



## ASX ANNOUNCEMENT

### **Dendrimer-Oxaliplatin shows better anti-cancer efficacy and less toxicity**

**Melbourne, Australia; Wednesday 11 September 2013:** Starpharma Holdings Ltd (ASX: SPL, OTCQX: SPHRY) today announced it had achieved improved tumour-inhibiting efficacy and reduced overall toxicity using a dendrimer enhanced version of the blockbuster cancer drug, oxaliplatin (ELOXATIN®).

These positive results were demonstrated in a pre-clinical study, which examined dendrimer-enhanced nanoparticle versions of oxaliplatin compared with ELOXATIN® (oxaliplatin) in a colon cancer model (xenograft).

Oxaliplatin is sold as ELOXATIN® by Sanofi and achieved sales of approximately US\$2B in 2012. It is primarily used to treat colon and colorectal cancer. Bone marrow toxicities (including the serious white blood cell disorder, neutropenia<sup>1</sup>) are reported in a high proportion of patients receiving Oxaliplatin – with rates in excess of 70%<sup>2</sup>.

The observation that Starpharma's Dendrimer-Enhanced Oxaliplatin nanoparticles substantially reduced neutropenia, a life threatening and dose-limiting toxicity is an important finding, both for this drug candidate (Dendrimer-Enhanced Oxaliplatin) and potentially also for Starpharma's platform more broadly.

"These are impressive results - that demonstrate Starpharma's dendrimer technology can be used to both enhance the efficacy and improve the safety profile of oxaliplatin, a widely used cancer treatment," said Starpharma CEO Dr Jackie Fairley.

Dendrimer-enhanced oxaliplatin is being developed as part of Starpharma's internal drug delivery program. The most advanced drug candidate in this program - a dendrimer enhanced nanoparticle of the leading anti-cancer drug docetaxel – is set to enter a Phase 1 clinical trial later this year.

These positive results achieved with Starpharma's Dendrimer-Enhanced Oxaliplatin nanoparticles are the subject of a new patent filing and given the obvious commercial potential, Starpharma now intends to advance Dendrimer-Enhanced Oxaliplatin formulations into development. Additional studies are ongoing to further explore the positive impact on bone marrow toxicity and the potential for the Dendrimer-Enhanced nanoparticles to reduce certain other clinically important toxicities.

---

<sup>1</sup> Neutropenia is an abnormally low level of neutrophils in the blood. Neutrophils are white blood cells (WBCs) produced in the bone marrow that ingest bacteria. Neutropenia is a serious disorder because it makes the body vulnerable to bacterial and fungal infections.

<sup>2</sup> ELOXATIN® Product Information; Sanofi-Aventis.co.uk

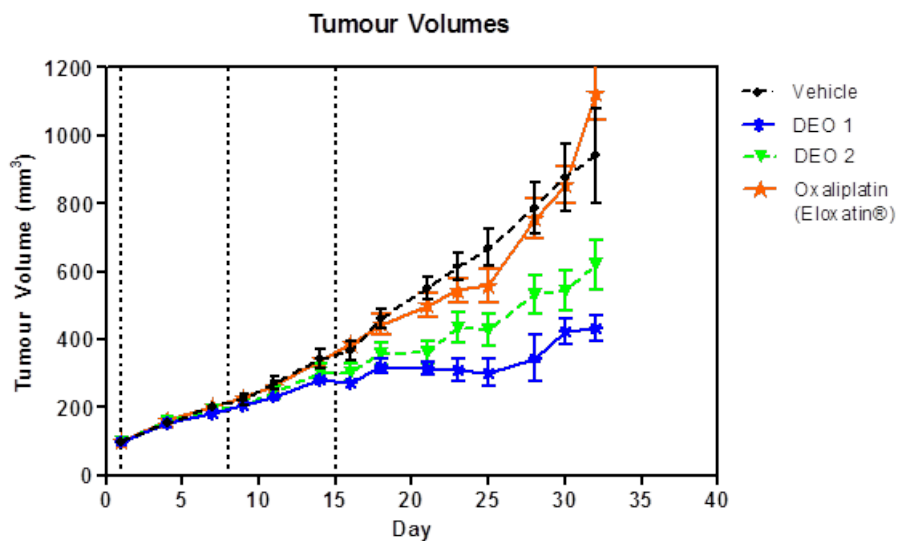
“These results and other studies indicate that Starpharma’s Dendrimer-Enhanced Oxaliplatin delivers better efficacy compared to oxaliplatin - as well as reduced neutropenia and myelosuppression<sup>3</sup> more broadly,” said Dr Fairley.

“Currently patient outcomes with oxaliplatin in colon cancer are negatively impacted by these toxicities so the clinical and commercial potential of an improved oxaliplatin product which offers both enhanced efficacy and reduced bone marrow toxicity is very significant. The fact that we also observed good anti-cancer activity in a colon cancer model that is refractory to oxaliplatin is also an impressive result for the Dendrimer-Enhanced Oxaliplatin formulations.”

### **Study Description and Findings**

The efficacy and tolerability of ELOXATIN<sup>®</sup> and two Dendrimer-Enhanced Oxaliplatin formulations (DEO1 and DEO2) were assessed using a model of human colon cancer (xenograft) in mice. Mice were implanted with human colon cancer cells (SW620). The implants were allowed to grow to tumours of a predetermined size (100mm<sup>3</sup>) and the mice (12 per group) were dosed on days 1, 8 and 15 with one of either Dendrimer-Enhanced Oxaliplatin, ELOXATIN<sup>®</sup> (oxaliplatin), or saline. Tumour volume was then assessed by manual measurement and mean tumour volume plotted against time, as shown in figure 1. Blood was collected from the mice on days 0, 7, 14, 26 and analysed for number of white blood cells (including neutrophils) and platelets per volume of blood.

### **Improvement in Efficacy**



**Figure 1 – Mouse xenograft – colon cancer (SW620) Mean Tumour volume vs time.**

**Both Dendrimer Enhanced Oxaliplatin formulations were found to be effective at inhibiting tumour growth, despite the non-responsive nature of this cancer model to ELOXATIN<sup>®</sup> oxaliplatin alone.**

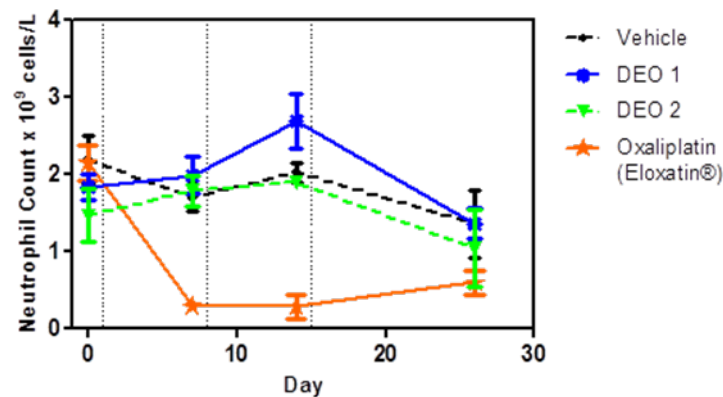
It was found that whilst the response of the colon cancer xenografts to ELOXATIN<sup>®</sup> alone was very limited (ie. it was unresponsive or refractory to oxaliplatin), the two Dendrimer-Enhanced Oxaliplatin formulations (DEO1 and DEO2) both showed good efficacy as measured by inhibition of tumour growth.

<sup>3</sup> Myelosuppression is suppression of bone marrow activity, resulting in reduction in the number of platelets, red blood cells, and blood white cells. Myelosuppression is a cause of neutropenia and low platelet numbers (thrombocytopenia).

## **Reduced Bone Marrow Toxicity (Neutropenia and Thrombocytopenia)**

In the experiment tumour-bearing mice treated with Dendrimer-Enhanced Oxaliplatin also exhibited less bone marrow toxicity than those treated with ELOXATIN® (oxaliplatin).

As shown in Figure 2 ELOXATIN® (oxaliplatin) treated mice suffered a rapid and severe drop in neutrophil count (neutropenia) as is typical in the use of that drug at effective dosing levels. In contrast, the Dendrimer-Enhanced Oxaliplatin group showed normal white cell counts and a lack of neutropenia.



**Figure 2 – Oxaliplatin treated mice exhibited severe neutropenia during the study. Neutropenia was not seen with Starpharma’s Dendrimer Enhanced Oxaliplatin.**

These observations regarding a lack of neutropenia with the Dendrimer-Enhanced Oxaliplatin formulations are consistent with separate studies which also showed that they caused less bone marrow toxicity than ELOXATIN® (oxaliplatin) alone. A similar picture, reduced toxicity with the Dendrimer-Enhanced Oxaliplatin formulations, was also observed with other white blood cell types including lymphocytes which, like neutrophils, play an important role in the functioning of the immune system.

As shown in Figure 3 and in keeping with the finding that the dendrimer formulations result in reduced bone marrow toxicity, the Dendrimer-Enhanced Oxaliplatin groups also had normal platelet counts whereas the ELOXATIN® group exhibited thrombocytopenia<sup>4</sup> (low platelet numbers).

<sup>4</sup> Thrombocytopenia means a low blood platelet count. Platelets (thrombocytes) are blood cells that play an important role in blood clotting and low levels of these cells can result in bleeding.

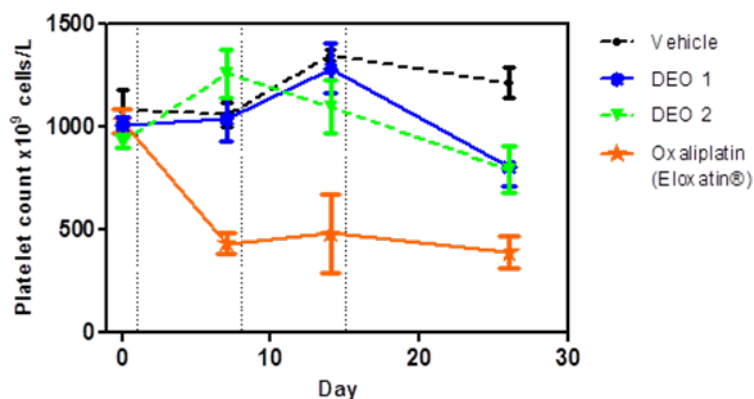


Figure 3 – Oxaliplatin treated mice exhibited severe thrombocytopenia during the study. In contrast, thrombocytopenia was not seen with Starpharma’s Dendrimer Enhanced Oxaliplatin.

### Conclusion and next steps

In addition to Starpharma’s lead internal drug delivery product, a dendrimer-docetaxel nanoparticle, the company is exploring dendrimer enhanced versions of a selected group of pharmaceuticals, including these candidates. Following the impressive results presented here and obvious commercial potential, the company intends to advance Dendrimer-Enhanced Oxaliplatin derivatives into development.

Starpharma’s internal programs have now demonstrated that its dendrimer technology has been able to yield improved efficacy with reduced toxicity for examples from three classes of major anticancer drugs: docetaxel (taxanes), Dendrimer-Enhanced Oxaliplatin (platinums) and doxorubicin (anthracyclines).

More widely, Starpharma’s drug delivery collaborations with pharmaceutical partners continue to make positive progress and the commercially attractive findings reported here add to the growing list of advantages offered by the company’s proprietary dendrimer nanoparticle technology. These advantages include: reduction in toxicity, improved solubility, tumour targeting, half-life extension, product stability, high particle loading, scalability, ease of manufacture and enhanced efficacy.

*Starpharma’s Dendrimer-Enhanced Oxaliplatin formulations are protected by a portfolio of filed and granted patents, both for the molecules themselves, and on Starpharma’s underlying drug delivery technology.*

## 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 uses. Starpharma has three core development programs: VivaGel® portfolio, drug delivery, and agrochemicals with the Company developing a number of products internally and others via commercial partnerships.

Starpharma's lead product is VivaGel® (SPL7013 Gel), a gel-based formulation of a proprietary dendrimer. VivaGel® is under clinical development for the treatment and prevention of bacterial vaginosis (BV) and also as a vaginal microbicide to prevent the transmission of sexually transmitted infections including HIV and genital herpes. Starpharma has also signed separate licence agreements with Ansell Limited (ASX:ANN) and Okamoto Industries Inc (Tokyo Stock Exchange) to market a value-added, VivaGel®-coated condom. Ansell manufactures and sells leading condom brands worldwide, including Lifestyles®, ZERO® and SKYN®. Okamoto is the market leader for condoms sold in Japan, the world's second largest condom market.

In the wider pharmaceutical and life science fields, Starpharma has both partnered and internal programs in Drug Delivery. Drug Delivery partners include GSK, Lilly and AstraZeneca. In its internal program Starpharma has announced significant tumour-targeting results in its docetaxel (Taxotere®) program, with animal studies showing its dendrimer-enhanced version of docetaxel to have significantly superior anti-cancer effects across a range of important cancer types including breast, prostate, lung and ovarian tumour, when compared to Taxotere® (docetaxel).

In agrochemicals Starpharma has a series of partnerships with leading industry players including Nufarm (ASX:NUF) and Makhteshim Agan as well as internal programs including an enhanced version of glyphosate (the active ingredient in Roundup®).

#### FOR FURTHER INFORMATION

##### **Media:**

##### **Buchan Consulting**

Rebecca Wilson

Mob: +61 417 382 391

[rwilson@buchanwe.com.au](mailto:rwilson@buchanwe.com.au)

Danny Rose

Mob: +61 407 25 00 88

[drose@buchanwe.com.au](mailto:drose@buchanwe.com.au)

##### **Starpharma:**

Dr Jackie Fairley, Chief Executive Officer  
+61 3 8532 2704

Ben Rogers, Company Secretary

[ben.rogers@starpharma.com](mailto:ben.rogers@starpharma.com)

[www.starpharma.com](http://www.starpharma.com)

#### **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.