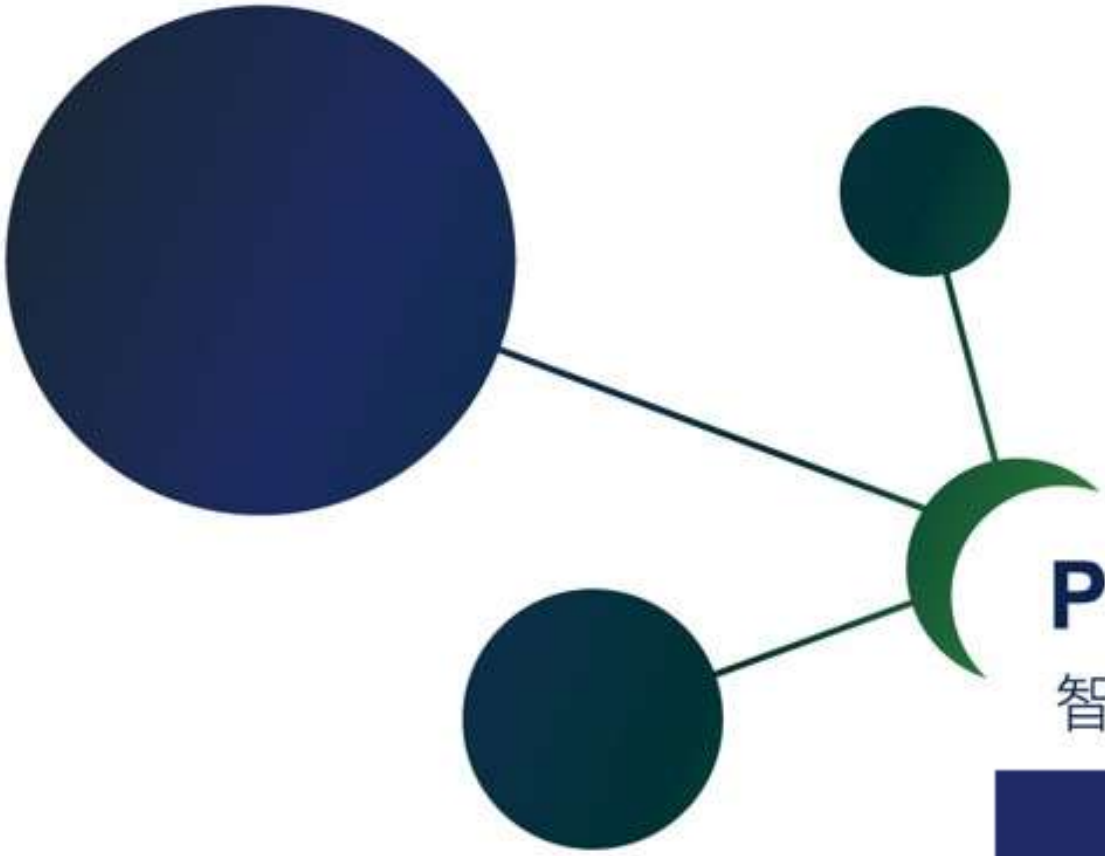

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智 擎 生 技 製 藥

智擎生技4162.TWO 法人座談

2023/08/01

免責聲明

- 本簡報中所提及之預測性資訊包括營運展望、財務狀況以及業務預測等內容，乃是建立在本公司從內部與外部來源所取得的資訊基礎。
- 本公司未來實際所可能發生的營運結果、財務狀況以及業務成果，可能與這些明示或暗示的預測性資訊有所差異。其原因可能來自於各種因素，包括市場風險、市場需求，以及本公司持續推出新藥產品專案等因素。
- 本簡報中對未來的展望，反應本公司截至目前為止對於未來的看法。對於這些看法，未來若有任何變更或調整時，本公司將盡力隨時再度提醒或更新。

議程

1. 1H 2023 營運亮點
2. 1H 2023 營運概況
3. 產品專案進度
   - ONIVYDE®
   - PEP07
4. 2023年營運展望
5. Q&A

1H 2023 營運亮點--公司維持營收穩定與價值創造

市場端

ONIVYDE® 新適應症延伸

1. 智擎向台灣 FDA提出胰腺癌一線用藥之新適應症申請
2. Servier已向歐洲EMA提出新適應症申請; IPSEN也已向美國FDA提出新適應症申請

研發端

新產品研發進程逐步加快

1. PEP07已獲澳洲及台灣核准進行第一期人體臨床試驗 (血液腫瘤)
2. 與外部新藥研發平台合作數項早期研發項目，研發進度符合預期

營運端

公司營運穩健成長

1. 獲得經濟部審定為〝生技醫藥公司〞
2. +20% 營收投入新藥研發
3. 1H 2023現金及約當現金暨按攤銷後成本衡量之金融資產達新台幣38億元
4. 穩定的股利配發策略
   - 2022年現金股利新台幣2.0元/股

1H 2023 營運概況


安能得®
onivyde®
(irinotecan liposome injection)
Liposomal Formulation
Do Not Substitute

ONIVYDE®營收趨勢

單位: 新台幣仟元

項目 / 年份	2017年度	2018年度	2019年度	2020年度	2021年度	2022年度	1H 2023 (較2022年同期成長率)
台灣銷貨收入	40,651	87,384	180,389	214,828	235,469	277,594	144,639 (+7%)
歐亞銷貨權利收入	63,526	109,825	133,651	271,584	419,366	376,789	189,764 (-8%)
里程碑金/授權金收入	749,500	96,221	0	569,600	0	0	0
合計	853,677	293,430	314,040	1,056,012	654,835	654,383	334,403 (-2%)

Taiwan Sales belongs to PharmaEngine, Inc.

Tiered royalties (high single – low double digit) in Europe/Asia (excl. TW) from Servier/IPSEN

1H 2023 營運概況

單位:新台幣仟元	1H 2023	1H 2022	Amount Change	% Change
營業收入	334,403	341,028	(6,625)	(1.94)
營業成本	26,256	23,948	2,308	9.64
營業毛利	308,147	317,080	(8,933)	(2.82)
推銷費用	19,770	15,807	3,963	25.07
管理費用	46,935	45,405	1,530	3.37
研究發展費用	106,941	42,024	64,917	154.48
營業費用	173,646	103,236	70,410	68.20
營業利益	134,501	213,844	(79,343)	(37.10)
營業外收入(支出)	40,165	12,557	27,608	219.86
稅前淨利	174,666	226,401	(51,735)	(22.85)
所得稅費用	18,170	48,697	(30,527)	(62.69)
本期淨利	156,496	177,704	(21,208)	(11.93)
基本每股盈餘(元)	1.09	1.24	(0.15)	(12.10)

產品專案進度

- 一線胰線癌藥證申請
- PEP07 將於澳洲及台灣進行一期臨床試驗
- 偕同外部AI/CADD技術，持續研發數項新專案

NAPOLI-3 安能得®合併 5-FU / LV / oxaliplatin (NALIRIFOX) *vs.* 一線標準治療 Gemcitabine + Nab-Paclitaxel (Gem + NabP)，對罹患晚期胰腺癌尚未接受治療的病患之全球樞紐性臨床試驗

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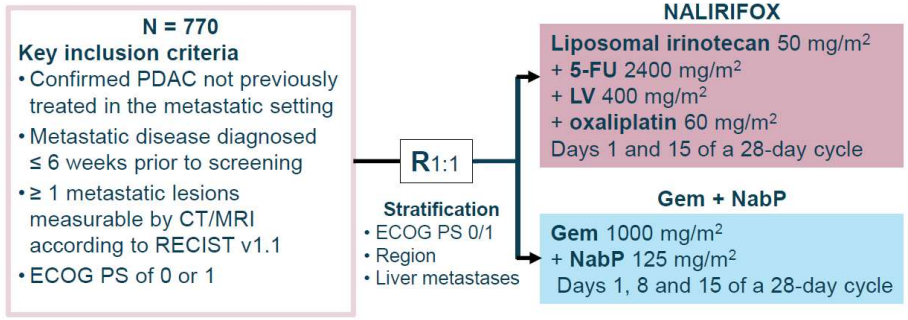
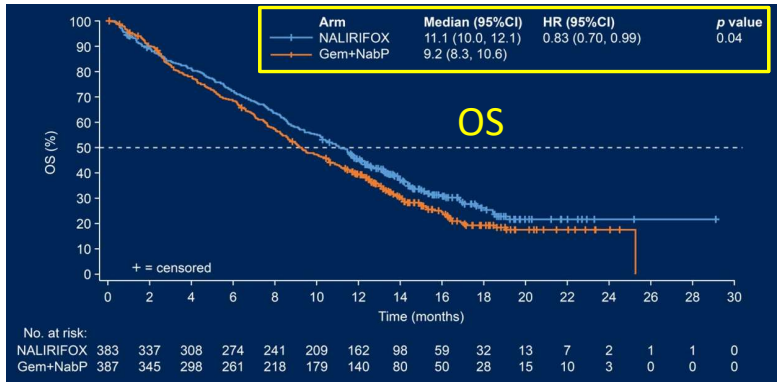
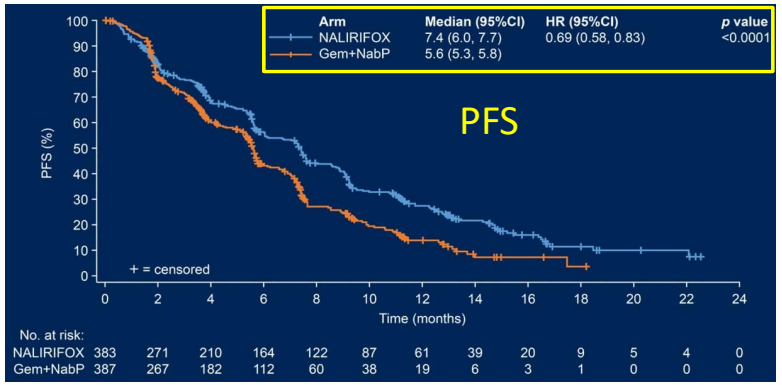
- NALIRIFOX (n = 383) vs. Gem + NabP (n = 387)，全球共770位病患
- 試驗終點:
  - 主要 - 總存活期（Overall Survival, OS）
  - 次要 - 無惡化存活期（Progression Free Survival, PFS），客觀緩解率（Objective Response Rate, ORR）
- 試驗期間: 2020年2月納入第一位病患，數據收集至2022年7月
- 試驗結果於2023年在舊金山，美國臨床腫瘤學會胃腸癌（ASCO GI）發表







- 試驗結論
  - 主要療效指標結果顯示，NALIRIFOX治療的 OS中位數為11.1個月，較Gem + NabP治療的9.2個月延長**1.9個月**，且達統計學顯著意義（p = 0.04）。
  - 次要評估指標的無疾病惡化存活期（PFS），NALIRIFOX組中位數為7.4個月，較Gem + NabP組的5.6個月延長**1.8個月**，也達到統計學顯著意義 （p < 0.0001）；客觀緩解率（ORR）分別為41.8%與36.2%。
  - 安全性方面，NALIRIFOX組不良事件比例為 99.7%，Gem + NabP組為99.2%；與藥物有關且Grade ≥ 3的不良反應，NALIRIFOX為70.8%，Gem + NabP 為68.1%。整體來說，NALIRIFOX治療的安全性可控，且在NAPOLI-3試驗中並沒有觀察到新的不良事件。

Frontline Regimens for Patients With Metastatic Pancreatic Cancer

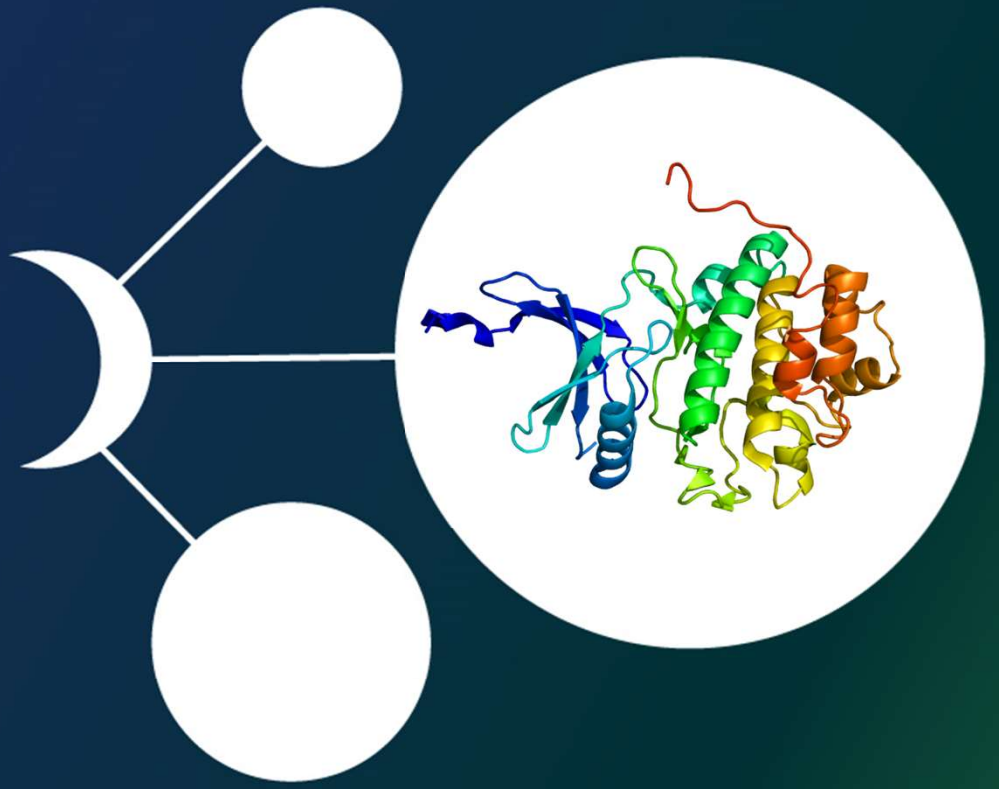
Study	Phase III NAPOLI 3		Phase III MPACT		Phase II/III ACCORD 11	
Drug	**NALIRIFOX (Onivyde)**	**Gemcitabine + Nab-Paclitaxel**	**Abraxane + Gemcitabine**	**Gemcitabine**	**FOLFIRINOX**	**Gemcitabine**
Source	ASCO GI 2023		Von Hoff et al 2013 (NEJM)		Conroy et al 2011 (NEJM)	
Baseline Characteristics						
n	383	387	431	430	171	171
Age (median)	64	65	62	63	61	61
ECOG 0	41.8%	43.4%	ND	ND	37%	39%
ECOG 1	58.0%	56.6%	ND	ND	62%	61%
Median no. of metastatic sites	2	2	2	2	2	2
Efficacy						
n	383	387	431	430	171	171
ORR	41.8%	36.2%	23%	7%	32%	9%
CR	0.3%	0.3%	<1%	0	1%	0%
DCR	67.6%	62.3%	48%	33%	70%	51%
mDoR(months)	NA	NA	ND	ND	5.9	3.9
mPFS(months)	7.4	5.6	5.5	3.7	6.4	3.3
mOS (months)	11.1	9.2	8.5	6.7	11.1	6.8

Source : ASCO-GI 2023; NEJM 2013; NEJM 2011

Note: ORR= Overall Response Rate ; CR=Complete Response ; DCR=Disease Control Rate; mDoR=median Duration of Response; mPFS=median Progression-Free Survival; mOS= median Overall Survival

PEP07 (CHK1 抑制劑)

- 早期同類型開發項目的國際授權案熱度增加
- PEP07 前臨床試驗成果發表
- 2H 2023 於澳洲及台灣進行一期臨床試驗



早期同類型開發項目的國際授權案熱度增加

Date	Licensor	Licensee	Target	Pipeline Stage	Deal Size
2020.05.26	Repare	BMS	Undisclosed x 10	Discovery	• Upfront: $65M • Milestone: $3.0bn • Royalties: high SD - Low DD
2021.02.02	Ribon Therapeutics	Ono	PARP7	Phase I	• Upfront: $16.3M • Milestone: $132M • Japan, South Korea, Taiwan and ASEAN countries
2021.04.07	Artios	Novartis	Undisclosed x 3	Discovery	• Upfront: $20M • Milestone: $1.3bn
2022.03.21	Volastra	BMS	Undisclosed	Discovery	• Upfront: $30M • Milestone: $1.1bn
2022.04.27	Zentalis	Pfizer	WEE1	Ph I/II	• $25M • Equity investment
2022.05.16	Atrin	Aprea	ATR, WEE1	Pre-clinical	• Buy out
2022.06.02	Repare	Roche	ATR	Ph I/II	• Upfront: $125M • Milestone: $1.2bn • Royalties: high SD- High teens
2022.09.21	Nerviano Medical Sciences	Merck	PARP1	Ph I	• Upfront and Option: $65M
2023.06.01	Impact Therapeutics	Eikon Therapeutics	PARP1	Pre-clinical	• Undisclosed

Upfront size: US$16-125M

PEP07 – Potential Best in Class CHK1 Inhibitor

PEP07 is a brain penetrating oral inhibitor which is more potent, selective, specific than the competitors.

	Drug	Stage	Potency	Selectivity	Specificity	Oral Bioavailability
Acrivon (Eli Lily)	Prexasertib	Ph II	Excellent	Fair	Fair	Poor
Genetech	GDC-0575	Discontinued	Good	Fair	Good	Good
gsk (Sierra Oncology)	SRA-737	Ph I/II (Complete)	Fair	Good	Unknown	Good
Esperas Pharma	LY2880070	Ph I/II (Complete)	Unknown	Unknown	Unknown	Unknown
PharmaEngine	PEP07	Ph I Ready	Excellent	Good	Good	Good

Excellent Good Fair Poor Unknown

PEP07: 新一代可穿透血腦障壁之小分子口服細胞損傷調控酵素抑制劑 (Chk1 Inhibitor)用於治療血液腫瘤 – 6th Annual DDR Inhibitors Summit 2023

PEP07: A novel, brain penetrant oral Chk1 inhibitor for the treatment of AML and MCL

Bettice Chen[1], Kyla Grimshaw[2], Jack Cheng[1], Allen Lee[1], Mel Liu[1], Meriel Major[2], Bob Boyle[2], Hong-Ren Wang[1]

Abstract

Chk1 is a key modulator of the cell division cycle and DNA damage response (DDR) signaling. Inhibition of Chk1, in conjunction with additional genetic alterations and/or addition of a DNA damaging agent, results in mitotic catastrophe and apoptosis of cancer cells, offering an attractive approach to treat cancer[3].

Acute myeloid leukemia (AML) is characterized by a deranged DDR pathway and high Chk1 expression that is associated with poor patient outcomes[4]. Mantle cell lymphoma (MCL) is a rare and aggressive form of Non-Hodgkin lymphoma with the genetic hallmark of a chromosomal translocation leading to the over expression of cyclin D1. Since Chk1 regulates cdk1/cyclin activity, Chk1 inhibitors have been proposed as a novel therapeutic approach in this cancer[5].

Here, we present PEP07, an orally available brain penetrant selective Chk1 inhibitor that is entering first in human clinical studies in AML and MCL.

In vitro properties of PEP07

PEP07 is a potent and selective Chk1 inhibitor with over 1000-fold selectivity vs Chk2. PEP07 treatment causes inhibition of Chk1 autophosphorylation and activation of the DDR and apoptotic pathways leading to cancer cell death.

a)

Target	IC50, nM
Chk1	1
Chk2	1630
Flt-3	37
Rsk3	42
Rsk2	83
RET	81
Rsk4	86
Rsk1	125
MAP4K4	242

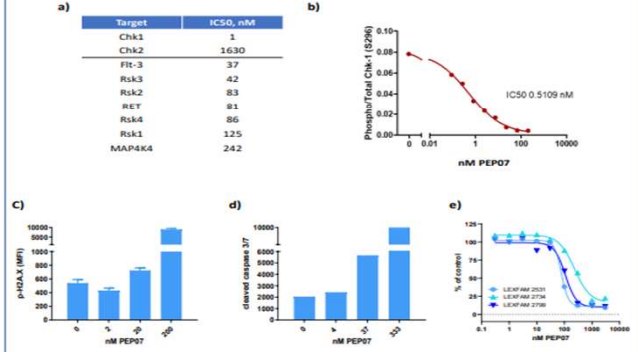


Figure 1. a) IC50s from ZLYTE FRET-based kinase assay b) Cellular IC50 as measured by autophosphorylation of pChk1 S296/total Chk1 in HT29 cells following 18h drug treatment c) phospho-H2A.X S139 in THP1 AML cell line following 18h drug treatment d) caspase 3/7 induction in Jeko-1 cell line following 18h drug treatment d) antiproliferative effects in AML patient derived cell models following 72h drug treatment.

PEP07 causes regressions in AML and MCL xenografts

PEP07 has been dosed orally as a single agent using a variety of dosing schedules, where it induces anti-tumor activity and tumor regressions and is well tolerated.

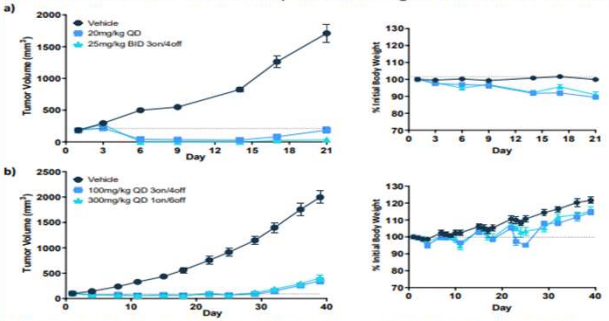


Figure 2. a) Jeko-1 MCL xenograft model. Mice were dosed with PEP07 daily for 21 days at 20mg/kg or BID 25mg/kg 3 days on followed by 4 days off. b) MV411 AML xenograft model. Mice were dosed with PEP07 once a week at 300mg/kg, or 100mg/kg for 3 days followed by 4 days off. Dosing was for 4 cycles.

PEP07 combines with cytarabine in AML xenografts

PEP07 combines with cytarabine in the cytarabine-sensitive MV411 model, and the cytarabine-insensitive THP1 model.

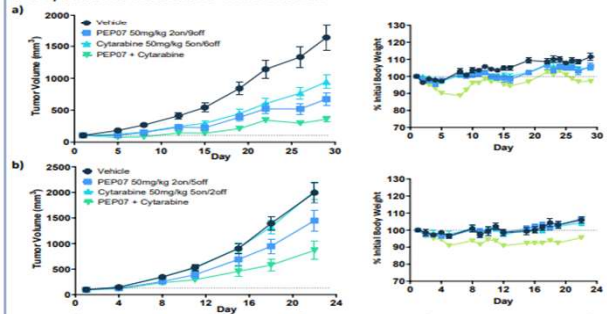


Figure 3. a) MV411 AML xenograft model and b) THP1 AML xenograft model, dosed as per the figure legends. PEP07 dosed PO and cytarabine dosed IP. Dosing was for 3 cycles.

PEP07 Tumor/Brain Penetration

Comparable exposures of PEP07 in the brain and plasma were observed in MV411 AML model, which suggests that PEP07 can penetrate the BBB in vivo. PEP07 significantly accumulates in the tumor.

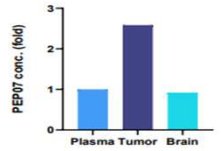
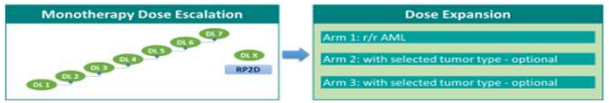


Figure 4. Following a 6-week efficacy experiment, 4 mice were treated with PEP07 and samples collected at 1h after dosing. LC-MS/MS analysis of PEP07 concentration in blood, tumor, and brain samples was conducted.

PEP07 Clinical Trial Design

The phase 1 clinical study for PEP07 comprises a dose escalation phase in relapsed/refractory (r/r) AML and MCL followed by a dose expansion phase in patients with r/r AML and/or selected tumor types. Patients will receive oral PEP07 treatment until disease progression or un-tolerable adverse event and DLTs will be evaluated during the first treatment cycle. Combination arms will follow to investigate PEP07 combination treatment in patients with r/r AML. The trial will be run in Australia and Taiwan which is aiming to begin patient recruitment in Q1 2023.

a) Study Design



b) Study schedule

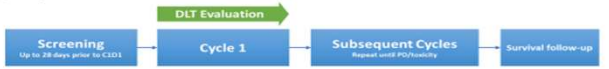


Figure 5. A schematic of the study design and schedule. a) Dose escalation and expansion with r/r AML and selected tumor, b) Study schedule contains screening, treatment and survival follow up period. The DLT is evaluated at cycle 1.

Conclusions

- PEP07 is a highly selective and potent Chk1 inhibitor that inhibits Chk1 auto-phosphorylation and induce apoptosis in cancer cell models
- PEP07 induces significant anti tumor efficacy as a single agent in models of AML and MCL
- PEP07 effectively combines with cytarabine in AML models
- PEP07 is advancing into Phase 1 clinical studies to treat patients with AML or MCL

PEP07 具有多項組合療法的潛力

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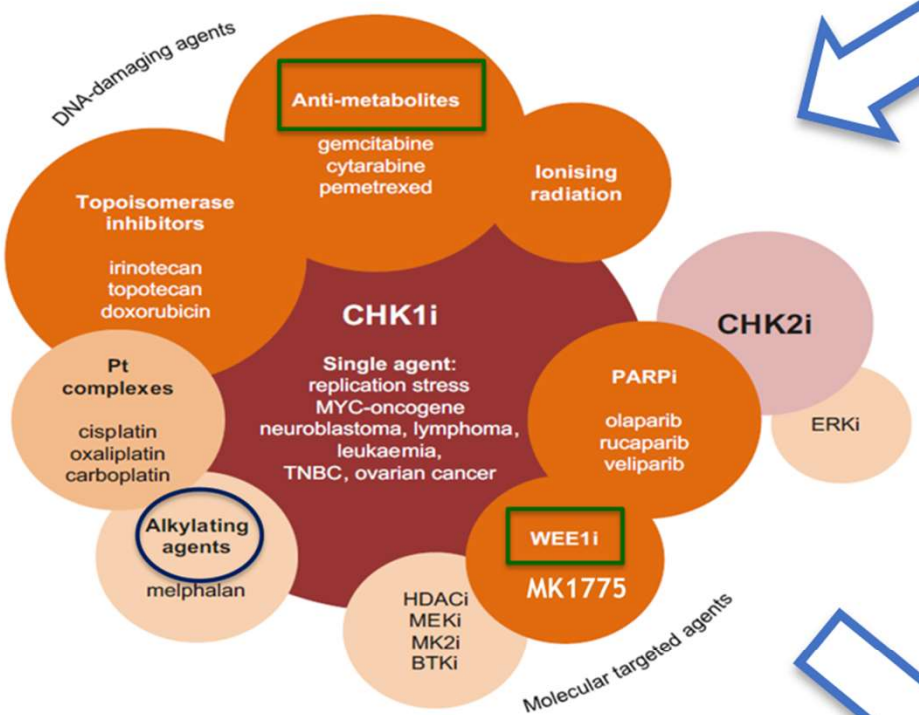

In vitro Combo treatment

SoC agents	Indication	Cell line
Ara-C	AML	MV4-11 / THP-1
Gemcitabine	NSCLC	NCI-H1703
5-Fu	Esophagus	KYSE-270
5-Fu	Stomach	MKN-45, SNU-16, SNU-5,
5-Fu	CRC	DLD-1, HT-29, SW480
TMZ	Brain	IMR-32
Sorafenib	RCC	A498

Green: Synergism ; Blue: Additivity

Clinical Trial Designs and Indications Guidance

：Synergistic effect verified in PEP07

：Additive effect observed in PEP07

Targeting the DNA Damage Response for Anti-Cancer Therapy 241-276, 2018

PEP07 早期臨床試驗規劃

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Ph1b monotherapy, dose escalation/expansion in AML and MCL

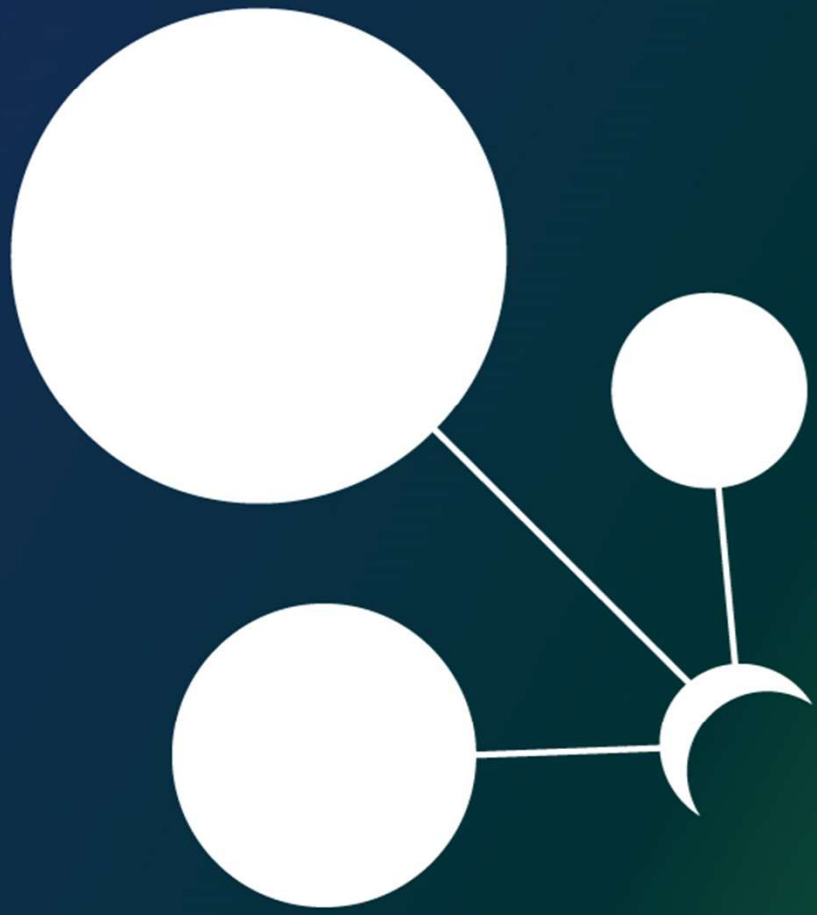
→ Ph1b Combo, dose escalation/expansion in selected hematologic cancer, e.g., AML or MCL

Ph1 monotherapy, dose escalation/expansion in advanced or metastatic solid tumor

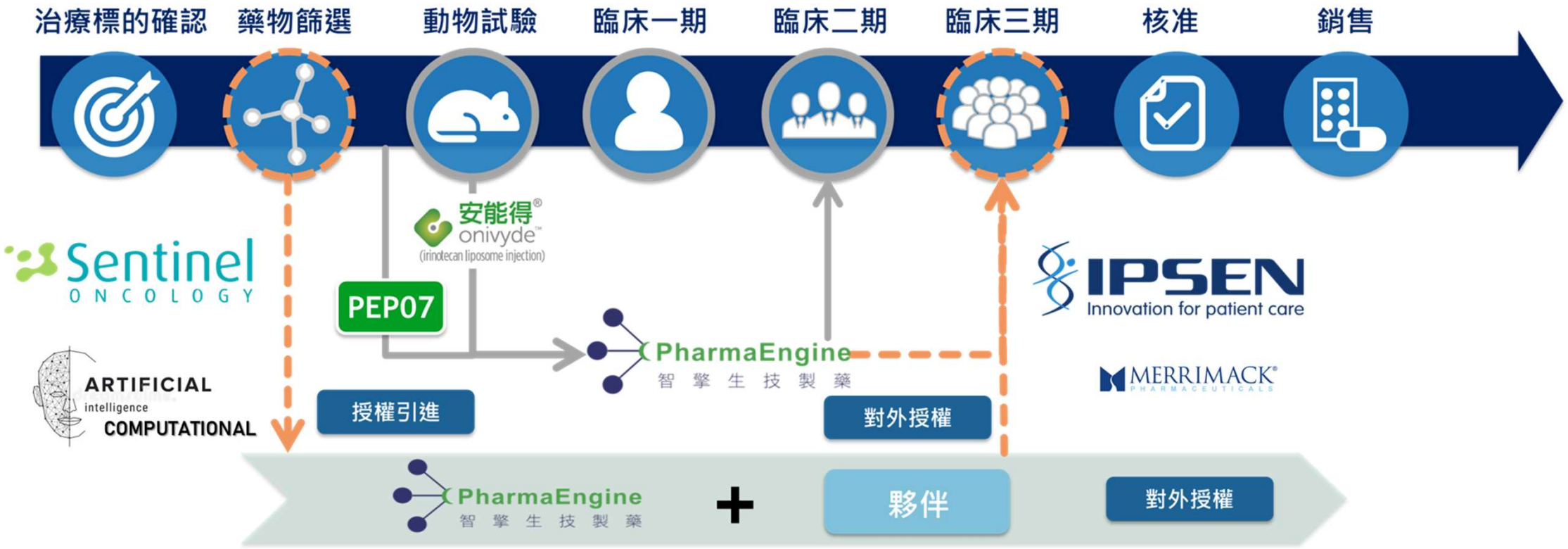
→ Ph1b Combo, dose escalation/expansion in selected solid tumors

Preclinical biomarker study is ongoing for further design of clinical trials

2023年
營運展望



Virtual Pharmaceutical Company 營運模式



產品組合聚焦在癌症精準醫療

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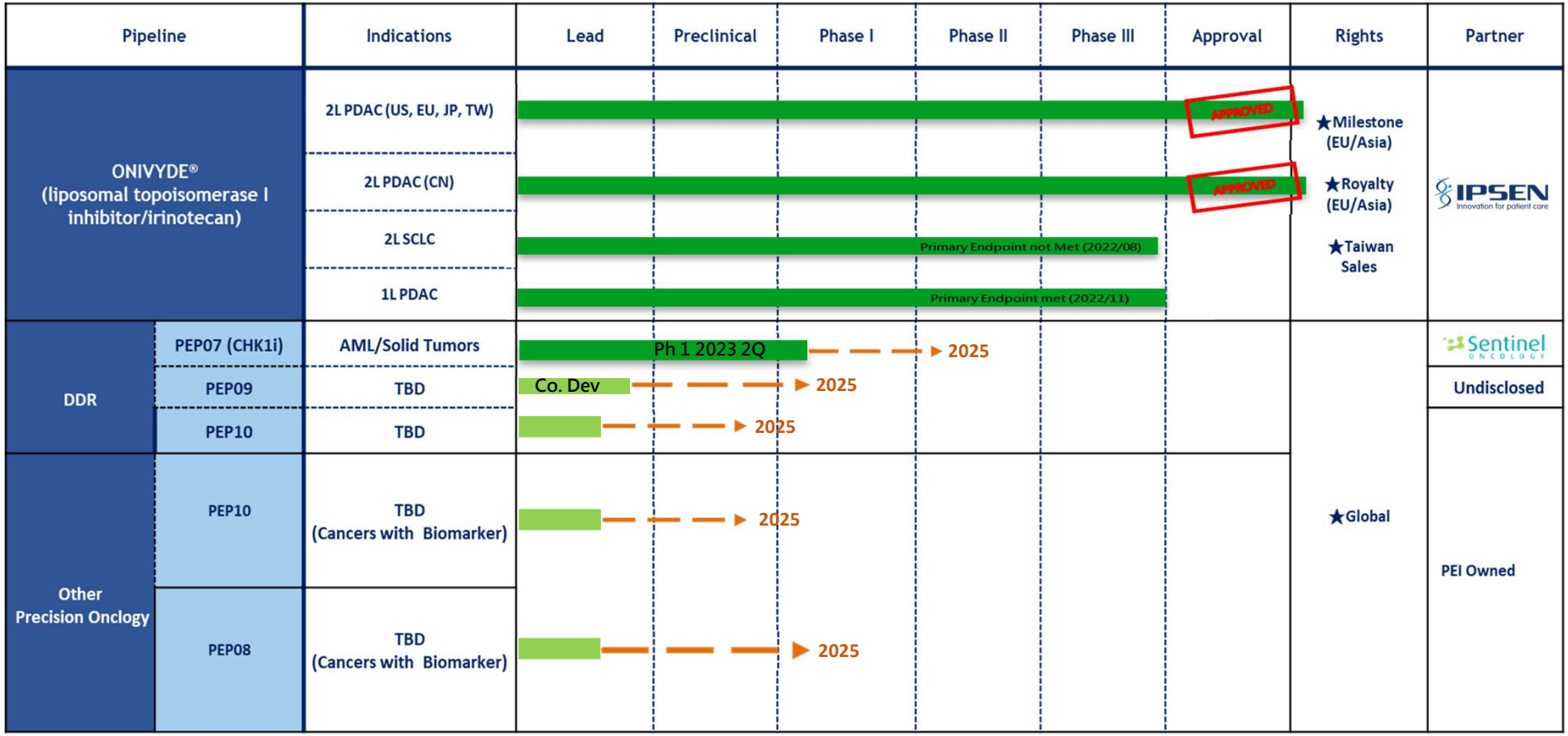

DDR: DNA Damage Response (BRCA ½, CHK ½, Wee1, etc...)

2023年 營運目標

ONIVYDE®產品生命週期的延展

1. 一線胰腺癌三期臨床詳細數據發表 (202301)
2. 一線胰腺癌申請藥證: PE (台灣) (202306)

早期在研產品線的推動與擴增

1. 進行兩個PEP07第一期臨床試驗針對急性骨髓性白血病(AML)及被套細胞淋巴瘤(MCL)的血液腫瘤與實體腫瘤(solid tumor)
2. 持續進行PEP07多項血液及實體腫瘤之前臨床有效性試驗及生物標記探索
3. 新世代DDR標靶藥物(PEP09/10)的開發推進和合成致死藥物(PEP08/10)準備進入前臨床階段


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