



SINGAPORE INSTITUTE OF ADVANCED MEDICINE HOLDINGS LTD.
(Company Registration No. 201134046D)
(Incorporated in the Republic of Singapore)

MINUTES OF THE ANNUAL GENERAL MEETING OF SINGAPORE INSTITUTE OF ADVANCED MEDICINE HOLDINGS LTD. (THE “COMPANY”, AND TOGETHER WITH ITS SUBSIDIARIES, THE “GROUP”) HELD AT 1 BIOPOLIS DRIVE, AMNIOS, SINGAPORE 138622, LEVEL 2, AUDITORIUM ON FRIDAY, 27 DECEMBER 2024 AT 2.30 P.M. (THE “AGM” OR “MEETING”)

1. CHAIRMAN

Mr Khoo Tiam Hock Vernon, the Chairman and Independent Director of the Company (the “**Chairman**”), took the chair of the AGM. On behalf of the Board of Directors (the “**Board**”), the Chairman extended a welcome to shareholders of the Company (each a “**Shareholder**” and collectively, the “**Shareholders**”) for their attendance at the AGM.

The Chairman introduced the other members of the Board who attended the AGM, as follows:

Dr Djeng Shih Kien	- Executive Director and Chief Executive Officer
Mr Yeo Seng Lye Paul	- Executive Director and Chief Operating Officer
Ms Vivienne Cheng Chi Fan	- Non-Executive and Non-Independent Director
Mr Gurdip Singh S/O Boor Singh	- Independent Director
Ms Sumei Shum	- Independent Director

Dato’ Lee Kok Chuan, a Non-Executive and Non-Independent Director of the Company, sent his apologies for being unable to attend the AGM.

2. QUORUM

Having ascertained that a quorum was present, the Chairman called the Meeting to order at 2.30 p.m.

3. NOTICE OF MEETING

The Notice of AGM dated 12 December 2024 (the “**Notice**”), having been despatched to Shareholders and made available on SGXNet and the Company’s website, was taken as read.

4. SPEECH BY EXECUTIVE DIRECTOR AND CHIEF EXECUTIVE OFFICER

Dr Djeng Shih Kien (“**Dr Djeng**”) delivered a speech discussing the Group’s performance during the financial year ended 30 June 2024 (“**FY2024**”). Dr Djeng acknowledged that while the Group has made significant progress with new and advanced treatments, it has faced challenges in meeting revenue expectations. One of the primary reasons for this has been the slower-than-expected patient acquisition since the appointment of three local radiation oncologists less than a year ago, compared to competing healthcare centres with longer-tenured doctors. Additionally, the limited insurance empanelment of the Group and its doctors during FY2024 has resulted in a reduced patient base, with many patients seeking treatment at other centres where their insurance policies are accepted, which contributed to the shortfall in the Group’s revenue. However, the Group and its doctors have recently been empanelled with two insurance companies, which will make the Group’s medical services more accessible to patients covered by these insurers.

To address the challenges, Dr Djeng outlined a number of strategies aimed at improving the Group's financial performance. These include enhancing marketing efforts, strengthening relationships and expanding partnerships with healthcare providers. The Group is also exploring new opportunities with research companies, which will help provide long-term revenue streams. In addition, the Group is introducing new services, such as a non-surgical treatment for non-melanoma skin cancers, available at the Group's medical centres and clinics. Further details on this treatment can be found in the presentation slides (see paragraph 5 below).

As a token of appreciation for the support of Shareholders, Dr Djeng announced at the AGM that the Group offered a 10% discount on all medical services and free flu vaccination (the "Offer") for Shareholders and attendees. A copy of the Letter to Shareholders and attendees of the AGM, containing the details of the Offer as published via SGXNet on 27 December 2024, is annexed hereto as "**Appendix A**".

5. PRESENTATION BY EXECUTIVE DIRECTOR AND CHIEF OPERATING OFFICER

Mr Yeo Seng Lye Paul ("**Mr Paul Yeo**") presented slides sharing updates on the Group's ongoing efforts to increase patient flow and strengthen its revenue streams, highlighting the Group is focusing on improving its existing business while exploring new technologies and business opportunities to support future growth and development. He mentioned the importance of building on the Group's current business operations and discussed several future developments. These include advancements in proton therapy, oncology treatments, and radioisotope distribution.

Additionally, Mr Paul Yeo shared that the Group is finalising a Master Services Agreement with OncoBeta Therapeutics Pty Ltd for supply, sales, training, and research of related medical products and services across 18 countries, including China and India, with exclusive access in 16 of these regions. This partnership is expected to further support the Group's strategic goals for growth and market expansion.

A copy of Mr Paul Yeo's presentation slides regarding the detailed updates on the Group's therapeutic developments, strategic collaborations, and future initiatives, as presented at the AGM and published via SGXNet on 27 December 2024, is annexed hereto as "**Appendix B**".

6. QUESTIONS FROM SHAREHOLDERS

The Chairman informed that the Company had received questions from the Shareholders, the Securities Investors Association (Singapore) in relation to the Company's Annual Report for the financial year ended 30 June 2024, prior to the AGM, and the Company has responded to the questions via announcement released on SGXNet and the Company's website on 22 December 2024.

The Chairman invited Shareholders present at the AGM to ask questions during the question-and-answer session. Shareholders then posed their questions and the following key matters were discussed between the Shareholders and the Directors:

- (a) In response to a Shareholder's queries regarding the Group's health insurance empanelment, particularly why certain insurance companies have not empanelled the Group and its doctors and whether any reasons were provided, Dr Djeng explained that the Group had made applications for empanelment with several major health insurance companies in Singapore. Some insurance companies responded with a flat refusal, while others indicated that their insurance panels were already full. Additionally, there were instances where no response was received at all. Despite these challenges, the Group and its doctors have recently been empanelled with two insurance companies after many months of discussions and meetings and will continue to engage with other insurance companies to expand its insurance empanelment.

In addition to Dr Djeng's explanations on why the Group and its doctors have not been empanelled by certain insurance companies, the Chairman added that each insurance company likely has its own criteria for empanelment. While these reasons may vary, the Chairman emphasized the Group is working towards getting empanelled with a broad range of insurance companies, considering the beneficial interests of the insurance companies, patients and the Group.

- (b) A Shareholder raised a potential issue regarding insurance companies' lack of awareness about the medical services and treatment options available at the Group's medical centres. He suggested that the Company organize seminars and events to raise awareness of the Group's proton therapy services, the differences in capabilities among the three proton centres in Singapore, and the treatment options available to patients. Mr Paul Yeo responded that the Group is already engaged in such outreach programs to showcase its services and treatment options at its medical centres and will continue to expand these efforts to reach a wider audience and enhance public awareness.
- (c) A Shareholder suggested that the Company consider relocating its medical centre from Biopolis to a more accessible location, similar to other medical centres at Orchard Road, to improve its visibility and attract patients. Mr Paul Yeo responded that the Group also operates two medical clinics on Orchard Road, at Lucky Plaza and Mount Elizabeth Medical Centre. Nevertheless, the Group will continue to strengthen its outreach to increase recognition of its medical centres and clinics.

7. POLL VOTING

The Chairman informed Shareholders that in accordance with Rule 730A(2) of the Listing Manual Section B: Rules of Catalist of the Singapore Exchange Securities Trading Limited ("**SGX-ST**") (the "**Catalist Rules**"), all motions tabled at the AGM would be voted on by way of a poll pursuant to Regulation 73(1) of the Company's Constitution. All the proposed resolutions would require a simple majority of votes for them to be carried.

The Chairman further informed that he had been appointed as proxy by certain Shareholders to vote on their behalf in his capacity as the Chairman of the Meeting and would vote in accordance with such Shareholders' instructions. The Chairman directed that the poll on each resolution be conducted after all the resolutions had been formally proposed and seconded.

8. ORDINARY RESOLUTION 1: ADOPTION OF THE DIRECTORS' STATEMENT AND THE AUDITED FINANCIAL STATEMENTS OF THE COMPANY AND THE GROUP FOR THE FINANCIAL YEAR ENDED 30 JUNE 2024 AND THE AUDITOR'S REPORT THEREON

The Chairman presented Ordinary Resolution 1 on the Notice, which was to receive and adopt the Directors' Statement and the Audited Financial Statements of the Company and the Group for the financial year ended 30 June 2024 and the Auditor's Report thereon.

The Chairman put the following motion to the Meeting:

"That the Directors' Statement and the Audited Financial Statements of the Company and the Group for the financial year ended 30 June 2024 and the Auditor's Report thereon be received and adopted."

The motion was duly proposed and seconded by a Shareholder, respectively.

9. ORDINARY RESOLUTION 2: APPROVAL OF PAYMENT OF DIRECTORS' FEES OF S\$88,334 FOR THE FINANCIAL YEAR ENDED 30 JUNE 2024

As Ordinary Resolutions 2 and 3 on the Notice related to the payment of Directors' fees to Independent Directors of the Company, the Chairman passed the chairmanship of the Meeting to Dr Djeng, the Executive Director and Chief Executive Officer of the Company.

Ordinary Resolution 2 on the Notice was to seek Shareholders' approval for the payment of Directors' fees for the financial year ended 30 June 2024. The Board recommended the payment of Directors' fees of S\$88,334 for the financial year ended 30 June 2024.

Dr Djeng put the following motion to the Meeting:

"That the payment of Directors' fees of S\$88,334 for the financial year ended 30 June 2024, be approved."

The motion was duly proposed and seconded by a Shareholder, respectively.

10. ORDINARY RESOLUTION 3: APPROVAL OF PAYMENT OF DIRECTORS' FEES OF S\$205,348 FOR THE FINANCIAL YEAR ENDING 30 JUNE 2025

Ordinary Resolution 3 on the Notice was to seek Shareholders' approval for the payment of Directors' fees for the financial year ending 30 June 2025, to be paid half-yearly in arrears. The Board recommended the payment of Directors' fees of S\$205,348 for the financial year ending 30 June 2025.

Dr Djeng put the following motion to the Meeting:

"That the payment of Directors' fees of S\$205,348 for the financial year ending 30 June 2025, be approved."

The motion was duly proposed and seconded by a Shareholder, respectively.

11. ORDINARY RESOLUTION 4: RE-ELECTION OF MR YEO SENG LYE PAUL AS DIRECTOR

Ordinary Resolution 4 on the Notice was to seek Shareholders' approval for the re-election of Mr Paul Yeo, who was retiring by rotation pursuant to Regulation 119 of the Company's Constitution, as a Director of the Company. Mr Paul Yeo had indicated his consent to continue in office.

The Chairman put the following motion to the Meeting:

"That Mr Yeo Seng Lye Paul be re-elected as a Director of the Company."

The motion was duly proposed and seconded by a Shareholder, respectively.

12. ORDINARY RESOLUTION 5: RE-ELECTION OF DATO' LEE KOK CHUAN AS DIRECTOR

Ordinary Resolution 5 on the Notice was to seek Shareholders' approval for the re-election of Dato' Lee Kok Chuan ("**Dato' Lee**"), who was retiring pursuant to Regulation 119 of the Company's Constitution, as a Director of the Company. Dato' Lee had indicated his consent to continue in office.

The Chairman put the following motion to the Meeting:

"That Dato' Lee Kok Chuan be re-elected as a Director of the Company."

The motion was duly proposed and seconded by a Shareholder, respectively.

13. ORDINARY RESOLUTION 6: RE-ELECTION OF MR GURDIP SINGH S/O BOOR SINGH AS DIRECTOR

Ordinary Resolution 6 on the Notice was to seek Shareholders' approval for the re-election of Mr Gurdip Singh S/O Boor Singh ("**Mr Gurdip Singh**"), who was retiring pursuant to Regulation 119 of the Company's Constitution, as a Director of the Company. Mr Gurdip Singh had indicated his consent to continue in office.

The Chairman put the following motion to the Meeting:

“That Mr Gurdip Singh S/O Boor Singh be re-elected as a Director of the Company.”

The motion was duly proposed and seconded by a Shareholder, respectively.

14. ORDINARY RESOLUTION 7: APPOINTMENT OF MESSRS FOO KON TAN LLP AS AUDITOR

Ordinary Resolution 7 on the Notice was to seek Shareholders’ approval for the appointment of Messrs Foo Kon Tan LLP as the Auditor of the Company, in place of the retiring Auditor, Messrs PricewaterhouseCoopers LLP, and to authorise the Directors to fix their remuneration.

The Chairman put the following motion to the Meeting:

“That Messrs Foo Kon Tan LLP be appointed as the Auditor of the Company, to hold office until the conclusion of the next annual general meeting of the Company, and the Directors of the Company be authorised to fix their remuneration.”

The motion was duly proposed and seconded by a Shareholder, respectively.

On behalf of the Board and Management, the Chairman expressed appreciation for the professionalism provided by Messrs PricewaterhouseCoopers LLP over the past several years.

15. ORDINARY RESOLUTION 8: AUTHORITY TO ALLOT AND ISSUE SHARES AND CONVERTIBLE SECURITIES

Ordinary Resolution 8 was the last resolution on the Notice and was to seek Shareholders’ approval to authorise and empower the Directors to allot and issue new shares and convertible securities of the Company pursuant to Section 161 of the Companies Act 1967 of Singapore and the Catalist Rules. The proposed Ordinary Resolution 8 as set out in the Notice was taken as read.

The Chairman put the following motion to the Meeting:

“That pursuant to Section 161 of the Companies Act 1967 of Singapore (“**Companies Act**”) and Rule 806 of the Listing Manual Section B: Rules of Catalist of the Singapore Exchange Securities Trading Limited (“**SGX-ST**”) (“**Catalist Rules**”), the Directors be authorised and empowered to:

- (a) (i) allot and issue shares in the capital of the Company (“**Shares**”) whether by way of rights, bonus or otherwise; and/or
- (ii) make or grant offers, agreements or options (collectively, “**Instruments**”) that might or would require Shares to be issued, including but not limited to the creation and issue of (as well as adjustments to) options, warrants, debentures or other instruments convertible into Shares,

at any time and upon such terms and conditions and for such purposes and to such persons as the Directors may at their absolute discretion deem fit; and

- (b) (notwithstanding the authority conferred by this Resolution may have ceased to be in force) issue Shares in pursuance of any Instrument made or granted by the Directors while this Resolution was in force,

provided that:

- (1) the aggregate number of Shares (including Shares to be issued in pursuance of Instruments made or granted pursuant to this Resolution) to be issued pursuant to this Resolution does not exceed 100% of the total number of issued Shares (excluding treasury shares and subsidiary holdings) (as calculated in accordance with sub-paragraph (2) below), of which the aggregate number of Shares (including Shares to be issued in pursuance of Instruments made or granted pursuant to this Resolution) to be issued other than on a *pro rata* basis to shareholders of the Company does not exceed 50% of the total number of issued Shares (excluding treasury shares and subsidiary holdings) (as calculated in accordance with sub-paragraph (2) below);
- (2) (subject to such manner of calculation as may be prescribed by the SGX-ST) for the purpose of determining the aggregate number of Shares that may be issued under sub-paragraph (1) above, the total number of issued Shares (excluding treasury shares and subsidiary holdings) shall be based on the total number of issued Shares (excluding treasury shares and subsidiary holdings) at the time this Resolution is passed, after adjusting for:
 - (a) new Shares arising from the conversion or exercise of convertible securities;
 - (b) new Shares arising from exercising share options or vesting of share awards, provided the options or awards were granted in compliance with Part VIII of Chapter 8 of the Catalist Rules; and
 - (c) any subsequent bonus issue, consolidation or subdivision of Shares.

Adjustments in accordance with sub-paragraphs (2)(a) and (2)(b) above are only to be made in respect of new Shares arising from convertible securities, share options or share awards which were issued and outstanding or subsisting at the time of the passing of this Resolution;

- (3) in exercising the authority conferred by this Resolution, the Company shall comply with the provisions of the Catalist Rules for the time being in force (unless such compliance has been waived by the SGX-ST), the Companies Act and the Constitution for the time being of the Company; and
- (4) (unless revoked or varied by the Company at a general meeting) the authority conferred by this Resolution shall continue in force until the conclusion of the next AGM of the Company or the date by which the next AGM of the Company is required by law and the Catalist Rules to be held, whichever is earlier; or in the case of shares to be issued in pursuance of the Instruments, made or granted pursuant to this resolution, until the issuance of such shares in accordance with the terms of the Instruments."

The motion was duly proposed and seconded by a Shareholder, respectively.

16. POLL RESULTS

The Company had appointed Boardroom Corporate & Advisory Services Pte. Ltd. as Polling Agent and CNP Business Advisory Pte. Ltd. as Scrutineer for the poll. The Chairman invited the Scrutineer to brief the Shareholders on the poll voting process.

As all the motions on the resolutions to be considered at the Meeting had been duly proposed and seconded, the Shareholders proceeded to vote on the resolutions by poll pursuant to Regulation 73(1) of the Company's Constitution. Shareholders then handed the completed poll voting papers to the Polling Agent.

The Chairman adjourned the Meeting at 3.50 p.m. to allow the Polling Agent to complete the counting of the votes.

SINGAPORE INSTITUTE OF ADVANCED MEDICINE HOLDINGS LTD.

(Company Registration No. 201134046D)

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The Chairman called the Meeting back to order and the Meeting resumed at 4.05 p.m.

The Chairman announced the poll results as follows:

ORDINARY RESOLUTION NUMBER	NO. OF SHARES FOR	% FOR	NO. OF SHARES AGAINST	% AGAINST
Resolution 1	719,726,619	100%	0	0%
Resolution 2	717,886,869	99.74%	1,839,750	0.26%
Resolution 3	717,886,869	99.74%	1,839,750	0.26%
Resolution 4	719,716,619	100%	10,000	0%
Resolution 5	719,676,619	99.99%	50,000	0.01%
Resolution 6	719,676,619	99.99%	50,000	0.01%
Resolution 7	719,726,619	100%	0	0%
Resolution 8	717,876,869	99.74 %	1,849,750	0.26%

Based on the poll results, the Chairman declared all the resolutions carried.

17. END OF MEETING

As no notice was received in respect of any other business that may be properly transacted at the Meeting, the Chairman declared the Meeting closed at 4.10 p.m. and thanked all present for attending the Meeting.

Signed as a correct record,

Khoo Tiam Hock Vernon
Chairman of the Meeting

Singapore Institute of Advanced Medicine Holdings Ltd. (the "**Company**") was listed on Catalist of the Singapore Exchange Securities Trading Limited ("**SGX-ST**") on 16 February 2024. The initial public offering of the Company was sponsored by PrimePartners Corporate Finance Pte. Ltd. (the "**Sponsor**").

This announcement has been reviewed by the Sponsor. It has not been examined or approved by the SGX-ST. The SGX-ST assumes no responsibility for the contents of this document, including the correctness of any of the statements or opinions made or reports contained in this announcement.

The contact person for the Sponsor is Ms. Ng Shi Qing, 16 Collyer Quay, #10-00 Collyer Quay Centre, Singapore 049318, sponsorship@ppcf.com.sg.

Appendix A

Letter to Shareholders and attendees of the AGM

Singapore Institute of Advanced Medicine Holdings Ltd
1 Biopolis Drive #02-01 Amnios Singapore 138622

Website: <https://advancedmedicine.sg/>

Date: 27th December 2024

To: Shareholders and attendees of Annual General Meeting 2024

Subject: 10% Discount on Medical Services & Free Flu Vaccination

Dear shareholder and attendee,

We are pleased to announce an exclusive offer available to you. As part of our continued commitment to the health and well-being of our community, we are offering **10% off on all medical services** and **free flu vaccination** for a limited time.

Offer Details:

- **10% Discount** on all medical services provided at our **Advanced Medicine Imaging / Asia Healthpartners / Proton Therapy SG Medical Centre**
- **Free Flu Vaccination**

To qualify for this promotion, attendees must **register** by providing the following details:

1. **Full Name** (as per NRIC/ID)
2. **NRIC/ID Number**
3. **Contact Information** (Phone and Email)

How to Register:

To take advantage of this offer, please complete the registration form by scanning the QR code below.

Ensure that all the required information is provided.

Registration URL : <https://forms.gle/ye9ta2Eu26DhpbMY7>

OR

Scan to register:



Validity Period:

- The 10% Discount on all medical services is **valid until 31st December 2025**.
- The free flu vaccination offer is valid **valid until 31st January 2025 (while stock lasts)**
- Please note that medical services will be available subject to our operational hours and availability.

Important Notes:

- The offer is non-transferable and only applicable to shareholders of the Company from 27 December 2024, and registered attendees of Annual General Meeting 2024.
- Free flu vaccinations are subject to availability and eligibility.

We strongly encourage all attendees to register early to ensure you don't miss out on this health benefit.

Thank you for your continued support and partnership.

Warm regards,
Sales & Marketing team



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Appendix B

Presentation slides



Singapore Institute of Advanced Medicine Holdings



**All AGM attendees & shareholders: 10% discount and free flu vaccination
- please register after the AGM.**

***shareholder from 27 Dec 2024**



We are making inroads and continue our best efforts for increasing our existing patient flows and our revenue streams.

While we build on our existing business, these are some our future developments:

- **Flash Proton Therapy**
- **Oncobeta**
- **EnGeneIC**
- **Radioisotope distribution**



First-in-Class

Antibody-Nanocell-Drug Conjugate (ANDC)

meets Immunotherapy in one Therapeutic for multiple cancers

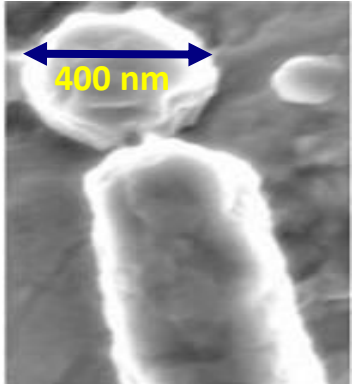
Fast Track to Market

December 2024

Technology Overview - EDV

1

Bacterially derived Nanocell



The Birth of an EDV™

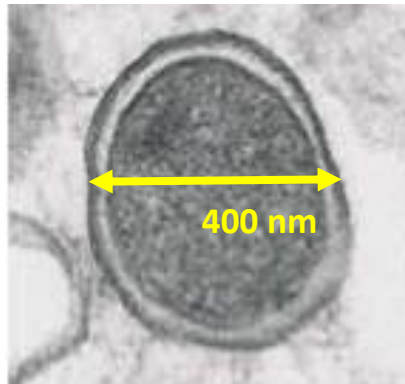
(**EnGeneIC Dream Vector**)

Non-living nanocells are generated by asymmetric cell division in genetically engineered safe strain (avirulent) of *Salmonella typhimurium* bacteria.

Cell division creates a uniform nanocell of 400 ± 20nm.

2

Transmission Electron Microscopy

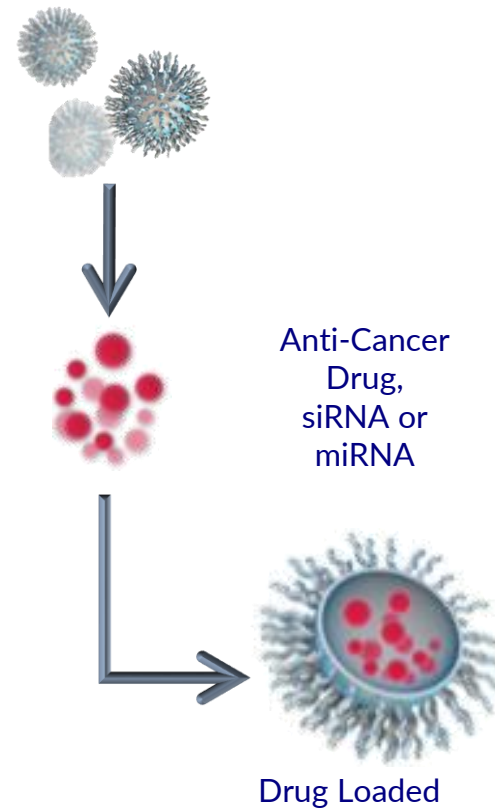


EDV is a non-living empty cytoplasmic sac with a robust double-walled membrane.

The EDV™ is sterile and non-toxic with no chromosome and no risk of replication or virulence.

3

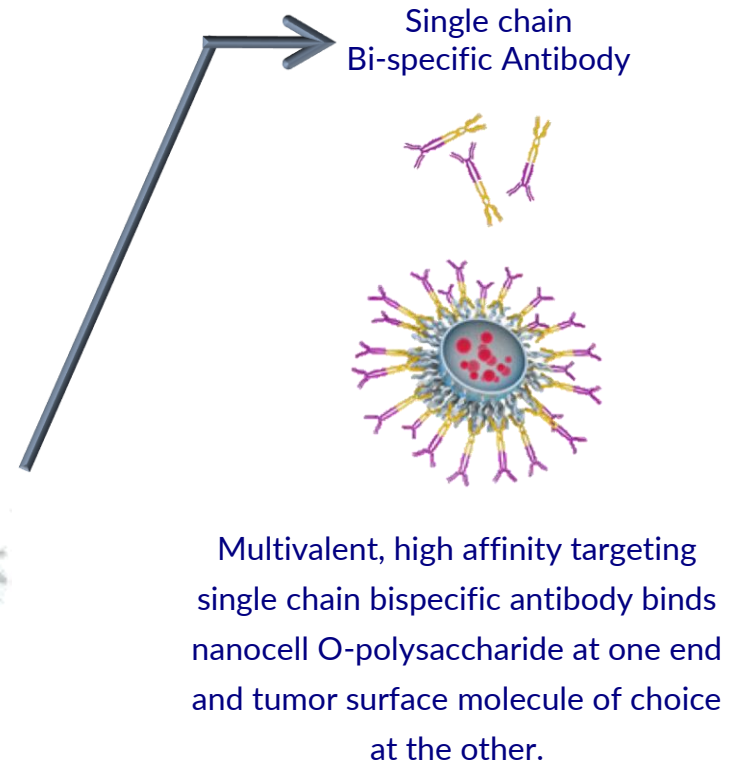
Unmatched Payload Capacity



EDVs™ can be readily packaged with diverse anti-cancer drugs or therapeutic nucleic acids or immune stimulating molecules: 0.5 - 1 million drug molecules or 10,000 siRNA copies per EDV.

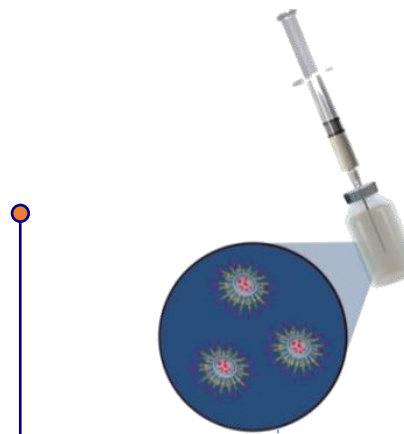
4

Bi-Specific Antibody Targeting to cancer cell surface receptor - Precision tumor targeting



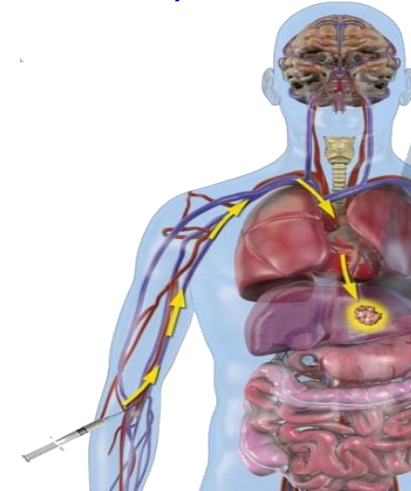
Multivalent, high affinity targeting single chain bispecific antibody binds nanocell O-polysaccharide at one end and tumor surface molecule of choice at the other.

Passive Accumulation in Tumor via Tumor-Associated Leaky Vasculature



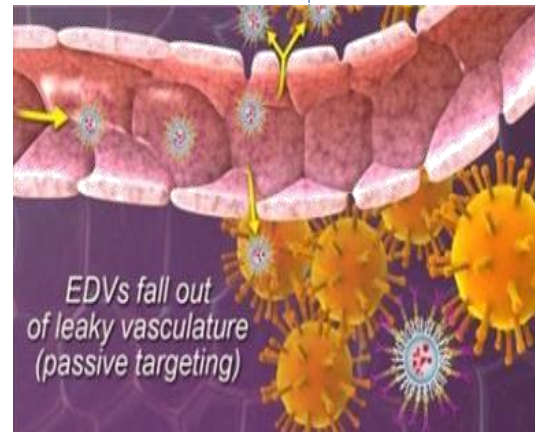
Leaky Vasculature

Antibody-targeted, drug-loaded EDVs™ accumulate passively in tumor tissue due to tumor-associated leaky vasculature



Simple Delivery

Transport of antibody-targeted, drug-packaged EDVs™ via bolus injection – 2ml



Passive Accumulation

EDVs extravasate and accumulate in the tumor microenvironment

Active Tumor Targeting = Direct killing of highly drug-resistant cancer cells

Once in the Tumor Environment, EDV™ Binds and Delivers Payload to Cancer Cell

Cancer Cell Article

Bacterially Derived 400 nm Particles for Encapsulation and Cancer Cell Targeting of Chemotherapeutics

Jennifer A. MacDiarmid,¹ Nancy B. Mugridge,¹ Jocelyn C. Weis,¹ Leo Phillips,¹ Adam L. Burn,¹ Richard P. Paulin,¹ Joel E. Haasdyk,¹ Kristie-Ann Dickson,¹ Vatsala N. Brahmabhatt,¹ Scott T. Pattison,¹ Alexander C. James,¹ Ghaleb Al Bakri,¹ Rodney C. Straw,² Bruce Stillman,³ Robert M. Graham,^{1,2} and Himanshu Brahmabhatt^{1*}

¹EnGeneic Pty Ltd, 105 Delhi Road, North Ryde, Sydney, NSW 2113, Australia
²Brisbane Veterinary Specialist Centre, Cnr. Old Northern Road and Keong Road, Albany Creek, Queensland 4035, Australia
³Cold Spring Harbor Laboratory, 1 Bungtown Road, Cold Spring Harbor, NY 11724, USA
^{*}Victor Chang Cardiac Research Institute, 384 Victoria Street, Darlinghurst, NSW 2010, Australia
[†]School of Biotechnology and Biomolecular Sciences, University of New South Wales, Kensington, NSW 2054, Australia
^{*}Correspondence: hbrahmabhatt@engeneic.com
 DOI 10.1016/j.ccr.2007.03.012

SUMMARY

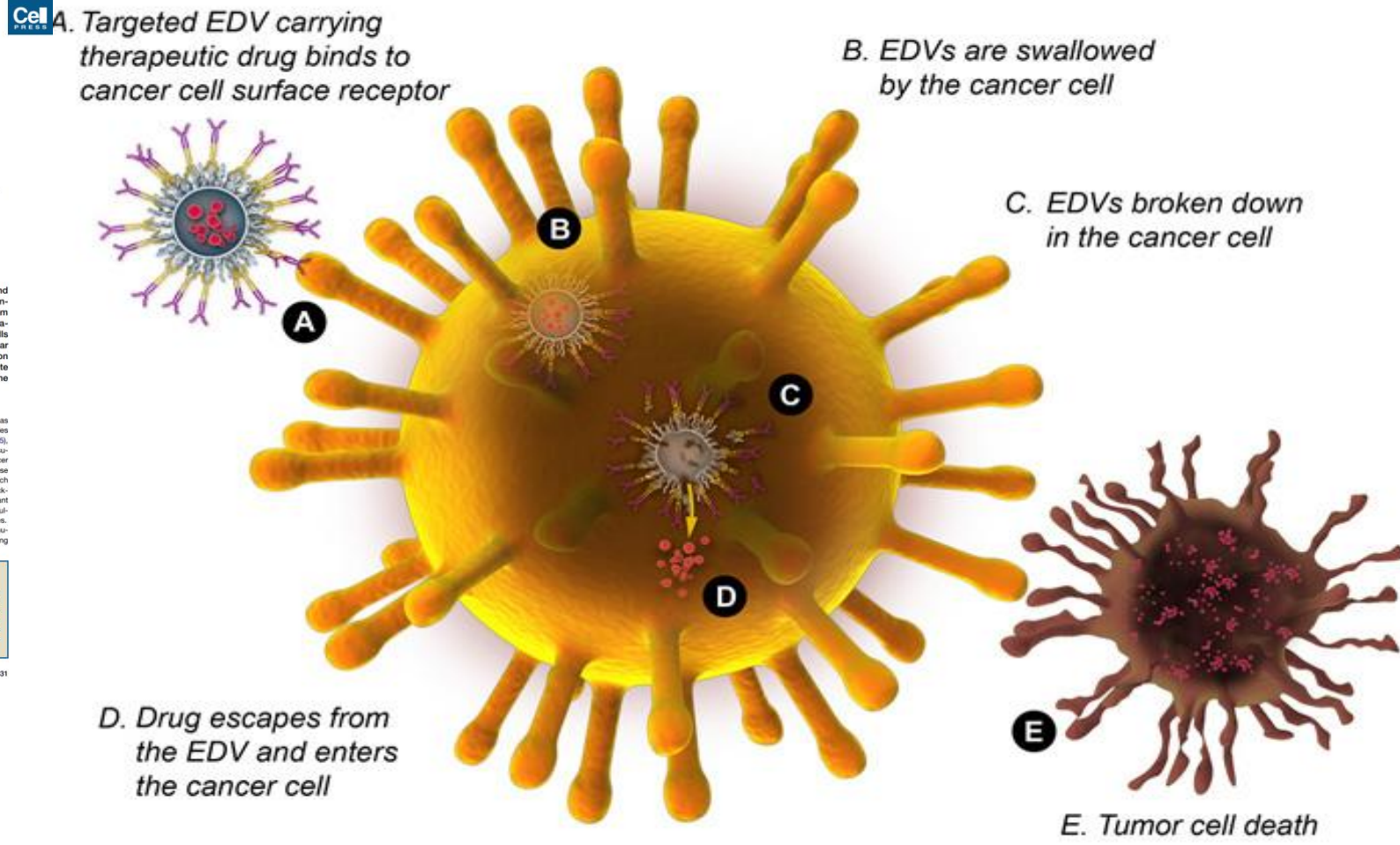
Systemic administration of chemotherapeutic agents results in indiscriminate drug distribution and severe toxicity. Here we report a technology potentially overcoming these shortcomings through encapsulation and cancer cell-specific targeting of chemotherapeutics in bacterially derived 400 nm minicells. We discovered that minicells can be packaged with therapeutically significant concentrations of chemotherapeutics of differing charge, hydrophobicity, and solubility. Targeting of minicells via bispecific antibodies to receptors on cancer cell membranes results in endocytosis, intracellular degradation, and drug release. This affects highly significant tumor growth inhibition and regression in mouse xenografts and case studies of lymphoma in dogs despite administration of minute amounts of drug and antibody; a factor critical for limiting systemic toxicity that should allow the use of complex regimens of combination chemotherapy.

INTRODUCTION

Severe toxicity remains a major factor limiting cancer chemotherapy. Lack of cancer cell specificity, indiscriminate drug distribution, and rapid clearance necessitate frequent administration of high doses of chemotherapeutics to elicit a satisfactory clinical response (Langer, 1998). Anticancer antibodies directed to overexpressed receptors on cancer cells, such as the epidermal growth factor receptor (EGFR; Nicholson et al., 2001) and HER2/neu (Rae and Lippman, 2004), are less toxic but do not possess the potency and wide spectrum antitumor activity of chemotherapeutic drugs. Efforts are being made to develop targeted drug delivery systems (DDS), such as stealth liposomes (Medina et al., 2004), nanoparticles (Brannon-Peugas and Bianchetti, 2004; Ferrari, 2005), and polymer therapeutics (Duncan, 2003), which encapsulate the cytotoxic drug in a vehicle and target it to cancer cells via tumor cell-surface receptors. However, these technologies are also hampered by shortcomings, such as drug leakage in vivo, lack of versatility in terms of packaging a diverse range of different drugs without significant derivatization, thereby reducing drug potency, and difficulties in production scale-up, particularly for nanoparticles. Here we show that bacterial minicells which are intrinsically nanoparticles produced as a result of inactivating

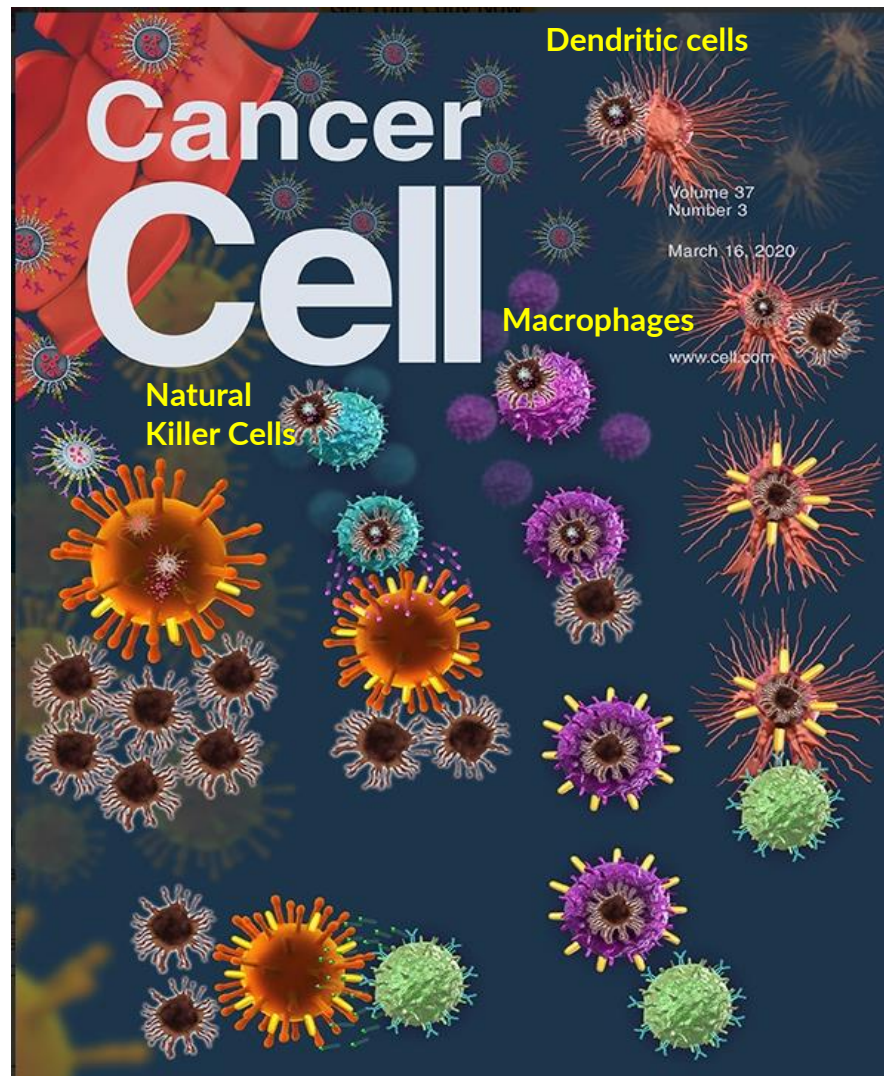
SIGNIFICANCE
 Nontargeted cancer chemotherapy is currently associated with severe toxicity. This report describes bacterially derived nano-sized particles (minicells) for encapsulation of a range of different chemotherapeutic drugs and specifically targeting the minicells to tumor cell-surface receptors via bispecific antibodies coating the minicells. Receptor engagement results in minicell endocytosis, intracellular degradation, and drug release. Consequently, highly significant tumor growth inhibition and regression is achieved despite administration of minute amounts of drug and antibody. The dramatic increase in therapeutic index may permit the use of multiring combinations to achieve an improved outcome for cancer therapy.

Cancer Cell 11, 431-445, May 2007 ©2007 Elsevier Inc. 431



Published:

- MacDiarmid, J.A., et al. Bacterially-derived 400nm particles for encapsulation and cancer cell targeting of chemotherapeutics. *Cancer Cell* 11: 431-445 (2007).
- MacDiarmid, J.A., et al. Sequential treatment of drug-resistant tumors with targeted minicells containing siRNA or a cytotoxic drug. *Nature Biotechnology* 27: 643-651 (2009).



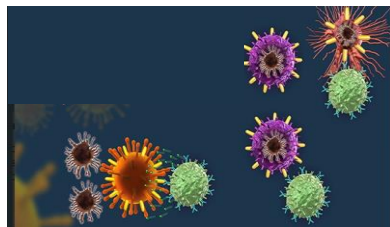
EDV (bacterial origin) activates main cells of the immune system

- **Dendritic cells**
- **Macrophages**
- **Natural Killer cells**

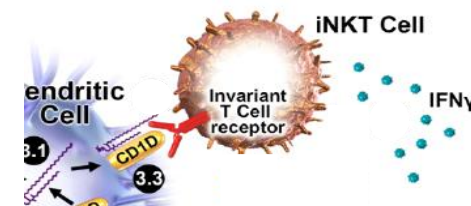
These cells swallow dying tumor cells and display tumor antigens on their surface



Tumor-specific CD8+ T cells

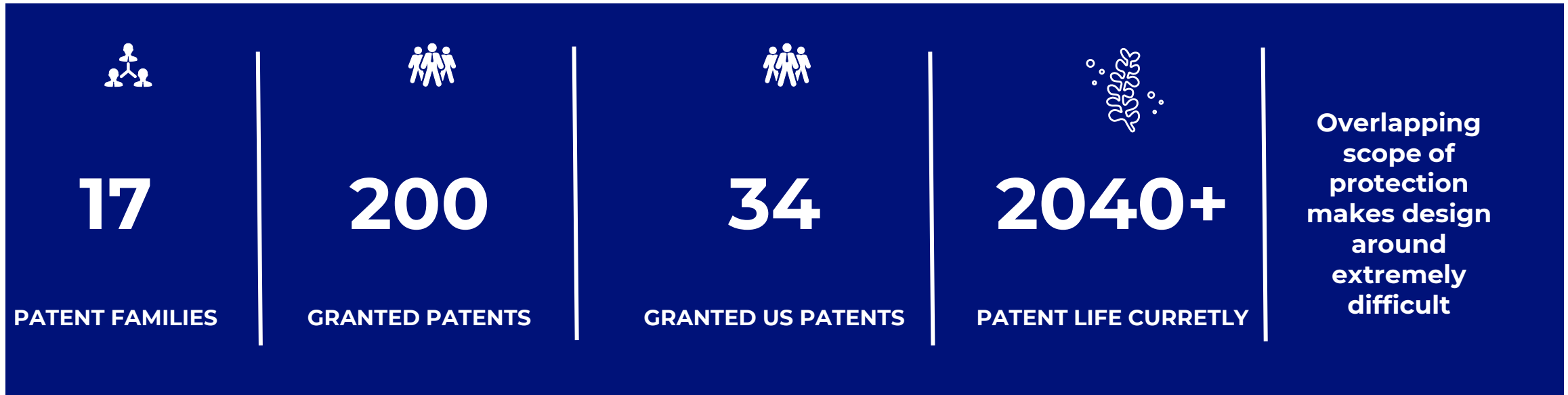


Tumor-specific iNKT cells



Only technology in the world that activates both major types of T cells to mount major killing of cancer cells

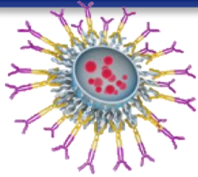
Globally Protected Patent Portfolio



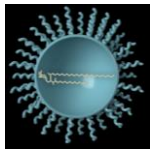
ENGeneIC = sole owner of entire patent portfolio

Foley & Lardner LLC (Washington DC) have handled all IP since inception

2ND generation EDV-based ANDC for Low Survival cancers



Antibody-targeted EDV carrying a **super-cytotoxic drug to overcome drug resistance**



α -galactosyl ceramide (glycolipid) to attract iNKT cells

End-stage pancreatic cancer patient



First Dose



Post Dose

8 doses over 8 weeks of EGFR^REDVs_{PNU-159682} + EDV _{α GC}

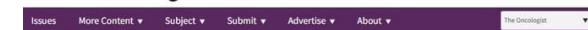
Single Patient IND (SPIND), Los Angeles

- Metastatic PDAC in pancreas, liver and lungs.
- Eligible for “Right to try” (SPIND) since she had exhausted all treatment options.
- Since start of EDV treatment – alive and well after 24 months.
- Excellent quality of life with two treatment breaks for holidays
- Scans from July 2023 to now show no measurable tumours =

COMPLETE RESPONSE



Oct 2024 publication The Oncologist



Article Contents

- Abstract
- Introduction
- Case report
- Discussion
- Acknowledgments
- Author contributions

JOURNAL ARTICLE

Recurrent pancreatic cancer treated with N-803 and PD-L1 t-haNK followed by an EGFR-targeted nanocell drug conjugate

Katayoun Moini, Tara Seery, Chaitali Nangia, Jennifer MacDiarmid, Himanshu Brahmibhatt, Patricia Spilman, Lennie Sender, Patrick Soon-Shiong

The Oncologist, oyae267, <https://doi.org/10.1093/oncolo/oyae267>

Published: 04 October 2024 Article history

US FDA has given “FAST-TRACK” designation for EDV therapeutics in pancreatic ductal adenocarcinoma (PDAC)

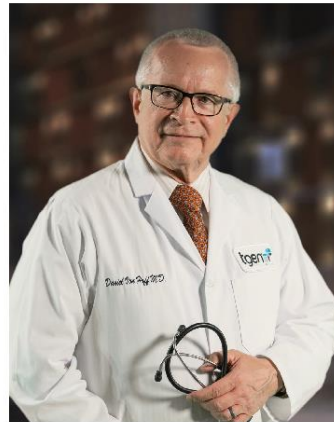
Phase II trials planned to start in Q1/Q2 Calender 2025 in the US

- Statistical Package being finalized by a top biostatistician at the Mayo Clinic (USA)
- Prof. Gulam Manji MD (Co-Director of Pancreas Center, Columbia University Herbert Irving Cancer Center (New York))



Source: EnGeneIC
October 01, 2024 08:00 ET

Distinguished Oncologist, Professor Daniel Von Hoff joins the Scientific/Clinical Advisory Board of EnGeneIC Cancer Therapeutics



SYDNEY and NEW YORK, Oct. 01, 2024 (GLOBE NEWSWIRE) — EnGeneIC, a clinical-stage biopharmaceutical company pioneering the development of a First-in-Class targeted nanocell for cancer therapy has today announced the appointment of Dr. Daniel Von Hoff to its Scientific/Clinical Advisory Board to advise EnGeneIC's on its upcoming trial in metastatic pancreatic cancer.

Professor Daniel Von Hoff, M.D., F.A.C.P., F.A.S.C.O., F.A.A.C.R. is an internationally recognized physician and scientist. He is currently Distinguished Professor at the Translational Genomics Research

- Prof Dan Von Hoff joined the EnGeneIC Scientific board in October 2025
- He is very experienced in bringing new cancer drugs to commercialization

7 Compassionate case studies – pancreatic ductal adenocarcinoma (PDAC) – Singapore with 3 oncology groups

1 Compassionate case study – Hong Kong - Osteosarcoma

3 Compassionate case studies – Melbourne - Glioblastoma

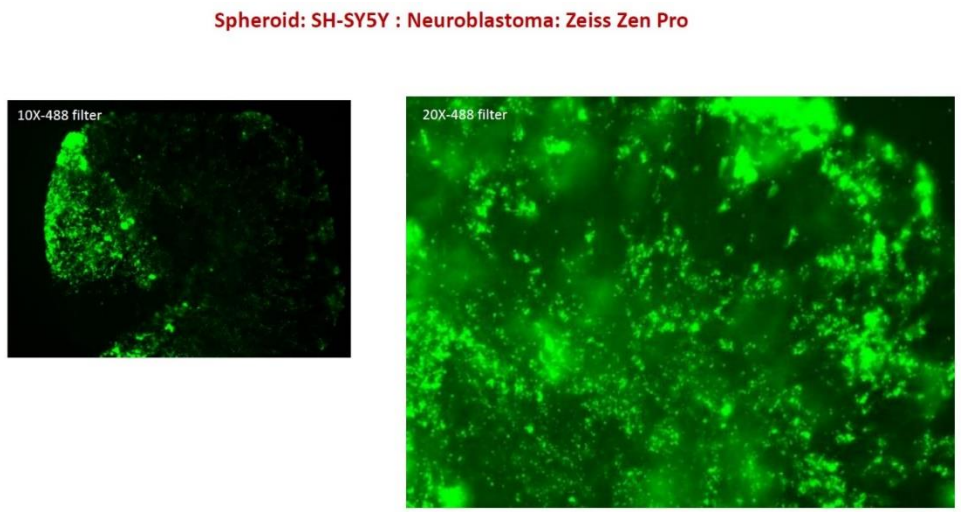
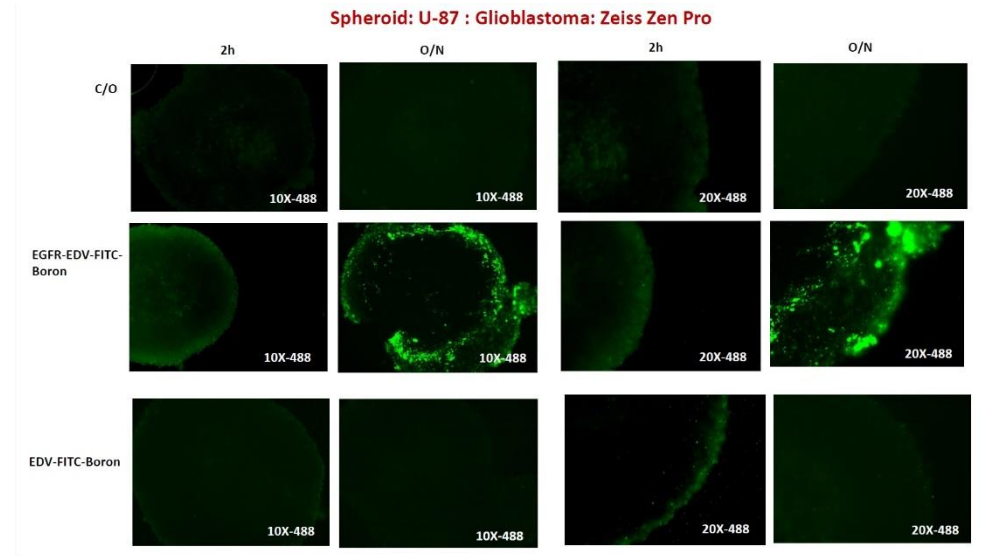
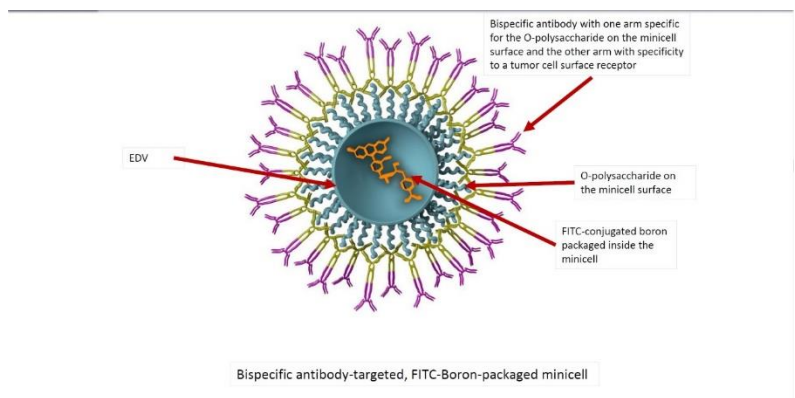
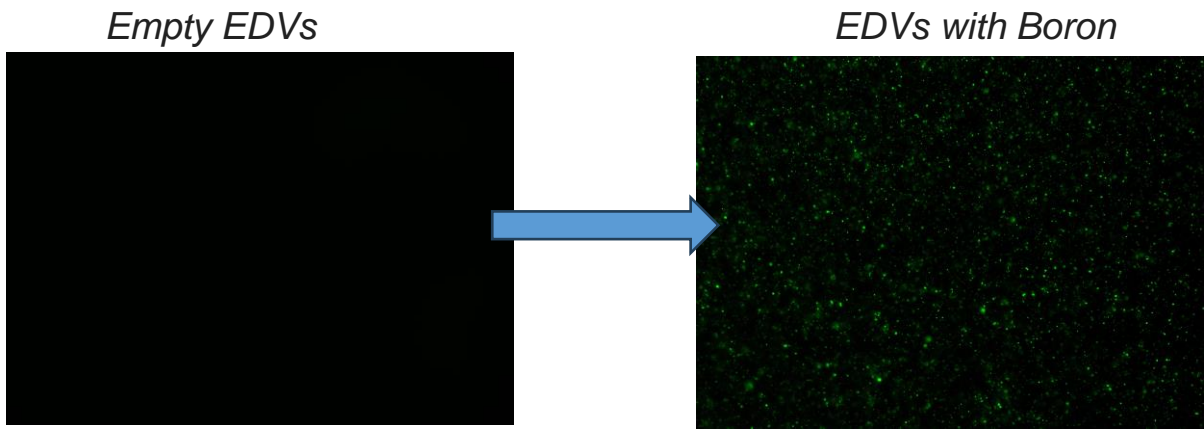
EDV doses associated with little to no toxic side effects ✓

November 2024: EnGeneIC received approval to start trials for many other cancers including: Lung, Breast, Bladder, Kidney cancer

Multiple other uses for EDV

- Boron-Proton & Neutron Capture Therapy
- Diagnostic Imaging Agent
- Theranostics
- Vaccines

World's first: Boron has been successfully packaged in EDVs & Cancer Spheroids





profit sharing and exclusive distribution rights to 17 countries including China and India.



For Immediate Release

Singapore Institute of Advanced Medicine Holdings enters into a strategic partnership with Australia-based biopharmaceutical company, EnGeneIC to revolutionize cancer treatment in Asia

- Dual-pronged expansion of revenue streams through profit-sharing agreement
 - SAM Holdings will have exclusive distribution rights for sales of EDV therapeutics in 17 countries within Asia.
 - Both parties will also collaborate on the development of EDV-based Theranostics to improve cancer outcomes and SAM Holdings will be granted exclusive distribution rights worldwide.
- Investing into next generation technology to achieve our core vision
 - First-in-class antibody nanocell drug conjugate platform for delivering a range of therapeutic payloads via antibody-targeting a cancer cell's surface, with minimal toxicity.
 - EDV-based theranostics can provide precise, personalized care, enabling early detection and targeted therapy, which aligns with the Group's vision.
- The partnership will bring the latest cancer treatment innovation to Singapore and increase Singapore's attractiveness as the medical tourism hub of Asia.

Singapore, 10 June 2024 – Singapore Institute of Advanced Medicine Holdings Ltd. ("SAM Holdings" or the "Company", and together with its subsidiaries, the "Group"), has entered into a strategic partnership with EnGeneIC Pty Limited ("EnGeneIC"), an Australia-based clinical-stage biopharmaceutical company pioneering the development of a First-in-Class targeted nanocell for cancer therapy. The partnership aims to revolutionize the cancer treatment landscape in Asia and provide better outcomes of life for our patients.

Under the partnership, the Group will collaborate with EnGeneIC on a profit-sharing basis for:
- Manufacturing and distribution of anti-cancer products based on EnGeneIC's proprietary technology platform, EnGeneIC Dream Vector ("EDV-based Products"); and
- Development of EnGeneIC Dream Vector-based theranostics for use in the imaging and treatment of various cancers ("EDV-based Theranostics").

EDV-based Products

The Group will help EnGeneIC secure funding and regulatory authorizations for building a manufacturing plant in Singapore for the manufacture of EDV-based Products, conduct clinical



trials in Singapore, and obtain regulatory authorization to market and sell the EDV-based Products. In turn, SAM Holdings will be granted exclusive distribution and marketing rights of these products in 17 countries within Asia.

EDV-based Theranostics

Leveraging on the Group's experience in theranostics, it will collaborate with EnGeneIC for pre-clinical testing of EDV-based Theranostics and obtain regulatory approval for commercialization and sale of EDV-based Theranostics. Subsequently, the Group will be granted exclusive distribution rights worldwide for EDV-based Theranostics.

Commenting on the partnership, Dr Djeng Shih Kien, Executive Director and CEO, and founder, of SAM Holdings, said, "We have always been committed to providing our patients with easier access to the latest cancer treatment technologies and our partnership with EnGeneIC is another step forward in that direction. We are excited at the prospect of bringing cutting edge EDV-based therapeutics to Singapore and Asia and collaborating on the development of EDV-based Theranostics. Our experience in cancer treatment coupled with EnGeneIC's advanced medical innovations will propel us forward in our journey to provide early diagnosis and better outcomes for our patients throughout the region."

- - End - -

Singapore Institute of Advanced Medicine Holdings Ltd. (the "Company") was listed on Catalyst of the Singapore Exchange Securities Trading Limited ("SGX-ST") on 16 February 2024. The initial public offering of the Company was sponsored by PrimsPartners Corporate Finance Pte. Ltd. (the "Sponsor").

This press release has not been examined or approved by the SGX-ST. The SGX-ST assumes no responsibility for the contents of this document, including the correctness of any of the statements or opinions made or reports contained in this press release.

The contact person for the Sponsor is Ms. Ng Shi Qing, 16 Collyer Quay, #10-00 Income at Raffles, Singapore 049318, sponsorship@ppcf.com.sg.

ONCOBETA[®]
epidermal radioisotope therapy

 **Rhenium-SCT**[®]



SAM

Singapore Institute of Advanced Medicine Holdings

Rhenium-SCT



What is Rhenium-SCT[®]?

- **Rhenium-SCT[®]** or **Rhenium-Skin Cancer Therapy (SCT)** is a medical device* for the treatment of non-melanoma skin cancer (NMSC), including basal and squamous cell carcinoma (BCC / SCC).
- Rhenium-SCT[®] utilises the Beta-emitting radioisotope, rhenium-188, to deliver a painless, non-surgical, single-session treatment that preserves functionality and cosmesis.
- Rhenium-SCT is administered as a paste allowing conformal application to complex surfaces.

NMSC: Can have a dramatic impact on quality of life¹

NMSC can be **difficult to treat** due to:

- Lesion size and location (face, lips, ears, genitals, etc.)

Treatment **can be unsatisfactory** due to:

- Disfigurement
- Loss of function
- Need for reconstruction
- Recurrence
- Pain
- Complications
- Waiting lists and/or recovery time

An effective, non-invasive, single-session treatment is a valuable option.





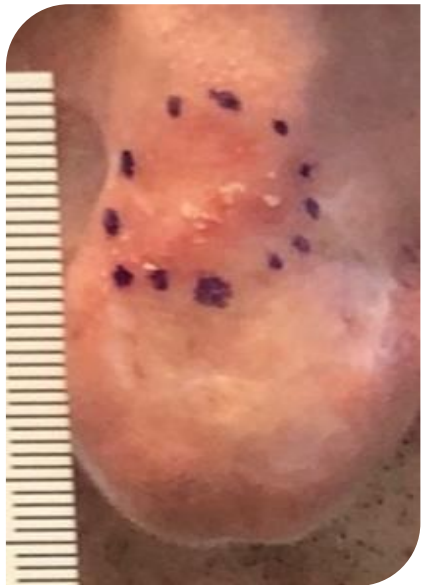
What is Rhenium-SCT?

- The Rhenium-SCT[®] is a resin/paste utilising the beta emitter radioisotope Rhenium-188 for the treatment of Non-Melanoma Skin Cancer.
- Mechanism of action is same as other radiation therapy modalities.

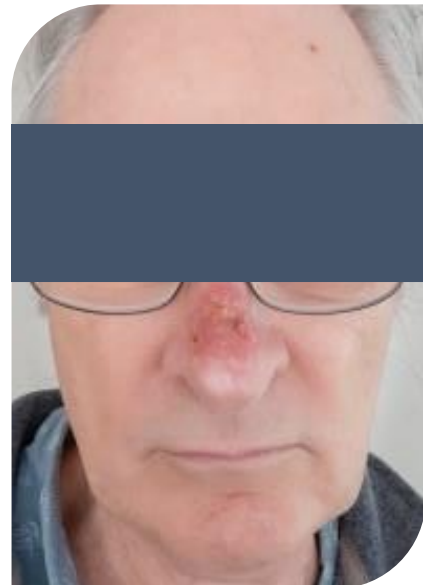
References: 1. Sedda AF, et al. Dermatological high-dose-rate brachytherapy for the treatment of basal and squamous cell carcinoma. *Clin Exp Dermatol.* 2008;33(6):745-749. doi: 10.1111/j.1365-2230.2008.02852.x 2. Cipriani C, et al. Personalized irradiation therapy for NMSC by rhenium-188 skin cancer therapy: a long-term retrospective study. *J Dermatolog Treat.* 2020:1-7. doi: 10.1080/09546634.2020.1793890. 3. Castellucci P, et al. High dose brachytherapy with non sealed 188Re (rhenium) resin in patients with non-melanoma skin cancers (NMSCs): single center preliminary results. *Eur J Nucl Med Mol Imaging.* 2021;48(5):1511-1521. doi: 10.1007/s00259-020-05088-z. 4. Cipriani C, et al. Personalized high-dose-rate brachytherapy with non-sealed rhenium-188 in non-melanoma skin cancer. *Int J Nucl Med.* 2017;114-112.

Rhenium-SCT: Skin reactions / cosmesis

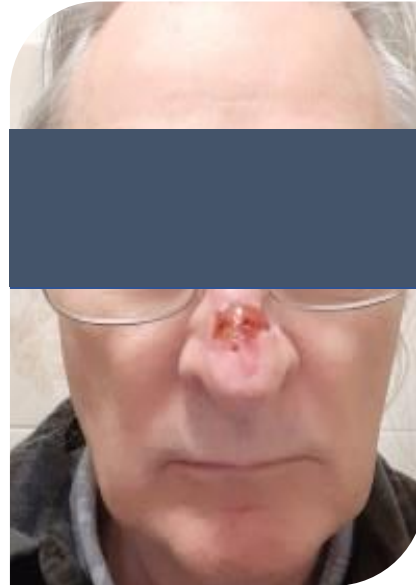
Results in areas with cosmetic considerations: BCC



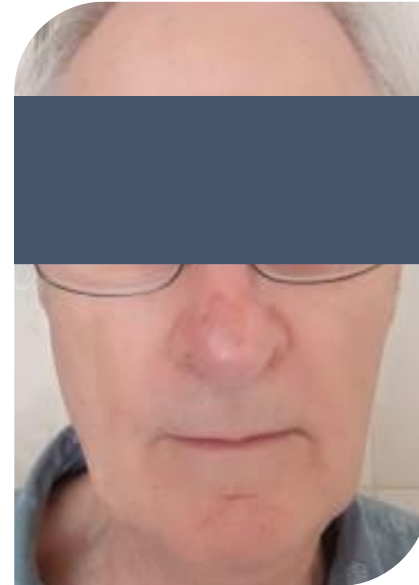
Before
Rhenium-SCT



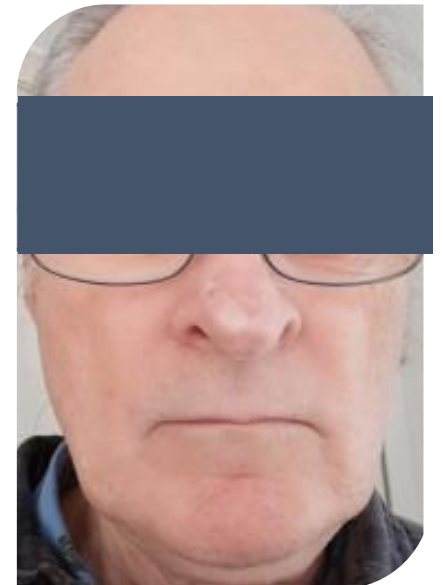
2 weeks



4 weeks



6 weeks



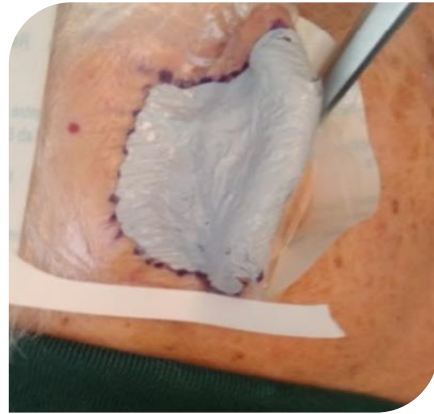
12 weeks

Rhenium-SCT: Lesions in areas with cosmetic considerations

Results in areas that have cosmetic considerations: SCC



Pre-treatment



Pre-treatment



Day 14



Day 30



Day 30



Day 48



Day 90



1 year

Male, 93 years-old

- SCC
- 2mm thickness
- No prior treatment

Rhenium-SCT: Lesions in areas with cosmetic considerations

Results in areas that have cosmetic considerations: BCC

Female, 92 years-old

- BCC
- 0.4mm thickness
- 3.3cm²
- Prior Mohs therapy



Pre-treatment



Day 14



Day 28



Day 180

Rhenium-SCT: Lesions in areas with cosmetic considerations

Results in areas that have functional considerations: BCC

Male, 84 years-old

- SCC
- 0.6mm thickness
- 2.5cm² treatment area
- Prior CO₂ laser, cryotherapy



Pre-treatment



Day 14



Day 28



Day 60



Day 90



finalizing a Master Services Agreement with Oncobeta for supply and sales, training and research for 18 countries including China and India, with exclusivity for 16 countries

ONCOBETA®
epidermal radioisotope therapy

Master Services
Agreement

OncoBeta Therapeutics Pty Ltd (ABN 39 624 903)

Singapore Institute of Advanced Medicine
Holdings Ltd
(Company Registration No. 201134046D)



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This presentation has been reviewed by the Sponsor for compliance with the relevant rules of the SGX-ST. It has not been examined or approved by the SGX-ST, and the SGX-ST assumes no responsibility for the contents of this presentation, including the correctness of any of the statements or opinions made or reports contained in this presentation.

The contact person for the Sponsor is Ms. Ng Shi Qing, 16 Collyer Quay, #10-00 Collyer Quay Centre, Singapore 049318, sponsorship@ppcf.com.sg