

Carna Biosciences, Inc.

February 10, 2022



Stock Code: 4572

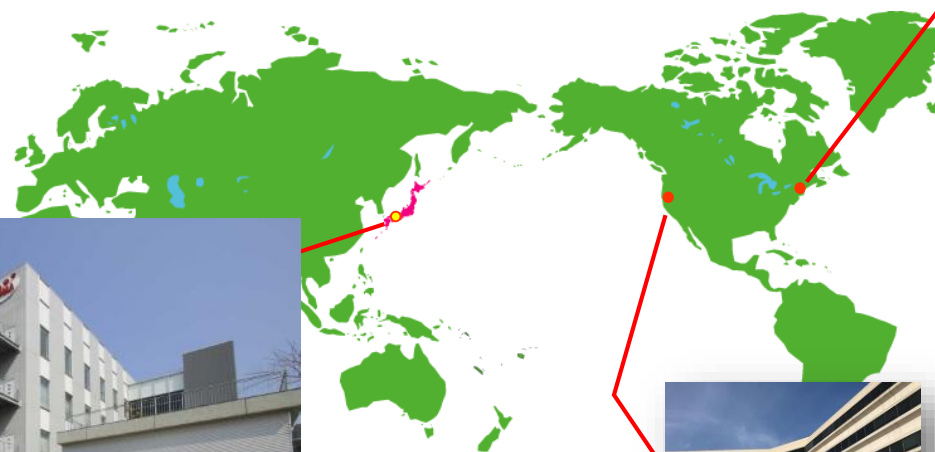
Company Overview

Company Overview

- ❑ Founded in April 2003 (spin-out company from N.V. Organon [MSD])
- ❑ Initial Public Offering (JASDAQ 4572) in March 2008
- ❑ 82 people
- ❑ Offices:
 - Carna Biosciences, Inc. - Kobe, Japan;
 - CarnaBio USA, Inc. - Natick, MA
 - Clinical Development Office – South San Francisco, CA



Carna Biosciences, Inc.
(Kobe, Japan)



CarnaBio USA
(Natick, MA)

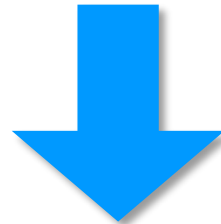


Clinical Development Office
(SSF, CA)

(As of February 1, 2022)

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

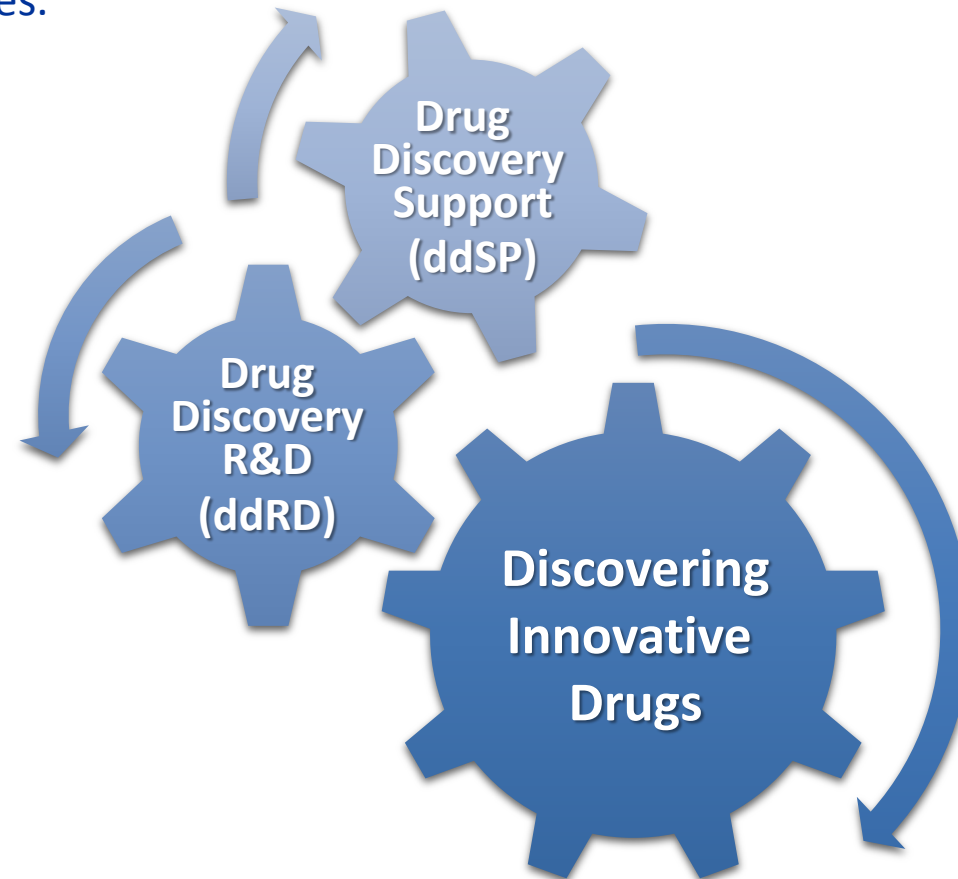
Carna's powerful drug discovery engine invents a drug from scratch and drives our pipeline expansion



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



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

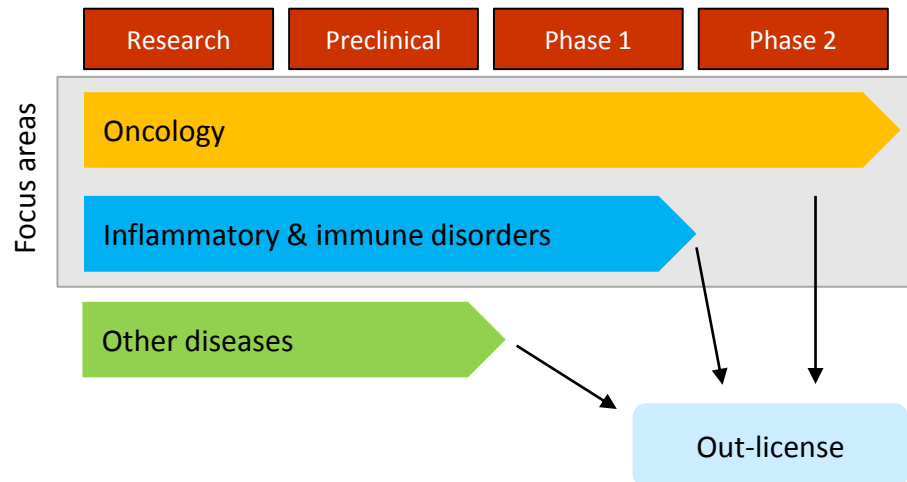


Business Model of Drug Discovery R&D (ddRD) Business



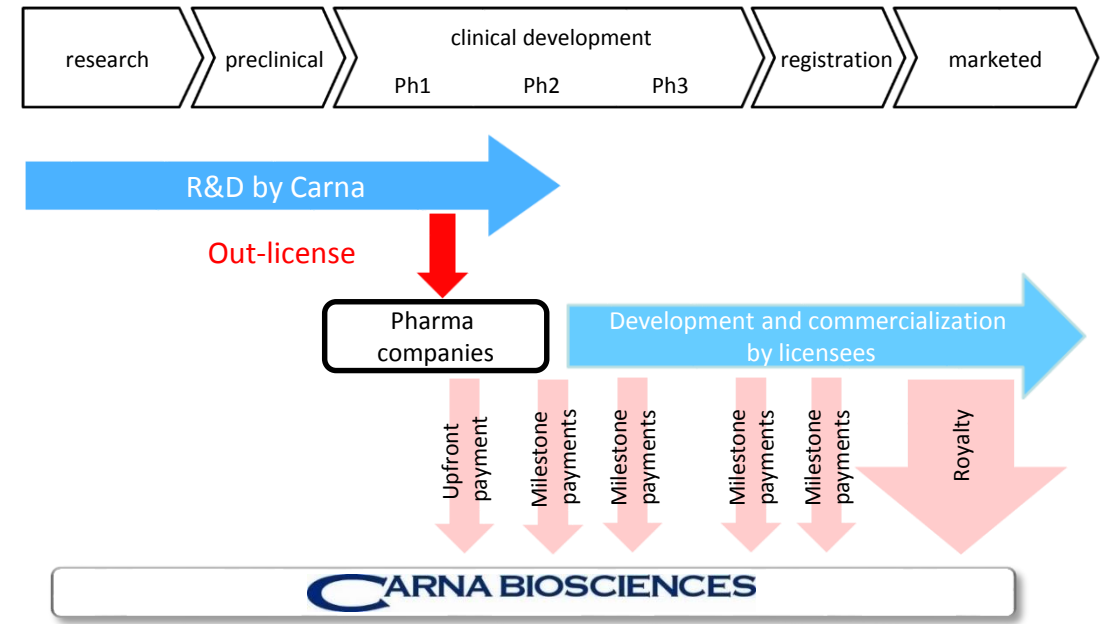
<R&D focus areas>

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



<Earnings model>

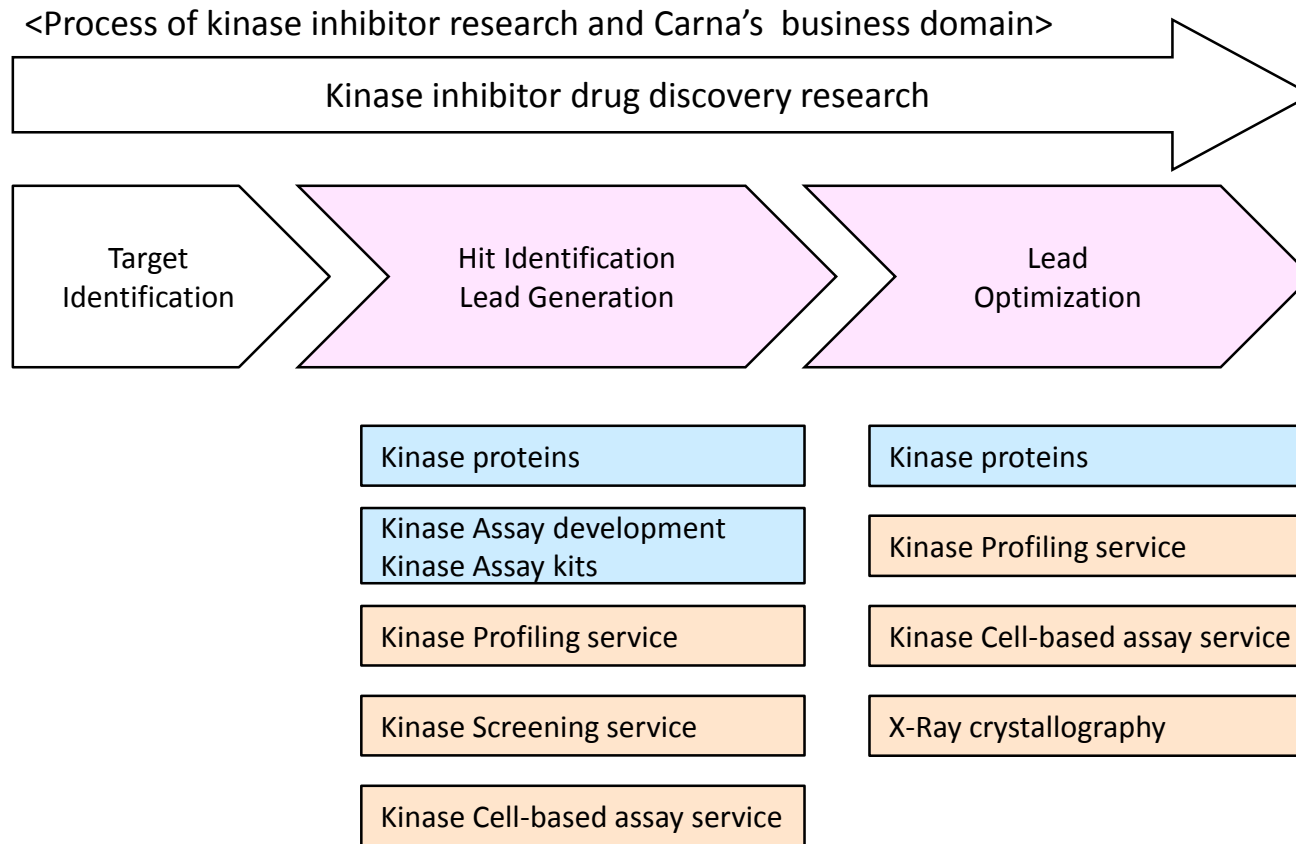
- We license our drug pipelines to pharma companies to generate revenue through upfront payments, milestone payments, and royalties on the resulting product sales.
- We intend to build long-term value by developing our own drug pipelines up to Phase 2 clinical trial on a fully burdened cost or in collaborations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



Business Model of Drug Discovery Support (ddSP) Business



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



Carna's products and services



Kinase proteins



Kinase Assay kits

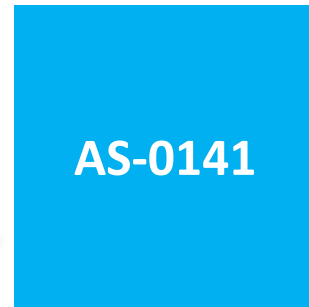
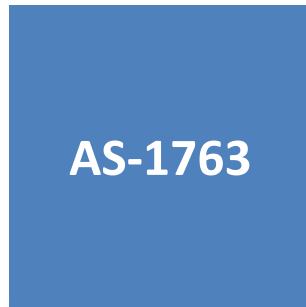


Kinase Profiling and screening service

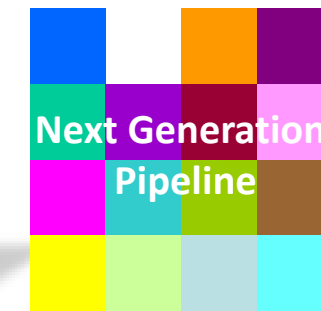
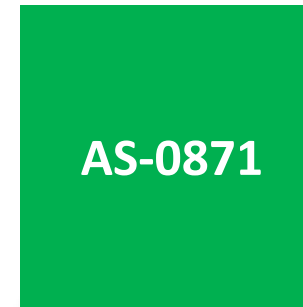
Drug Discovery R&D (ddRD) Business

Robust Drug Pipeline

Cancer



Immune-inflammatory diseases



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		
AS-1763	BTK	Blood Cancer			
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		
AS-0871	BTK	Immune-inflammatory diseases			
Small Molecule	N/A	Malaria			
Small Molecule	STING	Immune-inflammatory diseases	Out-licensed to Gilead		

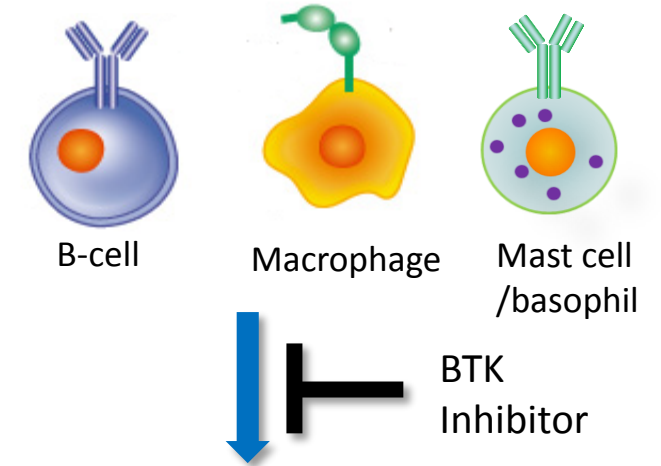
✓ As of Feb. 2022.

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

BTK Inhibitor Program

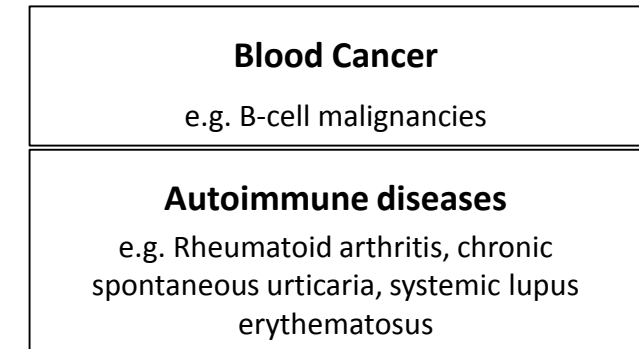
Bruton's Tyrosine Kinase (BTK)

- ✓ BTK is one of the crucial kinases for the B-cell maturation and macrophage activation
- ✓ BTK has been recognized as a validated therapeutic target since the success of Ibrutinib, the first FDA approved BTK inhibitor
- ✓ The expected peak sales of Ibrutinib is > \$10 billion*



<Sales of BTK inhibitors in market>

Launch	Product	Company	Target	2020	2026 Est.
2013	Ibrutinib	AbbVie/J&J	Blood cancer	\$8.4B	\$10.7B*1
2017	Acalabrutinib	Astra Zeneca	Blood cancer	\$522M*2	



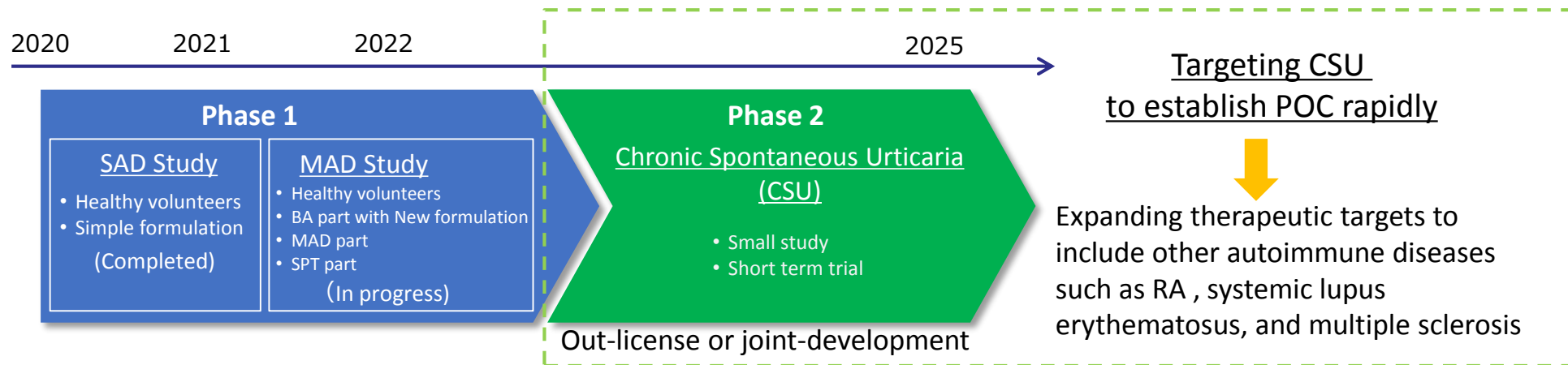
- In January 2019, Loxo Oncology, developing kinase inhibitors including non-covalent BTK inhibitor LOXO-305, was acquired by Eli Lilly for \$8.0 billion.
- In December 2019, ArQule, developing non-covalent BTK inhibitor ARQ 531, was acquired by Merck for \$2.7 billion.



High potential of non-covalent BTK inhibitors for sizable license deals

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



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



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

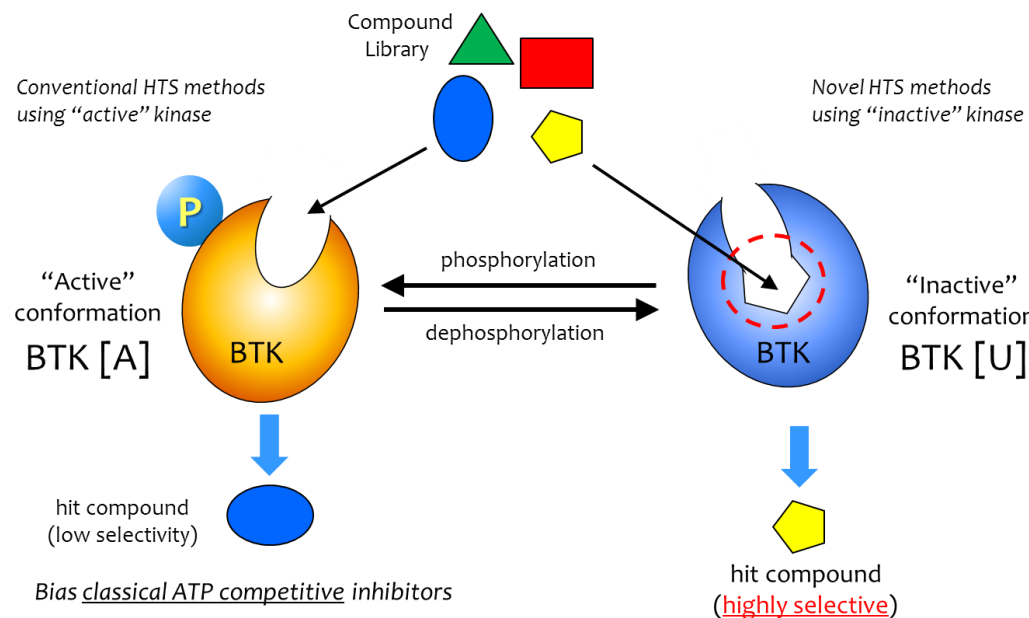
Tokiko Asami¹, Wataru Kawahata, Masaaki Sawa

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

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

Wataru Kawahata,¹ Tokiko Asami, Takao Kiyoi, Takayuki Irie, Haruka Taniguchi, Yoko Asamitsu, Tomoko Inoue, Takahiro Miyake, and Masaaki Sawa²

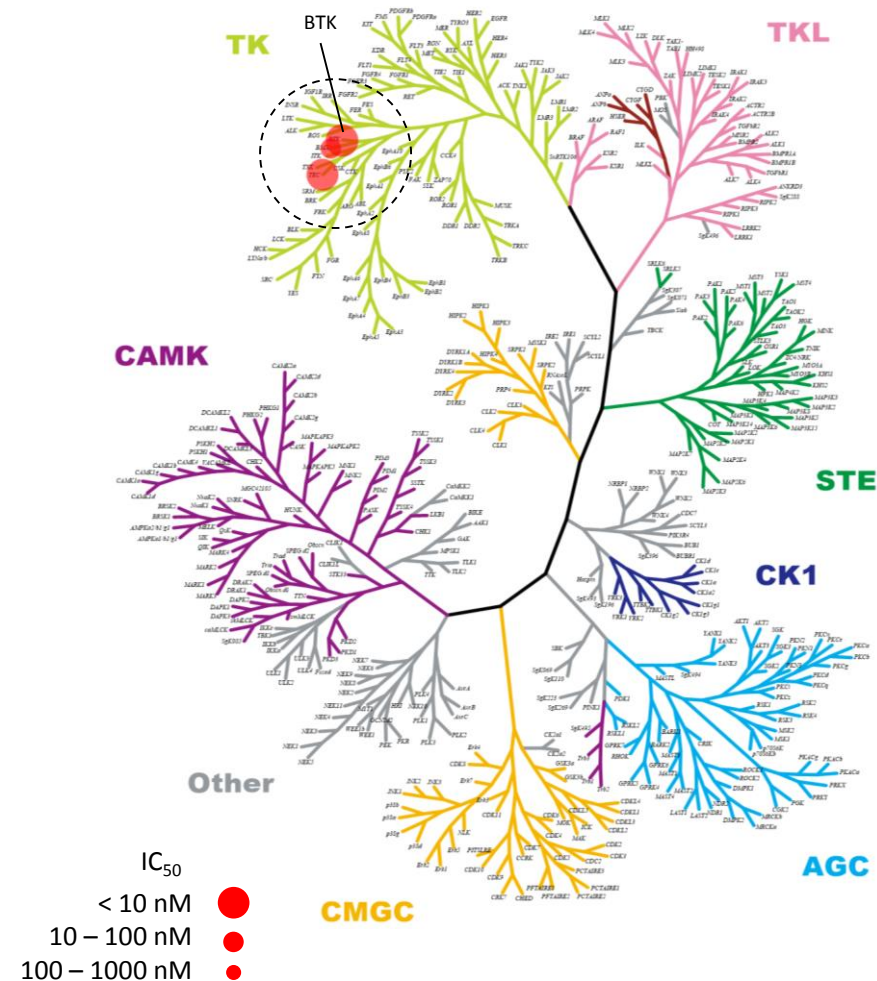
Research and Development, Carina Biosciences, Inc., 3rd Floor, BMA, 1-5-5 Minatogima-Minamimachi, Chuo-ku, Kobe 650-0047, Japan



	BTK IC ₅₀ (nM)	
	BTK [A]	BTK [U]
AS-0871	3.4	0.3

◆ Kinase Selectivity Profiling

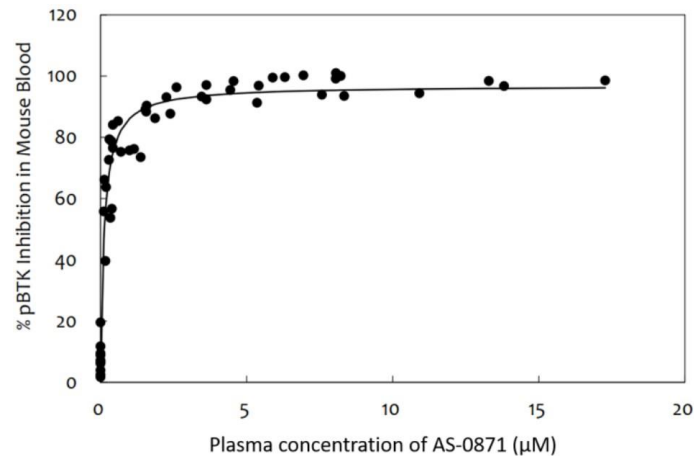
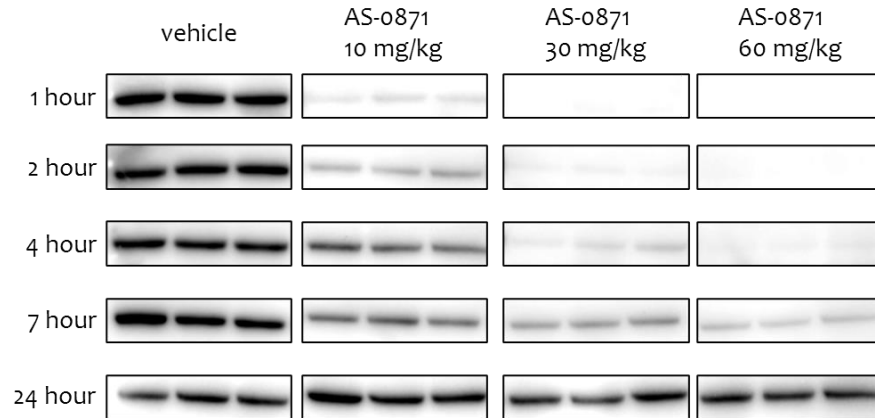
Only inhibited 2 other kinases in a total of 312 kinases tested at 0.3 μM concentration.



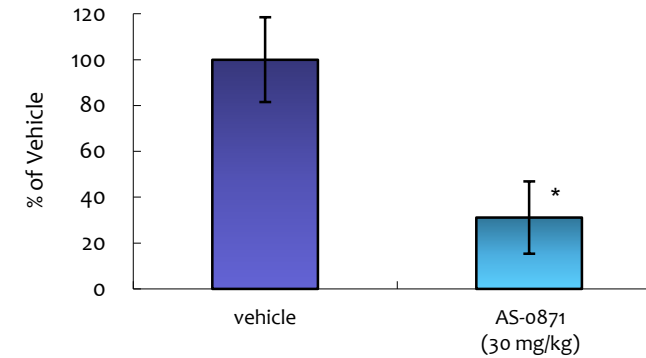
AS-0871: In Vivo Therapeutic Efficacy

◆ PK/PD Study

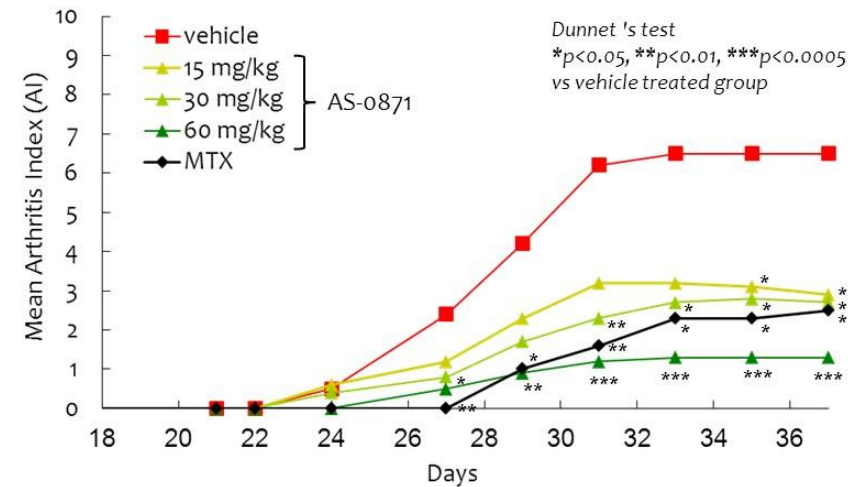
Auto-phosphorylation status of BTK was measured following oral single administration of AS-0871



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

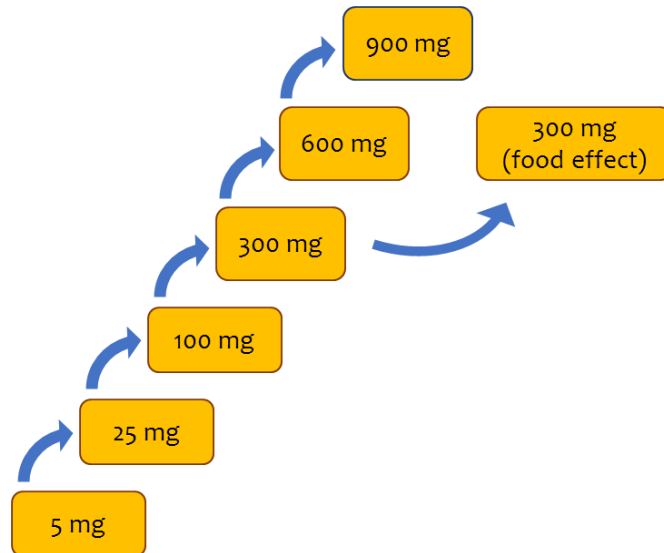


◆ Collagen-induced arthritis (CIA) mouse model (n=10)



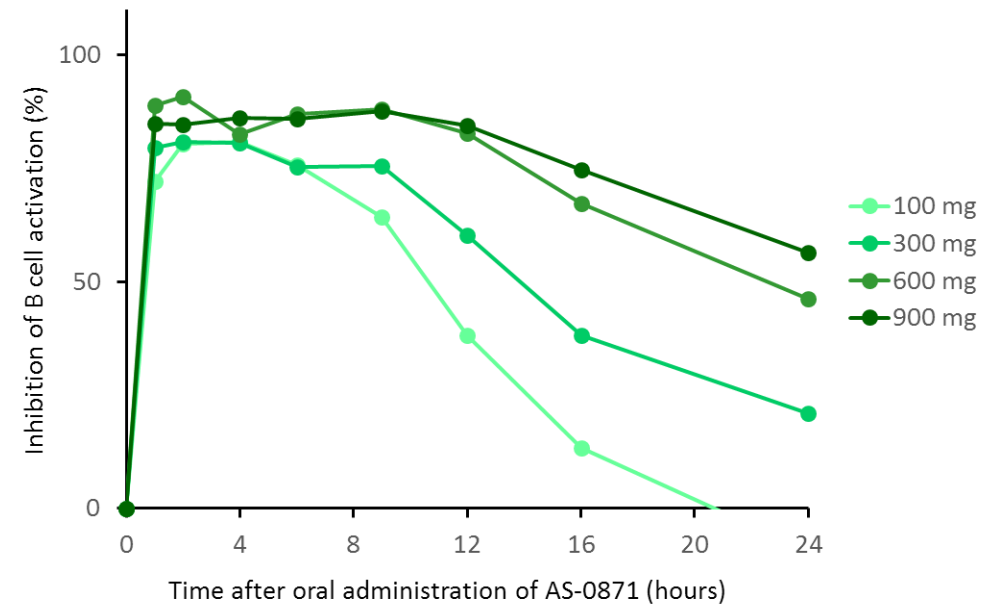
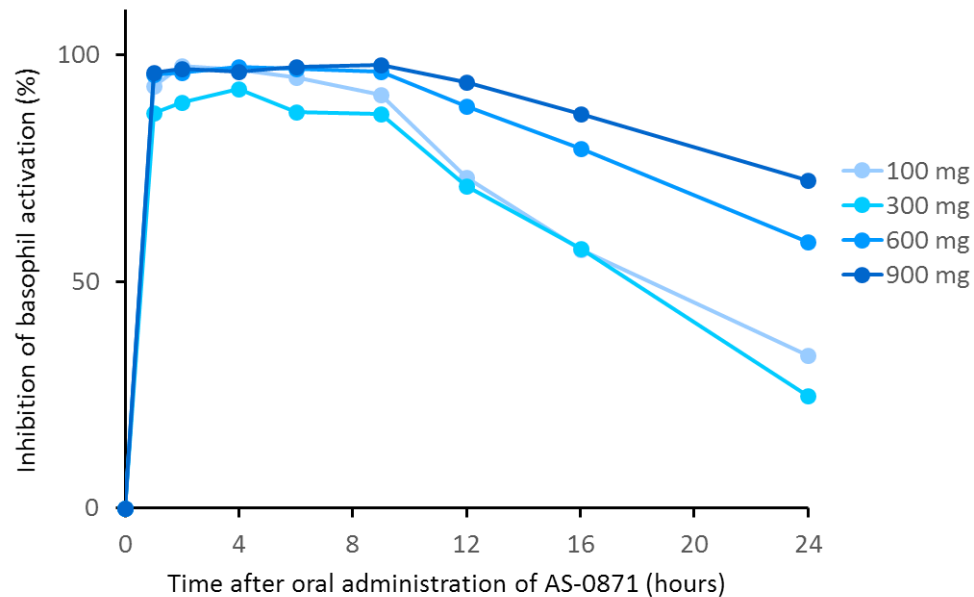
SAD Part (Completed)

Step 1 Single Ascending Dose Study (SAD)	Step 2
<ul style="list-style-type: none">• 6 dose levels (8 subjects/cohort)• Placebo controlled (6 active / 2 placebo)• Safety and tolerability• Pharmacokinetics and pharmacodynamics	<ul style="list-style-type: none">• 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.

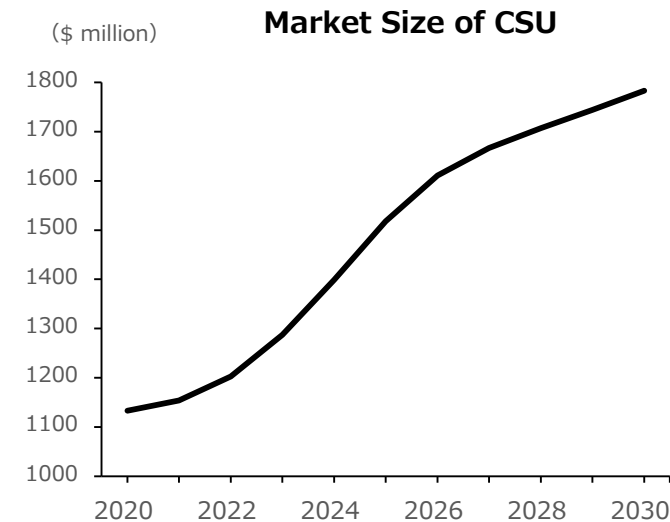
- ✓ Pharmacodynamic study demonstrated that subjects who received AS-0871 showed dose proportional inhibitions in basophil and B-cell activations, and significant and sustained inhibitory effects were observed at 100 mg and above.
- ✓ Oral administration of AS-0871 achieved therapeutic plasma levels needed to inhibit B cells and basophils activation, suggesting that AS-0871 has a potential to become a new treatment option for inflammatory diseases.



- ◆ Fenebrutinib is the only non-covalent BTK inhibitor under development targeting autoimmune diseases.
- ◆ No non-covalent BTK inhibitors under development targeting Chronic Spontaneous Urticaria.

Compound	Company	Development Phase
Fenebrutinib (GDC-0853)	Roche / Genentech	P3 Multiple Sclerosis

- ✓ Chronic Spontaneous Urticaria (CSU) is one of most frequent skin diseases with unmet medical needs since curative treatment is not available.
- ✓ CSU is a distressing skin disorder that characterized by itching and hives lasting for more than 6 weeks, which has major detrimental effects on quality of life with sleep deprivation and other conditions.
- ✓ An underlying cause is rarely detected and symptoms can be exacerbated by infectious diseases or stress.
- ✓ The lack of efficacy of approved standard therapy (antihistamines) in many patients is another major problems.
- ✓ Omalizumab, humanized anti-IgE anti IgE antibodies, has been approved as the third-line therapy, but the drug is very expensive (\$1874 per 4 weeks on average).
- ✓ The market size of CSU in 2020 was estimated as \$1,133 million in major seven countries. The market size excluding antihistamines was \$1,062 million.
- ✓ The market size of CSU is expected to become \$1,783 million in 2030 with launch of several humanized anti-IgE anti IgE antibodies competing with omalizumab.
- ✓ There are no approved BTK inhibitors targeting CSU.



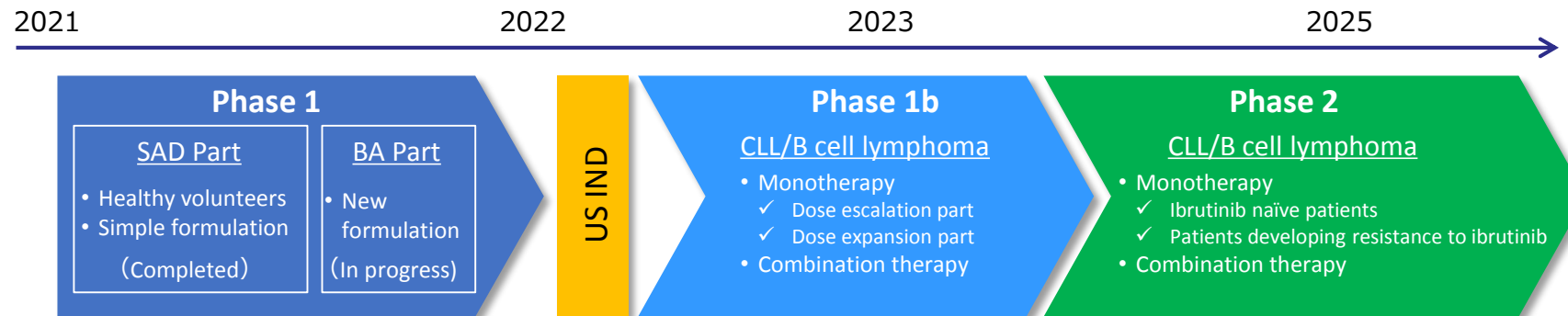
Source: DelevelInsight

*1 Market size of CSU is estimated by DelevelInsight.

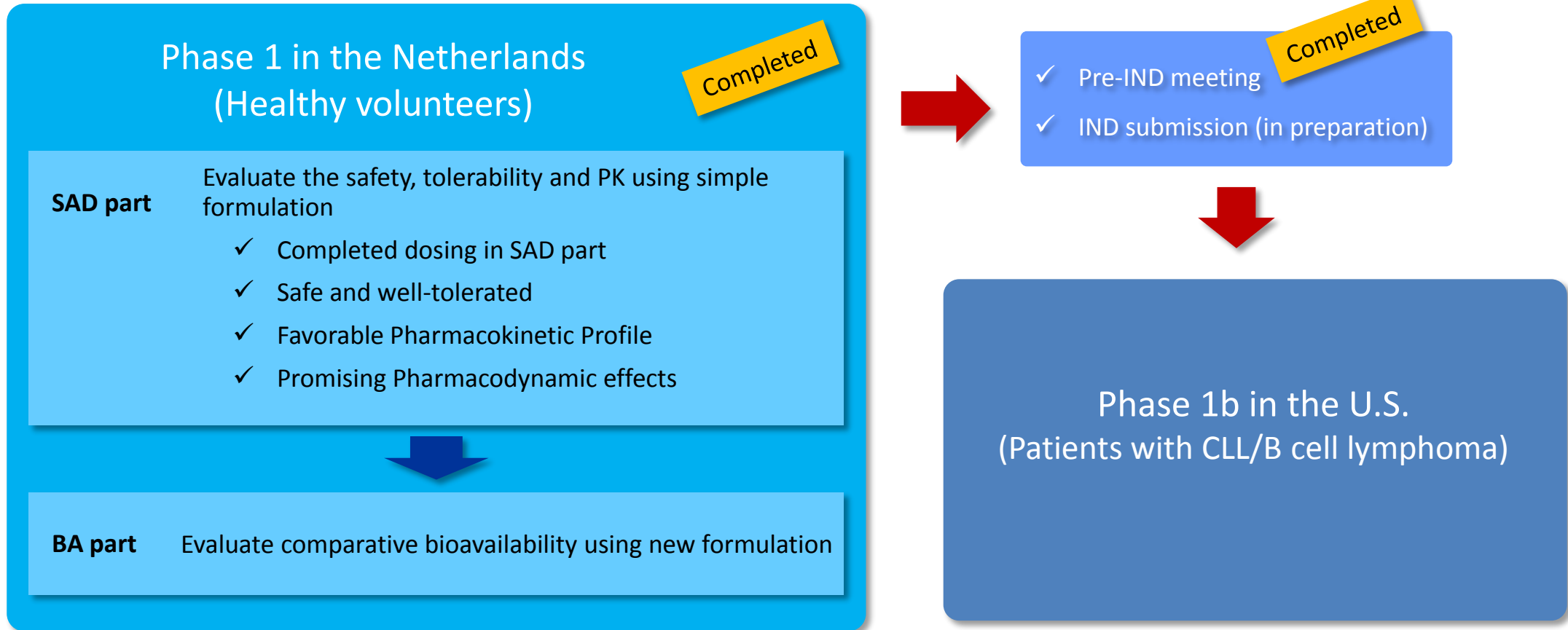
*2 Major seven countries include US, Germany, France, Italy, Spain and Japan.

AS-1763 : Targeting Blood Cancer

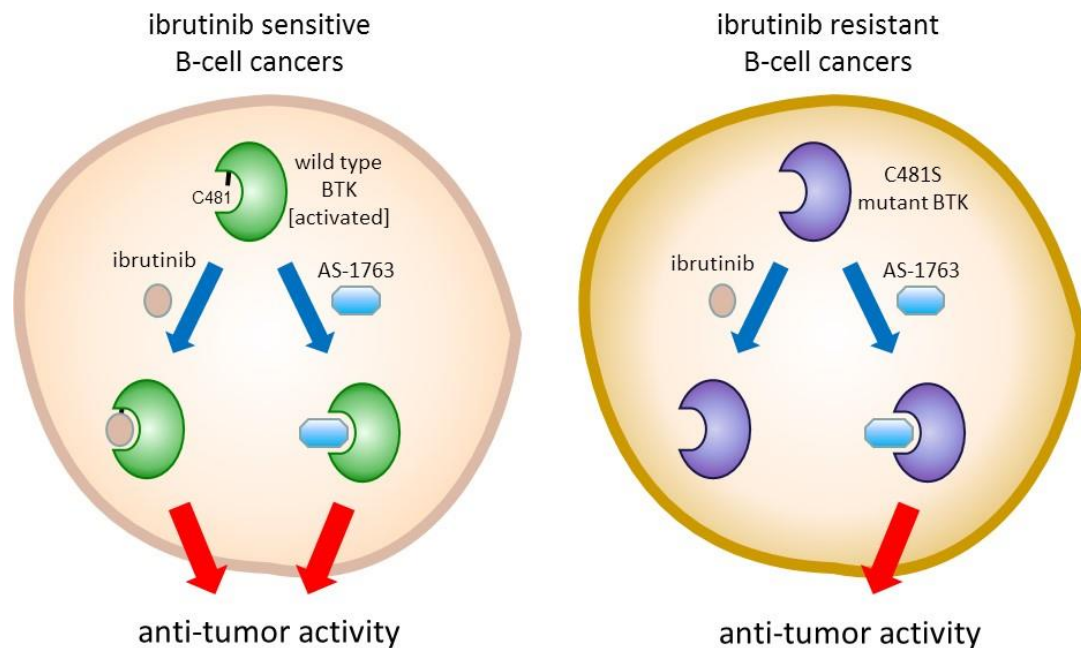
- Small molecule BTK inhibitor
- Non-covalent/reversible
- High kinase selectivity
- Inhibits both BTK wild type and ibrutinib resistant BTK C481S mutants
- Orally available
- Displayed strong anti-tumor effects in lymphoma model with both wild type and C481S mutant BTK
- Displayed efficacy in immuno-oncology 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



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



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

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◆ IC₅₀ 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.

◆ In vitro pharmacological activities of AS-1763

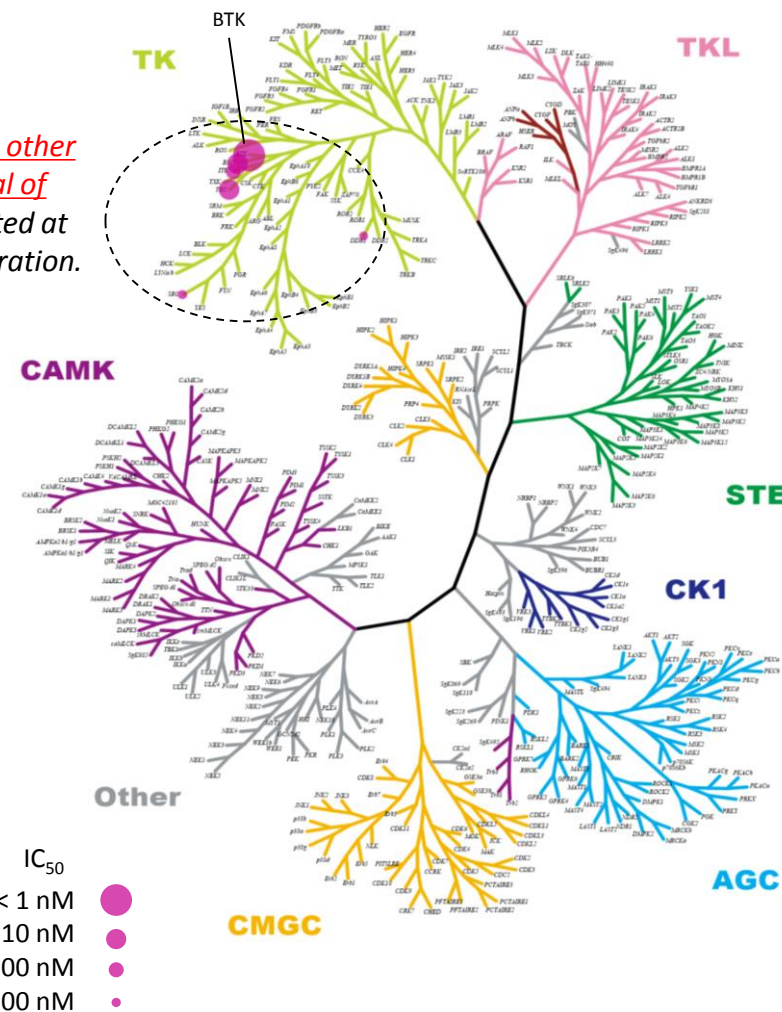
	IC ₅₀ (nM)	
	AS-1763	ibrutinib
Autophosphorylation BTK (Ramos)	1.4	1.1
CD69 activation (Human whole blood)	11	8.1
Cancer cell growth OCI-Ly10 cells	1.8	0.75
Cancer cell growth OCI-Ly10 [BTK C481S] cells	20	1030
Normal cell growth HEL299 cells	6370	6870

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

◆ Kinase selectivity profiling

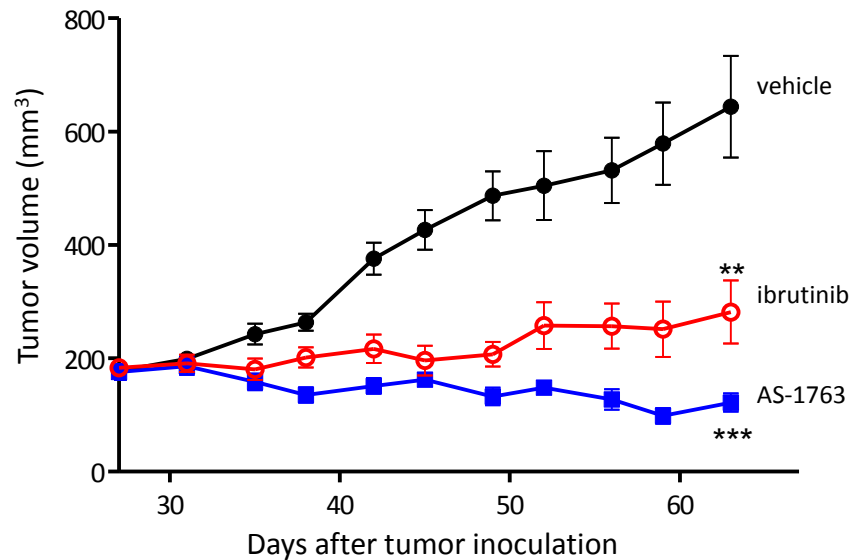
Only inhibited **6 other kinases** in a total of **291 kinases** tested at 0.3 μM concentration.



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



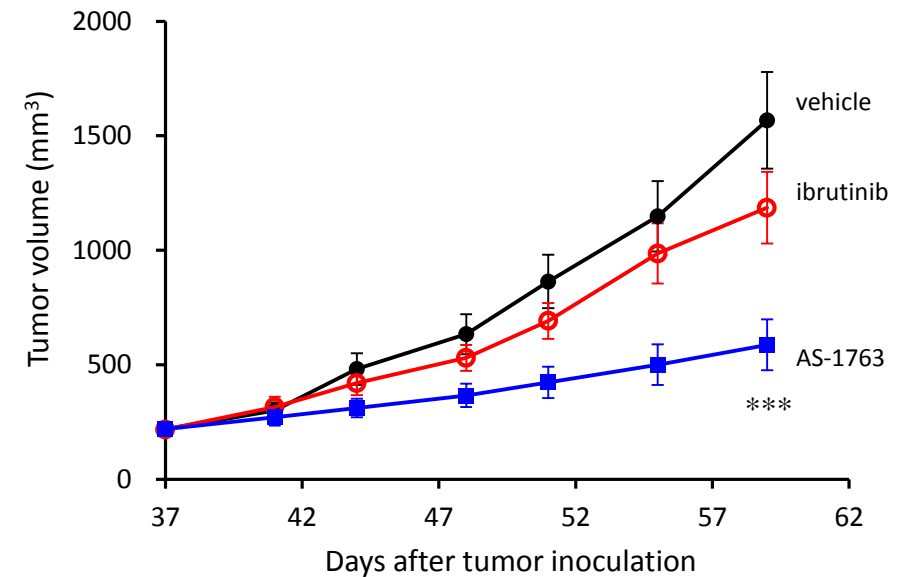
- ◆ In vivo antitumor effects of AS-1763 on human B-cell non-Hodgkin lymphoma cell line, OCI-LY10 tumor xenograft mouse model (n=8-10)



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

- First generation covalent BTK inhibitors
 - ✓ First generation covalent BTK inhibitors including ibrutinib are key therapeutic options for patients with B cell malignancies including chronic lymphocytic leukemia (CLL).
 - ✓ Sales of the first generation BTK inhibitors, ibrutinib, acalabrutinib, and zanubrutinib, totaled over \$9 billion in 2020. Sales of ibrutinib is expected to be over \$10 billion according to an estimate by Evaluate Pharma.
 - ✓ However, patients are reported to develop resistance during the treatment as more first generation BTK inhibitors are prescribed.

<Sales of first generation BTK inhibitors>

(\$million)	Development/ Marketing	2019	2020	2026Est.
Ibrutinib	AbbVie + J&J	7,291	8,433	10,722
Acalabrutinib	AstraZeneca	164	522	n.a.
Zanubrutinib	BeiGene	1	41	n.a.

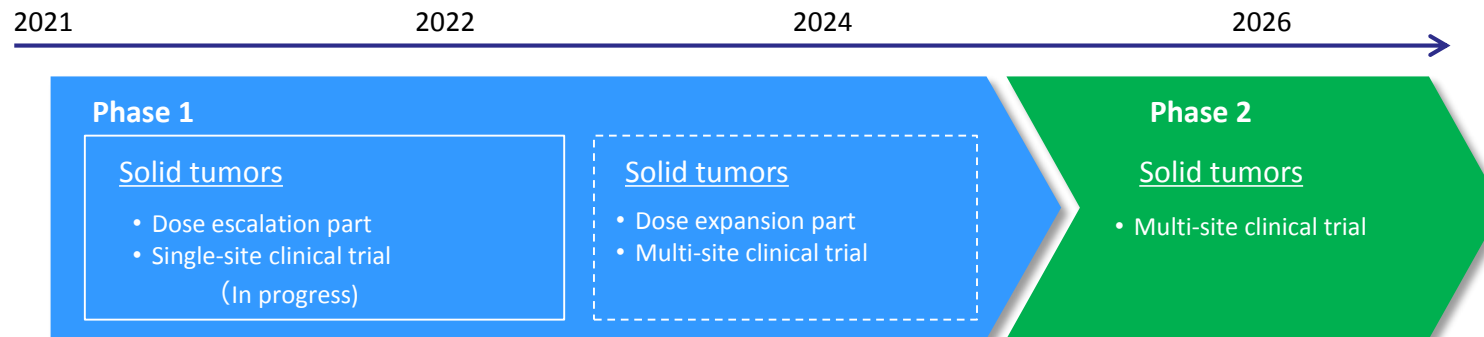
Source: Financial report of the companies for historical data. Estimate for 2026 is based on EvaluatePharma.

- A high unmet medical need for new therapeutic approaches to overcome the BTK C481S-mediated resistance
- ✓ Patients treated with ibrutinib are reported to develop resistance during the treatment due to substitution of cysteine residue at 481 position with serine (C481S mutation) in BTK, which prevents the covalent binding of the first generation irreversible BTK inhibitors.
- ✓ AS-1763 significantly abrogates cell proliferation in both wild type and C481S mutant BTK lymphoma cells, strongly suggesting that AS-1763 will be a new therapeutic option for treating patients with B cell malignancies both having wild type and C481S mutation in BTK.
- ✓ Inhibitors for BTK C481S-mediated resistance have not been launched, therefore there is a high unmet medical need for new therapeutic options.
- ✓ Two non-covalent BTK inhibitors to treat patients with BTK C481S mutation are currently under development. ArQule and Loxo that originally developed the programs were acquired by big pharma.

Compound	Company	Development Phase
ARQ531	Merck (ArQule)	P2
LOXO-305	Loxo / Lilly	P3

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



■ 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.

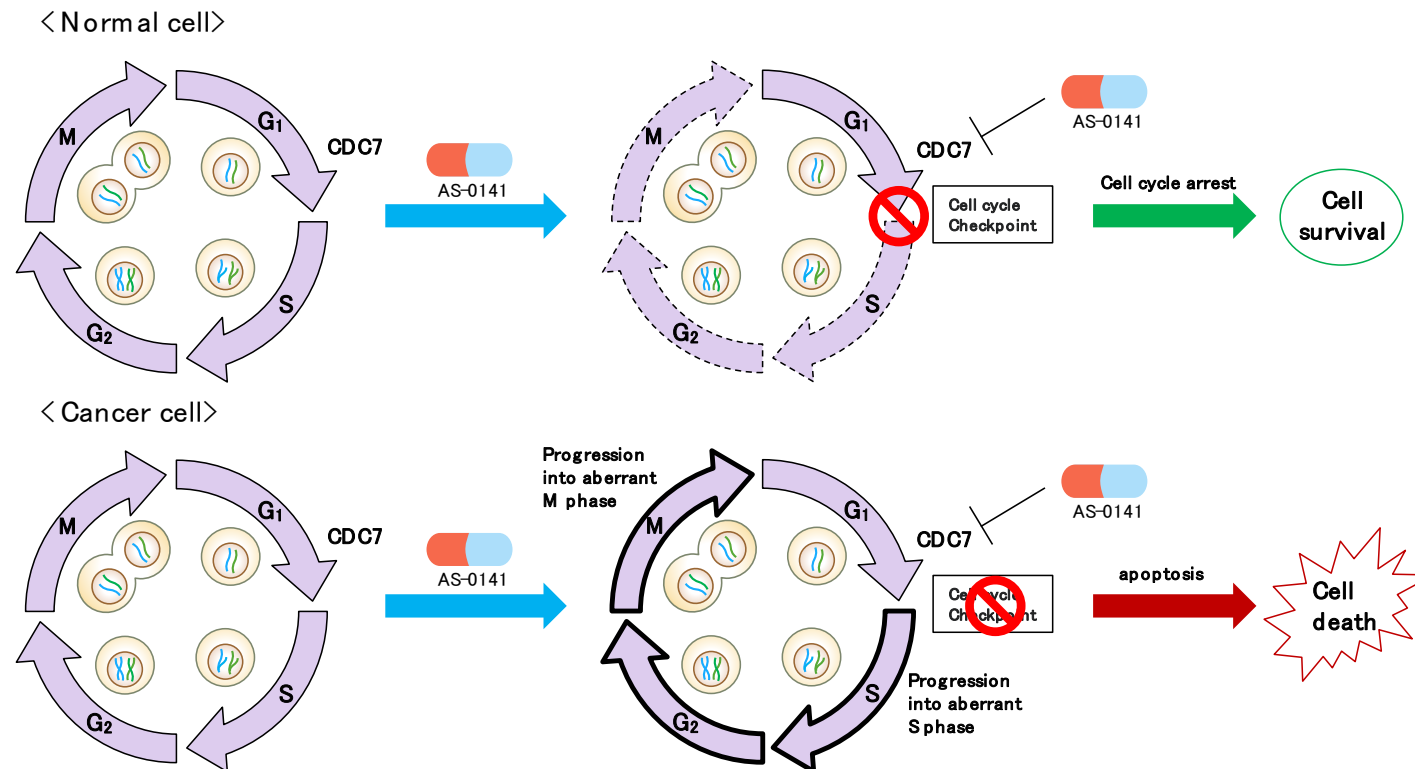
■ Clinical Development Plan

- ✓ 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)

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



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Drug Annotation

Research paper

Discovery of novel furanone derivatives as potent Cdc7 kinase inhibitors

Takayuki Irie^{a,b}, Tokiko Asami^a, Ayako Sawa^a, Yuko Uno^a, Mitsuharu Hanada^a, Chika Taniyama^b, Yoko Funakoshi^c, Hisao Masai^c, Masaaki Sawa^d

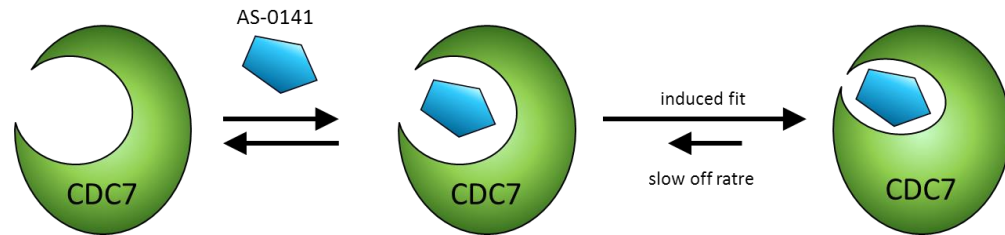
^a Research and Development, Carina Biosciences, Inc., 2F BMA, 1-5-5 Minatogima-Minamimachi, Chuo-ku, Kobe, 650-0047, Japan
^b Research and Development Department, SRI Biotech Co., Ltd., Ezumi Garden Tower B1F, 1-6-1 Aoyoguchi, Minato-ku, Tokyo 106-6018, Japan
^c Department of Genome Medicine, Tokyo Metropolitan Institute of Medical Science, 2-1-6 Kamikiazawa, Setagaya-ku, Tokyo 158-8501, Japan

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

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

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

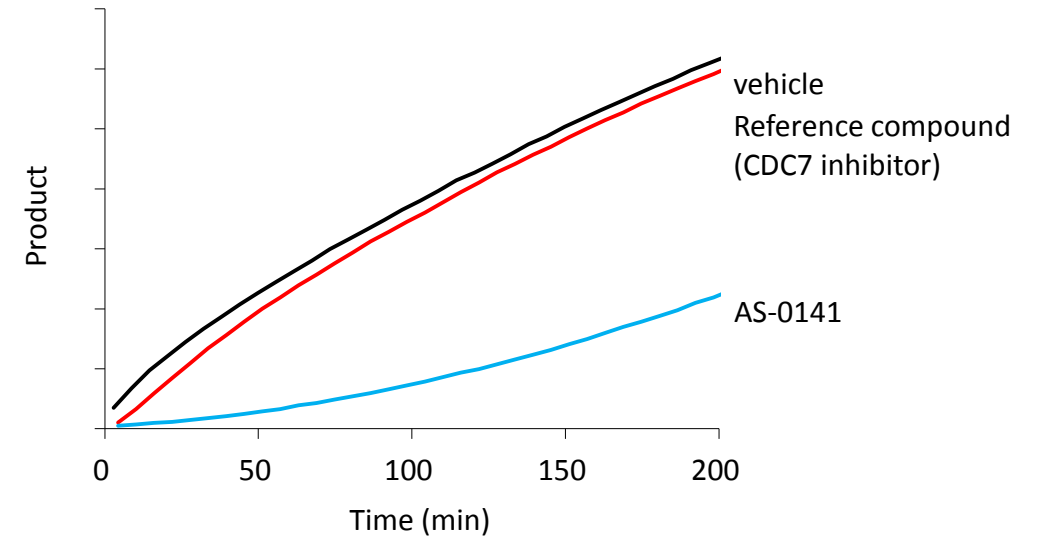
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Inhibitory potency (IC₅₀) for CDC7 in the presence of 1 mM ATP

Without Preincubation	With Preincubation
503 nM	2.4 nM

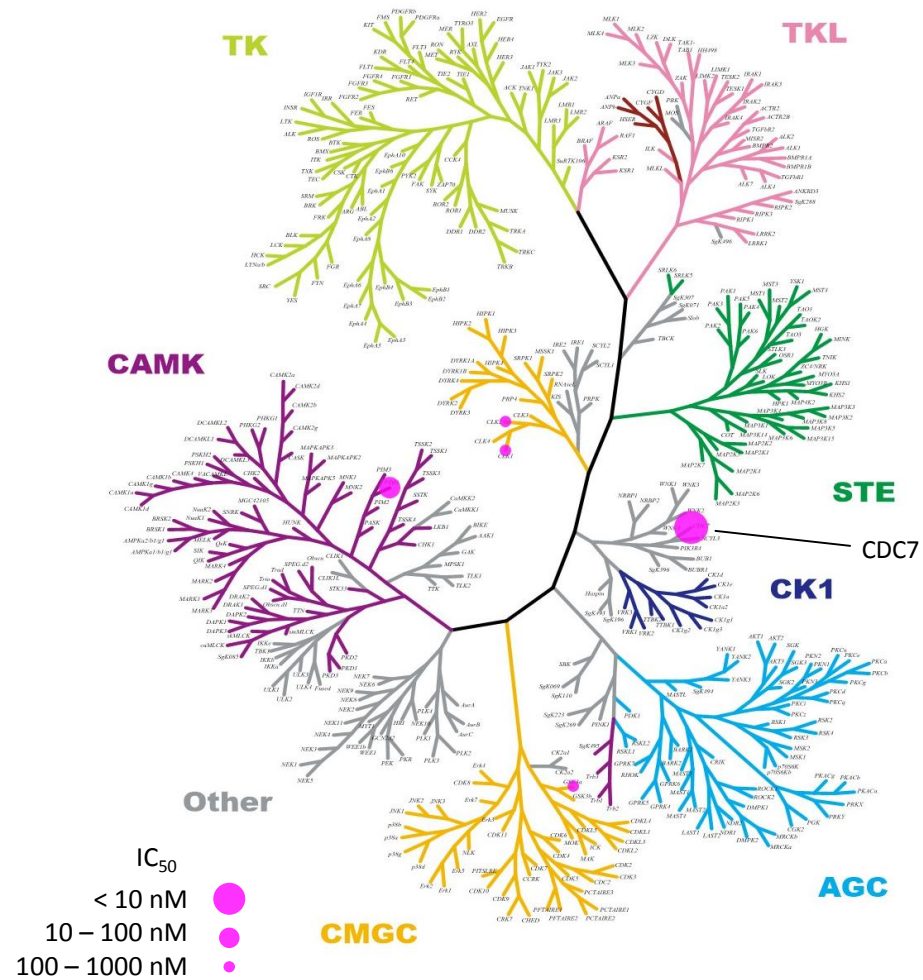
Rapid dilution assay for Cdc7 inhibitors. Recovery of enzymatic activity was monitored by formation of the phosphorylated product.



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

◆ 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
GSK3a	189	251

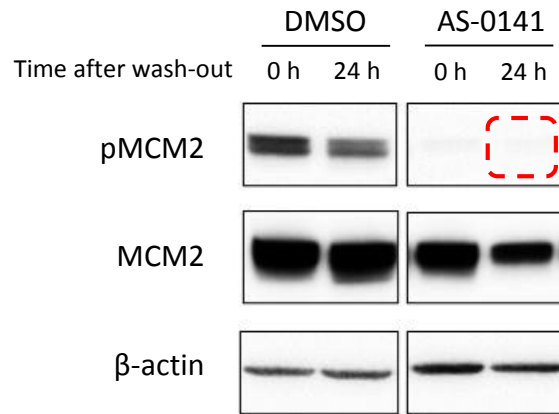
210-fold

CDC7 is the only kinase that shows preincubation effect

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

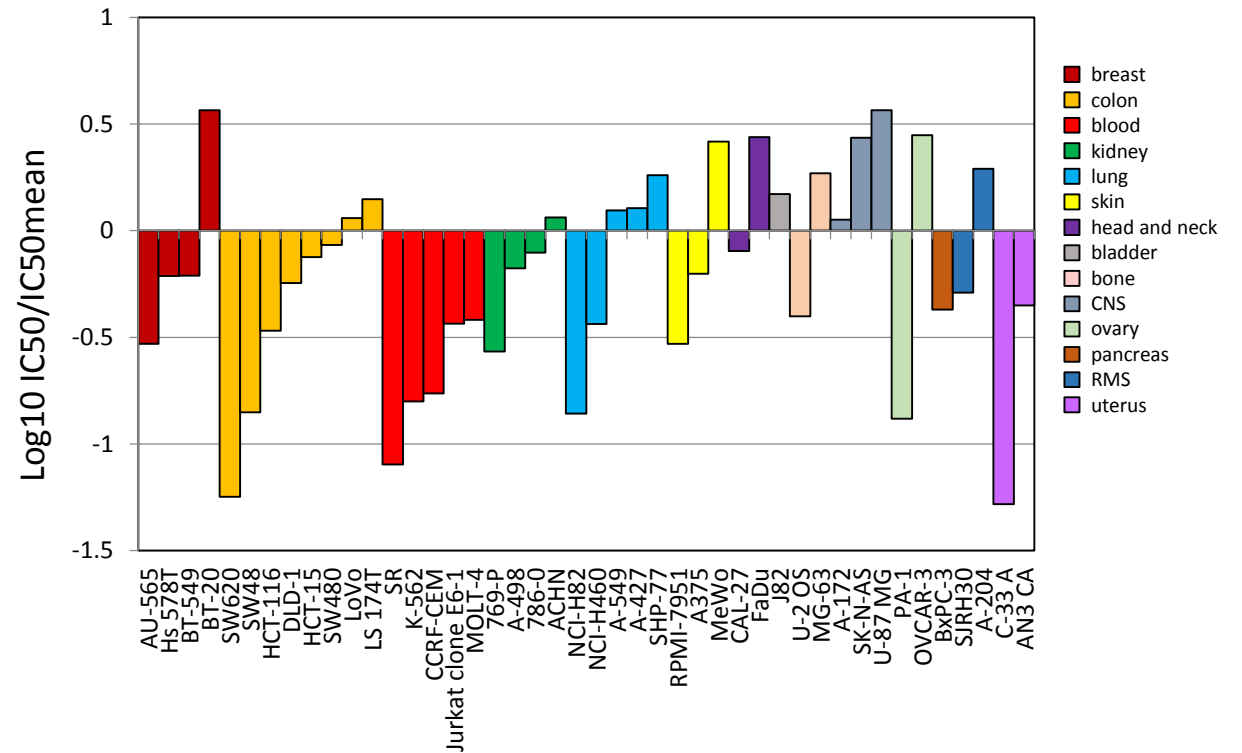
◆ Prolonged inhibition in cells

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.



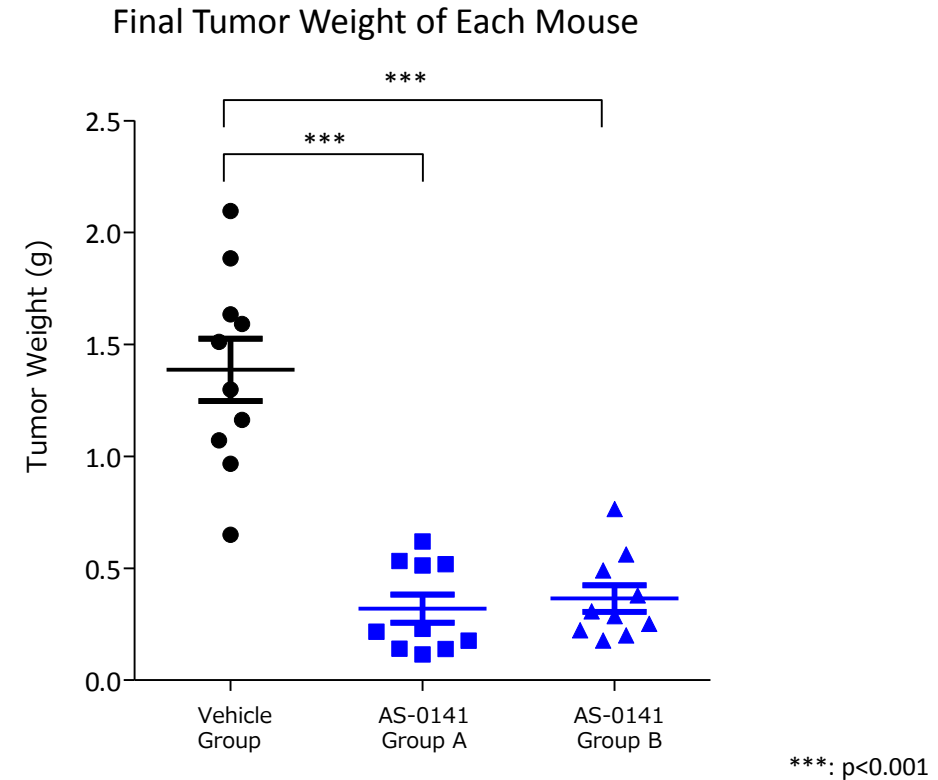
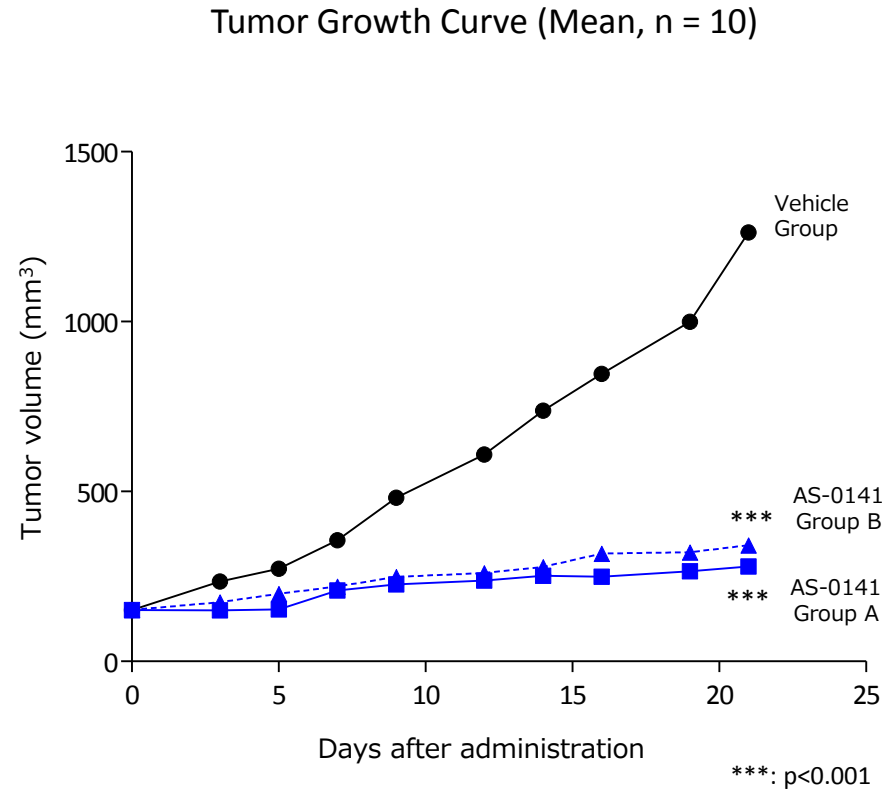
the inhibitory effect of AS-014 on the phosphorylation of MCM2 in cells continued up to 24 h after washing out

◆ 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)

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



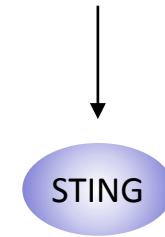
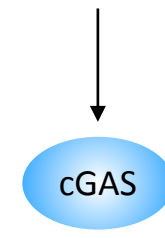
AS-0141 group A: 60 mg/kg TID, 4d ON/2d OFF
AS-0141 group B: 120 mg/kg QD

- ✓ 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.

Cytosolic DNAs produced by microbial infection or cellular stress



Type 1 INF production

Induce innate immunity

Potential Revenue from Out-licensed Programs



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

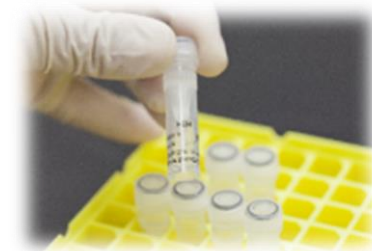
< License/joint research agreements with pharmaceutical companies >

Partner	Compound (Target)	Upfront payment	Total milestone payments expected	Royalty	Region	Contract date
Sumitomo Dainippon Pharma (Joint research)	Kinase inhibitor (Psychiatric and neurological disorders)	JPY80M (including research milestone)	JPY10.6B	Undisclosed	Worldwide	Mar. 2018
Gilead Sciences (Out-license)	Kinase inhibitor (Immuno- oncology)	\$20M	\$450M	Undisclosed	Worldwide	Jun. 2019
BioNova Pharmaceuticals (Out-license)	AS-1763	Undisclosed	\$205M	Up to two digits %	Greater China	Mar. 2020
Brickell Biotech (Out-license)	STING Antagonist	\$2M	\$258M	Up to 10%	Worldwide	Feb. 2022

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

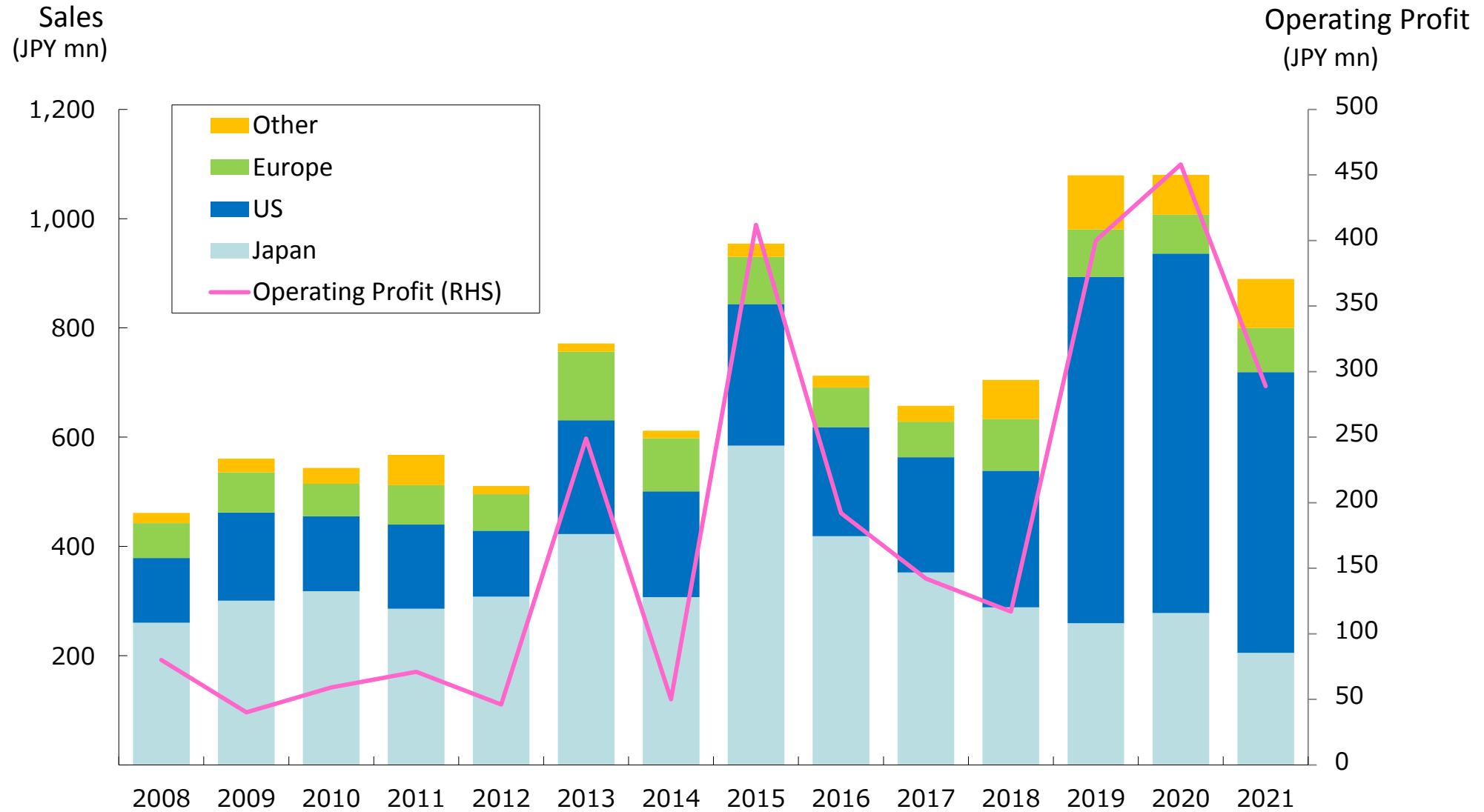
Drug Discovery Support (ddSP) Business

- ddSP business offers scientists worldwide key resources for their kinase inhibitor research including kinase proteins, assay kits, profiling and screening services, and cell-based assay services.
 - Our customers include top 10 pharmaceutical companies and biotech companies worldwide.
 - Our commitment to quality, including enzyme activity, purity, variability among others, leads to repeat orders and helps keeping our corporate image.
-
- High quality kinase proteins
 - ✓ *Lineup of approximately 460 products that are important for drug discovery research*
 - ✓ *Biotinylated Kinases of 130 kinds.*
 - Accurate profiling service
 - ✓ *Validated Kinase Panel that well cover the Human kinome (>300 kinases)*
 - Assay kits and assay development that satisfy customer needs
 - Cell-based assay services that provide further support to customers
 - ✓ *NanoBRET™ TE Intracellular Kinase Cell-Based Assay*
 - ✓ *ACD's Tyrosine Kinase Cell-Based Assay*
 - ✓ *NTRC's Oncolines™, panel of cancer cell lines*



- ✓ The demand for kinase inhibitor research services is strong in North America and China. More stable demand in Japan.
- ✓ Major competitors include Thermo Fisher Scientific(US), Eurofins(EU), SignalChem(Canada), and Reaction Biology(US) while no competitors exist in Japan.
- ✓ Carna is the only drug discovery support service provider specialized in kinase inhibitors.
- ✓ Carna is the only major player who offers biotinylated Kinases.
- ✓ Accurate assays, detailed technical support, and product development by researchers who have experiences in drug discovery.
- ✓ Focusing on cell-based assay services including NanoBRET™ TE Intracellular Kinase Assays, assay service licensed from Promega Corporation for which Carna recently launched a new full panel service.

Sales and Operating Profit of Drug Discovery Support (ddSP) Business



Business Plan

➤ *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)
<ul style="list-style-type: none"> Established in-house research capability Established pipeline 	<ul style="list-style-type: none"> Out-licensed multiple programs Initiated clinical trials 	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> 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

(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

Key Milestones for 2022



Business		Key Milestones		
		2021	2022	2023 and beyond
ddRD	AS-0871	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Initiate Ph1 MAD part (H2 2021) <i>(Achieved in Dec. 2021)</i> 	<ul style="list-style-type: none"> <input type="checkbox"/> Start partnering activity 	<ul style="list-style-type: none"> <input type="checkbox"/> Out-license
	AS-1763	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Initiate Ph1 (H1 2021) <i>(Achieved in Apr. 2021)</i> 	<ul style="list-style-type: none"> <input type="checkbox"/> Initiate Ph1b (US) 	<ul style="list-style-type: none"> <input type="checkbox"/> Proceed clinical trial and partnering activity
	AS-0141	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Initiate Ph1 (H1 2021) <i>(Achieved in Jun. 2021)</i> 	<ul style="list-style-type: none"> <input type="checkbox"/> Initiate Ph1 expansion part 	<ul style="list-style-type: none"> <input type="checkbox"/> Proceed clinical trial and partnering activity
	Research program	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Bring one or more programs in preclinical stage <i>(Achieved in Dec. 2021)</i> 	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Bring one or more programs in preclinical stage or license a program <i>(Achieved in Feb. 2022)</i> 	<ul style="list-style-type: none"> <input type="checkbox"/> Bring one or more programs in preclinical stage
ddSP		<ul style="list-style-type: none"> <input type="checkbox"/> Achieve sales target of JPY920 mn <input checked="" type="checkbox"/> Launch new products <input checked="" type="checkbox"/> Expand NanoBRET service <input type="checkbox"/> Propose project-based service to collaborate with clients, leveraging Carna's drug discovery technology 	<ul style="list-style-type: none"> <input type="checkbox"/> Expand sales of in-house developed products and services <input type="checkbox"/> Expand line-up of protein kinase products <input type="checkbox"/> Increase target kinases to expand profiling service <input type="checkbox"/> Seek collaboration opportunities to boost Carna's business 	<ul style="list-style-type: none"> <input type="checkbox"/> Expand sales of in-house developed products and services <input type="checkbox"/> Expand line-up of protein kinase products <input type="checkbox"/> Increase target kinases to expand profiling service <input type="checkbox"/> Collaboration opportunities to boost Carna's business

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

Achieved
 Plan or to be achieved

- In order to advance clinical trials, we aim to maintain adequate cash position by generating cash from Drug Discovery Support(ddSP) business and licensing, as well as by raising funds from capital markets.

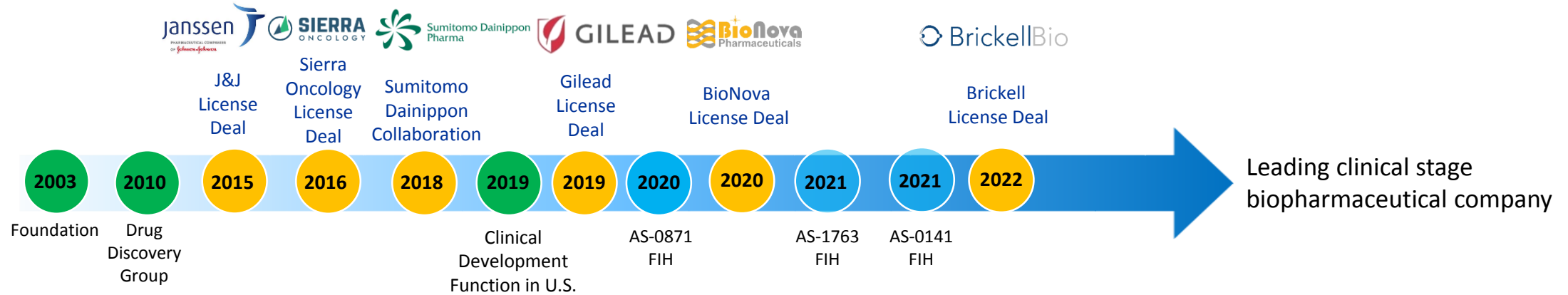
(JPY million)	As of Dec. 31, 2020	As of Dec. 31, 2021	Change
Current assets	4,708	5,318	+610
Cash and deposits	4,299	3,817	-481
Non-current Assets	127	114	-13
Total assets	4,835	5,432	+597
Current liabilities	727	774	+47
Non-current liabilities	284	342	+58
Total liabilities	1,011	1,116	+105
Total net assets	3,824	4,315	+491
Total liabilities and net assets	4,835	5,432	+597

Appendix

Building Long-Term Value



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



2003 - 2021	2022 Plan	Long term plan
<ul style="list-style-type: none"> ● Founding members who had expertise in kinase drug discovery technology spun out from Nippon Organon and established Carna. ● Started offering kinase proteins and screening services to pharmaceutical companies for kinase inhibitor drug discovery. ● In 2010, Drug Discovery Group was established to conduct internal drug discovery. ● Entered into four license agreements and one joint-development agreement with pharmaceutical companies. ● Initiated FIH study of BTK inhibitor AS-0871. 	<ul style="list-style-type: none"> ● Conducting Phase 1 studies of BTK inhibitor AS-0871, AS-1763, and CDC7 inhibitor AS-0141. ● Strengthening global clinical development capability. ● Advance research programs and initiate preclinical development. 	<ul style="list-style-type: none"> ● Advance clinical studies of AS-0871, AS-1763, and AS-0141 and earn upfront payments and milestone payments from out-licensing the pipelines. ● Receive milestone payments and royalties from licensees and strengthen financial position. ● Create next wave of pipeline.

FIH: First in Human

Directors



Kohichiro Yoshino, Ph.D. President & Chief Executive Officer, Representative Director

Dr. Yoshino founded Carna Biosciences in 2003 as a spin-out venture from Nippon Organon, a subsidiary of N.V. Organon where he was the head of the Osaka Research Center. As a member of Organon Research Committee, Dr. Yoshino contributed to research and development of NV Organon. Before joining Nippon Organon, he engaged in the research and development of small molecule drugs at Kanebo Corporation Inc. From 2004 to 2008, he was a Visiting Professor at Center for Advanced Science and Innovation, Osaka University. He earned M.S. in Chemistry from the Graduate School of Tokyo Institute of Technology and Ph.D. from Kyoto University.



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

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



Masaaki Sawa, Ph.D. Chief Scientific Officer, Director

Dr. Sawa built the current drug discovery group at Carna. Before joining Carna, he held positions at Sumitomo Dainippon Pharma. Prior to that, he was a medicinal chemist at Nippon Organon, a subsidiary of N.V. Organon. From 2004 to 2006, he was a visiting scientist at the Scripps Research Institute in San Diego. Dr. Sawa was a Visiting Professor at Graduate School of Medicine, Kobe University from 2013 to 2015. He received his Ph.D. from Kyoto University.



Emi Yamamoto Chief Financial Officer, Director, President of CarnaBio USA, Inc.

Ms. Yamamoto joined Carna Biosciences in 2004 after engaged in fund administration at CSK Venture Capital. She built Carna's accounting and business management group and held a responsible role in Carna's IPO. Since 2017, she leads administration group, in charge of accounting, finance, human resources, and corporate planning. Ms. Yamamoto holds a bachelor's degree in Business Administration from Aoyama Gakuin University, and a Certified Public Accountant.

Directors



Atsuo Arita Outside Director

Before joining the Board of Directors in 2020, Mr. Arita served as External Auditor of Carna Biosciences from 2004 to 2020, overseeing its management as a full-time company auditor. He held various responsible roles in accounting, finance, and sales management at Kanebo Corporation Ltd. and was the head of business management at Kanebo. He holds a bachelor's degree in Business and Commerce from Keio University.



Tsuguo Ogasawara Outside Director

Mr. Ogasawara served as External Auditor of Carna Biosciences from 2005 to 2020 before joining the Board of Directors in 2020. He has brought Carna his extensive experience in international business. He was a Director at Chugai Pharmaceutical Co. Ltd., in charge of international business. Prior to that, he was engaged in business management, finance, and international business at Toray Industries, Inc. He holds a bachelor's degree in Economics from Keio University.



Teruo Takayanagi, Ph.D. Outside Director

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



Takao Matsui Outside Director

Mr. Matsui served as External Auditor of Carna Biosciences since 2019 to 2020 before joining the Board of Directors in 2020. He has over 35 years of experience in financial audit and related advisory business. He served as Certified Public Accountant at KPMG AZSA LLC. from 1982 to 2018. Mr. Matsui also currently serves as Outside Director of AIR WATER, INC. He was a Specially Appointed Professor at School of Accountancy, Kansai University since April 2018 to March 2020. He is a part-time lecturer at Kansai University and School of Accountancy, Kansai University since April 2020.

Mr. Matsui holds a bachelor's degree in School of Business Administration from Kwansei Gakuin University, and a Certified Public Accountant.



“Carna” is a goddess of Roman mythology who takes care of human health, protecting the human heart and other organs as well as everyday life, and is said to be the root for the word “cardiac.”

The word “biosciences” is derived from the words 'biology' and 'life sciences.'

Carna Biosciences has created contemporary Carna goddess with protein kinase.

Carna Biosciences, Inc.

Corporate Planning

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