ASX Announcement

# DEP® irinotecan phase 2 commences after positive phase 1 results

- **Phase 1 part of the DEP® irinotecan phase 1 / 2 trial successfully completed, with phase 2 to commence immediately**
- **DEP® irinotecan was well-tolerated and patients generally experienced less severe side effects, including no cases of severe diarrhoea, which is particularly problematic (FDA black box warning) with the marketed form of irinotecan, Camptosar®**
- **Encouraging efficacy signals observed in 50% of evaluable patients to date - not only in patients with colorectal cancer, for which conventional irinotecan is approved, but also in patients with breast and pancreatic cancer**
- **Recruitment into phase 2 now underway with two new sites expected to be added shortly**

**Melbourne, Australia; 7 May 2020:** Starpharma (ASX: SPL, OTCQX: SPHRY) today announced successful completion of the phase 1 component of its phase 1 / 2 trial for DEP® irinotecan. The trial met its objective of evaluating safety, tolerability, pharmacokinetics and preliminary efficacy data, and identifying a recommended phase 2 dose. The trial will now transition seamlessly into phase 2, with recruitment activities underway at three sites. Two additional sites, The Beatson West of Scotland Cancer Centre (the Beatson) and the Kinghorn Cancer Centre in Sydney are also expected to commence recruitment shortly.

The phase 1 part of the trial enrolled 7 patients with colorectal cancer, pancreatic cancer and breast cancer, who were each dosed with up to 10 cycles of DEP® irinotecan. Encouraging efficacy signals have been observed in 50% of evaluable patients to date, and in all three tumour types enrolled, despite the fact conventional irinotecan is not approved for breast or pancreatic cancers and that enrolled patients were heavily pre-treated. All but one patient enrolled in the study had been previously treated with at least 10 cycles of prior anticancer therapy, with an average of 28 cycles (median 15), and one patient had as many as 114 cycles of 11 different cancer treatments.

DEP® irinotecan is a novel, patented dendrimer formulation of SN-38, the active metabolite of irinotecan. Irinotecan, a widely used cancer drug marketed by Pfizer as Camptosar® or Campto®, is used alone or in combination with other drugs for the treatment of colorectal cancer (CRC). Despite US FDA “Black Box” warnings for both neutropenia and severe diarrhoea, Camptosar® achieved peak annual sales of US$1.1 billion. The clinical use of irinotecan is limited by these toxicities. The objective for DEP® irinotecan is to improve the clinical utility of conventional irinotecan by reducing important toxicities and/or improving its efficacy in treating CRC and potentially other cancer types, thus expanding its use.

DEP® irinotecan was well tolerated by trial participants who experienced generally less severe side effects with no cases of severe diarrhoea, which is a particularly problematic side effect (FDA black box warning) with the marketed form of irinotecan, Camptosar®. With conventional irinotecan, diarrhoea occurs in the majority of patients[1], with severe diarrhoea in 20-40% of patients (grade 3 - hospitalisation indicated and grade 4 - life-threatening). Severe diarrhoea is one of the most significant side effects of Camptosar® and often limits its use.

[1] https://www.cancernetwork.com/review-article/gastrointestinal-toxicity-irinotecan; Camptosar® label

Commenting on the results, Starpharma CEO, Dr Jackie Fairley, said, “We’re excited to advance our third DEP® product to phase 2. We are very pleased to see activity in a range of tumour types and that none of the patients treated with DEP® irinotecan experienced the debilitating diarrhoea commonly seen with Camptosar®. It is also pleasing to have achieved this milestone of commencement of phase 2 earlier than originally estimated.We look forward to sharing these results with commercial partners and are also discussing a number of value-adding combinations.”

Recruitment activities are now underway for the phase 2 study at The Christie, The Royal Marsden and Newcastle Freeman Hospital, and additional trial sites are expected to commence recruitment shortly (the Beatson and the Kinghorn Cancer Centre, Sydney).

Starpharma thanks the DEP® irinotecan trial patients, their families and caregivers, and the study staff, investigators and consultants for their participation in the first phase of this trial, and achieving these milestones, particularly in the challenging COVID-19 environment.

## Phase 1 trial results

A total of 7 patients were enrolled into the phase 1 part of the study and received DEP® irinotecan at a range of doses up to 12.5 mg/m$^2$ [2] and up to 10 cycles of treatment each.

### Efficacy Signals

Whilst the primary objective of the phase 1 trial was not an assessment of efficacy, and patients were very heavily pre-treated with other anticancer agents (up to 114 cycles), encouraging signs of efficacy were observed in 50% of evaluable[3] patients treated with DEP® irinotecan. Evaluable patients are those who have received at least 1 dose of DEP® irinotecan and had a tumour response assessment. The efficacy signals observed in the study included prolonged stable disease and substantial tumour shrinkage in a range of tumour types including CRC, pancreatic and breast cancer.

### Safety and Tolerability

Patients treated with DEP® irinotecan generally experienced less severe side effects than typically associated with Camptosar®, with no cases of the severe high-grade diarrhoea which is experienced by 20-40% of patients with conventional irinotecan and often requires hospitalisation.

Conventional irinotecan (Camptosar®) has two FDA black box warnings (severe diarrhoea and neutropenia) and is associated with a high frequency of adverse events (AEs), including nausea, vomiting, alopecia and neutropenia. The AEs observed with DEP® irinotecan treatment were consistent with those seen in Camptosar® and generally less severe and mostly mild (grade 1). AEs observed with DEP® irinotecan included nausea, vomiting, alopecia and neutropenia.

The selection of the recommended phase 2 dose (RP2D) of DEP® irinotecan was determined taking account of the overall safety, tolerability, pharmacokinetics and preliminary efficacy results for DEP® irinotecan in the trial. The RP2D of DEP® irinotecan has been confirmed as 12.5 mg/m$^2$ administered intravenously once every three weeks.

---

[2] DEP® irinotecan is a dendrimer version of SN-38, the active metabolite of irinotecan, therefore, DEP® irinotecan doses are not directly comparable with conventional irinotecan (e.g. Camptosar®).

[3] Evaluable patients are those patients who have received ≥1 dose DEP® irinotecan and have had a tumour response assessment conducted post treatment to determine radiological and/or biochemical response.

## Phase 2 clinical trial

The phase 2 part of the DEP® irinotecan trial is being conducted at multiple sites including The Christie, The Royal Marsden and Newcastle Freeman Hospital, The Beatson and the Kinghorn Cancer Centre in Sydney. Starpharma may also add additional sites as the trial progresses.

The phase 2 study is an open-label trial, with the objective of establishing anti-tumour activity (efficacy) and safety of DEP® irinotecan at the RP2D. The first stage will enrol approximately 20-30 patients with CRC and other cancers. The study will further explore efficacy in selected tumour types and recruitment numbers may be adjusted based on results in certain patient cohorts.

DEP® irinotecan is one of Starpharma's clinical stage DEP® assets being developed internally, alongside DEP® docetaxel and DEP® cabazitaxel. Starpharma also has several partnered DEP® programs including a multiproduct DEP® licence with AstraZeneca, which includes the development and commercialisation of two novel oncology compounds - one of which (AZD0466, a novel Bcl2/xL inhibitor) is currently in a phase 1 trial in the US.

### *About DEP® irinotecan & colorectal cancer*

DEP® irinotecan is a novel, patented nanoparticle formulation of SN-38, the active metabolite of irinotecan, delivered using Starpharma's proprietary DEP® technology. DEP® irinotecan has shown a number of benefits compared to the original form of irinotecan, including significant improvements in anti-cancer efficacy and improved survival in multiple human cancer models (colorectal, pancreatic and breast).

CRC is one of the most common cancers in the world, affecting more than 1 million individuals annually, and is the fourth-leading cause of cancer-related death. The efficacy of Camptosar® in the treatment of cancer is dependent on the conversion of irinotecan in the liver to the active metabolite, SN-38, and this process can be highly variable within and between patients. The variability can lead to difficulties in patient management and dosing.

---

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 several products internally and others via commercial partnerships.

VivaGel®: Starpharma's women's health product - VivaGel® BV is based on SPL7013, astodrimer sodium, a proprietary dendrimer. VivaGel® BV for bacterial vaginosis (BV), is available for sale under the brand names Betafem® BV Gel (UK), Betadine BV™ (Europe), Betadine™ BV Gel (Asia) and Fleurstat BVgel (Australia and New Zealand) and a new drug application has been submitted to the US FDA. Starpharma has licensed the sales and marketing of VivaGel® BV to ITF Pharma for the US; Mundipharma for Europe, Russia, CIS, Asia, the Middle East, Africa and Latin America; and to Aspen Pharmacare for Australia and New Zealand. Starpharma also has licence agreements to market the VivaGel® condom (an antiviral condom which includes VivaGel® in the lubricant) in several regions, including Australia, Europe, Canada, China and Japan (Okamoto). The VivaGel® condom has been launched in Japan under Okamoto's 003 brand, and in Australia and Canada under the LifeStyles Dual Protect® brand. The VivaGel® condom is approved in Europe.

DEP® - Dendrimer Enhanced Product®: Starpharma's DEP® drug delivery platform has demonstrated reproducible preclinical benefits across multiple internal and partnered DEP® programs, including improved efficacy, safety and survival. Starpharma has three internal DEP® products – DEP® docetaxel, DEP® cabazitaxel and DEP® irinotecan - in clinical development in patients with solid tumours. Starpharma's partnered DEP® programs include a multiproduct DEP® licence with AstraZeneca, which involves the development and commercialisation of two novel oncology compounds, with potential to add more. In June 2019 Starpharma signed a Development and Option agreement with AstraZeneca for a DEP® version of one of AstraZeneca's major marketed oncology medicines.

Starpharma.com | Twitter | LinkedIn

Media:
WE Communications
Rebecca Wilson
Mob: +61 417 382 391
rwilson@we-worldwide.com

Arthur Chan
+61 2 9237 2805
arthurc@we-worldwide.com

Starpharma Holdings Limited
Dr Jackie Fairley, Chief Executive Officer
Nigel Baade, CFO and Company Secretary
+61 3 8532 2704
investor.relations@starpharma.com
4-6 Southampton Crescent
Abbotsford Vic 3067

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

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.