



# Disclaimer / 免责声明

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# Leading precision oncology company focused on DNA-damage response inhibitors (DDRi) / 专注于DNA损伤反应抑制剂(DDRi)的领先精准肿瘤学公司



**Lead pre-clinical candidate kt-3283, a novel dual-function DDRi;** under development for pediatric and adult solid tumors and expected in clinic H1' 2024 / 领先的临床前候选药物 **kt-3283**, 一种新型双功能DDRi; 正在开发治疗儿童和成人实体瘤, 预计将于2024年上半年进入临床



**Robust pipeline of novel DDRi-based therapeutics;** including kt-3000 series dual-function DDRi; kt-2000 series PARPi; and kt-4000 series alkylating-DDRi / 基于DDRi的新型疗法的强大管线; 包括kt-3000系列双功能DDRi; kt-2000系列PARPi; 和kt-4000系列烷基化-DDRi



**Powerful drug discovery and lead optimization platform** established in collaboration with **The University of British Columbia** / 与卑诗大学合作建立强大的药物发现和先导化合物优化平台



**Significant partnering opportunities** with Big Pharma investing more than **\$25 billion in DDRi technologies** to date / 与大型制药公司的重大合作机会, 迄今为止在DDRi技术上投资超过**\$250亿**



**>12 months working capital** to support research and development operations at end of June, 2023 / 截至2023年6月底, 有超过**12个月**的运营资金来支持研发业务

# Experienced team proven in drug discovery and development 有丰富药物发现和开发经验的团队

## Management Team / 管理层



**JEFFREY BACHA, BSC, MBA /**  
理学学士、工商管理硕士  
Executive Chairman/Director /  
执行董事会主席/董事



**DAVID HYMAN, CPA / 注册会计师**  
Chief Financial Officer / 首席财务官



**MADS DAUGAARD, PHD / 博士**  
President & Chief Scientific Officer /  
总裁兼首席科学官



**NEIL SANKAR, MD / 医学博士**  
Executive Medical Director / 执行医疗总监



**JOHN LANGLANDS, PHD / 博士**  
Chief Operating Officer / 首席运营官



## Scientific Advisors / 科学顾问



**DENNIS BROWN, PHD / 博士**  
Chair, Scientific Advisory Board (SAB)/Director: /  
科学顾问委员会 (SAB) 主席/董事:



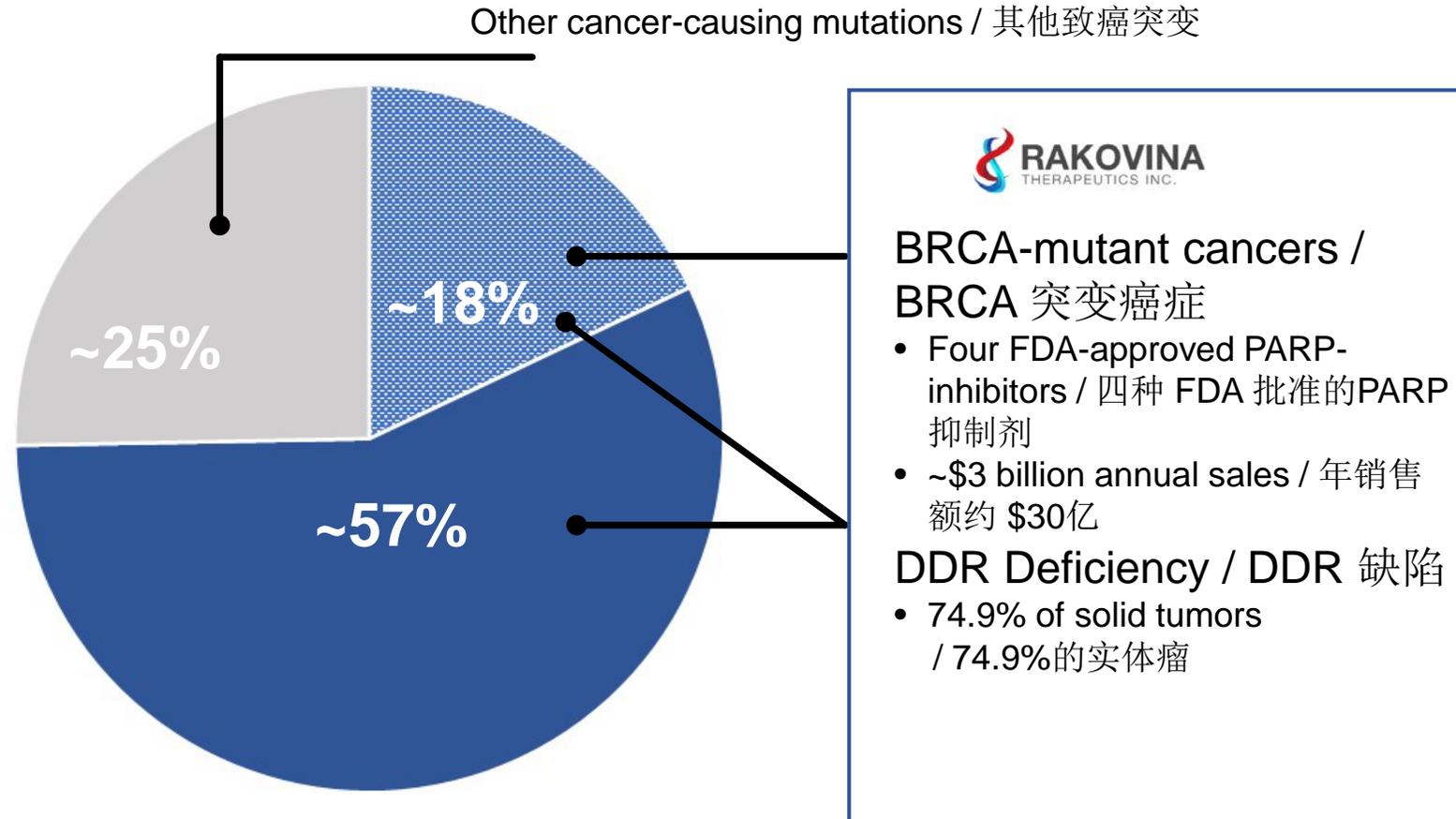
**LEONARD POST, PHD / 博士**  
SAB/Senior Drug Development Advisor /  
科学顾问委员会/高级药物开发顾问



**WANG SHEN, PHD / 博士**  
SAB/Senior Medicinal Chemistry Advisor /  
科学顾问委员会/高级药物化学顾问



# Focused on DNA-damage response – a major driver of many cancers / 专注于 DNA 损伤反应——许多癌症的主要驱动因素



nature  
REVIEWS CLINICAL  
ONCOLOGY

Targeting BRCA-deficient cancers using poly(ADP-ribose) polymerase (PARP) inhibitors is the archetype of synthetic lethality / 使用聚(ADP-核糖)聚合酶(PARP)抑制剂靶向BRCA基因缺陷癌症是合成致死的原型

Preclinical and clinical research with PARP inhibition has revealed multiple resistance mechanisms across a variety of cancer subtypes / PARP抑制剂的临床前和临床研究揭示了多种癌症亚型的多重耐药机制

The therapeutic landscape of DDR inhibitors is rapidly expanding (beyond BRCA mutations) to include inhibitors of other key mediators of DNA repair and replication / DDR抑制剂的治疗范围正在迅速扩大(超越BRCA突变),包括DNA修复和复制的其他关键介质的抑制剂

# Big Pharma has invested more than \$25 billion in DDRi technologies

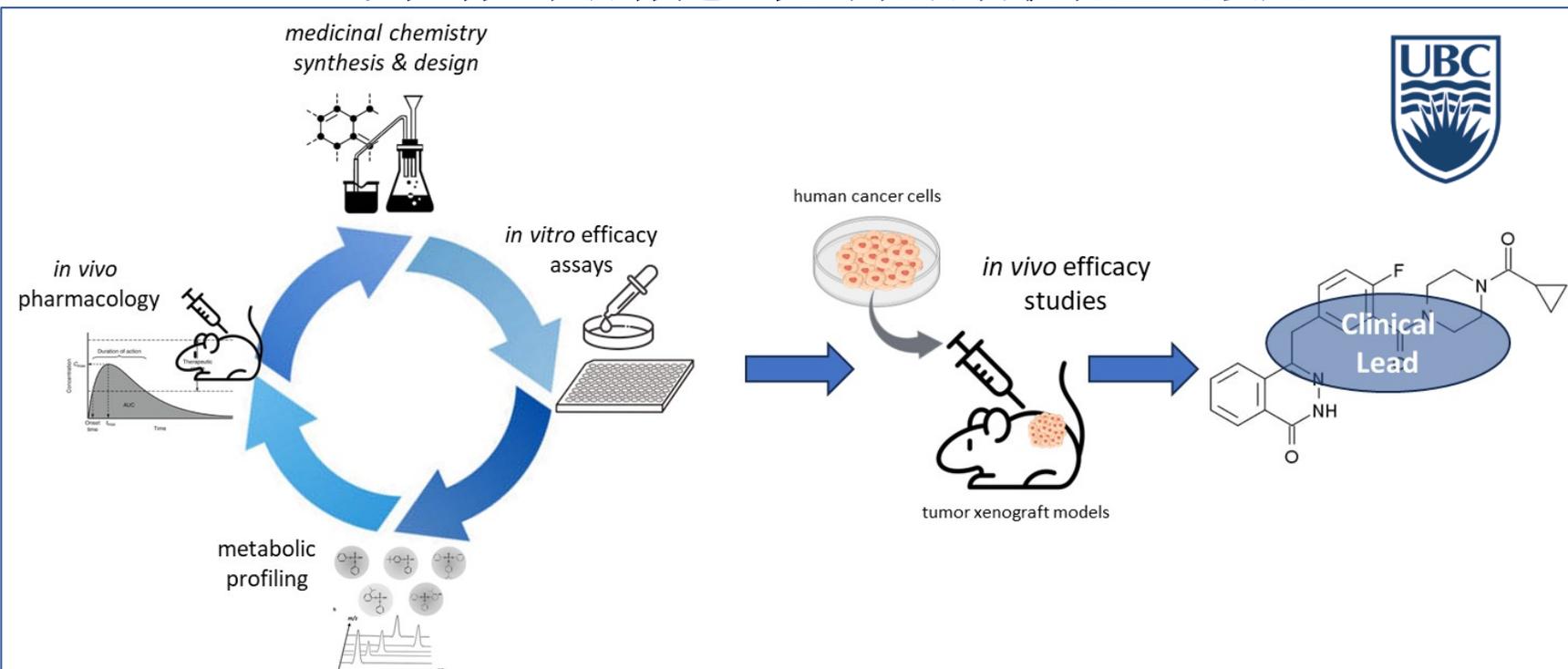
## 大型制药公司已在DDRi技术上投资超过\$250亿

	Biotech / 生物科技	Pharma / 药企	Deal Size / 交易规模	Year / 年份	Type / 类型	Development Stage / 开发阶段
<b>ACQUISITION OF FIRST GENERATION PARP-i / 收购第一代PARP-i</b>		AstraZeneca 	\$210M / \$2.1亿	2005	Acq. / 收购	preclinical / 临床前
		Pfizer 	\$14.0B / \$140亿	2016	Acq. / 收购	Phase 3 / 三期
		GSK 	\$5.1B / \$51亿	2019	Acq. / 收购	FDA Approved / FDA批准
<b>PRE-CLINICAL DEALS FOR NEXT-GENERATION DDR-i / 为下一代DDR-i进行的临床前交易</b>		Bristol Myers Squibb 	\$3.0B / \$30亿	2020	Invest. / 投资	Pre-clinical collaboration / 临床前合作
		GSK 	\$3.0B / \$30亿	2020	Invest. / 投资	Pre-clinical collaboration / 临床前合作
		NOVARTIS 	\$1.3B / \$13亿	2021	Invest. / 投资	Pre-clinical collaboration / 临床前合作

# Powerful Drug Discovery and Lead Optimization Platform

## 强大的药物发现和先导化合物优化平台

Lead optimization infrastructure established in collaboration with The University of British Columbia / 与卑诗大学合作建立先导化合物优化基础设施



Phase 1-2  
Clinical  
Trials / 1-2  
期临床试验

Pivotal  
Clinical  
Trials / 关  
键临床试验

# Robust pipeline of novel DNA-damage response inhibitors (DDRi)

## 强大的新型 DNA 损伤反应抑制剂 (DDRi) 管线

	Key Differentiator 关键差异化因素	Indication 适应症	Lead Optimization 先导化合物优化	Pre-clinical / IND enabling 临床前/ IND 启动	Phase 1/2 1/2期	Pivotal 关键	Upcoming Milestones / 即将到来 的里程碑
临床前 Pre-clinical	<b>kt-3000</b> Dual-function HDAC+PARP inhibition 双功能HDAC+PARP抑制剂	<ul style="list-style-type: none"> <li>Active against PARPi-resistant and HR-proficient tumors / 对 PARPi耐药和 HR 正常肿瘤具有活性</li> </ul>	Childhood and adult solid tumors / 儿童和成人实体瘤				Initiate Phase 1-2 clinical trials in H1'2024 / 2024 年上半年启动1-2期临床试验
先导化合物优化 Lead Optimization	<b>kt-2000</b> PARP1-selective inhibitors PARP1选择性抑制剂	<ul style="list-style-type: none"> <li>Improved side-effect profile / 改善副作用</li> <li>Improved CNS penetration / 改善中枢神经系统渗透性</li> </ul>	BRCA-positive tumors with brain metastases / BRCA阳性伴脑转移肿瘤				Pre-clinical lead selection; IND-enabling studies in 2024 / 临床前先导化合物选择; 2024年启动IND研究
	<b>kt-4000</b> DNA-alkylating PARP-inhibitor / DNA 烷基化PARP抑制剂	<ul style="list-style-type: none"> <li>Improved efficacy through synergistic effects / 通过协同效应提高疗效</li> </ul>	Solid Tumors / 实体瘤				<i>In vivo</i> proof-of-concept / 体内概念验证

**Lead Candidate**

**Dual Function DDRi kt-3283**

**先导候选双功能DDRi kt-3283**



# kt-3283: novel dual function DNA-damage response inhibitor

## kt-3283: 新型双功能DNA损伤反应抑制剂

**Oral inhibitor of PARP and HDAC to treat cancers resistant to FDA-approved PARP-inhibitors / 口服PARP和HDAC抑制剂，用于治疗对FDA批准的PARP抑制剂耐药的癌症**

**PARP is a cellular enzyme involved in repair of single-strand DNA breaks / PARP是一种参与修复单链DNA断裂的细胞酶**

**HDACs are proteins involved in DNA folding and cellular replication / HDAC是参与DNA折叠和细胞复制的蛋白质**

**FDA-approved PARP-inhibitors (PARPi) have become mainstay treatment in BRCA-mutated cancers / FDA 批准的PARP抑制剂 (PARPi) 已成为BRCA突变癌症的主要疗法**

**FDA-approved HDAC inhibitors (HDACi) are important in the treatment of blood-cancers, but use in solid tumors has been limited due to toxicity / FDA 批准的HDAC抑制剂 (HDACi)在治疗血癌中很重要，但由于毒性而在实体瘤中的应用受限**

**Compelling rationale for PARPi + HDACi combination therapy to overcome resistance to PARPi / PARPi + HDACi 联合疗法克服PARPi耐药的令人信服的理由**

**Clinical utility of this approach has been limited due to toxicity / 由于毒性，该方法的临床实用性受限**

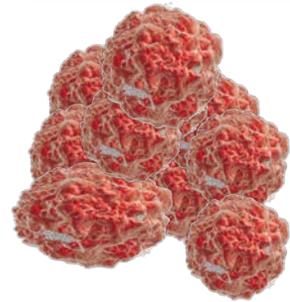
**kt-3283 differentiation driven by: / kt-3283 的差异化驱动因素:**

- **Enhanced chemical properties (potency & selectivity) / 增强的化学特性（功效和选择性）**
- **Activity against treatment-resistant phenotypes / 对抗治疗耐药表型的活性**
- **Observed synergy of dual function vs. single-agent treatments / 与单一疗法相比，观察到了双功能的协同作用**

# kt-3283: Overcoming PARPi treatment resistance

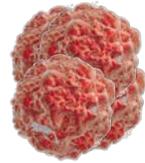
## kt-3283: 克服PARPi治疗的耐药性

### HR-deficient tumor / HR缺陷肿瘤



PARP-inhibitor therapy / PARP抑制剂治疗

Tumor shrinks / 肿瘤缩小



BRCA-gene regains function / BRCA基因恢复功能



Treatment-resistance & aggressive tumor regrowth / 治疗耐药性和侵袭性肿瘤再生

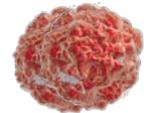


### kt-3283 dual function DDRi / kt-3283双功能DDRi

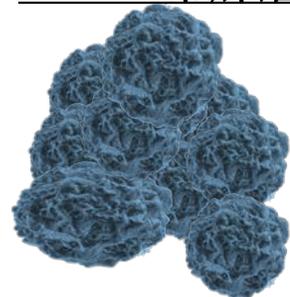
(1) HDAC-inhibition degrades BRCA-gene protein / HDAC抑制降解BRCA基因蛋白

(2) PARP-inhibition prevents DNA repair / PARP抑制防止DNA修复

Tumor Re-sensitized to treatment / 肿瘤对治疗重新敏感



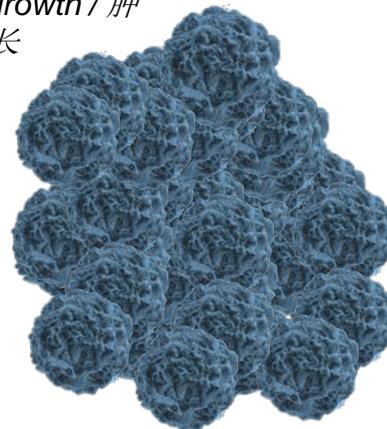
### HR-proficient tumor / HR正常肿瘤



PARP-inhibitor therapy / PARP抑制剂治疗

No effect / 无效果

Continued tumor growth / 肿瘤持续生长

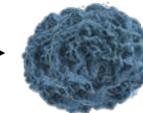


### kt-3283 dual function DDRi / kt-3283双功能DDRi

(1) HDAC-inhibition degrades BRCA-gene protein / HDAC抑制降解BRCA基因蛋白

(2) PARP-inhibition prevents DNA repair / PARP抑制防止DNA修复

Tumor responsive to treatment / 肿瘤对治疗有反应

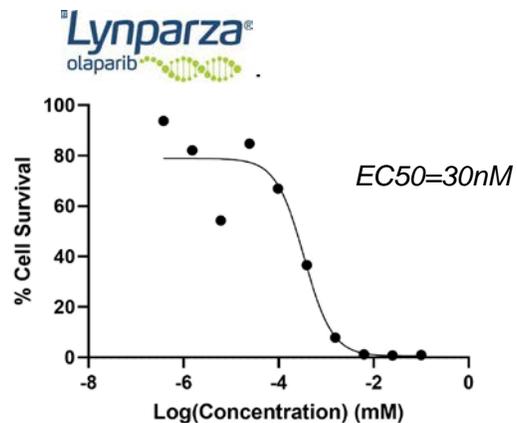
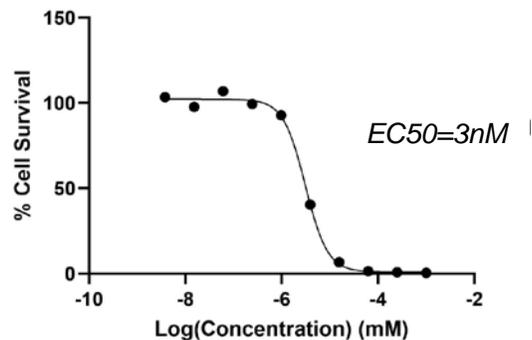


# kt-3283: Overcoming PARPi treatment resistance

## kt-3283: 克服 PARPi 治疗耐药性

### HR-deficient tumor (BRCA-mut) / HR缺陷肿瘤 (BRCA突变)

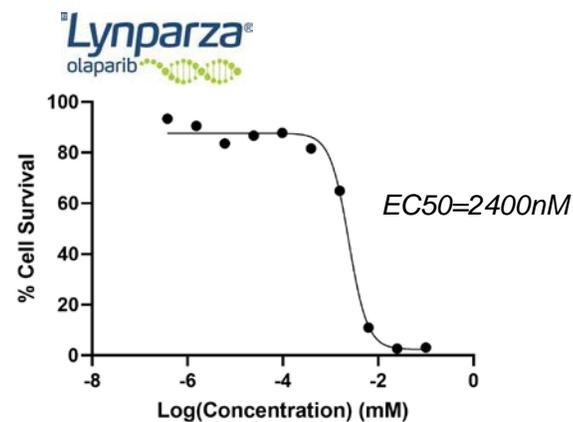
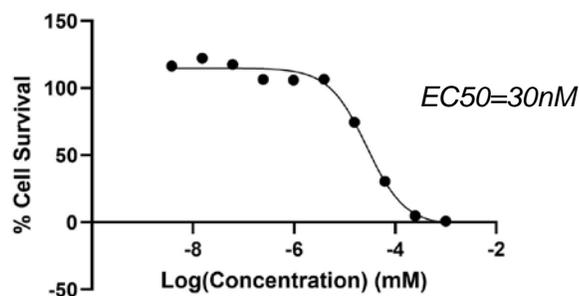
kt-3283



kt-3283 is **10x more potent** than FDA-approved PARPi Lynparza (olaparib) against **HR-deficient** tumor cells / 对比 FDA 批准的 PARPi Lynparza (olaparib), kt-3283 对抗**HR**缺陷肿瘤细胞的**功效超过10倍**

### HR-proficient tumor (BRCA-wt) / HR正常肿瘤 (BRCA野生型)

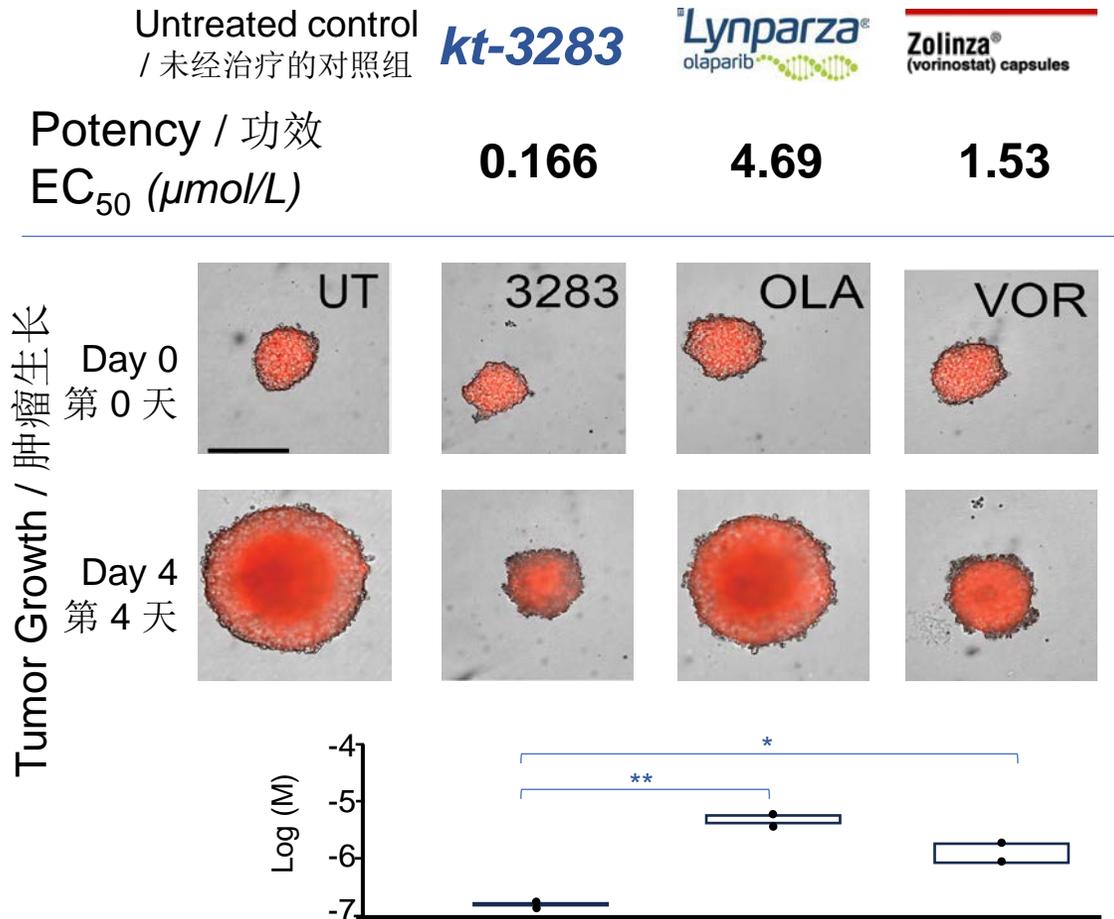
kt-3283



kt-3283 exhibits **potent anti-cancer activity** against **HR-proficient, PARPi-resistant** tumors / kt-3283 对**HR**正常、**PARPi**耐药肿瘤表现出**有效的抗癌活性**

# kt-3283: Overcoming PARPi treatment resistance

## kt-3283: 克服 PARPi 治疗耐药性



### CLINICAL CANCER RESEARCH

The Journal of Clinical and Translational Research

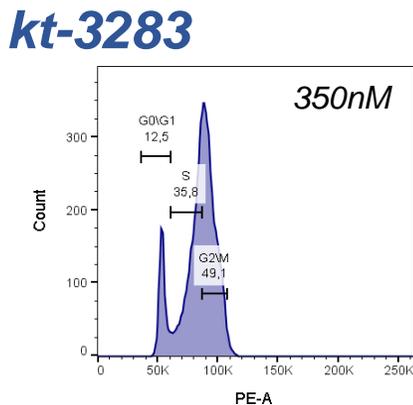
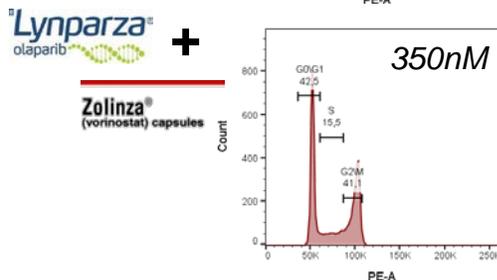
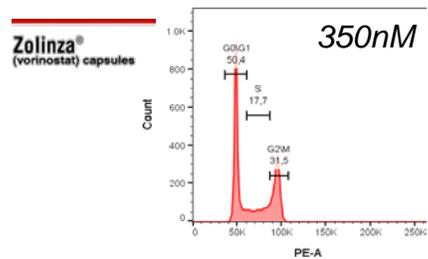
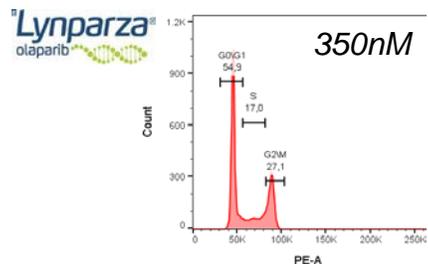
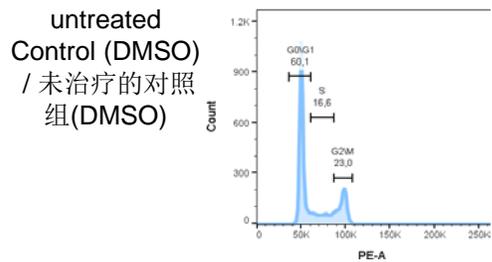
- kt-3283 inhibits metastasis and growth of treatment-resistant Ewing sarcoma tumors in mouse lung / kt-3283 抑制小鼠肺部难治性尤文肉瘤肿瘤的转移和生长
- kt-3283 exhibits >28x greater potency than Lynparza®(PARPi); and >9x potency than Zolinza®(HDACi) / kt-3283的功效比 Lynparza®(PARPi) 高 28 倍以上; 功效比 Zolinza®(HDACi) 高9倍以上
- Lynparza and Zolinza failed to inhibit significant tumor growth / Lynparza和 Zolinza未能显著抑制肿瘤生长

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AACR American Association for Cancer Research

# kt-3283: Achieving synergy to treat resistant cancers

## kt-3283: 实现耐药性癌症的协同治疗



AACR SPECIAL CONFERENCE: SARCOMAS

May 9 - 12, 2022  
Doubletree by Hilton Montreal  
Montreal, QC, Canada

kt-3283 dual function DDRi is highly effective against PARPi resistant cancer cells and achieves a synergistic effect superior to the combination of FDA-approved PARPi (Lynparza®) and HDACi (Zolinza®) at equimolar treatment doses. / kt-3283双功能DDRi对PARPi耐药癌细胞高度有效，并在等摩尔治疗剂量下实现优于FDA批准的PARPi (Lynparza®)和HDACi (Zolinza®)联合用药的协同作用。

### Affect on Ewing sarcoma cancer cells (cell cycle arrest) / 对尤文肉瘤癌细胞的影响（细胞周期停滞）

Treatment / 治疗	G0/G1	S	G2/M	conclusion / 结论
untreated (DMSO) / 未治疗 (DMSO)	60.1	16.6	23	
kt-3283	12.5	35.8	49.1	Highly effective / 非常有效
Lynparza®	54.9	17	27.1	No effect (resistant) / 无影响 (耐药)
Zolinza®	50.4	17.7	31.5	Moderately active / 适度活跃
Lynparza® + Zolinza®	42.5	15.5	41.1	Moderately active / 适度活跃

# DDRi Pipeline

## DDRi管线



# kt-2000 series: Potential best-in-class PARPi

## kt-2000 系列：潜在的同类最佳PARPi

Oral PARP-inhibitors designed for reduced side-effects and improved CNS penetration

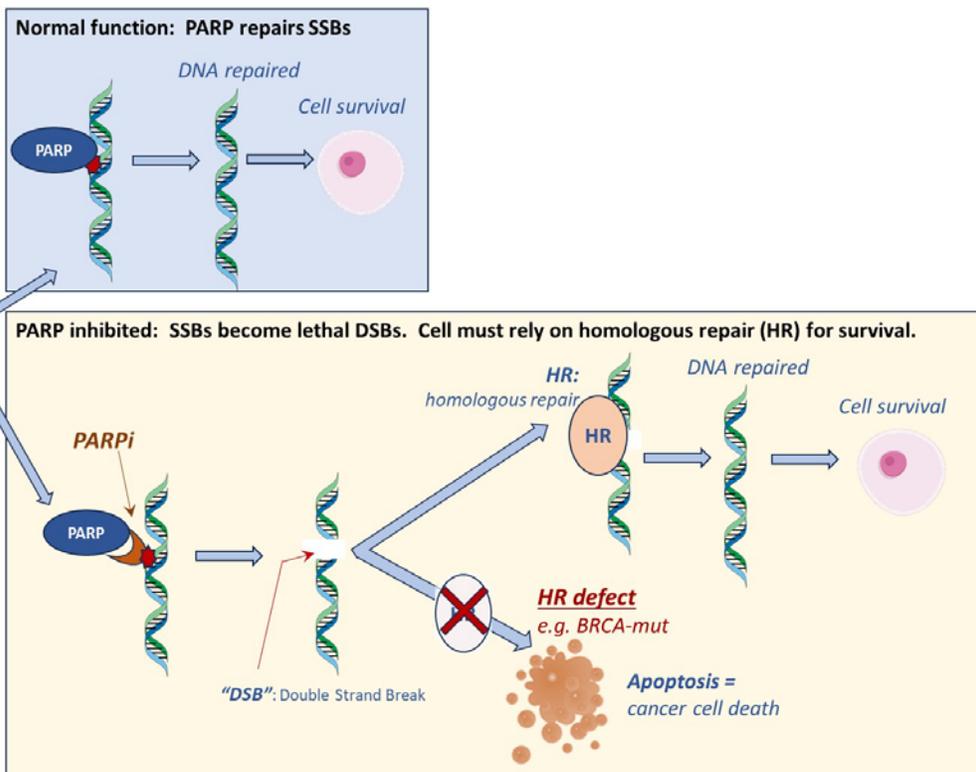
口服 PARP抑制剂，旨在减少副作用并提高中枢神经系统渗透性

FDA-approved PARPi harbor hematologic toxicity and poor brain penetration / FDA 批准的PARPi存在血液毒性和脑渗透性差

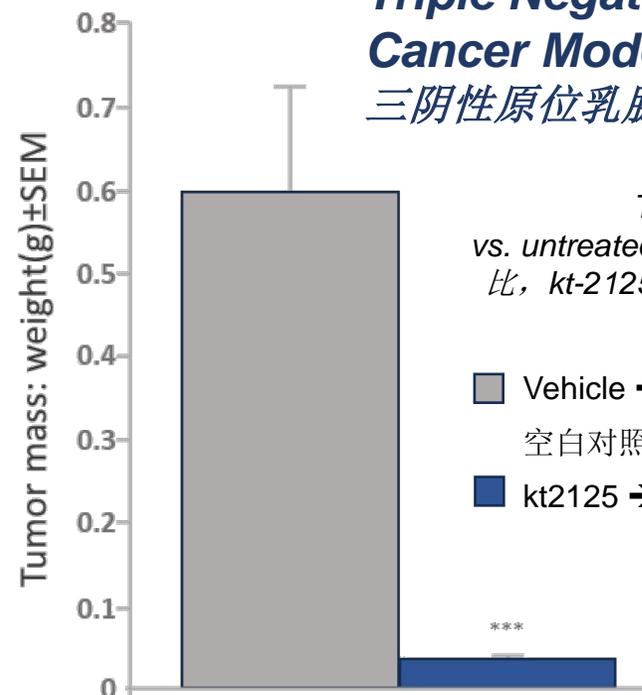
kt-2000 series drug candidates have demonstrated compelling anti-tumor activity in animal models / kt-2000系列候选药物在动物模型中表现出引人注目的抗肿瘤活性

kt-2000 series differentiation driven by: / kt-2000 系列的差异化驱动因素:

- PARP-1 v. PARP-2 selectivity / PARP-1与PARP-2 选择性
- Improved CNS penetration / 改善中枢神经系统渗透性



### Triple Negative Orthotopic Breast Cancer Model (MDA-MB-436) / 三阴性原位乳腺癌模型(MDA-MB-436)



Tumor size & weight kt-2125 vs. untreated control (day 29) / 与未治疗的对照组相比, kt-2125治疗后的肿瘤大小和重量 (第29天)

Vehicle →  
空白对照

kt2125 →



# kt-4000 series: DNA-alkylating PARPi

## kt-4000 系列: DNA 烷基化PARPi

### Oral PARP-inhibitors designed expand utility of PARPi beyond HR-deficient tumors

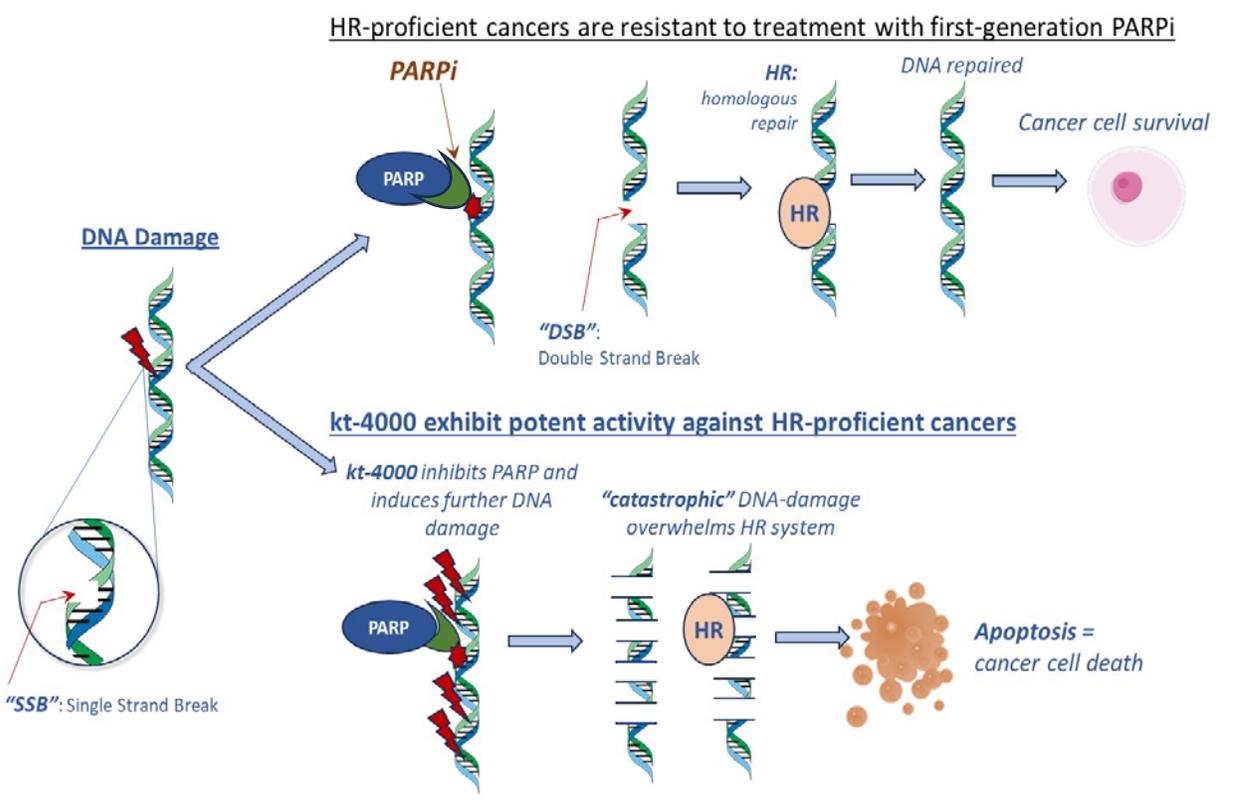
口服PARP抑制剂, 将PARPi的效用扩展到HR缺陷肿瘤之外

FDA-approved PARPi activity limited to cancers with underlying HR-defect / FDA 批准的PARPi活性仅限于具有潜在HR缺陷的癌症

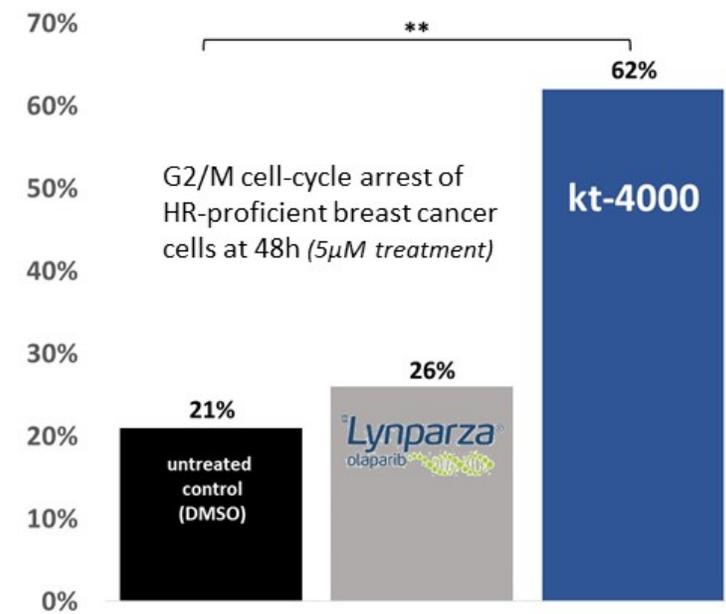
kt-4000 series drug candidates are rationally designed treat cancers not normally responsive to PARPi / kt-4000系列候选药物经过合理设计, 可治疗通常对PARPi无反应的癌症

kt-4000 series differentiation driven by: / kt-4000 系列的差异化驱动因素:

- DNA-alkylation function combined with potent inhibition of DNA-repair function / DNA烷基化功能与DNA修复功能的有效抑制相结合



- ✓ kt-4000 drug candidates alkylate DNA in a similar manner as temozolomide, an FDA-approved DNA alkylating agent / kt-4000候选药物烷基化DNA的方式与美国FDA批准的DNA烷基化药物替莫唑胺相似
- ✓ kt-4000 drug candidates demonstrate dose-dependent anti-cancer activity against PARPi-resistant cancers *in vitro* / kt-4000候选药物在体外对PARPi耐药性癌症具有剂量依赖性抗癌活性



# Highlights and Milestones

亮点和里程碑



# Financial Highlights / 财务亮点

**\$1.5M /  
\$150 万**

est. working capital /  
预计营运资金

as at 30-Jun 2023 /  
截至2023年6月30日

**~12 months  
/ 约12个月**

research funding /  
研究经费

expected runway with cash  
on hand / 手头现金预计用途

**69.8M /  
6980万**

basic & fully diluted  
shares outstanding /  
基本与完全摊薄后的  
发行在外股份

shares outstanding  
30-Jun 2023 / 截止2023年6  
月30日发行在外股份

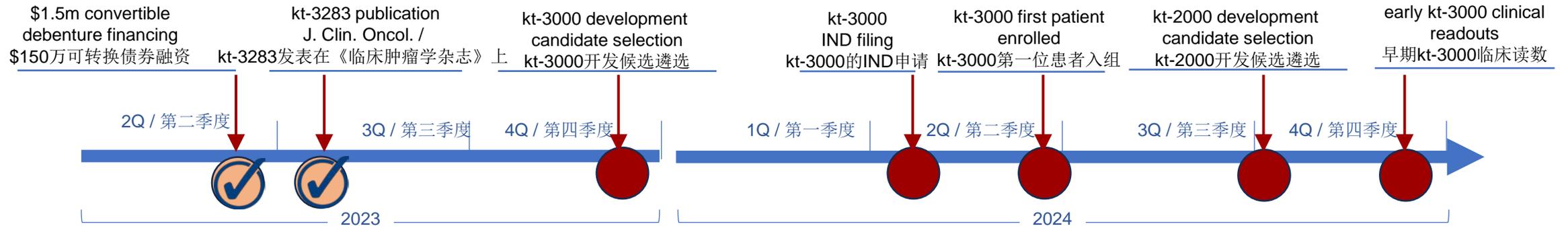
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insider held  
/ 内部人士持股

per yahoo finance / 来源于雅  
虎财经

# Recent progress and upcoming milestones

## 近期进展和即将到来的里程碑



# Rakovina Therapeutics: Summary of key differentiators

## Rakovina Therapeutics: 主要差异化因素总结:

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### Lead kt-3283 dual function DDRi / 领先 kt-3283双功能DDRi

- Differentiated to overcome PARPi resistance / 克服 PARPi 耐药性的差异化
- Targeted to enter human trials H1'24 / 目标是在24年上半年进入人体试验



### Pipeline / 管线

- Portfolio of novel DNA-damage response inhibitor technologies / 新型DNA损伤反应抑制剂技术组合



### Platform / 平台

- Robust drug discovery and lead optimization infrastructure / 强大的药物发现和先导化合物优化基础设施



### Balance sheet / 资产负债表

- Funded for multiple value-creating milestones / 为多个创造价值的里程碑提供资金

# Contact / 联系方式

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## Corporate

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## Auditor / 审计

