

## Starpharma to present at US Drug Delivery Conference

**Melbourne, Australia; 7 May 2019:** Starpharma (ASX: SPL, OTCQX: SPHRY) today announced that it will be presenting its DEP<sup>®</sup> platform at the 2<sup>nd</sup> Annual Drug Delivery West conference in San Francisco on 6-7 May 2019 (US time).

The Drug Delivery West conference is attended by senior licensing and development executives from large pharmaceutical and specialist drug delivery companies. Speakers include industry experts from companies such as Genentech, Allergan, GSK, Biogen, Amgen, Novartis, Eli Lilly and Bayer as well as representatives from leading drug delivery companies.

Starpharma's VP Business Development, Dr Tony Eglezos, will be presenting an overview of the benefits of the DEP<sup>®</sup> platform and its potential use in combination with immuno-oncology agents, as well as its application for radiopharmaceuticals and antibody-drug conjugates (ADCs). A copy of the presentation is attached and will be available on Starpharma's website at [www.starpharma.com](http://www.starpharma.com).

Starpharma will also be conducting partnering discussions with pharmaceutical companies at the conference.

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### 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<sup>®</sup> portfolio and DEP<sup>®</sup> drug delivery with the Company developing several products internally and others via commercial partnerships.

**VivaGel<sup>®</sup>:** Starpharma's women's health product - VivaGel<sup>®</sup> BV is based on SPL7013, astodimer sodium, a proprietary dendrimer. VivaGel<sup>®</sup> BV is approved for marketing in the EU and available for sale in Australia for bacterial vaginosis (BV) and a new drug application has been submitted to the US FDA. Starpharma has licensed the sales and marketing of VivaGel<sup>®</sup> 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<sup>®</sup> condom (an antiviral condom which includes VivaGel<sup>®</sup> in the lubricant) in several regions, including Australia, Europe, Canada, China and Japan (Okamoto). The VivaGel<sup>®</sup> condom has been launched in Australia and Canada under the Lifestyles<sup>®</sup> Dual Protect<sup>™</sup> brand.

**DEP<sup>®</sup> - Dendrimer Enhanced Product<sup>®</sup>:** Starpharma's DEP<sup>®</sup> drug delivery platform has demonstrated reproducible preclinical benefits across multiple internal and partnered DEP<sup>®</sup> programs, including improved efficacy, safety and survival. Starpharma has two internal DEP<sup>®</sup> products – DEP<sup>®</sup> docetaxel and DEP<sup>®</sup> cabazitaxel - in clinical development in patients with solid tumours, and further DEP<sup>®</sup> products approaching clinical development. Starpharma's partnered DEP<sup>®</sup> programs include a multiproduct DEP<sup>®</sup> licence with AstraZeneca, which involves the development and commercialisation of two novel oncology compounds, with potential to add more.

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

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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.



**Starpharma Holdings ASX:SPL**

**DEP<sup>®</sup> Drug Delivery:  
Developing Enhanced Therapies**



**May 2019**

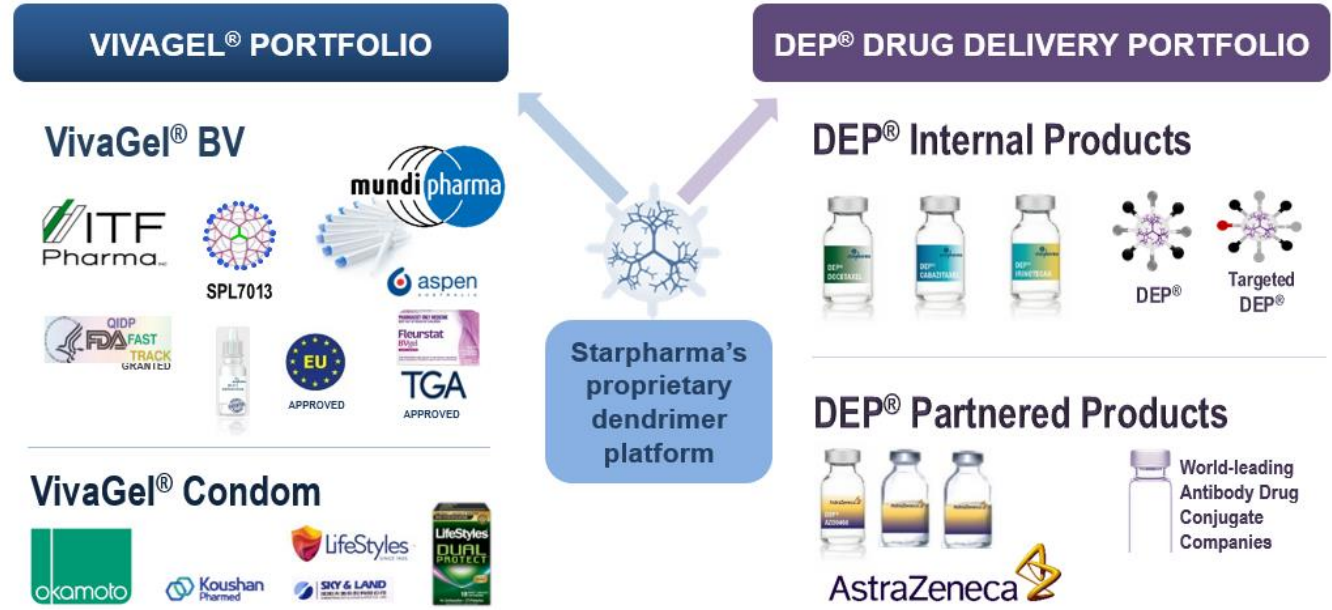
# Important notice and disclaimer

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# Starpharma has a deep portfolio of high-value global products with the potential to significantly improve patient outcomes



Starpharma is an ASX300 company (market cap ~A\$470M) with a **proven record of development & commercialisation** including successful partnerships with leading global companies



MULTIPLE HIGH VALUE COMMERCIAL OPPORTUNITIES UNDERPINNED BY 100+ PATENTS

- Starpharma's poly-lysine dendrimers**
- ✓ Well tolerated
  - ✓ Extremely pure (cGMP manufacture 30kg scale)
  - ✓ Prepared by standard chemical synthetic methods
  - ✓ Practical, easy to formulate
  - ✓ Cost effective

# Starpharma's deep pipeline of VivaGel® and DEP® products provides exceptional optionality

	Product	Indication	Preclinical	Clinical/Regulatory	Commercial
VIVAGEL®	VIVAGEL® BV	Bacterial Vaginosis			
	VIVAGEL® CONDOM	Anti-viral condom			
	SPL7013 OPHTHALMIC	Viral conjunctivitis			
INTERNAL DEP®	DEP® DOCETAXEL	Oncology			<p>Licence after proof-of-concept</p>
	DEP® CABAZITAXEL	Oncology			
	DEP® IRINOTECAN	Oncology			
	OTHER DEP®	Oncology			
	TARGETED DEP®	Oncology			
PARTNERED DEP®	AZ DEP® AZD0466	Oncology			
	AZ #2 DEP® CANDIDATE	Oncology			
	AZ #3 DEP® CANDIDATE	Undisclosed			
	ANTIBODY DRUG CONJUGATE (ADC) #1	Oncology			<p>Undisclosed Partner</p>
	ANTIBODY DRUG CONJUGATE (ADC) #2	Oncology			<p>Undisclosed Partner</p>

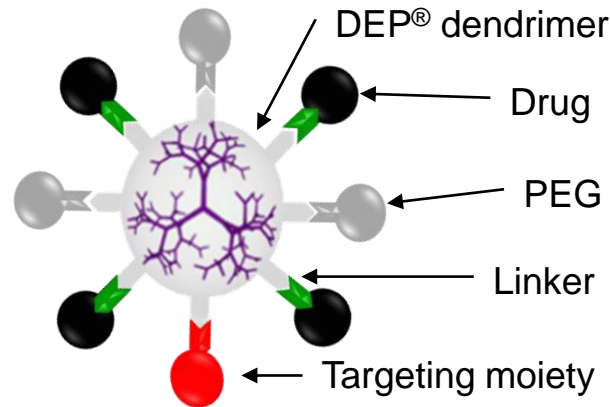
# DEP® PORTFOLIO



# Starpharma's DEP<sup>®</sup> platform enhances the commercial and therapeutic value of a wide range of drugs



**Improved efficacy<sup>1</sup>:** DEP<sup>®</sup> improves anti-cancer efficacy through better drug targeting & improved pharmacokinetics.



**Reduced side-effects<sup>1</sup>:** DEP<sup>®</sup> reduces important side effects such as bone marrow toxicity / low white blood cells (neutropenia) and alopecia (hair loss). Also removes need for steroid pre-treatment.



**Patent life:** In addition to the therapeutic and clinical benefits, DEP<sup>®</sup> also provides valuable commercial benefits by creating new intellectual property and extending patent life.

DEP<sup>®</sup> is potentially applicable to >70% of the top 200 pharmaceuticals (by sales)

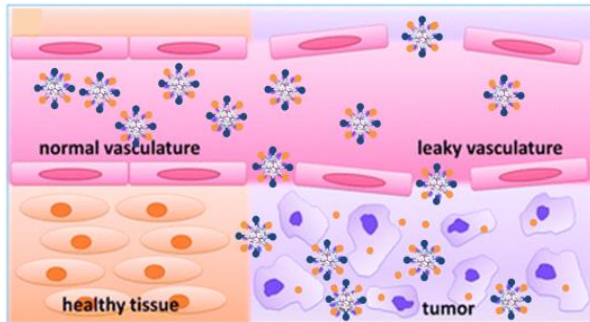
<sup>1</sup> Multiple preclinical studies have established improved efficacy, survival and safety with DEP<sup>®</sup> with many different drugs; clinical trials underway.



# DEP<sup>®</sup> conjugates accumulate in tumours via the EPR effect

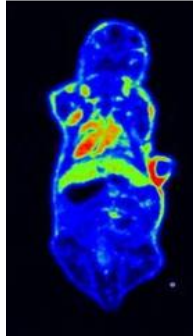
## EPR Effect

Through the EPR (Enhanced Permeability and Retention) effect, DEP<sup>®</sup> conjugates pass through the “leaky” vasculature in tumours and accumulate in these sites more than in normal tissues

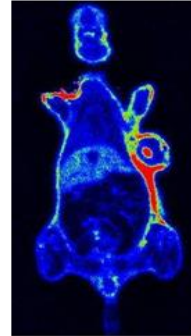


## Tumour Accumulation

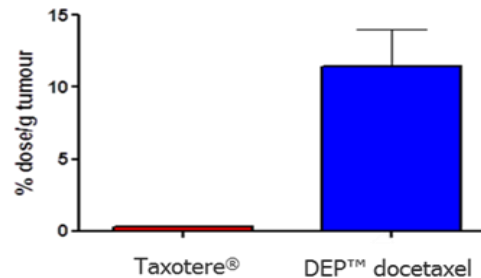
24 hr



168 hr



DEP<sup>®</sup> allows passive targeting of drugs to cancer tissue resulting in higher tissue levels – for DEP<sup>®</sup> docetaxel up to 70x more than Taxotere



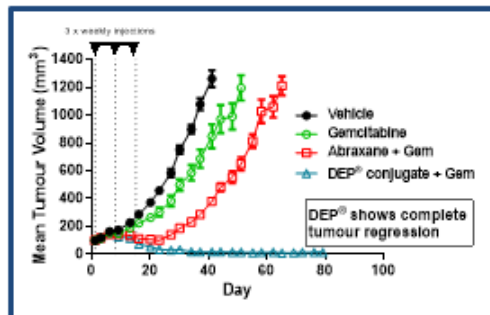
DEP<sup>™</sup> docetaxel shows preferential uptake into mouse MDA-MB-231 xenograft (45-70 fold)

## PET CT Image

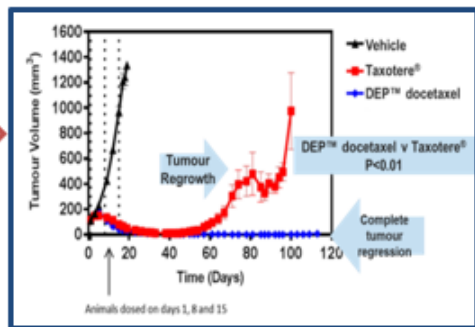


DEP<sup>®</sup> conjugate accumulates in the tumour of a mouse DU145 (human prostate cancer) xenograft 48 hours following injection, via the EPR effect.

# The DEP<sup>®</sup> platform has multiple benefits which are reproducible

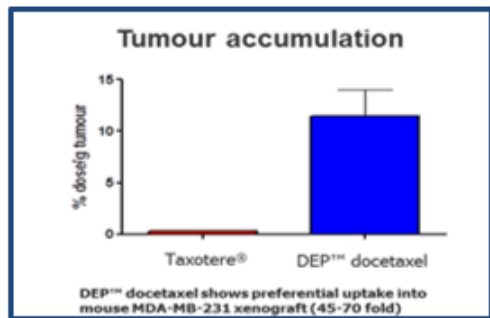
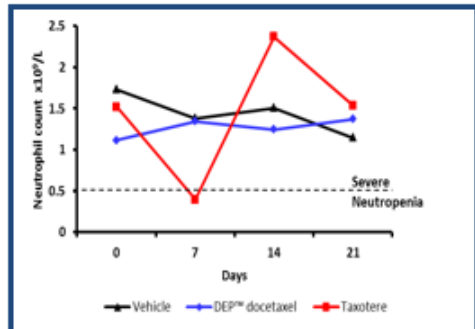


**Improved Efficacy**  
Reproducible results with many candidates & tumour types



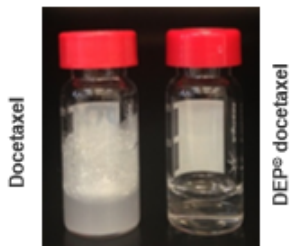
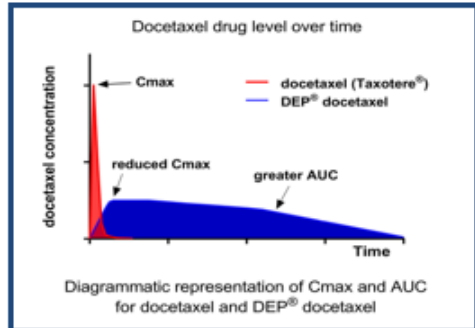
**Benefit in Combination**  
Enhanced efficacy as monotherapy or in combination approaches

**Improved Safety**  
Reduced neutropenia/BM toxicities



**Targeting Tumour Tissue**  
45-70 x more drug in tumour v original drug

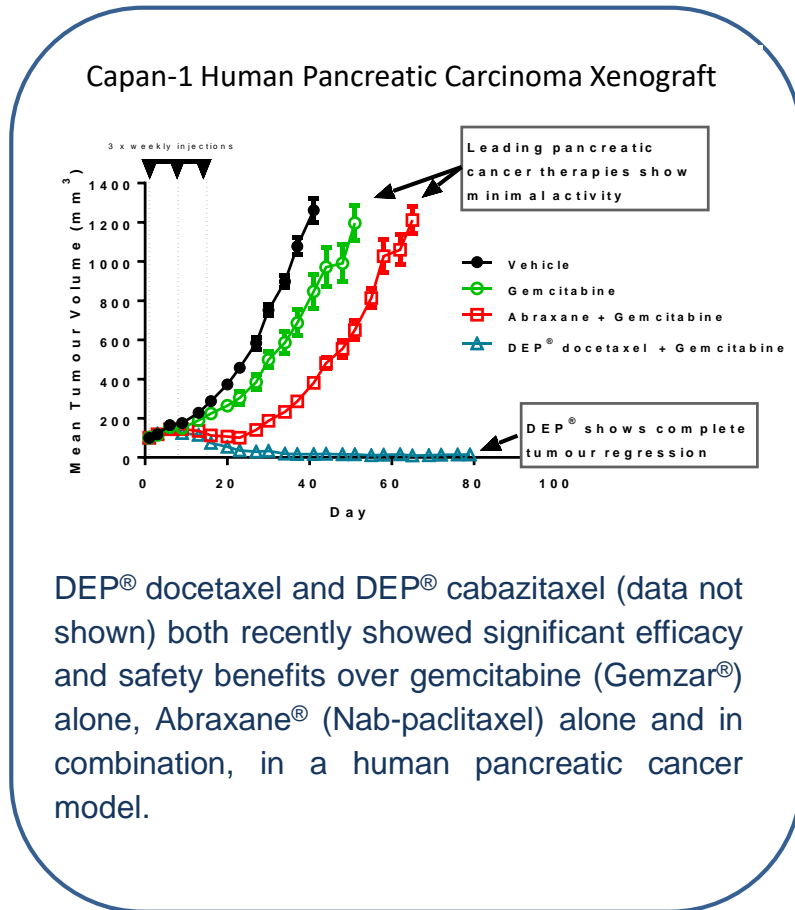
**Improved PK and Half-Life**  
Longer half life and lower C<sub>max</sub>



**Improved Solubility**  
Detergent Free Formulations for improved safety – 20,000 x solubility increase

# DEP<sup>®</sup> drugs are ideal candidates for combination therapy due to enhanced safety profile

Combination therapies are widely regarded as the future of oncology. Starpharma continues to add value to its DEP<sup>®</sup> portfolio through exploring DEP<sup>®</sup> products in combination with other oncology agents.



## DEP<sup>®</sup> THERAPEUTICS IN COMBINATION WITH IMMUNOONCOLOGY (IO) AGENTS

Starpharma's DEP<sup>®</sup> drugs are ideal candidates for combination therapy with IO agents.

- Successful immunotherapy requires a fully functional immune response
  - Unlike standard chemotherapy drugs which may cause immunosuppression, **DEP<sup>®</sup> drugs do not cause myelosuppression**
  - In a phase I study (n=27), DEP<sup>®</sup> docetaxel caused no neutropenia (compared to >>90% with Taxotere<sup>®</sup>)
- Many chemotherapy drugs require immunosuppressive steroid pre-treatment due to formulations containing detergent (e.g. polysorbate 80)
  - **DEP<sup>®</sup> products are water soluble**, with formulations not requiring polysorbate 80, **therefore patients do not require steroid pre-treatment**

# DEP<sup>®</sup> docetaxel, an enhanced version of the widely used cancer drug Taxotere<sup>®</sup>, is currently in phase 2

Docetaxel (Taxotere<sup>®</sup>) is a blockbuster cancer drug with peak global sales >US\$3.1B, used for a range of tumours including breast, lung and prostate.



Multiple US FDA “Black Box” warnings



## Advantages of DEP<sup>®</sup> docetaxel

- ✓ Reduction in major dose-limiting side effect (neutropenia)
- ✓ Detergent-free formulation (less toxic)
- ✓ Tumour-targeting (~70x more)
- ✓ Improved pharmacokinetics
- ✓ Improved efficacy



DEP<sup>®</sup> patents provide coverage to 2032

## Phase 1 Results

- **No steroid pre-treatment required** due to detergent-free formulation - unlike Taxotere<sup>®</sup>
- **No neutropenia** (compares to >>90% with Taxotere<sup>®</sup>)
- No protocol-defined Dose Limiting Toxicities; no reports of other problematic adverse events observed with docetaxel treatment, including anaphylaxis, fluid retention, diarrhoea and nail disorders
- Only one patient (1/27) with mild alopecia/hair loss – compared to ~75% with Taxotere<sup>®</sup>
- **Encouraging efficacy signals** in 13/27 patients (including lung, pancreatic, glioblastoma, gastroesophageal)

## Phase 2 Currently Recruiting

- 4 sites currently recruiting
  - Open-label, two-stage design exploring efficacy of DEP<sup>®</sup> docetaxel as monotherapy
  - In parallel, combination of DEP<sup>®</sup> docetaxel & nintedanib (Vargatef<sup>®</sup>) in lung cancer
  - Positive interim trial results for both arms show **notable lack of bone marrow toxicity (e.g. neutropenia)** and **encouraging efficacy signals**

# DEP<sup>®</sup> cabazitaxel, an enhanced version of leading prostate cancer drug Jevtana<sup>®</sup>, phase 1/2 trial underway

Cabazitaxel (Jevtana<sup>®</sup>) – estimated global sales of US\$500M for 2018, primarily used for prostate cancer and in development for other cancers including breast, bladder, head & neck.



Multiple US FDA “Black Box” warnings



## Advantages of DEP<sup>®</sup> cabazitaxel

- ✓ DEP<sup>®</sup> cabazitaxel significantly outperformed Jevtana<sup>®</sup> (cabazitaxel) in a human breast cancer model
- ✓ Detergent (polysorbate 80) free formulation
- ✓ Reduction of major dose-limiting side effect (neutropenia)



DEP<sup>®</sup> cabazitaxel patents and applications provide coverage to 2039

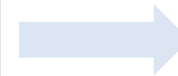
## Phase 1/2 Currently Recruiting

- Adaptive trial design
- Multi-site trial – recruiting at Guy’s Hospital London & UCLH (more sites to be added in the expansion phase)
- Planning to recruit ~35 patients with solid tumours
- As the trial progresses, tumour types will be selected and additional patients may be recruited to explore efficacy in specific tumours
- Efficacy signals at doses several-fold lower than Jevtana<sup>®</sup> dose

**Phase 1:** Open-label, dose-escalation to establish the MTD, DLTs, Recommended Phase 2 Dose & Pharmacokinetics

**Positive interim results: No dose-limiting toxicities (DLTs) or other significant toxicities associated with DEP<sup>®</sup> cabazitaxel have been observed**

Adaptive trial design

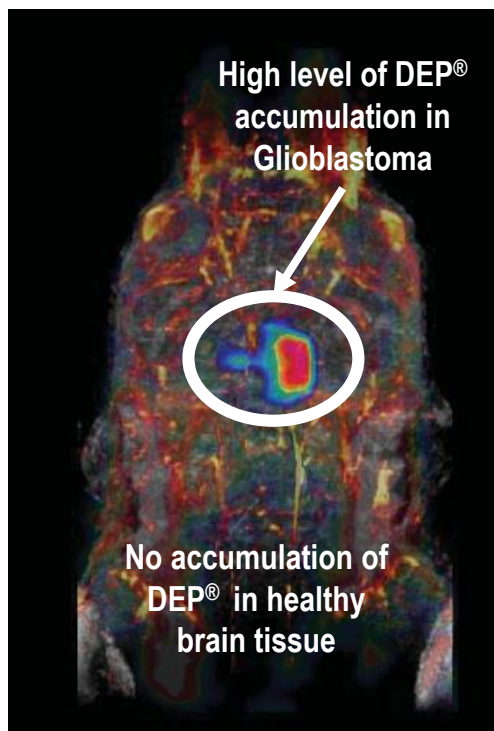


**Phase 2:** Dose expansion to establish efficacy

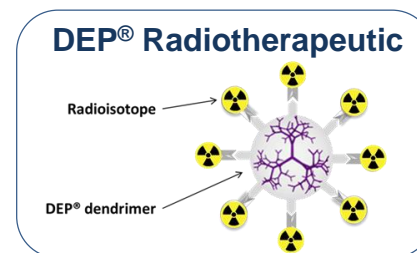
# DEP<sup>®</sup> shows significant accumulation in a glioblastoma (brain tumour) model

## About Glioblastoma Multiforme (GBM)

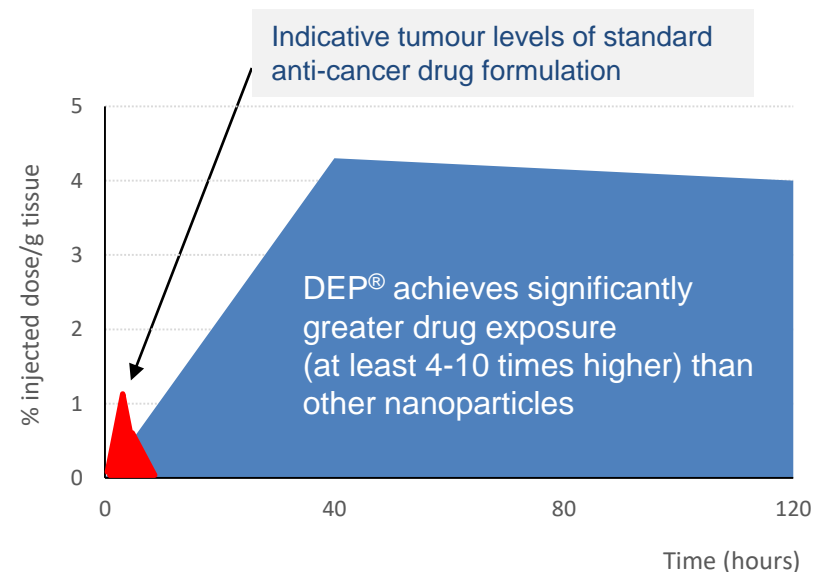
- GBM is the most common and aggressive malignant brain tumour
- GBM also has very poor survival rates with fewer than 10% of patients surviving more than 5 years
- GBM is considered to be incurable, with nearly 100% of patients experiencing disease relapse after initial treatment.



PET-MR image of GBM-bearing mouse 5 days post-injection of DEP<sup>®</sup> conjugate (details not disclosed pending IP filing)



## DEP<sup>®</sup> radiotherapeutic accumulation in GBM model

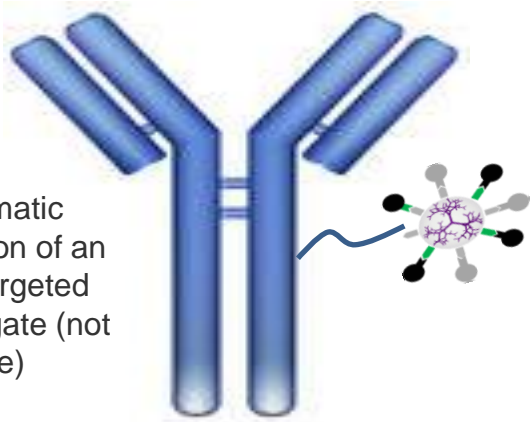


The accumulation of DEP<sup>®</sup> in this GBM model is of particular interest given the observation of stable disease (>10 weeks) in a patient with GBM treated with DEP<sup>®</sup> docetaxel (phase 1 trial)

# Targeted DEP<sup>®</sup> conjugates provide greater flexibility

Starpharma's Ab Targeted DEP<sup>®</sup> conjugates provide many benefits over existing ADCs and can overcome many issues faced today by existing ADC approaches, including:

- Greater **homogeneity**
- **Site specific** attachment of drug conjugate
- **High affinity**
- The delivery of **significantly higher payload** levels than conventional ADCs
- Overcome issues of payload **solubility** and aggregation



Diagrammatic representation of an Antibody targeted DEP<sup>®</sup> conjugate (not to scale)

## Targeting

- Flexibility in use of targeting molecule
  - Ab; Ab fragment; Non-Ab ligand; Small molecule

## DEP<sup>®</sup> drug conjugate

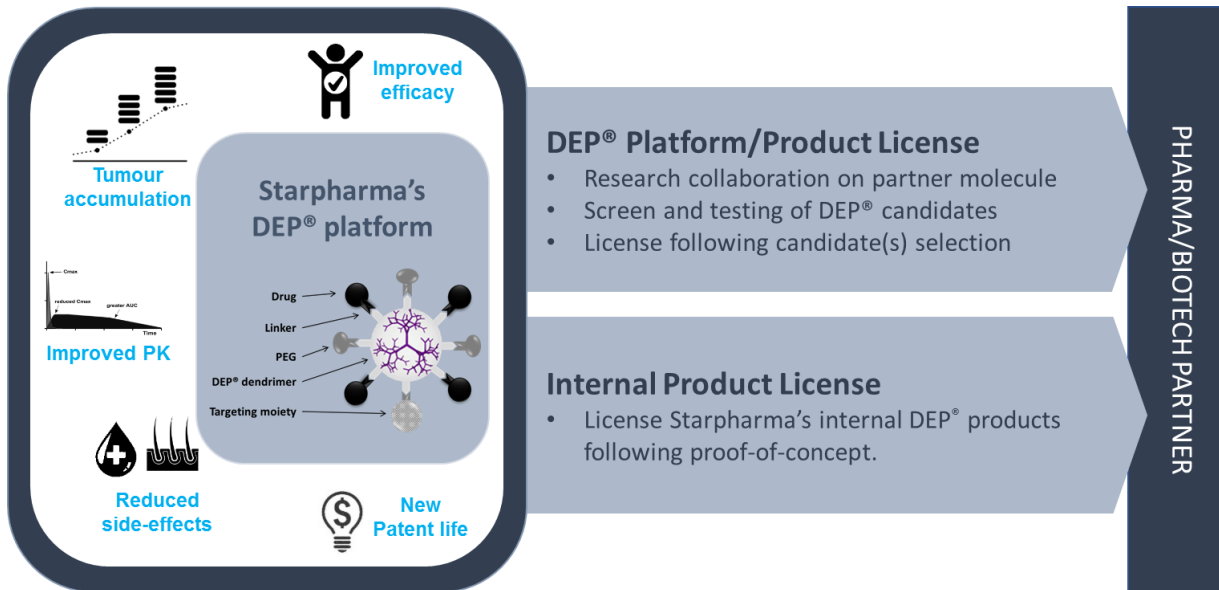
- Precisely manufactured poly-lysine dendrimer with attached drug/payload
- Dendrimer size easily scalable to deliver desired payload number (8, 16, 32...) per dendrimer conjugate
- Can deliver any type of payload - cytotoxic or ultratoxic
- Potential applications beyond cancer
- Drug-linker strategy easily tailored to meet drug release requirements
- Increase solubility and handling of payload

## Site specific attachment

- Precise and reproducible
- Ability to attach multiple dendrimers of differing size (payload number per dendrimer of 8, 16, 32...) on a single antibody - high Drug Antibody Ratio (DAR)
- Ability to achieve significantly higher DAR than other approaches

# The DEP<sup>®</sup> dual strategy involves partnering and developing internal products

Starpharma's dual DEP<sup>®</sup> strategy provides technical, IP and financial leverage, as well as increasing commercial opportunities, improving ROI and de-risking development



## DEP<sup>®</sup> Platform/Product License

- Research collaboration on partner molecule
- Screen and testing of DEP<sup>®</sup> candidates
- License following candidate(s) selection

## Internal Product License

- License Starpharma's internal DEP<sup>®</sup> products following proof-of-concept.

PHARMA/BIOTECH PARTNER

## PARTNERED DEP<sup>®</sup>

- Application to partners' drugs, both novel (eg. AZD0466) and existing
- Patent life extension
- Funded development
- Returns through licensing, milestones and royalties

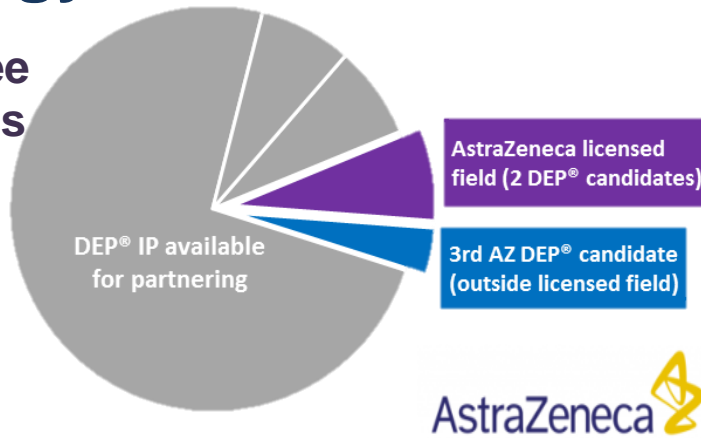
## INTERNAL DEP<sup>®</sup>

- Application to established drugs reduces risk and expedites development
- Patent life extension
- Self-funded
- Returns through licensing, milestones and royalties



# AstraZeneca's DEP<sup>®</sup> programs illustrate the value of the DEP<sup>®</sup> technology

AstraZeneca has three active DEP<sup>®</sup> programs

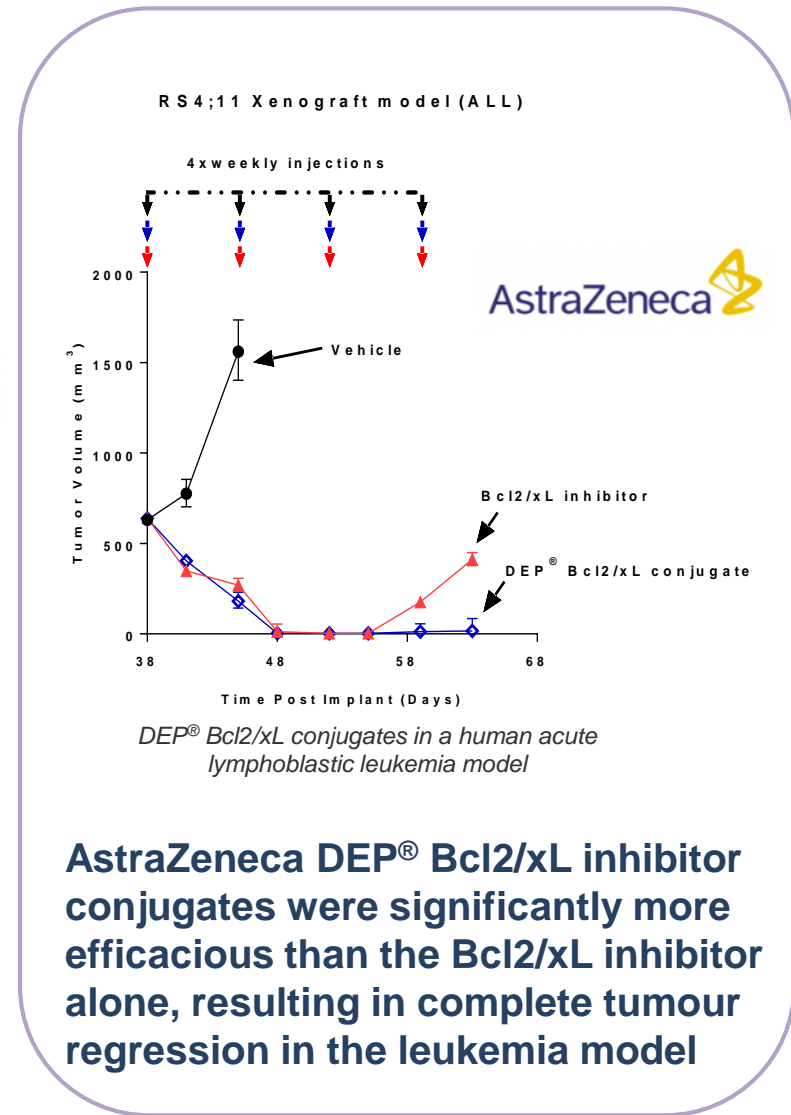


## AstraZeneca's multiproduct DEP<sup>®</sup> licence

- Development and commercialisation of two novel AstraZeneca oncology compounds with potential to add more
- The first DEP<sup>®</sup> product, AZD0466 (a Bcl2/xL inhibitor), is a potentially best-in-class drug with a broad combination opportunity in solid and haematological tumours
- AstraZeneca funds all development & commercialisation costs

*"This licence agreement will enable us to further harness the DEP<sup>®</sup> technology and evaluate its potential across novel molecules within our oncology portfolio."*

Dr Susan Galbraith, Head of the Oncology Innovative Medicines Unit at AstraZeneca



**AstraZeneca DEP<sup>®</sup> Bcl2/xL inhibitor conjugates were significantly more efficacious than the Bcl2/xL inhibitor alone, resulting in complete tumour regression in the leukemia model**



  
**starpharma**  
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