



starpharma



PODD Presentation

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Starpharma Holdings ASX: SPL

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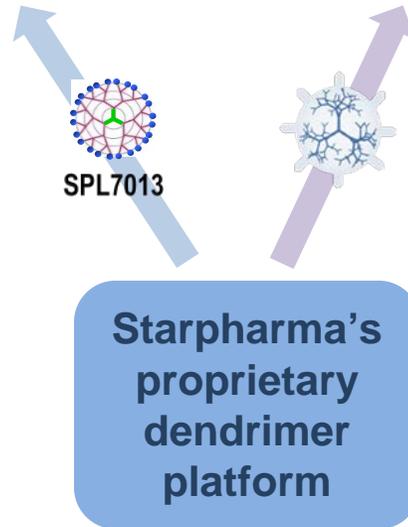
Starpharma's proprietary platform has enabled it to develop a deep portfolio of high-value healthcare products

VIVAGEL® PORTFOLIO

VivaGel® BV (on-market)

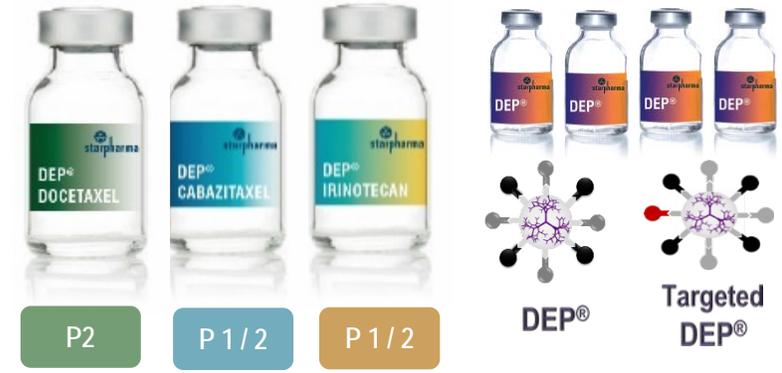


VivaGel® Condom (on-market)



DEP® DRUG DELIVERY PORTFOLIO

DEP® Internal Products (3 in clinical trials)



DEP® Partnered Products



MULTIPLE HIGH-VALUE COMMERCIAL OPPORTUNITIES UNDERPINNED BY 100+ PATENTS

Starpharma's DEP[®] drug delivery platform enhances the commercial and therapeutic value of many drugs with particular application in oncology

Improved efficacy and drug targeting¹

DEP[®] improves anti-cancer efficacy through better drug targeting, improved pharmacokinetics and controlled release.

Tuneable drug release and pharmacokinetics

Through the use of different drug linkers, dendrimer size and surface modification, DEP[®] provides the ability to tune drug release and dendrimer plasma half life.

Reduced side effects¹

DEP[®] reduces important side effects such as bone marrow toxicity / neutropenia and alopecia. No detergents in DEP[®] thus removes the need for pre-dosing with cortisone.

Benefits in Combination

DEP[®] products are ideal candidates for combination therapy including with immuno-oncology (IO) agents and other chemotherapy. DEP[®] products show synergistic benefits over the original versions and given they do not require pre-treatment with cortisone, they are particularly well suited to combine with IO.

Excellent stability and shelf life

DEP[®] provides excellent stability as a lyophilised powder with validated shelf life for DEP[®] products >4 years and ongoing.

Ease of manufacture

SPL dendrimer manufacture uses standard chemical processes and is readily scalable at approved CMO's, with batches of dendrimer prepared under cGMP at the >30 kg scale.

High drug loading with small size

DEP[®] provides a high dose equivalent of drug in a compact nanoparticle e.g. 25% w/w docetaxel in a particle with a measured diameter of 15 nm for DEP[®] docetaxel –less than 1/5 the size of liposomes.

High solubility

DEP[®] products are highly water soluble and easily reconstitute into aqueous solutions readily, with no need for toxic detergents such as polysorbate. However, they can also be formulated into oil based vehicles if desired.

Drug rescue

DEP[®] provides the ability to rescue drugs that for a variety of reasons can't progress into the clinic.

New formulations and ROA

The flexibility of the DEP[®] platform enables depot formulations to be considered using novel routes of administration (ROA) incl. IV, SC, IM, intravitreal, inhalation and topical. These may provide further drug targeting benefits.

Patent life

In addition to the therapeutic and clinical benefits, DEP[®] provides valuable commercial benefits by creating new intellectual property and extending patent life. This is of value for both new drugs but also for extending the patents for improvements to existing products.

Effective anti-generic strategy

The variety of commercial and therapeutic benefits allows for an effective anti-generic strategy, breathing new life into established marketed drugs.

DEP[®] is potentially applicable to a broad range of pharmaceuticals

¹ Multiple preclinical studies have established improved efficacy, survival and safety with DEP[®] with many different drugs; clinical trials underway.

Starpharma's DEP[®] platform enhances the commercial and therapeutic value of a wide range of drugs

3 x weekly injections

Mean Tumour Volume (mm³)

Day

Legend: Vehicle, Gemcitabine, Abraxane + Gem, DEP[®] conjugate + Gem

DEP[®] shows complete tumour regression

DEP[®] BENEFITS

Tumour Volume (mm³)

Time (Days)

Legend: Vehicle, Taxotere[®], DEP[™] docetaxel

Annotations: Tumour Regrowth, DEP[™] docetaxel v Taxotere[®] P<0.01, Complete tumour regression

Animals dosed on days 1, 8 and 15

Tumour accumulation

% dosed in tumour

Legend: Taxotere[®], DEP[™] docetaxel

DEP[™] docetaxel shows preferential uptake into mouse MDA-MB-231 xenograft (45-70 fold)

Improved Efficacy

Reproducible results with many candidates & tumour types

Neutrophil count x10⁹/L

Days

Legend: Vehicle, DEP[™] docetaxel, Taxotere

Annotation: Severe Neutropenia

Benefit in Combination

Enhanced efficacy as monotherapy or in combination approaches

% dosed in tumour

Legend: Taxotere[®], DEP[™] docetaxel

Improved Safety

Reduced neutropenia/BM toxicities

Docetaxel drug level over time

docetaxel concentration

Time

Legend: docetaxel (Taxotere[®]), DEP[®] docetaxel

Annotations: Cmax, reduced Cmax, greater AUC

Diagrammatic representation of Cmax and AUC for docetaxel and DEP[®] docetaxel

Targeting Tumour Tissue

45-70 x more drug in tumour v original drug

Docetaxel

DEP[®] docetaxel

Improved PK and Half-Life

Longer half life and lower Cmax

docetaxel concentration

Time

Legend: docetaxel (Taxotere[®]), DEP[®] docetaxel

Annotations: Cmax, reduced Cmax, greater AUC

Diagrammatic representation of Cmax and AUC for docetaxel and DEP[®] docetaxel

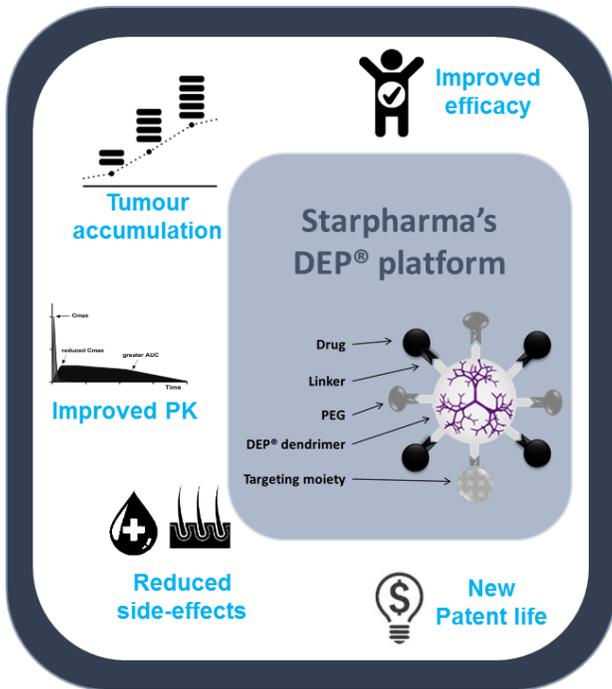
Improved Solubility

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

DEP[®] has demonstrated numerous reproducible benefits across multiple drugs

The DEP[®] dual strategy involves partnering and developing internal products

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



DEP[®] Platform/Product License

- Research collaboration on partner molecule
- Screen and testing of DEP[®] candidates
- License following candidate(s) selection

Internal Product License

- License Starpharma's internal DEP[®] products following proof-of-concept.

PHARMA/BIOTECH PARTNER

PARTNERED DEP[®]

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

INTERNAL DEP[®]

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

AstraZeneca's multiple DEP[®] programs illustrate potential returns from DEP[®] partnered products

Partnered-DEP[®]



Partner selects candidate – either novel or existing drug



Starpharma develops DEP[®] candidates under funded research collaborations



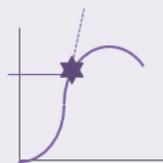
Partner funds development – creates a free carried interest for Starpharma



Starpharma is eligible to receive significant milestone payments & royalties on products

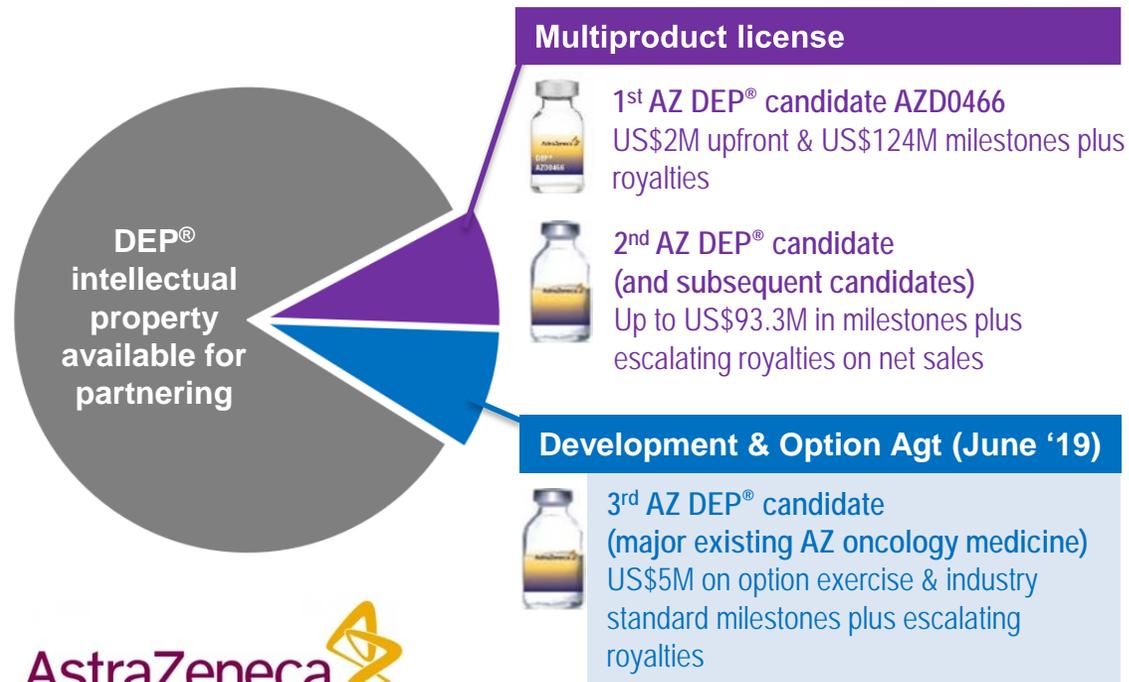


Licences are structured to allow for multiple partnered-DEP[®] programs to run in parallel



When DEP[®] is used for life-cycle management, it allows partners to achieve continued sales growth through differentiated product benefits & new IP

AstraZeneca has multiple commercial DEP[®] programs



"...the DEP[®] technology has enabled us to advance a very exciting novel oncology agent (AZD0466)..."

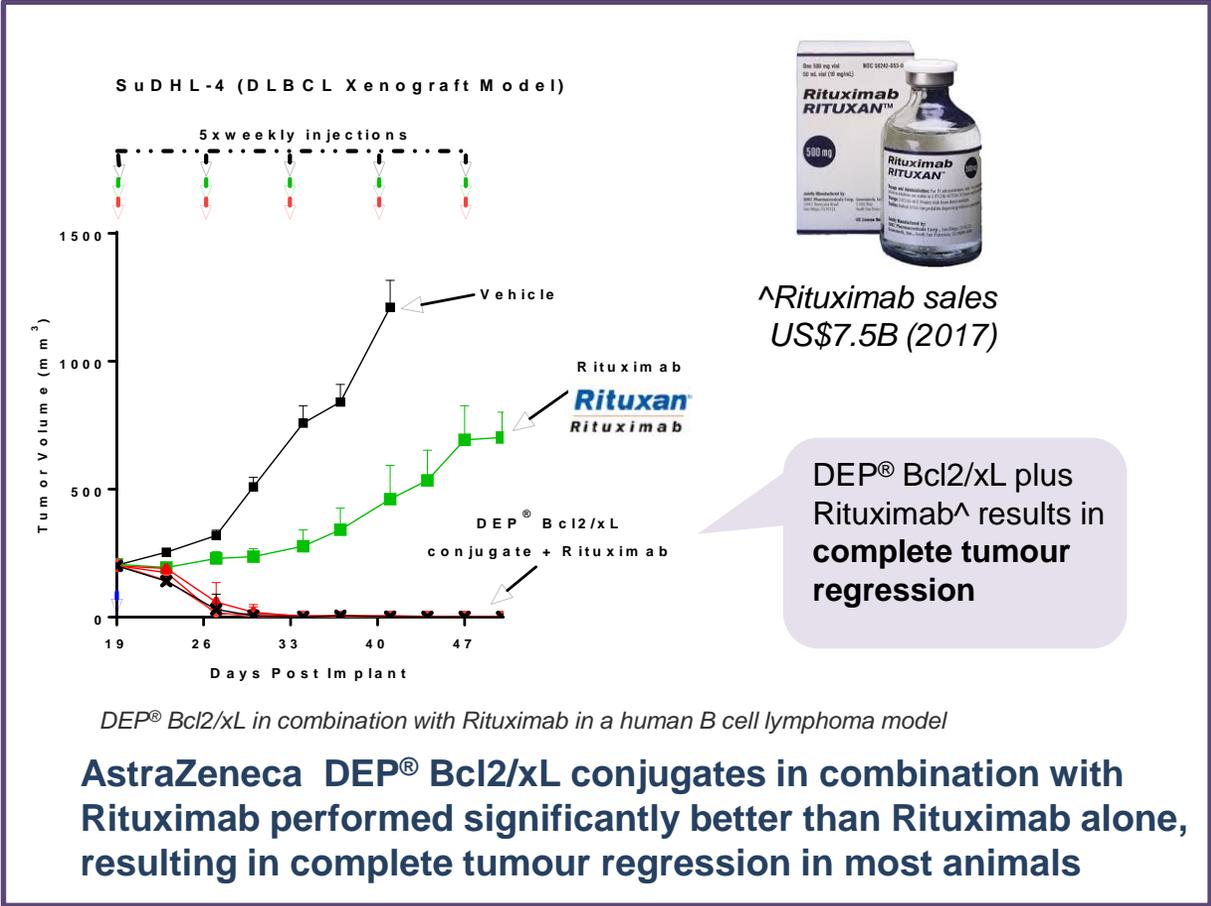
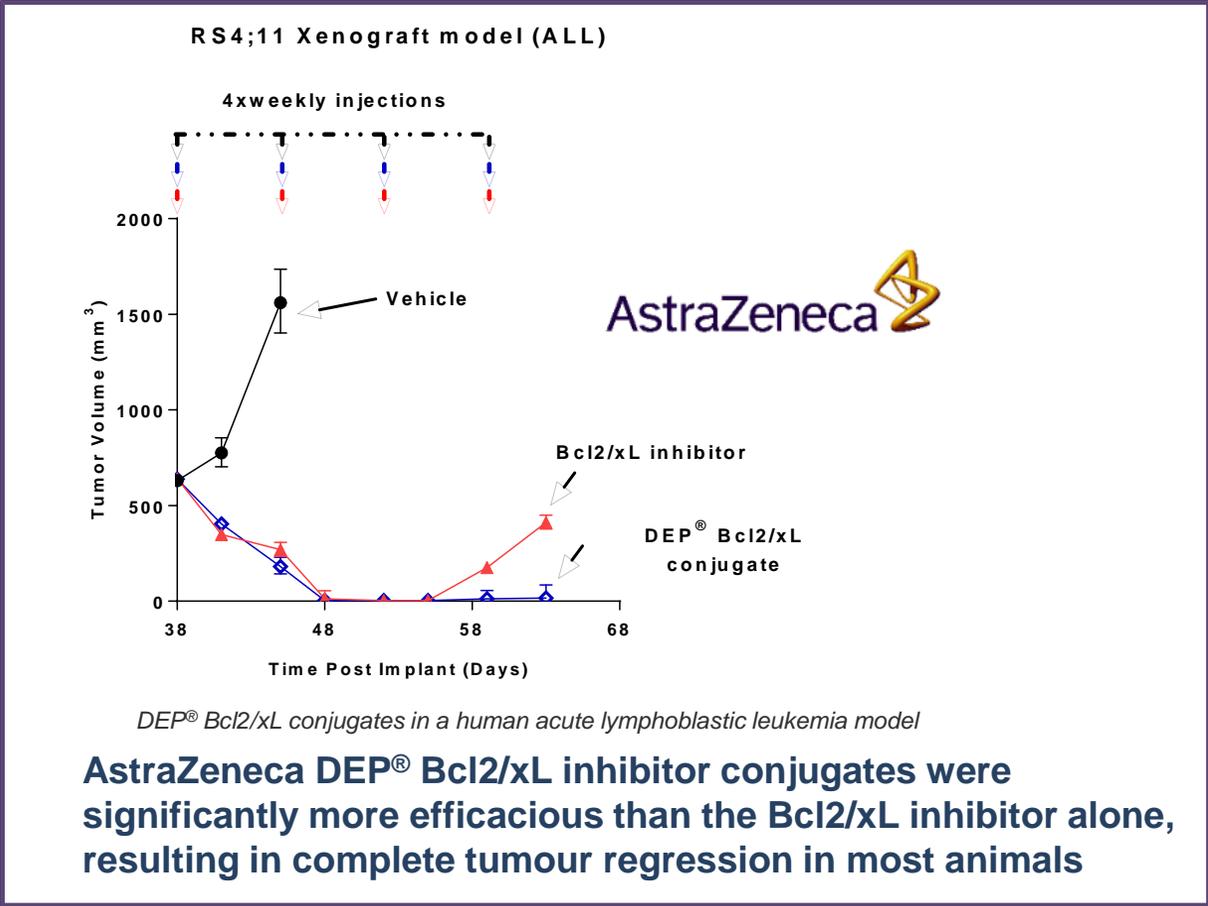
"[AZD0466] ...due to go into the clinic later this year"

Dr Susan Galbraith
Senior VP, Early Oncology, AstraZeneca



AstraZeneca DEP[®] Bcl2/xL conjugates in combination with Rituximab performed significantly better than Rituximab alone

AZD0466 is a highly optimized nanomedicine formulation of a novel dual Bcl2/xL inhibitor using Starpharma's DEP[®] delivery technology and is expected to enter the clinic later this year; IND allowed September 2019



DEP[®] platform has enabled Starpharma to build a deep internal pipeline of high-value products

DEP[®] docetaxel:
Detergent-free, enhanced version of widely used anti-cancer drug Taxotere[®]



Currently in Phase 2






Docetaxel (Taxotere[®]) had peak global sales >US\$3.1B despite having multiple US FDA “Black Box” warnings

PHASE 1 RESULTS (FY18)

- No neutropenia
- No steroid pre-treatment required
- Tumour-targeting (~70x more)
- No hair loss except one patient with mild alopecia
- No protocol-defined Dose Limiting Toxicities or anaphylaxis, fluid retention, diarrhoea and nail disorders

Encouraging efficacy signals in Ph1 & 2

DEP[®] cabazitaxel: Detergent-free, enhanced version of leading prostate cancer drug Jevtana[®]



Currently in Phase 1 / 2






Jevtana[®] had 2016 sales of ~US\$400M (est. US\$500M by 2018) despite having multiple US FDA “Black Box” warnings

EXCELLENT PRECLINICAL DATA

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

Encouraging efficacy signals & no DLTs in Ph 1 / 2

DEP[®] irinotecan: Enhanced version of leading anti-cancer drug Camptosar[®]



Currently in Phase 1 / 2






Irinotecan (Camptosar[®]) had peak sales of US\$1.1B despite having multiple US FDA “Black Box” warnings

EXCELLENT PRECLINICAL DATA

- DEP[®] irinotecan significantly outperformed Camptosar[®] (irinotecan) in multiple human colon cancer models – significantly better anti-tumour activity and increased survival

Outperformance in multiple cancer models – alone & in combination

Further internal DEP[®] candidates under development, including Targeted DEP[®]

Multiple preclinical studies have established improved efficacy, survival and safety with DEP[®] with many different drugs; clinical trials underway.

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DEP[®] docetaxel is an enhanced version of widely used cancer drug, Taxotere[®]



Enhanced version of docetaxel (Taxotere[®]) - one of the most widely used cancer drugs for a range of tumours including breast, lung and prostate



Docetaxel (Taxotere[®]) is a blockbuster cancer drug with peak global sales >US\$3.1B despite having multiple US FDA “Black Box” warnings



DEP[®] patents provide coverage to 2032



Advantages of DEP[®] docetaxel

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

vs



POSITIVE PHASE 1 RESULTS:

- No steroid pre-treatment required due to DEP[®] docetaxel’s detergent-free formulation - unlike Taxotere[®]
- No neutropenia (compares to >>90% with Taxotere[®])
- No protocol-defined Dose Limiting Toxicities and 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[®]
- Encouraging efficacy signals in 13/27 DEP[®] docetaxel patients including:
 - Stable disease (SD) in multiple patients with lung, pancreatic (SD>20 weeks), gastro-oesophageal (SD >18 weeks), glioblastoma (brain) and renal cancers

DEP[®] cabazitaxel is an enhanced version of leading prostate cancer drug, Jevtana[®]



Starpharma's patented DEP[®] cabazitaxel is an enhanced version of cabazitaxel (Jevtana[®]) – primarily used for prostate cancer and in clinical development for other cancers including breast and bladder



Cabazitaxel (Jevtana[®]) – estimated global sales of US\$500M for 2018 despite having multiple US FDA “Black Box” warnings (for neutropenia & anaphylaxis – due to polysorbate 80 in formulation)



DEP[®] cabazitaxel patents and applications provide coverage to 2039



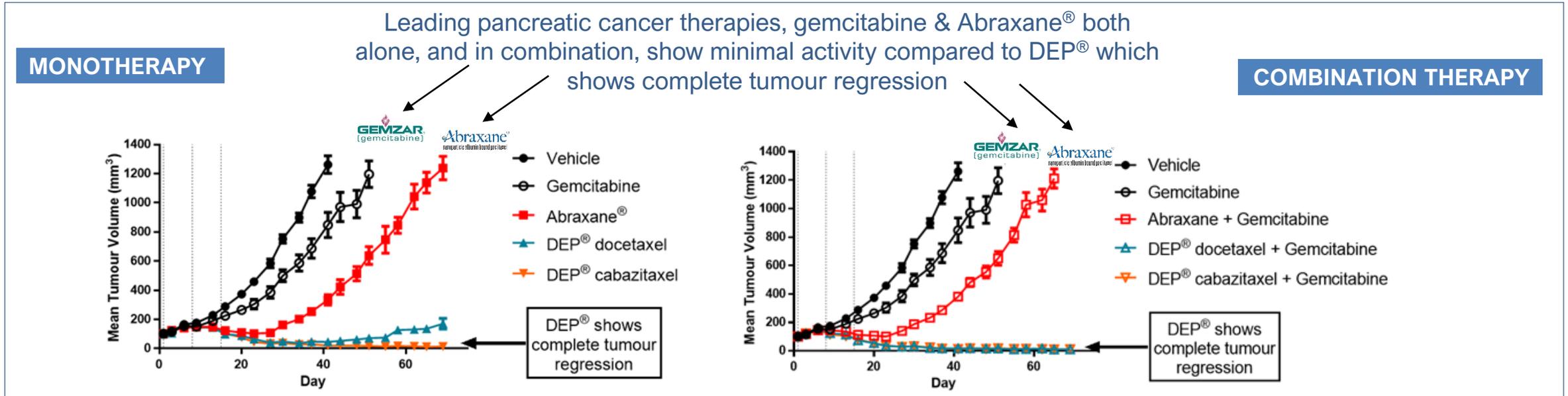
vs



Advantages of DEP[®] cabazitaxel

- ✓ DEP[®] cabazitaxel significantly outperformed Jevtana[®] (cabazitaxel) in a human breast cancer model with respect to efficacy, safety and survival
- ✓ Detergent (polysorbate 80) free formulation
- ✓ Reduction of major dose-limiting side effect (neutropenia)

DEP[®] docetaxel & DEP[®] cabazitaxel outperformed both gemcitabine & Abraxane[®] in human pancreatic cancer model



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
- ✓ These findings feed into the clinical development programs for DEP[®] docetaxel and DEP[®] cabazitaxel and combination studies

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

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

DEP[®] irinotecan: an enhanced version of widely used anti-cancer drug irinotecan (Camptosar[®])

Currently in Phase 1 / 2 trial



Irinotecan is a successful oncology agent – **Camptosar[®] peak sales US\$1.1B; Predominantly used for colorectal cancer**, also in combination for pancreatic, lung, ovarian, gastric & cervical cancer



Irinotecan has many significant issues including **black box warnings** for diarrhoea & myelosuppression



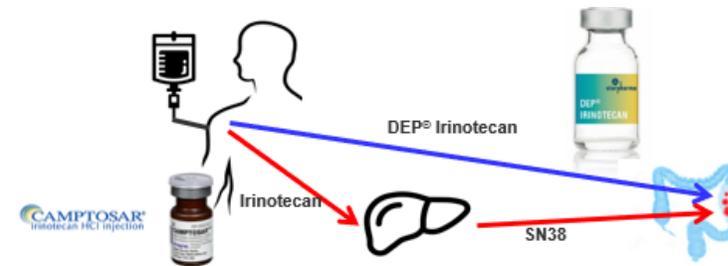
Irinotecan is a prodrug that must be converted to its active form, SN-38, to be effective and **displays wide patient-to-patient variability**



Irinotecan is increasingly being used **in combination with other anti-cancer drugs** with greater benefits



DEP[®] irinotecan incorporates the irinotecan active moiety (SN-38) and is an improved version of **Camptosar[®]** with improved efficacy, safety and tolerability demonstrated in multiple pre-clinical studies



DEP[®] drug delivery provides:

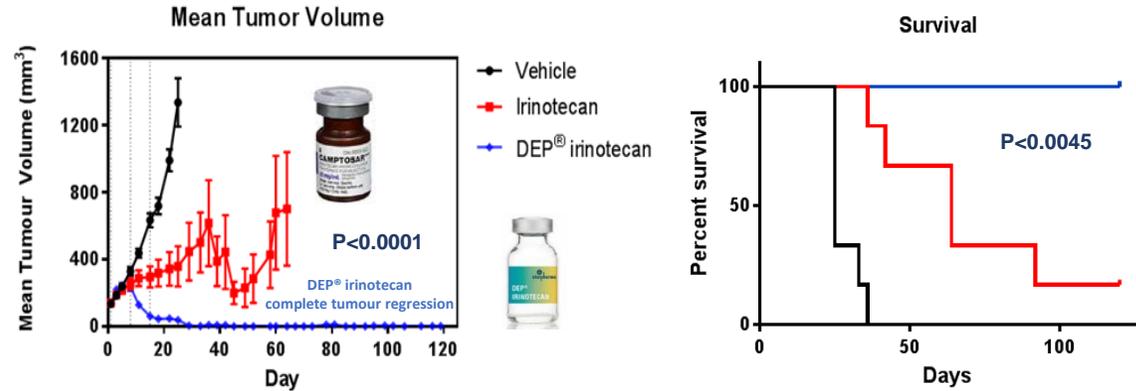
- the ability to solubilise the active metabolite SN38 directly thereby removing the need for liver metabolism
- protection of the active SN38 along with slow controlled release SN38
- targeting directly into solid tumours
- Improved efficacy and survival benefit (preclinical)

DEP[®] irinotecan outperformed standard irinotecan (Camptosar[®]) in human colon and pancreatic cancer models

Colon (colorectal) cancer:

- DEP[®] irinotecan demonstrated significantly better anti-tumour activity and increased survival compared with irinotecan (Camptosar[®]) in *multiple* human colon cancer models.

SW620 (human colon cancer) Xenograft

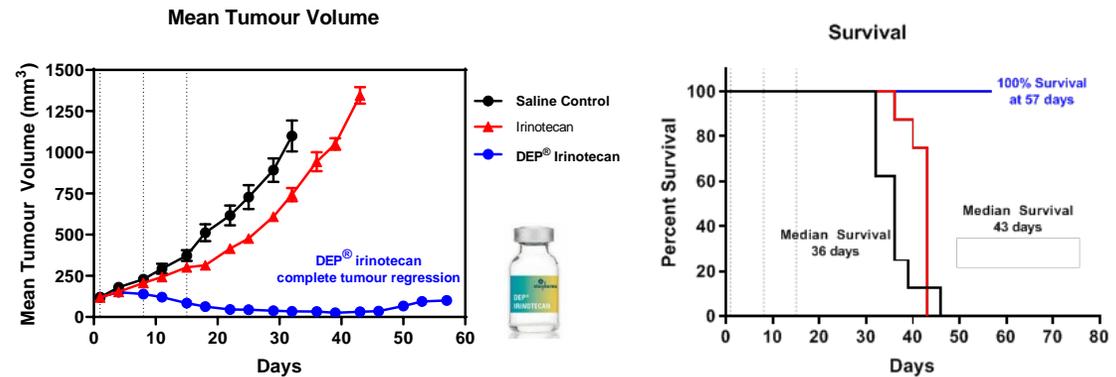


SW620 (colon cancer) mouse xenograft Balb/c nude mice (n=6 /group). IV dosing with Vehicle, DEP[®] irinotecan or irinotecan on days 1, 8 and 15.

Pancreatic cancer:

- DEP[®] irinotecan showed **complete tumour regression** and
- DEP[®] irinotecan showed **100% survival** in a human pancreatic cancer model

CAPAN-1 (human pancreatic cancer) Xenograft

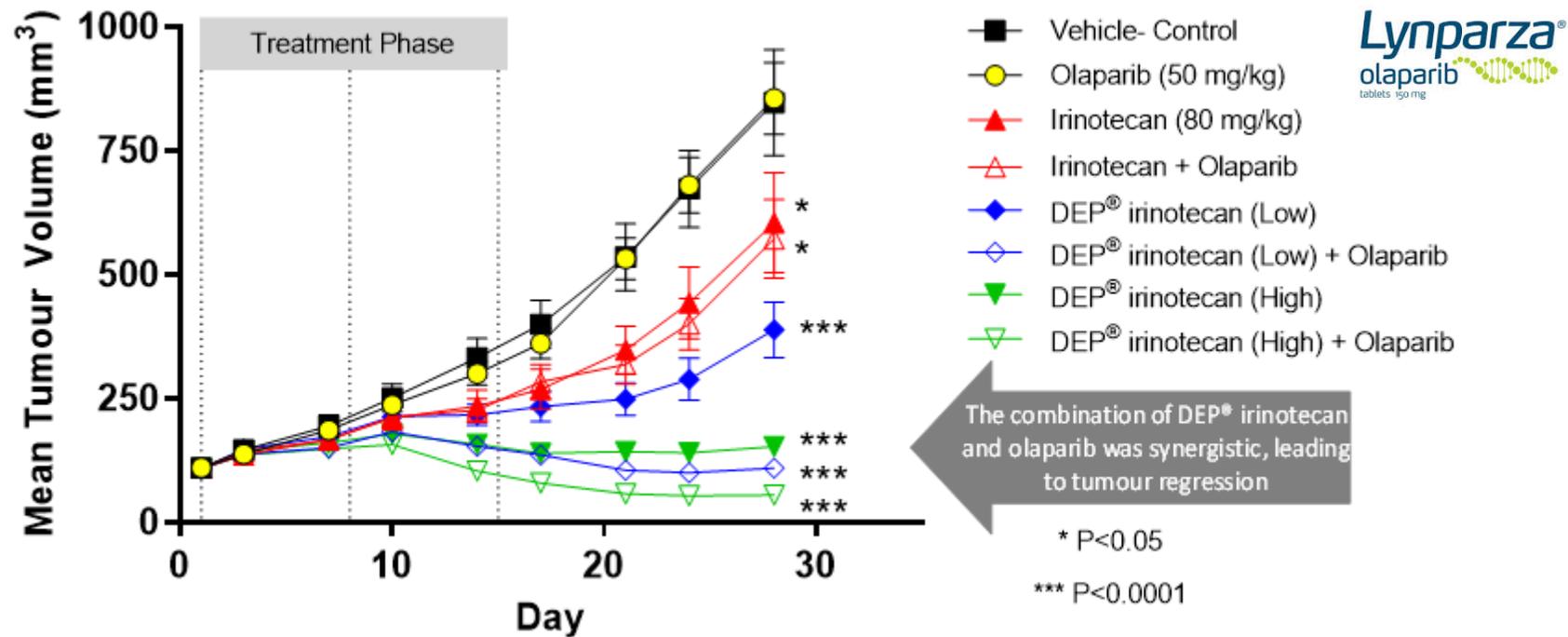


CAPAN-1 (human pancreatic cancer) xenograft in mice (n=8/group). IV dosing with Vehicle, DEP[®] irinotecan, irinotecan or irinotecan + 5-FU on days 1, 8 and 15

Kaplan Meier Survival Curve
DEP[®] irinotecan versus all other groups (P<0.0001 Log-rank Mantel Cox)

DEP[®] irinotecan synergistic with Lynparza[®] in refractory human colon cancer model

DEP[®] irinotecan, alone and in combination with Merck/AZ's Lynparza[®], showed significant anti-tumour efficacy and synergy compared with standard irinotecan (Camptosar[®]) and Lynparza[®] (olaparib) in an irinotecan-refractory human colon cancer model

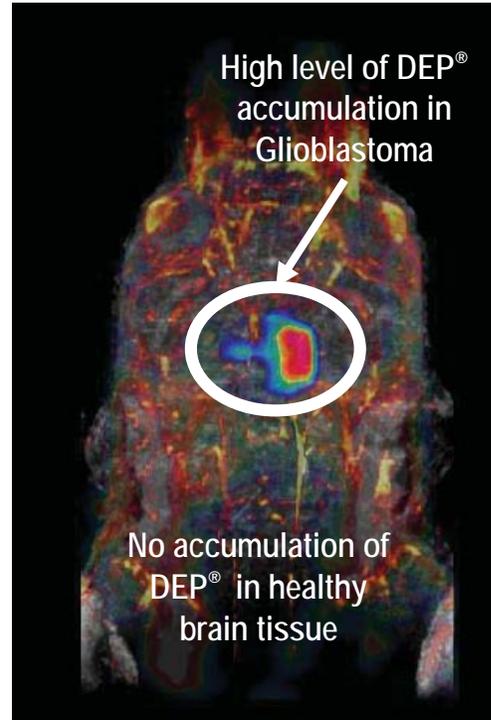


Balb/c mice were inoculated subcutaneously with the human colon cancer (HT-29) cell line (10 mice/group). Mice were dosed with saline (vehicle), DEP[®] irinotecan (low and high dose), and irinotecan (Camptosar[®]) (80 mg/kg) IV once per week. Olaparib (Lynparza[®] 50 mg/kg) dosed PO (per oral) five times per week (5 days on/2 days off). Irinotecan (Camptosar[®]) and olaparib (Lynparza[®]) were dosed at the pre-determined maximum tolerated dose for the combination; however, DEP[®] irinotecan doses were deliberately reduced in this experiment to allow for demonstration of synergy and were approximately one third (low dose) and approximately two thirds (high dose) of the maximum tolerated dose of single agent when used in this combination. Lynparza[®] doses were reduced if required in the highest DEP[®] irinotecan + olaparib dosing group (3/10 mice missed 1-2 olaparib doses during weeks 2 and/or 3 due to tolerability).

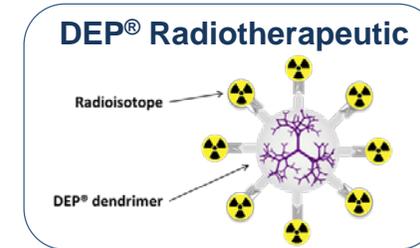
DEP[®] shows significant accumulation in a glioblastoma (brain tumour) model

About Glioblastoma Multiforme (GBM)

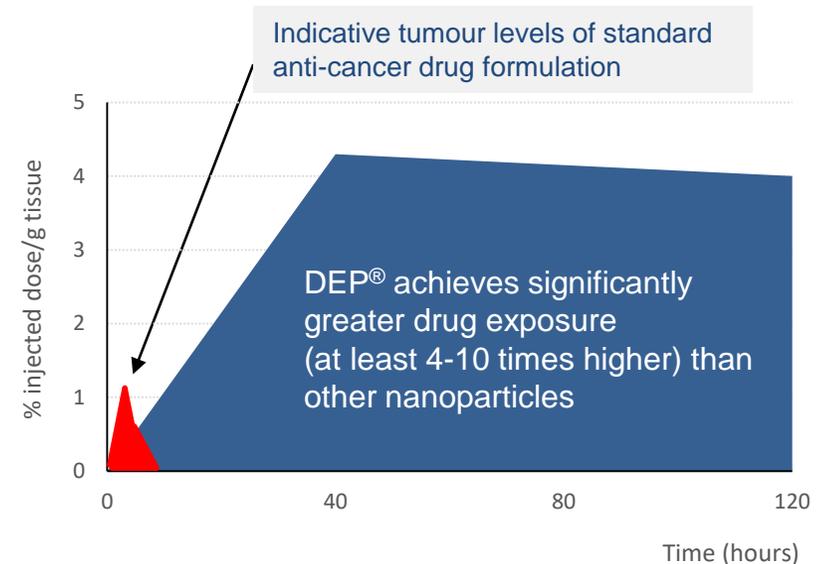
- GBM is the most common and aggressive malignant brain tumour
- GBM also has very poor survival rates with fewer than 10% of patients surviving more than 5 years
- GBM is considered to be incurable, with nearly 100% of patients experiencing disease relapse after initial treatment.



PET-MR image of GBM-bearing mouse 5 days post-injection of DEP[®] conjugate (details not disclosed pending IP filing)

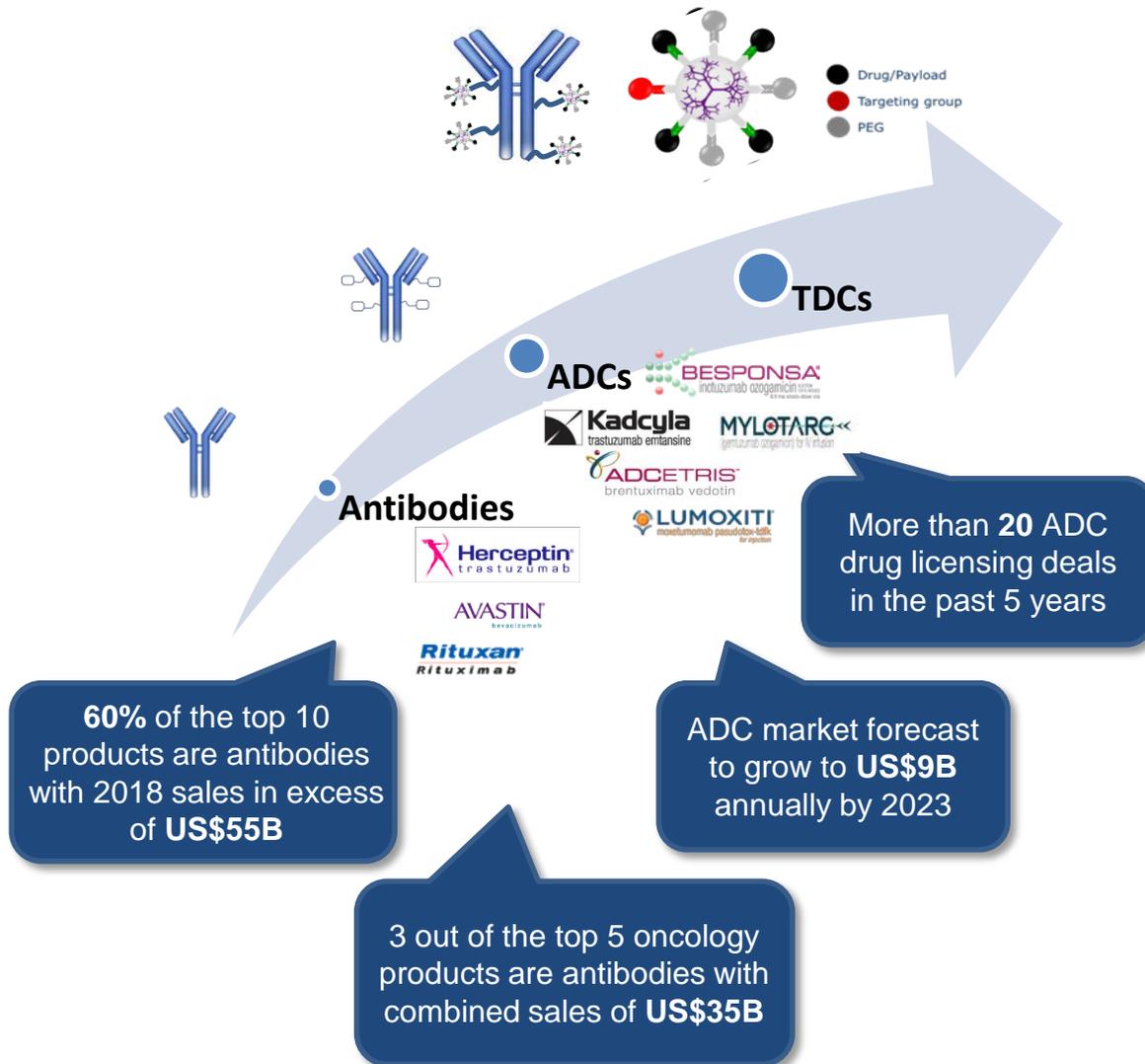


DEP[®] radiotherapeutic accumulation in GBM model



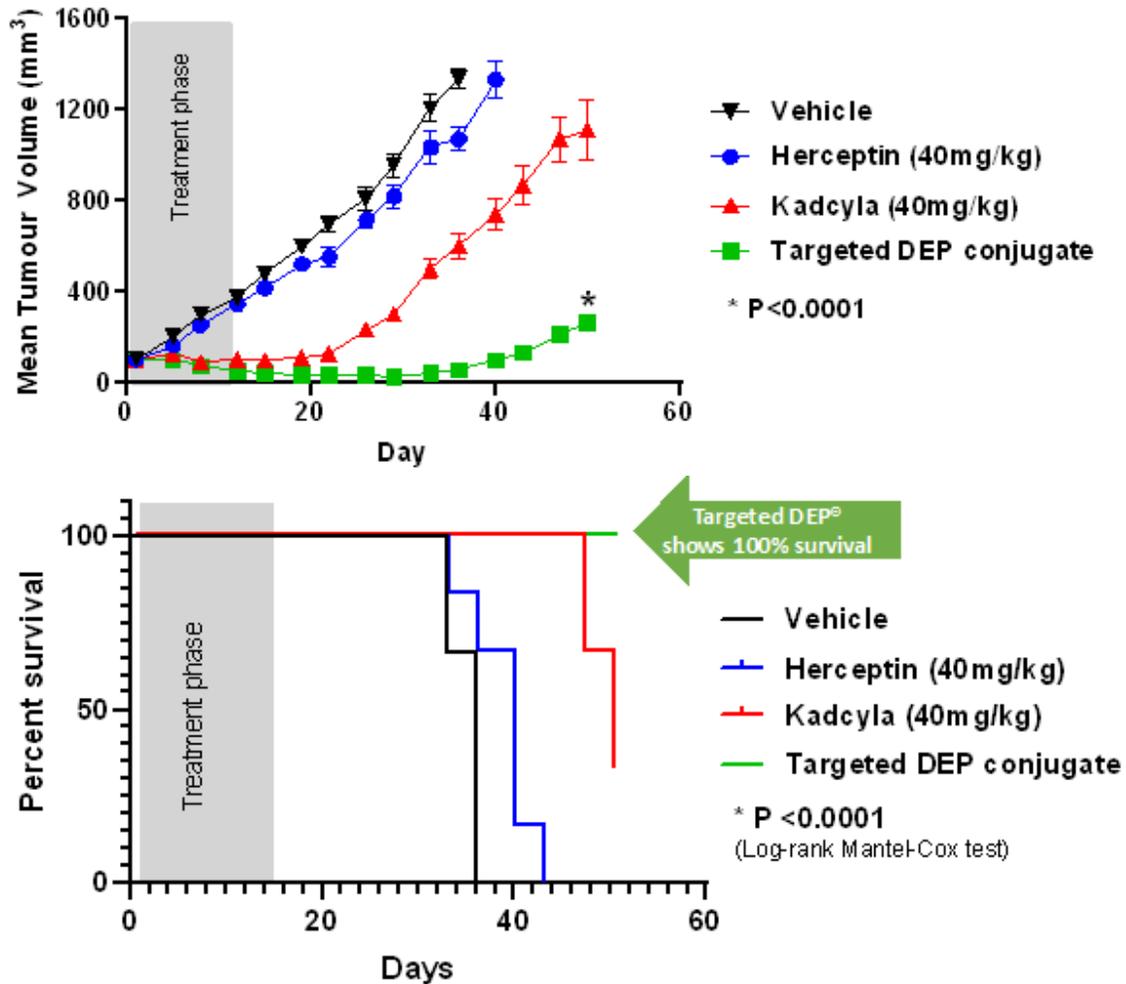
The accumulation of DEP[®] in this GBM model is of particular interest given the observation of stable disease (>10 weeks) in a patient with GBM treated with DEP[®] docetaxel (phase 1 trial)

Targeted DEP[®] conjugates (TDCs): a new approach to ADC design



Starpharma's Targeted DEP [®] conjugates	
Can use small molecule, whole antibody, antibody fragments or antibody mimetics	✓
Significantly higher drug loading than conventional ADCs	✓
Bind with high affinity and specificity	✓
Highly efficacious in cancer model in vivo	✓
Flexible and tailored to suit clinical requirements	✓
Homogeneous	✓
Standard chemistry yielding consistent, reproducible, stable molecules	✓
Platform already in the clinic and demonstrated to be safe and well tolerated	✓

Novel HER-2 Targeted DEP[®] significantly outperforms in human ovarian cancer model



Novel HER-2 Targeted DEP[®] conjugate:

- resulted in tumour regression and 100% survival, and
- significantly outperformed both Kadcylla[®] (T-DM1), a HER-2 targeted antibody-drug conjugate (ADC), and Herceptin[®] (Trastuzumab) itself,

in a human ovarian cancer model.





This experiment was conducted in a human ovarian cancer (SKOV-3) xenograft model in NOD SCID mice by an internationally recognised translational Cancer group. Groups of animals (6/group) were dosed once per week for 3 weeks with the novel HER-2 Targeted DEP[®] conjugate, Kadcylla[®], or a saline control. Another group of animals was treated with Herceptin[®] twice a week for 3 weeks. The tumour volume data represent the mean \pm standard error of the mean (SEM) and significance values determined using a Two-Way ANOVA (Tukey's post hoc). Survival analysis was carried out using Kaplan-Meier survival curves and the Log-rank test. (Note: If error bars do not display on the graphs, they are shorter than the height of the symbol and not visible.)



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