Starpharma presents positive results of clinical study of VivaGel™ in men at 4th International AIDS Society Conference

Melbourne, 24 July, 2007: Starpharma Holdings Limited (ASX:SPL, OTCQX:SPHRY) will today present results of a clinical trial indicating that 3% SPL7013 Gel (VivaGel™) was well-tolerated in men, and suitable for further development as a topical microbicide for the prevention of HIV and genital herpes.

The results are to be presented by Starpharma in Sydney today at the 4th International AIDS Society (IAS) Conference on HIV Pathogenesis, Treatment and Prevention, at which the research and development of microbicides is a key focus.

The study compared 36 circumcised and uncircumcised men who applied VivaGel™ (24 men) or a placebo gel (12 men) topically to their penis once daily for seven days. The trial was double blinded so that the participants, principal investigator and study staff did not know who was receiving placebo or VivaGel™.

Overall, this study demonstrated that VivaGel™ was safe and well tolerated, and comparable with placebo when applied to the penis of both circumcised and uncircumcised healthy male volunteers once daily for seven days, and left in place for approximately 9 hours. As seen in a previous completed clinical trial in women, there was no evidence of absorption of the active ingredient of VivaGel™, SPL7013, into the blood after topical application.

The most commonly reported genital adverse events in both treatment groups were considered to be mild and to be consistent with application to the surface of the penis of a substance which dries and is not washed off for a number of hours.

Acceptability was a secondary endpoint in this study and interviews indicated that VivaGel™ would be acceptable to participants if shown to be protective against sexually transmitted infections, and there were few concerns around the potential impact on sexual pleasure.

Detailed results of the study are included in the Appendix to this announcement.

The clinical study was conducted at the Melbourne Sexual Health Centre, in collaboration with the Burnet Institute and the National Centre in HIV Epidemiology and Clinical Research, and was funded with U.S. Federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH), Department of Health and Human Services (Contract No. HHSN266200500042C).

VivaGel™ is being developed as a topical vaginal microbicide for the prevention of HIV and genital herpes, and is currently under investigation in healthy female volunteers in two separate expanded safety clinical trials at four sites in the U.S. and Kenya. VivaGel™ also shows promise as a contraceptive agent.

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 is principally composed of two operating companies, Starpharma Pty Ltd in Melbourne, Australia and Dendritic Nanotechnologies, Inc in Michigan, USA. Products based on SPL's dendrimer technology are already on the market in the form of diagnostic elements and laboratory reagents.

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 the pharmaceutical field Starpharma has additional specific programs in the areas of Drug Delivery and ADME Engineering™ (using dendrimers to control where and when drugs go when introduced to the body), Polyvalency (using the fact that dendrimers can activate multiple receptors simultaneously) 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 with applications as diverse as adhesives, lubricants and water remediation.

SPL has a comprehensive IP portfolio that comprises more than 180 patents/applications issued and pending across 32 patent families - a unique level of IP concentration among nanotechnology companies.

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

Microbicides: A microbicide inactivates, kills or destroys microbes such as viruses and bacteria. Microbicides may be formulated as gels, creams, sponges, suppositories or films with the purpose of reducing significantly the incidence of STIs. They are intended for vaginal or rectal use to afford protection for varying periods, from several hours up to days. Microbicides may also be designed to have a contraceptive function.

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 is the depositary bank.

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CLINICAL TRIAL RESULTS APPENDIX – STUDY NO. SPL7013-002

This appendix contains a summary of the final analysis of the results of the clinical trial assessing the safety of 3% SPL7013 Gel (VivaGel™) on the penile epithelium, which was conducted in Australia under US Food and Drug Administration (FDA) Investigational New Drug Application (IND) No. 62,482.

Study Title	A phase 1, placebo controlled study of the safety of 3% w/w SPL7013 Gel, administered to the penis of healthy male volunteers once daily for seven days
Study Number	SPL7013-002
Study Design	The study was a single-centre, stratified, randomised, placebo controlled, repeat dose study. The objective of this trial was to compare the safety and tolerability of 3% SPL7013 Gel (VivaGel™) with placebo gel when applied to the penile epithelium of both circumcised and uncircumcised healthy men. This was the second study of the product in humans and was carried out in sexually abstinent, healthy male volunteers. The effectiveness of the drug in preventing HIV or genital herpes was not studied.
Blinding Status	Double-blind
Treatment Method	Volunteers were instructed to apply a 2g application of gel once daily each evening for seven consecutive days, and to leave the gel in place for 6 to 12 hours
Route of Admin	Topical, to the shaft and glans of the penis
Dose Level / Freq.	2g of 3% SPL7013 Gel or placebo gel, once daily for 7 days
Number of Trial Subjects	A total of 36 healthy male volunteers were stratified according to circumcision status (18 circumcised, 18 uncircumcised), randomised and treated
Subject Withdrawal or Dropout	One circumcised trial participant was withdrawn from the study after randomisation, but before administering study product, due to a genital skin condition detected at baseline. This participant was replaced by another circumcised participant. No other subjects were withdrawn or dropped out of the trial.
Subject Selection Criteria	Subjects were required to be healthy males, aged 18 years or older, free from sexually transmitted infections or genital conditions. In practice, the age of trial participants spanned 21-67 years.
Safety and Tolerability	The study showed that VivaGel™ is safe and well-tolerated when administered to the penis of both circumcised and uncircumcised healthy males once daily for seven consecutive days. There was no evidence of systemic absorption of SPL7013, and the gel was considered acceptable for use by study participants (i.e. a sample of Australian males). Detailed results for primary and secondary endpoints are shown below.

Primary Endpoint and Results	The primary endpoint was signs and symptoms of genital toxicity (i.e. incidence of genital adverse events (AEs)). The method of assessment and the results for this primary endpoint are described below.

Signs and Symptoms of Genital Toxicity

Background: Genital toxicity data was collected from reporting of solicited genital AEs (collected via a diary card) and non-solicited genital AEs (collected during genital examination and spontaneous reporting by participants) throughout the study. Each study participant was instructed to complete a daily diary card where they were to indicate the presence or absence of the following genital events: penile burning, penile pain, penile itch, penile redness, penile rash, penile swelling, penile discharge, pain upon urination, and any other genital symptoms. The diary card was regularly reviewed throughout the study. In addition, at set times throughout the study, the investigator conducted a detailed genital examination of each study participant to determine whether there was any evidence of toxicity, such as inflammation or irritation, to the penile epithelium. All genital AEs were coded according to MedDRA (Medical Dictionary for Regulatory Activities) standardised AE terms, and the severity graded from 1-4 according to the United States' Division of AIDS (DAIDS) toxicity table.

Result: The genital adverse events reported throughout the study were mild (grade 1) and benign in nature and most lasted for less than 24 hours.

A total of 12 genital AEs were reported by 33% of study participants in the VivaGel™ group (8 of 24 men), compared with 5 genital AEs reported by 33% of study participants in the placebo group (4 of 12 men). There was no difference in the incidence of genital events between the VivaGel™ and placebo groups when analysed either for all genital AEs or for those genital AEs deemed to have a potential causal relationship with study product.

The most commonly reported events were genital pruritus (penile itch) (12% participants in VivaGel™ group and 8% in placebo) and application site erythema (penile redness) (4% in VivaGel™ group and 25% in placebo). No patterns emerged in genital events between the circumcised and uncircumcised strata in either VivaGel™ or placebo treatment groups.

Secondary Endpoint and Results	The secondary endpoints for this study were: non-genital AEs; laboratory abnormalities; and plasma concentrations of SPL7013. The methods of assessment and the results for these secondary endpoints are described below.

Non Genital Adverse Events

Background: At set times throughout the clinical trial, the vital signs (e.g. temperature, pulse rate and blood pressure) for each volunteer were recorded, blood was drawn for laboratory measurements (*e.g.* haematology, coagulation and clinical chemistry) and, as for genital AEs, non-genital AEs were recorded according to MedDRA standardised AE terms and severity graded from 1-4 according to DAIDS toxicity tables. An AE can be any untoward medical occurrence in a clinical trial subject and does not necessarily have any causal relationship to the treatment administered.

Results: All measurements of vital signs and assessment of laboratory tests were deemed to be acceptable by the Principal Investigator.

There were no serious adverse events (SAEs) in any of the subjects during this study, nor any grade 3 or 4 AEs.

There was no evidence of systemic toxicity (as indicated by patterns of non-genital AEs) in either treatment group. Of the 32 non-genital AEs reported, 16 were deemed to have a potential causal relationship to study product (6 AEs were reported by 25% participants in the VivaGel™ treatment group, and 10 AEs were reported by 33% participants in the placebo group).

Three non-genital AEs were considered potentially related to study product and reported as “moderate” in intensity (grade 2), however all were reported by participants in the placebo treatment group. All other non-genital AEs deemed to be possibly related to study treatment were of mild intensity. The most commonly reported AE was headache with 13% participants reporting in the active group compared with 25% participants in the placebo group. All other non-genital AEs were reported in no more than one participant in each treatment group. These AEs were deemed not clinically significant by the Principal Investigator.

Level of SPL7013 in the Blood Following Penile Administration of SPL7013 Gel (Plasma Pharmacokinetics)

Background: The active ingredient of SPL7013 Gel, the dendrimer SPL7013, exerts its activity in the vagina during the initial stages of exposure to and infection with HIV or other sexually transmitted infections during heterosexual intercourse. The systemic safety profile of the product in male sexual partners of women using the product will be benefited if there is minimal absorption of SPL7013 through the penile epithelium into the blood system. If SPL7013 is absorbed into the blood, there may be systemic effects due to systemic exposure. The pharmacokinetics of SPL7013 absorption, if any, were determined in the current trial by analysing plasma samples collected from the participants during various study visits (4 samples in total per participant). In several non-clinical animal studies conducted prior to the clinical trial, SPL7013 was not detected in any plasma samples taken from the animals after vaginal administration of SPL7013 gels. In addition, no detectable absorption was seen after vaginal administration in the first clinical study, SPL7013-001.

Results: No SPL7013 was detected in any plasma sample at or above the lower limit of quantification of the validated bioanalytical assay method used. This finding in males adds to the body of non-clinical and clinical evidence, and suggests that SPL7013 is not absorbed into the blood following penile administration of SPL7013 Gel. This finding is promising from both a safety and efficacy viewpoint, because it means that exposure to the drug is localised to the place of administration and site of action in both women and men, without local irritation or systemic effects.

Acceptability

Background: Potential compliance with any preventative product is highly dependent upon the acceptability of the product to those who will use it. It is therefore important that VivaGel™ is acceptable by men for use during sexual intercourse as this will strongly influence the female partner's view of using the product. In order to determine the acceptability of the product a semi-structured interview was conducted with study participants before and after product administration to investigate the expectations of, and experiences with, the study gel.

Results: Qualitative analysis of the acceptability interviews indicated that VivaGel™ would be acceptable to participants if shown to be protective against sexually transmitted infections, and there were few concerns around the potential impact on sexual pleasure.

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