MIDATECH PHARMA

Right Time, Right Place; Micro- & Nano-particles for Drug Delivery

Dr Paul Seaman, Head of Sustained Delivery

UK HealthTech Conference 2016, Cardiff

A Rapidly Growing International Specialty Pharmaceutical Company

Organisation

UK-based public company (plc)

- c.110 employees across Europe & the US
- Diversified strategy and sources of revenue with innovative R&D pipeline
- Highly experienced pharma management team

Commercial Force

Established US Commercial Presence

- Six marketed products: potential aggregate peak sales of $50 million
- Double-digit top-line growth expected over the next 12 months
- Expect lead product Q-Octreotide to be filed for marketing authorisation H1 2018

R&D

Fully integrated R&D capabilities with two platform technologies

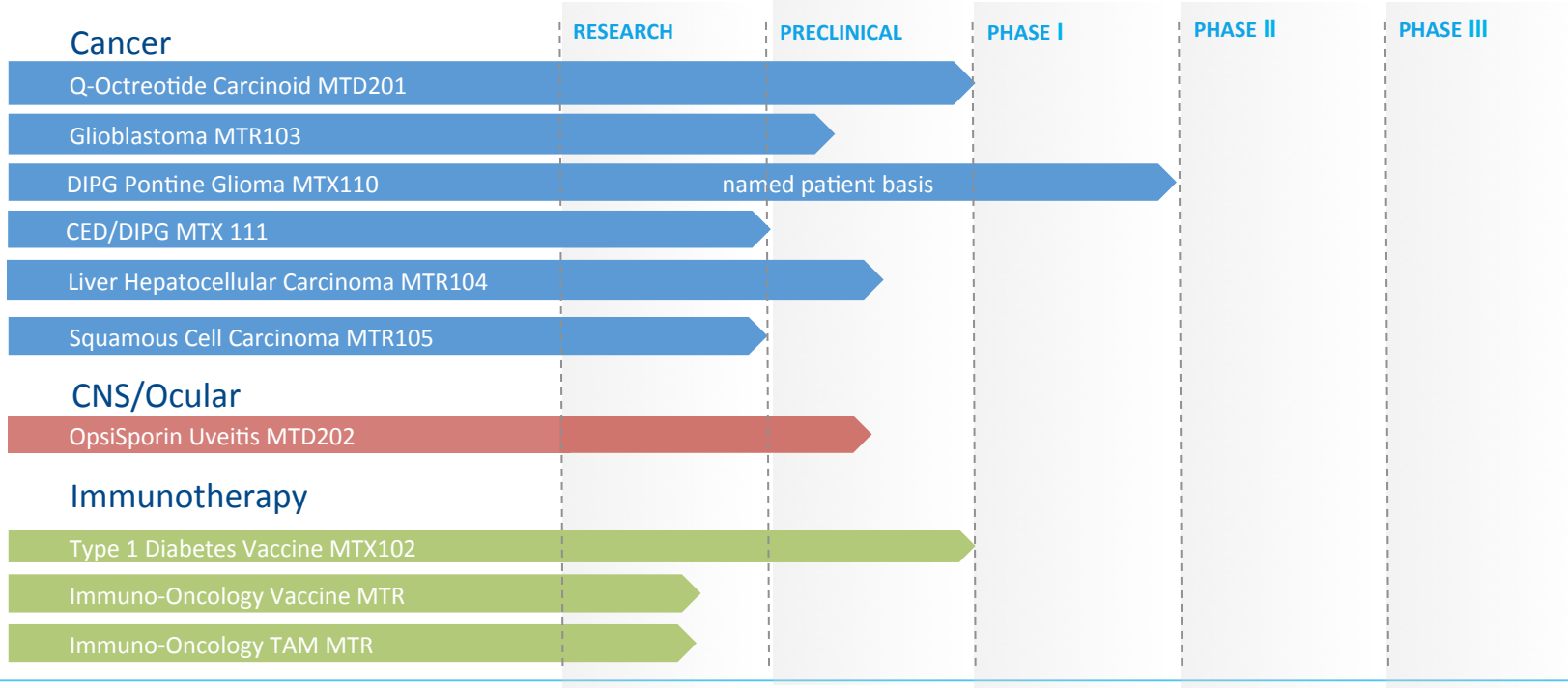
- Glycan coated gold nanoparticles (GNP)
- CAD “printed” sustained-release microparticles (Q-Sphera)
- Drives a novel, lower risk development pipeline based on known therapeutic agents
- 1500m² cGMP manufacturing facility located in Bilbao, Northern Spain

2016 H1 Operational Highlights

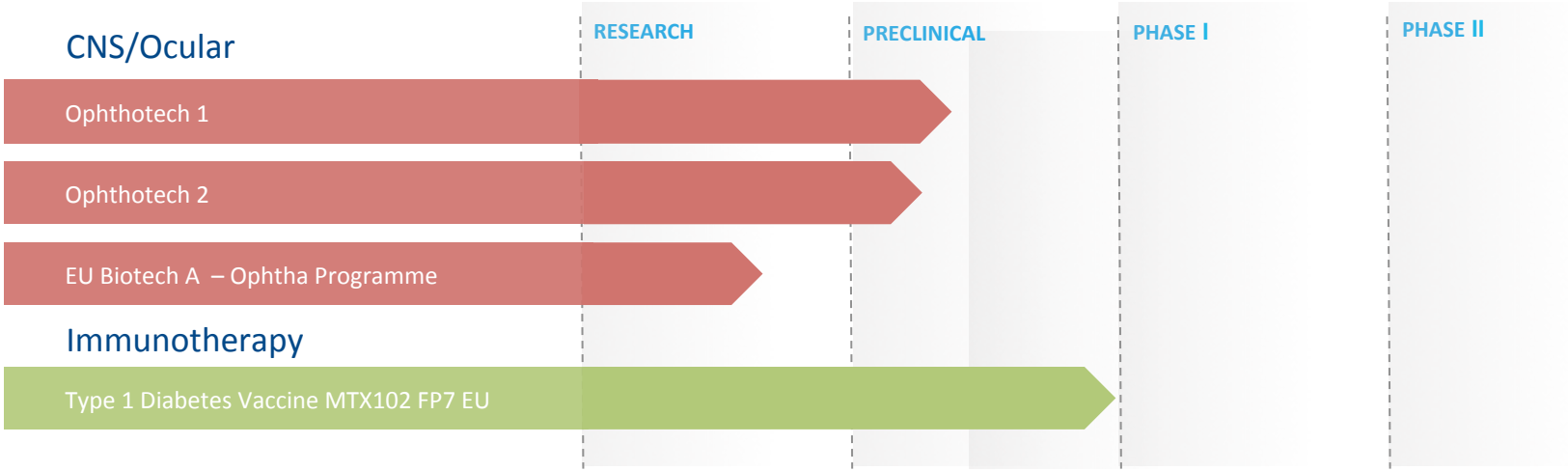
- Excellent integration and sales performance from our newly acquired US commercial business
  - Six months to June $4.58m (£3.19m), growth of 104% vs. H1 2015
- Launch of our anti-nausea product Zuplenz® in the US
  - Approved for use in multiple indications in a $10bn US market
- Preparation for final development & commercialisation of Q-Octreotide
  - GMP production capability started in H1 – £0.7m investment in our Bilbao facility
  - PI study to start H1 2017 and filing for first marketing authorisations anticipated in 2018
- Product candidate testing *in vivo* for glioblastoma (GBM) and hepatocellular carcinoma (HCC)
  - Both programmes on track for initial product selection by end of 2016
- Dosing due to commence in first immunotherapy Phase I study for Type I Diabetes
  - Consortium includes Cardiff University and King's College London
- Further positive progress seen in the OpsiSporin (MTD202) and MTX110/111 (DIPG) programmes

Development Pipeline: 10 Programs

Development of multiple, high-value, targeted therapies for major diseases with unmet medical need



Key Partnerships Pipeline



- Partnered development programmes for high-value, targeted therapies for further indications
- Partnerships and collaborations with specialty and major pharmaceutical companies and universities
- Already revenue generating

Right Time

- APIs with short $t_{½}$ require regular injection
- Sustained delivery technologies greatly increase dosing intervals
  - hours to months
  - Improved patient experience, ↑compliance and ↓clinician time
  - ↑efficacy/↓adverse effects
- Increase in biologics driving drug delivery challenges
- Polymer microsphere systems established for >30 years
  - Safe, effective, well received by patients and healthcare professionals
- Existing manufacturing technologies have significant drawbacks
  - Complex/slow to administer, difficult to tune release profile, limited API compatibility, class 2 solvents, limited drug loading, polydisperse, wasteful (CoGs), require substantial investment
- Midatech Pharma's Q Sphera technology addresses these needs
  - Long duration of action and tuneable release
  - Drug loading & size control enable reduced needle size/injection vol
  - Rapid resuspension and simple administration
  - Scalable, efficient and API-friendly manufacturing that uses only class 3 solvents

Q-Sphera – Midatech Pharma's SR Technology Platform

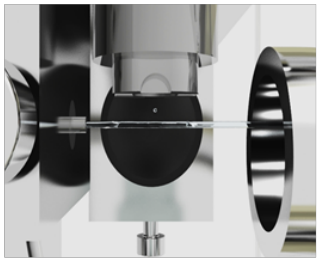
PROPRIETARY MICROSPHERE PLATFORM

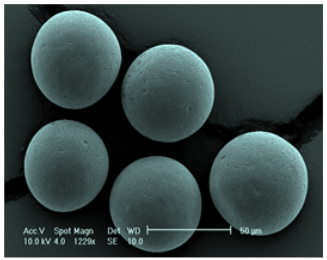
Precision encapsulation platform enabling tuneable sustained drug release for chronic diseases:

- Emulsion-free synthesis with product monodispersity
- Precise control over particle size, morphology, release kinetics
- High drug loading, minimal burst release, essential to development of safe & effective therapies

CONTROLLED RELEASE

- Control release of API over period of 2 weeks-6 months following single injection
- API released in predictable and consistent fashion



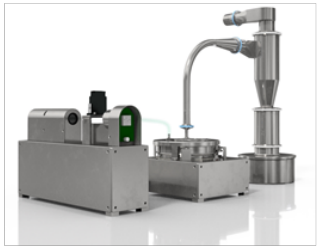


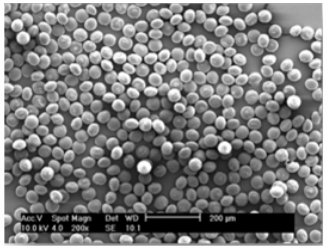
MICROPARTICLES

- Encapsulate drugs into micron sized particles - diameter ≈25µm
- Compatible with small molecules - peptides, oligonucleotides, proteins
- Tuneable using biodegradable polymers

"PRINTING" DRUGS AT SCALE

- Innovative adaptation of industrial inkjet technology to enable "printing" of uniform drug-containing microparticles
- Printing '000,000 particles per second
- Lab scale - commercial





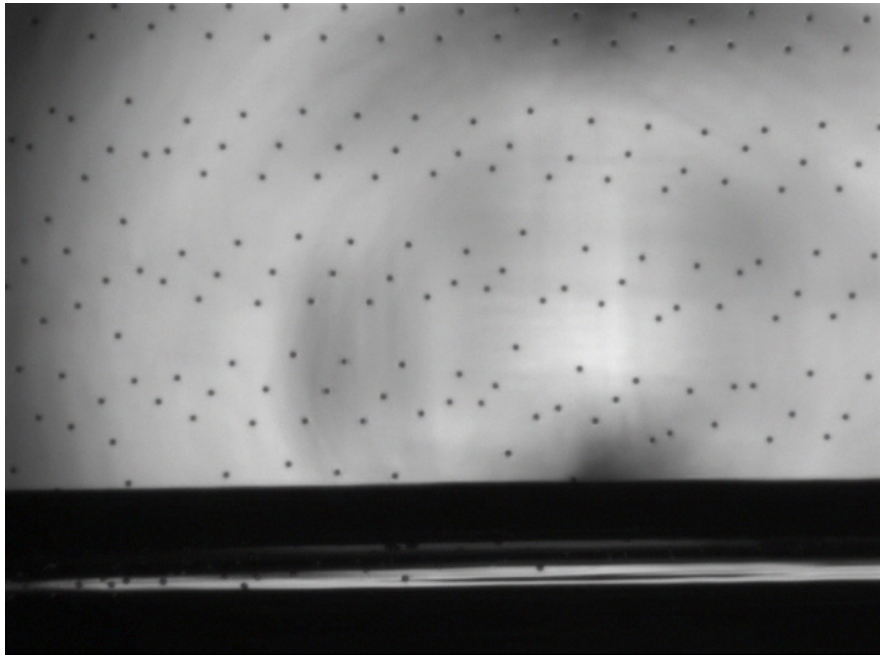
ADVANTAGES

- Readily injected via minimally-invasive needles as fine as 30G
- Minimal pain
- Eye and other difficult/complex routes
- Process and cost efficiency

Q-Sphera – Midatech Pharma's SR Technology Platform

Forming 30µm particles

@ ≈3 million per second



Q-Octreotide (MTD201)

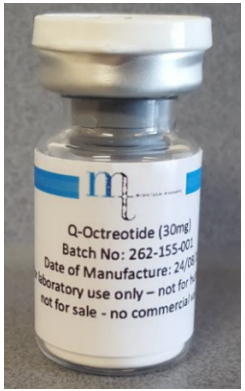
01 Currently in final stages pre-clinical development
- Formulation complete
- Entering bioequivalence or therapeutic equivalence studies Q1 2017
- Planned US launch in 2018/9

02 Long-acting formulation of Octreotide acetate for chronic treatment of carcinoid (cancer) & acromegaly

03 Manufactured in house
- Know-how and arising IP retained
- Investing now in preparation of full commercialisation

04 Peak market potential c.$100m pa
- Own sales targeted in the USA
- Centurion out-licence achieved for Turkish rights

05 Market worth over $2bn (Sandostatin LAR $1.6bn)



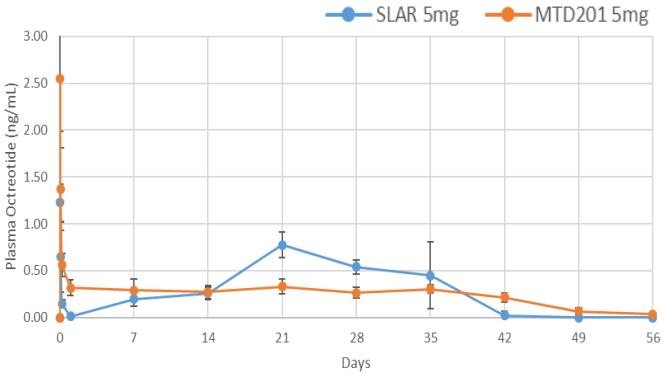
Advantages
- Quicker and easier to reconstitute/administer
- Smaller needle
- Fewer injection failures
- Clinical visit time significantly reduced
- More cost efficient

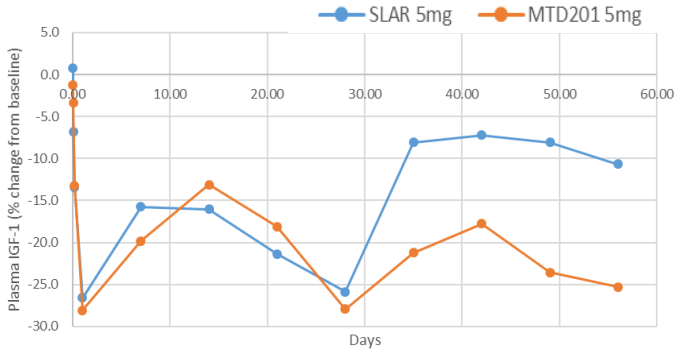
Positive pre-clinical data
- Compares favourably with Sandostatin LAR
- Pharmacokinetic data correlates well with PD effects
- Injections well tolerated with no site reaction

Steps to commercialisation
- Pilot human pharmacokinetic study planned Q1 2017, followed by bioequivalence or therapeutic equivalence programme in H1-2 2017
- Marketing authorisation submission anticipated in the period Q4/17 - Q4/18

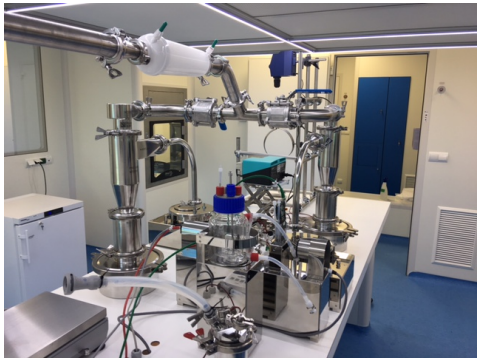
Q-Octreotide (MTD201)

- Positive non-clinical pharmacology
  - PK compares favourably with Sandostatin LAR (SLAR)
  - PK data correlates well with PD effects
  - Low variability
  - injections well tolerated





- GMP Manufacturing
  - in house production
  - terminal sterilisation
  - Investing now for full commercialisation 2018



OpsiSporin (MTD202)

01 **Successful PoC completed in several *in vivo* models**
- Clear dose response established in prophylactic model
- Efficacy established in therapeutic model
- PK supports 3-month duration of action

02 **OpsiSporin is injectable sustained release formulation of cyclosporine for treatment of non-infective uveitis**

03 **Intravitreal injection via 27-30G needle directly to vitreous with minimal transfer to the bloodstream**

04 **Orphan indication, application submitted Q3/16**

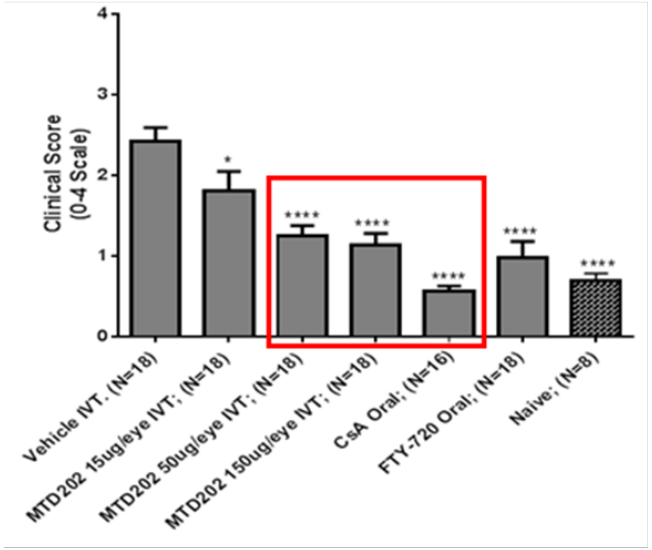
05 **Uveitis rapidly growing ≈$1.3bn market, current treated by eyedrops, steroids and immuno-suppressives**

Advantages
- Product will be steroid and immunosuppressant sparing
- Delivered intravitreal ≈1000 fold lower doses than oral
- Currently no approved intravitreal cyclosporine or other immunosuppressant treatment option available

Development pathway
- IND enabling to commence Q1 2017
- Toxicology program will complete approx. Q4 2017
- Phase I Q4 2017/Q1 2018

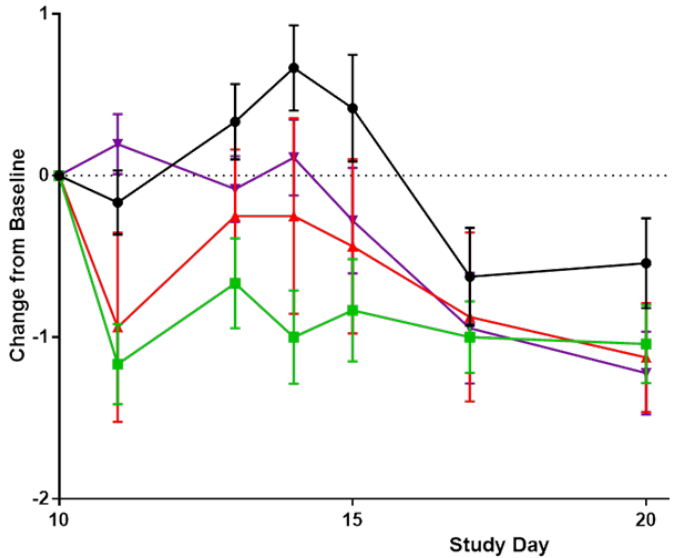
OpsiSporin Efficacy

Prophylactic Model



Dose response established

Therapeutic Model



Efficacy established, similar to oral CsA reference

Gold Nanoparticle (GNPs) Technology Platform

TARGETING

Multivalency - enables binding of several targeting and therapeutic agents to a single nanoparticle

THERAPEUTICS

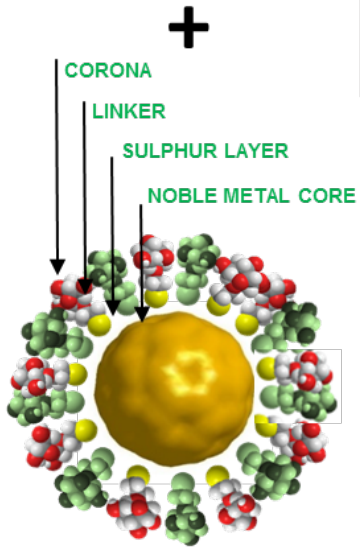
Payloads conjugated to form small (~5nm) medicines for targeted delivery

SOLUBILITY

Enable the transport of water insoluble and lipid soluble compounds to disease sites

RELEASABILITY

Designed to release the active compound inside the cell



Smallest particles in biomedical use: 10x-20x smaller than peers

MOBILITY

Small size ~1.5nm and defined charge allows transport to disease sites that are otherwise very difficult to reach

COMPATIBILITY

Ultra-small gold nanoparticles are bio-inert, non-toxic, non-immunogenic; do not generate immune-response

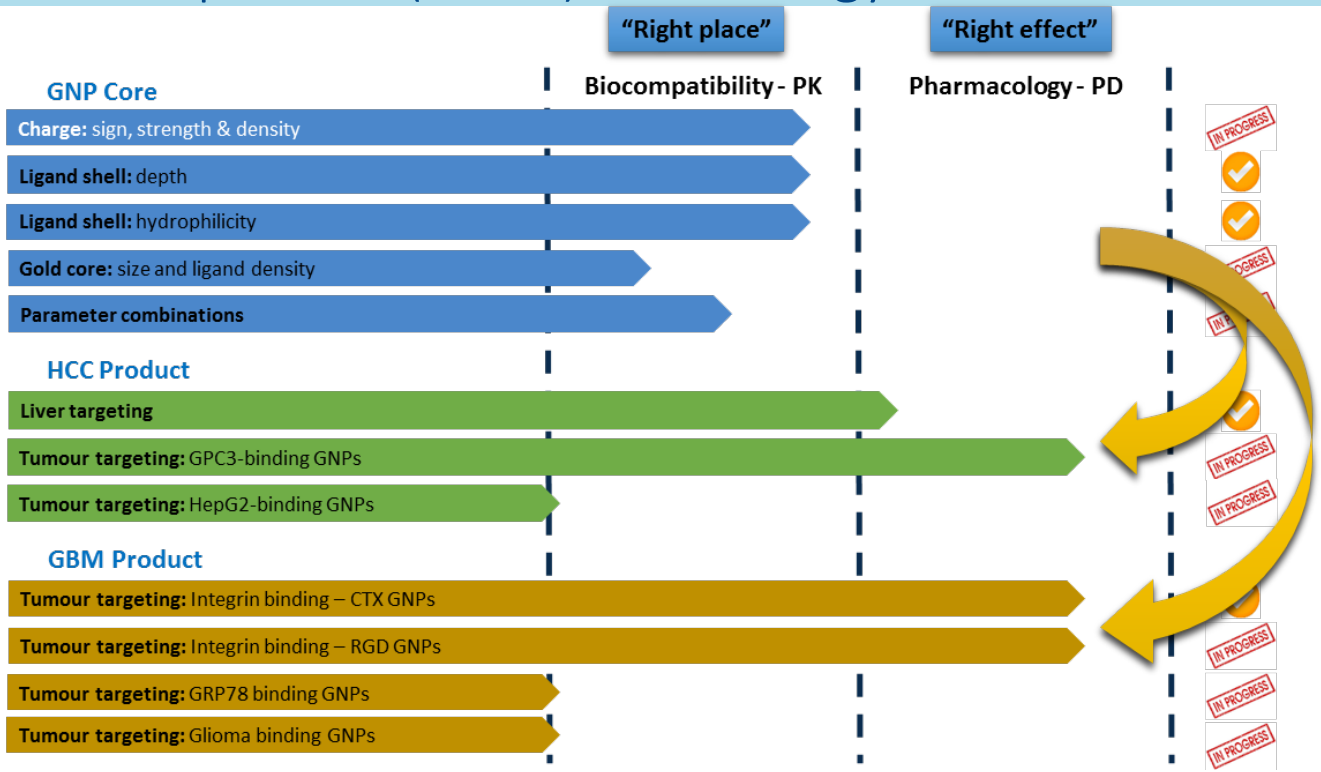
SCALABILITY

Internal GMP manufacturing facility

EXCRETABILITY

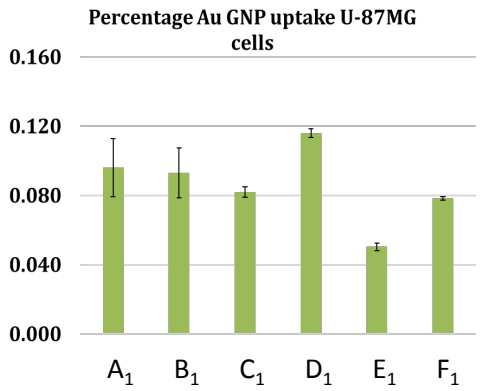
Drug conjugates eliminated via the kidneys and liver

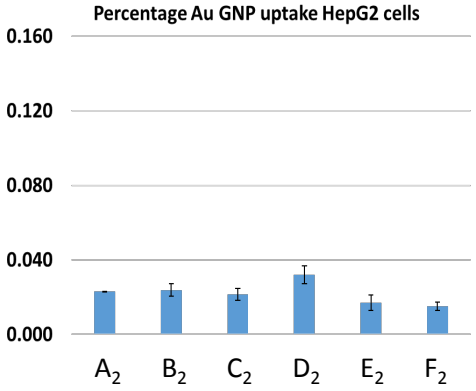
Gold Nanoparticle (GNPs) Technology Platform

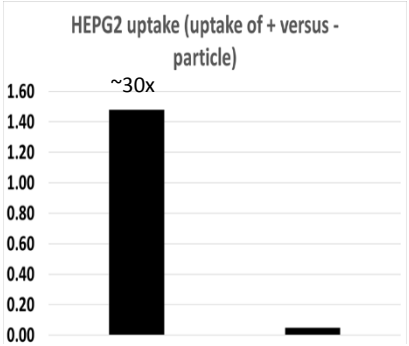


GNP Core Design

Cellular Affinity For GNPs: Comparison Of Different Glycan Coated Particle Uptake in GBM and HCC



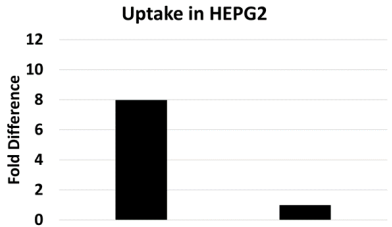


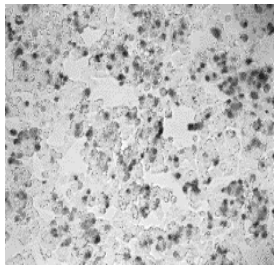


GNP design customised to maximise uptake for specific indication

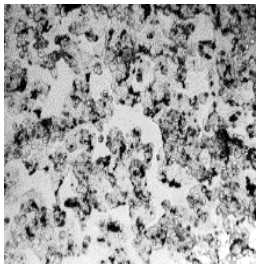
GNP Targeting – Hepatocellular Carcinoma (HCC)

Target Specific Delivery

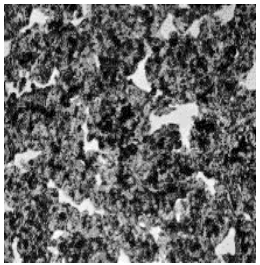




GNP construct

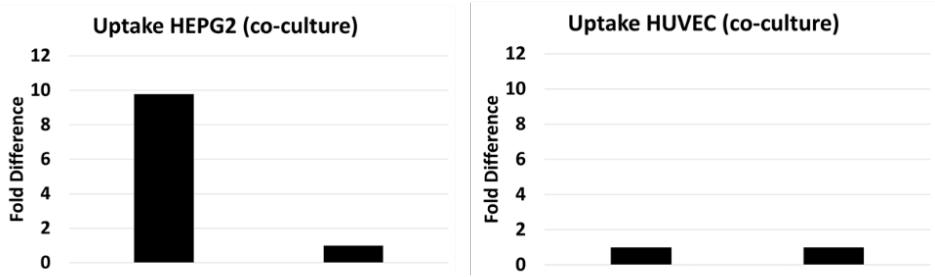


GNP-nonsense peptide

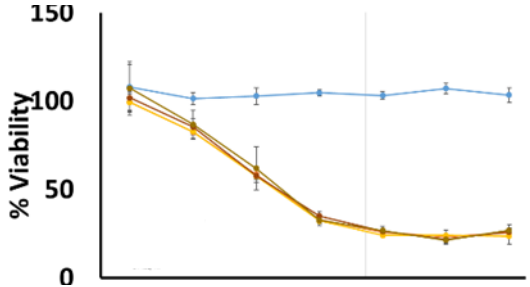


GNP-targeting peptide

Cancer selectivity



Cytotoxicity/Cytostasis



In vitro evaluation of Glypican 3 Targeted GNPs

Glioblastoma (GBM) (MTR103)

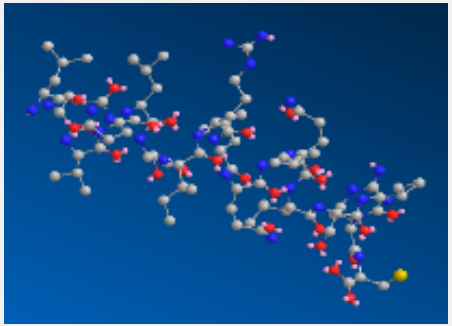
01 Combined targeting and therapeutic
- Development in conjunction with Dana Farber institute
- Initial candidate selection planned Q4 2016
- IND enabling to commence H1 2017
- Filing for marketing authorisation anticipated by 2020

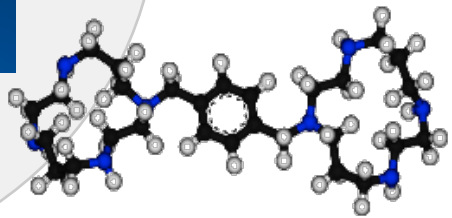
02 Worldwide estimated 240,000 cases of brain and nervous system tumours per year
- GBM is most common, and most lethal, of these tumours

03 Survival typically 12 to 15 months
- Less than 5% surviving greater than five years

04 Orphan indication, application to be submitted

05 Systemic and intra-tumoural administration





- GNP's targeted to bind tumour specific receptors on GBM cells; internalised GNPs developed to release therapeutic payload intracellularly
- GNP design customised to maximise uptake for specific GBM indication

Liver Hepatocellular Carcinoma (HCC) (MTR104)

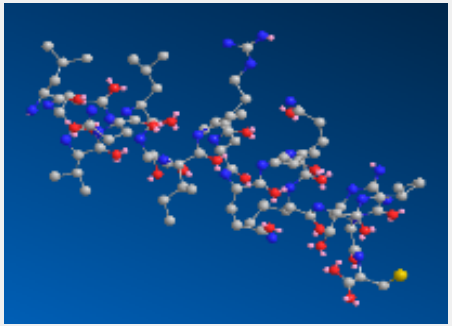
01 **Combined targeting and therapeutic**
- Initial candidate selection planned 2H 2016
- IND enabling to commence 1H 2017

02 **Sixth most frequent cancer globally and the second leading cause of cancer death**

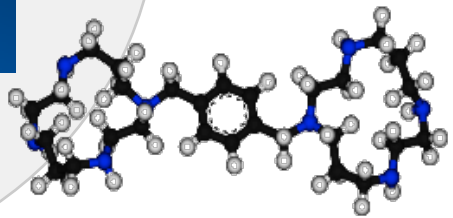
03 **Surgical resection major treatment option**
- But only 10 – 20% can be removed completely

04 **Current chemotherapeutic options too toxic**
- Opportunity to reduce through targeting

05 **Orphan indication**



- Target receptors on HCC tumour cells GPC3 to bind and internalise GNPs where the therapeutic payload would be released



DIPG: Diffuse Interstitial Pontine Glioma (MTX110)

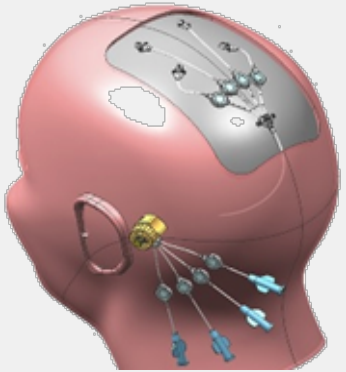
01 Midatech actively pursuing local delivery directly into the tumour through Convection Enhanced Delivery (CED) that delivers therapeutic constructs via a series of catheters fixed into the substance of the tumours

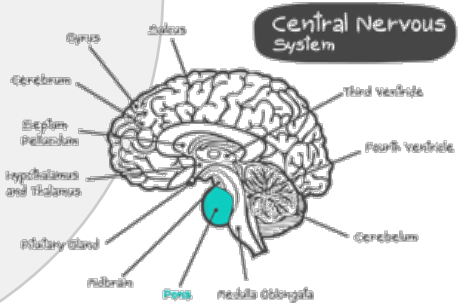
02 Ultra rare childhood brain tumour
- c1,000 cases / year worldwide
- Average survival, 7 months; universally fatal

03 Ultra-high unmet need, potential orphan indication

04 Compassionate use/named patient program: MTX110 (non-GNP nano-formulation solubilising)
- UK: two DIPG children treated monthly doses – encouraging safety and efficacy according to physician
- US: one DIPG patient received first dose MTX110

05 Research & Development next steps:
- Regulatory interactions through 2016 – high level of support for program by regulatory agencies
- Evaluating clinical trial for successful candidate constructs





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Thank you

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