股號:6492

# 生華生物科技股份有限公司

## 次世代DDR與HH/IO癌症新藥

# 法人說明會

宋台生 總經理

日期: 2019年12月16日

# 免責聲明

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# 簡報大綱

公司概況

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# 生華生物科技

## 次世代DDR與HH癌症新藥開發

**股票代號: 6492TW**

- 總部: 台灣新北市
- 臨床業務總部: 美國聖地牙哥
- 股本: 台幣7.44億元
- 市值: 台幣50億元(11/30/19)
- 現金及約當現金: 台幣9.15億元(2019Q3)

成立於2012年，專注於開發市場首見(First in class)之創新小分子抗癌藥物

經營團隊擁有豐富的藥物開發經驗，與過往成功紀錄

兩大產品 CX-4945 和 CX-5461 具有創新的治療機制(MOA)，能作為單一用藥，或與其他已上市產品進行合併治療，以解決未被滿足的醫療需求。

與世界頂尖科學家、醫學研究機構密切合作(CCTG,PMCC, PBTC), 受到全球聲譽卓著的機構頒予補助 SU2C/CBCF,CTEP(NCI).

# 癌症新藥產品線及開發進程

| Program | Indication | Phase 1 / Expansion Cohorts | Phase II | Pivotal Trial | Approval | Partner |
|---|---|---|---|---|---|---|
| CX-5461 | 乳癌 | CA | | | | CCTG |
|  | 乳癌/卵巢癌/胰臟癌等實體腫瘤 | | CA/USA | | | |
| | 血癌 | AUS | | | | PMCC |
| CX-4945 | 膽管癌 | USA, KR, TW | | | | |
| | 基底細胞癌 (BCC) | USA | | | | |
|  | 髓母細胞瘤 | USA | | | | PBTC, Stanford H |

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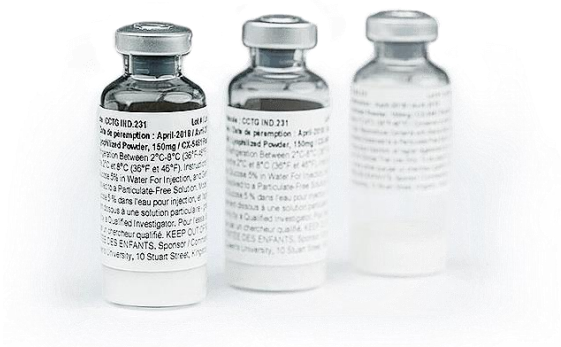
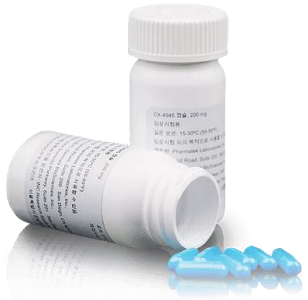
# 研發概況



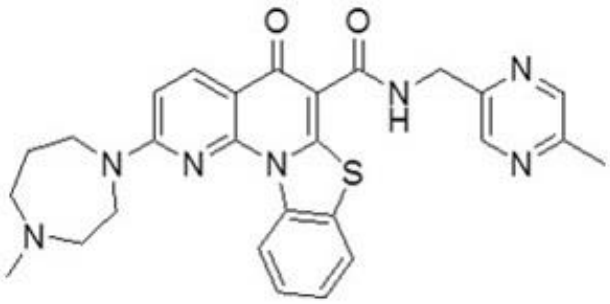
(First-in-class G4 stabilizer)

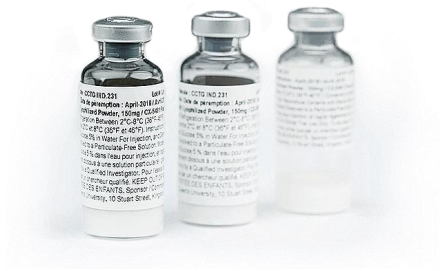


(First-in-class CK2 inhibitor)

# CX-5461

(市場首見新藥)



- Human efficacy
- Cisplatin resistant tumor
- PARP inhibitor resistant tumor
- Combination Potential

Canadian Cancer Trials Group

SABCS SAN ANTONIO BREAST CANCER SYMPOSIUM December 10-14, 2019 Henry B. Gonzalez Convention Center, San Antonio, Texas, USA

# CCTG IND.231: A phase 1 trial evaluating CX-5461, a novel first-in-class G-quadruplex stabilizer in patients with advanced solid tumors enriched for DNA-repair deficiencies

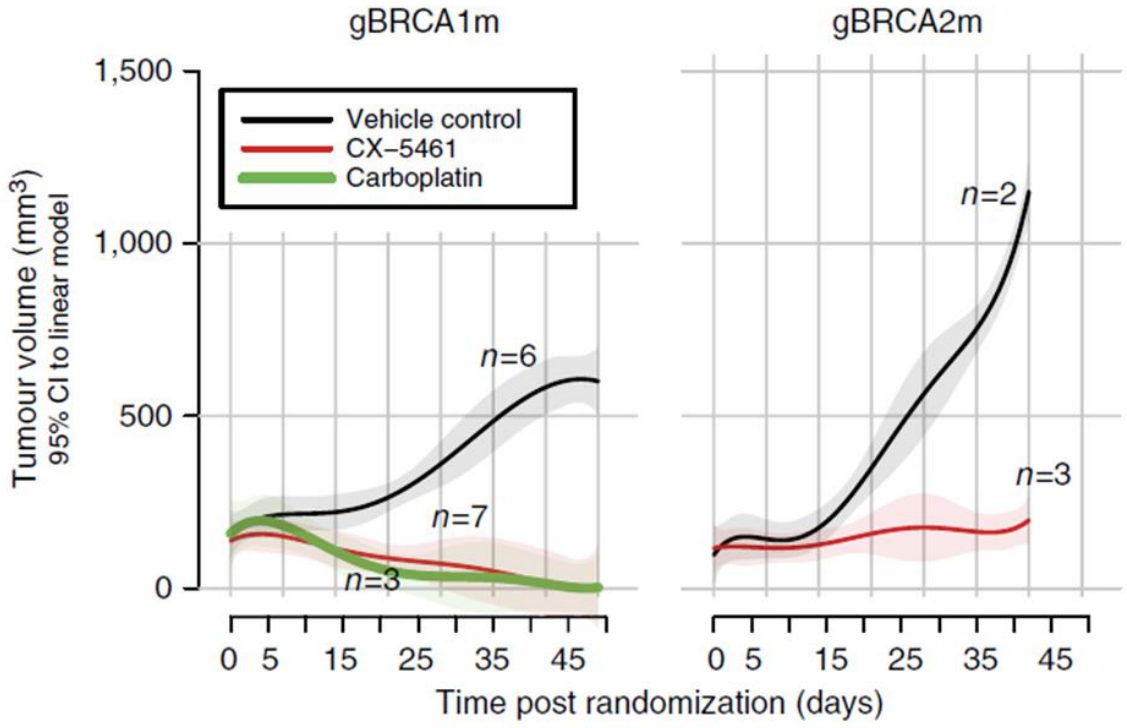

**Author List**

John Hilton, Karen Gelmon, David Cescon, Anna Tinker, Derek Jonker, Rachel Goodwin, Scott Laurie, Aaron Hansen, Samuel Aparicio, John Soong, Linda Hagerman, Hongbo Lui, Philippe Bedard, Kathleen Pritchard, Dongsheng Tu, Lesley Seymour


- 生華科合作夥伴-加拿大CCTG獲選以壁報(Poster)及口頭簡報形式，於2019聖安東尼國際乳癌大會SABCS之亮點發表會議(Spotlight Presentation)進行一期臨床數據發表。

# CX-5461有效抑制對platinum無反應三陰性乳癌細胞

- TNBC PDX model

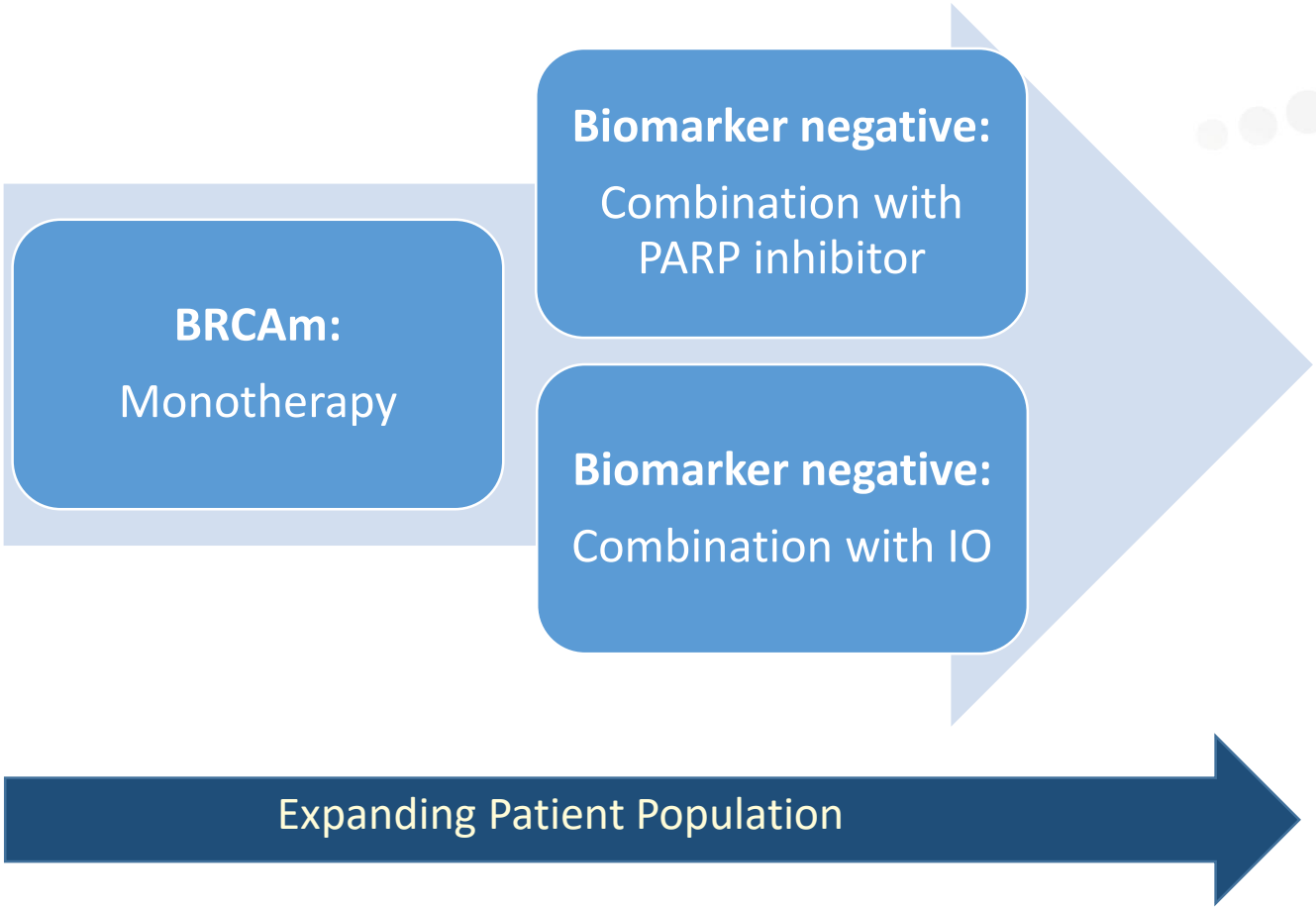



NATURE COMMUNICATIONS | 8:14432 | DOI: 10.1038/ncomms14432 | www.nature.com/naturecommunications

# Phase I patients with clinical benefit

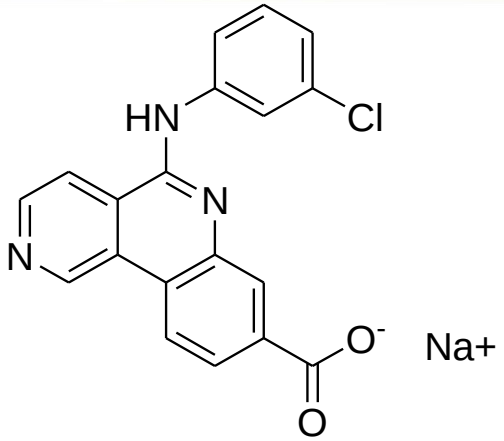
- 有效治療鉑類藥物抗藥性( platinum resistant) 的病人
- 有效展延無藥可醫的病人存活期(long Duration )
- 有效醫治特殊基因缺損族群病人(specific Pathogenic Gene Markers)
- Phase 1 收治的病人已無其它上市藥物可供選擇(最末線)

# CX-5461 Targeting DNA Damage Repair Beyond BRCA mutation



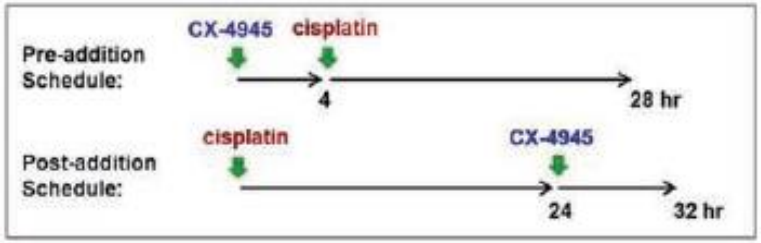
# CX-4945

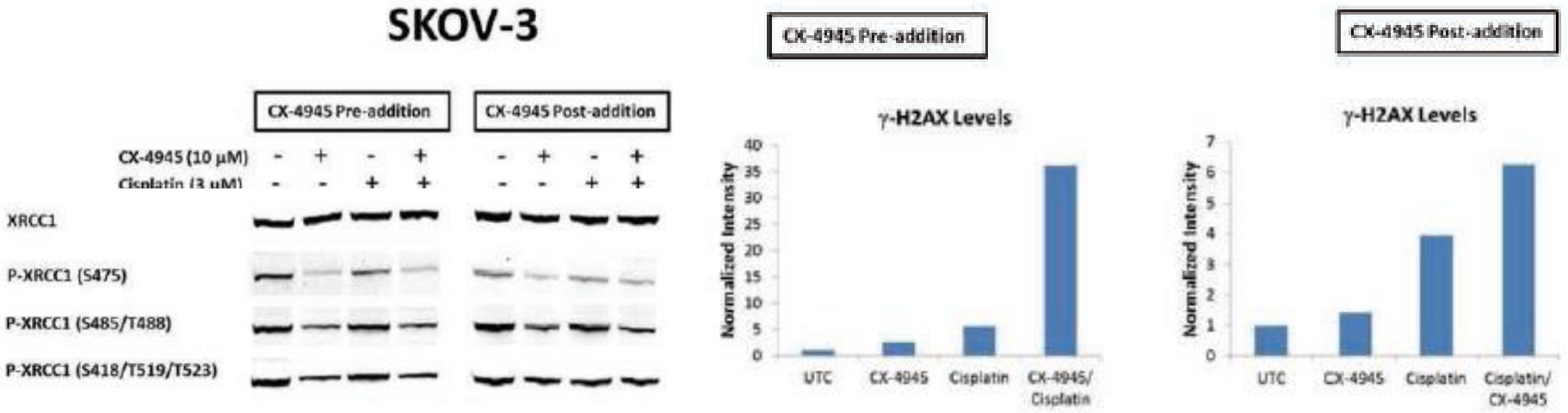
(市場首見新藥)




- Human efficacy in
  - Cholangiocarcinoma
  - Basal cell carcinoma
- Medulloblastoma

# CX-4945 Reduces XRCC1 and Increases Cisplatin Induced DNA Damage



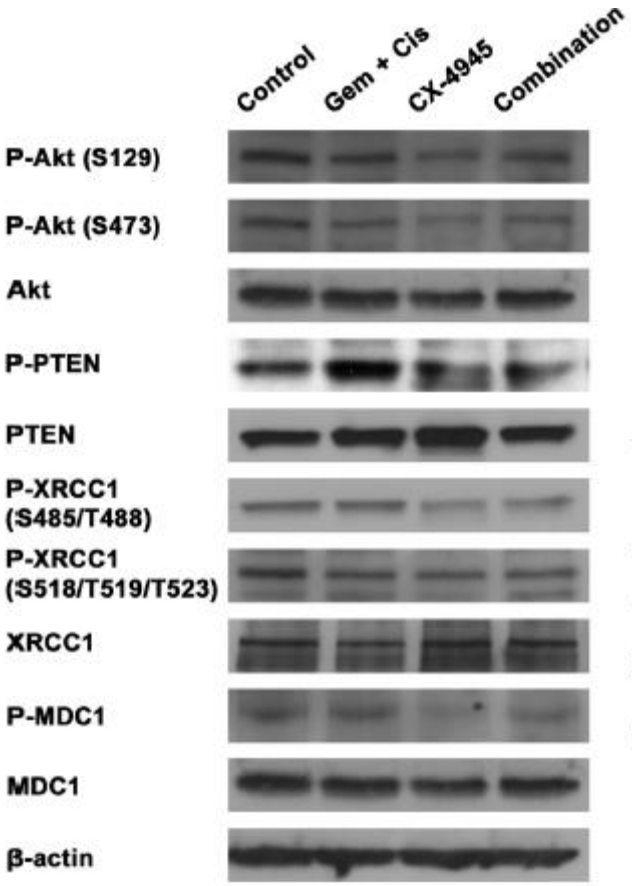



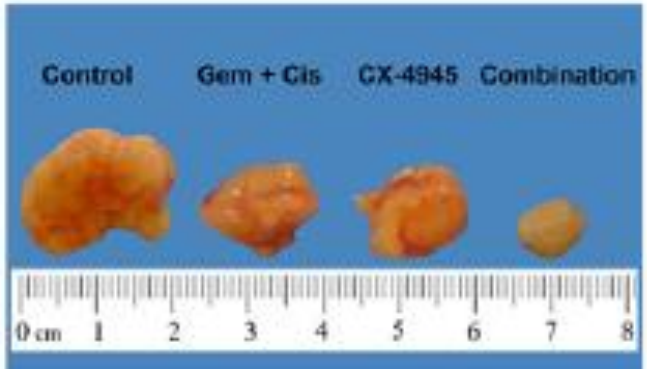

**Combining CX-4945/cisplatin in SKOV-3 cells**

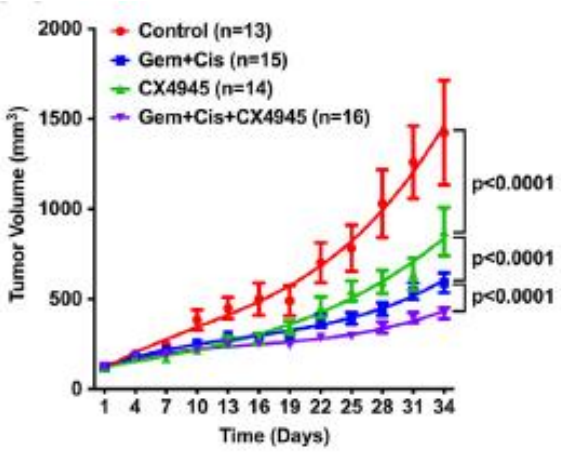
- Decreases XRCC1 phosphorylation
- Increases CHK 1/2 phosphorylation
- Increases γ-H2AX

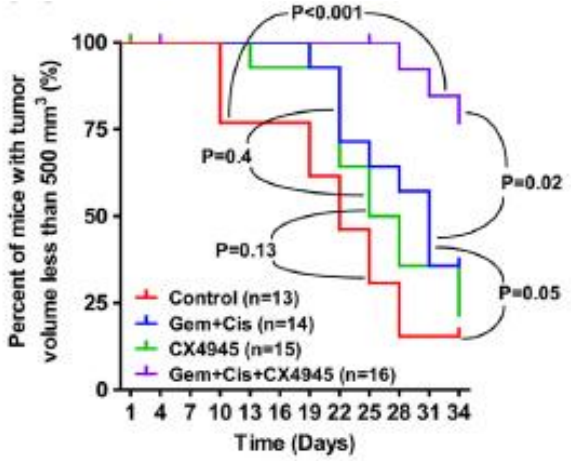
Mol Cancer Ther. 2012 ;11(4):994-1005.

# Preclinical In Vitro and In Vivo Evidence of an Antitumor Effect of CX-4945, a Casein Kinase II Inhibitor, in Cholangiocarcinoma




Source: Presented at DDW 2016. "The Casein Kinase II Inhibitor CX-4945 Has an Additive Effect With Gemcitabine and Cisplatin in Cholangiocarcinoma Xenografts". Miyabe et al.

# CX-4945 Phase I Data

# ADVANCED BILIARY TRACT CANCER

No practice-changing studies since 2010

**Best Supportive Care (no chemo)**

Median OS 2.5–4.5 months[1,2]

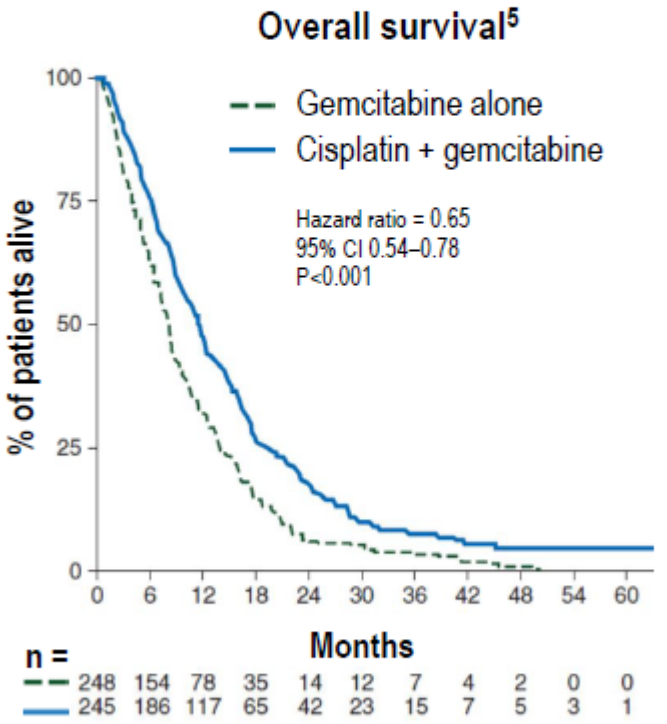
**Cisplatin and gemcitabine (CisGem) improves survival (over Gem alone)**

ABC-02 (n=410) OS 11.7 months[3]

BT-22 (n=84) OS 11.2 months[4]

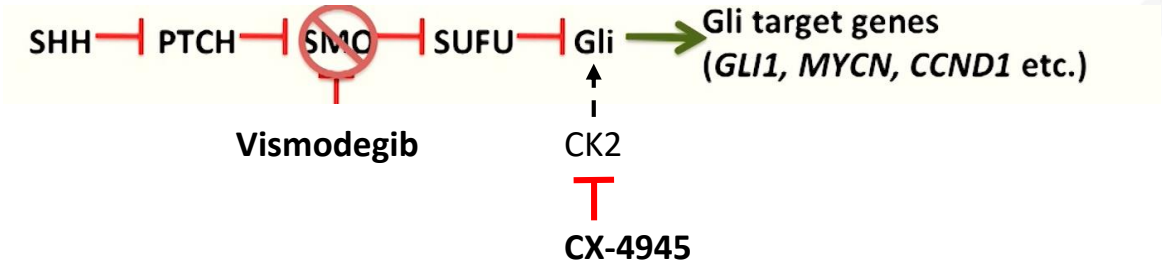
Meta-analysis OS 11.6 months[5]

**There is an urgent need to improve outcomes**




1. Glimelius Ann Oncol 1996;7(6):593–600.; 2. Sharma A, *et al.*, J Clin Oncol 2010;28(30):4581–6; 3. Valle JW, *et al.*, N Engl J Med 2010;362(14):1273–81; 4. Okusaka T, *et al.*, Br J Cancer 2010;103(4):469–74; 5. Valle JW, *et al.*, Ann Oncol 2014;25(2):391–8. By permission of Oxford University Press on behalf of the European Society for Medical Oncology.

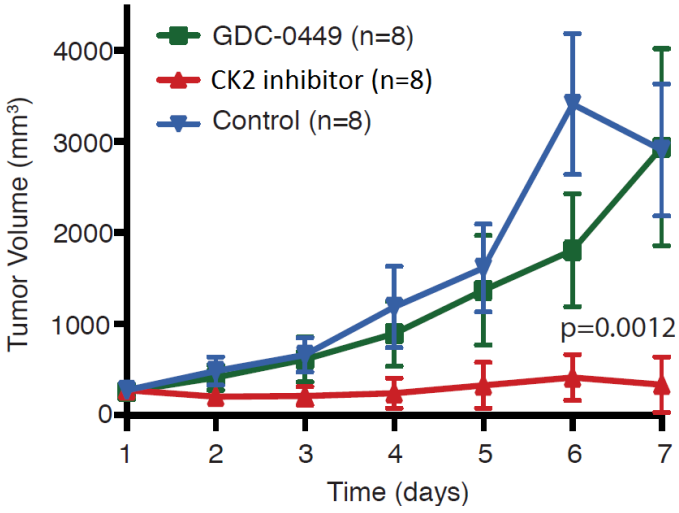
# CK2 regulates the activity of downstream proteins in the Hedgehog Pathway




- 85% of all SMO-treated BCC patients harbor SMO mutations post-treatment
- SMOi-resistant tumors maintain a high level of Gli expression
- **CX-4945 is a candidate in rescuing Hedgehog Pathway-driven cancers resistant to SMO inhibitor by targeting the terminal end of the Hedgehog pathway**
- SMO inhibitors bring significant tolerability challenges for patients on chronic administration, presenting a subsequent replacement opportunity for CX-4945

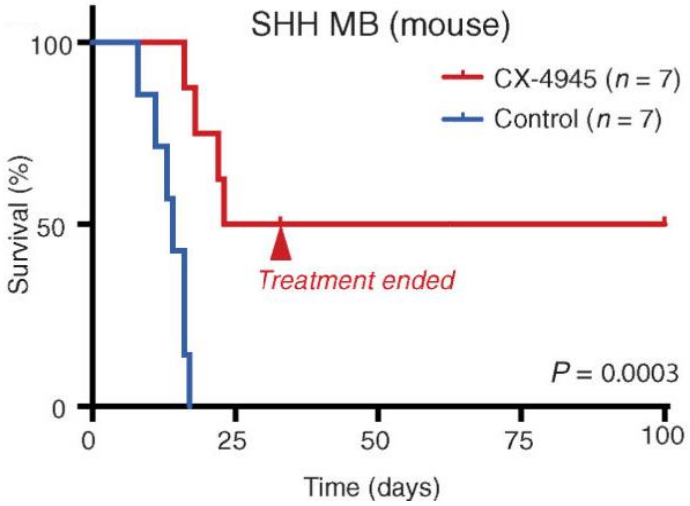
# Preclinical Efficacy of CX-4945 in an SMO inhibitor resistant mouse model of medulloblastoma

## Response where Vismodegib resistant




Shh Medulloblastoma mouse allograft with confirmed ***SmoD477G*** mutation.

## Response translates to prolonged survival




Kaplan-Meier survival analysis of n=7 per arm mice with Ptch+/−;Tpr53−/−;SmoD477G MB cerebellar allografts treated with CX-4945 or DMSO control.

***This data brought about the PBTC collaboration in medulloblastoma in May 2018.***

Source: Developmental phosphoproteomics identifies the kinase CK2 as a driver of Hedgehog signaling and a therapeutic target in medulloblastoma; Purzner et al - Sci Signal. ; 11(547):

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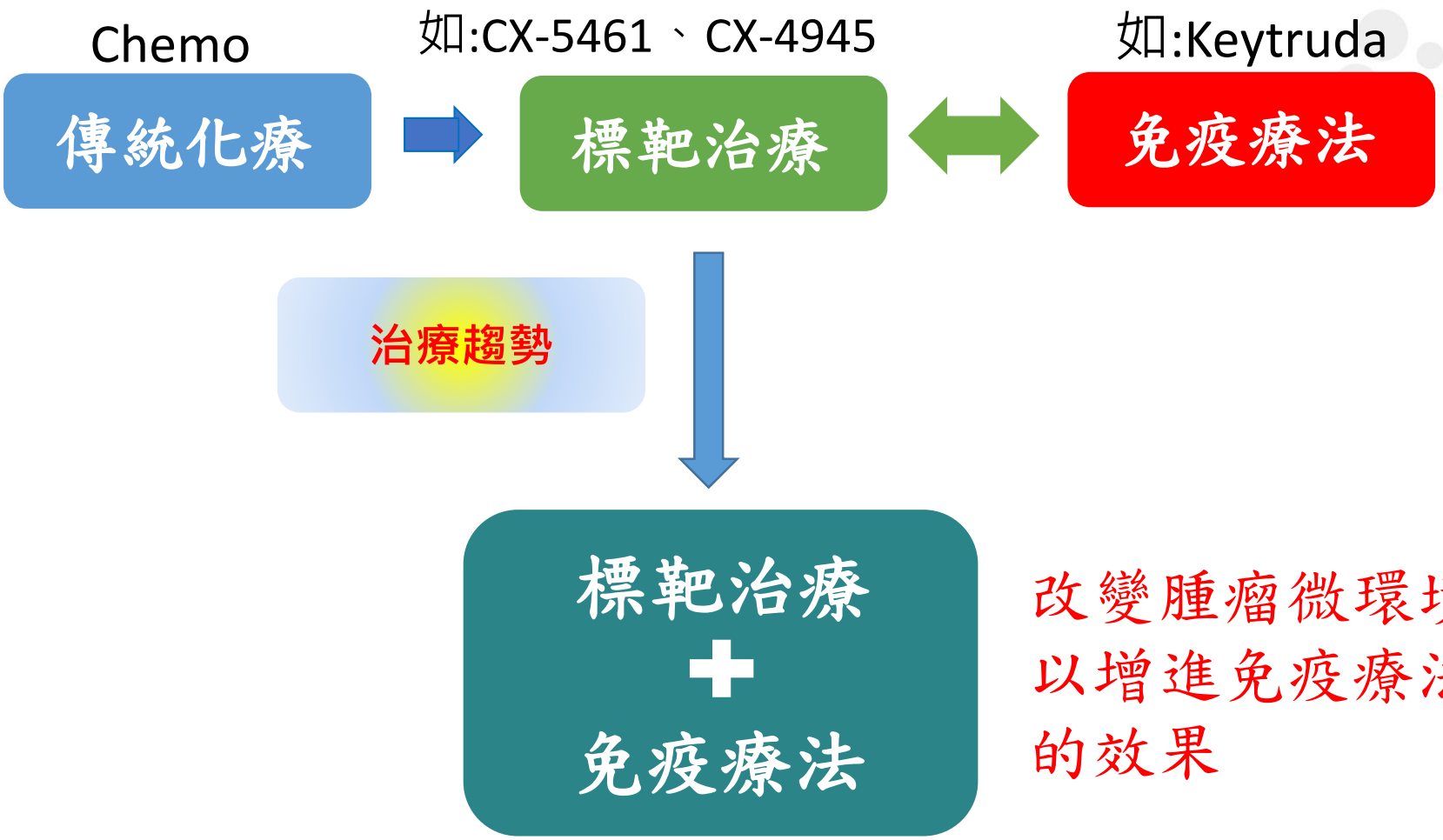
# 抗癌藥物的發展趨勢



# KOL Perspective

## PARP Inhibitor Resistance

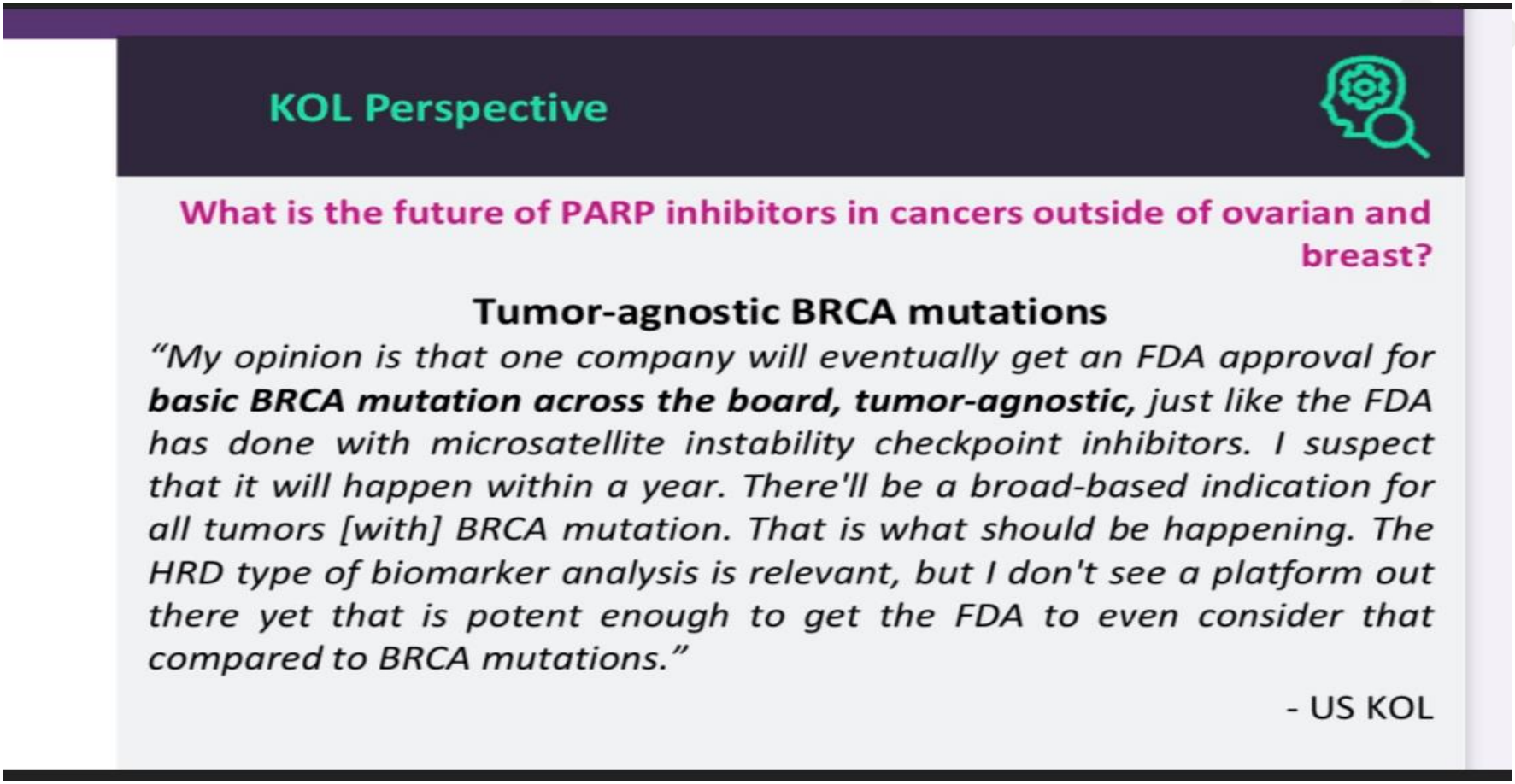
### Acquired Resistance Is a Key Factor in Treatment Failure

*"**Resistance is a big issue**, but this issue ultimately develops to all cancer drugs. I'm not aware of any particular methods to combat resistance, other than using different drugs or different PARPs. I don't know that anyone's been able to suggest one's better than the other or the newer ones are better than the older PARP inhibitors."*

US KOL

Sources: GlobalData

# KOL Perspective




Sources: GlobalData

# 標靶藥已進入高藥價時代

Forbes Billionaires Innovation Leadership Money Consumer Industry Lifesty



27,736 views | Nov 26, 2018, 08:45pm

## Loxo And Bayer's Amazing Drug Has An Expensive Price

**Matthew Herper** Forbes Staff
Healthcare
*I covered science and medicine, and believe this is biology's century.*

Forbes Billionaires Innovation Leadership Money Consumer Industry

cost of $32,800 a month for a 30-day supply of 100 milligram capsules. That's $393,600 annually. A liquid oral formulation for some children and adults will cost $11,000 a month for certain pediatric patients, Bayer says. This is not, Bayer insists, what patients will pay. The company says monthly out-of-pocket costs for the majority of patients will be $20 or less. "Bayer will ensure that no eligible patient with TRK fusion cancer will go without this highly effective therapy," the company said in a statement.

The company will help patients pay expensive co-pays, and will provide Vitrakvi for free while insurance details are worked out. If a patient can't afford the medicine, a charity funded by Bayer will provide the drug at no cost. The drug firm promises that if patients don't show a clinical benefit in the first three months of treatment, it will refund the money spent by insurers or government payers.

One reason the drug is so expensive: Patients who will benefit are rare. Bayer estimates 2,500 to 3,000 patients in the U.S. develop cancer due to a TRK fusion each year. What's more, these mutations are found only if doctors look for them by sequencing the DNA of tumors, a test that many patients still do not get, which means that building a market could be an expensive and arduous process. Drugs for rare diseases are often this expensive, and if they weren't, they probably wouldn't be developed.

Loxo的新藥上市，30天份藥價為美金$ 32,800、換算每年為$393,600！

Review article | Open Access | Published: 14 May 2018

Significance and implications of FDA approval of pembrolizumab for biomarker-defined disease

# “Tissue Agnostic” 將成為腫瘤藥物發展的新趨勢

## The Pipeline of Tissue-agnostic Cancer Treatments

| Tissue-agnostic Cancer Therapeutic | Indication | Status |
|---|---|---|
| Pembrolizumab (Keytruda) | Adult and pediatric patients with unresectable or metastatic solid tumors with MSI-H or dMMR | Approved by the FDA in May 2017 FDA APPROVED |
| Larotrectinib | Adult and pediatric patients with locally advanced or metastatic solid tumors harboring NTRK gene fusions | The FDA granted priority review in May 2018 and has set a target action date of Nov. 26, 2018 |
| Loxo-195 | Patients with TRK fusion–positive solid tumors | Drug under development; early clinical data available |
| Entrectinib | Pediatric and adult patients with recurrent or refractory extracranial solid tumors harboring NTRK1/2/3, ROS1, or ALK gene fusions | Drug under development; Phase I clinical data available |
| BLU-667 | Solid tumors with RET alterations | Drug under development; Phase I clinical data available |
| Loxo-292 | Solid tumors with RET alterations | The FDA granted breakthrough therapy designation on Sept. 5, 2018 |
| Anti-ERBB3 antibody | Solid tumors with NRG1-rearranged cancers | Preliminary clinical proof-of-principle data published |

Several other tissue-agnostic therapeutics, not listed here, are under investigation


AACR American Association for Cancer Research®

**Tissue Agnostic臨床試驗優點**

- 只要有可預測性的biomarker臨床結果，可加速新藥的上市!
- 以致病基因為導向，不分患病部位，可一次核准跨腫瘤類別的多項適應症!

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# 5年資產負債表

| NT$ Million | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 Q3 |
|---|---|---|---|---|---|---|
| **TOTAL ASSETS** | **918** | **746** | **532** | **1,626** | **1,246** | **941** |
| Cash | 839 | 734 | 514 | 1,601 | 1,229 | 916 |
| NR&AR | 3 | 3 | 1 | 1 | 1 | 1 |
| Inventory | - | - | - | - | - | - |
| Fixed Asset | 2 | 1 | 2 | 6 | 4 | 10 |
| **TOTAL LIABILITIES** | **14** | **16** | **21** | **58** | **37** | **35** |
| Bank Loans | - | - | - | - | - | - |
| NP & AP | 13 | 13 | 21 | 58 | 36 | 26 |
| **TOTAL EQUITY** | **904** | **731** | **512** | **1,568** | **1,209** | **906** |

| YoY(%) | | | | | |
|---|---|---|---|---|---|
| 2014 | 2015 | 2016 | 2017 | 2018 | 2019 Q3 |
| **11** | **(19)** | **(29)** | **205** | (23) | **(25)** |
| 11 | (13) | (30) | 212 | (23) | (25) |
| 63 | (3) | (50) | (1) | (26) | (46) |
| - | - | - | - | - | - |
| - | (24) | 33 | 200 | (33) | 150 |
| **(6)** | **15** | **34** | **178** | (36) | **(5)** |
| - | - | - | - | - | - |
| 17 | (4) | 62 | 178 | (38) | (28) |
| **11** | **(19)** | **(30)** | **206** | (23) | **(25)** |

# 5年損益表

| NT$ Million | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 Q3 | YoY(%) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 Q3 |
| Sales Revenue | 24 | - | 0 | - | 1 | 1 | (10) | (100) | - | (100) | 100 | (73) |
| Gross Profit | 0 | - | 0 | - | 1 | 1 | (107) | (100) | - | (100) | 100 | (32) |
| Operating Profit | (165) | (201) | (258) | (375) | (387) | (315) | 42 | 22 | 28 | 45 | 3 | (19) |
| Income before Tax | (157) | (191) | (254) | (371) | (378) | (313) | 39 | 22 | 33 | 46 | 2 | (17) |
| Net Income to Parent | (157) | (194) | (255) | (372) | (376) | (312) | 39 | 24 | 31 | 46 | 1 | (17) |
| EPS(NT$) | (2.48) | (2.96) | (3.89) | (5.18) | (5.05) | (4.20) | (4) | 19 | 31 | 33 | 3 | (17) |

Senhwa
BIOSCIENCES

www.senhwabio.com

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