巨生生醫 biomedical
MEGAPRO

股票代號:6827

巨生生醫股份有限公司

-奈米藥物平台專家

總經理：王先知博士
jassywang@megaprobio.com
www.megaprobio.com

免責聲明

這份簡報中所載的資訊是由巨生生醫股份有限公司編寫的。它有可能尚未得到充分核實，有待進一步更新、修訂。它是依據目前所獲得的主、客觀事實與依據進行撰寫，進展中的事情有可能持續變動中，無法充分保證不再更動。因此，並無法百分之百擔保本簡報所呈現的報告內容不再變動。新藥開發風險大，在醫藥法規部門未核定藥證前仍有眾多不確定風險，請投資人謹慎評估。

公司概況

✓設立時間：2014年11月

✓公司登記：中華民國

✓實收資本額：5.75億元

✓公司所在：新竹縣竹北市生醫五路66號10樓之1(生醫園區)

✓公司背景：從工研院奈米國家型計畫奈米生醫領域衍生的新創公司

✓產品/服務：以奈米藥物的臨床發展為核心

✓目標市場：將早期發展的候選藥物，經由前臨床、人體臨床試驗階段加值後，自行取證或再授權給藥廠。

✓員工人數： 21 位 / 研發 13位 (博士5位)

董事會

董事陣容堅強

蔣為峰 董事長/策略長
- 中興大學企管碩士
- 萬豐資本董事長

王先知 董事/總經理
- Iowa State University化學博士
- 經歷：
  奈米國家型計畫奈米生醫領域召集人
  工研院材化所副所長

許源宏 董事/研發副總
- 中興大學化工博士
- 經歷：
  工研院生醫所藥物傳輸技術部副理
  國家型奈米生醫計畫子項計畫主持人

中國化學製藥股份有限公司
法人董事

陳志隆 董事/轉譯科學協理
- 成功大學微生物與免疫研究所博士
- 經歷：
  工研院生醫所複合材料研究室副理
  國家型奈米生醫計畫子項計畫主持人

允成投資股份有限公司
(中橡旗下投資公司)
法人董事

吳朝同 獨立董事
- 中興大學企業管理學系
- 經歷：
  日盛聯合會計師事務所
  會計師

洪奇昌 獨立董事
- 台大公共衛生研究所醫學碩士
- 經歷：
  中華民國精神科專科醫師醫師
  立法院立法委員

傅祖聲 獨立董事
- 臺灣大學法學院法律系
- 經歷：
  國際通商法律事務所資深合夥律師

經營團隊

奈米技術優勢

王先知博士

總經理

- 奈米國家型計畫奈米生醫領域召集人
- 工研院材化所副所長
- 工研院歷練 25 年

許源宏博士

執行副總

- 智慧標靶藥物傳輸技術及應用
- 標靶奈米光動力藥物之轉譯研究
- SN38-PM技術及試量產GMP制程開發
- 新型抗腫瘤轉移之淋巴目標載體開發
- 熱誘導快速釋放之腫瘤標靶奈米載體

陳志隆博士

協理,
轉譯科學處

- 發展磁標定之幹細胞應用於脊髓損傷治療
- 建立人類幹細胞質量認證標準與流程
- 低能量光線與重力感應機制對小鼠骨髓間葉幹細胞生長活化之影響

陳永竹博士

處長,
產品研發與製造處

- 局部麻醉複方新劑型開發
- 長效口服過動症治療藥物開發
- 長效思覺失調治療藥物注射針劑開發

邱奕翔

財務副總

- 擅長財務、會計、審計及稅務規畫
- 臺灣IPO規劃與推動

奈米微粒產品特性

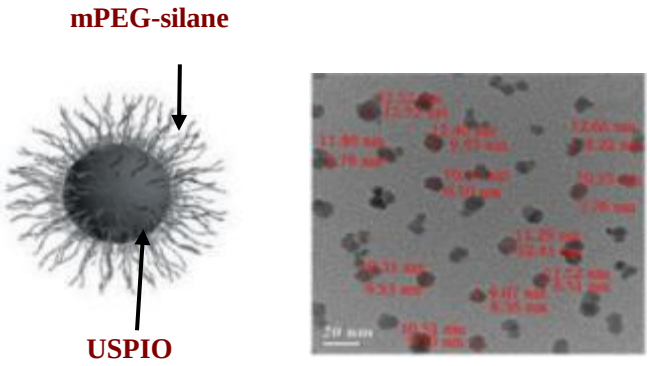
◆聚乙二醇化氧化鐵奈米顆粒 (PEGylated iron oxide nanoparticle)

主要特點:

a.非醣類製劑有較低的致敏性。
b.在T2影像下的MRI顯影劑中有較佳的 r2 橫向弛豫率(relaxivity)。
c.巨噬細胞吞噬效果佳，進入肝臟效率佳。
d.產生較低的游離鐵及氧化壓力。

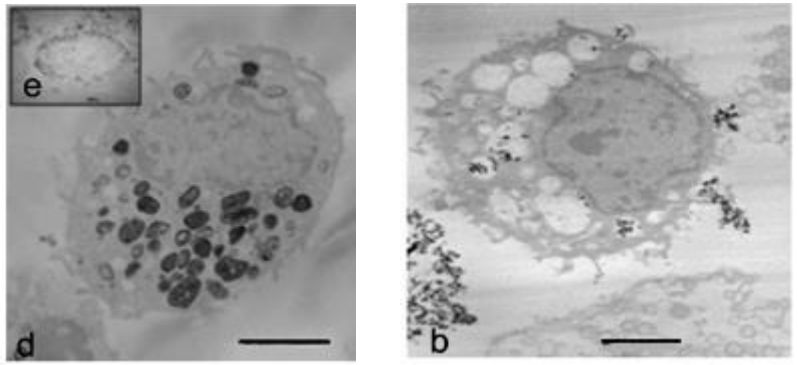
	IOP Injection	Feraheme
粒徑 (TEM)	10-12 nm	4.2 nm
r2 $(mM \cdot s)^{-1}$*	130~170	70

MegaPro: IOP Injection

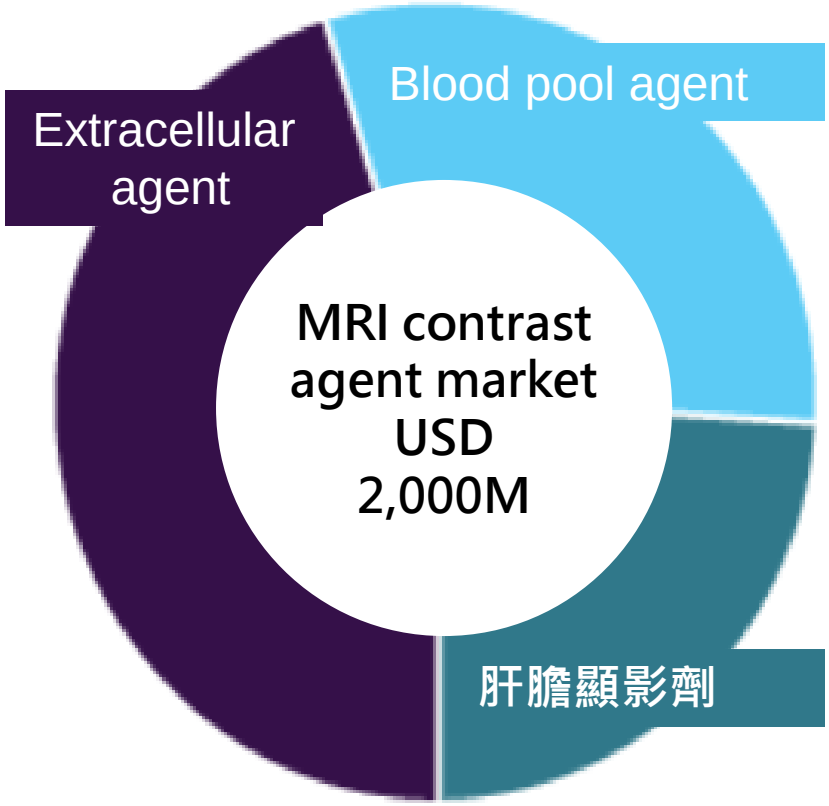


巨噬細胞吞噬效果佳

IOP Injection **Feraheme**



MPB-1523 被低估的肝癌檢測市場



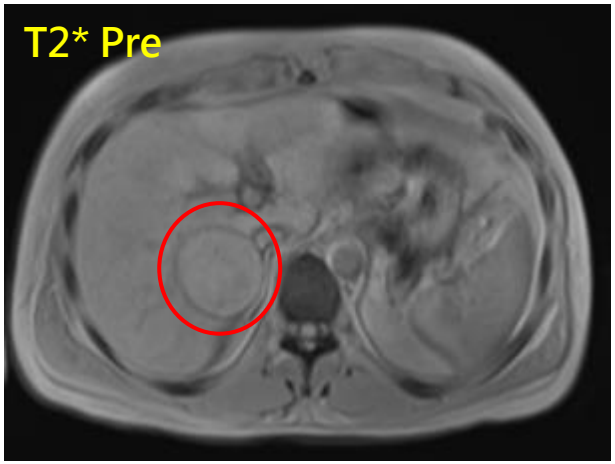
Source: www.grandviewresearch.com

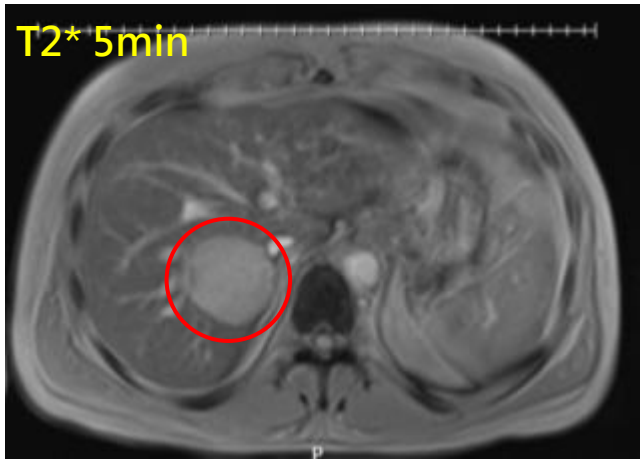
- 釓類顯影劑壟斷整個MRI顯影劑市場
- 釓類顯影劑用在腎功能不佳(eGFR<30)的病人，可能引起腎生性全身纖維化（Nephrogenic systemic fibrosis，簡稱 NSF）.
- **EMA's final opinion confirms restrictions on use of linear gadolinium agents in body scan** 21 July 2017
  ……. The intravenous linear agents gadoxetic acid and gadobenic acid can continue to be used for liver scans because they are taken up in the liver and meet an important diagnostic need. ……
- **MPB-1523已在今年6月獲得美國FDA孤兒藥資格認定，核准本MRI顯影劑用於肝細胞癌之追蹤**

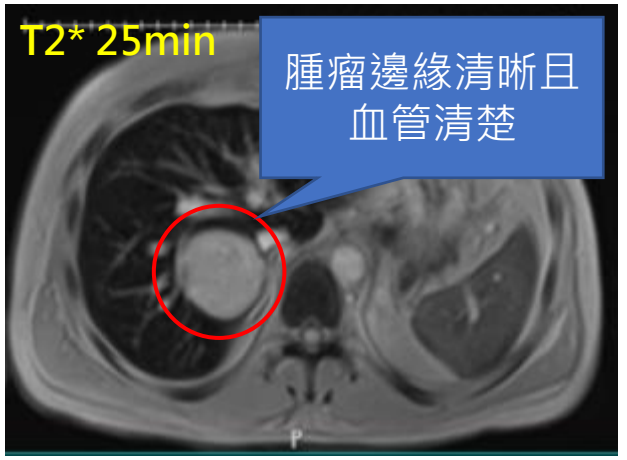
CT確診 vs MPB-1523

1-003-003

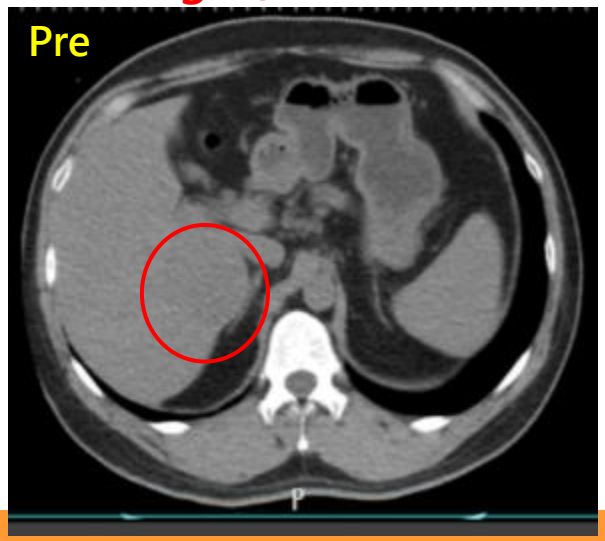
MPB1523 MR T2* image
(對比高所以腫瘤邊緣清楚，微細血管清晰，足以判斷是否已侵犯血管)

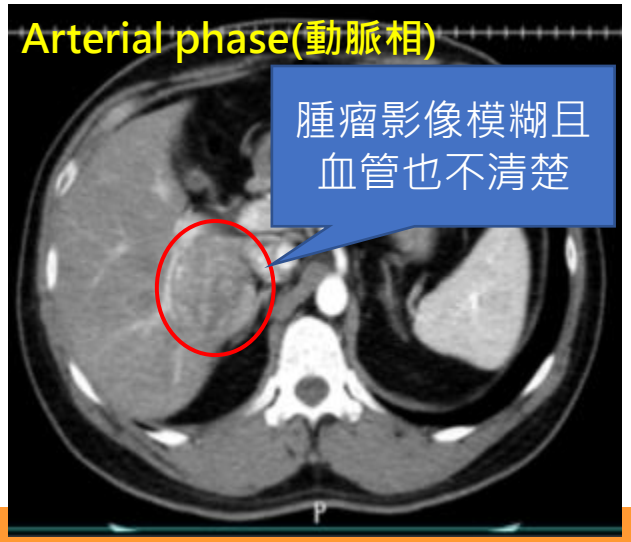


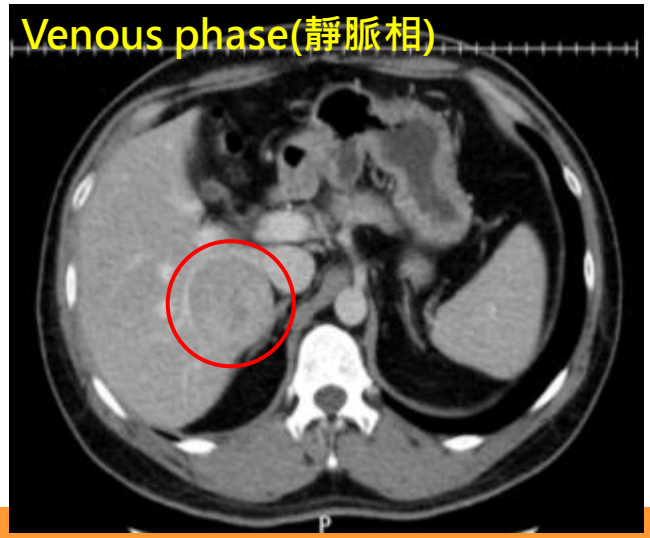




CT image (對比低，看不到微細血管)





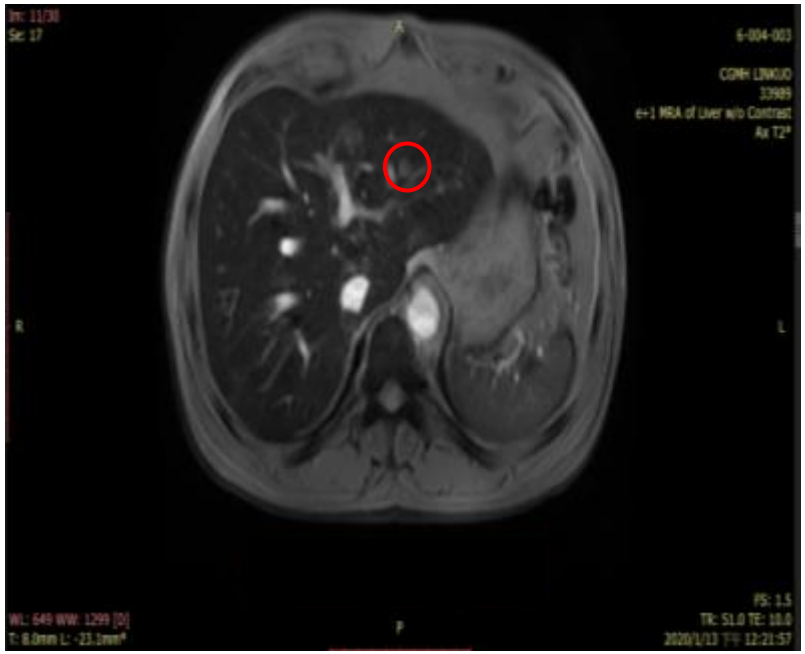


顯影效果卓越

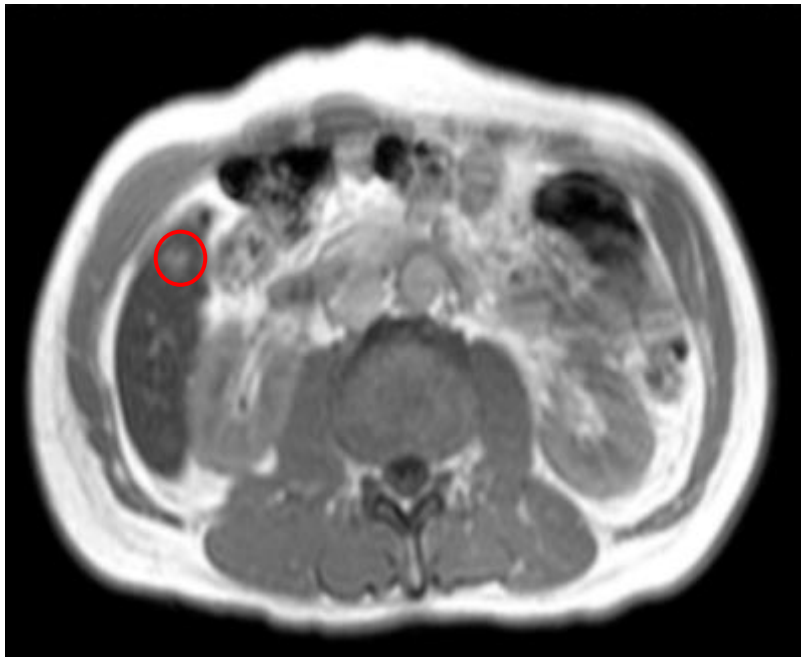
在各種分化程度下皆能偵測到小於1.5公分的腫瘤

在分化良好的 肝腫瘤 中，庫普弗細胞密度將保持不變，但與周圍肝臟相比，庫普弗細胞功能可能會降低，但是MPB-1523仍然可以清楚看到腫瘤影像。

Size: 1.5 cm * 1.0 cm
(分化良好)



Size 0.9 cm *0.7 cm
(中度分化)



MPB-1523 安全性及檢測率高

- MPB-1523 在臨床二期被判定與藥物相關的不良反應僅有2個:
  1個Grade 1 AE-紅疹 / 1個Grade 2 AE-皮膚搔癢，整體的不良反應僅有3.84%。
- 臨床二期試驗結果顯示腫瘤的陽性檢測率高達96%

Table 14.3.1.4 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Severity (Safety Population)

System Organ Class Preferred Term	Severity	Statistic	All Subjects (N =52)
Pruritus	Mild	n (%) E	0
	Moderate	n (%) E	1 (1.92) 1
	Severe or worse	n (%) E	0
Rash	Mild	n (%) E	1 (1.92) 1
	Moderate	n (%) E	0
	Severe or worse	n (%) E	0

E: Number of events; N: Number of subjects in the safety population; n: Number of subjects with adverse event with particular severity;
%: Calculated using the number of subjects in the safety population as the denominator (n/N*100).
All adverse events are coded using MedDRA version 20.0.

兩岸專家會議一致認同MPB-1523功效

- 某中國上市公司邀請了中國三甲醫院專家討論MPB-1523，對於MPB-1523的顯影效果十分驚豔。
- 認為MPB-1523可以鑑別肝硬化結節與腫瘤結節，競爭對手Primovist這方面效果差。
- MPB-1523臨床二期試驗中佔用機台時間與競爭對手Primovist相同皆為30分鐘，但是MPB-1523在試驗數據中有機會縮短。
- 轉移性的肝臟惡性腫瘤遠超過於原發性的肝癌，其主要大都來自於大腸直腸癌，因此也認同應用在轉移性肝臟惡性腫瘤診斷的必要性。
- 影像邊緣及血管的清晰對於判斷腫瘤特性十分重要，以往無法獲得這麼清晰的影像。

臨床2期結果發表於國際期刊

IOP Injection, A Novel Superparamagnetic Iron Oxide Particle MRI Contrast Agent for the Detection of Hepatocellular Carcinoma: A Phase II Clinical Trial

Chi-Feng Chiang, MD, PhD,[1] Yuan-Hung Hsu, PhD,[2] Wen-Yuan Hsieh, PhD,[2] Tzu-Hsin Liao, BS,[2] Chih-Lung Chen, PhD,[2] Yung-Chu Chen, PhD,[2] Po-Chin Liang, MD, PhD,[3,4*] and Shian-Jy Wang, PhD[2*]

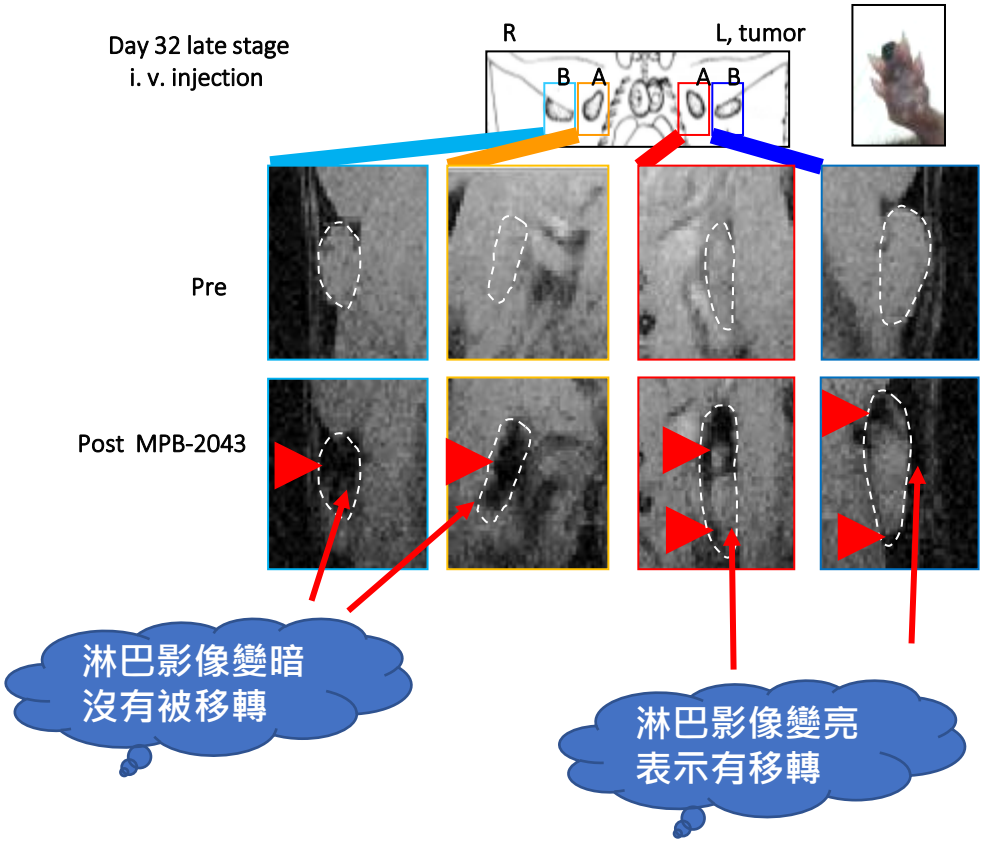
Background: MRI is crucial in diagnosing hepatocellular carcinoma (HCC). Superparamagnetic iron oxide particles (SPIO) are liver-specific contrast agents which enhance lesions in T_2-weighted images. Iron oxide nano-particle m-PEG-silane (IOP) Injection, a newly developed SPIO, showed promising imaging effects and good safety profile in preclinical studies and in phase I clinical trial.
Purpose: To evaluate the safety and clinical validity of IOP Injection as MRI contrast agent in diagnosing HCC.
Study type: Prospective.
Subjects: A total of 52 subjects (61.6 ± 11.05 years, 45 males/7 females) with suspected HCC.
Field Strength/Sequence: 1.5 T, T_1-weighted in/opposed phase, T_2*-weighted gradient echo, T_2-weighted fast spin echo, true fast imaging with steady-state free precession.
Assessment: Adverse effects and clinical monitoring were recorded throughout the 5-day study. Two independent readers (M.G.H. with 30 years of experience, S.P.K. with 26 years of experience) made the diagnosis. The diagnostic performance of IOP-enhanced MRI was evaluated with sensitivity and positive predictive value by comparing to the pathology reports from subsequent hepatic resection. The number of lesions with various sizes and degrees of differentiation detected by IOP-enhanced MRI was assessed. The relative change in signal intensities over time was indirectly measured from acquired images.
Statistical Tests: Sensitivity and positive predictive value were used to evaluate the diagnostic performance of IOP-enhanced MRI. Prevalence-adjusted and bias-adjusted κ coefficient was used to assess the interreader variability.
Results: No serious adverse event related to IOP Injection was found. IOP Injection enhanced the lesion-to-liver contrast ratio in T_2*-weighted images by 50.1% ± 4.8%. IOP-enhanced MRI detected HCC with 100% sensitivity by subject and 96% sensitivity by lesion. IOP Injection visualized subtle vascular invasion as filling defect within vessels in true fast imaging with steady-state free precession (TrueFISP) images.
Data Conclusion: IOP Injection was safe and efficacious as MRI contrast agent in diagnosing HCC in a limited group of subjects.
Evidence Level: 2.
Technical Efficacy: Stage 2.

J. MAGN. RESON. IMAGING 2023.

***JMRI*為MRI領域中的專業期刊，相關發表數據需要經過同儕覆核，公信力高，影響力點數5.1分。**

MPB-2043 市場規模龐大

MRI顯影劑-淋巴轉移診斷市場超過10億美金



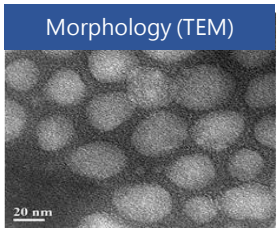
圈起來的部位為小鼠的淋巴結，施打MPB-2043後，淋巴結完全變暗代表沒有腫瘤細胞的存在，局部變暗或未變暗代表已被癌細胞轉移。

1. 淋巴結有無腫瘤細胞是癌症判斷期別及治療方式的重要依據
2. **精准的淋巴影像，可避免非必要的摘除，增加術後的恢復。**
3. 約有10-30% 的淋巴結在可取樣檢驗範圍外，造成診斷失誤。
4. 有影像可提供醫生精確的治療策略。
5. 幾乎所有發生率高的實體腫瘤都有淋巴轉移檢測的需求，**估計潛在市場超過10億美元。**

奈米微胞

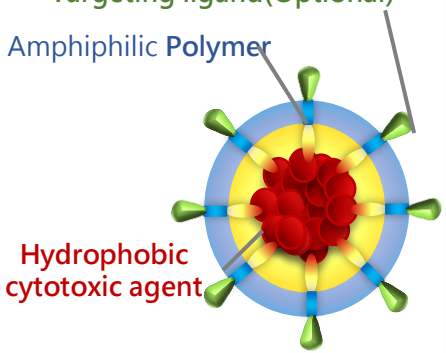
市場最佳的疏水性藥物針劑奈米載體技術

股票代號:6827



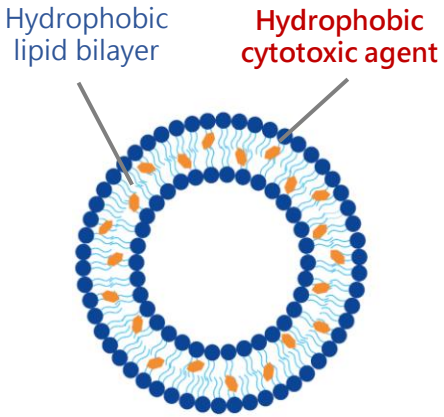
巨生獨家 高分子微胞技術

- 可應用於針劑型
- 物理包覆，疏水藥物載藥量大(>20%)
- 腫瘤的滲透能力佳(<70nm)
- 可再搭配靶向配體



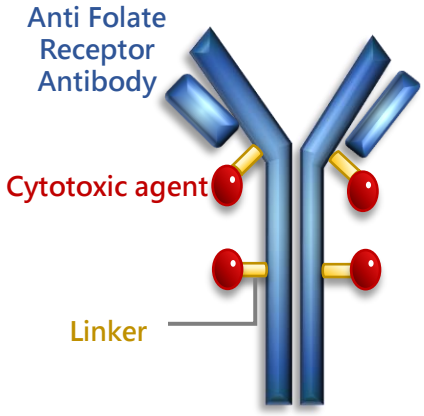
微脂體技術

- 可應用於針劑型
- 物理包覆，疏水性藥物載藥量約3~5%
- 通常粒徑範圍在100～200 nm



ADC

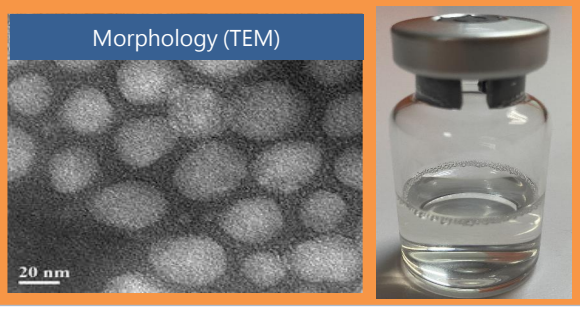
- 3-4小分子藥物
- 細胞標靶 + 小分子藥物



MPB-1734

可有效改善Jevtana(去癌達)缺點，並且擴大適應症範圍

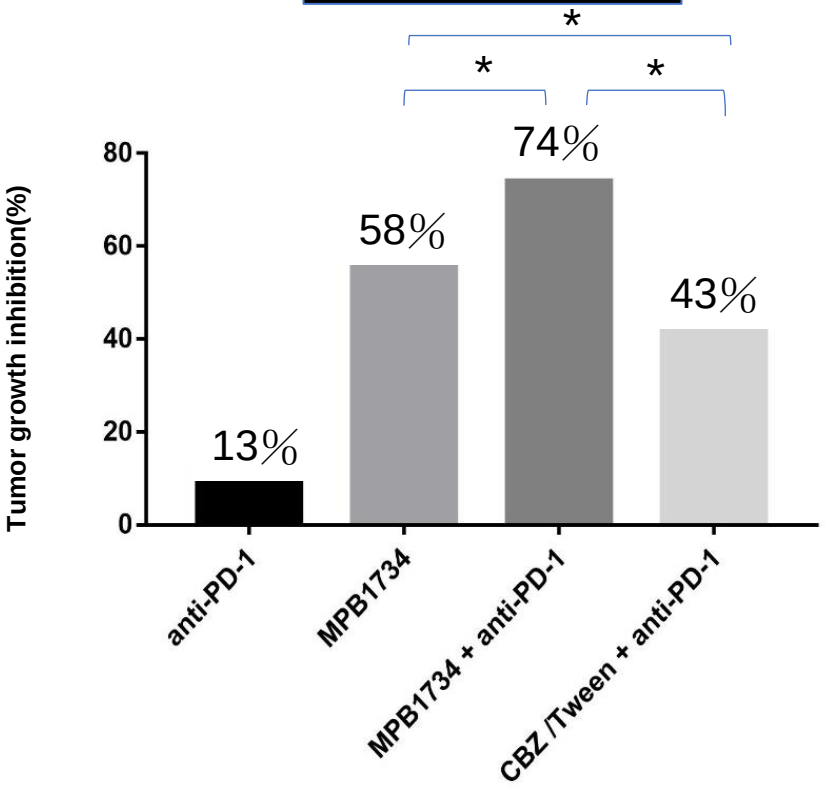
股票代號:6827

	巨生 MPB-1734	Sanofi Jevtana
		
專利	已於2022年11月取得美國成分專利,將以505B2申請藥證	API已經過期
水溶性	可溶於水	不溶於水 需要搭配Polysorbate 80與酒精
過敏反應	高分子膠束劑型，可溶於水不需要事前給予類固醇	Polysorbate 80具高致敏性，需要事前給予類固醇(黑盒警示)
嚴重嗜中性白血球低下	經過高分子膠束包覆後，已經大幅減少此問題	有嚴重嗜中性白血球低下問題，為劑量限制毒性 (黑盒警示)
適應症	目前將以卵巢癌、頭頸癌前列腺癌作為臨床申請	僅前列腺癌，2020年市場達USD 633M

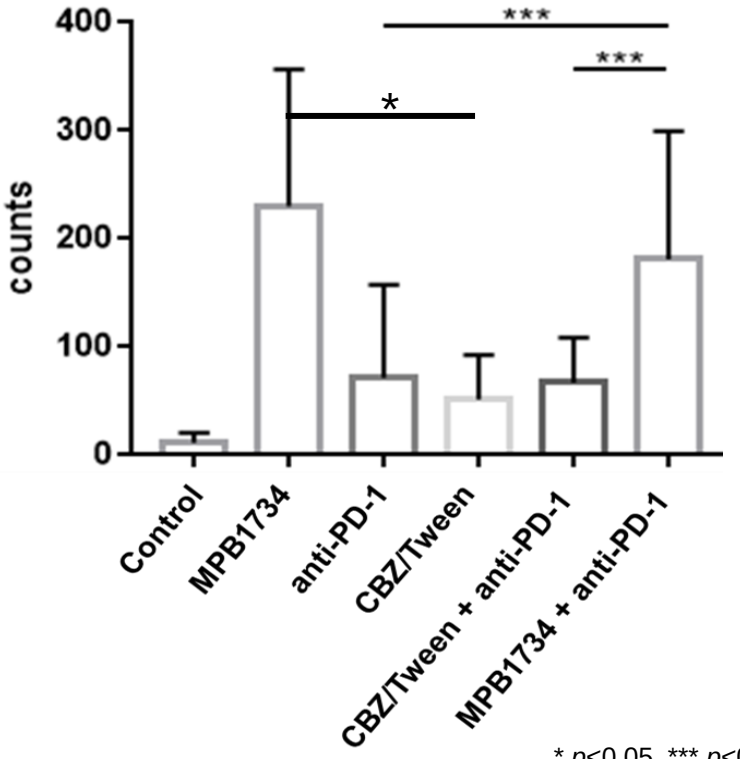
有機會併用免疫製劑

頭頸癌動物模式顯示
MPB1734 與anti-PD1抗體並用有加乘效果，腫瘤抑制效果顯著優於目前市售劑型，且治療後能夠顯著增加毒殺型T細胞進入腫瘤的量，讓原本對免疫治療療效不佳的”Cold Tumor”轉為”Hot tumor”

腫瘤抑制率比較



腫瘤內毒殺型T細胞比較



Cell line: MOCL2-1 (H&N cancer)

* $p<0.05$, *** $p<0.001$

MPB-1734 目前進度

1. 臨床一期試驗正在進行第二個劑量組的收案，預計明年中完成病人收案。
2. 2023/5 獲得 A+ 企業創新研發淬鍊計畫 - 快速審查臨床試驗計畫的支持，可獲得經費補助。
3. 臨床2期試驗規劃針對攝護腺癌、頭頸癌，並規劃與抗PD-1的藥廠合作，探討合併療法的可能性。

細胞治療 細胞治療發展

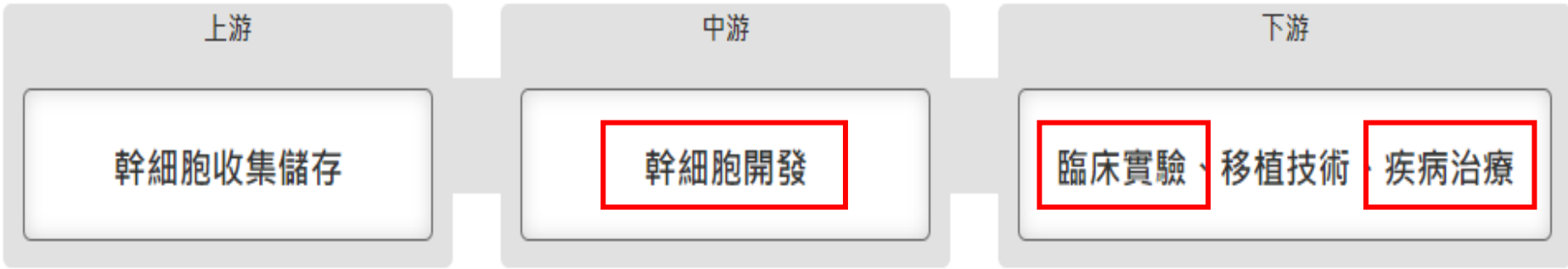
2018 TFDA發佈「特定醫療技術檢查檢驗醫療儀器施行或使用管理辦法」，開放6 項自體細胞治療技術

2022 TFDA已核准144 件細胞治療技術施行計畫。

2023 TFDA再生二法將細胞治療定義為藥品並且朝向規格化前進

2023 US FDA 至今已經核准了29種細胞與基因療法的產品。

https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products

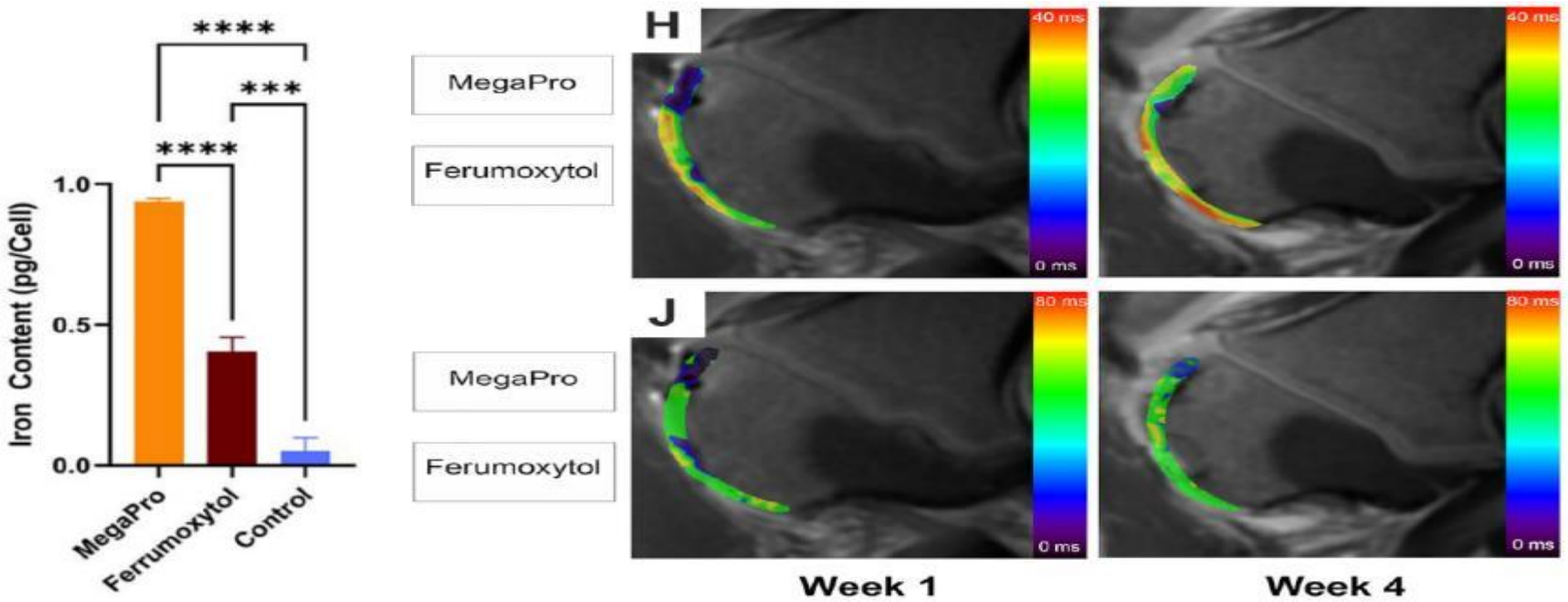


Cell therapy 奈米微粒應用在標示幹細胞

與美國史丹福大學合作的迷你豬軟骨幹細胞追蹤

試驗結果

- ✓ 巨生的奈米微粒在每個幹細胞的含量是其他產品的2倍以上。
- ✓ 植入幹細胞後其他產品在第二周訊號已經遞減，巨生的奈米微粒在第四周還能被偵測到.
- ✓ 巨生的奈米微粒是目前市面上可應用在人體臨床試驗最好的產品。



Cell therapy *Theranostics, 2023*

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Research Paper

MegaPro, a clinically translatable nanoparticle for *in vivo* tracking of stem cell implants in pig cartilage defects

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Abstract

Rationale: Efficient labeling methods for mesenchymal stem cells (MSCs) are crucial for tracking and understanding their behavior in regenerative medicine applications, particularly in cartilage defects. MegaPro nanoparticles have emerged as a potential alternative to ferumoxytol nanoparticles for this purpose.

Methods: In this study, we employed mechanoporation to develop an efficient labeling method for MSCs using MegaPro nanoparticles and compared their effectiveness with ferumoxytol nanoparticles in tracking MSCs and chondrogenic pellets. Pig MSCs were labeled with both nanoparticles using a custom-made microfluidic device, and their characteristics were analyzed using various imaging and spectroscopy techniques. The viability and differentiation capacity of labeled MSCs were also assessed. Labeled MSCs and chondrogenic pellets were implanted into pig knee joints and monitored using MRI and histological analysis.

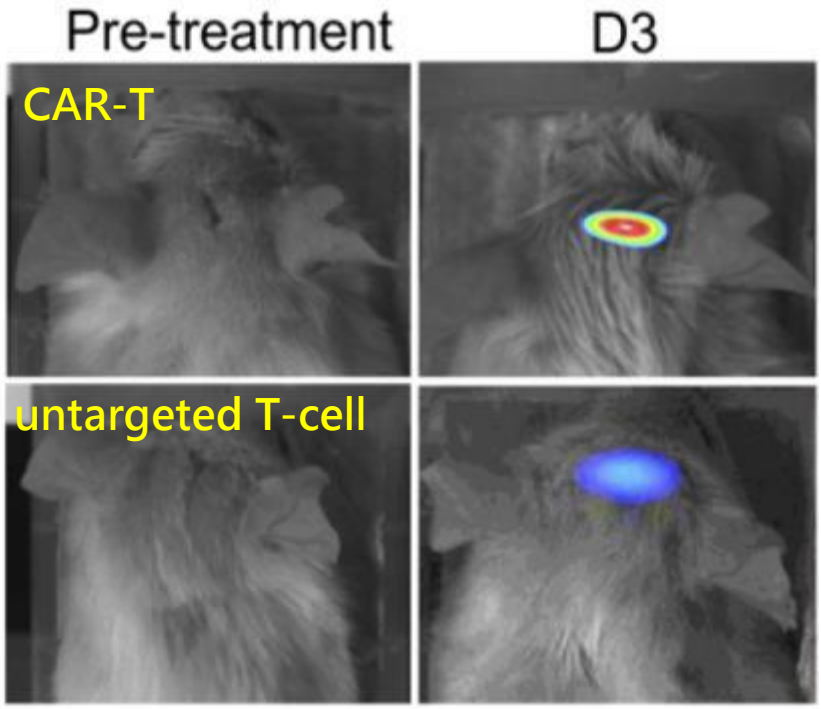
史丹福大學將與我們第一個合作的項目，發表在 *Theranostics* 專業期刊，並且強調可應用在人體臨床試驗中，該期刊影響力點數高達11.6分。

奈米微粒應用在標示CAR-T

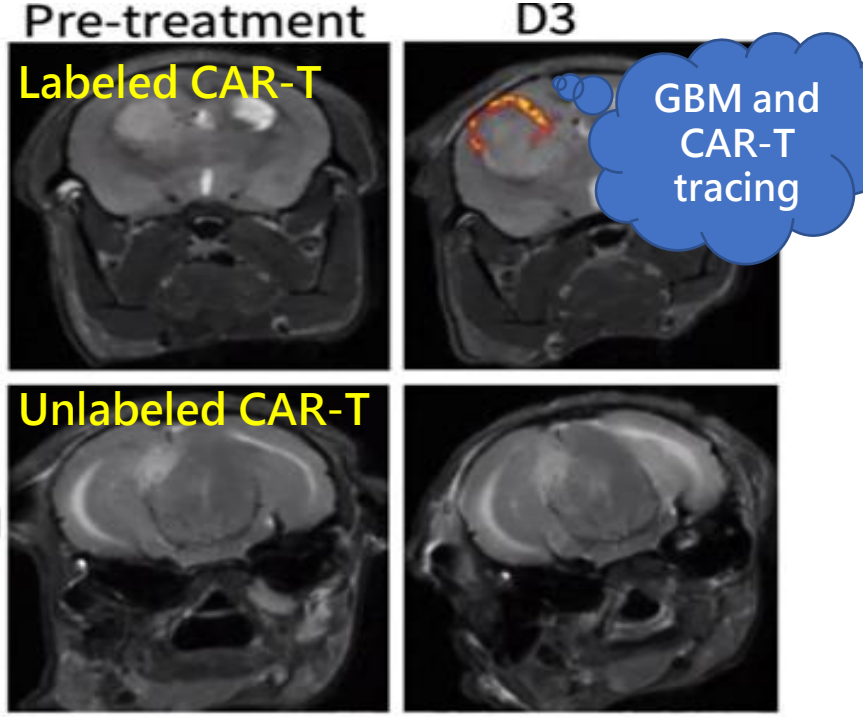
與美國史丹福大學合作的即時Cart-T細胞追蹤

- ✓ 臨床上缺乏可靠的 Car-T 細胞追踪技術，是Car-T細胞療法無法應用在實體瘤的主要障礙。
- ✓ 巨生的奈米微粒在Car-T的腦瘤動物試驗中，可以成功標示Car-T所在位置。

CAR-T vs untargeted T-cell



Labeled CAR-T vs unlabeled CAR-T



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Multimodal In Vivo Tracking of Chimeric Antigen Receptor T Cells in Preclinical Glioblastoma Models

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Abstract: Objectives: Iron oxide nanoparticles have been used to track the accumulation of chimeric antigen receptor (CAR) T cells with magnetic resonance imaging (MRI). However, the only nanoparticle available for clinical applications to date, ferumoxytol, has caused rare but severe anaphylactic reactions. MegaPro nanoparticles (MegaPro-NPs) provide an improved safety profile. We evaluated whether MegaPro-NPs can be applied for in vivo tracking of CAR T cells in a mouse model of glioblastoma multiforme.

Recent studies reported that a combination therapy of CXCR2-receptor targeted CAR T cells and ionizing radiation led to significant inhibition of GBM tumor growth in mouse models.[3] However, the tumor biology in clinical trials is far more heterogeneous in preclinical studies. Clinical experiences with other solid tumors have shown that the efficacy of CAR T-cell therapy varies substantially from patient to patient.[4] A non-invasive and clinically translatable imaging technique could help determine who might benefit from new CAR T-cell immunotherapies.

史丹福大學將與我們第2個合作的項目，發表在*Investigative Radiology*專業期刊，該期刊影響力點數高達10.1分，這兩份期刊的發表，已經讓2家在美國癌症專門領域的醫院找我們合作臨床試驗。

未來展望

短期目標

- 以多國多中心的方式，將MPB-1523及MPB-1514授權或是合作開發模式取得藥證。

中期目標

- 進入免疫治療及細胞療法的領域。
- 並且由巨生申請藥證。

長期目標

- 成為專業的 Specialty Pharma Company。
- 以奈米微粒和奈米微胞雙引擎，持續推動產品開發。

謝謝聆聽
敬請指教