Jacobio Pharma

2023 Interim Results Presentation

Aug 2023

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Key Milestones and Catalyst Events

2023 Interim Results

Core products

Glecirasib（KRAS G12Ci, JAB-21822)

- ***NSCLC*** *monotherapy* ***pivotal trial***
  Patient enrollment to **complete in Sep** 2023
- ***PDAC*** *monotherapy* ***pivotal trial***
  Approved and **granted BTD** by CDE
- ***CRC*** pivotal trial is under discussion with CDE.
  Data published at the 2023 JCA-AACR

JAB-3312（SHP2 inhibitor)

- *In combination with Glecirasib*
  More than 100 patients enrolled in the frontline, 2nd line, naïve and refractory setting
- *In combination with Sotorasib, osimertinib and anti-PD-1 antibody are ongoing*

Data Publications

2023 JAC-AACR

- Glecirasib plus cetuximab in CRC
  ORR 62.8%/DCR 93%

2023 AACR

- 3 preclinical studies
  - *$KRAS^{multi}$ inhibitor JAB-23425*
  - *CD73-STING iADC JAB-X1800*
  - *Aurora kinase A inhibitor JAB-2485*

Financial Performance

As of June 30, 2023:

- Bank Balances: RMB 1.3 billion
- Cash Runway: 24 months

- Revenue: RMB 40.3 million
- R&D Costs: RMB 230 million, increase by 5.5%

Financing Activities

- Public placing in Feb: RMB159 million
- Capital investment by Beijing E-town (亦庄国投) of RMB150 million

3 New INDs

- JAB-26766 (PARP7i)
- JAB-BX300 (LIF mAb)
- JAB-24114（GUEi）

New R&D Center

May 2023

- New Headquarters and R&D Center officially in operation
- Total area: 20,000 square meters

2023 H2 - 2024 H1 Key Milestones and Catalyst Events (1/2)

Event	Expected Timing
NDA	
Glecirasib (JAB-21822) monotherapy in NSCLC pre-NDA submission (CMC portion)	• 2023 Q4
Glecirasib (JAB-21822) monotherapy in NSCLC NDA submission	• 2024 H1
Pivotal Trials	
Glecirasib (JAB-21822) monotherapy in PDAC – Site activation	• 2023 September
Glecirasib (JAB-21822) combo w/ Cetuximab in patients with CRC *	• 2024 Q1
POC Readout	
JAB-3312 (SHP2i) Combo with Glecirasib (JAB-21822)– Oral presentation at ESMO	• 2023 Q4
Other Clinical Milestones	
JAB-8263 (BETi) RP2D	• 2023 H2
JAB-2485 (Aurora Ai) RP2D	• 2024
JAB-BX102 (CD73) RP2D	• 2024 H1

** CDE/FDA consulting meeting will be held to discuss the pivotal trials.*

2023 H2-2024 H1 Key Milestones and Catalyst Events (2/2)

Event		Expected Timing
New INDs		
JAB-23400 (KRAS^{multi})		• 2024 H1
JAB-30300 (P53 Y220C)		• 2023 Q4
Data publication		
ESMO	• Clinical data of JAB-3312 (SHP2i) plus Glecirasib	• October 2023
ASCO GI *(plan to submit)*	• Glecirasib monotherapy in PDAC and other tumor types	• January 2024

The Dilemma of Oncology Drug Development in the Past Decade

Target Therapy

In the last 15 years since 2001, the easier therapeutic targets have been largely developed, shifting the focus to previously considered undruggable targets.

Immuno-oncology

After the successful development of the anti-PD-1 antibody in 2013, there have been essentially no breakthrough in the field of immuno-oncology, particularly for “cold” tumors.

Our Strategy and Pipeline Layout (1/2)

Leveraging our IADD Platform for Developing Novel Drugs toward Undruggable Targets and Serving as Payloads for iADC

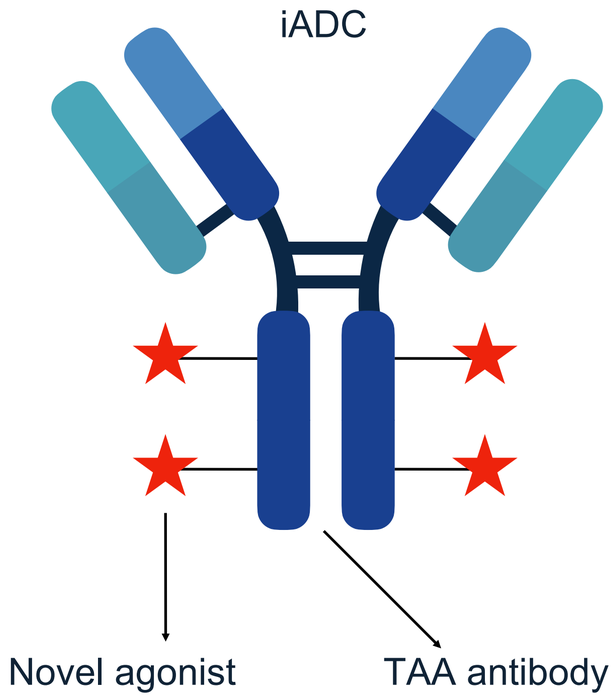
Jacobio's Induced Allosteric Drug Discovery ("IADD") Platform enables small molecules development toward undruggable targets including SHP2, KRAS, P53, Myc etc.

Development toward undruggable targets for classic oncogenic pathways

- **KRAS Pathway**
  JAB-21822 KRAS G12C
  JAB-3312 SHP2
  JAB-23400 KRAS^{multi}
  JAB-2485 Aurora A
  JAB-BX300 LIF
  JAB-22000 KRAS G12D
- **MYC Pathway**
  JAB-8263 BET
  JAB-2485 Aurora A
- **P53 Pathway**
  JAB-30300 P53 Y220C
- **Tumor Metabolic**
  JAB-24114 GUE

Our Strategy and Pipeline Layout (2/2)

Leveraging our IADD Platform for Developing Novel Drugs toward Undruggable Targets and Serving as Payloads for iADC



Development in Immuno-oncology

- **iADC**

  JAB-X400 HER2-STING agonist

  JAB-X1800 CD73-STING agonist

  …

- **Downstream targets of STING**

  JAB-26766 PARP7

In-house iADC platform with innovative payloads developed by utilizing IADD, promotes the filtration of immune cells to tumor and converts “cold” tumors to “hot” tumors.

9

Our Pipeline

Asset	Target	Pathway	Stage	IND	Indications	Global Ranking*	China Ranking	Note
JAB-3312 **JAB-3068**	SHP2	RAS&I/O	Phase II	2018	NSCLC, ESCC, other solid tumor	**2**	1	
JAB-21822	KRAS G12C	RAS	Phase II	2021	NSCLC, CRC, PDAC, other solid tumor		**2**	**Submit NDA in 2024**
JAB-8263	BET	MYC	Phase I	2020	solid tumor, MF, AML		**1**	The same target project $1.7 billion license-out
JAB-2485	Aurora A	RB	Phase I	2021	solid tumor	**2**	**1**	Eli Lily, Phase I/II
JAB-24114	GUE	Tumor Metabolic	IND approved	2023	solid tumor	**2**	**1**	Dracen, Phase I
JAB-BX300	LIF	RAS	IND approved	2023	solid tumor	**2**	**1**	AZ, Phase II
JAB-26766	PARP7	I/O	IND approved	2023	solid tumor	**2**	**1**	Ribon, Phase I
JAB-23400	$KRAS^{multi}$	RAS	IND-enabling	2024 H1	solid tumor	**1** (expect)	**1** (expect)	No products have entered clinical trials globally
JAB-30300	P53	P53	IND-enabling	2023 H2	solid tumor	**2** (expect)	**1** (expect)	PMV, Phase I
JAB-BX102	CD73	I/O	Phase I	2021	solid tumor			
JAB-BX400	HER2-STING iADC	I/O	Preclinical study	2024-2025		**2** (expect)	**1** (expect)	Mersana
JAB-X1800	CD73-STING iADC	I/O	Preclinical study	2024-2025		**1** (expect)	**1** (expect)	No products have entered clinical trials globally
JAB-22000	KRAS G12D	RAS	Lead optimization	2024		**2** (expect)	**1** (expect)	Mirati, Phase I

* Global ranking : Ranked by time of IND approval from FDA

Targeted Therapy Programs

- KRAS Pathway

Advancing Glecirasib in NSCLC

Regimen	Indications	IND	Phase I	Phase IIa	Phase IIb
Mono	NSCLC	***China trial (pivotal trial)***			
Combo w/JAB-3312	1L, 2L+ and KRAS G12Ci resistant NSCLC	***China trial***			
Mono	1L NSCLC w/ STK11 co-mutation	***China trial***			
Combo w/PD-1 mAb	NSCLC	***China trial***			
Mono	NSCLC	***Global trial***			

Robust enrollment from front line to late line NSCLC patients

- **Monotherapy: approximate 200 patients with KRAS G12C mutation have been enrolled in 100 sites.**
  - Pre-NDA submission in 2023Q4
  - NDA submission in 2024H1
  - BTD was granted by CDE in 2022
  - Phase II portion of global trial is enrolling NSCLC patients in Europe.

- **JAB-21822+JAB-3312: More than 100 patients were enrolled in study in various setting.**
  - Impressive clinical activity were observed in NSCLC, particularly frontline setting.
  - Results will be presented as oral presentation at 2023 ESMO.

Glecirasib has Superior Efficacy and Safety Profile in NSCLC

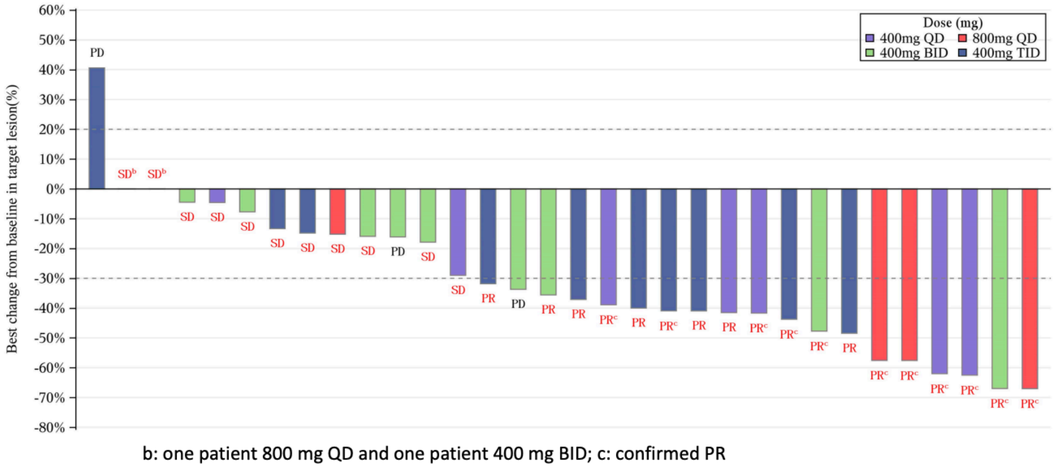
Efficacy

- In the early dose esc/exp trial, ORR was observed 56.3% (18/32) in NSCLC (2022 ASCO abstract).
- Promising response data in the frontline NSCLC was observed for JAB-21822+JAB-3312 trial (2023 ESMO Oral)

Safety

- JAB-21822, a weak base molecule with little stimulation to gastrointestinal tract, stands out for its minimal GI toxicity.
- Exploration of different dosing schedules (QD, BID and TID) led to the optimal daily dosing for all subsequent trials.
- Daily administration allows favorable toxicity profile (low Cmin) and potent anti-tumor activity (24 hours ERK suppression by its covalent binding)

Patients with KRAS G12C mutant NSCLC



b: one patient 800 mg QD and one patient 400 mg BID; c: confirmed PR

- **ORR 56.3% (18/32); DCR 90.6% (29/32)**
- QD COHORT (included 400mg & 800mg QD):
  - **ORR for 400 mg and 800 mg QD cohorts is 66.7% (8/12)**
  - **DCR for QD dosing 400 mg and 800 mg 100% (12/12)**

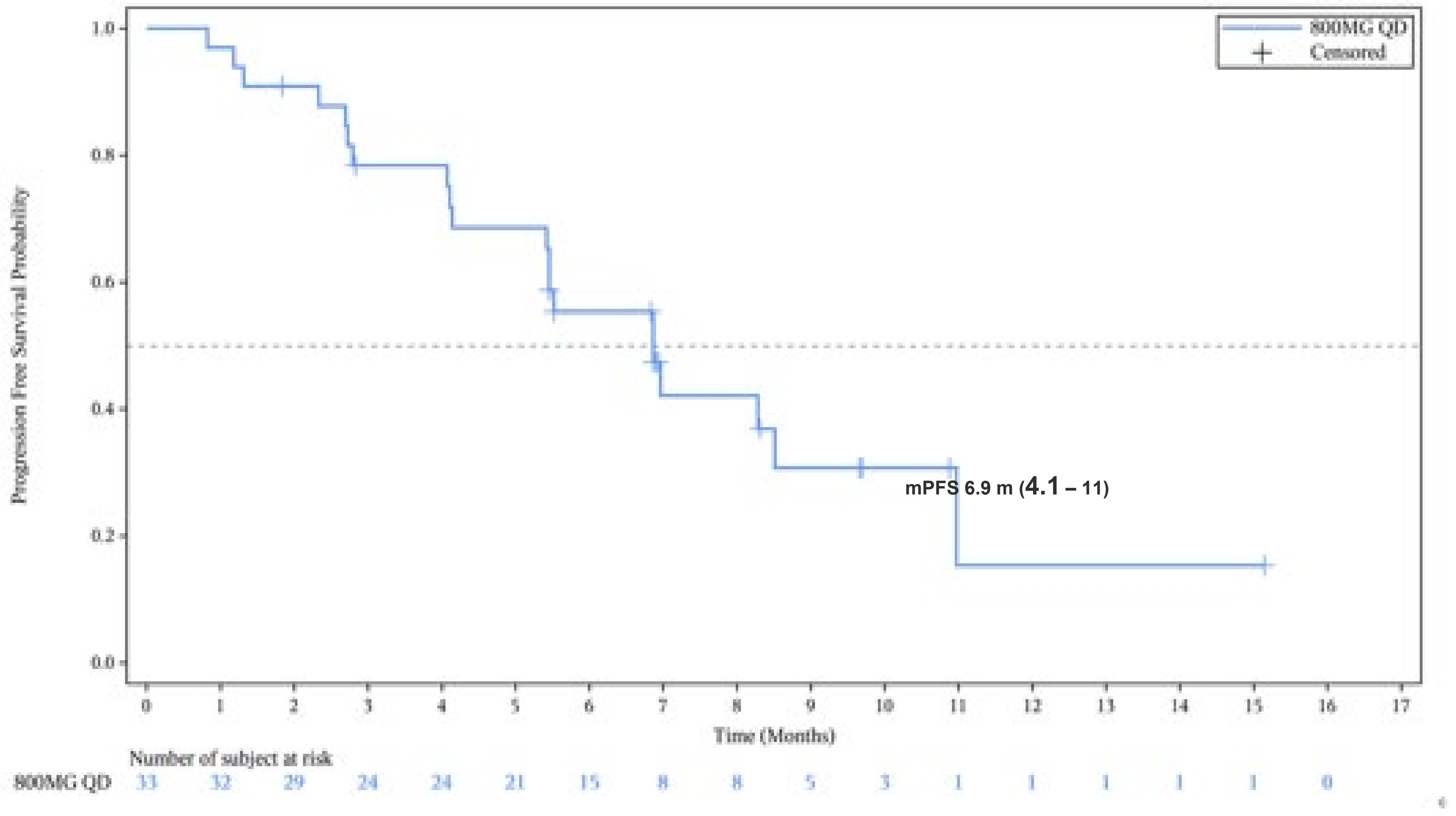
#3089, 2022 ASCO Poster, 8:00 AM-11:00 AM (CDT) 5 Jun 2022

Glecirasib has the BIC Potential in CRC

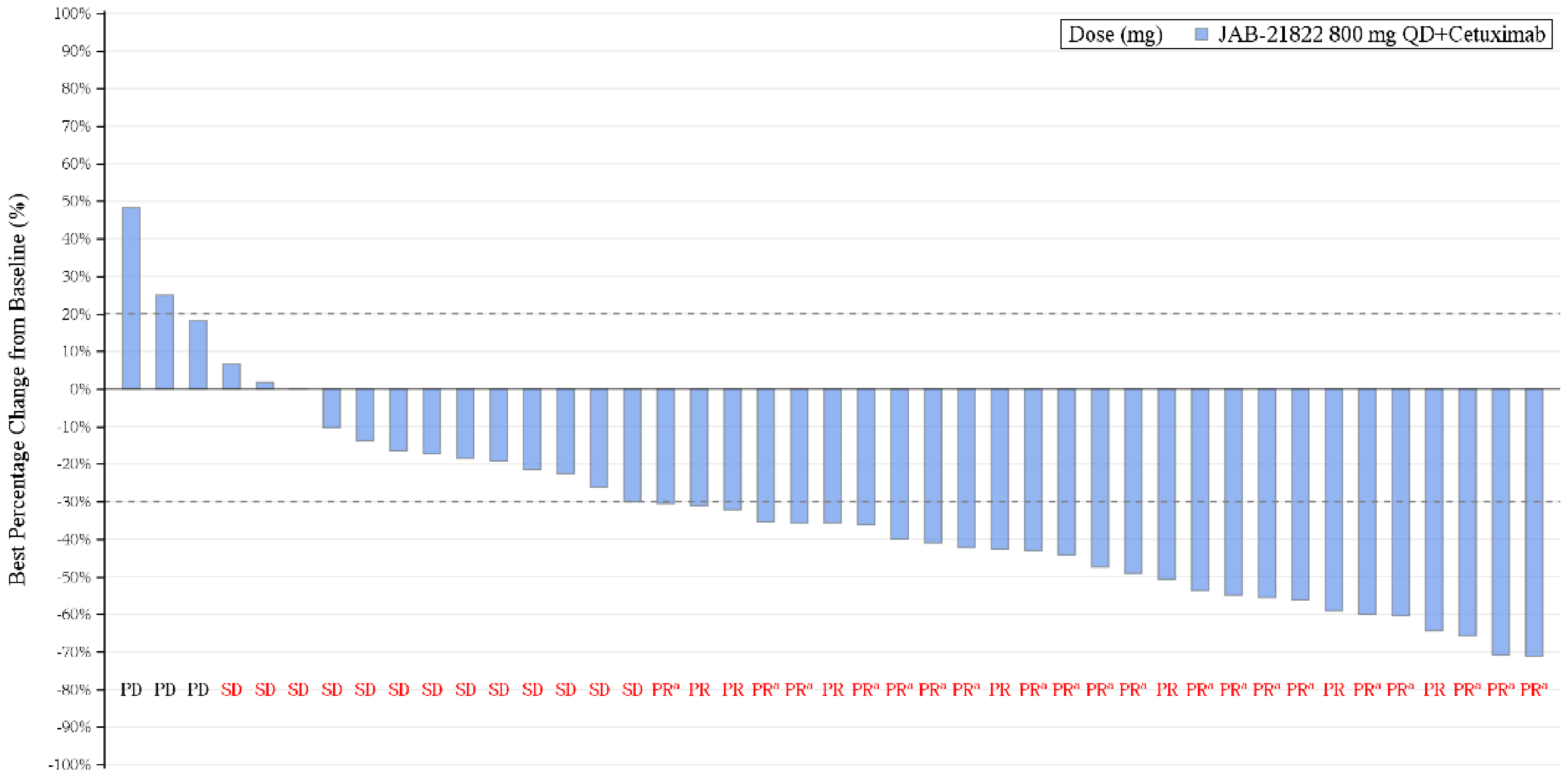
Efficacy and Safety shows superior advantage cross the competitors

- JAB-21822 has encouraging single agent activity in advanced CRC
  - ORR 33.3% (11/33), DCR 90.9% (30/33) and mPFS of 6.9 months.
- JAB-21822 + cetuximab produced promising clinical activity in advanced CRC
  - **ORR 62.8% (27/43) and DCR 93% (40/43).**
  - DOR and mPFS not reached
- Both single agent and combination therapy are safety and well tolerated.
- JAB-21822 plus cetuximab phase III pivotal study is in planning.

mPFS= 6.9m for JAB-21822 monotherapy



ORR=62.8% for JAB-21822+cetuximab



Glecirasib in Pancreatic Cancer Development

Monotherapy

Clinical Development Update

- The single arm **pivotal trial** in patients with PDAC harboring KRAS G12C mutation was **approved by the CDE. Site** is expected to be activated in September 2023.
- In August, Glecirasib was **granted BTD** for 2L + KRAS G12C mutant PDAC in China. This is the second BTD granted to Glecirasib apart from the one granted for 2L + KRAS G12C mutant NSCLC in China.
- Glecirasib is **the first KRAS G12Ci** which was approved for pivotal trial in PDAC globally.
- MRCT strategy is being explored with FDA.

Data Publication Plan

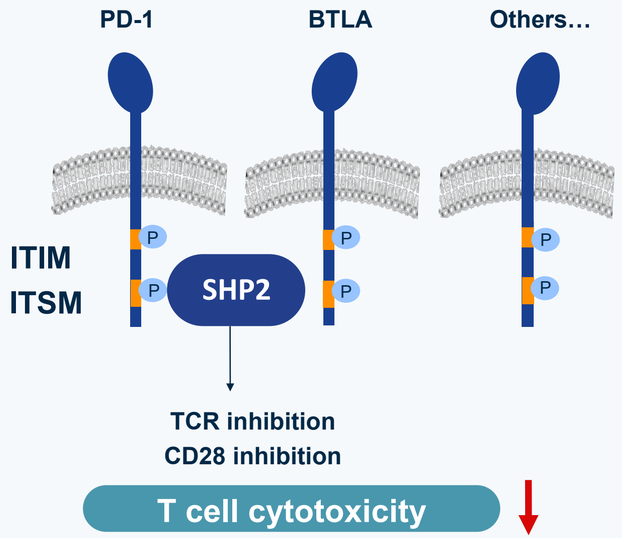
- With the promising tumor responding data, PDAC early result is planned to be submitted in the upcoming 2024 American Society of Clinical Oncology (ASCO) GI Annual Meeting, which will be held in January 2024.

SHP2 inhibitor

SHP2 Protein Phosphatase

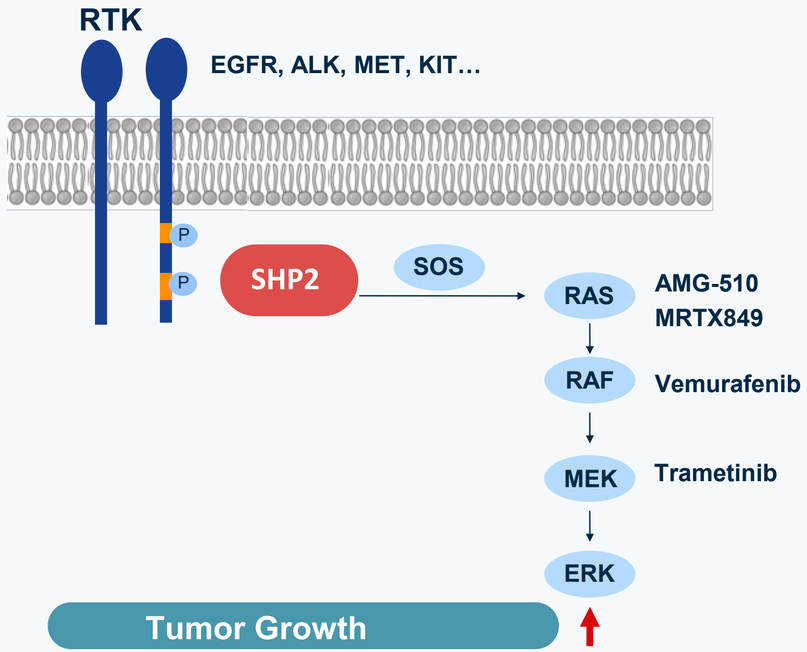
SHP2 effects are upstream of RAS and Programmed cell death protein 1 (PD-1)

Immune checkpoint in T cells



Ref: Science. 2017 31;355(6332):1428-1433.
Cell Rep. 2019 11;27(11):3315-3330.e7
Cancer Res. 75(3) February 1, 2015

KRAS pathway in tumor cells



Ref: Nat Med. 2018 24(7).
Sci Signal. 2019 28:12(583)

Clinical Application of SHP2 Inhibitors - SHPi+X combination therapy

SHP2 Inhibition Sensitizes Diverse Oncogene-Addicted Solid Tumors to Re-treatment with Targeted Therapy

- **SHP2 inhibitor overcome bypass-signaling-mediated resistance when combined with inhibitors of various oncogenic drivers**

1. Combo with KRAS G12C inhibitor: NSCLC,PDAC，CRC
2. Combo with ERK inhibitor (future multiple KRAS mutation inhibitor): KRASG12D-Mutant Ovarian Cancer.
3. Combo with ALK inhibitor: EML4–ALK Fusion–Positive Lung Cancer
4. Combo with Ros inhibitor: GOPC–ROS1 Fusion–Positive Pancreatic Cancer
5. Combo with BRAFV600E inhibitor: BRAFV600E-Mutant Colorectal Cancer

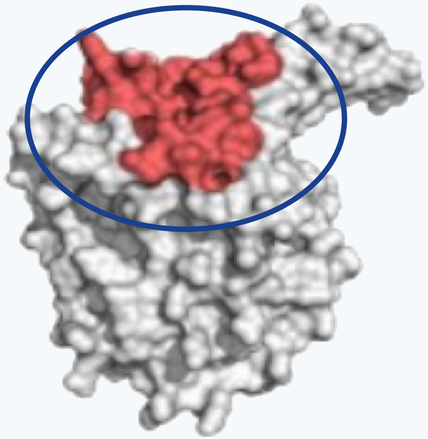
CANCER DISCOVERY, AUGUST 2023
By Memorial Sloan Kettering Cancer Center and Pfizer

JAB-3312 is the only second-generation SHP2i

First-generation SHP2i

JAB-3068
other clinical-stage compounds

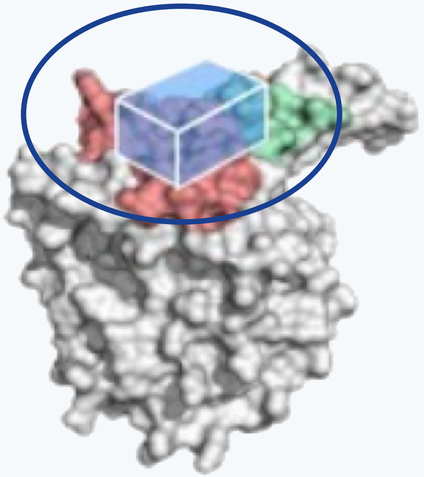
Biochemical assay IC_{50}: ~10nM
Cell viability IC_{50} ~100nM
Clinical dose up to 100-300mg/day



Second-generation SHP2i

JAB-3312

Biochemical assay IC_{50}: ~1.5nM
Cell viability IC_{50}: ~4nM
Clinical dose 2-4mg/day



Global Development Plan of SHP2 Inhibitors

Asset	Regimen	Indications	Phase I	Phase II
JAB-3312	Combination with JAB-21822	KRAS G12C mut solid tumors	*China trial*	
	Combination with sotorasib	KRAS G12C multi NSCLC	*Global trial*	
	Combination with Pembrolizumab (PD-1 mAb)	NSCLC, ESCC	*Global trial*	
	Combination with osimertinib	Osimertinib progressed NSCLC	*Global trial*	

SHP2i Development Highlight in 2022

- JAB-3312 + JAB-21822: Treatment responses were seen in KRAS G12Ci naïve and resistant patients both in first-line, second-line, and drug-resistant treatments, with over 100 patients enrolled. The preliminary clinical in the form of proffered paper presentation will be presented at the 2023 ESMO Congress in October 2023 in Spain.
- JAB-3312 + Pembrolizumab: Early efficacy signals were observed. Phase II trial is ongoing.
- JAB-3312 + Osimertinib: PhaseII trial is ongoing.

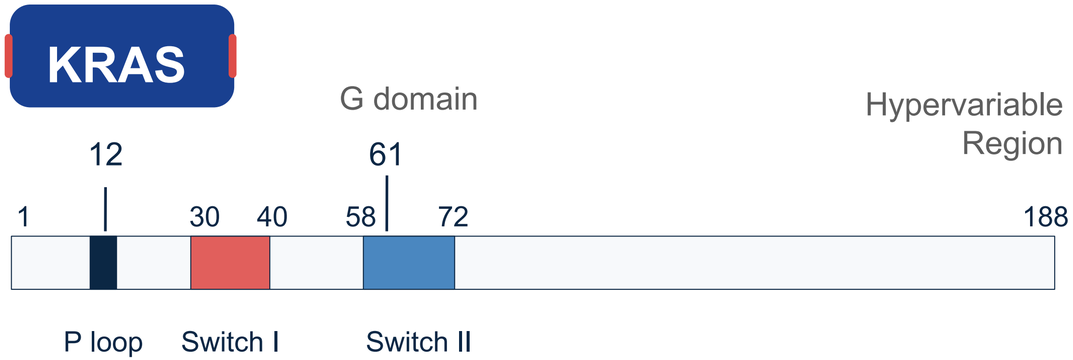
ESCC = esophageal squamous cell carcinoma; HNSCC = head and neck squamous cell carcinoma; NSCLC = non-small cell lung cancer; CC = cervical carcinoma; EC = Endometrial Cancer

JAB-23400: An Oral KRAS^{multi} Inhibitor

- **23% of** human cancers harbor KRAS mutations[1].
- **2,700,000** new cases per year with KRAS mutations in worldwide[2]

Differentiation of JAB-23400

- JAB-23400 inhibits **multiple KRAS mutants** (G12D, V, A, R, G13D, Q61H) in both RAS (ON) and RAS (OFF) states, but does not inhibit **HRAS and NRAS**. RMC-6236 inhibits not only KRAS but also HRAS and NRAS
- JAB-23400 binds to the **switch II pocket** of KRAS, while RMC-6236 binds to the pocket between KRAS and Cyclophilin A and forms **a Tri-complex**.



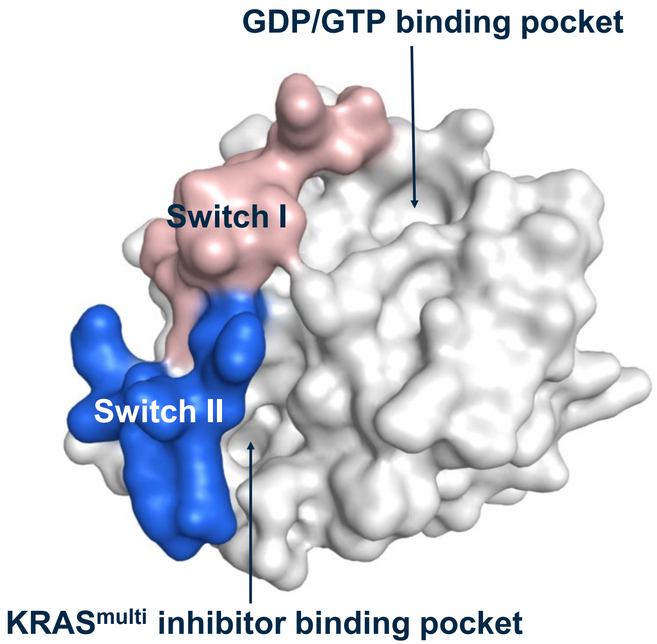


Image prepared by VMD 1.9.3

1. *npj Precis. Onc. 6, 91 (2022).*
2. *Numbers are estimated using the data from Estimated number of new cases in 2020, International Agency for Research on Cancer, World Health Organization*
3. *KRAS sequence from Comput Struct Biotechnol J. 2019 Dec 26;18:189-198.*

JAB-23400: An Oral KRAS^{multi} Inhibitor

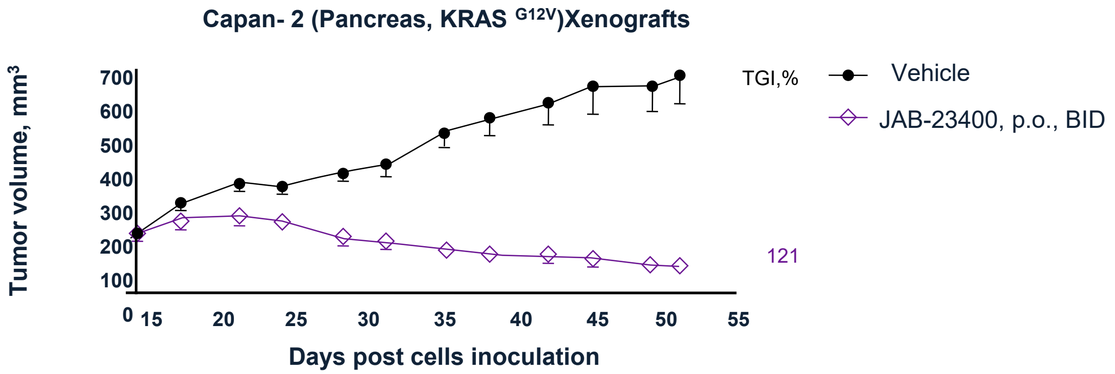
JAB-23400 Profile

- JAB-23400 inhibits the activity of multiple KRAS mutants **(G12D, V, A, R, G13D, Q61H)** in both RAS (ON) and RAS (OFF) states (binding affinity in pM for GDP and nM for GTP KRAS, slow K_{off} makes it behavior like a covalent inhibitor).
- JAB-23400 can potently inhibit the KRAS dependent cell line **(KRAS mutation/ WT amplification)**, while showing good selectivity to KRAS independent cell lines (KRAS WT without amplification in tumor and normal cells), which has **better safety windows.**
- JAB-23400 is an **oral bioavailable** KRAS inhibitor and exhibits **good PK properties**.
- **No inhibition** to HRAS and NRAS.
- **Tumor regression** is achieved in different KRAS mutant xenografts.

Inhibition of KRAS mutation profile

		Cell lines	pERK, IC_{50}, nM	Cell Viability, IC_{50}, nM
KRAS dependent cell lines	KRAS Mutation	AGS (KRAS G12D) SW620 (KRAS G12V) NCI-H747 (KRAS G13D)	**< 5**	**< 20**
	KRAS WT Amplification	MKN-1 (Stomach, CN=7) EBC-1 (Squamous, CN=5)	**< 5**	**< 20**
KRAS WT independent cell lines (no amplification)	KRAS WT (Tumor cell)	A375 (Skin)	>10000	>10000
		SK-MEL-2 (Melanoma)	>10000	>10000
		NCI-H1666 (Lung)	>10000	10000
	KRAS WT (Normal cell)	MRC-5 (Human Lung Fibroblast)	10000	>10000
		H9C2 (2-1) (Rat Heart)	9420	>10000

Strong antitumor activity



Targeted Therapy Programs - MYC Pathway

JAB-8263 Clinical Progress

- The Phase I dose escalation in solid tumors and hematological malignancies is ongoing in the U.S. and China simultaneously.
- Excellent safety and positive therapeutic signals.
- RP2D is expected to be determined in the second half of 2023.

JAB-2485 Clinical Progress

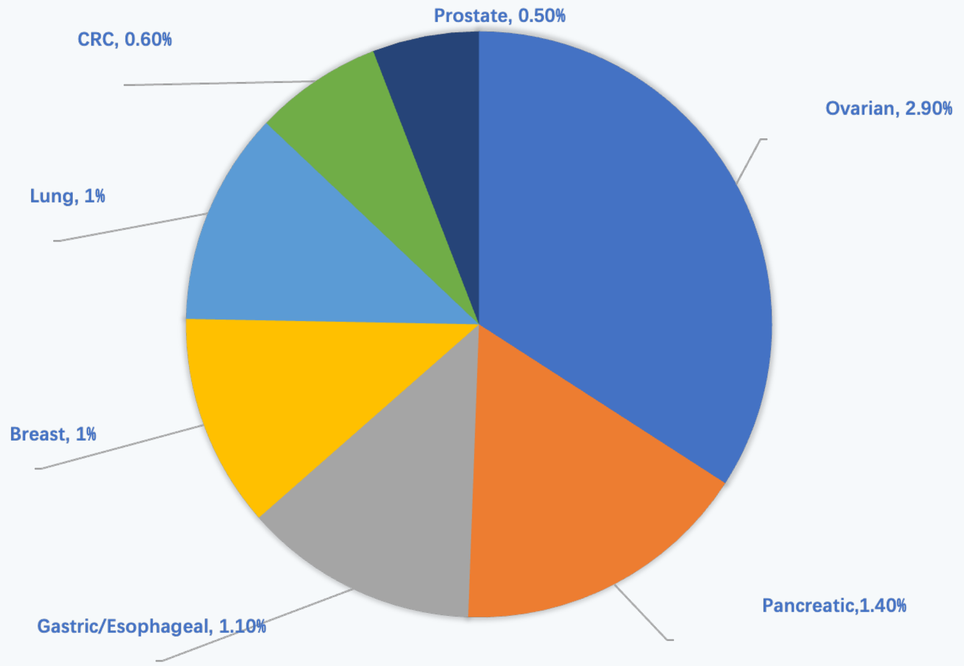
- The phase I/IIa global trial is on-going in the U.S. and China.

Targeted Therapy Programs

- P53 Pathway

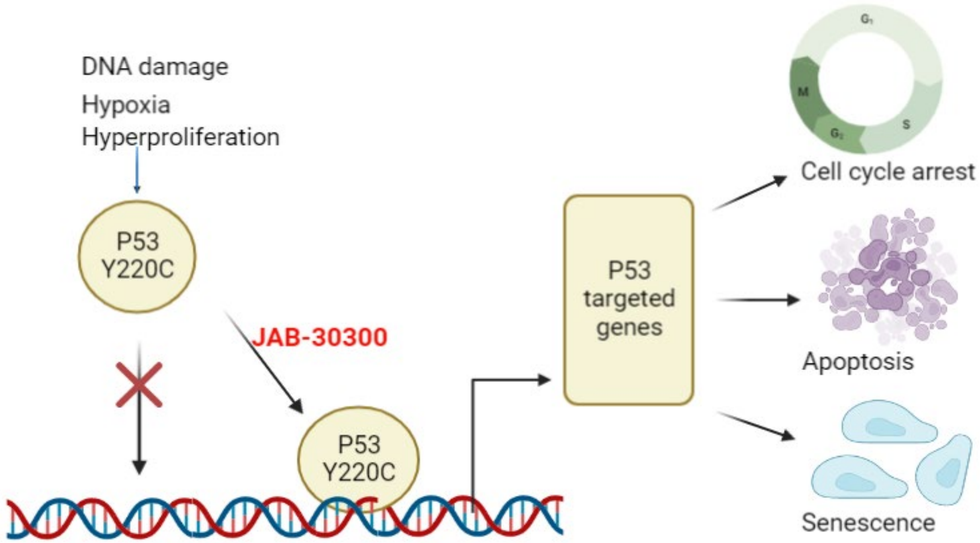
P53: Most Frequently Mutated Gene in Tumors

Frequency of P53 Y220C in solid tumors



- P53 is a key tumor suppressor that regulates various cell processes such as cell cycle arrest, DNA repair, apoptosis and aging.
- **About 50%** of cancer genomes contain P53 gene mutations
- P53 Y220C mutation is associated with **100,000** new cancer cases every year[1]

P53 Hotspot mutation	Frequency
Y220C	**1.80%**
R249S	2.00%
G245S	2.10%
R282W	2.80%
R273C	3.30%
R248W	3.50%
R273H	4.00%
R248Q	4.40%
R175H	5.60%



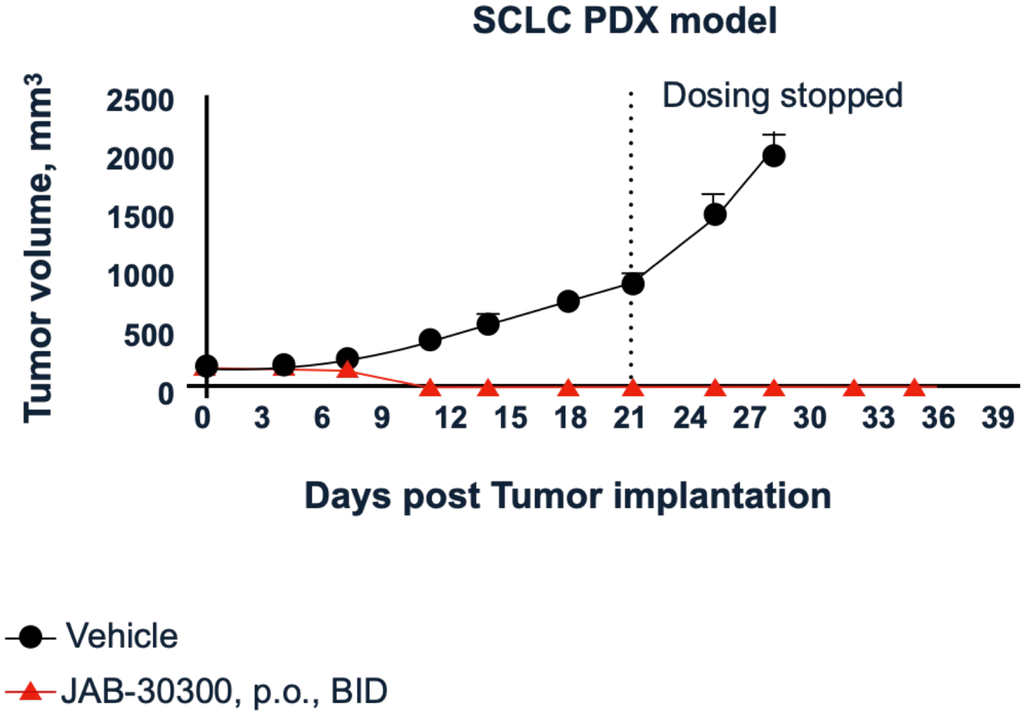
Ref: 1. ACS Pharmacol. Transl. Sci. 2022, 5, 1169−1180; 2. Data were obtained from the Catalogue of Somatic Mutations in Cancer (COSMIC) database

JAB-30300: An Oral P53 Y220C Activator

JAB-30300 Preclinical Profile

- JAB-30300 is **2-3 folds more potent than the competitor** (double digit nanomolar biochemical IC_{50})
- JAB-30300 demonstrates **>40% bioavailability** in mouse, rat, dog and monkey, and more than **3 folds higher** exposure in monkey than the competitor.
- Allometric scaling gives **low human clearance** prediction (<30% Qh).
- JAB-30300 crystalline shows high solubility in pH 1~7, and **100 folds higher** than the competitor at pH 6.5
- **Low risk** in hERG and CYP inhibition assays (IC50 >10 μM)
- JAB-30300 is predicted **a lower active human dose** than the competitor

Strong Antitumor Effect



Programs targeting other P53 mutations are also under development

Immuno-oncology

Clinical stage

- STING downstream target PARP7 inhibitor

Pre-clinical

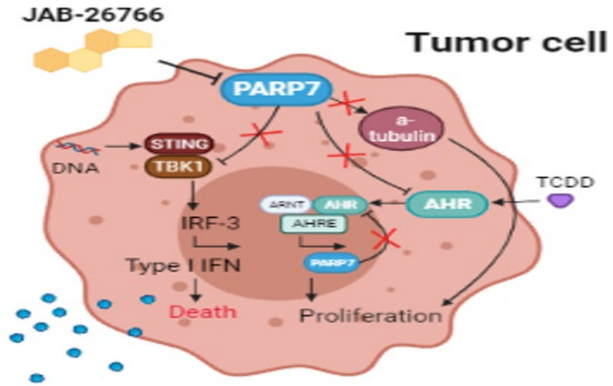
- iADC：Sting agonist as a Novel Payload

JAB-26766: An Oral PARP7 Inhibitor

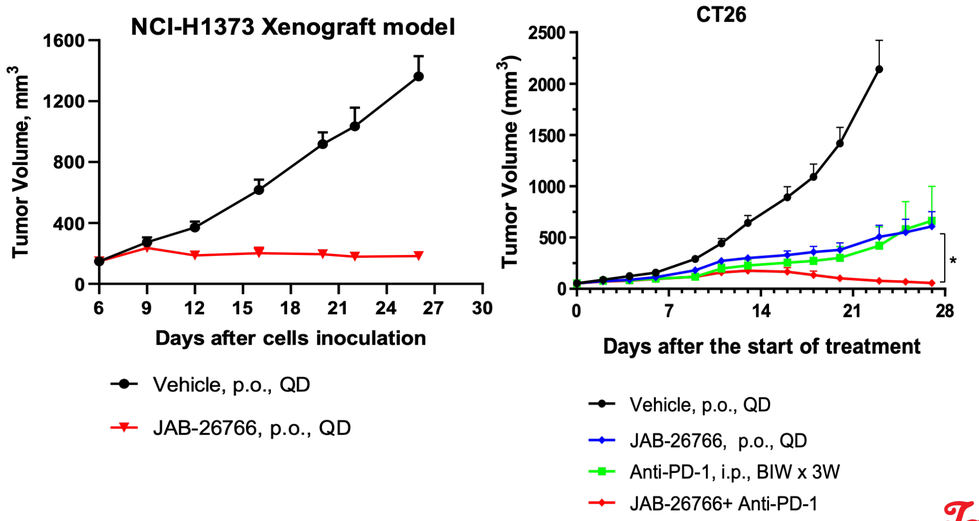
JAB-26766 Preclinical Profile

- PARP7 is frequently amplified in squamous cell carcinoma histologies, and inhibition of PARP7 restores the type I IFN response in tumor cells.
- JAB-26766 displays 3 folds higher potency in cellular assay, and 3-17 folds higher exposure in animals compared with the only competitor in clinical development.
- JAB-26766 demonstrates single agent anti-tumor activity in Xenografts. It synergizes with anti-PD-1, and also has the potential to combine with our iADC.
- JAB-26766 is predicted to have a lower active human dose than its competitor.

Role of PARP7



Strong Antitumor Effect



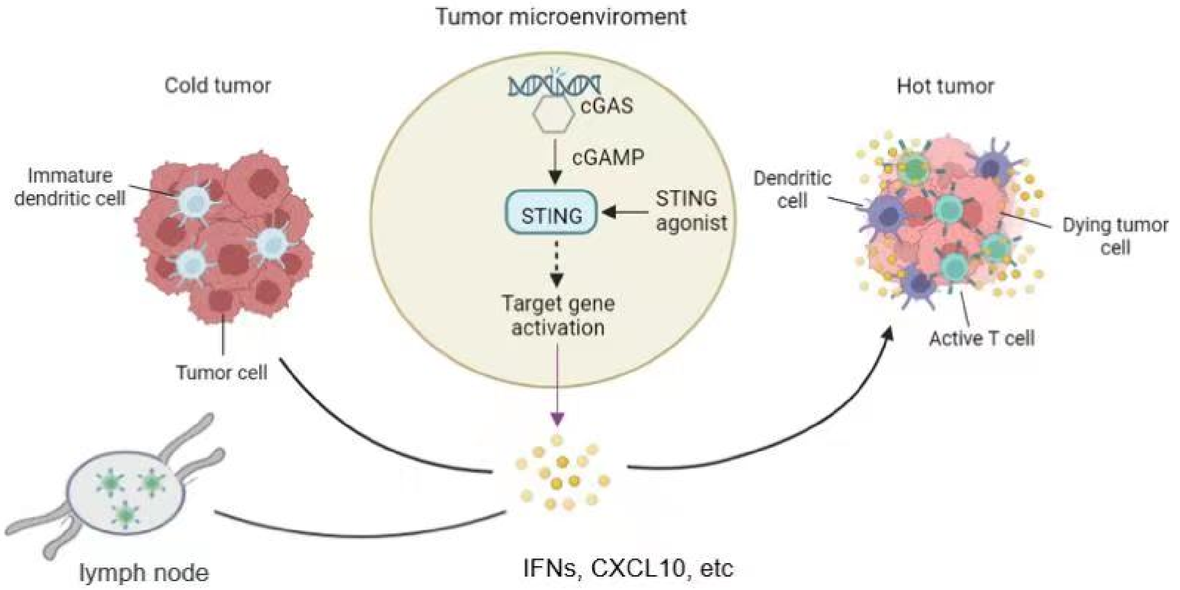
JAB-27670: STING Agonist as iADC Payload

Rationale

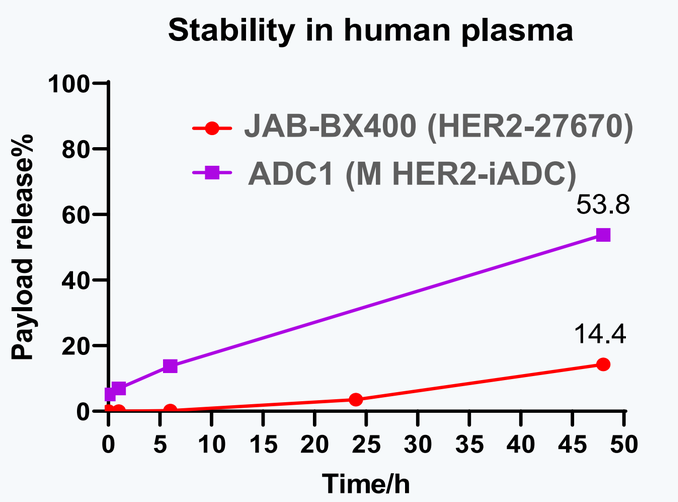
- STING agonist produces antitumor cytokine IFNs and T cell chemokine CXCL10, turning **“cold”** tumors into **“hot” tumors**.
- **Tumor-targeted delivery** of STING agonist is warranted to avoid toxicity by systemic administration.

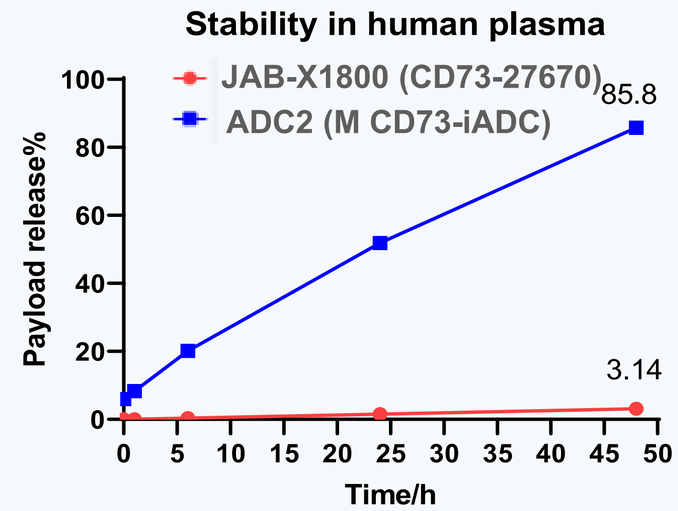
JAB-27670 Preclinical Profile

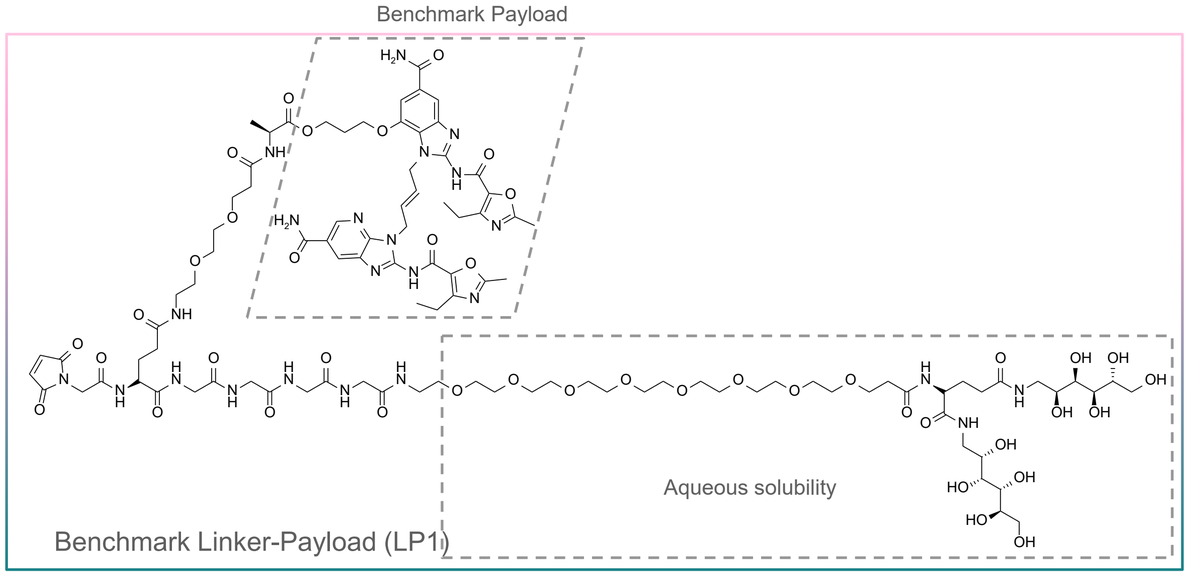
- **Non-CDN** small-molecule (good stability in tissue)
- **High potency** (IC_{50} <1nM)
- **High water solubility** (> 1 mg/mL @ pH 6~7)
- **Low permeability** ($Papp_{(A-B)} < 1 \times 10^{-6}$, cm/s)
- **Low hERG risk** (< 5% inhibition at 10 μM)



Stability of STING iADC agonists in plasma







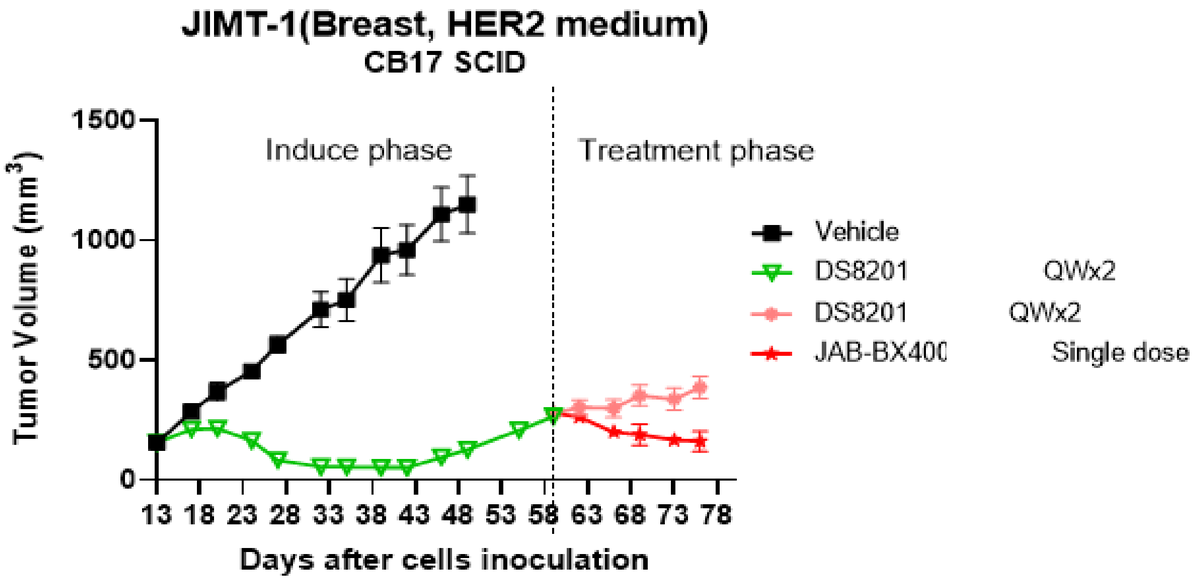
M iADC

Our iADC

- **No Payload release in plasma**
- **Favored safety** (no stimulation of inflammatory cytokine IL-6 in peripheral blood)

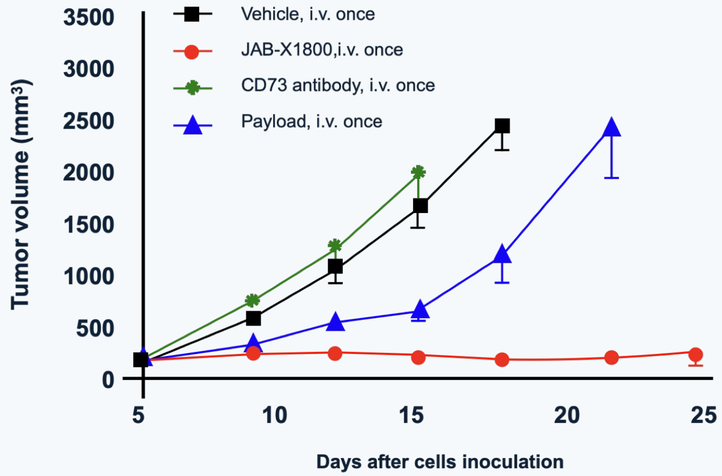
Our iADC Products

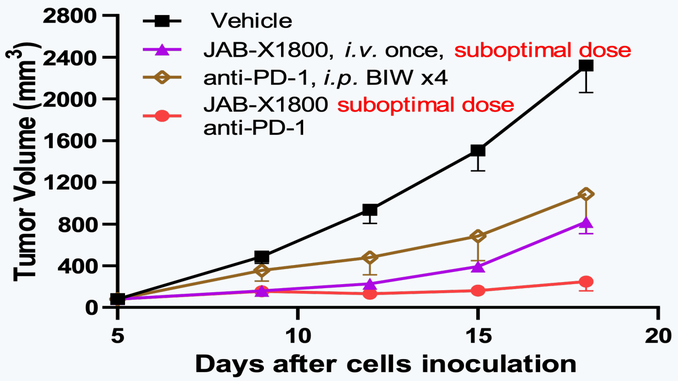
In pre-clinical studay, BX400 (HER2-27670) is effective to DS8201 resistance tumor models



We are developing **multiple STING iADCs with HER2** and other potential targets internally or through strategic collaborations.

High potency and Synergistic effect with anti-PD-1 hCD73-MC38 syngeneic (Colon, CD73- positive) hCD73- C57BL/6 mice

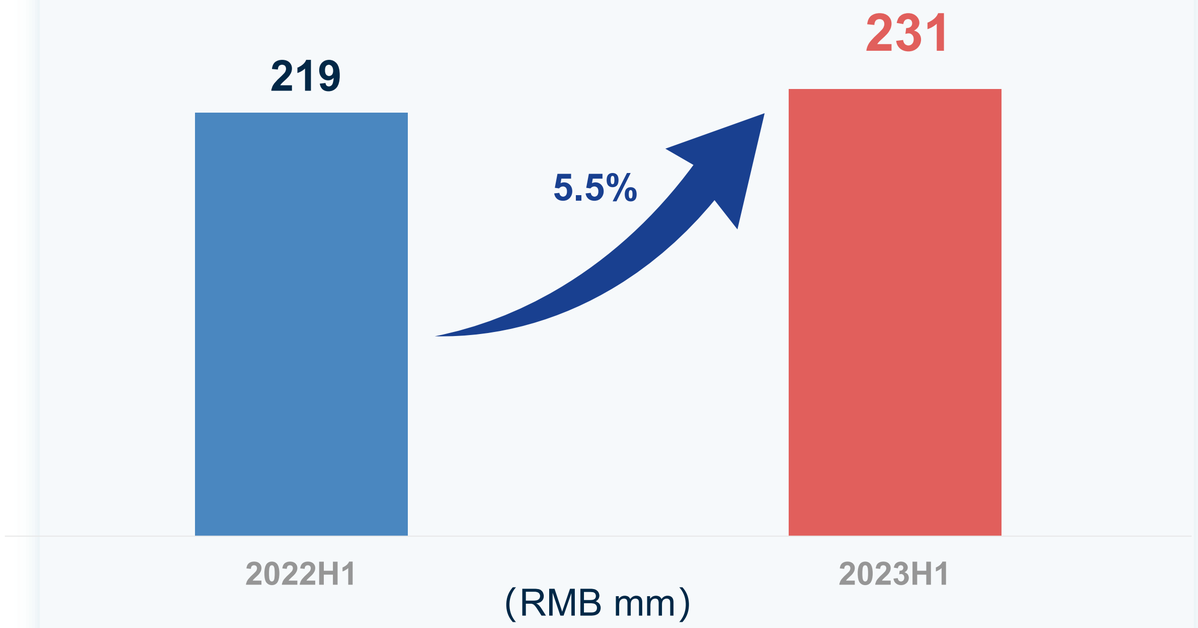




On Target to Capture the Global Market

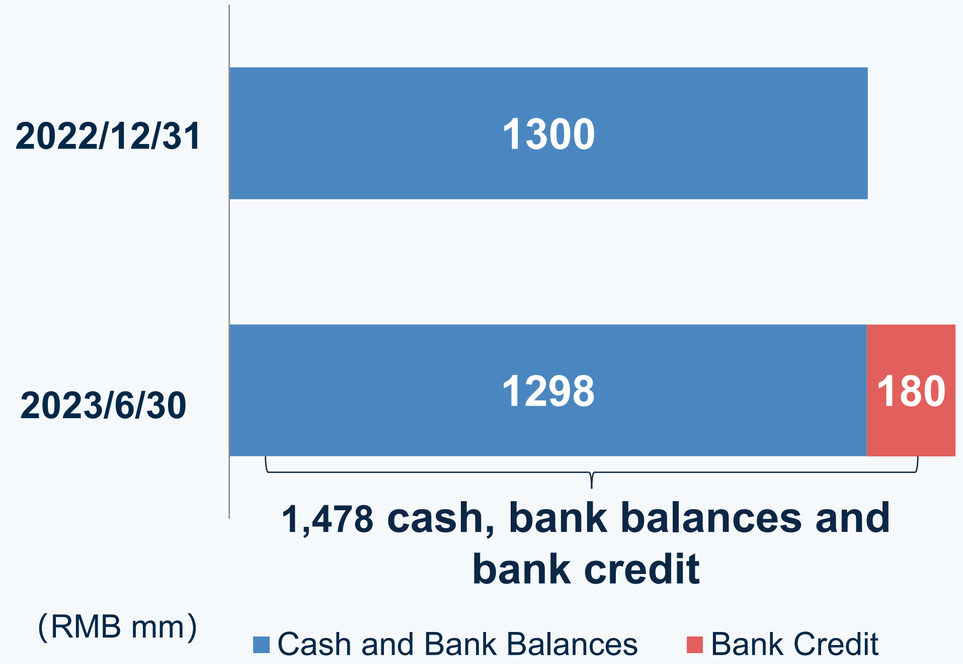
Financial Summary

R&D Costs [1]



1. R&D costs = Cost of revenue + Research and development expenses.
All R&D costs in relation to AbbVie Collaboration were recorded in "Cost of revenue" account.

Cash, Bank Balances and Bank Credit



Company Strategy

FIC & Global Top 3

Key projects on validated oncogenic signaling pathways are among the top three in the world

In-house R&D

Focus on in-house R&D by leveraging our IADD platform rather than relying on in-licensing

Full Function Pharma

Commercialization in China

Global Market

Explore MNC partnership to capture global market

http://www.jacobiopharma.com/