starpharma

ASX Announcement

Successful VivaGel® Phase 3 results and NDA planned for rBV

- **VivaGel® BV demonstrated statistically significant efficacy in two pivotal phase 3 trials**
- **VivaGel® BV consistently resulted in reduced rates of BV recurrence by the primary efficacy endpoint and five secondary efficacy measures, and delayed time to first recurrence**
- **VivaGel® BV resulted in sustained benefits 3 months after cessation of treatment**
- **The majority of women who used VivaGel® BV in both studies remained BV-recurrence-free during the 16-week treatment phase**
- **VivaGel® BV demonstrated excellent safety and tolerability, including very low rates of candidiasis**
- **These trial results strongly support marketing applications to US FDA and other regulators for rBV indication and add significant commercial value to VivaGel® BV**
- **FDA QIDP and Fast Track designations already granted for VivaGel® BV, providing significant commercial and regulatory advantages**
- **VivaGel® BV New Drug Application (NDA) is well-advanced for both BV indications (treatment and prevention of rBV)**
- **Phase 3 trial data significantly enhances the commercial opportunity for VivaGel® BV through the ongoing licensing process, facilitated by a global healthcare investment bank**

Melbourne, Australia; 7 August 2017: Starpharma (ASX: SPL, OTCQX: SPHRY) today announced that its two phase 3 trials of VivaGel® BV for prevention of recurrent bacterial vaginosis (rBV) achieved their primary objective demonstrating statistically significant superiority compared to placebo in preventing rBV based on topline data.

Starpharma intends to submit a marketing application to the FDA for VivaGel® BV for prevention of rBV based on these positive results. There are currently no approved products for the prevention of rBV, which is a significant unmet medical need.

The two double-blind, randomised, placebo-controlled trials, SPL7013-017 (017 US trial) and SPL7013-018 (018 European trial), were identical in design and enrolled 1,223 women who had a history of rBV. A history of rBV was defined as at least three episodes of BV in the preceding 12 months (i.e. average of at least one recurrence every 16 weeks). Trial participants used either VivaGel® BV (1% SPL7013 Gel) or placebo gel on alternate days for 16 weeks. The 017 US trial was conducted at sites in the US, Puerto Rico, Canada and Mexico, and the 018 European trial was conducted at sites mainly in Europe but also included some sites in Thailand and the US.

The primary endpoint of both studies was BV recurrence at or by week 16 as diagnosed by clinical findings (i.e. presence of three out of four Amsel criteria). For the primary efficacy analyses, any patients who failed to attend the Week 16 visit were deemed to have recurred i.e. were imputed to failure (even if in reality they remained BV free), making this a very rigorous efficacy result.

In the 017 US trial, the rate of BV recurrence at or by Week 16 (i.e. the primary endpoint) in the VivaGel® BV group was 44.2% (statistically significant versus placebo 54.3%, P=0.015, N=585) – see Figure A below. Actual BV recurrence rates, not imputing missing data to failure, were even lower at 34.9% for VivaGel® BV and 46.6% for placebo.

It has been observed in the literature that vaginally delivered placebos can have effect on BV, as was seen in both these trials. Therefore, in assessing the patient benefit of VivaGel® BV in this trial (apart from comparing to placebo) it is also useful to refer to expected rates of BV recurrence over a 16-week period without any intervention at all (i.e., placebo or active). Recurrence rates over 16-weeks in untreated rBV patients range between 65-85%[1] in the literature. In addition, a 16-week Historical Recurrence Rate (HRR) using the trial participants' historical BV recurrences immediately prior to commencing the trial was estimated. This 16-week Historical Recurrence Rate for the trial participants in the 017 US trial was approximately 65%.

In the 018 European trial, the rate of BV recurrence at or by Week 16 in the VivaGel® BV group was just 15.7% (statistically significant versus placebo 22.6%, P=0.027, N=636) – see Figure B below. In comparison, the 16-week Historical Recurrence Rate (without intervention) for the 018 European trial participants was approximately 50%.

Given the rates of BV recurrence in the 018 European trial were lower than expected, and low compared with the 017 US trial, an investigation was conducted prior to data unblinding, and efficacy analyses (additional analysis) were also conducted on a modified subset population. This additional analysis excluded a number of sites in countries (e.g., Ukraine and Romania) where recurrence rates were lower than anticipated. In this additional analysis, the same pattern of benefit of reduced recurrence was also demonstrated for VivaGel® BV compared with placebo as for the full analysis, although due to the reduced sample size in this subset compared with the full analysis, the difference was not statistically significant (VivaGel® BV recurrence rate 28.2% versus placebo 33.9%, P=0.266, N=327).

Figure A

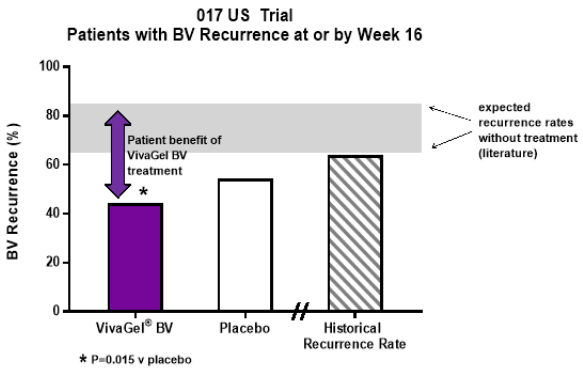
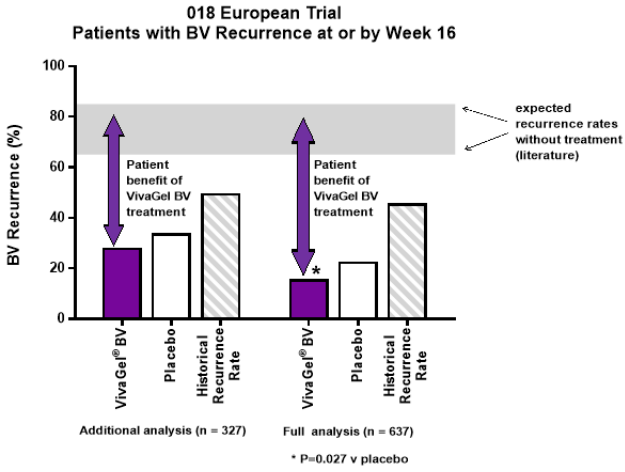


Figure B



In addition to the individual trial results reported above, when the data from both trials is combined, statistically significant differences between the rates of BV recurrence in the VivaGel® BV group versus placebo are also clearly demonstrated (017 US trial plus 018 European trial full analysis P=0.002, 017 US trial plus 018 European trial additional analysis P=0.014).

[1] According to key opinion leader (KOL) estimates and literature reports:
- Larsson, 1992; Boris et al, 1997; Vutyavanich et al, 1993

Further to the compelling benefits of VivaGel® BV in the primary endpoint, VivaGel® BV demonstrated statistically significant benefits compared with placebo in five secondary efficacy endpoints, including:

- **Time to recurrence of BV** (017 US trial P=0.007; 018 European trial full analysis P=0.009, additional analysis P=0.055);
- **Reduced recurrence of patient reported symptoms** of vaginal odour and/or discharge (017 US trial P<0.001; 018 European trial full analysis P=0.019, additional analysis P=0.032);
- **Reduced recurrence of BV by Nugent score of 7-10** (017 US trial P=0.012; 018 European trial full analysis P=0.002, additional analysis P=0.016);
- **Reduced recurrence of BV by clinical findings (i.e. 3 out of 4 Amsel criteria) and Nugent score greater than or equal to 4** (017 US trial P=0.008; 018 European trial full analysis P=0.014, additional analysis P=0.045); and
- **Reduced recurrence of individual Amsel criteria** as assessed by clinicians, including discharge (017 US trial P=0.015; 018 European trial full analysis P=0.011, additional analysis P=0.012), positive whiff test (017 US trial P=0.082; 018 European trial full analysis P=0.010, additional analysis P=0.022) and clue cells (017 US trial P=0.014; 018 European trial full analysis P=0.001, additional analysis P=0.008).

VivaGel® BV also resulted in sustained benefits well beyond cessation of treatment. Reduced recurrence of BV by the primary and secondary efficacy endpoints (including discharge, odour and clinical findings) were observed not only during the 16-week treatment period, but were also sustained during the 12-week follow-up period off-treatment.

Starpharma greatly appreciates the time and effort of the many women who volunteered for participation, along with the excellent support of clinicians and healthcare professionals in these trials.

Detailed results and the trial design are shown in Appendix 1, followed by a glossary of terms.

Results commentary

Dr Jackie Fairley, Starpharma Chief Executive Officer said: “We are delighted to report these successful phase 3 trial results, in which VivaGel® BV has demonstrated compelling efficacy in all six primary and secondary efficacy measures. Our NDA for VivaGel® BV for both treatment and rBV is well-advanced, and we’ll be using these data to complete the clinical package for submission to the FDA and other regulatory authorities.”

“There’s a desperate need for new therapeutic options for BV, a serious condition that affects nearly 1 in 3 women globally. The fact that VivaGel® BV is not a conventional antibiotic and specifically targets BV bacteria, makes it a particularly appealing solution for patients. It also represents a highly attractive commercial proposition especially given it will be first in class for the prevention of rBV. VivaGel® BV has potential to gain a significant share of this market, which is estimated to be in excess of US$1 billion per annum globally,” added Dr Fairley.

"Antibiotic resistance is a major issue globally and VivaGel® BV offers an alternative to conventional antibiotic therapies for BV. We know that patients and clinicians are very attracted to the non-antibiotic nature of the product, its novel mechanism of action on biofilm, and the fact that it is not absorbed into the bloodstream contributing to its excellent safety and tolerability profiles," concluded Dr Fairley.

Expert comments on VivaGel® BV and the trial results

Professor Jane Schwebke: "I have many patients who have recurrent BV and suffer from frequent episodes of the condition. It's very frustrating for these women and also for me as their physician that there are no effective therapies available, so the development of an efficacious BV preventative will be highly valued. In light of the importance of biofilm in the pathogenesis of BV, a therapy such as VivaGel® BV that disrupts biofilm would be most welcome for both the treatment and prevention of the condition."

Dr Jane Schwebke, MD is a Professor of Medicine in the Infectious Disease Division at the University of Alabama at Birmingham and Consultant for the Jefferson County Department of Health STD clinic, Key Opinion Leader, world authority in bacterial vaginosis and Principal Investigator in the 017 US trial.

Professor George Kinghorn: "BV is very common and often a persistent condition. Management of recurrent BV is problematic and there is a significant need for products that work differently to existing antibiotics and are suitable for use longer term.

In both phase 3 VivaGel® BV studies of rBV, the majority of VivaGel® BV treated women remained recurrence free during the 16-week treatment period. In addition, the product demonstrated consistent benefits in terms of improvements in patient symptoms and in objective clinician and bacteriologic assessments in those treated with VivaGel® BV as compared with placebo. The treatment was well tolerated and there was a very low rate of vaginal candidiasis. As a clinician, I'm impressed with the trial data for VivaGel® BV for rBV and believe that it will offer a new management tool for this very troublesome condition."

Dr George Kinghorn is an international expert in bacterial vaginosis having worked in the field for 40 years, most recently as Consultant Physician and Professor in the Department of Genitourinary Medicine, Royal Hallamshire Hospital, in Sheffield, UK.

Dr Philip McCloud: "The results for VivaGel® BV across these pivotal trials are strong. In the analyses VivaGel® BV demonstrated consistent and statistically significant benefits compared to placebo across multiple efficacy measures."

Dr Philip McCloud, International Biostatistics & Data Management Specialist, Director & Principal Statistician of McCloud Consulting Group. Dr Philip McCloud has 40 years' experience as an applied statistician at the top levels of the Pharmaceutical Industry, Government and Academia, overseeing the provision of expert statistical consulting and clinical data management. He was the biostatistician for these VivaGel® BV phase 3 trials.

Next Steps

These trial results strongly support marketing applications to the US FDA and other regulators for the BV prevention indication and add significant commercial value to VivaGel® BV.

The FDA new drug application (NDA) for VivaGel® BV for both treatment and rBV is well-advanced and data from the trials reported today will be incorporated to complete the clinical package. The NDA will be submitted to the FDA as soon as practicable with the initial sections of the rolling submission due for lodgement shortly. Throughout the preparation of the NDA, Starpharma continues to leverage the QIDP designation and Fast Track status

granted by the FDA for VivaGel® BV. These designations carry significant benefits for regulatory approval and commercialisation, including increased dialogue with the FDA, priority regulatory review and an additional five years of market exclusivity. Starpharma also has a Special Protocol Agreement in place from the FDA for VivaGel® BV which provides binding FDA agreement on the phase 3 trial design.

In addition, the data from these trials will also be submitted to other regulatory authorities including in Europe, to expand the indications for VivaGel® BV to include rBV.

Negotiations are continuing with a number of parties for regional and global commercial rights to VivaGel® BV. These trial results confirm the product's utility in both treatment and rBV and will have a significant positive impact on value. Starpharma has recently appointed a leading global healthcare investment bank to support the competitive process and for finalising commercial arrangements with potential partners.

About Bacterial Vaginosis (BV)
Bacterial vaginosis is the most common cause of vaginal infection for women of childbearing age, and affects around 30% of women in the US. It is a highly recurrent condition with 50-60% of sufferers having it recurrently. BV is caused by an imbalance of naturally occurring bacterial flora (the usual bacteria found in a woman's vagina). Smoking, the use of some hygiene products and several other risk factors are linked to a higher risk of developing BV. If left untreated, BV can cause a range of serious medical problems including pelvic inflammatory disease, infertility, premature delivery and miscarriage, low birth weights and uterine infection.BV also increases a woman's chance of acquiring HIV and other sexually transmitted infections and increases the likelihood that a woman will infect her partner with these conditions.

About VivaGel® BV
VivaGel® BV is a water based gel for topical treatment and rapid relief of bacterial vaginosis (BV). It is based on Starpharma's SPL7013, astodrimer sodium, a proprietary dendrimer that blocks certain bacteria involved in BV and also has potent antiviral activity against certain viruses (HIV, HSV, HPV, Zika).

The VivaGel® BV treatment product, which is already approved in Europe, targets an area of significant unmet medical need in a high-value market (est. US$750M) and has been licensed to Aspen Pharmacare with preparations underway for launch. A second VivaGel® BV product recently completed phase 3 clinical development for the prevention of recurrent BV which is another high value market (est. US$1B) for which there are currently no clinically approved products.

About Starpharma

Starpharma Holdings Limited (ASX: SPL, OTCQX:SPHRY), located in Melbourne Australia, is an ASX 300 company and is a world leader in the development of dendrimer products for pharmaceutical, life science and other applications.

Starpharma's underlying technology is built around dendrimers – a type of synthetic nanoscale polymer that is highly regular in size and structure and well suited to pharmaceutical and medical uses. Starpharma has two core development programs: VivaGel® portfolio and DEP® drug delivery with the Company developing a number of products internally and others via commercial partnerships.

VivaGel®: Starpharma's portfolio includes late stage women's health products based on VivaGel® (SPL7013, astodrimer sodium), a proprietary dendrimer. VivaGel® formulated as a water based gel and delivered vaginally - VivaGel® BV - has EU regulatory approval for topical treatment and rapid relief of bacterial vaginosis (BV) and has recently completed clinical development for the prevention of recurrent BV. Starpharma has signed a license agreement with Aspen Pharmacare Australia Pty Ltd for the sales and marketing of VivaGel® BV in Australia and New Zealand. Starpharma has also signed separate license agreements with Ansell Limited (ASX:ANN), Okamoto Industries. Inc., (TSE: JP3192800005), Sky and Land (China) and Koushan Pharmed (Iran) to market a value-added, VivaGel® condom. The VivaGel® condom is available for purchase in Australia and in Canada under Ansell's Lifestyles® Dual Protect™ brand. Ansell manufactures and sells leading condom brands worldwide, including LifeStyles®, Manix®, ZERO® and SKYN®. Okamoto is the market leader for condoms sold in Japan, which is the world's second largest condom market.

DEP®: The other major part of Starpharma's pharmaceuticals business is its proprietary DEP® drug delivery platform. Starpharma has both partnered and internal DEP® programs in Drug Delivery. A number of dendrimer-enhanced, or DEP® versions of existing drugs are under development by the Company. The most advanced of these is DEP® docetaxel, a dendrimer-enhanced version of docetaxel (Taxotere®), which is in clinical development in patients with solid tumours. In preclinical studies DEP® docetaxel has shown significant tumour-targeting and superior anti-cancer effects across a range of important cancer types including breast, prostate, lung and ovarian tumour, when compared to Taxotere® (docetaxel). In the partnered area, AstraZeneca has signed a licensing agreement with Starpharma for the use of its DEP® drug delivery platform in the development and commercialisation of a number of AstraZeneca oncology compounds.

Starpharma.com | Twitter | LinkedIn

Media
WE Buchan Consulting
Rebecca Wilson
Mob: +61 417 382 391
rwilson@buchanwe.com.au

Arthur Chan
+61 2 9237 2805
achan@buchanwe.com.au

Starpharma
Dr Jackie Fairley, Chief Executive Officer
Nigel Baade, CFO and Company Secretary
+61 3 8532 2704
investor.relations@starpharma.com

Forward Looking Statements

This document contains certain forward-looking statements, relating to Starpharma's business, which can be identified by the use of forward-looking terminology such as "promising", "plans", "anticipated", "will", "project", "believe", "forecast", "expected", "estimated", "targeting", "aiming", "set to", "potential", "seeking to", "goal", "could provide", "intends", "is being developed", "could be", "on track", or similar expressions, or by express or implied discussions regarding potential filings or marketing approvals, or potential future sales of product candidates. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no assurance that any existing or future regulatory filings will satisfy the FDA's and other authorities' requirements regarding any one or more product candidates nor can there be any assurance that such product candidates will be approved by any authorities for sale in any market or that they will reach any particular level of sales. In particular, management's expectations regarding the approval and commercialization of the product candidates could be affected by, among other things, unexpected trial results, including additional analysis of existing data, and new data; unexpected regulatory actions or delays, or government regulation generally; our ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry, and general public pricing pressures; and additional factors that involve significant risks and uncertainties about our products, product candidates, financial results and business prospects. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected. Starpharma is providing this information as of the date of this document and does not assume any obligation to update any forward-looking statements contained in this document as a result of new information, future events or developments or otherwise.

APPENDIX 1 – CLINICAL TRIAL SUMMARY AND RESULTS

Official Title: A phase 3, double-blind, multicentre, randomised, placebo-controlled study to determine the efficacy and safety of SPL7013 Gel (VivaGel®) to prevent the recurrence of bacterial vaginosis

Identifying Codes: Starpharma Protocol Numbers: SPL7013-017 and SPL7013-018

Primary Objective:
- To determine the efficacy of 1% SPL7013 Gel in reducing recurrent BV

Secondary Objective:
- To determine the safety and tolerability of 1% SPL7013 Gel

Primary Efficacy Endpoint:
- Recurrence of BV at or by the Week 16 visit

  (a diagnosis of BV is defined as the presence of at least 3 clinical findings, i.e., at least 3 of the 4 Amsel criteria: (i) the presence of homogenous vaginal discharge characteristic of BV; (ii) positive whiff test; (iii) clue cells representing at least 20% of total epithelial cells; (iv) vaginal fluid pH greater than 4.5)

Secondary Endpoints:

<u>Secondary Efficacy Endpoints</u>
- Time to recurrence of BV according to the primary efficacy endpoint definition
- Presence of patient-reported BV symptoms (vaginal odour and/or discharge) at or by the Week 16 visit
- Recurrence of individual Amsel criteria at or by the Week 16 visit
- Recurrence of BV as determined by presence of a Nugent score of 7-10 at or by the Week 16 visit
- Recurrence of BV according to the composite definition of at least 3 clinical findings and a Nugent score of at least 4 at or by the Week 16 visit

<u>Other Secondary Endpoints</u>
- Adverse events (AEs) during the Double-blind Treatment and Follow-up Phases

Study Design: Double-blind, multicentre, randomised, placebo-controlled, phase 3 studies.

After screening, eligible participants entered the Open-label Treatment phase and received a seven-day course of oral metronidazole (500 mg twice daily). At the Baseline visit for the Double-blind Treatment phase, eligible participants were randomised in a 1:1 ratio to receive either 1% SPL7013 Gel or hydroxyethyl cellulose (HEC) placebo gel at a dose of 5g administered vaginally at bedtime on alternate days for 16 weeks. Participants returned to the site at approximately 4-weekly intervals to the Week 16 visit.

During the Follow-up phase, participants returned to the site at approximately 4-weekly intervals to the End of Study visit (week 28).

Sites:

- SPL7013-017 was conducted at 66 sites in the US, Canada, Mexico and Puerto Rico.
- SPL7013-018 was conducted at 46 sites in Europe (UK, Bulgaria, Romania, Ukraine, Hungary, Czech Republic), US and Thailand.

Key Inclusion Criteria:

Enrolment into Open-label Treatment Phase:

- Women aged 18-45 years, inclusive
- Have a current episode of BV diagnosed by:
  - presence of at least 3 of the four Amsel criteria
  - Nugent score of ≥ 4
  - current patient reported symptoms consistent with BV or symptoms experienced within the previous three days in association with the current episode (i.e. any vaginal discharge, considered by the participant to be abnormal, and/or unpleasant vaginal odour)
- Have a history of recurrent BV, defined as at least three documented episodes in the previous 12 months, including the current episode
- Other than for the presence of BV, participant is of general good health
- Normal Pap smear at or documented within 2 years of screening

Enrolment into Double-blind Treatment Phase:

- As above, except participant's BV has resolved, as evidenced by absence of reported BV symptoms, and absence of the Amsel criteria regarding discharge, whiff test and clue cells

RESULTS

Sample Size:

- SPL7013-017: A total of 585 participants, aged 18 to 45 years, were randomised to receive 1% SPL7013 Gel (N=294) or placebo gel (N=291) and received at least one dose of study product.
- SPL7013-018: A total of 636 participants, aged 18 to 45 years, were randomised to receive 1% SPL7013 Gel (N=318) or placebo gel (N=318) and received at least one dose of study product and were included in the full analyses. The additional analyses as a result of site exclusions were conducted on a population limited to 327 participants randomised to receive 1% SPL7013 Gel (N=156) or placebo gel (N=171).

Efficacy: ***Primary Endpoint***

Table 1. Primary Endpoint – Recurrence of BV (defined as presence of at least 3 of the 4 Amsel criteria) at or by 16 weeks

Primary Endpoint Analyses	BV Recurrence Rate % (N)		*p*-value
	VivaGel® BV	Placebo	
017 US trial	44.2 (294)	54.3 (291)	0.015
018 European trial (full analysis)	15.7 (318)	22.6 (318)	0.027
018 European trial (additional analysis)	28.2 (156)	33.9 (171)	0.266

VivaGel® BV demonstrated benefit in terms of reduced rates of BV recurrence compared with placebo in all analyses. The differences were statistically significant in the US trial and the full analysis of the European trial. The difference did not reach statistical significance in the additional analysis of the European trial due to reduced sample size.

In assessing the patient benefit of VivaGel® BV in this trial (apart from comparing to placebo) it is also useful to refer to expected rates of BV recurrence over a 16 week period without any intervention at all (i.e., placebo or active). Recurrence

rates over 16 weeks in untreated rBV patients vary between 65-85% in the literature. In addition, a 16-week Historical Recurrence Rate (HRR) using the trial participants' historical BV recurrences immediately prior to commencing the trial was determined. This 16-week HRR for the trial participants was approximately 65% in the 017 US trial and approximately 50% for the 018 European trial participants. The "patient benefit" in Figures 1 and 2 is the difference between the expected recurrence rates and the rate of recurrence in the VivaGel® BV treatment arm.

Figure 1. Primary Endpoint – Patients with Recurrence of BV (defined as presence of at least 3 of the 4 Amsel criteria) at or by 16 weeks – 017 US trial

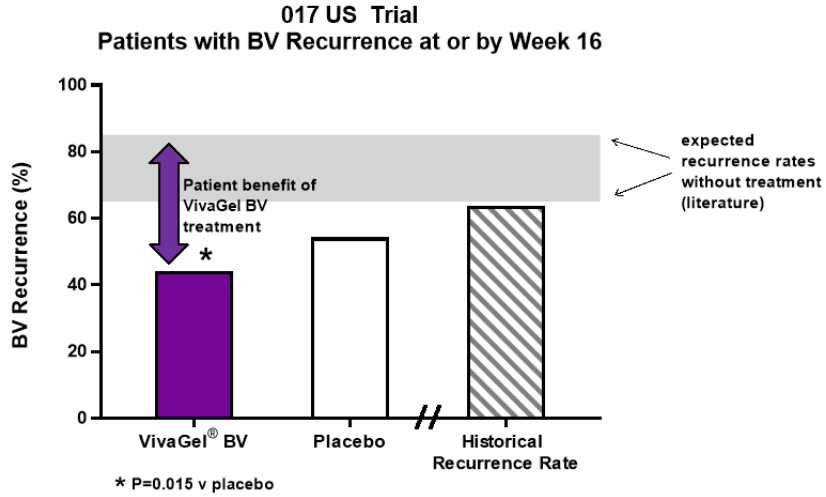
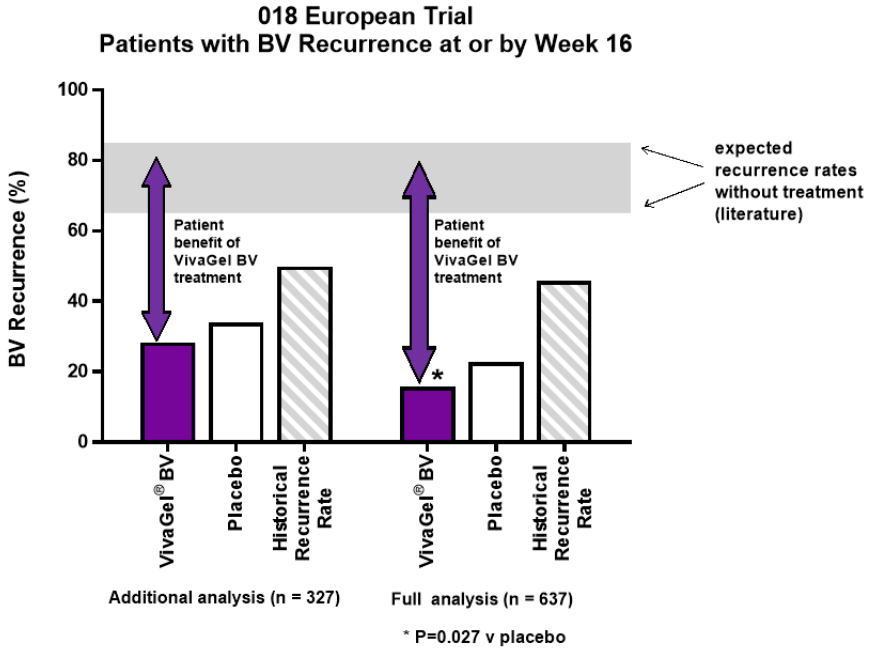


Figure 2. Primary Endpoint – Patients with Recurrence of BV (defined as presence of at least 3 of the 4 Amsel criteria) at or by 16 weeks –018 European trial



Secondary Endpoints

Further to the compelling benefits of VivaGel® BV in the primary endpoint, VivaGel® BV demonstrated statistically significant benefits compared with placebo in five secondary efficacy endpoints.

Figure 3. Secondary Endpoint – Time to Recurrence of BV (primary endpoint definition) – 017 US trial

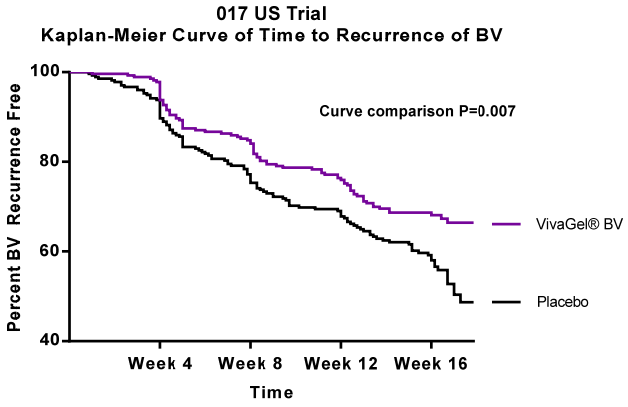
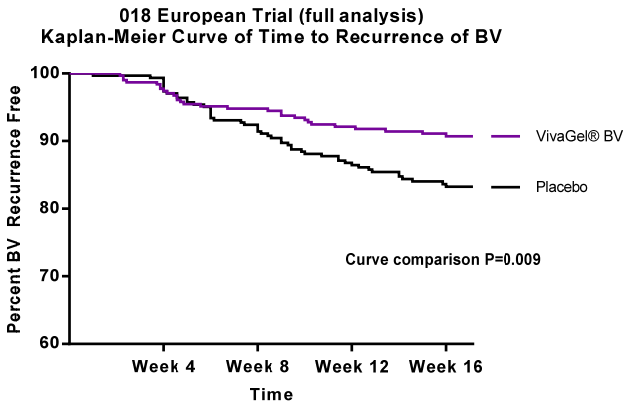


Figure 4. Secondary Endpoint – Time to Recurrence of BV (primary endpoint definition) – 018 European trial



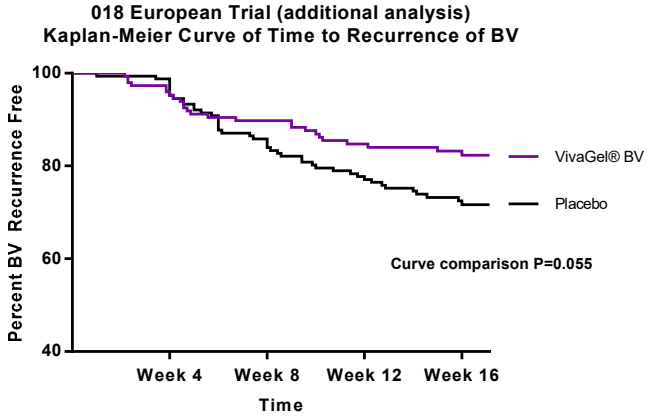


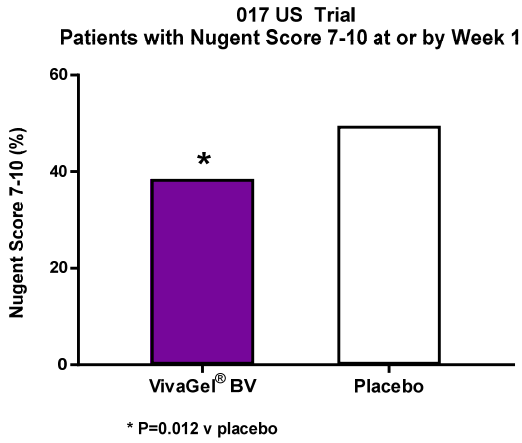
Table 2. Secondary Endpoint – Recurrence of BV (defined as presence of Vaginal Odour and/or Discharge) at or by 16 weeks

Secondary Endpoint Analyses Patient Reported Symptoms (Vaginal Odour and/or Discharge)	Recurrence Rate %		*p*-value
	VivaGel® BV	Placebo	
017 US trial	23.0	36.5	<0.001
018 European trial (full analysis)	14.4	21.7	0.019
018 European trial (additional analysis)	23.8	34.9	0.032

Table 3. Secondary Endpoint – Recurrence of BV (defined as presence of Nugent Score 7-10) at or by 16 weeks

Secondary Endpoint Analyses Nugent Score 7-10	Recurrence Rate %		*p*-value
	VivaGel® BV	Placebo	
017 US trial	38.5	49.5	0.012
018 European trial (full analysis)	14.4	24.6	0.002
018 European trial (additional analysis)	18.8	31.1	0.016

Figure 5. Secondary Endpoint – Recurrence of BV (defined as presence of Nugent Score 7-10) at or by 16 weeks



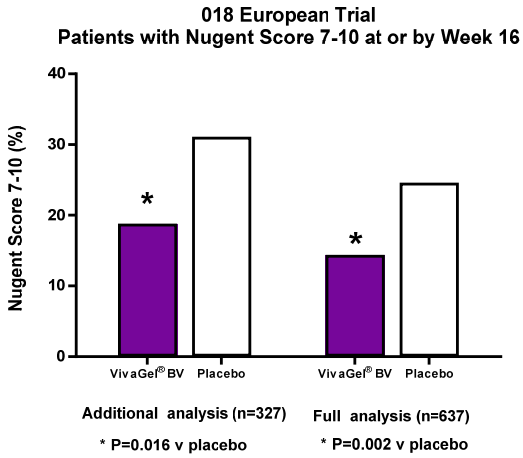


Table 4. Secondary Endpoint – Recurrence of BV (defined as presence of Clinical Findings [i.e. 3 out of 4 Amsel criteria] and Nugent Score ≥4) at or by 16 weeks

Secondary Endpoint Analyses Clinical Findings and Nugent Score ≥4	Recurrence Rate %		*p*-value
	VivaGel® BV	Placebo	
017 US trial	29.3	40.2	0.008
018 European trial (full analysis)	9.6	16.3	0.014
018 European trial (additional analysis)	17.2	26.7	0.045

Table 5. Secondary Endpoint – Recurrence of BV (defined as presence of Amsel criterion for discharge) at or by 16 weeks

Secondary Endpoint Analyses Amsel Criterion - Discharge	Recurrence Rate %		*p*-value
	VivaGel® BV	Placebo	
017 US trial	35.1	45.3	0.015
018 European trial (full analysis)	9.9	17.0	0.011
018 European trial (additional analysis)	16.6	28.5	0.012

Table 6. Secondary Endpoint – Recurrence of BV (defined as presence of Amsel criterion for whiff test) at or by 16 weeks

Secondary Endpoint Analyses Amsel Criterion – Whiff Test	Recurrence Rate %		*p*-value
	VivaGel® BV	Placebo	
017 US trial	35.9	43.1	0.082
018 European trial (full analysis)	10.9	18.3	0.010
018 European trial (additional analysis)	18.5	29.7	0.022

Table 7. Secondary Endpoint – Recurrence of BV (defined as presence of Amsel criterion for clue cells) at or by 16 weeks

Secondary Endpoint Analyses Amsel Criterion – Clue Cells	Recurrence Rate %		*p*-value
	VivaGel® BV	Placebo	
017 US trial	38.0	48.4	0.014
018 European trial (full analysis)	10.6	20.0	0.001
018 European trial (additional analysis)	18.5	31.7	0.008

Sustained Benefits

VivaGel® BV also resulted in sustained benefits well beyond cessation of treatment. Benefits in terms of reduced recurrence by the primary and secondary efficacy endpoints (including discharge, odour and clinical findings) were observed not only throughout the 16-week treatment period, but were also sustained throughout the 12-week follow-up period off-treatment.

Figure 6. Patients with Recurrence of BV (defined as presence of at least 3 of the 4 Amsel criteria) – 017 US trial

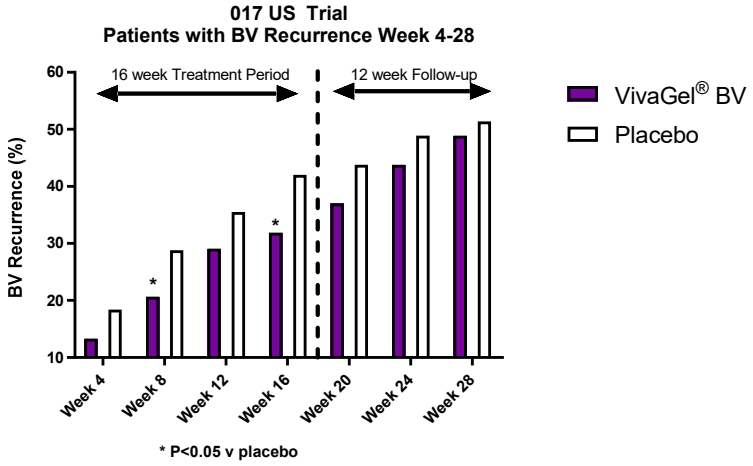


Figure 7. Patients with Recurrence of BV (defined as presence of at least 3 of the 4 Amsel criteria) – 018 European trial full analysis

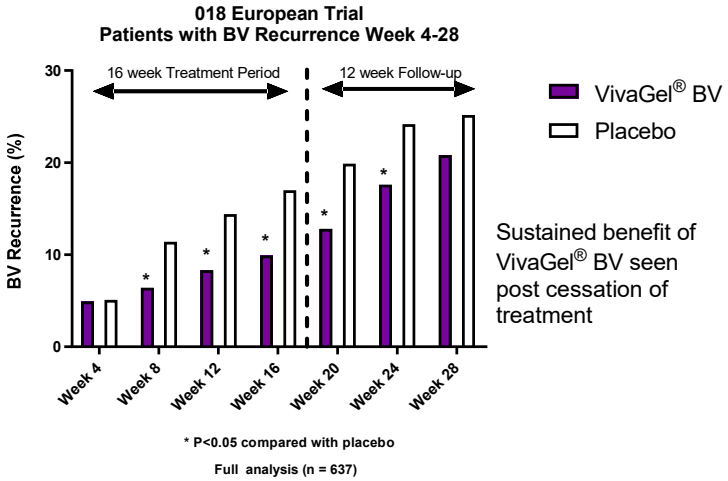


Figure 8. Patients with Recurrence of BV (defined as presence of vaginal odour and/or discharge) – 017 US trial

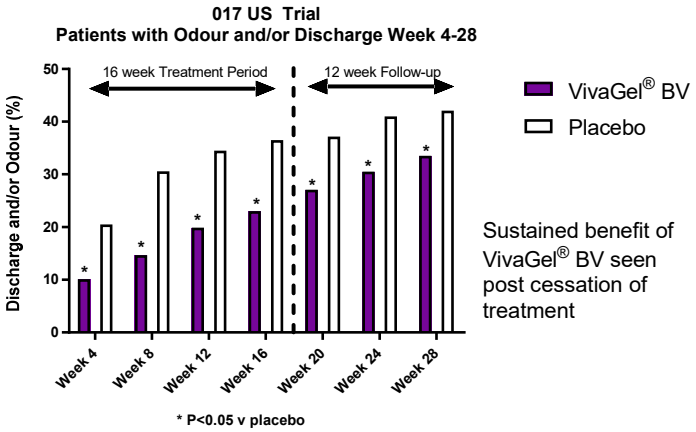
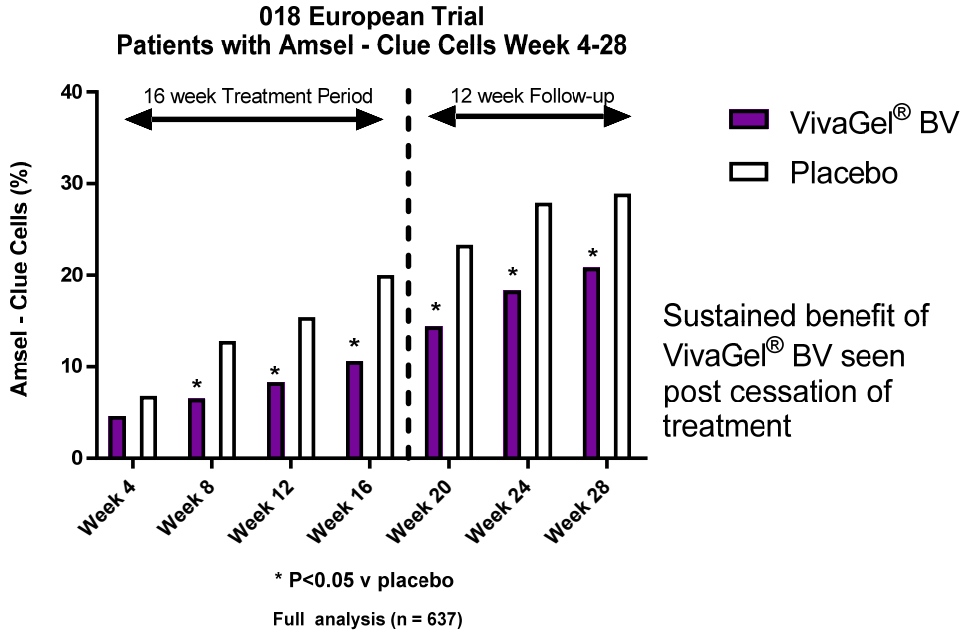


Figure 9. Patients with Recurrence of BV (defined as presence of clue cells) – 018 European trial



Safety and Tolerability:

Treatment Related Adverse Events (AEs)	017 US Trial				018 European Trial			
	During Treatment		Off Treatment		During Treatment		Off Treatment	
	VivaGel® BV	Placebo	VivaGel® BV	Placebo	VivaGel® BV	Placebo	VivaGel® BV	Placebo
Non-GU AEs	1.0%	1.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
GU AEs	10.9%	10.0%	1.4%	1.0%	1.6%	1.9%	0.3%	0.0%
Candidiasis	5.8%	2.7%	1.0%	0.0%	0.6%	0.9%	0.3%	0.0%

GU = genitourinary; During Treatment = Double-blind treatment phase; Off Treatment = Follow-up phase

Glossary of Terms

Amsel criteria	Refers to a set of four clinical assessments to objectively diagnose BV at the point of care. These four criteria are as follows: 1. Presence of an abnormal white-greyish vaginal discharge; 2. Whiff test, which consists of adding a few drops of a potassium hydroxide (KOH) solution to a sample of vaginal discharge to find out whether a strong fishy odor is produced; 3. Assessment of vaginal pH; the normal vaginal pH is 3.8 to 4.5. BV usually causes the vaginal pH to rise above 4.5; 4. Presence of "clue" cells on a wet mount; a sample of vaginal discharge is mixed with a saline solution after placing it on a microscope slide. The prepared slide is examined to identify the presence of unusual cells called clue cells. A diagnosis of BV is made if at least three of the four Amsel criteria are present.
BV Symptoms	Refers to abnormal vaginal discharge and odour, both clinical symptoms typically reported by women suffering from BV.
Clue cells	Cells from the vaginal epithelium with a distinctive stippled appearance due to the adherence of BV-related bacteria. The presence of clue cells is a sign used in the clinical diagnosis of BV.
Fast Track	Fast Track is a special designation for expedited review of drug candidates that are intended to treat a serious condition and fill an unmet medical need. The Fast Track designation enables more frequent interactions with the FDA, faster approval, and facilitates earlier market access for patients.
Imputed to failure	Imputing is a technique to complete missing study data. Having missing data is unavoidable and commonplace in clinical trials as a small proportion of participants will not attend all study visits. In this case, participants who were not able to be assessed for BV recurrence were considered to have recurred, thus imputed (or deemed) as failures.
NDA	NDA stands for New Drug Application. It is the regulatory vehicle to formally propose a new product for marketing approval in the US.
Nugent score	The Nugent score is a widely adopted standard scoring system for vaginal swabs to objectively diagnose BV. The Nugent score ranges from 0-10. A score of 7 to 10 is consistent with severe BV.
QIDP	QIDP stands for Qualified Infectious Disease Product. QIDP designation was created by the Generating Antibiotic Incentives Now (GAIN) Act in the US, and provides incentives for the development of new antimicrobial products. These incentives include priority regulatory review and an additional five years' of market exclusivity. Starpharma has been granted QIDP status for VivaGel® BV for both indications (treatment and rBV).
rBV indication	The use of VivaGel® BV to prevent repeated BV episodes in women suffering from recurrent BV. VivaGel® BV is applied every second day as a preventive therapy.

SPA	SPA stands for Special Protocol Assessment. An SPA is an advanced declaration from the Food and Drug Administration (FDA) that a Phase 3 trial is acceptable to support a marketing application for FDA approval. The purpose of an SPA is to allow a company to run or initiate a clinical trial of an experimental drug without risk that the FDA will object to the trial design itself, in the event that the company subsequently applies for product approval. Starpharma has an SPA for the VivaGel® BV rBV trials.
Statistical significance	*P<0.05
Treatment indication	The use of VivaGel® BV for the treatment of an acute episode of BV. VivaGel® BV is applied once a day for seven days.