Lessons in university intellectual property management: The secret to survivin’ or a train bound for nowhere?

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With apologies to Kenny Rogers
Disclaimer
The secret to survivin’:
Seven things that matter.

- Goals
- Metrics
- Size
- Timelines
- Strengths
- Relationships
- Value
Goals Matter

Reassess roles of university technology transfer offices. One size does not fit all.
You get what you measure. Measure the wrong thing and you get the wrong behaviors."

John H. Lingle
An example of poor intellectual property management driven by metrics.
SIZE MATTERS:
The World University Rankings 2014-2015

By Population

By GDP

Strengths
Matter
Infrastructure, research & human capacity
Timelines

Matter

Realistic assessment of contribution, transaction costs, & patent life

Translational Research from Basic through Clinical

1989
- Redirected T cell concept in vitro
  - Gross et al., PNAS

1998
- First HIV CAR patients treated (CD4 Zeta)
  - Persistence of CAR T cells up to 11 years post infusion (STM, 2012)

2008
- First Cancer Clinical Trials –poor T cell engraftment
  - Kershaw et al Clin Cancer Res; Lamers et al., J Clin Oncol

2004-2010
- T Cell Translational Research and First Clinical Trials: CD19 target in B cell malignancies

2014
- Chimeric Antigen Receptor T Cells for Sustained Remissions in Leukemia
  - N ENGL J MED 371:16 NEJM.ORG OCTOBER 16, 2014

Development of Clinical Scale T Cell Manufacturing Process

1987
- Discovery role of CD28 in T cell proliferation

1993
- CD3/CD28 beads produced (culture system)

1998
- Bead removal - passage over magnetic field

2010
- In-hospital production for T-cell infusion

2014-
- Scale-Out: Development of robotic systems (QC)

Adapted from Carl June:
2012 Chabner Colloquium – Collaboration in Cancer Drug Trials
https://www.youtube.com/watch?v=jQfFCC6i5_o
Relationships Matter
New funding calls for collaborative, multi-national, multi-disciplinary, and increasingly multi-sectorial research

Access to precompetitive research outputs raises the level of knowledge for all R&D actors.

Precompetitive research does not limit appropriation of innovation that is closer to practical application.

Avoids duplicative research.

Reduces negotiating costs associated with an abundance of intellectual property rights.

Promotes use of standard research tools and methods.
Value Matters
Look for opportunities.
Be flexible.

You've got to know when to hold 'em
Know when to fold 'em
Build on respective strengths:

Example 1 – Cellular Onco-Immunotherapy
Clinical translation is global
Plug knowledge/technology gaps

**Gap**
- Lack of cancer cell specific antigens causes off-target toxicity
- Need fully humanized CAR T-cell constructs
- Need more efficient genetic engineering methods
- Need robotic cell processing systems
- Need to control duration of immune response to limit adverse side-effects

**Plug**
- Target discovery is an academic strength
- Vector development is an academic strength
- CRISPR/Cas systems developed in academia and spun out to biotechnology companies
- Academic/industry co-development in bio-engineering
- Academic/industry co-development of suicide switch
Play a more effective role in assessing value.

Know when to walk away
And know when to run

Bringing regenerative medicines to the clinic: the future for regulation and reimbursement
More Medicine Goes Off Limits in Drug-Price Showdown
By Robert Langreth - Nov 25, 2014
Steve Miller is waging war on high-priced medicine, guiding decisions to ban drugs from the health plans of millions of Americans and sending companies reeling in a $270 billion market.
He and his colleagues at Express Scripts Holding Co. (ESRX) say they are just getting started.
Clinical development success rates for investigational drugs

Michael Hay, David W Thomas, John L. Craighead, Celia Economides & Jesse Rosenthal

Volume 32, Number 1, January 2014, Nature Biotechnology

Animal and/or Laboratory Studies

<table>
<thead>
<tr>
<th>Phase Success</th>
<th>Lead Indication</th>
<th>All Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1 to Phase 2</td>
<td>67%</td>
<td>64%</td>
</tr>
<tr>
<td>Phase 2 to Phase 3</td>
<td>39%</td>
<td>32%</td>
</tr>
<tr>
<td>Phase 3 to NDA/BLA</td>
<td>68%</td>
<td>60%</td>
</tr>
<tr>
<td>NDA/BLA to Approval</td>
<td>86%</td>
<td>83%</td>
</tr>
<tr>
<td>Approval to Post-market</td>
<td>86%</td>
<td>83%</td>
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I About 4.5 Years I About 8.5 Years I 1.5 Years
A framework for value evaluation

Translational Stage

Pre-clinical | Phase I | Phase II

Step 1: Headroom Analysis

Social Value Impact | Resource Impact | Health Impact

Technology & clinical landscapes | Confidence Adjustments

Value-Based Reimbursement Decisions for Orphan Drugs: A Scoping Review and Decision Framework

Mike Pawlison, Tania Stafinski, Devidas Menon, Christopher McCabe

Abstract

Background: The rate of development of new orphan drugs continues to grow. As a result, reimbursing orphan drugs on an exceptional basis is increasingly difficult to sustain from a health system perspective. An understanding of the value that societies attach to providing orphan drugs and the degree to which other health technologies are now recognised as an important input to policy debates.

Results: The scoping review identified 19 candidate decision factors, most of which can be characterised as either value-creating or ‘opportunity cost’-determining, and also a number of value propositions and pertinent sources of preference information. We were able to synthesise these into a coherent decision-making framework.

Conclusion: Our framework may be used to structure policy discussions to aid transparency about the values.
A framework for value evaluation

**Step 1: Headroom Analysis**
- Social Value Impact
- Resource Impact
- Health Impact

**Technology & clinical landscapes**

**Confidence Adjustments**

**Step 2: Macro Analyses – Cost-Effectiveness Modeling**
- Assesses assumptions cost of goods and effectiveness based on similar bio-therapeutics
- Clears Value Hurdle
  - YES
  - NO

**Step 3: Micro Analyses – Cost-Effectiveness Modeling**
- Cost of Goods
- Regulatory compliance
- Manufacturing Scale-up
- Structural barriers to implementation
- Effectiveness
- Safety profile
- IP and patent life
- YES
- NO

**De-risk Technology for Phase III Investment**
Value based reimbursement

Cost Effectiveness Plane

Incremental Value (QALYs)

Incremental Cost ($s)

BAD

NO

Good

YES

willingness to pay for health
### Evidence Matrix: Type 1 Diabetes

#### Unstable Type 1 Diabetes
**Islet beta cell transplantation – donor harvested**

- **Safety**
- **Effectiveness**
- **Cost of Goods**

<table>
<thead>
<tr>
<th>Islet Transplant?</th>
<th>Current</th>
<th>Future</th>
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</thead>
<tbody>
<tr>
<td>Beta Cell Transplant</td>
<td></td>
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<tr>
<td>Insulin</td>
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<tr>
<td>Insulin Pumps</td>
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<tr>
<td>Bone Marrow Transplant</td>
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<tr>
<td>Artificial Pancreas</td>
<td></td>
<td></td>
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<tr>
<td>Beta Cell 2</td>
<td></td>
<td></td>
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<tr>
<td>Intensive Insulin Therapy</td>
<td>X</td>
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<td>Insulin Pumps</td>
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“We” built a model and unpacked the Cost of Goods
Unpacking the problem: cost of beta cells

- Value of information modeling established max cost/dose for therapy in Canada @ $50,000/QALY and 5% discount rate.
- Was $17,344 without immunosuppression but -$36,039 with immunosuppression.
- Business model (scale-up or scale-out) and manufacturing to meet regulatory burden will determine minimum cost/dose.
- Need to factor in profit-margin.
- But immunosuppression will be major cost driver.
- Apply effort to immunosuppression-free technology prior to phase 3 trials.
More to life than money –
Destroying relationships.

You never count your money
When you're sittin' at the table
Are universities patent trolls?

- Practising/non-practising entities.
- Post-hoc rent seeking behaviour.
- Drives behaviour of risk averse institutions.
- May discourage commercial users.
- But litigation rare.
Decade of University Litigation

461 litigations
590 patents
Patent Trolls
Top 19 Institutions of 118

- University of Texas System
- Boston University
- Stanford University
- Duke University
- University of Utah
- Northwestern University
- National Cheng Kung University
- University of California
- University of Massachusetts
- University of Pennsylvania
- Johns Hopkins University
- Brandeis University
- Queen’s University
- Emory University
- Canada University
- University of Strathclyde
- State University of New York
- New York University

410 as plaintiffs
120 as defendants
Material Transfer Agreements

- MTAs are substantial disincentive to accessing and providing materials for basic and translational research.
- Problematic in context of research and funding timeframes.
- Complexity not proportional to value
- Rarely enforced
- Use simplified agreements.
Make deals to enable partnerships

There'll be time enough for countin'
When the dealin's done
• Operations started in June 2004
• Government agencies, Wellcome Trust, charities & leading pharma companies
• +300-strong team in six countries: Oxford, Toronto, Stockholm, Campinas (Brazil), Chapel Hill (US) & Frankfurt
• Open Access Policy:
  – Promptly placing results, reagents and know-how in the public domain
  – SGC scientists never file patents
Addressing herd behaviour

**A**

Citations in PubMed

**B**

WIPO Patents 2006-2009

Special Communication

*Unintended Consequences of Expensive Cancer Therapeutics—The Pursuit of Marginal Indications and a Me-Too Mentality That Stifles Innovation and Creativity*

The John Conley Lecture

Tito Fojo, MD, PhD, Sham Maitankody, MD, Andrew Lo, PhD

PRE-COMPETITIVE – NON PROPRIETARY

Public-Private-Patient Partnership

Public Domain

Tools & Basic Knowledge

NOVEL Proteins only!
- Structure
- Chemistry
- Antibodies
- Screening
- Cell Assays

Discovery and Exploration
- No patent
- No restriction on use
- Open access to tools and data.
- Target identification & validation

Drug Discovery and Development

Facilitated by access to increased amount of information in the public domain

- (re)Screening
- Lead Optimisation
- Pharmacology
- Metabolism
- Pharmacokinetics
- Toxicology
- Chemical development
- Clinical development

PROPRIETARY

Commercial

GSK
Boehringer Ingelheim
Janssen
Lilly
Bayer
Novartis
Pfizer
Takeda
AbbVie
Oxford
Harvard
UNC
Cambridge
SGC

FREE FROM RESTRICTIONS ON USE

SGC Foundation
Accelerating therapeutic development for Huntington's disease


ChD: Medicine News
Patent-free pact pushes the boundaries of precompetitive research

Elie Dolgin
Published online: 05 June 2014
Concluding thoughts

Every gambler knows
That the secret to survivin'
Is knowin' what to throw away
And knowin' what to keep
'Cause every hand's a winner
And every hand's a loser
And the best that you can hope for....
What does Canadian innovation success look like?
Conclusions

• New collaborative, translational research models gaining momentum, building on respective strengths of innovation stakeholders.
• Needs innovation and flexibility in technology transfer management of intellectual property.
• Specifically, attention on IP management best practices, appropriate metrics, and realistic attention to enforcement and evaluation of value.
• Especially important is enabling partnerships, build trust and enhance social capital.
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