

---

# *Starpharma Holdings Limited*

ASX:SPL

USOTC:SPHRY

eG Capital

Australian Bio-Investment Forum

14 June 2006

Dr Jackie Fairley – Chief Operating Officer

**“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 2005**

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

**Frost and Sullivan July 2005**

*This presentation contains forward-looking statements that involve risks and uncertainties. Although we believe that the expectations reflected in the forward-looking statements are reasonable at this time, Starpharma can give no assurance that these expectations will prove to be correct. Actual results could differ materially from those anticipated, because of various important factors, risks and uncertainties. These include risks associated with drug development and manufacture, risks inherent in the extensive regulatory approval processes mandated by regulatory authorities, delays in clinical trials, future capital needs and general economic uncertainty. Also, there can be no assurance that others will not independently develop similar products or processes or design around patents owned or licensed by the Company, or that patents owned or licensed by the Company will provide meaningful protection or competitive advantages.*

## *Outline*

---

1. Company Overview
2. VivaGel™ – Product Overview
3. VivaGel™ – Excellent Market Opportunities
4. Pipeline
5. Equity Holding in Dendritic Nanotechnologies Inc
6. Conclusion

# 1. *Company Overview*

## Company Overview

- Starpharma Holdings Limited ('Starpharma') (ASX:SPL) is a world leader in the development of nanotechnology based pharmaceuticals (dendrimers)
- Starpharma's lead product, **VivaGel™** is being developed as a microbicide to prevent the sexual transmission of **HIV** and **Genital Herpes**
- **US\$20.3m NIH funding** to develop VivaGel™ for HIV (Oct '05) **FDA Fast Track status** (Jan '06)
- **NIH clinical support** for Genital Herpes (Apr '06)
- Two **line extensions** to VivaGel™ also in development and broad **portfolio** of other dendrimer projects
- Equity stake in US company **DNT Inc.**
- Successful ADR program ~ **7.2% shares on issue**; growing at ~ 9% per month

### Financial Snapshot

Market Cap:	~ A\$60-70M
Institutional Investors:	~ 30%
Shares on Issue:	147M
Cash:	A\$15.4 M (March 06)

Starpharma is a world leader in developing dendrimers as pharmaceuticals

## *2. VivaGel™*

*Product Overview*

## *VivaGel™ – Lead Product for Prevention of STIs*

### VivaGel™ packaged into pre-filled applicators.

- 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 HIV and HSV-2 (genital herpes) virus by binding with the virus preventing it attaching to the host
- 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™ offers an attractive first line defence against the spread of HIV and genital herpes**

## *HIV – A Preventable, Life Threatening Disease*

---

- Human Immunodeficiency Virus (HIV) is the virus that causes AIDS (Acquired Immune Deficiency Syndrome)
- No cure for HIV/AIDS and may be transmitted by individuals that are asymptomatic
- 39 million people living with HIV; every day 7,000 women are newly infected
- The predominant route of transmission is via heterosexual contact
- More than 50 HIV vaccines have failed and estimates are that an effective vaccine is many years away
- Although when used condoms are effective in preventing HIV, in practice they are not used consistently or correctly

**HIV and AIDS (in the US): “Direct medical costs of up to \$15.5 billion per annum”**  
**“AIDS is the number one cause of death in African-American women aged 25-34”**

**““HIV prevention options as of 2005 are not enough”**  
**best option...technologies like microbicides which women can initiate and control”**

Source: Microbicide Development Act 2005: US Senate



## *Genital Herpes – Nasty, Incurable Disease*

- Genital herpes is the “un-recognised pandemic” of the industrialised world
  - **22%** of the US adult population has genital herpes; Est. cost (US) >\$1.5B pa
  - Without intervention the prevalence of genital herpes in the US is expected to increase to **39%** of men and **49%** of women by 2025
- Infection is life-long, drugs do not cure
- Results in painful blisters/ulcers
  - Ulcers last 3-4 weeks; 4-5 ulcerative episodes p.a
  - Increases affected individuals’ risk of HIV infection by 4-8x
- 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%
- Existing prevention methods have proven ineffective and developmental vaccines disappointing



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

## Product Offers Several Key Advantages

Market research indicates microbicide gels will have good uptake  
Female controlled, discreet and convenient  
Compelling competitive advantages: efficacy; non-irritant; broad activity\*  
Compatible with condoms

## Excellent Clinical Results in Human and Primate Trials

Human trials: VivaGel™ is non-toxic and non-irritating  
Potent activity in relevant HIV strains in very tough primate trials  
Potent activity against herpes in animal trials  
Viruses appear not to develop resistance to VivaGel™

## Excellent Drug Characteristics

Lower risk development – Topical gel, external to body  
Affordable – Low manufacturing costs  
Excellent IP position  
Passes key FDA hurdle – Well defined chemical entity

*\*See appendices for further detail as to how VivaGel™ compares to competitive products in development*

**US\$20.3m + of non-dilutive funding from US-based NIH**

- Funding is provided without downstream commercial obligations
- Funding will allow Starpharma to take product to market itself or secure a late-stage licensing deal

**Significantly ‘de-risks’ VivaGel™**

- NIH funding will support VivaGel’s development including:
  - Clinical (HIV and **now HSV-2**) and non-clinical trials,
  - Scale-up of manufacturing through to the final large-scale population study and
  - Access to world class clinical development expertise.

- FDA *Fast-Track* for VivaGel™ for HIV means:
  - Faster review of the NDA application( 6 months rather than 13)
  - Greater access to and input from the FDA into development program

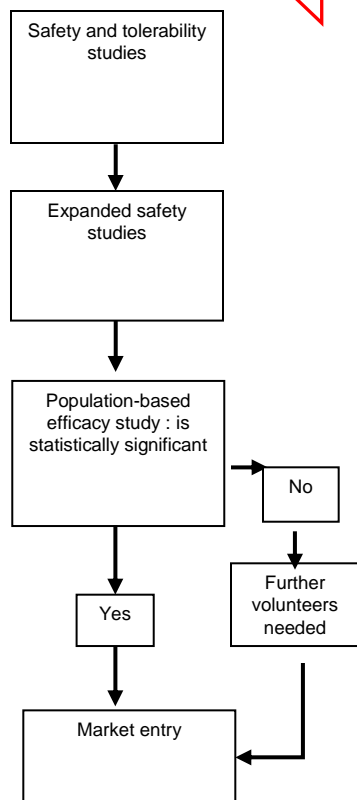
**Strong Endorsement of VivaGel™**

- The NIH selected VivaGel™ as the candidate for development support following a 12+ month evaluation period

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

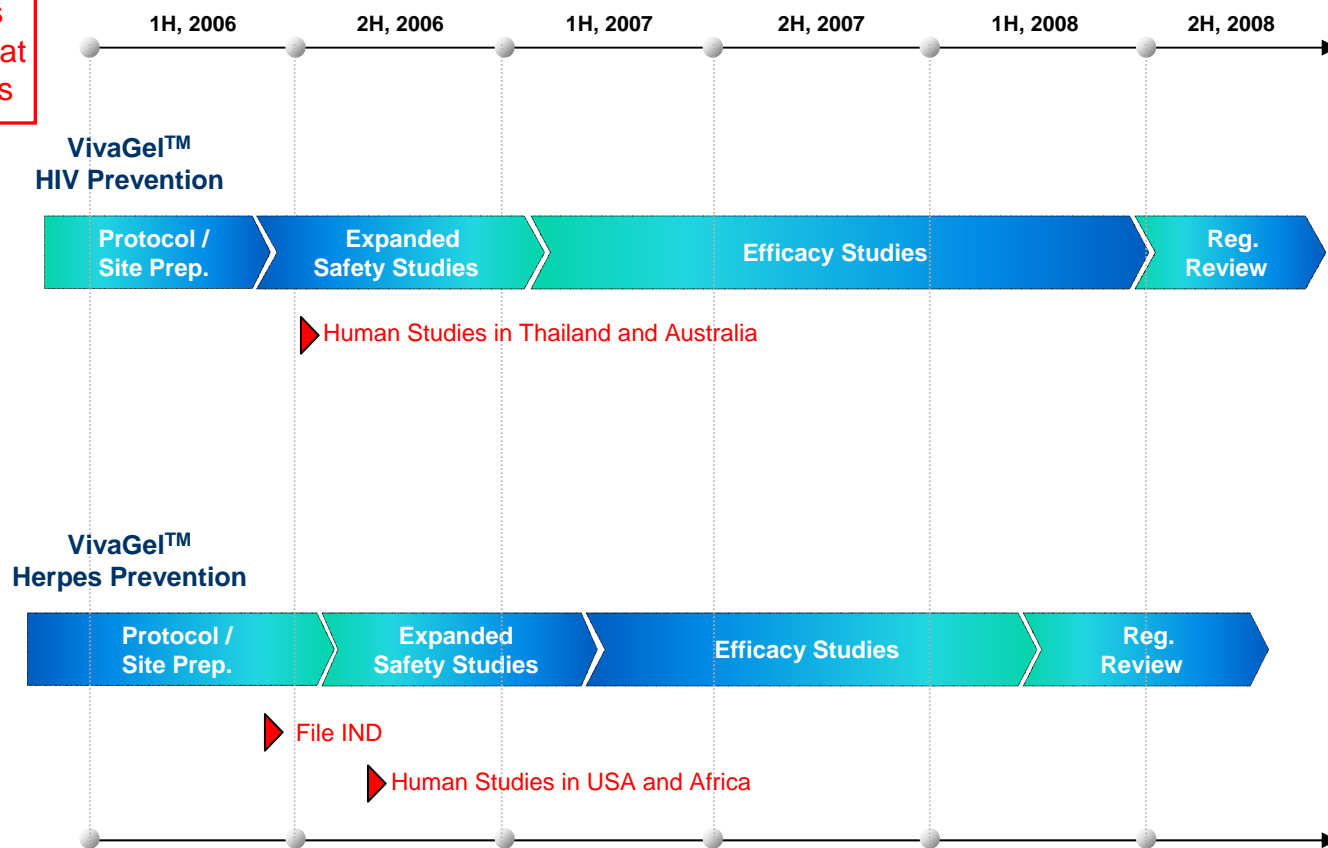
# VivaGel™ – Development Path

## MICROBICIDES DEVELOPMENT PATH (Prevention)



Development path for microbicides differs from that of other drugs

## SPL LEAD PRODUCTS DEVELOPMENT PLAN

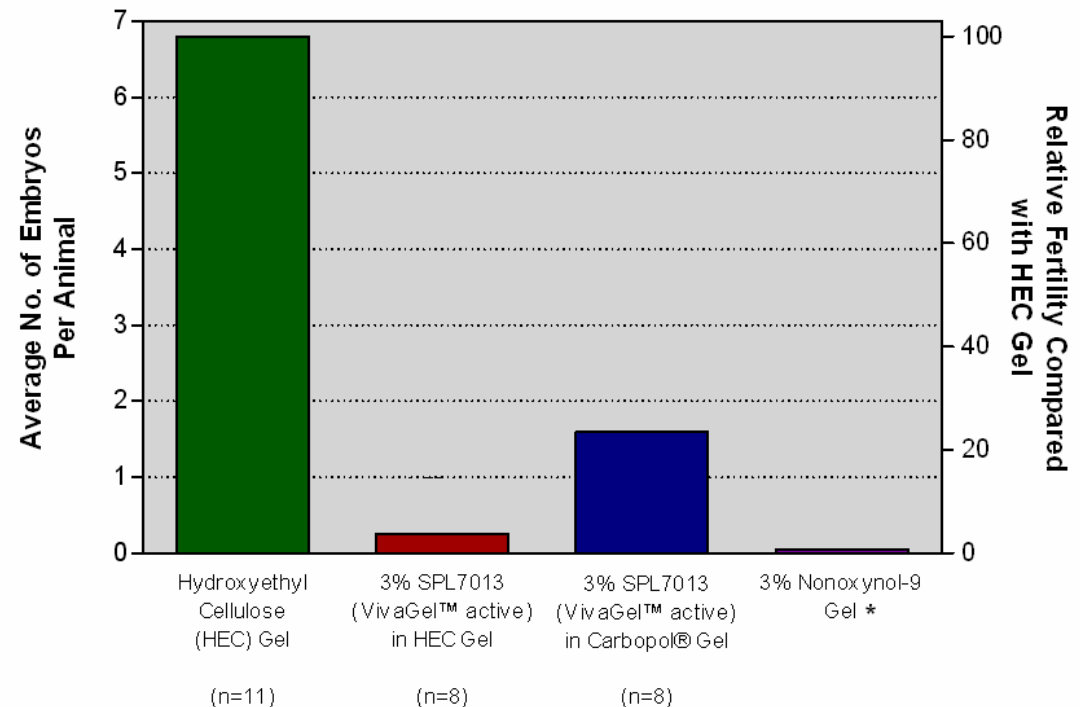


Lead products are entering significant clinical development phases in next 6 months

## VivaGel™ : Potent Contraceptive Activity in Rabbits

- Recent study has shown that SPL7013, the active ingredient in its VivaGel™, exhibits a potent contraceptive effect in rabbits
- Independent study undertaken at Johns Hopkins University under an NIH grant
- Fertility was reduced by more than 75% by SPL7013 in a VivaGel™ formulation and 95% in a HEC gel compared with an inactive gel
- If contraceptive activity is confirmed in humans it would allow for development with contraception as an additional claim
- Findings relevant to both the stand-alone gel and condom coating opportunities

Average No. of Embryos Conceived Per Animal Following Application of Vaginal Gels, and % Relative Fertility in Active Gel-Treated Rabbits Compared with HEC Control



\* N-9 figure based on published historical data, Castle et al, Contraception 1998;58:51-60, and Zeitlin et al, Sexually Transmitted Diseases, 2001;28:417-23

VivaGel™'s active ingredient is a potent contraceptive in animals

3. *VivaGel™*  
*Excellent Market Opportunities*

## *Commercial Opportunity for Microbicides*

---

- **Large, addressable markets:**
  - HIV primarily in developing countries
  - HSV-2 in both developing and developed countries
  
- **Increasing market “pull” for products**
  - US government firmly committed to development of safe and effective microbicides (Microbicides Development Act 2005)
  - US Opinion Leaders now calling for National Herpes Control Program
  
- **Several industry surveys have confirmed strong consumer demand:**
  - Over 20m women in US would use microbicide
  - 30-40% female US college students would buy microbicide; 70% with contraceptive properties
  - Strong market demand at 5x local condom price in various countries

*Source: World Bank; UNAIDS; EC AIDS survey; BCG analysis and various microbicide publications*

### 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 premium condoms

Likely less onerous regulatory path for VivaGel™ as a condom coating offering a shorter route to market.

### ComboGel

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

The 'ComboGel' will combine the active agents in ReProtect's BufferGel with VivaGel™ to generate a combination microbicide with potential to extend spectrum of activity.



## 4. *Pipeline*

## *Applications of Dendrimers in Life Sciences*

---

### ▪ **Pharmaceuticals**

- Polyvalent = multivalent presentation of covalently bound surface groups; activity due to multiple presentation of surface groups
- “Re-engineering” and/or re-formulation of existing drugs (technical & life-cycle management)

### ▪ **Drug Delivery**

- Small molecules occluded (non covalently) within the dendrimer architecture; alternative to liposomes
- Molecules attached to the dendrimer which are metabolically released; single molecule alternative to traditional polymer-drug conjugates

### ▪ **In vitro Diagnostics**

- A dendrimer is a key component of the Stratus CS instrument by Dade Behring [FDA - 510(k)]; detects certain protein biomarkers released in the blood stream as a result of heart muscle damage

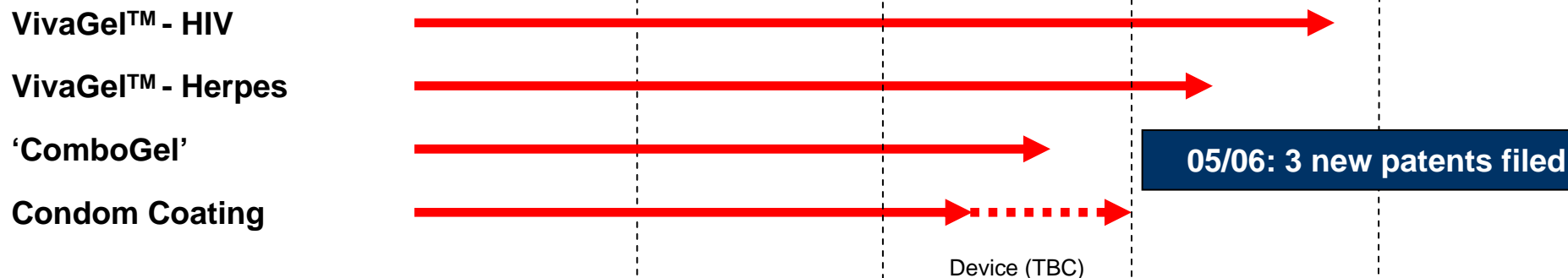
### ▪ **In vivo Diagnostics**

- MRI contrast agents e.g. Gadomer-17: Schering AG (24 gadolinium chelates covalently attached)
- Enhanced organ, tissue and/or tumor detection and resolution; optimized PK profile

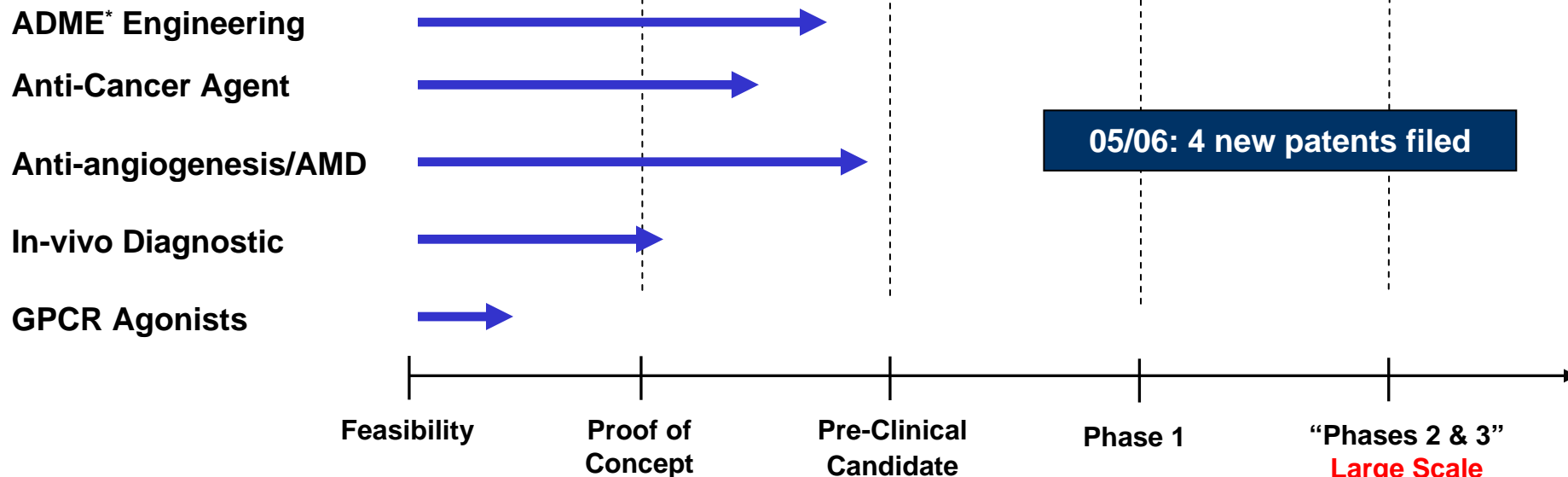
**Starpharma and DNT have an extremely broad IP portfolio in Dendrimers**

# Starpharma's Pipeline

## Development Pipeline



## Discovery Pipeline



\* ADME: Absorption Distribution Metabolism Excretion

**“Phases 2 & 3”  
Large Scale  
Efficacy Trials for  
Preventatives**

*5. Equity Holding in DNT*

# Dendritic Nanotechnologies Inc. (DNT)



- SPL has a 33% holding in a private US company DNT (The DOW Chemical Company holds 30% DNT equity)
- DNT has existing revenues streams from deals with leading companies including Pfizer Inc; Sigma Aldrich; General Dynamics Corp., Lumera, US Dept. Defense
- Valuable new synthetic methodology (Priostar™) for generating dendrimers cheaper and faster
- Short-term revenue generation opportunities for
  - Specialty Chemicals
  - siRNA (short interfering RNA) transfection reagents
- Longer-term potential to enhance existing drugs
  - solubility enhancement, life-cycle management
  - receptor-targeted diagnostic and therapeutic delivery technology for ovarian cancer

**MCaps of Listed US Nanomaterials Companies**

COMPANY	MCap (US\$m)
Orthovita	210
Altair	186
Nanogen	117
Nanophase	98
Lumera	57



<b>Initiatives</b>	<b>Status &amp; Funding</b>
<b>Receptor-targeted Diagnostic for Ovarian Cancer</b>	<b>Lead Candidate Screening</b> <ul style="list-style-type: none"><li>• National Cancer Institute contract (\$850k)</li><li>• Small Business Administration grant (\$820 k)</li><li>• NCL Collaboration</li></ul>
<b>Receptor-targeted Therapeutic Delivery for Ovarian Cancer</b>	<b>Lead Candidate Screening</b> <ul style="list-style-type: none"><li>–National Cancer Institute contract (\$850k)</li></ul>
<b>Transfection Reagents for siRNA Delivery</b>	<b>Final Product Testing</b> <ul style="list-style-type: none"><li>–Ongoing Collaborative Research Initiatives</li></ul>
<b>Specialty Commercial Products</b>	<b>Product Commercialization &amp; Scale Up</b> <ul style="list-style-type: none"><li>–Resins &amp; Adhesives</li><li>–Sanitizers &amp; Disinfectants</li><li>–Specialized Lubricants</li><li>–Water Remediation/Filtration</li></ul> <b>Ongoing Collaborative Research Initiatives</b>

siRNA Reagent Sales \$120 million in 2004 growing 15-18% annually

## *DNT: Exploiting dendrimer properties*

Dendrimers offer the potential for:

- Increased drug solubility
- Reduced drug toxicity
- Increased cellular retention times
- Attachment of targeting moieties
- Product life-cycle management

<b>Solubility Enhancement of Indomethacin and Paclitaxel</b>		
<b>Priostar Dendrimer</b>	<b>Drug</b>	<b>Solubility Enhancement</b>
<b>DNT-1900</b>	<b>Indomethacin (25 µg/mL)</b>	<b>77x</b>
<b>DNT-1910</b>	<b>Indomethacin</b>	<b>48x</b>
<b>DNT-1990</b>	<b>Paclitaxel (0.3 µg/mL)</b>	<b>20x</b>

# DNT's Business Partners



DADE BEHRING



Johnson & Johnson Research  
PTY. LIMITED



CALTECH



INSTITUTE FOR SOLDIER NANOTECHNOLOGIES



U.S. Army Research Laboratory



2005

FROST & SULLIVAN

Nanomaterials for Advanced Medical Applications  
Technology Innovation of the Year Award



## 6. *Conclusion*

## Starpharma: Investment Highlights

---

### Strong Financial Position:

- ✓ A\$15.4M cash (March 2006)

### Track Record Of Delivery / Internationally Recognised Clinical Program:

- ✓ US\$26m\* non-diluting funding from the NIH (off balance sheet) for VivaGel™ for HIV (Oct. 2005)
- ✓ Fast Track Status for VivaGel™ (Jan 2006)
- ✓ NIH also providing additional funding (confidential amount) for VivaGel™ clinical development for Herpes (*April 2006*)
- ✓ VivaGel™ Phase I trial successful; human trial preparation conducted in collaboration with NIH, trials to commence in Australia, US and Kenya in Q2/Q3 2006
- ✓ NIH to act as sponsor of the IND application for VivaGel™ for Herpes
- ✓ Continued strong uptake of ADRs (~7.2% shares)

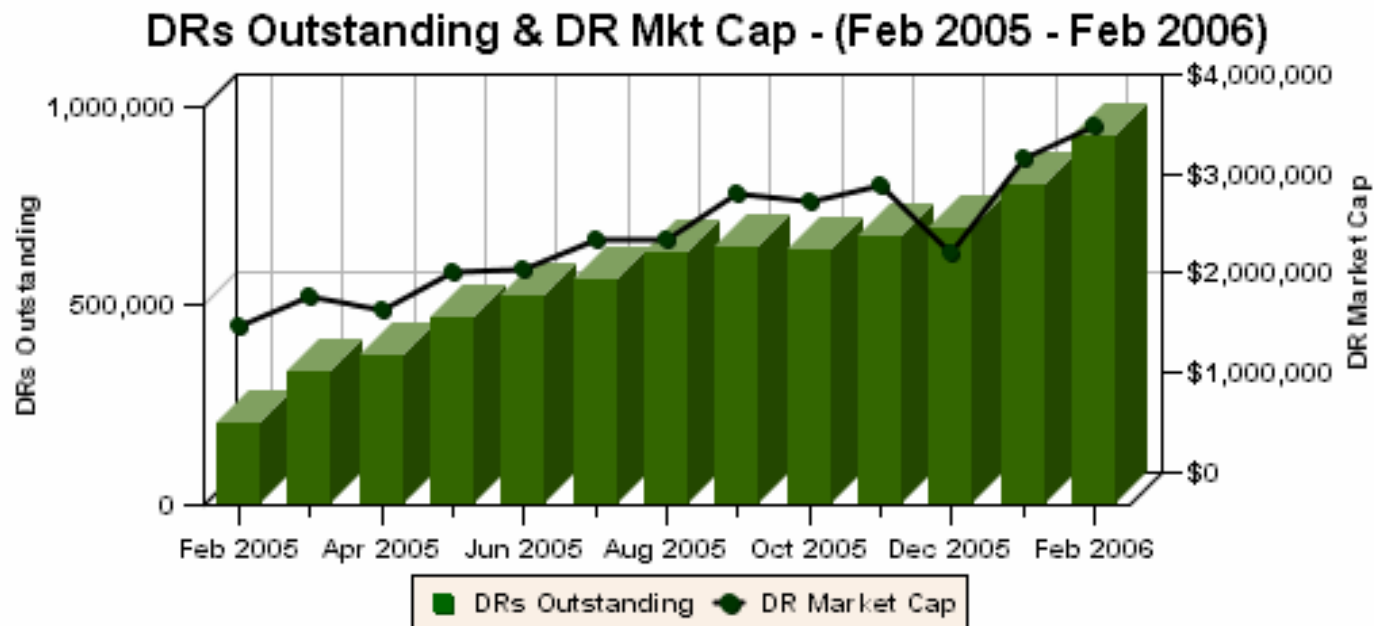
### Additional Commercial Opportunities:

- ✓ Progressing commercial arrangements/testing for condom coatings
- ✓ Dendrimer platform/pipeline and equity stake in Dendrimer Nanotechnologies (DNT) anticipated to yield multiple commercial opportunities

\* Two HIV grants: US\$20.3m contract + US\$5.4m grant (2004)

*For Further Information:*  
[jackie.fairley@starpharma.com](mailto:jackie.fairley@starpharma.com)

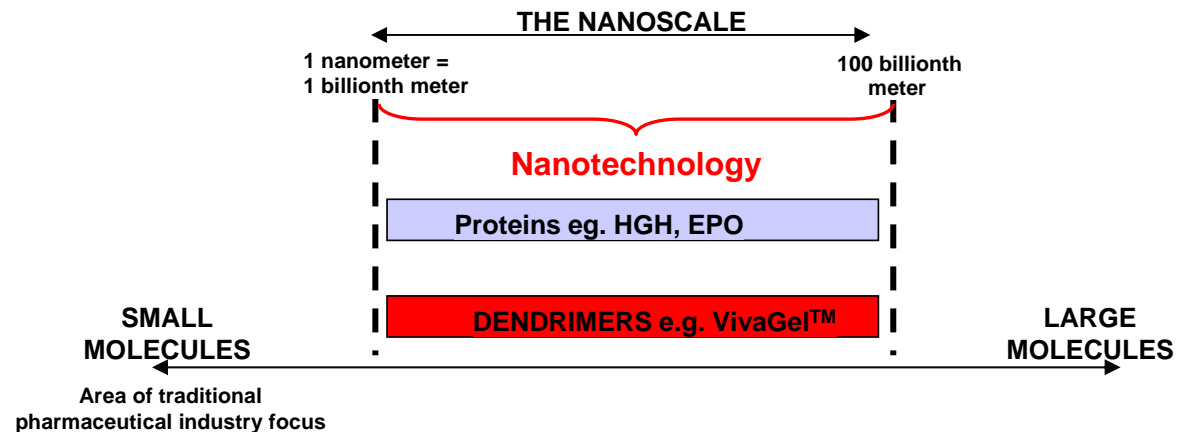
# *Appendices*



- Commenced: January 2005
- Issued by: The Bank of New York: USOTC:SPHRY
- DRs Outstanding: growing at a rate of 9% (compound) per month
- ADRs: represent ~7% of issued capital
- Major brokers: Merrill Lynch, Natexis Bleichroeder, Credit Lyonnais, Pershing LLC

## Starpharma is a Leader in 'Nanopharmaceuticals'

- Nanotechnology is the manipulation of matter smaller than 100 nanometres ('nm')
- Starpharma is a leader in developing dendrimers as drugs (VivaGel™ represented the first IND for a dendrimer)
- Dendrimers are highly branched macromolecules offering
  - Multiple binding sites: polyvalency
  - Precise manufacture: consistency of composition

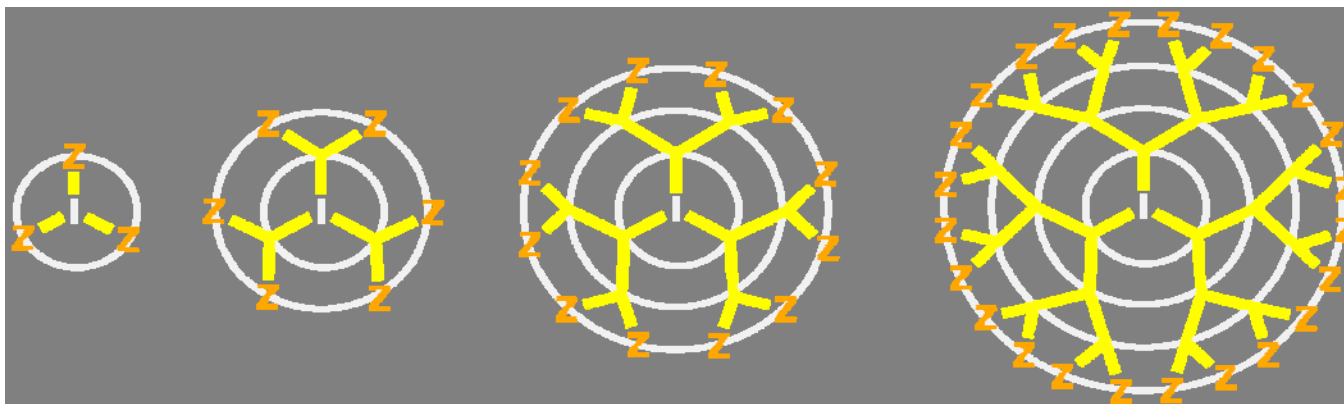


- Dendrimers also have life science applications in drug delivery (liposome-like), diagnostics and contrast agents

***“by 2014 16% of goods in healthcare and life sciences by revenue will incorporate emerging nanotechnology”***

Lux Research, October 2004

**Starpharma is a world leader in developing dendrimers as pharmaceuticals**



- I = Initiator or core
- Y = Branching unit
- L = Linker between Y and Z
- Z = Surface group

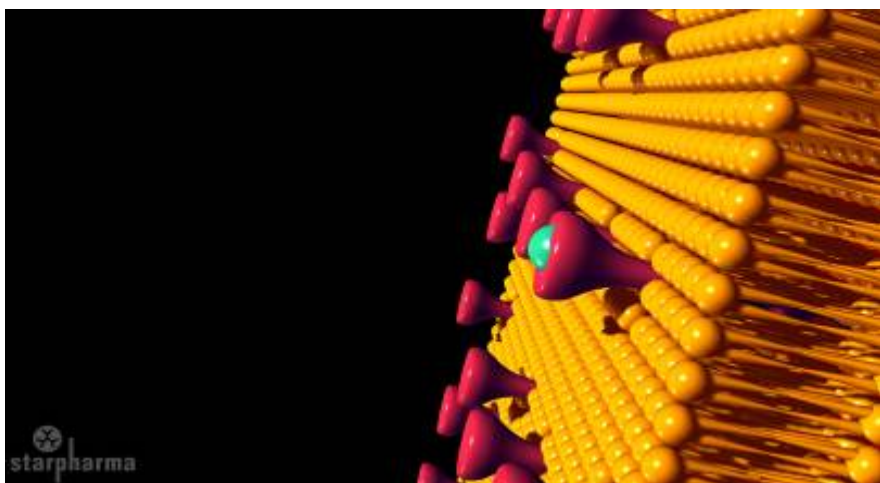
## Size

- Molecular weight
- Distance of span or volume

## Surface group/s

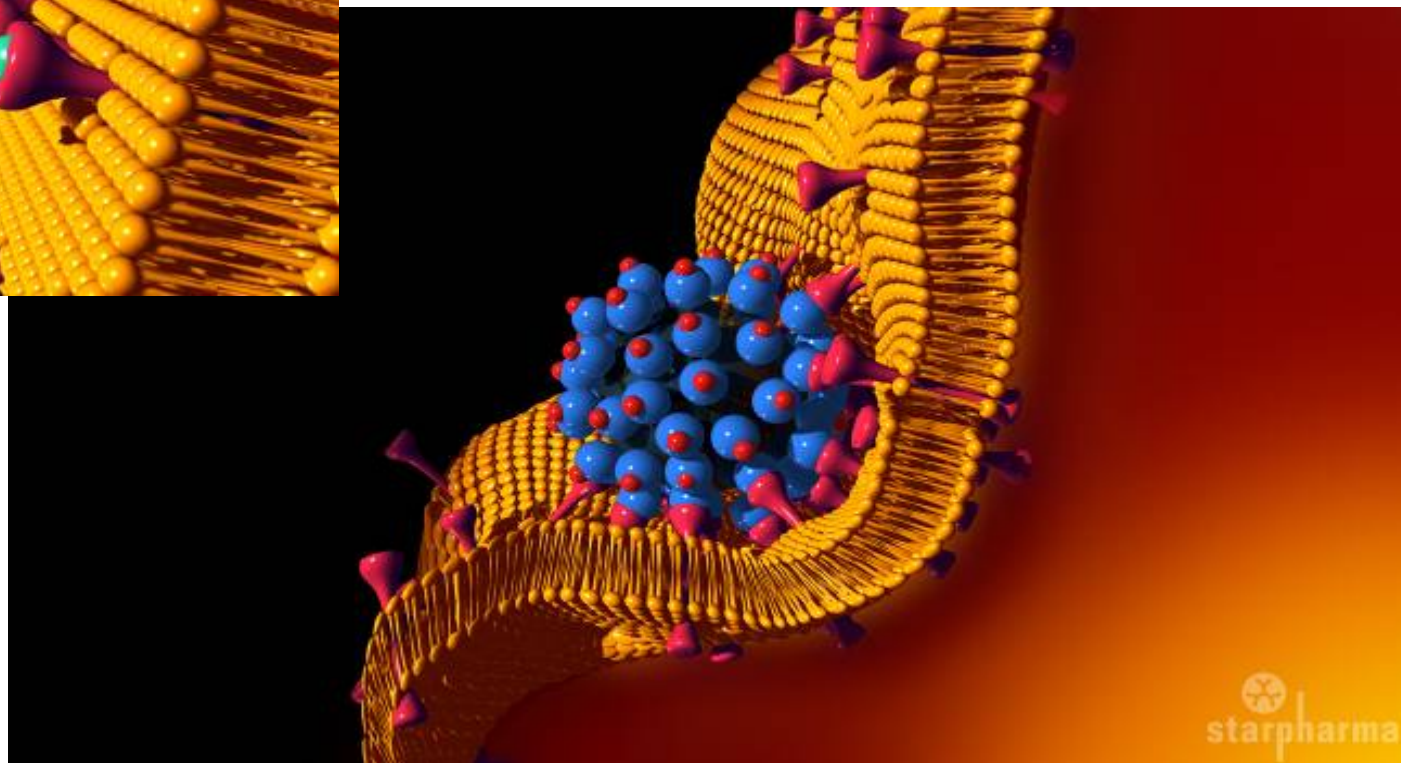
- Number
- Type

# *Dendrimers – a Platform for Polyvalent Interactions*



Traditional monovalent drug-receptor interaction.

Dendrimer nanodrug-receptor polyvalent interaction, mimics nature, and results in potentially enhanced activity compared with small molecules.





# *VivaGel™ – What is the Product Concept?*



# VivaGel™ – Excellent Market Opportunities

## Developed Countries:

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
  - Unit sale price circa US\$2
  - Usage rates according to published data

<p><b>Significant Advantages over Other Products in Development</b></p>	Competitor Category	Key Disadvantages	VivaGel™ Advantages
	Surfactants/ Detergents	<ul style="list-style-type: none"> <li>▪ Ulceration possible; potential incr. risk of HIV infection</li> </ul>	<ul style="list-style-type: none"> <li>▪ No surfactant properties; non-irritant; does not incr. infection risk</li> </ul>
	Sulphated carbohydrates	<ul style="list-style-type: none"> <li>▪ Not active against clinical HIV strains</li> </ul>	<ul style="list-style-type: none"> <li>▪ Highly active against all HIV strains tested</li> </ul>
	Reverse Transcript. Inhibitors and other anti-viral drugs	<ul style="list-style-type: none"> <li>▪ Drug resistance is an issue</li> <li>▪ Primary mode of action requires infection process to have begun</li> <li>▪ Not active against herpes</li> </ul>	<ul style="list-style-type: none"> <li>▪ Very high barrier to development of viral resistance</li> <li>▪ Primary mode of action is prevention of virus attachment</li> <li>▪ Potent activity against herpes</li> </ul>
	Sulphated Polymers	<ul style="list-style-type: none"> <li>▪ High cost of synthesis</li> <li>▪ Poor characterisation of the drug substance likely to present regulatory issues</li> </ul>	<ul style="list-style-type: none"> <li>▪ Excellent drug characteristics:                             <ul style="list-style-type: none"> <li>▪ Low manufacturing costs</li> <li>▪ Stable, well defined entity</li> </ul> </li> </ul>
	Acidity Control Agents	<ul style="list-style-type: none"> <li>▪ Acidity control: sufficient protection as mono-therapy?</li> </ul>	<ul style="list-style-type: none"> <li>▪ Potent activity against HIV and HSV-2 in animal models; non-irritant</li> </ul>