This presentation includes statements that are, or may be deemed, “forward-looking statements.” All statements, other than statements of historical facts, included in this presentation regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “anticipate,” “project,” “target,” “design,” “estimate,” “predict,” “opportunity,” “proposition,” “strategy,” “potential,” “ongoing,” “plan” or the negative of these terms and similar expressions intended to identify forward-looking statements.

These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Actual results may be materially different. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Forward-looking statements include, but are not limited to, statements about: the timing and success of preclinical studies and clinical trials; the ability to obtain and maintain regulatory approval of our product candidates; the scope, progress, expansion and costs of developing and commercializing our product candidates; our expectations regarding our expenses and revenue; the sufficiency of our cash resources and needs for additional financing; our ability to adequately manufacture our product candidates and the raw materials utilized therein; our ability to obtain and maintain intellectual property protection for our product candidates; our expectations regarding competition; the size and growth of the potential markets for our product candidates and the ability to serve those markets; the rate and degree of market acceptance of any of our product candidates; our anticipated growth strategies; the anticipated trends and challenges in our business and the market in which we operate; our ability to establish and maintain development partnerships; our ability to attract or retain key personnel; our expectations regarding federal, state and foreign regulatory requirements; and regulatory developments in the United States and foreign countries.
Investment Highlights

- **NeoCart®** - Potential to be the new standard of care in knee cartilage repair
  - Superiority over current standard of care demonstrated in Phase 2 clinical trial

- NeoCart® is a [novel innovative therapy](#) that creates [new cartilage](#) from:
  - Autologous cells + Scaffolding + Bioengineering + Bioadhesives

- Positioning new standard of care to meet [significant unmet need](#) in orthopedics

- U.S. Phase 3 clinical trial **enrolling under a Special Protocol Assessment with FDA**
  - Anticipated BLA filing H2 2017 and FDA approval in 2018: Possible first to market

- Robust commercialization pathway

- Technology platform & expertise drives [next-generation therapies](#)

- Completed Dec 2014 [IPO – Raised ~$70M](#) (Gross Proceeds)
NeoCart® Therapy from Biopsy to Implantation

**Surgical Steps**
- Assessment of defect & biopsy
- Shipping of Biopsy

**Manufacturing Steps**
- Cell isolation & expansion, followed by seeding of 3D scaffold (2 – 3 Weeks)
- Implant processing in bioreactor under joint-like conditions (1 Week)
- Continued growth in static culture (2 (Up to 4) Weeks)
- NeoCart® harvest & packaging (5 Days)

**End-to-end from Biopsy**
6-9 weeks

**Implantation into defect**
Significant Unmet Need in Cartilage Repair

Unlike bone & other tissue, joint cartilage does not heal on its own

- Knee joint cartilage injuries are symptomatic and debilitating
- NeoCart® target patient: Active and athletic adults with cartilage injury and are not candidates for total knee replacement surgery
  - 18-55 years old, otherwise healthy and active
  - Acute injury or repetitive trauma to the knee
  - Experiencing symptomatic pain and functional limitation
- Current therapies, including the standard of care, require extensive recovery time and are not effective long-term
- In spite of limitations, a large market exists already and can grow
  - Approx. 500,000 procedures are performed in the U.S. annually
  - Approx. 90% of the procedures are microfracture or debridement
- Surgeons and patients desire more effective therapies
## Current Patient Cartilage Treatment Paradigm

### First-Line Therapy

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Impact for Patient</th>
<th>Impact for Physician</th>
</tr>
</thead>
<tbody>
<tr>
<td>Debridement</td>
<td>Shaving of edges, removal of loose cartilage</td>
<td>Goal: Pain reduction – no cartilage repair</td>
</tr>
<tr>
<td>Microfracture</td>
<td>Perforation of bone to stimulate repair response</td>
<td>Variable outcomes &amp; longer recovery</td>
</tr>
</tbody>
</table>

### Second-Line Therapy

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Impact for Patient</th>
<th>Impact for Physician</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteochondral Graft</td>
<td>Bone/cartilage plugs transplanted into defect</td>
<td>Variable outcomes &amp; morbidity</td>
</tr>
<tr>
<td>Chondrocyte Implantation</td>
<td>Implantation of expanded cartilage cells</td>
<td>Technically challenging but reimbursed</td>
</tr>
</tbody>
</table>

Ideal Cartilage Therapy Is a Combination of Biologic and Engineered Components

<table>
<thead>
<tr>
<th>Elements of an Ideal Cartilage Therapy</th>
<th>Cells Only</th>
<th>Scaffold Only</th>
<th>Cells + Scaffold</th>
<th>Cells + Scaffold + Engineering</th>
</tr>
</thead>
<tbody>
<tr>
<td>Architecturally resembles hyaline cartilage</td>
<td>No</td>
<td>?</td>
<td>?</td>
<td>√</td>
</tr>
<tr>
<td>Biochemically functions like hyaline cartilage</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>√</td>
</tr>
<tr>
<td>Anatomically fills defect &amp; biologically integrates</td>
<td>No</td>
<td>?</td>
<td>?</td>
<td>√</td>
</tr>
<tr>
<td>Technically uncomplicated procedure and rehabilitation</td>
<td>No</td>
<td>?</td>
<td>?</td>
<td>√</td>
</tr>
</tbody>
</table>

Phase 3 Study Replicates Phase 2

1-Year Primary Endpoint for BLA Filing under SPA

Screening

n = 245

Randomization

Arm 1: NeoCart® Implantation (n = 163)

Arm 2: Microfracture (n = 82)

Endpoints at 1 Year

Key Inclusion Criteria:
- Age: 18-55
- Diagnosis: severe and symptomatic cartilage lesions (0.5-6cm²)

Key Exclusion Criteria:
- Prior lesion treatment
- High Body Mass Index
- Significant arthritis
- Concomitant surgeries
- Knee instability
- Meniscal insufficiency

Primary
- Knee pain/function improvement:
  - ≥12 pts KOOS pain
  - ≥20 pts IKDC Subjective

Secondary
- Time to full weight-bearing
- Failure rate:
  - >8 point deterioration in KOOS pain
  - Presence of mature collagen layering on MRI
NeoCart® Phase 3 Clinical Study – New Start

- **History:**
  - Trial Initiated 2010 with Special Protocol Assessment (SPA)
  - Initial Enrollment & Pauses – 2010 to 2013
- **New Start** - Targeting **H1 2016 Enrollment Completion**
  - First Patient back in clinic – March 2014
  - New clinical team in place – September 2014
  - Robust patient recruitment & screening efforts – September 2014
  - Site start-ups completed and fully functional – December 2014

---

**IPO Funding completed to enroll trial and obtain 1-year endpoint ~30+ Sites by December 2014 (up to 40 sites allowed per SPA)**

*as of November 14, 2014*
Phase 2 Study

**NeoCart® demonstrated significant improvement versus current standard of care**

- **NeoCart® patients demonstrated significant efficacy over standard of care**
  - Significant improvement in pain and function compared to baseline
  - Improvement was significantly better than microfracture improvement
  - Randomized (2:1), controlled trial at 6 U.S. centers
  - High-hurdle efficacy thresholds for pain and function to assess clinically meaningful benefit

- **Small number of patients, not powered for superiority outcomes**
  (n=30: 21 NeoCart®, 9 microfracture)

**Source:** J Bone Joint Surg Am. 2012;94:979-89.
NeoCart® Phase 2 Dual-Threshold Responder Rate Analysis Sets High Efficacy Threshold

Specific minimum improvement in two validated patient-reported outcome measures:

- >12 pts KOOS pain vs. baseline at 1 year AND
- >20 pts IKDC subjective vs. baseline at 1 year

Responder Analysis

Dual-Threshold Responder Rate Summary

- **NeoCart®**
- **Microfracture**

<table>
<thead>
<tr>
<th>Year</th>
<th>1 YR</th>
<th>2 YR</th>
<th>3 YR</th>
</tr>
</thead>
<tbody>
<tr>
<td>NeoCart®</td>
<td>*76%</td>
<td>*89%</td>
<td>69%</td>
</tr>
<tr>
<td>Microfracture</td>
<td>22%</td>
<td>44%</td>
<td>29%</td>
</tr>
</tbody>
</table>


- **NeoCart®** superiority at Y1
- Durability of response over time

*Evaluable Patients: 21 9 18 9 16 7*
Competitive Landscape in the U.S.

- First-mover advantage
- Potential for best-in-class as the new standard of care
- Possible barrier to entry created by superiority data & high-hurdle study design

<table>
<thead>
<tr>
<th>Key Cellular Products</th>
<th>Regulatory Path</th>
<th>Procedure</th>
<th>Cells</th>
<th>Cells + Scaffold</th>
<th>Cells + Scaffold + Engineering</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carticel®</td>
<td>FDA-approved</td>
<td>2-step</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DeNovo® NT</td>
<td>Sec.361, not FDA-cleared</td>
<td>1-step</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NeoCart®</td>
<td>Planned BLA for FDA approval with SPA</td>
<td>2-step</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>NovoCart® 3D</td>
<td>Planned BLA for FDA approval</td>
<td>2-step</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>MACI®</td>
<td>BLA (TBD)</td>
<td>2-step</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Revaflex®</td>
<td>Planned BLA for FDA approval</td>
<td>1-step</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: ClinicalTrials.gov; publicly available data / information.
Commercial Strategy

**Commercialization**

- Invest in a small, scalable U.S. commercial infrastructure for NeoCart®
- Specialty U.S. sales force targeting 4,000 to 5,000 orthopedic surgeons
- Selectively evaluate commercialization strategies outside of the U.S., including partnering

**Commercial & Production “Ready” Strategy**

- Scalable manufacturing based on demand, with gross margin upside
- Existing cGMP raw material supply and production expertise
- Active FDA feedback on scale-up & raw material strategy (Dec 14)
NeoCart® Seeks to Establish a Strong Value Proposition for Payers

- Leverage extensive existing coding options for NeoCart®
- Generating further “burden of proof” data to support value proposition & pricing – Jan 15 Protocol Approval to augment existing Phase 3 Data collection
- Limited barriers to adoption, economics for physicians and payers are positive

Better clinical outcomes for patients grow the market

- Faster return to work, functional and quality of life recovery
- Reduced physical therapy
- Durability of treatment effect

Better economic outcomes for physicians & payers

- Economics are comparable to existing therapies for physicians
- Lower procedural, treatment, and rehabilitation costs
- Failure Rates – Fewer re-operations and revisions

Data / Evidence Generation

- Phase 3 – Quality of Life (QOL), Pain, Function
- Patient Registry
- 5-Year Phase 2 Data
- Burden Study & Registry
- Utility & Productivity Data
- Cost Effectiveness / Quality Adjusted Life Years
Technology Platform and Internal Know-how Drives Future Pipeline

- New indications with existing NeoCart© technology (example: patella, ankles)
- Expand into other soft-tissue musculoskeletal areas within orthopedics

**INTREXON** Collaboration Announced in September 2014 w/ investment in IPO

- Improved manufacturing yields and one-step procedure
Intrexon chose Histogenics for exclusive partnership for cartilage repair therapies

- Leading synthetic biology & genetic engineering technologies from Intrexon (XON)
- Leverages Histogenics’ leading expertise in cellular & tissue processing and bio-engineering to create cartilage tissue

Potential Benefits

- Potential to revolutionize and grow the cartilage repair market
  - Enable access - grows the existing cartilage repair patient base
  - May enable a fundamental shift in knee treatment paradigm

- Enables expansion of existing manufacturing capabilities
  - May markedly increase volumes and supply capabilities
  - Improved scaling drives lower potential costs

- Leverage our cartilage franchise – potential to grow pipeline
  - Lead technological advancements in cartilage repair
  - Eliminate cell and donor availability issues

Collaboration Metrics:

- $10 million Tech Access Fee paid to Intrexon
- Intrexon Invested $20 M in Dec 14 IPO
- Reimbursement of R&D Expenses
- Back-end success milestones up to $34.5 million
- Low double-digit percentage royalty based on the gross profits
Use of IPO Proceeds (~$70M Gross/~$63 Net):

- Clinical trial enrollment & completion
- Mfg supply chain optimization & approval
- Reimbursement claims data generated
- Intrexon Collaboration

Key Financial Metrics:

- Market Value (Q1): ~$125M (13.2M shares outstanding)
- Avg. Volume: 40k (3m)
- Cash on Balance Sheet (YE14): ~$58M
- Cash Runway through mid-2017
- Expected Cash @ YE 2015: $33 – 35 million
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