ASX Announcement

DEP® Presentation at Radiopharmaceuticals Summit

Melbourne, Australia; 4 December 2024: Starpharma (ASX: SPL, US OTC: SPHRY) today announces a presentation that was delivered at the 6th Targeted Radiopharmaceuticals Summit Europe, in Amsterdam, Netherlands, showcasing the potential of its DEP® dendrimer technology in the delivery of targeted radiotheranostics.

Presented by Dr Jeremy Paull, Vice President of Development and Regulatory Affairs, the session demonstrated how DEP® dendrimers can serve as a versatile and customisable platform for enhancing the delivery of radiotheranostic payloads to cancerous tumours using novel targeting moieties. The presentation included an overview of the results from Starpharma's Phase II clinical programs of DEP® SN38 and DEP® cabazitaxel exemplifying the ability of the clinically validated DEP® platform to enhance delivery of cytotoxic payloads, and preclinical data in radiotheranostics.

Starpharma's dendrimers have the potential to offer a range of benefits in the delivery of targeted radiotheranostics compared with typical small molecule or large antibody approaches to delivery, most notably the ability to tailor the dendrimer physicochemical characteristics to achieve benefits including:

- Enhanced tumour penetration and retention,
- Tuneable solubility and pharmacokinetics, and
- Tuneable plasma and kidney clearance.

The dendrimer platform provides the flexibility to use a range of different targeting moieties, including bi- and multi-specific options, and can achieve multivalent targeting and payload presentation.

These advantages, combined with the broad applicability of Starpharma's DEP® platform across a range of therapeutic areas in drug development, are considered highly desirable characteristics for potential commercial partners and collaborators. The Targeted Radiopharmaceuticals Summit provides a unique opportunity for Starpharma to promote the potential benefits of its dendrimer technology to potential partners and collaborators.

Starpharma sees an opportunity to improve patient outcomes by applying its DEP® dendrimer technology in the development of optimised radiotheranostics and is advancing its preclinical pipeline of DEP® radiopharmaceuticals assets.

The Targeted Radiopharmaceuticals Summit presentation, **DEP® Dendrimers – a Platform for Novel Targeting Moieties and Payloads for Enhanced Radioisotope Specificity, Efficacy and Safety**, is appended.

About Starpharma

Starpharma ASX: SPL, OTCQX: 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.

DEP® Dendrimers – a Platform for Novel Targeting Moieties and Payloads for Enhanced Radioisotope Specificity, Efficacy and Safety

Dr Jeremy Paull, PhD

VP, Development and Regulatory Affairs

6th Annual TRP TARGETED RADIOPHARMACEUTICALS SUMMIT EUROPE

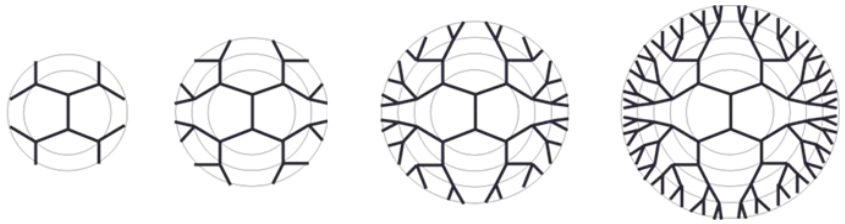
Workshop B

3 December 2024

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 provide 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.

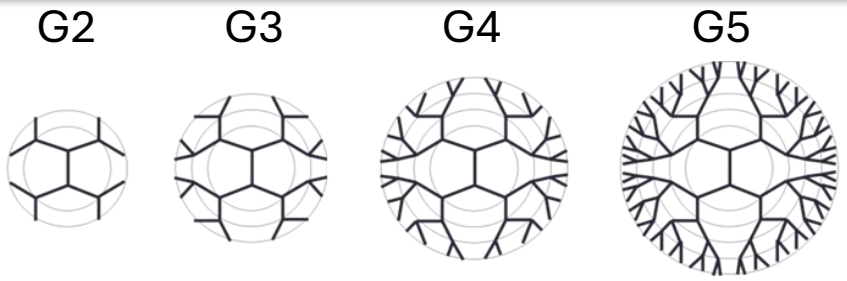
Strong intellectual property position
19 active patent families with over 150 granted and pending patents.

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

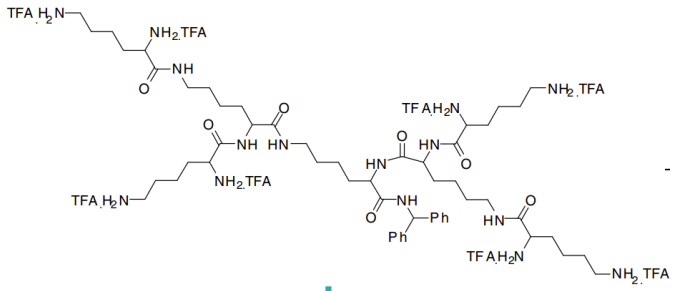
Improves drug performance

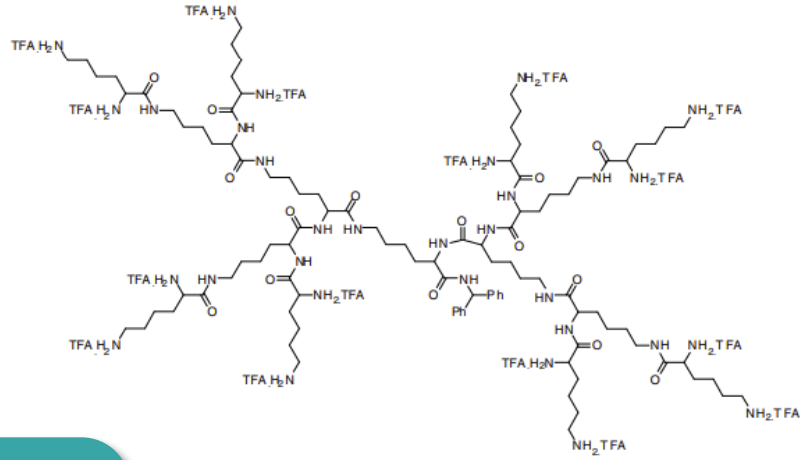
- Ability to design a dendrimer-drug conjugate to optimise both rate and site of payload release and clearance route
- Delivers up to 40-70x more drug in tumour vs. blood

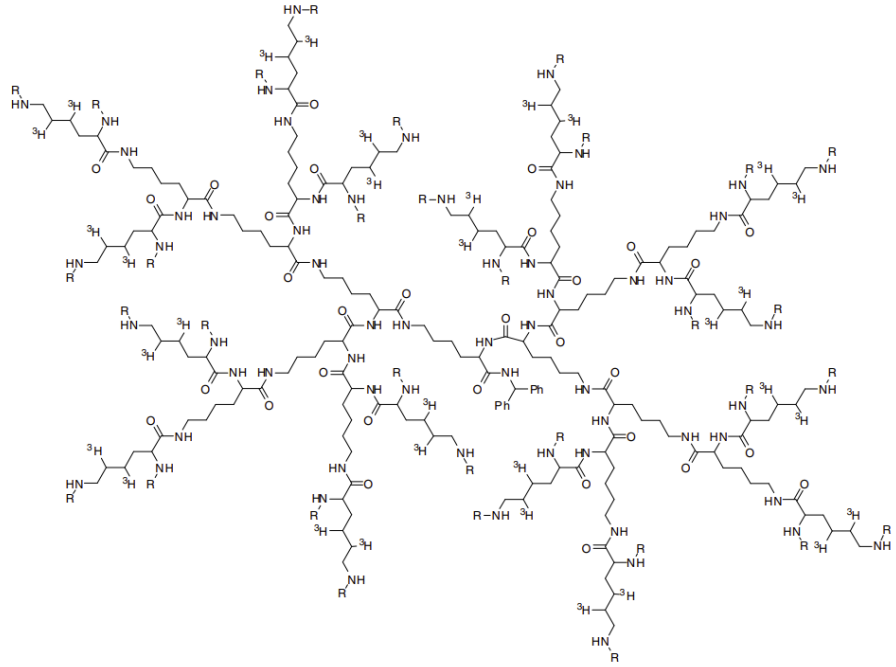
Broad applicability

- 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







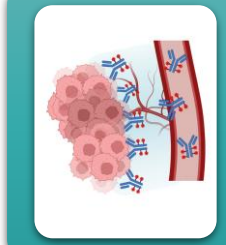
- Low polydispersity, near monomodal MW distributions
- Characterisation via standard methodologies, e.g., NMR, LCMS, HPLC, UPLC, SEC etc.

- 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.

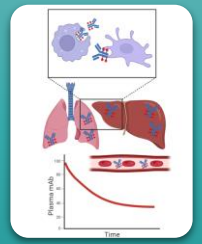
Why Dendrimers? Opportunities to Solve Complex Challenges Facing Traditional Small or Large Molecule Drug Conjugates

Large Molecules (e.g., mAb)



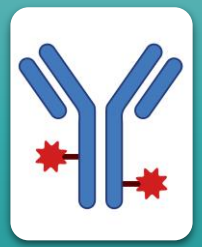
Efficacy Challenges

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



Toxicity / PK

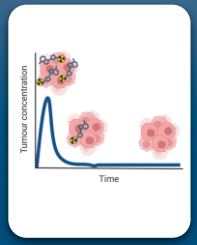
- On-target, off-tumour
- Off-target
- Antigen-independent toxicity
- Long half-life, circulation times



Chemistry

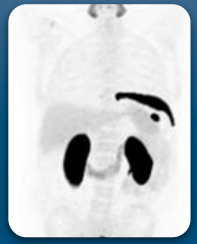
- Heterogeneous DAR, site-specific
- Solubility of lipophilic payloads
- Aggregation
- Manufacturing and scalability

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

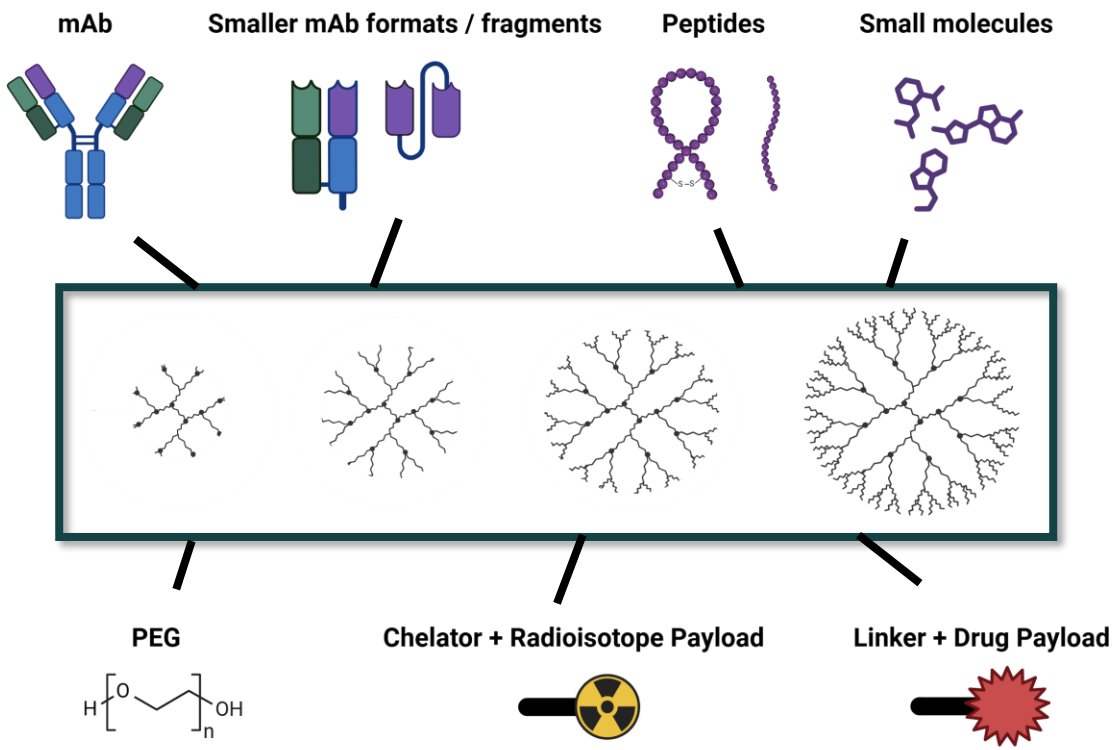
Chemistry

- 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



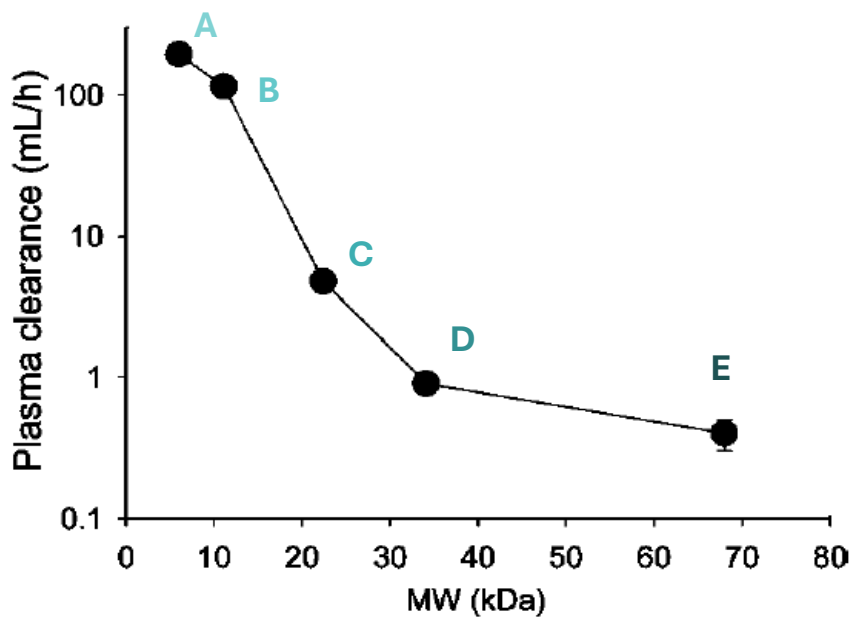
- Potential for improved tumour penetration and retention
- Tuneable solubility, PK
- Tuneable plasma / kidney clearance
- Range of targeting moieties (bi-/multi-specific)
- Multivalent targeting / payload presentation, linker selection
- Site-specific payload attachment, precise and reproducible DAR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

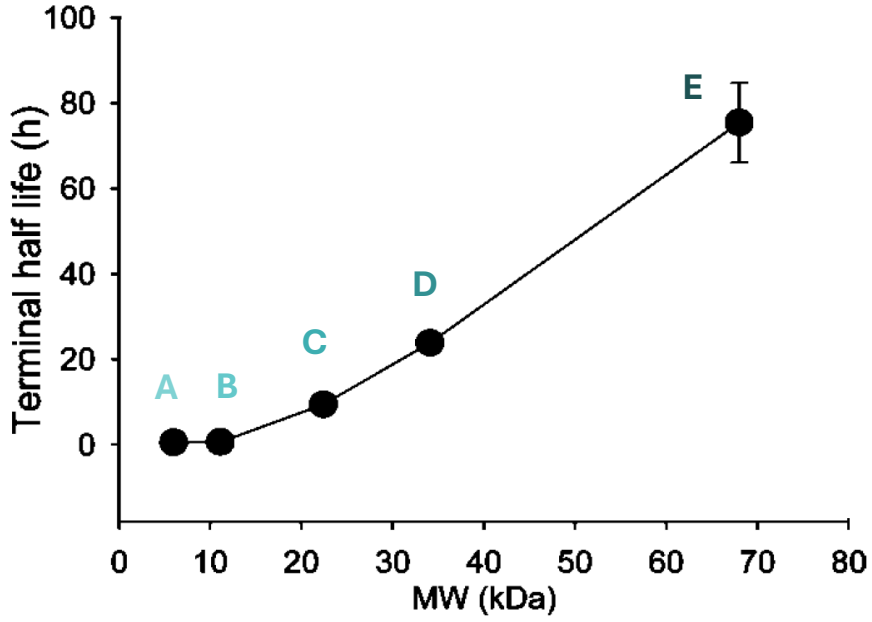
Images created in https://BioRender.com

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]



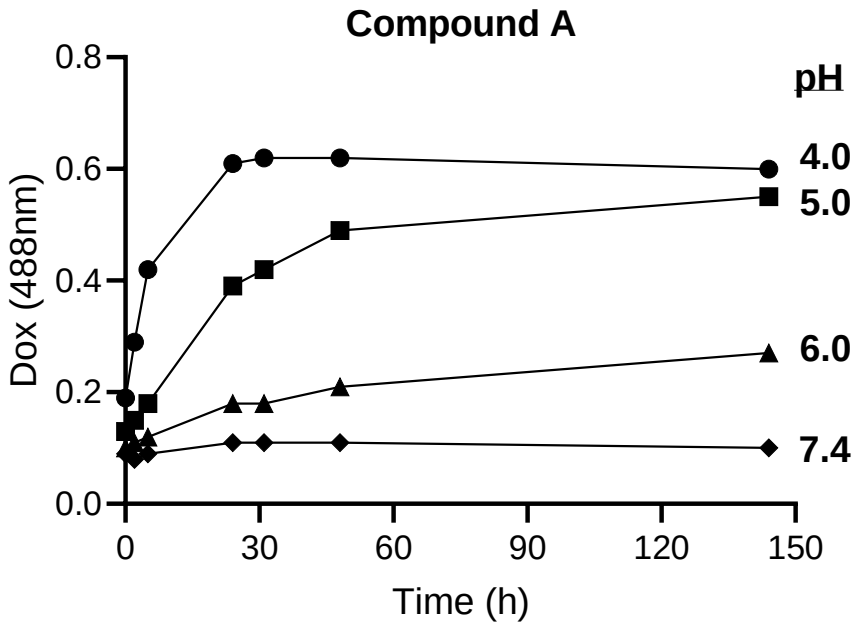


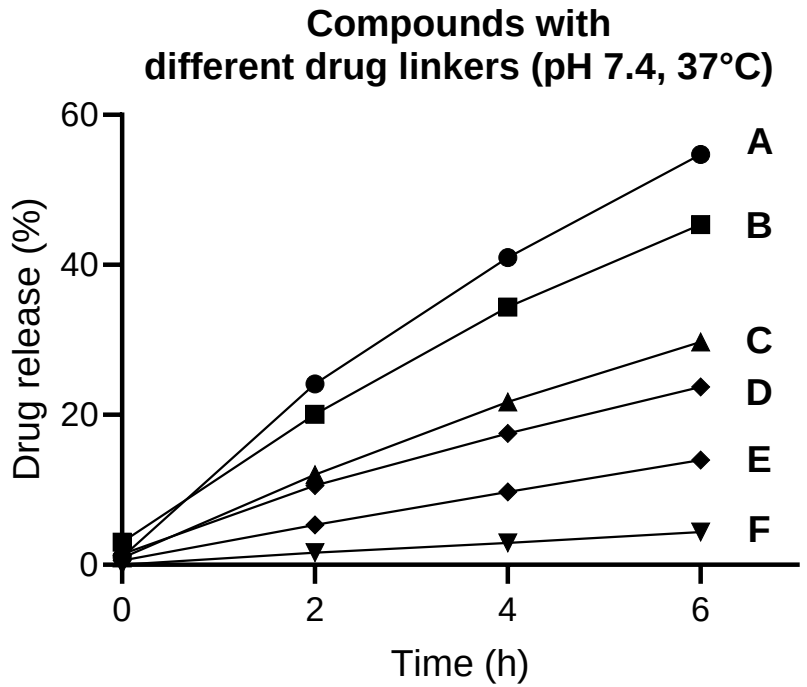
A DEP1 (PEG200)
B DEP2 (PEG200)
C DEP3 (PEG570)
D DEP4 (PEG2000)
E DEP5 (PEG2000)

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



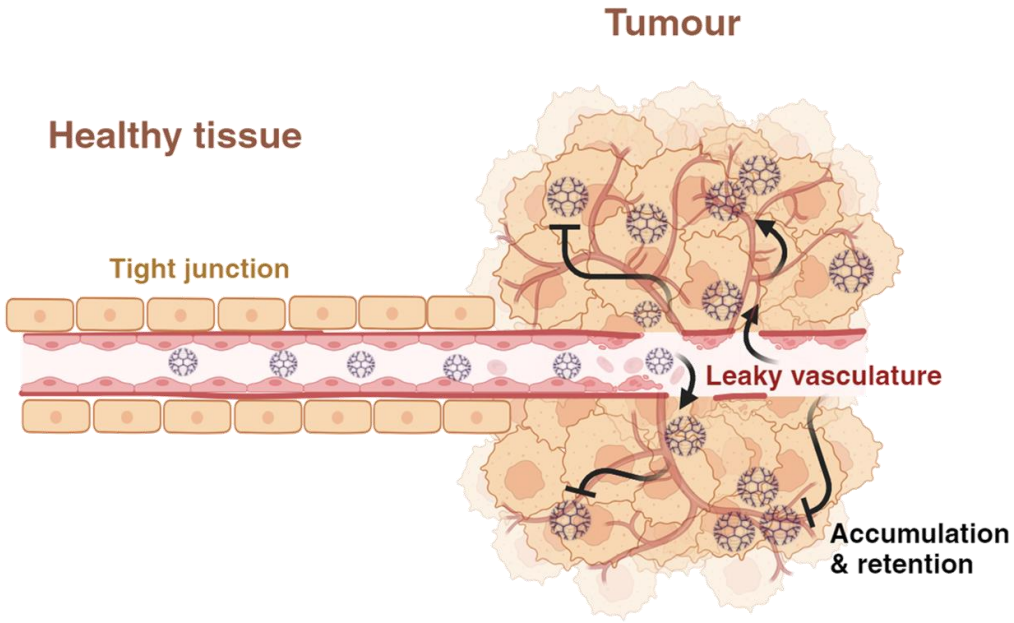


1. Kaminskas *et al.* Molecular Pharmaceutics 2008, 5(3), 449-463

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 the tumour due to leaky vasculature and poor lymphatic drainage
- → DEP® dendrimer size can be optimized to maximize the EPR effect
- → **e.g., DEP® SN38 and DEP® Cabazitaxel**



Biological targeting with wide range of targeting moieties

- → Large: mAb
- → Small: small molecules, peptides, small mAb fragments
- → Targeting molecules bound to the DEP® dendrimer surface
- → Monospecific, multi-valent and multi-specific targeting
- → **e.g., DEP® HER2-targeted radiotheranostic**

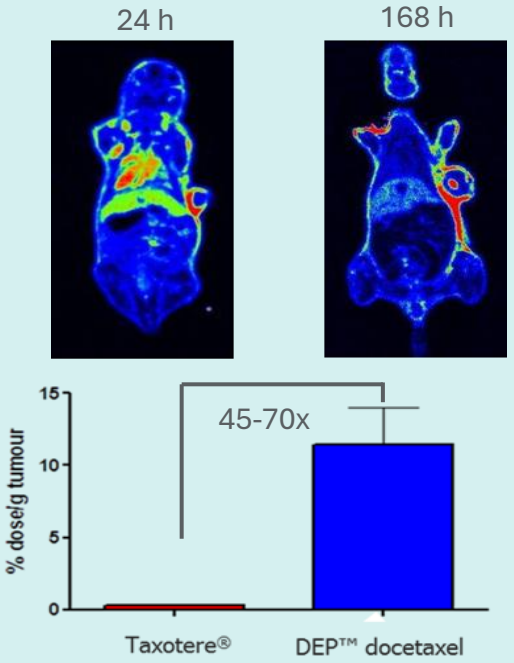
Physical Targeting	Biological Targeting
Exploits EPR effect	Uses specific tumour markers
Depends on tumour vasculature	Independent of EPR variability
No functionalisation needed	Requires ligand conjugation
DEP® dendrimers can combine both targeting mechanisms and thus, maximize therapeutic efficiency	

Images created in https://BioRender.com

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

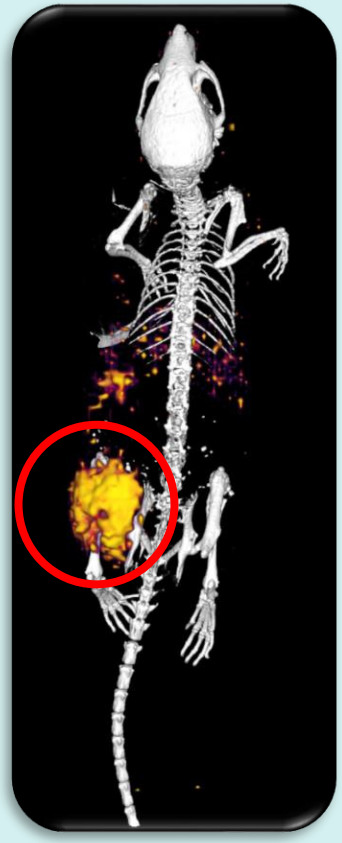
Tumour accumulation in human xenograft tumour models with "physically" targeted DEP® agents…

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

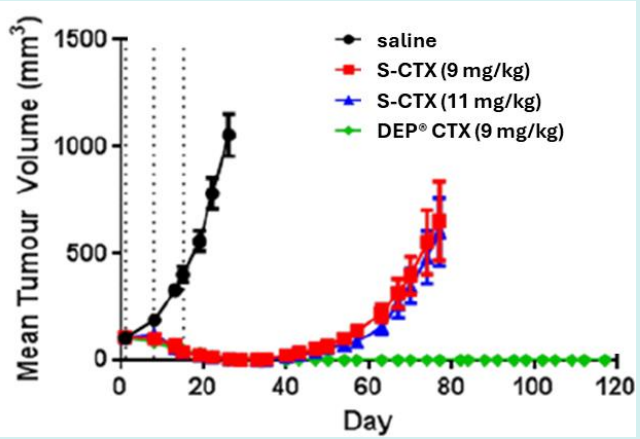


Radiolabelled DEP® dendrimer-drug conjugate accumulates in tumour via enhanced permeability and retention (EPR) effect

(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



Benefits of Starpharma's DEP® Platform Technology Demonstrated in the Clinic - Pipeline

Starpharma Internal DEP® Pipeline

Product	Target indication	Research	Pre-clinical	Phase I	Phase II	Phase III	Strategy
DEP® SN38	Ovarian and colorectal	*Phase II results reported*					License/co-develop – ovarian, colorectal
DEP® cabazitaxel	Prostate and gastro-oesophageal	*Phase II results reported*					License – prostate, ovarian
DEP® HER2 radiodiagnostic	Diagnostic						Optimise and accelerate to clinical
DEP® HER2 radiotherapeutic	Solid cancers						Advance to clinical
DEP® HER2 ADC	Solid cancers						Advance to preclinical
DEP® docetaxel	Pancreatic and other cancers	*Phase II results reported*					Lower priority

Partnered DEP® Programs

Genentech
A Member of the Roche Group

MSD

medicxi

DEP® Dendrimer Products on Market

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

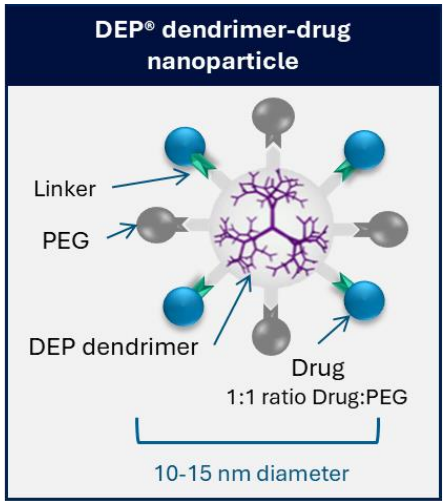
- Aqueous, detergent-free formulation; no steroid pre-treatment; improved tolerability; prolonged retention in tumour interstitium, improved efficacy

DEP® SN38

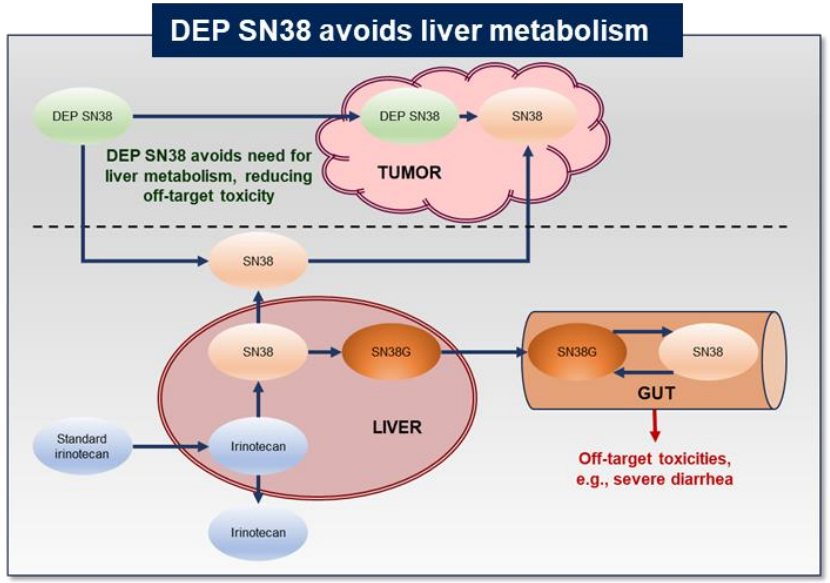
- Novel dendrimer-topoisomerase I (TOP1) conjugate of SN38, active metabolite of irinotecan (Camptosar®), which had peak sales of US$1.1B despite multiple US FDA "Black Box" warnings

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**

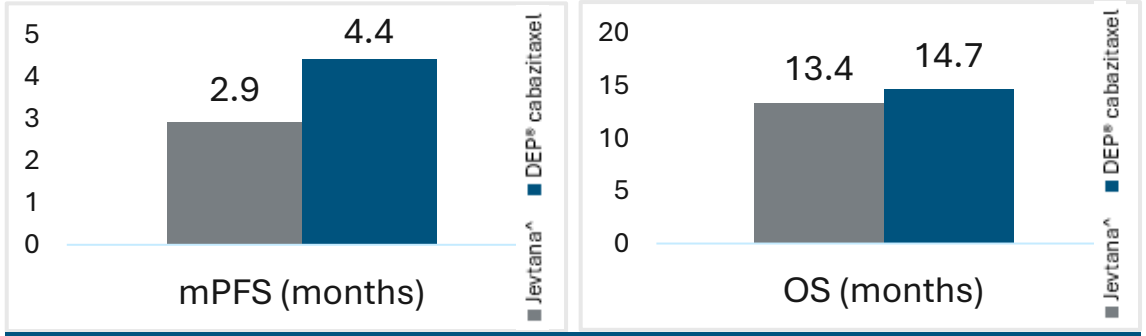


DEP® Cabazitaxel Achieves Highly Encouraging Efficacy in Late-Stage Patients, Compared to Standard Therapies

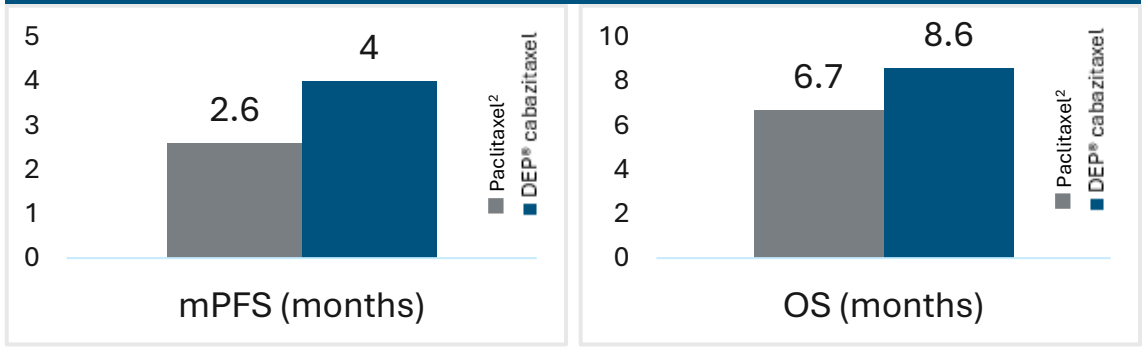
Results Presented at the 2024 ASCO Annual Meeting

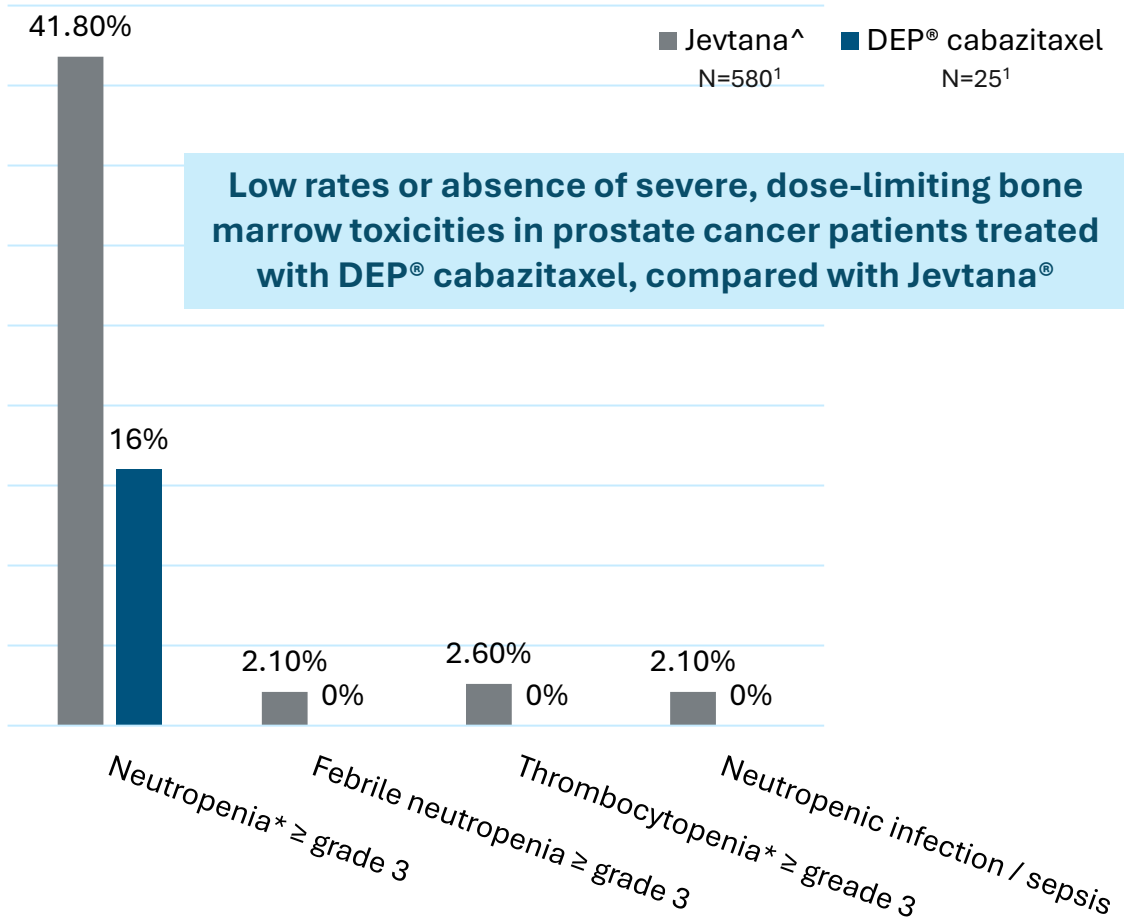
2024 ASCO ANNUAL MEETING

DEP® Cabazitaxel in Advanced Prostate Cancer



DEP® Cabazitaxel in Advanced Gastro-Oesophageal Cancers





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

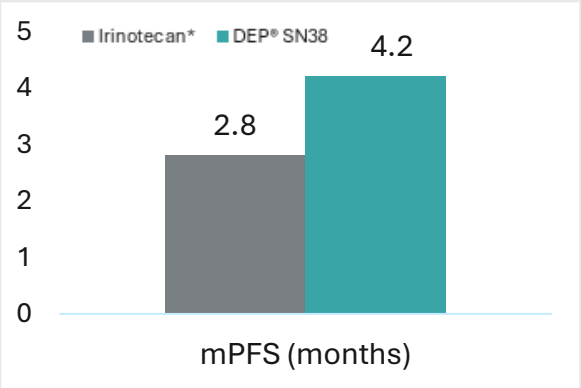
Full Phase II results reported in ASX Announcement dated 18 October 2023;
*Lab detected neutropenia or thrombocytopenia, regardless of whether event was reported as an adverse event; [1] Safety Population (received at least 1 dose); ^ Eisenberger, M, et al., *J Clin Oncol,* 2017; 35(28):3198-206; [2]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

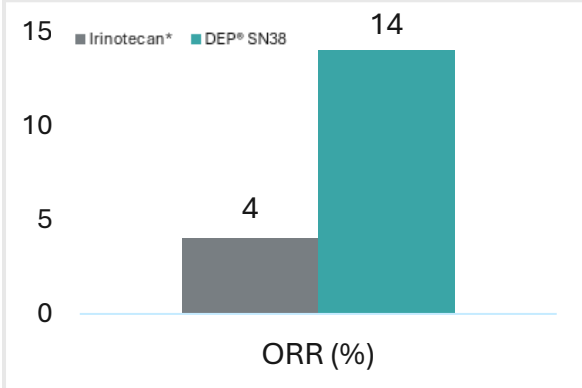
DEP® SN38 Phase II Study Shows Favourable Efficacy and Tolerability Data in Late-Stage Patients

Results Presented at the 2024 ASCO Annual Meeting

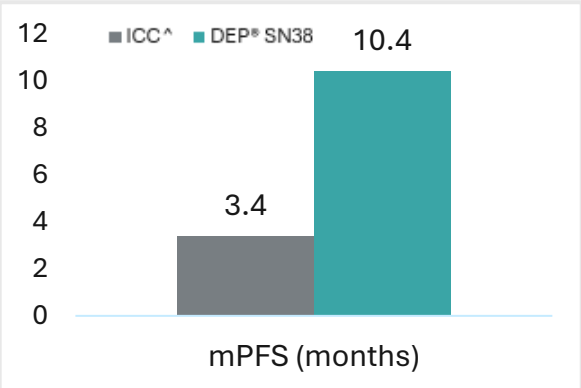
2024 ASCO ANNUAL MEETING

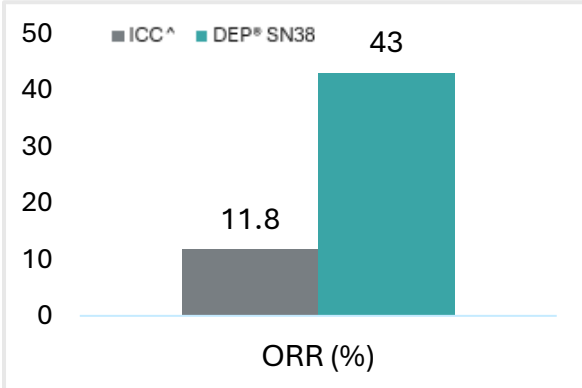
Advanced Colorectal Cancer



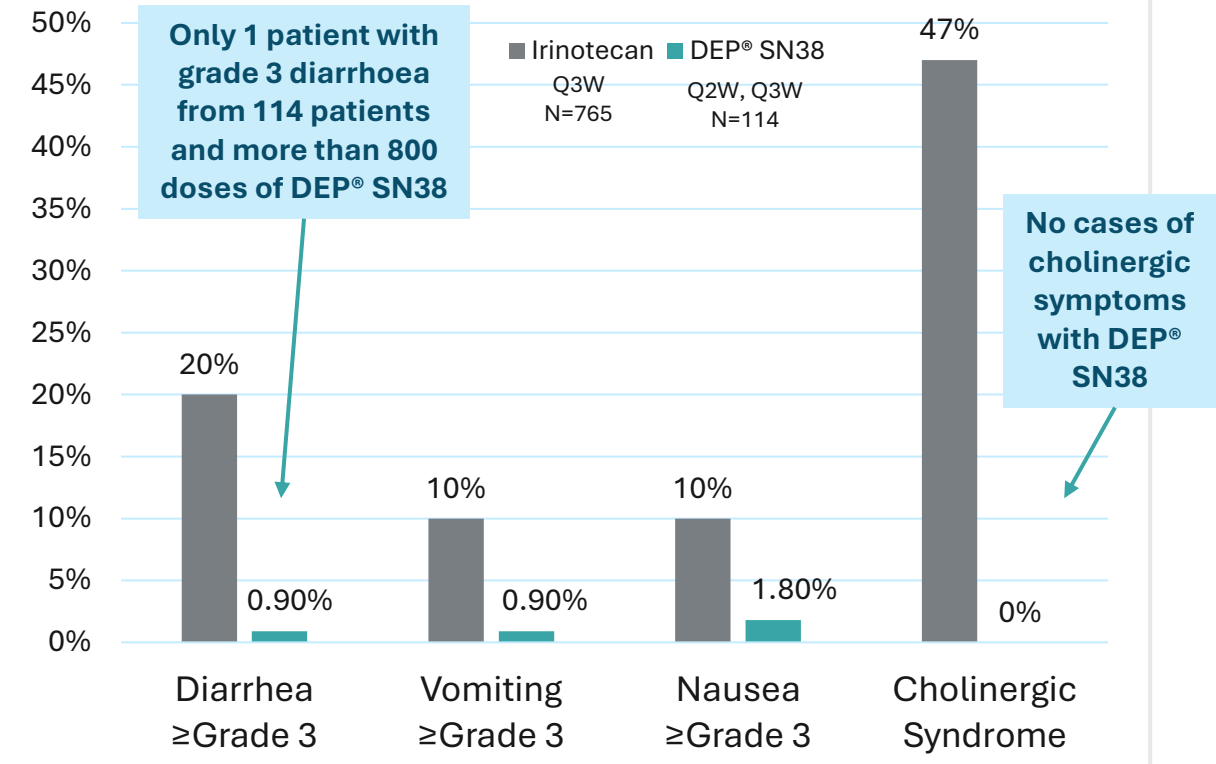


Advanced Platinum-Resistant Ovarian Cancer





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

Benefits of Starpharma's DEP® Platform Technology Extend to Radiopharmaceuticals - Pipeline

Starpharma Internal DEP® Pipeline							
Product	**Target indication**	**Research**	**Pre-clinical**	**Phase I**	**Phase II**	**Phase III**	**Strategy**
DEP® SN38	Ovarian and colorectal	*Phase II results reported*					License/co-develop – ovarian, colorectal
DEP® cabazitaxel	Prostate and gastro-oesophageal	*Phase II results reported*					License – prostate, ovarian
DEP® HER2 radiodiagnostic	Diagnostic						Optimise and accelerate to clinical
DEP® HER2 radiotherapeutic	Solid cancers						Advance to clinical
DEP® HER2 ADC	Solid cancers						Advance to preclinical
DEP® docetaxel	Pancreatic and other cancers	*Phase II results reported*					Lower priority

Partnered DEP® Programs

Genentech
A Member of the Roche Group

MSD

medicxi

DEP® Dendrimer Products on Market

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 therapeutic to address these needs**

HER2 Status, Imaging and Therapy

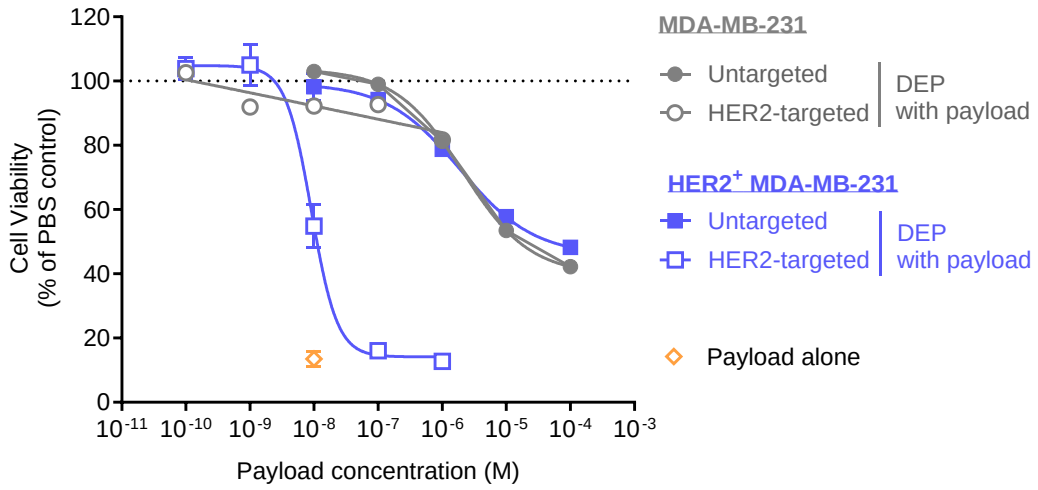
- **Decisions on HER2-targeted therapy may benefit from an accurate assessment of whole body HER2 status**
  - HER2-targeted therapies like Enhertu provide significant benefit to metastatic $HER2^{+}$ patients
  - Now expanding to include $HER2^{low}$ and $HER2^{ultra\ low}$ patient populations
  - HER2 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

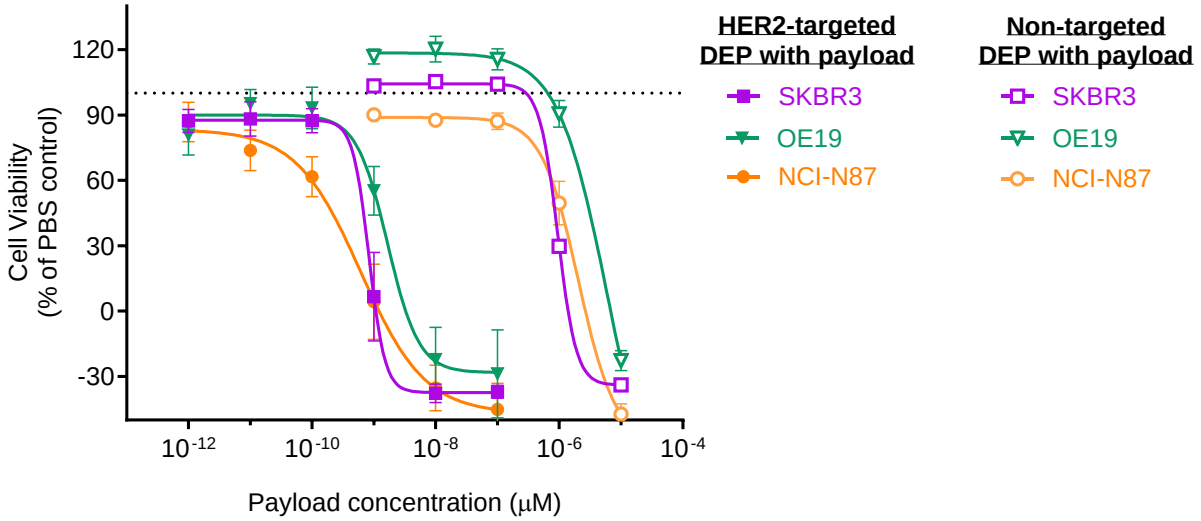
- **Starpharma is developing a DEP® HER2-targeted dendrimer-radio-diagnostic and therapeutic to address these needs**

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)

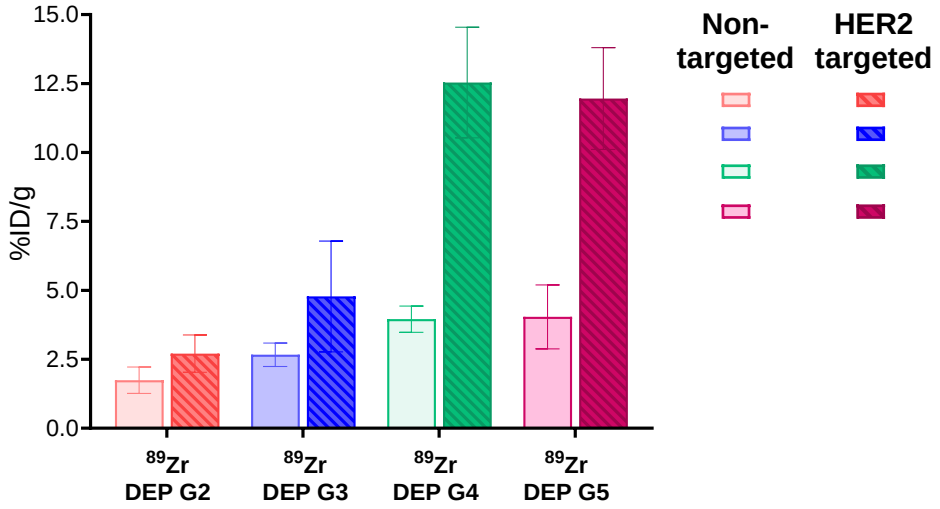


Assessed after 48h

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

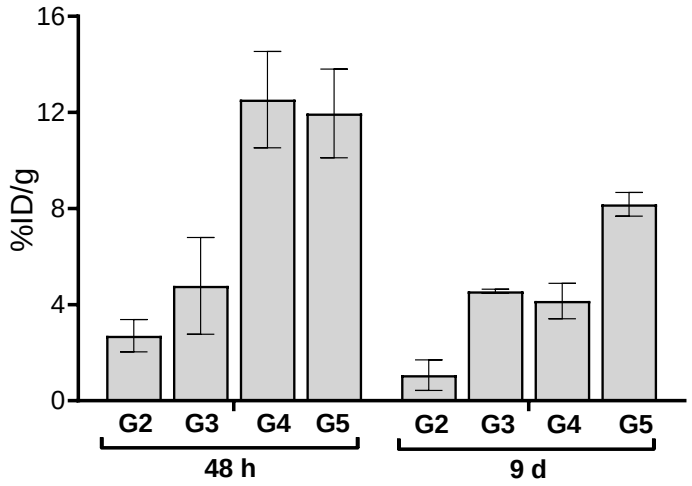
HER2⁺ BT474 tumours

48h



HER2 specificity vs dendrimer generation

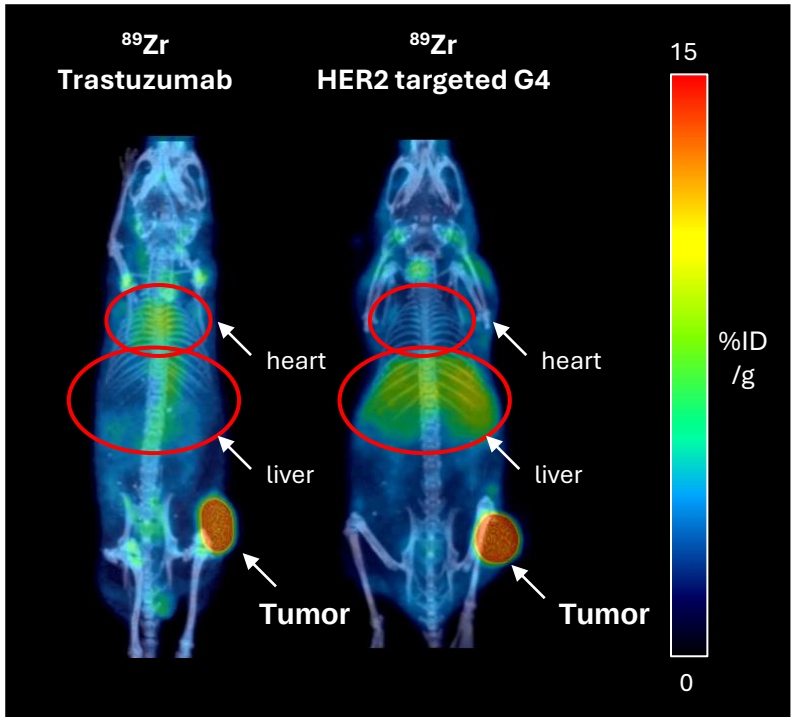
^{89}Zr HER2-targeted dendrimers



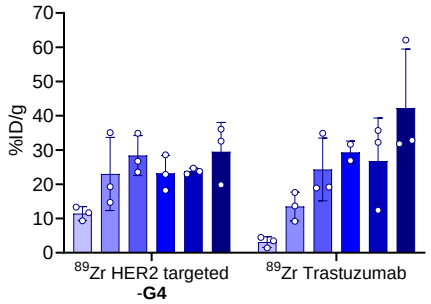
Increased and prolonged tumour accumulation

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

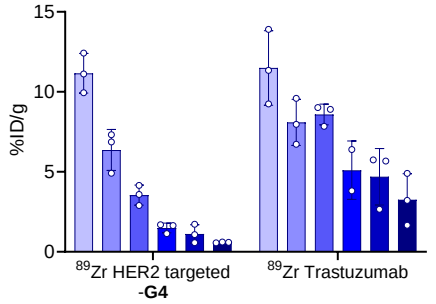
48h PET/CT - HER2⁺ BT474 tumour model



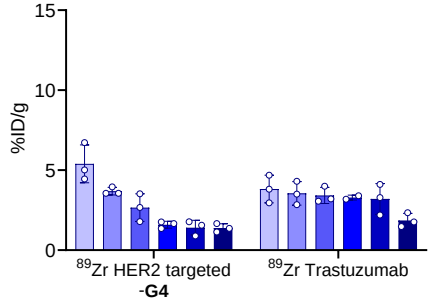
Tumour

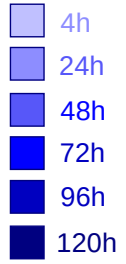


Blood



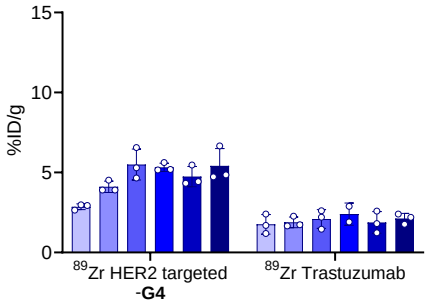
Lungs



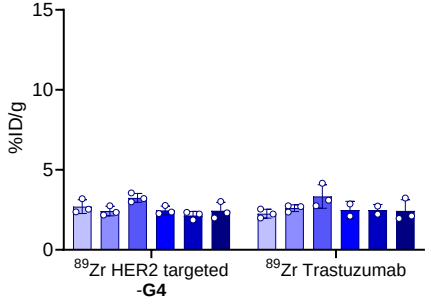


High + sustained tumour uptake out to 5d with HER2-targeted G4 dendrimer

Liver



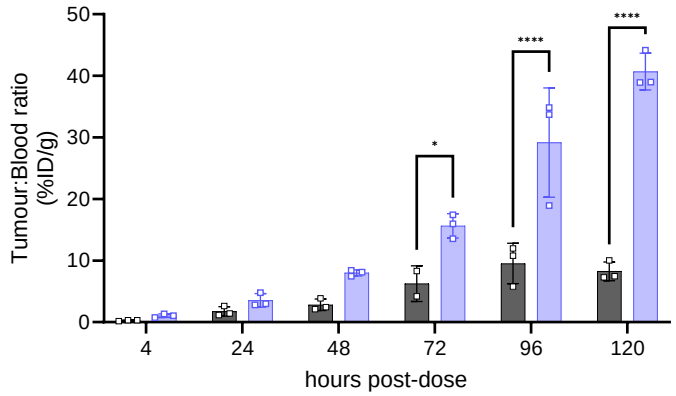
Kidneys



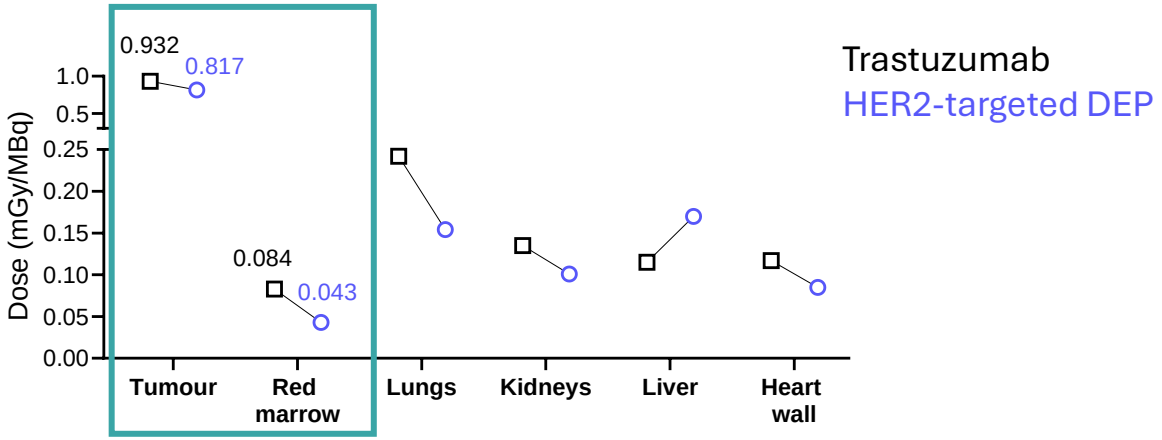
Ex vivo biodistribution in BT474-tumour bearing mice, each symbol = individual mouse

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

Tumour : blood ratio



Dosimetry: Absorbed doses



Consideration for radiotherapeutic:

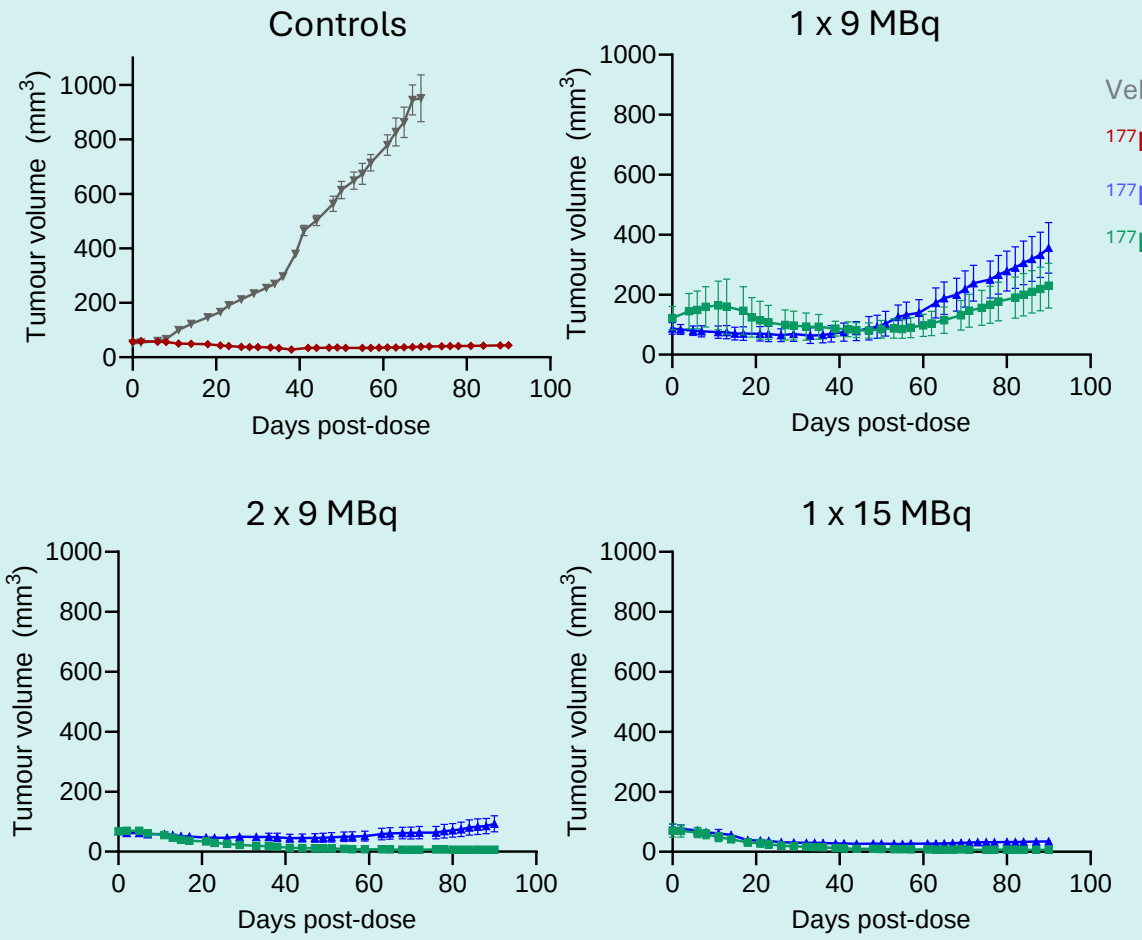
- Lower tumour : blood ratio with Trastuzumab
  → Higher adsorbed dose to bone marrow = dose-limiting organ (2Gy)
- When considering bone marrow dose limitations, HER2-targeted DEP® can be delivered at a higher dose, effectively achieving **~1.7-fold higher dose** to tumour vs. Trastuzumab

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.

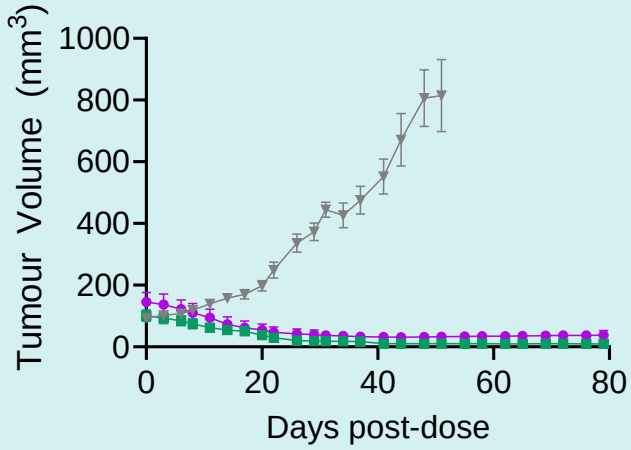
Delivered dose estimates assume DEP® HER2-zirconium and Trastuzumab have been labelled with ^{177}Lu

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



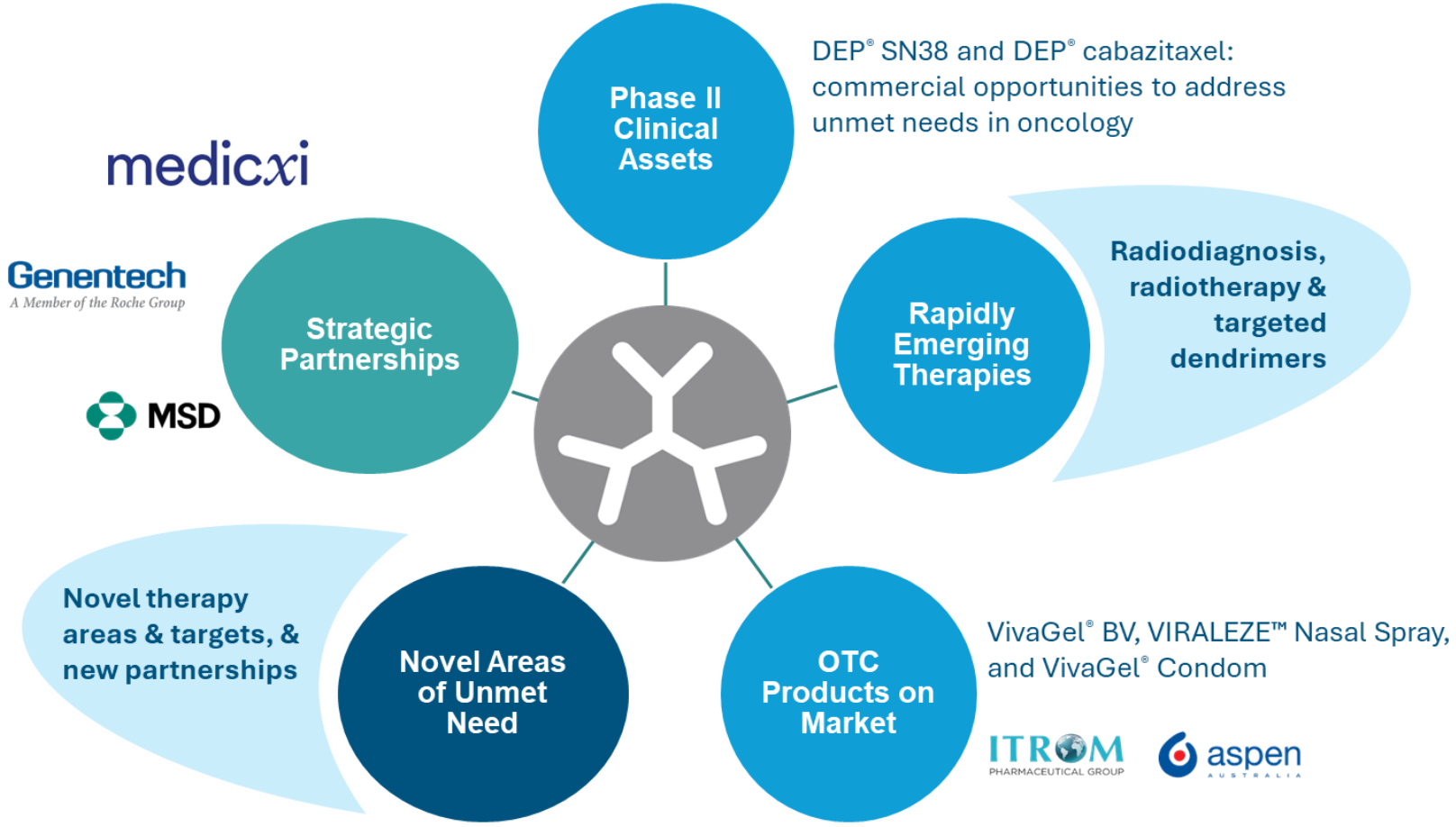
n=3-4 mice/group



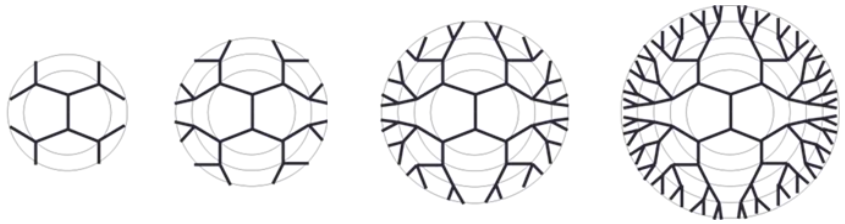
n=8 mice/group

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

Multiple Opportunities; Multiple Partnerships



Summary



- **DEP® dendrimers provide 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

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