

DEP[®] HER2-lutetium outperforms in human breast cancer model

- Radiotheranostics¹ represent an exciting and rapidly growing area of cancer therapy (radiopharmaceuticals) and diagnosis (radiodiagnostics)
- Starpharma's DEP[®] radiopharmaceuticals/diagnostics program has already generated several candidates including DEP[®] lutetium, DEP[®] zirconium, and most recently, DEP[®] HER2-lutetium
- Starpharma's newest radiopharmaceutical candidate, DEP[®] HER2-lutetium, showed complete tumour regression, outperforming Herceptin[®] labelled with lutetium, in a human breast cancer model
- Starpharma's earlier candidate, DEP[®] lutetium - an untargeted dendrimer-lutetium conjugate without a HER2 targeting group - also achieved better efficacy than Herceptin[®] labelled with lutetium, including 100% survival, in this model

Melbourne, Australia; 16 March 2021: Starpharma (ASX: SPL, OTCQX: SPHRY) today announced that its second radiopharmaceutical candidate, DEP[®] HER2-lutetium, achieved potent and durable anticancer activity, with complete tumour regression, outperforming Herceptin[®] (trastuzumab) labelled with lutetium, in a human breast cancer model (BT474).

Radiotheranostics is a rapidly developing area of cancer treatment and diagnosis, which has recently generated several high-value deals and sales in this category are estimated to grow to \$12–15 billion by 2030.² Recent deals include the acquisition of Endocyte by Novartis for US\$2.1 billion and the acquisition of Sirtex by CDH Genetech for ~A\$1.9 billion.

Worldwide, breast cancer is the most common cancer in women and the second most common cancer in the US. HER2 (human epidermal growth factor receptor 2) is a growth-promoting protein on the outside of all breast cells. Breast cancer cells with higher-than-normal levels of HER2 are called HER2-positive. These cancers tend to grow and spread faster than other breast cancers but are much more likely to respond to treatments with drugs that target the HER2 protein (such as Herceptin[®]).³ The HER2 receptor also exists in some other cancers such as gastric, colon, bladder and biliary cancers.

HER2 cancer treatments include Roche's Herceptin[®] and Perjeta[®] with sales of approximately US\$7 billion and US\$4 billion respectively.⁴

DEP[®] HER2-lutetium (Figure 1) is a proprietary dendrimer developed by Starpharma which incorporates the radioisotope lutetium-177 (¹⁷⁷Lu) and a novel HER2 targeting moiety (nanobody).

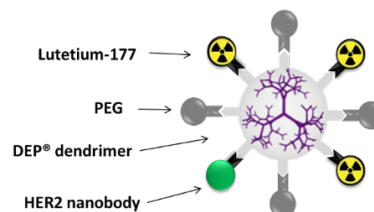


Figure 1: DEP[®] HER2- lutetium

¹ Theranostics is the systematic integration of targeted diagnostics and therapeutics. The theranostic platform includes an imaging component that "sees" the lesions followed by administration of the companion therapy agent that "treats" the same lesions. This strategy leads to enhanced therapy efficacy, manageable adverse events, improved patient outcome, and lower overall costs. Radiotheranostics refers to the use of radionuclides for the paired imaging and therapy agents. <https://pubmed.ncbi.nlm.nih.gov/29356634/>

² Nuclear medicine world market report & directory, MEDDraysintell, 2016

³ <https://www.cancer.org/cancer/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-her2-status.html>

⁴ Datamonitor HER2+ Breast Cancer publication December 2020, 2019 sales figures

This study evaluated the anticancer activity of different doses of DEP[®] HER2-lutetium and DEP[®] lutetium compared to Herceptin[®] labelled with lutetium in the BT474 human breast cancer model. The study was conducted at University of Queensland's Centre for Advanced Imaging.

Dr Jackie Fairley, CEO of Starpharma commented: "We and our specialist radiotheranostics clinical advisers are very excited by these latest data. Starpharma now has multiple potential DEP[®] products in the radiopharmaceuticals and radiodiagnostic area. We are delighted to continue working with Professor Kristofer Thurecht at the University of Queensland's Centre for Advanced Imaging, as well as building strong relationships with radionuclide specialists and clinicians."

About DEP[®] radiotheranostics

DEP[®] radiotheranostics (i.e., radio diagnostics and therapeutics) incorporate radioisotopes on to the DEP[®] scaffold. DEP[®] radiopharmaceutical conjugates selectively penetrate and accumulate within tumours and more effectively delivers radiation to kill tumour cells, that may be unreachable by conventional therapies. The addition of targeting groups, such as HER2, onto the DEP radiopharmaceutical can further enhance efficacy. Patent applications for DEP[®] lutetium, DEP[®] zirconium and DEP[®] HER2- lutetium have been filed.

Starpharma's DEP[®] platform

Starpharma's proprietary drug delivery platform technology, DEP[®], is being used to improve pharmaceuticals, to reduce key toxicities and enhance their performance. The DEP[®] platform is highly versatile and can be used with a wide range of targeting moieties (e.g., small molecules, peptides, antibodies, antibody fragments) and radioisotopes.

The Company has three clinical stage DEP[®] products, as well as numerous partnered programs. DEP[®] partnerships include oncology programs with AstraZeneca, with Merck in the area of Antibody Drug Conjugates (ADCs), with Chase Sun in the area of anti-infectives and other world leading pharmaceutical companies. Starpharma's partnered DEP[®] programs have the potential to generate significant future milestones and royalties.

Study results

Treatment with either a 1x15 MBq or 2x9 MBq dose of DEP[®] HER2-lutetium showed a potent anti-tumour effect resulting in complete tumour regression in the BT474 human breast cancer model. These results outperformed the antitumour activity of Herceptin[®] labelled with lutetium (1x15 MBq) (both DEP[®] HER2-lutetium doses p<0.0001 vs. Herceptin[®] labelled with lutetium)⁵ (Figure 2, showing 15 MBq dose groups only). All dose regimens of DEP[®] HER2-lutetium were extremely well tolerated. There were no deaths due to treatment or as a result of tumour growth in any treatment group.

⁵ All p-values obtained from a Mixed-effects Model with Repeated Measures (MMRM) analysis of tumour volume over time as a percentage of initial tumour volume. Groups 2 and 4: n=4, Groups 1 and 3: n=3

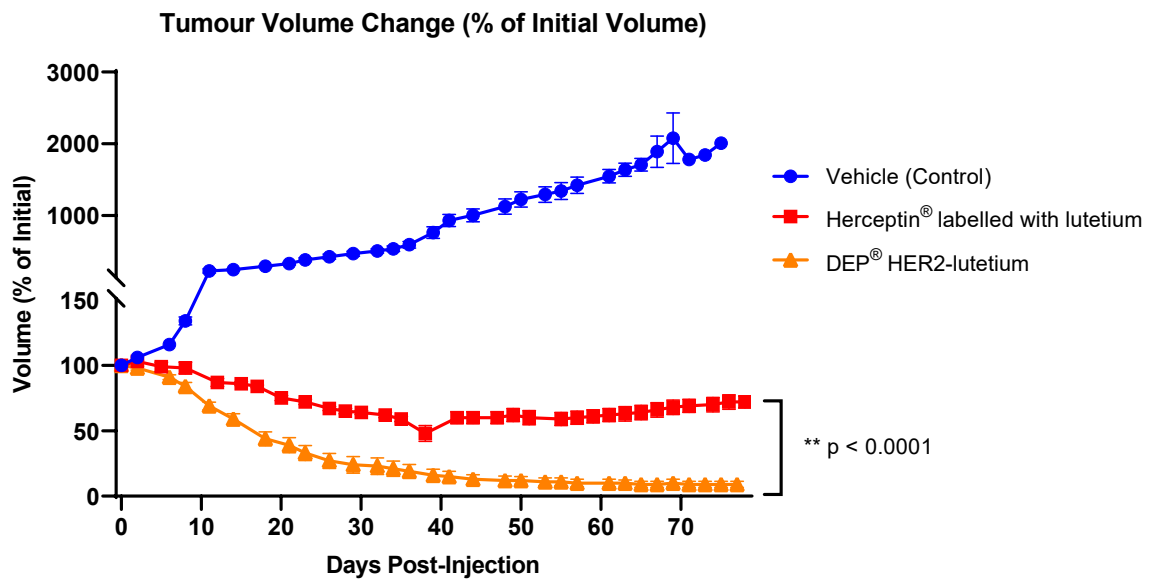


Figure 2: Comparative anticancer efficacy of DEP® HER2-lutetium (15 MBq) versus Herceptin® labelled with lutetium (15 MBq).

The study also compared DEP® lutetium (i.e., without HER2 targeting) (1x15 MBq) to Herceptin® labelled with lutetium (1x15MBq). The anticancer activity of DEP® lutetium was also better than the effect of Herceptin® labelled with lutetium ($p < 0.0001$)⁵ (Figure 3).

These data demonstrate that Starpharma's DEP® dendrimer (without HER2 targeting) has a potent anticancer effect which is greater than with Herceptin®, while the targeted DEP® HER2-lutetium provides even greater efficacy.

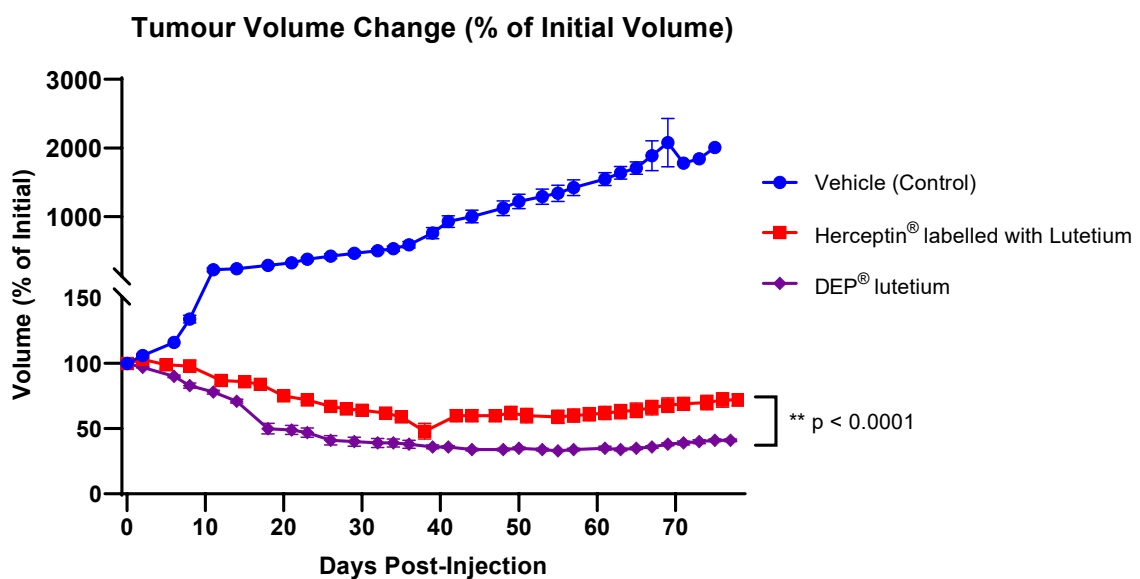


Figure 3: Comparative anticancer efficacy of DEP® lutetium (15 MBq) versus Herceptin® labelled with lutetium (15 MBq).

Study methods

This study was conducted in the laboratory of Professor Kristofer Thurecht at the University of Queensland's Centre for Advanced Imaging. This murine xenograft study implanted BT474 human mammary cancer cells in female Balb/c nude mice. Mice were injected subcutaneously in the breast mammary fat pad with BT474 cells and also received oestrogen. Tumours were measured 2-3 times weekly using electronic callipers. Tumour volume (mm³) was calculated at each timepoint. The tumour volume data represent the mean ± standard error of the mean (SEM).⁶

Following tumour establishment, mice were dosed intravenously as follows:

- Vehicle - days 1 and 15 (group 1)
- ¹⁷⁷Lu labelled Herceptin[®] (15 MBq ¹⁷⁷Lu) - day 1 (group 2)
- DEP[®] HER2- lutetium (15 MBq ¹⁷⁷Lu) - day 1 (group 3)
- DEP[®] lutetium (15 MBq ¹⁷⁷Lu) - day 1 (group 4)

About Starpharma

Starpharma Holdings Limited (ASX:SPL, OTCQX:SPHRY) is a global biopharmaceutical company and a world leader in the development of new pharmaceutical and medical products based on proprietary polymers called dendrimers, with programs for COVID-19, DEP[®] drug delivery and VivaGel[®]. Starpharma has developed VIRALEZE[™], an antiviral nasal spray for COVID-19, which is complementary to vaccines and other preventative measures such as distancing and PPE. VIRALEZE[™] is registered for sale in the UK/Europe, with launch of product expected in Q1 CY2021. SPL7013 is utilised in approved products - the VivaGel[®] condom and VivaGel[®] BV. VivaGel[®] BV has been licensed in >160 countries, is approved in >40 countries and available for sale in the UK, Europe, Japan, South East Asia, Australia and New Zealand.

As a leading company in dendrimer-based drug delivery, Starpharma's proprietary drug delivery platform technology, DEP[®], is being used to improve pharmaceuticals, to reduce toxicities and enhance their performance. There are numerous internal and partnered programs underway to develop DEP[®] versions of existing drugs, particularly in the area of anti-cancer therapies. DEP[®] partnerships include oncology programs with AstraZeneca, with Merck in the area of Antibody Drug Conjugates (ADCs), with Chase Sun in the area of anti-infectives and other world leading pharmaceutical companies. Starpharma's partnered DEP[®] programs have the potential to generate significant future milestones and royalties.

[Starpharma.com](https://www.starpharma.com) | [Twitter](#) | [LinkedIn](#)

Media: Summit Media

Grant Titmus
Mob: +61 419 388 161
grant@sumitmedia.com.au

Starpharma Holdings Limited

Dr Jackie Fairley, Chief Executive Officer
Nigel Baade, CFO and Company Secretary
+61 3 8532 2704
investor.relations@starpharma.com
4-6 Southampton Crescent
Abbotsford Vic 3067

Disclosure

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

⁶ Note: If error bars do not display on the graphs, they are not visible because they are shorter than the height of the symbol at this scale.

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.