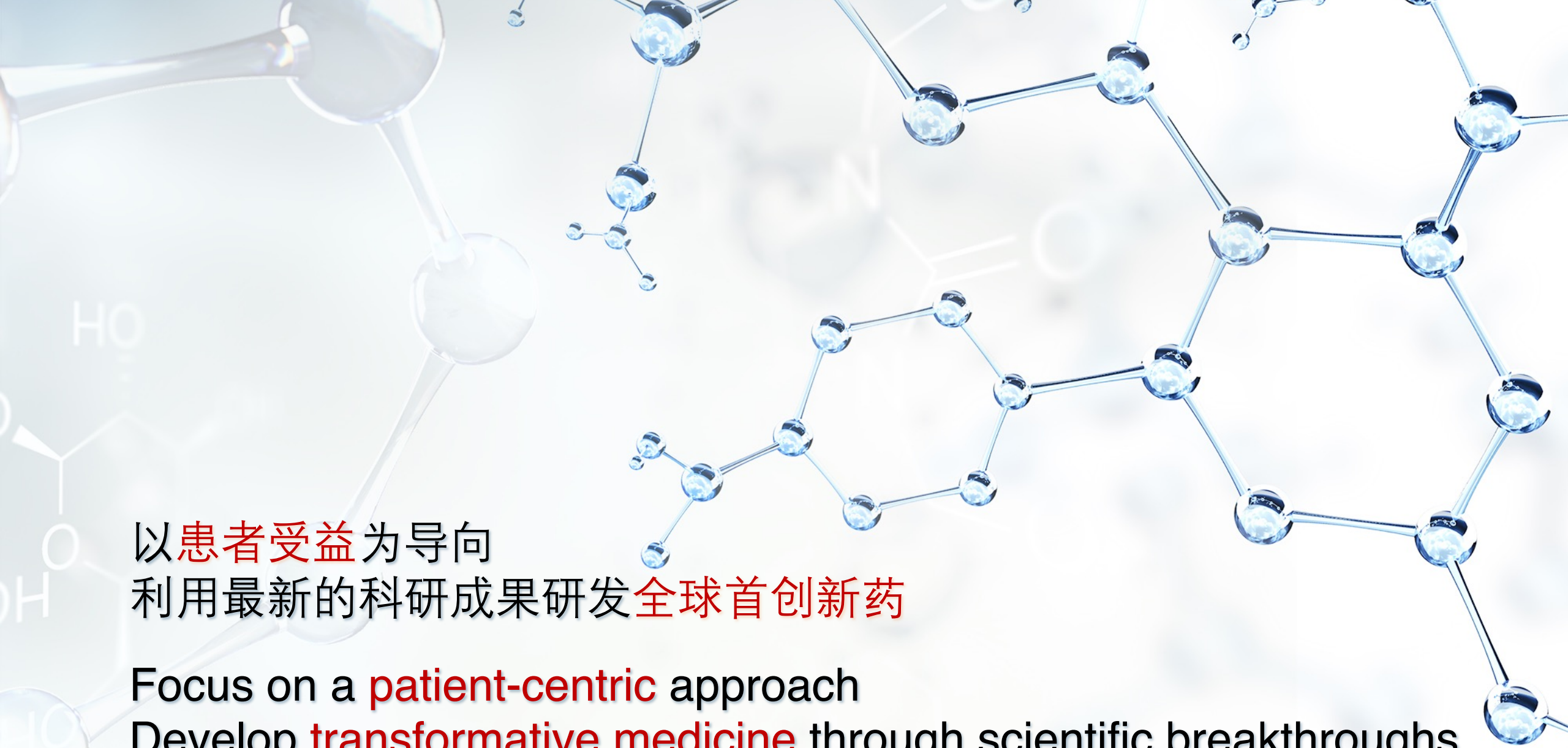
Jacobio Pharmaceuticals

2022 Interim Results



以患者受益为导向
利用最新的科研成果研发全球首创新药

Focus on a patient-centric approach
Develop transformative medicine through scientific breakthroughs and innovative technology

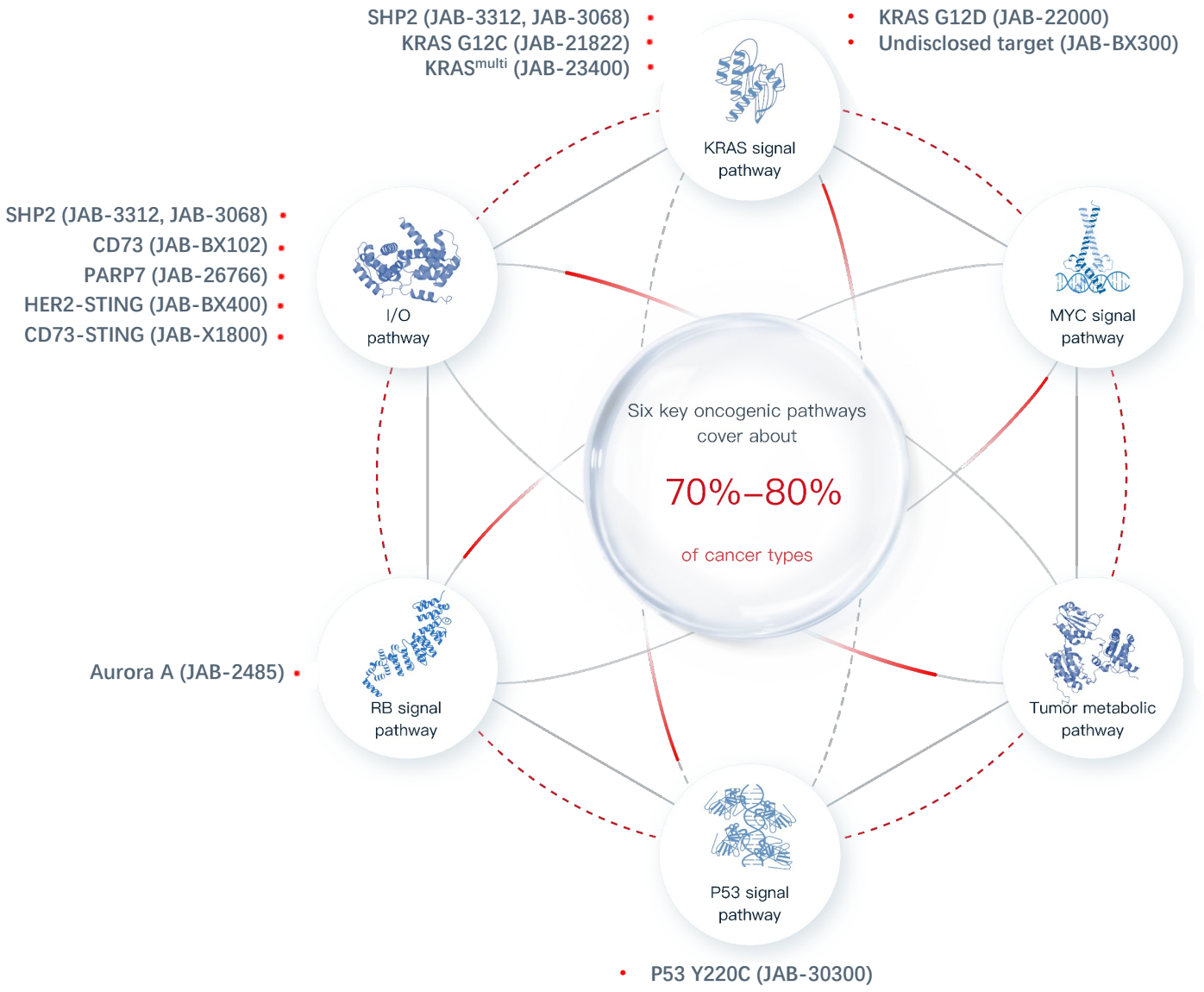
Our Induced Allosteric Drug Discovery Platform (“IADDP”)

Targeting undruggable proteins with significant clinical value, our **IADDP** integrates multiple proprietary techniques to:

- Identify possible allosteric sites
- Uncover potential allosteric mechanisms
- Design novel allosteric molecules, and
- Achieve the mission of “drugging the undruggable”

We have validated our **IADDP** in developing clinical-stage small-molecule drug candidates to modulate enzymes by binding to their allosteric sites.

Advance Novel Drug Development in Key Oncogenic Pathways



Progress and expand the pipeline targeting promising pathways - the "**BIG 6**" pathways cover 70%-80% cancer.

Our Diverse Pipeline Targeting Critical Pathways
- Clinical stage & 2022 INDs

Asset	Target	Modalities	Indications	Combo Strategy	Status	Pre-clinical	Phase I	Phase II
JAB-3312/ JAB-3068	SHP2 (RAS pathway, I/O)	Small molecule	NSCLC, HNSCC, ESCC, ACC	**KRASi**, PD-1, EGFRi	Phase II	*Global*		
JAB-21822	KRAS G12C (RAS pathway)	Small molecule	NSCLC, PDAC, CRC	**SHP2i**, PD-1, EGFR mAb	Phase II	*Global (NSCLC mono pivotal trial in China to start in 2022 H2)*		
JAB-8263	BET (MYC pathway)	Small molecule	Solid tumors, Hematological malignancies	**Aurora Ai**, JAKi, PD-1	Phase I	*Global*		
JAB-2485	Aurora A (RB pathway)	Small molecule	Solid tumors	**BETi**, **SHP2i**, **KRASi**	Phase I	*Global*		
JAB-BX102	CD73 mAb (I/O)	Monoclonal antibody	Solid tumors	PD-1	Phase I	*Global*		
JAB-26766	PARP7 (I/O)	Small molecule	Solid tumors	**SHP2i**, PD-1	2022 IND			
JAB-24114	Undisclosed (Tumor metabolic)	Small molecule	Solid tumors, Hematological malignancies	-	2022 IND			
JAB-BX300	Undisclosed (RAS pathway)	Monoclonal antibody	Solid tumors	-	2022 IND			

Clinical Stage ***IND-enabling Stage***

Our Diverse Pipeline Targeting Critical Pathways
- 2023 - 2024 INDs

Asset	Target	Modalities	Indications	Status	Lead Optimization	IND-enabling
JAB-23400	KRAS^{MULTI} (RAS pathway)	Small molecule	PDAC, CRC, NSCLC	2023 IND		
JAB-30300	P53 Y220C (P53 pathway)	Small molecule	Solid tumors	2023 IND		
JAB-BX400	HER2-STING (I/O)	**iADC**	Solid tumors	2024 IND		
JAB-X1800	CD73-STING (I/O)	**iADC**	Solid tumors	2024 IND		
JAB-22000	KRAS G12D (RAS pathway)	Small molecule	PDAC, CRC, NSCLC	2024 IND		

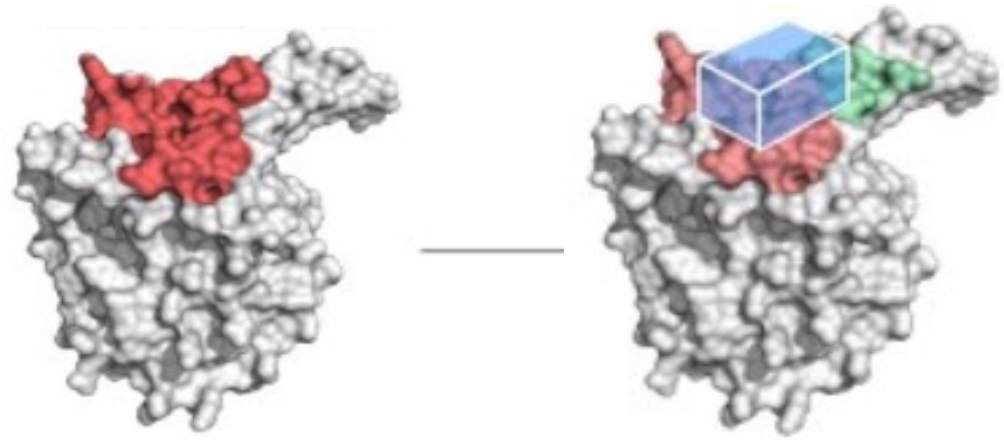
- Expertise in developing small-molecule drug candidates to modulate enzymes by **binding to allosteric sites** to address targets that lack easy-to-drug pockets where drugs can bind.
- Developing novel candidates with new modalities, **spanning from small molecule and monoclonal antibody to iADC**.
- As of June 30, 2022, we owned 228 patents or patent applications that are filed globally, in which 37 patents have been issued or allowed in major markets globally.

IND-enabling Stage *Lead Optimazition Stage*

Our SHP2 Inhibitor JAB-3312 as a Potential Best-in-Class Drug

Preclinical comparison

	JAB-3312	RMC-4550 In-house or ref
SHP2 biochemical IC_{50} (nM)	1.5	10.4
Binding kinetics KD (nM)	0.206	13.6
Cellular p-ERK IC_{50} in NCI-H358 (nM)	3.64	28 (ref)
Cellular p-ERK IC_{50} in KYSE-520 (nM)	0.32	9.1 (ref)
Cellular proliferation KYSE-520 IC_{50} (nM)	3.5	127



Clinical dose

JAB-3312
1-8mg QD

JAB-3068
50-300 mg QD

TNO-155
20-70 (or higher) mg QD 21/7

RMC-4630
20-80 mg QD
200mg D1/D2 weekly

SHP2 Inhibitor-Global Development Plan

Asset	Regimen	Indications	Phase I	Phase IIa	Recent development
JAB-3312 SHP2 abbvie	Combo w/KRAS G12Ci	KRAS G12C mut NSCLC	*Global trial*		Phase IIa initiated in Jul 2022
	Combo w/EGFRi	Osimertinib progressed NSCLC	*Global trial*		FPI in Jan 2022
	Combo w/PD-1 mAb	NSCLC, HNSCC, ESCC	*Global trial*		Phase IIa initiated with FPI in Feb 2022
	Mono	BRAF Class 3/NF1 LOF mutant solid tumers	*US and China trial*		
JAB-3068 SHP2 abbvie	Mono	ESCC, HNSCC, NSCLC, ACC	*US and China trial*		
	Combo w/PD-1 mAb	ESCC, HNSCC, NSCLC	*China trial*		

Key updates in the first half of 2022

- **JAB-3312 combo w/KRAS G12Ci**

  Global Study - *(combo w/Sotorasib)* Dose expansion portion in KRAS G12C treatment naïve NSCLC patients progressed on front-line treatment was initiated in July 2022.

  China Study - *(combo w/JAB-21822)* First patient was successfully dosed in May 2022. Dose escalation is ongoing. PR was observed in the first NSCLC patient enrolled in the first dose level. Both KRAS G12C treatment for naïve and resistant patients will be enrolled in expansion stage.

- **JAB-3312 combo w/EGFRi** - Dose escalation is ongoing. Early clinical response with confirmed PR was observed in one EGFR inhibitor resistant NSCLC patient.

- **JAB-3312 combo w/PD-1 mAb** - Dose exploration is being carried out in China. Early clinical response was observed in patients with certain tumor types.

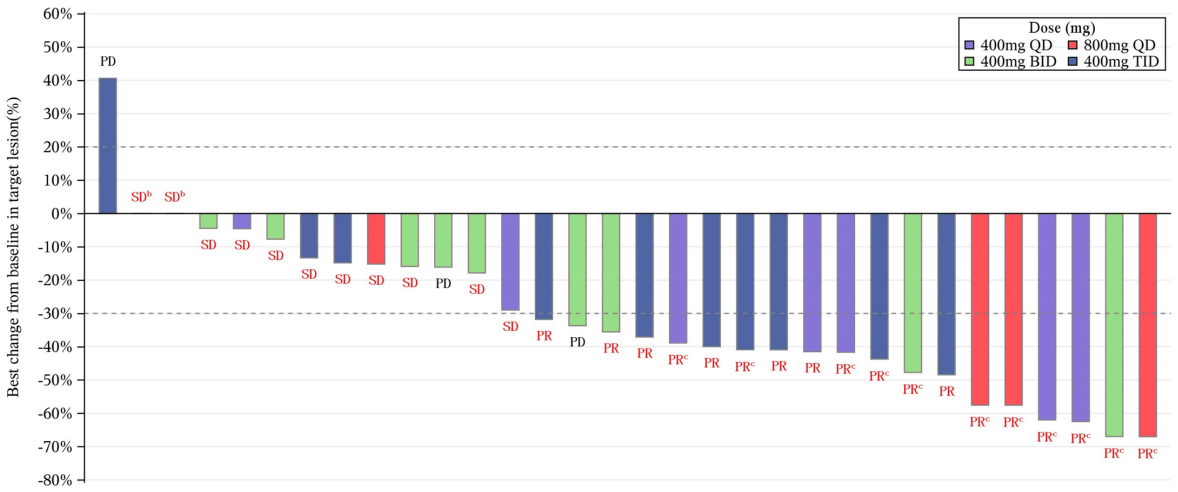
ESCC = esophageal squamous cell carcinoma; HNSCC = head and neck squamous cell carcinoma; NSCLC = non-small cell lung cancer

Our KARS G12C Inhibitor JAB-21822 with the Favorable Efficacy and Safety Profile – *2022 ASCO Data Readout*

Phase I preliminary clinical data of JAB-21822 monotherapy trial in China, especially in NSCLC cohort, was reported at the **2022 ASCO Annual Meeting** in June 2022.

Waterfall Plot (as of April 1, 2022)

Patients with KRAS^{G12C} NSCLC



a: Two NSCLC patients without KRAS ^{G12C} mutation were excluded; b: one patient 800 mg QD and one patient 400 mg BID; c: confirmed PR

Efficacy Summary

- **ORR 56.3% (18/32); DCR 90.6% (29/32)**

Safety Summary

- 72.2% (52/72) patients had at least one TRAE. 11.1% (8/72) patients had G3-4 TRAE.
- Overall, in 400mg and 800mg QD cohorts, Grade 3 or 4 TRAEs occurred in 2.5% (1/40) of patients.
- No Grade 3 or above GI AE was experienced in JAB-21822 Phase I trial.

KRAS G12Ci JAB-21822-Global Development Plan

Asset	Regimen	Indications	IND	Phase I	Phase II	Pivotal	Recent development	Upcoming Milestone (expected)
JAB-21822 KRAS G12C	Mono	NSCLC	China trial			2022 2H (Expected)	Phase II initiated with FPI in Mar 2022	
	Mono	CRC, PDAC and other solid tumors	China trial				Phase IIa initiated with FPI in Mar 2022	
	Mono Combo w/EGFR mAb	NSCLC, CRC, PDAC	Global trial				FPI (Sep 2021 in US, May 2022 in Europe)	Expansion portion to be initiated in 2022 2H
	Mono	1L NSCLC with STK11 co-mutation	China trial					FPI (Sep 2022)
	Combo w/SHP2i	Advanced solid tumors	China trial				FPI in May 2022	
	Combo w/EGFR mAb	CRC	China trial				Phase IIa initiated with FPI in Jul 2022	
	Combo w/PD-1 mAb	NSCLC	China trial					FPI (2023 1H)

Key updates in the first half of 2022

- **China Monotherapy** – Pivotal trial in NSCLC is expected to launch in 2022 Q3. Multiple cohorts are ongoing in parallel for CRC, PDAC and other solid tumor patients with KRAS G12C mutation.
- **Global Monotherapy** – Dose expansion to be initiated in 2H 2022.
- **1L Monotherapy in NSCLC Patients with STK-11 Co-mutation** – FPI of dose escalation stage is expected to be completed in in September 2022.
- **Combo w/EGFR mAb** – Dose escalation was completed in 1H 2022. FPI of dose expansion stage was achieved in July 2022.
- **Combo w/JAB-3312** – *Discussed in SHP2 section*

CRC = colorectal cancer; NSCLC = non-small cell lung cancer; 1H=First Half ; 2H=Second Half

KRAS G12C + SHP2

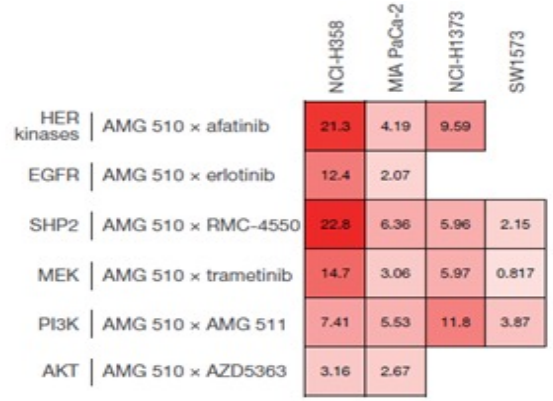
- Potentially Best Combo Strategy

KRAS G12C in combination with SHP2 strategy is supported by:

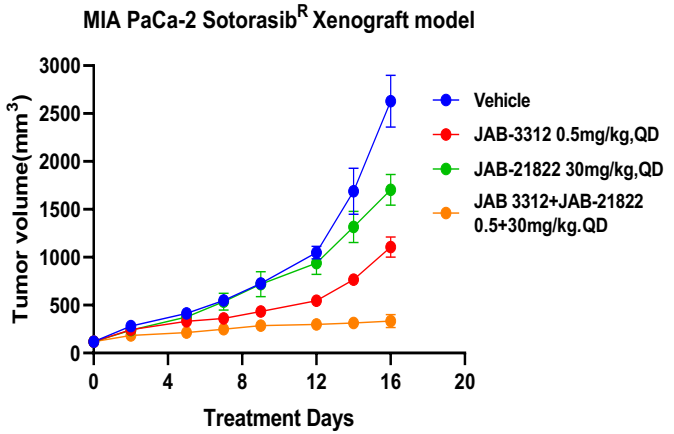
- Robust pre-clinical data
- Jacobio's preliminary clinical data
- Preliminary clinical data presented at IASLC 2022 World Conference of Lung Cancer by Amgen[1].
  - *Of the 6* ***KRASG12C inhibitor-naïve patients*** *with NSCLC who received the highest two doses of RMC-4630 in combination with sotorasib,* ***3 (50%) had a confirmed PR and 6 (100%) had disease control.***

Nature Publication

Ref: Jude Canon, Nature, 2019



Preclinical data in Sotorasib resistant model

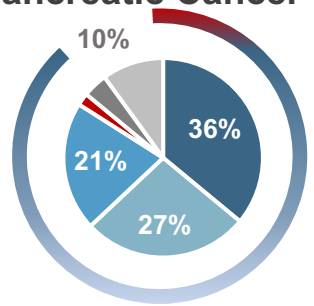


Note1: 2022 WCLC

Next Breakthrough

- Jacobio's KRAS^{multi} and KRAS G12D inhibitor

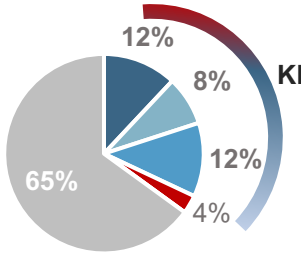
Pancreatic Cancer



KRAS ^{mt} total ~ 90%

KRAS G12D	~ 36%	KRAS G12V	~ 27%
KRAS G12R/S/A G13, Q61H	~ 21%	KRAS G12C	~ 2%

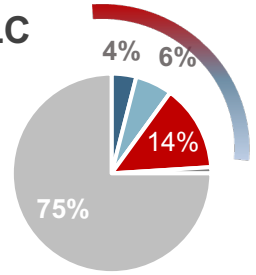
CRC



KRAS ^{mt} total ~ 35%

KRAS G12D	~ 12%	KRAS G12V	~ 8%
KRAS G12R/S/A G13, Q61H	~ 12%	KRAS G12C	~ 3-4%

NSCLC



KRAS ^{mt} total ~ 25%

KRAS G12D	~ 4%	KRAS G12V	~ 6%
KRAS G12C	~ 14%		

KRAS G12D | KRAS G12V | KRAS G12C | KRAS G12R/S/A, G13D, Q61H | Other KRAS ^{mt} | WT KRAS

JAB-23400

A first-in-class, orally bioavailable, KRAS^{multi} inhibitor.

Inhibit the activity of multiple KRAS mutants in both RAS (ON) and RAS (OFF) states, including KRAS G12X (G12D, G12V, G12R, G12S and G12A), G13D and Q61H.

- KRAS^{multi} inhibitor
- No multi-KRAS IND Globally *(1 RAS^{multi} (not KRAS selective) in PhI)*
- **2023 IND**

JAB-22000

A small-molecule KRAS G12D inhibitor.

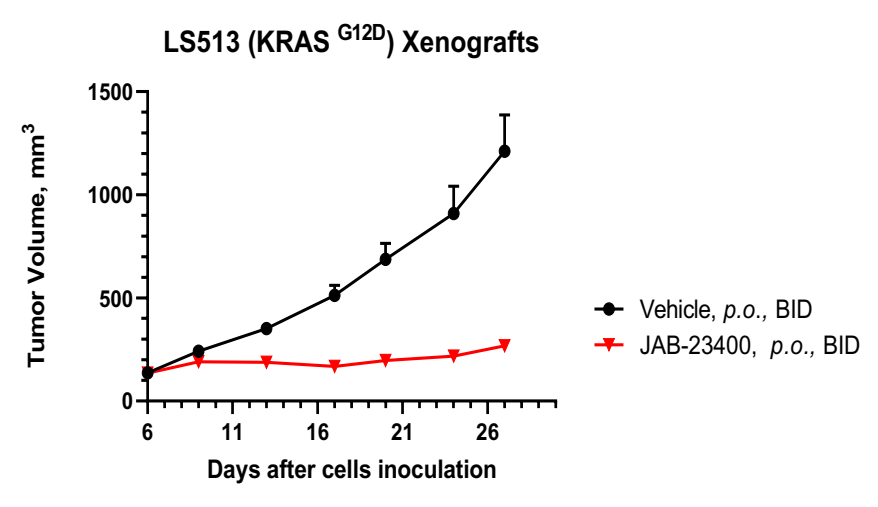
- KRAS G12D inhibitor
- No IND Globally
- **2024 IND**

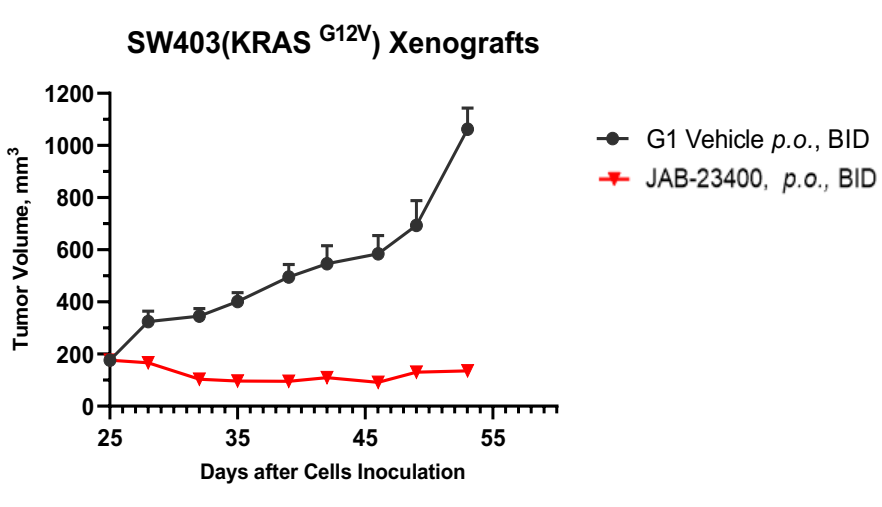
1. ZehirA, et al. Nat Med. 2017;23(6)703-713.
2. KrakstadC, et al. PLoSOne. 2012;7(12):e52795.
3. NIH TCGA: The Cancer Genome Atlas. February 11, 2021
5. Dunnett-Kane V, et al. Annals of Oncology, 2020, 31(7).
6. Prior I A, et al. Cancer Research, 2020, 80(14):canres.3682.2019.

Our KRAS^{MULTI} Inhibitor JAB-23400

Leveraging our Induced Allosteric Drug Discovery Platform ("**IADDP**"), we have designed JAB-23400 which can **Inhibit the activity of multiple KRAS mutants in both RAS (ON) and RAS (OFF) states, including KRAS** G12X (G12D, G12V, G12R, G12S and G12A), G13D and Q61H, with **no inhibition of HRAS and NRAS.**

Strong Antitumor Effect





- Tumor suppression or regression was achieved by oral administration in LS513 (KRAS G12D) and SW403 (KRAS G12V) models.
- Excellent anti-tumor effect in KRAS G12X (G12D, G12V, G12R, G12S and G12A), G13D, and Q61H mutant tumor xenografts.
- Exhibited an acceptable oral bioavailability both in rodents and non-rodents species.
- According to the preclinical data, it is predicted that JAB-23400 will have an acceptable exposure on human.

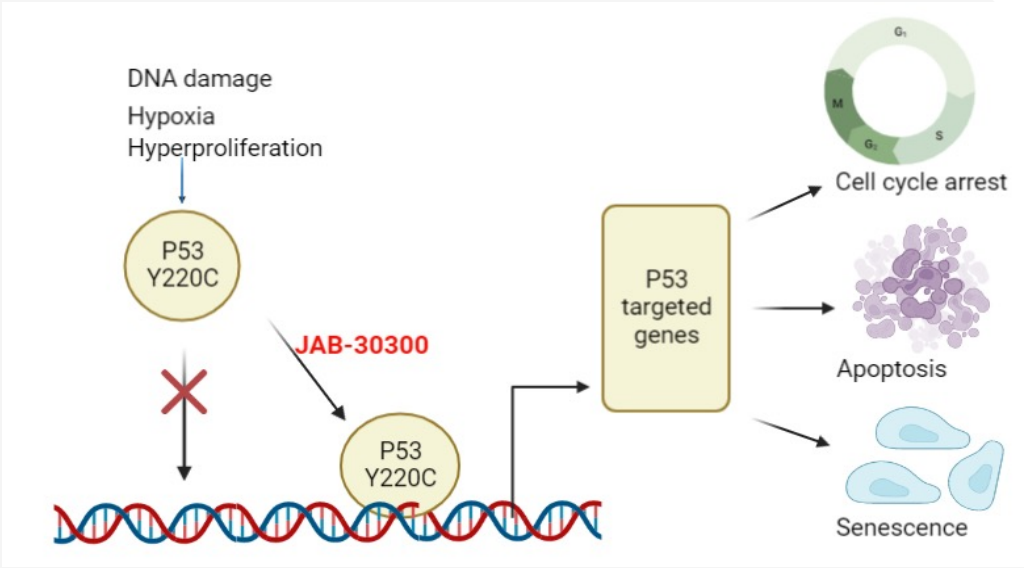
Competitive Landscape

To date, there is no small-molecule **KRAS^{multi}** inhibitor that targets both RAS (ON) and RAS (OFF) states in clinical stage globally.

Other Leading Pre-clinical Stage Drug Candidates – P53 Activator

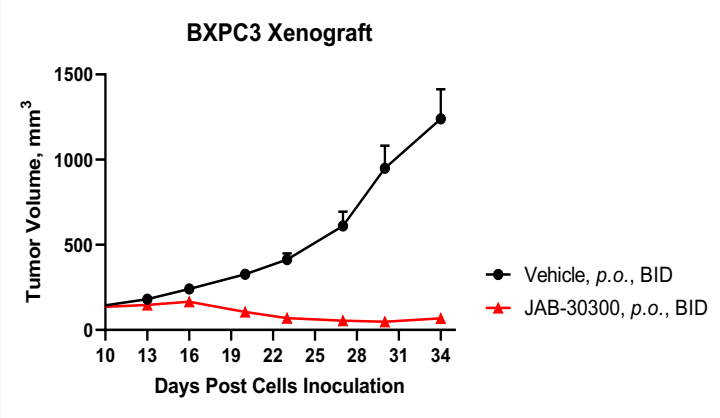
JAB-30300 is an orally available, **allosteric** small molecule for the treatment of patients with locally advanced or metastatic solid tumors harboring **P53 Y220C** mutation.
Projects targeting P53 mutations **other than Y220C** are also under development.

P53 is a classic tumor suppressor



- JAB-30300 increases the expression of p53-targeted genes and regulate cell cycle arrest, apoptosis, senescence and other processes by increasing the binding affinity of P53 Y220C with DNA.
- JAB-30300 was nominated as clinical candidate in 2022 Q2 and is currently in **IND-enabling stage**. (2023 IND)

Strong Antitumor Effect



- JAB-30300 is a highly potent and selective P53 Y220C activator.
- It has shown favorable PK properties in different species and tumor regression was achieved in different CDX mice models.

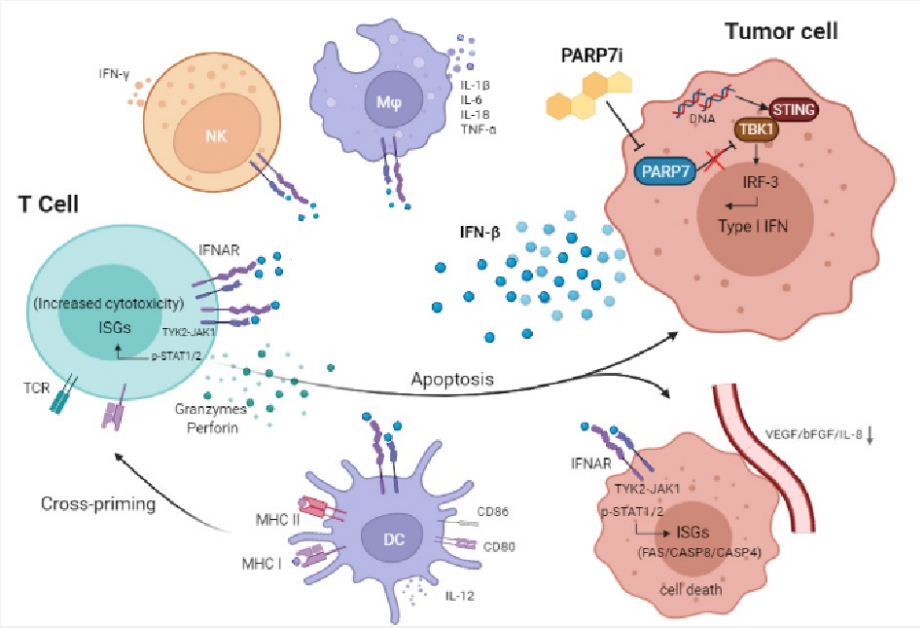
Competitive Landscape

- Currently, there is only one program in the Phase I clinical stage in respective drug classes globally.
- The TP53 Y220C mutation is associated with 0.5-3% of all cancers

Other Leading Pre-clinical Stage Drug Candidates – PARP7 Inhibitor

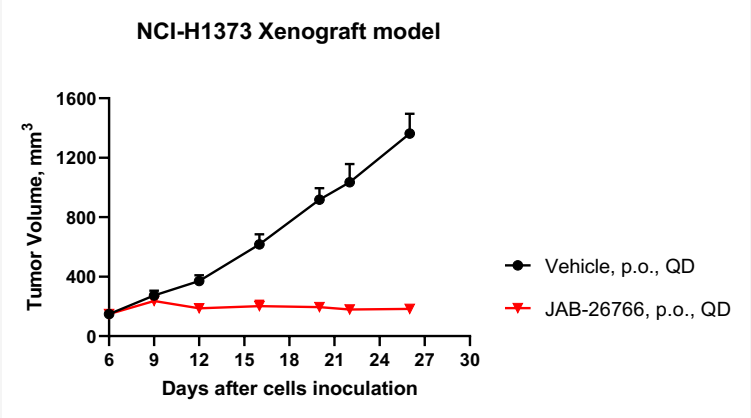
JAB-26766 - an orally bioavailable small-molecule **PARP7 inhibitor**, targeting immuno-oncology pathway for the treatment of a variety of solid tumors.

Role of PARP7



- PARP7 acts as a brake in type I IFN signaling in a TBK1-dependent manner. PARP7 is frequently amplified in squamous cell carcinoma
- By selectively inhibiting PARP7 in tumor cells, Type I IFN signaling to stimulate innate and adaptive antitumor immune response is restored.

Strong Antitumor Effect

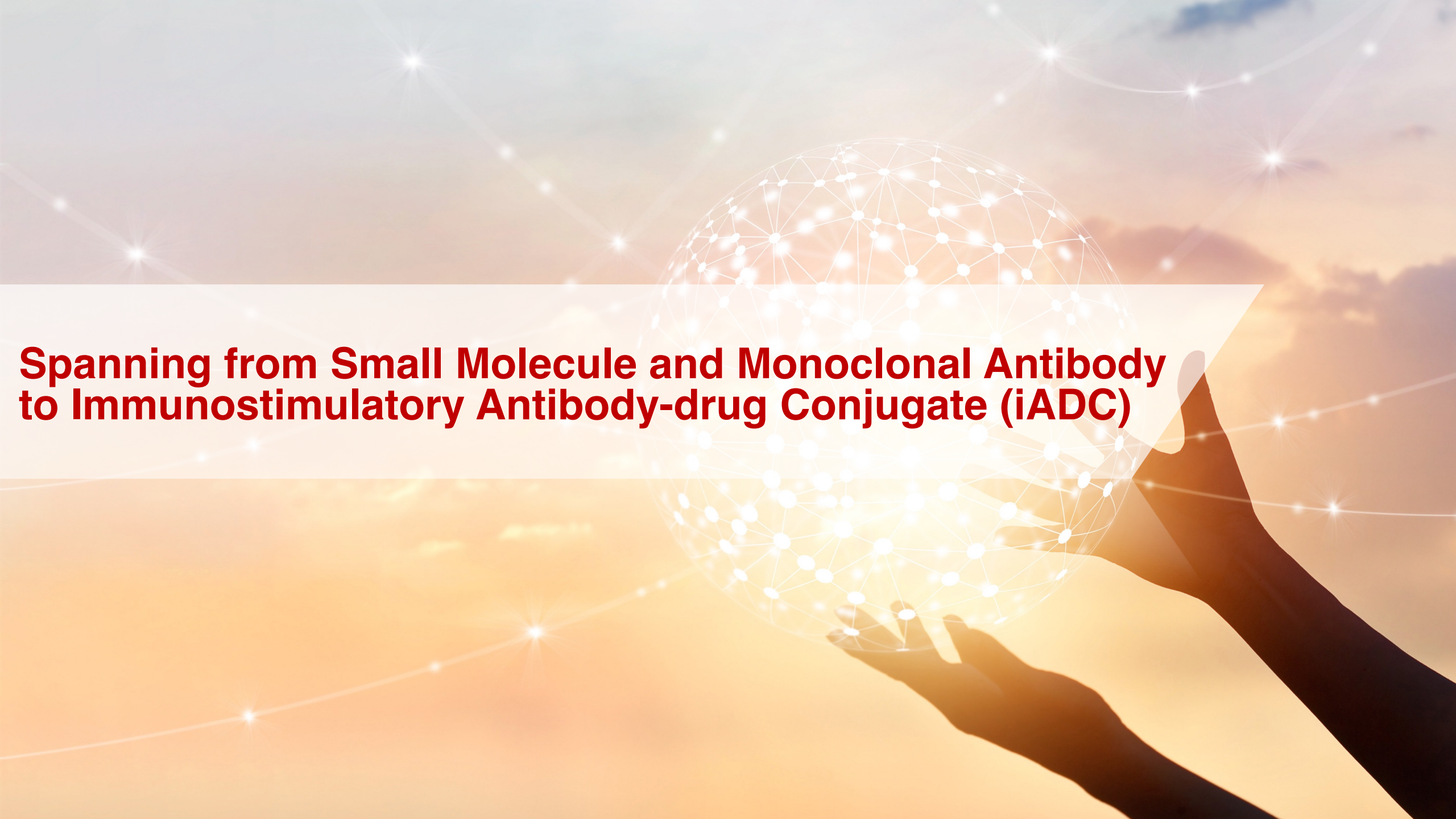


- JAB-26766 has exhibited favorable in vitro cell inhibition activities and selectivity.
- Higher exposure in mice and dog was seen for JAB-26766 per oral administration which led to substantial tumor inhibition activities in different tumor models.

Competitive Landscape

- Currently, there is only one program in the Phase I clinical stage in respective drug classes globally.
- IND application is expected to be submitted in the second half of 2022.

Spanning from Small Molecule and Monoclonal Antibody to Immunostimulatory Antibody-drug Conjugate (iADC)



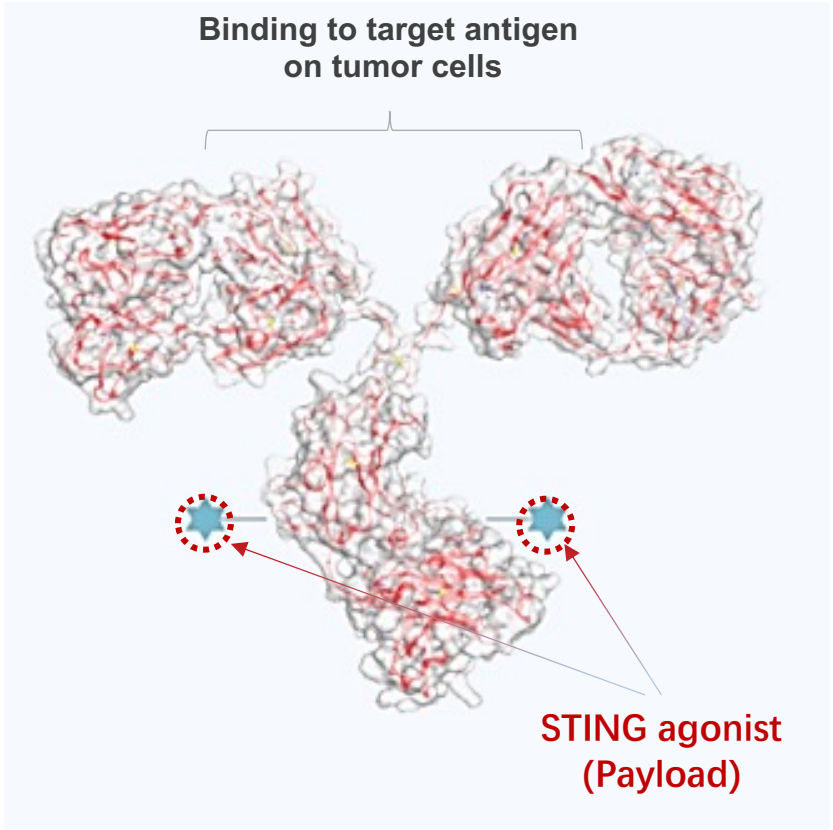
Our iADC Programs Supported by Unique Payloads

We believe the key of non-conventional ADCs is to find **the optimal payload and linker.** Leveraging our strength in small-molecule drug discovery and development, we have designed **innovative immune-stimulator as payloads to built our immunostimulatory antibody-drug conjugate (iADC) platform**.

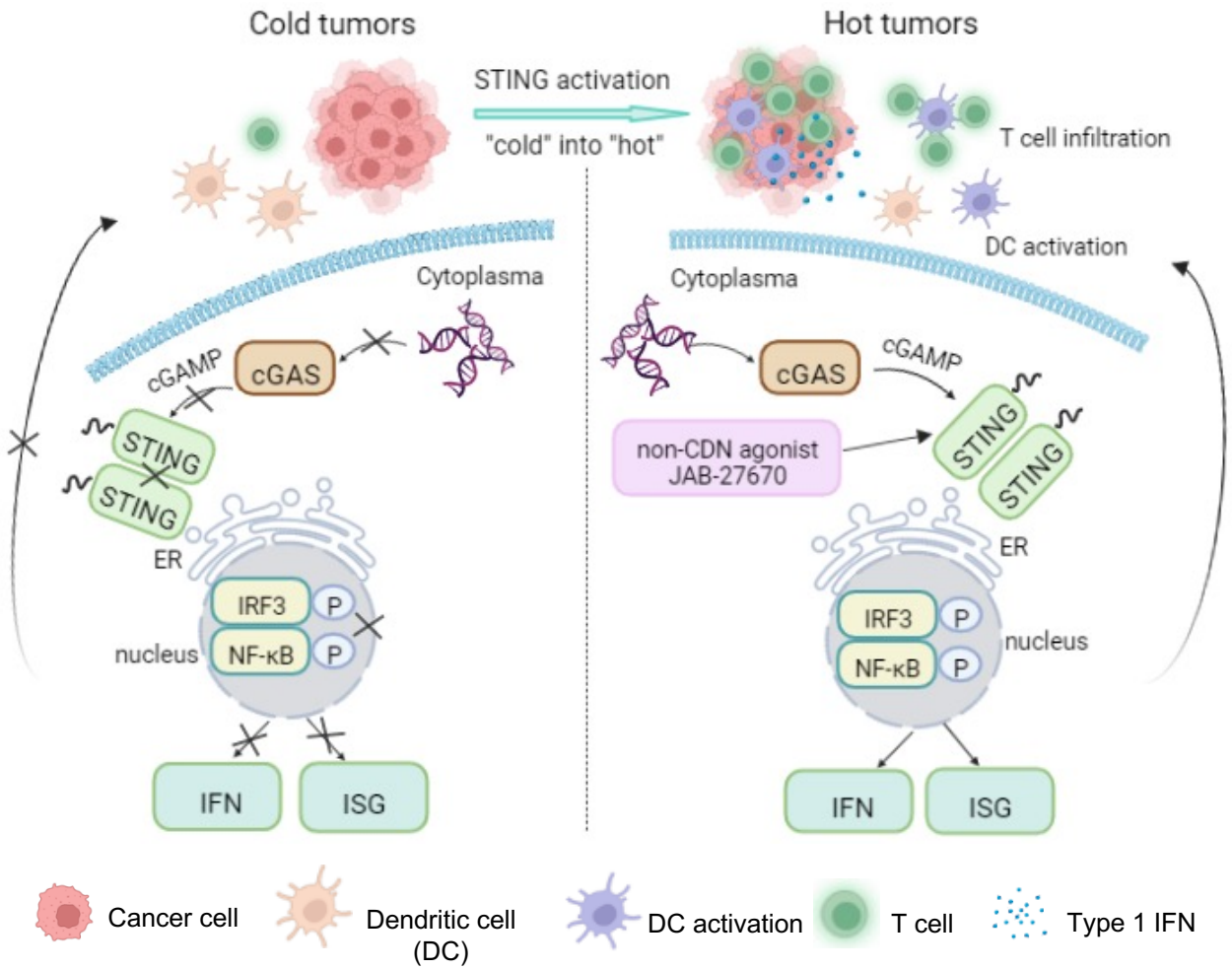
- **Conventional ADCs**, which **use toxins as payloads**, have demonstrated obvious **toxicity** due to the toxin molecules can be delivered to the normal tissues.
- In current immune-checkpoint blockade (**ICB**) therapy, "cold tumor" led to low response rate.

Our novel iADC program to address the challenges

- Our novel iADC program by targeted delivering immune-stimulators, including STING and other novel small-molecules, as payloads to the tumor has the potential to address the above challenges.



STING – Activate Anti-tumor Activity and Reshape the TME

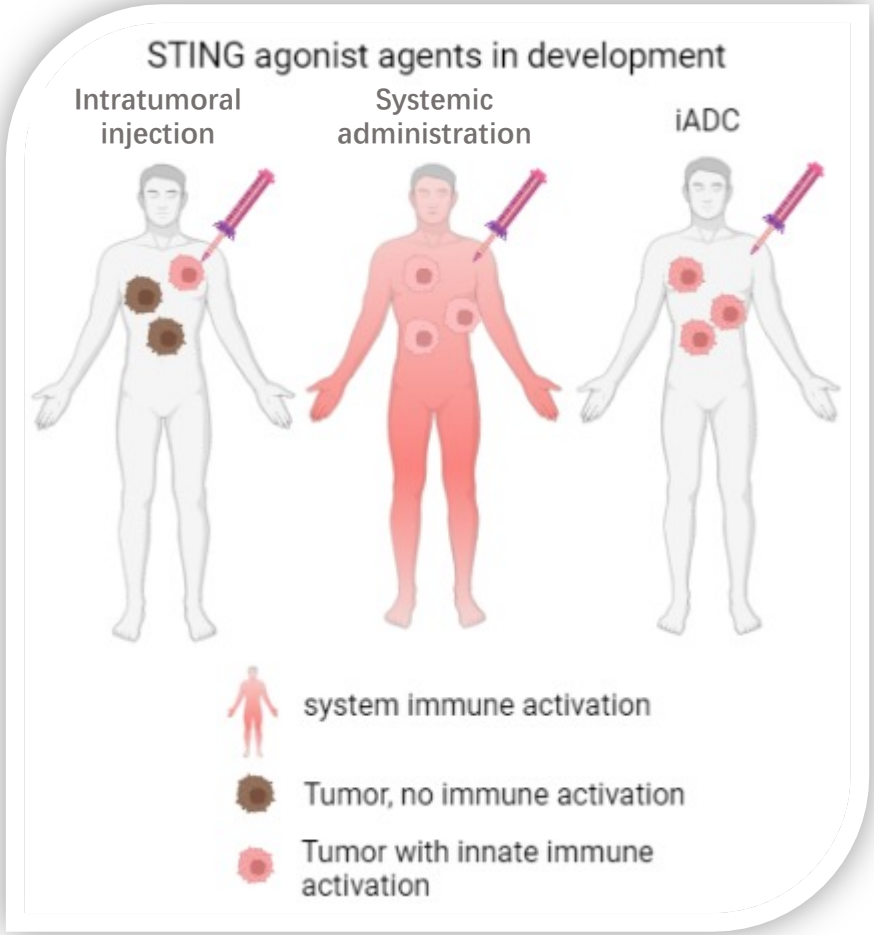


MOA in Tumor Microenvironment (TME)

- ***Immune cells — Turn "cold tumor" to "hot"***
  - "stimulating innate and adaptive immunity through cytokines such as type I IFN, promoting the maturation and production of immune cells such as T cells, DCs, and NK cells to trigger effective anti-tumor immune effects."
- ***Tumor cells — The expression of STING is inhibited in most tumors.*** *(*low expression in pancreatic cancer, defected in colon adenocarcinoma and other advanced tumors)
  - "when cGAS-STING pathway in tumor cells is activated, cytokines such as IL-6 and type I IFN are induced, leading to tumor cell apoptosis or death"

Note1: Li-Teng Ong et al., PNAS (2022).
Kewang Luo et al., Molecules (2022)

STING – Activate Anti-tumor Activity and Reshape the TME



Multiple projects in clinical stage evaluating the efficacy and safety of STING via

Intratumoral injection / **Systemic administration**

Restriction on tumor type, location or size

Systemic inflammation

ADCs are suited to overcome limitation of free agonist

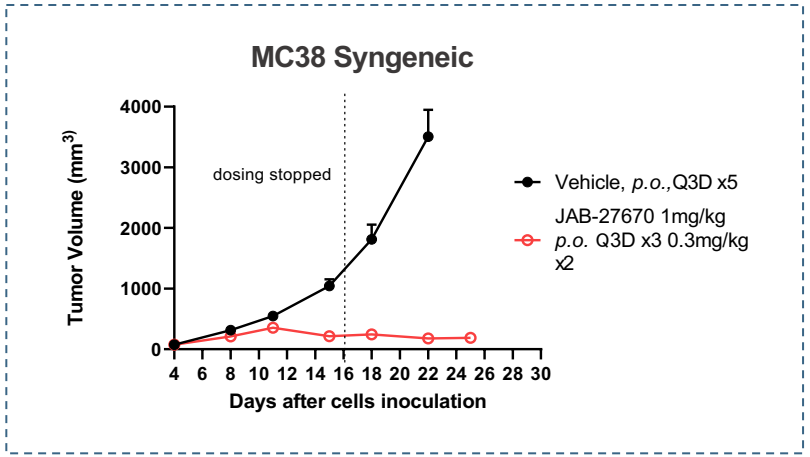
STING-iADC

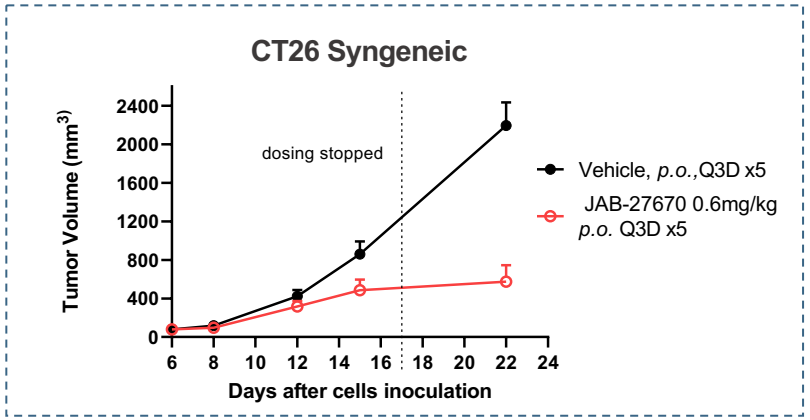
By **specifically delivering** highly potent STING agonist into tumor associated antigen (TAA) expressing tumor cell, rationale designed iADC could locally **activate anti-tumor activity** to boost the tumor specific **innate/adaptive immune response** and **avoid the risk of systemic immune-related adverse effect**.

Our Non-CDN STING Agonist

	Pharmacology studies	Jacobio STING agonist JAB-27670
Affinity	Human STING WT binding assay/IC_{50}	0.175nM
Cell-base function	Human IFN-β assay [b]/EC_{50}	17.9nM
	SK-OV-3 cancer cell /IC_{50}	69.2nM
Cell-base selectivity	MRC-5 human lung fibroblasts/IC_{50}	>30μM (>400 fold)
hERG	Inhibition% @10μM	4.86%
Safety panel	41 targets	No risk

- We have developed a **highly potent** novel non-cyclic dinucleotide ("**non-CDN**") small-molecule STING agonist designed with sub-nanomolar activity which is **suitable to be used as payload**.
- JAB-27670 STING agonist has exhibited **a potent and durable tumor inhibition** in CT26 and MC38 CDX models at a low dose (0.6 mg/kg, BIW) and was validated in CD73 and HER2 targets internally.

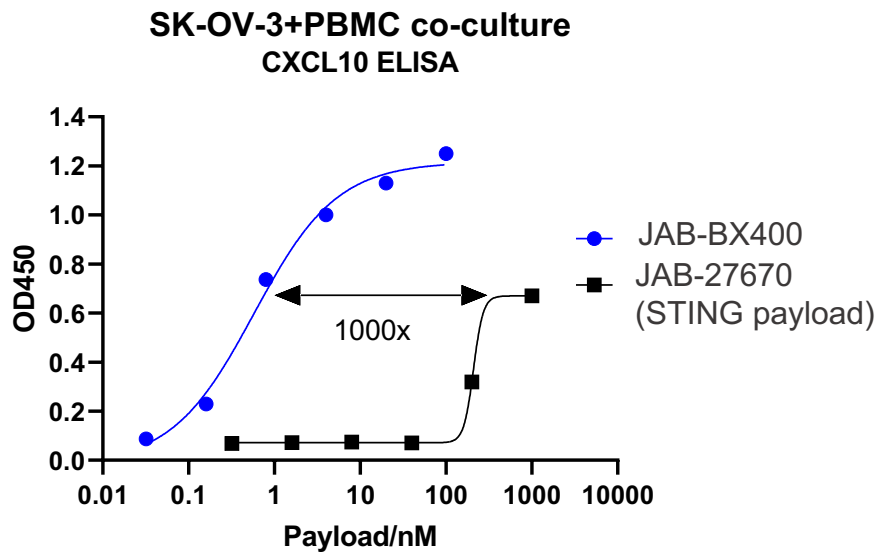




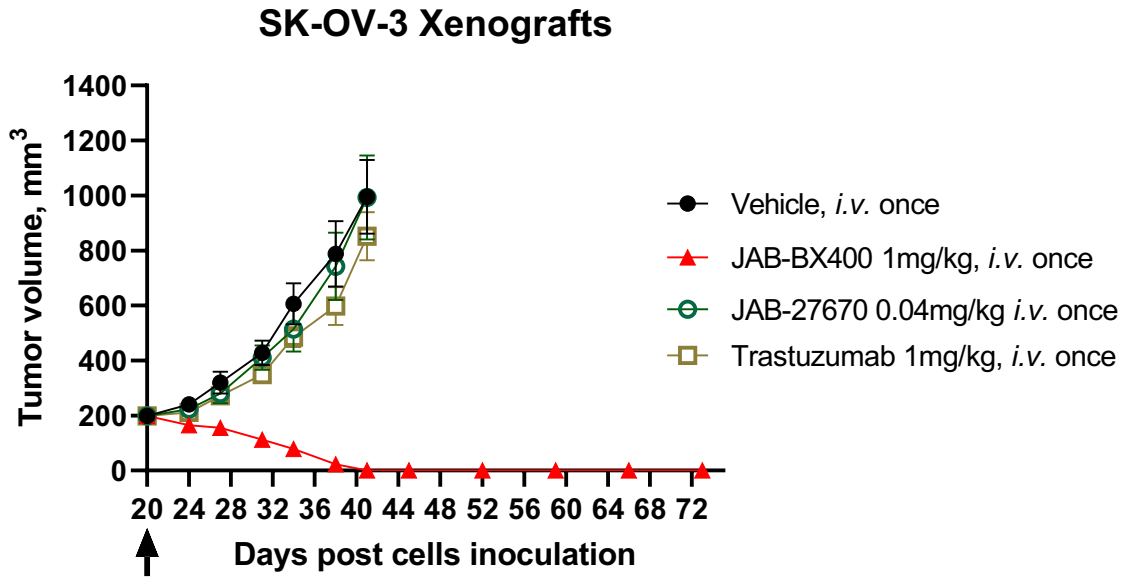
We are developing **multiple STING iADCs with HER2, CD73** and other potential targets internally or through strategic collaborations.

JAB-BX400 – a STING-iADC Product Candidate Targeting HER2

>1000 fold increase in potency of HER2-STING vs. Free payload (STING)



Superior Efficacy to Trastuzumab



- STING+HER2 rationale - The high proportion of trastuzumab resistance might arise from HER2 tumors having low IFI16, CXCL10, and CXCL11 expression.[1]
- A single dose (1 mg/kg) of our HER2 STING-iADC induces **complete and durable tumor regression** in SK-OV-3 CDX model, while 1 mg/kg trastuzumab induces limited tumor inhibition.

Note1: Li-Teng Ong et al., PNAS (2022).

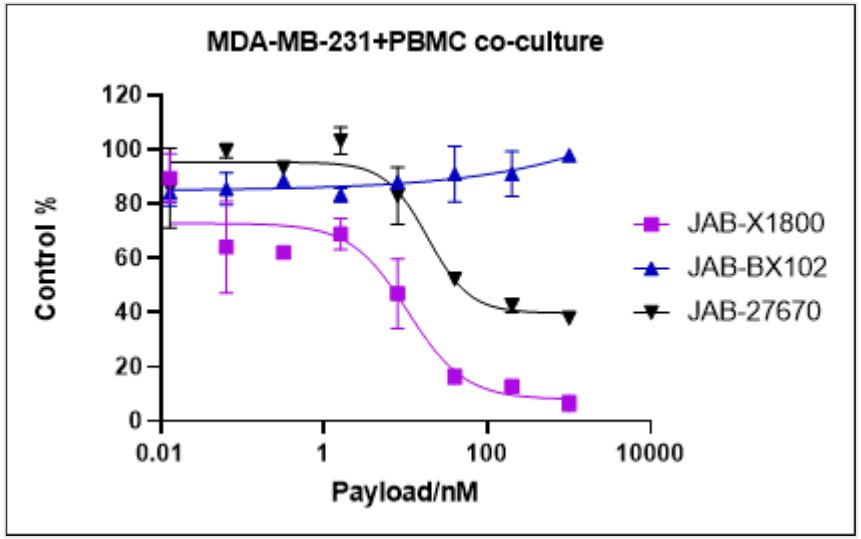
CD73 mAb (JAB-BX102) & CD73-STING iADC(JAB-X1800)

JAB-BX102 CD73 mAb

- JAB-BX102 in clinical stage - IND approved with FPI expected in Aug 2022
- To combo with PD-1 in clinical
- Direct inhibition of CD73 enzyme activity with better pre-clinical efficacy
- Efficiently elimate CD73 from the cell surface by inducing internalization of surface CD73
- In vivo PK/PD model, complete CD73 inhibition without the “hook effect”

JAB-BX1800 CD73-STING iADC

- CD73-STING iADC in lead optimization stage
- JAB-1800 with better MDA-MB-231 cancer cell-killing activity *in vitro* PBMCs co-cultures



On Target to Capture the Global Market

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

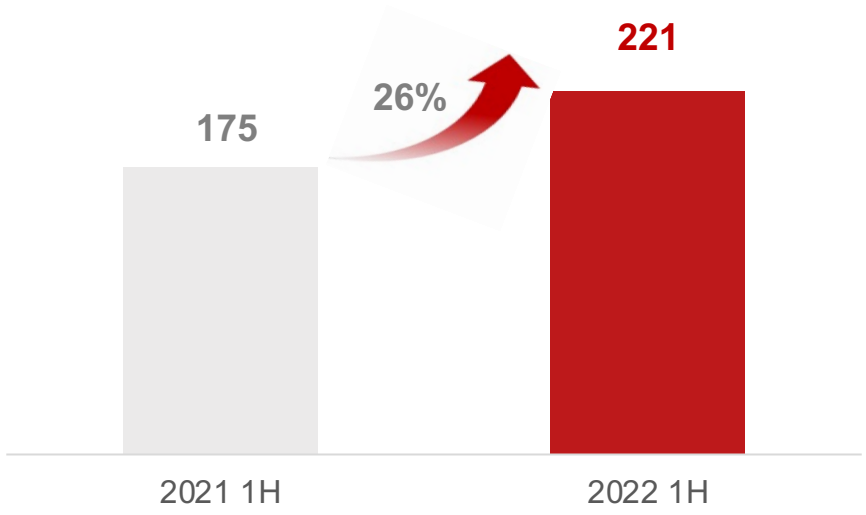
- **Upfront Payment (Received)**
  $45mm
- **Milestone Payments**
  up to $810mm - $20mm received
- **Royalties**
  Low-to-mid Double-digit percentages
- AbbVie will ***reimburse*** **costs of global clinical development** (incl. China) pre registrational trials
- Around ***RMB100 million cash inflow*** during 2022 1H

Financial Information

SELECT COMPANY FINANCIALS

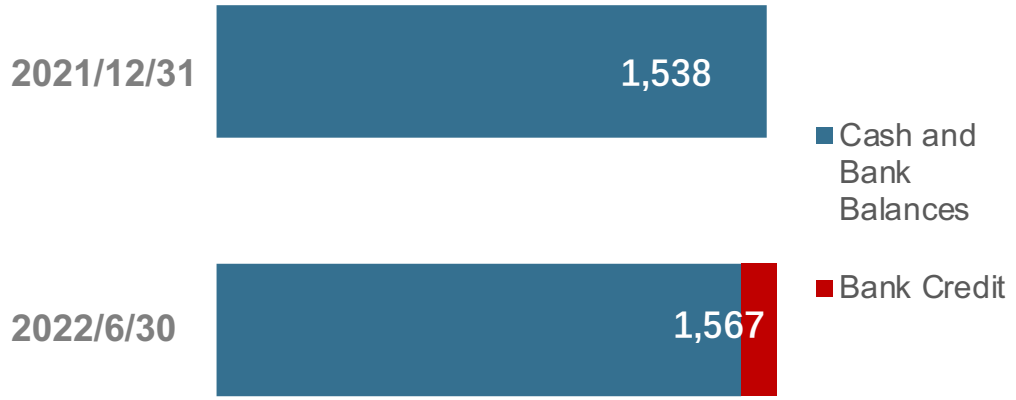
(RMB mm)

R&D costs [1]



(RMB mm)

Cash, Bank Balances and Bank Credit [2, 3]



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.

2 *As of June 30, 2022, the Group did not have any interest-bearing bank and other borrowing.*

3 *As of the date of our interim report, the Group have bank credit of RMB100 million.*

Our Expansion

Global Headquarter
Beijing, China

2022 HC: 285 employees

In-house R&D

Allosteric Inhibitor Tech Platform

Global FIC

6 Clinical Stage Assets (**2** Global TOP 3)

15+ Pipeline Assets (**9** Global TOP 3 Potential)

Global Market

Global Partnership License-out Deals

Full Function Pharma

First NDA in 2023-2024

Beijing Headquarter *(under construction)*

Beijing R&D Center

Beijing Clinical Office (Dazu)

Beijing Clincal office (Shoudong)

Shanghai Clinical Office

U.S. R&D Center in MA