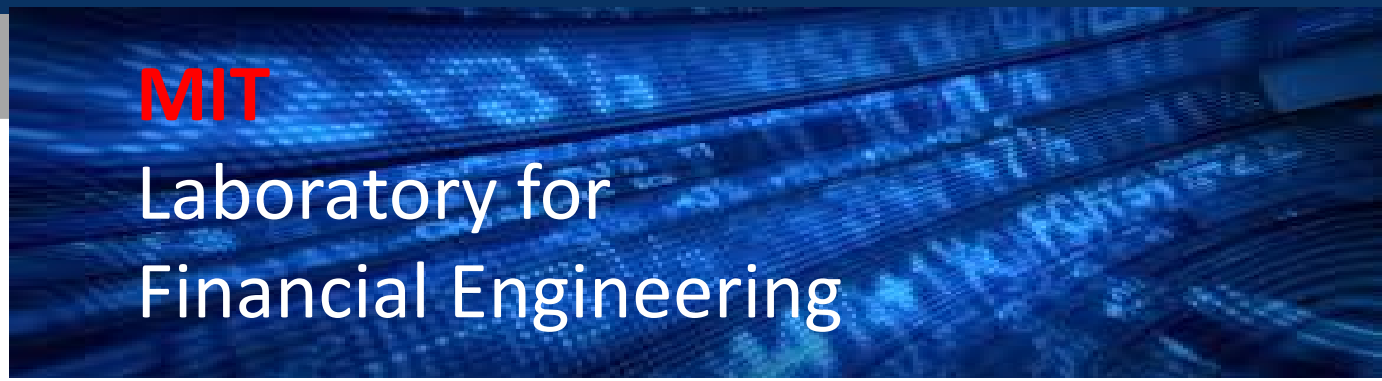
Can Financial Engineering Cure Cancer?

Andrew W. Lo, MIT

Tangerine Lecture in Finance

November 3, 2016



Paradox

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

So Why Is Funding Declining??

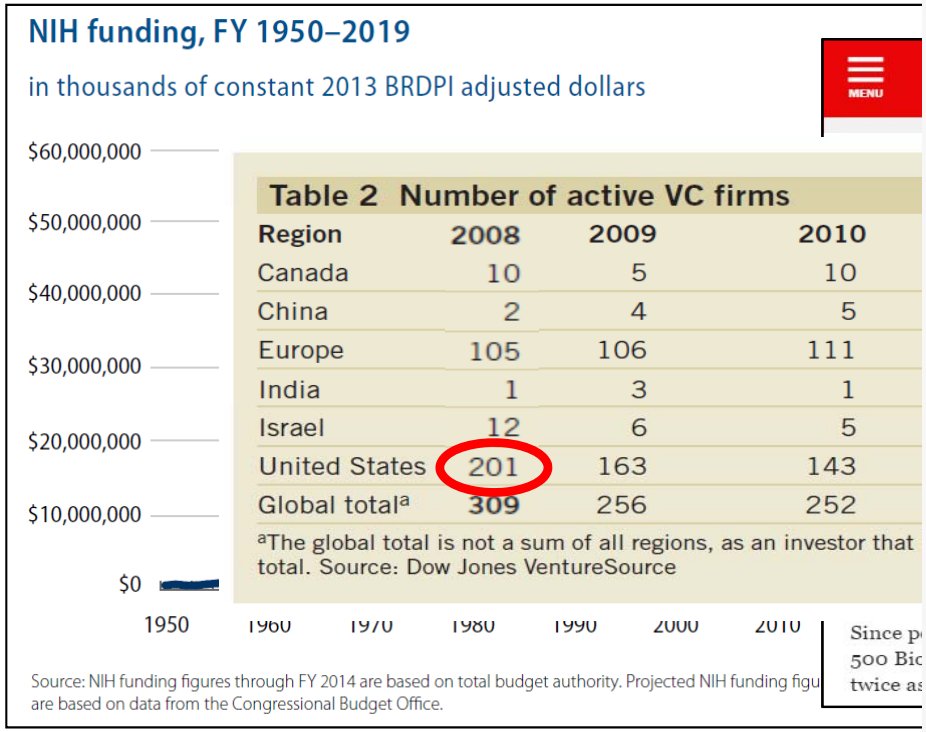
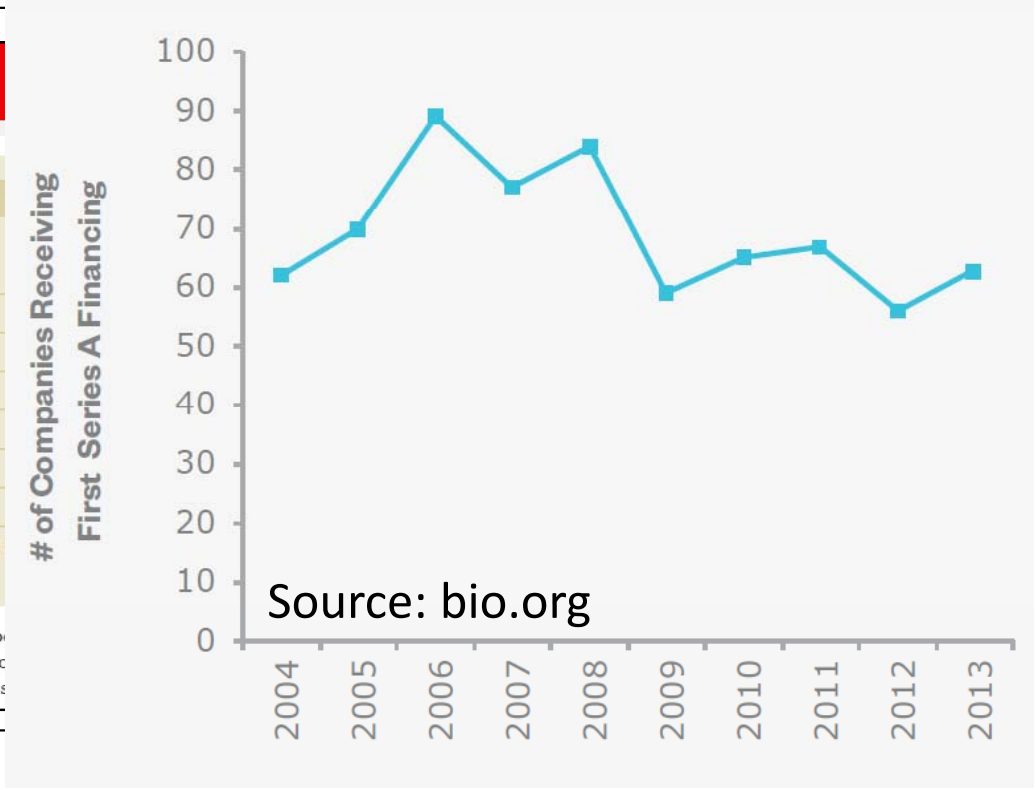


Table 2 Number of active VC firms

Region	2008	2009	2010
Canada	10	5	10
China	2	4	5
Europe	105	106	111
India	1	3	1
Israel	12	6	5
United States	201	163	143
Global total[a]	309	256	252

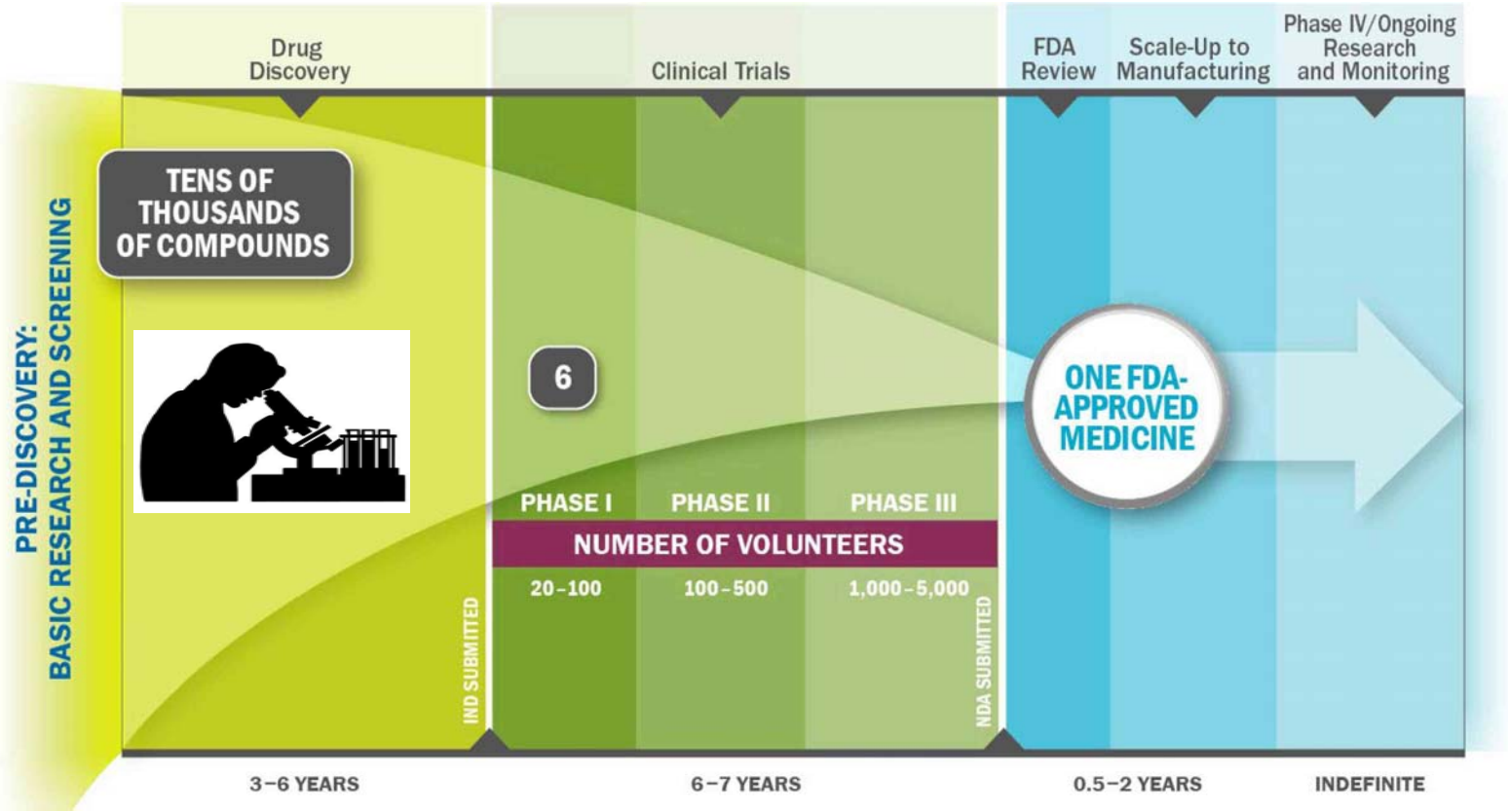
[a]The global total is not a sum of all regions, as an investor that total. Source: Dow Jones VentureSource



Why??

Increasing Risk and Uncertainty

The Challenge of Drug Development

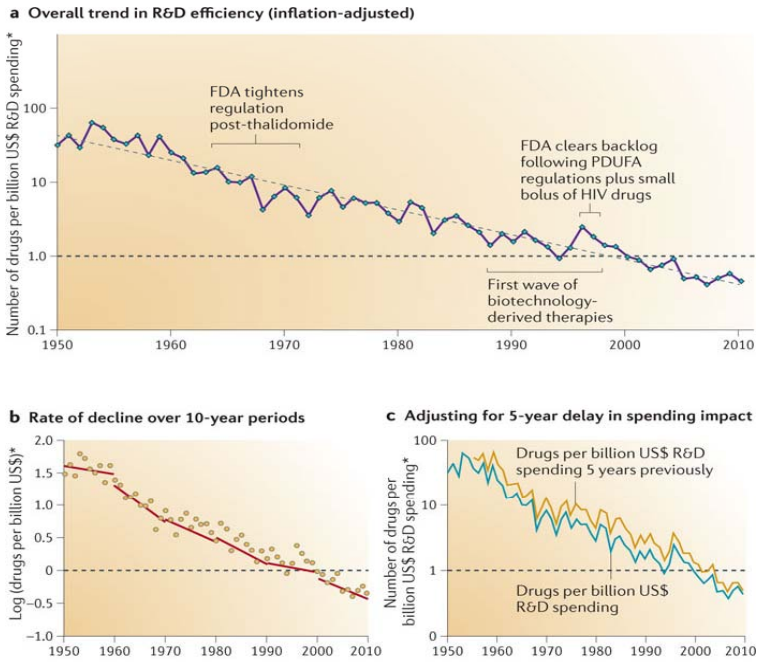


The Challenge of Drug Development

Example: Combination Therapies

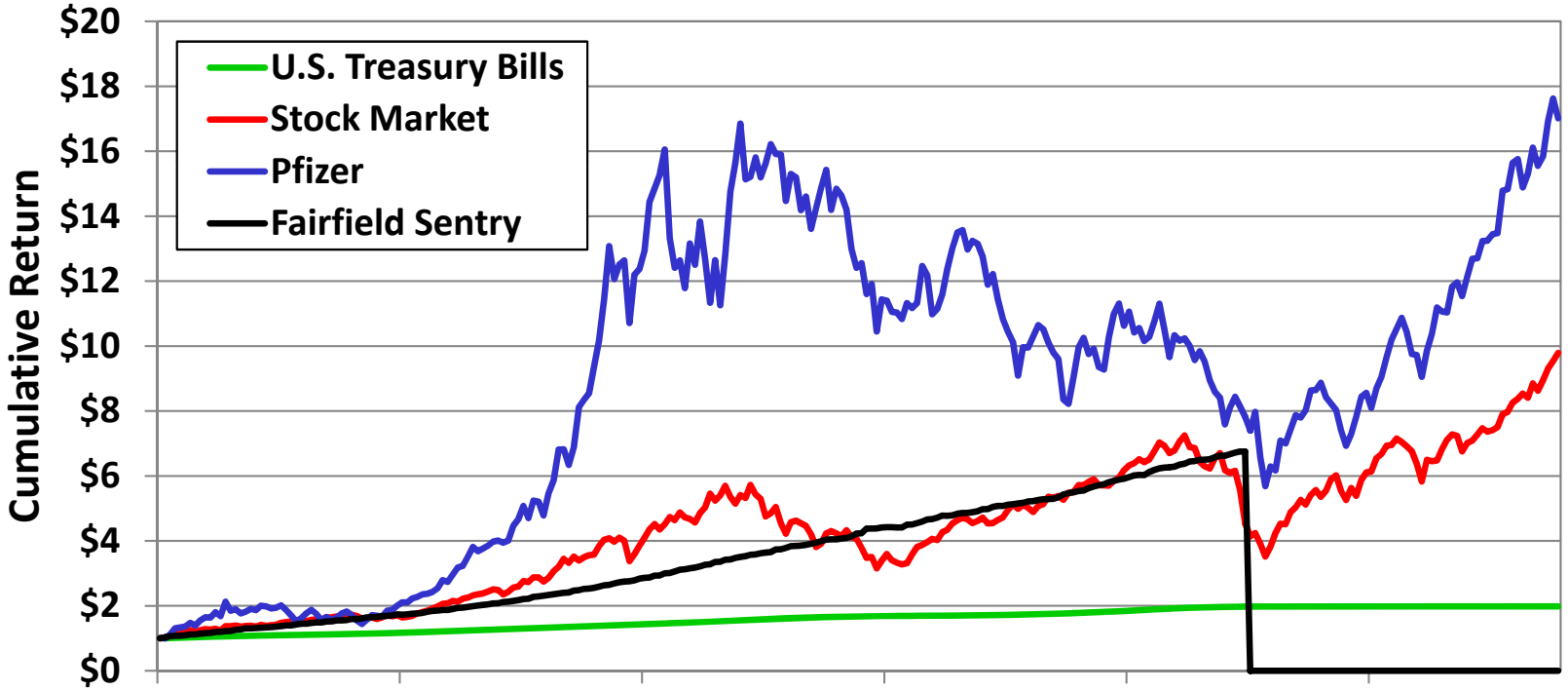
- 2,800 approved drugs
- 3,918,500 pairs
- 3,654,747,600 triples
- Other parameters:
  - Dosage regimens?
  - Biomarkers?
  - Resistance?
  - Side-effects, litigation?
  - Pricing, FDA, etc. ?

Eroom's Law



Source: Scannell et al. (NRDD 2012)

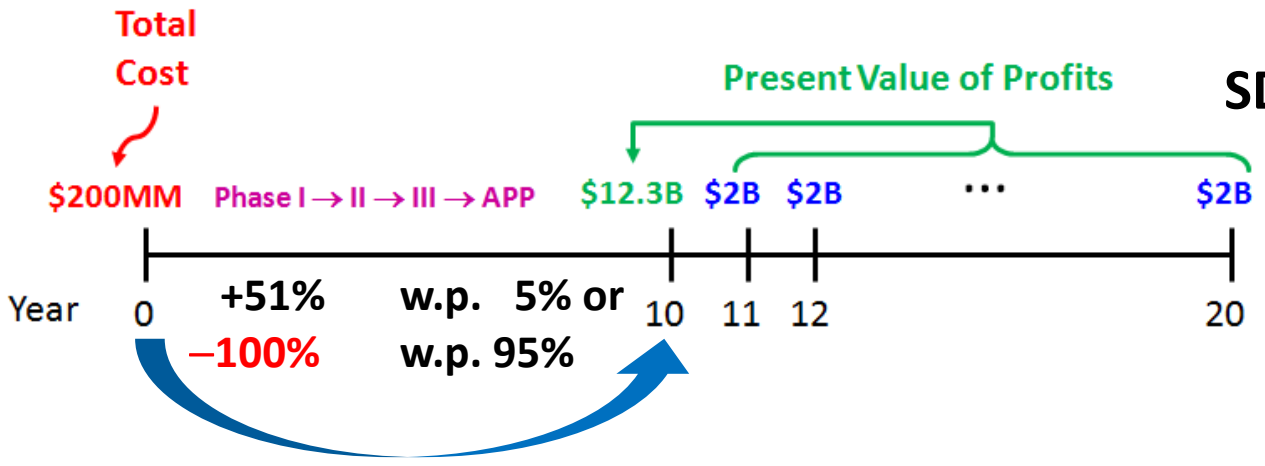
Risk and Reward



Risk and Reward

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



E[R] = 11.9%

SD[R] = 423.5%

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:

$$\mathrm{E}[R] = 11.9\%$$

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

- But can we raise $30B??
- It depends—how risky is it? (correlations matter here!)

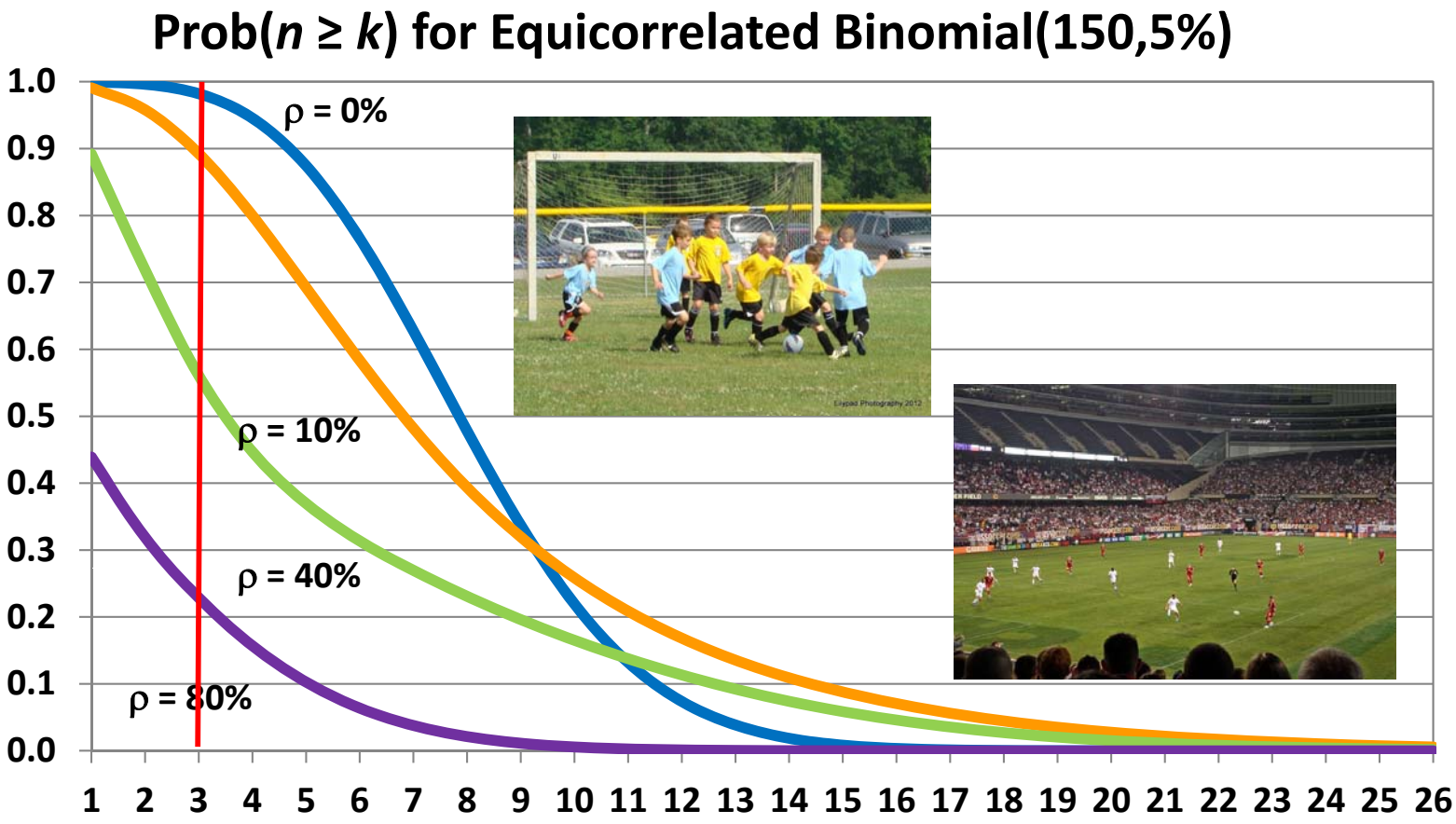
Financial Engineering Can Help

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 2.33% (BofAML AA 10-Yr as of 11/1/16)	Maximum Year-0 Proceeds at 2.65% (BofAML A 10-Yr as of 11/1/16)
At least 1 hit:	99.95%	$12,289	$9,761	$9,461
At least 2 hits:	99.59%	$24,578	$19,522	$18,922
At least 3 hits:	98.18%	$36,867	$29,283	$28,383
At least 4 hits:	94.52%	$49,157	$39,044	$37,844
At least 5 hits:	87.44%	$61,446	$48,805	$47,304

Financial Engineering Can Help



Financial Engineering Can Help

Other applications:

- Pool and securitize multiple biomedical projects to appeal to a new pool of investors (including pension funds, hedge funds, sovereign wealth funds, patient advocacy groups, etc.); $39 trillion vs. $199 billion
- Launch retail vehicles (BDCs) dedicated to specific diseases that allow individual investors to participate; $3,000 per household
- Offer new derivative securities to reduce the risk of the drug development process (guarantees, credit default swaps, “FDA swaps”, etc.)
- Explore public/private partnerships with government agencies, e.g., NCATS
- Develop better financial models of megafund risk and return

FAQs

- Do we really need $30 billion?
- Is there enough capital among investors?
- Can we afford these new therapies?
- Isn't pharma already doing this?
- 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?

Some Answers

- Cancer: Fernandez, Stein, Lo (NBT, 2012) **Open-source software**
- 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)
- Work-in-progress: FDA approval process, historical success rates, risk/reward of biopharma, case studies

Do We Really Need $30 Billion?

The Amount of Capital Needed Depends On:

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

→ Fernandez, Stein, Lo, (NBT 2012)

- Sourcecode available in R and Matlab

Finance and Biomedical Experts Must Collaborate

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

Orphan Diseases

- Often due to mutation in a single gene
- e.g. Huntington's, cystic fibrosis, Gaucher, paroxysmal nocturnal hemoglobinuria
- 25 million Americans suffer from all rare diseases
- Smaller population, urgent need, higher prices, lower development costs, higher success rates (20%), faster time to approval (3–7 years)
- $400–$500 million of capital and 10–20 projects sufficient

And Now The Bad News…

For Alzheimer's, $30 Billion May Not Be Enough!

- Lo, Ho, Cummings, Kosik (STM, 2014)
- 13-year development time, not 10; $500M to $600M in out-of-pocket costs; probability of success $\leq$ 5%
- But not enough "shots on goal" (beta amyloid, tau)
  - Correlated shots provide less risk reduction
- Basic science is not as developed as in oncology
- We have to "invest" in basic science of AD biology
- **The private sector will not do this**

And Now The Bad News…

How Many New Cancer Drugs Were Approved In 2015-2016? 30

How Many New AD Drugs Were Approved In 2015-2016? 0

How Many New AD Drugs Were Approved In 2014? 0

How Many New AD Drugs Were Approved In 2013? 0

How Many New AD Drugs Were Approved In 2012? 0

⋮

How Many New AD Drugs Were Approved In 2004? 0

How Many New AD Drugs Were Approved In 2003? 1

Role of Public/Private Partnerships

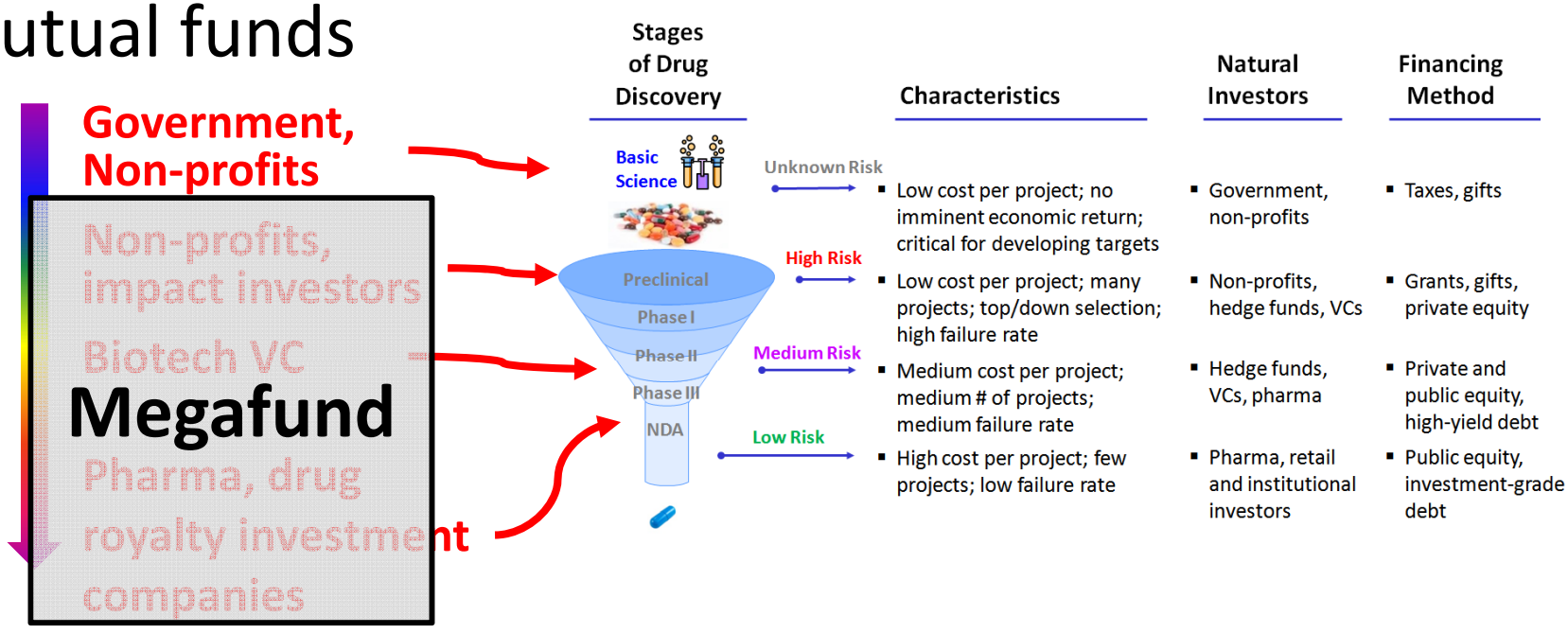
National Cancer Act of 1971
+
Human Genome Project
+
Biopharma R&D
+
Philanthropy

Orphan Drug Act of 1983
+
Human Genome Project
+
Philanthropy
+
Biopharma R&D

National Alzheimer's Project Act of 2011
+
BRAIN Initiative
+
Philanthropy
+
Biopharma R&D

New Business Models Are Emerging

- One size does not fit all—ideal business structures need not be pharma companies, CROs, biotech VCs, or mutual funds



Isn't Pharma Already Doing This?

Pfizer Balance Sheet 2015

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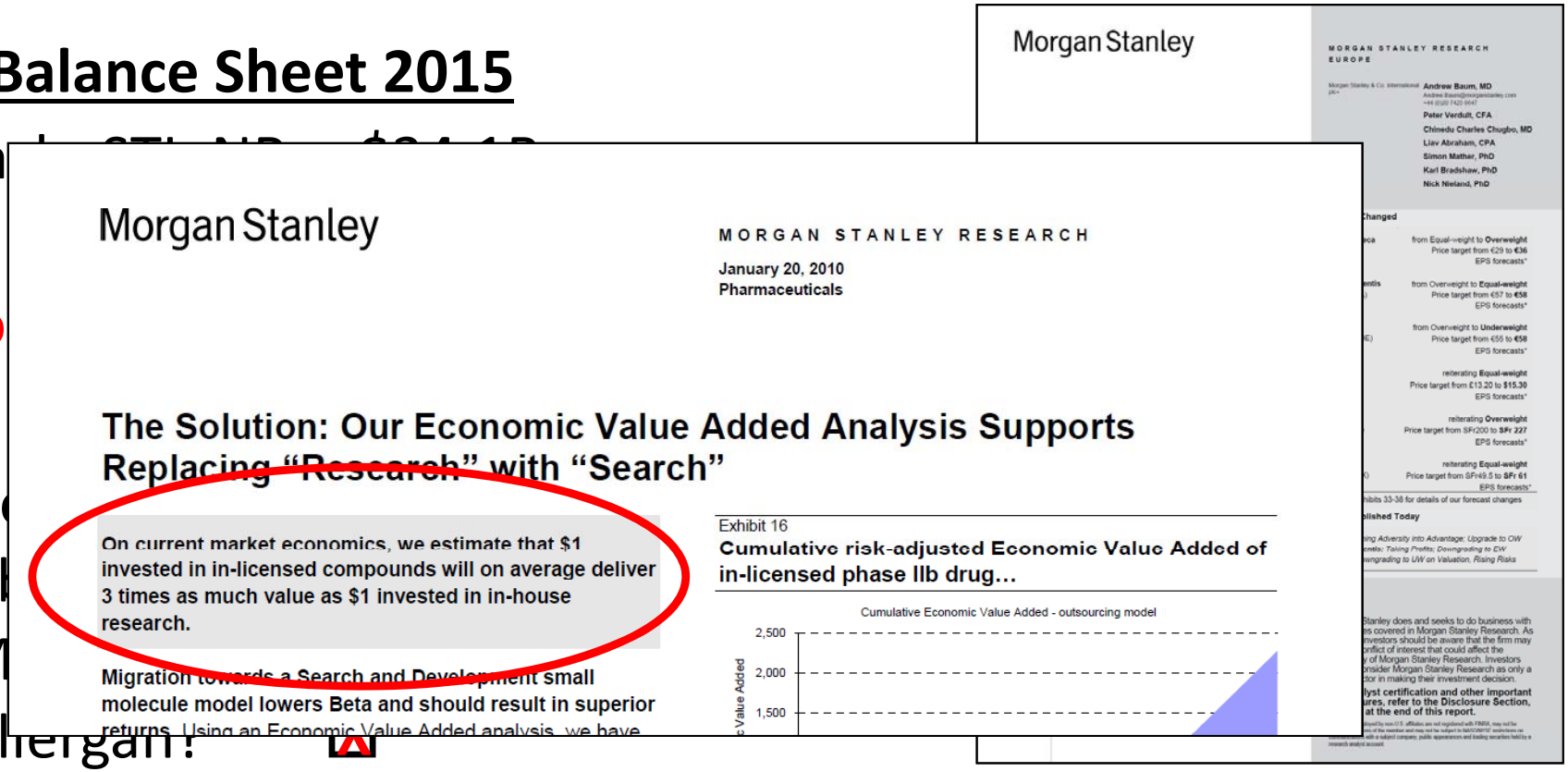


Isn't Pharma Already Doing This?

Pharma Job Cuts, 2008–2013

Company	Job Cuts
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

Company	Job Cuts

FiercePharma

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

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

October 21, 2015 | By Emily Wasserman

Source: Bloomberg

Is There Enough Capital?

Ivey

In 2015:

- U.S. bond market: $39.9T ($6.
  - Corporate bonds: $8.2T ($1.5T i
  - Mortgage-related: $8.7T ($1.7T
  - Asset-backed securities: $1.3T ($
  - Money-market funds: $2.8T
- Norwegian sovereign wealth fund: $873B
- CPPIB: $215B
- Target return of 126 public funds (2012): ~~8%~~ 7.5%


6/15/2014 MIT Borrows for the Long Run With a $750-Million 'Century Bond' - Administration - The Chronicle of Higher Education

THE CHRONICLE OF HIGHER EDUCATION
Administration

May 12, 2011

MIT Borrows for the Long Run With a $750-Million 'Century Bond'

By Goldie Blumenstyk

The Massachusetts Institute of Technology this week borrowed $750-million by issuing taxable bonds that it plans to repay not over 30 years, the usual term for capital borrowing by universities, but over 100 years.

In 2015, Total U.S. VC AUM Was? $165B

($7.6B invested in biotech)

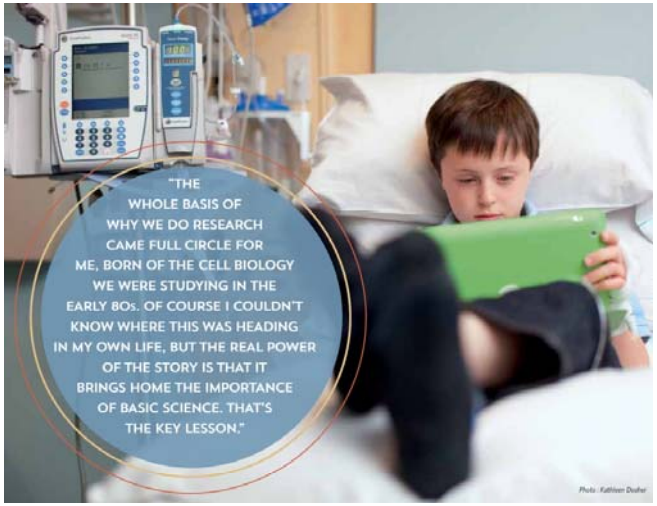
Next Steps

- Engaging various stakeholders and exploring business models and pilot program structures
- Getting more data, running more refined simulations, conducting case studies
- LFE/DFCI workshop on financing for curative therapies on Oct 14
- CanceRx 2016 on Oct 26–28 (cancerx.mit.edu)
- Education and outreach

→ **"Permissioning"**

Conclusion

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!

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