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ASX Announcement

Positive DEP® Cabazitaxel Phase 2 Results in Multiple Cancers

- DEP® cabazitaxel Phase 2 clinical trial met its objectives, with endpoints demonstrating positive anti-tumour efficacy in multiple cancers and confirming the product's favourable safety and tolerability profile.
- DEP® cabazitaxel demonstrated a number of key advantages compared to published data for conventional cabazitaxel (Jevtana®) in metastatic castrate-resistant prostate cancer (mCRPC) patients, or standard-of-care treatments for other tumour types, including advanced platinum-resistant ovarian and gastro-oesophageal cancers.
- These promising efficacy results in advanced prostate, ovarian, and gastro-oesophageal cancers create significant market opportunity for DEP® cabazitaxel.

Melbourne, Australia; 18 October 2023: Starpharma (ASX: SPL, OTCQX: SPHRY) today announces the final positive results from its completed Phase 2 open-label clinical trial of DEP® cabazitaxel. The trial met its objectives, with endpoints demonstrating positive anti-tumour efficacy of DEP® cabazitaxel in advanced, metastatic castrate-resistant prostate cancer (mCRPC), as well as other difficult-to-treat cancers, including platinum-resistant ovarian cancer and gastro-oesophageal cancers. The trial results also confirmed the favourable safety and tolerability profile of DEP® cabazitaxel.

Developed by Starpharma, DEP® cabazitaxel is a patented, dendrimer nanoparticle version of cabazitaxel (Jevtana®), which is widely used in the treatment of prostate cancer, with Jevtana® achieving peak sales of €433 million in 2021[1].

In Starpharma's Phase 2 trial, DEP® cabazitaxel achieved highly encouraging anti-tumour efficacy in multiple advanced solid cancers, including metastatic castration-resistant prostate cancer, platinum-resistant ovarian cancer, and gastro-oesophageal cancers.

Summary of key efficacy results:

- Heavily pre-treated, advanced **prostate cancer** patients (mCRPC) treated with DEP® cabazitaxel achieved a median progression-free survival (PFS) that was more than 50% longer and a median overall survival (OS) that was 10% longer than published data for Jevtana® at the same dose[2]. These final progression-free survival results improve upon the interim results on DEP® cabazitaxel reported by Starpharma at the ESMO (European Society of Medical Oncology) Congress 2022[3].
- In advanced, platinum-resistant **ovarian cancer** patients, who were heavily pre-treated with an average of 4 prior lines of chemotherapy, DEP® cabazitaxel achieved a disease control rate (DCR) of 66.7% and an objective response rate (ORR) of 17.6%, which compares favourably to standard-of-care therapies that report ORRs ranging from ~9 to 16%[4,5,6].
- In advanced **gastro-oesophageal cancer** patients, DEP® cabazitaxel achieved a median progression-free survival (PFS) and median overall survival (OS) that were 53.1% and 28.5% longer, respectively, than similar patient cohorts treated with standard-of-care paclitaxel[7].

These very encouraging DEP® cabazitaxel efficacy results were also clinically significant, given all patients had late-stage, hard-to-treat cancers, and had failed multiple therapies, including closely related taxanes[8], prior to entering this trial.

Furthermore, these positive efficacy results in prostate, ovarian, and gastro-oesophageal cancers demonstrate the significant market value and growth potential for DEP® cabazitaxel, not only in the approved prostate cancer indication of Jevtana®, but also in other cancers that have ahigh unmet medical need.

[1] Product sales for Jevtana®, Biomedtracker: https://www.biomedtracker.com/DrugReport.cfm?DrugID=10758#ProductSales.
[2] Eisenberger, M, et al., *J Clin Oncol*, 2017;35(28):3198-206.
[3] ASX Announcement dated 12 September 2022: Starpharma presents promising additional clinical data for DEP® cabazitaxel in prostate cancer.
[4] Taxol® (paclitaxel) Injection label, https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020262s049lbl.pdf.
[5] Mutch, DG, et al., *J Clin Oncol*, 2007;25(19):2811-2818.
[6] Pujade-Lauraine, E, et al., *J Clin Oncol*, 2014;32(13):1302-1308.
[7] Stockton, S, et al., *The Oncologist*, 2023;28(9):827–e822.
[8] Taxanes are a class of chemotherapy drugs, which include paclitaxel, docetaxel and cabazitaxel.

Importantly, DEP® cabazitaxel was also very well tolerated across the trial in patients who were often elderly, heavily pre-treated and had advanced disease. The overall rate of grade 3 or 4 non-haematological, treatment-related adverse events (AEs) across all DEP® cabazitaxel treated patients (21.3%) was approximately half that reported for Jevtana® (40%)[2] at the same dose. Unlike standard cabazitaxel, DEP® cabazitaxel is highly water soluble and does not contain toxic excipients (detergents) that can cause anaphylaxis, so patients do not need to be pre-medicated with steroids or antihistamines when using DEP® cabazitaxel, leading to an improved patient experience.

Commenting on the positive DEP® cabazitaxel Phase 2 results:

***Professor James Spicer, FRCP, MBBS, PhD, Professor of Experimental Cancer Medicine at King's College London and Consultant in Medical Oncology and the Principal Investigator for the trial at Guy's Hospital in London**, commented:*

"In our cancer early phase trials unit at Guy's Hospital, we conduct many studies of novel oncology therapeutics. The results with DEP® cabazitaxel clearly demonstrate promising and durable anti-cancer activity in very hard-to-treat cancer patients, not only in prostate cancer patients but also platinum-resistant ovarian cancer, and advanced gastro-oesophageal cancers. These advanced patients have few treatment options and we have had many patients who benefited from DEP® cabazitaxel therapy. It was also pleasing to see the limited impact on bone marrow function of this agent given these advanced patients are often at risk of complications of chemotherapy-induced bone marrow toxicity, especially low neutrophil counts."

***Dr David Pinato, MD, MRCP (UK), MRes, PhD, Clinical Reader and Consultant Medical Oncologist, Director of Developmental Cancer Therapeutics, and Investigator for the trial at Imperial College London**, said:*

"I am impressed with the data on Starpharma's novel dendrimer formulation of cabazitaxel, not only in prostate cancer patients, but in patients with other difficult-to-treat diseases such as advanced platinum-resistant ovarian and gastro-oesophageal cancers.

"DEP® cabazitaxel showed very encouraging efficacy signals in these heavily pre-treated patients who have few options remaining.

"For example, in elderly patients with prostate cancer who typically would not tolerate standard cabazitaxel due to low neutrophil counts and other adverse effects, treatment with DEP® cabazitaxel was possible due to its lack of significant effects on the bone marrow and its generally well tolerated safety profile, and achieved some excellent outcomes for these patients.

"Based on the data and my experience with DEP® cabazitaxel, it represents a well-tolerated and promising treatment alternative, not only to standard cabazitaxel for prostate cancer patients, but also for ovarian, gastro-oesophageal and potentially other cancers for which standard cabazitaxel is not indicated."

DEP® Cabazitaxel Efficacy Results

Prostate Cancer

Prostate cancer is the most commonly diagnosed cancer in Australia, with an estimated one in six males diagnosed by the age of 85; the average age at diagnosis is 70 years[9].

In heavily pre-treated advanced mCRPC patients (N=25) who had received a median of 4 lines and 70 cycles/months of prior anti-cancer treatment, DEP® cabazitaxel achieved a median progression-free survival (PFS) of 4.4 months, which is more than 50% longer than the published median PFS of 2.9 months for standard cabazitaxel (Jevtana®) at the same dose (20 mg/m^2)[2]. It is also more than 25% longer than the median PFS of 3.5 months at a higher dose of Jevtana® (25 mg/m^2) (Table 1).

DEP® cabazitaxel also achieved an improved median overall survival (OS)[10] of 14.7 months in these heavily pre-treated mCRPC patients, which also compares favourably with the published median OS of 13.4 months for Jevtana® at the same dose (20 mg/m^2)[2].

These improved and clinically meaningful outcomes were achieved with DEP® cabazitaxel despite these advanced prostate cancer (mCRPC) patients being significantly more heavily pre-treated prior to entry into this trial than patients in published clinical trials of Jevtana®. Notably, these responses were achieved

[9] Prostate cancer: https://www.cancer.org.au/cancer-information/types-of-cancer/prostate-cancer.
[10] Overall survival (OS) is defined as the time from start of treatment to death or last known contact with the patient.

despite 96% of patients in this trial cohort having received closely related taxane therapy, including up to 19 cycles of docetaxel and up to 10 cycles of conventional cabazitaxel (Jevtana®), prior to enrolment in the DEP® cabazitaxel trial.

Table 1. Longer PFS (median) observed in DEP® cabazitaxel mCRPC patients compared to published data on Jevtana®[11]

DEP® Cabazitaxel (20 mg/m²) (N=25)	Jevtana® (20 mg/m²) (N=598)[2]	Jevtana® (25 mg/m²) (N=602)[2]	Jevtana® (25 mg/m²) (N=378)[12]
4.4 months	**2.9 months**	**3.5 months**	**2.8 months**

Intent-to-treat (ITT) populations; PFS = Composite endpoint from date of randomisation to date of first tumour progression, PSA progression, or death.

In addition to the abovementioned efficacy outcomes relating to overall survival or progression of disease measured radiologically, 90% of evaluable[13] DEP® cabazitaxel patients achieved a reduction in the important cancer biomarker, prostate specific antigen (PSA), and more than half (52.4%) achieved a PSA reduction of at least 50% (PSA_{50}). This PSA_{50} result compares favourably with published data for Jevtana® at the same dose, where only 29.5% of patients achieved a PSA_{50}[2]**Error! Bookmark not defined.**.

DEP® cabazitaxel also achieved highly durable anti-tumour responses in 70.6% of prostate cancer (mCRPC) patients with assessable soft tissue lesions. Responses in these patients included partial responses (PR[14]) maintained for up to 55 weeks (Table 2) and disease control (stable disease, SD) maintained for up to 64 weeks. 100% of evaluable mCRPC patients[15] achieved a response to DEP® cabazitaxel in at least one measure of efficacy (soft tissue disease [SD or PR], PSA decrease, and/or no progression in bone disease).

Table 2. Key efficacy endpoints for DEP® cabazitaxel in prostate cancer

Cancer Type	Patients' Prior Anti-Cancer Therapy (Median)[16]	Disease Control Rate (DCR[13,17])	Objective Response Rate (ORR[13,18])	Median PFS
Prostate	**4 lines, 70 cycles/months**	**70.6%**	**16.7%**	**4.4 months**

The final DEP® cabazitaxel progression-free survival results in advanced mCRPC patients reported here improve upon the interim results reported by Starpharma at the ESMO Congress in September 2022[3]. Now that all patient cohorts have completed treatment, and final data analysis has been completed, overall survival (OS) results have also been calculated.

Platinum-resistant Ovarian Cancer

Ovarian cancer is a significant cause of morbidity and mortality worldwide, often diagnosed in an advanced stage where the 5-year survival rate is only 20–41%[19].

DEP® cabazitaxel also achieved highly encouraging efficacy results in patients with advanced platinum-resistant ovarian cancer (N=22), including tumour shrinkage of up to 40% and response durations of up to 34 weeks. The ovarian cancer patients in this study were also heavily pre-treated, having received a median

[11] Jevtana® studies also included pain progression.
[12] de Bono, JS, et al. *Lancet*, 2010;376(9747):1147-54.
[13] All efficacy response data reported in this announcement are for evaluable patients. Evaluable patients are those that received ≥1 dose cycle of DEP® cabazitaxel and had a CT scan, or other efficacy assessment (e.g., PSA in prostate cancer) as applicable, to assess response to treatment at ≥~8 weeks after commencement of treatment with DEP® cabazitaxel. PFS and safety data are reported for all patients who received treatment.
[14] Partial response (PR) is significant target tumour shrinkage of ≥30%.
[15] N=23.
[16] Median number of prior treatment lines and median number of prior cycles / months of treatment patients had received before enrolment into this trial.
[17] DCR = stable disease (SD) + partial response (PR).
[18] ORR = partial response (PR) + complete response (CR).
[19] https://ocrahope.org/get-the-facts/staging.

of 4 and up to 11 lines (with a median of 25 cycles) of prior anti-cancer treatment. All (100%) patients had received at least one prior taxane, with 45% having previously received 2 or more lines of taxane treatment.

DEP® cabazitaxel achieved a disease control rate (DCR) of 66.7% and an objective response rate (ORR) of 17.6% (Table 3) in evaluable ovarian cancer patients, despite this heavy pre-treatment. This ORR compares favourably to standard-of-care single-agent therapies that report ORRs ranging from ~9 to 16% (paclitaxel [Taxol®], topotecan [Hycamtin®], gemcitabine [Gemzar®] or pegylated liposomal doxorubicin [Caelyx®])[4,5,6]. DEP® cabazitaxel also achieved reductions of up to 95% in ovarian cancer biomarkers, CA125[20], or CEA[21], in 75% of evaluable ovarian cancer patients.

These durable efficacy responses (disease control, objective responses) in advanced ovarian cancer are highly encouraging, especially given these patients were so heavily pre-treated. Advanced platinum-resistant ovarian cancer represents a significant unmet clinical need and expanded market opportunity for DEP® cabazitaxel.

Table 3. Key efficacy endpoints for DEP® cabazitaxel in platinum-resistant ovarian cancer

Cancer Type	Patients' Prior Anti-Cancer Therapy (Median)[16]	Disease Control Rate (DCR[13,17])	Objective Response Rate (ORR[13,18])	Median PFS
Platinum-Resistant Ovarian	**4 lines, 25 cycles**	**66.7%**	**17.6%**	**3.1 months**

Gastro-oesophageal Cancers

Advanced gastro-oesophageal cancers[22] are a significant unmet medical need with a very poor prognosis and limited treatments. These cancers progress rapidly and have a one-year survival rate of only 20%[23,24].

In advanced gastro-oesophageal cancer patients, DEP® cabazitaxel achieved excellent efficacy responses, including a median progression-free survival (PFS) of 4.0 months and a median overall survival (OS) of 8.6 months (N=15). These results compare very favourably to standard-of-care paclitaxel treatment in patients with oesophageal or gastro-oesophageal junction cancers, with DEP® cabazitaxel achieving a more than 50% longer median PFS and a 29% longer median OS than paclitaxel administered weekly as a second-line treatment[7].

The majority of these gastro-oesophageal cancer patients were refractory to first-line therapy. Despite this refractory disease, DEP® cabazitaxel achieved a disease control rate (DCR) of 80.0%, and an objective response rate (ORR) of 30.0%, including stable disease (SD) for up to 27 weeks and partial responses (PR) for up to 17 weeks in evaluable gastro-oesophageal cancer patients (Table 4).

Table 4. Key efficacy endpoints for DEP® cabazitaxel in gastro-oesophageal cancers

Cancer Type	Patients' Prior Anti-Cancer Therapy (Median)[16]	Disease Control Rate (DCR[13,17])	Objective Response Rate (ORR[13,18])	Median PFS
Gastro-oesophageal	**1 line, 6 cycles**	**80.0%**	**30.0%**	**4.0 months**

[20] CA125: cancer antigen 125.
[21] CEA: carcinoembryonic antigen (in a patient with mucinous ovarian cancer).
[22] Gastro-oesophageal cancers include oesophagus, gastro-oesophageal junction, and stomach cancers.
[23] Survival for oesophageal cancer: https://www.cancerresearchuk.org/about-cancer/oesophageal-cancer/survival.
[24] Survival for stomach cancer: https://www.cancerresearchuk.org/about-cancer/stomach-cancer/survival.

Other Cancers

DEP® cabazitaxel also demonstrated promising efficacy responses in patients with a range of other cancer types, including head and neck cancer, cholangiocarcinoma and thymic carcinoma (total N=13). These responses included stable disease and tumour shrinkage of up to more than 30% (partial response, PR).

Standard cabazitaxel is currently only indicated for metastatic castrate-resistant prostate cancer. The efficacy responses of DEP® cabazitaxel in a broad range of cancer types, as demonstrated in the current study, demonstrate the potential clinical utility of DEP® cabazitaxel in additional indications, especially platinum-resistant ovarian cancer and advanced gastro-oesophageal cancers.

DEP® Cabazitaxel Safety and Tolerability

In the Phase 2 study, a total of 75 patients were treated with DEP® cabazitaxel at 20 mg/m^2 cabazitaxel administered intravenously (IV), once every 3 weeks, for up to 12 cycles. DEP® cabazitaxel was very well tolerated in patients enrolled in the study. Almost 90% of adverse events (AEs) deemed treatment-related were mild (grade 1, 63.9%) or moderate (grade 2, 24.8%), with very few severe (grade 3/4, 11.3%) events. Notably, the percentage of DEP® cabazitaxel-treated patients with grade 3 or 4 non-haematological, treatment-related AEs (21.3%) was approximately half that reported for Jevtana® (40%) at the same dose[2]**Error! Bookmark not defined.**.

Importantly, both the incidence and severity of bone marrow toxicity with DEP® cabazitaxel were markedly reduced compared to published data for Jevtana®. Only 16.0% of DEP® cabazitaxel treated prostate cancer patients experienced laboratory-detected grade 3 or 4 neutropenia, compared to 41.8% reported for Jevtana® at the same dose in prostate cancer patients[2].

DEP® cabazitaxel treated patients experienced especially low rates or absence of severe, dose-limiting neutropenia, febrile neutropenia and thrombocytopenia, events which are particularly problematic in older patients or patients with poorer health (Table 5). Given the older age of many patients with prostate cancer, this reduced bone marrow toxicity is an important benefit of DEP® cabazitaxel.

Table 5. Comparative bone marrow toxicity in prostate cancer patients treated with DEP® cabazitaxel vs published data on Jevtana®

Bone Marrow Toxicity	DEP® Cabazitaxel (20 mg/m^2) (N=25†)	Jevtana®[2] (20 mg/m^2) (N=580†)
Neutropenia* ≥ grade 3	16.0%	41.8%
Febrile neutropenia ≥ grade 3	0%	2.1%
Thrombocytopenia* ≥ grade 3	0%	2.6%
Neutropenic infection / sepsis	0%	2.1%

* Lab detected neutropenia or thrombocytopenia, regardless of whether event was reported as an adverse event
† Safety population (received at least 1 dose)

AEs observed for DEP® cabazitaxel are all reported with conventional cabazitaxel (Jevtana®). Patients treated with DEP® cabazitaxel had significantly fewer grade 3/4 non-haematologic treatment related AEs[25] compared to published data on Jevtana®[2]. AEs observed in ≥10% of DEP® cabazitaxel patients in Phase 2 included fatigue, neutropenia, anaemia, platelet count decrease, white blood cell decrease, constipation, diarrhoea, nausea, vomiting, peripheral neuropathy (PN) and decreased appetite. These AEs were generally well tolerated and manageable. Patients in the DEP® cabazitaxel study were heavily pre-treated with prior anti-cancer therapies, including taxanes, that have significant toxicities and can pre-dispose patients to toxicities such as myelosuppression (neutropenia) and PN, with subsequent treatments.

For many prostate cancer patients over 65 years old receiving Jevtana®, the recommendation is to receive prophylaxis with G-CSF[26] from the first cycle (primary prophylaxis) to prevent severe/life-threatening neutropenia. Despite the high mean age (73 years) of prostate cancer patients in this study, there was no

[25] Safety population (all patients who received at least 1 dose of study medication).
[26] Granulocyte-colony stimulating factor.

need to give any patients receiving DEP® cabazitaxel, primary G-CSF prophylaxis, including patients over 65. Furthermore, less than 10% of patients required any G-CSF therapy following an event of neutropenia.

Unlike Jevtana®, severe hypersensitivity reactions and anaphylaxis were not observed following DEP® cabazitaxel treatment. In addition, patients treated with DEP® cabazitaxel did not require routine pretreatment with steroids or antihistamines due to the absence of the detergent polysorbate-80 in Starpharma's DEP® cabazitaxel formulation. Daily treatment with oral corticosteroids was also not required with DEP® cabazitaxel. Avoidance of long-term steroid use is beneficial, particularly for patients with prostate cancer whose bone health can be a significant issue.

Dr Jackie Fairley, CEO, Starpharma, commented:

"Starpharma is delighted to report positive final results from our Phase 2 clinical trial of DEP® cabazitaxel, which showed both efficacy and tolerability benefits in advanced prostate cancer patients, compared with the published data for Jevtana®. DEP® cabazitaxel also achieved impressive efficacy responses in advanced platinum-resistant ovarian cancer and advanced gastro-oesophageal cancer patients. These outcomes illustrate the ability of the DEP® platform to expand the potential market of an already successful cancer treatment and offer new options for patients.

"These very positive results for DEP® cabazitaxel in three common and hard-to-treat cancers demonstrate its therapeutic and commercial value as well as its ability to address significant unmet medical needs. Many of the patients who participated in the trial had no or very few options, and DEP® cabazitaxel delivered clinically meaningful outcomes. We are deeply grateful to the patients who participated in this trial and to the clinical investigators and their site teams who contributed to the study."

Commercial Opportunity for DEP® cabazitaxel

The global prostate cancer drugs market was valued at more than US$12 billion in 2022 and is forecast to expand at a compound annual growth rate (CAGR) of 8.4% from 2023 to 2030[27]. Globally, prostate cancer cases reached more than 1.4 million diagnosed in 2020[28].

The global ovarian cancer drugs market was valued at an estimated US$3.4 billion in 2022 and is anticipated to grow at a CAGR of 6.6% from 2023 to 2030[29]. In 2020, a total of 313,959 new cases of ovarian cancer were recorded globally[30].

The global gastro-oesophageal cancer drugs market was valued at approximately US$4.6 billion in 2021 and is expected to expand at a CAGR of 4.58% from 2022 to 2030[31]. The number of cases globally is expected to grow from almost 1.7 million in 2020 to approximately 2.5 million by 2035[32].

These promising efficacy results for DEP® cabazitaxel in multiple common cancers demonstrate the significant market potential for DEP® cabazitaxel, not only in the approved prostate cancer indication of Jevtana®, but also in other cancers that have high unmet medical need. Starpharma is engaged in ongoing commercial/licensing discussions with potential partners for DEP® cabazitaxel, and these final results form part of these discussions.

Additional Study Information

The study was a multi-centre, open-label, Phase 1/2 trial designed to assess the safety and preliminary efficacy of DEP® cabazitaxel in patients with advanced, metastatic solid tumour cancers. DEP® cabazitaxel was administered intravenously (IV) once every three weeks (Q3W) at a dose of 20 mg/m^2 cabazitaxel. The objectives of the Phase 2 component of the trial were to further explore the anti-tumour efficacy in selected patient cohorts, and to further characterize the safety and tolerability of DEP® cabazitaxel.

Efficacy was assessed by radiographic imaging (CT [computerized tomography] scans) of tumours evaluated according to the Response Evaluation Criteria in Solid Tumours (RECIST) (version 1.1). The

[27] Prostate Cancer Therapeutics Market Size, Share & Trends Analysis Report: https://www.grandviewresearch.com/industry-analysis/prostate-cancer-therapeutics-market.
[28] Wang, L, et. al., *Front. Public Health,* 2022;10:811044.
[29] Ovarian Cancer Therapeutics Market Size, Share & Trends Analysis Report: https://www.grandviewresearch.com/industry-analysis/ovarian-cancer-drugs-market.
[30] Huang, J, et. al., *Cancers*, 2022;14(9):2230.
[31] Gastrointestinal Diagnostics Market Size, Share & Trends Analysis Report: https://www.grandviewresearch.com/industry-analysis/gastrointestinal-diagnostics-market-report.
[32] Global Cancer Observatory, GLOBOCAN 2020, International Agency for Research on Cancer 2023.

applicable aspects of the internationally recognised Prostate Cancer Working Group (PCWG3)[33] guidelines were also applied for the prostate cancer cohort. Tumour biomarkers, such as prostate specific antigen (PSA), CA125[20], and CEA[21] were also assessed as a measure of anti-tumour activity, where applicable for a selected cancer type. Adverse events were assessed and graded according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03.

Treatment of patients with DEP® cabazitaxel continued until their disease progressed or worsened, or withdrawal for other reasons (e.g., COVID-19). However, if the treating investigator determined that clinical benefits, such as reduced pain or improved symptoms, were being derived from the treatment, patients had the option to continue treatment beyond disease progression.

A total of 75 patients with advanced solid tumours were recruited into and received DEP® cabazitaxel in the Phase 2 part of this trial. Patients were enrolled across 5 trial sites in the UK and Australia, including Guy's Hospital, Imperial College and University College London Hospital (UCLH) in London, Velindre Cancer Centre in Cardiff, and the Kinghorn Cancer Centre at St Vincent's Hospital in Sydney.

Patients were enrolled into three main patient cohorts: metastatic castrate-resistant (Stage IV) prostate cancer (mCRPC) (N=25), advanced platinum-resistant ovarian cancer (N=22) and advanced gastro-oesophageal cancers (N=15). The remaining Phase 2 patients had advanced disease that could potentially benefit from a taxane such as cabazitaxel: head and neck cancer (N=7), cholangiocarcinoma (N=4), non-small cell lung cancer (NSCLC) (N=1) and thymic carcinoma (N=1).

The ages of patients in the three main cancer cohorts are shown in Table 6.

Table 6. Patient age by cancer type

Age (years)	Prostate	Ovarian	Gastro-oesophageal
Mean	73	62	59
Range	57 - 83	43 - 76	25 - 73

AEs observed for DEP® cabazitaxel are all reported with conventional cabazitaxel (Jevtana®). These AEs were generally well tolerated and manageable. AEs observed (all grades) in ≥10% of all DEP® cabazitaxel treated patients in Phase 2 include constipation (14.7%), diarrhoea (29.3%), nausea (48.0%), vomiting (29.3%), fatigue (60.0%), neutropenia (37.7%), anaemia (42.7%), platelet count decrease (17.3%), white blood cell decrease (13.3.%), peripheral neuropathy (PN, 60.0%), elevated liver enzymes (alanine aminotransferase, ALT 12.0%; aspartate aminotransferase, AST 18.7%), and decreased appetite (21.3%). Patients in this study were heavily pre-treated with anti-cancer therapies including cisplatin, oxaliplatin and taxanes that cause myelosuppression (neutropenia) and residual neurological toxicity (PN) and predispose patients to recurrence of these AEs with future treatments. The overall rate of laboratory-detected grade 3 or 4 neutropenia was 22.7%.

About DEP® cabazitaxel

Developed by Starpharma, DEP® cabazitaxel is a patented, dendrimer nanoparticle version of conventional cabazitaxel, which is marketed as Jevtana® and widely used in the treatment of prostate cancer. Unlike standard cabazitaxel, DEP® cabazitaxel is highly water soluble, does not contain toxic detergent-like excipients associated with anaphylaxis, and avoids the need for steroid pre-medication. In both preclinical and clinical studies, DEP® cabazitaxel has shown an improved side effect profile, notably markedly reduced bone marrow toxicity demonstrated by lower rates of severe neutropenia, thrombocytopenia, and severe anaemia, which are all reportedly experienced by a significant proportion of patients treated with Jevtana®.

About Starpharma's DEP® platform

Starpharma has developed a unique and valuable delivery platform known as DEP® (Dendrimer Enhanced Product), which utilises dendrimers to improve the effectiveness and safety of conventional and new drugs. DEP® has been widely applied in oncology but also has application to other classes of drugs, such as anti-infectives. DEP® opens new possibilities for more controlled and precisely targeted drug delivery, enhancing therapeutic and commercial opportunities and creating significant optionality. Additionally, the use of DEP® can create new intellectual property and extend the patent life for value-added versions of existing drugs.

[33] Scher, H.I., et al., Trial design and objectives for castration-resistant prostate cancer: updated recommendations from the Prostate Cancer Clinical Trials Working Group 3. *J Clin Oncol*, 2016, 34(12):1402-18.

Starpharma has developed an impressive pipeline of novel DEP® oncology assets. Its clinical-stage assets, DEP® cabazitaxel, DEP® docetaxel and DEP® irinotecan, are improved versions of commonly used chemotherapeutic drugs that have demonstrated improved anti-cancer effects and safety profiles. Additionally, Starpharma has a promising preclinical pipeline, including DEP® Antibody-Drug Conjugates (ADCs) and DEP® radiotheranostic products.

In addition to its internal programs, Starpharma has a number of partnered DEP® programs with global companies, including MSD, Genentech, Chase Sun, and AstraZeneca.

About Starpharma

Starpharma Holdings Limited (ASX: SPL, OTCQX: SPHRY) is a world leader in dendrimer technology for medical applications. As an innovative Australian biopharmaceutical company, Starpharma is focused on developing and commercialising novel therapeutic products that address significant global healthcare needs. Starpharma boasts a strong portfolio of products, partnerships, and intellectual property.

Starpharma's innovative technology is based on proprietary polymers called dendrimers, which are precise, synthetically manufactured, nanoscale molecules. The unique properties of dendrimers – including their size, structure, high degree of branching, polyvalency, and water solubility – are advantageous in medical and pharmaceutical applications.

Starpharma uses its dendrimer technology to develop novel therapeutics and to improve the performance of existing pharmaceuticals. Starpharma's portfolio includes multiple clinical-stage oncology products, which utilise its Dendrimer Enhanced Product ('DEP®') drug delivery technology, and marketed products, including VIRALEZE™ and VivaGel® BV, which utilise SPL7013, a proprietary dendrimer with antimicrobial properties.

Starpharma's DEP® drug delivery platform is being used to enhance the effectiveness of existing and novel therapies and to reduce drug-related toxicities through controlled and specified drug delivery.

In addition to Starpharma's internal DEP® programs, Starpharma has multiple DEP® partnerships with international biopharmaceutical companies, including AstraZeneca (oncology), MSD (Antibody-Drug Conjugates), Chase Sun (anti-infectives), and other world-leading pharmaceutical companies. Due to the broad applicability and optionality of Starpharma's DEP® platform, partnered DEP® programs have the potential to generate significant future milestones and royalties.

Starpharma's topical antiviral nasal spray, VIRALEZE™, is now registered in more than 35 countries*, including Europe, the UK, and Asia. Starpharma's novel non-antibiotic vaginal gel, VivaGel® BV, for the treatment of bacterial vaginosis (BV) and prevention of recurrent BV, is registered in more than 50 countries, including in the UK, Europe, Southeast Asia, South Africa, Australia and New Zealand.

For more information about Starpharma, visit www.starpharma.com or connect with Starpharma on LinkedIn.

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Disclosure
This ASX Announcement was authorised for release by the Chair, Mr Rob Thomas.

Forward Looking Statements
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