Can Financial Engineering Cure Cancer?

Andrew W. Lo, MIT
(joint work with Jose Maria Fernandez and Roger M. Stein)
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Great Progress In Biomedical R&D:

In Gene Sequencing Treatment for Leukemia, Glimpses of the Future

By GINA KOLATA

ST. LOUIS — Genetics researchers at Washington University, one of the world’s leading centers of work on the human genome, were devastated. Dr. Lukas Wartman, a young, talented and accomplished colleague, had the very cancer he had devoted his career to studying. He was deteriorating fast. No known treatment could save him. And no one, to their knowledge, had ever investigated the complete genetic makeup of a cancer like his.

- 2012: Dr. Lukas Wartman, Wash U. “cured” of acute lymphoblastic leukemia via RNA analysis
  - FLT3 gene overexpressed; using drug-gene interaction database, identified Sutent
Conundrum

Weak Performance In Biopharma Investments

- January 2002 to January 2012, NYSE/ARCA Pharma Index return: $-1.2\%$
- 2001 to 2010 VentureXpert average biotech IRR: $-1.0\%$

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Conundrum

Why??

- Conjecture: biopharma business model may be broken
- As we get smarter, business risk *increases* (why?)
- Additional uncertainty due to recent economic events
- VC, private equity, and public equity are not ideal

⇒ Funding is declining despite/because of better science

Financial Engineering May Offer A Solution

- Portfolio theory
- Securitization
To get back to long-run average, we need 45% real drop (= 35% nominal drop)

Lessons From The Financial Crisis?

### U.S. Bond Market Debt Issuance ($Billions)

<table>
<thead>
<tr>
<th>Year</th>
<th>Municipal</th>
<th>Treasury¹</th>
<th>Mortgage-Related²</th>
<th>Corporate Debt³</th>
<th>Federal Agency Securities</th>
<th>Asset-Backed</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>185.2</td>
<td>612.4</td>
<td>479.7</td>
<td>343.7</td>
<td>277.9</td>
<td>168.4</td>
<td>2,067.2</td>
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<tr>
<td>1997</td>
<td>220.7</td>
<td>540.0</td>
<td>577.6</td>
<td>466.0</td>
<td>323.1</td>
<td>223.1</td>
<td>2,350.5</td>
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<tr>
<td>1998</td>
<td>286.8</td>
<td>438.4</td>
<td>1,118.1</td>
<td>610.7</td>
<td>596.4</td>
<td>286.6</td>
<td>3,336.9</td>
</tr>
<tr>
<td>1999</td>
<td>227.5</td>
<td>364.6</td>
<td>985.4</td>
<td>629.2</td>
<td>548.0</td>
<td>287.1</td>
<td>3,041.8</td>
</tr>
<tr>
<td>2000</td>
<td>200.8</td>
<td>312.4</td>
<td>660.0</td>
<td>587.5</td>
<td>446.6</td>
<td>281.5</td>
<td>2,488.8</td>
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<tr>
<td>2001</td>
<td>287.7</td>
<td>380.7</td>
<td>1,663.9</td>
<td>776.1</td>
<td>941.0</td>
<td>326.2</td>
<td>4,375.6</td>
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<tr>
<td>2002</td>
<td>357.5</td>
<td>571.6</td>
<td>2,283.0</td>
<td>636.7</td>
<td>1,041.5</td>
<td>373.9</td>
<td>5,264.2</td>
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<tr>
<td>2003</td>
<td>382.7</td>
<td>745.2</td>
<td>3,084.3</td>
<td>775.8</td>
<td>1,267.5</td>
<td>461.5</td>
<td>6,717.0</td>
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<tr>
<td>2004</td>
<td>359.8</td>
<td>853.3</td>
<td>1,879.0</td>
<td>780.7</td>
<td>881.8⁽⁴⁾</td>
<td>651.5</td>
<td>4,524.3</td>
</tr>
<tr>
<td>2005</td>
<td>408.2</td>
<td>746.2</td>
<td>2,182.4</td>
<td>752.8</td>
<td>669.0</td>
<td>753.5</td>
<td>5,512.1</td>
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<tr>
<td>2006</td>
<td>386.5</td>
<td>788.5</td>
<td>2,088.8</td>
<td>1,058.9</td>
<td>747.3</td>
<td>753.9</td>
<td>5,823.9</td>
</tr>
<tr>
<td>2007</td>
<td>429.3</td>
<td>752.3</td>
<td>2,186.2</td>
<td>1,127.5</td>
<td>941.8</td>
<td>509.7</td>
<td>5,946.8</td>
</tr>
<tr>
<td>2008</td>
<td>389.5</td>
<td>1,037.3</td>
<td>1,362.2</td>
<td>707.2</td>
<td>984.5</td>
<td>139.5</td>
<td>4,620.2</td>
</tr>
<tr>
<td>2009</td>
<td>409.8</td>
<td>2,185.5</td>
<td>2,041.4</td>
<td>901.8</td>
<td>1,117.0</td>
<td>150.9</td>
<td>6,806.4</td>
</tr>
<tr>
<td>2010</td>
<td>433.1</td>
<td>2,303.9</td>
<td>1,742.7</td>
<td>1,062.7</td>
<td>1,032.6</td>
<td>109.4</td>
<td>6,684.5</td>
</tr>
</tbody>
</table>

¹ Interest bearing marketable coupon public debt.
² Includes GNMA, FNMA, and FHLMC mortgage-backed securities and CMOs and private-label MBS/CMOs.
³ Includes all non-convertible debt, MTNs and Yankee bonds, but excludes CDs and federal agency debt.
⁴ Beginning with 2004, Sallie Mae has been excluded due to privatization.

Source: SIFMA
Lessons From The Financial Crisis?

Who Benefited From This Trend?:

- Commercial banks
- Credit rating agencies (S&P, Moody’s, Fitch)
- Economists
- Government sponsored enterprises
- Homeowners
- Insurance companies (multiline, monoline)
- Investment banks and other issuers of MBSs, CDOs, and CDSs
- Investors (hedge funds, pension funds, mutual funds, others)
- Mortgage lenders, brokers, servicers, trustees
- Politicians
- Regulators (CFTC, Fed, FDIC, FHFA, OCC, OTS, SEC, etc.)

“A Rising Tide Lifts All Boats”
Lessons From The Financial Crisis?

Crises Are Not New (see Reinhart and Rogoff, 2008):

- 18 times since 1974
- 5 big bank-related crises:
  - 1977: Spain
  - 1987: Norway
  - 1991: Finland
  - 1991: Sweden
  - 1992: Japan
- Common themes:
  - Rising housing and stock markets
  - Capital inflows
  - Large public debt
  - Financial liberalization and innovation
Finance Is Becoming More Important
Why?

Innovation Requires Financial Infrastructure!

- Private investment
- Accounting, legal, regulatory structures
- Systemic stability
- Well-functioning capital markets
- Proper design of securities

⇒ Incentives

Fear Works Faster, But Greed Lasts Longer
Why?

Example: The DARPA Network Challenge

- Find 10 red balloons in fixed locations in U.S.
- $40K prize to first team to find all 10 locations
- MIT team won
- 8:52:41!
- How??

⇒ Financial engineering!

- $4,000 per balloon if they won
  = $2,000 to locator +
    $1,000 to person who asked locator +
    $500 to person who asked person + ... 
    + remainder to charity
The Power of Global Capital Markets

Real Home Price Index (1890-2006)

What If We Could Focus This Power For “Good”? 

- Financial engineering with a “conscience”
- Apply expertise to solving society’s biggest challenges
- Finance facilitates collaboration; collective intelligence
- With the proper financial engineering, I believe we can **solve** the following problems in 20 years or less:
  1. Cancer
  2. Energy Crisis
  3. Global Warming

How?
Curing Cancer: Would You Invest?

Typical Drug Development Program:
- $200MM out-of-pocket costs, 10-year approval process
- Probability of success in oncology is 5%
- If successful, annual profits of $2B for 10-year patent
Curing Cancer: Would You Invest?

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- Probability of success in oncology is 5%
- If successful, annual profits of $2B for 10-year patent

\[
E[R] = 11.9\%
\]
\[
SD[R] = 423.5\%
\]
Curing Cancer: Would You Invest?

What If We Invest In 150 Programs Simultaneously?:

- Requires $30B of capital
- Assume programs are IID (can be relaxed)
- Diversification changes the economics of the business:

\[
E[R] = 11.9\%
\]

\[
SD[R] = \frac{423.5\%}{\sqrt{150}} = 34.6\%
\]

- But can we raise $30B??
Curing Cancer: Would You Invest?

What If We Invest In 150 Programs Simultaneously?:

- Given the reduction in risk, debt-financing is possible!

<table>
<thead>
<tr>
<th>Event</th>
<th>Probability</th>
<th>Minimum Year-10 NPV</th>
<th>Maximum Year-0 Proceeds at 3.85% (Aaa as of 2/12)</th>
<th>Maximum Year-0 Proceeds at 5.14% (Baa as of 2/12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least 1 hit:</td>
<td>99.95%</td>
<td>$12,289</td>
<td>$8,423</td>
<td>$7,445</td>
</tr>
<tr>
<td>At least 2 hits:</td>
<td>99.59%</td>
<td>$24,578</td>
<td>$16,846</td>
<td>$14,889</td>
</tr>
<tr>
<td>At least 3 hits:</td>
<td>98.18%</td>
<td>$36,867</td>
<td>$25,268</td>
<td>$22,334</td>
</tr>
<tr>
<td>At least 4 hits:</td>
<td>94.52%</td>
<td>$49,157</td>
<td>$33,691</td>
<td>$29,778</td>
</tr>
<tr>
<td>At least 5 hits:</td>
<td>87.44%</td>
<td>$61,446</td>
<td>$42,114</td>
<td>$37,223</td>
</tr>
</tbody>
</table>

- $16.8B of Aaa debt can be issued
- With securitization, debt capacity is even larger
Simulations

Simulate Historical Investment Performance

- Cost assumptions:

- Historical data for revenues (valuations) and transitions:
  - DEVELOPMENT optimizer (Deloitte Recap, LLC), Center for the Study of Drug Development (Tufts); January 1990 to January 2011: +2,000 ⇒ 733 compounds
  - Bloomberg

- Seven-state Markov chain (PreC, Phases I–III, NDA, APP, WD)
  - Simulation A (PreC to Phase II), Simulation B (Phase III to APP)
  - run 500,000 simulations for each

- Financial structure of the megafund:
  - Senior tranche (5% coupon), junior tranche (8% coupon), equity tranche
  - 7.5-year tenor
  - 0.5% annual management fee,
  - $5B for Simulation A (2:1 leverage), $15B for Simulation B (2.5:1 leverage)
Table 4: Performance summary statistics of the biomedical megafund simulations

<table>
<thead>
<tr>
<th>Variable or summary statistic</th>
<th>Simulation A</th>
<th>Simulation B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All equity</td>
<td>Research-backed obligations</td>
</tr>
<tr>
<td>Number of compounds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preclinical</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Phase 1</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Phase 2</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Phase 3</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Research impact</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of compounds to reach phase 2</td>
<td>52.8</td>
<td>101.7</td>
</tr>
<tr>
<td>Number of compounds sold in phase 3 and NDA</td>
<td>0.9</td>
<td>2.3</td>
</tr>
<tr>
<td>Number of compounds sold once APP</td>
<td>0.6</td>
<td>1.0</td>
</tr>
<tr>
<td>Liabilities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capital ($ millions)</td>
<td>2,500</td>
<td>5,000</td>
</tr>
<tr>
<td>Sonior tranche ($ millions)</td>
<td>—</td>
<td>1,250</td>
</tr>
<tr>
<td>Junior tranche ($ millions)</td>
<td>—</td>
<td>1,250</td>
</tr>
<tr>
<td>Equity tranche ($ millions)</td>
<td>2,500</td>
<td>2,500</td>
</tr>
<tr>
<td>Equity tranche performance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average annualized return on equity</td>
<td>7.2%</td>
<td>8.9%</td>
</tr>
<tr>
<td>Prob. (return on equity &lt; 0 )</td>
<td>17%</td>
<td>20%</td>
</tr>
<tr>
<td>Prob. (return on equity &gt; 5% )</td>
<td>61%</td>
<td>68%</td>
</tr>
<tr>
<td>Prob. (return on equity &gt; 15%)</td>
<td>15%</td>
<td>35%</td>
</tr>
<tr>
<td>Debt tranche performance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senior tranche: default prob., expected loss (bp)</td>
<td>—</td>
<td>1, &lt;1</td>
</tr>
<tr>
<td>Junior tranche: default prob., expected loss (bp)</td>
<td>—</td>
<td>87, 27</td>
</tr>
</tbody>
</table>

bp, units of basis points or 0.01%; prob., probability.

Matlab and R software is available! Source: Fernandez, Stein, Lo (2012)
Is This Realistic?

Drug Royalty Investment Companies Already Exist

- Royalty Pharma, $8B in assets, 19 full-time employees
  - But it only invests in approved (and Phase III) drugs
Is This Realistic?

With Some Imagination, We Can Do Better!

- Imagine creating a $30B “Cure For Cancer” megafund
- Imagine creating an advisory board of experts:
  - Francis Collins, Al Gilman, Eric Lander, Bob Langer, Phil Sharp, Harold Varmus;
- Imagine 10MM households investing $3,000 each
- Imagine corporate pension funds, foundations, endowments, insurance companies investing as well
- Imagine government tax incentives, credit enhancement, etc. (think Fannie Mae, Freddie Mac!)
Is This Realistic?

Is There Capacity From Investors? In 2010:

- U.S. bond market: $35T
- Mutual funds: $12T
- Money-market funds: $1T
- Norwegian sovereign wealth fund: $537B
- CalPERS: $226B
- Target return of 126 public funds (2010): 8%

In 2010, the Size of the Entire VC Industry Was: $176B

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Is This Realistic?

What Are Some of the Potential Challenges?

- **Size**: managing large portfolios of complex R&D projects may require new management and governance structures (e.g., Manhattan Project)
- **Centralization**: must preserve the benefits of diversity as scale increases
- **Capacity**: is the talent pool large enough to match the scale of this venture?
- **Complexity**: can investors understand the risks and rewards of RBOs?
- **Excesses**: if successful, the potential for abuse will also increase
- **Ethics**: how to balance profit motive vs. social objectives for cures?
Conclusion

Don’t Declare War On Cancer...

Put A Price Tag On Its Head Instead!

With Sufficient Scale, We Can Do Well By Doing Good
"Can We Afford Not To Try?"

- heart disease, Alzheimer’s, dementia, diabetes, obesity, H1N1, energy crisis, climate change, solar flares

With the Proper Financial Structure, **Anything** Is Possible!
Thank You!