

# **Starpharma Dendrimer Reduces Toxicity of Cancer Drug**

**Melbourne, Australia; 17 December 2008:** Starpharma Holdings Ltd (ASX:SPL, OTCQX:SPHRY) today reported an important advance in its dendrimer-based drug-delivery program.

A Starpharma dendrimer combined with a widely-used cancer drug (doxorubicin) has achieved a significant extension of the drug's plasma half-life and a marked reduction in drug toxicity compared to administration of the drug alone. In this proof-of-concept animal study the efficacy of the dendrimer-drug construct was equivalent to that of the drug alone.

Doxorubicin was selected to illustrate the delivery technique because of its wide use as an anticancer agent, having application in Hodgkin's lymphoma, some leukemias, as well as cancers of the breast, lung, and ovaries. The clinical use of doxorubicin is often constrained by its cardiac toxicity which may result in congestive heart failure and dilated cardiomyopathy.

In Starpharma's recent study, an animal cancer-model ("xenograft") showed that Starpharma's dendrimer-doxorubicin construct (SPL8181) achieved the same inhibition of human breast-cancer tissue as doxorubicin alone (Figure 1), but with markedly reduced cardiac toxicity. Blinded histopathological examination of cardiac tissue samples from the dosed animals revealed (Figure 2) significantly lower cardiotoxicity (p=0.019) in the dendrimer-doxorubicin construct treatment group (toxicity in 14% of samples) compared to a doxorubicin-only treatment group (toxicity in 86% of samples). Signs of reduced toxicity in other organs were also observed for the animals dosed with the dendrimer-based molecule compared to doxorubicin alone.

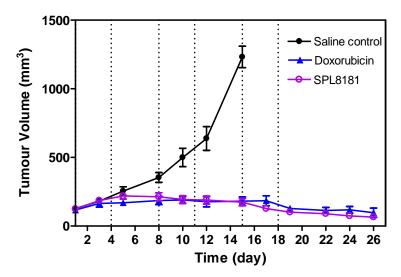
Starpharma's delivery technology works by attaching multiple drug molecules to the surface of a dendrimer nanoparticle. The result is that the dendrimer nanoparticle can target the drug to the tumour, in preference to other organs. This effect is illustrated for a second cancer molecule in Figure 3. Additionally Starpharma's proprietary dendrimer technology has been engineered to allow for the drug payload to be preferentially released from the nanoparticle in close proximity to the tumour.

Starpharma CEO, Dr Jackie Fairley said "Starpharma has already formed a number of partnerships based on its drug-delivery technology, including a dermal program with Stiefel Laboratories. The technology has application for both small molecule drugs and protein therapeutics and Starpharma is in advanced discussions with additional potential partners who have an interest in using it to improve the delivery, efficacy, and toxicity profile of their products."

The animal studies were conducted in collaboration with Associate Professor Chris Porter of the Victorian College of Pharmacy and Dr Carleen Cullinane of the Peter MacCallum Cancer Centre.

Starpharma has already taken a dendrimer-based drug into clinical trials conducted to US FDA requirements: VivaGel® vaginal microbicide is currently in Phase II clinical trials, and is the subject of a license agreement with Durex® condoms for use as a condom coating.

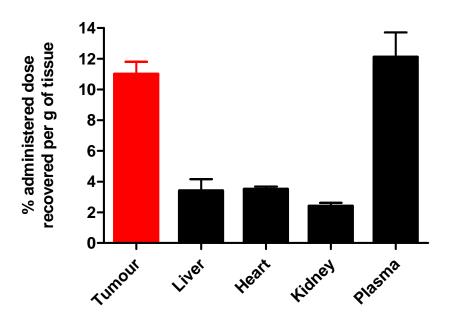
# Figures:



**Figure 1:** Results from a mouse xenograft tumour model of human breast cancer showing that the doxorubicin-containing dendrimer construct, SPL8181, is equivalent to doxorubicin alone in inhibiting tumour growth. The graph represents tumour volume (mm³) over time (days) following dosing with a saline control (n=5), doxorubicin (n=4), or SPL8181 (n=5). Doses were administered twice a week for three weeks on days 0, 4, 8, 11, 15 and 18 (dotted lines).

	Cardiac Toxicity		
	Yes	No	
Saline control (n=4)	0	4	
Doxorubicin (n=7)	6	1	
SPL8181 (n=7)	1	6	

**Figure 2**: Results from blinded histopathological examination of mouse cardiac tissue following dosing with saline control, doxorubicin, or SPL8181 in a mouse xenograft tumour model of human breast cancer. There was a highly significant difference between the number of animals showing cardiac toxicity, as indicated by vacuolation of myocardial fibres, inflammatory cell infiltrates and loss of cross-striation. The SPL8181-treated group showed lower toxicity (1 out of 7) compared with the group treated with doxorubicin alone (6 out of 7) (\*p=0.019, by a logistic regression analysis (pairwise) with a Bonferroni adjustment). These results indicate that cardiac toxicity caused by doxorubicin alone was significantly reduced by delivery of the drug as the doxorubicin-containing dendrimer construct, SPL8181.



**Figure 3.** Results from a tissue distribution study of a methotrexate-containing dendrimer construct in a mouse xenograft tumour model of human colon cancer (n=5). In this study, the construct was preferentially localized in tumour compared with liver, heart and kidney.

#### **About Starpharma**

Starpharma Holdings Limited (ASX:SPL, OTCQX:SPHRY) is a world leader in the development of dendrimer nanotechnology for pharmaceutical, life-science and other applications. SPL has two operating companies, Starpharma Pty Ltd in Melbourne, Australia and DNT, Inc in the USA. Products based on SPL's dendrimer technology are already on the market in the form of diagnostic elements and laboratory reagents through licence arrangements with partners including Siemens and Merck KgA.

The Company's lead pharmaceutical development product is VivaGel® (SPL7013 Gel), a vaginal microbicide designed to prevent the transmission of STIs, including HIV and genital herpes. In September 2008 Starpharma signed a full licence agreement with SSL International plc (LSE:SSL) to develop a VivaGel® coated condom. SSL manufactures and sells Durex® condoms, the market-leading condom brand worldwide. Starpharma's receipts under the agreement are estimated to exceed A\$100m comprising royalties on SSL sales, further milestone payments, and development support.

In the wider pharmaceutical field Starpharma has specific programs in the areas of Drug Delivery and Drug Optimisation technologies (using dendrimers to control where and when drugs go when introduced to the body) and Targeted Diagnostics (using dendrimers as a scaffold to which both location-signalling and targeting groups are added to allow location of specific cell type, such as cancer cells). More broadly the company is exploring dendrimer opportunities in materials science applications including water remediation.

**Dendrimer:** A type of precisely-defined, branched nanoparticle. Dendrimers have applications in the medical, electronics, chemicals and materials industries.

American Depositary Receipts (ADRs): Starpharma's ADRs trade under the code SPHRY (CUSIP number 855563102). Each Starpharma ADR is equivalent to 10 ordinary shares of Starpharma as traded on the Australian Stock Exchange. The Bank of New York Mellon is the depositary bank. Starpharma's ADRs are listed on International OTCQX (<a href="www.otcqx.com">www.otcqx.com</a>), a premium market tier in the U.S. for international exchange-listed companies, operated by Pink Sheets, LLC.

### **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.

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