

# Starpharma's Dendrimer-Docetaxel eliminates neutropenia

**Melbourne Australia**; 24 October 2013 - Starpharma Holdings Ltd (ASX: SPL; OTCQX: SPHRY) today announced additional positive results for its dendrimer formulation of the major chemotherapeutic, docetaxel (Taxotere<sup>®</sup>), ahead of its advancement into clinical trials later this year.

In the preclinical study, animals treated with Starpharma's Dendrimer-Docetaxel formulation exhibited a lack of neutropenia. In contrast, animals treated with Taxotere<sup>®</sup> in this study exhibited severe neutropenia, a sign of bone marrow toxicity and the most important dose-limiting side effect of Taxotere<sup>®</sup>.

Docetaxel, which is now generic, has reported annual sales of \$3.1 billion. The originator is marketed worldwide under the trade name Taxotere<sup>®</sup>.

Severe neutropenia (abnormally low circulating neutrophil numbers) is a life threatening toxicity that occurs in more than 75% of patients<sup>1</sup> treated with docetaxel (Taxotere<sup>®</sup>). Neutrophils are a type of white blood cell, so severe neutropenia exposes the patient to a high risk of serious infection and requires modification to dosing schedules, rescue therapy with expensive drugs, and additional clinical management. Taxotere<sup>®</sup> has an FDA "black box" warning in its product information regarding neutropenia including contraindications and management requirements for certain patients.

"These latest results are really very positive for our Dendrimer-Docetaxel formulation in the lead up to its move into the clinic," said Starpharma Chief Executive Officer, Dr Jackie Fairley.

"We have now shown that Starpharma's dendrimer technology can prevent neutropenia as observed in independent studies of two leading cancer drugs, docetaxel and oxaliplatin. These findings suggest that the ability to avoid these important toxicities is likely to be a feature of the dendrimer platform and therefore, could also be anticipated with other cancer drugs."

Starpharma's proprietary Dendrimer-Docetaxel formulation has also previously been reported to show other significant benefits compared to Taxotere<sup>®</sup>. In its preclinical development, the Dendrimer-Docetaxel formulation has been shown to:

• be water soluble (removing the need for Polysorbate 80, a detergent which is present in Taxotere<sup>®</sup> and most other formulations of docetaxel, and which causes the serious toxicity, anaphylaxis)

<sup>&</sup>lt;sup>1</sup> Taxotere<sup>®</sup> Approved Product Information

- have excellent drug targeting to tumour tissue (more than 40 times greater levels than Taxotere<sup>®</sup>)
- have a markedly extended half-life (60 fold increase in plasma half-life), and
- have significantly enhanced anticancer effect when compared to Taxotere<sup>®</sup>.

"When all these advantages and clinically significant benefits of the Starpharma Dendrimer-Docetaxel formulation are placed alongside the latest findings of a lack of neutropenia, it places the dendrimer formulation in a very compelling competitive position. It is particularly pleasing to have these latest findings ahead of taking the product into the clinic later this year," said Dr Fairley.

## **Description of Study**

This study was conducted as part of the pre-clinical program ahead of commencement of clinical trials. The relative toxicities of the Dendrimer-Docetaxel formulation and Taxotere<sup>®</sup> were compared in a study where equivalent doses (based on docetaxel; 9mg/kg) were administered to male and female rats by intravenous injection on Day 0. Blood samples were taken at day 0 prior to dosing, then at days 7, 14 and 21. The level of neutrophils, expressed as the mean absolute count across all animals in the dose group (n=6 per group), at each time point are shown in Figure 1.



Figure 1: Neutrophil levels as measured weekly over 21 days, showing the lack of neutropenia in animals treated with the Dendrimer-Docetaxel formulation. In contrast, Taxotere<sup>®</sup> treated mice show marked neutropenia and the typical rebound neutrophilia, which follows.

As can be seen from Figure 1, the neutrophil counts of the Dendrimer-Docetaxel formulation treated rats remained normal throughout the study. Rats treated with Taxotere<sup>®</sup> exhibited a significant neutropenia resembling the neutropenia that is commonly seen in humans. These results indicate that the Dendrimer-Docetaxel formulation did not cause neutropenia.

In this study, the Dendrimer-Docetaxel formulation treated rats were also free from other bone marrow toxicities such as thrombocytopenia (low platelets) which were observed in Taxotere<sup>®</sup> treated animals.

"The potential to be able to use docetaxel with reduced need for expensive rescue therapies or additional hospital stays represents an important advance for patient care. Apart from better patient outcomes, the potential savings for constrained health-care budgets are also very attractive," Dr Fairley added.

Whilst Starpharma's most advanced drug delivery program is docetaxel, the technology has value more broadly as it can be applied to a wide variety of drugs (including proteins, antibodies, hormones) in addition to being particularly valuable in cancer treatments. The company recently announced its dendrimer-enhanced formulation of oxaliplatin, a leading treatment for colon and colorectal cancer, significantly reduced bone marrow toxicity and neurotoxicity in preclinical studies.

### 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<sup>®</sup> 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<sup>®</sup>) 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<sup>®</sup> (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<sup>®</sup>).

#### 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 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 health authorities' requirements regarding any one or more product candidates nor can there be any assurance that such product candidates will be approved by any health 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 clinical trial results, including additional analysis of existing clinical data, and new clinical 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.