



VivaGel[®] Vaginal Microbicide

Product Summary (Non-Confidential)

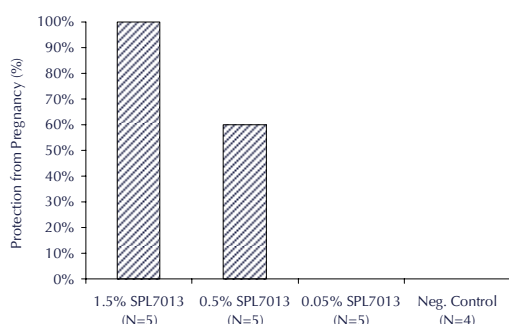
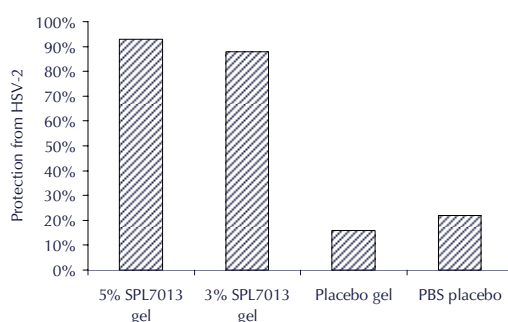
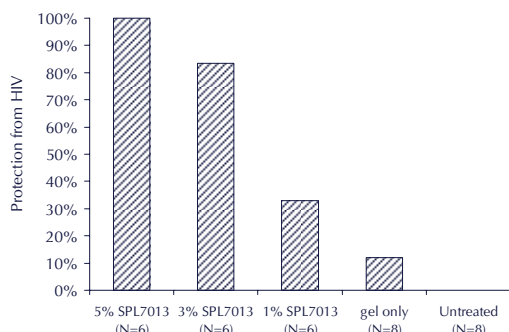


Product Description	VivaGel [®] (SPL7013 Gel) is a topical vaginal microbicide under development by Starpharma Holdings Ltd for the prevention of infection with HIV and HSV-2. It also has potential application for other sexually transmitted infections and as a contraceptive.								
Motivation	HIV and HSV-2 are widely prevalent diseases with no known cure. Condoms can only protect when used, and condom usage rates are relatively low. Studies suggest that a microbicidal gel with appropriate characteristics is associated with an “intent to purchase” probability of up to 69% in young US women. Independent data shows a strong causal link between HIV and HSV-2, so that protection against one may help avoid subsequent infection by the other, hence a dual action gel.								
Drug Substance	SPL7013 is assembled by the addition of lysine molecules in layers onto a central core to form a dendrimer, the surface of which is derivatised with sodium naphthalene disulfonate.								
SPL7013 Gel Drug Product	VivaGel [®] is a 3% w/w formulation of SPL7013 in a Carbopol [®] based, aqueous gel. The formulation was selected for its muco-adhesive properties and its similarity to existing, marketed vaginal products. Apart from SPL7013, all ingredients of the gel are standard pharmaceutical excipients that have Generally Recognized As Safe (GRAS) status.								
Presentation	VivaGel [®] is supplied in single-use, pre-filled vaginal applicators made from polypropylene. The applicators are made by HTI Plastics and are the subject of a drug master file with the US FDA.								
Indications - by Stage of Development	<table border="0"> <tr> <td>HIV</td> <td>(Phase I/II—“expanded safety”)</td> </tr> <tr> <td>HSV-2</td> <td>(Phase I/II—“expanded safety”)</td> </tr> <tr> <td>HPV</td> <td>(positive <i>in vitro</i> data: <u>activity observed beyond strains addressed by vaccines</u>)</td> </tr> <tr> <td>Contraception</td> <td>(positive <i>in vitro</i> and <i>in vivo</i> data)</td> </tr> </table>	HIV	(Phase I/II—“expanded safety”)	HSV-2	(Phase I/II—“expanded safety”)	HPV	(positive <i>in vitro</i> data: <u>activity observed beyond strains addressed by vaccines</u>)	Contraception	(positive <i>in vitro</i> and <i>in vivo</i> data)
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Mechanism of Action	The mechanism of action for SPL7013 for both pathogens is believed to be prevention of attachment of the virus to human cells. In the case of HIV it is believed that this is achieved by attachment to viral membrane protein gp120, inhibiting binding of virus to CD-4 receptors on human T-cells. The mechanism is believed to be analogous for HSV-2 and Glycoprotein B. VivaGel’s contraceptive effect appears to be based on several mechanisms including hyaluronidase inhibition and stimulation of acrosomal loss.								
Clinical Program	VivaGel [®] is being developed for HIV and HSV-2 under two FDA INDs. Two safety and tolerability trials have been successfully completed, providing data for both male and female safety. A third study has completed recruitment and data analysis is underway. A fourth, expanded, safety trial has commenced. Data from all trials is consistent with continuation of the development of VivaGel [®] . Efficacy will be determined in population-based studies. VivaGel [®] has received Fast Track development status from the FDA for its HIV indication.								
Commercial Position	<p><i>Applicator Presentation:</i> VivaGel[®]’s development is supported by > US\$26m from the US NIH. This funding does not encumber the product commercially and it is currently available for licensing.</p> <p><i>Condom Coating Presentation:</i> In October 2007 Starpharma announced a co-development agreement with SSL International, the manufacturers of Durex[®] condoms for condom coating applications of VivaGel[®]. The agreement does not restrict Starpharma from licensing the “stand-alone” applicator presentation of the gel.</p>								
Further Reading	VivaGel [®] non-confidential brochure (20pp approx)								

continued overleaf...



Efficacy Data



HIV Study.

in vivo - Macaque

Experiment design: To increase risk of infection, hormone was used to thin the vaginal epithelium prior to challenge. 1000µl of gel was applied vaginally. After 20 minutes 500µl of SHIV_{89.6P} was introduced into the vagina at a viral titre judged to be far higher than would be encountered clinically. Animals assessed for 36 weeks post-challenge for signs of infection and disease.

HSV-2 Study

in vivo - Guinea pig

Experiment design: (N=18 per arm). To increase risk of infection, hormone was used to thin the vaginal epithelium prior to challenge. 200µl of gel or placebo was applied intravaginally. After 5 minutes virus (200µl of strain MS; 10⁶ plaque forming units) was introduced into the vagina. Animals were assessed over several days post infection for signs of continued intravaginal infection and disease (e.g. lesions, swelling).

Contraception Study

In vivo - Rabbit

Experiment design: Test agents were delivered to the cervico-vagina using a flexible cannula, and 5 minutes later the inseminating dose was delivered in the same manner. Fertilisation = number of embryos formed per doe. Other studies suggested that a contraceptive effect continued at 24 and 48 hours.

HPV Study

in vitro - Pseudovirion uptake assay

Strong activity observed in strains HPV-5, 6, 16 and 45 at concentrations of SPL7013 low compared to that found in VivaGel®. No marketed vaccine has a registered indication for the HPV-45 strain.

Patent Coverage

	Description	Filing Date	Publication No	Granted Patents	Applications Pending
SPL-1	Active ingredient in VivaGel® (SPL7013)	1995	WO95/34595	Australia, Austria, Brazil, Canada, China, Europe, Hong Kong, Mexico, New Zealand, Singapore, South Korea, USA (6,190,650)	Japan
SPL-4	Method for the treatment of microbial or parasitic agents using SPL7013	1999	WO00/15240	Australia, Europe, New Zealand, Singapore, South Korea, USA (6,464,971)	Brazil, Canada, China, Mexico, South Korea, USA (CIP- 10/227,538)
SPL-6	The use of SPL7013 for the treatment of STD's	2002	WO02/079299	Australia, China, Europe, NZ, Singapore	Brazil, Canada, South Korea, USA (10/472,439)
SPL-8	Condom carrying SPL7013	2006	WO07/045009	-	Argentina, Australia, China, Europe, India, Japan, Malaysia, Mexico, New Zealand, South Korea, Taiwan, USA
SPL-14	SPL7013 for use as a contraceptive	2007	WO07/106944	-	International (PCT)

CONTACT

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