

Commercializing Regenerative Medicine Products

The Academia-Industry Partnership

Strategic Biotech Innovation Venturing

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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? ”

Ideal safety and efficacy attributes

**Sensing
and
responding
properties**

Large safety margin	Similar effects in a large range of doses
Activated only in diseased areas of the body	Manufactured and distributed as any biologic

**Robustness and
industrialization
attributes**

Allogeneic mesenchymal stem cells appear to have the potential to deliver the characteristics above at least in the Inflammation Disease area

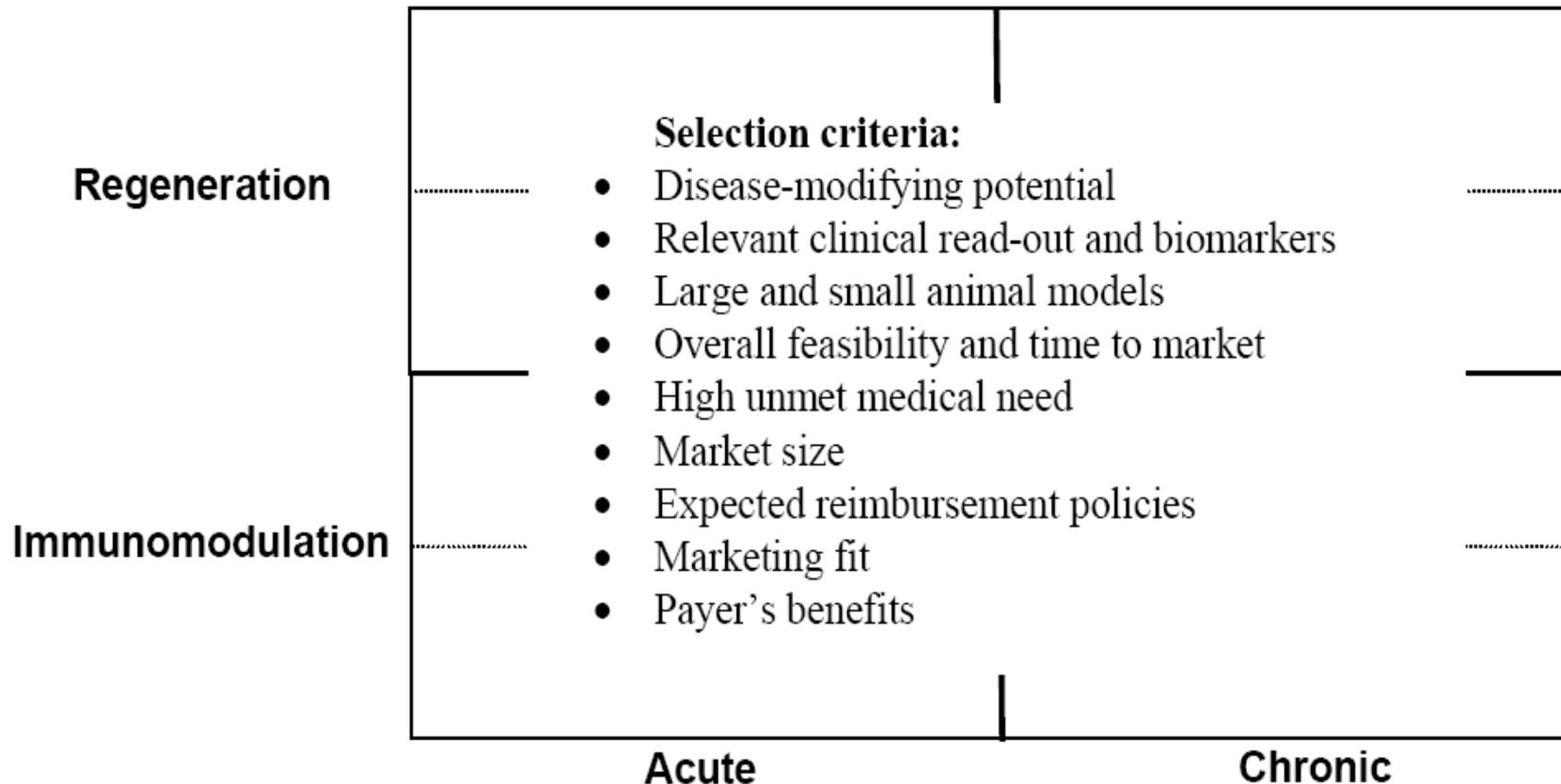
Market and Implementation Perspectives

Portfolio hurdles

Demonstration of safety	High	<p>Indications discovery</p> <ul style="list-style-type: none"> • Expand therapeutic uses • Extend patent life 	<p>Best-in-class</p> <ul style="list-style-type: none"> • Lowest risks of failure • Highest returns
	Low	<p><i>Terra incognita</i></p> <ul style="list-style-type: none"> • Highest risks • Uncertain returns • Lead to first-in-class • Intrinsic strategic value as market leader 	<p>Clinical precedent</p> <ul style="list-style-type: none"> • Build-in improved safety in compounds exhibiting efficacy • Lead to best-in-class • Defensive and offensive strategic values
		Low	High
		Demonstration of mechanism	

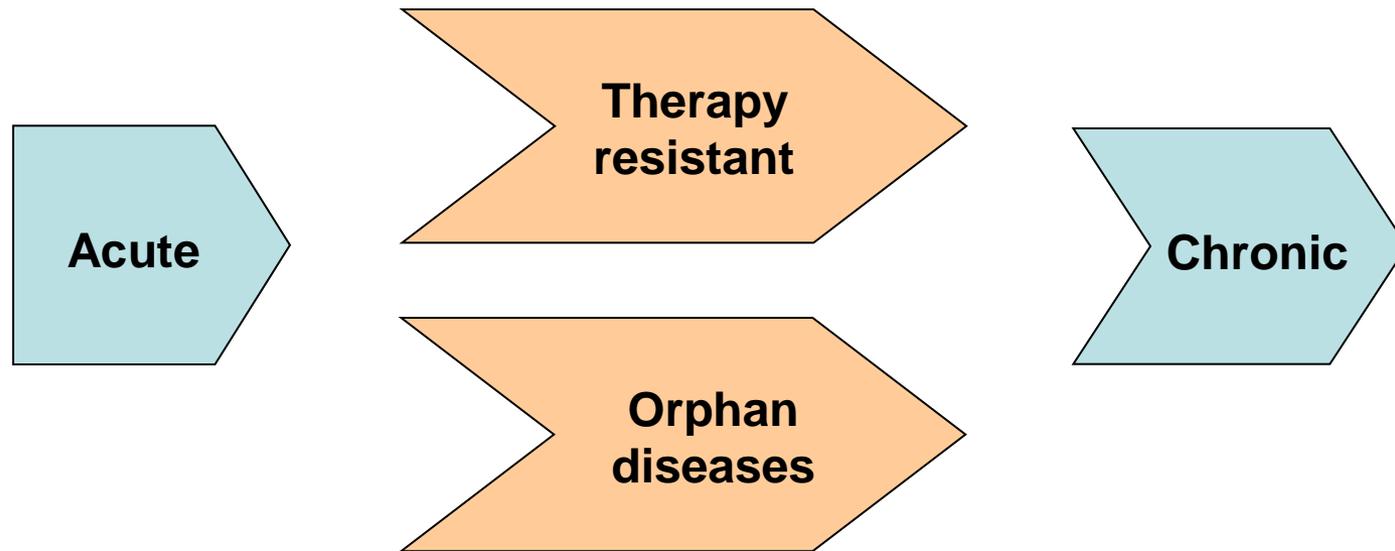
Market and Implementation Perspectives

Indication decision filters



Market and Implementation Perspectives

Franchise transformation maps

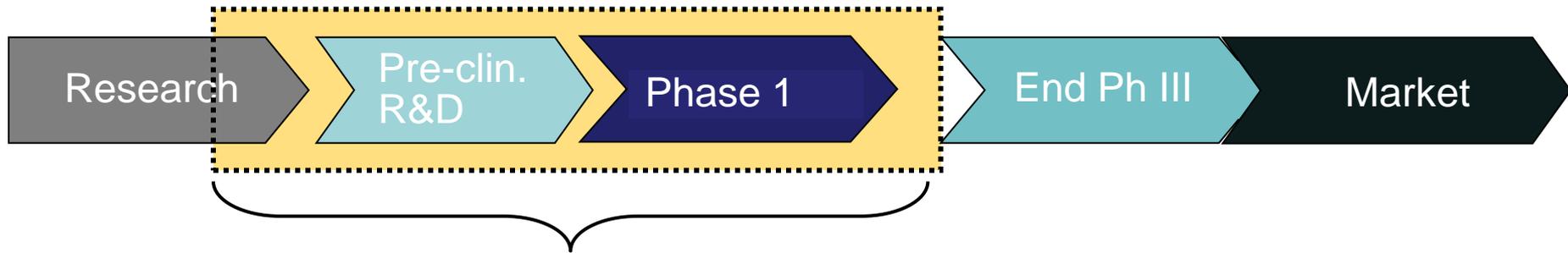


Immunomodulation
Cell replacement

Regeneration

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

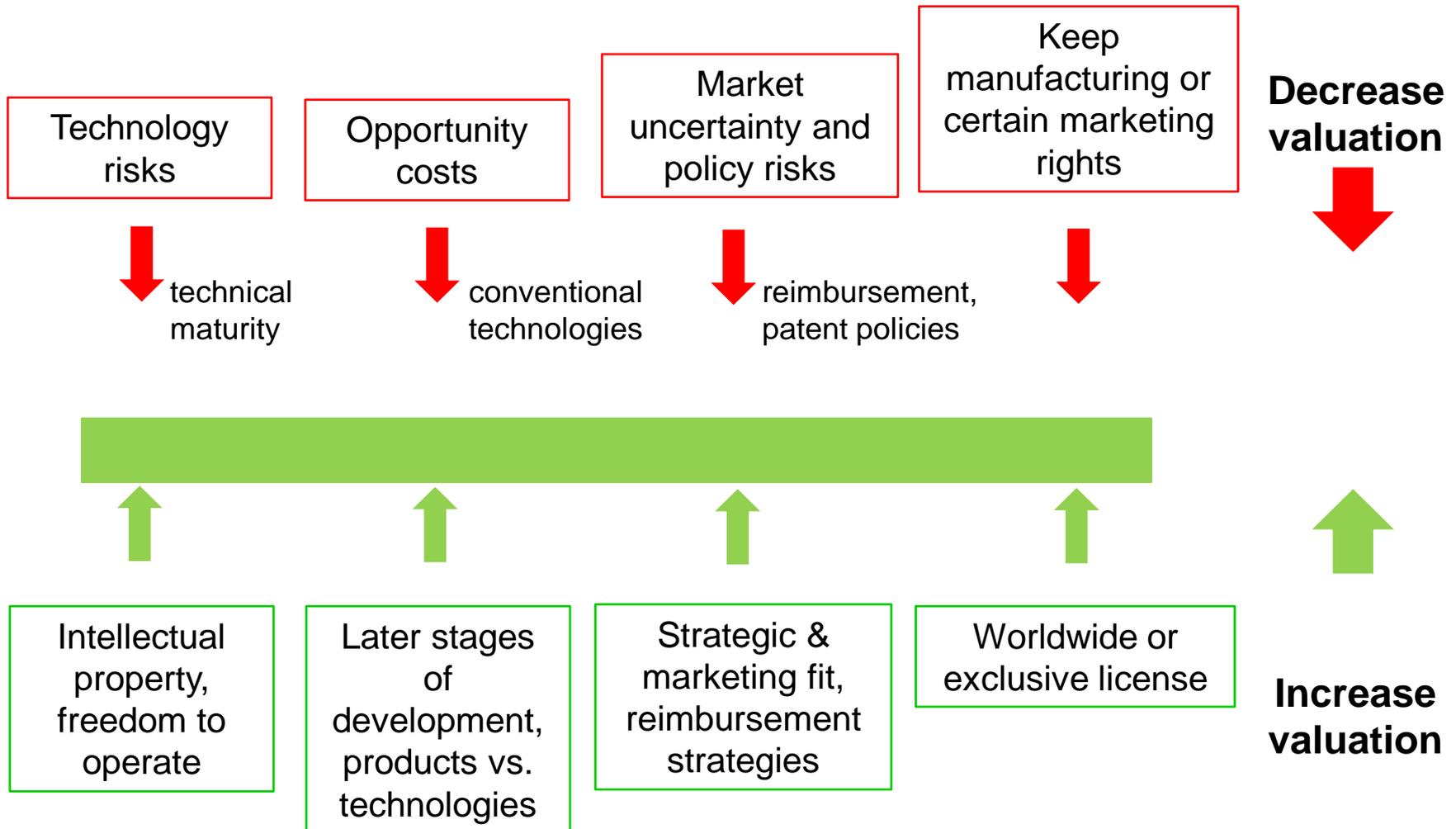
trend of declining first sequence capital in 2011

Funding Gap

More acute in emerging technology fields
Challenge = Opportunity

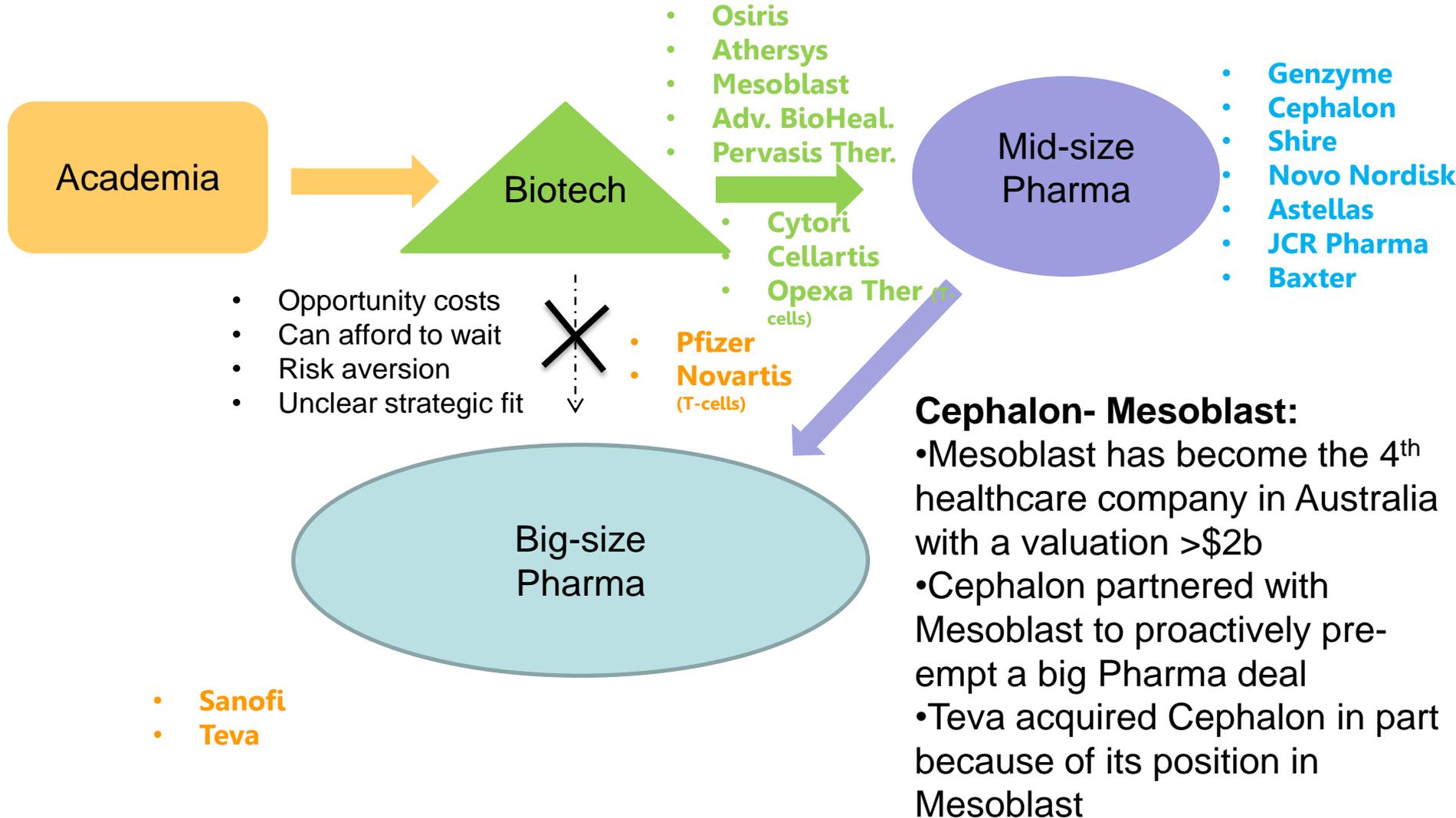
Licensing Valuation

Constraints model



Stem Cells Partnerships and M&A activities

Mechanisms at play and predicted trends



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

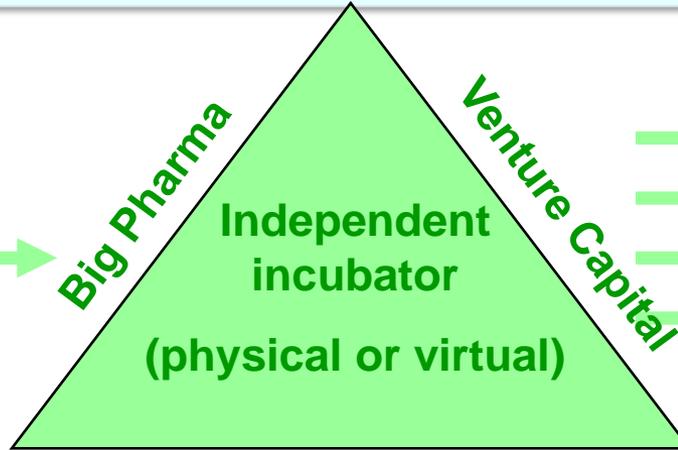
Recombinant antibodies

Syndicate Innovation Venturing: Basic model

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

- Technology awareness
- Rights for preferential access to IP and FTO

Joint R&D project or start-up proposals



Tangible assets such as compounds or independent biotechs



Strategy:

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

Co-investment:

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

- Capital gains or event payments and royalty streams
- Faster exit and higher ROI by tailored approach focused on Pharma needs

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Alliance management mechanisms

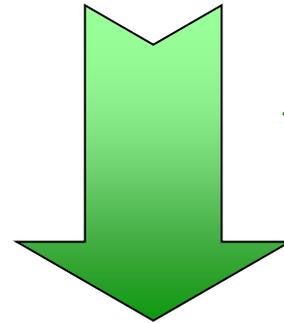
- **Objective**
 - Design **new models** to access academic innovation while minimizing resource commitment and maximizing reach
- **Concept**
 - Form a syndicate of stakeholders with **aligned incentives** for optimizing technology commercialization
 - Generate product **options**
 - Absence of **zero-sum games**

New Opportunities Channeling Mechanisms

Attract

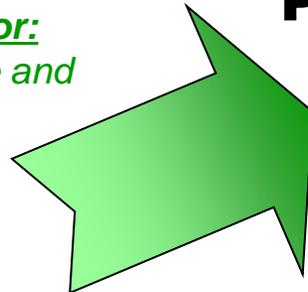
Beacon of visibility to bring VCs, entrepreneurs and scientists within the Big Pharma sphere of influence

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

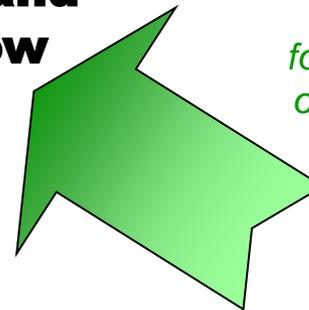


Project and deal flow

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



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



Scout & leverage

Systematic search for scientific projects of outstanding potential

Design

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

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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

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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:**
 - VC invests \$Ym
 - The hosting incubator company invests \$Ym
 - The project is financed in part by the government via a competitive loan or grants of \$Y
 - Big Pharma provides a grant of \$Ym
 - Big Pharma has a Right of First Negotiation
 - 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**

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Model description: reference

Open Access

Syndicate Innovation Venturing: *Translating Academic Innovations Into Commercial Successes*

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VALUE POTENTIAL OF NEW OPPORTUNITIES: COMPARABLES

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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

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Case studies: mature technologies (II)

- **Biologics**

- Peptides: **Aileron**

- Founded in 2005, \$61m raised in total, series D in 2009
 - Technology: stabilize peptides, drug undruggable 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

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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

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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

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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

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Value proposition

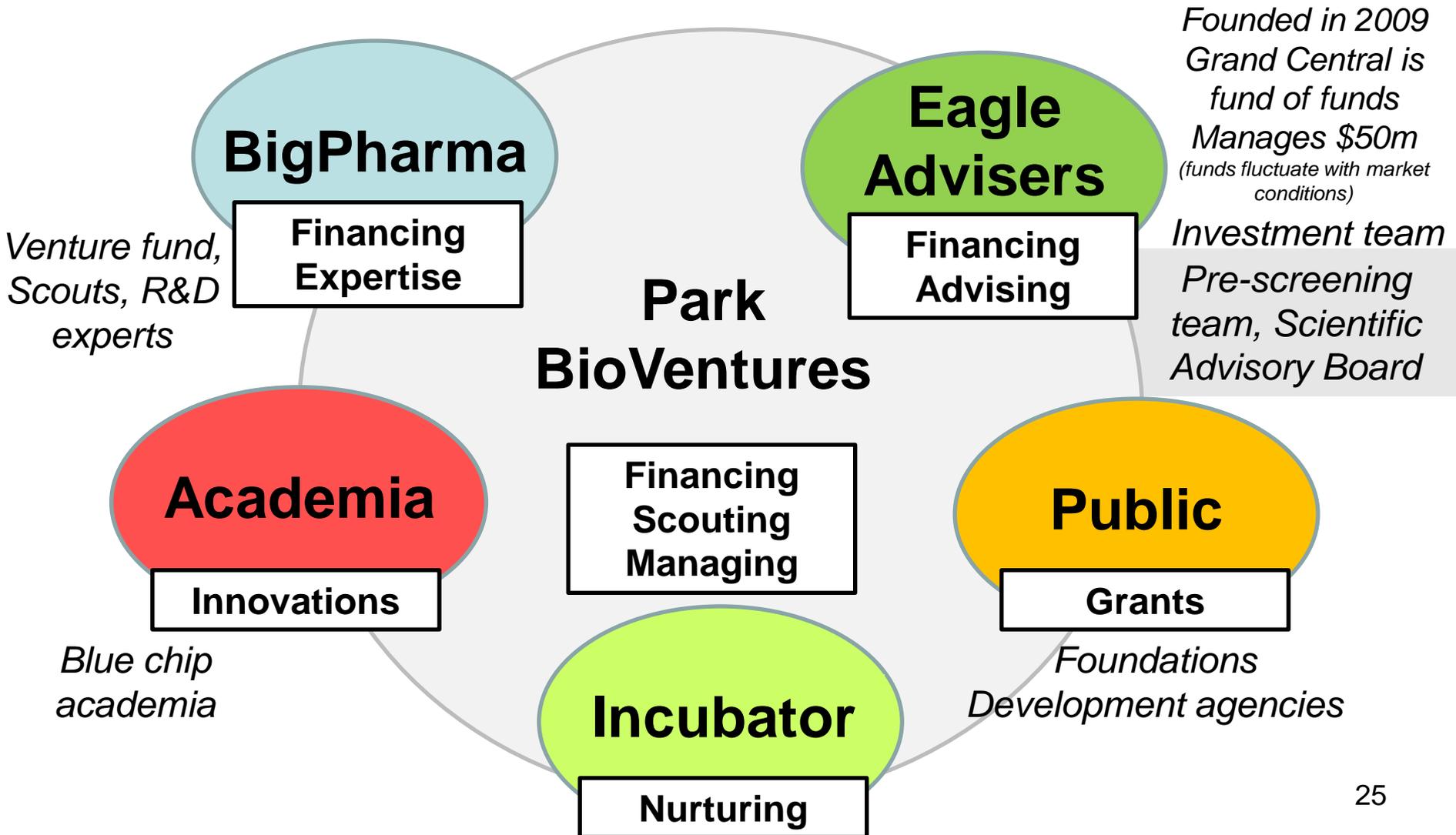
- **Business case for funding new opportunities**
 - **assess for blockbuster potential**
- *De-risking*
- *Selecting areas that address fundamental technical issues*
 - *new mechanism*
 - *new target*
 - *new platform*
 - *new disease area*
- *Externalizing R&D to create valuable product options*
- *Maximizing probability of strategic alliances with big Pharma*
- *Maximizing probability of exit via M&A*

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IMPLEMENTATION

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Potential partners in New York



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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

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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