UCLA CTSI Drug Development Series

From the Bench to the Clinic: Therapeutic Drug Development

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Mondays at 4pm

UCLA: NRB auditorium
Charles Drew Univ: Augustus Hawkins Room - 3071
LA BioMed/Harbor: RB3, Room 213

UCLA CTSI

Office of Investigator Services Seminar Series

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Clinical and Translational Research Center and Laboratory - Westwood

Thur March 21, 2013 3:00 – 5:30 pm
Services, funding opportunities, food, raffles and giveaways
CHS BE-144, near the “O” elevators

For more information:  www.ctsi.ucla.edu (310) 794-CTSI  or ois@ctsi.ucla.edu
UCLA CTSI Drug Development Series
From the Bench to the Clinic: Therapeutic Drug Development

The Business of Therapeutics
March 4, 2013

Michael Palazzolo, MD, PhD
UCLA Visiting Professor

www.ctsi.ucla.edu
What is the Goal of this Series?

• Drug discovery is not an academic discipline
  – It is learned by working in Pharma or Biotech
• Life, Morality, Science, and Drug Discovery are all idiosyncratic activities
• This series is my idiosyncratic approach to drug discovery
• I am not trying to convince you that mine is correct
• I am trying to lay a foundation so that you can build your own idiosyncratic approach
• Idiosyncratic strategies are most successful when they are informed and revised by data.
• My underlying idiosyncracy: From the Clinic To the Bench To the Clinic
Overview of Series in Six Parts

• **Business**
  • Drug Discovery Process
  • Targets and Biomarkers
  • Process Mapping and Project Management
  • Strategic Planning
  • Therapeutic Antibodies
Overview of Today’s Presentation on The Business of Drug Discovery

- What are some of the key differences between business and academia?
- What is the process of drug discovery as a scientific enterprise?
- What is the process of drug development as a business enterprise?
What are some of the key differences between business and academia?
- Goals
- Teamwork
- Importance of the clinic trial
- Advisory boards
- Systems approach and platforms

What is the process of drug discovery as a scientific enterprise?

What is the process of drug development as a business enterprise?
Setting Goals

• Research in academia is typically unstructured with a goal of achieving insight.
• Research in industry is about developing products – especially blockbuster products.
A cathedral was a monumental undertaking and took anywhere from 100 to 600 years to complete. Try to imagine this: men and women spent their whole lives working on a project that they would never see completed.
The Interdisciplinary Team

- Therapeutic Specialists
- Disease Specialists
- Legal
- Advisors
- Business
Humans need to see signal in the noise.

Academics publish papers if they can present credible data that suggests sufficient signal.

Drug industry signal has to correlate with and be predictive of success in the clinic.
Almost all biotech company startups and venture capital firms have **SABs**

SABs are composed of people with extensive **track records** of successful product development

Important for **guidance** and **conflict resolution**

Gladwell’s *Outliers*: **10,000 hours** to be world class at something
Amgen’s Secreted Factor Program – 1990s

- Assumptions
  - Most therapeutic proteins were homeostatic regulators
  - Only 1/3 of the genome had been sequences
  - Should be about two dozen more potential products

- Strategy
  - EST sequencing, clone full length, transgenic overexpression, pseudo-clinical workup, targeted translation

- Advantages
  - Directed therapeutic approach
  - Go/No Go decision points

- Was it successful?
Business Overview

• What are some of the key differences between business and academia?

• **What is the process of drug discovery as a scientific enterprise?**
  – Drug discovery
  – Drug development

• What is the process of drug development as a business enterprise?
Clinic to the Bench to the Clinic

Drug Discovery

Drug Development

Celgene

Medscape © http://www.medscape.com
What are some of the key differences between business and academia?

What is the process of drug discovery as a scientific enterprise?

What is the process of drug development as a business enterprise?

- Process and players
- Venture capitalists
- Types of biotech companies
- Value (IP, revenue, profit margin, market cap, royalties)
- Stress in the system
- How can universities benefit?
The **technological bottleneck** is the mechanistic understanding of a disease that can be used to validate therapeutic intervention points. This happens largely in the university. However, the **value transition point** occurs at proof-of-concept in clinical trials in phase I or phase II. This currently takes place in Biotech and Pharma.
What do Venture Capitalists Do?

- Raise money from investors by promising a significant return on their investment.
- Identify new opportunities
- Due diligence
- Assess value
- Build investment syndicates
- Startup companies (board seats)
- Help manage companies to exit
What are the Different Types of Biotech Companies?

- Drug Discovery with Platforms
- Drug Discovery
- Tool/Service Companies
- Devices
- Diagnostics
• Utility Patent:
  A patent granted for one of the following types of inventions: a process, a machine, a manufacture, or a composition of matter (such as new chemical).

• Process:
  A method, operation, or series of actions intended to achieve some end or result. “A process is a way of doing something. If the process is patentable, the result of that process – the something getting done – need not of itself be useful or non-obvious. In other words, the result of an inventive process need not be an invention itself.” *Intellectual Property: Patents, Trademarks, and Copyright in a Nutshell, Miller & Davis, (West Group 2000).*

• Machine:
  A device or apparatus consisting of fixed or moving parts that work together to form some function.

• Manufacture:
  A thing that is made or built by a human being (or by a machine), as distinguished from something that is a product of nature. Examples of manufactures are chairs and tires.

• Composition of Matter:
  A patentable compound of material composed of two or more different substances; a product containing two or more substances, including all composite articles, whether resulting from chemical union or from mechanical mixture, and whether the substances are gases, fluids, powders or solids.

• Dominant & Subservient Patents:
  The language in §101 which permits patents for “any new and useful improvement” of an existing process or product is limited to the new use. The patent for the original process/product is referred to as the *dominant patent* while the patent for the new use is the *subservient patent.*

http://nationalparalegal.edu
Leading Drugs

• Consensus sales forecasts for world's top 10 drugs in 2014:
  1. Avastin (cancer)  Roche  $8.9 bln
  2. Humira (arthritis)  Abbott (ABT.N)  $8.5 bln
  3. Enbrel (arthritis)  Pfizer(PFE.N)/Amgen(AMGN.O)  $8.0 bln
  4. Crestor (cholesterol)  AstraZeneca (AZN.L)  $7.7 bln
  5. Remicade (arthritis)  Merck(MRK.N)/J&J(JNJ.N)  $7.6 bln
  6. Rituxan (cancer)  Roche  $7.4 bln
  7. Lantus (diabetes)  Sanofi-Aventis (SASY.PA)  $7.1 bln
  8. Advair (asthma/COPD)  GlaxoSmithKline (GSK.L)  $6.8 bln
  9. Herceptin (cancer)  Roche  $6.4 bln
  10. NovoLog (diabetes)  Novo Nordisk (NOVO.B.CO)  $5.7 bln

• Consensus forecasts for 2010:
  1. Lipitor (cholesterol)  Pfizer  $11.7 bln
  2. Plavix (anticlotting)  Sanofi/Bristol (BMY.N)  $9.6 bln
  3. Advair (asthma/COPD)  GlaxoSmithKline  $9.0 bln
  4. Remicade (arthritis)  Merck/J&J  $7.4 bln
  5. Enbrel (arthritis)  Pfizer/Amgen  $7.1 bln
  6. Humira (arthritis)  Abbott  $6.8 bln
  7. Avastin (cancer)  Roche  $6.7 bln
  8. Rituxan (cancer)  Roche  $6.1 bln
  9. Diovan (hypertension)  Novartis  $6.0 bln
  10. Crestor (cholesterol)  AstraZeneca  $5.8 bln

http://www.reuters.com
Profit Margins in Health Care

Gilead Sciences (biotechnology): 37.6 percent
Amgen (biotechnology): Profit margin, 30.6 percent
Johnson & Johnson (drug manufacturer): 20.8 percent
GlaxoSmithKline (drug manufacturer): 17.4 percent
Baxter International (medical equipment): 17.5 percent
Pfizer (drug manufacturer): 16.3 percent
Medtronic (medical equipment): 14.9 percent
Covidien (medical equipment): 12.3 percent
Celgene Corp. (biotechnology): 11.9 percent

Quest Diagnostics (healthcare services): 8.7 percent
Unitedhealth Group (healthcare plans): 4.1 percent
WellPoint (healthcare plans): 4 percent
Aetna (healthcare plans): 3.9 percent
Express Scripts (healthcare services): 3.7 percent
MedcoHealth Solutions (healthcare services): 2.1 percent

http://www.healthbeatblog.com
### Top 20 Pharma

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<tr>
<th></th>
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<th>Revenue</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Pfizer</td>
<td>$58,523</td>
</tr>
<tr>
<td>2</td>
<td>Novartis</td>
<td>$44,420</td>
</tr>
<tr>
<td>3</td>
<td>Merck &amp;Co.</td>
<td>$39,811</td>
</tr>
<tr>
<td>4</td>
<td>Sanofi</td>
<td>$37,403</td>
</tr>
<tr>
<td>5</td>
<td>GlaxoSmithKline</td>
<td>$36,156</td>
</tr>
<tr>
<td>6</td>
<td>AstraZeneca</td>
<td>$32,515</td>
</tr>
<tr>
<td>7</td>
<td>Johnson &amp;Johnson</td>
<td>$22,396</td>
</tr>
<tr>
<td>8</td>
<td>Eli Lilly &amp;Co.</td>
<td>$21,685</td>
</tr>
<tr>
<td>9</td>
<td>Abbott Laboratories</td>
<td>$19,894</td>
</tr>
<tr>
<td>10</td>
<td>Bristol-Myers Squibb</td>
<td>$19,484</td>
</tr>
<tr>
<td>11</td>
<td>Teva</td>
<td>$16,121</td>
</tr>
<tr>
<td>12</td>
<td>Takeda Pharma</td>
<td>$14,829</td>
</tr>
<tr>
<td>13</td>
<td>Bayer Schering</td>
<td>$14,485</td>
</tr>
<tr>
<td>14</td>
<td>Boehringer-Ingeheim</td>
<td>$12,883</td>
</tr>
<tr>
<td>15</td>
<td>Astellas</td>
<td>$11,161</td>
</tr>
<tr>
<td>16</td>
<td>Daiichi-Sankyo</td>
<td>$10,794</td>
</tr>
<tr>
<td>17</td>
<td>Eisai</td>
<td>$8,542</td>
</tr>
<tr>
<td>18</td>
<td>Otsuka Pharmaceutical</td>
<td>$8,440</td>
</tr>
<tr>
<td>19</td>
<td>Gilead Sciences</td>
<td>$7,390</td>
</tr>
<tr>
<td>20</td>
<td>Mylan</td>
<td>$5,404</td>
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### Top 20 Device Companies

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<tr>
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<td>Johnson and Johnson</td>
<td>$17.7B</td>
</tr>
<tr>
<td>2</td>
<td>GE Healthcare</td>
<td>$12.1B</td>
</tr>
<tr>
<td>3</td>
<td>Medtronic</td>
<td>$10.1B</td>
</tr>
<tr>
<td>4</td>
<td>Baxter International</td>
<td>$9.8B</td>
</tr>
<tr>
<td>5</td>
<td>Cardinal Health</td>
<td>$9.8B</td>
</tr>
<tr>
<td>6</td>
<td>Tyco Healthcare</td>
<td>$9.5B</td>
</tr>
<tr>
<td>7</td>
<td>Siemens Medical Solutions</td>
<td>$9.2B</td>
</tr>
<tr>
<td>8</td>
<td>Philips Medical Systems</td>
<td>$7.5B</td>
</tr>
<tr>
<td>9</td>
<td>Boston Scientific</td>
<td>$6.3B</td>
</tr>
<tr>
<td>10</td>
<td>Stryker</td>
<td>$4.9B</td>
</tr>
<tr>
<td>11</td>
<td>B. Braun</td>
<td>$3.9B</td>
</tr>
<tr>
<td>12</td>
<td>Guidant Corp.</td>
<td>$3.6B</td>
</tr>
<tr>
<td>13</td>
<td>3M Healthcare</td>
<td>$3.5B</td>
</tr>
<tr>
<td>14</td>
<td>Zimmer Holdings</td>
<td>$3.3B</td>
</tr>
<tr>
<td>15</td>
<td>Becton, Dickinson &amp; Co.</td>
<td>$3B</td>
</tr>
<tr>
<td>16</td>
<td>St. Jude Medical</td>
<td>$2.9B</td>
</tr>
<tr>
<td>17</td>
<td>Kodak Health Group</td>
<td>$2.7B</td>
</tr>
<tr>
<td>18</td>
<td>Hospira</td>
<td>$2.6B</td>
</tr>
<tr>
<td>19</td>
<td>Fresenius</td>
<td>$2.5B</td>
</tr>
<tr>
<td>20</td>
<td>Smith &amp; Nephew</td>
<td>$2.4B</td>
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Patent Issues

• Patents last 20 years – from filing
• Composition of matter is patentable – not targets
  – Pharma tries to invent around competitor compounds and develop me-too drugs
• Generic drug companies move in when patents run out
VCs, Biotech, and Pharma are Under Stress

• “However, although investment in pharmaceutical research and development has increased substantially...the lack of a corresponding increase in terms of new drugs begin approved indicates that therapeutic innovation has become more challenging.

• “venture financing for biotech has been in decline...Some venture capitalists have stopped funding new biotech altogether.”
Who Will Seize the Opportunity in a Changing Landscape?

- If Biotech shrinks and its ability to supplement Pharma’s pipeline is weakened, can a university take advantage and recover value currently captured by VCs and Biotech?

Yes, if it develops an **ecosystem** that **develops** products that have qualities resembling those that emerge from Biotech. In other words, the **IP has to move up to the value transition point**. Can Universities develop drugs comparable to what comes out of biotech?
What are UCLA’s Goals?

- Facilitate the efficiency of translation for society’s benefit
- Do so in a way that increases UCLA’s IRR so that the process moves towards being self-sustaining
  - Had UCLA performed at Columbia’s level in 2009, UCLA would have realized nearly $308,000,000 in licensing income. *
  - Columbia also found that most of their licensing revenues come from a few, rare “blockbusters”*. 
- Blockbusters means therapeutics.

* From Bill Ouchi’s Ecosystem Report
What are the Practical Implications of Moving Down the Value Chain?

- How do these entities fit together to increase efficient translation?
- What are definitions, goals, metrics, methods of coordination?
- This is a much larger discussion.
- The focus of the remainder of this discussion includes some potential concepts for the DGSOM Accelerator.
Recent History of Accelerators

- Harvard
- MIT
- Michigan
- Ontario Genomics Institute
- Campbell Family Institute

- Money, space, and quality of the science are not the rate limiting features to translation. They are necessary but not sufficient.
What do you want the accelerator to do? What will go in it? What are its goals?

• Support the goals of the Ecosystem for Innovation
  – Key goal is to be top tier in IRR
  – Secondary goal is to meet medical needs that are important but will not be met in a strictly commercial environment

• **Accelerator should identify and fill gaps in the Ecosystem to support translation from invention to exit**
Conclusions

• Importance of focused goals
• Interdisciplinary teamwork and management
• Therapeutics biggest potential payoff but higher risk and longer development time
• To reap the highest rewards UCLA should try and move projects to clinical proof of concept where possible and practical
UCLA Clinical and Translational Science Institute

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