Buying Cures vs. Renting Health

Andrew W. Lo, MIT

(based on joint work with Jayna Cummings, David Fagnan, John Frishkopf, Jose-Maria Fernandez, Carole Ho, Austin Gromatzky, Ken Kosik, John McKew, Vahid Montazerhodjat, Roger Stein, Richard Thakor, David Weinstock, Nora Yang)

MIT Sloan Reunion Weekend
June 4, 2016
Jimmy Carter says he no longer needs cancer treatments

Former U.S. President Jimmy Carter said on Sunday that he will no longer need treatment for melanoma, a type of skin cancer that had spread to his liver and brain, a spokeswoman said.


REUTERS/SINIEL HALL
"CONVERGENCE: THE FUTURE OF HEALTH" - REPORT RELEASE

Event to be held at the following time, date, and location:

Friday, June 24, 2016
from 9:00 AM to 12:30 PM (EDT)

National Academies of Sciences, Engineering, and Medicine
The Lecture Room
2101 Constitution Avenue, N.W.
Washington, DC 20418
Biomedicine Is At An Inflection Point
Biomedicine Is At An Inflection Point

NYSE/ARCA Pharma, Biotech, and S&P 500 Indexes
5 Dec 1994 to 27 May 2016
Biomedicine Is At An Inflection Point

NYSE/ARCA Pharma, Biotech, and S&P 500 Indexes
5 Dec 1994 to 27 May 2016

S&P 500*
Pharma*
Biotech*

MIT Life Sci Envtc

© 2016 by Andrew W. Lo
All Rights Reserved
So Why Is Funding Declining??

Why??

NIH funding, FY in thousands of
$60,000,000 — $50,000,000 — $40,000,000 — $30,000,000 — $20,000,000 — $10,000,000 — 0

© 2016 by Andrew W. Lo
All Rights Reserved
4 June 2016
The Challenge of Drug Development

Drug Discovery

Clinical Trials

FDA Review

Scale-Up to Manufacturing

Phase IV/Ongoing Research and Monitoring

PRE-DISCOVERY:
BASIC RESEARCH AND SCREENING

TENS OF THOUSANDS OF COMPOUNDS

6

PHASE I

PHASE II

PHASE III

NUMBER OF VOLUNTEERS

20–100

100–500

1,000–5,000

ONE FDA-APPROVED MEDICINE

INDEFINITE

3–6 YEARS

6–7 YEARS

0.5–2 YEARS
The Challenge of Drug Development

Example: Combination Therapies

- 2,800 approved drugs
- 3,918,500 pairs
- 3,654,747,600 triples
- Dosage regimens?

Additional Complexities

- Biomarkers
- Resistance
- Side-effects, litigation
- Pricing, FDA, etc.

Eroom’s Law

- 2,800 approved drugs
- 3,918,500 pairs
- 3,654,747,600 triples
- Dosage regimens?

Additional Complexities

- Biomarkers
- Resistance
- Side-effects, litigation
- Pricing, FDA, etc.
Risk and Reward

Cumulative Return

- U.S. Treasury Bills
- Stock Market
- Pfizer
- Fairfield Sentry
CAPM Betas for Pharma and Biotech, 1926-2014
Daily Returns, 2-Year Rolling Windows

- Pharma
- Biotech
Executive Summary

- Evidence shows that the Cost of Capital for venture backed early stage companies in life sciences is high:
  - Many estimates suggest 20% or higher
- This reflects investors’ expectation of a return sufficient to compensate them for taking on extraordinary risk
Consider The Following Investment Opportunity:

- $200MM investment, 10-year horizon
- Probability of positive payoff is 5% (failure rate = 95%)
- If successful, annual profits of $2B for 10-year patent

\[ \text{E}[R] = 11.9\% \]
\[ \text{SD}[R] = 423.5\% \]
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??
- It depends on the portfolio’s risk/reward profile (correlations are key)
What If We Invest In 150 Programs Simultaneously?:

- With reduced risk, debt-financing is feasible!

<table>
<thead>
<tr>
<th>Event</th>
<th>Probability</th>
<th>Minimum Year-10 NPV</th>
<th>Maximum Year-0 Proceeds at 2.41% (BofAML AA 10-Yr as of 6/1/16)</th>
<th>Maximum Year-0 Proceeds at 2.77% (BofAML A 10-Yr as of 6/1/16)</th>
<th>Maximum Year-0 Proceeds at 4.67% (BofAML Baa 10-Yr as of 6/1/16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least 1 hit</td>
<td>99.95%</td>
<td>$12,289</td>
<td>$9,685</td>
<td>$9,351</td>
<td>$6,136</td>
</tr>
<tr>
<td>At least 2 hits</td>
<td>99.59%</td>
<td>$24,578</td>
<td>$19,370</td>
<td>$18,702</td>
<td>$12,272</td>
</tr>
<tr>
<td>At least 3 hits</td>
<td><strong>98.18%</strong></td>
<td>$36,867</td>
<td>$29,055</td>
<td>$28,053</td>
<td>$18,408</td>
</tr>
<tr>
<td>At least 4 hits</td>
<td>94.52%</td>
<td>$49,157</td>
<td>$38,740</td>
<td>$37,404</td>
<td>$24,543</td>
</tr>
<tr>
<td>At least 5 hits</td>
<td>87.44%</td>
<td>$61,446</td>
<td>$48,425</td>
<td>$46,755</td>
<td>$30,679</td>
</tr>
</tbody>
</table>
Financial Engineering Can Help

Prob($n \geq k$) for Equicorrelated Binomial(150,5%)
Details, Details...

- Do you really need $30 billion?
- Isn’t pharma already doing this?
- Can we afford these new therapies?
- Is there enough capital among investors?
- Are there enough projects and people?
- How do you manage 150 projects?
- Shouldn’t the government be doing this?
- Why hasn’t this already been done?
The Amount of Capital Needed Depends On:

- Cost per shot
- Probability of success
- Duration of trials
- Correlation of shots
- Profits per success

Finance and Biomedical Experts Must Collaborate

- Cultures are very different
- Value created in being able to bridge this gap

Fernandez, Stein, Lo, (NBT 2012)
- Sourcecode available in R and Matlab
Financing translation: Analysis of the NCATS rare-diseases portfolio

David E. Fagnan,¹,2* N. Nora Yang,³ John C. McKew,³† Andrew W. Lo¹,2,4,5†

The portfolio of the National Center for Advancing Translational Sciences (NCATS) rare-diseases therapeutic development program comprises 28 research projects initiated at the preclinical stage. Historical data reveal substantially lower costs and higher success rates but longer preclinical timelines for the NCATS projects relative to the industry averages for early-stage translational medical research and development (R&D) typically cited in literature. Here, we evaluate the potential risks and rewards of investing in a portfolio of rare-disease therapeutics. Using a “megafund” financing structure, NCATS data, and valuation estimates from a panel of industry experts, we simulate a hypothetical megafund in which senior and junior debt yielded 5 and 8%, respectively. The simulated expected return to equity was 14.7%, corresponding to a modified internal rate of return of 21.6%. These returns and the likelihood of private-sector funding can be enhanced through third-party funding guarantees from philanthropies, patient advocacy groups, and government agencies.
Do We Really Need $30 Billion??

Prob($n \geq k$) for IID Binomial(20,$p$)

$p = 30\%$
$p = 15\%$
$p = 10\%$
$p = 5\%$

But can you earn a decent rate of return on investment??
Isn’t Pharma Already Doing This?

The Solution: Our Economic Value Added Analysis Supports Replacing “Research” with “Search”

On current market economics, we estimate that $1 invested in in-licensed compounds will on average deliver 3 times as much value as $1 invested in in-house research.

Migration towards a Search and Development small molecule model lowers Beta and should result in superior returns. Using an Economic Value Added analysis, we have...

- Mylan?
- Allergan? ✗
Abbott 5,900
AstraZeneca 25,733
Bristol-Myers Squibb 5,285
Eli Lilly 6,250
GlaxoSmithKline 8,687
Johnson & Johnson 9,200
Merck & Co. 46,140
Novartis 5,390
Pfizer 16,517
Roche 6,750
Sanofi 7,684
Total 143,536

Source: Bloomberg

Isn't Pharma Already Doing This?

Pharma Job Cuts, 2008–2013

Biogen axes 800-plus jobs to keep Tecfidera sales engine running

Published on FiercePharma (http://www.fiercepharma.com)

October 21, 2015 | By Emily Wasserman
Isn’t Pharma Already Doing This?

NYSE/ARCA Pharma, Biotech, and S&P 500 Indexes
5 Dec 1994 to 27 May 2016
Published on FierceBiotech (http://www.fiercebiotech.com)

**PureTech banks $171M in a London IPO to fund its biotech bets**

June 19, 2015 | By Damian Garde
“...its plan is to acquire majority or significant minority equity positions in private, pre IPO, pre trade sale operating businesses in the life sciences industry.”

Malin raises €330m in stock exchange debut
Flotation of life sciences company is first for Irish Stock Exchange in 2015

Fiona Reddan

“The Ireland Strategic Investment Fund (ISIF), a government fund aimed at supporting economic activity and employment in Ireland, is a 15 per cent shareholder in the company, having invested €50m in Malin’s IPO.”
New Business Models Are Emerging

GEN News Highlights: Jun 25, 2015

London Mayor Proposes $15.7B Biopharma "Megafund"

London Mayor Boris Johnson today invited biopharmas, investors, and other stakeholders to discuss his proposal for a £10 billion ($15 billion) “megafund” intended to support drug development in his city and across the U.K.
New Business Models Are Emerging

April 28, 2016

UBS, MPM Seek Big ‘Impact’ in Cancer Drugs with $471M Fund
By Marie Powers, News Editor, BioWorld Today, April 28, 2016

UBS Wealth Management is getting into the cancer game.

Oct 9, 2015 | Press Release

Washington, D.C. (October 9, 2015) - Today, Rep. Thomas J. Rooney (FL-17) and Rep. Juan Vargas (CA-51) introduced the Rare Disease (RaD) Fund Act of 2015 (H.R. 3731). The creation of this Fund would transform the life sciences industry by implementing a novel financial structure for early stage development. The bill seeks to act as a bridge to the ever-widening funding gap that currently exists between basic research and clinical development.

"The life sciences industry desperately needs help to overcome the "valley of death,"" said Rep. Vargas. "Recent advancements in genetics and biomedicine are leading to incredible research projects and novel therapies with the possibility of changing the lives of many patients who suffer from rare diseases. However, the current lack of financing is leaving many promising therapies gathering dust when they could be saving lives. The RaD Fund would allow for a larger number of biomedical projects to be funded, and thereby increase the likelihood for new cures to be found faster, more efficiently and with greater efficacy."
Can We Afford These Therapies?

DEVELOPING STORY

CEO SLAMMED FOR DRUG "PRICE GOUGING"
CLINTON WEIGHS IN ON "OUTRAGEOUS" 5000% JUMP
There’s a difference between price-gouging and genuine breakthrough therapies

Example: hepatitis C

12-week treatment cures it!

– Cost of liver transplant: $577,000 in 2011
– Value of statistical life: $9.1 million × 2/3?

But 3 million U.S. patients have hepatitis C!
Can We Afford These Therapies?

Sovaldi Is A Bargain, But The Cost Impact Is Huge!

- Suppose we “mortgaged” Sovaldi?

$$84,000 = \frac{P}{r/12} \left[ 1 - \frac{1}{(1 + r/12)^{12n}} \right] \Rightarrow P = \frac{84,000 r/12}{1 - \frac{1}{(1+r/12)^{12n}}}$$

### Monthly Payment

<table>
<thead>
<tr>
<th>Years</th>
<th>1%</th>
<th>3%</th>
<th>5%</th>
<th>10%</th>
<th>15%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$7,038</td>
<td>$7,114</td>
<td>$7,191</td>
<td>$7,385</td>
<td>$7,582</td>
</tr>
<tr>
<td>5</td>
<td>$1,436</td>
<td>$1,509</td>
<td>$1,585</td>
<td>$1,785</td>
<td>$1,998</td>
</tr>
<tr>
<td>10</td>
<td>$736</td>
<td><strong>$811</strong></td>
<td>$891</td>
<td>$1,110</td>
<td>$1,355</td>
</tr>
<tr>
<td>15</td>
<td>$503</td>
<td>$580</td>
<td>$664</td>
<td>$903</td>
<td>$1,176</td>
</tr>
<tr>
<td>30</td>
<td>$270</td>
<td>$354</td>
<td>$451</td>
<td>$737</td>
<td>$1,062</td>
</tr>
</tbody>
</table>
Buying cures versus renting health: Financing health care with consumer credit

Vahid Montazerhodjat,1,2 David M. Weinstock,3,4* Andrew W. Lo

A crisis is building over the prices of new transformative therapies for cancer, HIV, viral infection, and rare diseases. The clinical imperative is to offer these therapies promptly and rapidly as possible. We propose a practical way to increase drug affordability: to establish health care loans (HCLs)—the equivalent of mortgages for large health care providers that allow patients in both multipayer and single-payer markets to access a broad array of therapeutics, including expensive short-duration treatments that are curative in nature. These loans can be paid as a percentage of the clinical benefit they provide, and should help lower per-patient cost while still allowing development of transformative therapies rather than those that offer smaller incremental benefits. Moreover, we propose the use of securitization—a well-known financial engineering method—to finance a large diversified pool of HCLs through both diversified institutional funds and individual households. Numerical simulations suggest that securitization is viable for a wide range of underlying environments and cost parameters, allowing a much broader patient population to access transformative therapies while also aligning the interests of patients, payers, and the maceutical industry.

Senior tranche: 2.1%
Junior tranche: 2.5%
Equity tranche: 12.5%
I Want To Be Harvey Lodish!

Finance Doesn’t Have To Be A Zero-Sum Game

- We can do well by doing good
Thank You!
Additional References


Additional References
