

AstraZeneca's DEP Bcl2/xL inhibitors show compelling efficacy and synergy in combination

- AstraZeneca's first of several patent applications on Starpharma's DEP[®] dendrimer with AstraZeneca's Bcl2/xL inhibitors has been published, showing compelling results
- DEP[®] Bcl2/xL conjugates demonstrate better anti-cancer activity than Bcl2/xL inhibitor alone in multiple cancer models
- DEP[®] Bcl2/xL conjugates in combination with leading current anti-cancer treatments provide substantial improvements in efficacy in multiple leukemia models

Melbourne, Australia; 31 August 2018: Starpharma (ASX: SPL, OTCQX: SPHRY) today announced AstraZeneca's first patent application on DEP[®] Bcl2/xL conjugates has been published by the World Intellectual Property Organisation. These DEP[®] Bcl2/xL conjugates combine Starpharma's innovative DEP[®] delivery technology with AstraZeneca's novel Bcl2/xL inhibitor for treating various cancers, including leukemias.

The published patent application shows compelling efficacy data on DEP[®] Bcl2/xL conjugates, both alone and in combination with other leading current anti-cancer treatments, in various preclinical human tumour models.

As announced on [28 September 2017](#), AstraZeneca describes its DEP[®] Bcl2/xL conjugate, AZD0466, as "best-in-class" with a broad combination opportunity in both solid and haematological tumours (blood cancers)¹. Bcl2 is a clinically validated oncology target with the leukemia drug venetoclax (Venclexta[®] - AbbVie/Genentech) approved by the US FDA in 2016. Peak global sales of venetoclax are projected to be greater than US\$7 billion². However, venetoclax has only anti-Bcl2 activity and its efficacy may be limited because cancer cells are potentially able to exploit a parallel survival mechanism³. Therefore, targeting *both* Bcl2 and Bcl/xL (as AstraZeneca's novel DEP[®] Bcl2/xL conjugate AZD0466 does), and using it in combination with other therapies, are attractive strategies that may overcome problematic drug resistance which occurs in many human cancers and thereby provide better efficacy.

Starpharma CEO, Dr Jackie Fairley commented: "AstraZeneca's impressive data published today demonstrates that the DEP[®] Bcl2/xL conjugates are highly effective across a range of cancer types both alone and in combination with other anti-cancer agents. Especially exciting for Starpharma is the combination with blockbuster products such as Rituximab, where the DEP[®] Bcl2/xL conjugates, including AZD0466 showed a strong synergistic effect. Given the synergy appears to also occur with other leading anti-cancer drugs this could represent an important additional benefit for the DEP[®] platform".

"The data published in this patent demonstrates that AstraZeneca's science-driven approach to identifying optimal combinations for its oncology portfolio has delivered outstanding results. We're very pleased that Starpharma's DEP[®] technology makes an important contribution to the performance of these exciting oncology candidates. This first patent application incorporating the novel DEP[®] Bcl2/xL conjugates developed under our

¹ 3rd AstraZeneca-MedImmune-CRUK Cambridge Centre Symposium 2017 presentation

² <http://www.fiercepharma.com/marketing/abbvie-roche-look-for-blockbuster-boost-from-110k-leukemia-med>

³ https://www.astrazeneca.com/content/dam/az/Our-Science/IMED-Biotech-Unit/IMED_Annual%20Review_2016.pdf

multiproduct licence with AstraZeneca is a great illustration of the commercial value that can be created using the DEP[®] platform and further validates DEP[®]'s significant benefits and utility", added Dr Fairley.

The publication of this patent application results from the highly successful collaborative research effort between Starpharma and AstraZeneca and names inventors from both companies.

Under the AstraZeneca multiproduct DEP[®] licence, Starpharma is eligible to receive potential development, launch and sales milestones of US\$124 million for the first DEP[®] product, and US\$93.3 million for each subsequent qualifying product. Starpharma will also receive tiered royalties on net sales, and AstraZeneca funds development costs of DEP[®] AstraZeneca products, including these DEP[®] Bcl2/xL conjugates.

Summary of the Published Data

In one study utilising an Acute Lymphoblastic Leukemia model, AstraZeneca compared its Bcl2/xL inhibitor alone to two DEP[®] Bcl2/xL conjugates. The model uses the human Acute Lymphoblastic Leukemia cell line RS4;11. Figure 1 shows that DEP[®] Bcl2/xL inhibitor conjugates were more efficacious than the Bcl2/xL inhibitor alone.

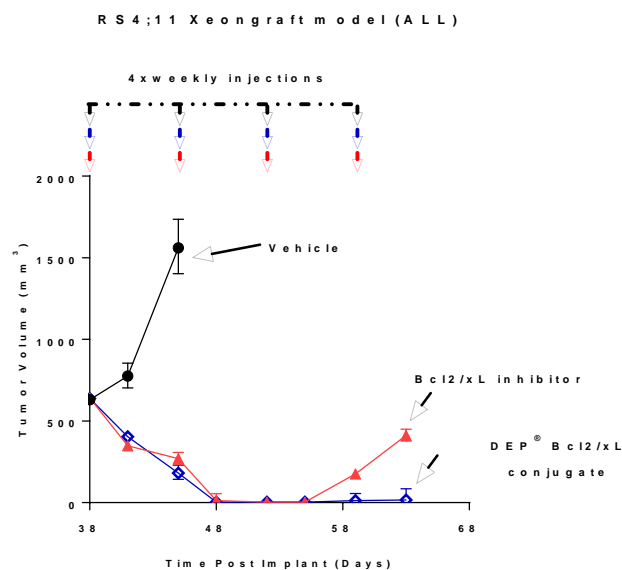


Figure 1 *In vivo* anti-tumor activity of DEP[®] Bcl2/xL conjugates in a human Acute Lymphoblastic Leukemia model

Combination therapy is extremely common in cancer treatment to improve efficacy outcomes. The recently published patent also explored the performance of the novel DEP[®] Bcl2/xL conjugates in combination with leading anti-cancer drugs including Rituximab and AstraZeneca's acalabrutinib (Calquence) in lymphoma models. The efficacy of the DEP[®] Bcl2/xL conjugates in combination with these widely used cancer drugs was extremely impressive, showing significant synergistic effects compared to the drugs alone. This finding is significant, particularly given the fact that this strongly synergistic effect is seen reproducibly.

In a study utilising a B cell Lymphoma model (SuDHL-4), DEP[®] Bcl2/xL conjugates in combination with Rituximab performed much better than Rituximab alone. The combination

significantly inhibited tumor growth and resulted in complete tumor regression in most animals, whereas none was seen with single drug treatment (Figure 2).

Rituximab is a leading leukemia therapy sold under the brand names Rituxan and Mabthera. In 2017 Rituximab had sales of approximately US\$7.5 billion and is primarily used to treat non-Hodgkin's lymphoma and chronic lymphocytic leukemia⁴.

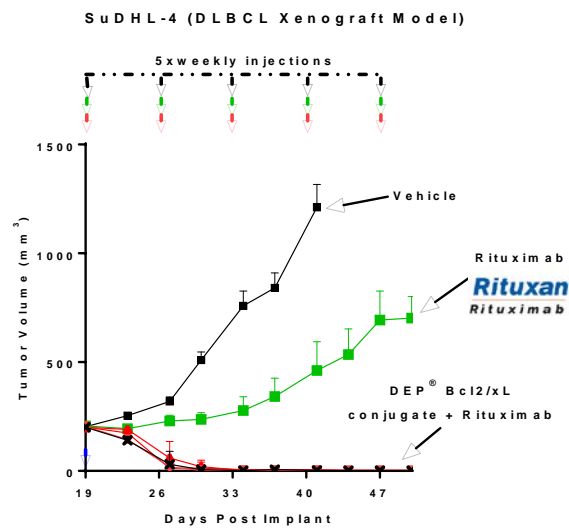


Figure 2 *In vivo* anti-tumour activity of DEP® Bcl2/xL in combination with Rituximab in a human lymphoma model

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, astodimer sodium, a proprietary dendrimer. VivaGel® BV is approved for marketing in the EU and Australia for bacterial vaginosis (BV) and a new drug application is under Fast Track review by the US FDA. Starpharma has licensed the sales and marketing of VivaGel® BV to 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 Australia and Canada under the Lifestyles® Dual Protect™ brand.

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 two internal DEP® products – DEP® docetaxel and DEP® cabazitaxel - in clinical development in patients with solid tumours, and further DEP® products approaching clinical development. 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.

Starpharma.com | [Twitter](https://twitter.com/Starpharma) | [LinkedIn](https://www.linkedin.com/company/starpharma)

⁴ Medtrack Database, August 2018



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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.