



15.482 Healthcare Finance

Spring 2017

Andrew W. Lo, MIT

Unit 0, Part 1: Current Challenges in
Healthcare Finance

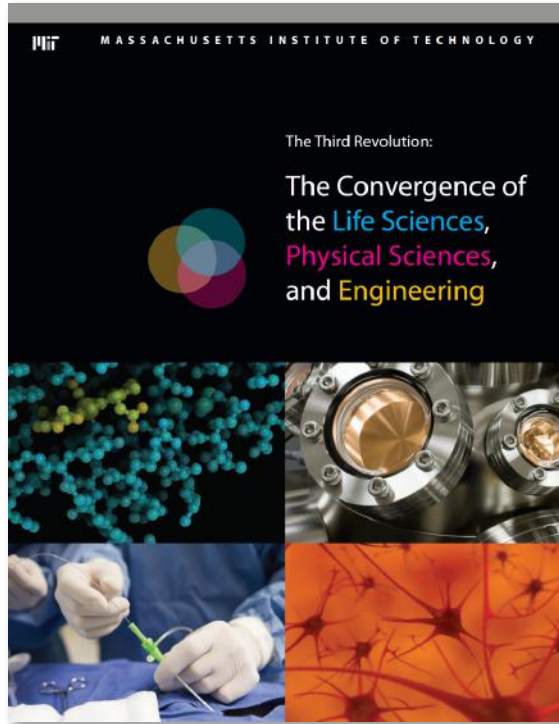
INCURABLE

A Life After Diagnosis



Charles Harris

Biomedicine Is At An Inflection Point



"CONVERGENCE: THE FUTURE OF HEALTH" - REPORT RELEASE

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

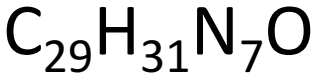
Friday, June 24, 2016
from 9:00 AM to 12:30 PM
(EDT)

**National Academies of
Sciences, Engineering, and
Medicine**

The Lecture Room
2101 Constitution Avenue, N.W.
Washington, DC 20418



Biomedicine Is At An Inflection Point



1998



2001



\$4.7 Billion in 2015



Nicholas Lydon



Brian Druker



Biomedicine Is At An Inflection Point

Series of Breakthroughs In Biomedicine:

- 2001: Gleevec, first of a new class of drugs based on molecular biology (tyrosine kinase inhibitor)
- 2004: Avastin, angiogenesis inhibitor (VEGF)
- 2006: Sutent, approved for RCC and GIST simultaneously
- 2008: First cancer genome (leukemia) sequenced by Wash U. Genome Institute, Nature 456 (2008):66-72.
- 2012: Dr. Lukas Wartman, Wash U. “cured” of acute lymphoblastic leukemia via RNA analysis and Sutent
- 2012: David Aponte “cured” of same type of leukemia using immunotherapy (T-cells targeting CD19)
- 2014: Keytruda approved, PD-1 immunotherapy



Biomedicine Is At An Inflection Point

Series of Breakthroughs In Biomedicine:



FOR IMMEDIATE RELEASE
Aug. 12, 2016

The New York Times

U.S.

Former President Jimmy Carter Is Free of Cancer

By ASHLEY SOUTHWELL

Former 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 EDITION U.S.

HOME BUSINESS MARKETS WORLD POLITICS TECH OPINION BREAKINGVIEWS MONEY LIFE PICTURES VIDEO

Jimmy Carter says he no longer needs cancer treatments

PHOTOS OF THE WEEK

Our top news photography this week. [Slideshow »](#)

[Separatist clashes in Azerbaijan](#)

[Going hungry in Yemen](#)

[The art of Shaolin](#)

[Creatures caught on camera](#)

Former U.S. President Jimmy Carter delivers a lecture on the eradication of the Guinea worm, at the House of Lords in London, Britain February 3, 2016. REUTERS/NEIL HALL

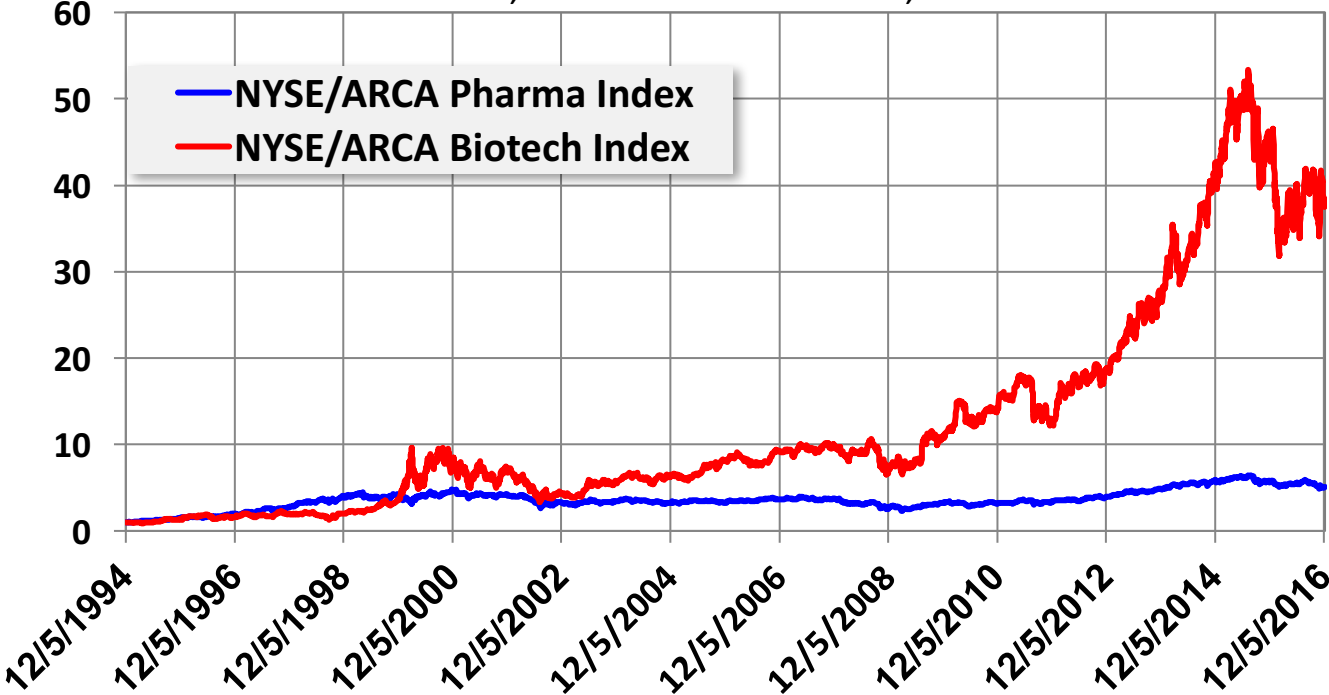
Former U.S. President Jimmy Carter said on Sunday that he will no longer need treatment for melanoma, a type of skin cancer that had spread to his liver and brain, a spokeswoman said.




Biomedicine Is At An Inflection Point

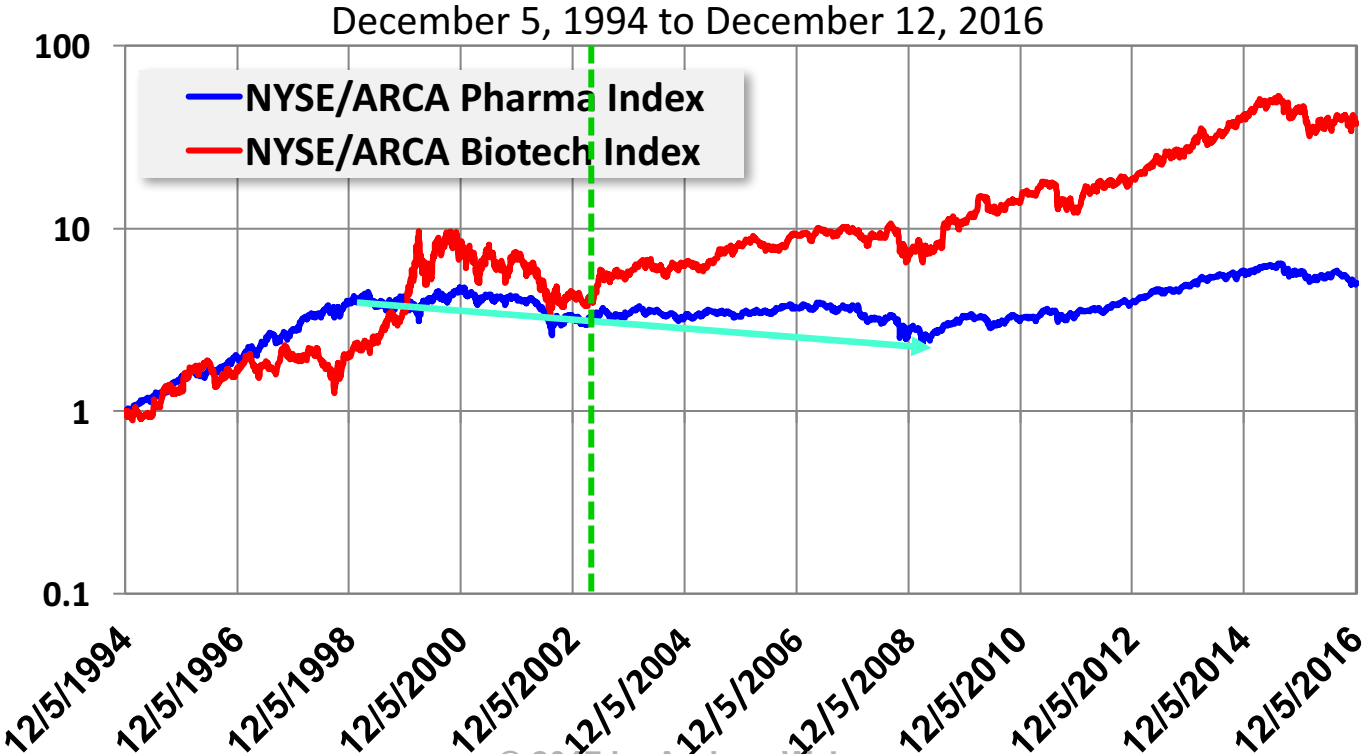
Pharma vs. Biotech

December 5, 1994 to December 12, 2016

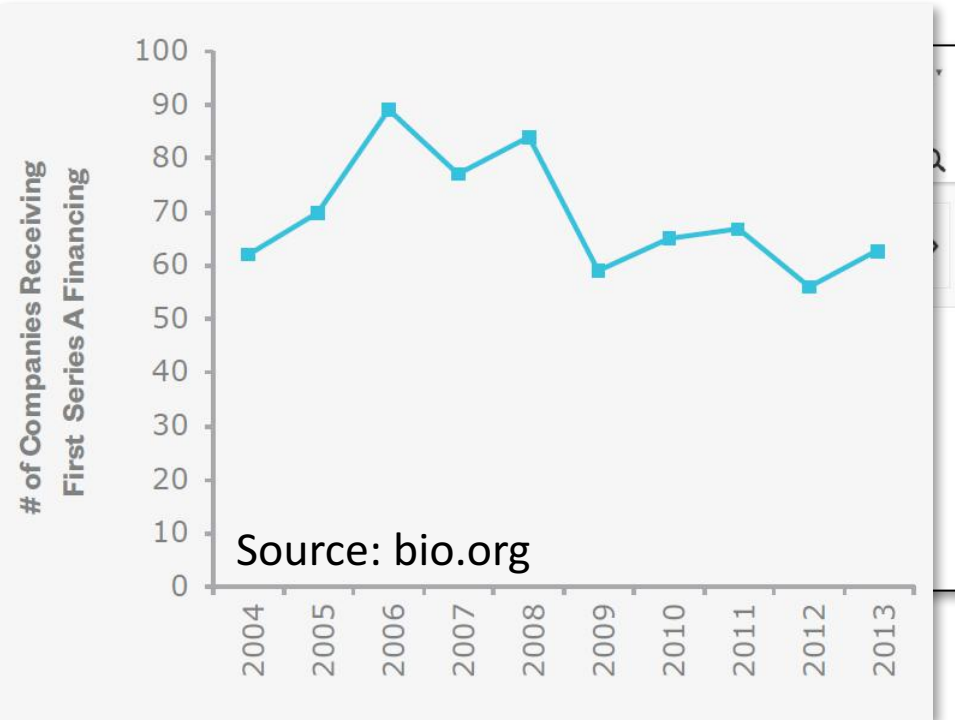
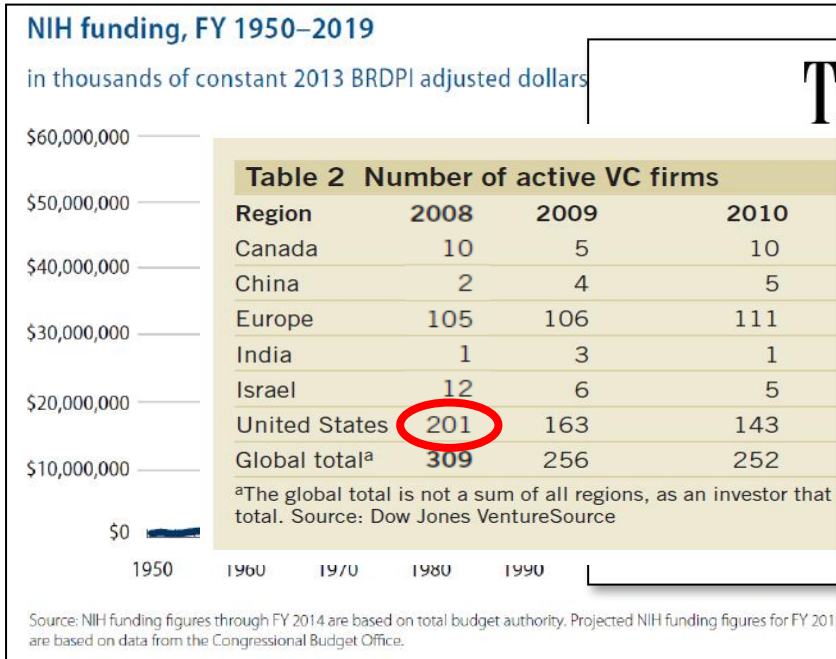


Biomedicine Is At An Inflection Point

Pharma vs. Biotech



So Why Is Funding Declining??



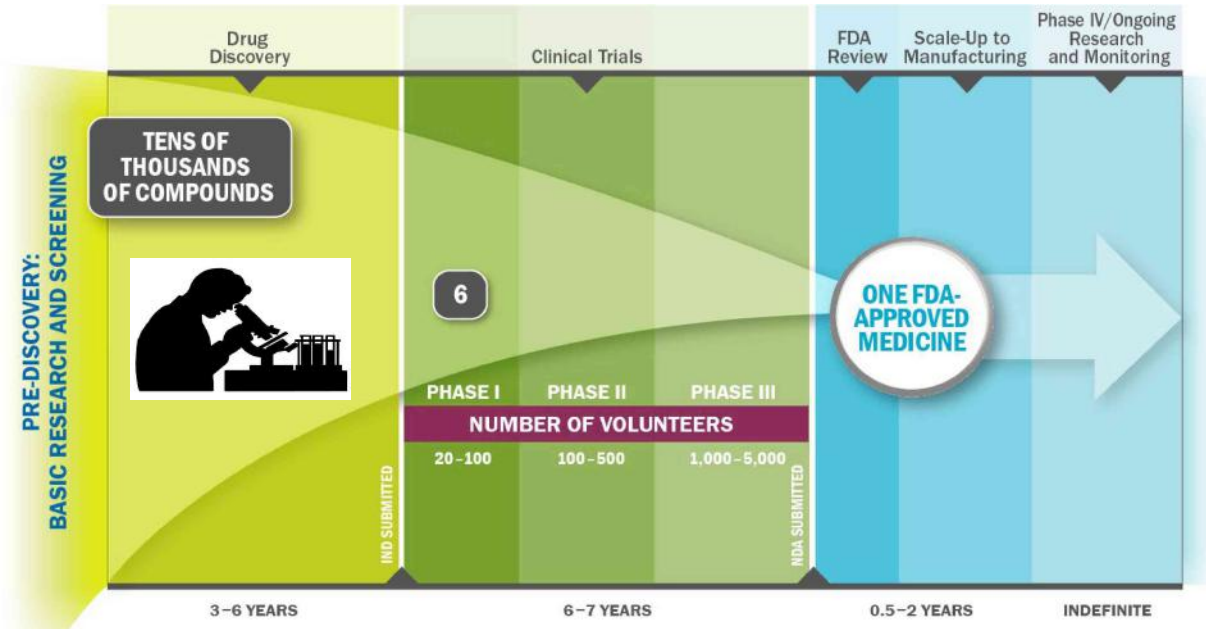
Increasing Risk and Uncertainty

Why??



The Challenge of Drug Development

15.482



3 Features:

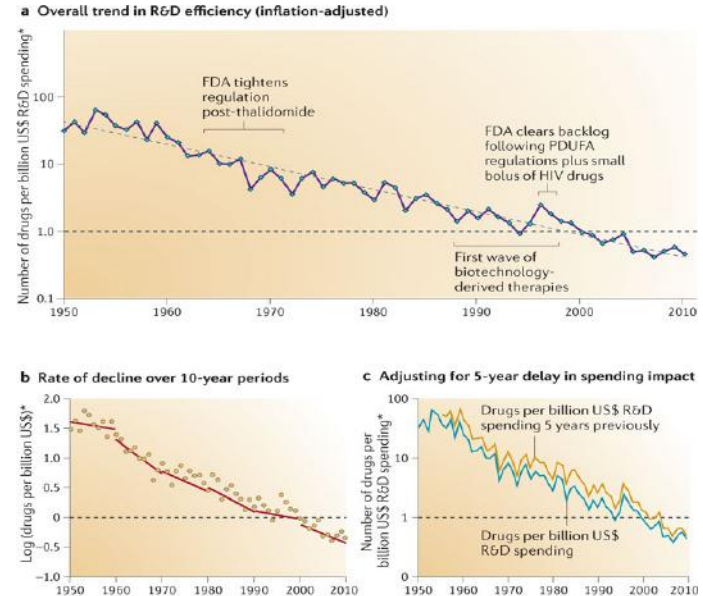
1. Costly
2. Low PoS
3. Long duration

The Challenge of Drug Development

Example: Combination Therapies

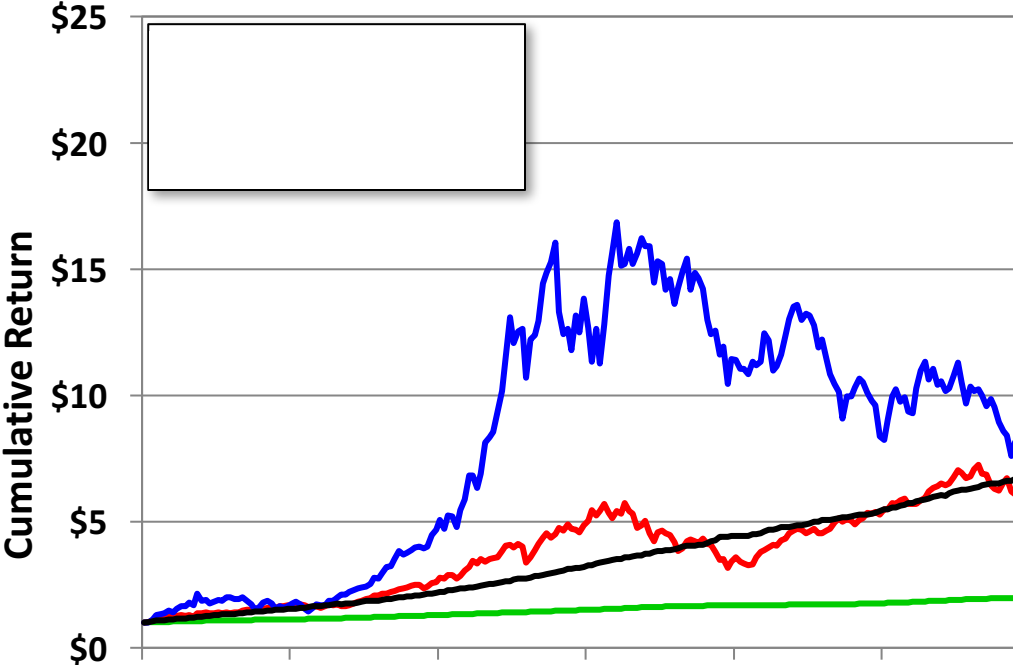
- 2,800 approved drugs
- 3,918,500 pairs
- 3,654,747,600 triplets
- 1,429,081,599,400,560 quintuplets
- Other parameters:
 - Dosage regimens
 - Biomarkers
 - Resistance
 - Side-effects, litigation
 - Pricing, FDA, etc.

Eroom's Law



Source: Scannell et al. (NRDD 2012)

Investment Pop Quiz #1



Investment Pop Quiz #2

Urn A contains 100 balls:

- 50 red, 50 black
- Pick a color, then draw a ball
- If you draw your color, \$10,000 prize
- Which color would you prefer?
- How much would you pay to play?

Investment Pop Quiz #2

Urn B contains 100 balls:

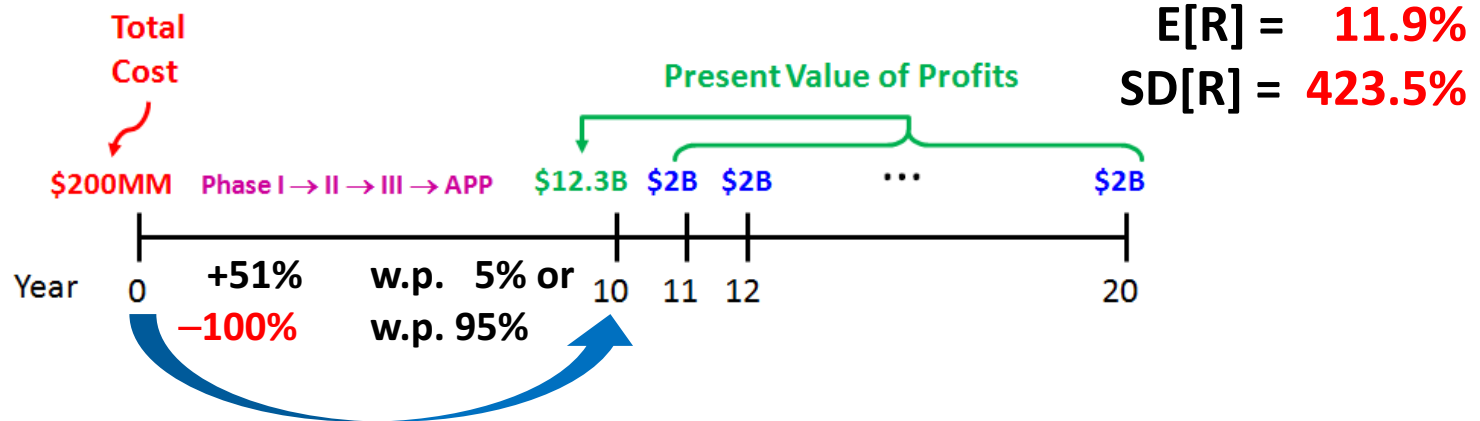
- **Unknown proportion** of black and/or red balls
- Pick a color, then draw a ball
- If you draw your color, \$10,000 prize
- Which color would you prefer?
- How much would you pay to play?

Investors Hate **Uncertainty More Than Risk!**

Investment Pop Quiz #3

Consider The Following Investment Opportunity:

- \$200MM investment, 10-year horizon
- Probability of positive payoff is 5%
- If successful, annual profits of \$2B for 10-year patent



The Consequences of Risk and Uncertainty

| Stakeholder | Challenge | Response |
|-----------------------|---|--|
| Big pharma | Decreasing productivity of R&D, increasing complexity, greater competition, patent cliff, regulatory and political uncertainty | Sell mature drugs, raise cash, reduce R&D, acquire new technologies via in-licensing and M&A |
| Biotech VC | Higher startup costs, longer time to milestones, increasing complexity, lower risk tolerance of LPs, uncertainty of second-round financing, competition | Re-allocate investments away from biotech toward better-performing lower-cost sectors such as software, energy, infrastructure, etc. |
| Biotech Entrepreneurs | Scarcer startup capital, less patient capital, more onerous terms, fewer “home runs” | Focus on “hot” areas, propose less challenging targets with clearer market value |
| NIH | Declining funding, increasing real cost of research, increasing risk of government dysfunction and oversight | Award grants to PIs with “proven” track records, shorter time-to-delivery, less speculative research |
| Academia | Less grant money, fewer job opportunities, uncertain career paths | Take finance at Sloan and go to Wall Street |

What Do Investors Want?



High Returns and Low Risk ➔ High Sharpe

Example: which would you prefer as an investor?

- “me-too” oncology drug in Phase 3
- blinatumomab + chemo to **cure** ALL

What Do Investors Want From Biotech?

The Cost of Capital for Stage Biotechnology

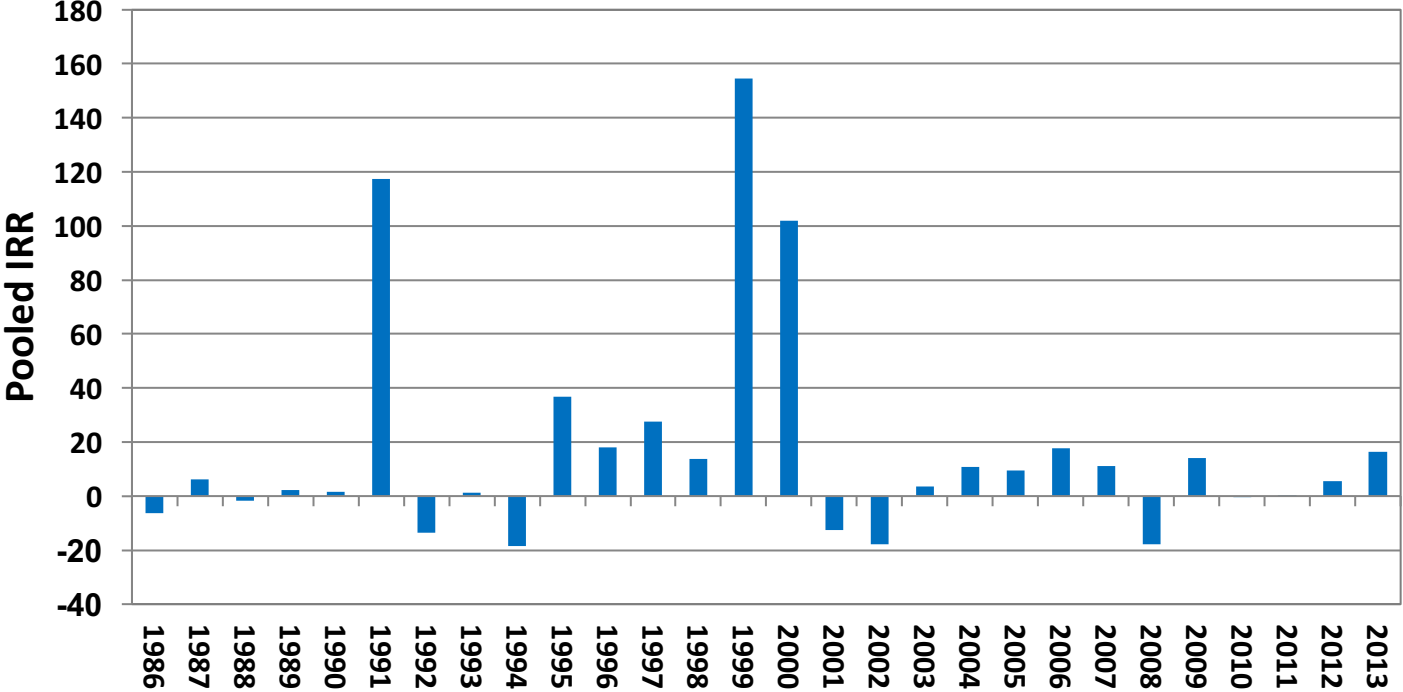
Iain Cockburn and Josh
Boston University and Harvard

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

What Do Investors Want From Biotech?

VentureXpert Biotech VC Pooled IRR



What Do Investors Want From Pharma?



Contents lists available at [ScienceDirect](#)

Journal of Corporate Finance

journal homepage: www.elsevier.com/locate/jcorpfin



New estimates of the cost of capital for pharmaceutical firms[☆]

Carmelo Giaccotto^{a,*}, Joseph Golec^b, John Vernon^{c,d}

^a Department of Finance and Center for Healthcare and Insurance Studies, University of Connecticut, School of Business, 2100 Hillside Road, Unit 1041, Storrs, CT 06269-1041, United States

^b Center for Healthcare and Insurance Studies, University of Connecticut, School of Business, 2100 Hillside Road, Unit 1041, Storrs, CT 06269-1041, United States

^c Department of Health Policy and Management, University of North Carolina at Chapel Hill, United States

^d National Bureau of Economic Research (NBER), United States

***Journal of Corporate Finance* 2011(17), 526–540.**

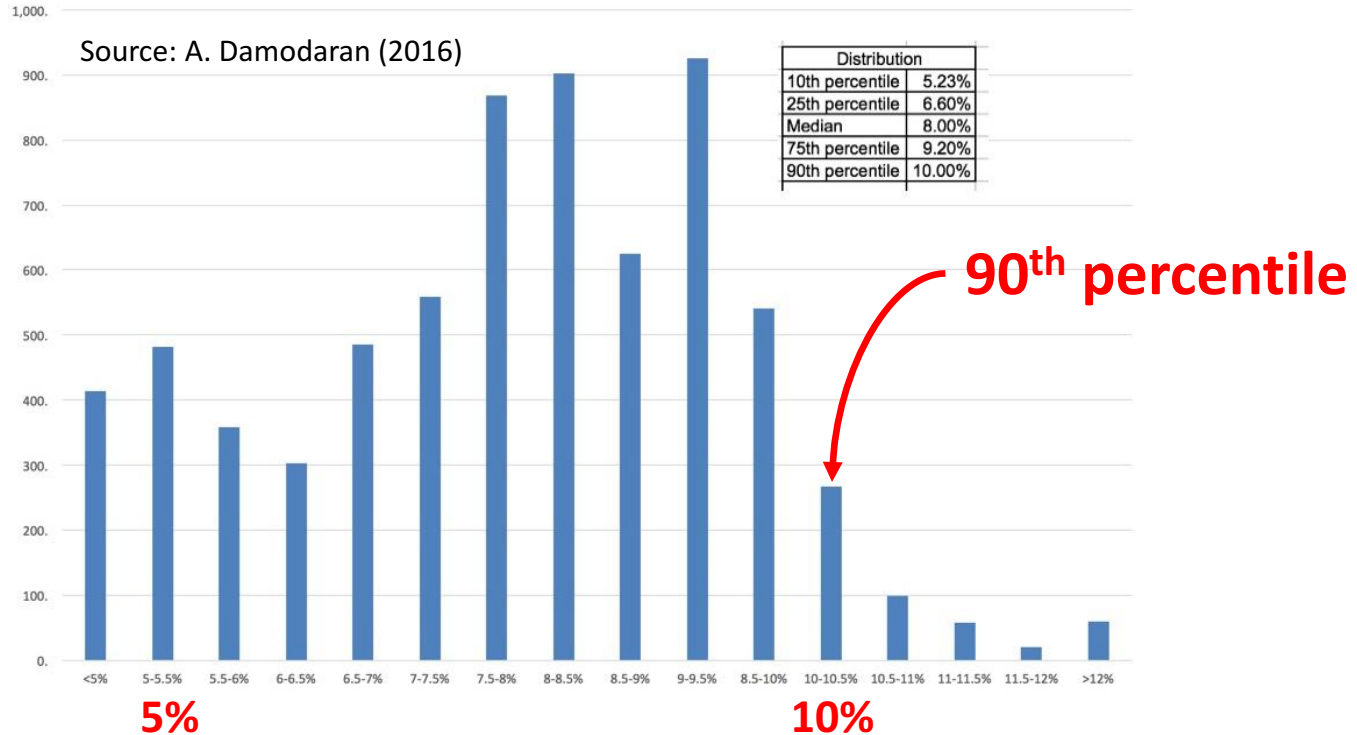
What Do Investors Want From Pharma?

| Company | 10-Year Estimated Cost of Capital | 90% Confidence Interval |
|--------------------------|--|------------------------------------|
| Abbott Labs | 10.5% | [8.8% , 12.2%] |
| Balchem Corp | 10.7% | [8.6% , 12.5%] |
| Bausch & Lomb | 11.3% | [9.3% , 13.4%] |
| Bristol Myers Squibb | 10.5% | [9.1% , 12.7%] |
| Chattem | 13.6% | [10.9% , 15.4%] |
| Eli Lilly | 11.5% | [9.1% , 13.2%] |
| Forest Labs | 13.9% | [11.6% , 16.6%] |
| Johnson & Johnson | 10.0% | [8.4% , 11.9%] |
| Merck | 10.8% | [8.7% , 12.3%] |
| Mylan Labs | 12.4% | [10.0% , 14.7%] |
| Nabi Biopharmaceuticals | 13.0% | [10.3% , 15.2%] |
| Novo Nordisk | 10.4% | [8.6% , 12.0%] |
| Pfizer | 12.0% | [9.8% , 14.9%] |
| Pharmacia | 12.9% | [10.5% , 15.7%] |
| Schering-Plough | 10.7% | [8.8% , 12.6%] |
| Sigma-Aldrich | 10.3% | [8.1% , 11.6%] |
| Wyeth | 11.1% | [9.2% , 13.0%] |
| Value-Weighted Portfolio | 11.3% | [9.5% , 12.9%] |

Source: Giaccotto, Golec, Vernon (2011, Table 3)

What Do Investors Want From Pharma?

Cost of Capital for U.S. Companies, Jan 2016



Financial Engineering Can Help

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:

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

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

- But can we raise \$30B??
- It depends on the portfolio's risk/reward profile (correlations?)

Financial Engineering Can Help

What If We Invest In 150 Programs Simultaneously?:

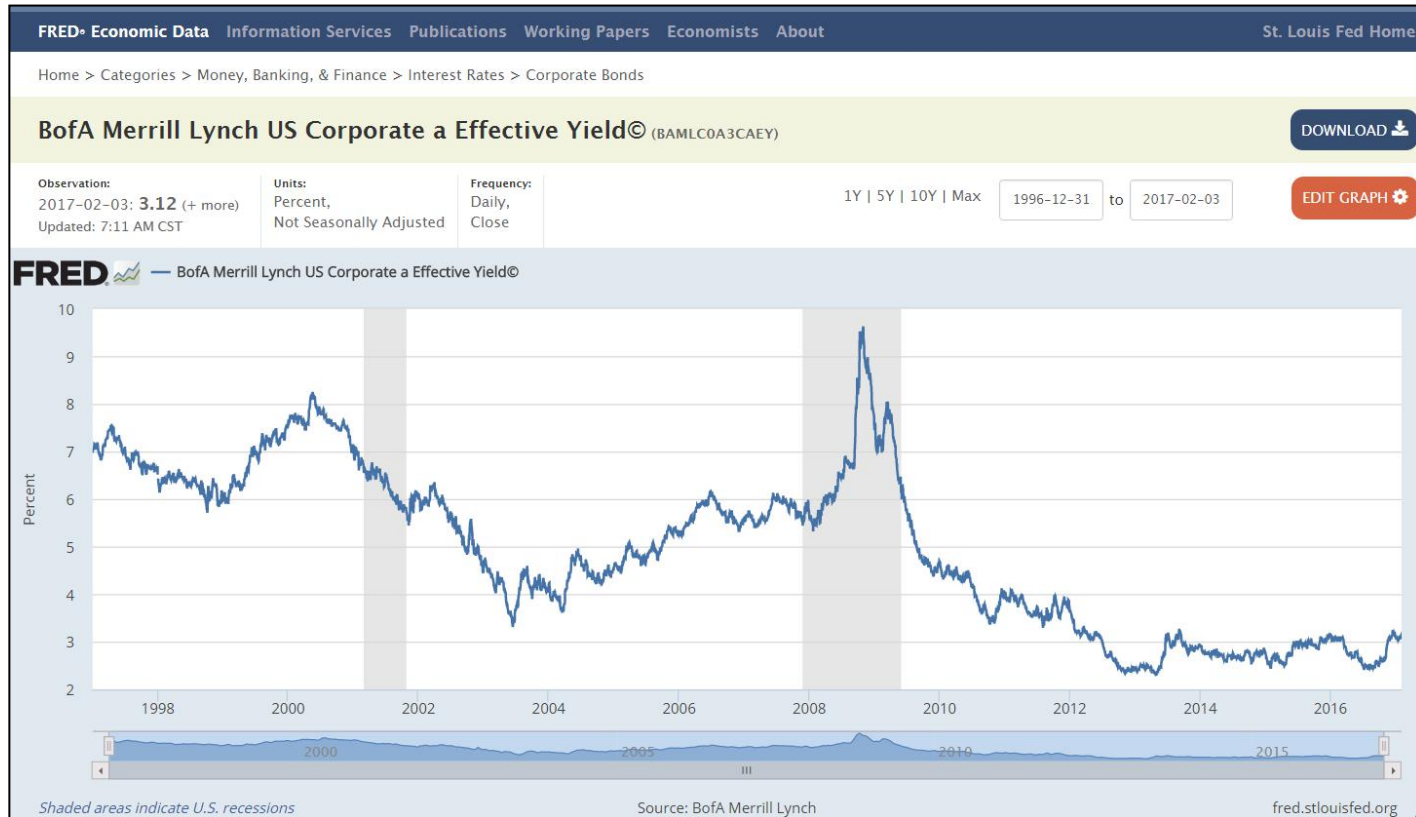
- With reduced risk, debt-financing is feasible!



| Event | Probability | Minimum Year-10 NPV | Maximum Year-0 Proceeds at 2.76% (BofAML AA 10-Yr as of 2/2/17) | Maximum Year-0 Proceeds at 3.11% (BofAML A 10-Yr as of 2/2/17) | Maximum Year-0 Proceeds at 3.77% (BofAML BBB 10-Yr as of 2/2/17) |
|------------------|-------------|---------------------------|--|--|---|
| At least 1 hit: | 99.95% | \$12,289 | \$9,360 | \$9,047 | \$6,465 |
| At least 2 hits: | 99.59% | \$24,578 | \$18,720 | \$18,094 | \$12,930 |
| At least 3 hits: | 98.18% | \$36,867 | \$28,080 | \$27,142 | \$19,395 |
| At least 4 hits: | 94.52% | \$49,157 | \$37,440 | \$36,189 | \$25,860 |
| At least 5 hits: | 87.44% | \$61,446 | \$46,800 | \$45,236 | \$32,325 |

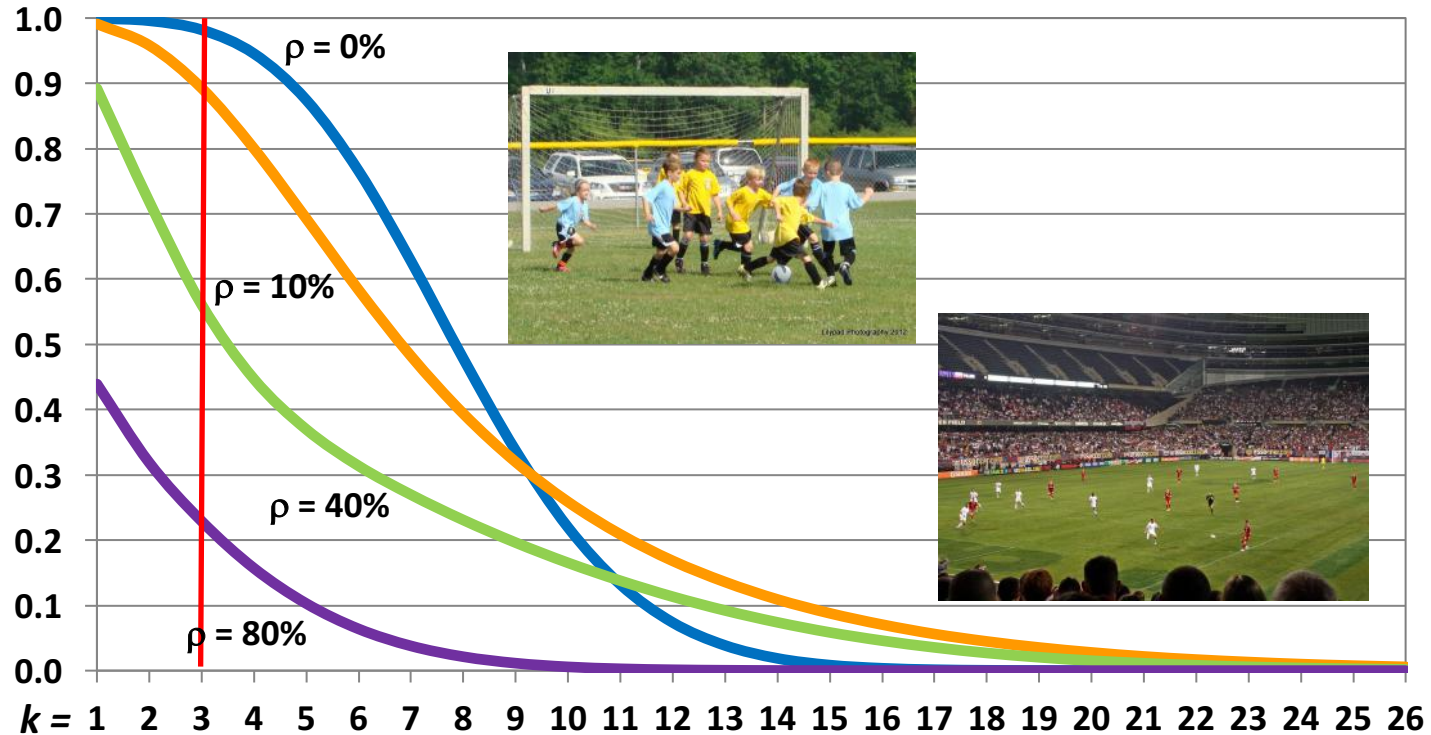
Financial Engineering Can Help

15.482



Financial Engineering Can Help

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



FAQs (details, details...)

- Do we really need \$30 billion?
- What's the market failure; why hasn't this been done already?
- Isn't pharma already doing this? If not, isn't government doing it?
- Is there enough capacity (projects, capital, and people)?
- Isn't biomedicine too complex to manage as a large portfolio?
- Are there any other similar industries that use these techniques?
- How about drug pricing? Can we afford these therapies?
- What role can/should government play?
- Are there existing examples of megafunds?

Short Answer

15.482



Short Answer

15.482

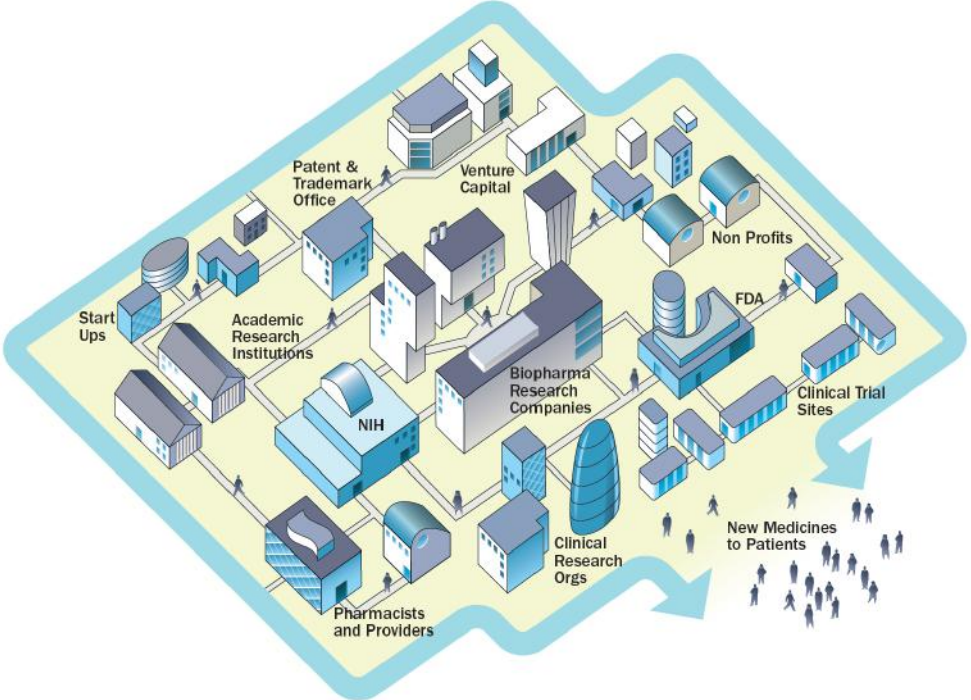


Long Answer

- Cancer: Fernandez, Stein, Lo (NBT, 2012)
- Guarantees: Fagnan, Stein, Fernandez, Lo (AER, 2013)
- Orphan drugs: Fagnan, Gromatzky, Stein, Lo (DDT, 2014)
- Alzheimers: Lo, Ho, Cummings, Kosik (STM, 2014)
- NCATS: Fagnan, Yang, McKew, Lo (STM, 2015)
- Dynamic leverage: Montazerhodjat, Frishkopf, Lo (DDT, 2015)
- Drug mortgages: Montazerhodjat, Weinstock, Lo (STM, 2016)
- Current research: FDA approval process, historical success rates, risk/reward of biopharma, case studies, etc.

 **15.482 Healthcare Finance**

Biopharma Ecosystem



Source: TEconomy/BIO, 2016, *The Value of Bioscience Innovation in Growing Jobs and Improving Quality of Life*, Figure 15.