Regenerative medicine for a mobile, active life
Why orthopaedics is more like dentistry than one might think
What would you expect an x-ray of a 50-year-old’s mouth to look like if it were taken in…

…1979?
What would you expect an x-ray of a 50-year-old’s mouth to look like if it were taken in...

...1979?
What would you expect an x-ray of a 50-year-old’s mouth to look like if it were taken in…

…1979?

…2009?
What would you expect an x-ray of a 50-year-old’s mouth to look like if it were taken in...

...1979?

...2009?

...2029?
Increased awareness and adoption of multiple technologies to restore chemical, biomechanical, biological condition of the healthy mouth

- Increasing availability of advanced metal implants
- Drug delivery systems adapted for dental treatments
- Application advanced of in-situ curing ceramic
- Increasing emphasis on treatments for gum disease
- FDA approval of YAG laser technology

<table>
<thead>
<tr>
<th>1940s</th>
<th>1950s</th>
<th>1960s</th>
<th>1970s</th>
<th>1980s</th>
<th>1990s</th>
<th>2000s</th>
<th>2010s</th>
<th>2020s</th>
<th>2030s</th>
</tr>
</thead>
</table>

- First fluoride toothpaste
- Dental Health Act (USA)
- FDA approval of YAG laser technology
What would you expect an x-ray of a 50-year-old’s mouth to look like if it were taken in…

…2029?

Is this realistic?
What would you expect an x-ray of a 70-year-old sports-injury patient’s knee to look like if it were taken in…

…1999?
What would you expect an x-ray of a 70-year-old sports-injury patient’s knee to look like if it were taken in...

...2009?
What would you expect an x-ray of a 70-year-old sports-injury patient’s knee to look like if it were taken in...

...2009?

...2029?
What would you expect an x-ray of a 70-year-old sports-injury patient’s knee to look like if it were taken in...

...2009?

...2029?

...2049?
Increased awareness and adoption of multiple technologies to restore chemical, biomechanical, biological condition of the healthy articular joint.

<table>
<thead>
<tr>
<th>1960s</th>
<th>1970s</th>
<th>1980s</th>
<th>1990s</th>
<th>2000s</th>
<th>2010s</th>
<th>2020s</th>
<th>2030s</th>
<th>2050s</th>
<th>2050s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marrow stimulation techniques for articular cartilage repair developed</td>
<td>Increasing availability of advanced alloys</td>
<td>Tissue preservative implants emerge</td>
<td>First application of autologous cell treatments for articular cartilage</td>
<td>Reimbursement for regenerative medical treatments clarified?</td>
<td>Resorbable polymers developed</td>
<td>Cell, scaffold and molecular treatments showing promise</td>
<td>Marrow stimulation techniques for articular cartilage repair developed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
INCREASED AWARENESS AND ADOPTION OF MULTIPLE TREATMENTS WITH THE GOAL OF TREATING THE ARTICULAR JOINT AS A COMPLETE ORGAN

Marrow stimulation techniques for articular cartilage repair developed
Increasing availability of advanced alloys
Resorbable polymers developed
Tissue preservative implants emerge
Cell, scaffold and molecular treatments showing promise
Emergence of total joint replacement
First application of autologous cell treatments for articular cartilage
Reimbursement for regenerative medical treatments clarified?

<table>
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<tr>
<th>1960s</th>
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<th>1990s</th>
<th>2000s</th>
<th>2010s</th>
<th>2020s</th>
<th>2030s</th>
<th>2050s</th>
<th>2050s</th>
</tr>
</thead>
</table>

[Images of knee joints]
Background
Orthomimetics is the First Technology Spin-Out from the Cambridge-MIT Institute (“CMI”)

- ~£4.0m in funding from 2002-2006
- Access to facilities and expertise at Cambridge, MIT and Harvard
- Links to world-renowned surgeons, scientists and engineers who had previously developed products used in over 500,000 patients

Key Milestones Achieved Under CMI Funding

1. Development of a patent-protected technology platform
2. Production of working prototypes of two products
3. Successful completion of two large-animal, pre-clinical trials of lead product
Orthomimetics’ Key Milestones

- Closed **£5.0m in Series A funding** from consortium of blue-chip investors
- Recruited an **experienced executive team** and a **world-class medical advisory board**
- Achieved commercial-scale **ISO-13485 certified manufacturing capabilities**
- Developed a **minimally invasive delivery system** for the Company’s lead product
- Raised **>£2.3m in non-dilutive grant funding** to support development of the Company’s pipeline products
- Received **CE-mark approval** for Chondromimetic on 8th December 2008
- Commenced **post-marketing clinical study** (Recruitment on track; 9 procedures as of 1st August 2009)
- Distribution and clinical development agreement with leading orthopaedic distributor in **Italy**
- Heads of terms for distribution and clinical development agreements in negotiation for **Germany, Benelux, UK/Ireland, South Africa and South Korea**
The business of joint preservation
Technology
OM Aims to be a Leading Global Provider of High-Margin Products that **Reduce the Risk of Degenerative Joint Disease**

### Key Statistics – Worldwide

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Annual expenditure on total joint replacement</td>
<td>$36bn</td>
</tr>
<tr>
<td>Annual expenditure on revision joint replacement</td>
<td>$4.5bn (12.5%)</td>
</tr>
<tr>
<td>Average life of a total joint replacement for a 65-year-old patient</td>
<td>17 years</td>
</tr>
<tr>
<td>Average life of a total joint replacement for a 45-year-old patient</td>
<td>10 years</td>
</tr>
</tbody>
</table>
OM’s Products are Poised to **Raise the Standard of Care** for Patients Suffering from Sports Injuries and Other Orthopaedic Trauma

OM’s proprietary technology platform enables the production of high-margin products that support the regenerative repair of soft tissues (such as cartilage, ligaments and tendons) and the bone to which they are anchored.
The ability to heal both cartilage and subchondral bone provides a major advantage for the treatment of patients treated only several months after injury.

Healthy subchondral bone

Subchondral bone 6 months after articular cartilage injury
Chondromimetic, the first product
Chondromimetic is a Porous, Resorbable Tissue Regeneration Scaffold that Supports the **Separate Yet Simultaneous** Repair of Articular Cartilage and the Underlying Bone.

Defect prepared to create a cylindrical osteochondral recipient site. Chondromimetic scaffold inserted into defect. Blood containing marrow-derived stem cells impregnate the scaffold. Cells implement repair, replacing scaffold with newly formed tissue. Defect filled with newly formed bone and cartilage.
Chondromimetic is a Porous, Resorbable Tissue Regeneration Scaffold that Supports the *Separate Yet Simultaneous* Repair of Articular Cartilage and the Underlying Bone.

Defect prepared to create a cylindrical osteochondral recipient site

Chondromimetic scaffold inserted into defect

Blood containing marrow-derived stem cells impregnate the scaffold

Cells implement repair, replacing scaffold with newly formed tissue

Defect filled with newly formed bone and cartilage

Chondral layer: collagen/GAG

Osseous layer: collagen/GAG/calcium phosphate
…and Produced a Surgeon-Designed Procedure Pack Harnesses these Properties to Ensure **Rapid, Accurate Delivery.**

- Site preparation tool prepares defect site
- Hydration portal enables hydration with any sterile fluid
- Thumb-activated delivery ensures simple delivery

Procedure pack
A Single-Centre Clinical Study is Underway to Demonstrate Preliminary Safety and Efficacy Data for Chondromimetic

- World renowned cartilage surgeon (Laszlo Hangody)

- 15 patients (10 mosaicplasty backfill, then 5 primary sites)

- Primary endpoint at 6 months including MRI and biopsy data

- 9 Patients Enrolled as of 1st August 2009

- Lead investigator states that ‘patients are doing well and 3-month MRI results have shown promising outcomes’
Chondromimetic Has Shown Strong Potential for Use Either *Alone* or in *Combination* with Other Treatments

- Chondromimetic with marrow stimulation…
  - …improves quality of repair
- Chondromimetic with osteochondral autograft…
  - …reduces donor site morbidity
- Chondromimetic with autologous chondrocyte implantation…
  - …improves product efficiency

... as a stand-alone treatment
... as a tissue-specific controlled-release vehicle
... as a tissue-specific scaffold for cell-based therapies

1<sup>st</sup> Generation | 2<sup>nd</sup> Generation | 3<sup>rd</sup> Generation
A device that makes a Drug

Point-of-Service Combination of Chondromimetic with Platelet Rich Plasma

- Strong activation of platelet rich plasma
- No need for bovine or autologous thrombin
- Easy-to-implant, point-of-treatment solution

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Growth Factor Release</th>
<th>Safety</th>
<th>Ease of Delivery to Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chondromimetic and PRP</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PRP + Bovine Thrombin</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>PRP + Autologous Thrombin</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>Synthetic Scaffold + PRP</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Custom Delivery of Active Molecules

Orthomimetics has developed its implants to provide a highly favorable environment for cells for combination therapy applications with:

- Delivery of a range of active molecules
- Control and accuracy of delivery
- Flexible ‘Point-of-Service’ application empowering surgeon choice in theatre.

Superior Features of OM Scaffolds

High Loading Efficiency

Scaffolds bind active molecules directly to their structure at up to 73.4% efficiency. This means active molecules do not escape from the scaffold with their liquid carrier.

Superior Retention

Scaffolds release active molecules in a highly sustained manner, with 74.3% of certain commercial molecules remaining in the scaffold after two weeks.

Preserved Activity

A range of growth factors delivered on the scaffolds exhibit no alteration upon release. This means molecules retain their activity upon release.

Confocal microscopy image showing binding throughout 3D implant structure
Cell Based Therapy

- Scaffold pore structure allows cell migration into core.
- The material composition favours cell initiated repair mechanism.
- Mineralised and un-mineralised scaffolds can selectively attract different cell types i.e. Osteoblasts or Chondrocytes.
- Cell phenotype and viability remain intact providing sustainable healing efficacy
- High growth levels with no differentiation or cell death

Chondromimetic Scaffolds: A highly favorable environment for cells for combination therapy applications
The competitive environment and competitive advantages
There are **Two Distinct Segments** to the Articular Cartilage Repair Market

**Small-Lesion Segment**
- Cost-effective treatments
- Single intervention
- Easy to implant

**Large-Lesion Segment**
- Dominated by ACI and other cell-based treatments
- All products in this segment are priced >$6,000

Lesions Warranting Only Minimal Intervention
- Currently treated with simple shaving, lavage and debridement

---
- border between small and large lesions generally accepted to be between 2.0cm² and 3.0cm² depending on patient and depth of lesion
Chondromimetic Follows Two Other Products in the Market For Small Lesions

1. **TruFit**
   - Smith & Nephew
   - Osteochondral plug
   - 510(k) as BVF (Q3 2004)
   - CE-Mark (Q1 2005)

2. **OsseoFit**
   - Kensey Nash/Biomet
   - Osteochondral plug
   - 510(k) as BVF (2006)
   - CE-Mark (Q4 2008/Q1 2009)

3. **Chondromimetic**
   - Orthomimetics
   - Osteochondral plug
   - 510(k) as BVF (Q1 2009)
   - CE-Mark (Q4 2008)

4. **BST-CarGel**
   - BioSyntech
   - In-situ setting cartilage gel
   - In clinical trials
   - Approval schedule unclear
Q: What is Chondromimetic’s Main Competitive Advantage Over ACI and Other Large-Lesion Products

A: Cost Effectiveness.
- Single intervention
- Efficient delivery system
- COGS < £100 (~83% instrumentation)
All-Natural Composition Yields a Substitution Mechanism of Resorption that Matches the Rate of New Tissue Formation
Good Results from Leading Synthetic, Better Results from Chondromimetic

- **Six-month data**
  - Skeletally mature goat model

- **Histology from Chondromimetic at six months**

**Graphs:**
- **Higher histology scores**
- **Mechanical properties statistically equal to natural tissue**
- **Higher gross morphology scores**

**Vastly lower incidence of adverse tissue responses**

<table>
<thead>
<tr>
<th></th>
<th>Synthetic</th>
<th>Chondromimetic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bone Cysts</strong></td>
<td>33%</td>
<td>33%</td>
</tr>
<tr>
<td><strong>Widening of Defect</strong></td>
<td>100%</td>
<td>0%</td>
</tr>
</tbody>
</table>

*Orthomimetics*
All of Orthomimetics’ Regulatory and Commercial Activities Will Focus on **Maximising Long-Term Value in the US Market**

<table>
<thead>
<tr>
<th>Market Attractiveness (Size, Global Peer Influence)</th>
<th>Risk/Cost of Entry (Regulatory, Reimbursement, Legal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S Europe</td>
<td>E Europe, Turkey, S Africa, Balkans</td>
</tr>
<tr>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>UK, Germany, France</td>
<td>Australia, Benelux, Canada, Scandinavia, Taiwan, South Korea</td>
</tr>
<tr>
<td>US</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td></td>
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</table>

- **Collect Strong Clinical Data**
- **Maintain Distribution Flexibility**
- **Position Chondromimetic for Long-Term Revenue Generation**
Orthomimetics’ Clinical, Regulatory and Commercial Timelines

<table>
<thead>
<tr>
<th>Stage 1: Pilot Clinical</th>
<th>Stage 2: Clinical Register</th>
<th>Stage 3: Pivotal US Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>2010</td>
<td>2011</td>
</tr>
<tr>
<td>Clinical &amp; Regulatory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1: Pilot Clinical</td>
<td>Stage 2: Clinical Register</td>
<td>Stage 3: Pivotal US Trial</td>
</tr>
<tr>
<td>2009</td>
<td>Clinical Register</td>
<td>Pivotal US Trial</td>
</tr>
<tr>
<td>Pilot Clinical</td>
<td>(Co-Ordinated by Cleveland Clinic)</td>
<td>Objective: Optimize pivotal trial, strengthen ex-US post-marketing data set</td>
</tr>
<tr>
<td>Proof of Concept Trial (Budapest)</td>
<td>Objective: Data sufficient to support IDE</td>
<td></td>
</tr>
<tr>
<td>Targeted Sales</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited sales in up to 10 centres</td>
<td>Objective: Maintain control of distribution</td>
<td></td>
</tr>
<tr>
<td>Full Ex-US Sales</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sales in all ex-US territories (excl Japan)</td>
<td>Objective: Rapid increase in sales revenues, maximise ex-US sales</td>
<td></td>
</tr>
<tr>
<td>Full US Sales</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sales in all US territories</td>
<td>Objective: Sales growth</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CE-Mark</th>
<th>510(k)</th>
<th>IDE Application</th>
<th>Full Ex-US Launch</th>
<th>Pre-Market Approval</th>
<th>Full US Launch</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>2010</td>
<td>2011</td>
<td>2012</td>
<td>2013</td>
<td>2014</td>
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</table>
Orthomimetics Continues to Harness Surgeon Expertise Through its **World-Class Medical Advisory Board**

<table>
<thead>
<tr>
<th>Medical Advisory Board</th>
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<tbody>
<tr>
<td><strong>International</strong></td>
</tr>
<tr>
<td>Anthony Miniaci, The Cleveland Clinic, USA</td>
</tr>
<tr>
<td>Laszlo Hangody, Uzoki Hospital, Budapest</td>
</tr>
<tr>
<td>Neil Rushton, Addenbrooke’s Hospital, Cambridge, UK</td>
</tr>
<tr>
<td>William Long, Insall Scott Kelly Clinic, New York, USA</td>
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</tbody>
</table>

*Source: Orthomimetics*
Orthomimetics has a Strong Pipeline of Scaffolds for the Regeneration of a Variety of Musculoskeletal Tissues

- **Product:** Chondromimetic (small chondral/osteochondral lesions)
  - CE Mark
  - Controlled EU Introduction
  - Full Ex-US Launch
  - PMA and US Launch

- **Product:** Ligamimetic (RTR donor site for ACI reconstruction)
  - Prototype
  - CE Mark

- **Product:** Teneomimetic (large and massive rotator cuff tears)
  - Prototype
  - CE Mark
  - Full Ex-US Launch
  - Global Launch

- **Product:** Meniscosomimetic (partial meniscal tears)
  - Prototype
  - CE Mark
  - Full Ex-US Launch
  - PMA and US Launch

- **Product:** Osteomimetic (w PMN) (high tibial osteotomy, other bone void filling)
  - CE Mark
  - Full Ex-US Launch
  - Global Launch
OM’s Corporate Partnering Approach Seeks to Accelerate and Reduce Cost of OM’s Clinical, Regulatory and Commercial Strategy

Small Geographically Focused Distribution Partners with Strong Track Record with Clinical Trials

Small Third-Parties; Independent Local Distributors

Global Partners with Extensive Sales Networks and Capable of Funding US Pivotal Trial

Mid to Large Orthopaedics and Sports Medicine Companies

Control Distribution

Gather High-Quality Data

Target Key Opinion Leaders

Maximise Sales Volume

Expand Geographical Coverage

Access All Surgeons
Regenerative medicine for a mobile, active life

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