Commercializing Regenerative Medicine Products
The Academia-Industry Partnership

Strategic Biotech Innovation Venturing

Alain Vertès, PhD-MBA
London Business School
avertes.sln2004@london.edu

TERMIS, Vienna, Austria, 5-8 September 2012
Park BioVentures, 230 Park Avenue, Suite 539, New York, NY 10169
Strategic Breakthrough Question

Reasons to believe

1. Cell therapy is not a passing fad, it will transform medicine
2. Cells are not only transplants: they can be drugs
3. Cell therapy’s first paradigm changing application is in treating inflammation / autoimmune disease
4. It is possible to protect the intellectual property of these new drugs
5. These medicines offer the prospect of stunning efficacy with significantly reduced side-effects
6. It is possible to consistently and cost-economically manufacture these new therapies and maintain their intrinsic attributes throughout the distribution chain
Strategic Breakthrough Question
Perspective on adaptive medicines

“Bacteria sense and respond to their local microenvironments. Can medicines be developed that mimic this fundamentally natural property of living things to optimize molecular responses to disease environments?”

<table>
<thead>
<tr>
<th>Sensing and responding properties</th>
<th>Ideal safety and efficacy attributes</th>
<th>Robustness and industrialization attributes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Large safety margin</td>
<td>Similar effects in a large range of doses</td>
</tr>
<tr>
<td></td>
<td>Activated only in diseased areas of the body</td>
<td>Manufactured and distributed as any biologic</td>
</tr>
</tbody>
</table>

Allogeneic mesenchymal stem cells appear to have the potential to deliver the characteristics above at least in the Inflammation Disease area.
Market and Implementation Perspectives

Portfolio hurdles

<table>
<thead>
<tr>
<th>High</th>
<th>Indications discovery</th>
<th>Best-in-class</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Expand therapeutic uses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Extend patent life</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td><strong>Terra incognita</strong></td>
<td>Clinical precedent</td>
</tr>
<tr>
<td>• Highest risks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Uncertain returns</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Lead to first-in-class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Intrinsic strategic value as market leader</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Demonstration of mechanism</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Market and Implementation Perspectives

Indication decision filters

Selection criteria:
- Disease-modifying potential
- Relevant clinical read-out and biomarkers
- Large and small animal models
- Overall feasibility and time to market
- High unmet medical need
- Market size
- Expected reimbursement policies
- Marketing fit
- Payer’s benefits

Source: Vertès, 2010, London Business School
Market and Implementation Perspectives
Franchise transformation maps

Acute

Therapy resistant

Orphan diseases

Increasing complexity

Immunomodulation
Cell replacement

Regeneration

Chronic
Escaping the Valley of Death
Seed Funding

$1,400m private equity invested in 2009-2010 in conventional oncology products vs. $200m in stem cell technologies

trend of declining first sequence capital in 2011

Funding Gap
More acute in emerging technology fields
Challenge = Opportunity
Licensing Valuation

Constraints model

- **Technology risks**
  - technical maturity

- **Opportunity costs**
  - conventional technologies

- **Market uncertainty and policy risks**
  - reimbursement, patent policies

- **Keep manufacturing or certain marketing rights**

---

**Increase valuation**

- Intellectual property, freedom to operate
- Later stages of development, products vs. technologies
- Strategic & marketing fit, reimbursement strategies
- Worldwide or exclusive license

---

**Decrease valuation**
Stem Cells Partnerships and M&A activities
Mechanisms at play and predicted trends

Academia

Biotech

• Opportunity costs
• Can afford to wait
• Risk aversion
• Unclear strategic fit

Mid-size Pharma

• Osiris
• Athersys
• Mesoblast
• Adv. BioHeal.
• Pervasis Ther.
• Cytori
• Cellartis
• Opexa Ther (T-cells)

Big-size Pharma

• Pfizer
• Novartis (T-cells)

Cephalon- Mesoblast:
• Mesoblast has become the 4th healthcare company in Australia with a valuation >$2b
• Cephalon partnered with Mesoblast to proactively preempt a big Pharma deal
• Teva acquired Cephalon in part because of its position in Mesoblast

• Sanofi
• Teva

• Genzyme
• Cephalon
• Shire
• Novo Nordisk
• Astellas
• JCR Pharma
• Baxter
Syndicate Innovation Venturing

Definition

**Syndicate Innovation Venturing:**

*Bringing together actors from complementary economic sectors in a ‘non-zero sum game’ partnership to conduct seed funding in technology areas with blockbuster potential*

Applications to emerging technologies and disruptive innovation

- Regenerative medicine and therapeutic stem cells
- Stem cells for research
- Recombinant antibodies
Syndicate Innovation Venturing: Basic model

- Independent incubator located at or near an academic center
- Incubator company
  - Big Pharma as a strategic partner

Joint R&D project or start-up proposals

Strategy:
- Big Pharma white space areas
- Emerging technologies
- Fundamental technologies

Independent incubator (physical or virtual)

Co-investment:
- risk sharing decreased evaluation burden
- decreased investment requirements and operational burden
- alignment of incentives (company management)

Co-investment:
- Technology awareness
- Rights for preferential access to IP and FTO
- Tangible assets such as compounds or independent biotechs
- Capital gains or event payments and royalty streams
- Faster exit and higher ROI by tailored approach focused on Pharma needs
Syndicate Innovation Venturing
Alliance management mechanisms

• **Objective**
  – Design **new models** to access academic innovation while minimizing resource commitment and maximizing reach

• **Concept**
  – Form a syndicate of stakeholders with aligned incentives for optimizing technology commercialization
  – Generate product **options**
  – Absence of **zero-sum games**
New Opportunities Channeling
Mechanisms

**Attract**
Beacon of visibility to bring VCs, entrepreneurs and scientists within the Big Pharma sphere of influence

*Key success factor:* quality of the people and their business or scientific plans

---

**Scout & leverage**
Systematic search for scientific projects of outstanding potential

*Key success factor:* quality of the science and teamwork

---

**Design**
Organize creativity in areas of priority with both robust business and scientific cases

*Key success factor:* focused goals and quality of the innovative thinking

---

**Project and deal flow**
Syndicate Innovation Venturing

Key benefits

• De-risked access to emerging technologies
• Bridge to “white space” disease areas
• Cost effective access to entrepreneurship, knowledge and competences outside the boundaries of the firm
• Low level of investment
• No de facto ‘obligation’ to follow up investments in start-ups
• Early establishment of sound bases to eventual future alliances or team integration in new technologies or white space areas
Syndicate Innovation Venturing
Field test (e.g. Pontifax-Roche) & typical terms

• **Big Pharma establishes areas of interest** (platform-to-product or white space disease areas)
• **Within these guidelines, VC scouts and suggests a deal flow**
• **For each selected project:**
  o VC invests $Ym
  o The hosting incubator company invests $Ym
  o The project is financed in part by the government via a competitive loan or grants of $Y
  o Big Pharma provides a grant of $Ym
  o Big Pharma has a Right of First Negotiation
  o Big Pharma has the option to transform its initial grant into shares of the NewCo upon completion of a Series A financing round achieving a pre-set funding target
• **The agreement is non-exclusive**
• **The term of the agreement is 5 years**
• **Either party may terminate the agreement with 6 months notice**
• **4 start-ups created within 6 months of agreement signature**
Open Access

Syndicate Innovation Venturing: Translating Academic Innovations Into Commercial Successes

ISSN 2078-1547

www.mdpi.com/journal/challenges
VALUE POTENTIAL OF NEW OPPORTUNITIES: COMPARABLES
Syndicate Innovation Venturing
Case studies: mature technologies (I)

• Small molecules
  – Big pharma out-licenses: Actelion
    • Founded in 1997
    • Technology: focus on endothelium-related conditions
    • IPO in 2000 raised $247m, 2010 market cap: $6.6b, 2010 operating profit: $457m
  – Novel targets: Sirtris
    • Founded in 2004, raised $82m in total
    • Technology: sirtuins (mitochondrial targets)
    • M&A by Glaxo in 2008 for $720m
• Biologics
  – Peptides: **Aileron**
    • Founded in 2005, $61m raised in total, series D in 2009
    • Technology: stabilize peptides, drug undrugable targets
    • Deal with Roche in 2010: $25m upfront, up to $1.1b in event payments
  – Monoclonal antibodies: **Medarex**
    • Founded in 1987
    • Technology: fully human monoclonal antibodies
    • IPO in 1991, deal with BMS in 2004: $50m upfront, up to $480m in event payments, M&A by BMS in 2009 for $2.1b
Syndicate InnovationVenturing
Case studies: emerging technologies (I)

• Nucleic acids
  – siRNA: **Alnylam**
    • Founded in 2002
    • Series B raised $15m in 2002, $17.5m invested in total by 2003, IPO in 2004 raised $26m, deal with Roche in 2007, $331m upfront comprising a 5% equity investment, up to $1b in event payments
  – siRNA: **Sirna**
    • Founded (refocus of Ribozyme Pharma, on RNAi) in 2003
    • Series A raised $48m in 2003, M&A by Merck in 2006 for $1.1b
Syndicate Innovation Venturing
Case studies: emerging technologies (II)

• Research tools
  – Stem cells: Cellular Dynamics (CDI)
    • Founded in 2004
    • Technology: stem cell-based research tools
    • Series A raised $18m, series B raised $40.6m in 2010, deal with Roche signed in 2008
Syndicate Innovation Venturing
Case studies: emerging technologies (III)

• Therapeutic stem cells
  – Mesenchymal stem cells: **Mesoblast/Angioblast**
    • Founded (Angioblast) in 2001
    • Technology: therapeutic adult allogeneic mesenchymal stem cells
    • IPO (Mesoblast) in 2004 raised $21m, deal with Cephalon in 2011: $220m (20%) equity investment, $130m upfront and up to $1.7b in event payments
    • 2011 valuation $2b-2.5b
Syndicate Innovation Venturing
Value proposition

→ Business case for funding new opportunities
  • assess for blockbuster potential

• De-risking
• Selecting areas that address fundamental technical issues
  • new mechanism
  • new target
  • new platform
  • new disease area
• Externalizing R&D to create valuable product options
• Maximizing probability of strategic alliances with big Pharma
• Maximizing probability of exit via M&A
Syndicate Innovation Venturing
Potential partners in New York

BigPharma
- Financing
- Expertise

Academia
- Innovations
- Blue chip academia

Incubator
- Nurturing

Eagle Advisers
- Financing
- Advising

Park BioVentures
- Financing
- Scouting
- Managing

Public
- Grants

Venture fund, Scouts, R&D experts

Grand Central is fund of funds
Manages $50m (funds fluctuate with market conditions)

Investment team
Pre-screening team, Scientific Advisory Board

Founded in 2009

Development agencies
Syndicate Innovation Venturing
Critical Success Factors: creating & nurturing

- **Deal flow sourcing**
  - Academic network
  - VC scouting and beacon of visibility to sustain calls for proposals

- **Assessment**
  - Key opinion leader committees
  - Business development committees

- **Financing**
  - Big Pharma, Eagle Adviser, incubator companies, other VC partnerships (e.g. academia venture funds or other big Pharma venture funds)

- **Implementation and nurturing**
  - Incubator New York / New Jersey
  - Entrepreneurs in residence

- **Value realization**
  - Right of First Negotiation (big Pharma)
  - Strategic alliances, IPO, M&A, and trade sales
Syndicate Innovation Venturing

Critical Success Factors: 3 key focus areas

• Technology focus
  – Emerging technologies
    • **Therapeutic stem cells**
    • Other cell therapeutics including cancer vaccines
    • **Stem cell-based research tools and stem cell-based diagnostics**
    • Therapeutic peptides
    • **Recombinant antibodies**
    • Intracellular delivery (peptides, liposomes, blood-brain barrier, etc.)
    • miRNA
    • Epigenetics
    • Gene therapy
  – White space disease areas
    • Dermatology
    • Bone and cartilage repair
    • Rare and orphan diseases
    • Emerging diseases of the developed world
  – Small molecules at early clinical phases
  – Biologics at early clinical phases