加科思药业集团有限公司
2024年度业绩

JACOBIO PHARMACEUTICALS GROUP CO., LTD.

2024 Annual Results

股份代码：01167.HK

2025.03

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加科思 Jacobio

聚焦具有重大临床价值的难成药靶点

强大的研发管线

- **经典肿瘤信号通路布局**
  重点KRAS和STING iADC，覆盖约70%-80%的癌症类型
- **核心项目以全球前三为目标**
  目前13款在研项目，10款处于临床阶段，其中已有9款处于全球前三，预计5年内3-4个NDA的产品

可持续的创新能力

- 创始团队行业经验丰富，成功领导第一个靶向抗肿瘤药上市
- 双平台驱动创新：诱导变构药物发现平台和iADC药物研发平台
- 全球专利申请数量达到360+项，其中126项专利已在全球主要市场获得授权

全球化布局

- 项目临床试验申请（IND）中美双申报，30+IND获批
- 在全球范围内进行临床试验，公司已在中国、美国及欧洲等多国启动多项临床试验；核心管线的临床进度及临床效果均列第一梯队
- 通过对外授权、共同开发等方式将产品推向全球市场，推动药物全球商业化

财务状况稳健

- 资金储备可覆盖未来4年的支出
- 截至2024年12月31日，公司拥有现金、银行余额和银行授信14.6亿元；2024年8月将戈来雷塞和SHP2抑制剂的中国权益以约9亿人民币首付款+里程碑付款及两位数分级销售分成授权给上海艾力斯，已收到2亿元近期付款，为公司提供了稳定的现金流支持

2024年度业绩

1
新药生产上市申请（NDA）

3
关键注册临床研究

2
中、美一期临床完成

2
中、美新药临床试验申请（IND）获批

13
数据发表

1
临床候选分子

1
BD授权合作

360+
专利申请

126
专利授权

（截至2024年12月31日）

3.2亿人民币
资金流入

A级
ESG获MSCI

加科思产品管线布局（一）：聚焦KRAS信号通路

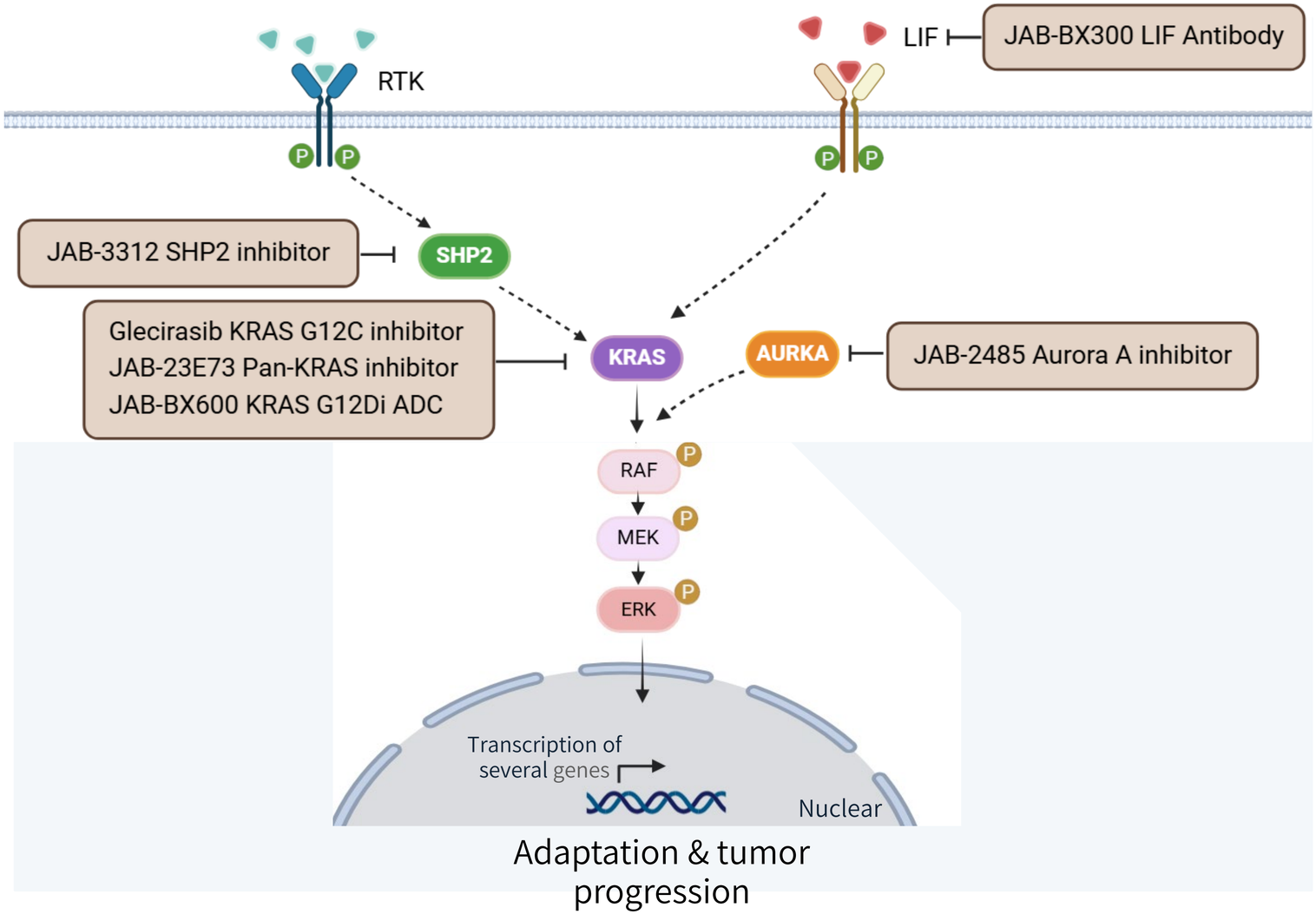
临床阶段产品

- 戈来雷塞（JAB-21822 KRAS G12C抑制剂，NDA阶段）
- JAB-3312 SHP2抑制剂，Phase III
- JAB-2485 Aurora A抑制剂，Phase I
- JAB-23E73 Pan-KRAS抑制剂，Phase I
- JAB-BX300 LIF mAb， IND获批

临床前研发阶段产品

以高活性的KRAS G12D inhibitor为payload的ADC

- JAB-BX600 KRAS G12Di ADC



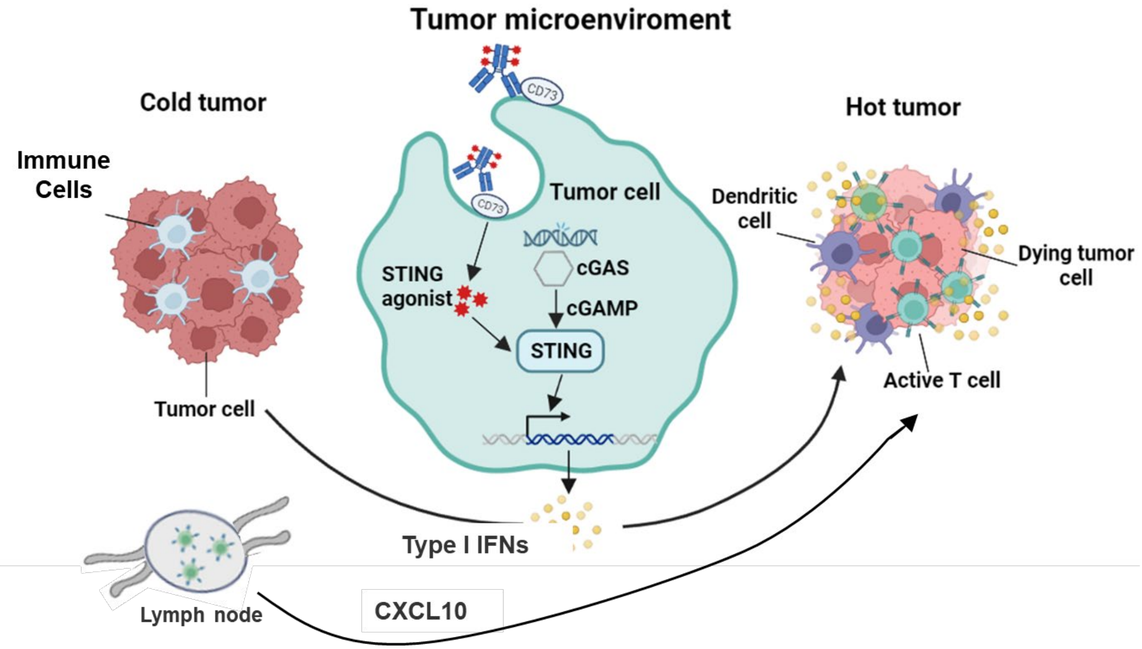
加科思产品管线布局(二）：iADC肿瘤免疫2.0

iADC：肿瘤免疫2.0

- PD-1之后肿瘤免疫靶点鲜有突破，70%以上的患者对PD-1单药无响应（冷肿瘤）
- 依托小分子药物设计优势，创新性地将特异性STING激动剂作为iADC的载荷（payload），通过精准重塑肿瘤微环境（TME）实现免疫细胞浸润，将冷肿瘤转变为热肿瘤，解决冷肿瘤对PD-1单药无响应的治疗困境
- STING相关研究获2024年拉斯克医学奖（Lasker Medical Research Awards）

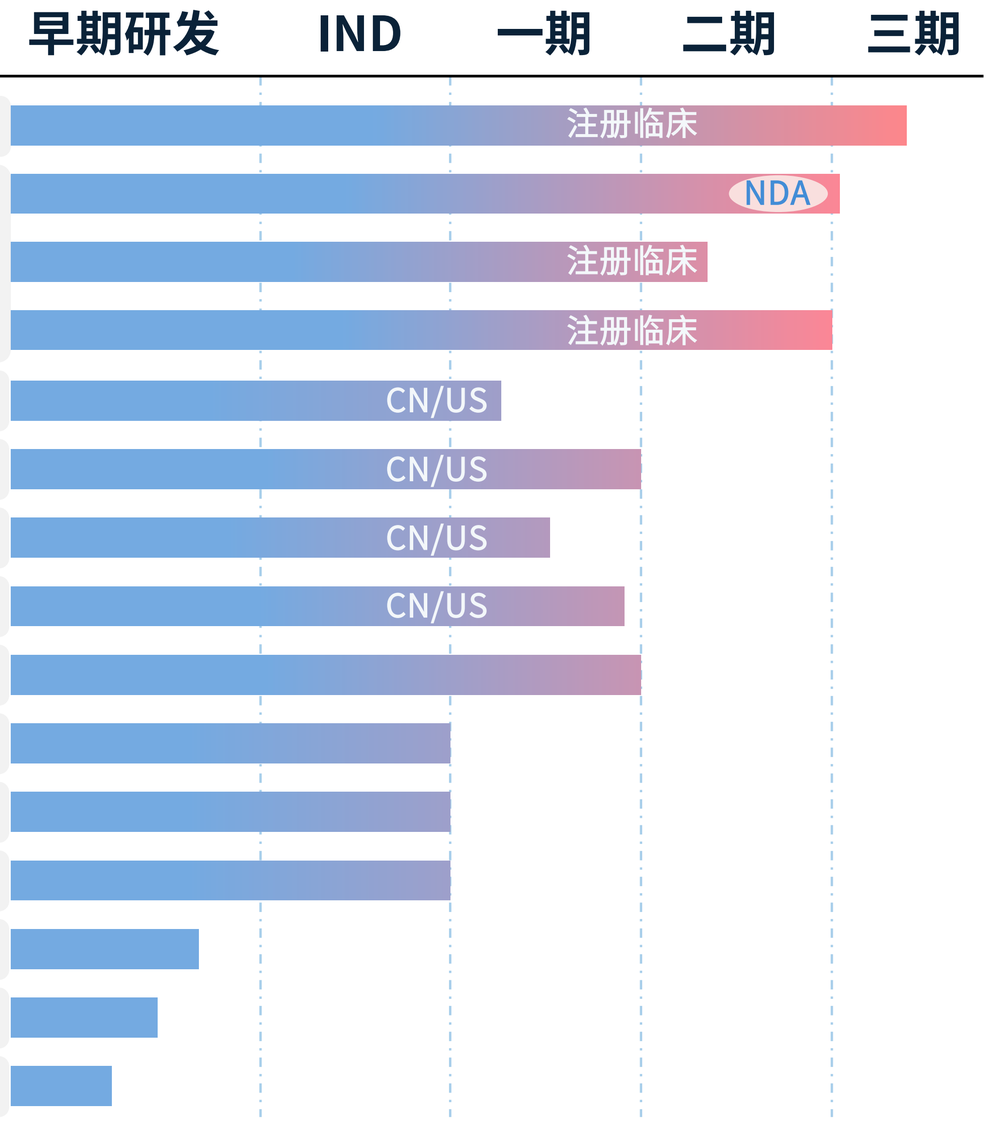
- JAB-BX467 HER2-STING（已经确定临床候选化合物，2026年IND）
- 其他抗体偶联iADC

iADC促进免疫细胞浸润到TME，激活肿瘤免疫



产品管线布局：核心管线进度全球前三

项目	靶点	适应症
JAB-3312*/Glecirasib	SHP2/KRAS G12C	一线非小细胞肺癌
Glecirasib*	KRAS G12C	二线及以上非小细胞肺癌 二线及以上胰腺癌及泛瘤种** 结直肠癌
JAB-23E73	pan-KRAS（口服）	实体瘤
JAB-8263	BET	实体瘤、血液瘤
JAB-30355	P53 Y220C	实体瘤
JAB-2485	Aurora Kinase A	实体瘤
JAB-BX102	CD73	实体瘤
JAB-BX300	LIF	实体瘤
JAB-24114	GUE***	实体瘤、血液瘤
JAB-26766	PARP7	实体瘤
JAB-BX467	HER2-STING iADC	实体瘤
JAB-BX600	KRAS G12Di ADC	实体瘤
JAB-BX700	Undisclosed ADC	实体瘤



- **戈来雷塞及JAB-3312的中国权益于2024年8月30日授权给艾力斯*
- ***泛瘤种：除NSCLC，PADC，CRC以外的其他癌种，如胆道癌，胃癌，小肠癌，阑尾癌，宫颈癌，头颈癌，卵巢癌，滑膜肉瘤，纵隔肿瘤等*
- ****GUE: glutamine utilizing enzymes*

我们的管线

Jacobio

戈来雷塞≥ 2L非小细胞肺癌（NSCLC）

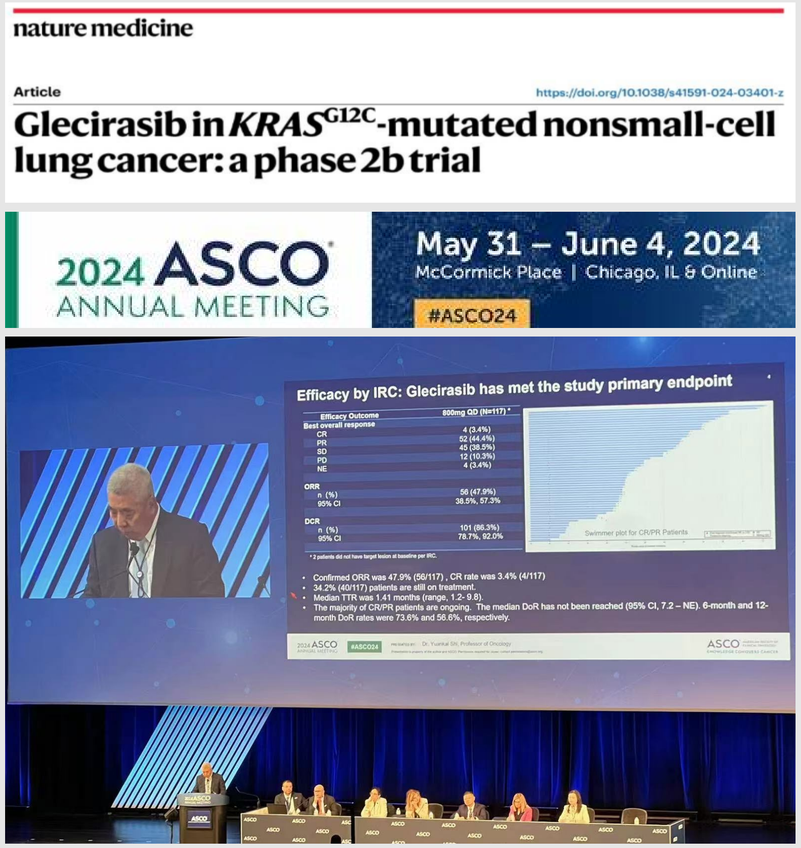
2025年Nature Medicine（自然医学）上发表注册性临床数据
2024 ASCO* Plenary Series全体会议和2024 ASCO年会（口头报告）

- 戈来雷塞单药二线及以上治疗KRAS G12C突变NSCLC患者

  报道117位患者数据

  - cORR 47.9%（56/117），DCR 86.3% (101/117)，mPFS 8.2个月，mOS 13.6个月
  - 耐受性良好，消化道相关不良事件显著低于其他KRAS G12C抑制剂

- KRAS抑制剂戈来雷塞于2024年5月在中国提交新药生产上市申请（NDA），预计于2025年Q2获批上市。



PI: 石远凯院长

*ASCO：美国肿瘤年会

戈来雷塞+JAB-3312 一线非小细胞肺癌（NSCLC）

2024年美国临床肿瘤学会（ASCO）年会（口头报告）

- 戈来雷塞联合JAB-3312（SHP2抑制剂）治疗KRAS G12C突变的一线NSCLC患者

  报道194位患者数据，其中一线NSCLC患者102例

  - cORR 64.7% (66/102)，DCR 93.1% (95/102)，mPFS 12.2个月
  - 最优剂量组（戈来雷塞800 mg每天 + JAB-3312 2 mg [1/1]）：cORR 77.4% (24/31)，54.8% (17/31)肿瘤缩小超过50%

- 戈来雷塞联合JAB-3312用于一线治疗NSCLC患者的注册性3期临床研究，正在中国进行中。
- 2024年欧洲肿瘤学学会（ESMO）（壁报）
- 2025年联用转化研究数据被国际学术杂志接收

一线治疗KRAS G12C阳性且PD-L1<1%的NSCLC：全球仅加科思和Amgen进入注册性3期临床研究

KRAS G12C突变的NSCLC患者
(4% 的中国NSCLC患者，14%的欧美NSCLC患者)

- **一线标准疗法 PD-L1 TPS <1%：**

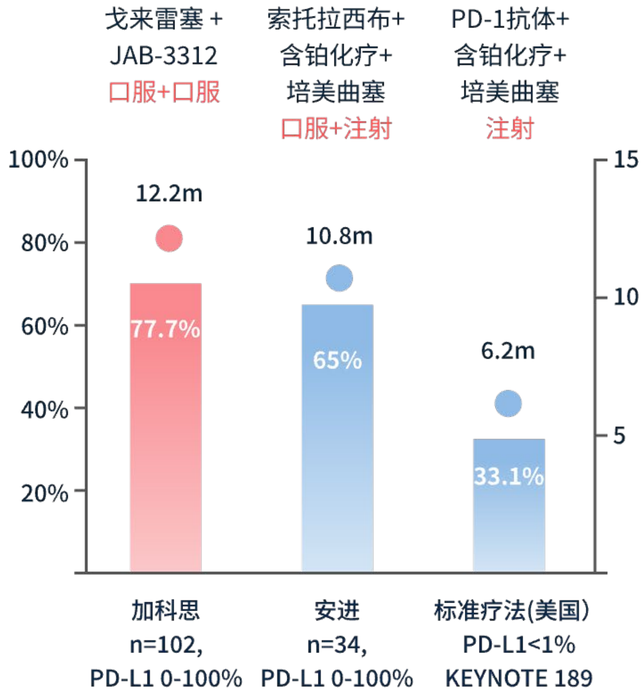
标准疗法	PD-1抗体注射+含铂化疗注射+培美曲塞注射
加科思	戈来雷塞口服+ JAB-3312口服
Amgen	索托拉西布口服+含铂化疗注射+培美曲塞注射

- **真实世界疗效数据**

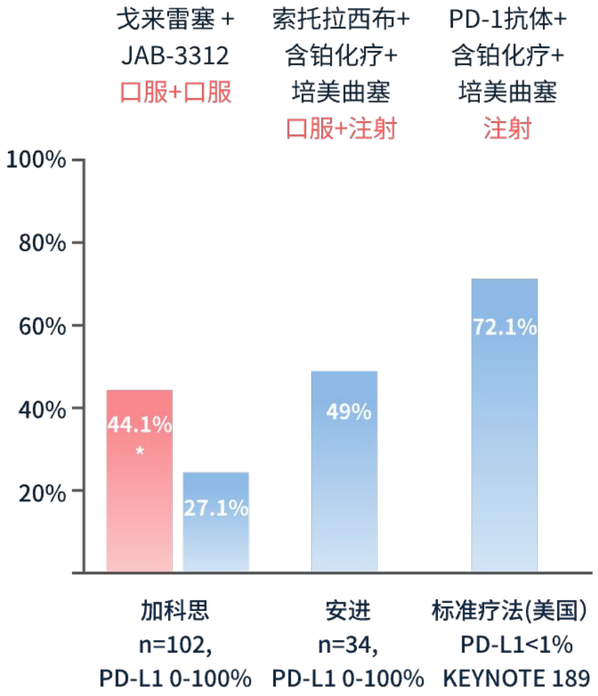
KRAS G12C突变，且PD-L1<1%的NSCLC，一线标准疗法mPFS 6.2月[1]

早期临床数据对比

疗效：cORR和mPFS



安全性：≥Gr3 TRAE



*含17%甘油三酯指标升高

1. *Elkrief, Arielle, et al. "Outcomes of Combination Platinum-Doublet Chemotherapy and Anti-PD (L)-1 Blockade in KRASG12C-Mutant Non-Small Cell Lung Cancer." The Oncologist 28.11 (2023): 978-985.*

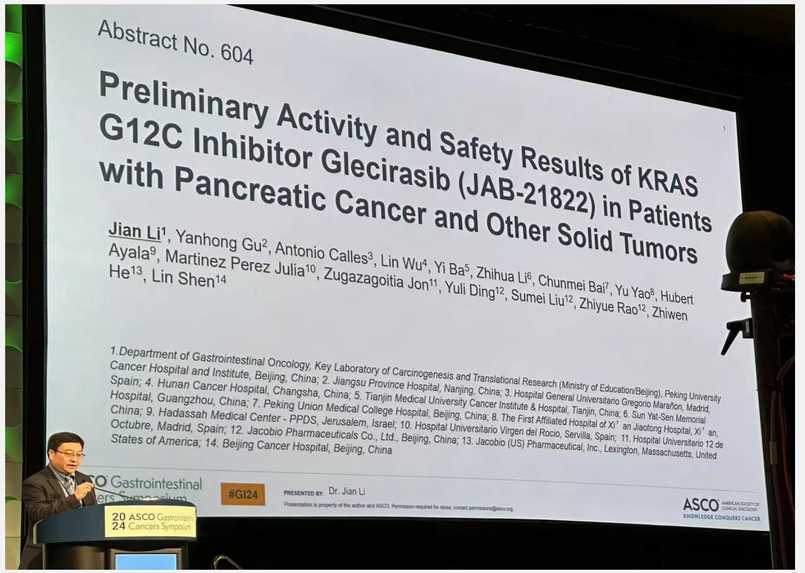
戈来雷塞≥ 2L 胰腺癌（PDAC）和泛瘤种

2024年美国临床肿瘤学会胃肠癌研讨会年会（ASCO GI）（口头报告）

- 戈来雷塞单药二线及以上治疗KRAS G12C突变胰腺癌（PDAC）和泛瘤种

  报道50位患者数据

  - PDAC：ORR 41.9% (14/31)，mPFS 5.6 m，mOS 10.7 m
  - 泛瘤种：cORR 57.9 (11/19)，DCR 84.2% (16/19)
  - 单药和联合用药的治疗相关性不良事件（TRAE）主要为1-2级。



- 胰腺癌及泛癌种单臂2期注册性临床研究在中国进行中；
- 获CDE授予突破性疗法认定;
- 获FDA及EMA孤儿药认证。

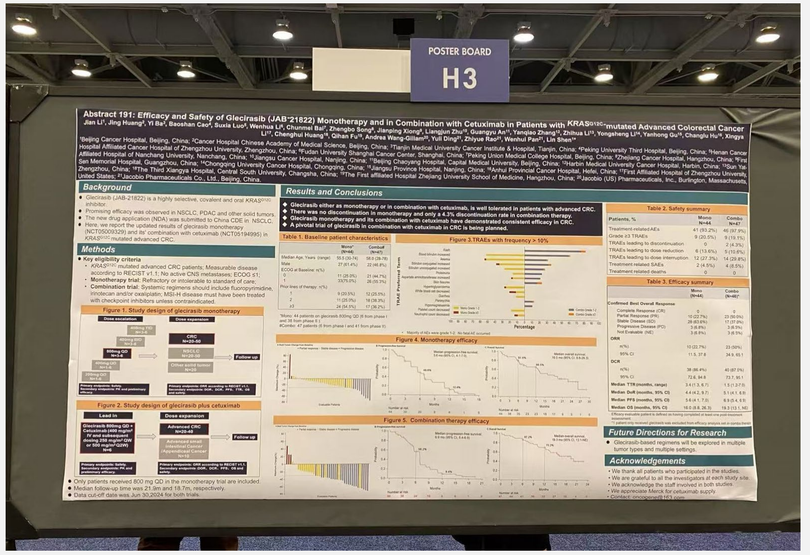
戈来雷塞联合西妥昔单抗晚期结直肠癌(CRC)

2025年美国临床肿瘤学会胃肠癌研讨会年会（ASCO GI）

- 戈来雷塞（JAB-21822）与西妥昔单抗联合用药治疗KRAS G12C突变晚期结直肠癌（CRC）的临床数据

  - 联用：ORR 50% (23/46)
    DCR 87.0%(40/46)
    mPFS 6.9m
    mOS 19.3m

  - Glecirasib联合西妥昔单抗治疗晚期KRAS G12C突变晚期结直肠癌的疗效优于Glecirasib单药治疗，同时保持良好的安全性。



- 注册性3期临床研究方案于2024年5月获CDE批准；
- 获CDE授予突破性疗法认定。

戈来雷塞及JAB-3312的授权合作

戈来雷塞+JAB-3312

中国权益

艾力斯

包括中国大陆、香港、澳门和台湾地区

首付款及其他近期付款

约2亿元人民币

里程碑付款

7亿元人民币

销售提成

两位数比例的净销售分级提成，
其中JAB-3312净销售额提成最高为20%

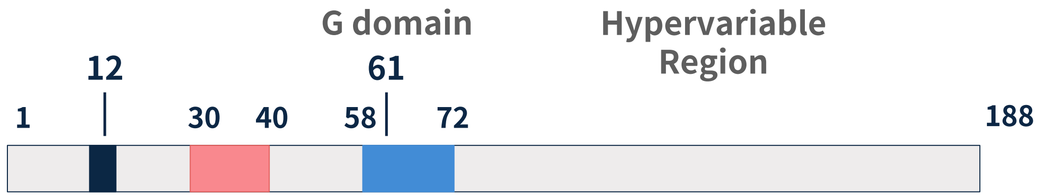
JAB-3312

SHP2项目

SHP2项目（JAB-3312及JAB-3068）于2020年5月与艾伯维（AbbVie）达成超过8.55亿美元的战略合作协议，2023年7月双方终止合作，加科思重新获得SHP2全球权益，公司共获得1.2亿美元的合作付款。

泛KRAS抑制剂的开发

KRAS的结构[3]



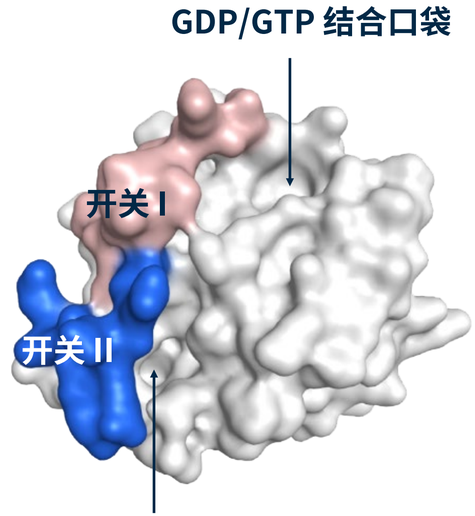
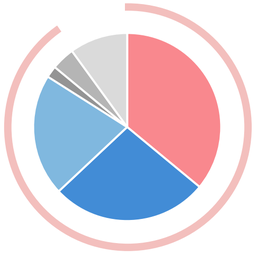


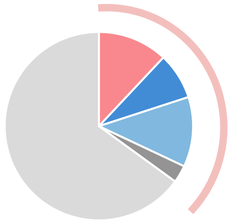
Image prepared by VMD 1.9.3

- 23%的人类癌症带有KRAS突变[1]
- 每年全球有2,700,000的带有KRAS突变的新增病例[2]



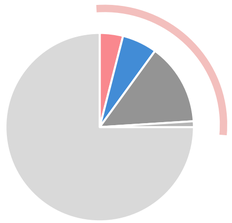
PDAC
KRAS ^{mt} total ～90%

KRAS G12D	~ 36%	KRAS G12V	~ 27%
KRAS G12R/S/A G13D, Q61H	~ 36%	KRAS G12C	~ 2%



CRC
KRAS ^{mt} total ～35%

KRAS G12D	~ 12%	KRAS G12V	~ 8%
KRAS G12R/S/A G13D, Q61H	~ 12%	KRAS G12C	~ 3-4%



NSCLC
KRAS ^{mt} total～10%-25%

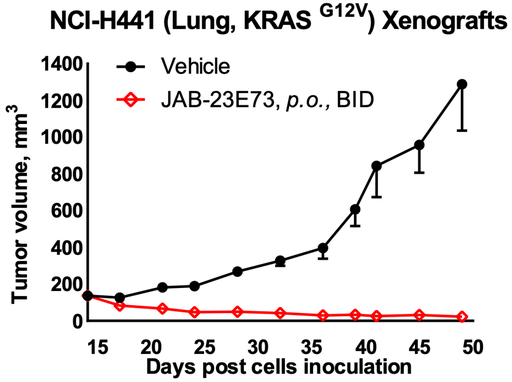
KRAS G12D	~ 4%	KRAS G12V	~ 6%
KRAS G12C	~ 14%		

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

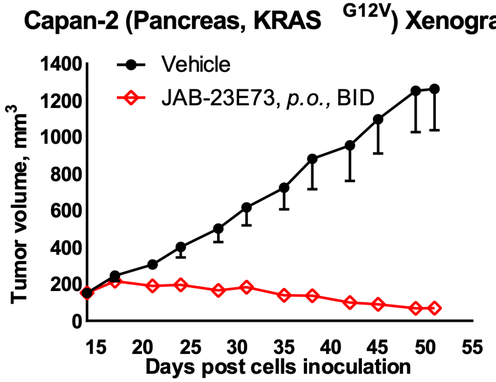
1. *npj Precis. Onc. 6, 91 (2022).*
2. *Numbers are estimated using the data from Estimated number of new cases in 2020, International Agency for Research on Cancer, World Health Organization*
3. *KRAS sequence from Comput Struct Biotechnol J. 2019 Dec 26;18:189-198.*

JAB-23E73在多种KRAS突变肿瘤上，实现肿瘤消退

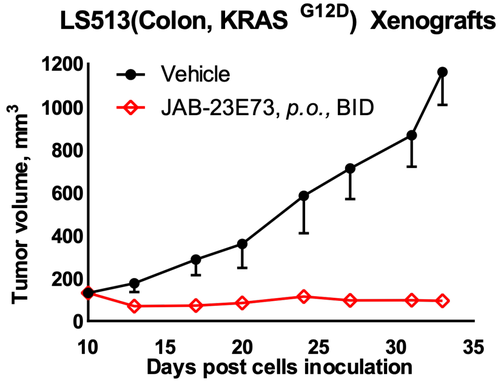
肺癌



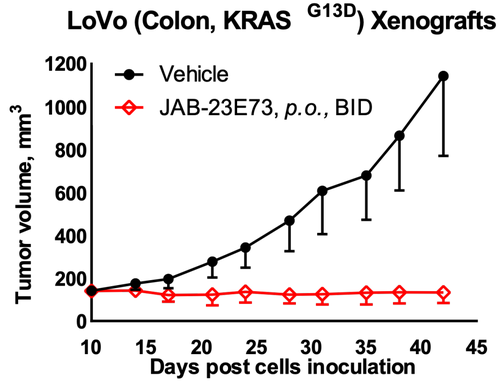
胰腺癌



结直肠癌



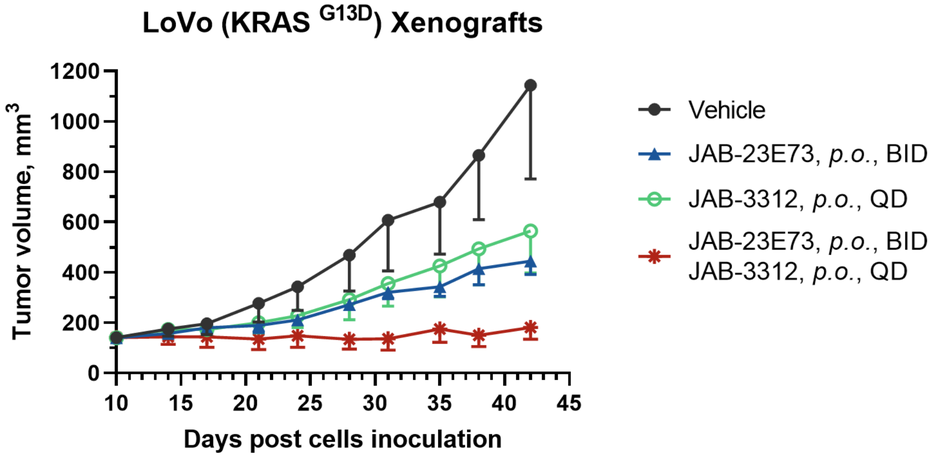
结直肠癌



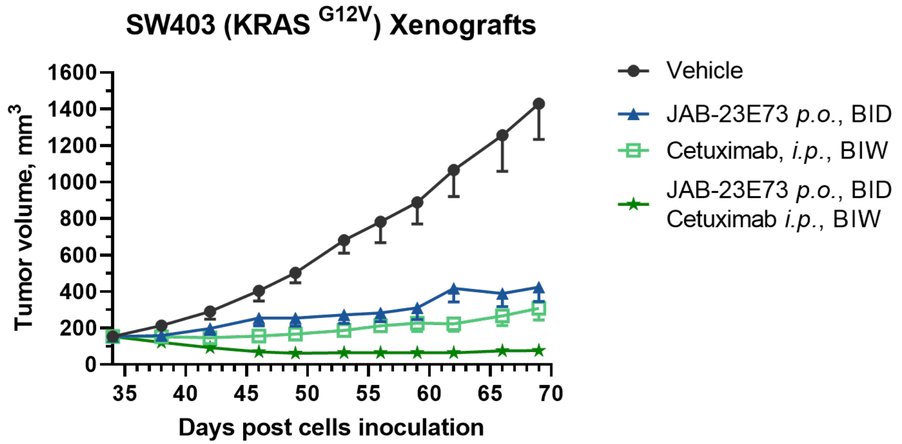
- 临床前研究显示，JAB-23E73在多种KRAS突变的肿瘤模型中，引起肿瘤消退
- JAB-23E73在小鼠中耐受性良好

JAB-23E73与JAB-3312或EGFR抗体联用在KRAS突变肿瘤中具有协同作用

结直肠癌（与JAB-3312联用）

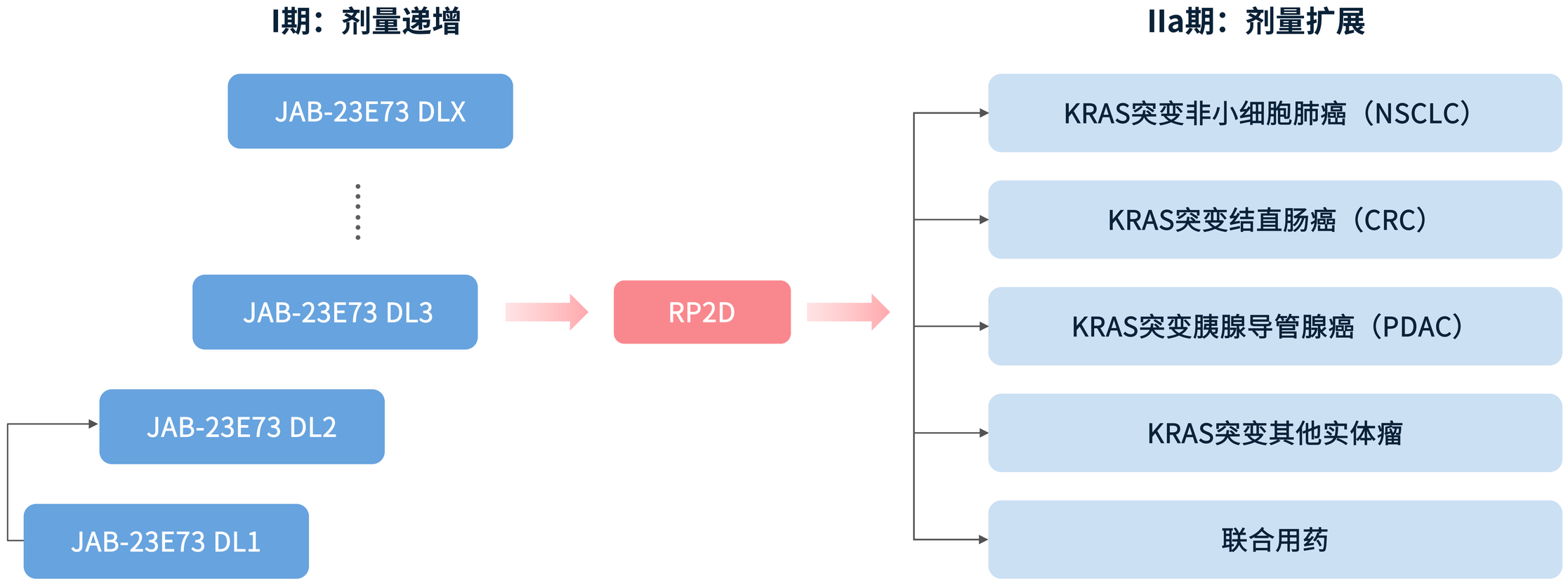


结直肠癌（与EGFR抗体联用）



- 临床前研究显示，JAB-23E73联合JAB-3312或EGFR抗体在KRAS突变的肿瘤模型中，引起肿瘤消退

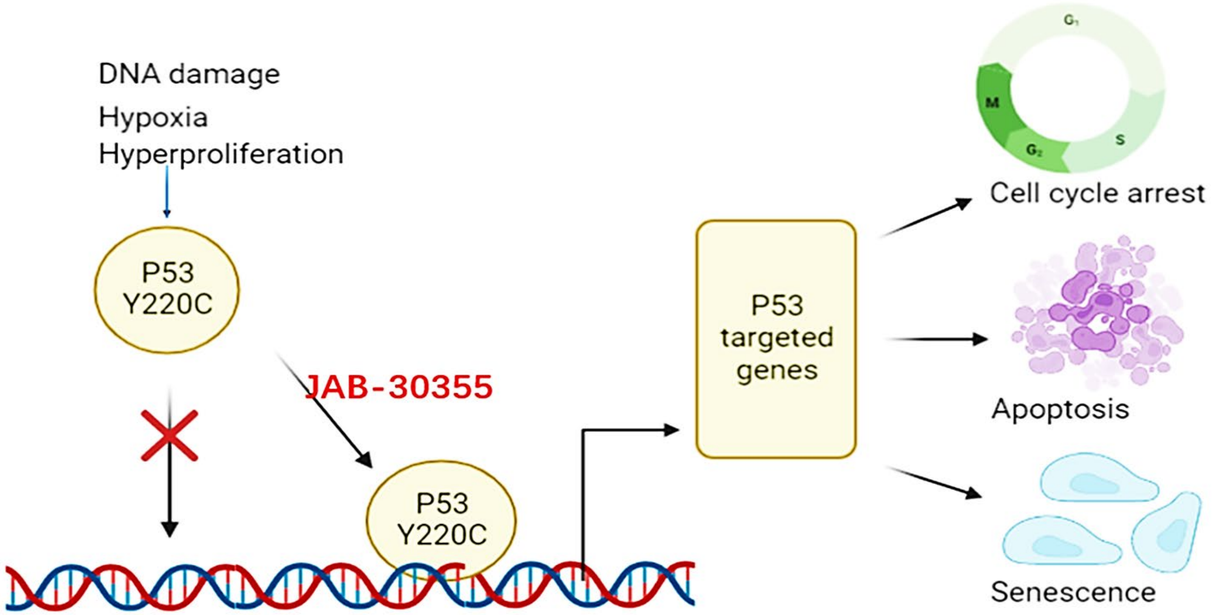
JAB-23E73在实体瘤中的临床试验



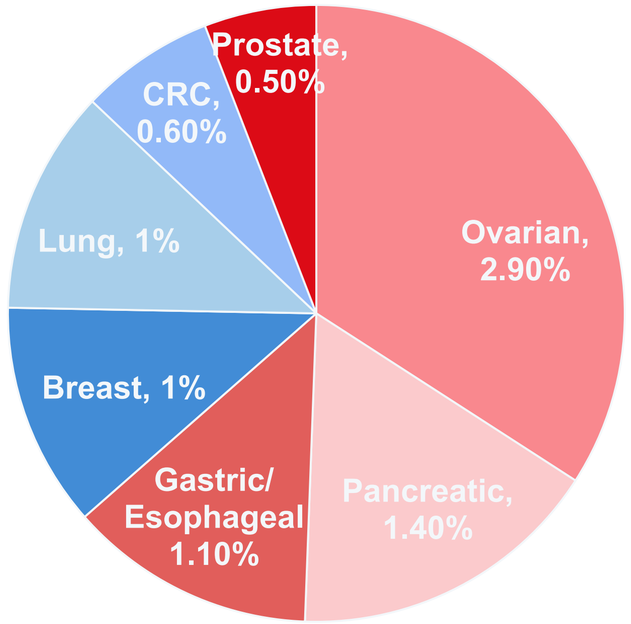
- JAB-23E73首次人体研究（编号：JAB-23E73-1001）在中国进行中
- 2024年11月实现首例患者入组（FPI）
- 美国IND已获批，研究启动相关工作正在有序推进中

P53: 肿瘤中最常见的突变基因

JAB-30355治疗肿瘤机制



p53 Y220C 在不同肿瘤中突变频率



https://tp53.isb-cgc.org/

- P53是一种关键的肿瘤抑制因子，可调节细胞周期阻滞、DNA修复、细胞凋亡和衰老等多种细胞过程
- P53 Y220C突变每年与10万例新的癌症病例相关
- P53 Y220C突变携带患者占所有实体瘤患者的1%，存在于超过30种不同的肿瘤类型

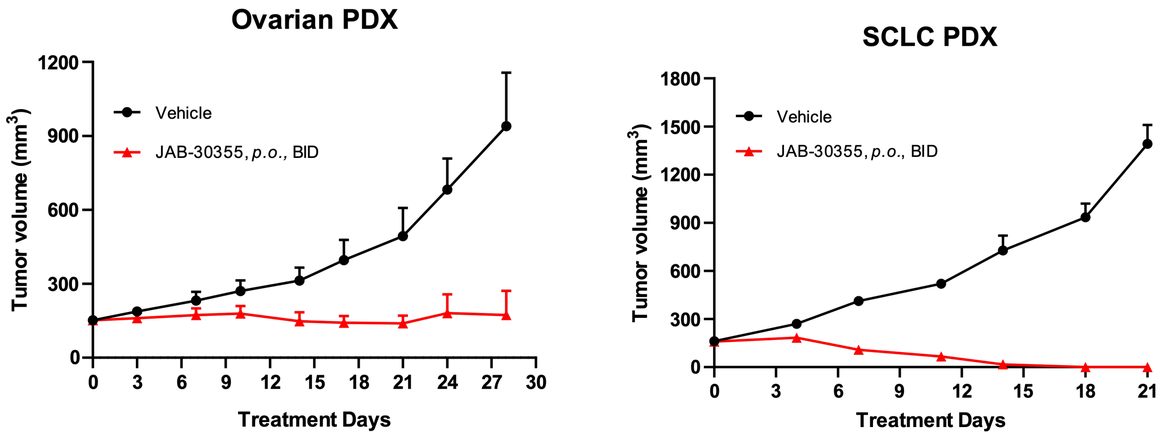
JAB-30355: 口服P53 Y220C激动剂

JAB-30355概要

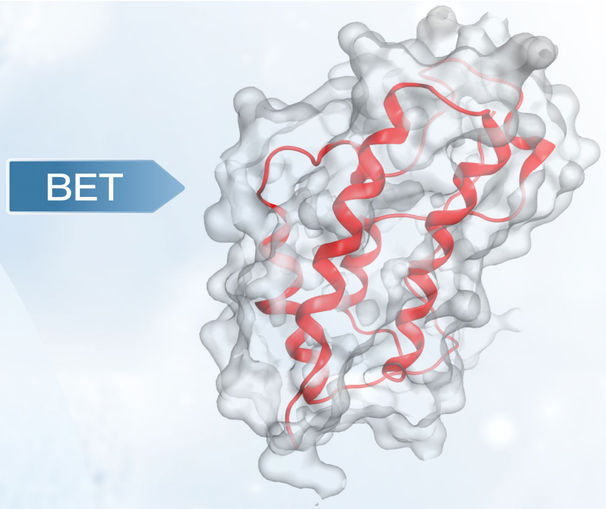
- 全球尚无靶向p53 Y220C的药物上市。目前仅JAB-30355和PMV公司的PC14586在临床阶段
- PMV于2024年一季度启动P53 Y220C激活剂PC14586的单臂2期关键临床。2期推荐剂量为2000毫克/日。PC14586单药或与AZA联用治疗AML/MDS计划启动
- JAB-30355的亲和力比PC14586高2-3倍（纳摩尔级生化活性）
- JAB-30355的预测有效临床剂量为PC14586的一半
- JAB-30355项目IND申请在2024年3月由FDA批准， 2024年6月由CDE批准
- 第一例中国患者已于2024年7月入组接受治疗
- 中美临床一期计量爬坡在进行中

Assay		JAB-30355	PMV-cmpd
Biophysics SPR assay	Affinity KD (nM)	1.68	7.95
	EC50 (nM)	69.70	154
	Maximal recovery of p53 active conformation	76.2%	58.7%
Biochemical HTRF assay	EC50 (nM)	23.29	35.50

在多种PDX模型上，实现肿瘤抑制



JAB-8263: 临床阶段活性最强的BET抑制剂之一



项目介绍:

BET (Bromodomain and extra-terminal domain) 在多种肿瘤中过表达，招募转录因子，调节基因表达，如癌基因Myc。

JAB-8263

临床剂量：0.3~0.4毫克每天连续给药

Pelabresib[1]

临床剂量：125毫克每天给药14天停药7天

INCB057643[2]

临床剂量：4~12mg QD consecutive

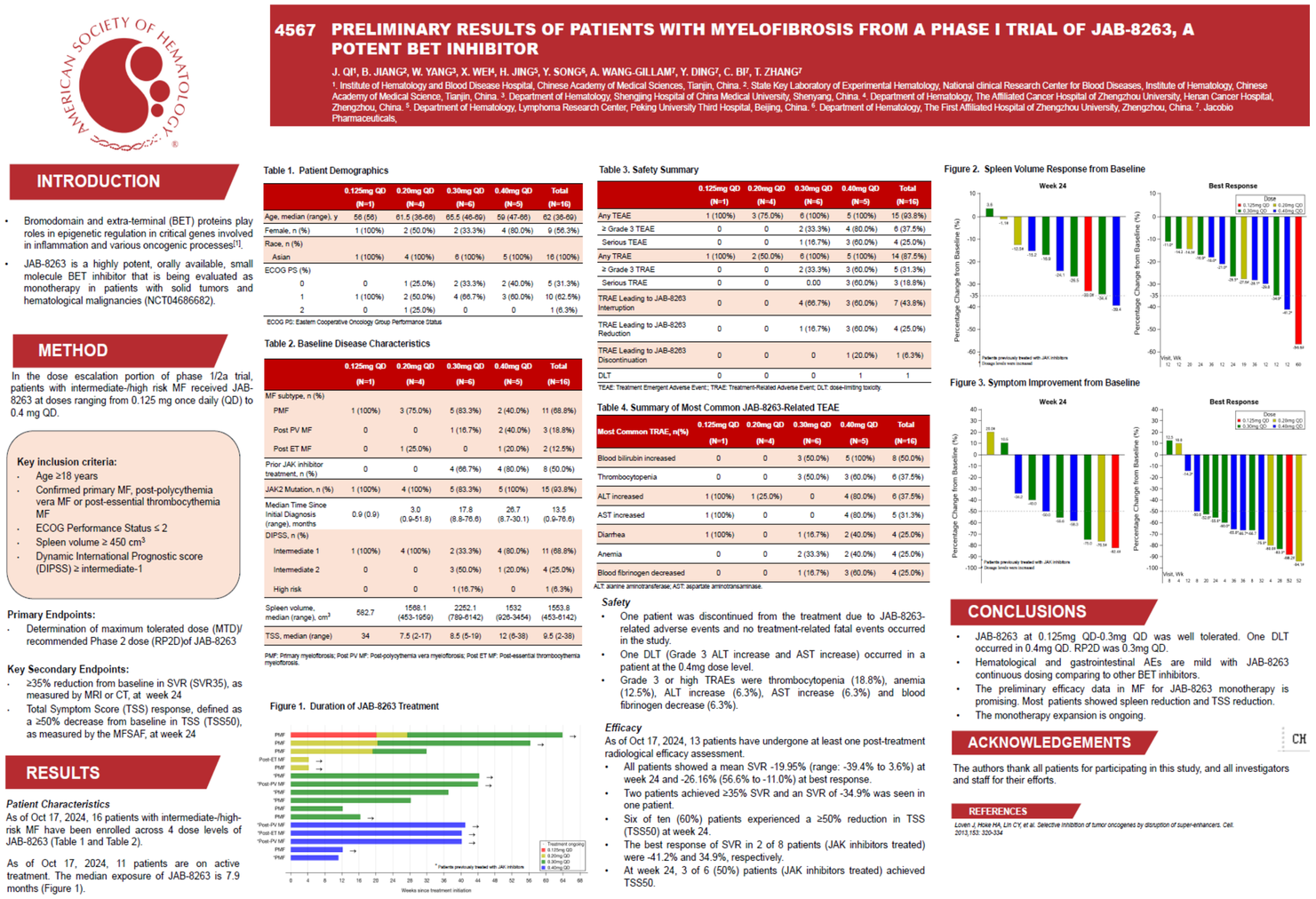
- MorphoSys 公司的 pelabresib（CPI-0610）与芦可替尼联用在一线骨髓纤维化患者的3期注册研究取得阳性结果，数据发表在2025年2月Nature Medicine，NDA在计划中；
- 基于 pelabresib 的成功，诺华于2024年2月以29亿美元收购MorphoSys。

1. *2023 ASH. Pelabresib in combination with ruxolitinib for JAKi treatment-naïve patients with myelofibrosis: results of the MANIFEST-2 randomized, double-blind, Phase 3 study*
2. *2023 ASH. Bromodomain and Extra-Terminal Inhibitor INCB057643 (LIMBER-103) in Patients with Relapsed or Refractory Myelofibrosis and Other Advanced Myeloid Neoplasms: A Phase 1 Study.*

JAB-8263：强效BET抑制剂

临床研究

- 1期临床剂量递增研究在中国和美国完成，RP2D剂量0.3mg QD
- JAB-8263用于治疗MF的I期研究结果发表在2024年第66届美国血液学会（ASH）年会
  - 13例MF患者平均的脾脏体积缩小（SVR）26.16%，24周的平均SVR值为19.95%；
  - 2例经JAK抑制剂治疗的患者SVR达到41.2%和34.9%；
  - 60%（6/10）患者在24周时的总体症状评分下降达到50%以上（TSS50）；
  - 患者安全耐受性良好，只有1例患者因JAB-8263相关的AE而永久停药。



4567 PRELIMINARY RESULTS OF PATIENTS WITH MYELOFIBROSIS FROM A PHASE I TRIAL OF JAB-8263, A POTENT BET INHIBITOR

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INTRODUCTION

- Bromodomain and extra-terminal (BET) proteins play roles in epigenetic regulation in critical genes involved in inflammation and various oncogenic processes[1].
- JAB-8263 is a highly potent, orally available, small molecule BET inhibitor that is being evaluated as monotherapy in patients with solid tumors and hematological malignancies (NCT04686682).

METHOD

In the dose escalation portion of phase 1/2a trial, patients with intermediate-/high risk MF received JAB-8263 at doses ranging from 0.125 mg once daily (QD) to 0.4 mg QD.

Key inclusion criteria:
- Age ≥18 years
- Confirmed primary MF, post-polycythemia vera MF or post-essential thrombocythemia MF
- ECOG Performance Status ≤ 2
- Spleen volume ≥ 450 cm^3
- Dynamic International Prognostic score (DIPSS) ≥ intermediate-1

Primary Endpoints:
- Determination of maximum tolerated dose (MTD)/ recommended Phase 2 dose (RP2D)of JAB-8263

Key Secondary Endpoints:
- ≥35% reduction from baseline in SVR (SVR35), as measured by MRI or CT, at week 24
- Total Symptom Score (TSS) response, defined as a ≥50% decrease from baseline in TSS (TSS50), as measured by the MFSAF, at week 24

RESULTS

Patient Characteristics

As of Oct 17, 2024, 16 patients with intermediate-/high-risk MF have been enrolled across 4 dose levels of JAB-8263 (Table 1 and Table 2).

As of Oct 17, 2024, 11 patients are on active treatment. The median exposure of JAB-8263 is 7.9 months (Figure 1).

Table 1. Patient Demographics

	0.125mg QD (N=1)	0.20mg QD (N=4)	0.30mg QD (N=6)	0.40mg QD (N=5)	Total (N=16)
Age, median (range), y	56 (56)	61.5 (36-66)	65.5 (46-69)	59 (47-66)	62 (36-69)
Female, n (%)	1 (100%)	2 (50.0%)	2 (33.3%)	4 (80.0%)	9 (56.3%)
Race, n (%)					
Asian	1 (100%)	4 (100%)	6 (100%)	5 (100%)	16 (100%)
ECOG PS (%)					
0	0	1 (25.0%)	2 (33.3%)	2 (40.0%)	5 (31.3%)
1	1 (100%)	2 (50.0%)	4 (66.7%)	3 (60.0%)	10 (62.5%)
2	0	1 (25.0%)	0	0	1 (6.3%)

ECOG PS: Eastern Cooperative Oncology Group Performance Status

Table 2. Baseline Disease Characteristics

	0.125mg QD (N=1)	0.20mg QD (N=4)	0.30mg QD (N=6)	0.40mg QD (N=5)	Total (N=16)
MF subtype, n (%)					
PMF	1 (100%)	3 (75.0%)	5 (83.3%)	2 (40.0%)	11 (68.8%)
Post PV MF	0	0	1 (16.7%)	2 (40.0%)	3 (18.8%)
Post ET MF	0	1 (25.0%)	0	1 (20.0%)	2 (12.5%)
Prior JAK inhibitor treatment, n (%)	0	0	4 (66.7%)	4 (80.0%)	8 (50.0%)
JAK2 Mutation, n (%)	1 (100%)	4 (100%)	5 (83.3%)	5 (100%)	15 (93.8%)
Median Time Since Initial Diagnosis (range), months	0.9 (0.9)	3.0 (0.9-51.8)	17.8 (8.8-76.6)	26.7 (8.7-30.1)	13.5 (0.9-76.6)
DIPSS, n (%)					
Intermediate 1	1 (100%)	4 (100%)	2 (33.3%)	4 (80.0%)	11 (68.8%)
Intermediate 2	0	0	3 (50.0%)	1 (20.0%)	4 (25.0%)
High risk	0	0	1 (16.7%)	0	1 (6.3%)
Spleen volume, median (range), cm^3	582.7	1568.1 (453-1959)	2252.1 (789-6142)	1532 (926-3454)	1553.8 (453-6142)
TSS, median (range)	34	7.5 (2-17)	8.5 (5-19)	12 (6-38)	9.5 (2-38)

PMF: Primary myelofibrosis; Post PV MF: Post-polycythemia vera myelofibrosis; Post ET MF: Post-essential thrombocythemia myelofibrosis.

Figure 1. Duration of JAB-8263 Treatment

Table 3. Safety Summary

	0.125mg QD (N=1)	0.20mg QD (N=4)	0.30mg QD (N=6)	0.40mg QD (N=5)	Total (N=16)
Any TEAE	1 (100%)	3 (75.0%)	6 (100%)	5 (100%)	15 (93.8%)
≥ Grade 3 TEAE	0	0	2 (33.3%)	4 (80.0%)	6 (37.5%)
Serious TEAE	0	0	1 (16.7%)	3 (60.0%)	4 (25.0%)
Any TRAE	1 (100%)	2 (50.0%)	6 (100%)	5 (100%)	14 (87.5%)
≥ Grade 3 TRAE	0	0	2 (33.3%)	3 (60.0%)	5 (31.3%)
Serious TRAE	0	0	0.00	3 (60.0%)	3 (18.8%)
TRAE Leading to JAB-8263 Interruption	0	0	4 (66.7%)	3 (60.0%)	7 (43.8%)
TRAE Leading to JAB-8263 Reduction	0	0	1 (16.7%)	3 (60.0%)	4 (25.0%)
TRAE Leading to JAB-8263 Discontinuation	0	0	0	1 (20.0%)	1 (6.3%)
DLT	0	0	0	1	1

TEAE: Treatment Emergent Adverse Event;; TRAE: Treatment-Related Adverse Event; DLT: dose-limiting toxicity.

Table 4. Summary of Most Common JAB-8263-Related TEAE

Most Common TRAE, n(%)	0.125mg QD (N=1)	0.20mg QD (N=4)	0.30mg QD (N=6)	0.40mg QD (N=5)	Total (N=16)
Blood bilirubin increased	0	0	3 (50.0%)	5 (100%)	8 (50.0%)
Thrombocytopenia	0	0	3 (50.0%)	3 (60.0%)	6 (37.5%)
ALT increased	1 (100%)	1 (25.0%)	0	4 (80.0%)	6 (37.5%)
AST increased	1 (100%)	0	0	4 (80.0%)	5 (31.3%)
Diarrhea	1 (100%)	0	1 (16.7%)	2 (40.0%)	4 (25.0%)
Anemia	0	0	2 (33.3%)	2 (40.0%)	4 (25.0%)
Blood fibrinogen decreased	0	0	1 (16.7%)	3 (60.0%)	4 (25.0%)

ALT: alanine aminotransferase; AST: aspartate aminotransaminase.

Safety
- One patient was discontinued from the treatment due to JAB-8263-related adverse events and no treatment-related fatal events occurred in the study.
- One DLT (Grade 3 ALT increase and AST increase) occurred in a patient at the 0.4mg dose level.
- Grade 3 or high TRAEs were thrombocytopenia (18.8%), anemia (12.5%), ALT increase (6.3%), AST increase (6.3%) and blood fibrinogen decrease (6.3%).

Efficacy

As of Oct 17, 2024, 13 patients have undergone at least one post-treatment radiological efficacy assessment.
- All patients showed a mean SVR -19.95% (range: -39.4% to 3.6%) at week 24 and -26.16% (56.6% to -11.0%) at best response.
- Two patients achieved ≥35% SVR and an SVR of -34.9% was seen in one patient.
- Six of ten (60%) patients experienced a ≥50% reduction in TSS (TSS50) at week 24.
- The best response of SVR in 2 of 8 patients (JAK inhibitors treated) were -41.2% and 34.9%, respectively.
- At week 24, 3 of 6 (50%) patients (JAK inhibitors treated) achieved TSS50.

Figure 2. Spleen Volume Response from Baseline

Figure 3. Symptom Improvement from Baseline

CONCLUSIONS
- JAB-8263 at 0.125mg QD-0.3mg QD was well tolerated. One DLT occurred in 0.4mg QD. RP2D was 0.3mg QD.
- Hematological and gastrointestinal AEs are mild with JAB-8263 continuous dosing comparing to other BET inhibitors.
- The preliminary efficacy data in MF for JAB-8263 monotherapy is promising. Most patients showed spleen reduction and TSS reduction.
- The monotherapy expansion is ongoing.

ACKNOWLEDGEMENTS

The authors thank all patients for participating in this study, and all investigators and staff for their efforts.

REFERENCES

Lovén J, Hoke HA, Lin CY, et al. Selective inhibition of tumor oncogenes by disruption of super-enhancers. Cell. 2013;153: 320-334

以STING激动剂为payload的iADC

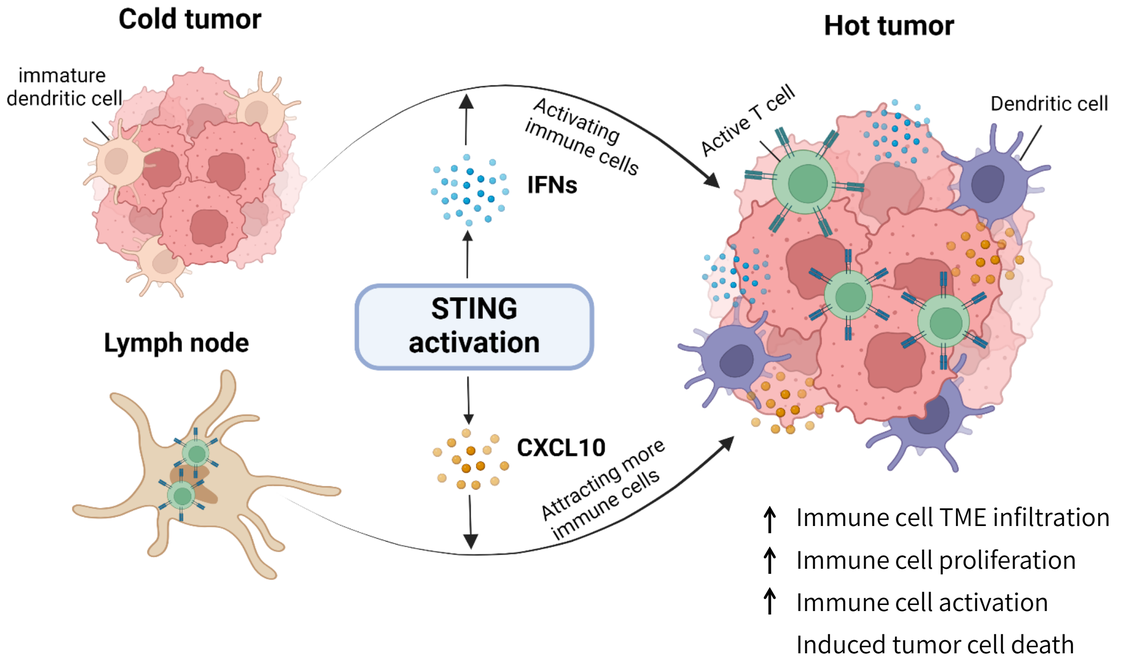
iADC作用机制

- iADC将STING激动剂特异性的递送到肿瘤细胞
- 促进肿瘤细胞分泌趋化因子CXCL10，招募更多免疫细胞浸润到肿瘤微环境，将“冷肿瘤”转化成“热肿瘤”，治疗PD-1抗体无效的患者
- 促进肿瘤细胞分泌细胞因子type Ⅰ IFNs，激活免疫细胞杀伤肿瘤细胞

加科思自主研发的STING激动剂作为payload的优势

- 非CDN小分子化合物：良好的组织稳定性
- 高亲水性：> 1 mg/mL @ pH 6~7，稳定性好，安全性高
- 低渗透性：Papp (A-B) < 1 ×10^{-6}, cm/s，free-payload不能自由穿透细胞膜

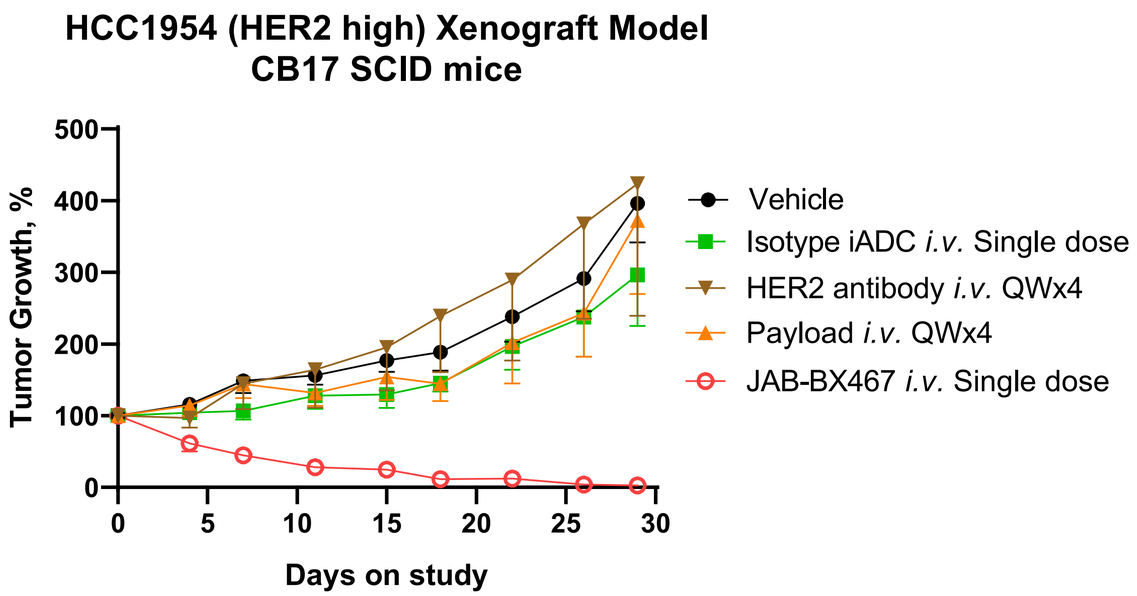
iADC促进免疫细胞浸润到TME，激活肿瘤免疫



- JAB-BX467 HER2-STING iADC已确定临床候选分子

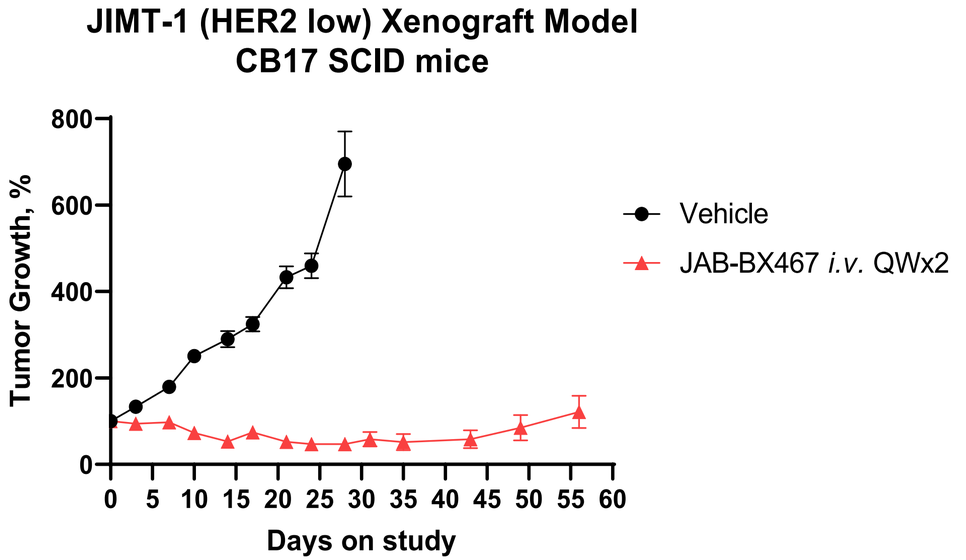
JAB-BX467 (HER2-STING) 体内对不同HER2表达量的人肿瘤细胞具有明显且持久的杀伤作用

HER2高表达的肿瘤



- JAB-BX467在HER2高表达模型（免疫缺陷鼠，缺失T）中，单次注射给药即可导致肿瘤完全消退，而对应剂量的单抗/isotype iADC/payload没有显示抗肿瘤作用

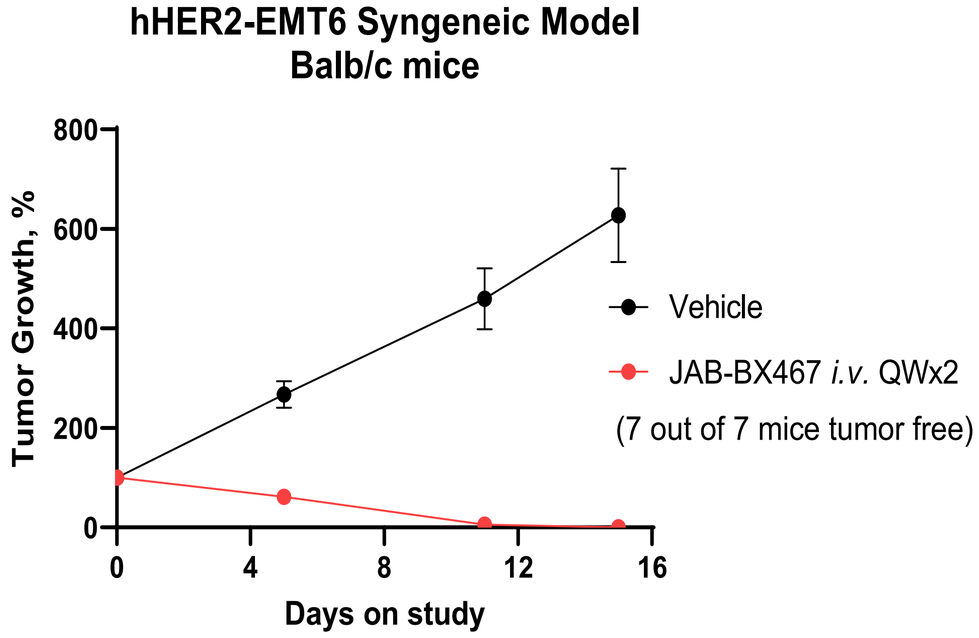
T-DM1耐药/HER2低表达的肿瘤



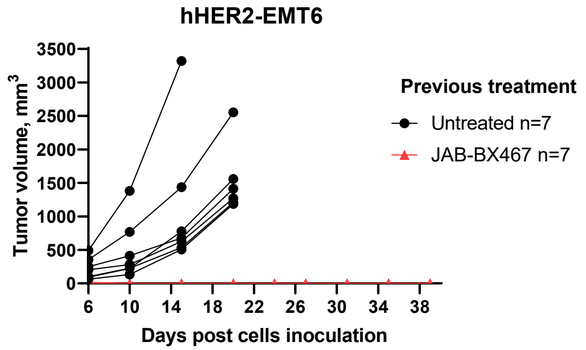
- JAB-BX467两次注射给药在T-DM1耐药/HER2低表达模型中（免疫缺陷鼠，缺失T），可以持久抑制肿瘤生长，停药后肿瘤反弹较慢

JAB-BX467 (HER2-STING) 对冷肿瘤有效，提高免疫细胞浸润，介导免疫记忆

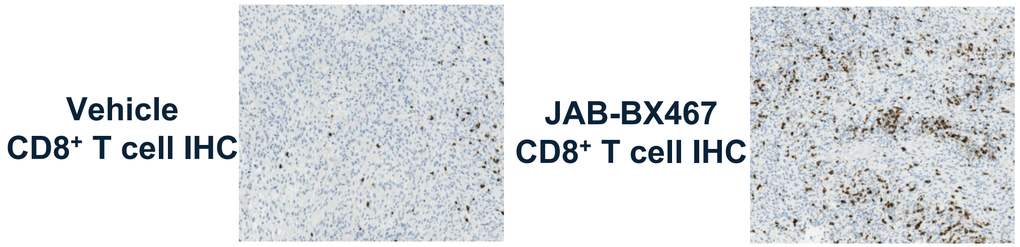
Efficacy study



Re-challenge study



CD8⁺ T cell infiltration



表达人HER2的EMT6模型（免疫健全小鼠，冷肿瘤）：

- JAB-BX467低剂量注射给药即可导致肿瘤完全消退
- 药效研究实验中，肿瘤完全消失的动物，再接种hHER2-EMT6（红色），采用相同周龄的动物接种hHER2-EMT6（黑色）作为对照，具有JAB-BX467给药史的动物再接种后，肿瘤在体内不能生长，而对照组生长正常，因此JAB-BX467具有介导免疫记忆的作用
- JAB-BX467诱导肿瘤内免疫细胞浸润

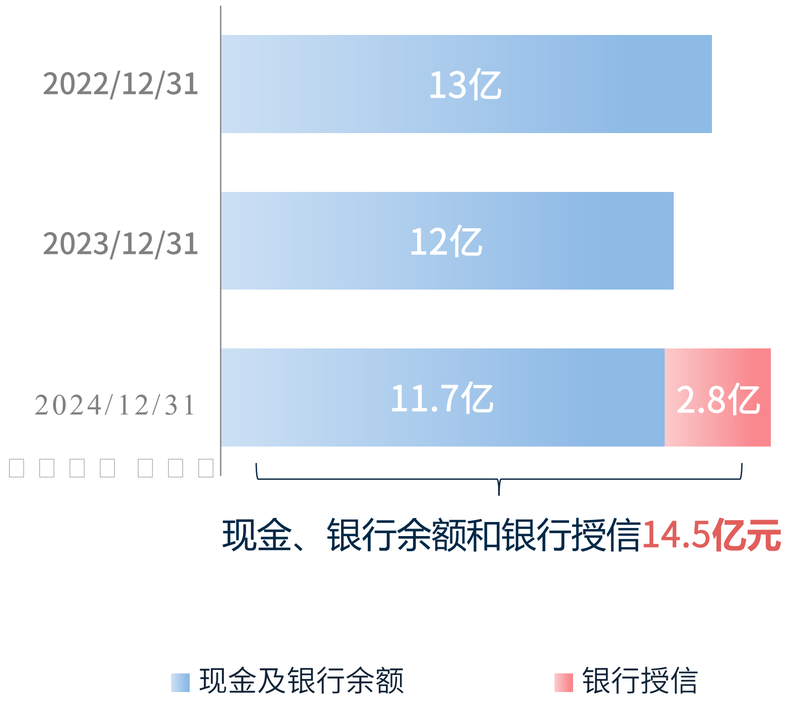
迈向全球市场

财务总结

2024年度主要财务数据

- 2024年研发费用3.3亿元，占总支出的约90%
- 经营及融资资金流入3.2亿元
  - 艾力斯合作收款2.13亿元
  - 与亦庄国投签订北京加科思1.5亿元融资协议，获得第二笔4500万元投资。剩余4500万元已于2025年1月收到
  - AbbVie合作尾款约940万元
  - 政府补助及返还约2100万元
  - 利息收款约3000万
- 融资资金流出500万港元
  - 用于回购293万股

资金余额稳定，可支撑未来约4年的支出



2025年里程碑时间预期

项目	里程碑	预期时间
戈来雷塞	KRAS G12C抑制剂戈来雷塞用于二线非小细胞肺癌在中国的商业化许可（NDA）获批 触发中国权益License- out里程碑付款	2025 Q2
戈来雷塞与 JAB-3312	KRAS G12C+SHP2联用转化研究数据文章发表	2025 H1
JAB-23E73	Pan-KRAS抑制剂完成中美临床I期剂量爬坡并确定II期临床推荐剂量（PR2D）	2025 H2
JAB-30355	完成剂量爬坡	2025 H2
JAB-2485	Aurora A抑制剂完成中美临床I期剂量爬坡并确定II期临床推荐剂量	2025 H1
JAB- BX467 HER2- STING	IND-enabling启动	2025 H1
JABX600	KRAS G12D ADC确定PCC	2025 H2

未来收入来源

戈来雷塞及JAB-3312中国权益授权合作里程碑及销售分成

- 戈来雷塞和JAB-3312中国权益License- out里程碑收款
- 戈来雷塞单药：肺癌II线中国销售分成（2025年开始）
- 戈来雷塞单药：泛瘤种II线中国销售分成
- 戈来雷塞和JAB-3312联用：肺癌I线中国销售分成

管线项目中潜在的BD授权收入

公司战略

谢谢！

Jacobio