



## ASX ANNOUNCEMENT

### **DEP<sup>®</sup> irinotecan outperforms irinotecan in multiple cancer models**

- **Starpharma's DEP<sup>®</sup> irinotecan significantly outperforms Camptosar<sup>®</sup> (irinotecan) in multiple human colon cancer models**
- **DEP<sup>®</sup> irinotecan targets colorectal cancer - a significant unmet need and attractive market**
- **Further development activities for DEP<sup>®</sup> irinotecan now underway**

**Melbourne, Australia; 6 June 2017:** Starpharma (ASX: SPL, OTCQX: SPHRY) today announced that its proprietary DEP<sup>®</sup> irinotecan has demonstrated significantly better anti-tumour activity and increased survival compared with irinotecan in a variety of human colon cancer models.

DEP<sup>®</sup> irinotecan is Starpharma's dendrimer version of the already marketed major cancer drug, irinotecan, and one of several Starpharma internal DEP<sup>®</sup> candidates under development (others include DEP<sup>®</sup> docetaxel and DEP<sup>®</sup> cabazitaxel).

Irinotecan is primarily used to treat colorectal cancer, which, although one of the most common cancer types, remains an area of significant unmet need with few treatment options. Irinotecan was originally commercialised under the brand name Camptosar<sup>®</sup> and achieved peak sales of US\$1.1 billion prior to losing patent exclusivity. Irinotecan has a US FDA "Black Box" warning for severe diarrhoea and myelosuppression (including neutropenia).

In Starpharma's studies, a single treatment cycle of DEP<sup>®</sup> irinotecan administered on days 1, 8 and 15 significantly improved anti-tumour activity and enhanced survival compared to irinotecan (Camptosar<sup>®</sup>) in all cancer models tested. In the SW-620 colon cancer model, DEP<sup>®</sup> irinotecan resulted in complete tumour regression and 100% survival.

Following these impressive results for DEP<sup>®</sup> irinotecan, the Company is expediting its development and scaling up the drug for further pre-clinical studies prior to clinical trials.

Starpharma is presenting these results and other DEP<sup>®</sup> clinical programs in meetings with clinicians and partners at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago this week. ASCO brings together more than 35,000 oncology professionals, including internationally recognised oncologists, and a wide range of global pharmaceutical companies.

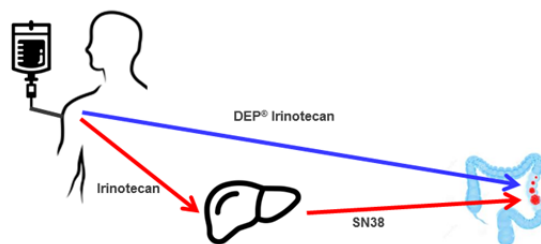
Starpharma CEO, Dr Jackie Fairley, commented: "These impressive results for DEP<sup>®</sup> irinotecan are promising in their own right, and more so when coupled with the mounting data from both our internal and partnered DEP<sup>®</sup> programs, which consistently demonstrate reproducible benefits in efficacy and tolerability from our DEP<sup>®</sup> platform using a range of anti-cancer drugs. The optionality associated with our DEP<sup>®</sup> technology is enabling us to build a pipeline of enhanced drugs, such as DEP<sup>®</sup> irinotecan, and represents a very attractive commercial scenario for Starpharma.

“We are focused on rapidly building value across the DEP<sup>®</sup> portfolio and our recently commissioned internal scale-up facilities will allow us to manufacture DEP<sup>®</sup> irinotecan, as well other internal and partnered DEP<sup>®</sup> candidates, to accelerate their development,” concluded Dr Fairley.

DEP<sup>®</sup> irinotecan is one of several anti-cancer DEP<sup>®</sup> products being developed internally by Starpharma, along with DEP<sup>®</sup> docetaxel, which is currently in the advanced stages of phase 1 clinical trial and will soon enter phase 2, and DEP<sup>®</sup> cabazitaxel, which will enter clinical trials later this year. Starpharma also has a number of partnered DEP<sup>®</sup> programs, including multiple compounds in drug development with AstraZeneca and world-leading antibody-drug conjugate companies.

### **About Irinotecan**

Conventional irinotecan is a pro-drug, which, following intravenous administration, needs to be converted in the liver to the active anti-cancer agent, known as SN-38. In contrast, Starpharma’s DEP<sup>®</sup> irinotecan incorporates the active irinotecan derivative (i.e., SN-38), avoiding the need for hepatic conversion. DEP<sup>®</sup> irinotecan is expected to accumulate preferentially in tumour tissue to exert its superior anti-tumour effect, as is seen with DEP<sup>®</sup> docetaxel and other DEP<sup>®</sup> conjugates (Diagram 1).



*Diagram 1: Graphical representation of conversion of irinotecan to SN-38 by the liver, and the direct delivery of DEP<sup>®</sup> irinotecan to the tumour*

Irinotecan is used as a component of first line therapy for the treatment of colorectal cancer (CRC), which is one of the most common cancers in the world, affecting more than 1 million individuals annually. CRC is the third most common cancer to affect both men and women, and the third-leading cause of cancer-related death, accounting for 8% of all annual cancer mortalities<sup>1</sup>.

### **Study Methods and Results**

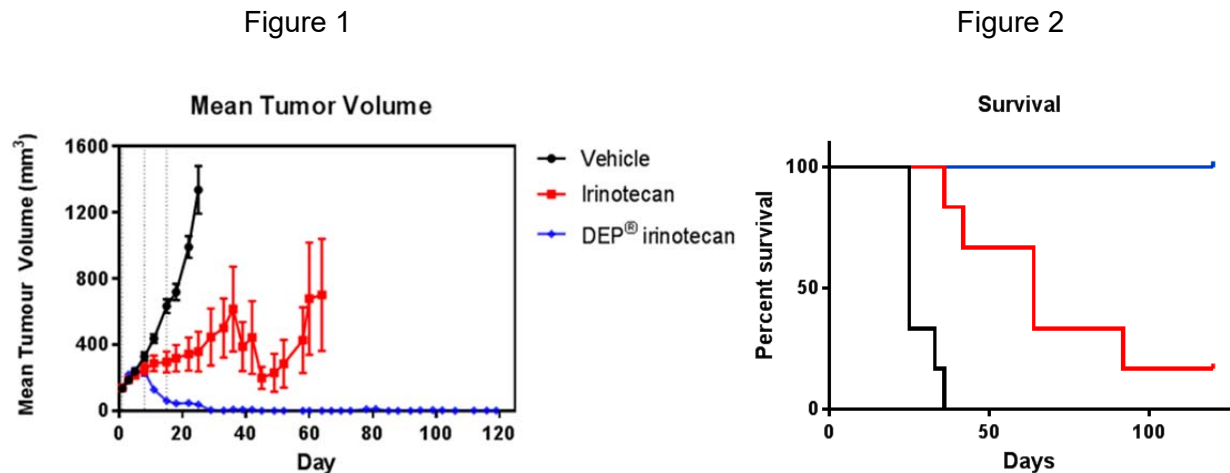
Two xenograft studies (using HT-29 and SW-620 – human colon cancer cells) were conducted for Starpharma by an internationally recognized translational cancer group as part of a wider program of studies to assess DEP<sup>®</sup> conjugates. A xenograft study uses human cancer cells, which are then implanted in a mouse, and is a well-established means of assessing efficacy of anti-cancer therapies.

Balb/c mice were inoculated subcutaneously with either the HT-29 or SW-620 cancer cell line (10 and 6 mice/group, respectively). Mice were dosed with saline (vehicle), DEP<sup>®</sup> irinotecan (25mg/kg) and irinotecan (90mg/kg) on days 1, 8 and 15 (all drug groups were dosed at the pre-determined maximum tolerated dose for each therapy). Tumour growth data were analysed in GraphPad Prism for ANOVA followed by Dunnett’s post-hoc test. The tumour volume data represent the mean  $\pm$  standard error of the mean (SEM). Kaplan-Meier survival curves were analysed using the Log-rank (Mantel-Cox) test.

<sup>1</sup> Datamonitor report – Colorectal cancer (Disease Coverage) – DMKC10877

## SW-620 Xenograft:

Complete tumour regression and 100% survival was observed in DEP<sup>®</sup> irinotecan treated animals bearing the colon cancer tumour cell line, SW-620. The tumour inhibition and survival effects of DEP<sup>®</sup> irinotecan were markedly improved compared with the irinotecan treated group and the differences were highly statistically significant ( $P < 0.0001$  and  $P < 0.0045$ , respectively) (see Figures 1 and 2).



Figures 1 and 2: Efficacy (anti-tumour effect – mean tumour volume) and survival curves comparing DEP<sup>®</sup> irinotecan to irinotecan and saline (vehicle) control. DEP<sup>®</sup> irinotecan showed markedly enhanced efficacy and survival rates compared to irinotecan and the differences were highly statistically significant ( $P < 0.0001$  and  $P < 0.0045$ , respectively).

In DEP<sup>®</sup> irinotecan-treated animals, complete tumour regression was seen as early as day 29 after the first dose and maintained to the end of the study at day 119 (Figure 3). In this model, there was no tumour regression seen with irinotecan (the anti-cancer effect was limited to a delay in tumour growth). DEP<sup>®</sup> irinotecan was well tolerated in the model.

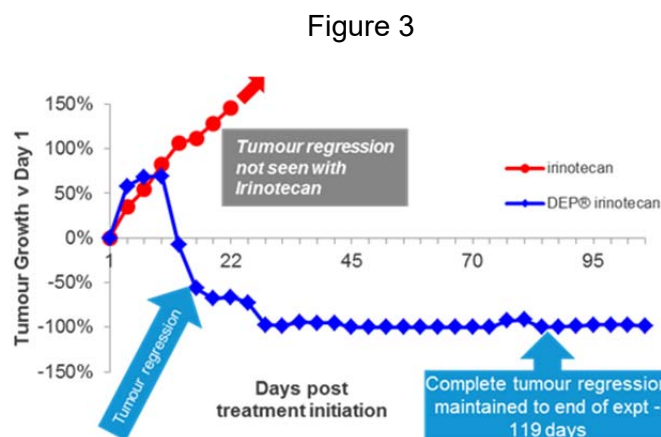
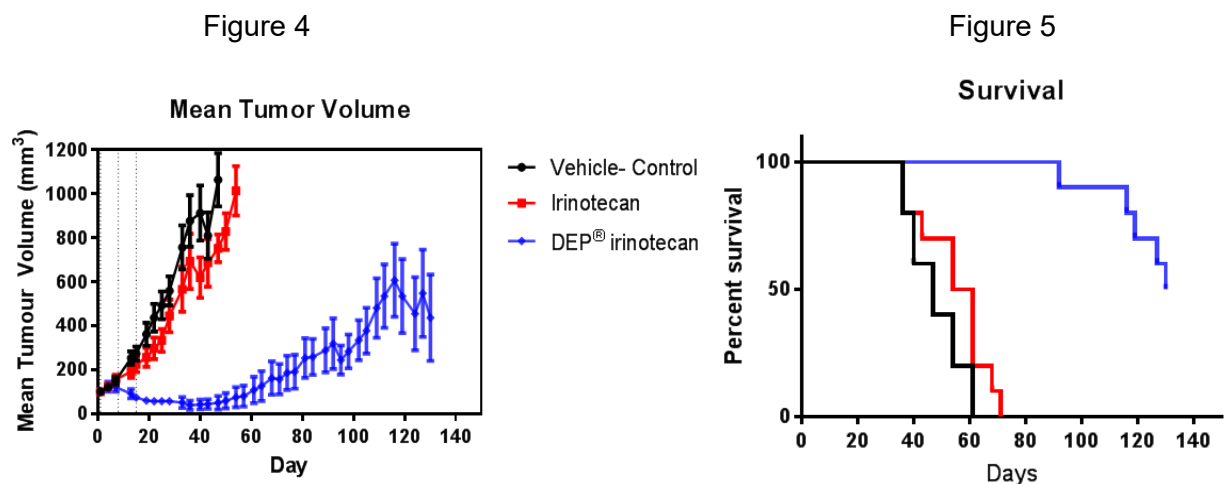


Figure 3: Tumour regression – SW-620 xenograft: DEP<sup>®</sup> irinotecan induced complete tumour regression in all mice tested, an effect that was sustained until the end of the study (day 119). This enhanced effect was highly statistically significant compared with the effect of irinotecan ( $P < 0.0001$ ). In contrast to treatment with DEP<sup>®</sup> irinotecan, tumour regression was not observed following treatment with irinotecan, and irinotecan only induced a delay in tumour growth compared with vehicle.

## HT-29 Xenograft:

DEP<sup>®</sup> irinotecan was also shown to be very effective in this colon cancer (HT-29) tumour model, which typically responds poorly to irinotecan (Figures 4 and 5). DEP<sup>®</sup> irinotecan treatment resulted in an 11.8-fold improvement in survival compared with irinotecan (Table 1).

In this study, irinotecan did not achieve appreciable anti-cancer activity compared to saline, whereas DEP<sup>®</sup> irinotecan exhibited a significant anti-cancer effect (Figure 4). DEP<sup>®</sup> irinotecan was significantly more effective than irinotecan ( $P < 0.0001$ ) for both enhanced efficacy and survival (see Figures 4 and 5). DEP<sup>®</sup> irinotecan was also well tolerated in this model.



Figures 4 and 5: Efficacy (anti-tumour effect – mean tumour volume) and survival curves comparing DEP<sup>®</sup> irinotecan to irinotecan and vehicle control. DEP<sup>®</sup> irinotecan showed enhanced efficacy and survival rates compared with irinotecan and the differences were highly statistically significant ( $P < 0.0001$  and  $P < 0.0001$ , respectively).

Table 1

Xenograft Model	Tumour type	Comparator Drug	Survival Improvement (x comparator)	Study Duration (Days)
HT-29	colorectal	irinotecan	11.8x	130

Table 1: The enhanced survival benefit seen in mice treated with DEP<sup>®</sup> irinotecan was an 11.8-fold improvement compared to that seen with irinotecan, with a 50% survival increase of 83 days over saline (vehicle). Irinotecan survival improvement was only 7 days more than that seen with vehicle.

The HT-29 cell-line is a cell-line in which irinotecan effectiveness is poor. Despite this, DEP<sup>®</sup> irinotecan was able to induce substantial tumour regression, which was not seen with irinotecan (Figure 6). A significantly enhanced tumour inhibition effect was seen with DEP<sup>®</sup> irinotecan compared with irinotecan ( $P < 0.0001$  – Dunnett's post-hoc test). At day 36, tumour growth inhibition versus saline (vehicle) was only 21% for irinotecan and 95% for DEP<sup>®</sup> irinotecan.

This significant differential anti-tumour effect of the two agents demonstrates the potential for DEP<sup>®</sup> irinotecan to overcome the lack of responsiveness to irinotecan in this model.

Figure 6

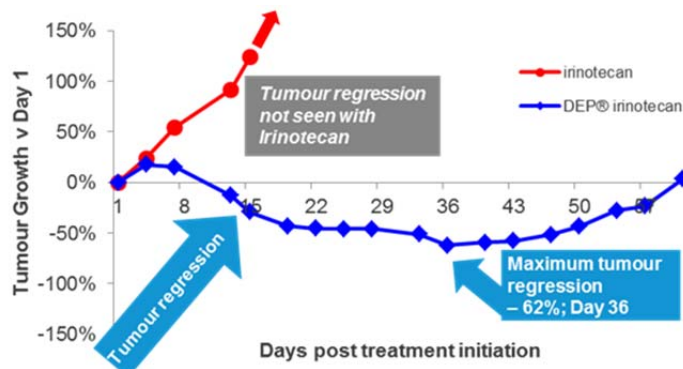


Figure 6: Tumour regression – HT-29 xenograft: DEP® irinotecan induced tumour regression in all mice tested, an effect that was observed until the end of the study (day 130). This enhanced effect was statistically significant compared with the effect of irinotecan ( $P < 0.0001$ ). In contrast to treatment with DEP® irinotecan, tumour regression was not observed following treatment with irinotecan, and irinotecan only induced a very short transient delay in tumour growth compared with vehicle.

## 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® portfolio, DEP® 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, astodimer sodium), a proprietary dendrimer. 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 signed a license agreement with Aspen Pharmacare Australia Pty Ltd for the sales and marketing of VivaGel® BV in Australia and New Zealand. Starpharma has also signed separate license agreements with Ansell Limited (ASX:ANN), Okamoto Industries, Inc., (TSE: JP3192800005), Sky and Land (China) and Koushan Pharmed (Iran) to market a value-added, VivaGel® condom. The VivaGel® condom is available for purchase in Australia and in Canada under Ansell's Lifestyles® Dual Protect™ brand. Ansell manufactures and sells leading condom brands worldwide, including LifeStyles®, Manix®, 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® versions of existing drugs are under development. The most advanced of these is DEP® docetaxel, a dendrimer-enhanced version of docetaxel (Taxotere®), which is in clinical development in patients with solid tumours. In preclinical studies DEP® 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® 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](http://www.starpharma.com)

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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 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.