



康宁杰瑞 (9966.HK)
2023年中期业绩发布会
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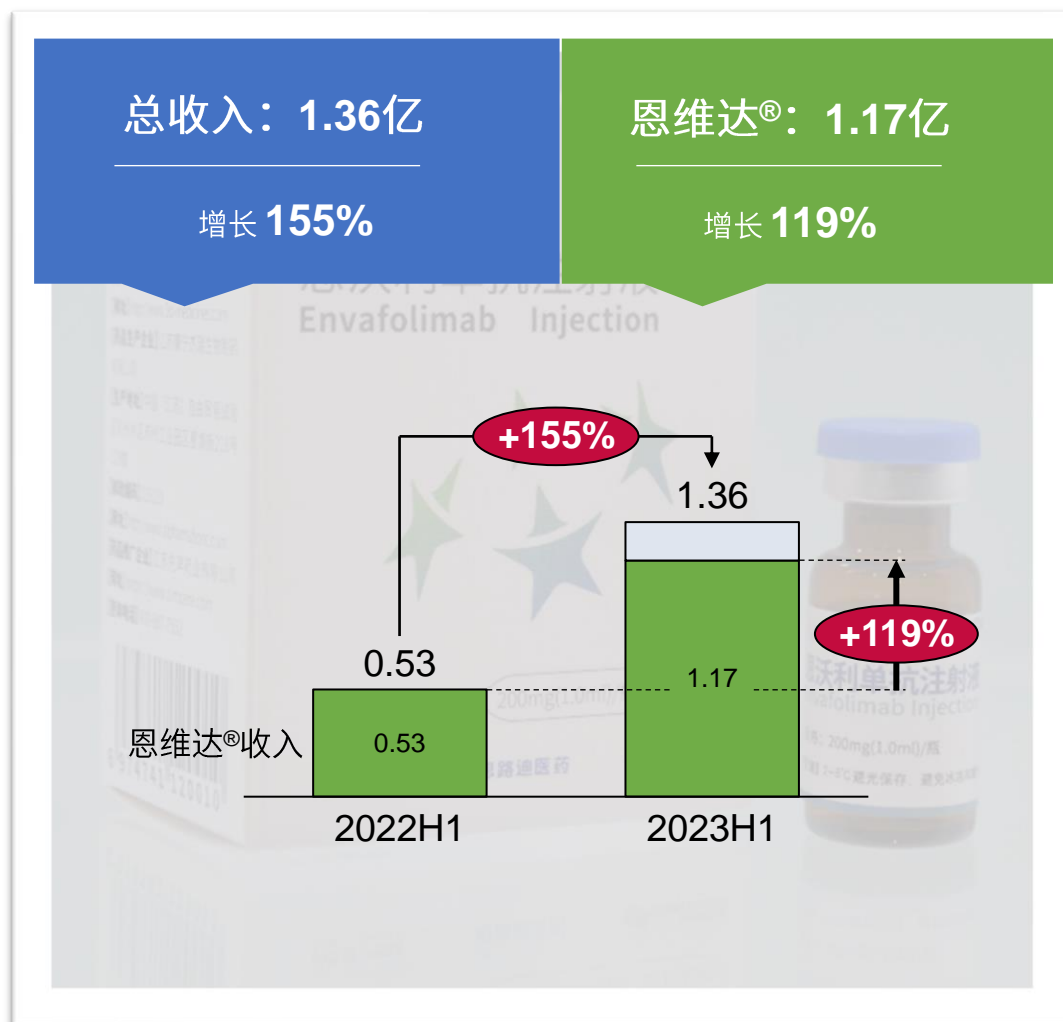
- 1 2023H1 财务概况
- 2 业务进展
- 3 2023H2 公司展望
- 4 临床进展
- 5 研发战略
- 6 Q&A

01

2023H1财务概况

主要财务数据概览

(人民币: 亿)



综合损益表

(RMB'000)	截至2023年6月30日止	
	2023年	2022年
收入	136,465	53,569
销售成本	(33,165)	(14,820)
毛利	103,300	38,749
其他收入	42,979	21,686
其他损益	48,751	63,628
研发开支	(194,681)	(216,399)
行政开支	(33,244)	(44,097)
融资成本	(6,967)	(10,876)
税前亏损	(39,862)	(147,309)
所得税	-	-
期内亏损	(39,862)	(147,309)

02 业务进展

2023年1月至7月核心业务进展

1月



7月

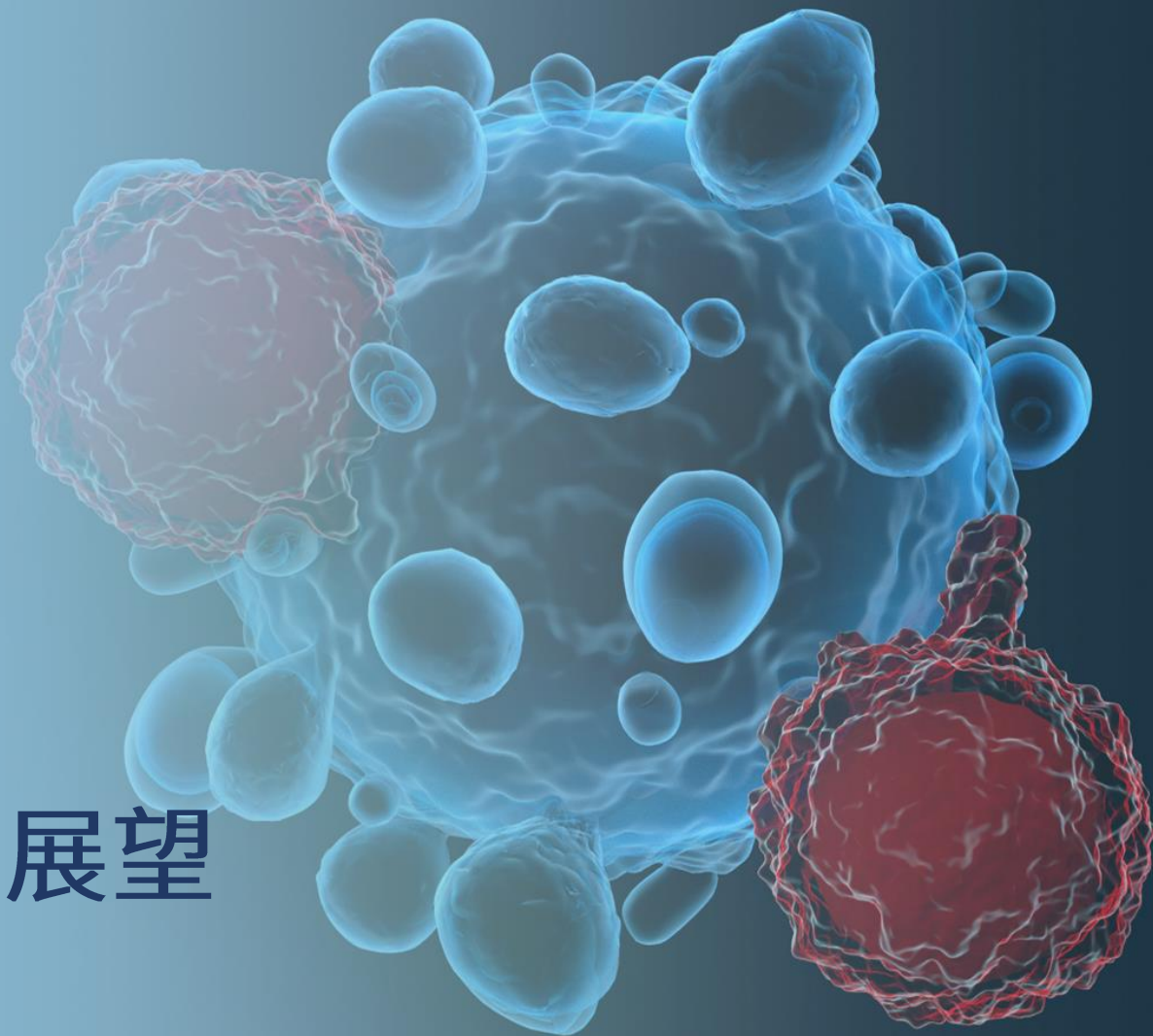
- 01 2023年1月, KN026针对 $\geq 2L$ HER2阳性GC/GEJ三期临床研究顺利进行
- 02 2023年3月, JSKN003 (HER2双抗ADC) I期临床研究完成中国首例患者给药
- 03 2023年3月, KN046-303胰腺癌三期临床研究完成患者入组
- 04 2023年5月, KN046-209试验 KN046+阿昔替尼针对PD-(L)1经治NSCLC患者首例患者给药
- 05 2023年5月, KN026联合化疗(HB1801)一线治疗HER2阳性BC三期临床研究获得临床批件; 7月该三期试验完成首例患者给药



- 06 2023年6月, 恩沃利单抗针对肉瘤在超过80例患者中的第二次期中分析取得了阳性结果
- 07 2023年6月, 双抗ADC JSKN016完成临床前研究
- 08 2023年7月, JSKN003澳洲I期临床研究进入8.4mg/kg剂量组; 中国I期临床研究进入6.3mg/kg剂量组
- 09 2023年7月底, JSKN003启动国内II期临床研究, 截至7月底中澳I期临床研究共入组超过30例患者
- 10 KN052(PD-L1/OX40) AACR 发布临床前研究数据
KN046+KN026 II期临床 ASCO HER2阳性实体瘤

03

2023H2 公司展望





关键临床

- KN046+化疗, 1L鳞状NSCLC: 2024年H1 OS数据读出
- KN046+化疗, 1L 胰腺癌: Q4数据读出、启动Pre-BLA
- KN046+阿昔替尼, 1L PD-L1阳性NSCLC: 年内完成 II 期临床试验入组
- KN046+阿昔替尼, PD-(L)1经治NSCLC: 年内完成II期临床试验大部分患者入组
- KN026+化疗, HER2+1L 乳腺癌: 推进 III 期优效设计临床试验入组
- KN026+化疗, ≥2L GC/GEJ: 推进 III 期优效设计临床试验入组
- JSKN003单药, Q4启动注册临床试验
- KN035, 软组织肉瘤: 美国注册临床试验完成全部患者给药, 并进行第三次期中分析



临床数据发布

ESMO (计划发布: 2023年10月)



- 1) KN046+阿昔替尼: II期临床, 1L PD-L1阳性NSCLC
- 2) KN046单药: II期临床, 后线 胸腺癌
- 3) KN046单药: II期, PD-(L)1经治驱动基因野生型 NSCLC
- 4) KN046单药: II期, EGFR-TKI 经治驱动基因突变NSCLC
- 5) KN026+多西他赛: II期, 新辅助 HER2+乳腺癌
- 6) KN026+多西他赛: II期, 1L HER2+乳腺癌

CSCO (计划发布: 2023年9月)



- 1) JSKN003: 澳洲 I 期临床, HER2表达实体瘤

SABCS (计划发布: 2023年12月)



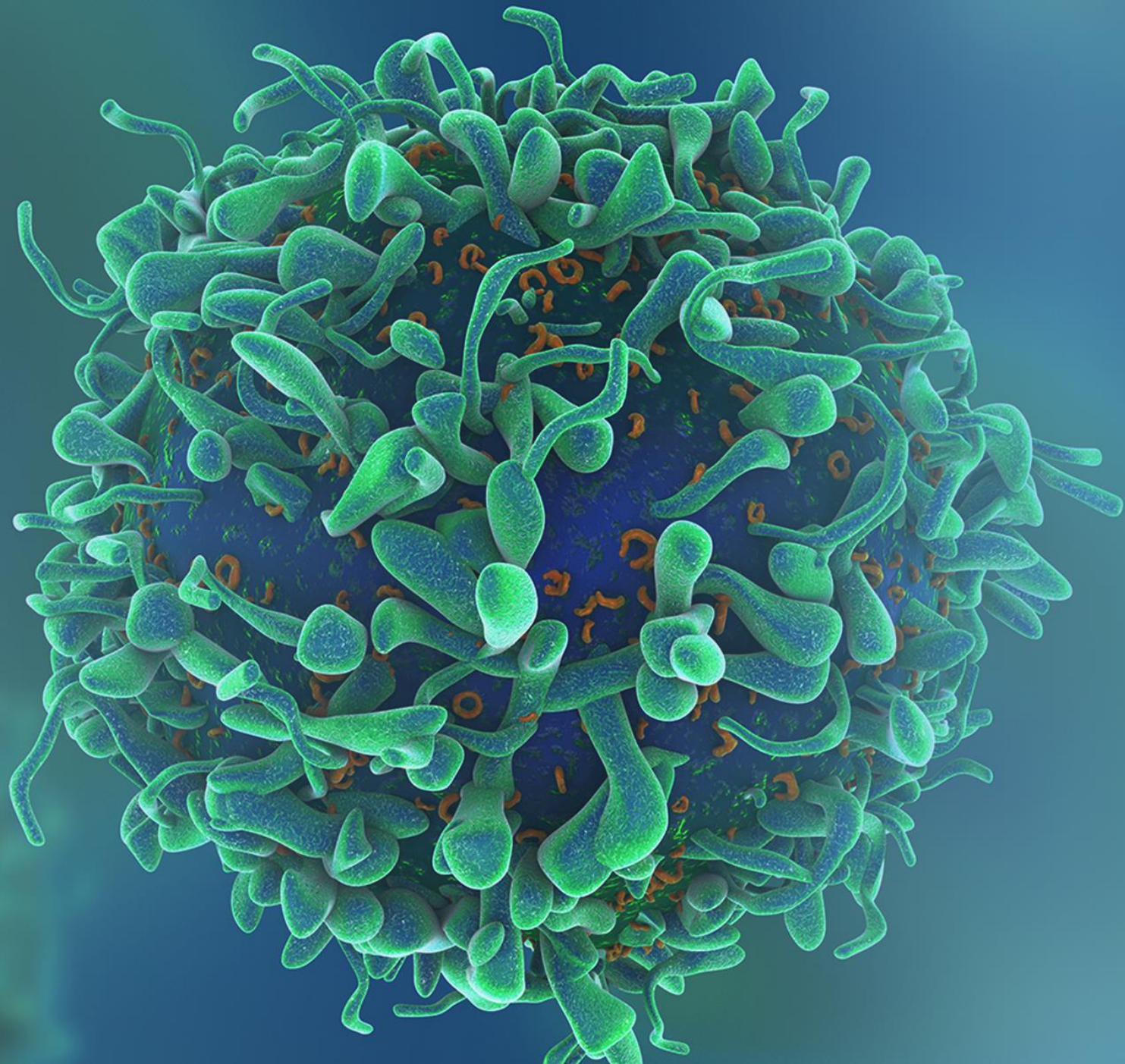
- 1) JSKN003: 澳洲 I 期&中国 I/II期临床, HER2表达实体瘤



新药管线进展和其他

- **KN052**: 完成 I 期临床剂量爬坡
- **JSKN016**: 年底申报 IND
- 新增2个临床候选化合物
- 推动生产工艺的变革性升级

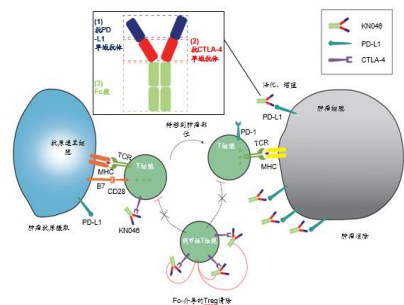
04
临床进展



KN046

双重阻断PD-L1和CTLA-4

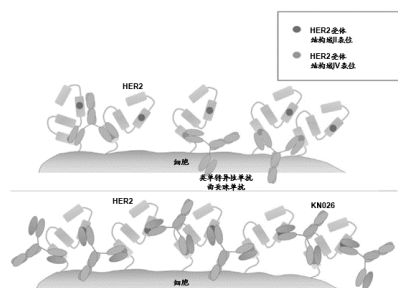
- PD-(L)1经治实体瘤
- PD-(L)1响应不充分



KN026

双重阻断HER2 II和IV表位

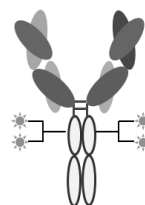
- HER2高表达实体瘤
- 定位一线及围手术期



JSKN003

HER2双抗ADC

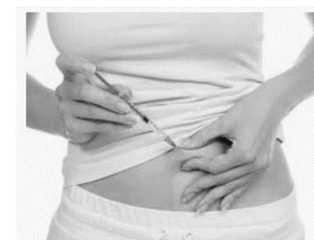
- 抗HER2治疗响应不充分的高表达肿瘤
- HER2低表达实体瘤
- 与其他机制药物联用



KN035

皮下注射PD-L1单抗

- 全球唯一可用于皮下注射的PD-(L)1单抗



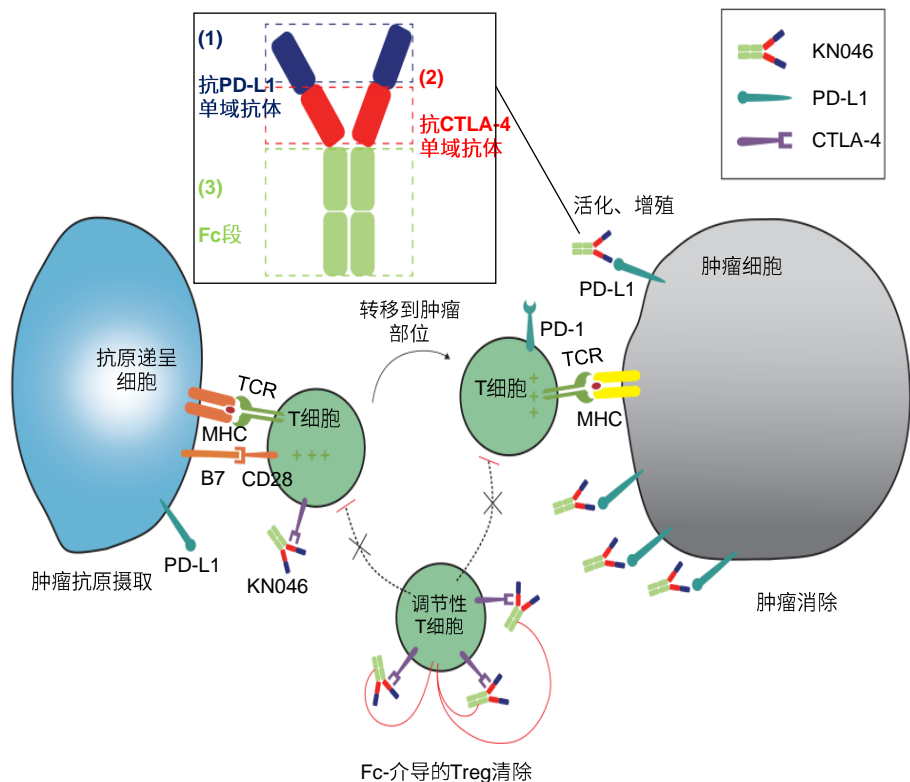
KN052

PD-L1/OX40双抗

- PD-L1拮抗剂和OX40激动剂串联结构
- 作为佐剂与肿瘤疫苗和细胞治疗联合使用



药物机理



药物优势

- ☑ 靶向药物传递
 - 蛋白质工程使得抗PD-L1单域抗体主导药物呈递
 - 靶向药物呈递到肿瘤微环境，有效降低非肿瘤组织的药物暴露
- ☑ 不同的CTLA-4结合表位
 - 我们的抗CTLA-4单域抗体通过空间位阻阻断CTLA-4/B7通路
 - 使得KN046具有潜在更优的安全性
- ☑ 保留Fc介导的效应功能
 - 保留完整的Fc功能以清除调节性T细胞
- ☑ 坚实的科学基础支持通过双特异性抗体靶向PD-L1和CTLA-4

KN046 主要临床试验

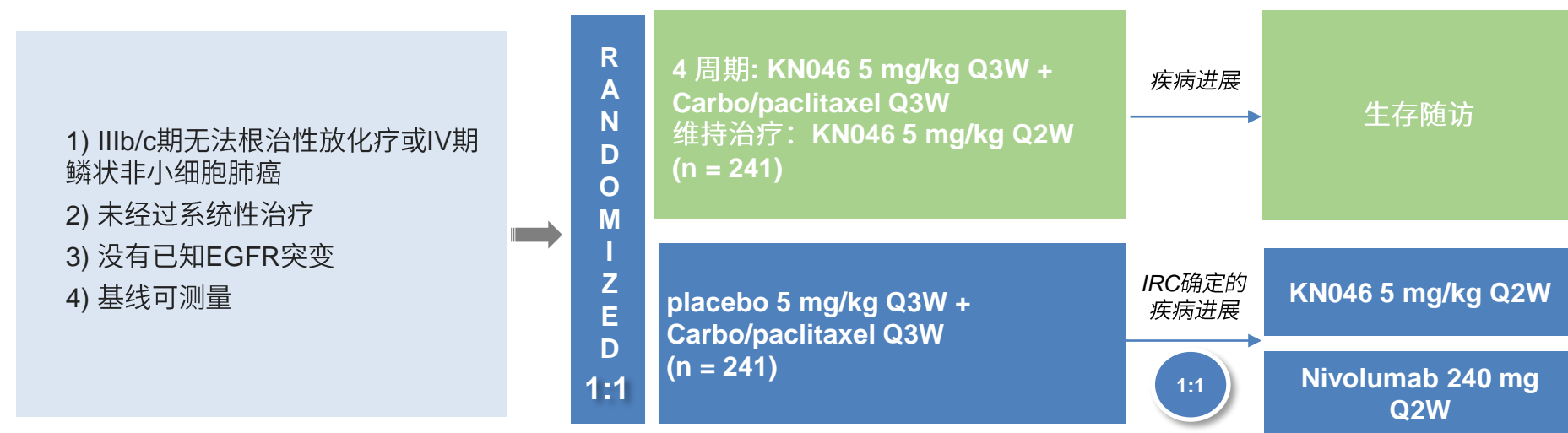
适应症	组合疗法	IND	概念验证	关键临床	NDA
1L 鳞状NSCLC	+化疗	Pre-NDA			
1L 胰腺癌	+化疗				
1L PD-L1阳性NSCLC	+阿昔替尼				
PD-(L)1 经治NSCLC	+阿昔替尼				

KN046 临床结果概览

适应症 有效性和 安全性	KN046 (超过 1,200 例患者已参加临床研究)				
	sq-NSCLC 1L (n=87)	胰腺癌 1L (n=53)	肝癌 1L (n=55)	三阴乳腺癌 1L (n=27)	食管鳞癌 1L (n=15)
组合疗法	+化疗	+化疗	+仑伐替尼	+化疗	+化疗
总生存期 OS	26.6 个月	12 个月	--	30.92 个月 (未成熟)	--
中位无进展 生存期 PFS	5.7 个月	6 个月	11 个月	7.33 个月	--
客观缓解率 ORR	50%	47.9%	45.5%	44%	58.3%
疾病控制率 DCR	80.6%	93.5%	89.1%	96%	91.6%
TRAE ≥Grade3	34.5%(TEAE)	27.6%	47.3%	66.7%	29.4% (KN046相关)

KN046-301 (III期) 1L NSCLC (ENREACH-LUNG-01)

纳入标准 实验设计





- 分层**
- PD-L1 表达水平(PD-L1<1%对PD-L1≥1%)
 - 肿瘤分期

- 主要终点:**
- 无进展生存期(PFS)
 - 总生存期(OS)

- 次要终点:**
- 客观缓解率(ORR)
 - 疾病控制率(DCR)
 - 缓解持续时间 (DOR)等

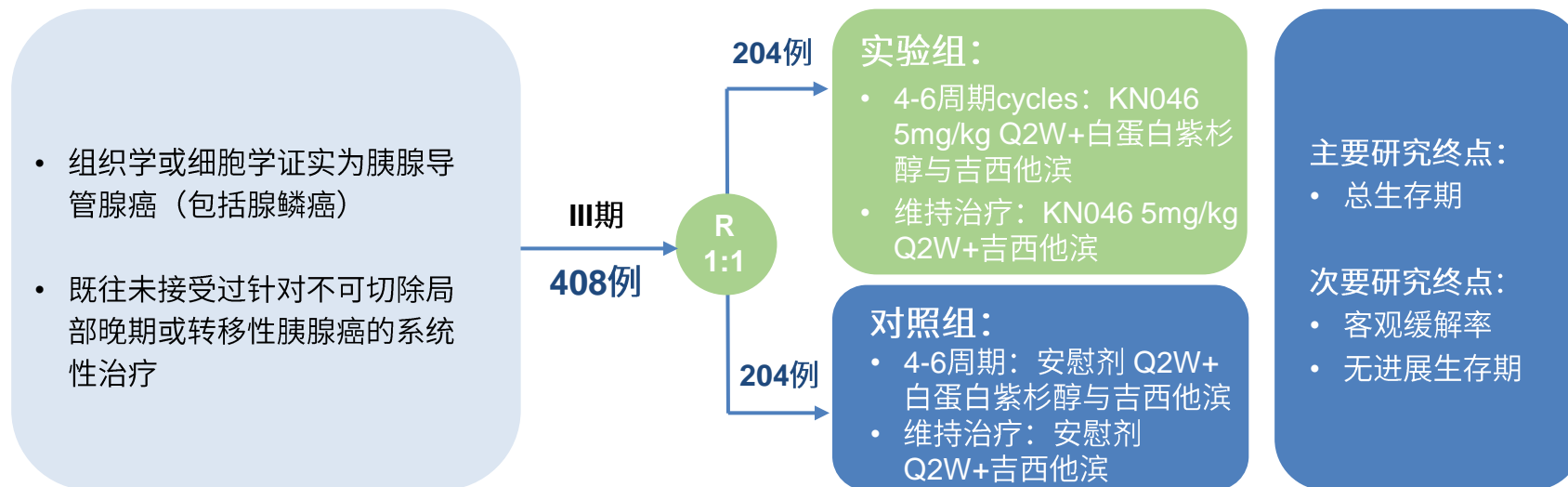
KN046-303 (III期) 1L PDAC 试验方案设计 (2022 ASCO)

 **KN046-IST-04 试验设计 (II期)** : 入组 53 例初治患者 (cohort 2) , 给予KN046联合吉西他滨+白蛋白紫杉醇治疗, 直至疾病进展或出现不可耐受毒性

 **KN046-IST-04 试验疗效 (II期)** : 53例可评估患者, ORR **47.9%¹**, mPFS **6个月**, mOS近 **12个月²**。基于该II期试验疗效, 设计和开展了KN046-303 III期注册临床试验 (ENREACH-PDAC-01)

纳入标准

实验设计

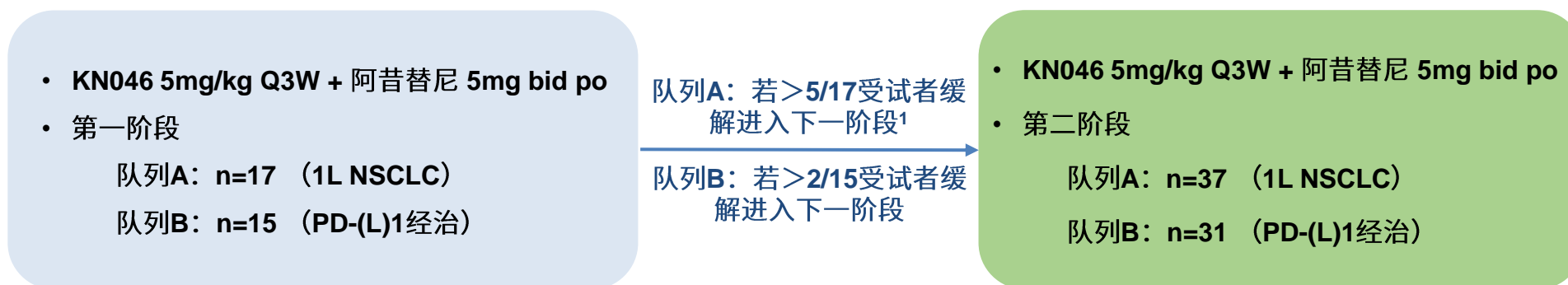


- KN046-303 是一项多中心、随机、双盲、安慰剂对照 III 期临床研究
- 已完成原计划设定的临床入组样本量, Q4 总生存期(OS)数据读出

注: 1. 数据截至2022年5月26日; 2. 近70%患者为 IV 期晚期胰腺癌患者, 包括基线相对差的患者

KN046-209 无化疗方案入排标准概况

- ✓ IIIB-IV期非小细胞肺癌
- ✓ PD-(L)1+ (TPS≥1%) (仅针对队列A)
- ✓ 无驱动基因突变



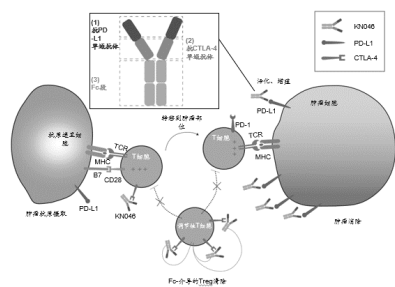
- ✓ 队列A: 针对初治局部晚期 (不能手术切除且不能接受根治性放化疗) 或转移性且未经系统性治疗的PD-L1阳性非小细胞肺癌 (NSCLC) 受试者。
- ✓ 队列B: 针对PD-(L)1经治后进展的非小细胞肺癌受试者。

注: 1. 队列A已进入第二阶段

KN046

双重阻断PD-L1和CTLA-4

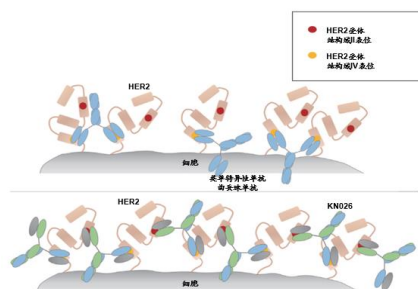
- PD-(L)1经治实体瘤
- PD-(L)1响应不充分



KN026

双重阻断HER2 II和IV表位

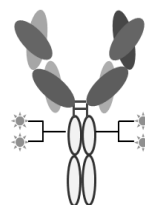
- HER2高表达实体瘤
- 定位一线及围手术期



JSKN003

HER2双抗ADC

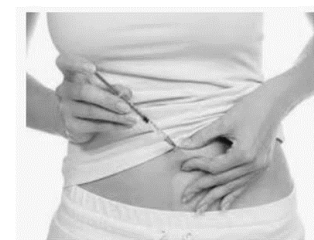
- 抗HER2治疗响应不充分的高表达肿瘤
- HER2低表达实体瘤
- 与其他机制药物联用



KN035

皮下注射PD-L1单抗

- 全球唯一可用于皮下注射的PD-(L)1单抗



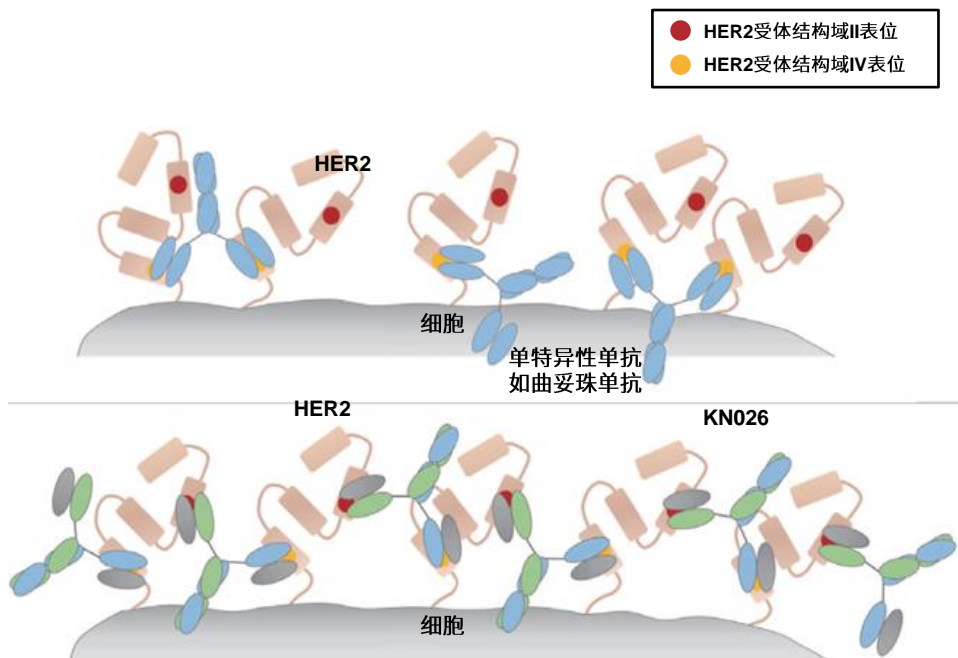
KN052

PD-L1/OX40双抗

- PD-L1拮抗剂和OX40激动剂串联结构
- 作为佐剂与肿瘤疫苗和细胞治疗联合使用





药物机理



药物特点

- 双重阻断HER2相关信号通路
- 增强多个HER2受体结合和内吞
- 具有完整效应功能的基于Fc的双特异性抗体

KN026主要临床试验: HER2阳性实体瘤


适应症	组合用药	IND	概念验证	关键临床	NDA
1L 乳腺癌	+ 白蛋白多西他赛			2023年7月FPI	
≥ 2L GC/GEJ	+ 化疗			2023年1月进入第二阶段	
乳腺癌新辅	+多西他赛				
未线结直肠癌	+ KN046				


- 于2021年8月，就KN026的中国权益与石药集团达成合作，涉及首付款1.5亿元，里程碑金额8.5亿元及双位数的销售佣金
- 石药集团在联合开发委员会下负责临床开发及注册申报，并承担所有临床研发费用，涉及乳腺癌和胃癌两大适应症

KN026 临床结果概览

适应症 有效性和 安全性	KN026 (超过 300 例患者已参加临床研究)				
	HER2+ 乳腺癌 1L (n=57)	HER2+ 乳腺癌 新辅助 (n=30)	HER2+ 胃癌 1L (n=39)	HER2+ 胃癌 ≥2L (n=39)	HER2+ 结直肠癌 ≥3L (n=15)
组合疗法	+化疗	+化疗	+KN046	单药	+KN046
总生存期 OS	91.2% (24个月)	--	--	16.3 个月	--
中位无进展生存期 PFS	25.4 个月 (未成熟)	--	10.9 个月	8.3 个月	12.2个月
客观缓解率 ORR	76.4%	60.7% (tpCR)	71.8%	56.0%	53.3%
疾病控制率 DCR	100%	100%	92.6%	76.0%	93.3%
≥Grade3 AE	KN026相关 TEAE 38.6%	TEAE 53.3%	TRAE 16.1%	TRAE 11.1%	胆红素升高 7.7% AST 升高7.7%


KN026-202 (II期) ≥2L GC/GEJ (2022 ASCO)

 **试验设计:** 45 例 HER2 表达经治患者, **42%**接受过至少二线系统性治疗, 给予KN026 (10 mg/kg QW, 20 mg/kg Q2W, or 30 mg/kg Q3W) 单药治疗, 直至疾病进展或出现不可耐受毒性

 **疗效:** 25例**HER2高表达 (IHC3+ or IHC 2+ ISH+)** 可评估患者中, ORR **56%**, DCR **76%**

14例**HER2低表达 (IHC 1+/2+ ISH- or IHC 0/1+ISH+)** 可评估患者中, ORR **21%** , DCR **29%**

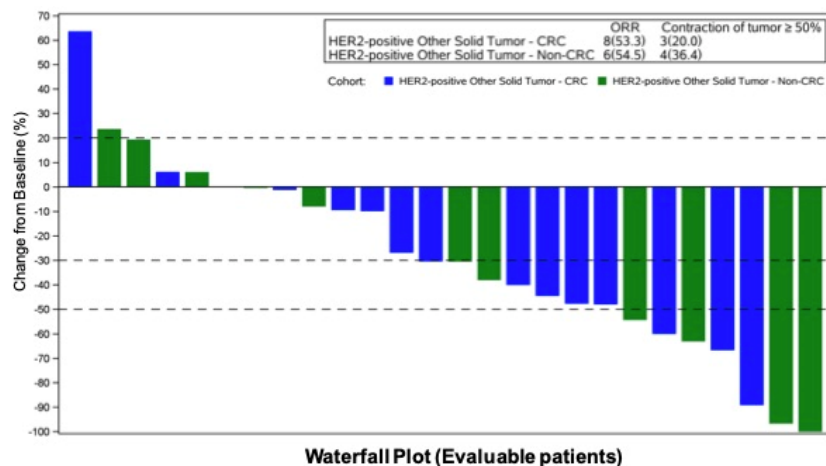
≥2L HER2+GC	KN026单药		DS-8201		KN026单药
HER2水平	HER2高表达		HER2高表达		HER2低表达
对比实验	KN026-202 ¹		DESTINY-Gastric01 ²	DESTINY-Gastric02 ³	KN026-202 ¹
患者人数	25		187 (日本79.7%、韩国20.3%)	79 (白种人)	14
	Total n=25	曲妥珠经治 n=14	55.6%患者经2L治疗	中位线数 2L	
ORR	56%	50%	42.9%	41.8%	21%
mPFS	8.3 个月	5.5个月	5.6 个月	5.6个月	1.4 个月
mOS	16.3 个月 (11.3-NE)	14.9个月 (11.0-NE)	12.5个月	12.1个月	9.2 个月

 **安全性:** 45例患者中, 4例患者出现5项与KN026治疗相关≥3级不良事件 (TRAE)

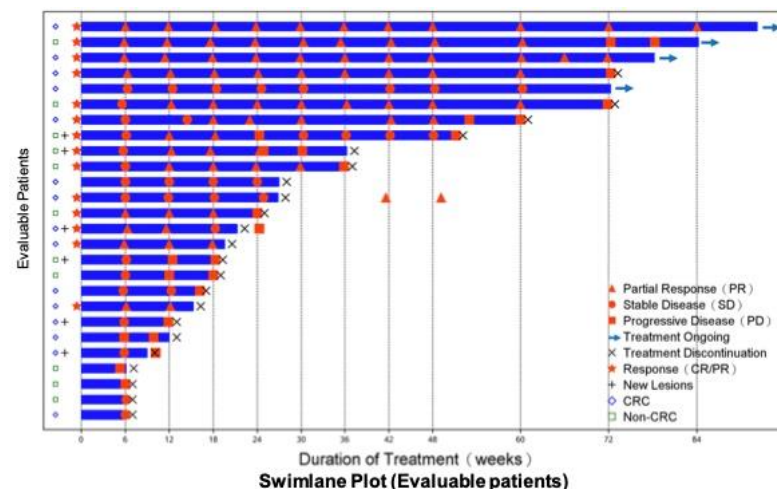
注: 1. 目前 KN026-202 试验进行中, 数据截至2022年5月31日; 2. ≥3级AE发生率85.6%, 其中中性粒细胞下降发生率51%、贫血38%、所有级别ILD发生率12.8%; 3. ≥3级TEAE发生率55.7%, 治疗期间永久性停药发生率19.0%, 所有级别ILD发生率10.1%。

KN026-203 (II期) KN046+KN026 ≥3L HER2阳性小瘤种 (2023 ASCO)

瀑布图



泳道图



共入组26例患者，包括15例结直肠癌，5例非小细胞肺癌，4例胆囊癌，1例肾盂癌以及1例胰腺癌患者，92.3%的患者(及所有结直肠癌患者)接受过至少2线前线治疗。

疗效： 总体确认的ORR 53.8%，DCR 88.4%，mPFS 5.6m，12个月OS rate为80.4%；其中15例结直肠癌中，ORR 53.3%，DCR 93.3%，mPFS 12.2m，12个月OS rate为80.0%

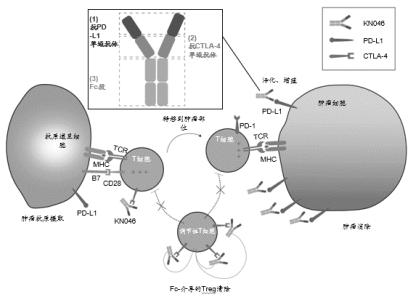
安全性： 34.6%的患者发生过至少1次≥3级TRAE，常见的所有级别TRAE为输液相关反应（38.5%）、腹泻（19.2%）、贫血、AST/ALT升高等

注：1. 试验进行中，数据截至2022年11月10日，中位随访时间16.6个月

KN046

双重阻断PD-L1和CTLA-4

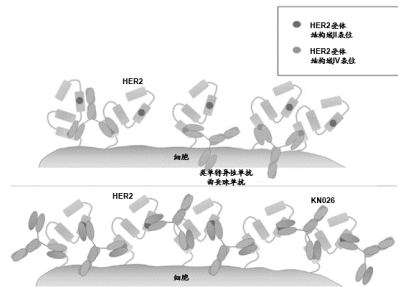
- PD-(L)1经治实体瘤
- PD-(L)1响应不充分



KN026

双重阻断HER2 II和IV表位

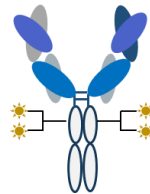
- HER2高表达实体瘤
- 定位一线及围手术期



JSKN003

HER2双抗ADC

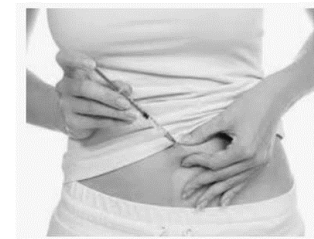
- 抗HER2治疗响应不充分的高表达肿瘤
- HER2低表达实体瘤
- 与其他机制药物联用



KN035

皮下注射PD-L1单抗

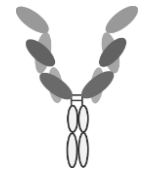
- 全球唯一可用于皮下注射的PD-(L)1单抗



KN052

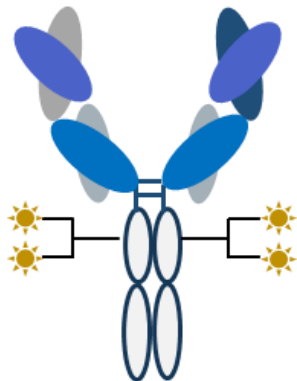
PD-L1/OX40双抗

- PD-L1拮抗剂和OX40激动剂串联结构
- 作为佐剂与肿瘤疫苗和细胞治疗联合使用



JSKN003: 抗HER2双特异性抗体偶联药物

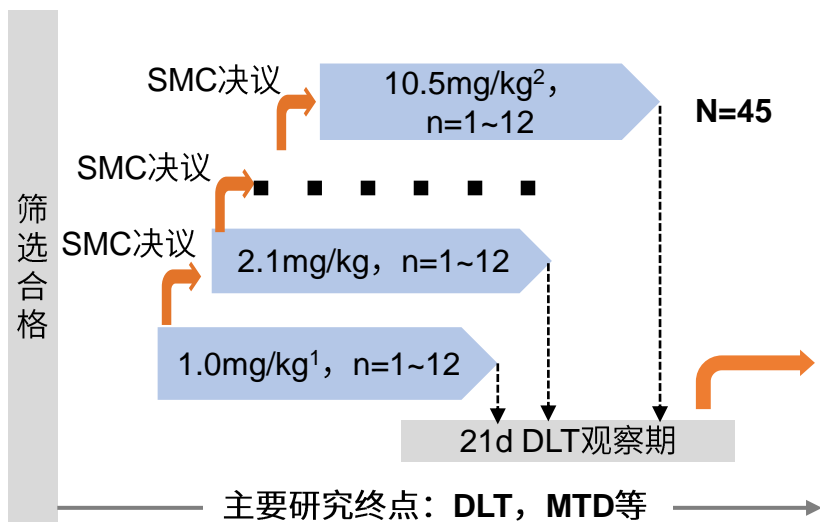
药物结构



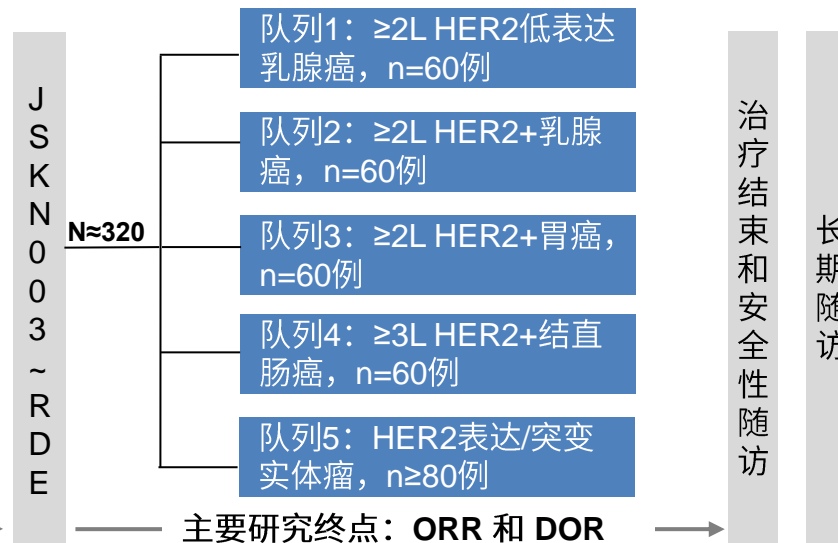
药物特点和临床策略

- 靶向HER2 (KN026) 的两个不同表位
- 糖基定点偶联, DAR 3-4
- 更好的血清稳定性
- 对标DS8201, 多个药效模型与DS8201可比
- 临床前研究显示良好的耐受性
- HER2表达全覆盖
- 后线快速上市和前线研究同步推进

I 期剂量递增阶段-加速滴定的BOIN设计



II 期RDE³剂量下的队列扩展阶段



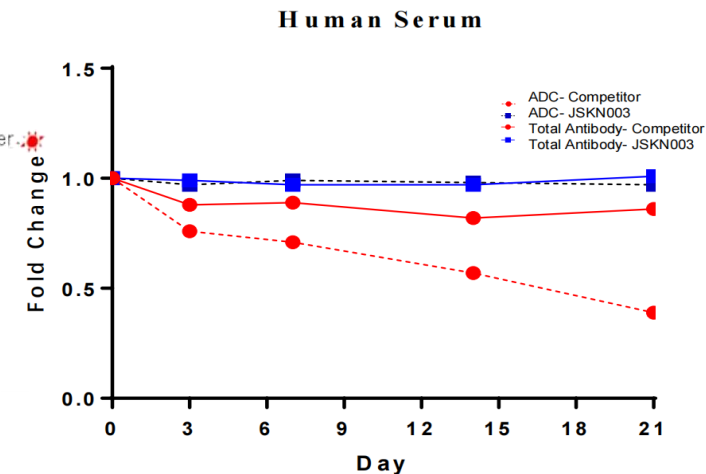
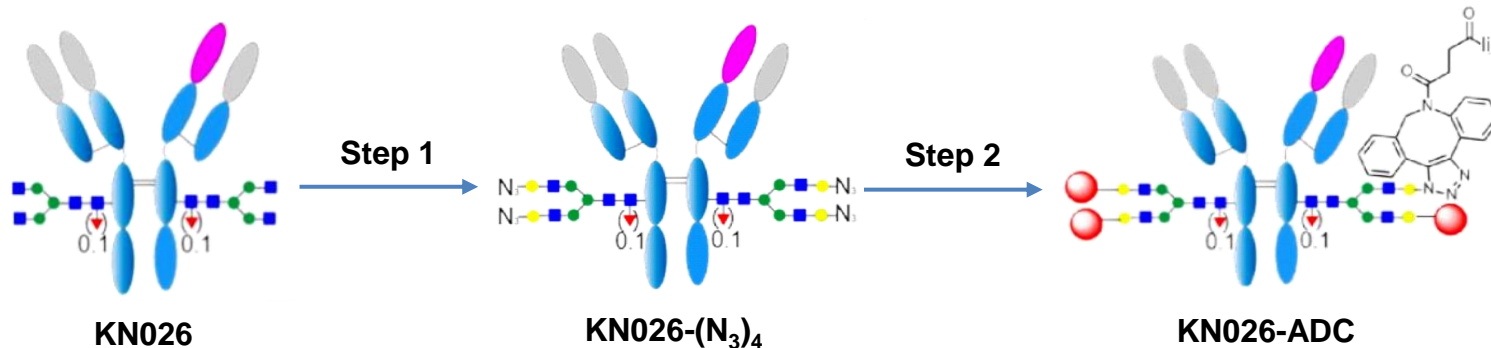
备注: 1. 共预设9个剂量组, 起始剂量为1.0mg/kg

2. 若剂量递增至10.5mg/kg时仍未达到MTD, 由SMC决定是否继续进行剂量递增

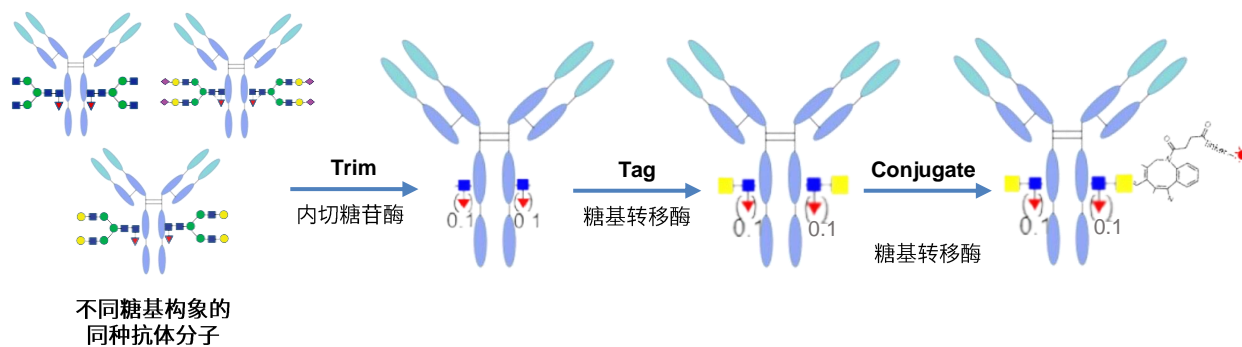
3. RDE: 队列扩展推荐剂量, 由SMC根据Ia期数据选择, 不同队列/瘤种可选择不同的RDE进行扩展

JSKN003偶联工艺更高效、产物更稳定

康宁杰瑞 一酶两步法 JSKN003



Synaffix 两酶三步法

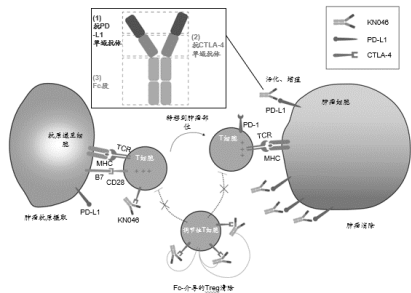


- JSKN003 血浆循环更稳定，体内暴露特点更类似抗体
- DS-8201 21天血浆循环中毒素脱落率近70%
- 康宁杰瑞ADC平台采用自研的一酶两步糖基定点偶联工艺，较Synaffix的工艺更高效

KN046

双重阻断PD-L1和CTLA-4

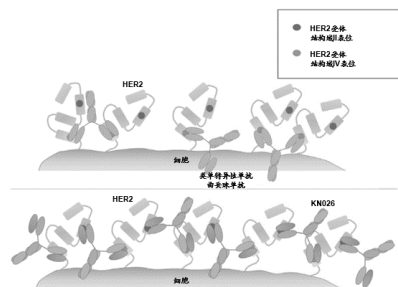
- PD-(L)1经治实体瘤
- PD-(L)1响应不充分



KN026

双重阻断HER2 II和IV表位

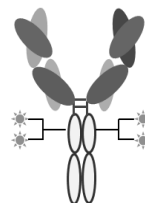
- HER2高表达实体瘤
- 定位一线及围手术期



JSKN003

HER2双抗ADC

- 抗HER2治疗响应不充分的高表达肿瘤
- HER2低表达实体瘤
- 与其他机制药物联用



KN035

皮下注射PD-L1单抗

- 全球唯一可用于皮下注射的PD-(L)1单抗



KN052

PD-L1/OX40双抗

- PD-L1拮抗剂和OX40激动剂串联结构
- 作为佐剂与肿瘤疫苗和细胞治疗联合使用



恩维达®(KN035)同步开展多个临床试验



适应症	组合用药	IND	概念验证	关键临床	NDA
≥2L MSI-H/dMMR晚期实体瘤	单药	2021年11月25日在中国上市			
≥2L 软组织肉瘤	单药	全球			
1L 胆道癌	+化疗				

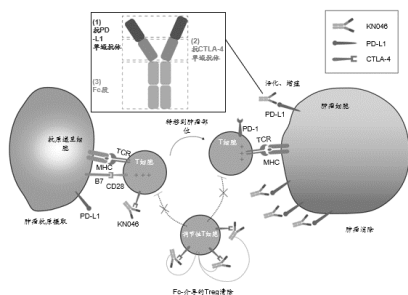
- 2023年上半年恩维达®计入康宁杰瑞的收入达1.17亿元
- 纳入2022版CSCO六大指南，包括胃癌、结直肠、免疫检查点抑制剂、子宫内膜癌、宫颈癌及卵巢癌诊疗临床应用指南
- 2023年6月19日，美国合作伙伴Tracon公告，二期单臂注册临床研究ENVASARC¹中，经IDMC对超过80例患者的疗效及安全性进行评估，无论单药还是联合伊匹木单抗，恩沃利单抗针对≥2L肉瘤的期中分析均取得了阳性结果（两位数的ORR），且单药治疗组无一例患者发生>2级的TRAE。

注：1. 该研究的主要研究终点为ORR至少达到11.25%，目前针对软组织肉瘤唯一的治疗药物帕唑帕尼(pazopanib) ORR仅为4%且存在黑框警告

KN046

双重阻断PD-L1和CTLA-4

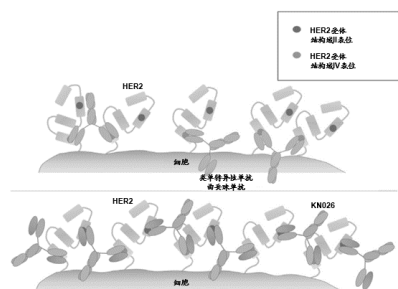
- PD-(L)1经治实体瘤
- PD-(L)1响应不充分



KN026

双重阻断HER2 II和IV表位

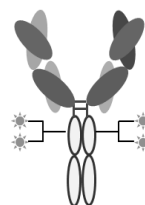
- HER2高表达实体瘤
- 定位一线及围手术期



JSKN003

HER2双抗ADC

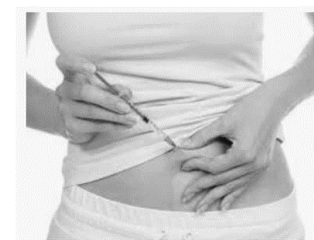
- 抗HER2治疗响应不充分的高表达肿瘤
- HER2低表达实体瘤
- 与其他机制药物联用



KN035

皮下注射PD-L1单抗

- 全球唯一可用于皮下注射的PD-(L)1单抗



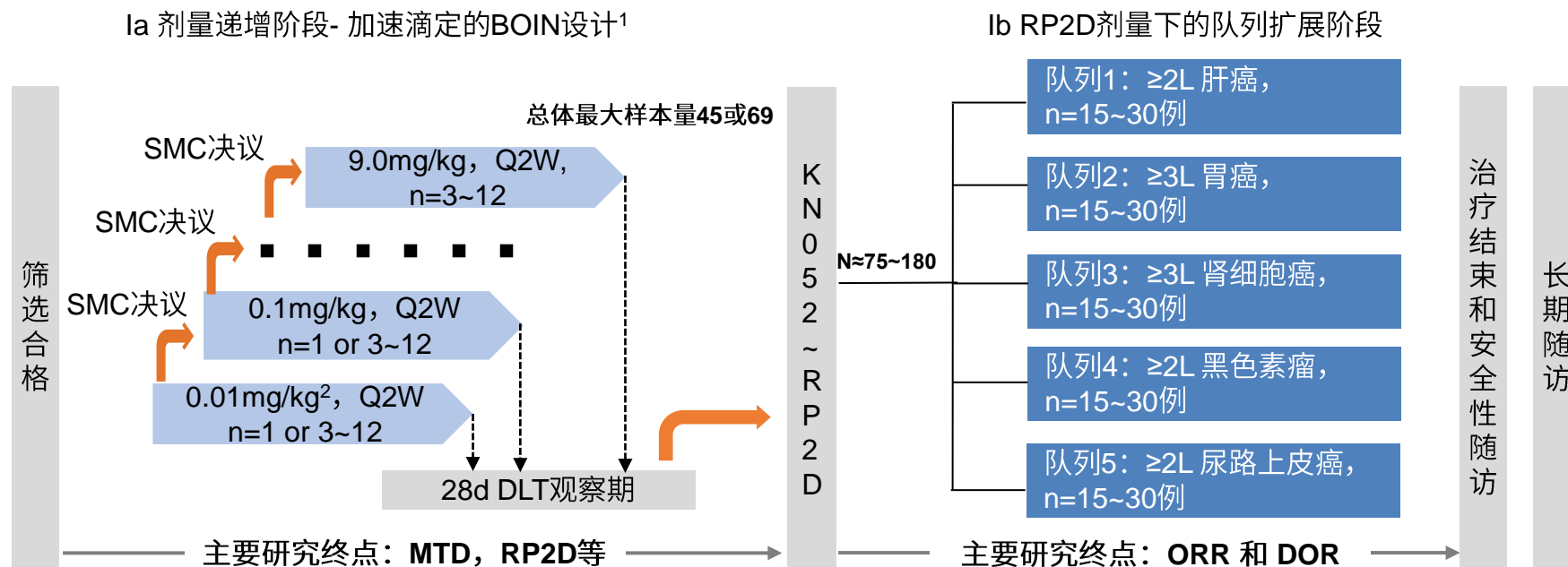
KN052

PD-L1/OX40双抗

- PD-L1拮抗剂和OX40激动剂串联结构
- 作为佐剂与肿瘤疫苗和细胞治疗联合使用



KN052: 抗PD-L1/OX40双特异性抗体



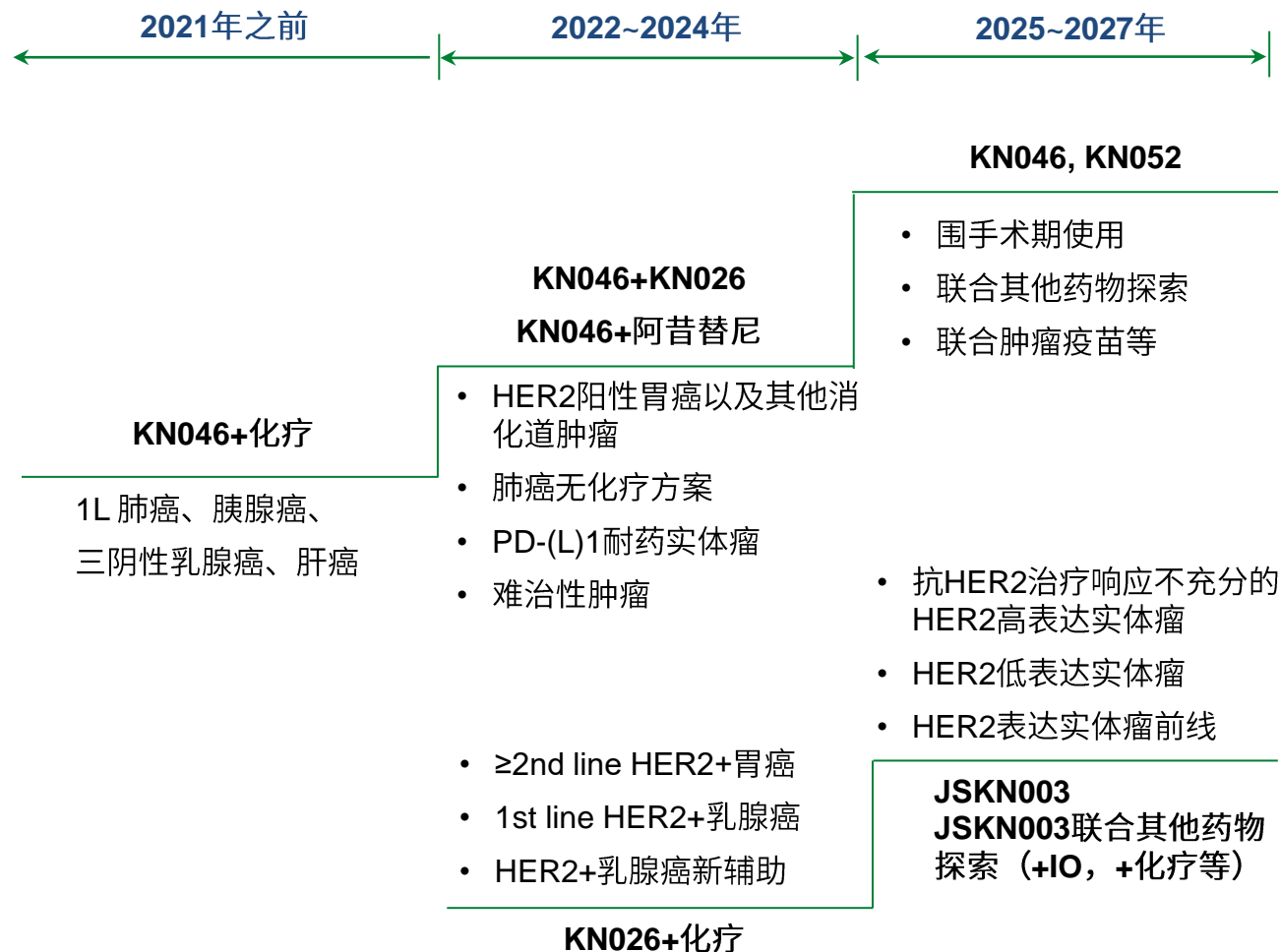
药物特点和OX40的临床价值

- PD-L1拮抗剂和OX40激动剂在同一分子中产生活性，此串联结构用于抗原结合结构域排列以减弱抗 OX40毒性，保留完整Fc功能的野生型IgG1 Fc
- OX40是一类关键的T细胞共刺激分子，OX40和OX40L结合增加效应T细胞和记忆T细胞的存活和扩增，增加细胞因子的分泌、降低Tregs的免疫活性
- 可作为佐剂与肿瘤疫苗和细胞治疗联合使用

备注: 1. Ia期采用加速滴定的BOIN设计, 起始剂量时每次仅入组1人, 直到出现DLT或第二个≥2级毒性出现, 或达到最高剂量
2. 共预设8个剂量组, 起始剂量为0.01mg/kg

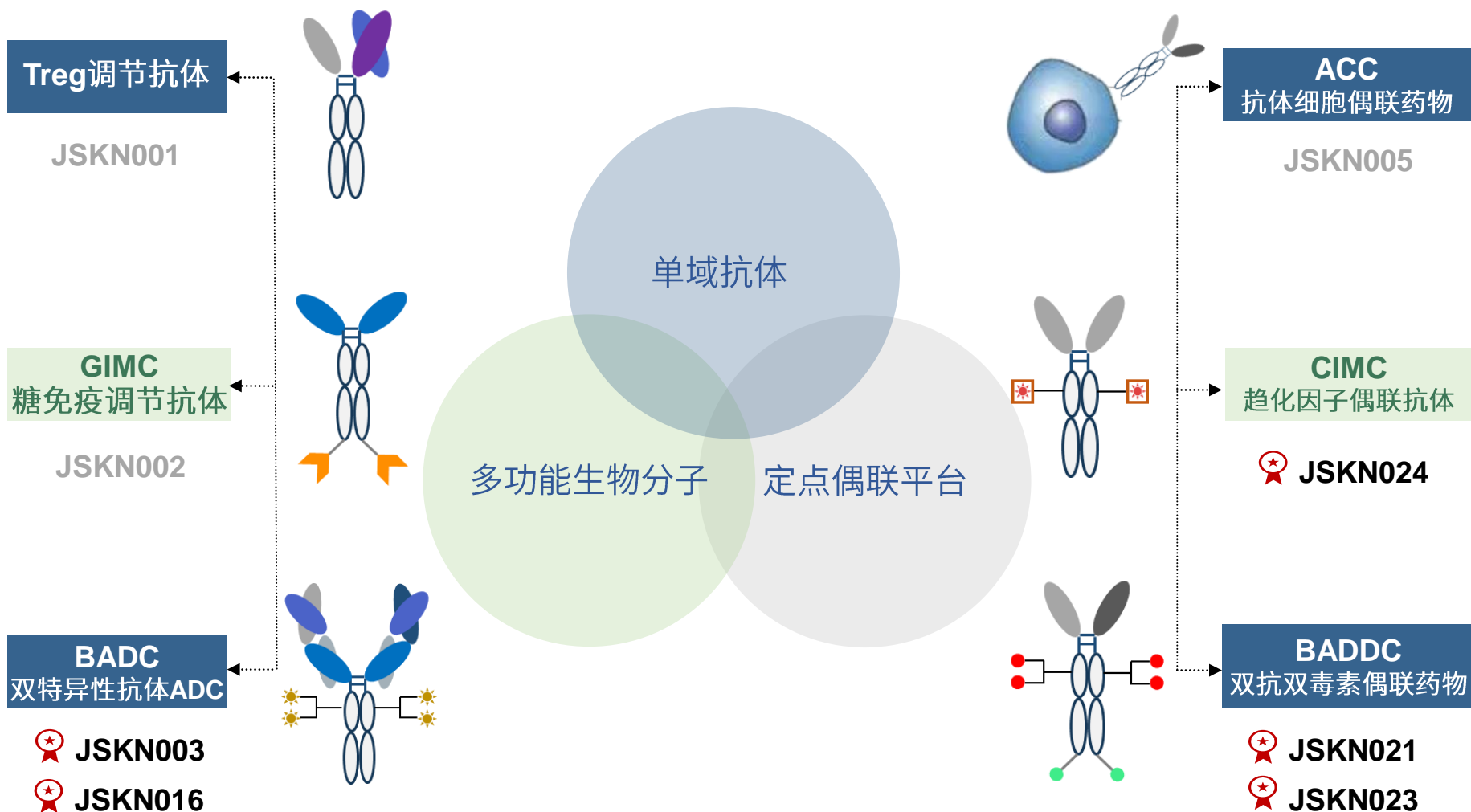
05

研发战略



研发战略：模块化的多功能大分子开发平台；推动核心产品升级换代，提高产品的疗效及安全性；以创新思维推动肿瘤无化疗方案探索

扩展多模块、多功能新产品开发平台





谢谢

Q&A