Senhwa Biosciences, Inc.

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

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總經理

Bringing Hope to Life

2023年 12月

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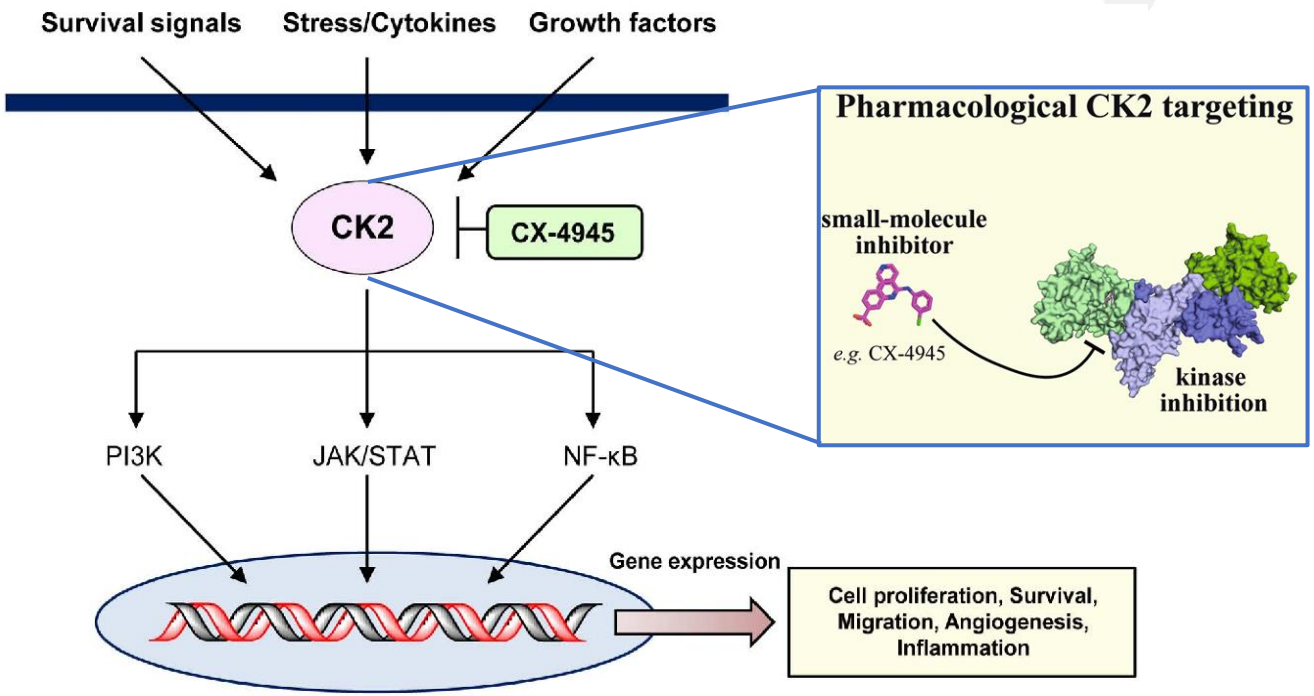
Current Pipeline

Program	Indication	Phase I / Expansion	Phase II	Pivotal Trial	Approval	Sponsor/ Funded
Pidnarulex (CX-5461) 	乳癌	CA				SU2C/CBCF*
	乳癌/ 卵巢癌/胰臟癌等實體腫瘤	USA/CA				
	血癌	AU				NHMRC/ CCV /PMCC**
	攝護腺癌 (和 PARPi抑制劑併用)	AU				PCF/Pfizer***
	HRD/Non-HRD 實體腫瘤	USA				NCI-NExT
Silmitasertib (CX-4945) 	膽管癌	USA, KR, TW				
	基底細胞癌 (BCC)	USA				
	髓母細胞瘤	USA				NIH/CTEP****
	新冠及社區性肺炎	TW/USA				

Bringing Hope to Life

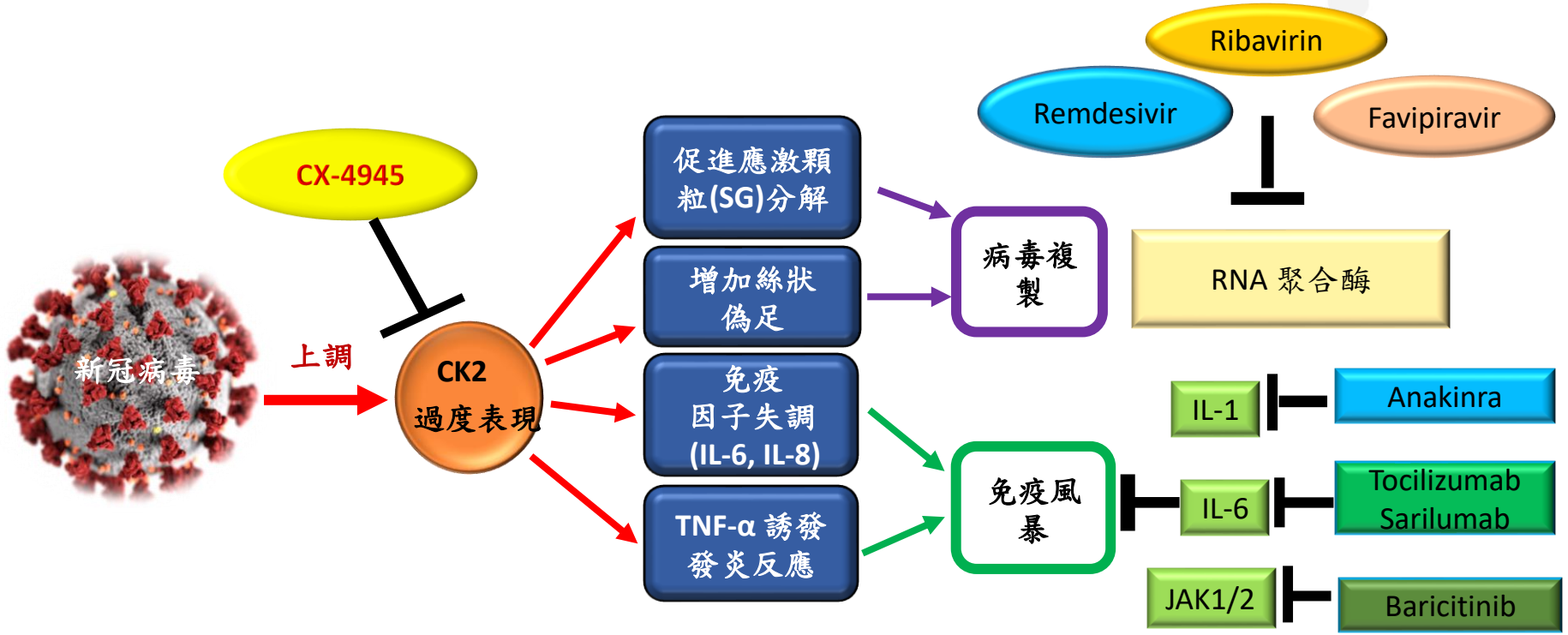
Silmitasertib

(First-in-class CK2 inhibitor)



Multiple pathways, multiple mechanism, toward multiple indications

CX-4945 併用其他抗病毒藥物 具治療Covid-19加乘潛力



免疫負債、共病威脅
細菌抗藥性海嘯席捲全球

免疫負債：

- 新冠疫情下減少活動，戴口罩勤洗手，病毒感染下降，造成免疫力降低．隨著疫情趨緩，各國解封，人類活動增加，包括**流感**、**呼吸道融合病毒(RSV)**感染增加，連帶繼發性細菌感染增加，如**肺炎鏈球菌**等．

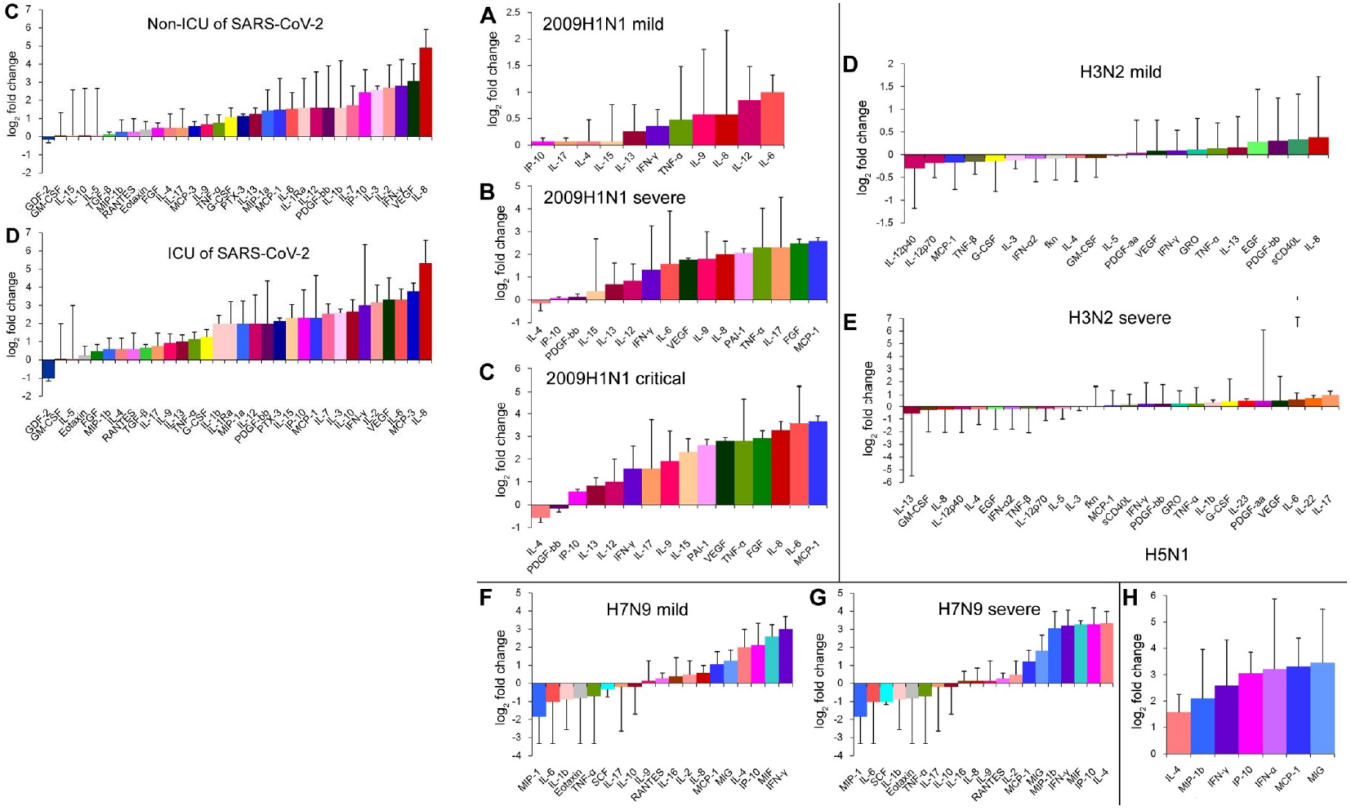
共病威脅：

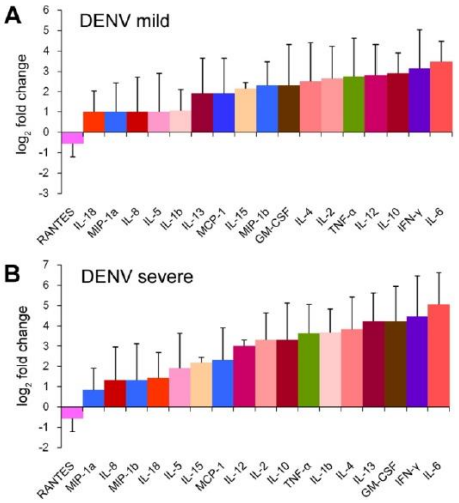
- 新冠肺炎 plus 癌症、代謝疾病、感染疾病…
- 新冠肺炎 induce 中風、真菌重複感染…

新冠疫後時代人類面臨：

- 病毒感染、抗藥性細菌、真菌感染、黴漿菌感染和結核病…

Alterations In Cytokine Production Following Viral Infection





Quantification of Cytokine Storms During Virus Infections

Shu Yuan[1†], Si-Cong Jiang[2†], Zhong-Wei Zhang[1†], Yu-Fan Fu[1†], Jing Hu[3] and Zi-Lin Li[4]

ORIGINAL RESEARCH
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frontiers in Immunology

Update

美國CARE新冠二期臨床試驗

- 試驗結果顯示Silmitasertib與對照組相比具統計和臨床意義，可加速患者康復時間(time to recovery)和臨床體徵正常化時間(time to normalization of clinical sign)等
- 10位試驗組患者在療程中都僅接受Silmitasertib單藥治療，並未同步接受其他EUA藥物治療
- 安全性 - 未顯示任何與 Silmitasertib 相關的嚴重不良事件 (SAE)
- 此2期試驗達到作為Silmitasertib治療COVID-19的臨床概念驗證 (Clinical Proof-of-Concept)

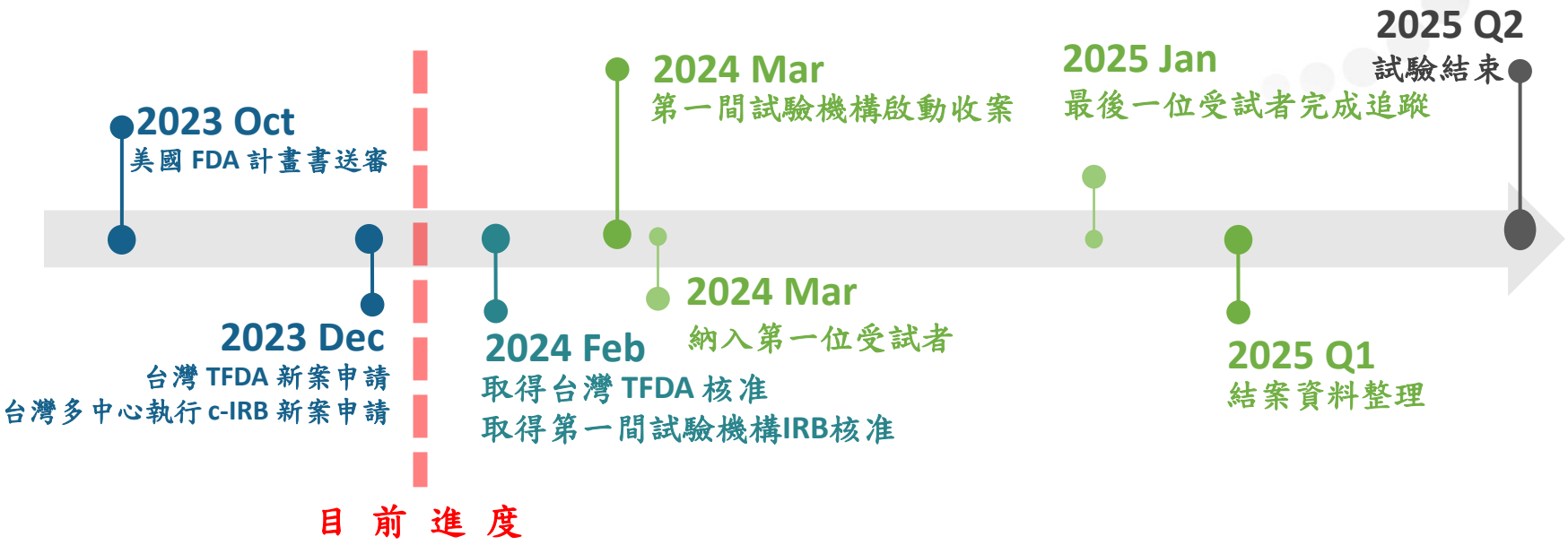
Update

Silmitasertib Community Acquired Pneumonia 臨床試驗 – 合作醫院

試驗機構	科別
國立台灣大學醫學院附設醫院 (NTUH)	感染科
國立臺灣大學醫學院附設醫院癌醫中心分院 (NTUCC)	綜合內科部
醫療財團法人徐元智先生醫藥基金會亞東紀念醫院 (FEMH)	感染科
三軍總醫院 (TSGH)	感染及熱帶醫學科
衛生福利部桃園醫院 (TYGH)	感染科

Update

Silmitasertib CAP 臨床試驗– 試驗時程



Bringing Hope to Life

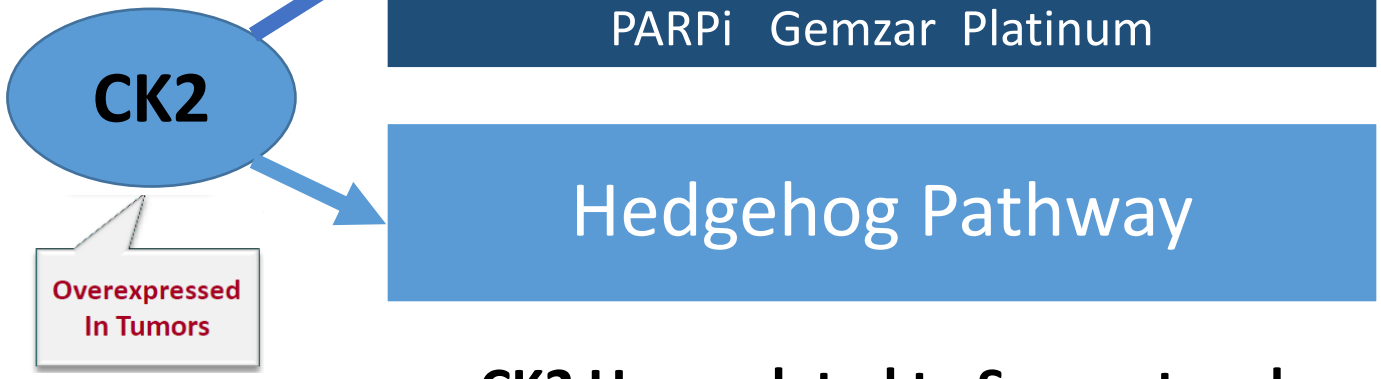
Interleukin Inhibitors Global Market

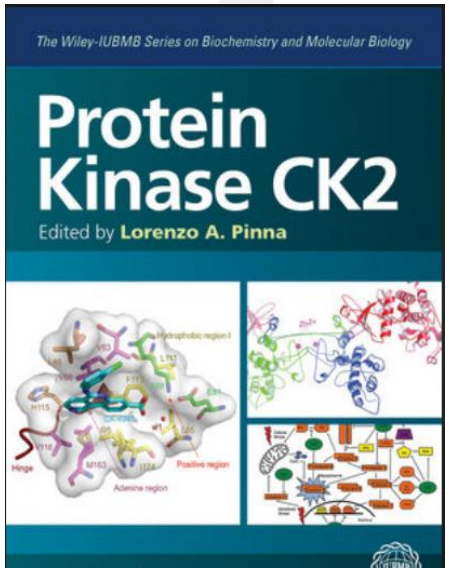
- 主要的細胞激素抑制劑(抗介白素)包括 IL-17, IL-23, IL-1, IL-5, IL-6和其他, 透過抗發炎和調節免疫效果達到治療
- 介白素抑制劑的全球市場預測: 從2022 年的 317.3 億美元增長到 2023 年的 369.6 億美元，複合年增長率 (CAGR) 為 16.5%
- 由Roche旗下Regeneron和Sanofi共同開發的IL-6單株抗體Actemra(tocilizumab, 安挺樂)已核准用於治療包括類風溼性關節炎以及幼年型慢性關節炎
- Major players: Roche, Regeneron, Sanofi, GSK, Novartis, Johnson & Johnson, Eli Lilly, AstraZeneca, Teva

Actemra (CHFm)	Q	2021	%
GLOBAL SALES	Q	3,562	24.6%
US Sales	Q	1,761	45.3%
Rest of World Sales	Q	1,801	9.4%

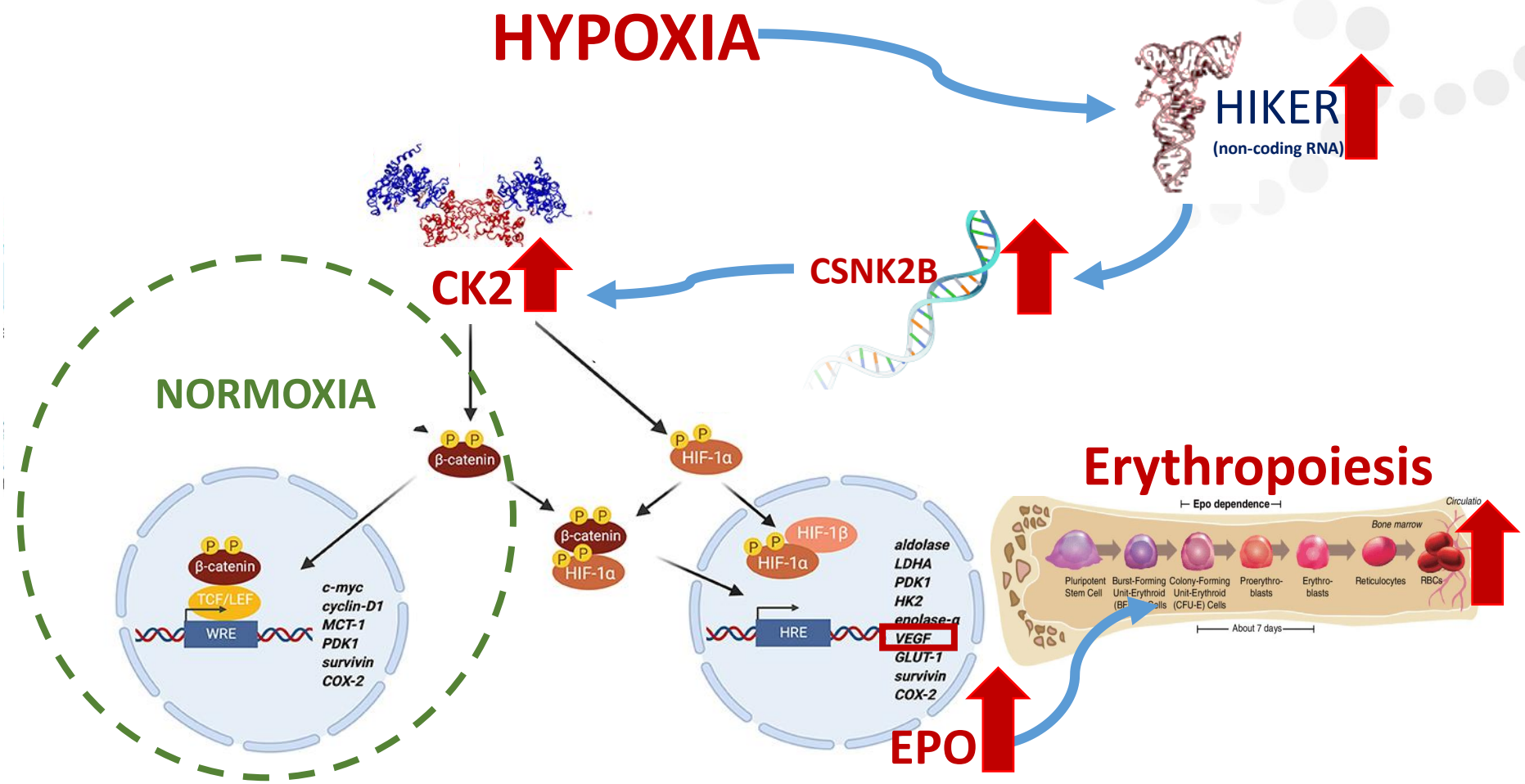
Actemra (CHFm)	Q	2022	%
GLOBAL SALES	Q	2,701	-24.2%
US Sales	Q	1,196	-32.1%
Rest of World Sales	Q	1,505	-16.4%

CK2 Drives Multiple Oncogenic Pathways
We have focused on 2 areas for development





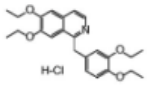
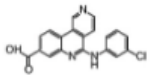
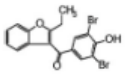
CK2 Upregulated to Support and Maintain these Activities in Cancer Cells



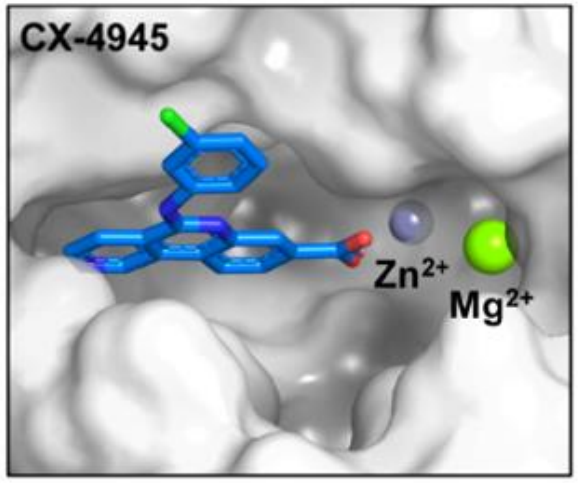
Source: J Clin Invest. 2023; Long noncoding RNA HIKER regulates erythropoiesis in Monge's disease via CSNK2B.

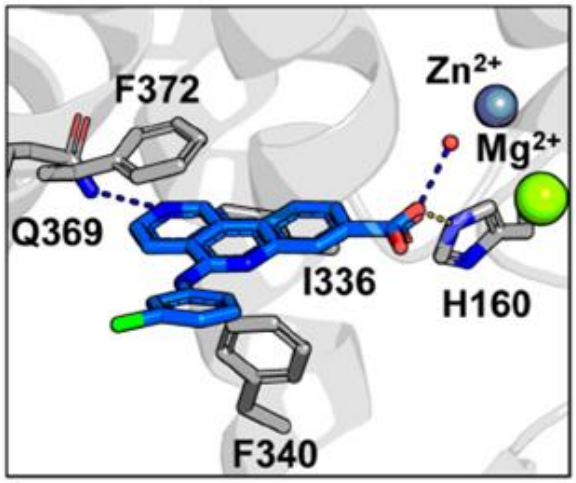
實驗證明CX-4945會off-target到PDE4 (磷酸雙酯酶4型) CX-4945抑制CK2或是PDE4皆達到抗發炎效果

Table 1
IC_{50} of 11 compounds against PDE4 determined by the SPA assay.

Stages	Compounds	Original target	Chemical structures	IC_{50} to PDE4
Approved drug	Ethaverine hydrochloride	MAO		0.41 ± 0.03 μM
Approved drug	CX-4945	CK2		1.00 ± 1.13 μM
Approved drug	Benzbromarone	URAT1		2.10 ± 1.61 μM
Clinical candidate	CVT-313	CDK2		0.42 ± 0.03 μM

C

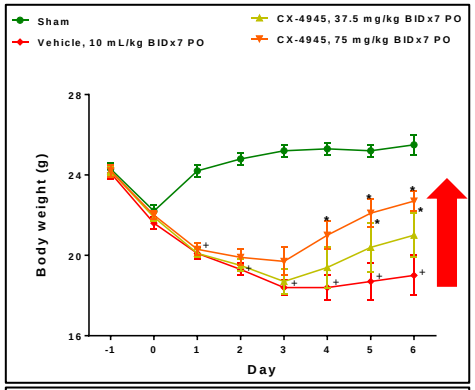


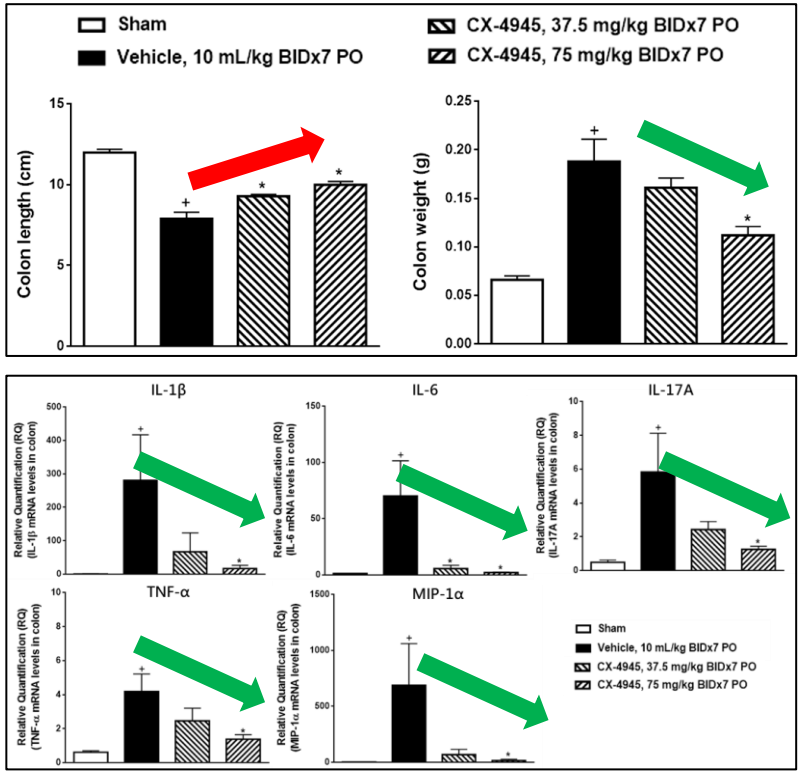


Ref. European Journal of Medicinal Chemistry

CX-4945顯著改善
大腸結腸炎小鼠動物模型症狀

- CX-4945顯著改善小鼠大腸結腸炎症狀，包括：體重上升，大腸長度增長和大腸重量增加
- CX-4945降低大腸內促發炎細胞因子釋放

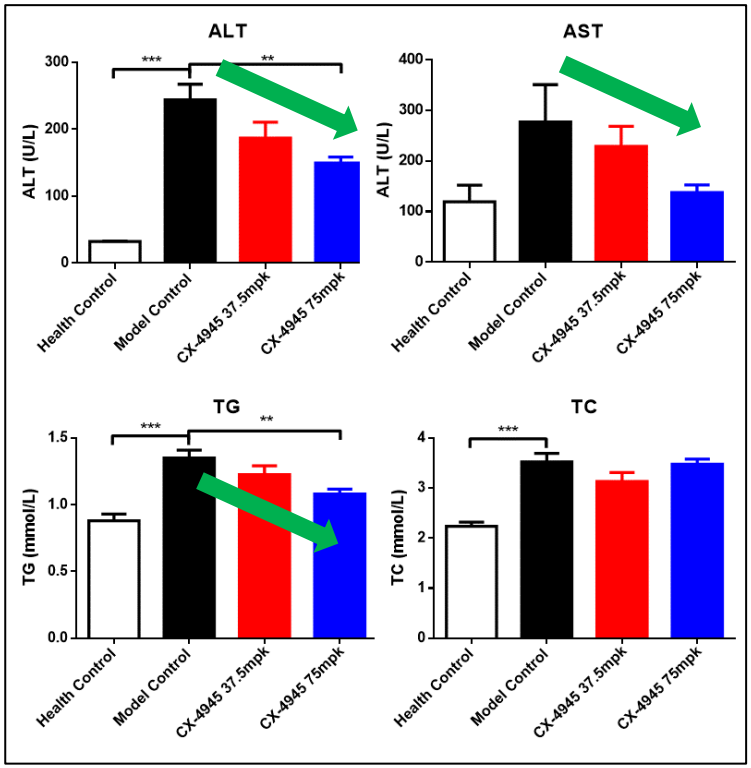


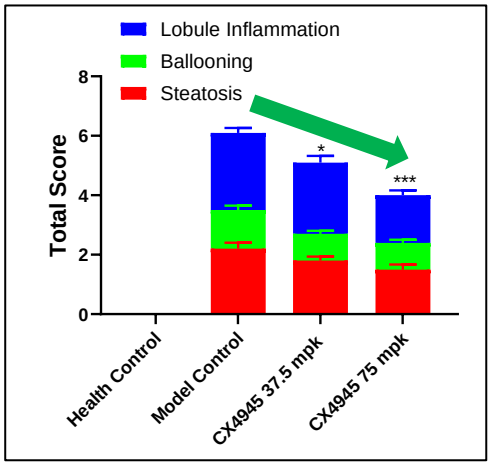


†p< 0.05, vs sham control;
*p< 0.05, vs vehicle control

CX-4945顯著改善
非酒精性脂肪肝小鼠動物模型症狀

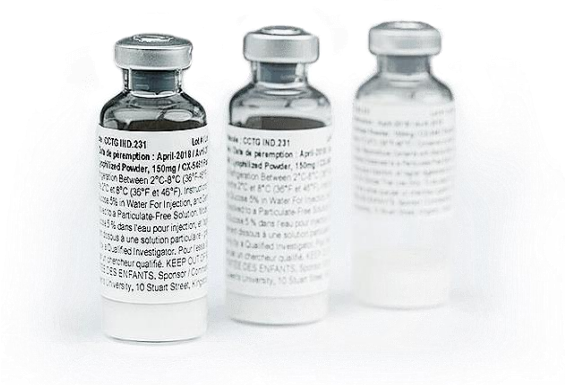
CX-4945顯著改善肝發炎指數(ALT和AST)、三酸甘油脂和NASH 發炎積分系統分數

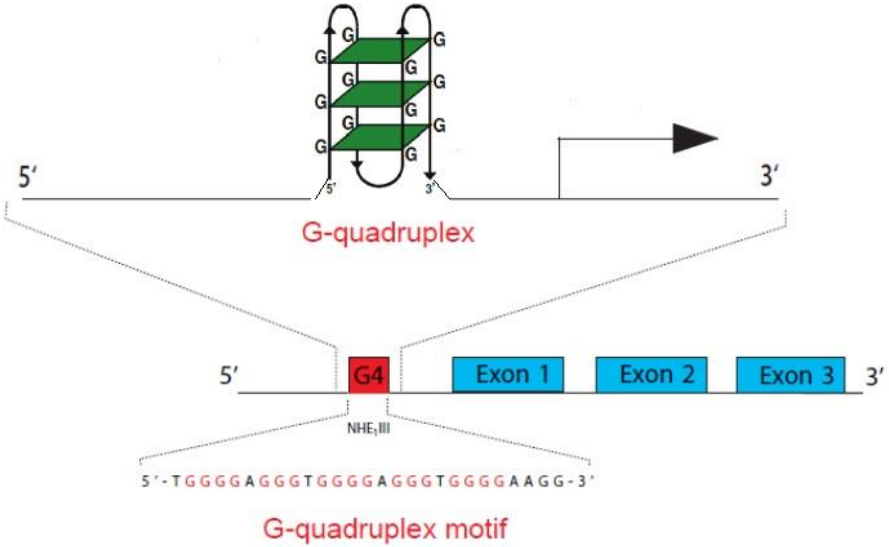




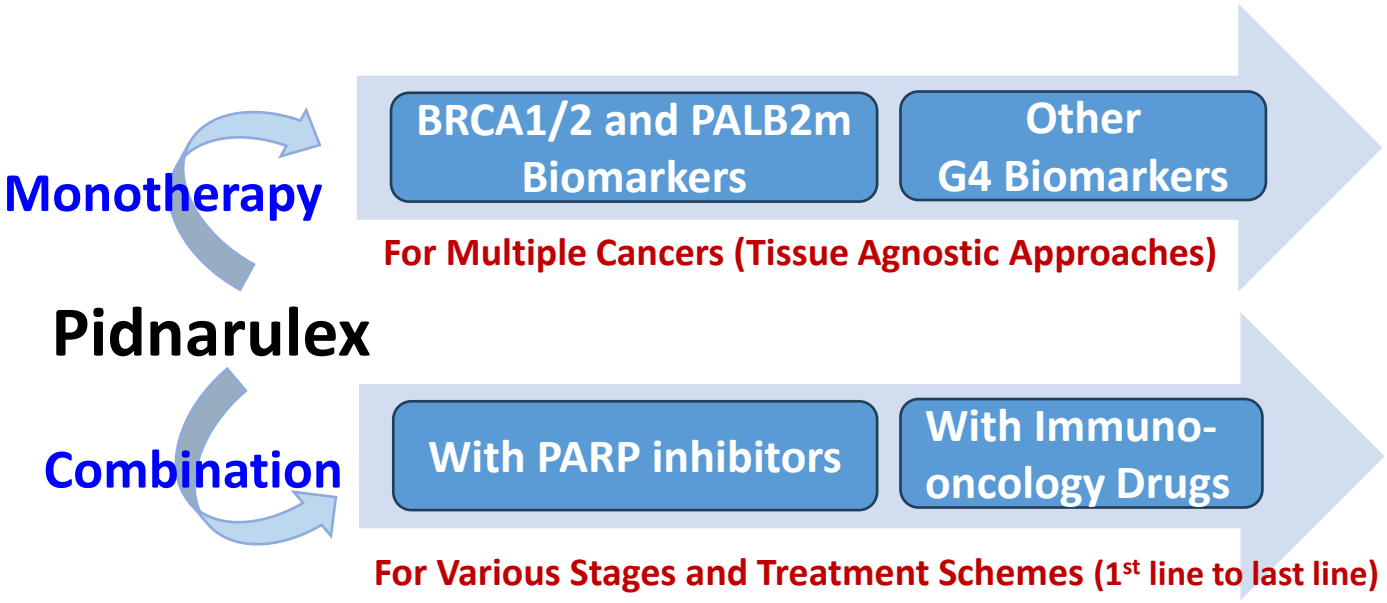
Pidnarulex

(First-in-class G4 stabilizer)





Pidnarulex (CX-5461) Targeting DNA Damage Repair Beyond BRCA1/2 and PALB2 mutation Expanding Patient Population and Intervention Priority



2016

- CX-5461 won SU2C Breast Cancer Dream Team Grant ($9m CAD)

2021-2024

- Phase Ib BRCA1/2 and PALB2m Solid Tumor Study
- Phase I study combination with PARP inhibitors

2023-2027

- Clinical studies through NExT Program
- Exploratory studies in colorectal cancers (CRC)

CX-5461(G4)

G-quadruplex stabilizer-CX-5461

CX-5461, a synthetically derived small molecule, is supplied as a lyophilized drug with intravenous (IV) administration.

Bringing Hope to Life

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.

NATIONAL CANCER INSTITUTE
DCTD Division of Cancer Treatment & Diagnosis
CCR Center for Cancer Research

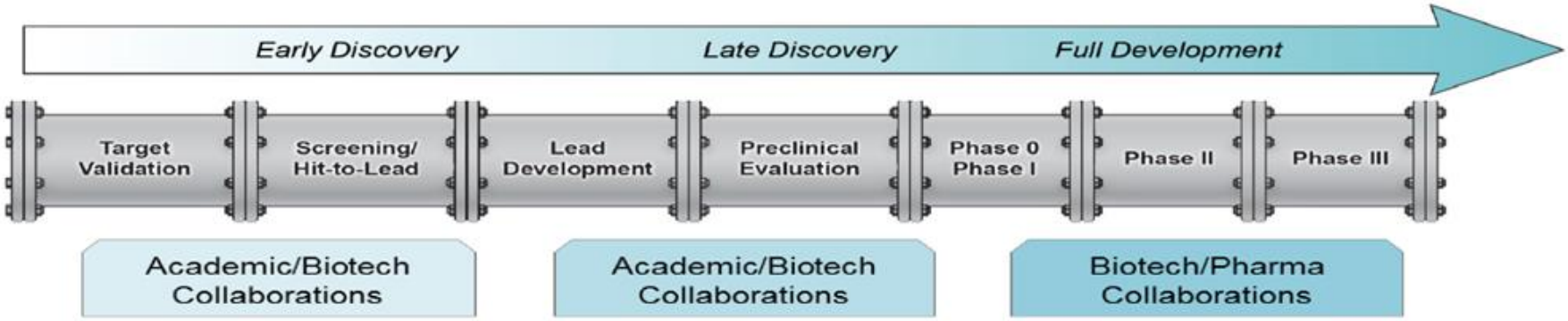
NExT NCI Experimental Therapeutics Program

- ***NExT*** 計劃是由美國政府支持，所有 NExT 計劃申請都由一個特別重點小組 (Special Emphasis Panel, SEP) 進行評估， SEP 成員透過五個標準：科學價值(scientific merit)、可行性(feasibility)、使命(mission)、新穎性(novelty)及醫療需求(clinical need)評選出最適新藥進入下個階段開發。
- 獲選進入NExT 計劃之新穎藥物，不限於資金贊助，可獲媒合各項臨床試驗所需人才和物力等整合式廣大資源，並以加速達到新藥成功上市的里程碑為終極目標，迎來造福全球癌症患者的創新治療

NExT Review Process

NExT- 加速新穎治療上市

- 美國食品藥物管理局(FDA) 核准上市的所有**抗癌藥物**中，約有 ***70%*** 是和 NIH旗下相關計畫有關，包括: 全球國際大廠包括***AZ (Olaparib)***、***Pfizer(Talazoparib)***、***Merck(Pembrolizumab)***、**Tekeda/Millennium*(Bortezomib)***、**BMS *(Ipilimumab)*** 等上市藥物
- NExT 申請計畫僅***10%-14% 成功獲選率***
- 目前逾上百個臨床試驗進行中，包括80多個和製藥以及生技公司的臨床合作協議。全美約3,300個機構、高達11,000名研究人員參與、每年約收治30,000名患者



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Update

CX-5461 NExT Program-臨床試驗意向書 (LOI)

計畫名稱	CX-5461在晚期實體腫瘤患者之藥效動力學(PD) 先導性試驗		
適應症	晚期實體腫瘤		
臨床階段	第一階段	**試驗人數**	共40人/20 位同源修復缺陷(HRD)之病患： 20 位無同源修復缺陷 (non-HRD)之病患

HPLC 純度檢測比較
SPT V.S MCE

Impurity profile (%Area)

			SPT	HY-13323		
Component	RT	RRT	#71763AA001	#134166	#282370	#08634
	6.928	0.254	N.D.	N.D.	N.D.	LT QL (0.03%)
CX-5461-529D	9.723	0.361	N.D.	0.13%	LT QL (0.03%)	0.24%
	10.760	0.395	N.D.	LT QL (0.04%)	N.D.	0.05%
	11.572	0.424	N.D.	0.05%	N.D.	0.10%
	12.520	0.459	N.D.	0.05%	N.D.	0.05%
	12.933	0.473	N.D.	N.D.	LT QL (0.04%)	N.D.
	13.332	0.489	N.D.	LT QL (0.03%)	N.D.	N.D.
	13.871	0.509	N.D.	1.34%	0.39%	1.45%
	14.983	0.549	N.D.	0.15%	0.14%	0.18%
	15.680	0.573	N.D.	0.11%	0.11%	0.14%
	16.204	0.594	N.D.	N.D.	N.D.	LT QL (0.04%)
CX-5461-407A	17.861	0.653	LT QL (0.03%)	N.D.	N.D.	0.08%
	18.313	0.665	N.D.	N.D.	N.D.	0.28%
	20.050	0.735	N.D.	N.D.	N.D.	0.18%
CX-5461-499A	20.635	0.755	0.05%	0.47%	0.12%	0.61%
	22.540	0.824	N.D.	N.D.	0.08%	N.D.
	24.515	0.899	N.D.	0.08%	2.71%	0.10%
	28.403	1.031	N.D.	N.D.	N.D.	0.10%
	28.497	1.045	N.D.	0.15%	0.08%	0.09%
CX-5461-527A	30.205	1.114	N.D.	0.04%	0.05%	0.04%
CX-5461-560A	33.330	1.219	N.D.	0.13%	0.27%	0.20%
	42.221	1.544	0.05%	0.17%	0.07%	0.63%
	43.689	1.602	N.D.	LT QL (0.04%)	LT QL (0.03%)	N.D.
Total impurity			0.10%	2.87%	4.02%	4.52%

Note: Each impurity is calculated by %area and corrected with RRF according to following table from

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