



ASX ANNOUNCEMENT

## **Dendrimers improve anticancer efficacy in lung metastasis model**

**Melbourne Australia; 4 March 2013** – Starpharma Holdings Ltd (ASX:SPL;OTCQX:SPHRY) today announced the results of an animal study which shows that a dendrimer-based formulation of doxorubicin was substantially more efficacious in treating secondary tumours of breast cancer (metastases) in lungs than the drug alone.

The study involved a dendrimer formulation of the widely used cancer drug doxorubicin delivered via intra-tracheal administration, and was substantially more efficacious than doxorubicin alone in treating lung metastases of breast cancer.

The study was conducted as part of an ARC (Australian Research Council) funded collaboration with Monash Institute of Pharmaceutical Sciences (MIPS). It utilised a rat model which uses lung-resident secondary tumours (or metastases) derived from breast cancer cells. Lung metastases are particularly difficult to treat with conventional chemotherapeutic drugs, leading to a mortality rate of approximately 85% within 5 years, and existing treatments may often be considered palliative in nature. Commonly used treatments include doxorubicin, either alone or in combination with other agents.

In addition to the improvement in efficacy, the study also found that the dendrimer-doxorubicin formulation tended to remain in the lungs rather than passing into the body of the animal. This distribution pattern also creates the potential for reduced side effects, which are a significant problem with many cancer drugs, including doxorubicin.

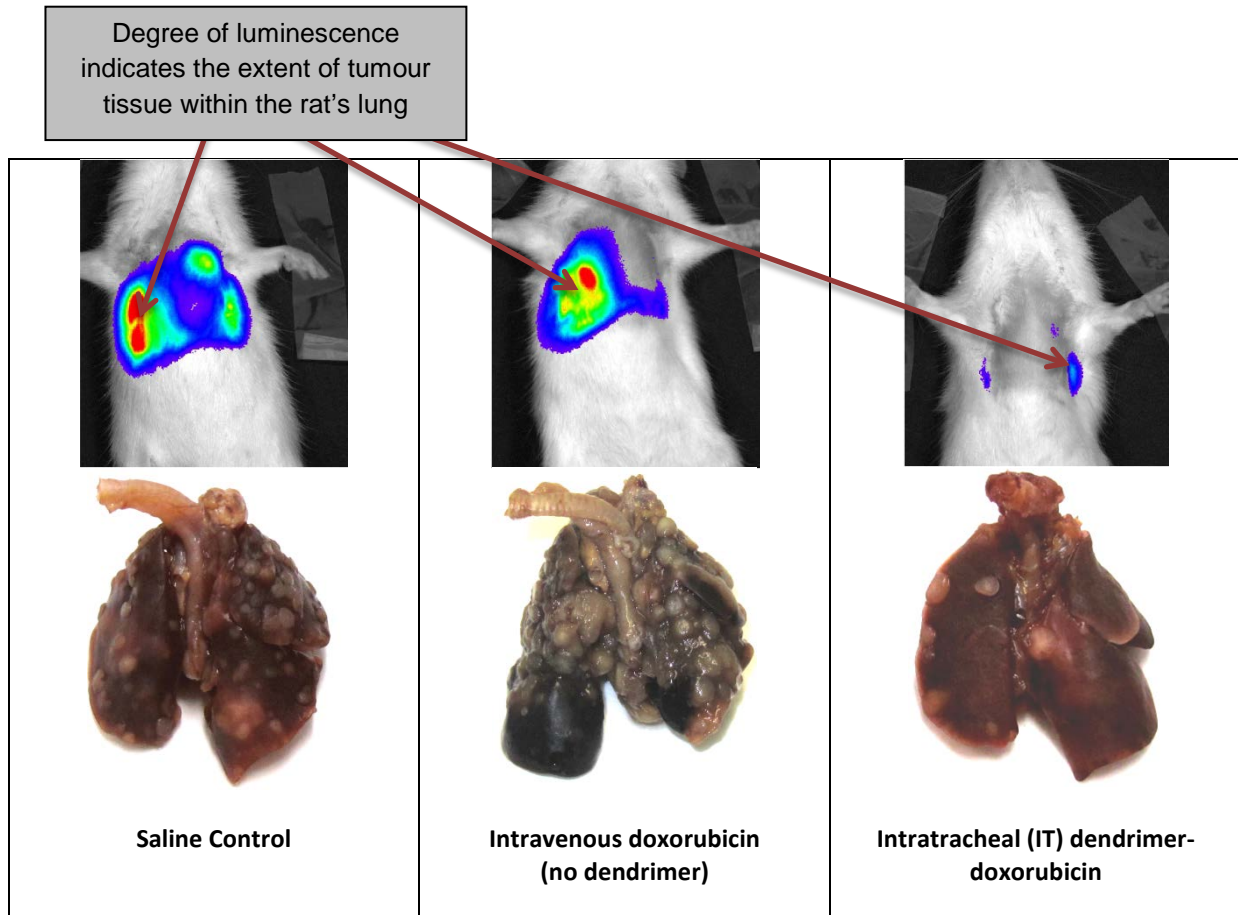
Dr Jackie Fairley said: "The combination of Starpharma's dendrimers, an existing cancer drug and direct lung administration appears to yield a substantially more efficacious agent for treating lung metastases than the drug alone. Given the clinical management of lung metastases is an area of significant medical need, and current drugs often provide poor results, this finding has the potential to create a valuable and important application for Starpharma's proprietary dendrimer formulations."

Starpharma has recently filed a new patent based on these results as a precursor to further discussions with commercial partners.

### **Results and Methods**

This rat lung metastasis model is intended to replicate the situation in humans in which breast cancer cells separate from the primary breast tumour and "metastasize" or spread, seeding new tumours to multiple points throughout a lung.

Figure 1 shows results from the study in which rats with lung-resident tumours derived from breast cancer cells were treated with either saline (left panel), intravenous doxorubicin (centre panel), or intra-tracheal dendrimer-doxorubicin (right panel). [Note: results from intra-tracheal delivery of doxorubicin alone could not be generated as this route of administration proved too toxic for the drug in the absence of dendrimer.]



**Figure 1 – Rat Lungs: Bioluminescent Images and Gross Pathology**

The figure shows both the gross appearance of the rat lungs and bioluminescent images of the chest at the end of the experiment (day 18-21). The degree of luminescence indicates the extent of tumour tissue within the rat's lungs (top), and a photograph of the exterior of the lungs (bottom) is also shown.

As can be seen by both gross appearance of the lungs and the bioluminescent images, the extent of lung metastases was greatly reduced in the intra-tracheal dendrimer-doxorubicin group compared with other treatment groups (intravenous doxorubicin and a saline control).

To conduct the study, rats were dosed with breast cancer cells by tail vein injection (Day 0). These tumour cells had been transfected with the luciferase gene allowing imaging of resultant tumours by a technique known as bioluminescent imaging. Following administration, breast cancer cells migrated to the lungs, lodged there and began to replicate, initially without treatment. From Day 7 different treatment formulations were administered to the rats twice a week for two weeks. At the end of the experiment (day 18-21, depending on the extent of tumour growth) all rats were sacrificed and an assessment

was made of their lung pathology and degree of metastasis using both visual inspection of the gross pathology and bioluminescent imaging.

Work is now underway to further explore these findings, including examination of the effect of dosage in metastatic models and the testing of other dendrimer drug combinations. Starpharma is also investigating potential explanations for this finding including the observation that its dendrimer nanoparticles appear to be selectively concentrated in tumour tissue and within the lymphatic system - which plays an important role in tumour spread.

The work was conducted as part of an on-going collaboration between Starpharma and Professor Chris Porter, Dr Lisa Kaminskis, and their colleagues at MIPS. The collaboration is funded through the ARC linkage scheme and is exploring a range of novel applications of dendrimers as drug delivery systems. Data generated under this program also supports Starpharma's in-house oncology program including its proprietary dendrimer-docetaxel formulation being developed for intravascular use and due to enter the clinic later this year.

Starpharma's internal oncology program sits alongside a number of partnered drug delivery programs (including for a range of indications with Lilly, GSK and AstraZeneca), and Starpharma's development programs and commercial relationships based on VivaGel® in BV (bacterial vaginosis) and as a condom coating (licensed to Ansell and Okamoto).

## 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. 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).” The company is also exploring dendrimer opportunities in agrochemicals in a series of industry partnerships with leading industry players including Nufarm (ASX:NUF) as well as with internal programs including an enhanced version of glyphosate (the active ingredient in Roundup®).

## FOR FURTHER INFORMATION

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### Forward Looking Statements

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