



# ASX ANNOUNCEMENT

# Targeted DEP™ shows sustained superior performance in ovarian cancer model

Melbourne, Australia; 2 February 2016: Starpharma (ASX: SPL, OTCQX: SPHRY) today announced the final results of the preclinical study of its HER2-targeted DEP™ conjugate, which achieved complete tumour regression at the last study time point of 120 days post dosing. These results are an extension of the previously announced findings that showed complete tumour regression at 60 days post dosing with the HER2-targeted DEP™ conjugate.

Starpharma's HER2-targeted DEP™ conjugate also significantly outperformed all other treatment groups, including Kadcyla® (Trastuzumab-DM1), a Herceptin® antibody-drug conjugate (ADC) currently marketed by Roche, with respect to both tumour regression and survival.

In the study, 100% of mice treated with Starpharma's HER2-targeted DEP<sup>™</sup> conjugate were tumour-free within three weeks of the commencement of treatment and remained that way for the total duration of the study. In contrast, only tumour stasis was observed during treatment in the Kadcyla<sup>®</sup> group, with a maximum tumour volume inhibition of 32%<sup>1</sup> with significant tumour regrowth occurring soon after the completion of dosing.

Starpharma Chief Executive, Dr Jackie Fairley, commented, "We are very excited by these latest results for our Targeted DEP™ conjugates and the feedback from commercial parties on the study data has been very positive indeed. Both the extent and the sustained nature of the anticancer effect seen with Starpharma's DEP™ candidate have been considered most impressive. Discussions are now underway with a number of leading pharmaceutical companies in relation Targeted DEP™ conjugates and the application of Starpharma's Targeted DEP™ platform to their proprietary drugs."

This study was conducted for Starpharma by an internationally recognised cancer organisation, as part of a wider program of studies to assess various Targeted DEP™ conjugates. The study was conducted using a well-established ovarian cancer model for assessing efficacy of therapies against HER2-positive cancer cell lines.

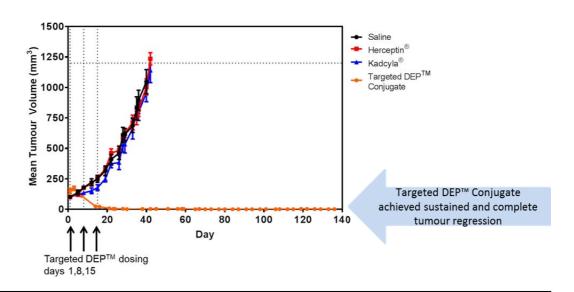
The results from this study clearly demonstrate significant and long term survival benefits for the Targeted DEP™ conjugate compared to other treatment groups, including Kadcyla<sup>®</sup>.

<sup>&</sup>lt;sup>1</sup> See Figure 3. Percentage Tumour Inhibition

The top 3 antibody based treatments in cancer (Rituxan<sup>®</sup>, Avastin<sup>®</sup> and Herceptin<sup>®</sup>) had total sales in excess of \$US20 billion in 2014. Targeted therapies for cancer, such as the ADCs Kadcyla<sup>®</sup> and Adcetris<sup>®</sup>, had combined sales in excess of US\$1 billion in 2014, with Kadcyla<sup>®</sup> sales growing at 144% versus the previous year. The market for ADCs is expected to grow to US\$9 billion annually by 2023.<sup>2</sup>

Anticancer efficacy and survival curves are illustrated in the graphs below.

Figure 1. Efficacy of HER2-targeted DEP™ Conjugate vs Kadcyla® and Herceptin® in an Ovarian\* Cancer Model

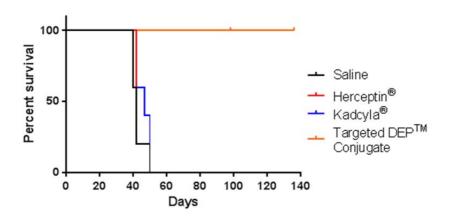


\*SKOV-3 Ovarian cancer xenograft in NOD-SCID mice (5-6/group)
Saline, Kadcyla® (10mg/kg) and Targeted DEP™ conjugate were dosed once/wk for 3 wks; Herceptin®
(20mg/kg) dosed twice/wk for 3 wks. Statistical analysis at day 40. Kadcyla® vs Targeted DEP™; P <0.0001.

(ANOVA followed by Tukey's post hoc test).

Figure 2. Kaplan Meier Survival Curve<sup>3</sup>:

Targeted DEP™ Conjugate vs Kadcyla® and Herceptin®



<sup>&</sup>lt;sup>2</sup> Roots Analysis, Antibody Drug Conjugates Market,

<sup>&</sup>lt;sup>3</sup> Statistical analysis Kadcyla<sup>®</sup> vs Targeted DEP™; *P* = 0.0011 (Mantel Cox log rank test).

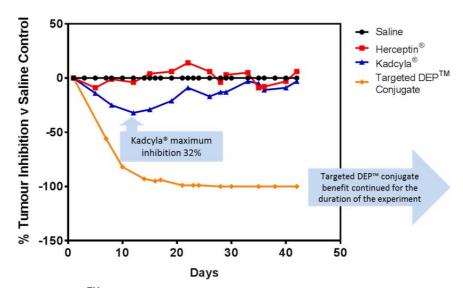


Figure 3. Percent Tumour Inhibition Compared to Saline control

\*The HER-2 targeted  $DEP^{TM}$  conjugate continued to display complete tumour inhibition for the duration of the experiment.

# **About the Study**

These latest results are an extension of the previously announced 16<sup>th</sup> November 2015 xenograft study results at 60 days post dosing with the HER2-targeted DEP™ conjugate.

Groups of animals were dosed once per week for 3 weeks with the HER2-targeted DEP™ conujgate, Kadcyla®, or a saline control. Another group of animals was treated with Herceptin® twice a week for 3 weeks.

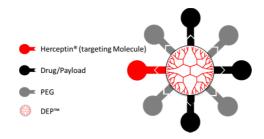
The animals treated with the HER2-targeted DEP<sup>™</sup> conjugate showed vastly superior anticancer effectiveness compared with the saline, Kadcyla<sup>®</sup> and Herceptin<sup>®</sup> treated control groups, demonstrating significant ablation of the tumours even after the first dose. Subsequent dosing resulted in 100% of mice being completely tumour-free within three weeks after the commencement of treatment and remained such for the total duration of the study. All mice in the HER2-targeted DEP<sup>™</sup> conjugate group remained within the acceptable body weight range during dosing and gained weight post dosing.

In contrast, only tumour stasis was observed during treatment in the Kadcyla<sup>®</sup> group, with a maximum tumour volume reduction, as measured at study day 12, of 32% compared with the saline control group, with significant tumour regrowth occurring soon after the completion of dosing. In accordance with ethical requirements the Kadcyla<sup>®</sup> and other control groups were discontinued at 42 days post dosing due to body weight loss and extensive tumour growth.

## Targeted DEP™ Conjugates

Starpharma's proprietary targeted DEP™ conjugate in this experiment consists of a dendrimer scaffold, a targeting group (in this case the monoclonal antibody, trastuzumab (Herceptin®)) and a "payload" of anticancer drug.

Targeted DEP™ conjugates have a number of important advantages over standard ADCs including higher drug loading and manufacturing advantages.



#### **ABOUT STARPHARMA**

Starpharma Holdings Limited (ASX:SPL, OTCQX:SPHRY), located in Melbourne Australia, is an ASX 300 company and is a world leader in the development of dendrimer products for pharmaceutical, life science and other applications.

Starpharma's underlying technology is built around dendrimers – a type of synthetic nanoscale polymer that is highly regular in size and structure and well suited to pharmaceutical and medical uses. Starpharma has three core development programs:  $VivaGel^{\circ}$  portfolio,  $DEP^{TM}$  drug delivery, and agrochemicals with the Company developing a number of products internally and others via commercial partnerships.

Starpharma's lead products are based on VivaGel® (SPL7013, astodrimer sodium), a proprietary dendrimer which has antimicrobial properties. VivaGel® formulated as a water based gel and delivered vaginally now has EU regulatory approval for topical treatment and rapid relief of bacterial vaginosis (BV) and is under clinical development for the prevention of recurrent BV. Starpharma has also signed separate licence agreements with Ansell Limited (ASX:ANN) and Okamoto Industries. Inc., (TSE: JP3192800005) to market a value-added, VivaGel® condom. The VivaGel® condom is available for purchase in Australia under Ansell's Lifestyles® Dual Protect™ brand. Ansell manufactures and sells leading condom brands worldwide, including LifeStyles®, ZERO® and SKYN®. Okamoto is the market leader for condoms sold in Japan, which is the world's second largest condom market.

In the wider pharmaceutical field, Starpharma has both partnered and internal programs in Drug Delivery. A number of dendrimer-enhanced, or DEP<sup>TM</sup> versions of existing drugs are under development. The most advanced of these is DEP<sup>TM</sup> docetaxel, a dendrimer-enhanced version of docetaxel (Taxotere®), which is in clinical development in patients with solid tumours. In preclinical studies DEP<sup>TM</sup> docetaxel has shown significant tumour-targeting and superior anti-cancer effects across a range of important cancer types including breast, prostate, lung and ovarian tumour, when compared to Taxotere® (docetaxel). AstraZeneca has signed a licensing agreement with Starpharma for the use of its DEP<sup>TM</sup> drug delivery platform in the development and commercialisation of an AstraZeneca oncology compound, with potential for follow on compounds directed at a defined family of targets.

In agrochemicals Starpharma has a series of partnerships with leading industry players including global leader Adama (formerly Makhteshim Agan) as well as internal programs including an enhanced version of glyphosate (the active ingredient in Roundup®). For more information please visit: www.starpharma.com

#### FOR FURTHER INFORMATION

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#### **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 fillings 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.