ASX Announcement

Starpharma showcases DEP® dendrimer platform at PepTalk Targeted Radioligand Therapies Conference

Melbourne, Australia; 16 January 2025: Starpharma (ASX: SPL, US OTC: SPHRY), an innovative biotechnology company with two decades of experience in advancing dendrimer technology from the lab to the patient, today announces that a DEP® presentation was delivered at Cambridge Healthtech Institute's 24th Annual PepTalk conference, which focuses on advancements in biotherapeutic discovery and development, held in San Diego overnight. This presentation was part of the Targeted Radioligand Therapies, Precision Medicine for Cancer program, which featured at the conference for the first time and highlighted the latest advancements and opportunities in the rapidly emerging radiotheranostics space.

Presented by Dr Jeremy Paull, Vice President of Development and Regulatory Affairs, the session showcased the potential of DEP® dendrimers in achieving the targeted delivery of radiotheranostic payloads to cancerous tumours. The presentation also highlights the opportunity for the DEP® platform to be used to improve upon the delivery of radioisotopes using a wide array of novel targeting moieties. Compared with the standard approach of using small molecules or large antibodies alone, which have limitations and challenges such as excessive kidney exposure or long blood circulation times, Starpharma's DEP® platform allows for biological targeting at the same time as optimising the biodistribution profile of a radioisotope for different applications. The potential benefits of this approach include improved biodistribution, enhanced diagnostic and efficacy profiles, better tumour penetration and retention, faster clearance from the bloodstream, and increased specificity.

Key companies in the radiotheranostic field attended the meeting, including Telix Pharmaceuticals, RayzeBio (a Bristol Myers Squibb Company), and Clarity Pharmaceuticals. Conferences such as PepTalk provide an excellent platform for Starpharma to engage with potential commercial partners and research collaborators in this exciting and rapidly evolving area of research.

The PepTalk presentation, titled **Dendrimer Nanoparticles (DEP®) Enable Targeted Precision Delivery and Customized Biodistribution for Cancer Radiotheranostics**, is appended.

About Starpharma

Starpharma ASX: SPL, US OTC: SPHRY) is an innovative biotechnology company with two decades of experience in advancing dendrimer technology from the lab to the patient. Our mission is to help patients with significant illnesses, such as cancer, achieve improved health outcomes and quality of life through the application of our unique dendrimer technology.

Dendrimers are precise, synthetically manufactured, nanoscale molecules. Their unique properties—including their size, structure, high degree of branching, polyvalency, and water solubility—are advantageous in medical and pharmaceutical applications.

Starpharma's portfolio of dendrimer-based products includes three clinical-stage DEP® (dendrimer enhanced product) assets, preclinical radiopharmaceutical assets, research collaborations, and three commercially marketed over-the-counter (OTC) products.

For more information about Starpharma, visit www.starpharma.com or connect with Starpharma on LinkedIn.

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Disclosure
This ASX Announcement was authorised for release by the Chair, Mr Rob Thomas.

Forward-Looking Statements
This document contains certain forward-looking statements, relating to Starpharma's business, which can be identified by the use of forward-looking terminology such as "promising", "plans", "anticipated", "will", "project", "believe", "forecast", "expected", "estimated", "targeting", "aiming", "set to", "potential", "seeking to", "goal", "could provide", "intends", "is being developed", "could be", "on track", or similar expressions, or by express or implied discussions regarding potential filings or marketing approvals, or potential future sales of product candidates. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no assurance that any existing or future regulatory filings will satisfy the FDA's and other authorities' requirements regarding any one or more product candidates, nor can there be any assurance that such product candidates will be approved by any authorities for sale in any market or that they will reach any particular level of sales. In particular, management's expectations regarding the approval and commercialization of the product candidates could be affected by, among other things, unexpected trial results, including additional analysis of existing data, and new data; unexpected regulatory actions or delays, or government regulation generally; our ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry, and general public pricing pressures; and additional factors that involve significant risks and uncertainties about our products, product candidates, financial results and business prospects. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated, or expected. Starpharma is providing this information as of the date of this document and does not assume any obligation to update any forward-looking statements contained in this document as a result of new information, future events or developments or otherwise. Clinical case studies and other clinical information given in this document are given for illustrative purposes only and are not necessarily a guide to product performance and no representation or warranty is made by any person as to the likelihood of achievement or reasonableness of future results. Nothing contained in this document, nor any information made available to you is, or shall be relied upon as, a promise, representation, warranty or guarantee as to the past, present or the future performance of any Starpharma product.

Dendrimer Nanoparticles (DEP®) Enable Targeted Precision Delivery and Customized Biodistribution for Cancer Radiotheranostics

Dr Jeremy Paull, PhD

VP, Development and Regulatory Affairs

NOVEL TARGETING MECHANISMS AND EMERGING TARGETS

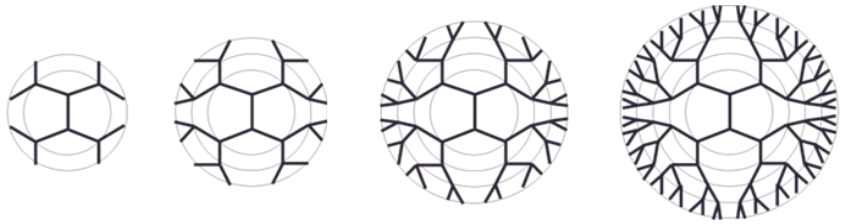
Targeted Radioligand Therapies

15 January 2025

Disclaimer and Forward-Looking Statements

This presentation contains forward-looking statements that involve risks and uncertainties. Although we believe that the expectations reflected in the forward-looking statements are reasonable at this time, Starpharma can give no assurance that these expectations will prove to be correct. Actual results could differ *materially* from those anticipated. Reasons may include risks associated with drug development and manufacture, risks inherent in the regulatory processes, delays in clinical trials, risks associated with patent protection, future capital needs or other general risks or factors.

Summary



- **DEP® dendrimers are a versatile, customisable platform for enhancing delivery of radiotheranostic payloads to tumours using novel targeting moieties**

❑ Proprietary DEP® platform – **clinically validated** via 4 clinical programs, multiple drug classes

❑ Starpharma's are the only **marketed** dendrimer-based products

❑ DEP® platform:

- ✓ Unique design provides **flexibility** for utilising a **wide range of payloads and chelating agents**
- ✓ Selected characteristics tailored to achieve **preferential delivery** to tumour microenvironment, e.g., size
- ✓ Can be precisely engineered and **functionalised** to carry a **wide range of targeting moieties**
- ✓ Highly **customisable** for desired **biodistribution / excretion profile**

❑ Targeted DEP® can achieve **improved biodistribution and diagnostic/efficacy** profiles vs. antibody or small molecule targeting for radiotheranostics

Starpharma...

An innovative, biopharmaceutical company and leader in dendrimer technology

Focus: Dendrimer Drug (DEP®) Delivery Technology

Clinically validated technology
More than 350 patients treated with DEP® across multiple clinical programs.

Uniquely experienced team
Expertise in dendrimer science and manufacturing, cancer biology, clinical product development.
Staff of ~40 people.

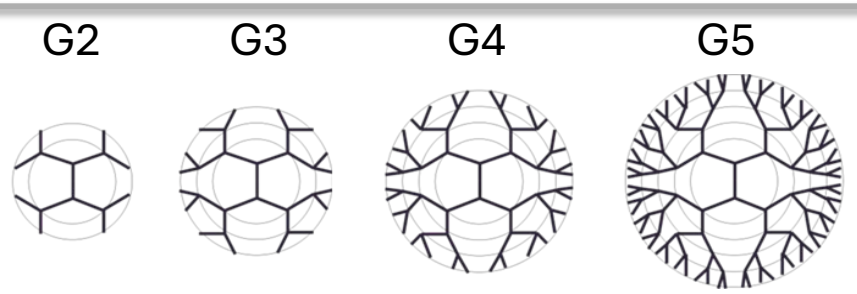
Strong intellectual property position
19 active patent families with over 150 granted and pending patents.

Pipeline of products and partnerships
Portfolio includes clinical-stage assets, early-stage research, partnerships, and commercial products.

Starpharma's Validated DEP® Platform

DEP® dendrimers have a unique construction based on concentric layers (generations) of lysine monomers

- *Synthetic, reproducible, scalable, precise*
- *Customisable size, generation and surface*



Clinically validated

- Phase II oncology studies demonstrated favourable tolerability and efficacy outcomes with cytotoxic payloads
- Range of therapeutic classes

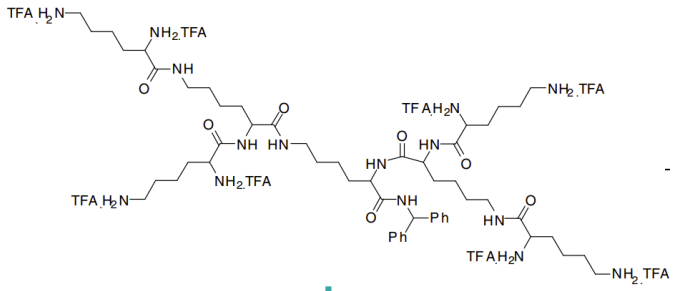
Improves drug performance

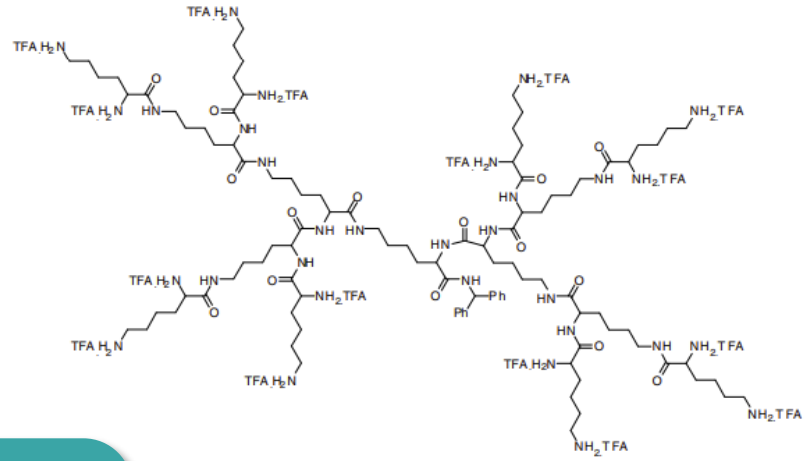
- Ability to design a dendrimer-drug conjugate to optimise both rate and site of payload release and clearance route
- Delivers up to 40-70x more drug in tumour vs. blood

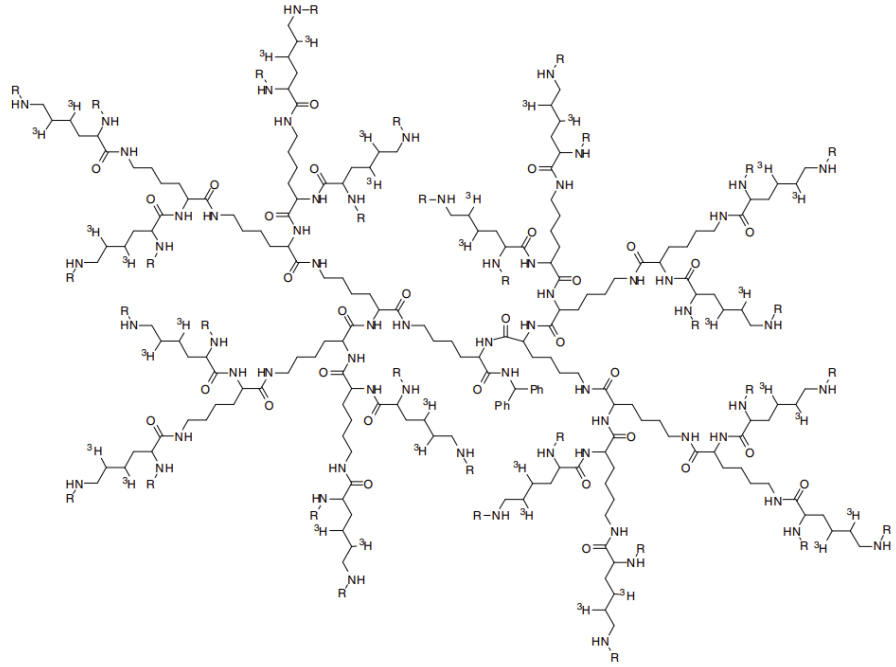
Broad applicability

- Applicable to a wide range of therapeutic areas, treatment modalities and applications, including targeted radiotheranostics, dendrimer-drug conjugates, targeted therapies (~ADCs), and drug rescue

Dendrimers – Synthetic Molecules, With Precise Architecture, Customizable Size, Generation and Surface Functionality







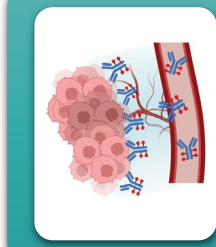
- Low polydispersity, near monomodal MW distributions
- Characterisation via standard methodologies, e.g., NMR, LCMS, HPLC, UPLC, SEC etc.

- Standard synthetic chemistry methods and processes
- Controlled and reproducible
- Scalable, GMP

Kaminskas et al. Mol Pharm. 2008;5(3):449-63. doi: 10.1021/mp7001208.

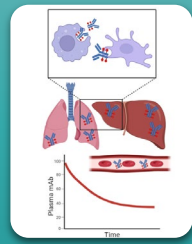
Why Dendrimers? Opportunities to Solve Complex Challenges Facing Traditional Small or Large Molecule Drug and Radio Conjugates

Large Molecules (e.g., mAb)



Efficacy Challenges

- Limited tumour penetration
- Limited "DAR" achievable
- Need for highly toxic payloads



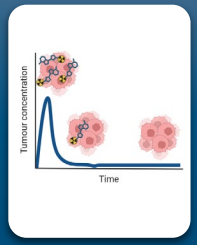
Toxicity / PK

- On-target, off-tumour
- Off-target
- Antigen-independent toxicity
- Long half-life, circulation times

Chemistry

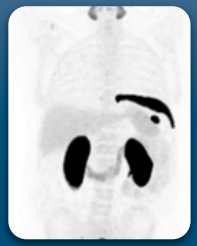
- Heterogeneous DAR, site-specific
- Solubility of lipophilic payloads
- Aggregation
- Manufacturing and scalability

Small Molecules (e.g., small molecules, peptides)



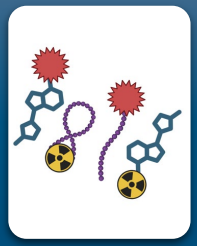
Efficacy Challenges

- Limited tumour exposure
- Limited amount of payload possible
- Need for highly specific / high affinity binding



Toxicity / PK

- On-target, off-tumour
- Off-target
- Short half-life, rapid clearance
- Kidney exposure / uptake



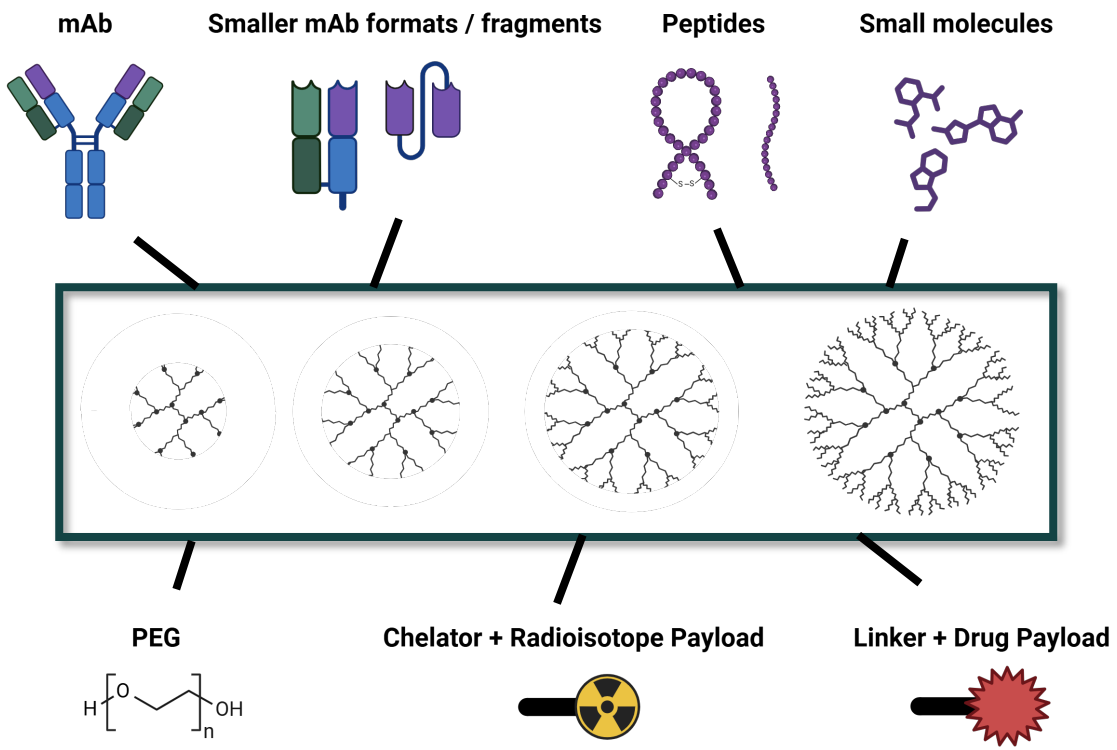
Chemistry

- Solubility of lipophilic payloads
- Instability
- 1:1 "DAR", "Target"

Images created in https://BioRender.com

DEP® Dendrimers – A Unique Solution to Solving Complex Payload/Target Delivery Challenges

DEP® dendrimers bridge the gap between small and large molecule targeting and payload delivery



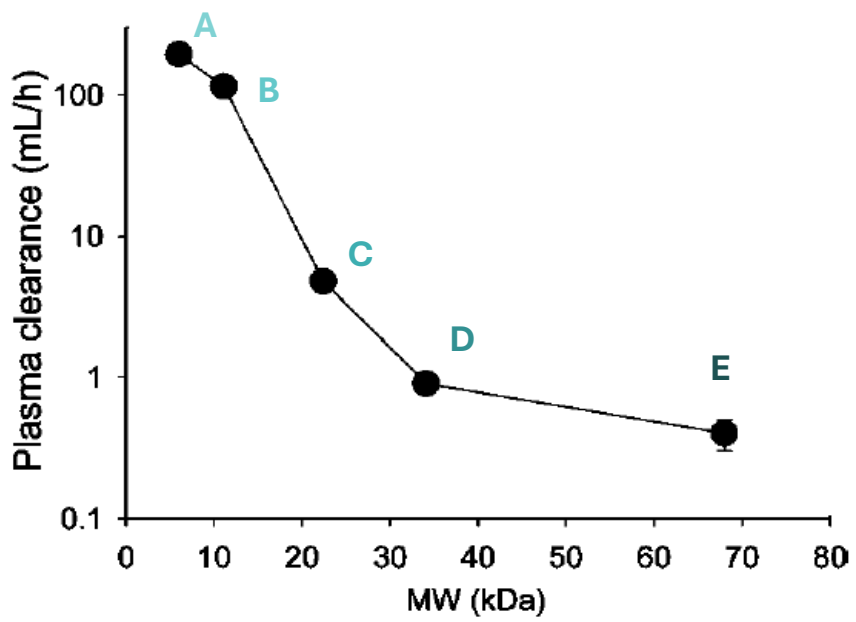
- Potential for improved tumour penetration and retention
- Tuneable solubility, PK
- Tuneable plasma / kidney clearance
- Range of targeting moieties (bi-/multi-specific)
- Multivalent targeting / payload presentation, linker selection
- Site-specific payload attachment, precise and reproducible DAR
- Scalable, reproducible, commercial scale under GMP

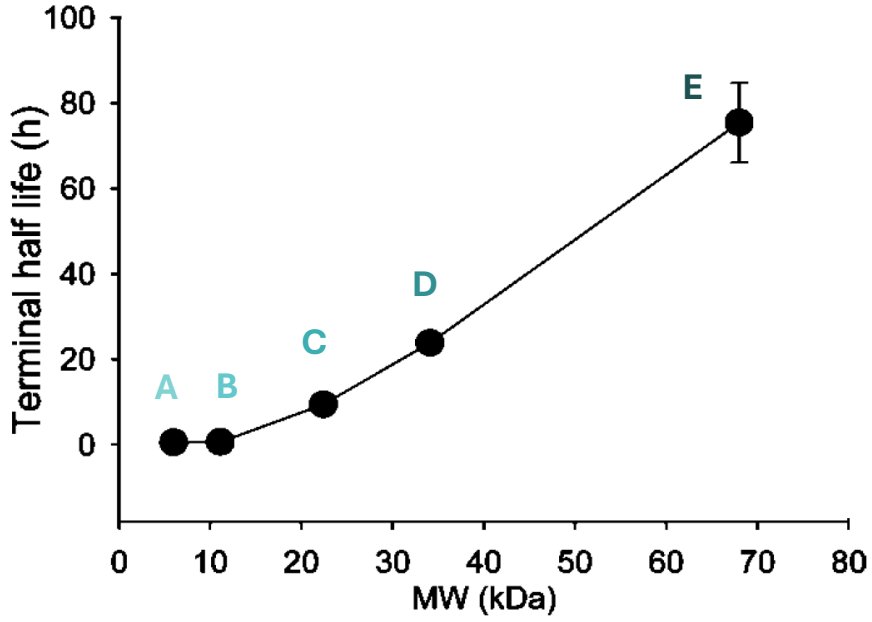
Images created in https://BioRender.com

DEP® Offers Highly Specialised Tuneable PK and Plasma Clearance Profile

- **Plasma clearance and half-life can be tailored with specific dendrimer generation (size) and surface properties, including PEG**

Non-targeted Poly-L-Lysine dendrimers in rats (IV dose)[1]



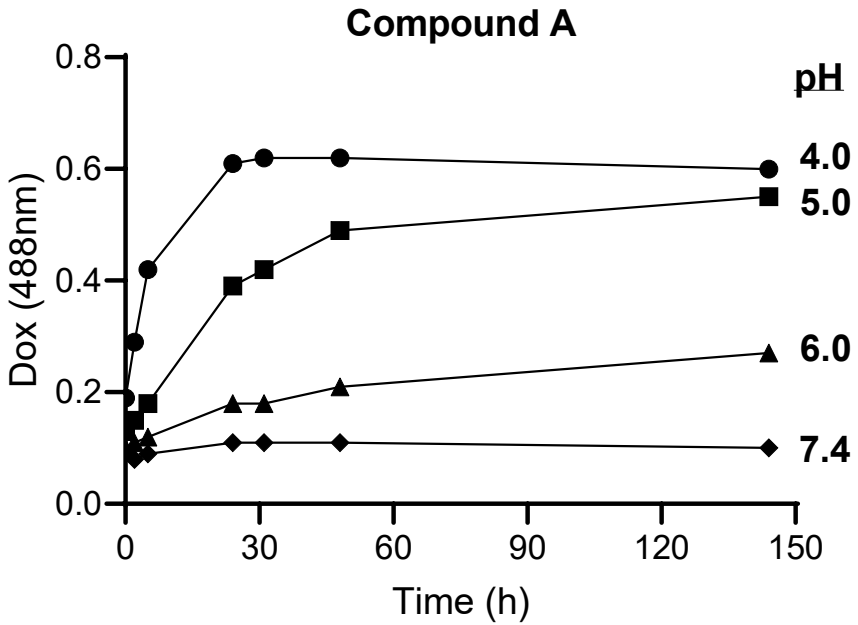


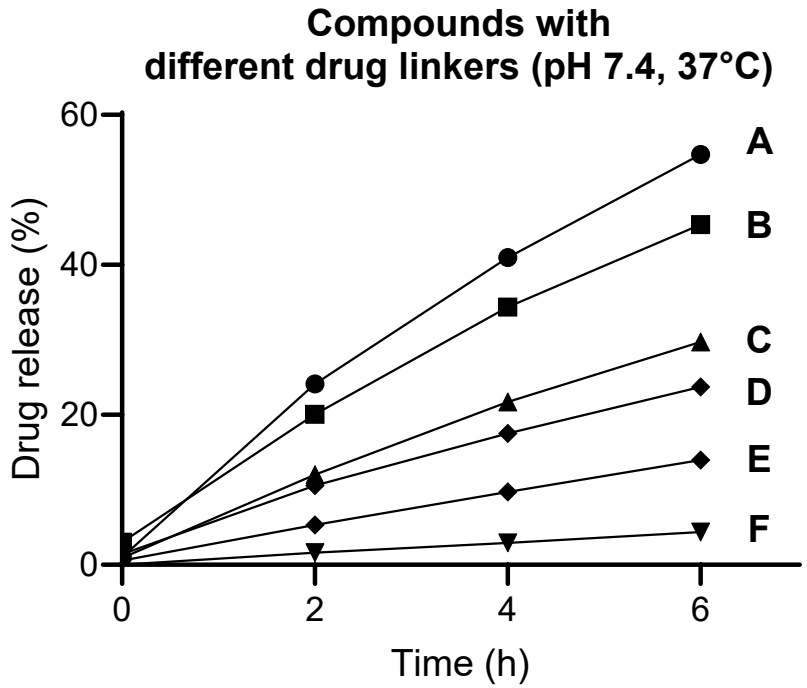
A DEP1 (PEG200)
B DEP2 (PEG200)
C DEP3 (PEG570)
D DEP4 (PEG2000)
E DEP5 (PEG2000)

1. Kaminskas *et al.* Molecular Pharmaceutics 2008, 5(3), 449-463

DEP® Dendrimer Payload Release with Different Linkers to Achieve Custom PK Profile

- Tuneable drug release profile using different linker chemistry



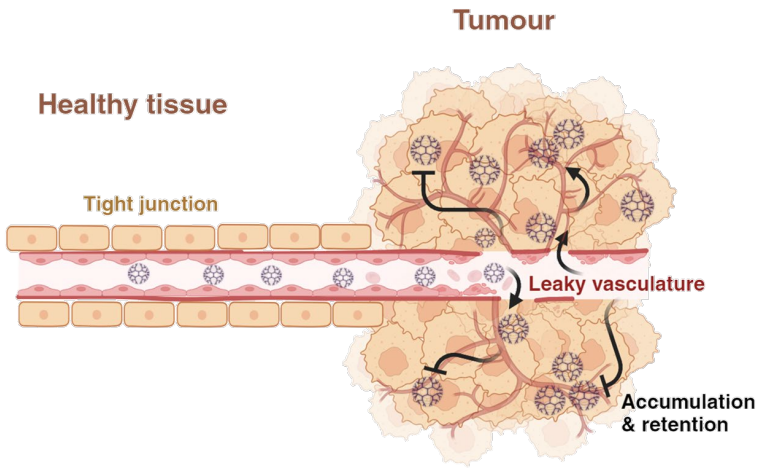


1. Kaminskas *et al.* Molecular Pharmaceutics 2008, 5(3), 449-463

DEP® Dendrimers Achieve Tumour Targeting via Complementary Mechanisms

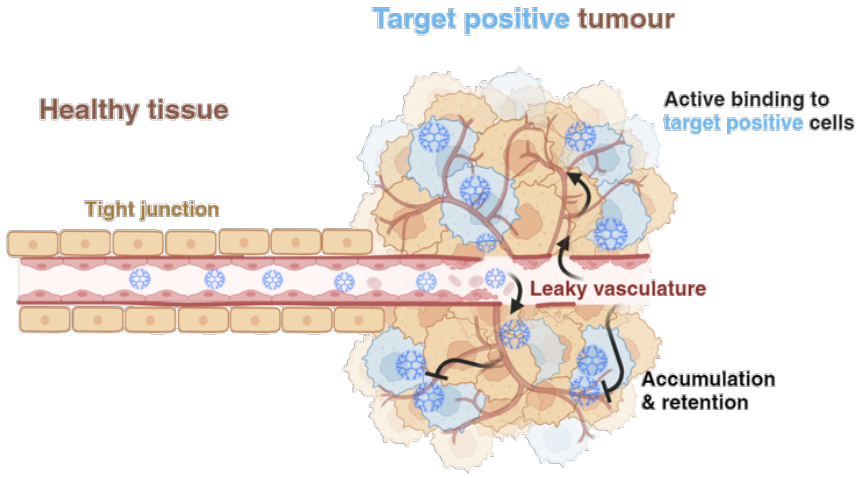
Physical targeting based on size and EPR effect

- EPR: Enhanced permeability and retention
- Allows dendrimers to accumulate in tumour due to leaky vasculature and poor lymphatic drainage
- DEP® dendrimer size can be optimized to maximize EPR effect
- **e.g., DEP® SN38 and DEP® Cabazitaxel**



Biological targeting with wide range of targeting moieties

- Targeting moieties (e.g., mAb, small molecules, peptides, small mAb fragments) bound to DEP® dendrimer surface
- Mono-specific, multi-specific, multi-valent targeting
- Independent of EPR variability
- **e.g., DEP® HER2-targeted radiotheranostic**

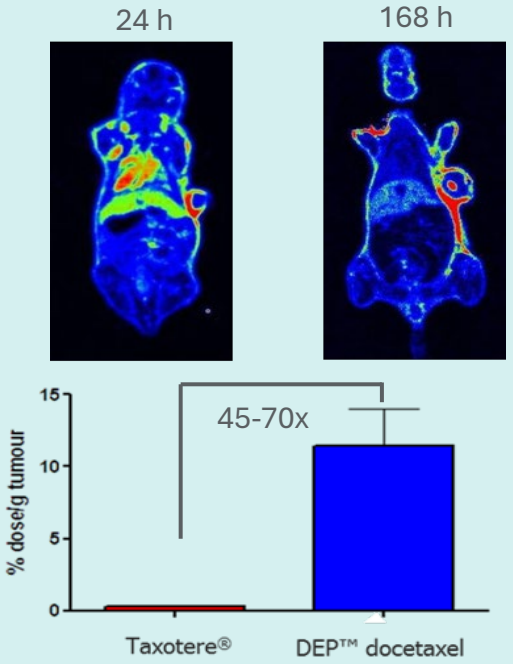


DEP® dendrimers can combine both targeting mechanisms and thus, maximize therapeutic efficiency

Dendrimers Achieve Selective Tumour Accumulation by Virtue of Size and EPR Effect, Leading to Improved Efficacy

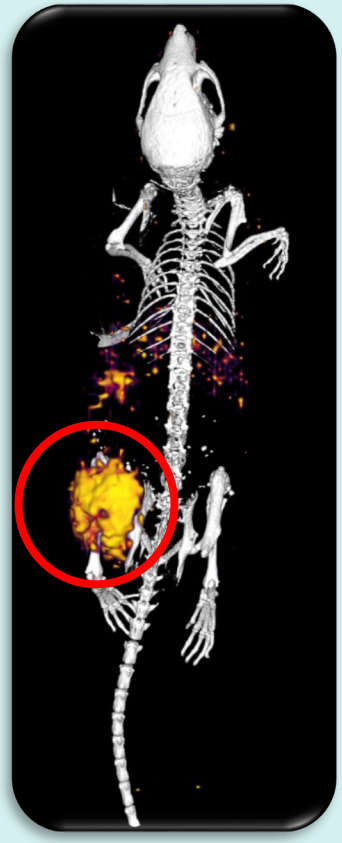
Tumour accumulation in human xenograft tumour models with "physically" targeted DEP® agents…

MDA-MB-231 breast cancer model



DEP® size allows "physical" targeting of drugs to cancer tissue resulting in higher tissue levels

DU145 prostate cancer model

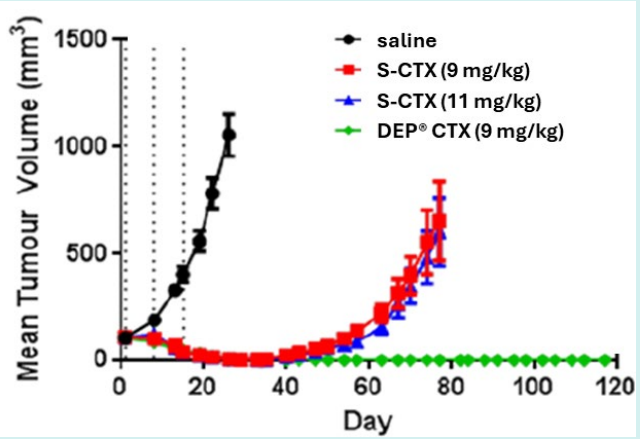


Radiolabelled DEP® dendrimer-drug conjugate accumulates in tumour via enhanced permeability and retention (EPR) effect

(image obtained 48 hours post-injection)

Translates to enhanced efficacy in human xenograft tumour model

DEP® cabazitaxel shows enhanced efficacy and vs. standard cabazitaxel in SCID mice, DU145 prostate cancer xenograft model



Starpharma's Internal DEP® Oncology Portfolio

Multiple Clinical Stage Assets with Significant Commercial Potential to Address Unmet Need

DEP® Cabazitaxel

- Dendrimer version of leading prostate cancer drug, cabazitaxel (Jevtana®), which had global sales of ~US$500M for 2021 despite multiple US FDA "Black Box" warnings

Advantages of DEP® cabazitaxel

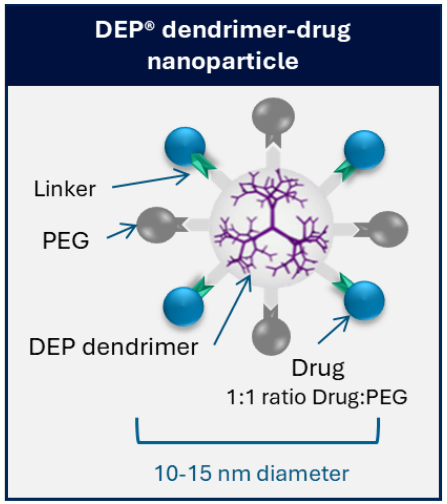
- Aqueous, detergent-free formulation; no steroid pre-treatment; improved tolerability; prolonged retention in tumour interstitium, improved efficacy

DEP® SN38

- Novel dendrimer-topoisomerase I (TOP1) conjugate of SN38, active metabolite of irinotecan (Camptosar®), which had peak sales of US$1.1B despite multiple US FDA "Black Box" warnings

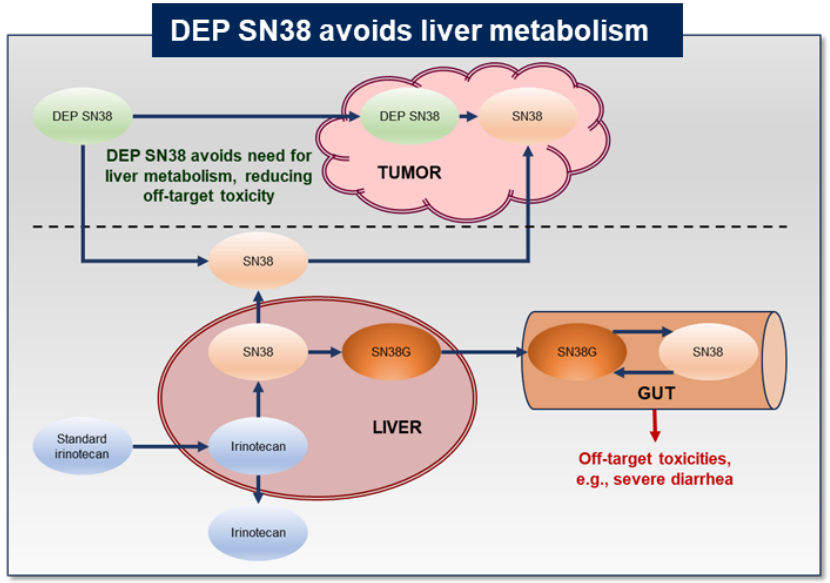
Advantages of DEP® SN38

- Solubility, direct dosing of SN38; avoids liver conversion; reduced toxicity, variability; prolonged retention in tumour interstitium, improved efficacy



Insoluble drug payload

DEP® solubilised drug payload

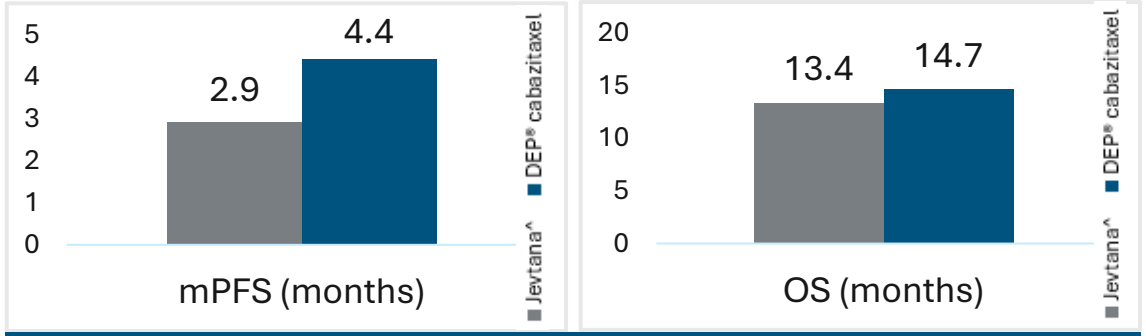


DEP® Cabazitaxel Achieves Highly Encouraging Efficacy in Late-Stage Patients, Compared to Standard Therapies

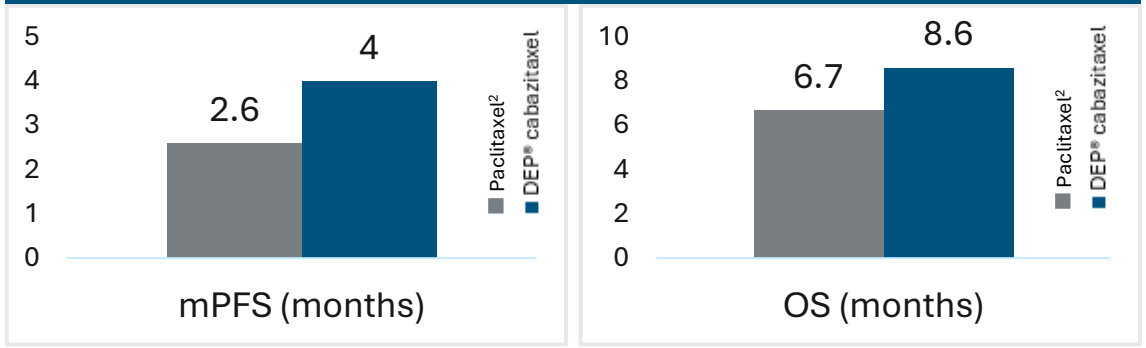
Results Presented at the 2024 ASCO Annual Meeting

2024 ASCO ANNUAL MEETING

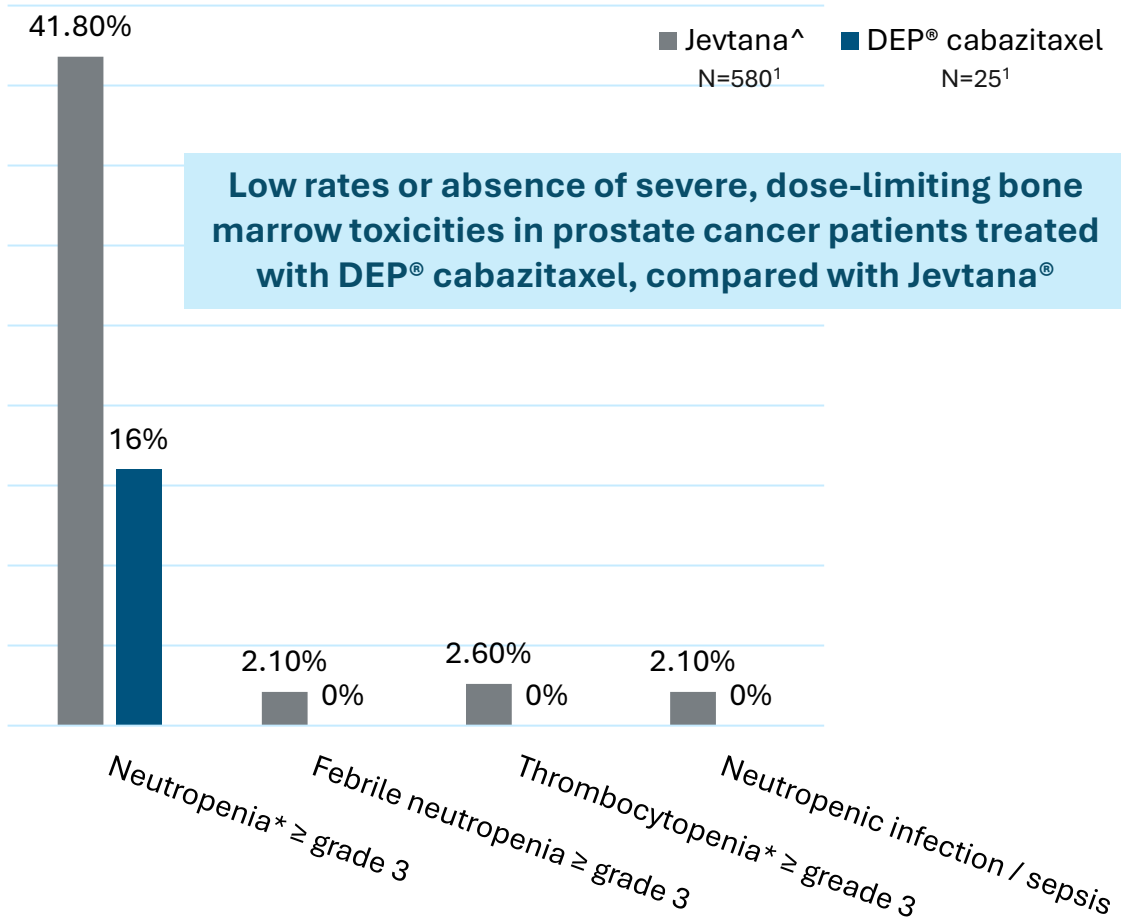
DEP® Cabazitaxel in Advanced Prostate Cancer



DEP® Cabazitaxel in Advanced Gastro-Oesophageal Cancers



Full Phase II results reported in ASX Announcement dated 18 October 2023;
*Lab detected neutropenia or thrombocytopenia, regardless of whether event was reported as an adverse event; [1] Safety Population (received at least 1 dose); ^ Eisenberger, M, et al., *J Clin Oncol,* 2017; 35(28):3198-206; [2] Stockton, S et al., *The Oncologist,* 2023;28(9):827-e822.



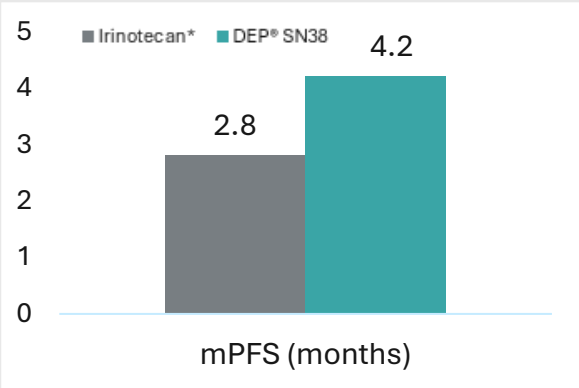
Low rates or absence of severe, dose-limiting bone marrow toxicities in prostate cancer patients treated with DEP® cabazitaxel, compared with Jevtana®

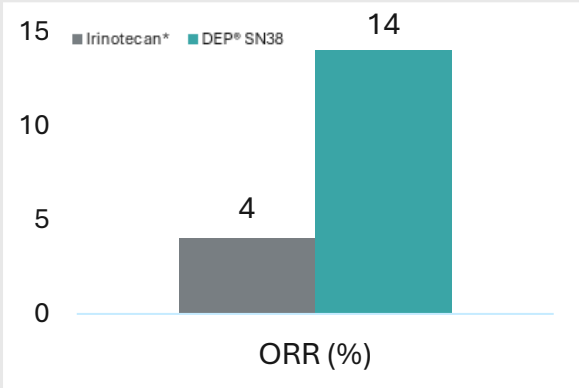
DEP® SN38 Phase II Study Shows Favourable Efficacy and Tolerability Data in Late-Stage Patients

Results Presented at the 2024 ASCO Annual Meeting

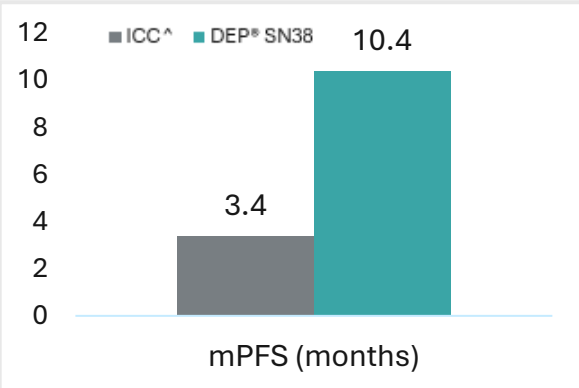
2024 ASCO ANNUAL MEETING

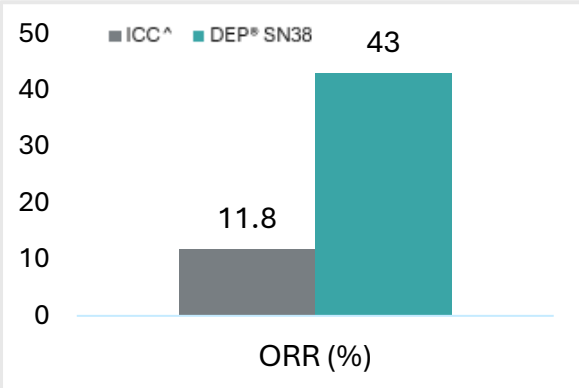
Advanced Colorectal Cancer



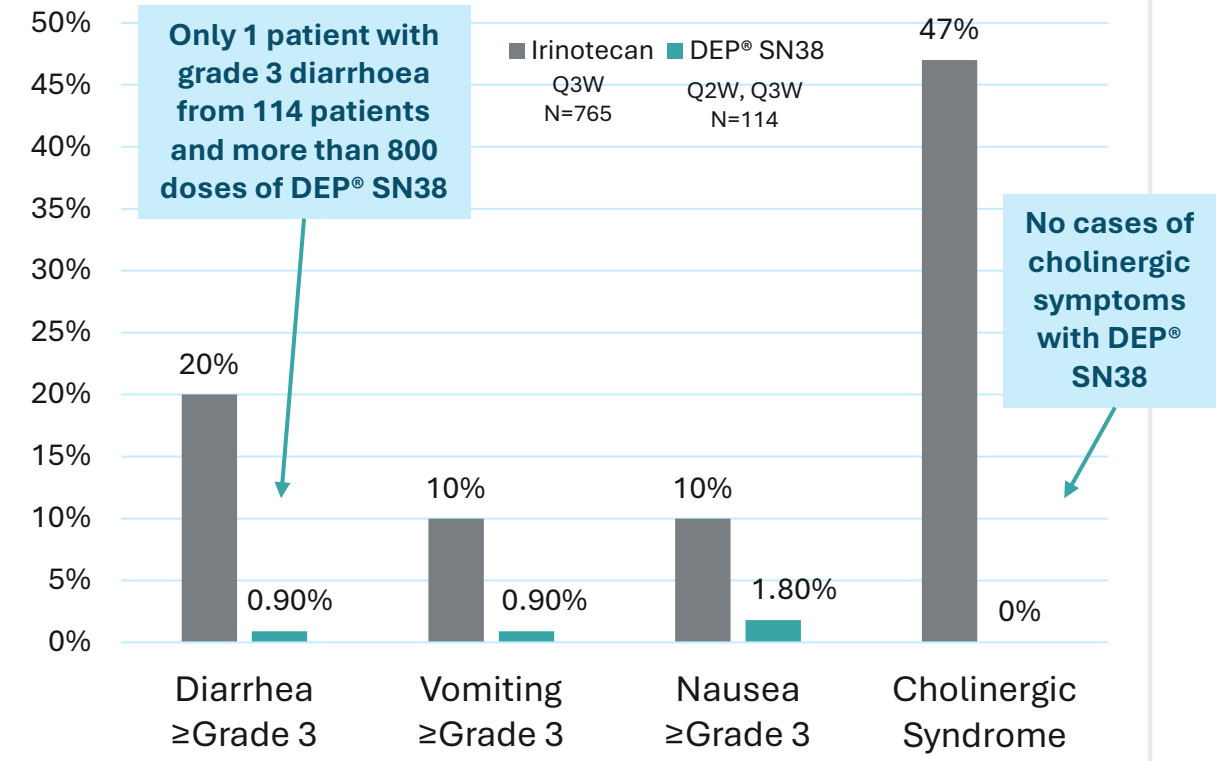


Advanced Platinum-Resistant Ovarian Cancer





Gastrointestinal Toxicity Profile Significantly Improved with DEP® SN38 Treatment, Compared to Published Data on Irinotecan#



Data for DEP® SN38 in combination with 5-FU/LV; Full Phase II results reported in ASX Announcement dated 27 May 2024; *From published data on irinotecan in combination with 5-FU/LV, Tournigand et al., *Clin Oncol,* 2023, 41(19):3469-3477; # https://www.medicines.org.uk/emc/product/6506- UK SmPC April 2022; ^From published data on ICC (investigator chemotherapy of choice) (pegylated liposomal doxorubicin, paclitaxel, or topotecan), Pujade-Lauraine E, et al., *J Clin Oncol,* 2014, 32(13):1302-1308

HER2 Status, Imaging and Therapy

- **Importance of understanding HER2 heterogeneity to drive appropriate treatment**
  - HER2 status is diagnosed using HER2 IHC ± ISH on a tumour biopsy
  - Results drive treatment decisions/planning (e.g., HER2-targeted therapy)
  - A biopsy may not be representative of HER2 expression across an entire tumour or across metastatic lesions due to HER2 heterogeneity

- **HER2 imaging has been assessed in humans**
  - mAb, affibodies and nanobodies have been radiolabeled with radioisotopes for both PET and SPECT imaging
  - Some of these are currently being assessed in clinical trials (Affibody, GE Healthcare, ASCINT and various academic institutes/hospitals)

- **Starpharma is developing a DEP® HER2-targeted dendrimer-radio-diagnostic and radiotherapeutic to address these needs**

HER2 Status, Imaging and Therapy

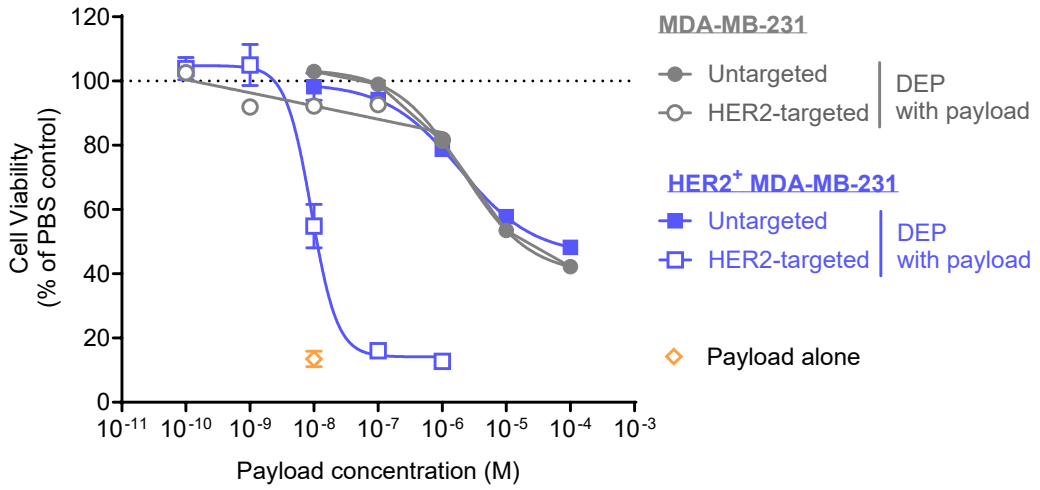
- **Decisions on HER2-targeted therapy may benefit from an accurate assessment of whole body HER2 status**
  - HER2-targeted therapies like Enhertu provide significant benefit to metastatic $HER2^{+}$ patients
  - $HER2^{low}$ and $HER2^{ultra\ low}$ patient populations identified by IHC
  - HER2 imaging may help to better identify patients who would benefit (or not) from HER2-targeted therapy

- **A HER2-targeted radiotherapeutic could provide an alternate option to overcome resistance for those who progress on current HER2-targeted therapies like Enhertu**
  - No approved HER2-targeted radiotherapies exist
  - Potential to address wide range of HER2+ cancers (e.g., breast, gastro-oesophageal)
  - Radioisotopes like ^{177}Lu have bystander effect to overcome heterogeneity of HER2 expression

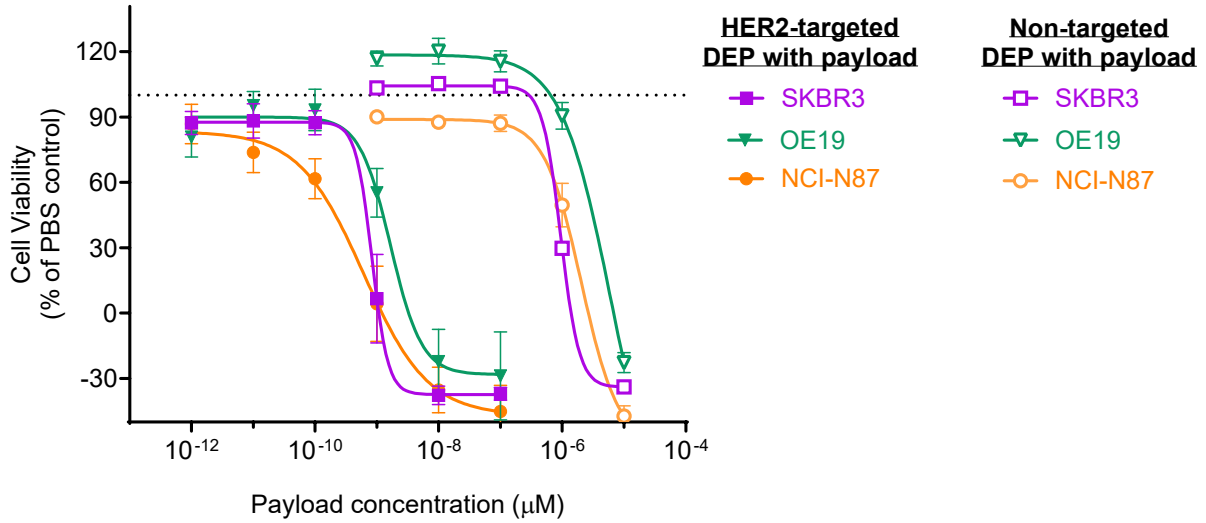
- **Starpharma is developing a DEP® HER2-targeted dendrimer-radio-diagnostic and radiotherapeutic to address these needs**

HER2-Targeted Dendrimers Enable Enhanced Killing of HER2$^+$ Cells

HER2-targeted dendrimers with cytotoxic payload induce HER2-specific cytotoxicity



Cytotoxicity induced in range of HER2$^+$ cell lines: breast (SKBR3), oesophageal (OE19) and gastric (NCI-N87)

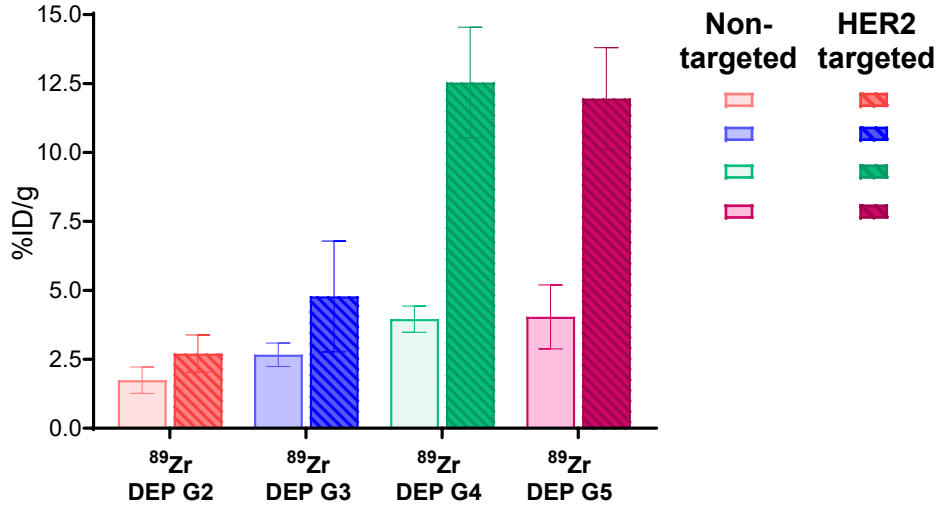


Assessed after 48h

Higher Generation Targeted Dendrimers Achieve HER2⁺ Specific Tumour Accumulation, Sustained via EPR Effect

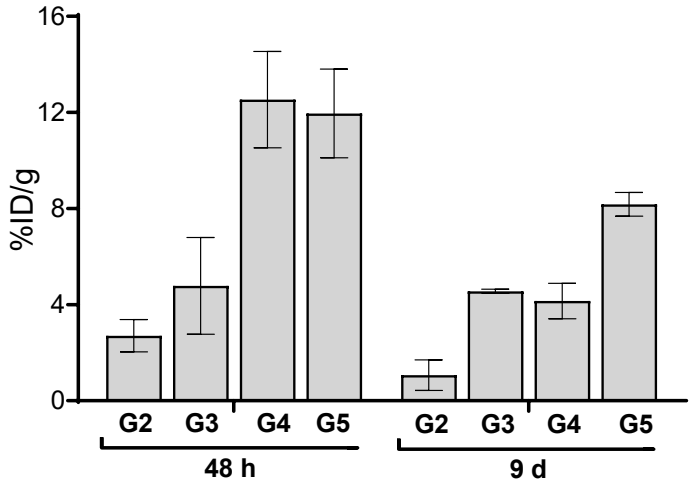
HER2⁺ BT474 tumours

48h



HER2 specificity vs dendrimer generation

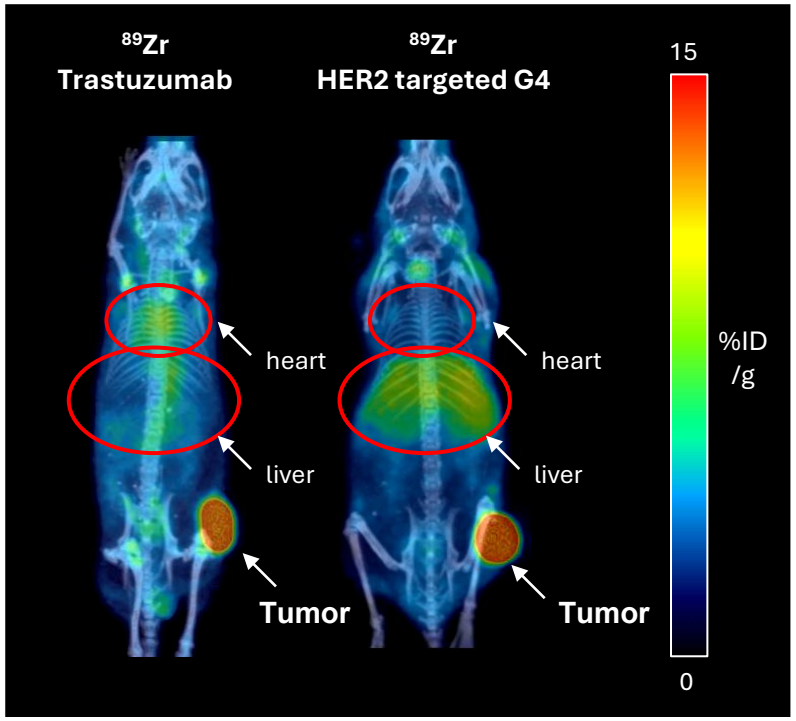
^{89}Zr HER2-targeted dendrimers



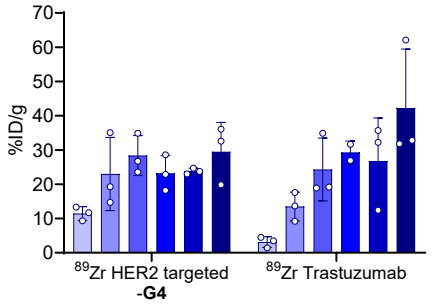
Increased and prolonged tumour accumulation

HER2-Targeted, Larger Generation Dendrimers (~50kDa) Accumulate in Tumours Similarly to HER2-mAb, Trastuzumab, with a Biodistribution Profile Showing More Rapid Clearance From Blood and Lungs

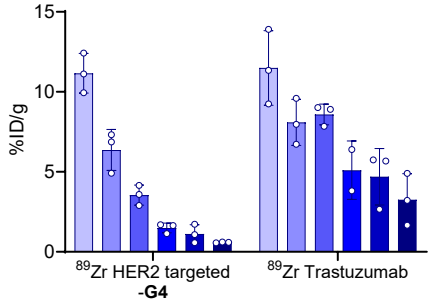
48h PET/CT - HER2⁺ BT474 tumour model



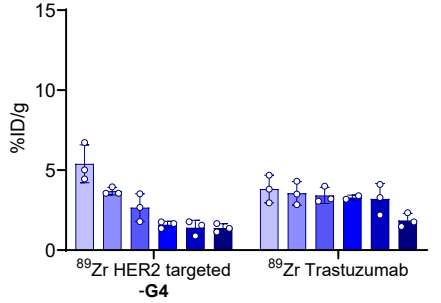
Tumour

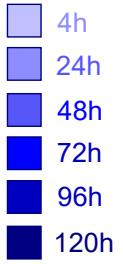


Blood



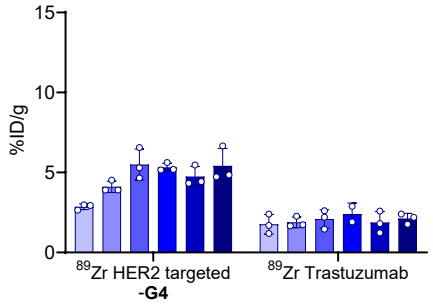
Lungs



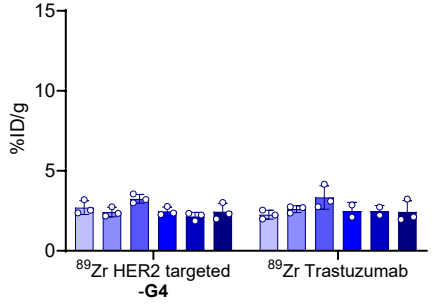


High + sustained tumour uptake out to 5d with HER2-targeted G4 dendrimer

Liver



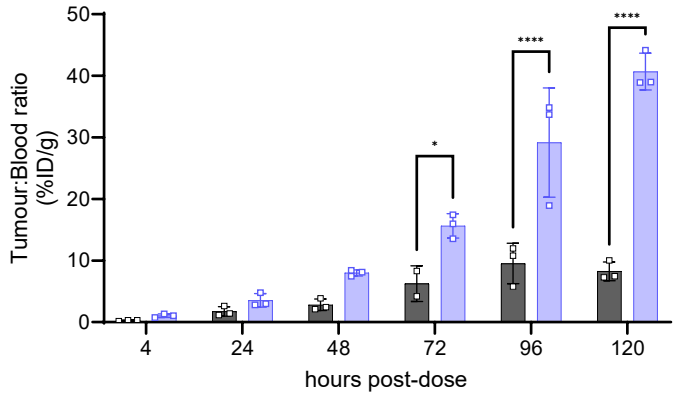
Kidneys



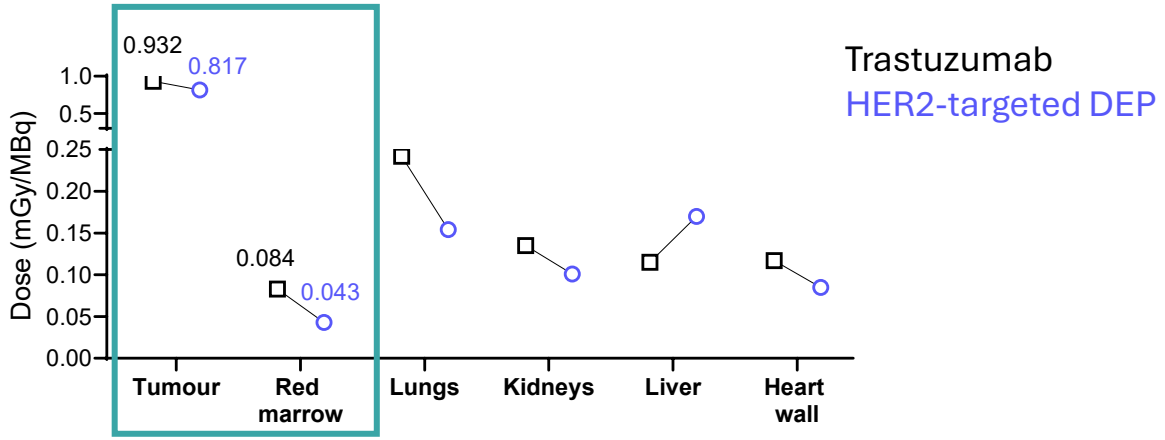
Ex vivo biodistribution in BT474-tumour bearing mice, each symbol = individual mouse

HER2-targeted Dendrimer Biodistribution Profile Indicates a Higher Radiation Dose can be Delivered to Tumour with DEP® vs mAb

Tumour : blood ratio



Dosimetry: Absorbed doses



Consideration for radiotherapeutic:

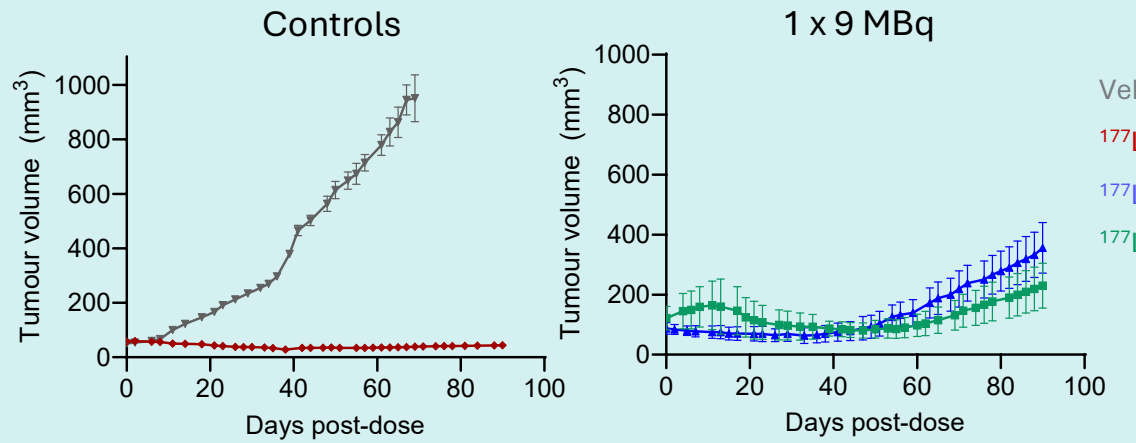
- Lower tumour : blood ratio with Trastuzumab
  → Higher adsorbed dose to bone marrow = dose-limiting organ (2Gy)
- When considering bone marrow dose limitations, HER2-targeted DEP® can be delivered at a higher dose, effectively achieving ~**1.7-fold higher dose** to tumour vs. Trastuzumab

Dosimetry analysis notes:
Delivered dose estimates derived from the activity curves obtained from *ex vivo* dataset (0-288h). Delivered dose estimates from the PET dataset (0-120h) or from activity data extrapolated to infinity are in line with results presented here.

Delivered dose estimates assume DEP® HER2-zirconium and Trastuzumab have been labelled with ^{177}Lu

Red bone marrow doses estimated based on blood measured activity as per methodology described by Wessels et al (J Nucl Med. 2004 Oct;45(10):1725-33)

Efficacy Observed With Dendrimer Constructs Radiolabeled With ^{177}Lu, Achieving Similar Efficacy to ^{177}Lu-Trastuzumab in HER2^{+} BT474 Xenograft Tumour Model



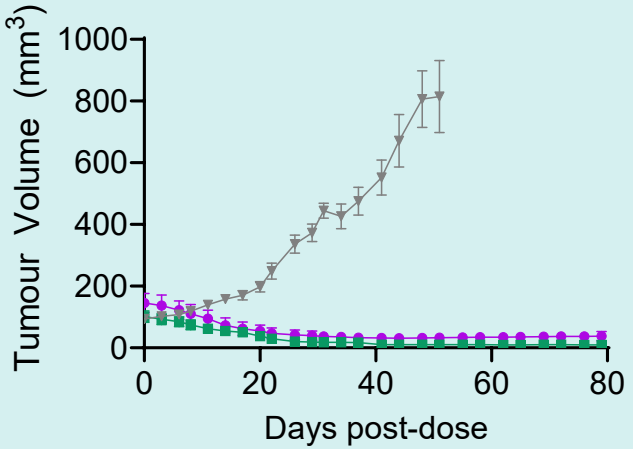
Vehicle

^{177}Lu Trastuzumab (15 MBq)

^{177}Lu non-targeting DEP 1

^{177}Lu HER2-targeting DEP 1

n=3-4 mice/group



Vehicle

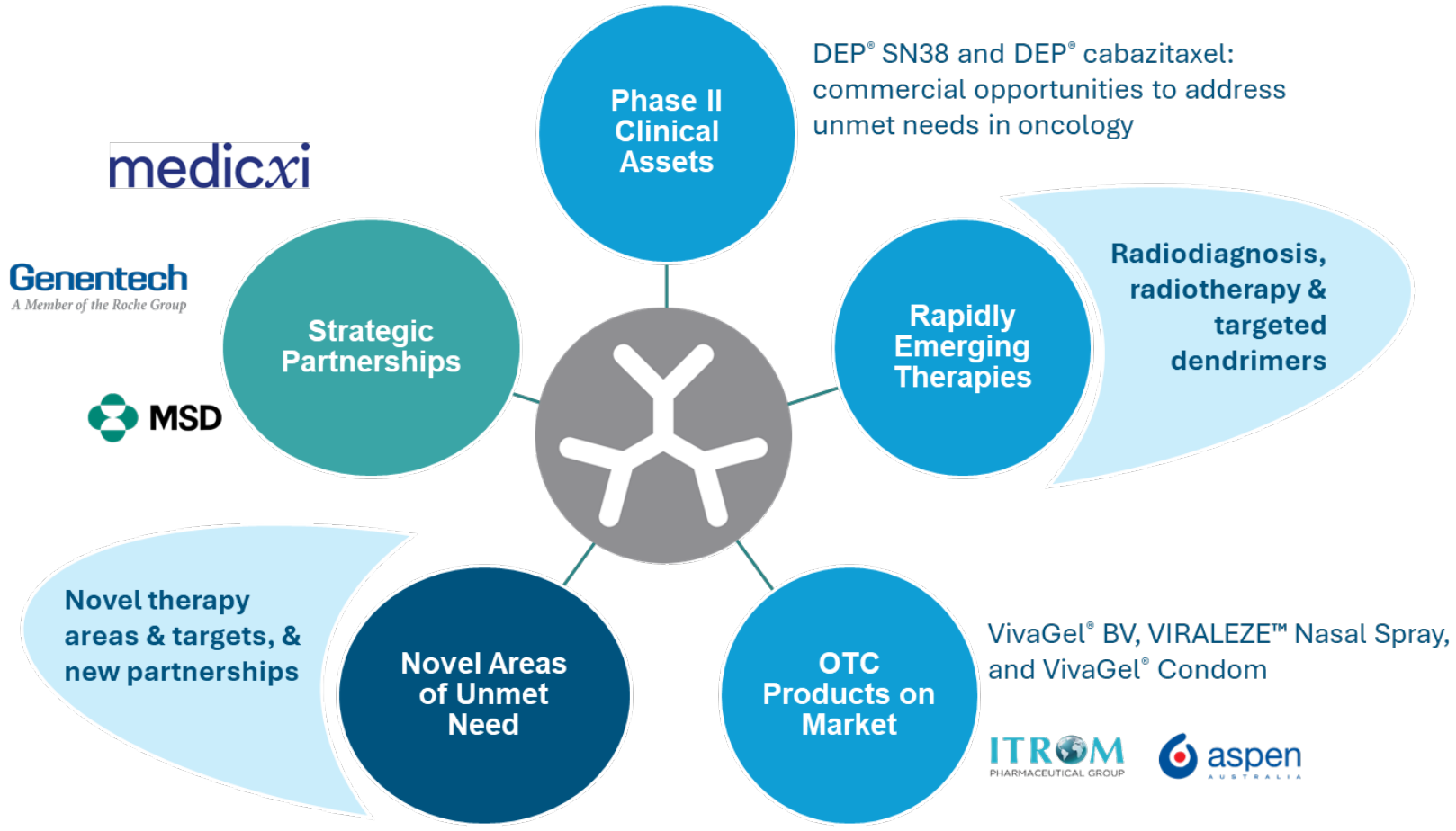
^{177}Lu HER2-targeting DEP 1 (1x 15 MBq)

^{177}Lu HER2-targeting DEP 2 (1x 15 MBq)

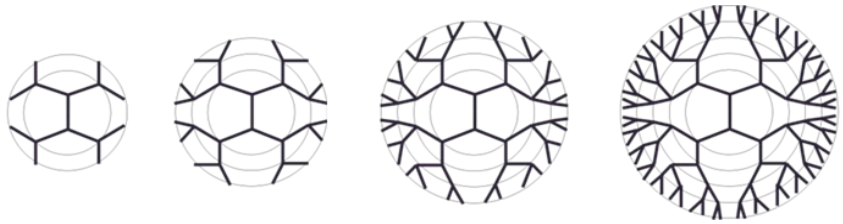
n=8 mice/group

Starpharma's DEP® Platform Technology: Versatile and Multifunctional for Delivery of Therapeutics & Diagnostics

Multiple Opportunities; Multiple Partnerships



Summary



- **DEP® dendrimers are a versatile, customisable platform for enhancing delivery of radiotheranostic payloads to tumours using novel targeting moieties**

❑ Proprietary DEP® platform – **clinically validated** via 4 clinical programs, multiple drug classes

❑ Starpharma's are the only **marketed** dendrimer-based products

❑ DEP® platform:

- ✓ Unique design provides **flexibility** for utilising a **wide range of payloads and chelating agents**
- ✓ Selected characteristics tailored to achieve **preferential delivery** to tumour microenvironment, e.g., size
- ✓ Can be precisely engineered and **functionalised** to carry a **wide range of targeting moieties**
- ✓ Highly **customisable** for desired **biodistribution / excretion profile**

❑ Targeted DEP® can achieve **improved biodistribution and diagnostic/efficacy** profiles vs. antibody or small molecule targeting for radiotheranostics

Acknowledgements

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Thank you.

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