股號:6492

生華生物科技股份有限公司

次世代DDR與HH癌症新藥

Bringing Hope to Life

日期: 2019年6月20日

Senhwa Biosciences

Next Generation DDR/HH Pathway Therapeutics

TPEx Ticker : 6492

- **Headquarter:** TPE, TW
- **Subsidiary:** San Diego, USA
- **Shares:** **74.5** Million
- **Mkt Cap: US$ 168** MM (2019/06/10)

A clinical-stage pharmaceutical company focused on developing *First in Class, Next Generation DDR and HH Pathway* therapeutics for patients with unmet medical needs in oncology.

Strong experienced management team with a proven track record of successes.

Lead compounds CX-4945 and CX-5461, each designed with a unique Mechanism of Action (MOA) have potential as a monotherapy or combination with marketed regimens.

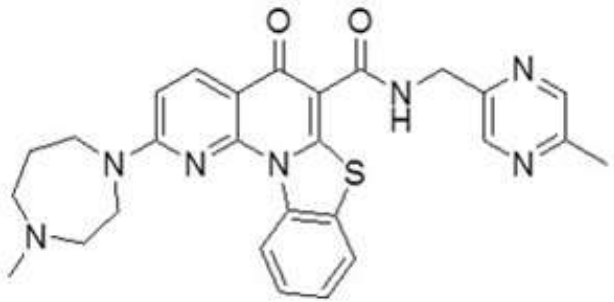
Collaboration with world class research institutions(CCTG,PMCC, PBTC) and awarded premier science recognitions including SU2C/CBCF and CTEP(NIH-NCI).

Product pipeline

Program	Indication	Phase I	Expansion Cohorts/ Phase II	Pivotal Trial	Approval	Partner
CX-5461 	Breast Cancer	CA				CCTG
	Ovarian cancer		CA/USA			
	Pancreatic cancer		CA/USA			
	Hematologic Malignancies	AUS				PMCC
CX-4945 	Cholangio-carcinoma	USA, KR, TW				
	Basal Cell Carcinoma		USA			
	Medulloblastoma		USA			PBTC

CX-5461

(First-in-class)

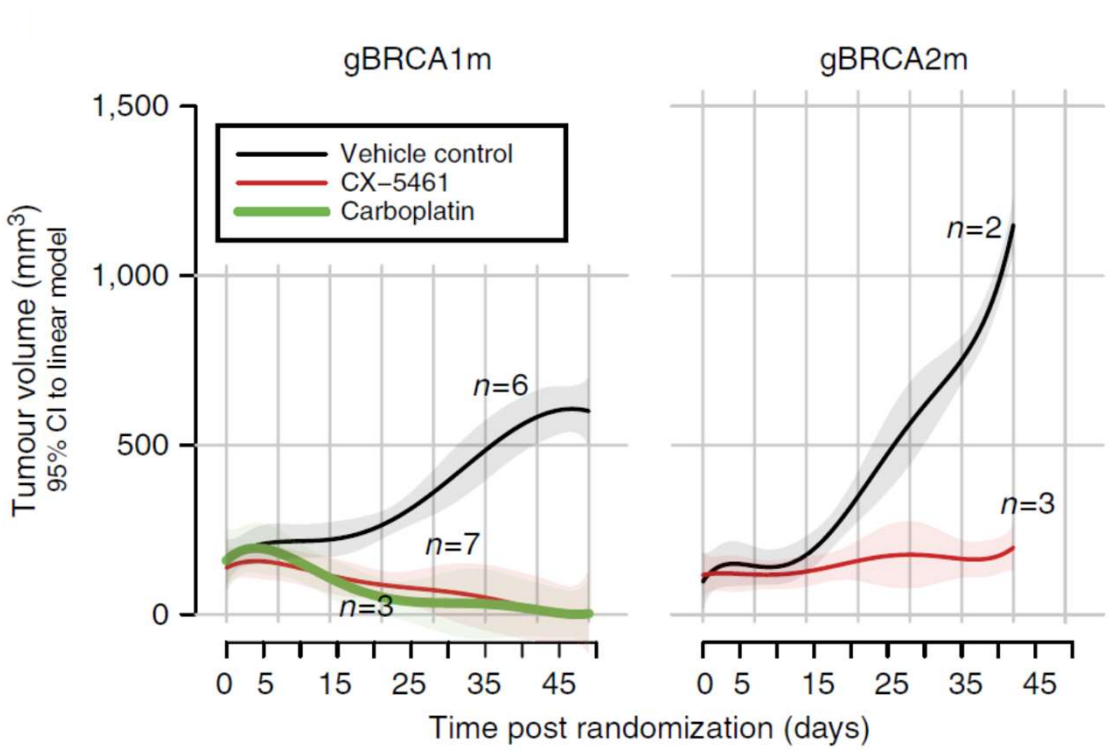


CX-5461 CA Phase I Results

- Small molecule G4 (G-quadruplex) stabilizer
  - *New target for DNA damage repair disruption*
- MAD(Maximum Administered Dose) has been reached at Dose level 9.
- All patients enrolled in the Phase I study had reached the end of the line in terms of treatment. These patients have no other available treatments.
- Phase I results show preliminary safety, tolerability data and anti-tumor activity in specific genes mutant solid tumors.
- The tumor responses lean heavily in patients harboring specific genes mutation. The response to CX-5461 is deep and with long duration.
- Tumor response data still needs time to mature before the final report is released.
- Phase 1 expansion to enroll patients with specific gene deficiency in breast cancer is on-going. Multiple expansion cohorts to test other indications are in planning.

CX-5461 is effective in treating platinum-resistant TNBC PDX

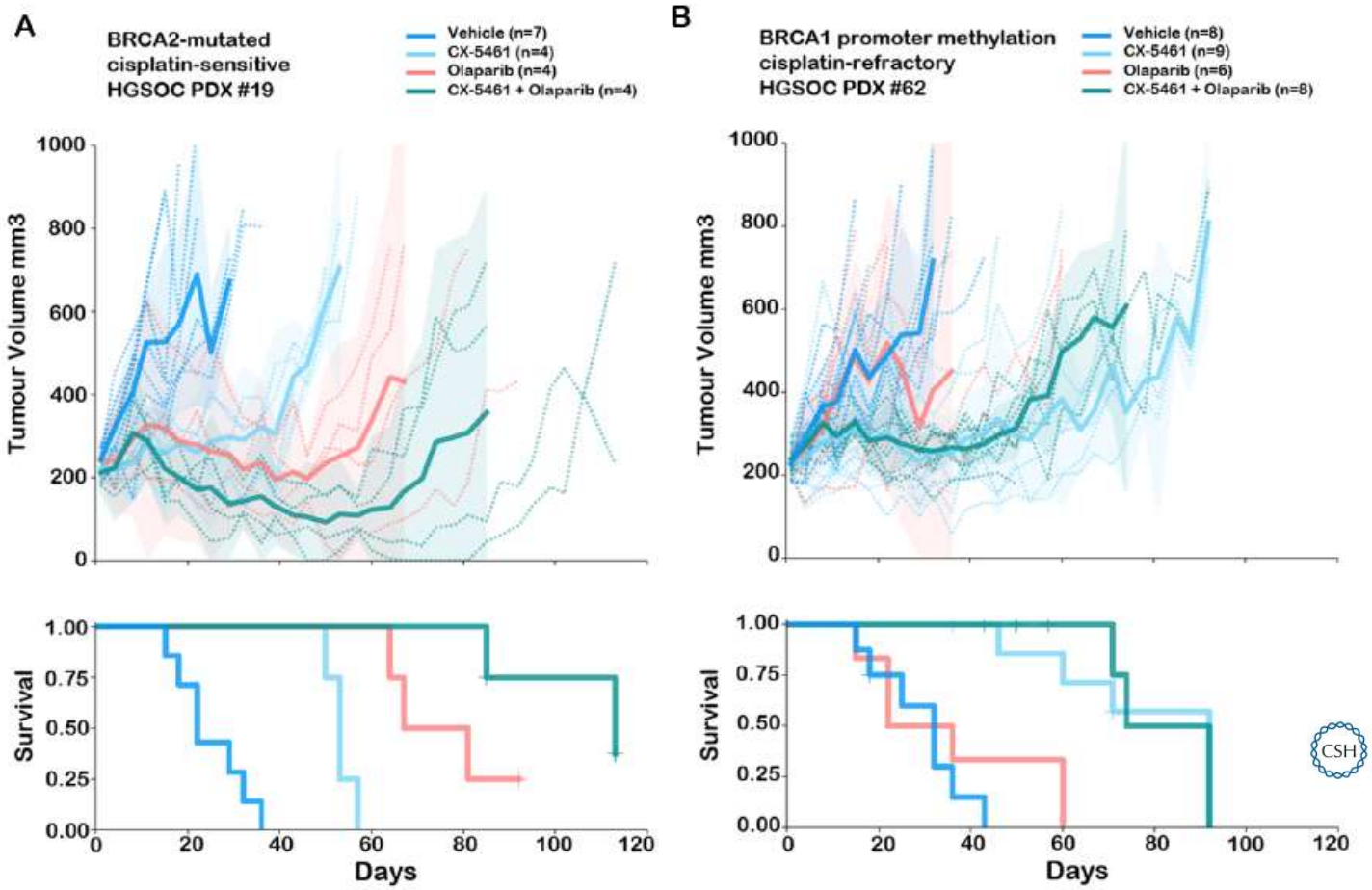
- Cisplatin-sensitive TNBC PDX CFIBNB02
- Cisplatin-resistant TNBC PDX CFIB-70620



Nature Comm. 2017 8:14432

•CX-5461 can benefit the efficacy of Olaparib in BRCA2-mutated *Ovarian PDX*

•*CX-5461 is effective in treating platinum-resistant Ovarian PDX*

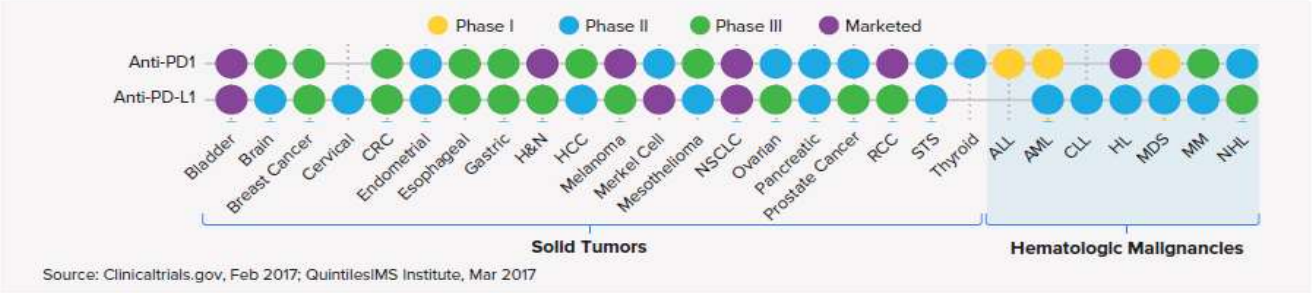


DDR drugdeal

AZ /Merck	Tesaro/Tekeda	Tesaro/GSK
Lynparza (olaparib)	Zejula (niraparib) (僅授權東北亞)	Zejula (niraparib)
• Global co-develop/market rights • **Deal Size US$ 8.5Bn** • Upfront US$ 1.6Bn • License options US$ 750m • Milestone US$ 6.15Bn • Gross profit shared equally	• Regional Licensing including Japan, S. Korea, Taiwan, Russian and Australia . • **Deal Size US$ 241m** • Upfront US$ 1m • Millstone US$ 240m • Royalty 15%~30%	• **Buyout** • **Deal Size US$ 5.1Bn (Cash)** BUYOUT
2017/7/26	2017/7/27	2018/12/3

PD1/PD-L1 inhibitors : USD40 Bn market across all tumor types

Chart 12: Next Generation Immuno-Oncology MoAs in Development



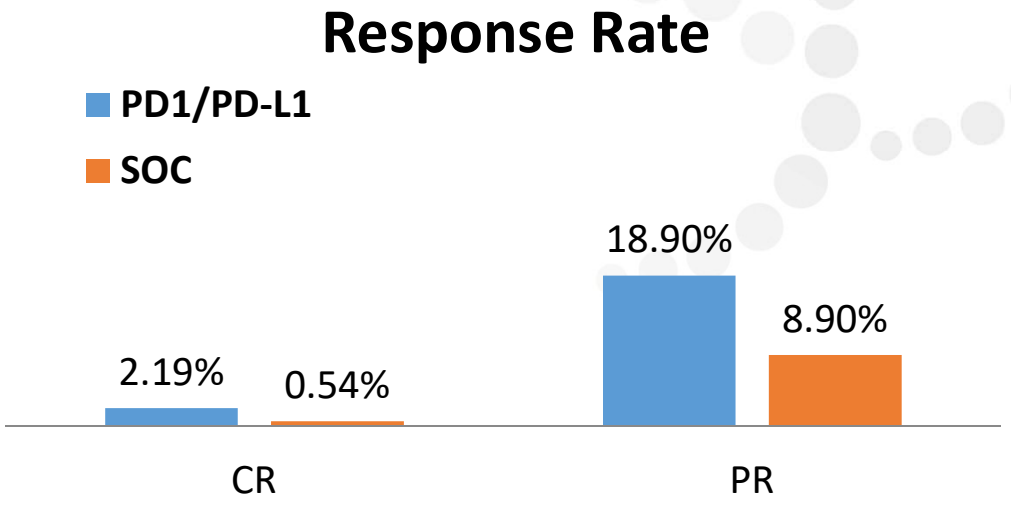
Source: Clinicaltrials.gov, Feb 2017; QuintilesIMS Institute, Mar 2017

Class	US, Millions	廠商	US approvol	2016	2017	2018	2019E	2020E	2021E	2022E	2023E	2024E
PD-1	Nivolumab (Opdivo)	BMY	2014	3,774	4,948	6,735	6,957	7,421	8,283	9,051	9,854	10,538
PD-1	Pembrolizumab (Keytruda)	Merck	2014	1,402	3,809	7,171	9,522	11,447	13,046	14,380	15,524	16,754
PD-1	LIBTAYO (cemiplimab)	Regeneron	2018			15	190	382	542	667	829	983
PD-L1	Atezolizumab (Tecentriq)	Roche	2016	157	487	772	1,632	2,599	3,287	3,748	4,300	4,826
PD-L1	Durvalumab (Imfinzi)	AstraZeneca	2017		19	633	1,332	2,106	2,688	3,120	3,362	3,603
PD-L1	Bavencio (avelumab)	Pfizer	2017			71	244	449	636	793	969	1,114
SUM				5,333	9,263	15,397	19,877	24,404	28,482	31,759	34,838	37,818

Source: GlobalData.

僅有2成的病患對PD-1抗體有療效，其餘8成的病患仍屬unmet medical need

Oncotarget, 2018, Vol. 9, (No. 9), pp: 8706-8715



Best overall response	Nivolumab, No.	Median OS, months	(95% CI)	Do
Patients with squamous NSCLC (CheckMate 017)				
Overall	135	9.2	(7.3 to 12.6)	
Complete/partial response*	27	NR	(30.5 to NR)	
Stable disease	39	11.9	(9.2 to 17.1)	
Progressive disease	56	4.9	(4.2 to 5.7)	

對PD-1 抗體有反應的2成病患，存活時間比其他病患或者化療病患多活兩年以上

Mechanisms by which DNA damaging agents affect the immunogenicity of tumours

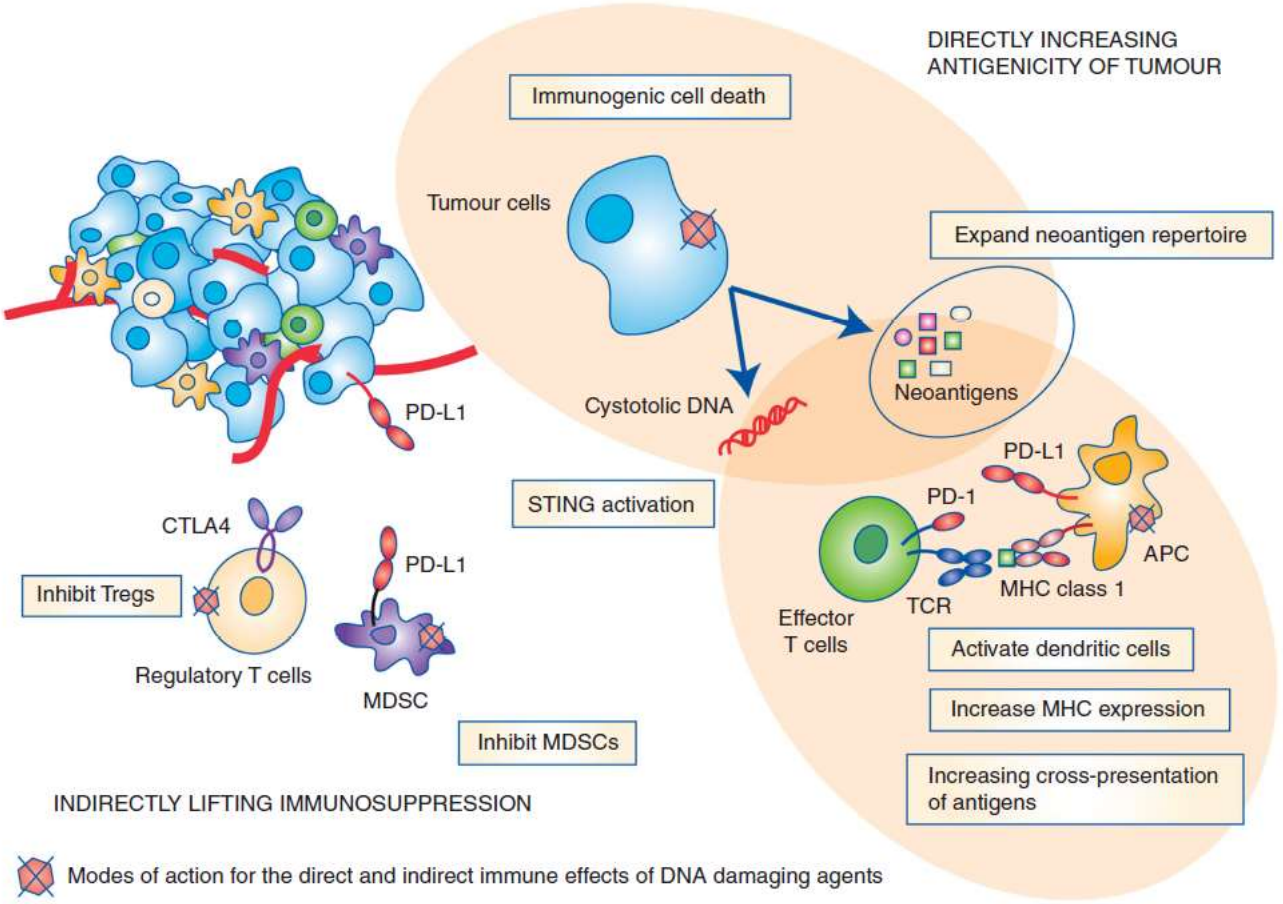
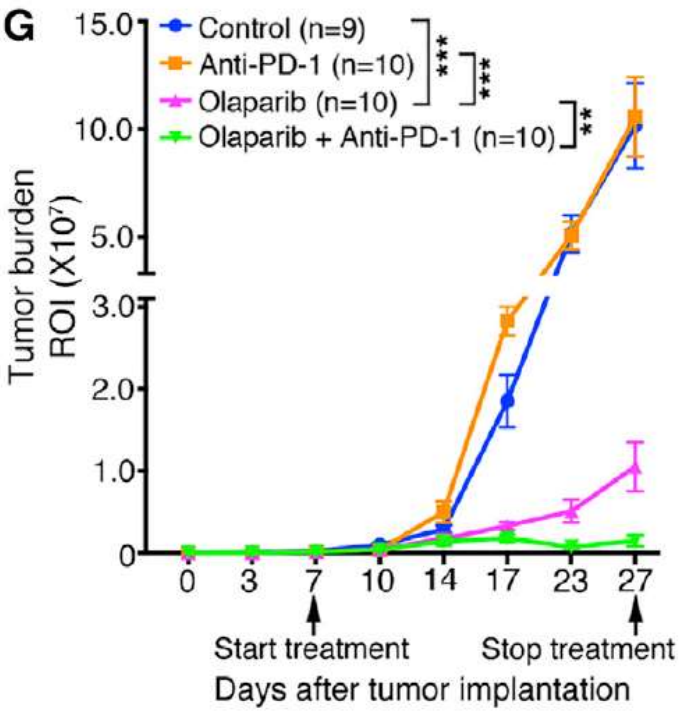


Figure 1. Mechanisms by which DNA damaging agents affect the immunogenicity of tumours. See text for details.

PD-1 Combo Olaparib is only effective in BRCA muation cancer cells

BRCAm



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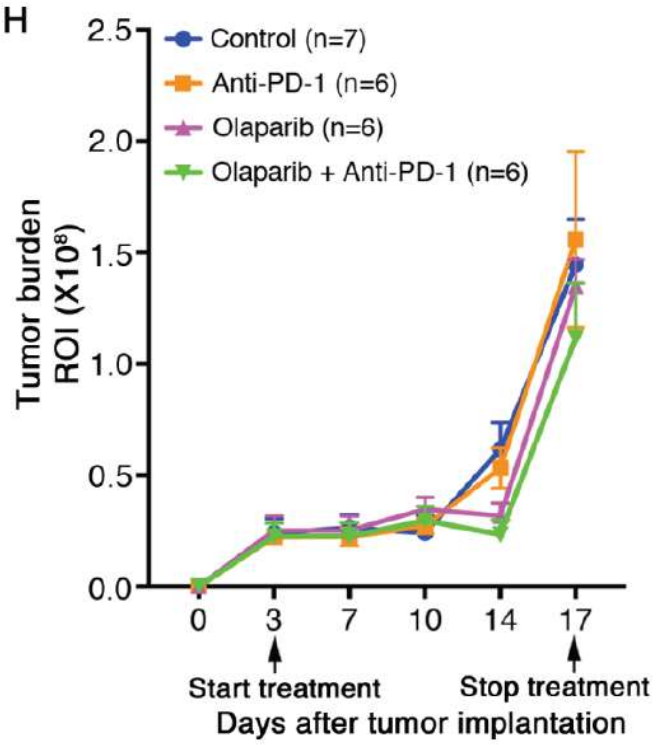
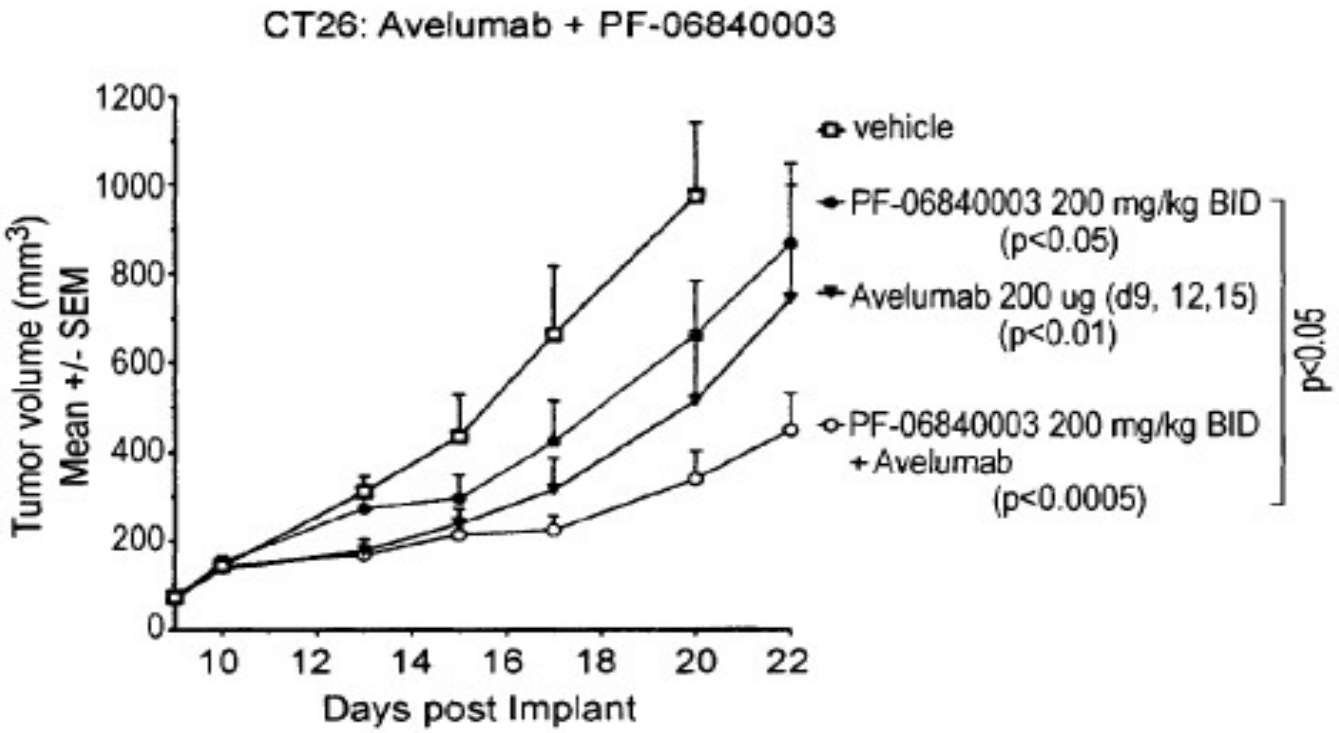


IDO1 inhibitor combo with anti-PD-L1

FIG. 5A

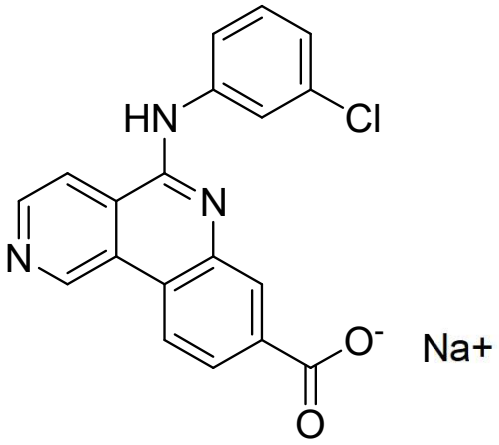


PD-1 combination drug deal

發生日期	藥品名稱	機制	買方	賣方	Upfront	Milestone	Royalty	交易時臨床階段
2018/2/14	NKTR-214	CD122-biased agonist	BMS	Nektar	1.85bn	1.8bn	65% Profit	Phase 1/2
2016/7/19	JTX-2011	anti-ICOS	Celgene	Jounce	225m	2.3bn	mid-teen	phase 2
2014/11/24	FPA008	anti-CSF1R	BMS	Five Prime	350m	1.4bn	double-digit	phase 1
2014/10/20	NLG919	IDO inhibitor	Roche	Newlink	150m	1bn	double-digit	phase 1
2018/4/4	OSE-172	anti-SIRP-alpha	Boehringer Ingelheim	OSE	18m	1.4bn	無揭露	Preclinical
2015/3/30	ADUS-100	STING agonist	Norvatis	Aduro	225m	0.5bn	mid-teen	Preclinical
2017/8/3	STING and NLRP3 agonist	STING and NLRP3 agonist	BMS	IFM	300m	1bn	無	Preclinical

CX-4945

(First-in-class)



Senhwa BIOSCIENCES

CX-4945 CCA Phase I Results

- Small molecule CK2 (Casein Kinase 2) inhibitor
  - *Hedgehog pathway inhibition via Gli (downstream of SMO)*
  - *CK2 also impacts immunomodulation via T Cell proliferation*

Data compiled in this slide deck is not final; verification through onsite monitoring and data cleaning activities are still ongoing. There is no planned interim analysis so only the CSR should be used for regulatory authority review or publication.

CX-4945 combo-Cholangiocarcinoma

	Median OS Time	OS Post Progression
Gemcitabine＋Cisplatin	11.7month	3.6~4.4
CX-4945 +Gemcitabine+Cisplatin	• Significantly prolonged the lives of patients. • Among the evaluable patients the median duration of PFS and OS are significantly better than patients who received SOC.	

*Pts still under monitor.

Resource: Cisplatin plus Gemcitabine versus Gemcitabine for Biliary Tract Cancer *N Engl J Med* 2010; 362:1273-1281

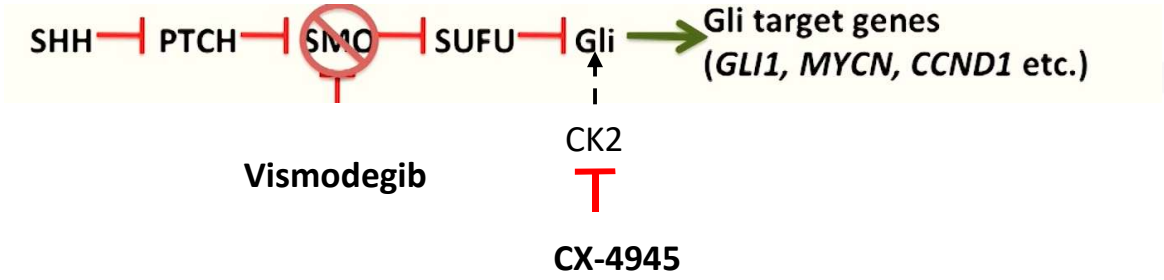
Current unmet medical need
Cholangiocarcinoma（膽管癌）

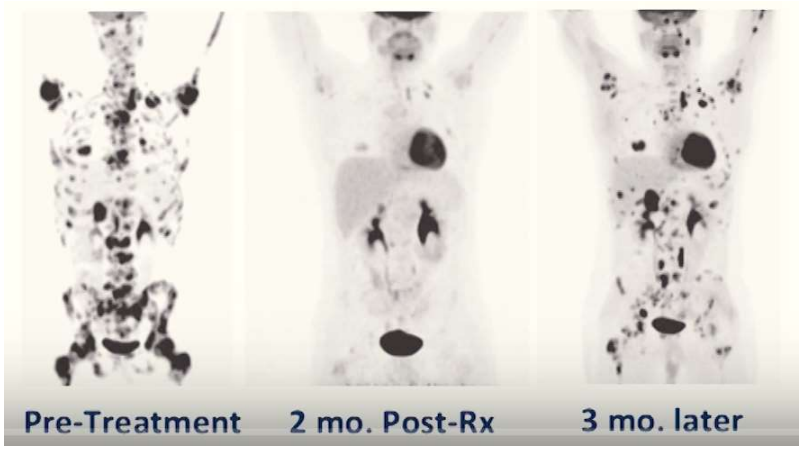
- Standard of Care (SOC): Gemcitabine and Cisplatin
- Median progression-free survival (mPFS): **8.0 months**
- Median overall survival (mOS): **11.7 months**

Valle J, Wasan H, Palmer DH, et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med 2010; 362:1273-1281

CX-4945: A Rescue Medicine for SHH-driven cancer

SMO inhibition vs. CK2 inhibition





After 3 months of Vismodegib in Medulloblastoma

- 69-77% SMO-treated BCC patients harbor SMO mutations post-treatment [1]
- SMOi-resistant tumor lacking SMO mutation maintain high level *Gli* expression [1]
- Some SMOi-resistance may be due to mutations downstream of SMO [1]
- CX-4945 is a candidate in rescuing SHH-driven cancer

資料來源 Dr. Teresa Purzner, Stanford University

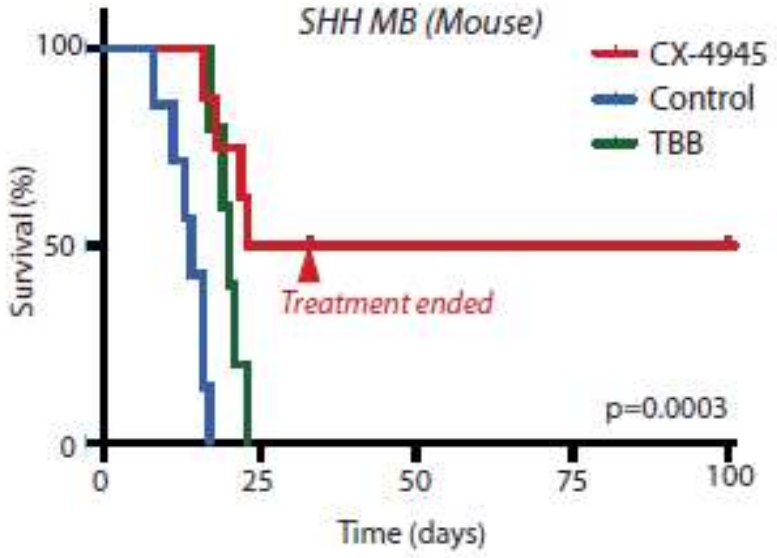
CX-4945 Potential in Medulloblastoma

Trial Design: Blinding and randomization, SMO resistant mice.

The Result:

1. Control group mortality @100% after 17 days vs. CK2i group 50% survival up to 100th day after treatment stopped at day 30th.
2. Mouse sacrificed discovered “Zero” tumor cell in tissue.
3. Rest CK2i treated mice continued surviving to 12m surpassing Vismodegib recurrent time @ appx 3m(100days).

CX-4945–One of the most potent treatment of MB brought about the collaboration of PBTC vs. Senhwa on 2018, 05.23.



PhI/II expected at 2019H1.

資料來源 Dr. Teresa Purzner, Stanford University

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www.senhwabio.com

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