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2022 YTD Earning Result

2023/03/03

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This presentation contains certain forward-looking statements.

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Agenda

1. FY 2022 Operational Highlights
2. FY 2022 Operational Overview
3. Research and Development
   - ONIVYDE®
   - PEP07
4. Vision for 2023
5. Q&A

Keep Deliver Sustainable Growth and Enhanced Value

Commercial

ONIVYDE ® market and new indication expansion

1. ONIVYDE® 2L PDAC treatment got China NMPA approved.
2. ONIVYDE® 1L PDAC phase III trial success

Pipeline

New project licensing and RD progress accelerated

1. PEP07 preclinical progress meets expectation
2. PEP07 officially licensing in from Sentinel Oncology
3. Multiple Projects Under Evaluation with External AI/CADD collaboration
4. Early stage projects under evaluation

Operation

Operation with a sustainable growth

1. +20% revenue as RD expenses
2. FY22 Cash and cash equivalents: NT$3.6 bn
3. Long-lasting dividend payout : NT$2.0/share for 2022

FY 2022 Operational Overview

FY 2022 Financial Results

NT$ (000)	FY 2022	FY 2021	Amount Change	% Change
Operating revenue	654,383	654,835	(452)	0%
Operating costs	49,699	37,073	12,626	34%
Gross profit	604,684	617,762	(13,078)	(2%)
Sales expenses	45,104	36,731	8,373	23%
G&A expenses	94,960	80,498	14,462	18%
R&D expenses	181,881	136,887	44,994	33%
Total operating expenses	321,945	254,116	67,829	27%
Operating income	282,739	363,646	(80,907)	(22%)
Total non-operating income and expenses	109,726	181,749	(72,023)	(40%)
Income before income tax	392,465	545,395	(152,930)	(28%)
Income tax expense	73,682	119,364	(45,682)	(38%)
Profit for the period	318,783	426,031	(107,248)	(25%)
EPS(NT$)	2.22	2.95	(0.73)	(25%)

Sales and Royalties Drives Long-term Growth

NT$(000)

Items / Year	2017	2018	2019	2020	2021	FY 2021 / FY 2022 YoY (%)
Taiwan Sales	40,651	87,384	180,389	214,828	235,469	277,594 (18%)
Royalties from Europe and Asia	63,526	109,825	133,651	271,584	419,366	376,789 (-10%)
Milestone	749,500	96,221	0	569,600	0	0
Total	853,677	293,430	314,040	1,056,012	654,835	654,383 (0%)

Taiwan Sales belongs to PharmaEngine, Inc.

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

Research and Development

- Positive topline ONIVYDE® 1L PDAC Phase III Readout at YE22
  - PEP07 Officially Licensing in from Sentinel Oncology
  - PEP07 File IND at YE22
- Multiple Projects Under Evaluation with External AI/CADD collaboration

NAPOLI-3

A randomized, open label phase 3 study of liposomal irinotecan + 5-FU/LV + oxaliplatin (NALIRIFOX) versus nab-paclitaxel + gemecitabine in treatment-naïve patients with metastatic pancreatic ductal adenocarcinoma

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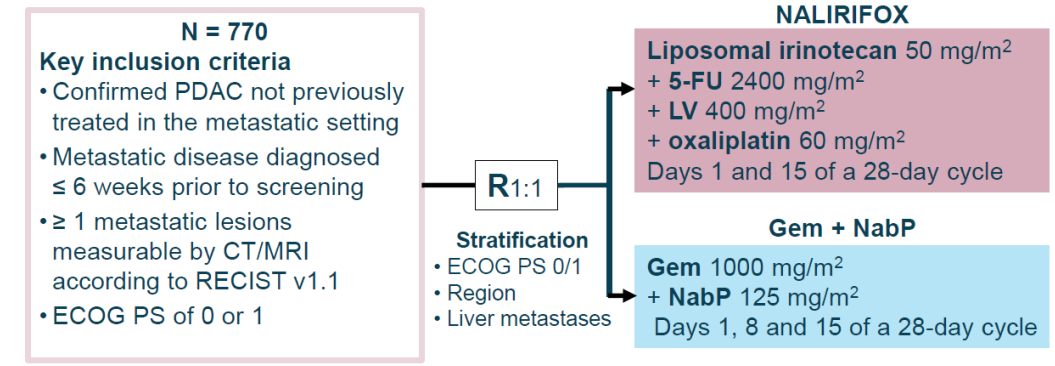
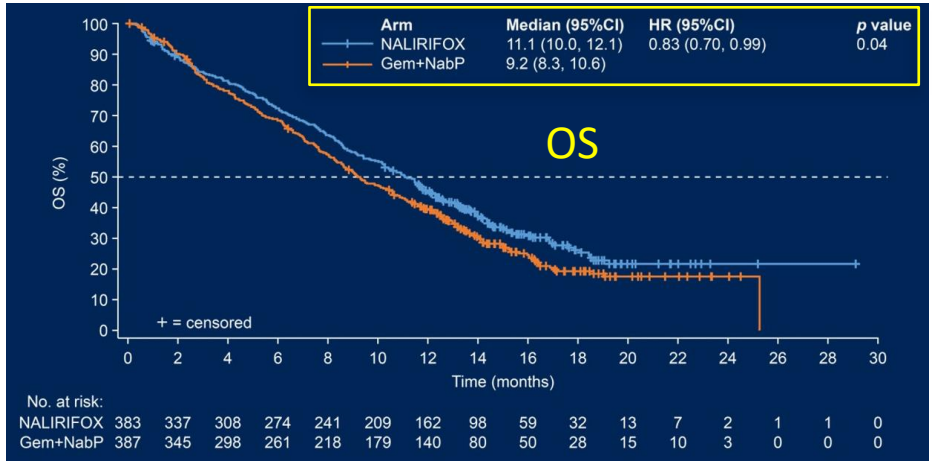
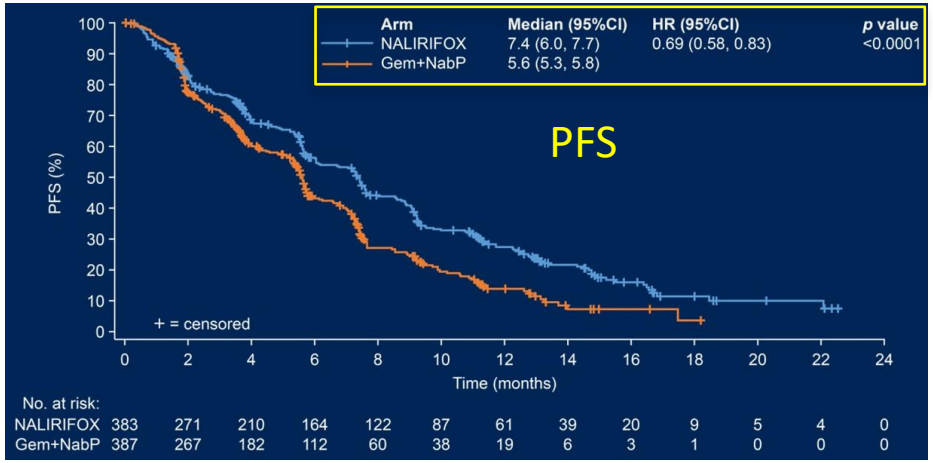
- NALIRIFOX (n = 383) vs. Gem + NabP (n = 387), 770 patients enrolled
- Study endpoints:
  - Primary endpoint – OS (Overall Survival)
  - Secondary endpoints – PFS (Progression Free Survival), ORR (Objective Response Rate)
- First Patient Enrolled: Feb. 2020; Data cut-off: July 23, 2022
- Topline results presented in 2023 ASCO GI







- Conclusion
  - The NALIRIFOX regimen met its primary endpoint demonstrating a statistically significant improvement in OS of 11.1 in months compared to 9.2 months for patients treated with Gem + NabP (HR 0.83 [95% CI 0.70–0.99]; p=0.04).
  - The trial met its secondary endpoint showing patients treated with NALIRIFOX had a statistically significant improvement in mPFS of 7.4 months versus 5.6 months for Gem + NabP (p < 0.0001); ORR was 41.8% (36.8%-46.9%; 95% CI) for patients treated with the NALIRIFOX versus 36.2% with Gem + NabP (31.4%-41.2%; 95% CI).
  - Overall, the safety profile of NALIRIFOX in NAPOLI 3 was manageable. No new safety concerns with the NALIRIFOX regimen were identified.

Frontline Regimens for Patients With Metastatic Pancreatic Cancer

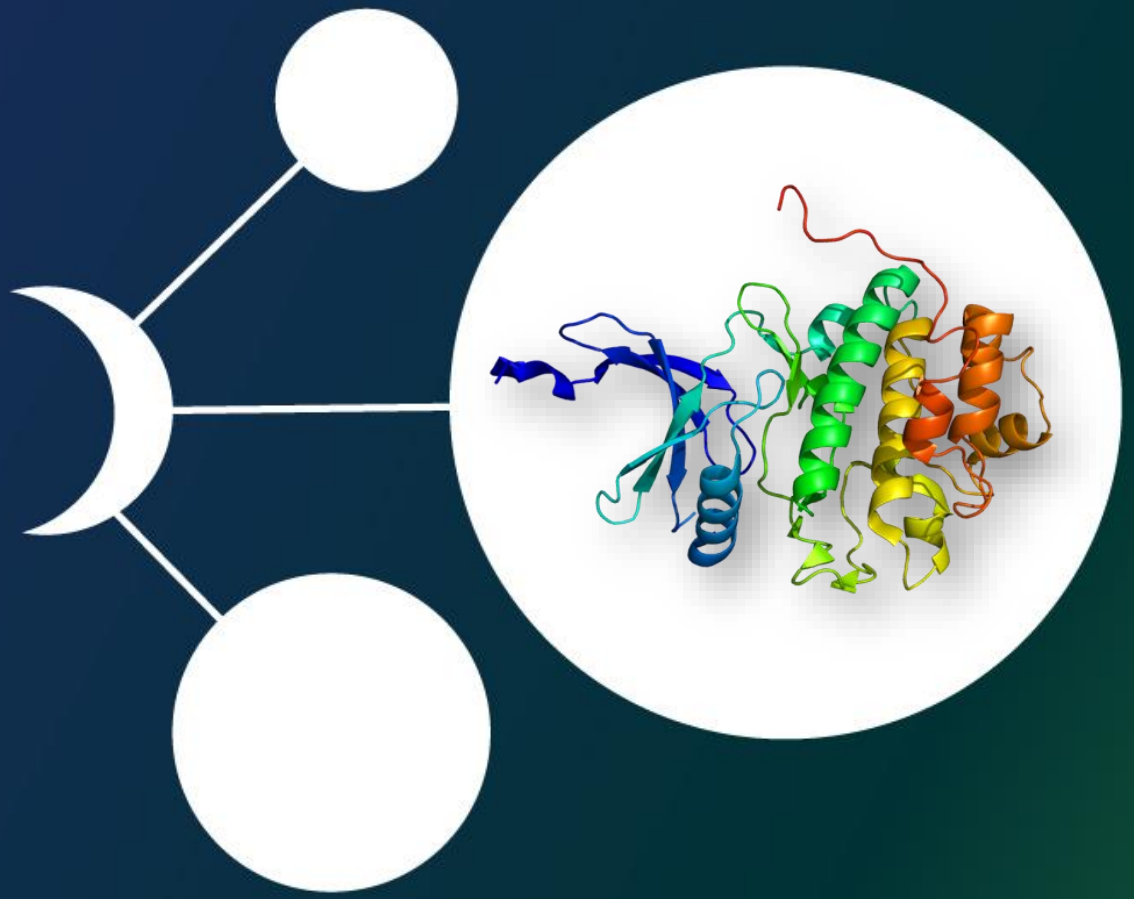
Study	Phase III MPACT		Phase III MPACT		Phase II/ III ACCORD 11	
Drug	NAIRIFOX (Onivyde)	Gemcitabine + Nab-Paclitaxel	Abraxane + Gemcitabine	Gemcitabine	FOLFIRINOX	Gemcitabine
Source	ASCO GI 2023		Von Hoff et al 2013 (NEJM)		Conroy et al 2011 (NEJM)	
Baseline Characteristics						
n	383	387	431	430	171	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	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

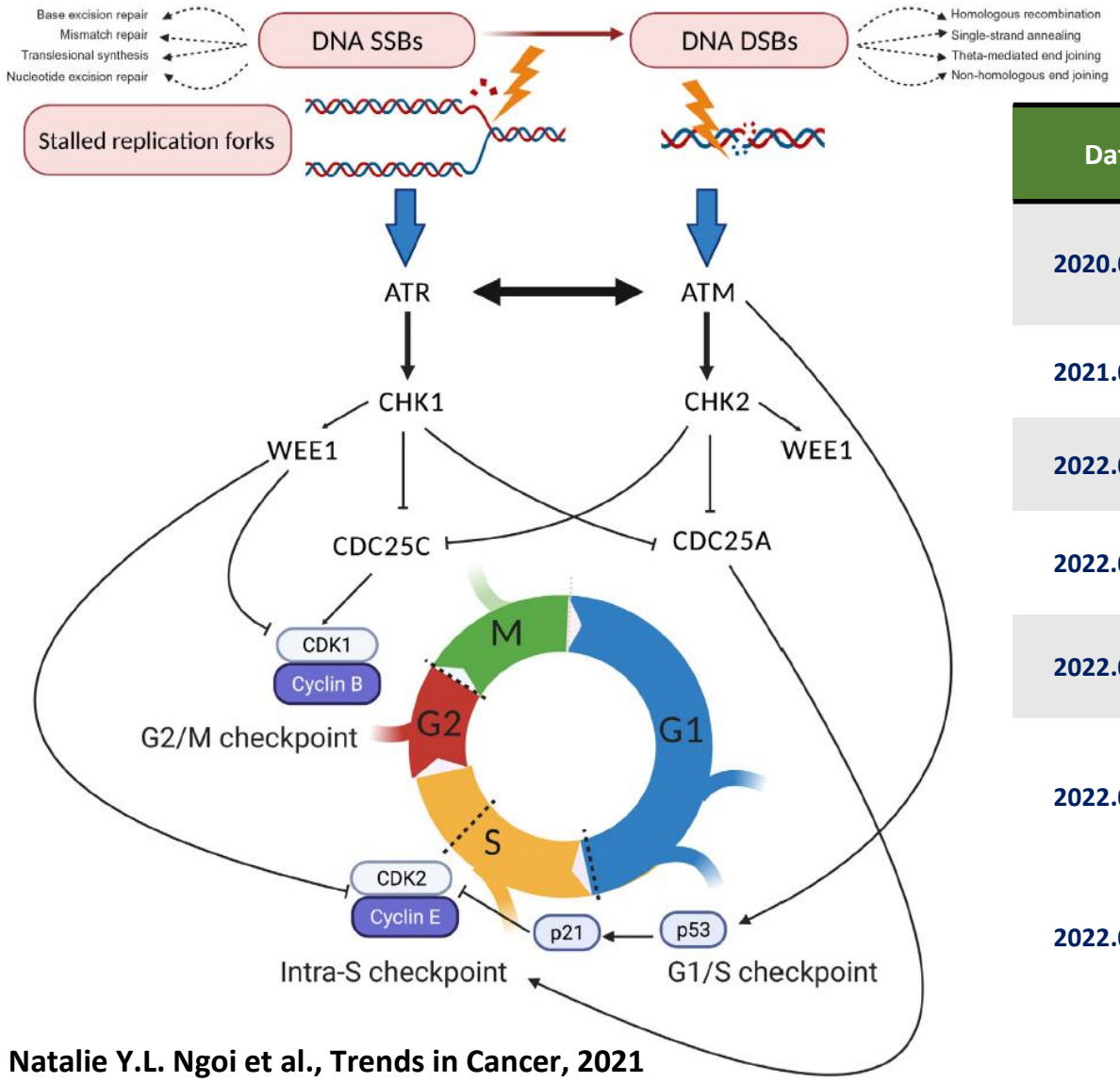
Note: ORR= Overall Response Rate ; CR=Complete Response ; DCR=Disease Control Rate; mDoR=median Duration of Response; mPFS=median Progression-Free Survival; mOS= median Overall Survival

PEP07 (CHK1 inhibitor)

- PEP07 Officially Licensing in from Sentinel Oncology
- Early-stage DDR Project Transactions Became Hotter
- Keep Moving Forward to Phase I IND



DNA Damage Repair
One Critical Pathway, Multiple Targets



Natalie Y.L. Ngoi et al., Trends in Cancer, 2021

DDR deal transactions became hotter

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
2021.04.07	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

Deep understanding and targeted query of DDR pathways may identify novel therapeutic opportunities and biomarkers for optimal patient selection

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				
Genetech	GDC-0575	Discontinued				
GSK (Sierra Oncology)	SRA-737	Ph I / II (Complete)				
Esperas Pharma	LY2880070	Ph I / II (Complete)				
PharmaEngine	PEP07	Ph I Ready				

Excellent Good Fair Poor Unknown

PEP07: A novel, brain penetrant oral Chk1 inhibitor for the treatment of AML and MCL – 6th Annual DDR Inhibitors Summit 2023

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

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Sentinel ONCOLOGY

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

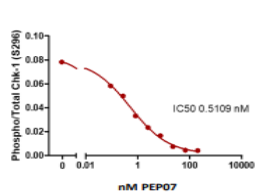


Figure 1. a) IC50s from ZLYTE FRET-based kinase assay b) Cellular IC50 as measured by autophosphorylation of pChk1 S296/total Chk1 in HT29 cells following 18h drug treatment c) phospho-H2A.X S139 in THP1 AML cell line following 18h drug treatment d) caspase 3/7 induction in Jeko-1 cell line following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

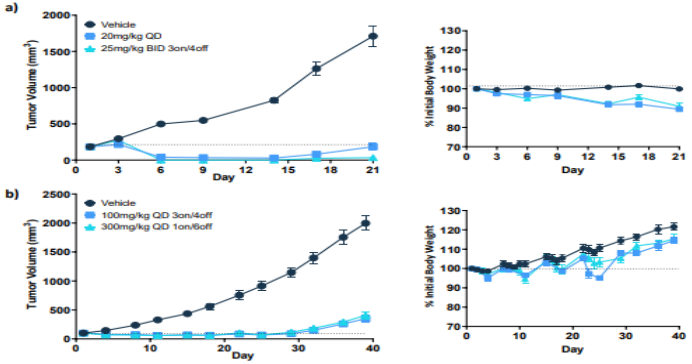


Figure 2. a) Jeko-1 MCL xenograft model. Mice were dosed with PEP07 daily for 21 days at 20mg/kg or BID 25mg/kg 3 days on followed by 4 days off. b) MV411 AML xenograft model. Mice were dosed with PEP07 once a week at 300mg/kg, or 100mg/kg for 3 days followed by 4 days off. Dosing was for 4 cycles.

PEP07 combines with cytarabine in AML xenografts

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

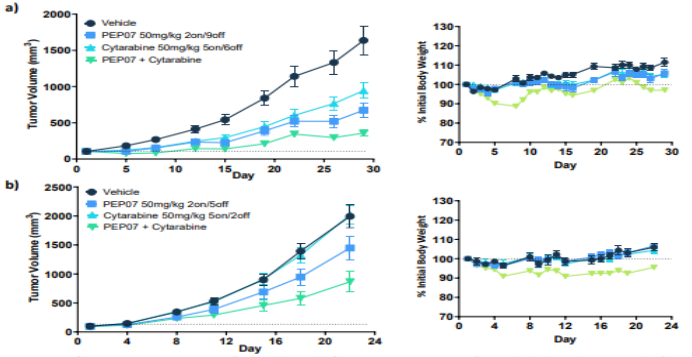


Figure 3. a) MV411 AML xenograft model and b) THP1 AML xenograft model, dosed as per the figure legends. PEP07 dosed PO and cytarabine dosed IP. Dosing was for 3 cycles.

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.

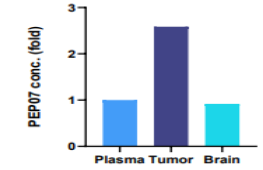
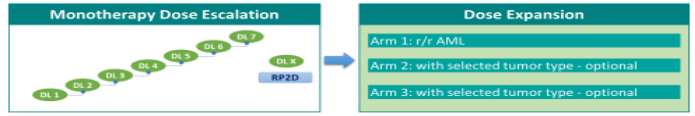


Figure 4. Following a 6-week efficacy experiment, 4 mice were treated with PEP07 and samples collected at 1h after dosing. LC-MS/MS analysis of PEP07 concentration in blood, tumor, and brain samples was conducted.

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



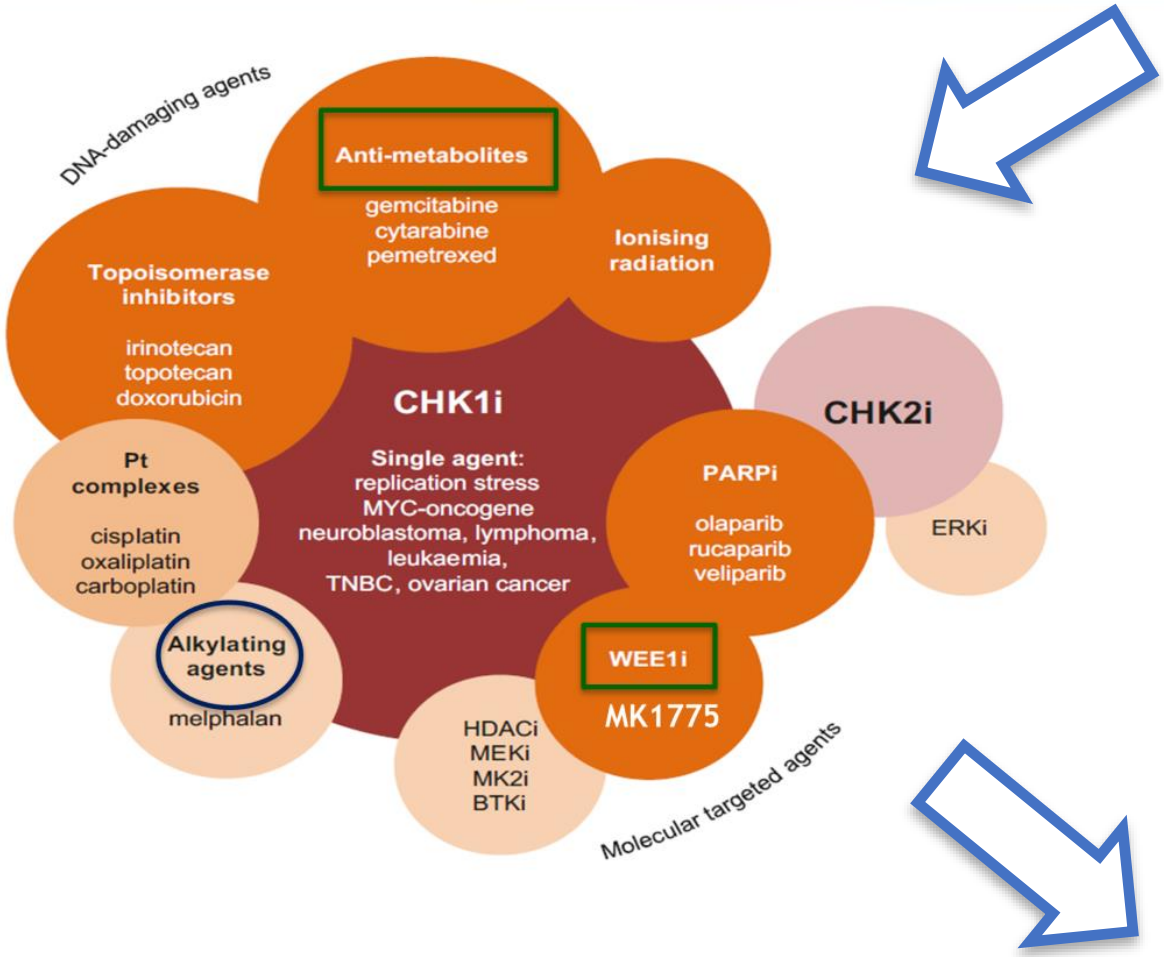
b) Study schedule

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 for Potential Combination Therapies



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 Early-Stage Clinical Development Strategy

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Ph1b monotherapy, dose escalation/expansion in AML and MCL

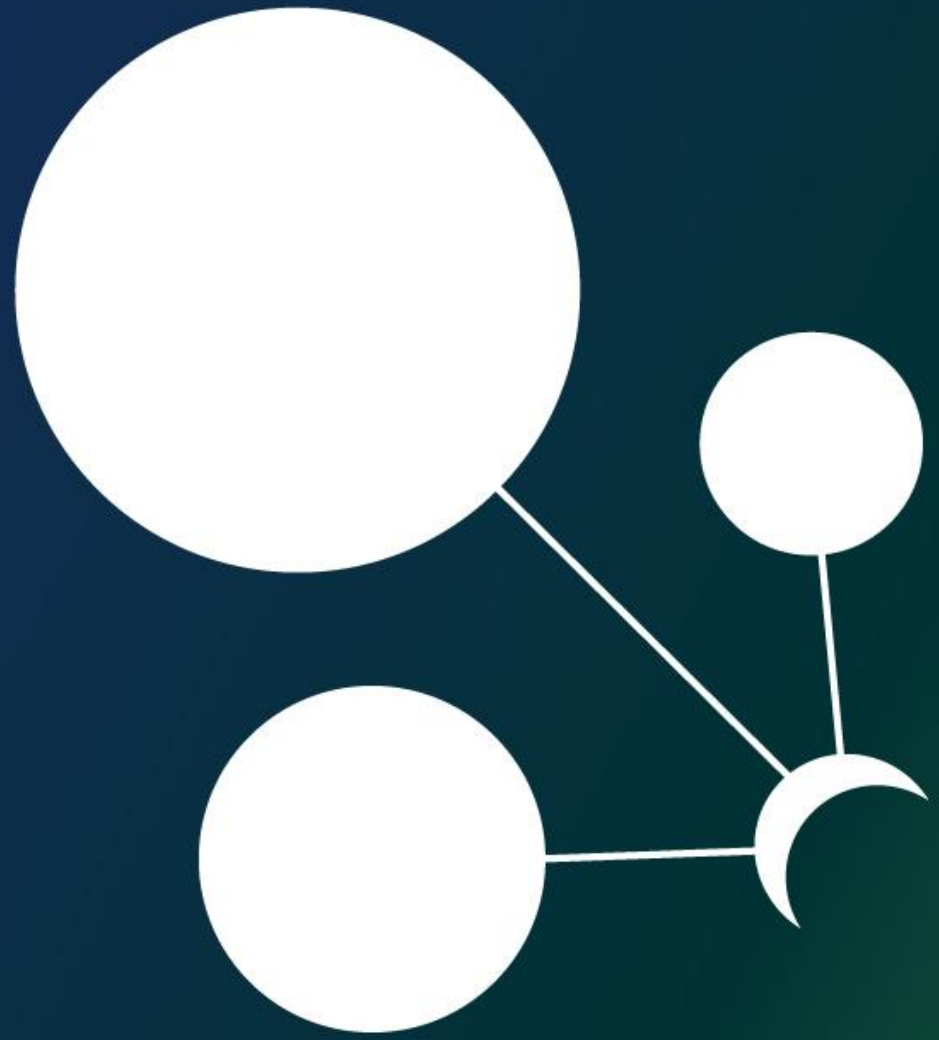
→ **Ph1b Combo, dose escalation/expansion in selected hematologic cancer, e.g., AML or MCL**

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

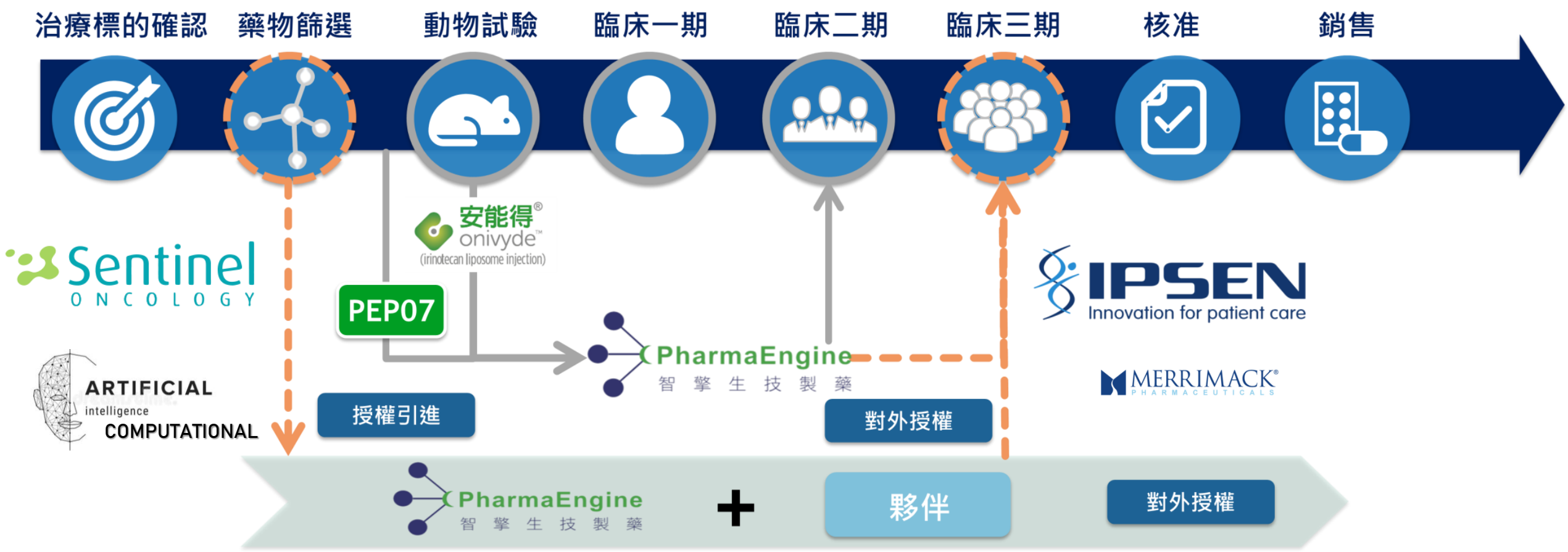
→ **Ph1b Combo, dose escalation/expansion in selected solid tumors**

Preclinical biomarker study is ongoing for further design of clinical trials

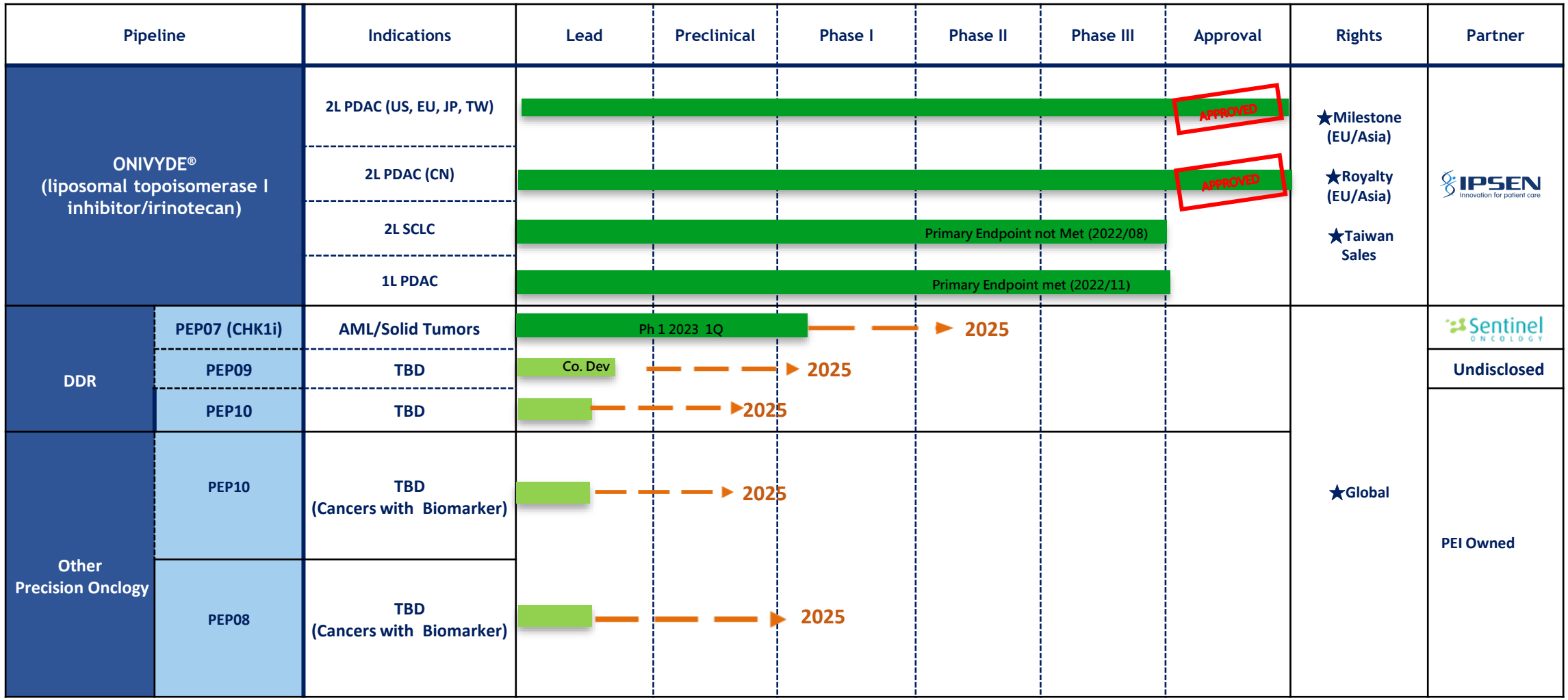
Vision for 2023



Virtual Pharmaceutical Company Business Model



Pipeline Portfolio Focus on Precision Oncology



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

2023: Year of Revitalization and Marching Forward

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Growth through ONIVYDE® life cycle management

1. 1L PDAC Phase III data readout (1Q23)
2. 1L PDAC file NDA in Taiwan and other countries

Advancement and growth of early-stage pipeline

1. Start PEP07 Phase 1 studies and aim in AML and MCL
2. Additional efficacy studies in animal models and biomarker evaluation of PEP07 for different oncology indications
3. Develop more DDR targets: PEP09, PEP10
4. Develop next generation target therapy : PEP08, PEP10
5. Initiate other precision oncology projects development

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