

# SHAREHOLDER Update

**JANUARY 2019**

**VIVAGEL® BV**

**VIVAGEL®**

**>> FDA requests further data for VivaGel® BV approval in the US**

Upon completion of its review of the New Drug Application for VivaGel® BV, the US FDA advised Starpharma on 27 December 2018 that it requires confirmatory clinical data prior to approval of the product.

Starpharma has commenced the process of securing a meeting with the FDA as soon as practicable to discuss the data required. The meeting, which is expected to be scheduled during the next six-to-eight weeks, will allow the Company to clarify what clinical data will be required and whether this will be through the generation of new confirmatory clinical data, or whether the requirement can be satisfied by additional analyses of existing clinical data. In parallel and as part of the preparation for the FDA meeting, Starpharma is working closely with expert FDA consultants in the US, which include former senior FDA personnel, to expedite the path to approval.

Starpharma retains the Fast Track status and QIDP designation granted to VivaGel® BV and is keen to work with the FDA to secure approval with minimal delay to allow access to the product in the US.

**>> VivaGel® BV licensed to ITF Pharma in the US**

In December 2018, Starpharma signed a licence for the sales and marketing rights to VivaGel® BV in the US.

Under the licence, Starpharma is eligible to receive up to US\$101M in milestone payments in addition to escalating double-digit royalties on sales. The milestones comprise US\$20M in regulatory approval milestones for the two BV indications and up to US\$81M in commercial milestones.

**>> Launch of VivaGel® BV in multiple territories**

Advanced launch activities for VivaGel® BV are underway by both Mundipharma and Aspen in preparation for launches in multiple territories during the first half of 2019.

Starpharma and its manufacturers are also well advanced in manufacturing and supply chain activities in support of product launch. These supply activities have been occurring in parallel with extensive sales training, promotional activities, launch meetings (including with Key Opinion Leaders) and other marketing activities by Starpharma's partners (Mundipharma and Aspen).



*(continued on page 2)*

ITF Pharma is the US subsidiary of the leading private multinational pharmaceutical company, Italfarmaco SpA which employs around 3,100 people globally and has annual sales turnover of more than €720M.



**DEP® DRUG DELIVERY**

**>> Progress with internal DEP® drugs & AstraZeneca-DEP® patent published**



Positive interim trial results for DEP® docetaxel phase 2 trial; Four UK sites recruiting patients



Positive interim trial results for DEP® cabazitaxel phase 1 / 2 trial; Two UK sites recruiting patients in dose escalation phase



DEP® irinotecan outperforms in pancreatic cancer model; Phase 1 / 2 trial expected to commence FY19



DEP® docetaxel & DEP® cabazitaxel outperform in pancreatic cancer models



Patent published for AstraZeneca DEP® drugs & compelling data on Bcl2/xL conjugates



*(continued on page 3)*

**ANALYST COVERAGE**

**>> Macquarie initiates coverage of Starpharma**

On 16 January 2019, Macquarie initiated formal research coverage of Starpharma.



**VIVAGEL® BV**

**>> Launch of VivaGel® BV in multiple territories**

*(continued from page 1)*

Starpharma continues to be impressed with the speed at which Mundipharma is progressing with its registration and launch plans for multiple territories, including the launch in Europe.

Starpharma is working closely with its partners through participation in Key Opinion Leader briefings and sales/marketing training programs with its partners' teams. Optimal launch timings are being scheduled taking account of key

in-market factors, such as new product / sales cycles in the relevant outlets, but ultimately final timing is determined by Starpharma's partners.

With multiple international launches of VivaGel® BV planned, Starpharma is now set to move to a new phase with revenue growth expected to occur over time, as the product is rolled out globally.

In addition to revenue share and royalties, Starpharma is also eligible for milestone payments of up to US\$24.7 million from Mundipharma based upon certain events, such as regulatory approvals, market launches and sales thresholds.



Above: Headquarters of Mundipharma's Global Consumer Healthcare business in Singapore, where the Asian Regional Advisory Board Meeting for VivaGel® BV was recently held.

**VivaGel® BV licence & regulatory status - Launches planned in multiple markets in 2019**



**United States**  
Escalating, double-digit royalties + up to US\$101M in milestones



VivaGel® BV has been licensed in over 160 countries globally. The global market is estimated to be >US\$750M for BV treatment and >US\$1B annually for BV prevention.

**Rest of World (RoW)**

Europe, Russia, CIS, Asia, Middle East, Africa, Latin America  
Attractive revenue share + up to US\$24.7M in milestones



Regulatory activities underway in other Mundipharma territories



**VIVAGEL® CONDOM**

**>> VivaGel® condom approved in Japan**

The VivaGel® condom has received final regulatory approval and can now be sold in Japan by Okamoto, Japan's leading marketer of condoms. Okamoto has commenced key launch preparations, including labelling and manufacturing activities, and plans to launch the VivaGel® condom in the first half of 2019.

Okamoto is Japan's leading marketer of condoms with a majority share of the

Japanese condom market, which is one of the world's largest condom markets and estimated to be in the order of US\$500 million per annum.

Okamoto has sales revenue of more than US\$1.1 billion and around 2,600 employees.

In addition to its dominant position in the Japanese condom market, Okamoto also holds strong market positions in several other Asian markets, including Korea, Taiwan, Malaysia, Singapore and China.

Starpharma will be eligible to receive royalty payments under its licence with Okamoto.

Condoms with functional coatings and gels represent the next wave of innovation in the Japanese condom market following on from a previous focus on condom thinness.

"We are very pleased to be in a partnership with Starpharma for this innovative product and excited about its upcoming launch."

Mr. Keiji Ikeda,  
Okamoto's senior managing director





**INTERNAL DRUG DELIVERY**

**>> Clinical trials for internal DEP® products progressing well**



**DEP® docetaxel**

Approximately 70% of the initial cohort of the monotherapy arm in the DEP® docetaxel phase 2 trial have now been recruited. The positive interim trial results for this arm show continued lack of neutropenia and encouraging efficacy signals, including stable disease and tumour shrinkage, in patients with lung and prostate cancer. Based on investigator interest, Starpharma is also investigating other tumour types for the DEP® docetaxel trial.

Recruitment is being expanded in the DEP® docetaxel + nintedanib combination arm in non-small cell lung cancer based on positive interim results. These include efficacy signals and no protocol-defined Dose Limiting Toxicities and no neutropenia. The efficacy signals observed include stable disease and tumour shrinkage.

**DEP® DOCETAXEL PHASE 2 TRIAL DESIGN**

- Four sites currently recruiting
- Monotherapy arm: Open-label, two-stage design (20+20 patients) to allow for exploration of efficacy of DEP® docetaxel as a monotherapy
- Combination arm: combination of DEP® docetaxel & nintedanib (Vargatef®) in lung cancer



**DEP® cabazitaxel**

The positive interim results for this trial include: no neutropenia; no protocol-defined Dose Limiting Toxicities; and efficacy signals have been observed in prostate cancer despite a low dose of DEP® cabazitaxel (due to being in the dose escalation phase).

The adaptive phase 1 / 2 trial design for DEP® cabazitaxel is in place to enable a seamless transition from phase 1 to phase 2, to explore efficacy as early as possible.

**DEP® CABAZITAXEL PHASE 1 / 2 TRIAL DESIGN**

- Two sites recruiting (more sites to be added in the expansion phase)
- Planning to recruit ~35 patients with solid tumours
- As the trial progresses, decisions will be made as to which tumour types to focus on



**DEP® irinotecan:** Recent data showed impressive efficacy and safety benefits of DEP® irinotecan over standard irinotecan in combination with 5-FU in a human pancreatic cancer model. DEP® irinotecan achieved complete tumour regression and 100% survival.

The final stages of preclinical work for the DEP® irinotecan phase 1 / 2 trial are now complete and trial preparations are well advanced with the trial planned to commence in FY19. The trial will be open to patients with a range of cancers, including colon and pancreatic, where impressive efficacy has been shown in preclinical models.

**PARTNERED DRUG DELIVERY**

**>> Patent published for AstraZeneca-DEP® drugs: DEP® Bcl2/xL inhibitors show compelling efficacy & synergy in combination**

AstraZeneca's first patent application on DEP® Bcl2/xL conjugates was recently published by the World Intellectual Property Organisation.

The published patent application represents the first disclosure of the compelling efficacy data on DEP® Bcl2/xL conjugates, both alone and in combination with market-leading anti-cancer treatments including Rituximab, in various human leukemia models.

The data published showed that the DEP® Bcl2/xL inhibitor conjugates were significantly more efficacious than the Bcl2/xL inhibitor alone, resulting in complete tumour regression in most animals. Additionally, AstraZeneca DEP® Bcl2/xL conjugates in combination with Rituximab performed significantly better than Rituximab alone, resulting in complete tumour regression in most animals.

Clinical trials for AZD0466 are funded by AstraZeneca and are expected to commence in 2019.



AstraZeneca

**>> DEP® docetaxel & DEP® cabazitaxel outperformed both gemcitabine & Abraxane®**

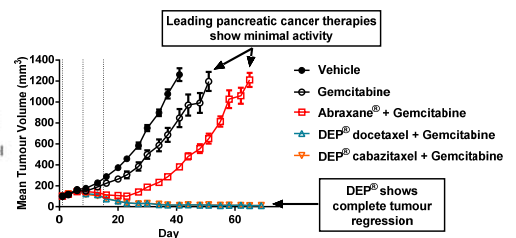
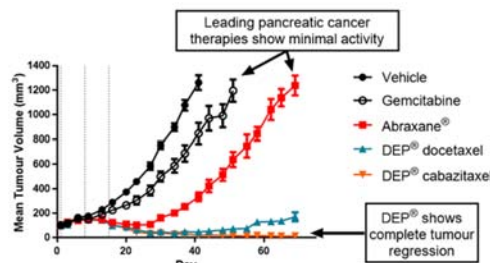
Starpharma continues to add value to its DEP® portfolio through exploring its DEP® products in combination with other oncology agents. DEP® docetaxel and DEP® cabazitaxel both recently showed significant efficacy and safety benefits over gemcitabine (Gemzar®) alone, Abraxane® (Nab-paclitaxel) alone and in combination, in a human pancreatic cancer model.



DEP® cabazitaxel, both alone and in combination with gemcitabine, showed complete tumour regression and 100% survival.



DEP® docetaxel, alone, and in combination with gemcitabine significantly outperformed gemcitabine and/or Abraxane® and showed 100% survival.



Gemcitabine (peak sales US\$1.7B) is frequently used alone and in combination with Abraxane® (2017 sales US\$1.2B) in pancreatic cancer as a first line drug treatment.

Pancreatic cancer is a leading cause of cancer death, with a 1-yr survival rate of 20%, and a 5-yr survival of only 7%

These impressive DEP® efficacy results were despite the fact that standard pancreatic cancer treatments, gemcitabine and/or Abraxane®, showed limited activity in this model. This data will feed into the clinical development programs for DEP® docetaxel and DEP® cabazitaxel.

PRECLINICAL & PIPELINE

>> **Starpharma's dendrimer platform continues to yield further valuable product opportunities**

**SPL7013 eye drops for viral conjunctivitis**

The US Patent and Trademark Office recently granted Starpharma a patent for SPL7013 ophthalmic drops for viral conjunctivitis. The patent has been granted with broad claims for treating and preventing microbial infections of the eye and the patent term is to 2033.

SPL7013 is a proprietary dendrimer which is the active ingredient in Starpharma's VivaGel® products. SPL7013 ophthalmic drops have already demonstrated compelling efficacy in animal models of viral conjunctivitis. The drops have shown potent anti-viral activity, decreased infectivity and are non-irritating.

Starpharma recently completed independent market research with US Physicians / Ophthalmologists and Payers regarding the opportunity for SPL7013 ophthalmic drops. Findings from the research were extremely positive and have been of particular interest in discussions with potential partners.

SPL7013 ophthalmic drops elicited positive responses in 87% of clinicians surveyed<sup>1</sup>:

- Clinicians felt that SPL7013 "addresses a major unmet need" for Viral Conjunctivitis
- Clinicians described its novel mechanism of action as "compelling"
- Clinicians were impressed by its ability to inhibit spread of disease



<sup>1</sup> Results and verbatim quotes from independent US market research conducted with 18 Physicians/Ophthalmologists/Payers. Sep 2018.

Viral conjunctivitis is the most common cause of infectious conjunctivitis, affecting approximately 6 million people in the US and approximately 4 million in Europe each year.

The viral conjunctivitis market is estimated to be around US\$700 million annually. There are currently no approved therapies for viral conjunctivitis and it remains an area of significant unmet medical need globally.

OUTLOOK

>> **VivaGel® portfolio**



Launch of VivaGel® BV in Europe, Australia & other international markets



Meeting with FDA to address request for confirmatory data



Further regulatory approvals for VivaGel® BV



Revenue from VivaGel® BV milestones & sales



Launch of VivaGel® condom in Japan and additional regions, such as Europe and China

>> **DEP® portfolio**



Progress with DEP® docetaxel & DEP® cabazitaxel clinical trials



DEP® irinotecan trial commencement



Other DEP® program developments, including new candidates, e.g. DEP® radiotherapeutics



AstraZeneca program developments, AZD0466 advanced to the clinic & revenue from milestones; further compounds advanced/nominated



New partnered DEP® deals and program developments, including for Targeted DEP®

CORPORATE

>> **Partnering activities**

>> In early January 2019, Dr Jackie Fairley, CEO and Dr Tony Eglezos, VP Business Development, attended the annual J.P. Morgan Healthcare Conference. Based in San Francisco, this is one of the largest annual healthcare conferences in the US.

In association with the conference, Starpharma held multiple partnering meetings with teams from new and existing partners. These included major multinational and US pharmaceutical companies focussing primarily on Starpharma's DEP® (oncology, targeted and other areas) and viral conjunctivitis opportunities. These meetings are expected to yield a number of new partnerships and programs which are currently being discussed.



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