股號:6492

生華生物科技股份有限公司

次世代DDR與HH/IO抗癌與抗病毒新藥

法人說明會

宋台生 總經理

日期: 2020年12月01日

免責聲明

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公司概況

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未來展望

生華生物科技

次世代DDR與HH癌症與抗病毒新藥開發

股票代號: 6492TT

- 總部: 台灣新北市
- 臨床業務總部: 美國聖地牙哥
- 股本: 台幣8.97億元
- 市值: 台幣211億元(11/05/20)

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).

Current Pipeline

Program	Indication	Phase I / Expansion	Phase II	Pivotal Trial	Approval	Sponsor/ Funded
Pidnarulex (CX-5461) 	Breast Cancer	CA				SU2C/CBCF*
	Breast Cancer/ Ovarian/ Prostate/ Other Solid Tumors	CA/USA				
	Haem Cancer	AU				NHMRC/ CCV /PMCC**
	Prostate Cancer (Combination studies with PARPi)	AU				PCF/Pfizer***
Silmitasertib (CX-4945) 	**Cholangio-carcinoma**	USA, KR, TW				
	Basal Cell Carcinoma	USA				
	Medullo-blastoma	USA				NIH/CTEP****
	COVID-19		USA (IIT)			

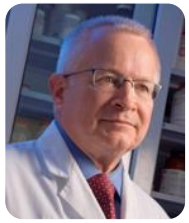
* Stand Up To Cancer Grant Winner of 2016. SU2C funded phase I study conducted by Canadian Clinical Trial Groups (CCTG). Also funded by Canadian Breast Cancer Foundation (CBCF).

** Supported by the National Health and Medical Research Council (NHMRC) of Australia Development grant, Cancer Council Victoria (CCV) grants-in-aid and the Peter MacCallum Cancer Foundation.

***2019 The Prostate Cancer Foundation (PCF)-Pfizer Global Challenge Awards.

**** Fully funded by NIH/CTEP and conducted by Pediatric Brain Tumor Consortium (PBTC).

臨床醫學團隊



Daniel D. Von Hoff, M.D., FACP.

- Physician in Chief and Director of Translational Research at Translational Genomics Research Institute (TGen)
- Professor of Medicine, Mayo Clinic
- Chief Scientific Officer, VGPCC Clinical Trails Program at Scottsdale Healthcare

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- Ex Director of Office of Generic Drugs (OGD), US FDA
- Senior advisor, Cornerstone Intellectual Property Foundation
- President & CEO, GloboAsia LLC
- Professor of NTU, NYMU and NCCU

John Soong, M.D., FCAP

Chief Medical Officer, US Office

- Fellow of the College of American Pathologists (FCAP)
- In charge of clinical trial design, medical writing and supervise clinical programs

Olga Titova, M.D., SPM

- 19 years experience as Clinical Medical Monitor at Syneos

Mohamed Elgendy, M.D., SCA

- 10 years experience as Senior Clinical Manager at Syneos

Emmet Tse, Pham.D., SPM

- 16 years experience in oncology at Pfizer

Santhosh Karunakaran, Ph.D., Associate Director , US Office

- Regulatory Affairs

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Thomas Malefyt, Ph.D.

- Ph.D., University of California, Santa Barbara
- CEP, DesErrata LLC
- VP, CMC Operations, Syntex Research
- In-depth knowledge of strategic and tactical CMC plans and regulatory for US FDA

Beverly M. Dixon

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- Over 2 decades of QA & regulatory experiences
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Bella Bleza, US Office

Jimmy Chen, Taiwan Office

Amy Lai, Taiwan Office

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CMC製備團隊與品質監控

Kimberly Barcega US Office

Howard Hu, Taiwan Office

Dennis Phung US Office

Stella Wu, Taiwan Office

國際權威機構認可贊助–降低burn rate

Pidnarulex (CX-5461)

Canadian Clinical Trial (NCIC)

- **SU2C Award**
- **breast cancer dream team**

Australia Clinical Trial (PMCC)

NHMRC's Research Grant

PCF-Pfizer Global Challenge Awards

Sponsor PARPi + Pidnarulex combination in prostate cancer

Grant funded by Canadian Ovarian Cancer Foundation.

- **Study led by PMH, Canada**

Silmitasertib (CX-4945)

Pediatric Brain Tumor Consortium (PBTC)

- The National Institutes of Health Grant

Banner Health

- **Phase II** IIT/ Expanded Access IND

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抗癌藥物的產業發展趨勢

Future

- Targeted Therapy + Targeted Therapy
- Targeted Therapy + Immunotherapy
- Biomarker driven precision anticancer drug

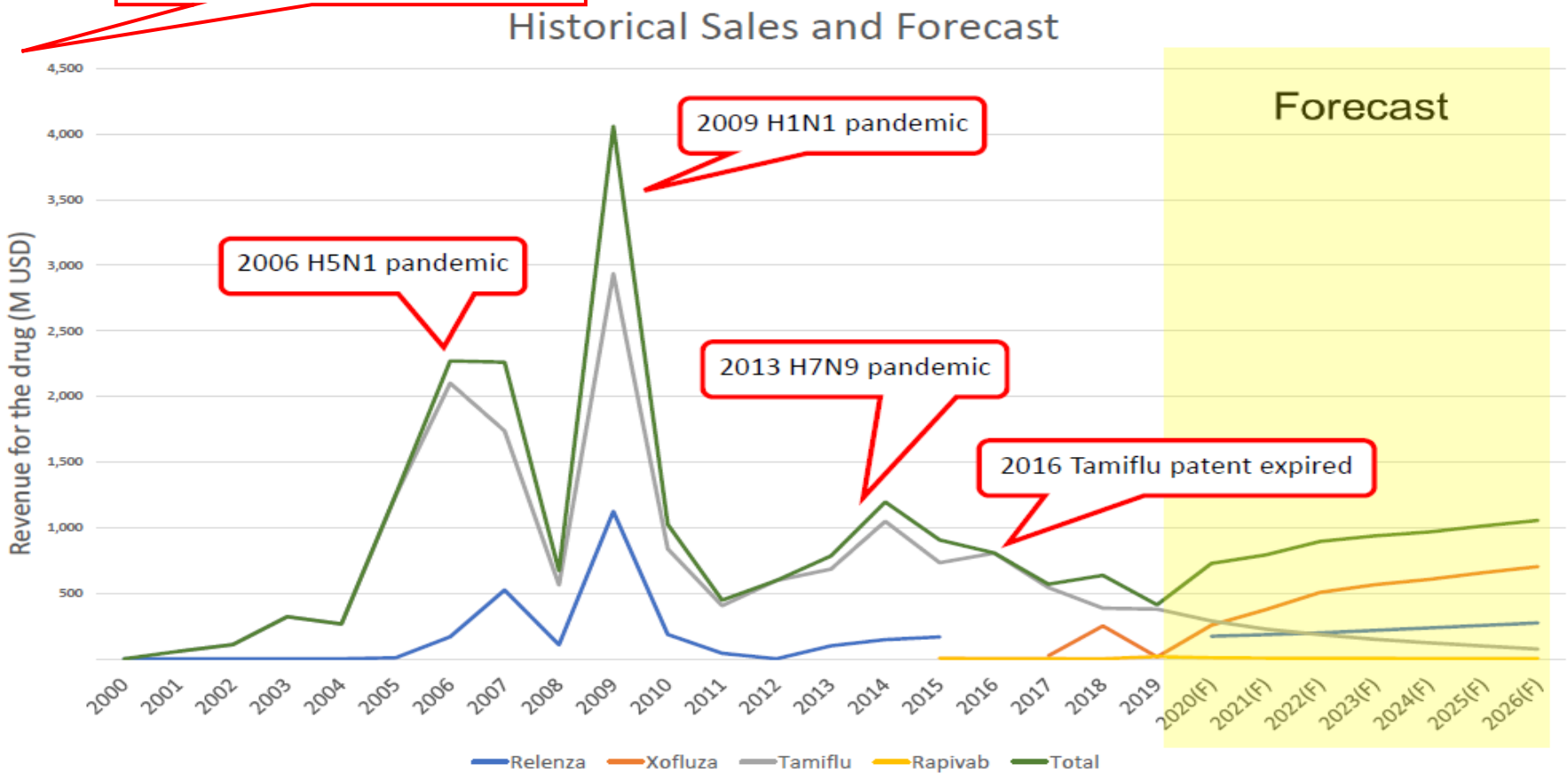
Biomarker driven targeted therapeutics to treat cancer

- Pidnarulex (CX5461) has identified specific biomarkers associated closely with tumor responses in phase I study.
- Now, we filed IND in both US and Canada on Nov 24, 2020, to initiate phase Ib expansion trial to further confirm:
  - Lower dose responses.
  - Cisplatin resistant vs sensitive patient responses.
  - Parp inhibitor resistant vs sensitive patient responses.
  - Results will lead to FDA approved tissue agnostic trials to facilitate biomarker driven approval for all tumors.

新冠疫苗雖現曙光 解封仍靠治療藥物

- Antiviral drugs are always in demand regardless of any vaccine in market.

1978 the first trivalent vaccine

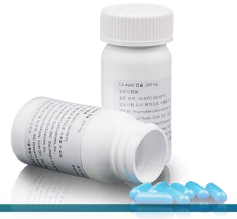


Antiviral drugs are in high demand today, regardless of vaccine development

1. Greater than 75% vaccination may achieve herd immunity. This is unlikely to achieve.
2. Vaccination may drive viral mutation.
3. FDA continues to grant EUA for new antibody drugs to be used in mild and moderate stage patients recently after the announcement of vaccines. There is no new drug for severe and hospitalized patients except Remdecivir, which is not recommended by WHO lately for a lack of benefit.
4. There is no oral anti covid19 drug available. We are developing oral drug to treat both moderate and severe stage patients.
5. Merck recently has just acquired two small biotech companies to treat Covid19, OncoImmune which has developed an antibody to reduce respiratory failure or death for 425 million dollars, and VelosBio for 2.75 Billion dollars. They are willing to bet on little known efficacy of covid19 treatments. Pharma knows clearly, drug is the key to end this covid pandemic, not by vaccine alone.

We still need a COVID treatment in the future for the following reasons

1. Immunosuppressed patients may not generate a strong enough immune response to the vaccine and may still be at risk of serious disease, necessitating future treatment.
2. The virus has already begun mutating which may lead to loss of vaccine efficacy over time.
3. Protective antibodies may decline in patients at differing rates over time and patients may not know they have lost Ab protection.
4. Different patient populations may respond differently to vaccines, leaving some at risk of developing severe disease. (similar concept as the first bullet)
5. We don't yet know if the vaccine produces sterilizing immunity (i.e. vaccines can't transmit infection) or whether it just prevents morbidity. If the latter, there will be continued spread of the virus and undoubtedly new cases, although at a lower rate.



Senhwa focuses in developing therapy for covid19

1. Developing an oral formulation drug to treat covid19 at moderate stage and severe stages.
2. Silmitasertib is a dual action drug, reduce viral replication and cytokine storm. This is the only drug to demonstrate its activities and widely reported worldwide.
3. First human data was proven its efficacy for severe patient under eIND in early September.
4. More clinical trials are underway to treat moderate and severe patients in parallel studies.
5. Silmitasertib is to treat virus through host directed approach, which will not be affected by new mutants or new virus sharing the same CK2 target to replicate.

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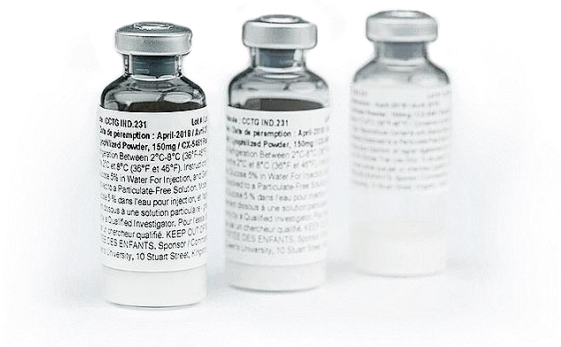
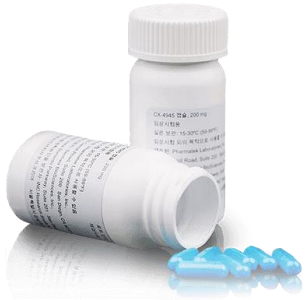
研發概況



(First-in-class G4 stabilizer)

Pidnarulex (CX-5461)

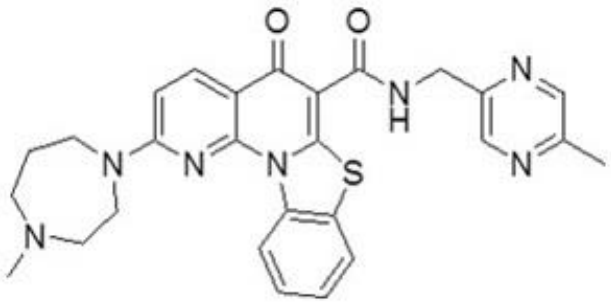


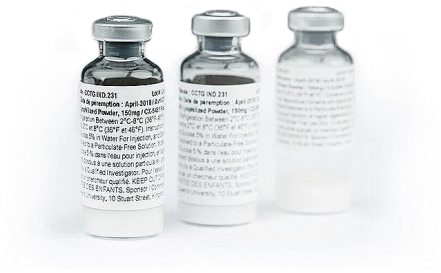
(First-in-class CK2 inhibitor)

Silmitasertib (CX-4945)

Pidnarulex (CX-5461)

(市場首見 G4 stabilizer)





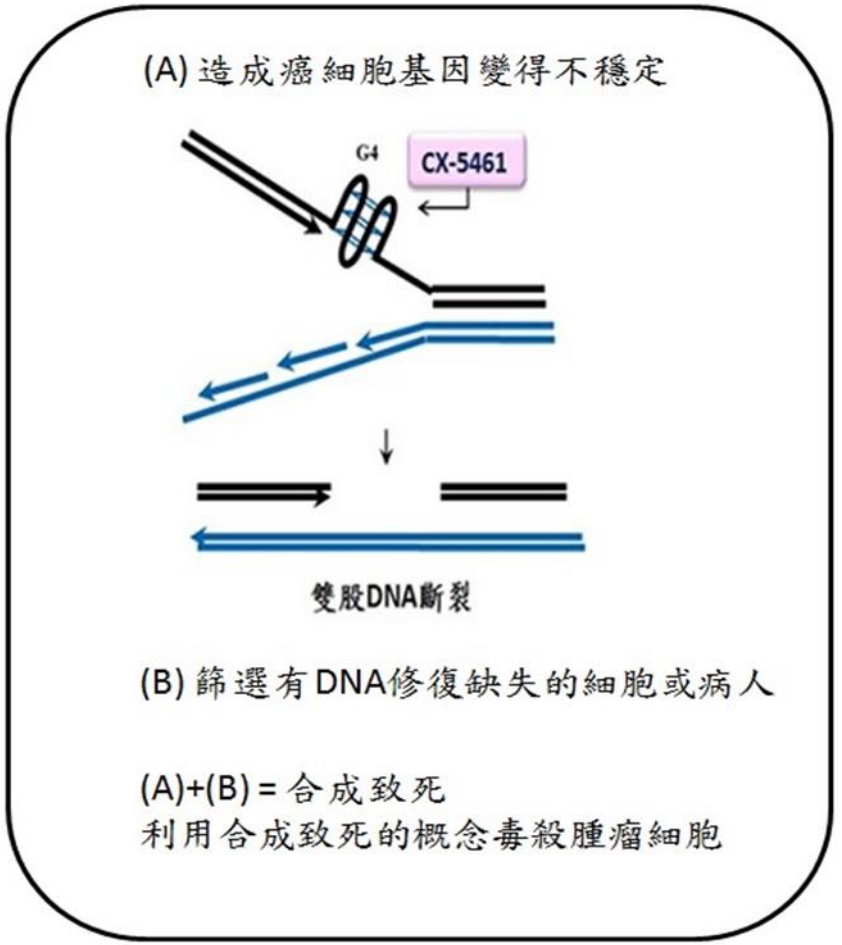
- Confirmed human efficacy
- Cisplatin resistant tumor
- PARP inhibitor resistant tumor
- Combination Potential
- High recognition worldwide, received grants from SU2C, CBCF, PMCC, PCF, COVF, etc.
- Pfizer grant to explore combination potential

Pidnarulex (CX-5461)次世代 DDR藥物

Next Generation DDR, new targeted therapy is essential to change medical practice

瞄準G-四聯體(G4) 結構

- G-四聯體 (G4) 穩定劑 –造成複製叉停滯，使得癌細胞的基因組出現不穩定性，進而產生DNA斷裂
- 若搭配篩選具有DNA修復缺陷(BRCA或HR突變) 的病人，會使得受損的DNA比較不容易被修復，**Pidnarulex (CX-5461)** 即是利用此合成致死(synthetic lethality)的概念(A+B)，促使癌細胞死亡



Pidnarulex (CX-5461)機制

Phase I 臨床試驗觀察到的療效

Author List

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

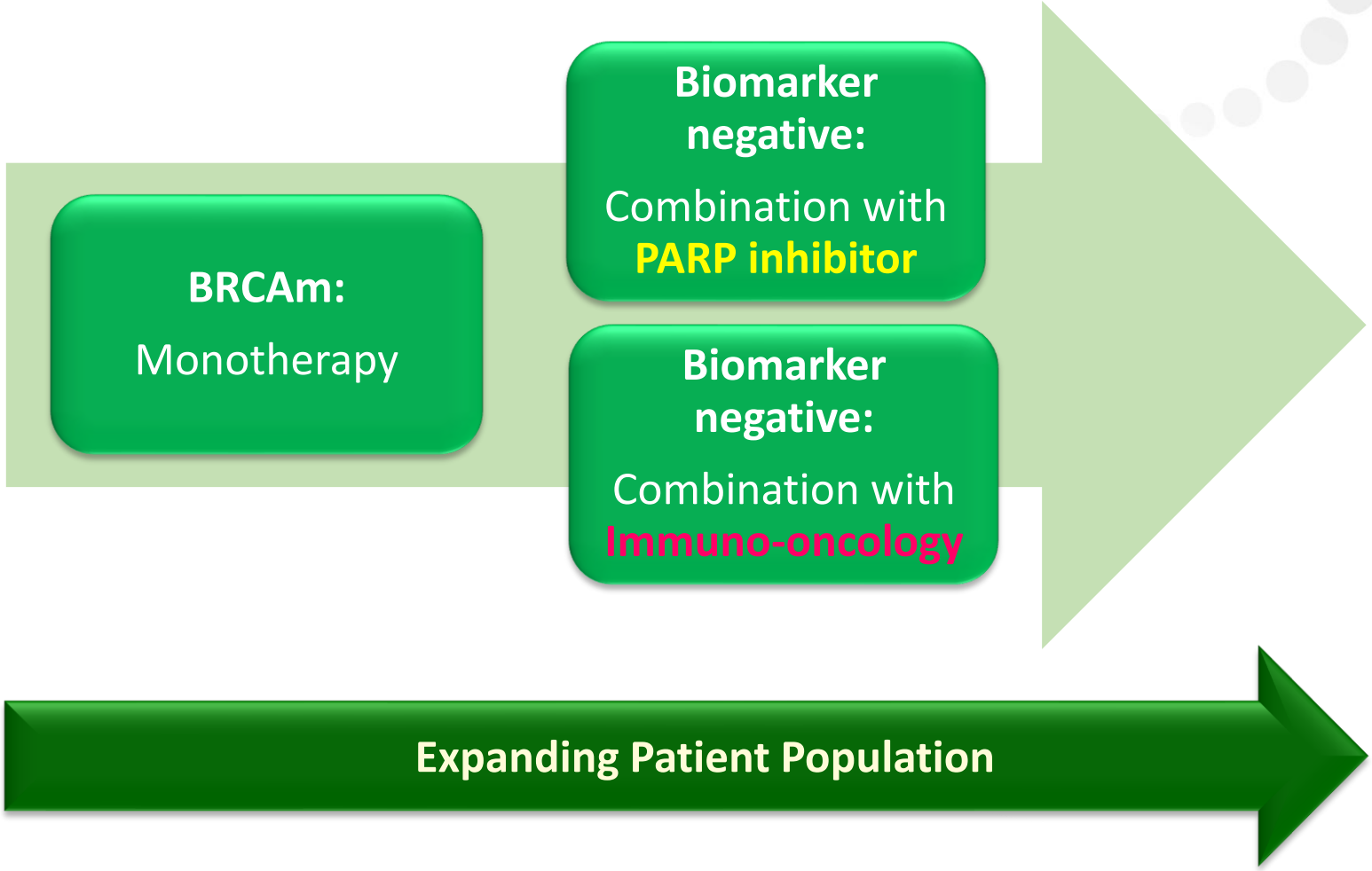
John Hilton, Karen Gelmon, David Cescon, Anna Tinker, Derek Jonker, Rachel Goodwin, Scott Laurie, Aaron Hansen, Samuel Aparicio, John Soong, Linda Hagerman, Hongbo Lui, Philippe Bedard, Kathleen Pritchard, Dongsheng Tu, Lesley Seymour

- 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。
  - 確認第二期臨床試驗投藥劑量
  - 明確觀察到有四位病人病情獲得部分緩解(PR) (3位乳癌、1位卵巢癌；3位BRCA2m、1位PALB2m)。All of these responders are platinum resistant.
  - 獲得部分緩解 (PR) 的病人具有較長存活期，有一位病人經歷16 cycles (換算為15個月) 註：這些末線病人身體已非常虛弱，存活期通常不超過3個月
  - 第一期臨床試驗主要在探討安全性，並無事先篩選病人，也未事先設計基因篩選，所有病人的分析資料均為事後分析的結果。

Pidnarulex (CX-5461) / Solid Tumor 實體腫瘤

- Study Title: **Phase Ib expansion study of CX-5461 in patients with solid tumors and BRCA2 or PALB2 mutation; enroll patients with platinum sensitive and resistant, PARPi sensitive and resistant**
- IND number: 149195 (US)
- Sponsor: Senhwa
- Study sites: CA & US

Pidnarulex (CX-5461) Targeting DNA Damage Repair Beyond BRCA Mutation



PCF-Pfizer Global Challenge Awards

Winner of PCF-Pfizer Global Challenge Awards

- Pidnarulex is newly granted (informed on 2020/7/17) the PCF-Pfizer Global Challenge Awards and will be combined with Pfizer's PARP inhibitor Talazoparib tested in human study for prostate cancer.

- The human study will be conducted and led by Senhwa's clinical partner PMCC (Peter MacCallum Cancer Centre) with several major hospitals in Australia

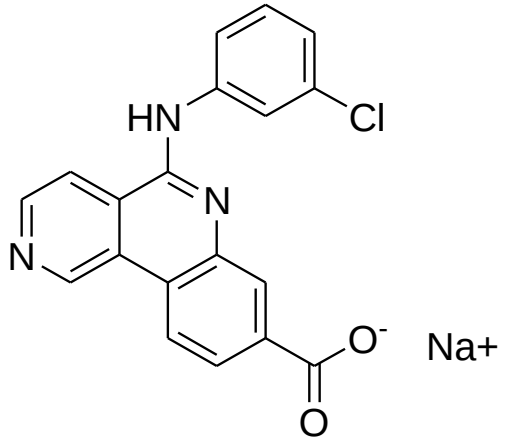
Area of Interest:

- Combination of talazoparib with novel agents
- Identifying resistance mechanisms to talazoparib with treatment strategies to avoid or overcome resistance

Funding Agency: Pfizer Inc.

Silmitasertib (CX-4945)

(市場首見CK2 inhibitor)



- Potential Anti-COVID-19
- Human efficacy in
  - Cholangiocarcinoma
  - Basal cell carcinoma
- Medulloblastoma

Bringing Hope to Life

生華科CK2抑制劑Silmitasertib (CX-4945)抗COVID-19開發進程

2020/03/30

- 美國加州大學舊金山分校定量生物科學研究所***(QBI-UCSF)***，透過大數據從***332***人體蛋白激酶篩選出生華科新藥Silmitasertib (CX-4945)，可調控及抑制受感染宿主細胞中蛋白激酶***CK2***活性，降低應激顆粒 ***Stress Granule (SG)***的分解，阻斷病毒在體內傳播，降低宿主細胞感染。

2020/04/9

- 生華科和美國國衛院旗下國家過敏和傳染病研究所***(NIAID)***簽訂合作協議，啟動新藥Silmitasertib (CX-4945)抗新冠病毒的一系列臨床前試驗。

2020/04/23

- 美國猶他州立大學抗病毒研究所***(IAR-USU)***進行抗新冠病毒潛力藥物海選，從全球***1670***個已核准或臨床階段藥物中，生華科Silmitasertib (CX-4945)脫穎而出。

2020/06/26

- 美國***QBI-UCSF***所領軍跨國抗病毒研究80人科學家團隊，在國際頂尖科學期刊***《Cell》***發表重磅研究，科學家找出***5***個藥物可能**優於瑞德西韋**，包括生華科***CK2***抑制劑Silmitasertib (CX-4945)，因為新冠病毒磷酸化的過程中，**人類蛋白激酶CK2是感染途徑的總開關**。

生華科CK2抑制劑Silmitasertib (CX-4945)抗COVID-19開發進程

2020/08/04

- 和**全美最大醫療體系之一**、也是亞利桑那州最大的醫療機構***Banner Health***

簽署合作意向書，展開新藥Silmitasertib首次用於新冠臨床.

2020/08/10

- 生華科和美國喬治亞州先進研究和教育中心醫療機構正式簽訂合作備忘錄，將申請新藥Silmitasertib(CX-4945)用於由研究者主導的人體臨床試驗(IIT)治療新冠肺炎患者。

2020/08/27

- 生華科新藥Silmitasertib(CX-4945)已獲美國食品藥物監督管理局FDA核准緊急人體臨床(EIND)治療新冠患者，為台灣第一家生技公司新藥首次用於治療新冠患者。

2020/09/03

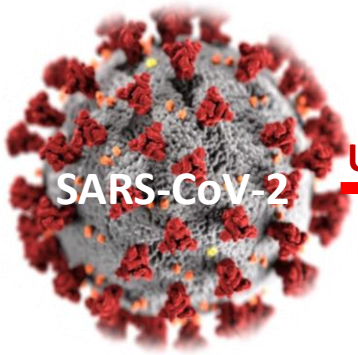
- 全球首位接受生華科新藥Silmitasertib(CX-4945)緊急臨床之新冠肺炎重症患者，**經過5天治療後康復出院**。

2020/11/04

- **美國喬治亞州先進研究和教育中心醫療機構申請新藥Silmitasertib(CX-4945)用於由研究者主導的人體臨床試驗(IIT)獲FDA核准，將用於治療中症患者。**

Antiviral and Anti-inflammatory effects of CK2 inhibition by Silmitasertib (dual actions)

CK2 inhibition has the potential to reduce viral replication AND cytokine storm severity.



Upregulation

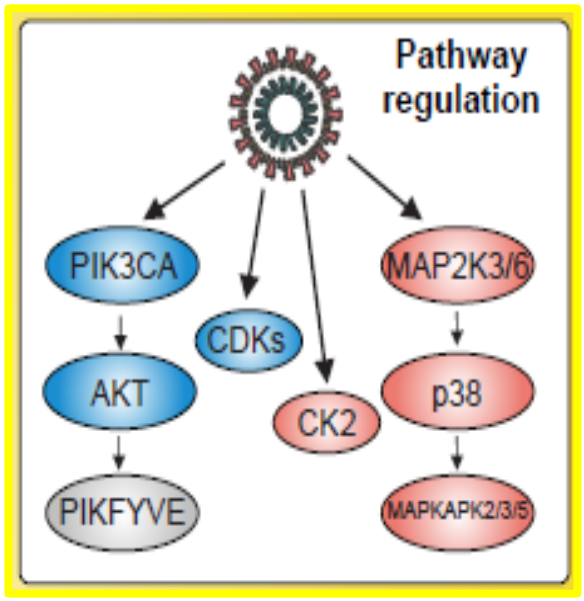
CK2
overexpression

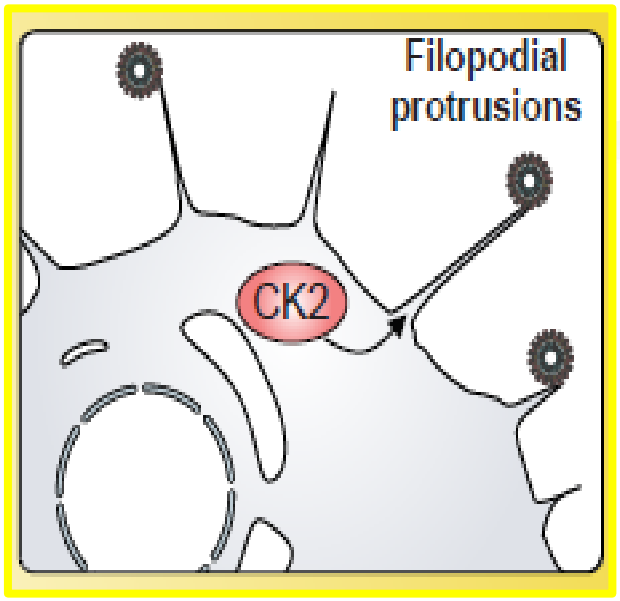
- Stress Granule disassembly
- Type I IFN response dysregulation
- Pro-inflammatory cytokine dysregulation (IL-6, IL-8)
- TNF-α – induced inflammation
- T-cells differentiation (Th17↑/Treg ↓), IL-17 production

→ Viral replication

→ Cytokine storm

Colocalization of CK2 and Viral Proteins at Actin Protrusions





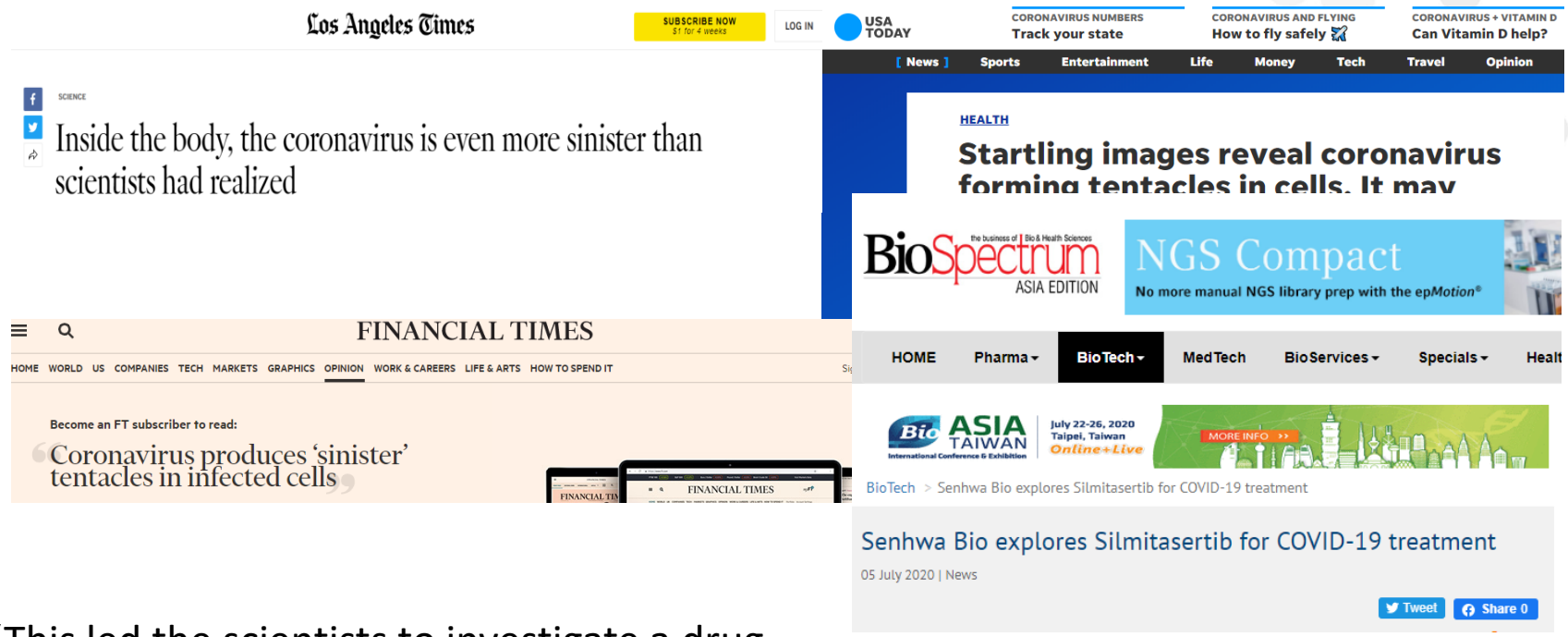
- At 24 hours, infected cells showed CK2 expression along the thin filopodia protrusions, partially co-localized with SARS-CoV-2 N protein.
- The CK2 inhibitor displayed robust antiviral activity, suggesting a role for this kinase in regulating the SARS-CoV-2 life cycle.

Source: https://www.sciencedirect.com/science/article/pii/S0092867420308114

根據美國加州大學舊金山分校定量生物科學研究所(QBI-UCSF)最新新冠研究成果顯示：

CK2 is the **Achilles Heel** of COVID19 virus.
By blocking the target will inhibit replication

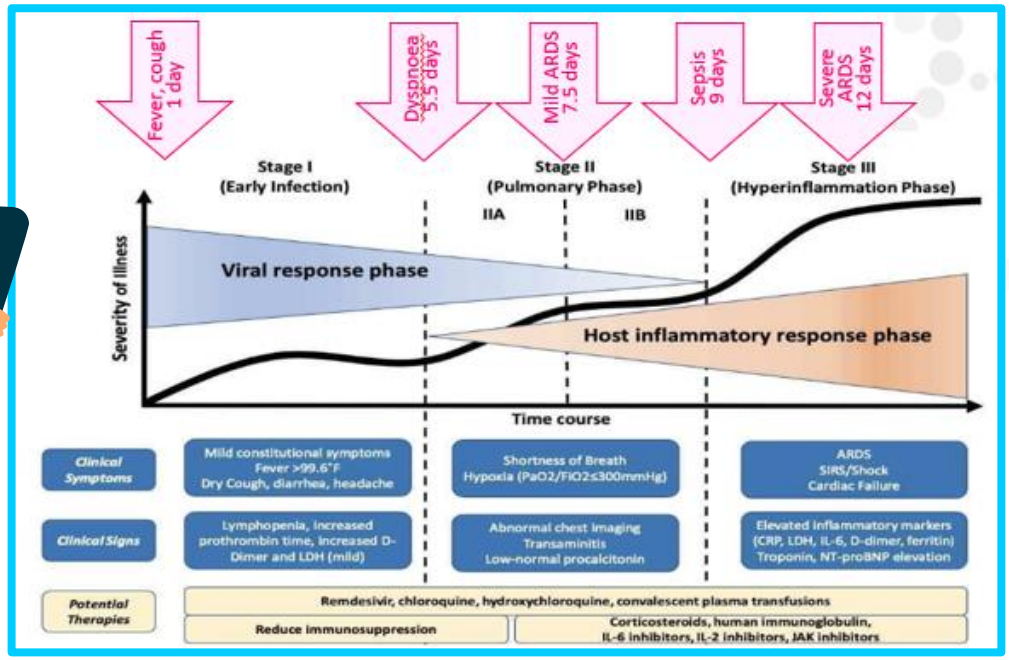
生華科Silmitasertib具抗新冠潛力登上國際媒體版面



"This led the scientists to investigate a drug called ***Silmitasertib***. Tests found this drug ***inhibits CK2 and eliminates the new coronavirus***." (摘自 *Milwaukee Journal Sentinel*, 2020/6/26)

"Potential drugs include ***silmitasertib***, made by Taiwan-based Senhwa Biosciences - which is working with the NIH on trials in the US. The drug works by ***inhibiting the CK2 enzyme which is used to build the tubes***. The drug is one of five which were found to be **more effective against the virus than Gilead's remdesivir**" (摘自 *Financial Times,* 2020/6/27)

臨床治療分期



1. 感染初期，應給予強效的**抗病毒藥物**治療；
2. Mid stage, need to control both viral load and inflammation
3. 重症狀態下，應給予強效的**抗發炎藥物**進行治療

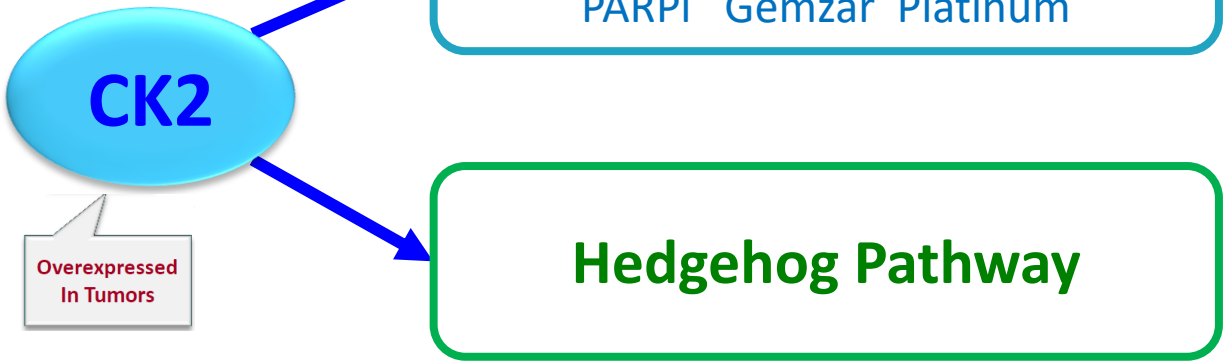
Ongoing Silmitasertib Clinical SARS-CoV-2 Studies

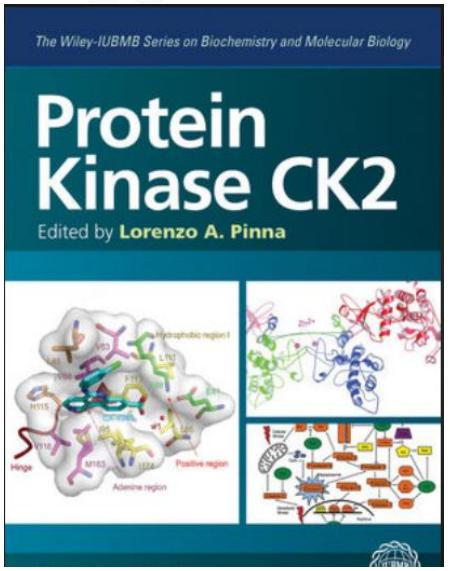
Organization/ Institution	Location	Experiment Outline
University of Arizona College of Medicine/ Banner* – Uni. Medical Center Phoenix.	AZ, US	Phase II multi-center, randomized, two-arm controlled interventional prospective IIT study to assess the safety, clinical benefit, and anti-viral activity of Silmitasertib in up to 40 patients with **severe** COVID-19.
Center for Advanced Research and Education (CARE)	GA, US	Phase II, investigator-initiated, two-arm controlled clinical investigation of the safety and clinical benefit of silmitasertib in 20 patients with **moderate** COVID-19.

* Banner Health System, 3 medical centers and 28 hospitals across 6 States, HQ in Arizona

CK2 Drives Multiple Oncogenic Pathways

We have focused on 2 areas for development





CK2 Upregulated to Support and Maintain these Activities in Cancer Cells

Silmitasertib: CCA Phase I/II(interim analysis) to be presented at ASCO GI in Jan, 2021

	Median OS Time	OS Post Progression
Gemcitabine＋Cisplatin	11.7month	3.6~4.4
Silmitasertib +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.	

簡報大綱

公司概況

產業概況

營運概況

未來展望

未來展望

- **Partnering Activities with Big Pharma**
- **Proof of Concept of Pidnarulex**
- **Proof of Concept of Pidnarulex +PARPi/ Pidnarulex +IO**
- **Proof of Concept of Silmitasertib to treat Covid-19 patients**
- Develope Next Generation CK2i for Anti-virus

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