Tackling Osteoarthritis: Matriptase Inhibitor as a Disease Modifying Therapy

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Tackling Osteoarthritis

Osteoarthritis (OA) is the most common joint disorder

- OA affects approximately 60% of over 65 year olds
  - OA causes pain, joint stiffness and poor mobility
  - OA often reduces independence and quality of life in sufferers

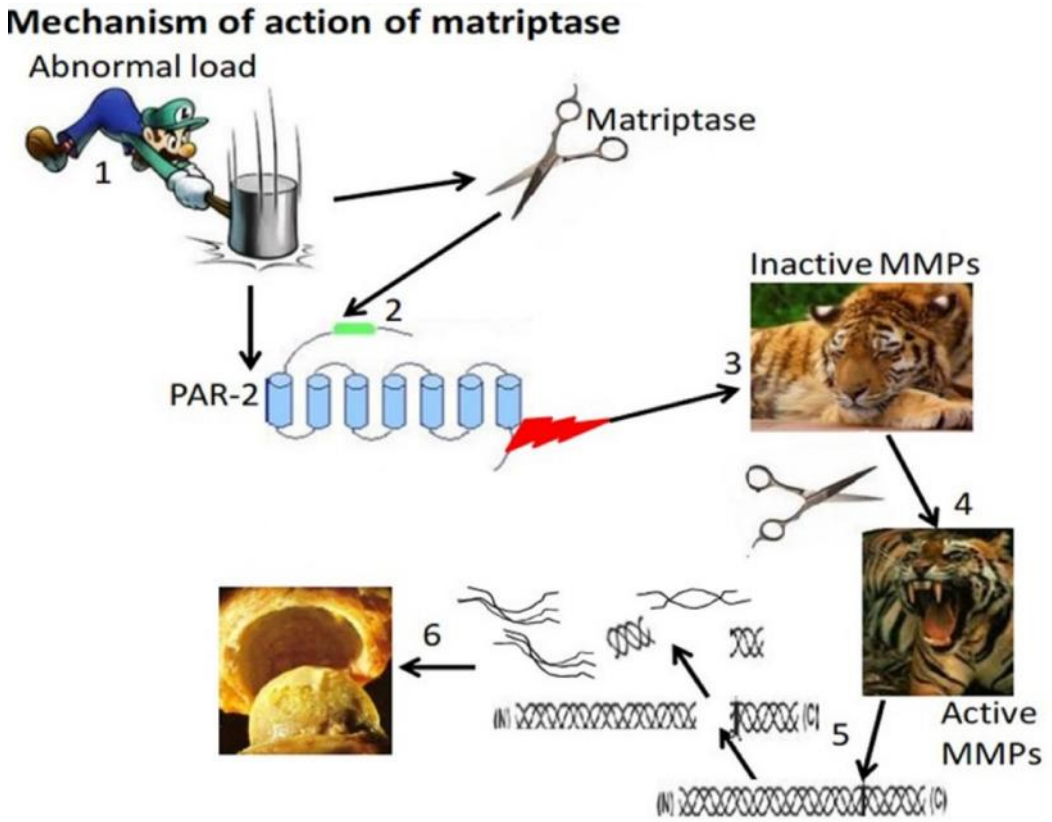
- **Q:What is the cause?**
- **A: Gradual breakdown of cartilage and bone within the affected joints, the most commonly affected being the knees and hips.**

- Current Treatments do not slow the progression of disease
- Prevalence will grow: Age and obesity are risk factors

Tackling Osteoarthritis: Matriptase Inhibitor as a Disease Modifying Therapy(DMT)

- **Our Approach:**
- An effective 'disease-modifying OA drug' would target a detrimental protein present in an OA joint but not the normal joint
- Our research has identified such a protein, an enzyme which promotes cartilage degradation in OA

- **This enzyme is Matriptase**



Tackling Osteoarthritis:
Matriptase Inhibitor –The Invention

- **Our Approach:**
- **Our research has enabled the validation of matriptase as a therapeutic target for osteoarthritis**
- We have create novel small molecule inhibitors of Matriptase
- Achieve selective targeting of osteoarthritic joint by:
  1. Selection of matriptase as a validated target for diseased joints
  2. Creating molecules with selectivity for Matriptase over other key proteolytic enzymes
  3. Local delivery of matriptase inhibitor to the joint

Tackling Osteoarthritis: Matriptase Inhibitor as a Disease Modifying Therapy (DMT)

- **Commercial Potential:**
- Prevalence is rising. **Diagnosed Prevalent Population (Symptomatic) (7MM), from 36M (2016) to 41M (2026).**
- Market was valued at $1.6 billion in the 7MM in 2016, and is expected to increase to $3.5 billion in 2026
- An effective ‘Disease-Modifying OA drug' will deliver structural alteration of the disease linked to clinical benefit
- Our current approach to commercial translation is to develop and progress a DMT that will be delivered via *ia* injection into relevant joints at relevant dosages and time intervals
- The launch of new biologic therapies priced at a substantial premium to small-molecule therapies will drive overall market growth
- Local delivery may alleviate some of the cost of goods “headwinds” associated with new disease-modifying therapies

Tackling Osteoarthritis: Matriptase Inhibitor as a DMT

- **Differentiation in the Development pipeline and Market Place:**
- Few Disease Modifying Therapies (DMT) are being developed
- DMT as currently-available therapies offer only symptom relief
- Most “competition” emerges from analgesics with innovative MOAs—including anti-nerve growth factors (anti-NGFs), a new class of opioids (CR845), an intra-articular formulation of capsaicin (CNTX-4975)
- Potential DMT are now in development. These drugs include a small molecule therapy, SM04690, and two cell-based DMT- Invossa and ReJoin
- Evolution of the OA pipeline products will lead to the OA market landscape changing radically over the next 20 years.
- **Our solution: small molecule inhibitors designed to inhibit a target that has DMT potential with systemic effects being limited by local (ia) delivery**

Tackling Osteoarthritis: Matriptase Inhibitor as a DMT

- **Development Status:**
- Composition of matter identified
- Potent inhibitors of Matriptase identified
- Selectivity against key enzymes confirmed
- Some *in vivo* PoC complete. Further compound characterisation ongoing in 2018

- **IP status:**
- A UK provisional application (1720145.0) has been filed describing a series of hit compounds and a family of derivatives.

Matriptase Inhibitor as a DMT: Risks and bottle necks

- **Risks:**
  - Translation of rodent findings into human
  - Adoption into market/clinical pathway (Vs a “pill”)
  - Territorial approaches to OA therapy (but also an opportunity)
- **Bottlenecks:**
  - Finding the right partner
  - Progressing to next stage of development with appropriate data set

Matriptase Inhibitor as a DMT: Resources Needed

- **Next step for development:**

- Currently strengthening the *in vivo* data package obtained with lead molecules
- Looking for potential partners who wish to conduct diligence/evaluation from 2Q2018

- **Partners sought:**

- Licensees sought
- Global rights available
- Rights granted could be based on territories (Asia-Pacific ;US & European)
- Ideal partner would take project to human PoC

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