

Dendrimers in Drug Delivery

Starpharma's DEP™ technology

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Safe Harbour Statement & 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.

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Starpharma Dendrimer Pipeline

A platform technology with broad optionality and applicability

			Res	PC	PhI	PhII	PhIII	Reg.	Mkt	
Antimicrobial / Antiviral (SPL7013)*	VivaGel®	BV Symptomatic Relief**	→						→	
	VivaGel®	BV Prevention of Recurrence	→						→	
	VivaGel® (SPL7013)*	Viral Conjunctivitis	→							
	VivaGel®	VivaGel® Coated Condom	→							
Oncology (Internal)	Drug Delivery	DEP™ docetaxel (various cancers)	→				→			
	Drug Delivery	DEP™ oxaliplatin (various cancers)	→		→					
	Drug Delivery	Various oncology	→							
Undisclosed	Partnered programmes	Drug Delivery - Various	→							

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Completed



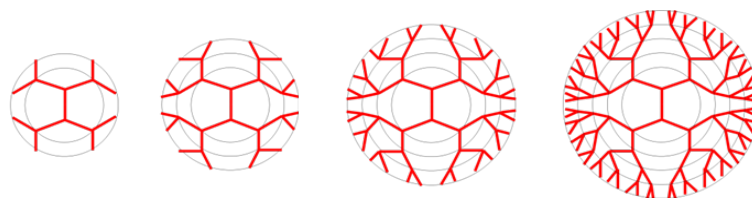
Planned

* VivaGel® supported by a full FDA CMC package for an NDA

** Alternative symptomatic claim strategies being pursued



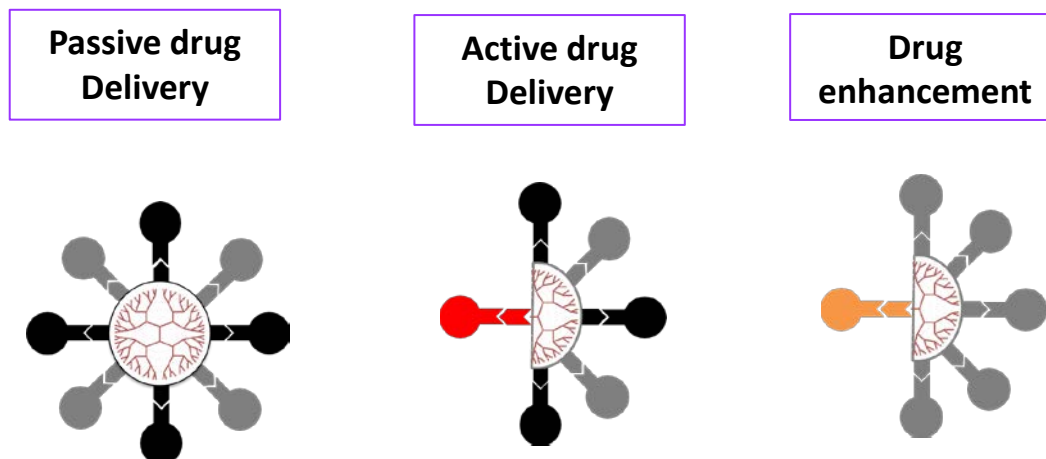
What is a Dendrimer



- Starpharma's dendrimers are based on lysine have a precise and defined size
- A dendrimer is a highly branched, approximately spherical macromolecule.
- Multiple layers (Generations) of polymer built around a central core, size 1-100 nm diameter, commonly 5-15 nm
- Starpharma's dendrimers are already in the clinic
- have been demonstrated to be well tolerated
- Current cGMP manufacture (30kg scale) provides dendrimers that are extremely pure
- Dendrimers are prepared by standard chemical synthetic methods: practical, easy to formulate and cost effective

Starpharma's DEP™ platform

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DEP™ dendimer	Precisely manufactured poly-lysine dendrimer (variable size) Manufactured using standard chemistry
Toxin/Drug/Payload	Small molecule, Cytotoxic, Ultratoxic
Targeting group	Whole antibody, fragment, mimetic, small molecule
PEG	Provides stealth; solubility; control clearance; flexibility in size
Drug to be enhanced	Molecule requiring enhanced PK, PD, solubility or elimination of off target toxicities , expansion of therapeutic window

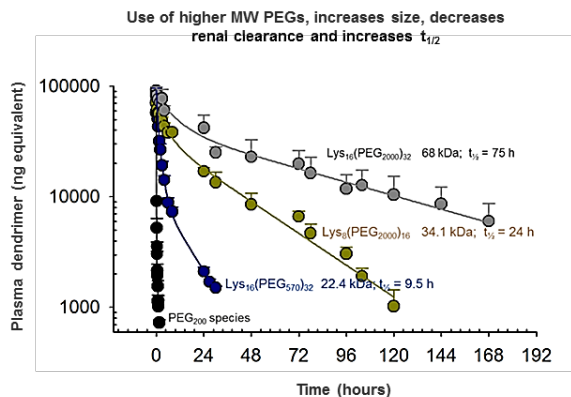


Starpharma's DEP™ platform

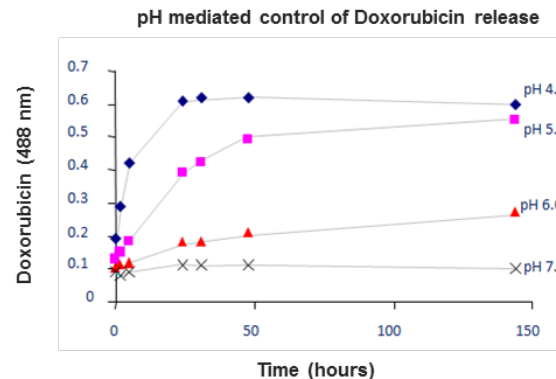
A flexible approach to enhancing therapeutics

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Stealth with enhancement of PK and $T_{1/2}$

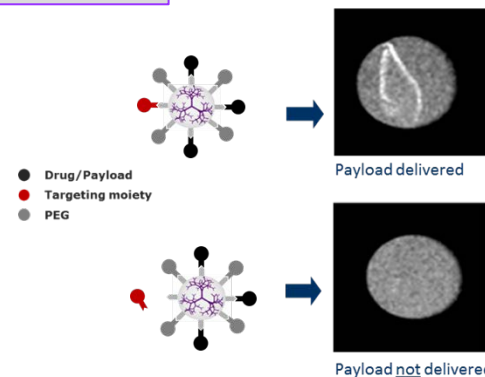
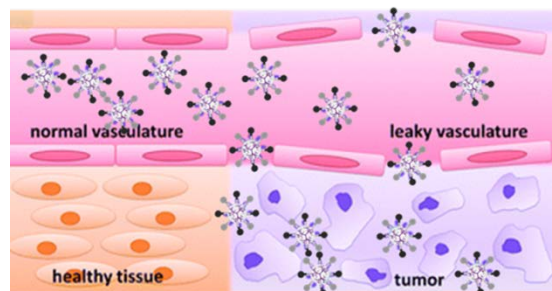


Controlled release of drug in target environment



Use of larger dendrimer constructs attached to insulin increased both PK and $T_{1/2}$

Preferential accumulation in target tissue (passive/ targeted)



Starpharma's DEP™ drugs

Multiple benefits in Oncology

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Attribute	DEP™ docetaxel	DEP™ oxaliplatin	DEP™ doxorubicin
Elimination of major dose-limiting toxicity	✓ (neutropenia)	✓ (neurotoxicity)	✓ (cardiotoxicity)
Water soluble – Polysorbate 80 free	✓ (x20,000)	NA	NA
Tumour-targeting (passive)	✓ (>40-fold)	✓ (>40-fold)	✓ (>40-fold)
Extended half-life	✓ (x60)	✓ (x60)	✓ (x60)
Efficacy	✓ (various cancer models)	✓ (colon cancer model)	✓ (MTD twice that of originator)
Patents	Patents are granted or pending in major markets		
Development Stage	Phase 1	Pre Clin	Pre Clin

DEP™ docetaxel

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Enhanced solubility

Enhanced safety

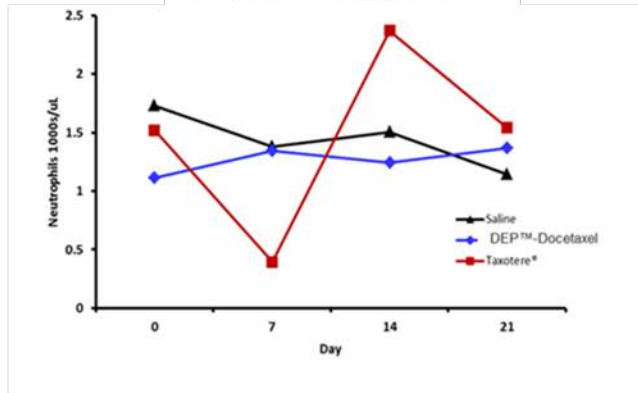
Enhanced efficacy

Docetaxel DEP™ docetaxel



- solubility >↑ 20,000x
- polysorbate 80-free

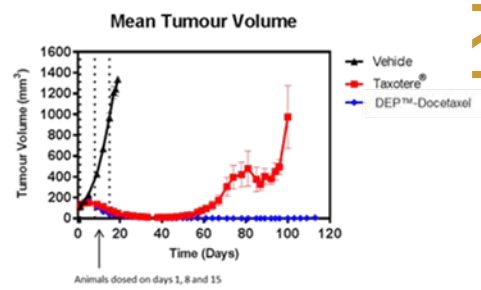
Reduced neutropenia with DEP™ docetaxel



DEP™ docetaxel Efficacy: Mouse Breast Cancer Model*



PBS 19d DEP™ docetaxel 19d



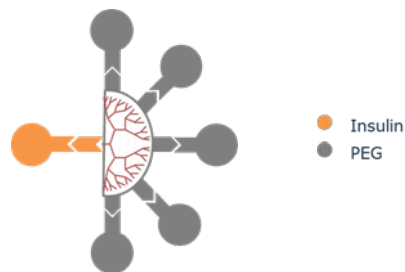
*Mouse Xenograft (MDA-MB 231); N= 10/group; p< 0.0001

DEP™ docetaxel is in Phase 1 Clinical studies:
 “A phase I dose-escalation study to evaluate the safety, tolerability and pharmacokinetics of DEP™ docetaxel in patients with advanced solid tumours”



Starpharma's DEP™ drugs

Multiple benefits in Diabetes



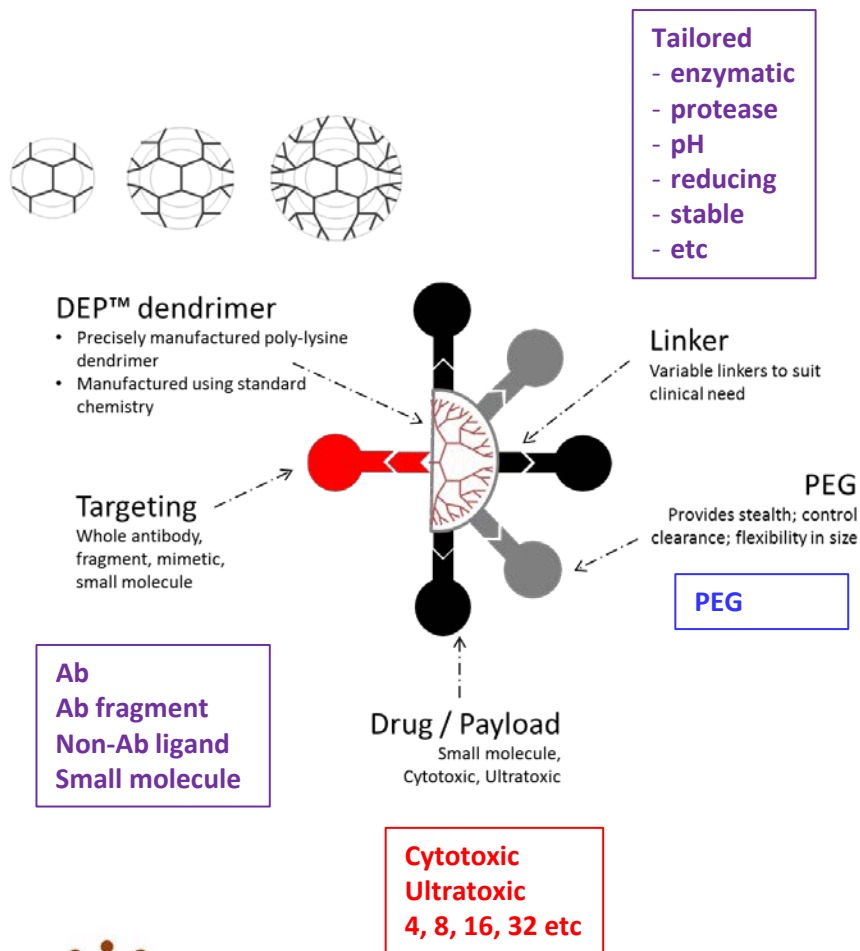
Attribute	DEP™ insulin
Solubility	<p>✓</p> <p>Patient friendly administration / low sting - high aqueous solubility, low viscosity and is non-acidic</p>
Extended half-life	<p>✓</p> <p>Tunable duration PK of insulin can be extended to achieve desired half -life half life extension from 1 day to 1 week</p>
Efficacy	<p>✓</p>
manufacturing	Standard chemistry yielding consistent, reproducible stable molecules
Patents	Patents are granted or pending in major markets

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Targeted DEP™ Conjugates

A flexible approach to drug conjugate design and development

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Can use small molecule, whole antibody, antibody fragments or antibody mimetics	✓
Bind with high affinity and specificity	✓
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	✓

Targeted DEP™ Conjugates

A new approach to drug conjugate design and development

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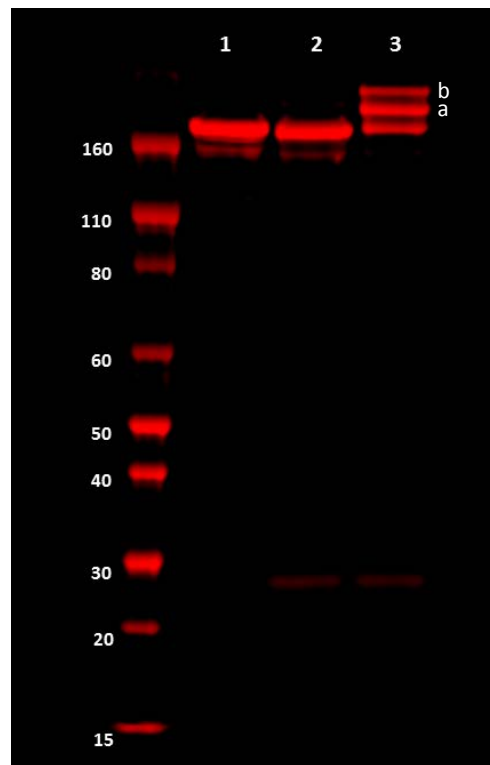
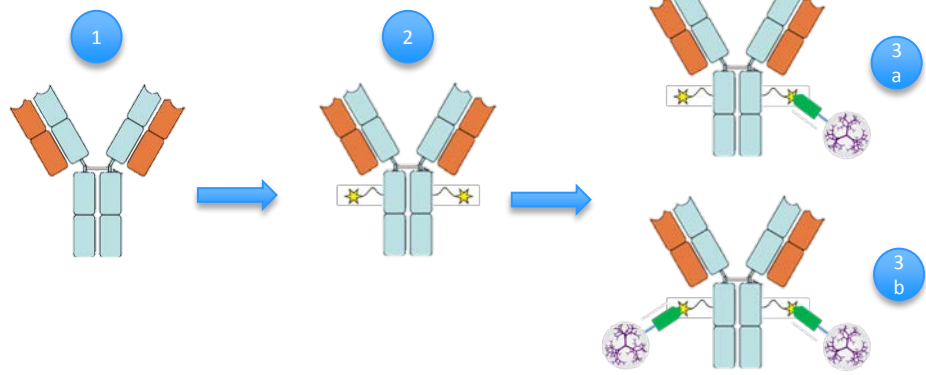
Traditional ADC's - Limitations	Targeted DEP™ Conjugates Attribute	Targeted DEP™ Conjugates Benefit
Heterogeneity	Homogeneous	Specific attachment of targeting molecule and payload gives a homogeneous molecule – easier characterisation, regulatory path and manufacture
Low payload to Ab ratio	High payload to targeting molecule ratio	Single targeting moiety bound to DEP™ dendrimer <ul style="list-style-type: none"> • with high and scalable target/payload ratio • allowing flexibility in number of drug molecules and type of payload used
Need for ultratoxic	Cytotoxic, small molecule, ultratoxic	Flexibility in choice of type of drug or payload used High payload to target ratio does not limit to use of ultratoxic payload
High cost of Antibody production	Lower cost potential	Ability to use small molecule, antibody fragment or mimetic for targeting, in addition to whole antibody
Manufacturing and Analytical complexity	Efficient Manufacturing Easier Analytical Characterisation	Lower COGS associated with <ul style="list-style-type: none"> • ability to use a diverse range of low cost targeting molecules • High payload to target ratio – less targeting molecule required



Targeted DEP™ Conjugates

A new approach to drug conjugate design and development

Full length Ab (HER-2 targeting) molecule



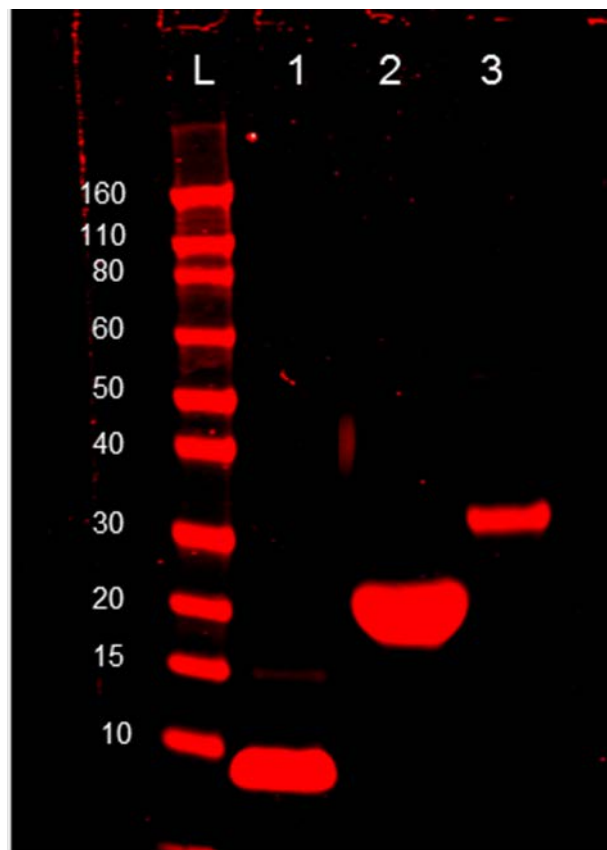
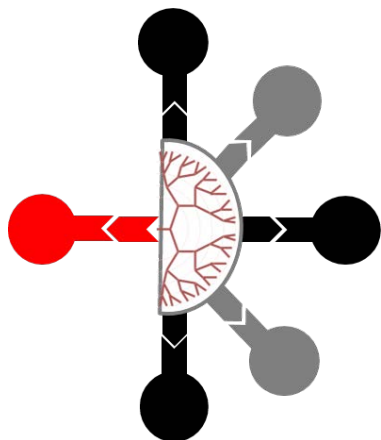
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Targeted DEP™ Conjugates

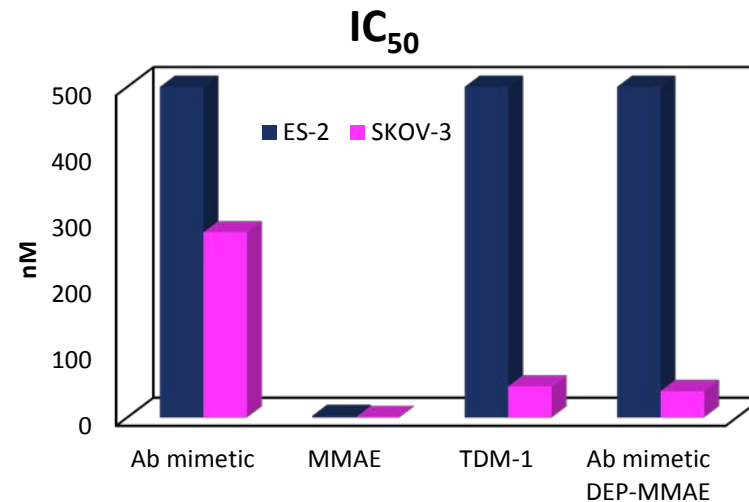
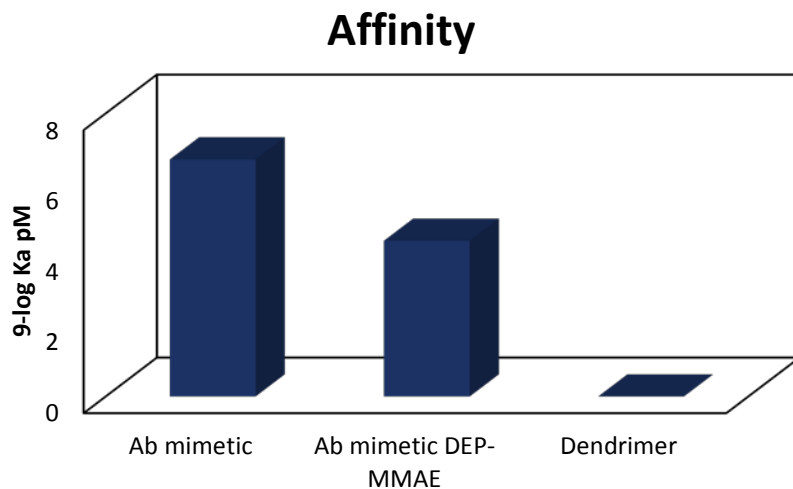
A new approach to drug conjugate design and development

Small molecular weight (HER-2 targeting) molecule



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Maintenance of affinity and specificity



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Dendrimers in drug delivery: Nanoparticles with multiple advantages

Maximising commercial opportunity through differentiation and value add

- Starpharma’s dendrimer nanoparticle DEP™ technology has broad applicability
 - NCE’s and existing therapeutics
- Analysis shows dendrimers applicable to >50% of leading pharmaceuticals
- Significant potential in oncology
 - Other areas include Endocrinology, Ophthalmology, Immunology/Inflammation
- Proof of concept in docetaxel, doxorubicin, paclitaxel, platinumums
- Also Suited to:
 - Small molecules, Proteins, peptides; Targeted Drug Conjugates

Therapeutic Performance	Increased Bioavailability	✓
	Enhanced Pharmacokinetics	✓
	Enhanced Efficacy	✓
	Novel Targetability	✓
	Better Side Effect profile	✓
Commercial Performance	Patent Protection	✓
	Indication Expansion	✓
	Competitive advantages	✓
	Innovative treatment options	✓
	Accelerated development	✓
	Elevated ROI	✓
	Robust, scalable manufacturing and logistics	✓

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