starpharma

ASX Announcement

# DEP® HER2-radiodiagnostic shows imaging benefits

- HER2[1] is a well-characterized oncology target that is prevalent in ~30% of breast and gastric cancers, as well as other cancers.
- HER2-based antibody products had total sales of ~US$11 billion in 2022[2], which included Herceptin® (or trastuzumab), marketed by Roche/Genentech.
- Starpharma is developing a targeted radiodiagnostic called **DEP® HER2-zirconium** designed to diagnose, stage, and monitor HER2-positive (HER2+) cancers with improved sensitivity.
- DEP® HER2-zirconium has demonstrated imaging benefits in a HER2+ breast cancer model, including:
    - More rapid tumour accumulation and superior pharmacokinetics (PK) than HER2 monoclonal antibody (mAb), trastuzumab, labelled with zirconium (trastuzumab-zirconium);
    - A favourable biodistribution profile, with excellent imaging contrast between tumour and normal tissues;
    - Highly desirable "fast-in"/"fast-out" kinetics, meaning it accumulates rapidly in the tumour and is cleared quickly from the bloodstream;
    - High tumour-to-organ ratios, delivering excellent specificity in imaging the tumour in HER2+ breast cancer.
- Additionally, DEP® HER2-zirconium resulted in higher tumour-to-blood ratios, demonstrating the DEP® technology may also deliver superior performance as a radiotherapeutic, compared to mAb-based radiotherapeutics.
- Starpharma is planning to conduct clinical testing of DEP® HER2-zirconium and other DEP® radiotheranostics and is also engaging in discussions with potential partners in this area.

**Melbourne, Australia; 21 July 2023: Starpharma** (ASX: SPL, OTCQX: SPHRY) today announces that **DEP® HER2-zirconium**, its HER2-targeted radiodiagnostic candidate, has demonstrated a favourable biodistribution profile, with excellent imaging contrast between tumour and normal tissues, as well as rapid uptake and high levels of tumour accumulation in a HER+ breast cancer model. These are important features for a radiodiagnostic product for accurate diagnosis and monitoring of tumour lesions using PET-CT imaging. The study details and results are reported below.

Starpharma's DEP® HER2-zirconium is a radiodiagnostic product that belongs to the rapidly growing "radiotheranostic" category – which includes both radiodiagnostic and radiotherapeutic products. DEP® HER2-zirconium is designed to specifically diagnose, stage, and monitor HER2+ cancers with greater sensitivity, meaning that patients suffering from these cancers could be diagnosed earlier, more accurately, and monitored more closely during cancer treatment.

The study results are very encouraging as they confirm the optimised binding properties of DEP® HER2-zirconium for targeted delivery and preferential uptake by cancer cells, and support a precision medicine approach for cancer patients. The combined effect of the novel pharmacological properties of DEP® HER2-zirconium gives it an advantage in the promotion of selective tumour cell entry and support its targeted delivery mechanism to tumour cells, leaving normal cells relatively untouched.

[1] HER2: Human epidermal growth factor receptor 2
[2] Disease Analysis: HER2+ Breast Cancer | Datamonitor Healthcare. Database accessed on 20 July 2023.

Commenting on the significance of these findings, Clinical Pharmacology and Oncology specialist, Dr Paul Wabnitz, (MD, FRACP)[3], said:

"Translated clinically, this technology has the potential to detect cancer cells at very low levels and better guide therapeutic decisions at earlier stages and at levels that were previously undetectable by current radiological methods. This has several advantages, including dose optimisation and better identifying the minimal dose level for an efficacious response, thereby minimising toxicity and promoting the quality of life and care of cancer patients undergoing therapy."

Dr Jackie Fairley, CEO of Starpharma, commented:

"Radiotheranostics and HER2 therapeutics are both rapidly growing categories with a number of highly successful product launches in recent years. The application of Starpharma's DEP® technology in the radiotheranostic area presents a substantial opportunity to expand the commercial opportunity for DEP®. The DEP® platform offers greater flexibility which allows a wide range of radioisotopes to be utilised."

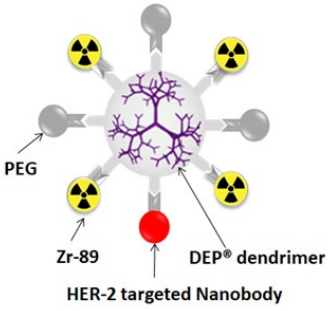
## HER2 and radiotheranostics market

The global radiotheranostics market was US$1.8 billion in 2022 and is expected to grow by over 10% annually to US$4.2 billion by 2030. There are already several successful marketed radiodiagnostics, such as Pylarify® and Illuccix®, which detect prostate cancer through PET-CT scans, with others in development.

HER2-based antibody products had total sales of ~US$11 billion in 2022, which included Herceptin® (or trastuzumab), marketed by Roche/Genentech and the highly successful AstraZeneca product, Enhertu®.

## DEP® HER2-zirconium study details and results

DEP® HER2-zirconium utilises a novel single-domain antibody (sdAb), or nanobody, which is smaller than a full mAb, to target and bind to HER2+ tumour cells.




The study assessed the biodistribution and imaging (diagnostic) performance of DEP® HER2-zirconium compared with a HER2-targeted full antibody (trastuzumab/Herceptin®), labelled with zirconium-89. Zirconium-89 is a radioisotope used for PET-CT imaging in cancer patients.

A HER2+ human breast cancer cell line (BT474) was grown as a tumour subcutaneously in mice. Biodistribution was measured by *in vivo* PET-CT imaging and quantitative *ex vivo* gamma counting at time points ranging from 4 hours to 120 hours after dosing with either DEP® HER2-zirconium or trastuzumab-zirconium, with a target radioactivity of 3 MBq (megabecquerel) per dose.

In this study, DEP® HER2-zirconium:

- Showed significant accumulation in tumour (>25% of the injected dose per gram [ID/g] of tumour);
- Was cleared more rapidly from the blood, and highly perfused organs such as heart and lung, than HER2 mAb trastuzumab-zirconium (see Figure 1);
- Demonstrated a significantly higher tumour-to-blood ratio than trastuzumab-zirconium; and

[3] Dr. Wabnitz (BSc (Hons), PhD, MD, MBA, FRACP) is a specialist physician with extensive experience in medical oncology, pharmacology, and drug development experience in industry (Pfizer and Parke-Davis).

- Resulted in high tumour-to-organ ratios, delivering excellent specificity in imaging the HER2+ breast cancer model (see Figure 2).

**Figure 1. Injected dose in blood over time, demonstrating more rapid clearance of DEP® HER2-zirconium versus trastuzumab-zirconium.**

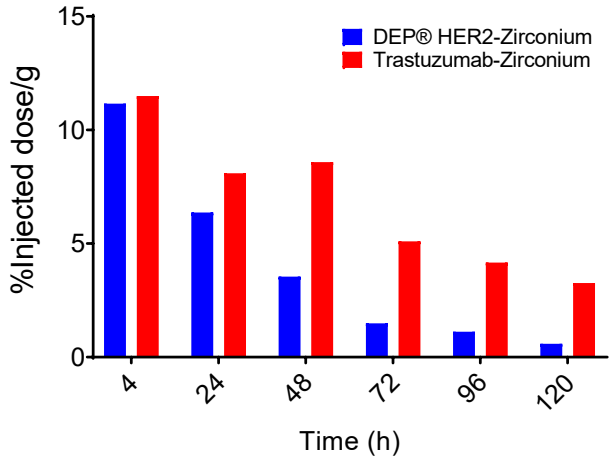
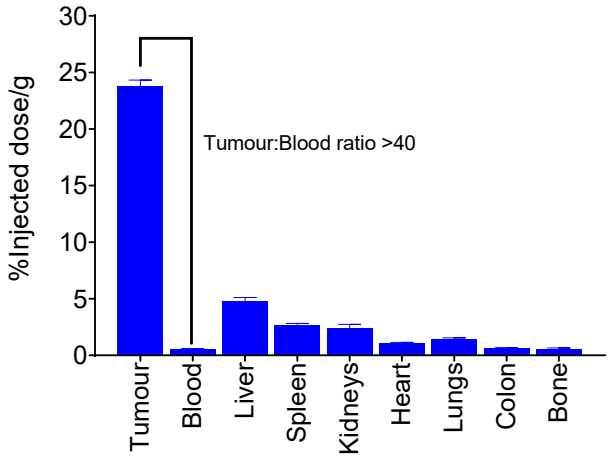



**Figure 2. Tumour and normal tissue levels of DEP® HER2-zirconium at 120 hours.**




In summary, the data reported here for DEP® HER2-zirconium highlight its promise in radiotheranostics, due to its efficiency of tumour delivery and favourable PK and biodistribution characteristics. The study results demonstrate positive characteristics that are relevant to both radiodiagnostic and radiotherapeutic DEP®-based products.

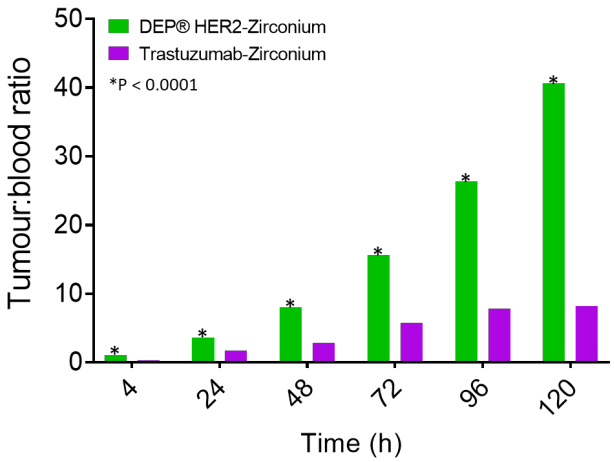
## Starpharma's DEP® radiotheranostics programs

In addition to the imaging/diagnostic results reported above, the study results also highlight the potential benefits of DEP® technology in radiotherapeutic, or treatment, applications.

Radiotherapeutics seek to deliver radiation directly to cancer cells as a treatment while minimising adverse effects on other organs in the body. Radiotherapeutics utilising mAbs are often associated with dose-limiting haematological toxicities, such as neutropenia and thrombocytopenia, due to the slow clearance of mAbs from the body.

In this study, DEP® HER2-zirconium demonstrated highly desirable “fast-in”/”fast-out” kinetics, meaning it accumulates rapidly in the tumour and is cleared quickly from the bloodstream. DEP® HER2-zirconium achieved 40 times more drug in tumour versus blood, while at the same time point, trastuzumab-zirconium was only 8 times more in the tumour than in the blood (Figure 3).

**Figure 3: Tumour-to-blood ratio over time for DEP® HER2-zirconium is significantly larger than trastuzumab-zirconium.**




Furthermore, rapid clearance of DEP® HER2-zirconium from the blood suggests that the corresponding DEP® HER2-lutetium radiotherapeutic would be expected to have reduced haematological toxicity compared with mAb-based radiotherapeutics.

For therapeutic applications, Starpharma is developing DEP® HER2-lutetium, which has demonstrated a more favourable PK and tissue biodistribution than a full mAb. This profile has the potential to reduce specific toxicities associated with mAb-based radiotherapeutics. Starpharma has previously reported results for DEP® HER2-lutetium demonstrating enhanced delivery of radioisotopes to solid tumours in pre-clinical studies. These prior data for the DEP® radiotheranostics also demonstrated durable anti-tumour responses, enhanced survival, and high levels of tumour uptake, including in a glioma (brain cancer) model. These two products, DEP® HER2-lutetium and DEP® HER2-zirconium, constitute a HER2 “theranostic pair”.

## About Starpharma

Starpharma Holdings Limited (ASX: SPL, OTCQX: SPHRY) is a biopharmaceutical company focussed on the development of pharmaceutical and medical products for unmet patient needs, including in the areas of oncology and infectious diseases.

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 in Europe, in the UK, and in Asia. Starpharma's novel non-antibiotic vaginal gel, VivaGel® BV, for treatment of bacterial vaginosis (BV) and prevention of recurrent BV, is registered in more than 50 countries, including in the UK, in Europe, in Southeast Asia, South Africa, Australia and New Zealand.

* Note: VIRALEZE™ is not approved for use or supply in Australia.

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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.