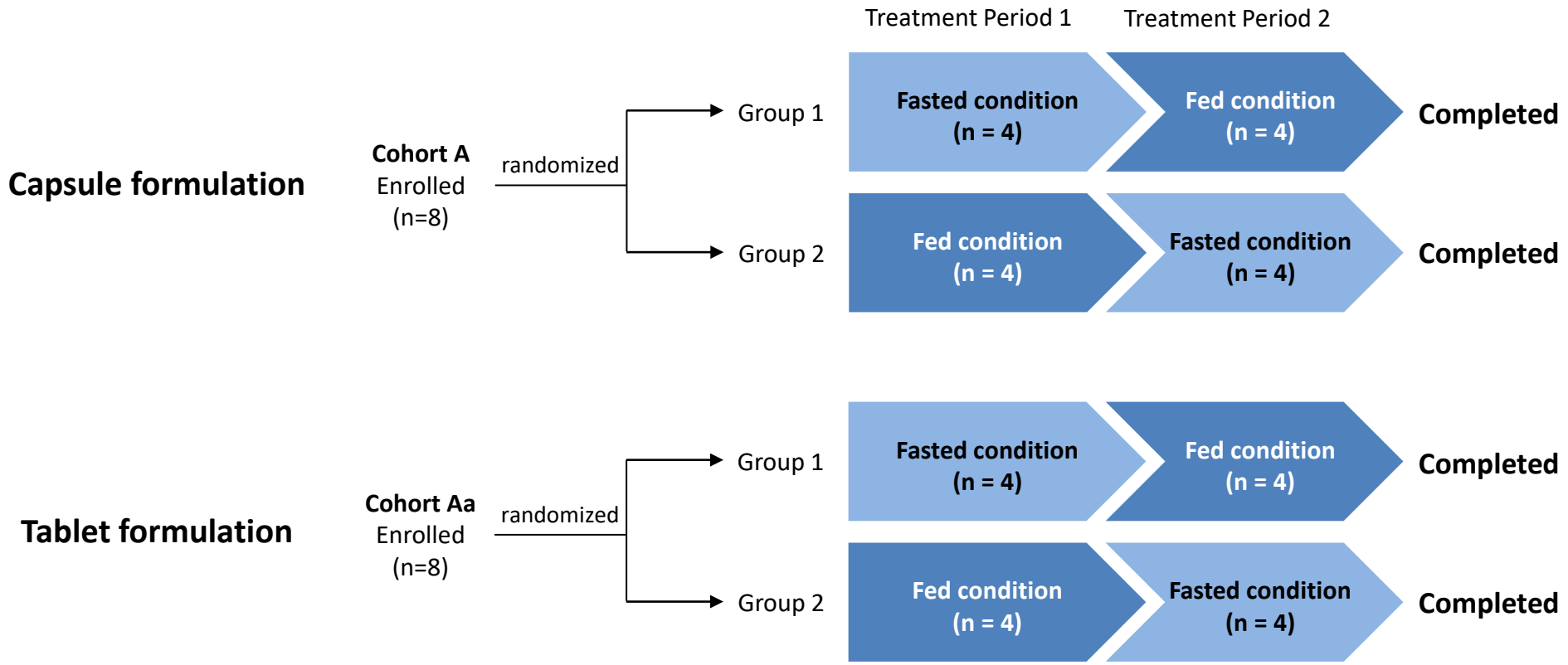




AS-0871: Phase 1 MAD Study: BA part

Study Design of rBA/FE part

PK, safety, and tolerability after single-dose oral administration of AS-0871, formulated as capsules or tablets, were be evaluated under fasted and fed conditions in an open-label, randomized, 2-period crossover design. Eight healthy subjects (Cohort A or Cohort Aa) were randomized to either Group 1 or Group 2 (4 subjects per group).

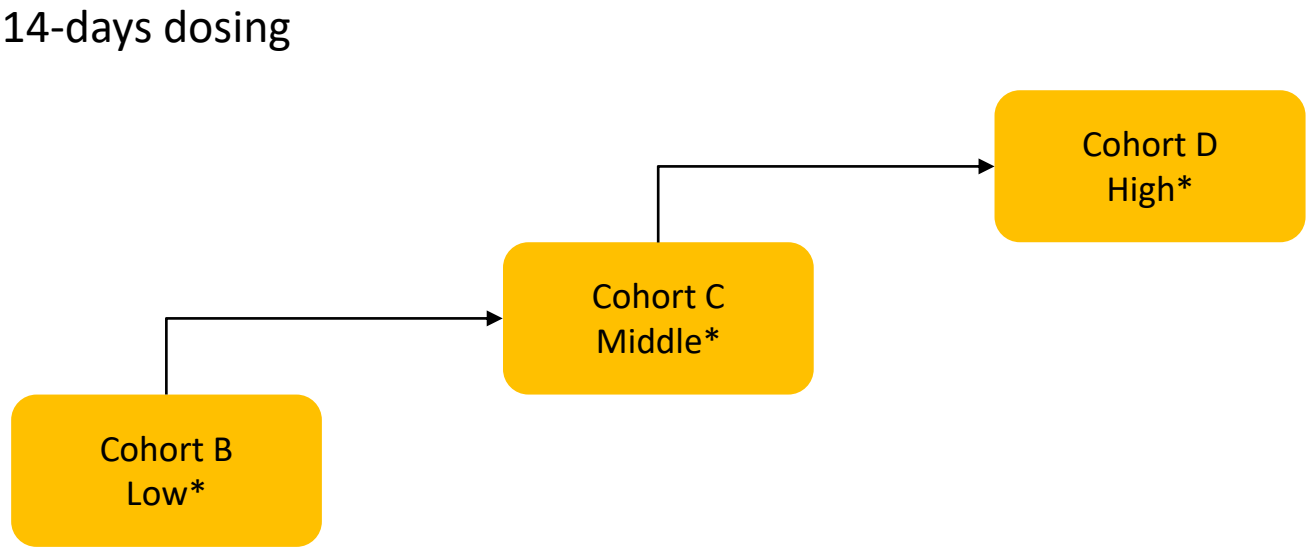


*One subject vomited after dosing (considered not related to study drug), excluded from the PK analysis.
**One subject withdrew from the study due to personal reasons before dosing.

AS-0871: Phase 1 MAD Study: MAD part

Study Design of MAD part

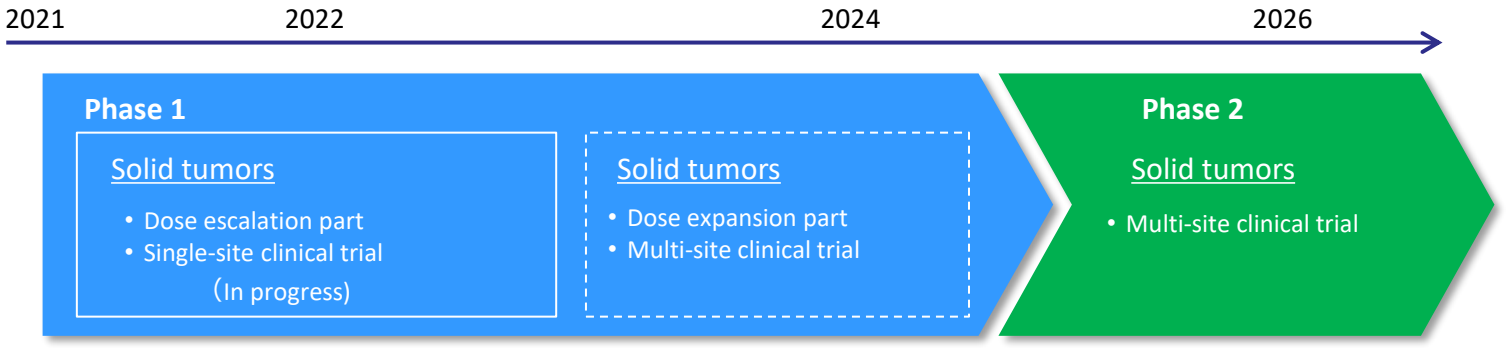
- In the MAD part, safety, tolerability, PK, and PD of 3 multiple ascending doses of AS 0871, following 14 day multiple dose oral administration of AS-0871, will be investigated using a double blind, placebo-controlled, randomized design in 3 cohorts of 8 healthy subjects each.
- Dosing will be completed in Q1 2023.
- The results are expected in H2 2023.



*The dose levels may be adjusted for the MAD part to match with projected exposure levels depending on the results of the BA part.

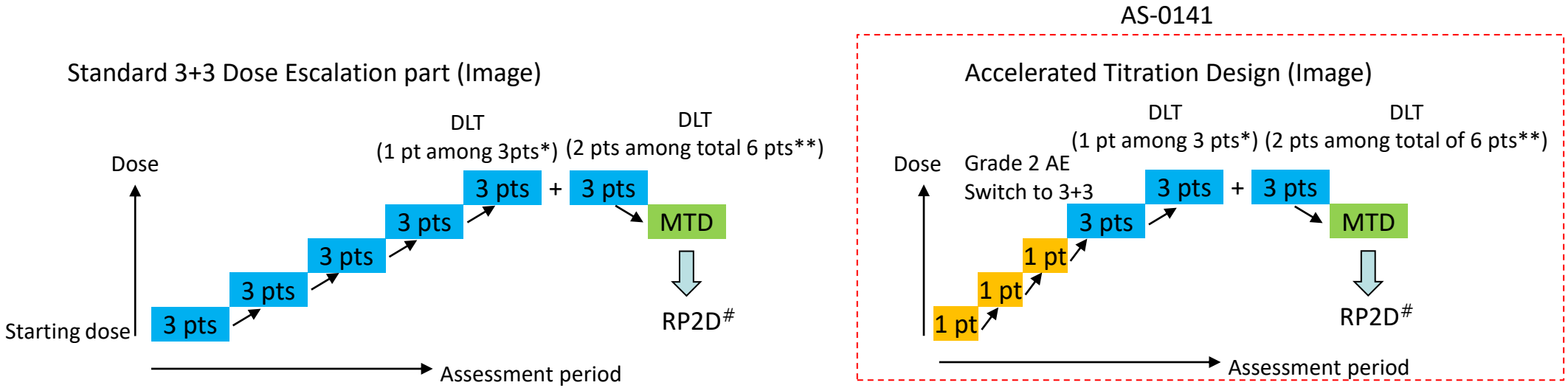
AS-0141: CDC7 Inhibitor

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
  - ✓ 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

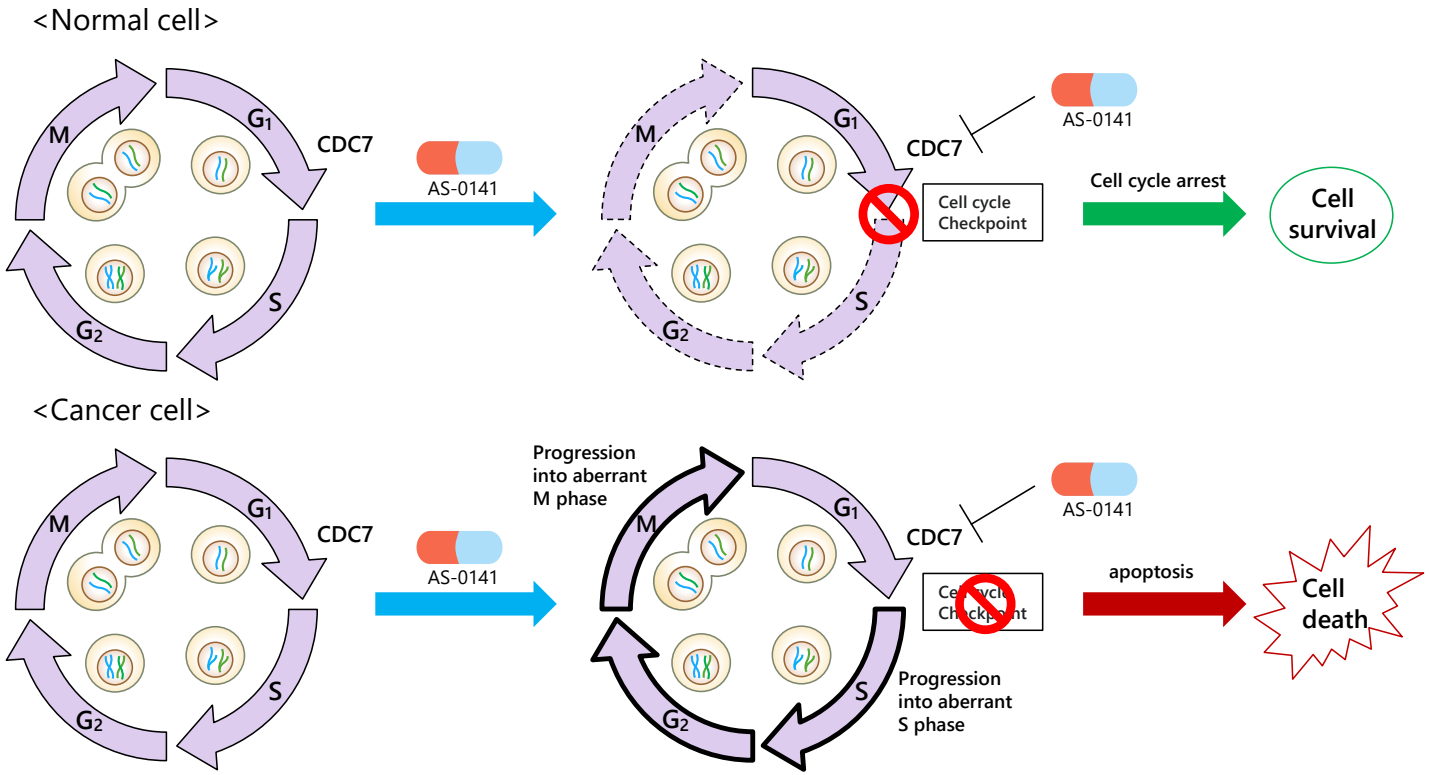
Cohort	Dose level (5d on/2d off)		Status
1	20 mg BID	N=1	No G2 AE/No DLT
2	40 mg BID	N=1	No G2 AE/No DLT
3	80 mg BID	N=1	No G2 AE/No DLT
4	150 mg BID	N=1	No G2 AE/No DLT
5	250 mg BID	N=1	No G2 AE/No DLT
6	300 mg BID (switched to 3+3 design)	N=3	DLT（2/3 pts）
	< 300 mg BID (3+3 design)		

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

AS-0141: Highly Selective CDC7 Inhibitor

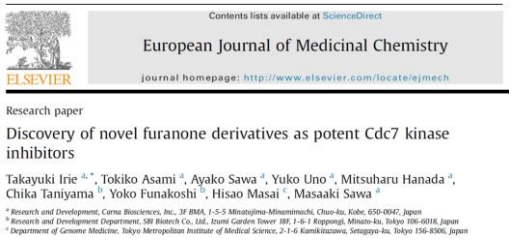
■ CDC7 kinase inhibitor

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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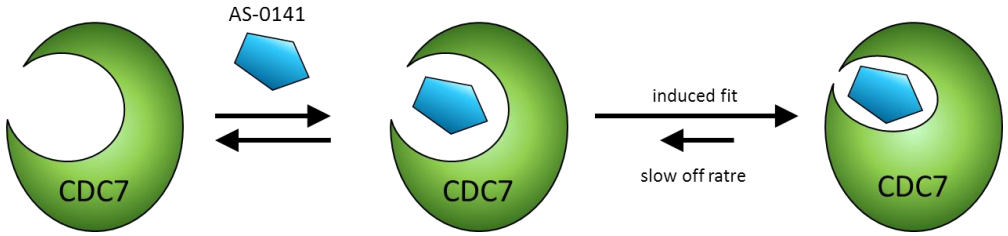


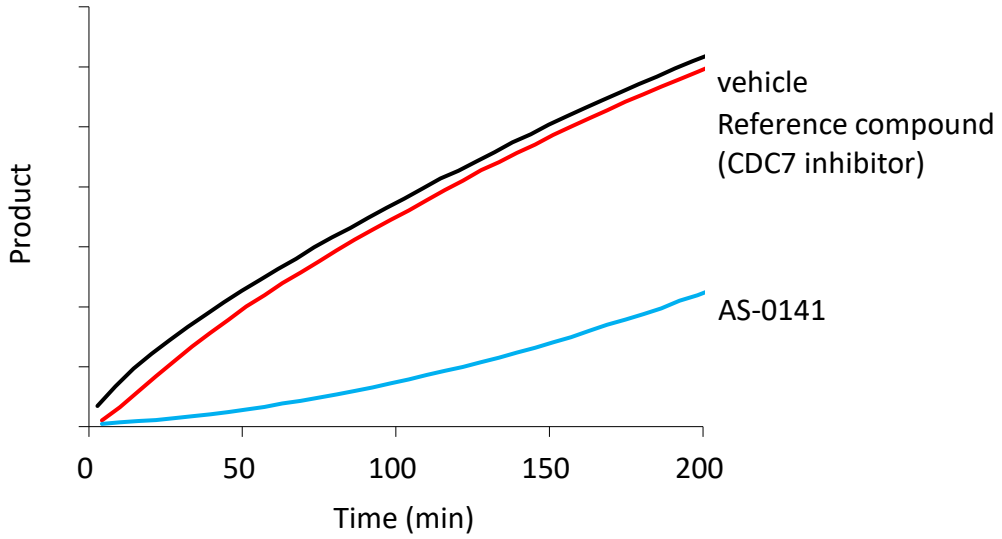
Inhibitory potency (IC_{50}) for CDC7 in the presence of 1 mM ATP

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

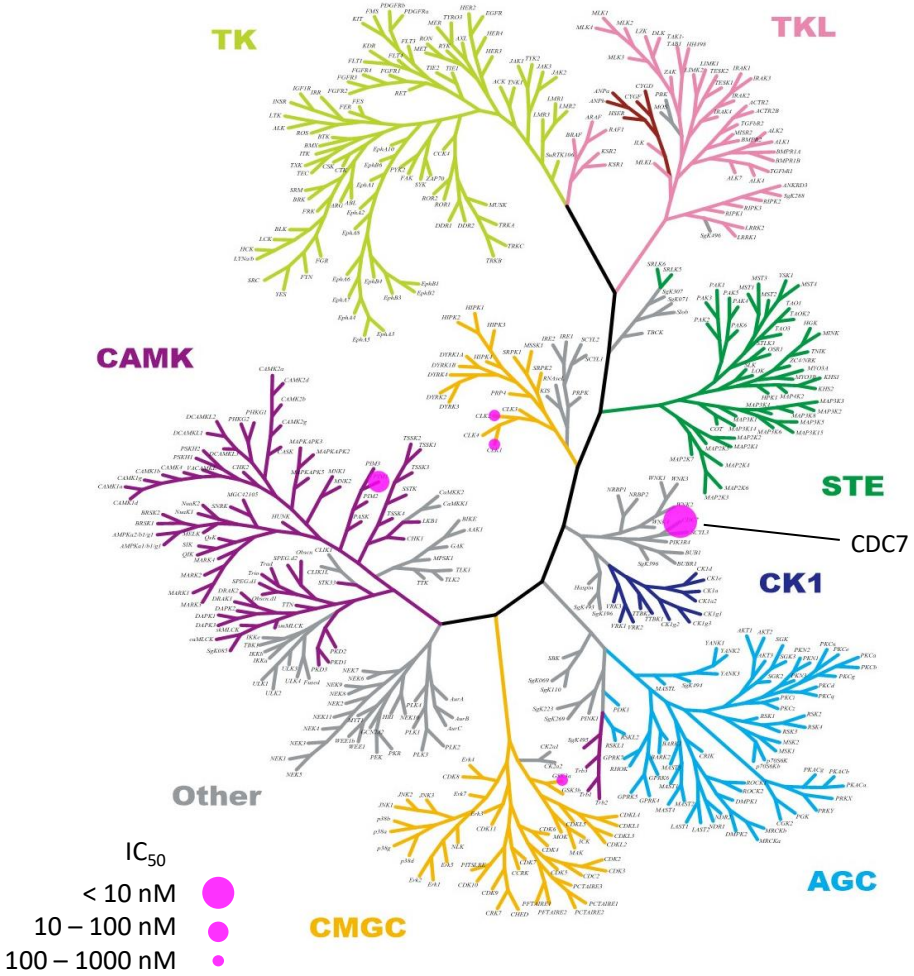
Rapid dilution assay for Cdc7 inhibitors. Recovery of enzymatic activity was monitored by formation of the phosphorylated product.



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

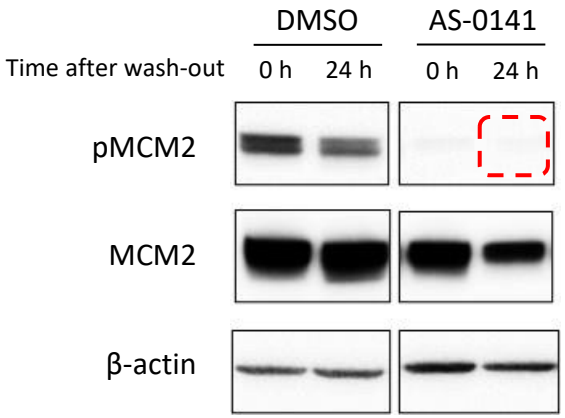
CDC7 is the only kinase that shows preincubation effect

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

AS-0141: Strong Cellular Activity

◆ Prolonged inhibition in cells

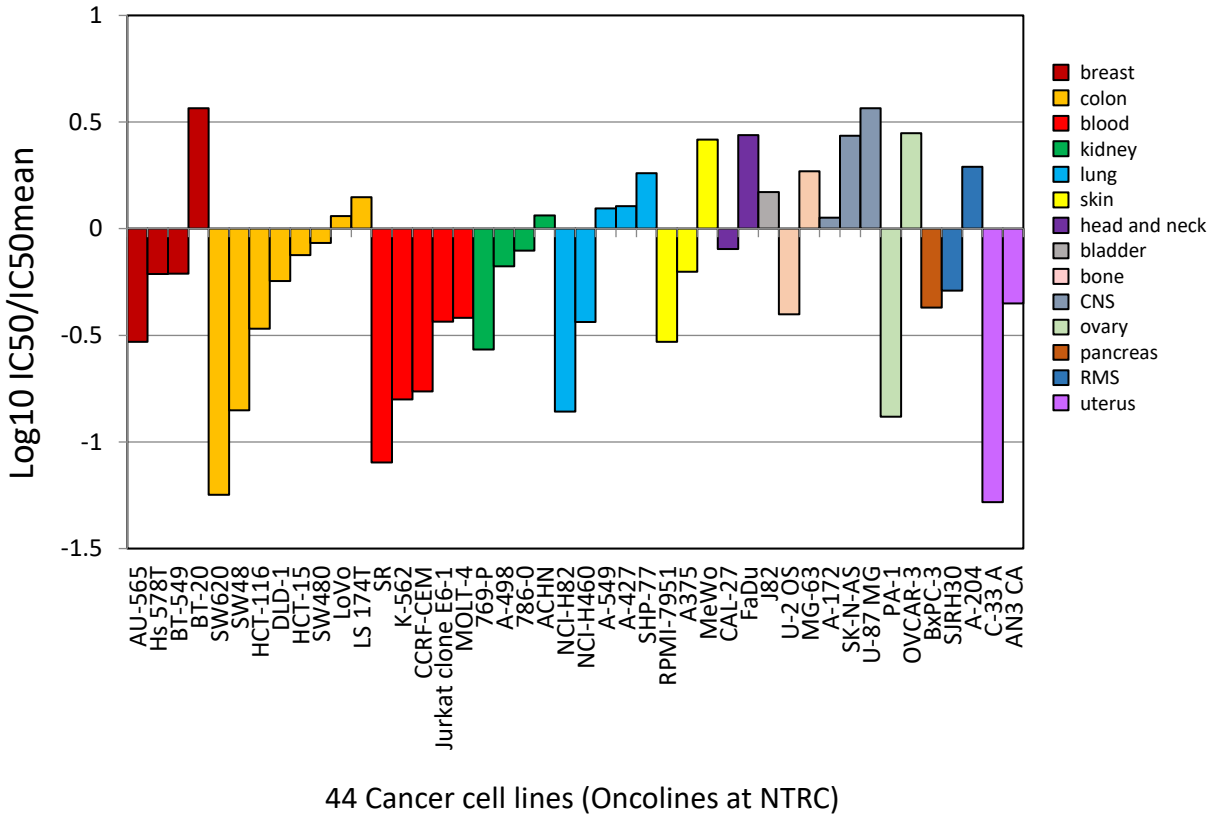
Human colon cancer cell line, Colo-205 cells were treated with DMSO control or AS-0141. After washout of the inhibitor, the cells were further incubated in the same media for 0 or 24 h and subjected to western blot analysis.



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

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

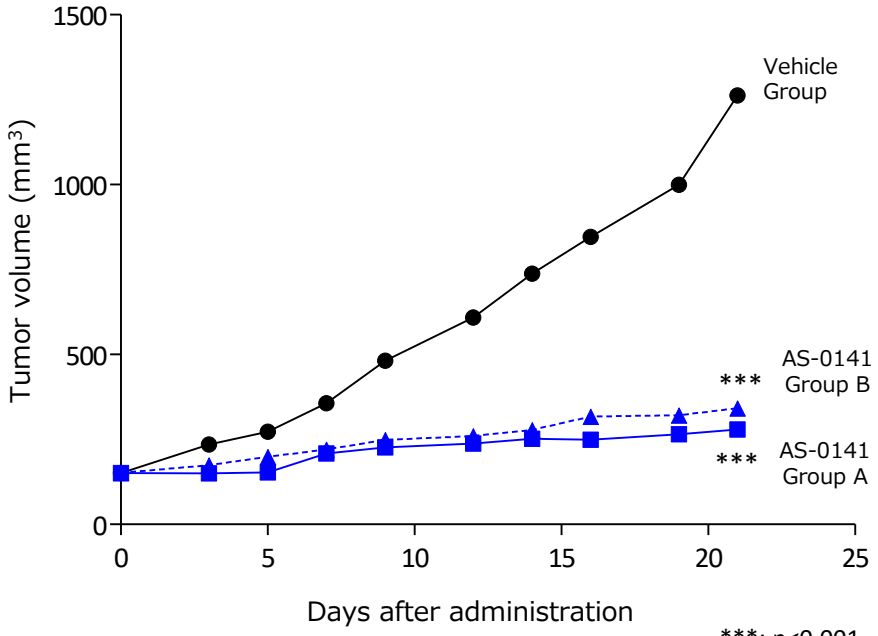


44 Cancer cell lines (Oncolines at NTRC)

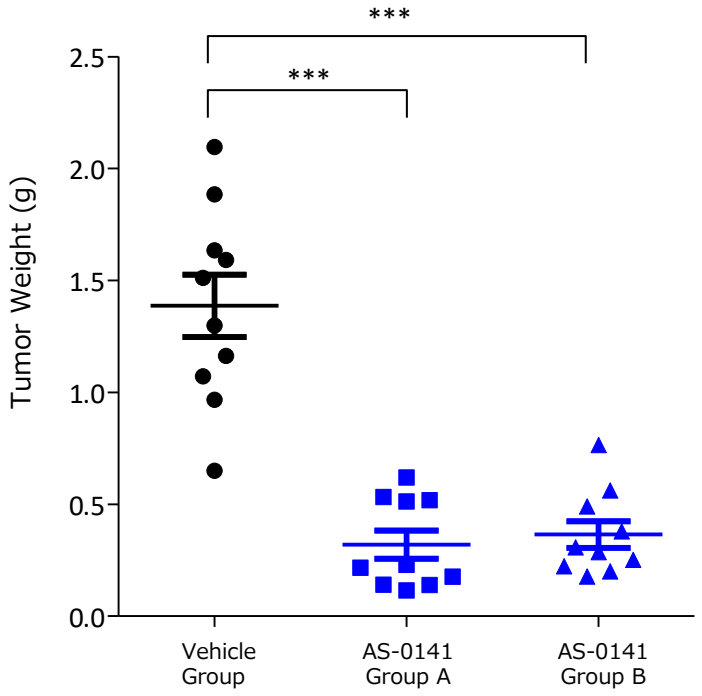
AS-0141: Robust In Vivo Antitumor Efficacy

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

Tumor Growth Curve (Mean, n = 10)



Final Tumor Weight of Each Mouse



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.

Deal with FRTX for STING Antagonist

In Feb. 2022, Carna and Fresh Tracks Therapeutics (FRTX) entered into a license agreement to grant FRTX 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.)

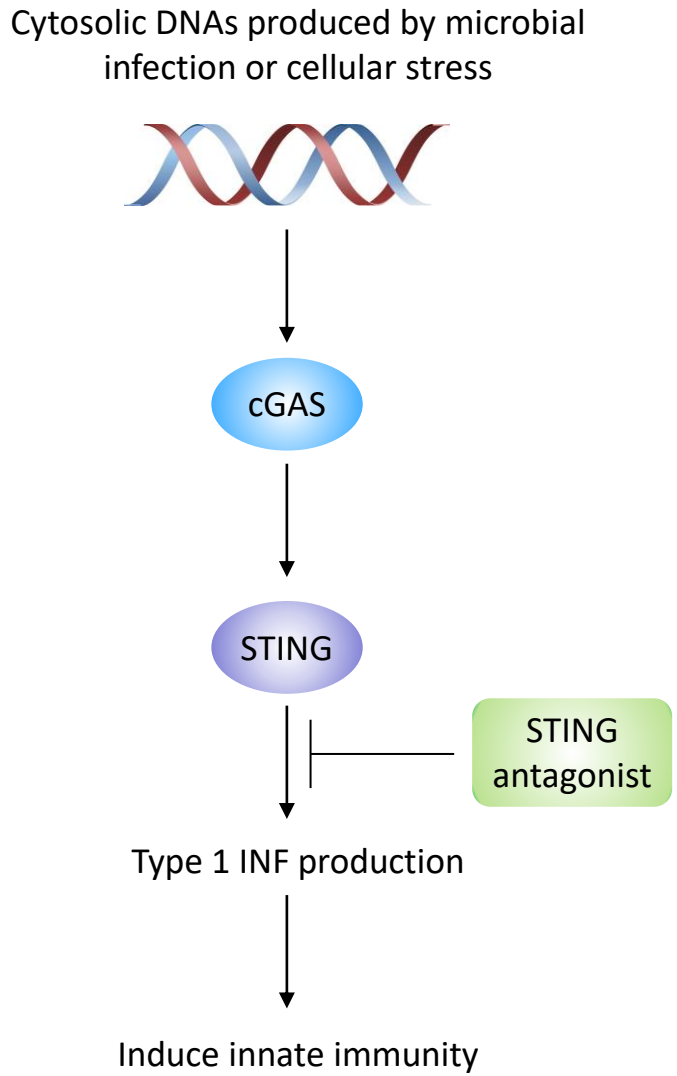
Successfully licensed non-kinase target project in a short period of time.

↓

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

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

- Achieved record-high sales of JPY1,100 mn (+23.7% yoy).
  - ✓ In North America, sales increased 22.2% yoy. Sales of kinase proteins, especially biotinylated proteins, were strong. Demand from biotech companies including AI-driven drug discovery companies has been strong. In addition we received large orders from contracted research organizations (CROs) and major pharmaceutical companies. Sales to Gilead also contributed until Q3.
  - ✓ In Japan, sales increased 6.7% yoy. While overall demand has been weak, cell-based assay service (agent business) was robust and sales of kinase proteins were flat yoy.
  - ✓ In other area including China, sales increased 103.2% yoy. Sales of kinase proteins were strong thanks to the continued expansion of the market in China. Sales in South Korea also increased.
  - ✓ In Europe, sales decreased 11.1% yoy. Demand was weak and the logistics was unstable due to the war in Ukraine. The logistics has stabilized after changing the logistic company and sales were sold in H2.
- Expanding lineup of kinase proteins and profiling service
  - ✓ 36 kinase protein products, including high-demand mutant kinase biotinylated kinases, have been newly added to the line-up.
  - ✓ Launched Chinese website to boost sales in China.
- 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.

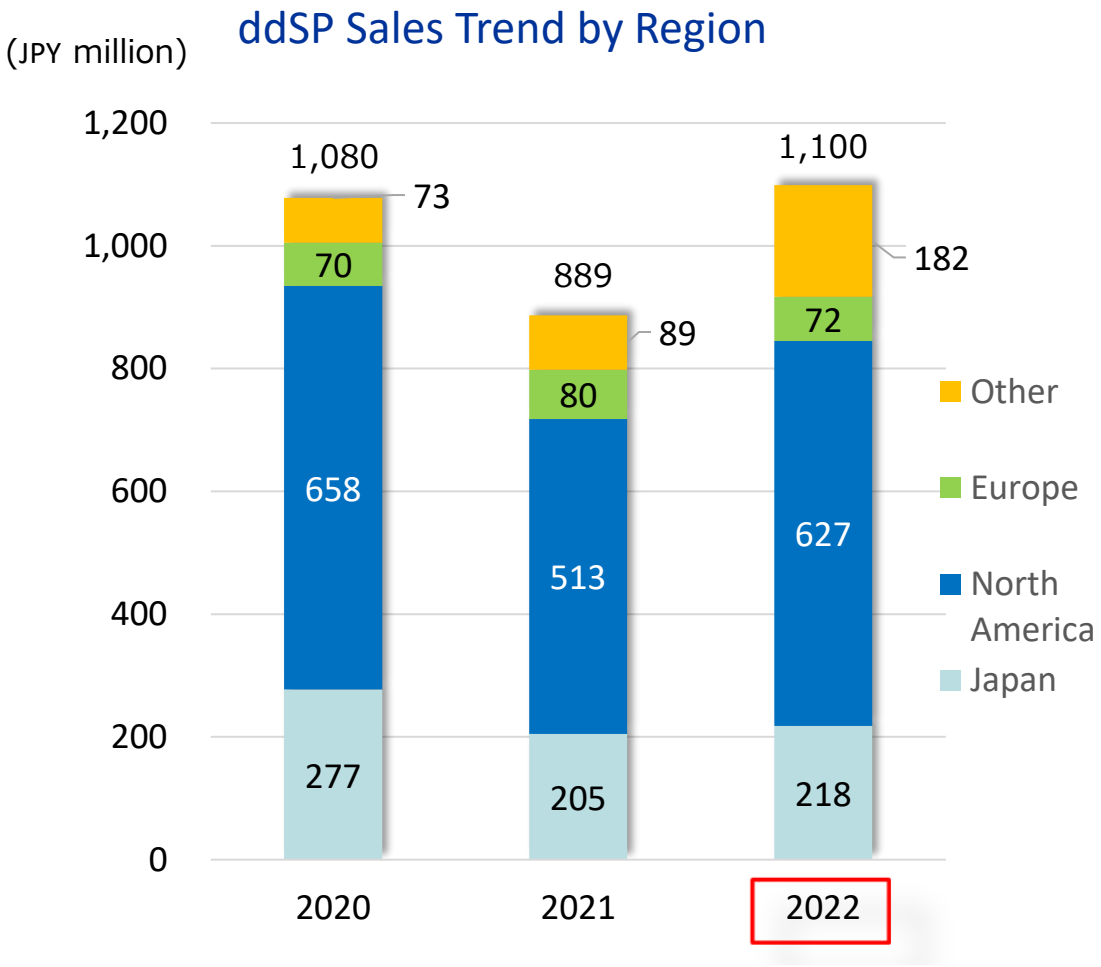
FY2022 Financial Results

FY2022 Consolidated Financial Results

(JPY million)	FY2021 Actual	**FY2022 Actual**	YoY Change	FY2022 May 10 Revised Plan	FY2022 Dec. 14 Revised Plan	
Total Sales	2,017	**1,386**	-630 -31.3%	1,186	1,363	
ddSP business	889	**1,100**	+211 +23.7%	900	1,077	- Sales of kinase proteins were strong in the U.S. and China.
ddRD business	1,128	**286**	-841 -74.6%	286	286	- Received an upfront payment from FRTX and a milestone payment from BioNova. - Received a milestone payment from Gilead in Q4 2021.
Total Operating Loss	(531)	**(1,269)**	(738)	(1,672)	(1,451)	
ddSP business	289	**452**	+163 +56.7%	300	435	- Sales of high-margin kinase proteins were strong.
ddRD business	(820)	**(1,722)**	(902)	(1,972)	(1,887)	- Sales decreased yoy compared to 2021 when we received a milestone payment from Gilead.
Ordinary Loss	(522)	**(1,278)**	-755	(1,685)	(1,451)	
Net Loss	(534)	**(1,349)**	-815	(1,740)	(1,513)	- Impairment loss of JPY44 million was recognized for lab equipment.
R&D cost	1,841	**1,882**	+40 +2.2%	2,166	2,046	- Actual R&D cost was lower than the forecast due to a timing of recording as costs.

Note 1: Rounded down to the nearest million yen.
Note 2: ddRD: Drug Discovery R&D business, ddSP: Drug Discovery Support Business

FY2022 Discovery Support (ddSP) Business Sales by Region



- Japan: Increased 6.7% YoY
  - Cell-based assay service, crystallography and NanoBRET™ service were robust.
  - Sales of kinase proteins were flat yoy while profiling service was weak.
- North America: Increased 22.2% YoY
  - Sales of kinase proteins were strong.
- Europe: Decreased 11.1% YoY
  - Sales declined as both kinase proteins and profiling service were weak.
- Other: Increased 103.2% YoY
  - Sales of kinase proteins were strong in China.
  - Sales in South Korea also increased.

Consolidated Balance Sheet

(JPY million)	As of Dec. 31, 2021	As of Dec. 31, 2022	Change	Reason for changes
Current assets	5,318	4,104	-1,214	Accounts receivable-trade -1,061 Cash and deposits -438
Cash and deposits	3,817	3,379	-438	
Non-current Assets	114	162	+48	
Total assets	5,432	4,266	-1,166	
Current liabilities	774	436	-338	
Non-current liabilities	342	188	-154	Long term loans payable -119 Bonds payable -32
Total liabilities	1,116	624	-492	
Total net assets	4,315	3,641	-673	Capital stock and capital surplus +650, Retained earnings -1,349
Total liabilities and net assets	5,432	4,266	-1,166	

Shareholders' equity ratio	79.3%	85.0%
BPS	323.5 yen	255.0 yen
PBR	3.4x	2.0x
Share price of Carna	1,102 yen	520 yen

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

<20th Subscription Rights to Shares >

	Dec. 2022	Jan. 2023	Total
Amount raised (JPY)	300 mil.	600 mil.	900 mil.
No. of shares exercised (Shares)	550,000	1,300,000	1,850,000
No. of Exercised rights/No. of total rights issued	16.2%	38.4%	54.6%

Business Plan for FY2023

Key Milestones for 2023

Business		Key Milestones		
		Milestones for 2022	Achievement in 2022	Milestones for 2023
ddRD	AS-0871	☐ Start partnering activity	☑ Started partnering activity	☐ Complete Ph1 MAD study ☐ Prepare a package for licensing
	AS-1763	☐ Initiate Ph1b (US)	☑ Completed IND (US) ☐ FPI is expected in Q1 2023	☐ Ph1b FPI (US)
	AS-0141	☐ Initiate Ph1 expansion part	☑ Switched to 3+3 design in Ph1 dose escalation part ☐ Plan to initiate Ph1 expansion part in H2 2023	☐ Initiate Ph1 expansion part
	Research program	☐ Bring one or more programs in preclinical stage or license a program.	☑ STING antagonist was licensed to FRTX	☐ Bring one or more programs in preclinical stage or license a program.
ddSP		☐ 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	☑ Strong sales in North America and Asia. ☑ Launched 36 new kinase protein products ☑ Added 5 new PIK3 mutant targets to profiling service and 12 new targets to 1 mM assay ☑ Started discussion with potential collaboration partners	☐ Expand sales of in-house developed products and services in North America and Asia ☐ Increase line-up of protein kinase products ☐ Expand sales of cell-based assay

FPI: First Patient In
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 • Earn revenue from new license deals • Receive milestone payments from the out-licensed programs and deliver profits • Initiate pre-clinical and clinical studies of new pipelines	• Receive milestone payments and royalty income from the out-licensed programs and expand profits • Earn revenue from new license deals • Initiate pre-clinical and clinical studies of new pipelines

<ddRD>
- ✓ Advance clinical trials of AS-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)	FY2022 Actual	**FY2023 Plan**	**Outlook for 2024 - 2026**
Total Sales	1,386	**902**	
ddSP business	1,100	**902**	Maintain stable sales
ddRD business	286	**—**	Revenue from milestone payments and upfront payments
Total Operating Loss	(1,269)	**(1,890)**	
ddSP business	452	**221**	Maintain stable profit while investing in product developments
ddRD business	(1,722)	**(2,111)**	Continue to invest in R&D and deliver profits depending on the size of milestone payments and upfront payments
Ordinary Loss	(1,278)	**(1,911)**	
Net Loss	(1,349)	**(1,936)**	

(JPY million)	FY2022 Actual	**FY2023 Plan**	**Outlook for 2024 – 2026**
R&D Cost	1,882	**1,968**	Invest in R&D (JPY1 bn to 2.5 bn) for the future growth.
Capex	125	**6**	Invest in equipment for R&D and IT system (JPY20 mn to 100 mn)

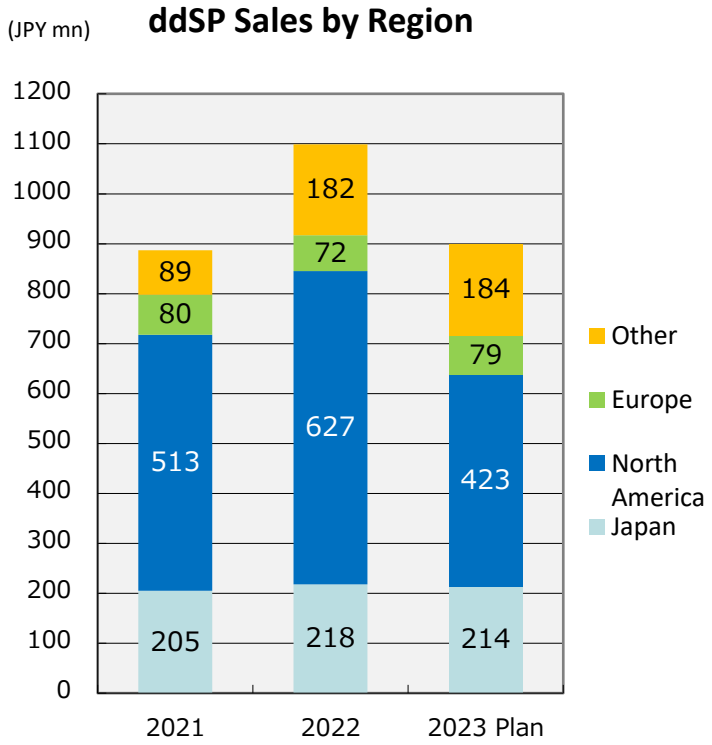
- Business plan for FY2023 dose not include potential milestone payments or upfront payments as the timing or the amounts are difficult to predict.
- Numerical targets for 2024-2027 are not disclosed for the same reason.

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

Drug Discovery Support (ddSP) Business: Sales by Region/Products

(JPY mn)	FY2021 Actual	FY2022 Actual	FY2023 Plan
ddSP	889	1,100	**902**
Kinase Proteins	323	592	**583**
Assay Development	274	178	**4**
Profiling & Screening	203	188	**192**
Cell-based Assay	57	64	**78**
Cell-based Assay (agent business)	12	49	**32**
Others	17	27	**10**

Exchange rate(US$):	109.9 yen	131.6 yen	**130 yen**
% of Overseas sales:	76.9%	80.1%	**76.2%**



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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