

Starpharma to present DEP® at Radiopharmaceuticals Summit

Melbourne, Australia; 6 December 2023: Starpharma (ASX: SPL, OTCQX: SPHRY) today announces it is presenting at the Targeted Radiopharmaceuticals Summit Europe, having been invited to present at the specialist radiotheranostics conference being held in Berlin, Germany, from 5 to 7 December 2023.

The Targeted Radiopharmaceuticals Summit also includes speakers from Novartis, Bayer, Bicycle Therapeutics, AstraZeneca, Bristol-Myers Squibb, Precirix, Telix, and Fusion Pharmaceuticals. The Summit brings together professionals to provide insights into the research, development, and commercialisation of radiopharmaceuticals, including novel targets and combination therapies.

Starpharma's Vice President of Development and Regulatory Affairs, Dr Jeremy Paull, will deliver a presentation on the application of Starpharma's DEP® platform for precision cancer radiotheranostics, including:

- the application, versatility, and benefits of the DEP® platform for targeted delivery of radiotheranostics; and
- an overview of Starpharma's two DEP® HER2-targeted radiotheranostic products, DEP® HER2-zirconium and DEP® HER2-lutetium.

Starpharma recently reported data on DEP® HER2-zirconium, a HER2-targeted radiodiagnostic candidate, demonstrating excellent tumour accumulation, a favourable biodistribution profile, with excellent imaging contrast between tumour and normal tissues, as well as rapid uptake in a HER+ breast cancer model. Starpharma's radiotherapeutic product, DEP® HER2-lutetium, has shown excellent anticancer activity, outperforming Herceptin® labelled with lutetium, in a human breast cancer model. These products are designed to assist in improving the diagnosis, staging, monitoring, and treatment of HER2+ cancers, which include breast and upper gastro-intestinal cancers. The data reported in the presentation have been generated from studies conducted in collaboration with the Monash Institute of Pharmaceutical Sciences (MIPS) and the University of Queensland.

The conference presentation, '*Branching Out: DEP® Dendrimer Nanoparticles as a Versatile Platform for Precision Cancer Radiotheranostics*', will take place on 6 December 2023 in Berlin as part of the Novel Targets stream.

A copy of the presentation is appended.



About Starpharma

Starpharma Holdings Limited (ASX: SPL, OTCQX: SPHRY) is a world leader in dendrimer technology for medical applications. As an innovative Australian biopharmaceutical company, Starpharma is focused on developing and commercialising novel therapeutic products that address significant global healthcare needs. Starpharma boasts a strong portfolio of products, partnerships, and intellectual property.

Starpharma's innovative technology is based on proprietary polymers called dendrimers, which are precise, synthetically manufactured, nanoscale molecules. The unique properties of dendrimers – including their size, structure, high degree of branching, polyvalency, and water solubility – are advantageous in medical and pharmaceutical applications.

Starpharma uses its dendrimer technology to develop novel therapeutics and to improve the performance of existing pharmaceuticals. Starpharma's portfolio includes multiple clinical-stage oncology products, which utilise its Dendrimer Enhanced Product ("DEP[®]") drug delivery technology, and marketed products, including VIRALEZE™ and VivaGel[®] BV, which utilise SPL7013, a proprietary dendrimer with antimicrobial properties.

Starpharma's DEP[®] drug delivery platform is being used to enhance the effectiveness of existing and novel therapies and to reduce drug-related toxicities through controlled and specified drug delivery.

In addition to Starpharma's internal DEP[®] programs, Starpharma has multiple DEP[®] partnerships with international biopharmaceutical companies, including AstraZeneca (oncology), MSD (Antibody-Drug Conjugates), Chase Sun (anti-infectives), and other world-leading pharmaceutical companies. Due to the broad applicability and optionality of Starpharma's DEP[®] platform, partnered DEP[®] programs have the potential to generate significant future milestones and royalties.

Starpharma's topical antiviral nasal spray, VIRALEZE™, is now registered in more than 35 countries*, including Europe, the UK, and Asia. Starpharma's novel non-antibiotic vaginal gel, VivaGel[®] BV, for the treatment of bacterial vaginosis (BV) and prevention of recurrent BV, is registered in more than 50 countries, including in the UK, Europe, Southeast Asia, South Africa, Australia and New Zealand.

For more information about Starpharma, visit www.starpharma.com or connect with Starpharma on [LinkedIn](https://www.linkedin.com/company/starpharma).

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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", "outlook", 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.

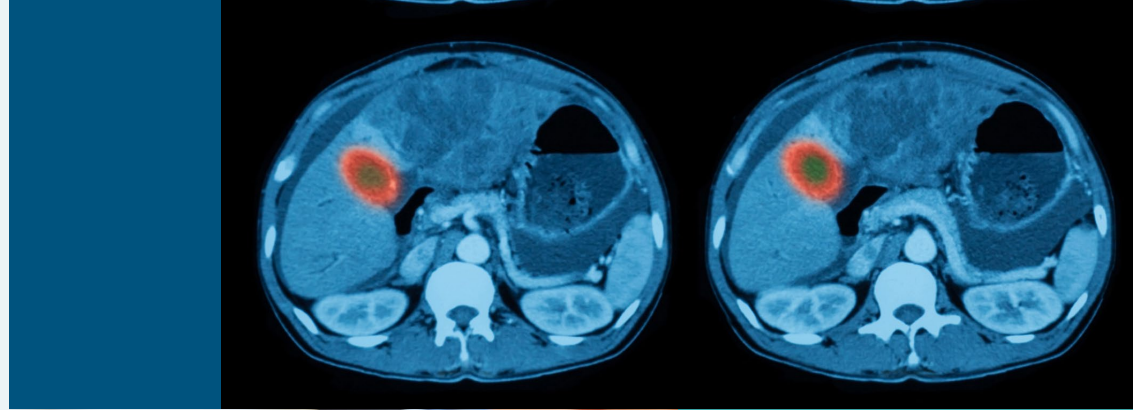


Branching Out: DEP[®] Dendrimer Nanoparticles as a Versatile Platform for Precision Cancer Radiotheranostics

Jeremy Paull, PhD
VP, Development and Regulatory Affairs

5th Annual Targeted Radiopharmaceuticals Summit Europe

6 December 2023



TARGETED
RADIOPHARMACEUTICALS
SUMMIT EUROPE

Important notice and disclaimer

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DEP[®] Dendrimers: A Versatile, Multifunctional Delivery Platform for Precision Cancer Radiotheranostics

KEY MESSAGES

- ❑ Proprietary DEP[®] platform – **clinically validated** via 4 clinical programs, multiple drug classes
- ❑ Starpharma's are the only **marketed** dendrimer-based products
- ❑ DEP[®] platform:
 - ✓ provides **flexibility** for a **wide range of payloads and chelating agents**
 - ✓ can achieve **preferential delivery** to tumours by virtue of size
 - ✓ can also be **functionalised** to carry a **wide range of targeting moieties**
 - ✓ provides **flexibility** for **customisation of biodistribution / excretion profile**
- ❑ Targeted DEP[®] can achieve **improved biodistribution and efficacy** profiles vs antibody targeting



DEP[®] DENDRIMERS: A VERSATILE, MULTIFUNCTIONAL PLATFORM FOR CUSTOMISATION OF PRECISION RADIOTHERANOSTICS FOR CANCER IMAGING AND THERAPEUTIC APPLICATIONS

Starpharma is an innovative biopharmaceutical company and leader in dendrimer technology



Innovative drug / multifunctional delivery platform, DEP®

Proprietary nanoparticle platform; ability to create innovative therapies and enhance existing drugs; significant optionality; accelerates path to market; and manages investment risk.

Deep portfolio of high-value assets

Three promising internal clinical-stage assets are under development: improved, patented versions of widely used cancer medications and a strong pipeline of preclinical-stage assets, including radiotheranostics.

Multiple products on market.

Multiple global pharma partnerships

DEP® partnerships with three of the world's top 10 pharmaceutical companies: MSD, Genentech and AstraZeneca. Starpharma generates returns via research fees, milestones and royalties. Funded by large pharma partners. DEP® platform offers the ability to partner widely without Starpharma funding programs.

Strong financial position

Strong balance sheet and runway with \$35.6 million cash at 30 September 2023, excluding the \$7.2 M R&D tax incentive refund received in October 2023.

Strong international institutional share register

Institutions include Allianz, UIL/ICM, Allan Gray, M&G, and Fidelity.



Starpharma's portfolio: multiple dendrimer-based clinical-stage assets, partnerships and products in market



DEP® Pipeline

Product	Target indication	Preclinical	Phase 1	Phase 2
DEP® cabazitaxel	Prostate and other cancers	Phase 2 complete & results reported		
DEP® irinotecan	Colorectal and other cancers	Phase 2 recruitment complete		
DEP® docetaxel	Pancreatic and other cancers	Phase 2 recruitment complete		
DEP® HER2 ADC	Solid cancers	▶		
DEP® HER2 radiotherapy	Solid cancers	▶		
DEP® HER2 radiodiagnostic	Diagnostic	▶		
Partnerships	Various	▶		



Partnered DEP® Programs

<p>Two DEP® ADC Research Agreements with MSD (Merck & Co., Inc.)</p>	<p>Two DEP® Research Agreements with Genentech</p>
<p>DEP® anti-infective research partnership with Chase Sun</p>	<p>Multi-product DEP® licence with AstraZeneca</p>

Commercialised Products

VIRALEZE™ Antiviral Nasal Spray



VivaGel® BV



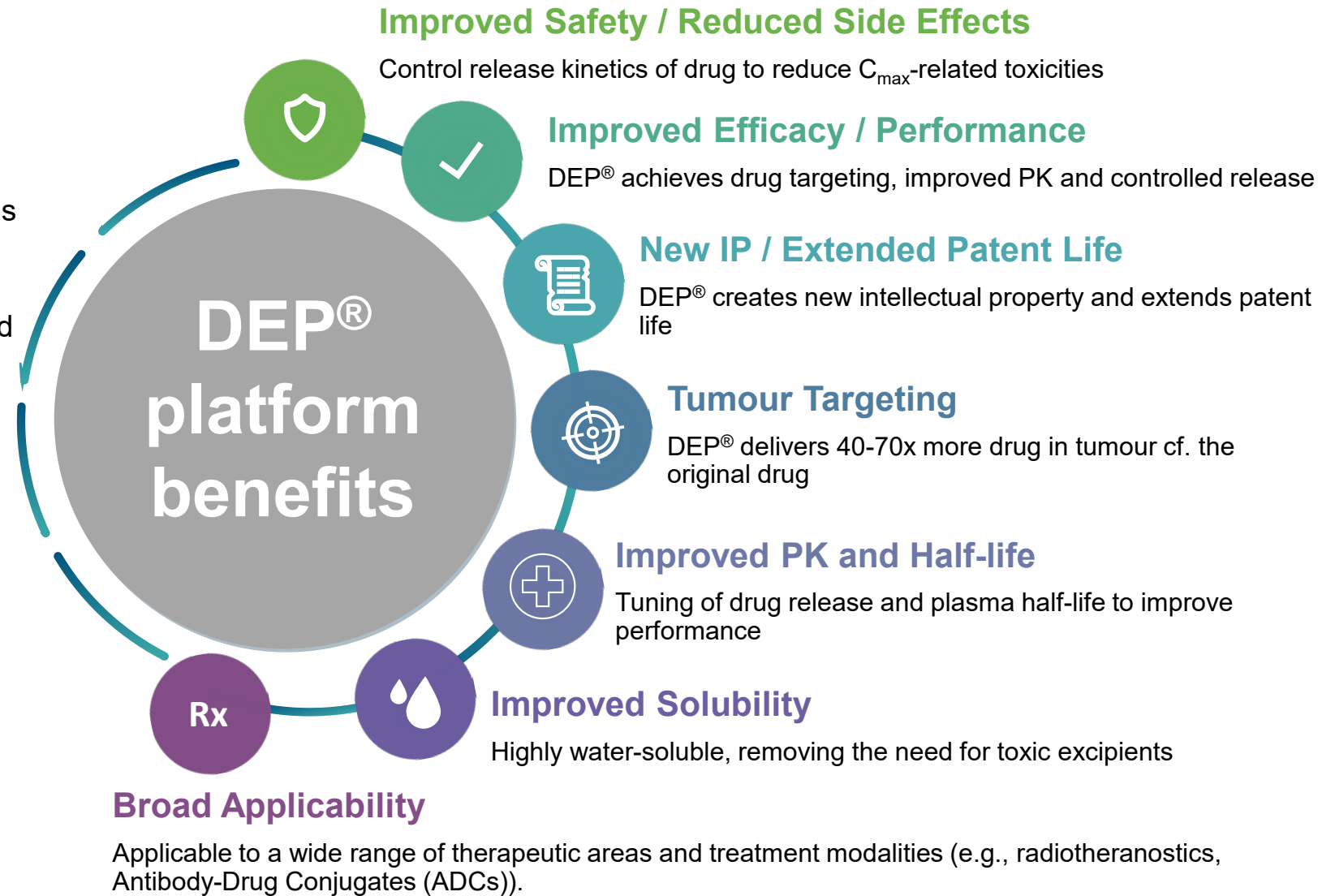
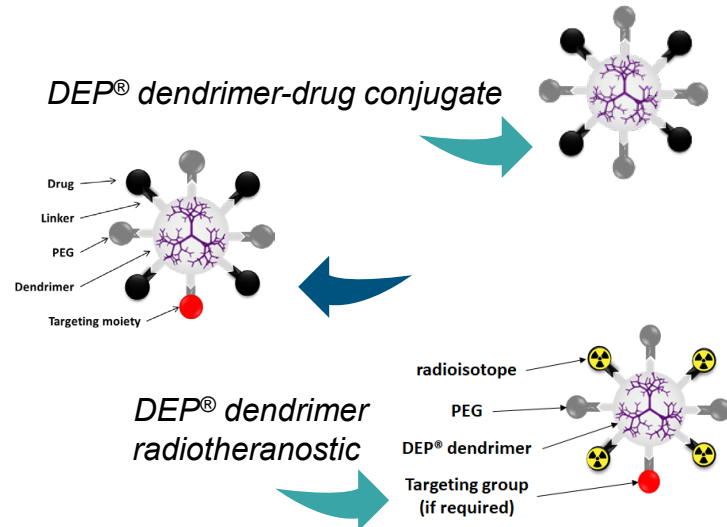
VivaGel® Condom



Starpharma's DEP[®] platform: highly versatile, enhancing the commercial and therapeutic value of a wide range of drugs

DEP[®] technology:

- Based on proprietary, branched polymers called dendrimers
- A platform with significant optionality – applicable to many different drugs / payloads
- Optimises drug properties and enables targeted therapy, creating differentiated products, managing a product's lifecycle and creating new intellectual property.



DEP[®] partnering creates significant commercial value and optionality

Benefits of DEP[®] partnerships

- Funded by partners
- Leverage existing and create new intellectual property
- Broaden the applications of DEP[®], creating multiple potential revenue streams
- DEP[®] platform offers significant optionality and leverage, enabling multiple licenses to run in parallel without Starpharma funding programs



Two DEP[®] ADC Research Agreements with MSD 

Two DEP[®] Research Agreements with Genentech 
A Member of the Roche Group

DEP[®] anti-infective research partnership with Chase Sun 
红日药业集团
CHASE SUN

Multiproduct DEP[®] licence and Option agreement with AstraZeneca 

Starpharma's DEP[®] platform enhances the commercial and therapeutic value of a wide range of drugs, creating multiple potential revenue streams and significant IP leverage

Starpharma's DEP[®] platform has broad applicability, creating multiple high-value commercial applications



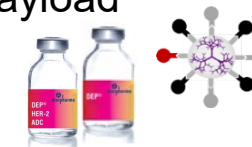
Chemotherapeutics

- Franchise extension
- Generic differentiation
- New chemical entities
- Combinations including immuno-oncology



Antibody-Drug Conjugates

- Flexible technology
- Increased drug antibody ratio
- Targeting group agnostic
- Site selective payload attachment

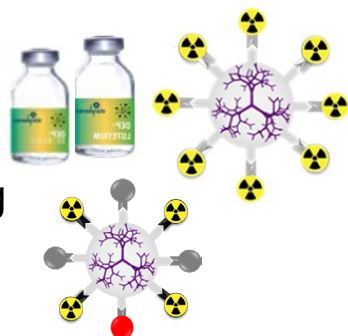


The DEP[®] platform can provide therapeutic and commercial value across a wide range of therapeutic areas and treatment modalities.



Radiotheranostics

- Radiotheranostic applications
- Can use a variety of isotopes and targeting approaches



Non-oncology

- Applicable to antivirals and anti-infectives
- Endocrinology



DEP[®] Dendrimer

- **Clinically validated**
- **Easily scalable**, precisely manufactured, GMP

Drug / Payload

- **Flexible** – **type** and **number** of payload molecules
- Can deliver high “DAR” (4, 8, 16, etc.), no impact on solubility

Linker / Pharmacokinetics

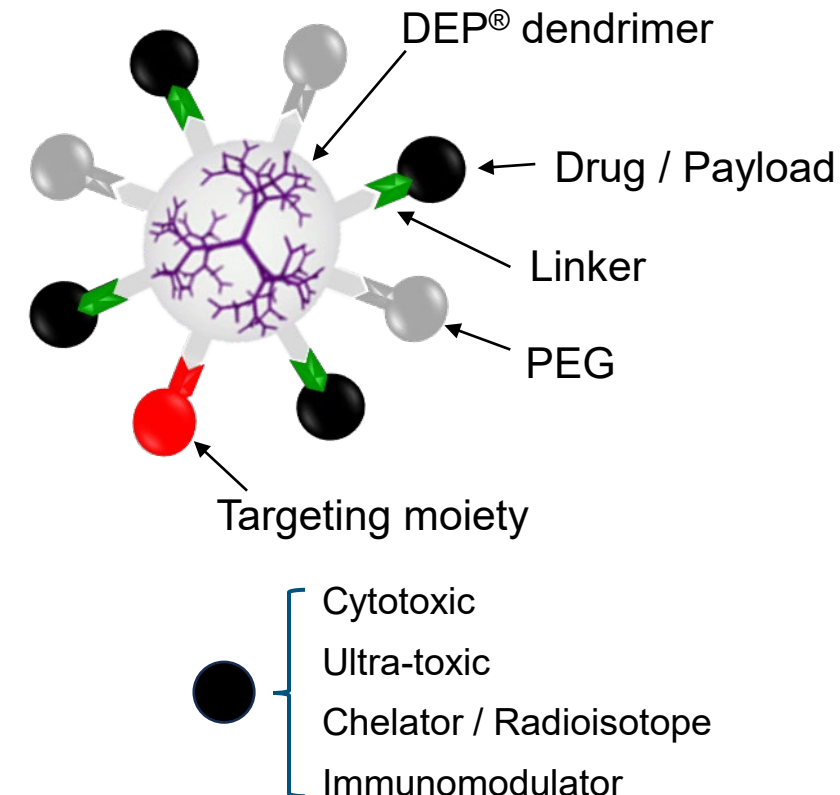
- Payload **release rate**, plasma **half-life tuneable**
- Dendrimer size and charge can be altered to **regulate kidney glomerular filtration**

PEG

- Provides stealth, controls clearance, solubility
- No observed adverse effects, ABC

Targeting (Option)

- **Flexible** choice of targeting moiety (e.g., antibody, antibody mimetics, peptide, small molecule)
- **Polyvalency**



Insoluble drug payload



DEP[®] solubilised drug payload

Starpharma's internal DEP[®] oncology portfolio

Multiple clinical-stage assets with high commercial value potential



DEP[®] cabazitaxel Phase 2



DEP[®] cabazitaxel – dendrimer version of leading prostate cancer drug, cabazitaxel (Jevtana[®])

Jevtana[®] global sales of ~US\$500M for 2021 despite multiple US FDA “Black Box” warnings

Advantages of DEP[®] cabazitaxel^{#*}
Improved tolerability profile; detergent-free formulation; no steroid pre-treatment; tumour-targeting, improved efficacy; patent filings to 2039 (plus up to an additional ~5 years)

DEP[®] irinotecan Phase 2



DEP[®] irinotecan – dendrimer version of irinotecan (Camptosar[®]) – commonly used to treat colorectal cancer

Camptosar[®] peak global sales of US\$1.1B despite multiple US FDA “Black Box” warnings

Advantages of DEP[®] irinotecan^{#*}
Tumour-targeting; DEP[®] solubilises SN38 active metabolite and allows direct dosing, avoiding need for liver conversion – reduced toxicity, variability; improved efficacy; patent filings to 2039 (plus up to an additional ~5 years)

DEP[®] docetaxel Phase 2



DEP[®] docetaxel – dendrimer version of docetaxel (Taxotere[®]), which is widely used to treat breast, lung and prostate cancer

Taxotere[®] was a blockbuster cancer drug with peak global sales of >US\$3B despite having multiple US FDA “Black Box” warnings

Advantages of DEP[®] docetaxel^{#*}
Reduction in neutropenia; detergent-free formulation; no steroid pre-treatment; tumour-targeting (~60x more drug in tumour); improved efficacy; improved PK; patent filings to 2032 (plus up to an additional ~5 years)

COMMERCIAL OBJECTIVE

Create value through clinical proof-of-concept (Phase 2)



License following Phase 2 clinical data; platform validation



Clinical data adds value to partnered programs



Utilise accelerated development/reg. pathways (i.e. 505(b)(2)) for optimal ROI

Clinical studies have demonstrated reduction in important side effects with DEP[®] such as bone marrow toxicity, anaphylaxis, severe diarrhoea and hair-loss

* Multiple preclinical studies have established improved efficacy, survival and safety with DEP[®] with many different drugs

DEP[®] cabazitaxel: Positive Phase 2 results across multiple tumour types, enhancing market potential



- **N=75**, positive final results reported

Summary of key efficacy results

- Heavily pre-treated, **advanced prostate cancer patients (mCRPC)**
 - median progression-free survival (PFS) >50% longer, median overall survival (OS) 10% longer than published data for Jevtana[®] at same dose¹
- Heavily pre-treated **advanced, platinum-resistant ovarian cancer patients**
 - disease control rate (DCR) 66.7%, objective response rate (ORR) 17.6%, which compares favourably to standard-of-care therapies that report ORRs ranging from ~9 to 16%^{2,3,4}
- **Advanced gastro-oesophageal cancer patients**
 - median PFS and median OS 53.1% and 28.5% longer, respectively, than similar patient cohorts treated with standard-of-care paclitaxel⁵

Results reported in Starpharma's ASX Announcement dated 18 October 2023.

1 Eisenberger, M., et al., PROSELICA. *J Clin Oncol*, 2017, 35(28):3198-206

2 Taxol[®] (paclitaxel) Injection label, https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020262s049lbl.pdf

3 Mutch, DG, et al., *J Clin Oncol*, 2007;25(19):2811-2818.

4 Pujade-Lauraine, E, et al., *J Clin Oncol*, 2014;32(13):1302-1308.

5 Stockton, S, et al., *The Oncologist*, 2023;28(9):827-e822.

All efficacy response data are for evaluable patients. Evaluable patients are those that received ≥1 dose cycle of DEP[®] cabazitaxel and had a CT scan, or other efficacy assessment (e.g., PSA in prostate cancer) as applicable, to assess response to treatment at ≥~8 weeks after commencement of treatment with DEP[®] cabazitaxel. PFS and safety data are reported for all patients who received treatment.

Longer PFS and OS in prostate cancer patients treated with DEP[®] cabazitaxel vs published data on Jevtana[®]

Key Efficacy Measures	DEP [®] cabazitaxel (20 mg/m ²) (N=25 [†])	Jevtana [®] (20 mg/m ²) (N=598 [†]) ¹
Median PFS	4.4 months	2.9 months
Median overall survival (OS)	14.7 months	13.4 months
PSA Reduction ≥50%	52.4%	29.5%

Comparative bone marrow toxicity in prostate cancer patients treated with DEP[®] cabazitaxel vs published data on Jevtana[®]

Safety Outcomes	DEP [®] cabazitaxel (20 mg/m ²) (N=25 [^])	Jevtana [®] (20 mg/m ²) ¹ (N=580 [^])
Neutropenia* ≥ grade 3	16.0%	41.8%
Febrile neutropenia ≥ grade 3	0%	2.1%
Thrombocytopenia* ≥ grade 3	0%	2.6%
Neutropenic infection / sepsis	0%	2.1%

*Lab detected neutropenia or thrombocytopenia, regardless of whether the event was reported as an adverse event; [^]Safety population (received at least 1 dose)

DEP[®] irinotecan Phase 2 trial

Positive interim results in multiple cancers



Monotherapy in heavily pre-treated advanced colorectal cancer (CRC) and ovarian cancer patients



Heavily pre-treated CRC patients (N=38)

- >97% of patients had progressed after prior treatment with conventional irinotecan

Positive interim results

- Durable efficacy responses for up to 72 weeks with a DCR 48%
- No severe diarrhoea or cholinergic syndrome, significantly fewer severe TRAEs

Heavily pre-treated ovarian patients (N=23)

- 100% of patients' cancer resistant or refractory to platinum-based therapies (standard-of-care)

Positive interim results

- DCR 100%, ORR 43% (Q2W)
- Tumour shrinkage of up to 60%
- Response durations up to 45 weeks

All efficacy response data reported are for evaluable patients. Evaluable patients are those that received ≥1 dose cycle of DEP[®] irinotecan and had a CT scan to assess response to treatment at ≥8 weeks after commencement of treatment with DEP[®] irinotecan.

Tournigand et al., *Clinical Oncology*, 2023;41(19):3469-3477.
<https://doi.org/10.1200/jco.22.02774>

Combination arm with 5-fluorouracil (5-FU) and leucovorin (LV) in advanced CRC patients

Positive interim results (N=5)

- DCR 100%, ORR 20% (vs. published data in advanced CRC patients – ORR of 4% for conventional irinotecan plus 5-FU/LV (FOLFIRI) as second-line therapy (i.e., less heavily pre-treated patients))
- Clinicians report significant clinical benefit in these heavily pre-treated patients, including durable responses for up to 35 weeks
- Very good tolerability

Safety Outcome	DEP [®] irinotecan*	Camptosar ^{®†^}
GASTROINTESTINAL		
Diarrhoea ≥ Gr 3	0	~20-40%
Nausea ≥ Gr 3	2%	~10%
Vomiting ≥ Gr 3	1%	~10%
NERVOUS SYSTEM		
Cholinergic Syndrome	0%	~47%

* N=112

^ N=765

†H. Bleiberg, & E. Cvitkovic. (1996) Characterisation and Clinical Management of CPT-11 (Irinotecan)-induced Adverse Events. *European Journal of Cancer*, Volume 32 Supplement 3.

*<https://www.medicines.org.uk/emc/product/6506-UK> SmPC April 2022

“...Our experience in treating more than 20 patients on the trial to date have shown promisingly low rates of severe gastrointestinal adverse events and absence of cholinergic toxicity, which are both common and problematic side effects of standard irinotecan therapy.

“I am also getting consistent feedback from several patients in the trial that they far prefer DEP[®] irinotecan plus 5-FU/LV compared to the standard FOLFIRI regimen, which uses conventional irinotecan.”

Dr Jenny Liu, MD, PhD, FRACP, Medical Oncologist and Principal Investigator
 Kinghorn Cancer Centre, St Vincent's Hospital in Sydney.

Clinical validation of DEP[®] platform benefits

- >350 patients treated across 4 DEP[®] product clinical programs
- DEP[®] clinical-stage products span multiple drug classes
- Excellent translation from preclinical findings (PK, efficacy and safety)
- DEP[®] achieves tumour accumulation / targeting in humans: >60x *higher* vs. blood
- Improved or comparable efficacy, including responses in patients who failed conventional formulations of these drugs
- Significantly lower rates or absence of severe AEs including:
 - FDA “Black Box” warnings – neutropenia, anaphylaxis, severe diarrhoea
 - cholinergic syndrome
 - myelosuppression
- Well tolerated; no new AEs due to DEP[®] (TRAEs associated with delivered drug)
- Solubilisation beneficial in clinical settings, allowing for improved formulation characteristics and clinical benefit (no polysorbate-80 infusion reactions, no steroids required)



Radiotheranostics and antibody-drug conjugates (ADCs)

Significant commercial activity continues

Radiotheranostics is a rapidly developing area of cancer treatment and diagnosis

- Global radiopharmaceutical market projected to reach US\$35 billion by 2031[^]
- Over US\$17 billion invested in M&A transactions between 2014 and June 2022⁺ in the radiopharmaceutical market
- **Starpharma's DEP[®] platform has yielded multiple radiotheranostic DEP[®] candidates;** Starpharma continues to evaluate licensing opportunities for its internal radiotheranostic candidates and engages in discussions with potential partners exploring access to Starpharma's DEP[®] platform

Significant corporate deals in radiotheranostics

 ~US\$2B Nov 2022	 €40M Apr 2023	 US\$1B Sept 2023	 US\$1.4B Oct 2023
 US\$3.9B Oct 2017	 US\$2.1B Oct 2018	 US\$300M Mar 2021	 €520M Dec 2021

Innovative therapeutic area of ADCs continues to grow, with many high-value deals signed in recent years

- The ADC market is expected to reach to more than US\$15 billion by 2030^{*}
- Significant scope to improve delivery, efficacy and safety profile of ADCs
- Starpharma's DEP[®] technology represents a valuable partnering platform with potential to generate revenue through royalties and milestones
- Starpharma has two DEP[®] research agreements with MSD for dendrimer-based ADCs using the DEP[®] technology



Significant corporate deals in ADCs



 US\$1.7B Feb 2022	 US\$936M Jul 2022	 US\$1.1B Feb 2023	 US\$4B + up to US\$22B Oct 2023
 US\$6B Jul 2020	 US\$2.75B Nov 2020	 €1.2B Dec 2020	 US\$3.1B Jun 2021

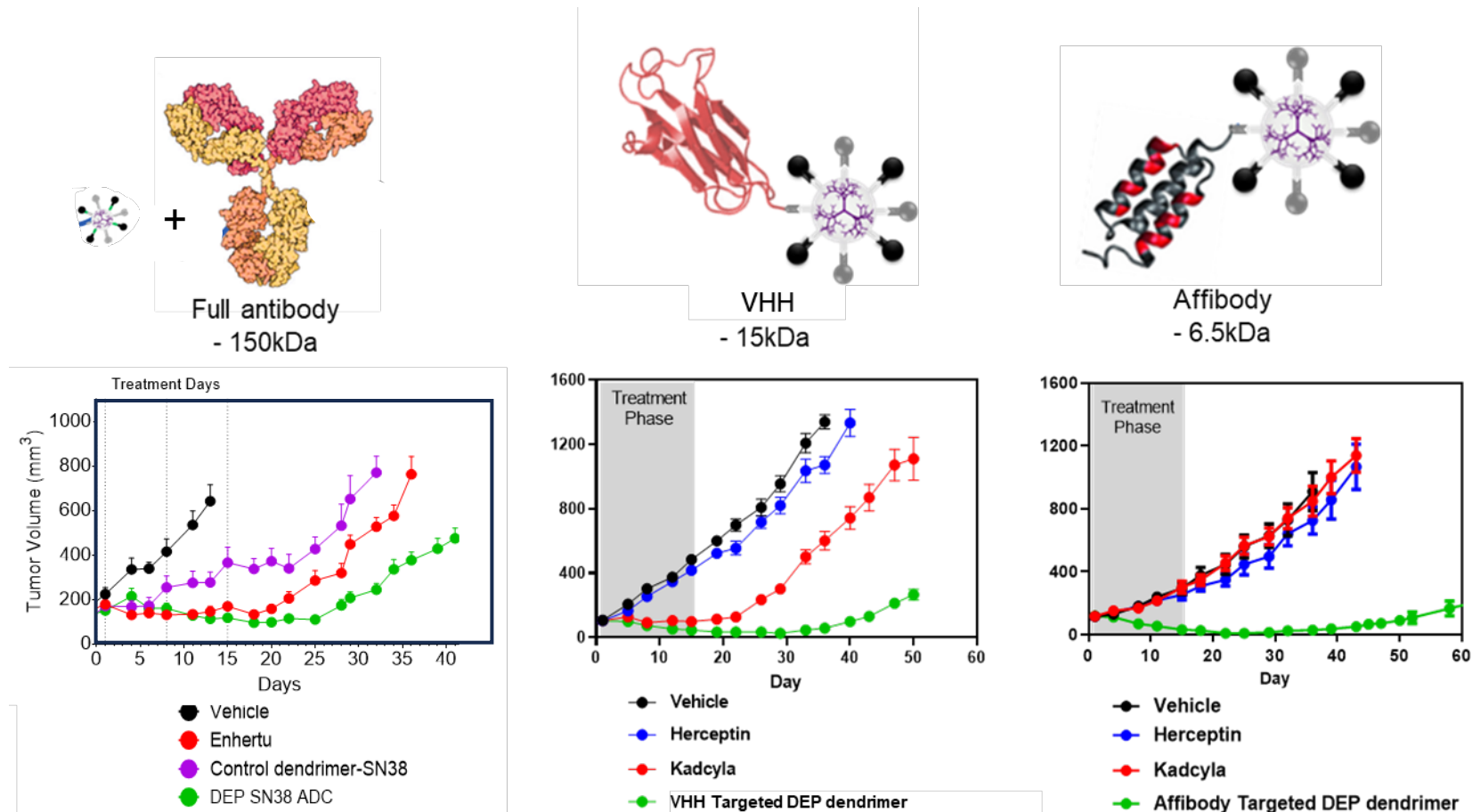
[^]MEDDraysintell Nuclear medicine report Edition 2022

^{*}https://www.medraysintell.com/_files/ugd/1beeab_6bc27b0bbe664527aca68f41bf7de2bc.pdf

⁺Colombo and Rich, The therapeutic window of antibody drug conjugates: A dogma in need of revision, Cancer Cell (2022), <https://doi.org/10.1016/j.ccell.2022.09.016>

Versatile DEP[®] platform for payload and targeting flexibility

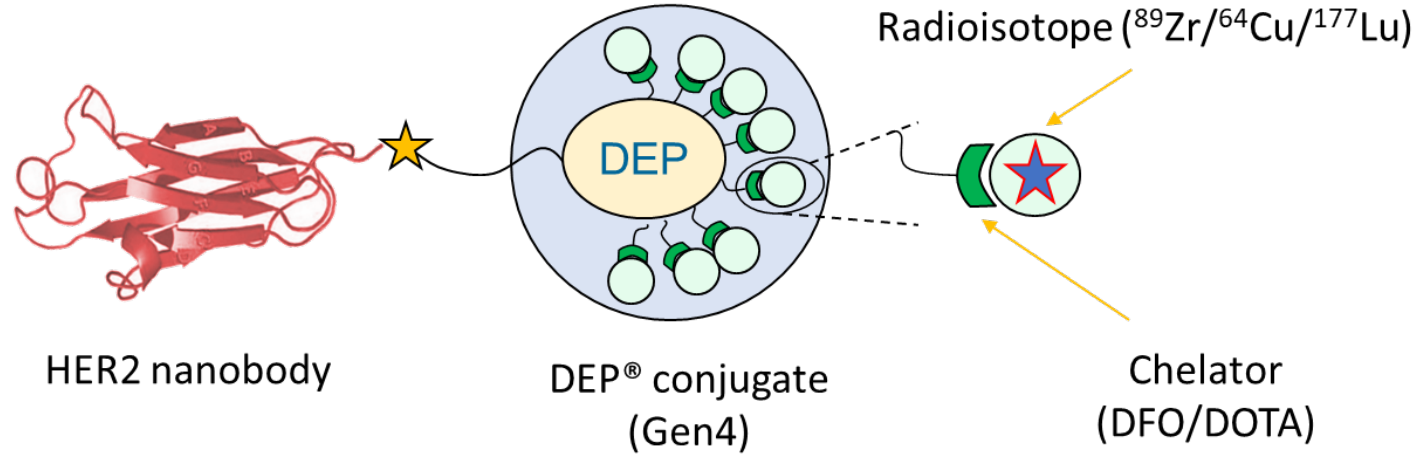
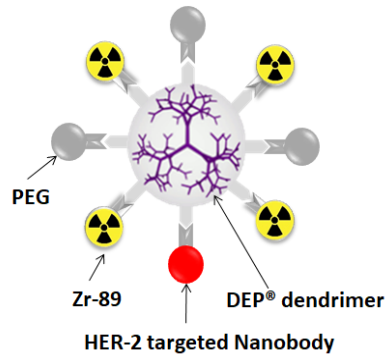
Starpharma's versatile DEP[®] technology provides advantages, including targeting moiety and payload flexibility, leading to enhanced safety and efficacy over conventional ADCs



These experiments were conducted in a human ovarian cancer (SKOV-3) mouse xenograft model

DEP[®] HER2-zirconium (radiodiagnostic): favourable imaging and biodistribution in a HER2⁺ breast cancer model

DEP[®] HER2-zirconium

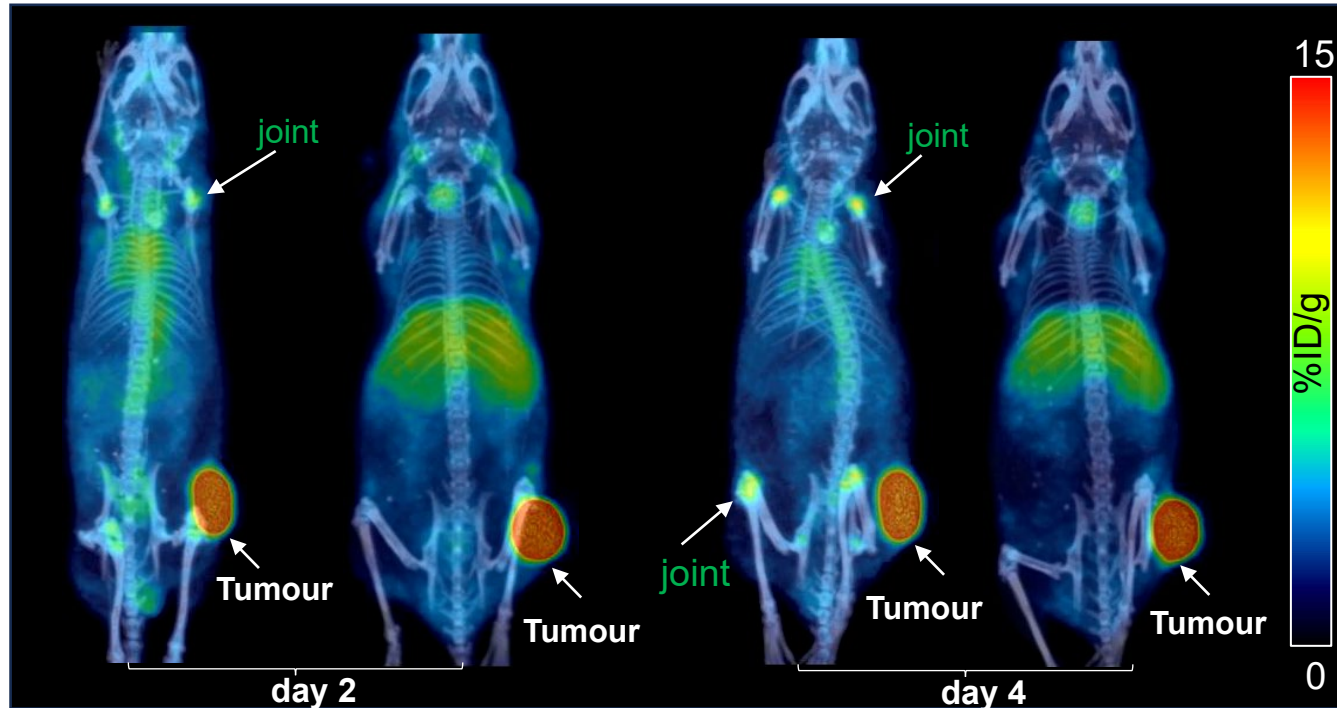


DEP[®] HER2 can be loaded with imaging or therapeutic radionuclides

- HER2-targeted radiotheranostics development is less advanced compared to other targets, such as PSMA
- In clinical studies involving [Trastuzumab](#), [myelosuppression](#) has emerged as a significant dose-limiting toxicity
- [DEP[®] HER2-zirconium](#) showed enhanced biodistribution and kinetics in BT474 HER2⁺ tumour bearing mice:
 - Potential for the clinical delivery of higher doses to tumours with lower risk of dose-limiting toxicity
 - Highly desirable “**fast-in**”/”**fast-out**” **kinetics**, with rapid accumulation in tumour and rapid clearance from the bloodstream
 - Excellent imaging contrast between tumour and normal tissues

DEP[®] HER2 vs. Trastuzumab: PET/CT imaging performance

Trastuzumab-⁸⁹Zr DEP[®] HER2-⁸⁹Zr Trastuzumab-⁸⁹Zr DEP[®] HER2-⁸⁹Zr



Maximum intensity projection (MIP) PET-CT images of BT474 HER2⁺ tumour-bearing mice dosed with either DEP[®] HER2-⁸⁹Zr or Trastuzumab-⁸⁹Zr

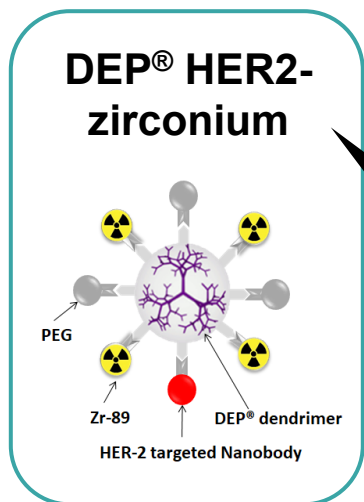
Radioconjugates administered at t=0

Representative mice shown at Day 2 (left side) or Day 4 (right side) after injection

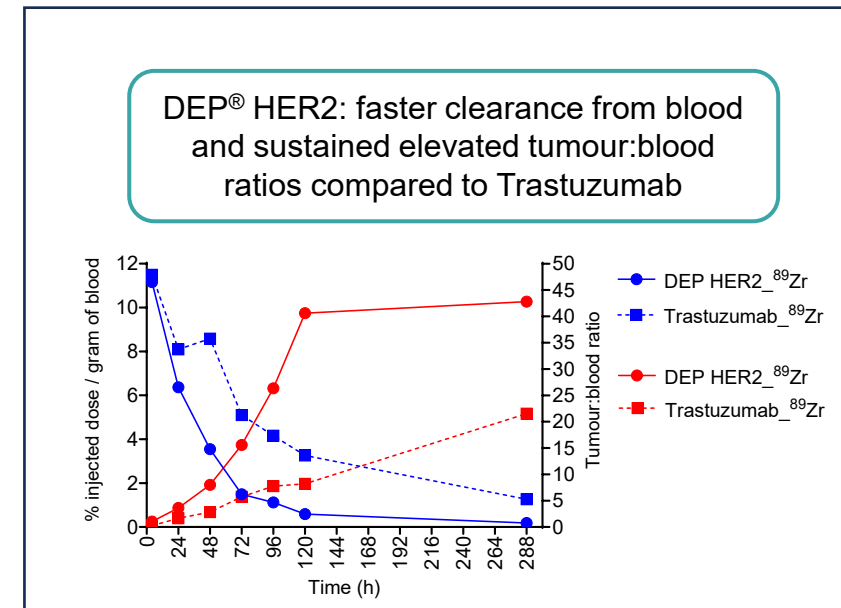
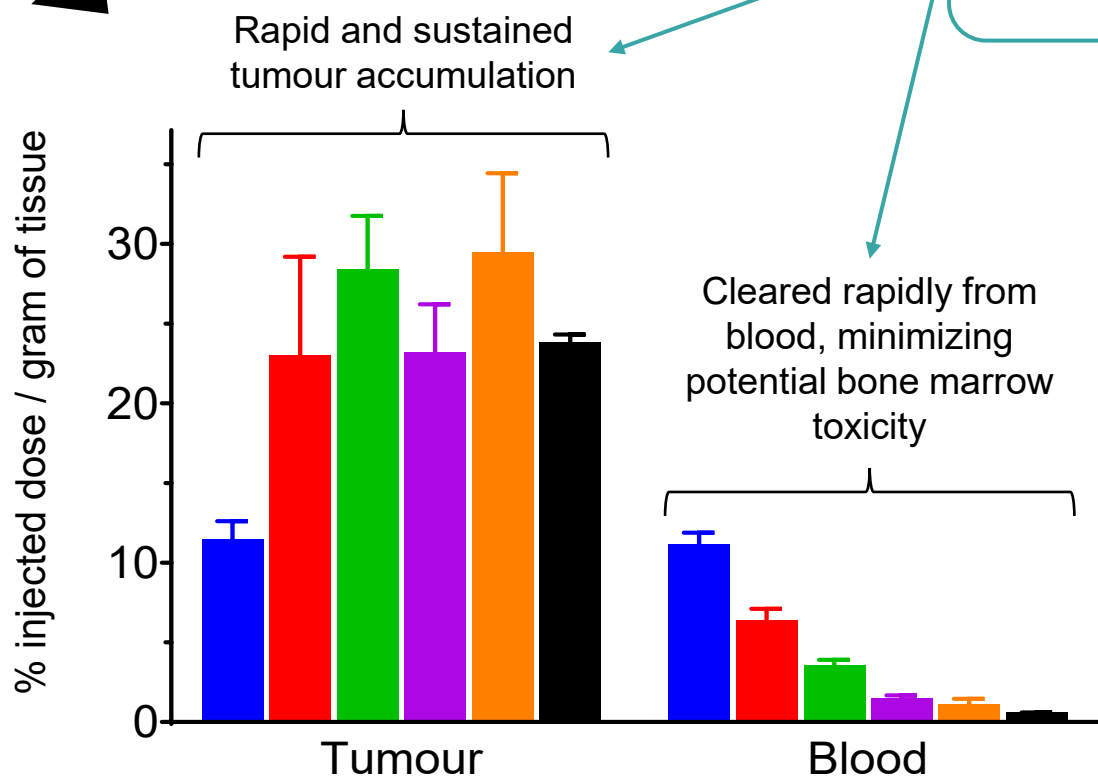
Scale bar (% ID/g) is shown to the right

- DEP[®] HER2 achieved excellent imaging contrast between tumour and normal tissue, similar to Trastuzumab
- Higher levels of activity are observed in heart for Trastuzumab at Day 2 and Day 4, consistent with *ex vivo* blood activity data,
- DEP[®] HER2 shows typical clearance by RES for nanoparticles
- Deposition in shoulder and hip joints was prominent for Trastuzumab but not DEP[®] HER2

DEP® HER2-zirconium (radiodiagnostic): favourable imaging characteristics in a HER2⁺ breast cancer model



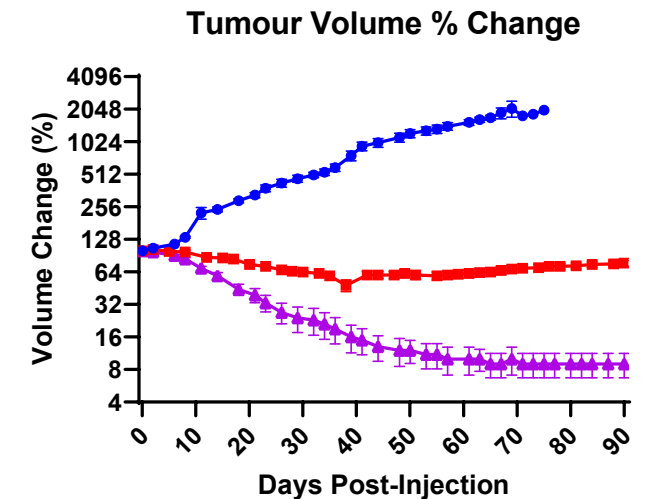
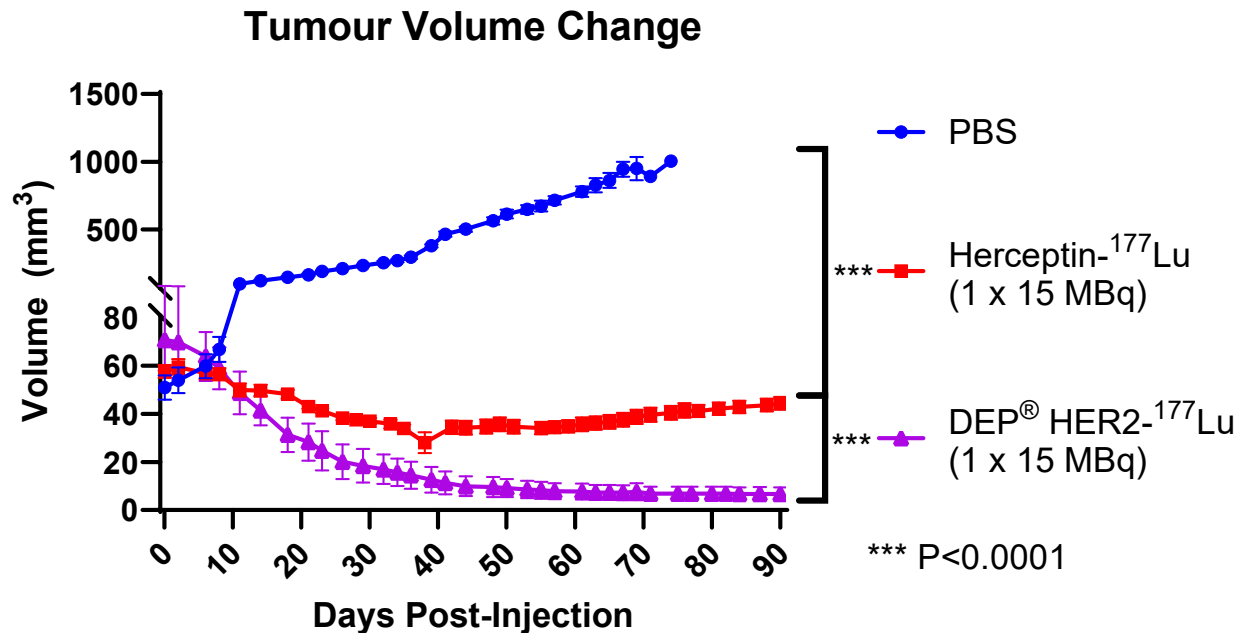
These characteristics are also desirable for a radiotherapeutic to maximise efficacy and minimise toxicity



DEP[®] HER2-lutetium radiotherapy outperforms in efficacy study in HER2+ breast cancer model

HER2-targeted DEP[®] dendrimer-nanobody radiotherapeutic, DEP[®] HER2-lutetium

- achieved significantly better efficacy than antibody in breast cancer model
- achieved complete tumour regression
- extremely well tolerated
- anti-tumour effect dose-dependent
- 100% survival

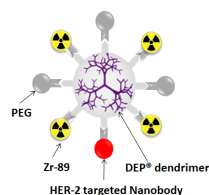


- HER2 overexpressed (HER2^{hi}) in ~20%-30% of breast, gastric & gastro-oesophageal cancers; also expressed at low levels (HER2^{lo}) in other carcinomas including colorectal, endometrial & lung
- HER2+ breast cancer treatment market \$9.7 billion[^] in 2021 and expected to increase to \$11.2 billion in 2025 (US, Japan, EU5)
- Global HER2-positive gastric cancer market is currently valued at ~US\$1.3 billion

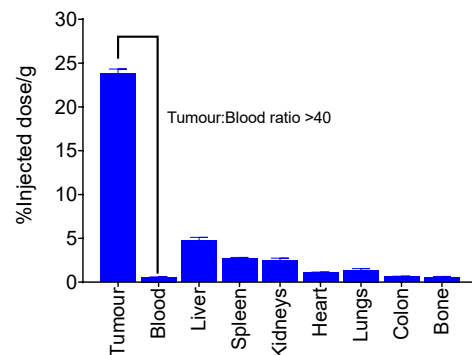
DEP[®] HER2-zirconium (radiodiagnostic)

DEP[®] HER2-zirconium demonstrated imaging benefits in a HER2⁺ breast cancer model, including:

- More **rapid tumour accumulation and superior PK** than HER2 mAb, trastuzumab (Herceptin[®]), labelled with zirconium;
- Favourable biodistribution profile, with **excellent imaging contrast between tumour and normal tissues**;
- High **tumour-to-organ ratios, delivering excellent specificity** in imaging HER2+ tumours; and
- Highly desirable “fast-in”/“fast-out” kinetics, meaning it accumulates rapidly in the tumour and is cleared quickly from the bloodstream.



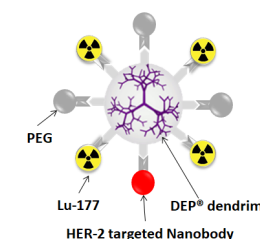
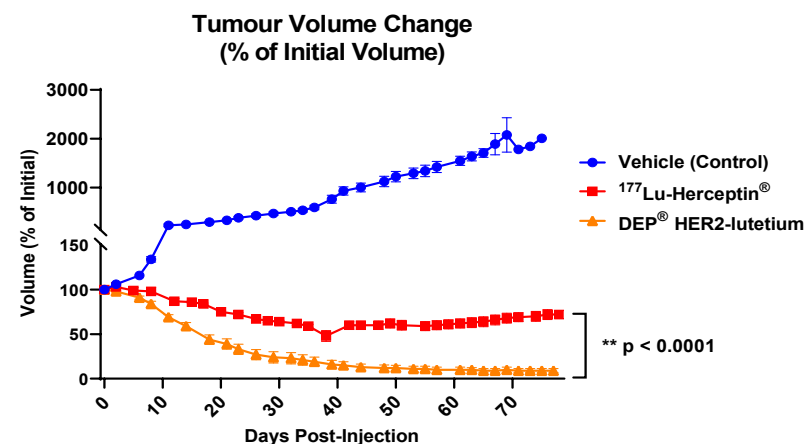
Tumour and normal tissue levels of DEP[®] HER2-zirconium at 120 hours.



DEP[®] HER2-lutetium (radiotheranostic)

DEP[®] HER2-lutetium demonstrated therapeutic benefits in a breast cancer model:

- **Achieved complete tumour regression**; well tolerated
- Anti-tumour effect was radiation dose-dependent
- 100% survival



HER2-targeted DEP[®] SN38 ADC outperforms in HER2+ human cancer model

A HER2-targeted DEP[®] ADC, utilising active metabolite of irinotecan, SN38, outperformed Enhertu[®], showing significantly greater anti-tumour activity and improved survival in a HER2+ human cancer xenograft model

Key advantages of Starpharma's DEP[®] platform for ADCs:

- Ability to achieve higher DAR, and higher drug payload than conventional ADCs;
- Improved solubility not impacted by higher DAR of poorly soluble drug payloads;
- Greater flexibility in terms of linker strategies to precisely control drug release profiles;
- Capacity to widen the therapeutic index of toxic drug payloads; and
- Flexibility in terms of compatible targeting agents, including biologics (whole antibodies and fragments), small molecules, peptides and other approaches.

ADCs represent an **innovative and growing area of cancer treatment**. The **global ADC market** grew from USD ~\$5.8 billion in 2021 to USD ~\$8.0 billion in 2022 and is **projected to reach USD ~\$22.9 billion in 2030**

HER2 ADCs Drug-to-Antibody Ratios, Drug Payload

HER2 ADC	Approximate Drug-to-Antibody Ratio (DAR)	Drug Payload
Kadcyla[®] (Genentech/Roche)	3.5	DM-1 (emtansine)
Enhertu[®] (AstraZeneca/Daiichi-Sankyo)	8	DXd (exatecan derivative)
HER2-targeted DEP[®] SN-38 ADC (Starpharma)	13	SN-38

Effect of HER2-targeted DEP[®] SN38 ADC vs. Enhertu[®] on Tumour Volume Over Time

DEP[®] Dendrimers: A Versatile, Multifunctional Delivery Platform for Precision Cancer Radiotheranostics

KEY MESSAGES

- ❑ Proprietary DEP[®] platform – **clinically validated** via 4 clinical programs, multiple drug classes
- ❑ Starpharma's are the only **marketed** dendrimer-based products
- ❑ DEP[®] platform:
 - ✓ provides **flexibility** for a **wide range of payloads and chelating agents**
 - ✓ can achieve **preferential delivery** to tumours by virtue of size
 - ✓ can also be **functionalised** to carry a **wide range of targeting moieties**
 - ✓ provides **flexibility** for **customisation of biodistribution / excretion profile**
- ❑ Targeted DEP[®] can achieve **improved biodistribution and efficacy** profiles vs antibody targeting



DEP[®] DENDRIMERS: A VERSATILE, MULTIFUNCTIONAL PLATFORM FOR CUSTOMISATION OF PRECISION RADIOTHERANOSTICS FOR CANCER IMAGING AND THERAPEUTIC APPLICATIONS

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 - Dr Martina Jones and colleagues
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 - Professor Christopher Porter and colleagues





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