Enhancing drug delivery

DEP® dendrimer platform

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PODD

starpharma

#PODD2021

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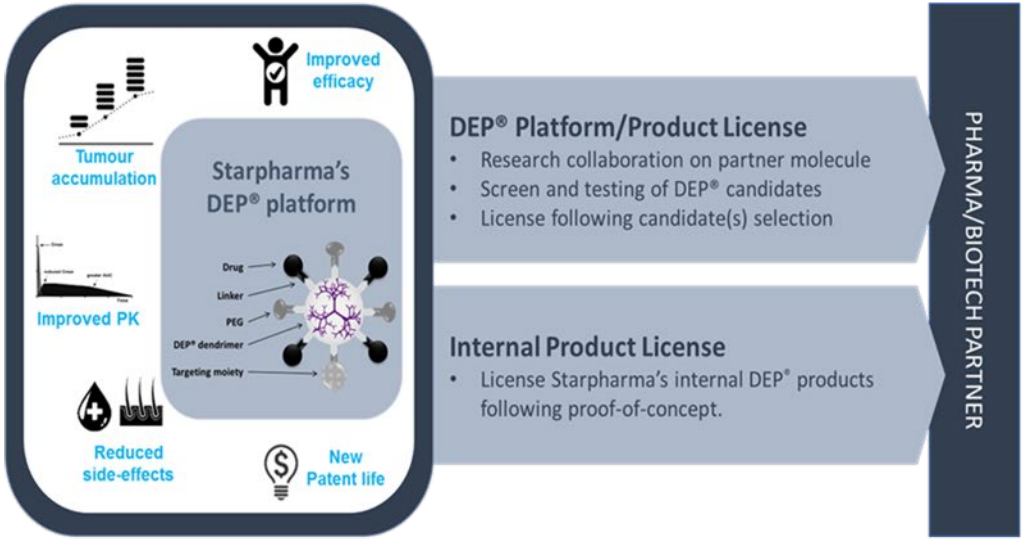
FLEURSTAT BVGEL (VivaGel® BV) for the treatment of BV and relief of symptoms: Ask your pharmacist – they must decide if this product is right for you. Always read the label. Follow the directions for use. Do not use for more than 7 days unless a doctor has told you to. See your doctor if symptoms persist after 7 days or recur within 2 weeks, and if you consider you may be at risk of an STI. See a doctor if you are diabetic or pregnant/breastfeeding (or plan to be).

Starpharma's DEP® strategy :

"To leverage our proprietary dendrimer platform to build high value products and partnerships that address significant unmet need"



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

Clinical-Stage Assets

Three internal phase 2 products

DEP® platform

Offers exceptional optionality for multiple programs to run in parallel

***DEP® treatment areas include:** Antivirals; Anti-infectives; Chemotherapeutics; Radiotheranostics; Antibody Drug Conjugates (ADCs); Endocrinology & other non-oncology areas*

Preclinical Pipeline

Developing new assets to progress to the clinic

Multiple DEP® Partnered Programs

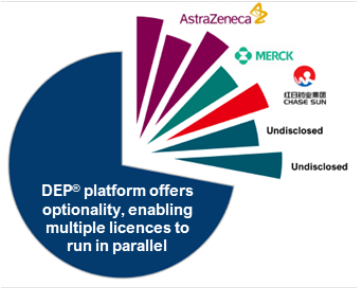
Potential to generate significant revenue through royalties and milestones

AstraZeneca MSD 红日药业集团 CHASE SUN

DEP® partnering creates significant value and optionality

Starpharma's DEP® platform enhances the commercial and therapeutic value of a wide range of drugs, creating multiple potential revenue streams and significant IP leverage

DEP® platform allows for multiple partnerships



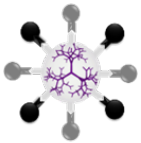
Starpharma has several disclosed/undisclosed partnered DEP® programs, including with large pharma companies: AstraZeneca, Merck and Chase Sun

AstraZeneca's novel DEP® nanoparticle AZD0466

AstraZeneca

- Dual Bcl2/xL inhibitor with DEP® significantly improving its therapeutic index
- Phase 1 trial significantly expanded and advanced in 2021, to a multi-region, global Phase 1/2 clinical trial
- The new phase 1/2 trial design is aimed at seamless transition to phase 2, to facilitate marketing approval.
- Data was also recently published showing the potent anti-cancer effects of AZD0466 in a malignant mesothelioma model.
- AZD0466 is the first candidate in Starpharma's multiproduct licence with AZ;
- Total AZD0466 deal up to US$124M + royalties

*AstraZeneca describes AZD0466 as having the **potential to be a "best-in-class" agent** with a **broad application** in both **solid and haematological tumours***



AZD0466 featured at AACR 2020 Meeting: https://starpharma.com/drug_delivery/dep-posters

MSD

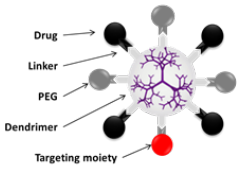
Starpharma has signed a DEP® research agreement with MSD for dendrimer-based ADCs using DEP® technology

Recent ADC deals demonstrate strong interest

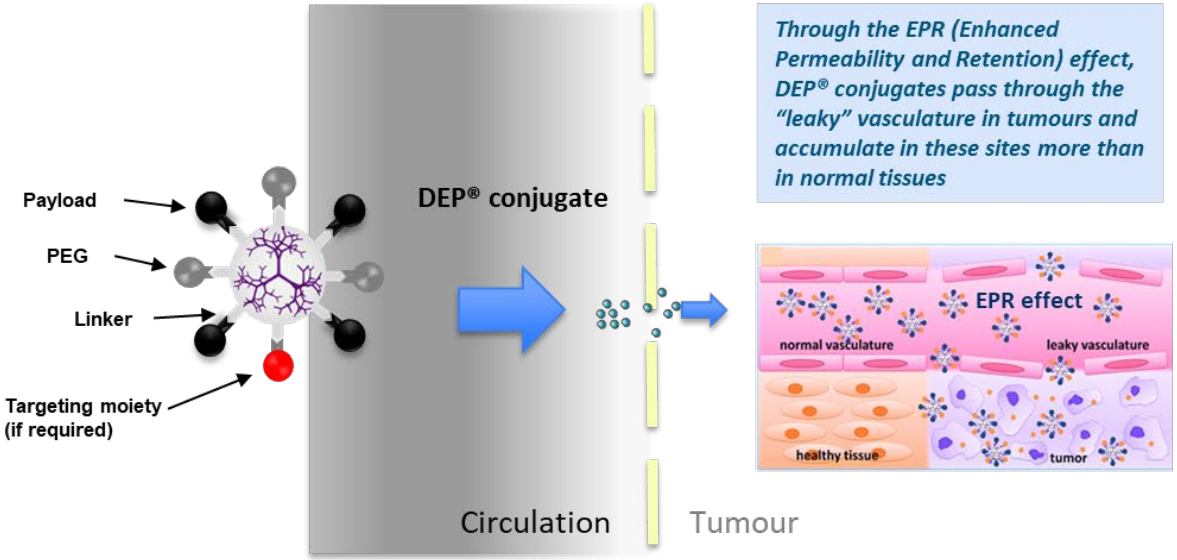
- AstraZeneca & Daiichi Sankyo, **US$6.9 billion,** *July 2020.*
- Gilead & Immunomedics, **US$21 billion,** *Sep 2020.*
- Seattle Genetics & Merck, **$6.8 billion,** *Sep 2020.*
- Merck & VelosBio, **$2.75B,** *Nov 2020.*
- Boehringer Ingelheim, **€1.2B ($1.5B),** *Dec 2020.*
- BMS & Eisai, **US$3.1B,** *June 2021.*

"MSD is a recognised leader in oncology, and we are delighted to have signed this new Research Agreement in such an innovative and valuable area"

Dr Jackie Fairley, CEO Starpharma



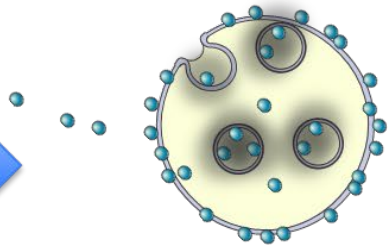
DEP® platform - preferential tumour accumulation ⟹ enhanced benefits



Through the EPR (Enhanced Permeability and Retention) effect, DEP® conjugates pass through the "leaky" vasculature in tumours and accumulate in these sites more than in normal tissues

DEP conjugate

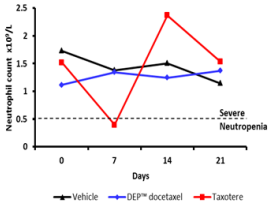
- Accumulation in tumour via EPR
- Interaction with cell
- drug release
- antitumour effect

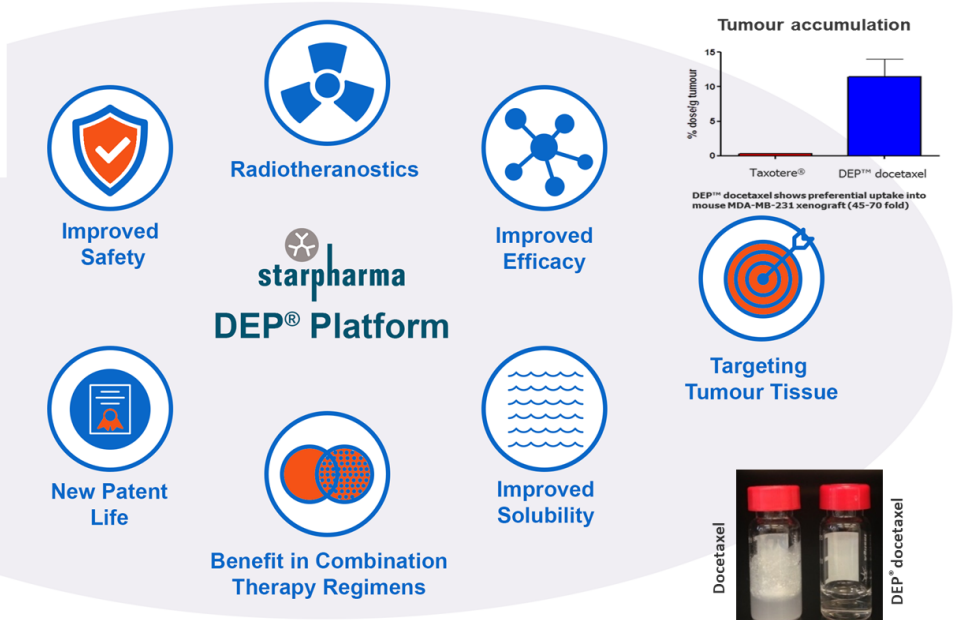


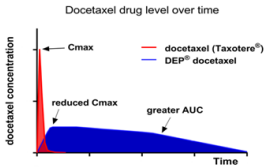
Targeted DEP® conjugate

- DEP ADC, DEP radiotherapy
- Targeting moiety helps binds to cell
- Binding increases retention and internalization at cells
- Increased internalization = increased drug release/activity

Starpharma's DEP® drug delivery platform enhances the therapeutic and commercial value of drugs





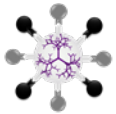


Diagrammatic representation of Cmax and AUC for docetaxel and DEP® docetaxel

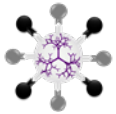
DEP® is a technology platform with multiple commercial opportunities in oncology and beyond

DEP® PLATFORM

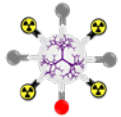
NON-ONCOLOGY
- Antiviral eg. DEP® remdesivir
- Anti-infective
- Endocrinology



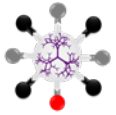
CHEMOTHERAPEUTICS
- Franchise extension
- Generic differentiation
- New Chemical Entities
- Combinations including immuno-oncology

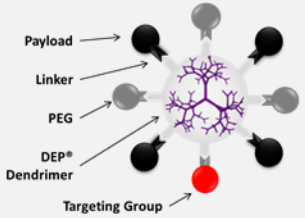


RADIOTHERANOSTICS
- Radiotheranostic applications
- Can use variety of radioisotopes



ANTIBODY DRUG CONJUGATES (ADCs)
- Flexible technology
- Increased drug antibody ratio
- Targeting group agnostic
- Site selective payload attachment





Improved efficacy

DEP® improves anti-cancer efficacy through better drug targeting & improved pharmacokinetics.

Reduced side-effects

DEP® 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® also provides valuable commercial benefits by creating new intellectual property and extending patent life.

DEP® internal oncology programs

Multiple clinical-stage assets with high commercial value potential

COMMERCIAL OBJECTIVE	Create value through clinical proof-of-concept in one or more cancer types – alone and/or in combination	License following proof-of-concept clinical data; platform validation	Utilise accelerated development / regulatory pathways (i.e. 505b2) for optimal ROI

PHASE 2 — TAXOTERE®

DEP® DOCETAXEL: Enhanced version of docetaxel (Taxotere®) – widely used for breast, lung & prostate cancer

Phase 2 trial ongoing, 50 patients recruited

- **Encouraging efficacy signals** observed, including prolonged stable disease and significant tumour shrinkage in patients with pancreatic, oesophageal, cholangiocarcinoma, and gastric cancer.
- **Notable lack of bone marrow toxicity** (e.g., neutropenia) and other common side effects inc. hair-loss, mouth ulcers, anaphylaxis and oedema

PHASE 2 — JEVTANA® (cabazitaxel) injection

DEP® CABAZITAXEL: Enhanced version of leading prostate cancer drug cabazitaxel (Jevtana®)

Phase 2, ongoing, 42 patients recruited

- **Encouraging efficacy signals** have been observed, including radiological responses, stable disease, significant target tumour shrinkage and substantial tumour marker reductions (e.g., PSA), in cancers including prostate, ovarian, lung, gastro-oesophageal, head and neck and other cancers.
- Significantly less toxicity than is usually associated with Jevtana®

PHASE 2 — CAMPTOSAR® irinotecan HCl injection

DEP® IRINOTECAN: Improved version of irinotecan (Camptosar®) - predominantly used for colorectal cancer

Phase 2, ongoing, 54 patients recruited

- **Encouraging efficacy signals** observed include prolonged stable disease, impressive tumour shrinkage and reductions in tumour marker levels for a number of tumour types, including breast, colorectal, ovarian, pancreatic, lung and oesophageal cancer
- **No severe high-grade diarrhoea seen with DEP® irinotecan** which is experienced by 20-40% of patients with conventional irinotecan & often requires hospitalisation

Starpharma's deep preclinical pipeline includes DEP® chemotherapeutic candidates including:

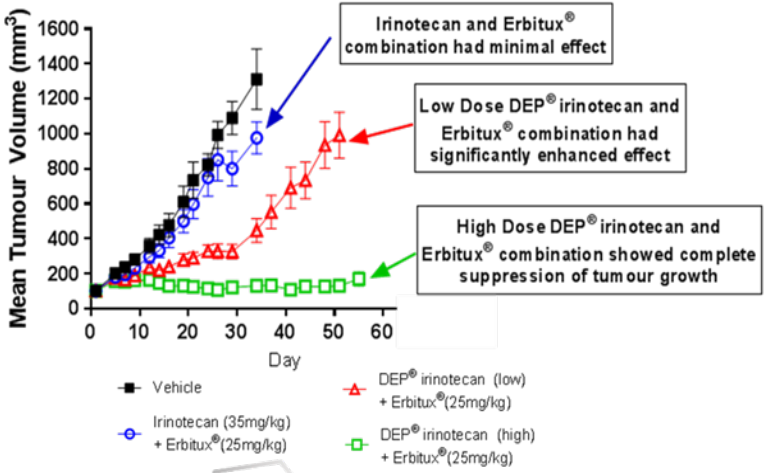
- DEP® gemcitabine
- DEP® radiotherapeutic candidates
- DEP® antibody drug conjugate (ADC) candidates
- Further therapeutic candidates

#Clinical studies have demonstrated reduction in important side effects with DEP® including bone marrow toxicity, anaphylaxis, oedema and hair-loss

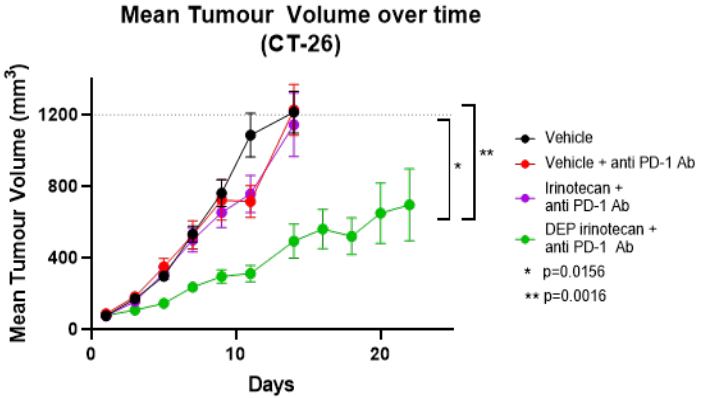
* Multiple preclinical studies have established improved efficacy, survival and safety with DEP® with many different drugs

DEP® drugs are also ideal candidates for combination therapy- conventional, targeted and Immuno-Oncology approaches

- DEP® irinotecan in combination with **Erbitux®** demonstrated significantly enhanced anti-cancer efficacy, and survival with **complete suppression of tumour growth and 100% survival in HT-29 colon cancer model**



- DEP® irinotecan + anti PD-1 Ab in combination
- showed significant enhancement of anti PD-1 antibody (anti PD-1 Ab) activity by DEP® irinotecan in both CT-26 and MC-38 colon cancer models

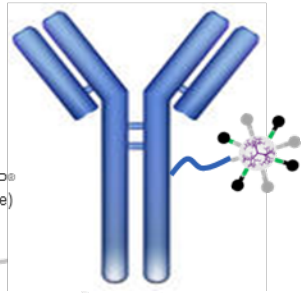


These results indicate that DEP® irinotecan in combination with an anti PD-1 antibody could boost the efficacy over anti PD-1 antibody alone, or immuno-oncology (IO) combinations with standard chemotherapeutic agents.

Targeted DEP® conjugates provide additional flexibility

Starpharma's Ab Targeted DEP® 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
- Versatility in payload type
- Overcome issues of payload **solubility** and aggregation



Diagrammatic representation of an Antibody targeted DEP® conjugate (not to scale)

Targeting

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

DEP® drug conjugate

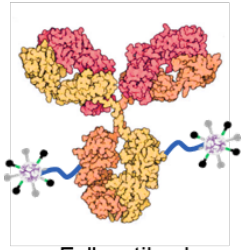
- Precisely manufactured poly-lysine dendrimer with attached drug/payload
- Dendrimer size easily scalable to deliver desired payload number (8, 16, 32…) per dendrimer conjugate
- Can deliver any type of payload – cytotoxic, ultratoxic, radioisotope
- Potential applications beyond cancer
- Drug-linker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

Site specific attachment

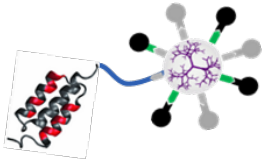
- Precise and reproducible
- Ability to attach multiple dendrimers of differing size (high DAR)
- Ability to achieve significantly higher DAR than other approaches

DEP® ADC / Radiotheranostic platform

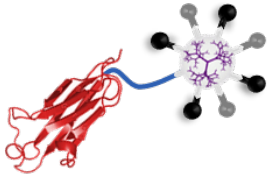
Flexibility in targeting approach – Flexibility in payload - Enhanced performance



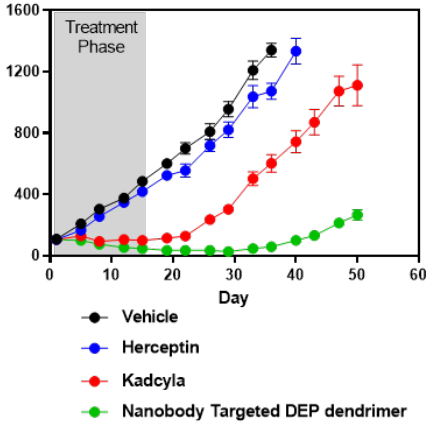
Full antibody
- 150kDa

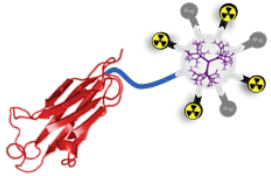


Affibody
- 6.5kDa

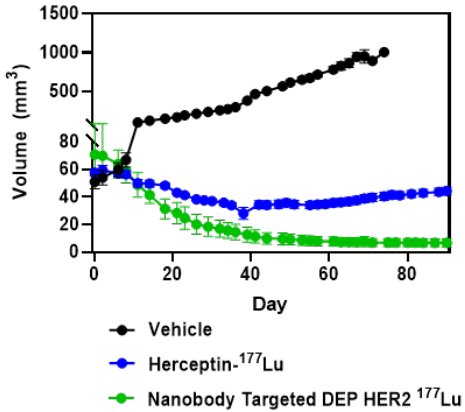


Nanobody
- 15kDa



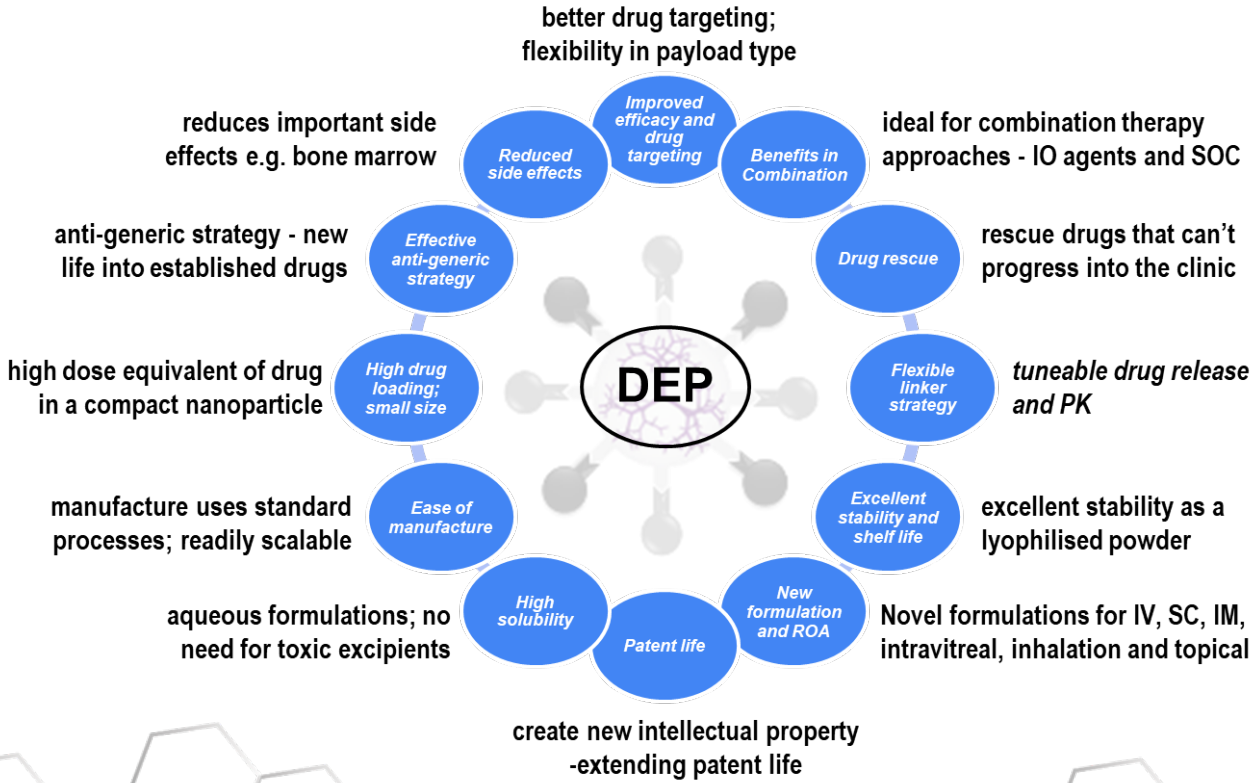


Nanobody
- 15kDa



These experiments were conducted in either a human ovarian cancer (SKOV-3) or human prostate cancer (DU-145) mouse xenograft model

DEP® platform – significant optionality, therapeutic and commercial benefits



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