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# Starpharma Holdings Limited

## (ASX:SPL)

### Market Update

### October 2005

#### “Top Nanotech Buys for 2005”

*“We expect great things to come from the company and its significant ownership in U.S.-based Dendritic Nanotechnologies, Inc.”*

Forbes/Wolfe

#### “Top 5 Nanotech Breakthroughs for 2004”

Forbes/Wolfe

#### “Growth Strategy Leadership Award in the World Nanobiotechnology Market”

Frost and Sullivan July 2005

1. Company overview and investment highlights
2. Vivagel™ and line extensions
  - Vivagel™ – HIV
  - Vivagel™ – Genital Herpes
3. NIH funding
4. Development pipeline
5. Equity investments
6. Board and senior management
7. Financial snapshot
8. Conclusion

- Starpharma Holdings Limited ('Starpharma') is a world leader in the development of nanotechnology based pharmaceuticals
- Starpharma's lead product, VivaGel™ is being developed as a microbicide to prevent the sexual transmission of HIV and genital herpes
- Following a 12-month evaluation period the National Institute of Health (NIH) recently awarded Starpharma US\$20.3m (A\$26.4m) to develop VivaGel™
  - Strong endorsement of VivaGel™ : NIH is one of the leading most significant research organisations in the world
  - Minimises funding and development risks: NIH contract fully funds development costs to the start of large scale efficacy trials and ensures access to world-class facilities and clinicians
- In addition, Starpharma has a number of other pharmaceutical applications for dendrimers under development and continues to explore M&A opportunities to further leverage its technology

# VivaGel™ and line extensions



- VivaGel™ is a microbicide being developed to prevent sexually transmitted infections (STIs) in women
- VivaGel™ is a gel-based formulation with a nanotech active, delivered privately via an applicator prior to sexual activity
- The active ingredient of VivaGel™ (SPL7013) inactivates the HIV and HSV-2 (genital herpes) virus by binding with the virus preventing it attaching to the host
- Unlike HPV vaccines, vaccines against HIV and genital herpes have thus far failed and there is a significant and growing recognition that microbicides offer the best alternative

VivaGel™ packaged into pre-filled applicators.



**VivaGel™ offers an attractive first line defence against the spread of HIV and genital herpes**

- The Microbicide Development Act 2005 introduced by H Clinton et al.
  - HIV and AIDS: “direct medical costs of up to \$15.5B per annum”
  - “AIDS is the number one cause of death in African-American women aged 25-34”
  - “The US Government is firmly committed to the development of safe and effective microbicides”
  - “HIV prevention options as of 2005 are not enough”
  - “best option...technologies like microbicides which women can initiate and control”

***“It is estimated that by age 25 half of all sexually active people in the United States can expect to be infected with a sexually transmitted disease (STD) ”***

**Microbicides provide a solution to strong demand for STD prevention measures in industrialised world**

- Human Immunodeficiency Virus (HIV) is the virus that causes AIDS (Acquired Immune Deficiency Syndrome)
- AIDS is the most serious stage of the HIV infection, it results from the destruction of the infected person's immune system
- There is no cure for HIV/AIDS. It may be transmitted by individuals that are asymptomatic.
- 37 000 000 adults living with HIV; every day 7000 women are newly infected
- Existing prevention methods to reduce the risk of infection have proven relatively ineffective:
  - Condoms (male controlled, cultural implications, user reservations)
  - More than 50 HIV vaccines have failed and estimates are that an effective vaccine is many years away

# Genital Herpes – Nasty, Incurable Disease

- Infection is life-long
- Results in painful blisters/ulcers
  - Ulcers last 3-4 weeks
  - Typically ~ 4-5 ulcerative episodes per annum (may > 20 episodes per annum)
- Frequently causes anxiety and depression in affected individuals
- Increases affected individuals risk of HIV infection 3-4x
- May be transmitted by individuals who have no visible ulcers
- Transmissible at birth:
  - Occular, neurological and respiratory disease
  - Long term complications in 40%; death in 14%

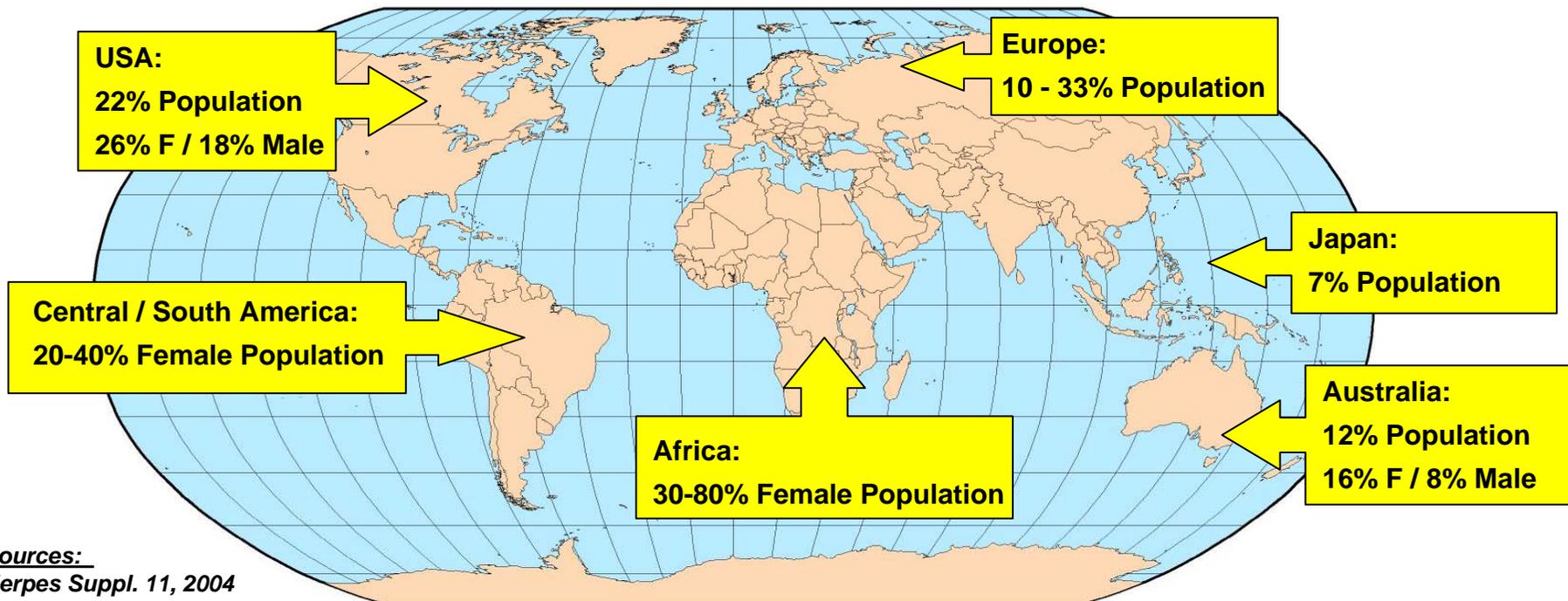


**Genital herpes is an incurable, life long condition that can be transmitted unknowingly**

# Genital Herpes – Large and Growing Market

- **22%** of the US adult population has genital herpes.
- Without intervention the prevalence of genital herpes in the US is expected to increase to **39%** of men and **49%** of women by 2025

Prevalence of Genital Herpes



Genital herpes is the “un-recognised epidemic” of the industrialised world

- Anti-viral therapeutics are used to treat people infected with acute genital herpes but do NOT cure the disease
- Genital herpes is a large, growing and expensive problem in the developed world
  - US costs of genital herpes is estimated at ~US\$1 billion per annum
  - Cost of neonatal genital herpes is estimated at up to US\$450K per case
- Without intervention the prevalence of genital herpes in the US is expected to increase to 39% of men and 49% of women by 2025
- The existing prevention methods have proven relatively ineffective:
  - Condoms (male controlled, cultural implications, user reservations)
  - Recent HSV-2 vaccine results have been disappointing: “unlikely to be available for many years”

## Product Offers Several Key Advantages

Female controlled (unlike condoms)  
Discreet (administered privately) with broad cultural acceptability  
Improved sensory characteristics c.f condoms  
Compatible with condoms

## Excellent Clinical Results

Potent activity in relevant HIV strains laboratory and primate trials  
Good activity against other STIs including HSV-2 (herpes)  
Non-toxic and non-irritating in human trials

## Superior Drug Characteristics

Affordable – Low manufacturing costs  
Passes key FDA hurdle – Well defined chemical entity  
Large and growing target market with major unmet needs  
Unlikely to be confounded by resistant HIV strains

**VivaGel™ has key competitive advantages as a preventative for HIV and Genital Herpes**

## Condom Coatings

The most common coating in premium condoms is nonoxynol-9 (N-9) that is meant to provide spermicidal protection and act as a microbicide

Recent studies have shown that the detergent N-9 actually results in an **increase** in the rate of infection by HIV and other viruses

Starpharma is already in discussions with a number of potential commercial partners who are exploring replacing N-9 with VivaGel™ as a coating for their premium condoms

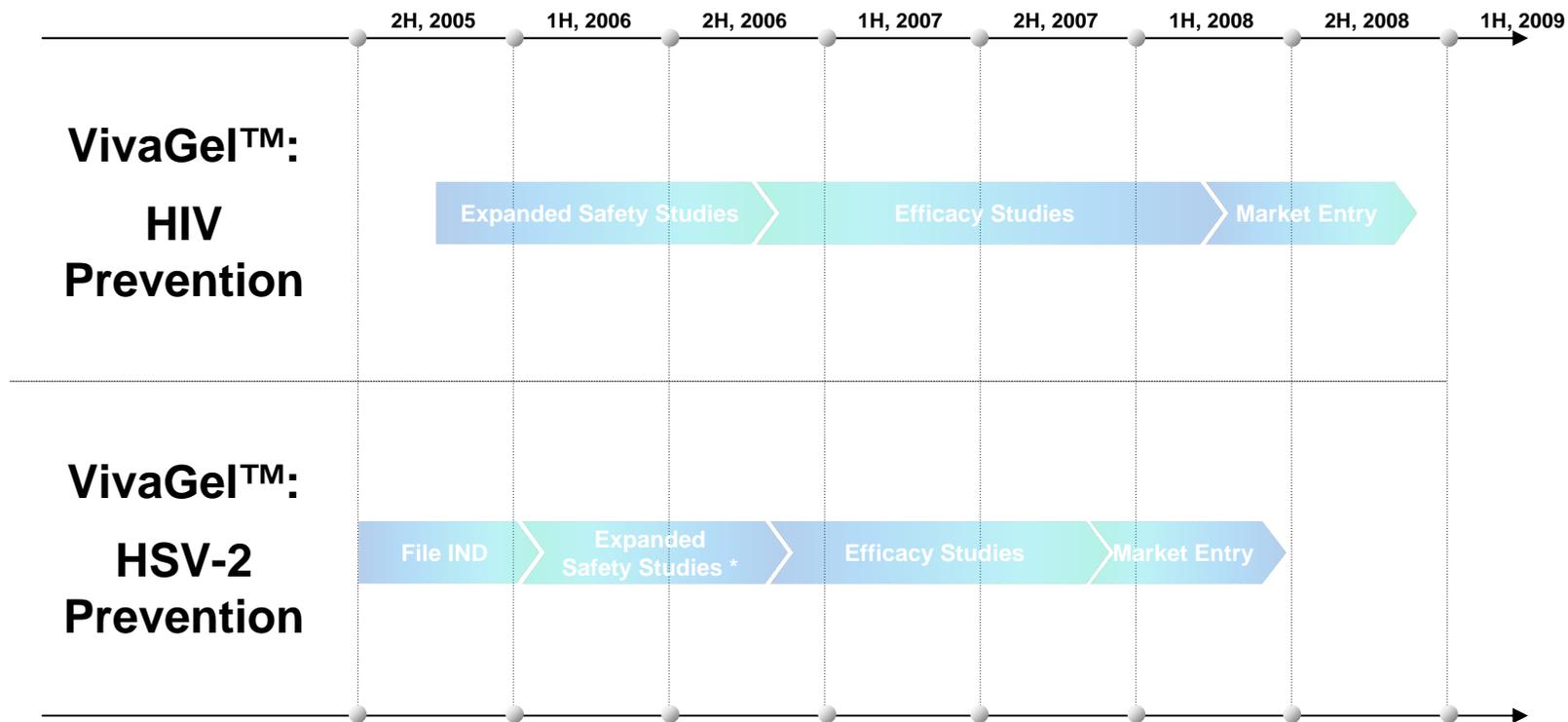
Less onerous regulatory path for VivaGel™ as a condom coating thereby offering a shorter route to market: **Market entry as early as 2H 2007**

## ComboGel

Starpharma **received US\$5.4m funding from the NIH** to develop the 'ComboGel' in partnership with a US company, ReProtect

'ComboGel' will combine the active components of ReProtect's BufferGel with VivaGel™ to generate a combination microbicide and contraceptive gel

# VivaGel™ Development Plan



\* It is anticipated that there will be significant crossover between expanded safety studies for the HIV and HSV-2 prevention indications.

VivaGel™ line extensions have potential market entry from CY2007

Market Penetration	Average Frequency of Use per Annum		
	25x	50x	100x
2.5%	US\$365m	US\$730m	US\$1460m
5.0%	US\$725m	US\$1450m	US\$2900m
10.0%	US\$1450m	US\$2900m	US\$5800m

- Key assumptions
  - 291m women of reproductive age (15-49) in developed countries
  - 115m (40%) of those unmarried (ignores use by 176m married women)
  - Unit sale price circa US\$2
  - Usage rates according to published data

- Starpharma is currently focused on four commercial applications of VivaGel™

Product	<p><b>VivaGel™ HIV Prevention</b></p> <hr style="border-top: 1px dashed black;"/> <p>Topical Microbicide</p>	<p><b>VivaGel™ Genital Herpes Prevention</b></p> <hr style="border-top: 1px dashed black;"/> <p>Topical Microbicide</p>	<p><b>Premium Condoms</b></p> <hr style="border-top: 1px dashed black;"/> <p>Microbicide Condom Coating</p>	<p><b>‘ComboGel’</b></p> <hr style="border-top: 1px dashed black;"/> <p>Combination Microbicide &amp; Contraceptive</p>
Est. Market Size	<p>&gt; US\$1bn</p>	<p>&gt; US\$1bn</p>	<p>\$US300-500M</p>	<p>&gt; US\$1.5bn</p>
Path to Market	<p>IND</p> <hr style="border-top: 1px dashed black;"/> <p>De-risked via NIH funding</p>	<p>IND</p> <hr style="border-top: 1px dashed black;"/> <p>Costs reduced and de-risked by utilising HIV safety studies</p>	<p>Device</p> <hr style="border-top: 1px dashed black;"/> <p>Already in discussions Likely less onerous regulatory approvals</p>	<p>IND</p> <hr style="border-top: 1px dashed black;"/> <p>De-risked via NIH funding</p>
Est. Market Entry	<p>~ 2H 2008</p>	<p>~ 1-2H 2008</p>	<p>2H 2007 Depends on Partner</p>	<p>&gt; 1H 2009</p>

Following the BRI transaction, Starpharma owns the underlying IP to VivaGel™ royalty free

NIH funding, Development pipeline,  
Equity investments,  
Board/Management, Financials



# SPL Awarded US\$20.3m Funding from the NIH



## **A\$26m+ of non-dilutive funding**

- Funding is provided without any downstream commercial obligations on future revenues generated from VivaGel™
- Funding will allow Starpharma to take product to market itself or secure a late-stage licensing deal

## **Strong Endorsement of VivaGel™**

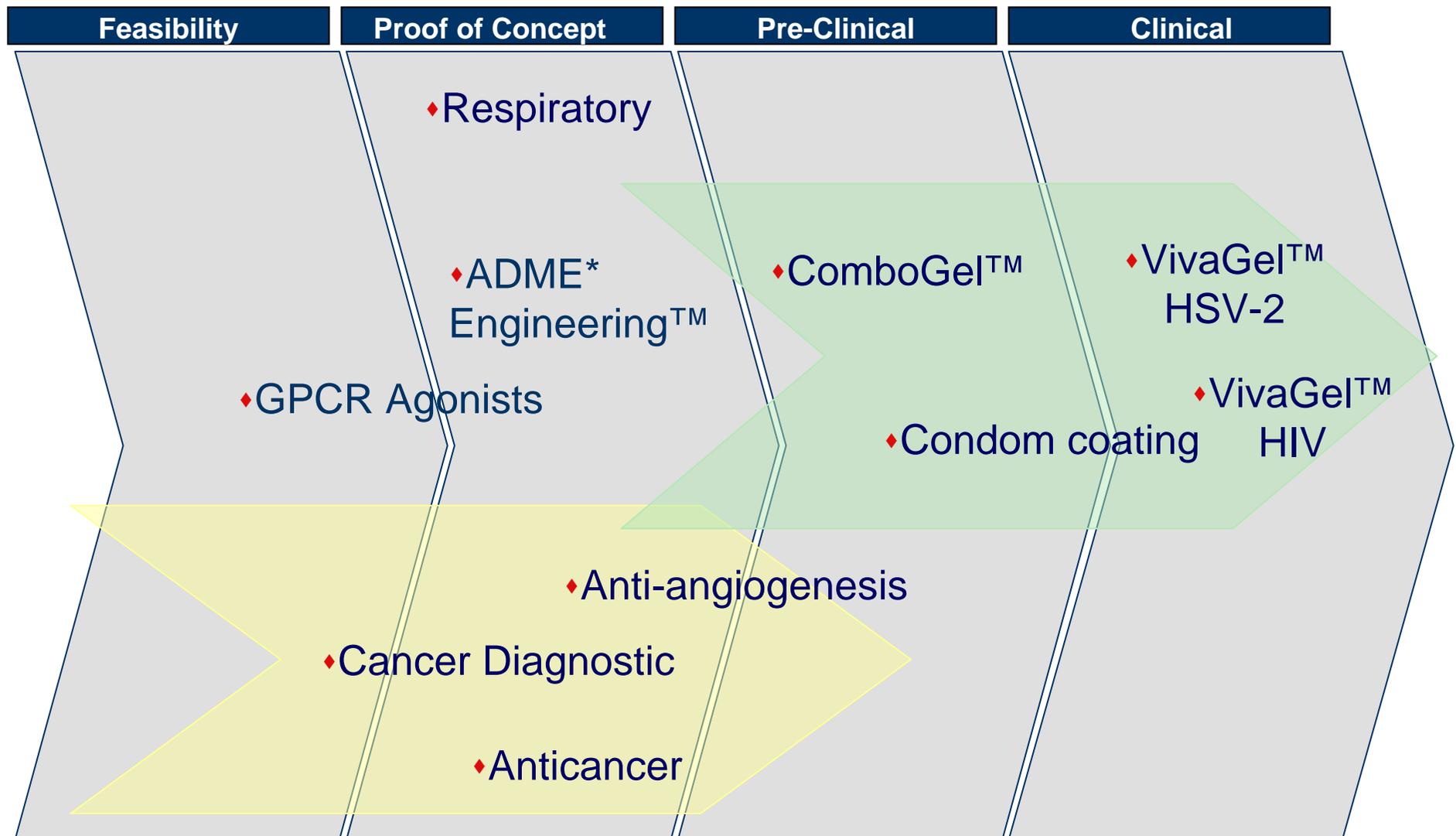
- The National Institute of Health (NIH) is one of the most significant research organisations in the world
- Following a 12+ month evaluation period NIH selected VivaGel™ as the candidate for development support

## **Significantly 'de-risks' VivaGel™**

- NIH funding will support VivaGel's preclinical and clinical development including scale-up manufacturing through to the final large-scale population study
- In addition to the funding, the NIH relationship ensures Starpharma can access world-class clinical development expertise, key clinicians and opinion leaders

**Significantly enhances probability that VivaGel™ will be successfully developed and commercialised**

# Starpharma's Pipeline



\*ADME: Absorption, Distribution, Metabolism, Excretion

- **ADME Engineering™**
  - Use of dendrimers to improve pharmacokinetics and safety of existing small molecule drugs and protein therapeutics
  - Potential as patent extension mechanism, improved dose efficiency
- **Respiratory**
  - Dendrimers for the treatment/prevention of RSV and other respiratory pathogens eg. influenza, exotic viruses
  - A natural extension of Starpharma's antiviral expertise.
- **Anti-angiogenesis Agent**
  - In vivo efficacy demonstrated
  - Potential for local delivery reducing dosing load and frequency
  - Non-cancer applications include: AMD, diabetic retinopathy, macular oedema.
- **Anticancer Agent**
  - Specific example of ADME engineering of existing anticancer drug to modify the pharmacokinetic and safety profile
- **Anti-cancer Diagnostic**
  - Faster and clearer imaging of cancer
  - Proof of concept studies underway in solid tumours
- **GPCR Agonist, eg Cancer**
  - Polyvalent engineering of existing small molecule GPCR ligands to improve efficacy and reduce toxicity.

# DNT is a Valuable and Strategic Asset

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- SPL has a 33% holding in a private Michigan based company Dendritic Nanotechnologies Inc (DNT)
  - Existing revenues streams from deals with leading pharmaceutical and biotechnology companies including Pfizer Inc; Johnson & Johnson; Sigma Aldrich; General Dynamics Corporation etc
  - Licensed two products generating royalty income
- The DOW Chemical Company (DOW) transferred its entire intellectual property portfolio in dendrimers to DNT in exchange for a 33% equity holding
- DNT recently announced major contract with the NCI for cancer diagnostic development
- SPL has exclusive commercialisation rights to DNT's technology for nanopharmaceuticals
- DNT is currently developing a number of products for near-term licensing and an exciting new synthetic methodology for generating dendrimers cheaper and faster

## Board of Directors

Mr Peter Bartels	Chairman
Prof. Peter Colman	Non-executive Director
Mr Ross Dobinson	Non-executive Director
Mr Leon Gorr	Non-executive Director
Dr Peter Jenkins	Non-executive Director
Dr John Raff	Executive Director/CEO

## Senior Management

Dr Jackie Fairley	Chief Operating Officer
Dr Tom McCarthy	Drug Development
Mr Tim Grogan	Commercial Dev
Dr Paul Barrett	Business Development
Dr Jeremy Paull	Regulatory and QA
Mr Ben Rogers	Co. Secretary/CFO
Dr Guy Krippner	Drug Discovery

- Starpharma's Management Team is focussed on drug development and commercialisation
- Recent recruits bring additional commercialisation focus to the Company

## Financial Snapshot

Share price: \$0.57 (as at 13 October 2005)

Market cap: \$67.5m

Cash: \$8.2m (as at 30 June 2005)

Shares on issue: • 118.4m\*  
• 5.7% of the shares on issue are traded in the US under SPHRY via a Level 1 ADR Program

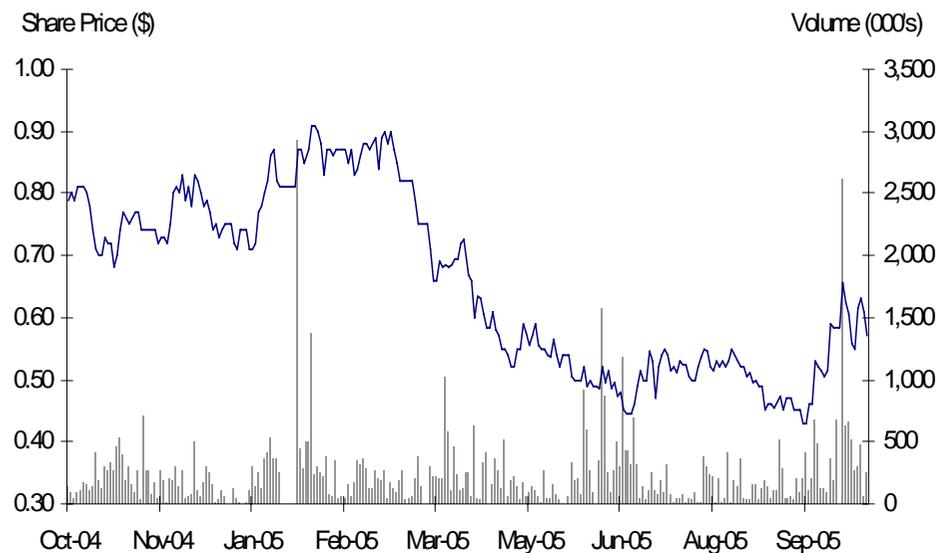
## Register

SPL Directors: ~ 20.0%

US Investors (via Level 1 ADR): ~ 5.7%

Top Twenty: ~ 50%

## 12 Month Share Price Performance



\* post recent royalty-equity swap with BRI

Market is yet to fully recognise the impact on SPL of the recent NIH funding

- Value uplift via VivaGel™ and line extensions development
  - NIH funding significantly de-risks VivaGel™ HIV development and commercialisation
  - Commence clinical trials of VivaGel™ in USA, Africa and Australia in 1HCY2006
- VivaGel™ and line extensions address a large, growing market with unmet needs
  - Global epidemic nature of HIV, genital herpes and other STIs
  - Strong probability of additional non-dilutive funding from international health organisations
- Significant value in Starpharma's equity investments
  - US private company, Dendritic Nanotechnologies (DNT)
  - Dimerix Bioscience
- Breadth and quality of dendrimer pipeline
  - Significant competitive advantage: Exclusive commercialisation rights to DNT's dendrimer technology for nanopharmaceuticals

**Strong news flow over the next 6 months from VivaGel™, DNT and the discovery pipeline**