

## Shareholder Update: May 2007

> This edition showcases the latest commercial deal for Starpharma subsidiary Dendritic Nanotechnologies (DNT) - the first since the acquisition was completed last year, and provides an insight into the other commercial opportunities for DNT currently being progressed. According to DNT President Robert Berry, DNT's technology even has applications in water purification. We hear from the Starpharma CEO on her recent investor trip to the United States and the progress being made there, and an update on the status of VivaGel<sup>™</sup> which continues to progress through the clinic.

## First DNT commercial milestone post acquisition – siRNA license and supply agreement with EMD Biosciences

In February, Starpharma announced its first commercial deal following the October 2006 acquisition of DNT - a worldwide exclusive license and supply agreement for dendrimers as small interfering RNA (siRNA) transfection reagents with EMD Biosciences, part of Merck KGaA's Performance and Life Science Chemicals division.

Under this deal DNT will supply EMD Biosciences its PrioFect<sup>™</sup> transfection reagents based on Priostar<sup>™</sup> proprietary dendrimers for the DNA and siRNA transfection research markets. The undisclosed terms of the agreement include royalties and milestone payments. Under the EMD agreement Starpharma has retained rights to the application of dendrimers in siRNA-based drugs and is actively progressing commercial discussions in this area.

DNT's PrioFect<sup>™</sup> transfection reagents will be launched later this year into the US\$200 million-market for nucleic acid, DNA and siRNA research. Many observers of the pharmaceutical and biotechnology sectors predict that the future application of siRNA technology will provide highly specific new drugs for the treatment of a wide range of diseases.

Small interfering RNA is a crucial component of a cellular process called RNA interference (RNAi) that causes degradation of specific RNA molecules and, as a result, prevents expression of the corresponding genes.

PrioFect<sup>™</sup> dendrimers have features which can overcome many of the limitations of commonly used siRNA transfection reagents. In addition, the surface of PrioFect<sup>™</sup> dendrimers can be modified to include chemical groups that allow targeting, a feature which is of great interest to developers of siRNA therapeutic agents.

## Financials for quarter ended March 2007

Cash at the end of the March quarter was A\$12.7 million, which is A\$1.5 million greater than the previous quarter. Receipts of A\$4.7 million for the quarter included grant funding payments, primarily from the U.S. National Institutes of Health (NIH), together with receipts from commercial relationships including the recently announced siRNA deal with EMD Biosciences



# Improved share access for US investors through premium trading site OTCQX



Starpharma's management continues to develop the company's investment profile in the United States by enhancing its listing

arrangements there. Over the last 18 months Starpharma has seen strong growth in the uptake of its ADRs trading as SPHRY. US investors now account for 10.8% of issued capital.

In March this year a new premium tier market for Level 1 ADRs was established and Starpharma was invited to join. Under the new programme daily volumes in SPHRY have increased by approximately 55% and several market makers including Merriman Curhan Ford, Hill Thompson, Jefferies, and Knight Capital are actively trading in the stock.

According to CEO Jackie Fairley, this encouraging level of US investor interest is driven primarily by the following factors:

- > Investor and consumer awareness of sexually transmitted infections (STIs) is particularly high in the US, where genital herpes already infects more than one in four women. Active direct-to-consumer advertising of herpes medications has resulted in US investors and consumers having an acute awareness of the risks of acquiring the disease. As a result, US investors readily understand the commercial opportunity offered by VivaGeI<sup>™</sup>, and the projected market estimates for microbicides support this potential.
- > There is growing concern over the significant healthcare costs and personal impact of STIs - including life-long drug treatment and the need for caesarean delivery where mothers are infected by genital herpes.

- > VivaGeI<sup>™</sup> has been the recipient of significant funding support from the highly regarded US National Institutes of Health (NIH). This funding support - in excess of US\$26m across the company's microbicide programs, is non-dilutive to shareholders, and is allowing the company to progress the clinical trial program of VivaGeI<sup>™</sup> as rapidly as possible and with the benefit of accessing the considerable expertise of the NIH.
- > With the completion of the integration of DNT Starpharma has a US subsidiary with a new siRNA deal with EMD Merck, revenue streams from existing commercial arrangements, and a number of valuable technology platforms and development programs.
- > The Dow Chemical Company (NASDQ:DOW) is now a major shareholder.



CEO Dr Jackie Fairley

"We see growing and active US investor support for Starpharma as being a catalyst to future short and long term shareholder value and believe a growing US profile will also establish a solid foundation for the commercialisation and launch of our products," said CEO Jackie Fairley.

As part of an active program to raise the investor profile of the company, Starpharma management recently

presented the company to US brokers and investors, and at a major healthcare investor conference. Additional US initiatives are planned in the coming months and are expected to further build demand and trading volumes.

## Status Update - VivaGel™

Starpharma is developing SPL7013 Gel (VivaGel<sup>™</sup>) as a topical microbicide for prevention of HIV and genital herpes. Topical microbicides are critical tools in the fight against the spread of HIV and other sexually transmitted infections for which vaccines and other preventive measures have so far been unsuccessful. In a recent *Nature Medicine* survey of leading scientists in the field, little hope was given of a safe and effective vaccine for HIV being developed any time in the next 10 years. This reaffirms the opportunity for an effective microbicide.

Starpharma is pleased to report that the clinical trial to assess the safety and acceptability of VivaGel<sup>™</sup> in males has now been completed and the product was very well tolerated. These results will advance the development of VivaGel<sup>™</sup> for prevention of both HIV and genital herpes and will support the use of VivaGel<sup>™</sup> in upcoming trials in sexually-active women. Data from the trial will be presented at international scientific conferences later this year.

The expanded safety study in females in San Francisco (UCSF) and Kisumu in Kenya continues to progress well. This trial, reported in the previous update, involves 60 sexually inactive, healthy women between the ages of 18 and 24 to test the effects of twice daily application of VivaGel<sup>™</sup> for 14 days.

The first trial of VivaGeI<sup>™</sup> in sexually active women is set to commence in the US shortly. The trial will assess the product's safety in addition to its acceptability and ease of use. (continued from page 2) This expanded safety study will be conducted at two US trial sites - the University of South Florida in Tampa, and the University of Puerto Rico in San Juan by the Microbicide Trials Network (MTN, an HIV/AIDS clinical trials network established and funded by the National Institute of Allergy and Infectious Diseases, part of the US NIH).

Preclinical aspects of the VivaGel<sup>™</sup> development program are progressing well and the active ingredient scale-up to 10kg batches is nearing completion.

#### Vivagel<sup>™</sup> as a condom coating

Development work on the exciting commercial opportunity for the VivaGeI<sup>™</sup> active (SPL7013) as a condom coating continues with high priority. Starpharma has been working with condom manufacturers to develop supporting data and establish the most effective commercial structure for this line extension of VivaGeI<sup>™</sup>. Recent months have seen substantial progress and Starpharma remains very positive about this commercial opportunity.

# Innovative dendrimer-based approaches to more effective drug treatments

#### Starpharma technology extends beyond VivaGel<sup>™</sup>.

Although Starpharma's best known and most advanced pharmaceutical product is VivaGel<sup>™</sup>, Starpharma is also developing its dendrimer technology to address important challenges in today's pharmaceutical and life science industries. Starpharma's dendrimers offer significant commercial potential through their application to drug delivery - the more effective delivery of existing drugs.

According to Dr David Owen, Starpharma's VP of Research, many drugs would be enhanced if more accurately directed to their target tissue.

"Dendrimers have the potential to improve various properties of drugs and the way in which they are administered to patients because of the large number of active groups that can be incorporated onto the surface of dendrimers during their synthesis. They can be made with high purity and a well-defined chemical composition – two important attributes for drugs."

Dendrimers can connect a number of different molecules together into a single, multifunctional particle. For example, a single dendrimer can carry beside the active drug, a recognition molecule that directs it to the desired target tissue, or a molecule that increases the time that a drug remains active in the bloodstream.

A common challenge in drug development is the successful delivery of the active compound to its target tissue with no adverse side effects. The pursuit of better ways to deliver new and established therapeutic compounds is an area of keen interest for pharmaceutical companies. They are also becoming increasingly focussed on finding new methods of delivering existing drugs in order to extend the life of patents. A solution to this challenge for a range of drugs would be extremely valuable.



Pharmaceutical companies are often interested in increasing the time that their drugs remain in the body (the socalled 'half life'). This is particularly true for biologicals, which are often broken down quickly by enzymes and removed from the body. Dendrimers have the potential to keep both small molecule drugs and biological agents (such as insulin, growth hormone or EPO) in the body for longer by decreasing

the rate of clearance by the kidney or the rate of drug metabolism. Starpharma refers to this technique as ADME (Absorption, Distribution, Metabolism, Excretion) Engineering<sup>™</sup>.



The company is currently in discussions with several well-known pharmaceutical and biotechnology companies to develop programs that will advance these compounds and provide them with a route to market.

Starpharma's dendrimer technology is a platform, meaning that it has the potential to be licensed multiple times. This situation is advantageous, potentially leading to a wide range of drugs that are enhanced using dendrimer technology, and, consequently, multiple royalty streams to Starpharma.



## Profile on DNT commercial opportunities

DNT's successful licensing of its PrioFect<sup>™</sup> technology to EMD Biosciences is the most recent example of the commercial opportunity of dendrimer technology. DNT also has a series of existing royalty bearing licensing agreements, and sales and distribution deals that are generating revenue. DNT currently has commercial licensing and supply agreements with Dade Behring, Sigma Aldrich and Qiagen generating approximately \$1m in revenue per annum. The prospect for further revenue growth is high as DNT progresses the development of its technology and secures new commercial partners.

The following provides a snapshot of some of the diverse applications of dendrimers being pursued at DNT – from improving Magnetic Resonance Imaging (MRI) contrast agents through to purifying water.

### Increasing the strength of fluorescent dyes

Fluorescent reagents are used extensively in a range of research applications, including high-throughput screening, diagnostic immunoassays, microarrays, fluorescence microscopy, genomics and proteomics. DNT's Priostar<sup>™</sup> dendrimer technology has recently been demonstrated to amplify the signal and increase the duration of the signal of existing products in the multi-billion dollar fluorescent reagents market. The Company has filed a patent based upon this discovery and is in discussions with existing suppliers of fluorescent reagents to establish a rapid route to market for these dendrimer-dye conjugates.

## Priostar<sup>™</sup> dendrimers in the cosmetic and personal care industry

In cosmetics, Priostar<sup>™</sup> dendrimers have been shown to improve the solubility, stability and adhesion of the active components in cosmetic formulations, and may also be used to control their release.

The US and Western European market for delivery systems for cosmetics – including products for personal care – and specialty actives were together estimated by Kline and Company at about US\$400 million in 2005, and growing rapidly.

DNT's US-based business development group has already initiated discussions with high-end cosmetic providers to explore these high margin commercial possibilities.

## Enhancing the signal from contrast agents used in Magnetic Resonance Imaging (MRI)

DNT has a US\$850,000-contract with the National Cancer Institutes (NCI) in the US to examine how dendrimers can improve the images captured by MRI. Early data have shown that attachment of a contrast agent to dendrimers before injection gives a stronger MRI signal, probably because multiple contrast molecules are concentrated on one dendrimer particle.

#### Dendrimers in water remediation

Through a collaboration with the Strategic Environmental Research and Development Program (SERDP) of the U.S. Department of Defense, DNT is exploring the use of dendrimers for water remediation, that is, using dendrimers to remove toxins and other impurities from water. The first project will explore the removal of perchlorate from drinking water, known to be a 'serious and growing problem' in some parts of the US and elsewhere. Other possible impurities that could be removed from water include heavy metals such as copper, lead and zinc.

### Supply Agreement with Sigma-Aldrich

In March DNT announced an expansion of its supply agreement with Sigma-Aldrich. DNT will initially supply the new STARBURST<sup>®</sup> dendrimer kits to Sigma-Aldrich for sale to research markets. *STARBURST<sup>®</sup>* is the product name for DNT's dendrimer technology in growing demand as a research tool for early stage drug discovery and development. The product has a range of applications, including improving the water solubility of drugs, enhancing the performance of metal catalysts, and providing precise nanoscale materials for researching material and biological phenomena.

#### **Further information**

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