Jacobio
2022 Annual Results Investor Presentation

March 2023

1167.HK

2022 Major Achievements

Clinical-Stage Programs

Glecirasib (KRAS G12Ci, JAB-21822)

- Monotherapy trial in China, US and Europe
- Pivotal trial in NSCLC FPI in 2022 Q3
- BTD granted from CDE in 2022 Q4
- Combo w/Cetuximab in CRC achieved POC
- PDAC and other solid tumor achieved POC

JAB-3312 (SHP2 inhibitor)

- JAB-3312+Sotorasib Phase II FPI in 2022 Q3
- JAB-3312+JAB-21822 trial initiated in KRAS G12C naïve and resistant setting
- JAB-3312 + Pembrolizumab RP2D determined in 2022 Q3

2 New MNC Partners

MERCK

- We have entered into a clinical trial collaboration agreement with Merck on clinical study of combination therapy between Jacobio's KRAS G12C inhibitor Glecirasib (JAB-21822) and Merck's epidermal growth factor receptor (EGFR) inhibitor Erbitux® (cetuximab).

Merck & Co., Inc

- We entered into a clinical collaboration with Merck & Co., Inc., Rahway, NJ, USA to evaluate the combination of Jacobio's CD73 mAb JAB-BX102 in combination KEYTRUDA® (pembrolizumab).

2 Presentations

Glecirasib (JAB-21822)

- Reported Phase I preliminary clinical data at 2022 ASCO

SHP2 inhibitor

- Reported the results of preclinical studies in combination with KRAS G12C inhibitor at 2022 ESMO-Asia

3 New INDs

JAB-2485 (Aurora Ai)

- IND approved by FDA and CDE
- The second drug entering clinical development globally

JAB-BX102 (CD73 mAb)

- IND approved by FDA and CDE

JAB-24114 (GUEi)

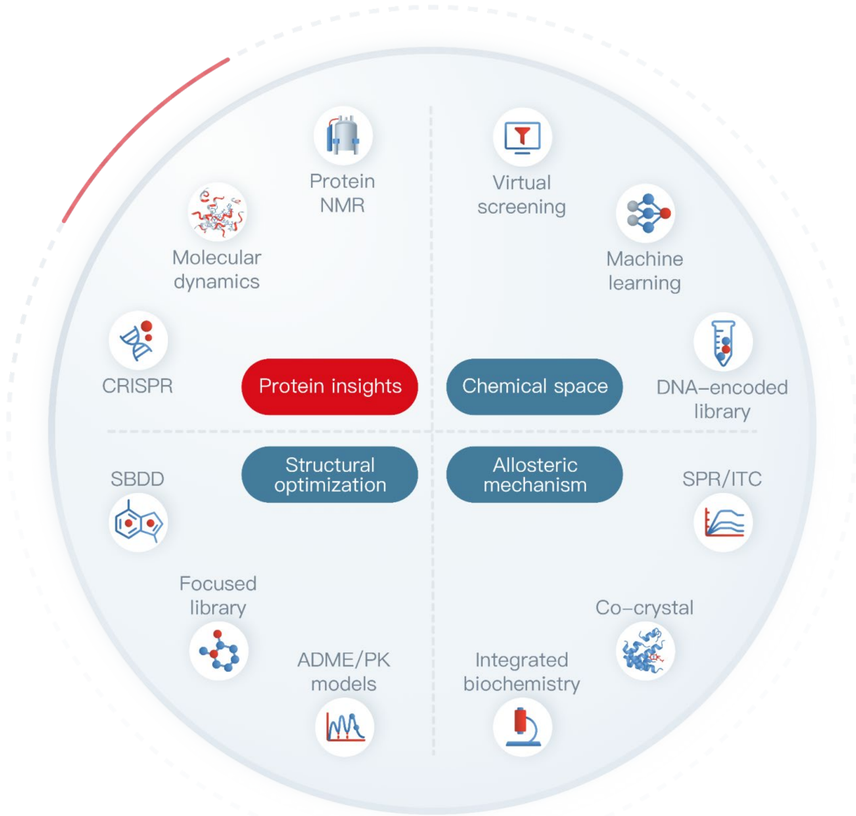
- IND approved by CDE
- The second drug entering clinical development globally

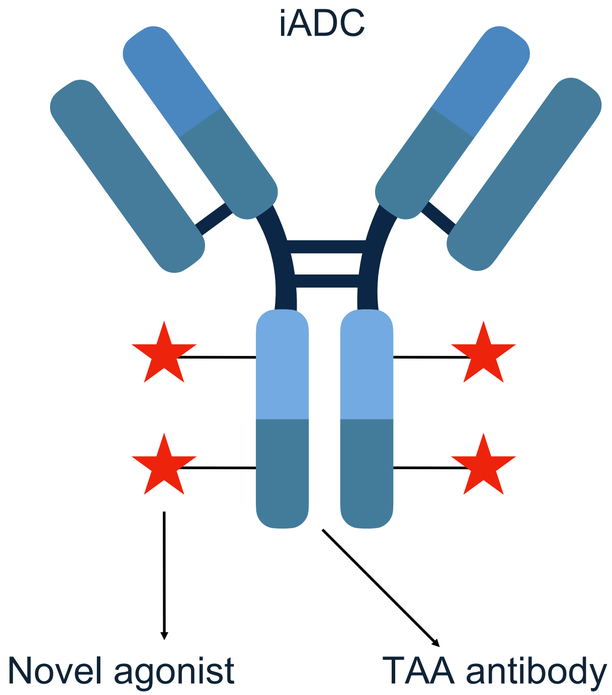
Rapid Advancements of Clinical-Stage Assets in 2022

Product	2022 Q1	2022 Q2	2022 Q3	2022 Q4
JAB-21822 KRAS G12C Inhibitor	JAB-21822 + Cetuximab FPI in China	JAB-21822 monotherapy FPI in EU JAB-21822 + Cetuximab RP2D	JAB-21822 Pivotal NSCLC trial FPI JAB-21822 NSCLC 1L STK11 Co-mut FPI	JAB-21822 + Cetuximab in CRC achieved POC
JAB-3312 SHP2 Inhibitor		JAB-3312 + JAB-21822 FPI in China	JAB-3312+ Sotorasib RP2D & Phase II FPI JAB-3312+Pembrolizumab RP2D	
JAB-8263 BET Inhibitor	JAB-8263 monotherapy FPI in China			
JAB-2485 Aurora A Inhibitor	JAB-2485 IND in US			JAB-2485 IND in China
JAB-BX102 Anti-CD73 mAb	JAB-BX102 IND in China		JAB-BX-102 Phase I trial FPI	

Our Strategy

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





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

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.

Targeted Therapy Programs

Glecirasib has BIC Potential with Superior Efficacy and Safety Profile

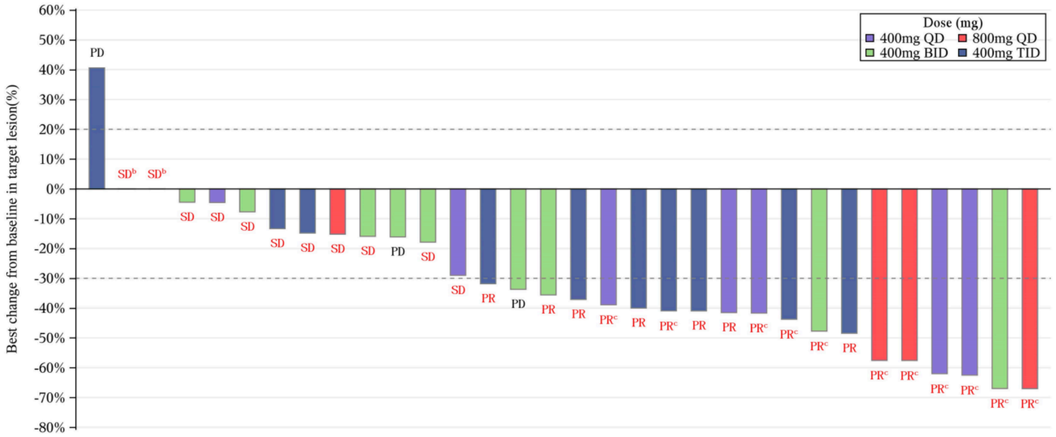
Efficacy

- Promising therapeutic benefits have been observed in multiple tumor types.
- ORR was 56.3% (18/32) in NSCLC (2022 ASCO abstract)
- Monotherapy efficacy in CRC, PDAC and other tumor types harboring KRAS G12C mutation.

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 C_{min}) and potent anti-tumor activity (24 hours ERK suppression by its covalent binding)

Patients with KRAS G12C mutant NSCLC

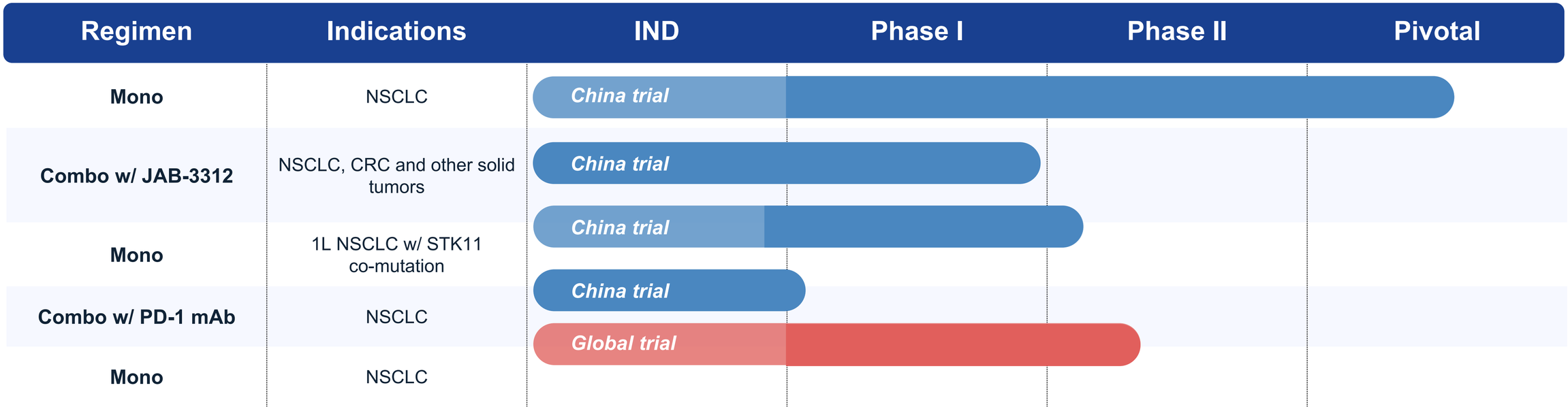


b: one patient 800 mg QD and one patient 400 mg BID; c: confirmed PR

- **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

Advancing Glecirasib in NSCLC

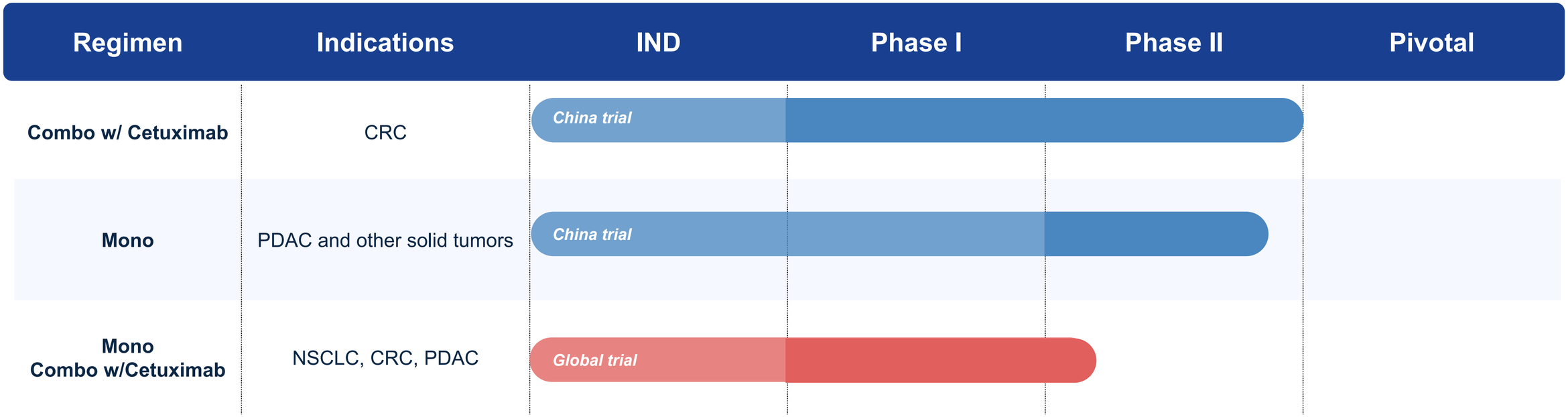


KRAS G12Ci Development Highlight

- **Monotherapy: approximate 200 patients with KRAS G12C mutation have been enrolled in 100 sites.**
  - Phase I/II study has been completed in China.
  - Pivotal study was greenlighted by CDE with FPI in Sep 2022
  - BTD was granted by CDE in Q4 2022
  - Phase II portion of global trial is enrolling NSCLC patients in Europe.

- **JAB-21822 + JAB-3312**
  - Preclinical data were presented at 2022 ESMO-Asia.
  - Treatment responses were observed in KRAS G12Ci naïve and resistant NSCLC.
  - Topline results will be presented at 2023 ESMO.

Glecirasib in GI Cancers



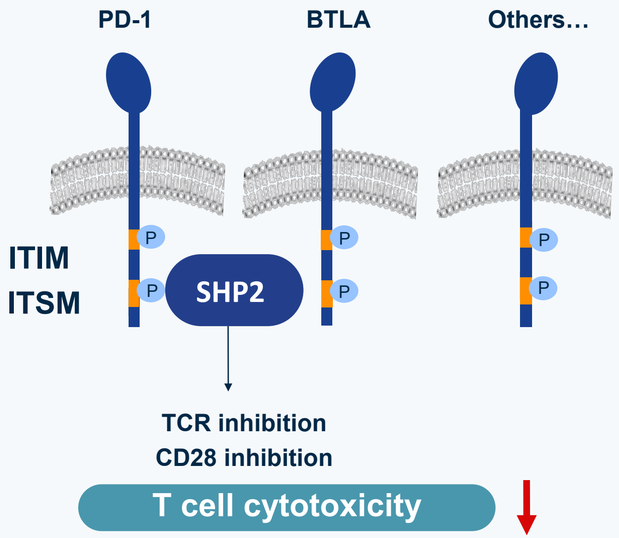
JAB-21822 Highlights

- **JAB-21822+ Cetuximab in CRC**
  - Phase I/II study was completed and POC was achieved in CRC.
  - Pivotal trial in CRC will be initiated in 2023.
- **Monotherapy**
  - PDAC and other solid tumors: promising responses were observed. A global pivotal trial is currently been planned.

SHP2 Exerts Dual Functions in PD-1 and KRAS Pathways

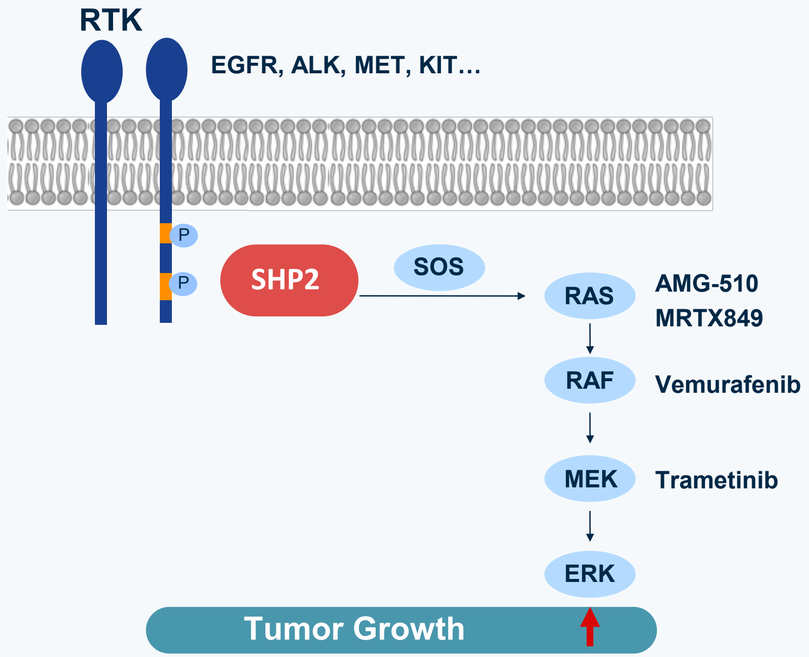
- Potential benefit in PD-1 primary and secondary resistant tumors
- Serve as backbone in combination with agents in I/O space and RAS pathways
- SHP2 and KRAS inhibitors cover 30-40% of cancer patients

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



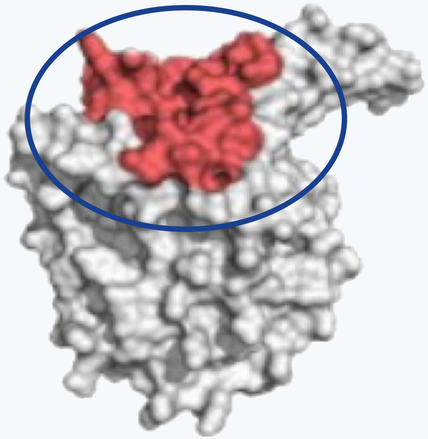
Ref: Nat Med. 2018 24(7).
Sci Signal. 2019 28:12(583)

JAB-3312 is the only second-generation SHP2i

First-generation SHP2i

JAB-3068
other clinical-stage compounds

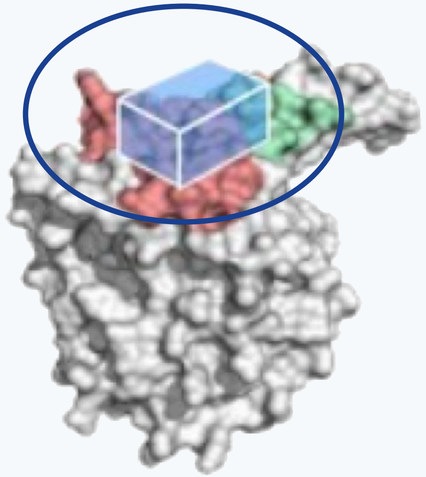
Biochemical assay IC_{50}: ~10nM
Cell viability IC_{50} ~100nM
Clinical dose up to 100-300mg/day



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
abbvie JAB-3312	Combo w/ JAB-21822	KRAS G12C mut solid tumors	China trial	
	Combo w/ sotorasib	KRAS G12C mut NSCLC	Global trial	
	Combo w/ osimertinib	Osimertinib progressed NSCLC	Global trial	
	Combo w/ Pembrolizumab	NSCLC, ESCC	Global trial	
	Mono	BRAF Class 3/NF1 LOF	US and China trials	
JAB-3068	Mono	ESCC, NSCLC, ACC	US and China trials	
	Combo w/ JS-001	ESCC, HNSCC, NSCLC	China trial	

SHP2i Development Highlight in 2022

- JAB-3312 + JAB-21822: Treatment responses were seen in KRAS G12Ci naïve and resistant patients .
- JAB-3312 + Sotorasib: RP2D was determined and phase II portion in KRAS G12Ci naïve NSCLC was initiated.
- JAB-3312 + Pembrolizumab: Early efficacy signals were observed. Phase II enrollment is ongoing.
- JAB-3312 + Osimertinib: Phase II portion is ongoing.
- JAB-3068 + JS-001 (anti-PD-1 mAb): Treatment responses with prolonged duration of responses were seen in Chinese patients.

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

AbbVie Partnership Expedited Our Global Development

Transformative Collaboration

- Leverage a partner's global clinical, regulatory, medical, patient advocacy and commercial footprint
- **Rights of Parties**

  AbbVie – Worldwide

  (except for PRC, Hong Kong and Macau)

  Jacobio - PRC, Hong Kong and Macau

Financial Arrangement

Upfront Payment (Received)

$45mm

Milestone Payments

up to **$810mm - $20mm** received

Royalties

Low-to-mid Double-digit percentages

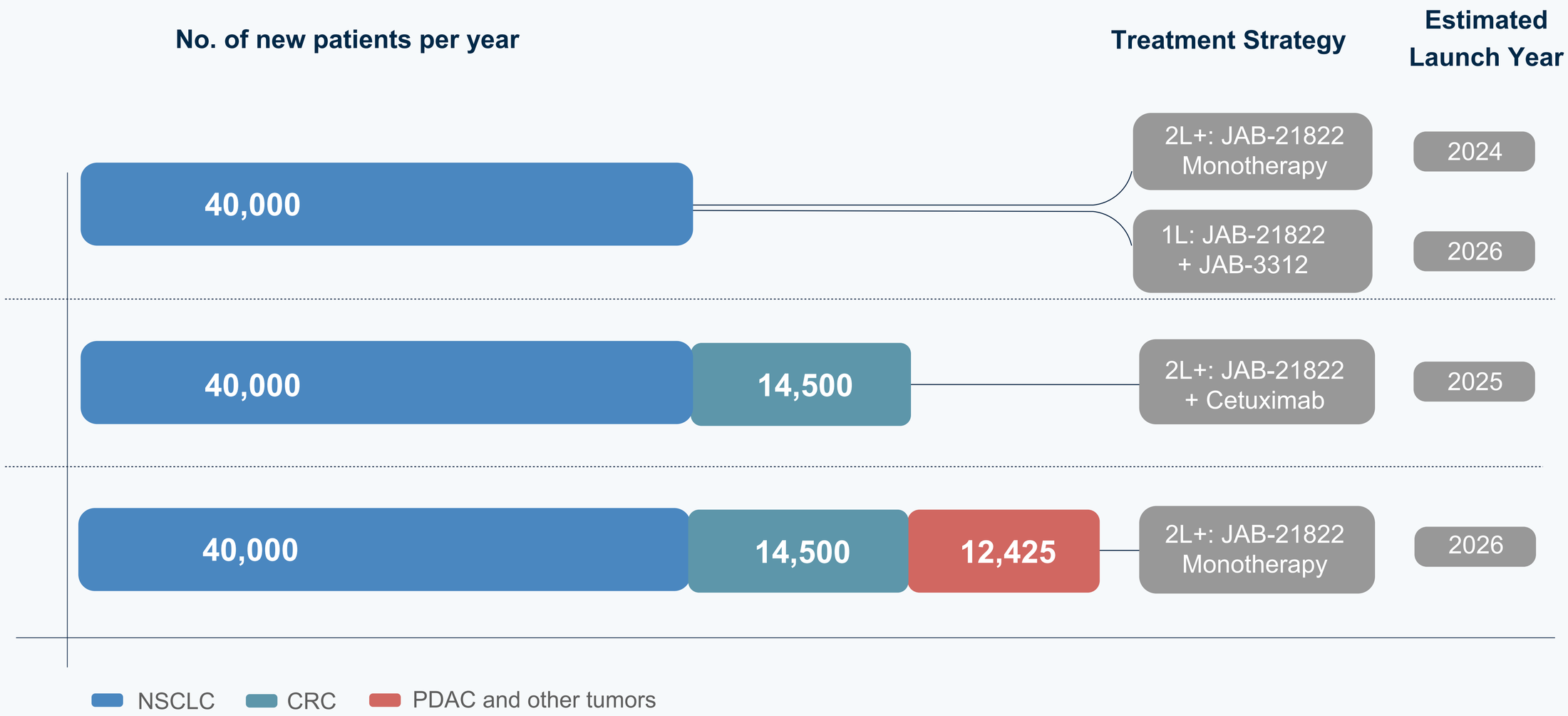
AbbVie will reimburse costs of global clinical development

2022 Cash inflow

Around

RMB150mm

Market Prospect of Glecirasib



1. GLOBOCAN 2020
2. KRAS G12C mutations in Asia: a landscape analysis of 11,951 Chinese tumor samples. Transl Lung Cancer Res. 2020 Oct;9(5):1759-1769

Robust Pipelines

Asset	Regimen	Indications	IND	Phase I	Phase II	Pivot trial	Recent development
	Mono	Solid tumors	US trial				
JAB-8263 BETi (MYC pathway)	Mono	Solid tumors	China trial				FPI in Feb 2022
	Mono Combo w/ JAKi	MF and AML	China trial				
JAB-BX102 CD73 mAb (I/O)	Mono Combo w/ anti-PD-1	Solid tumors	Global trial				FPI in Sep 2022
JAB-2485 Aurora Ai (RB pathway)	Mono	Solid tumors	Global trial				FPI in Jan 2023
JAB-26766 PARP7 (I/O)	Mono	Solid tumors	Global trial				IND (CDE) submitted in Mar 2023
JAB-24114 GUE (Tumor metabolic)	Mono	Solid tumors, Hematological malignancies	Global trial				IND (CDE) approved in Mar 2023
JAB-BX300 LIF mAb (RAS pathway)	Mono	Solid tumors	Global trial				IND (CDE) submitted in Jan 2023

Highlights in 2022

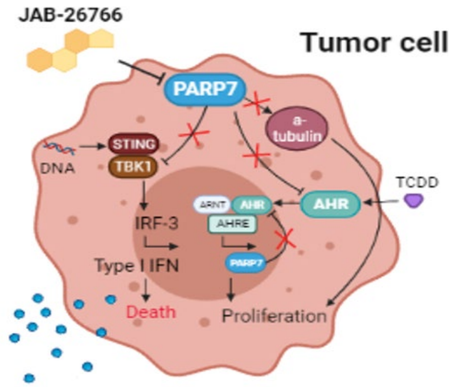
- JAB-2485 & JAB-BX102 received IND approval from FDA and CDE
- JAB-2485 & JAB-BX102 FPI were achieved
- JAB-24114 IND approved in Mar 2023
- JAB-2485 Global Phase I trial managed by the internal team

JAB-26766: An Oral PARP7 Inhibitor

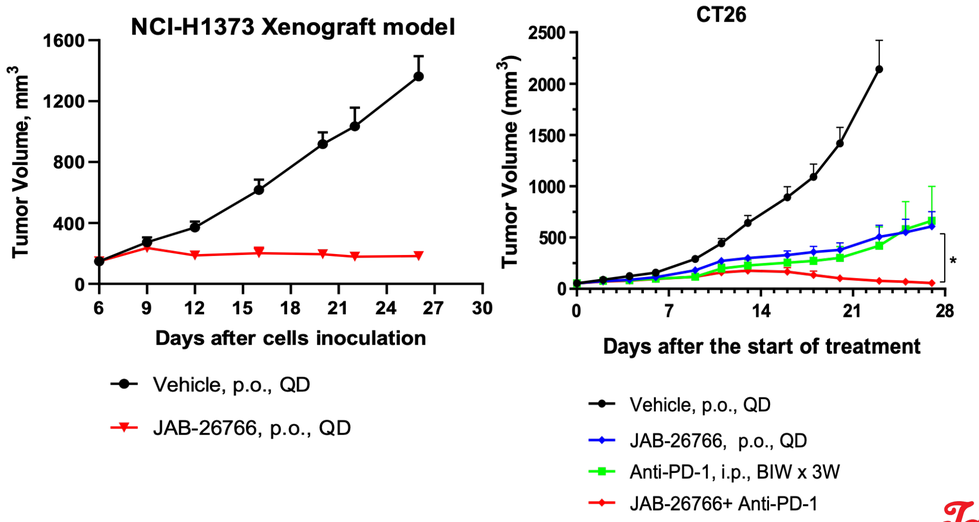
JAB-26766 Preclinical Profile

- 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

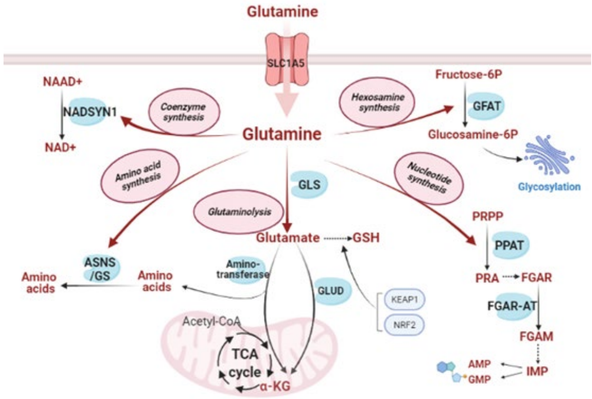


JAB-24114: Targeting Glutamine-Utilizing Enzymes (GUEs) in Tumor Metabolic Pathway

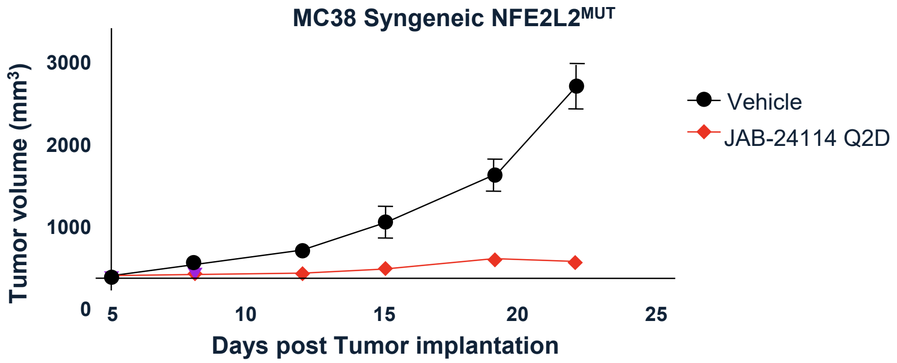
JAB-24114 Preclinical Profile

- JAB-24114 is a prodrug of L-6-Diazo-5-oxo-norleucine (DON).
- DON can block multiple glutamine-dependent pathways including glutaminolysis, nucleotide synthesis, hexosamine synthesis, coenzyme synthesis and amino acid synthesis, differentiating from glutaminase inhibitors which are only blocking the conversion of glutamine to glutamate
- JAB-24114 is preferentially distributed in tumors and can circumvent the GI toxicity caused by DON, further broaden the therapeutic window of DON.
- JAB-24114 demonstrates good plasma stability in human and is inactive in its prodrug form.
- IND was approved by CDE in March 2023

Signaling pathway



Strong Antitumor Effect

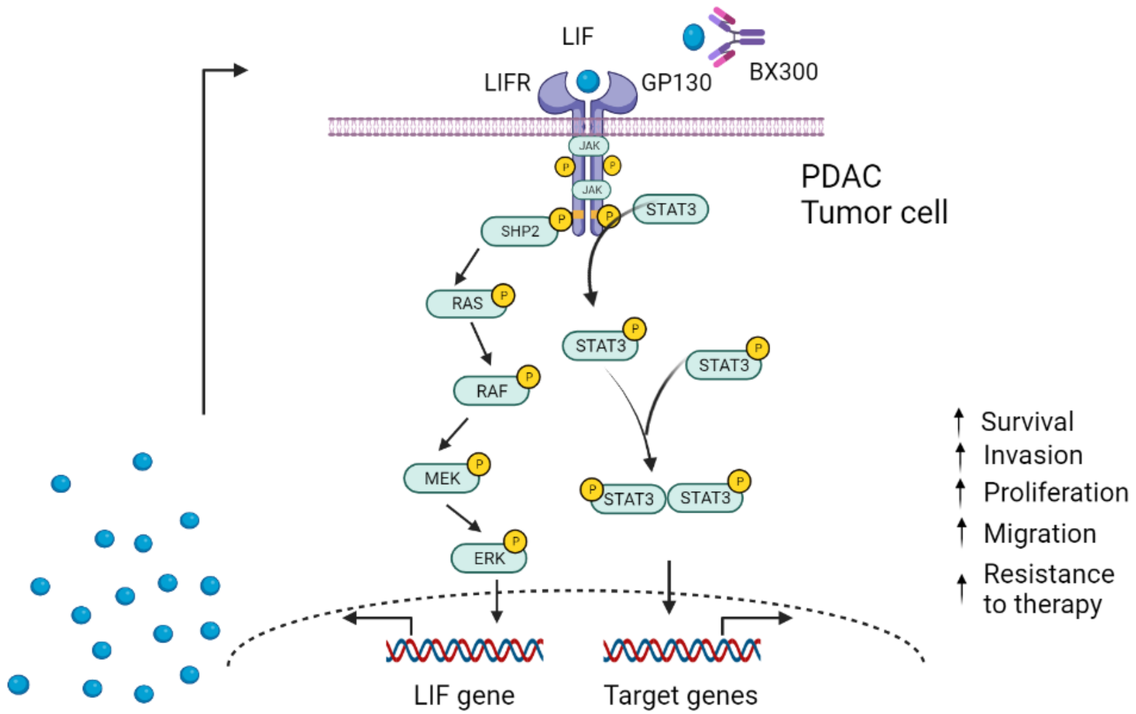


JAB-BX300: a Humanized anti-Leukemia Inhibitory Factor (LIF) mAb

JAB-BX300

- LIF is an attractive therapeutic target and serves as a **biomarker** in PDAC[1]. LIF is induced specifically by KRAS in PDAC[2].
- JAB-BX300 blocks **LIF/LIFR** interaction, while AZD0171 (in phase II trial in PDAC) blocks **LIF/GP130** interaction.
- JAB-BX300 shows **significant anti-tumor activity** in pancreatic cancer patient-derived xenografts in humanized PBMC mice. LIF antibody and KRAS inhibitor have the potential for **combinational therapy**.
- JAB-BX300 is expected to receive IND approval in 2023Q2.

Signaling pathway



Ref: Nature. 2019 May ; 569(7754): 131–135.
Nat Commun. 2019 Jul 11;10(1):3055.

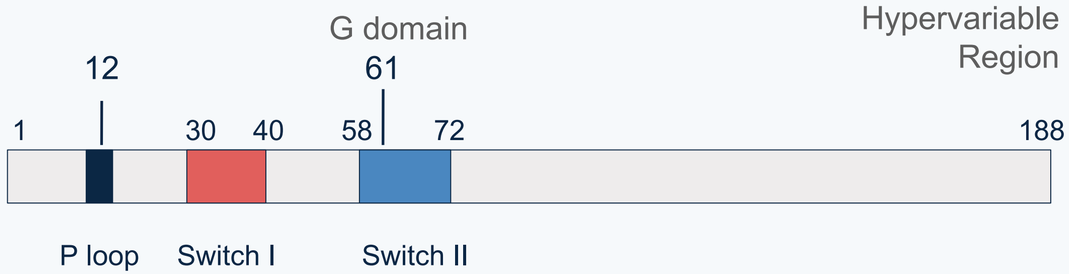
JAB-23400: An Oral KRAS^{multi} Inhibitor

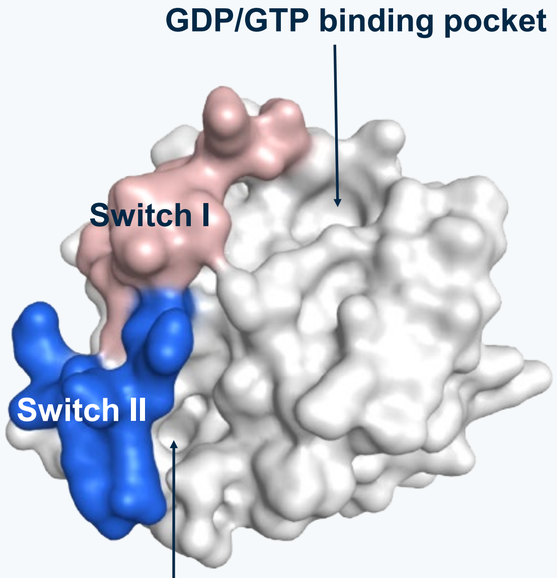
- **23% of** human cancers harbor KRAS mutations[1].
- **2,700,000** new cases per year with KRAS mutations in worldwide[2]

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**.

Structure of KRAS





KRAS^{multi} inhibitor binding pocket

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

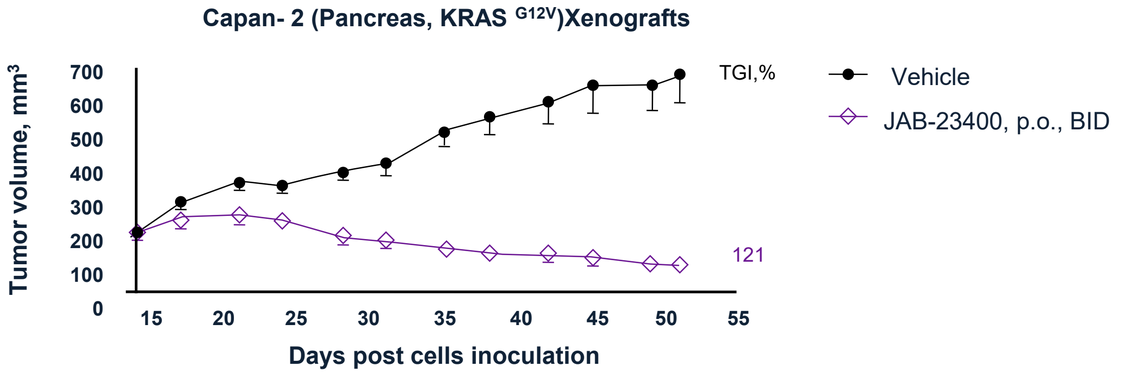
JAB-23400 Profile

- 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

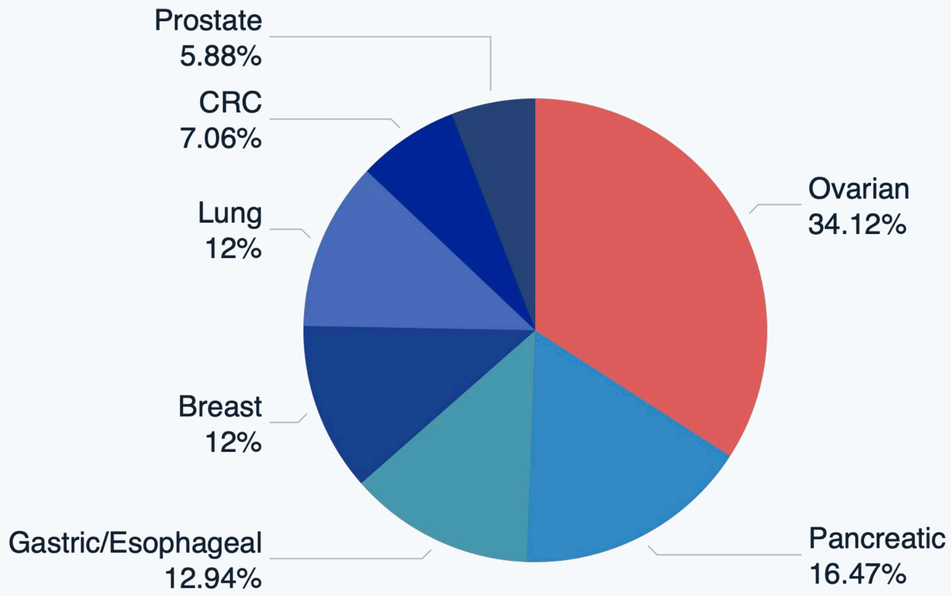
		Cell lines	pERK, IC_{50}, nM	Cell Viability, IC_{50}, nM
KRAS dependent cell lines	KRAS Mutation	AGS (KRAS G12D) SW620 (KRAS G12V) NCI-H747 (KRAS G13D)	**< 5**	**< 20**
	KRAS WT Amplification	MKN-1 (Stomach, CN=7) EBC-1 (Squamous, CN=5)	**< 5**	**< 20**
KRAS WT independent cell lines (no amplification)	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



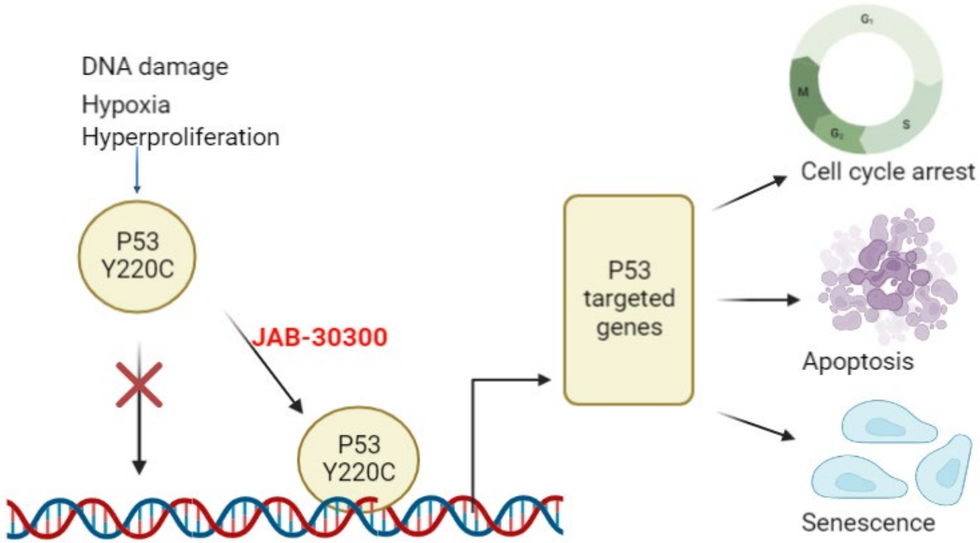
P53: Most Frequently Mutated Gene in Tumors

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%



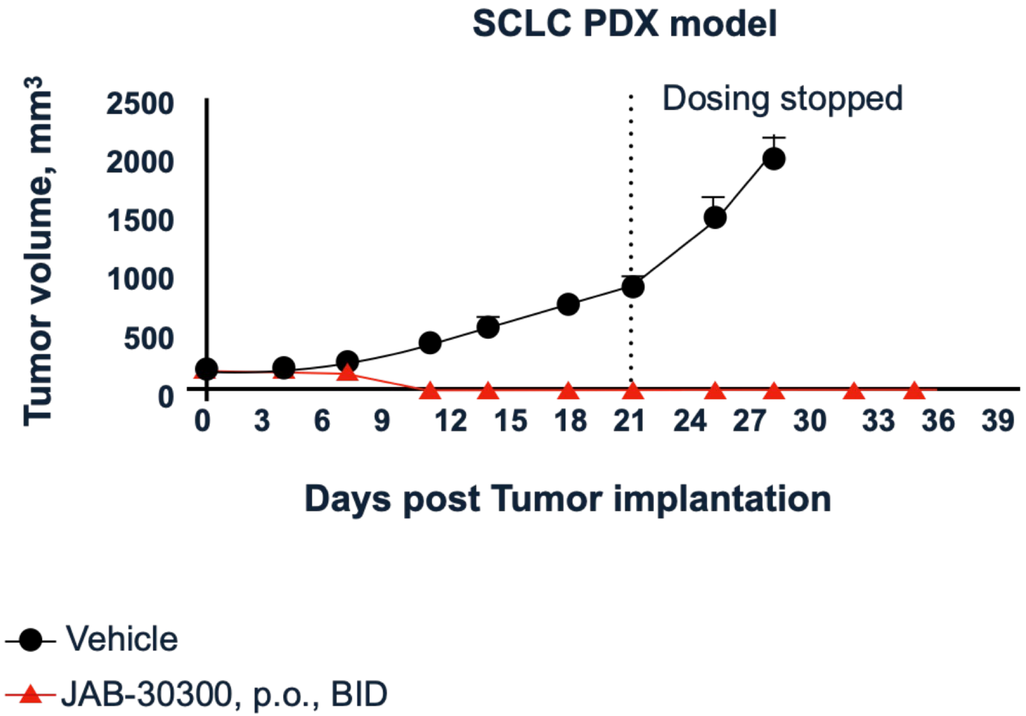
Ref: 1. ACS Pharmacol. Transl. Sci. 2022, 5, 1169−1180; 2. Data were obtained from the Catalogue of Somatic Mutations in Cancer (COSMIC) database

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.

Novel Payloads for Innovative iADC Platform

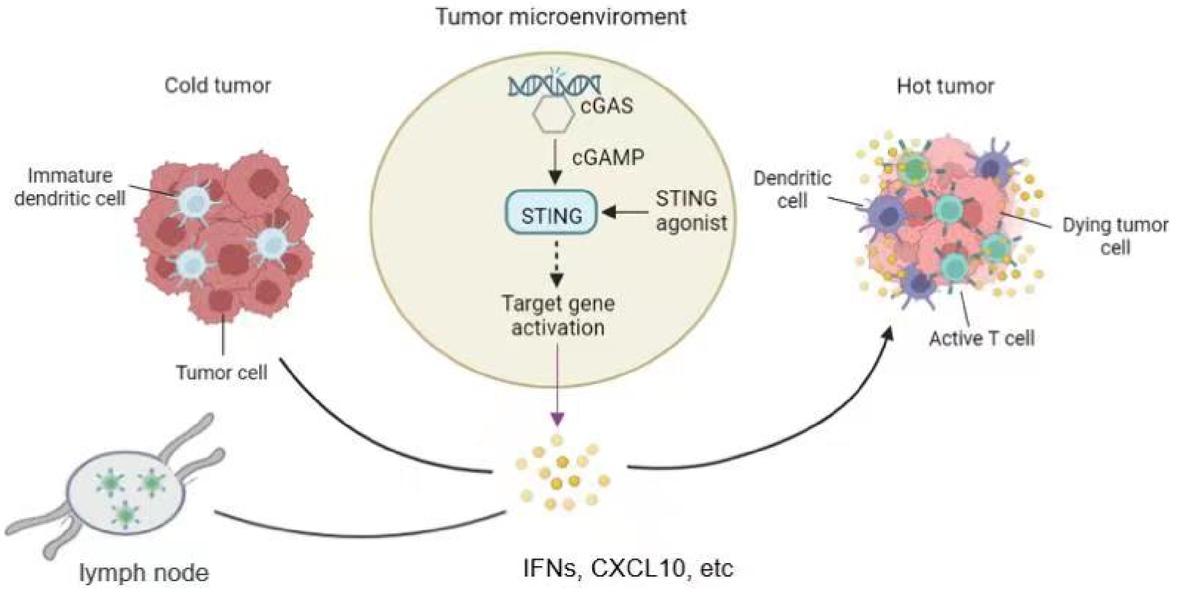
JAB-27670: STING Agonist as iADC Payload

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 ×10^{-6}, cm/s)
- **Low hERG risk** (< 5% inhibition at 10 μM)



JAB-X1800: CD73-STING agonist iADC

Rationale of JAB-BX102 for iADC conjugation

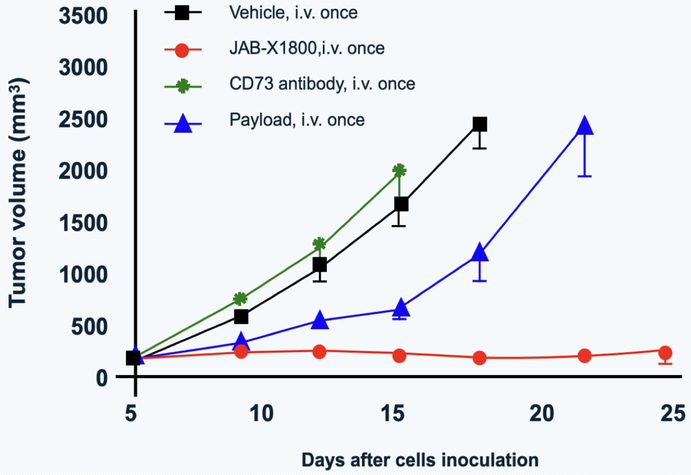
- **High expression of CD73** in **74%** of TNBC, in **50%** of Gastric cancer, Ovarian cancer and PDAC, and in **44%** of HNSCC.
- JAB-BX102 is a humanized anti-CD73 mAb with **strong internalization** activity, and is in Ph1 trial.

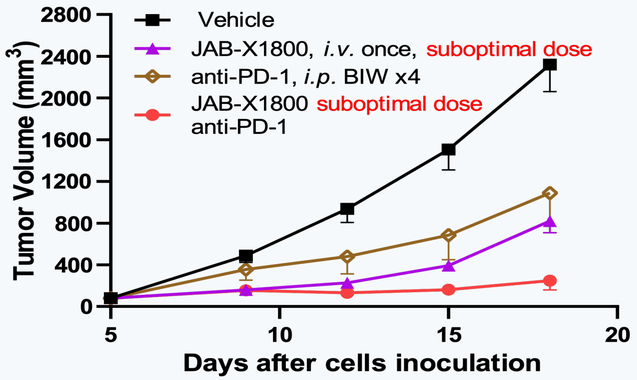
JAB-X1800 Preclinical Profile

- **No Payload release in plasma**
- **Favored safety** (no stimulation of inflammatory cytokine IL-6 in peripheral blood)
- **High potency and immune memory** (complete and durable tumor regression after single administration)
- **Synergistic effect with anti-PD-1**

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

hCD73-MC38 syngeneic (Colon, CD73- positive) hCD73- C57BL/6 mice





Jacobio Pipeline

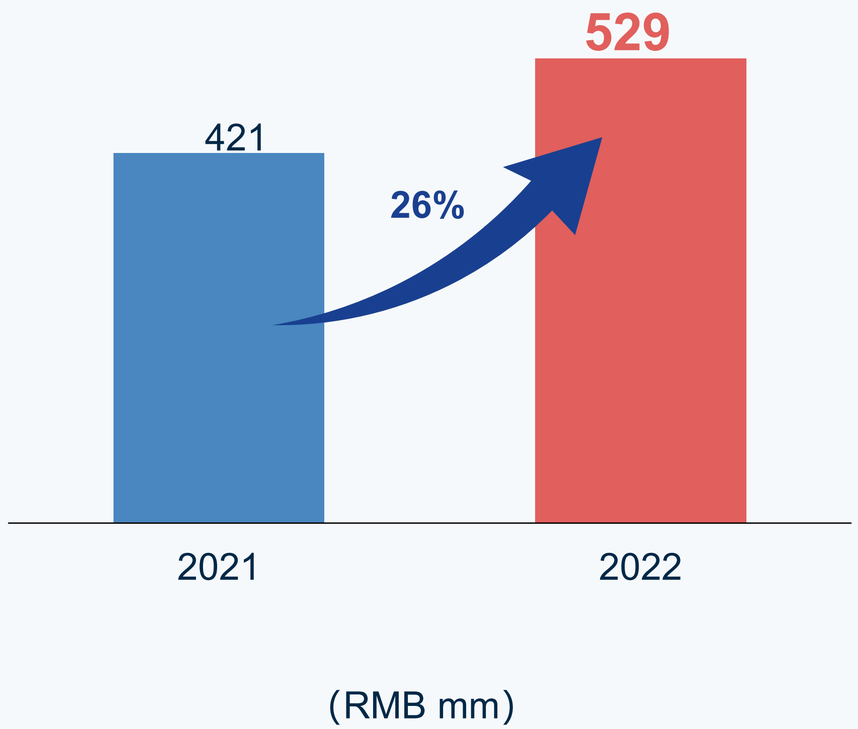
Asset	Target	Pathway	Stage	IND		No. of top 3 Globally & top 1 in China	No. of top 3 in China
JAB-3312 **JAB-3068**	SHP2	RAS, I/O	Phase II	2018			
JAB-21822	KRAS G12C	RAS	Phase II	2021			
JAB-8263	BET	MYC	Phase I	2020	2022	5	3
JAB-2485	Aurora A	RB	Phase I	2021			
JAB-26766	PARP 7	I/O	IND submitted	2023 H1			
JAB-24114	GUE	Tumor metabolism	IND approved	2023			
JAB-BX300	LIF	RAS	IND submitted	2023 H1			
JAB-23400	$KRAS^{multi}$	RAS	IND-Enabling	2023	2023	4	(The IND of the new pipeline is expected to be the top 3 Globally and the first in China)
JAB-30300	P53	P53	IND-Enabling	2023			
JAB-X1800	CD73-STING iADC	I/O	IND-Enabling	2024			
JAB-22000	KRAS G12D	RAS	Lead Optimization	2024	2024	2	(The IND of the new pipeline is expected to be the top 3 Globally and the first in China)

- Clinical trials are conducted in more than **70** hospitals in China, more than 30 sites in the US and Europe.
- Jacobio has started to internally manage global trial.
- Global ranking*: Ranked by time of IND approval from FDA

On Target to Capture the Global Market

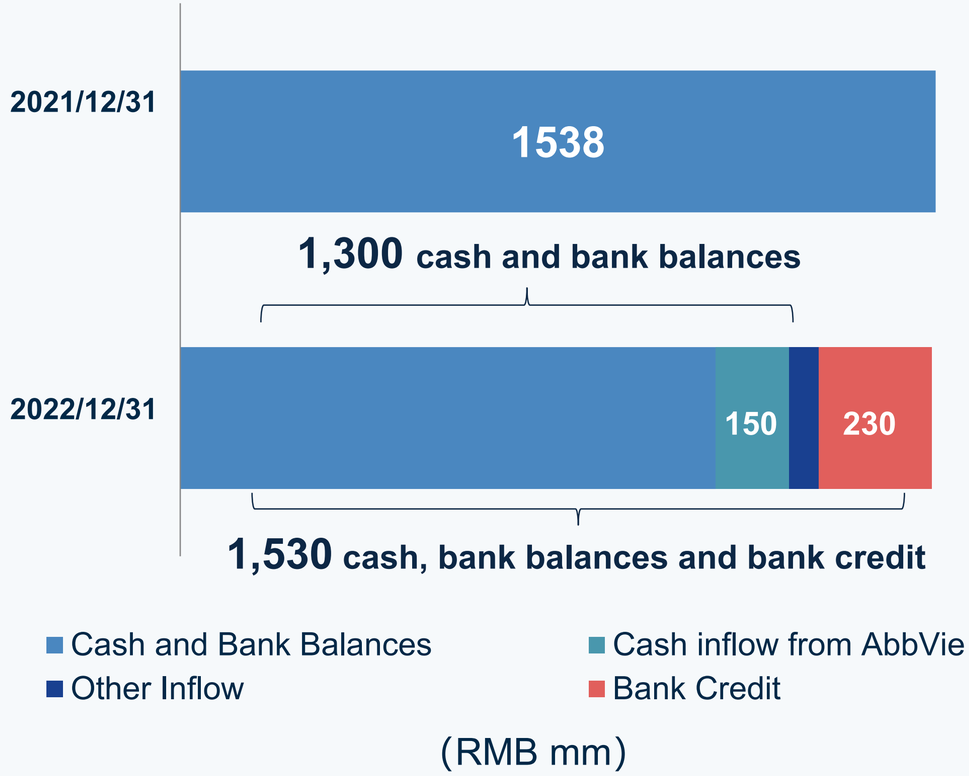
Financial Summary

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 [2, 3]



2. As of December 31, 2022, the Group did not have any interest-bearing borrowing.
3. As of the date of our annual report, the Group have bank credit of RMB230 million.

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 leveraging our allosteric inhibitor tech platform rather than in-licensing

Full Function Pharma

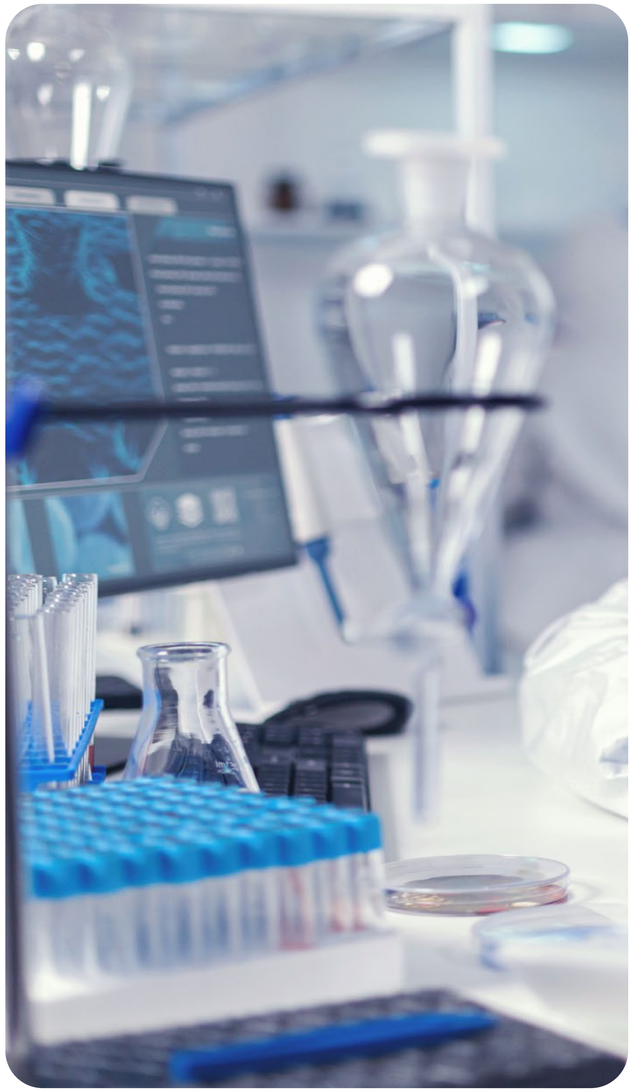
Commercialization in China

Global Market

Explore MNC partnership to capture global market

2023 Key Milestones and Catalyst Events

Events	Expected Timing
Submit NDA	
Glecirasib (JAB-21822) monotherapy in NSCLC submit NDA	2023 Q4
Pivotal Trials*	
Glecirasib (JAB-21822) combo w/ Cetuximab in patients with CRC	2023 H2
Glecirasib (JAB-21822) in patients with PDAC	2023 H2
POC Readout	
JAB-3312 (SHP2i) Combo with Glecirasib (JAB-21822) in patients with NSCLC	2023 Q4
Other clinical milestones	
JAB-8263 (BETi) RP2D	2023 H2
JAB-2485 (Aurora Ai) RP2D	2024
JAB-BX102 (CD73 mAb) RP2D	2023 H2
JAB-24114 (GUEi) IND approved	Mar 17, 2023
JAB-BX300 (LIF mAb) IND approval	2023 H1
JAB-26766 (PARP7i) IND approval	2023 H2



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

2023 Key Milestones and Catalyst Events

Events		Expected Timing
2+ New INDs		
JAB-23400 (KRAS^{multi}) IND submission		2023 Q4
JAB-30300 (P53) IND submission		2023 Q4
JAB-X1800(CD73 –STING mAb) IND submission		2023-2024
Data publication		
AACR (The poster has been accepted)	Preclinical data of JAB-23425 (KRAS^{multi})	April 2023
	Preclinical data of JAB-2485 (Aurora Ai)	
	Preclinical data of JAB-X1800 (CD73–STING iADC)	
ESMO (Under discussion with AbbVie, plan to submit in May)	Clinical data of JAB-3312 (SHP2i) Combo with Glecirasib (JAB-21822)	October 2023
ASCO GI	Glecirasib (JAB-21822) Mono PDAC and other solid tumor	February 2024

Jacobio in 2022 and Beyond: Q&A
March 2023