How Financial Engineering Can Cure Cancer

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(based on joint work with David Fagnan, Jose-Maria Fernandez, Austin Gromatzky, and Roger Stein)

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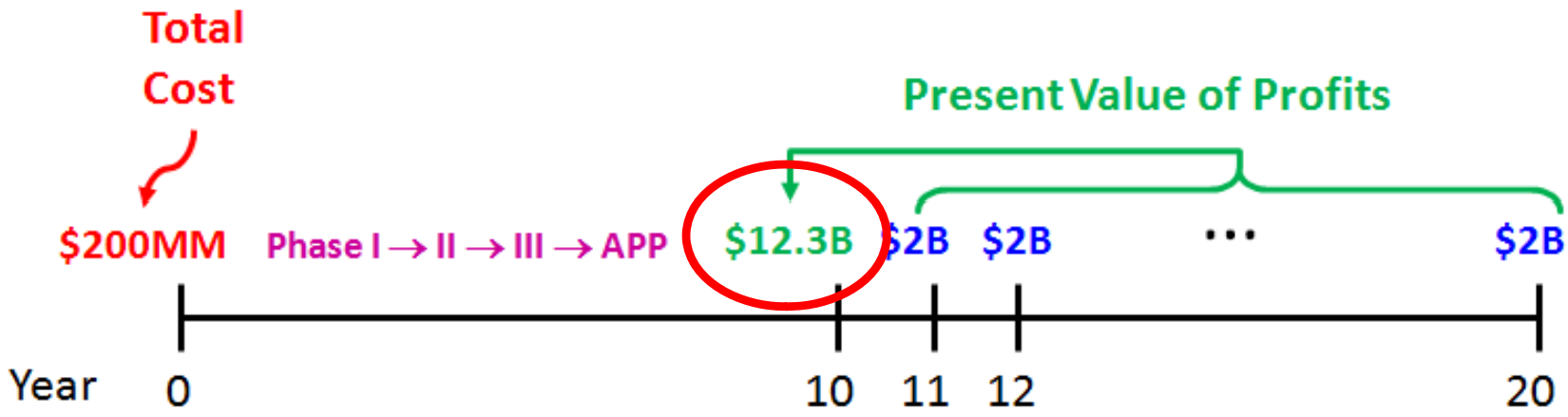
An Investment Problem

Consider the Following Investment Opportunity

- $200MM investment today, 10 years before payoff
- Probability of success is 5%
- If successful, annual profits of $2B for 10-year patent



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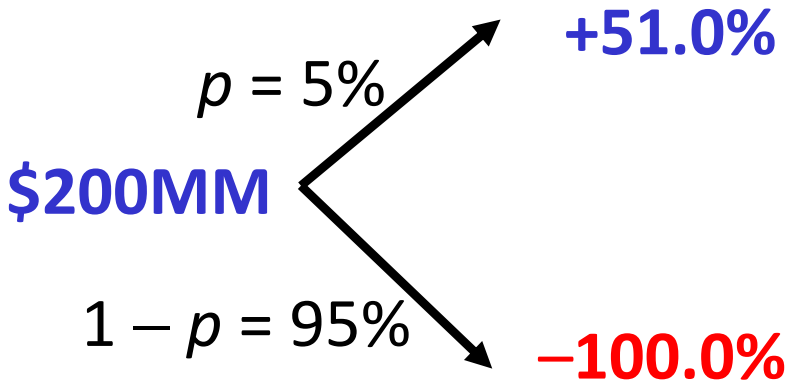


$$\Rightarrow \quad \begin{aligned} \mathrm{E}[R] &= 11.9\% \\ \mathrm{SD}[R] &= 423.5\% \end{aligned}$$

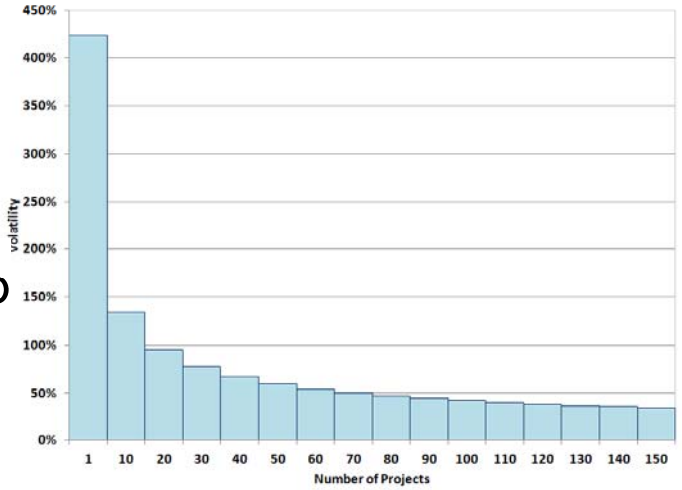
An Investment Problem

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??

An Investment Problem

What If We Invest In 150 Programs Simultaneously?:

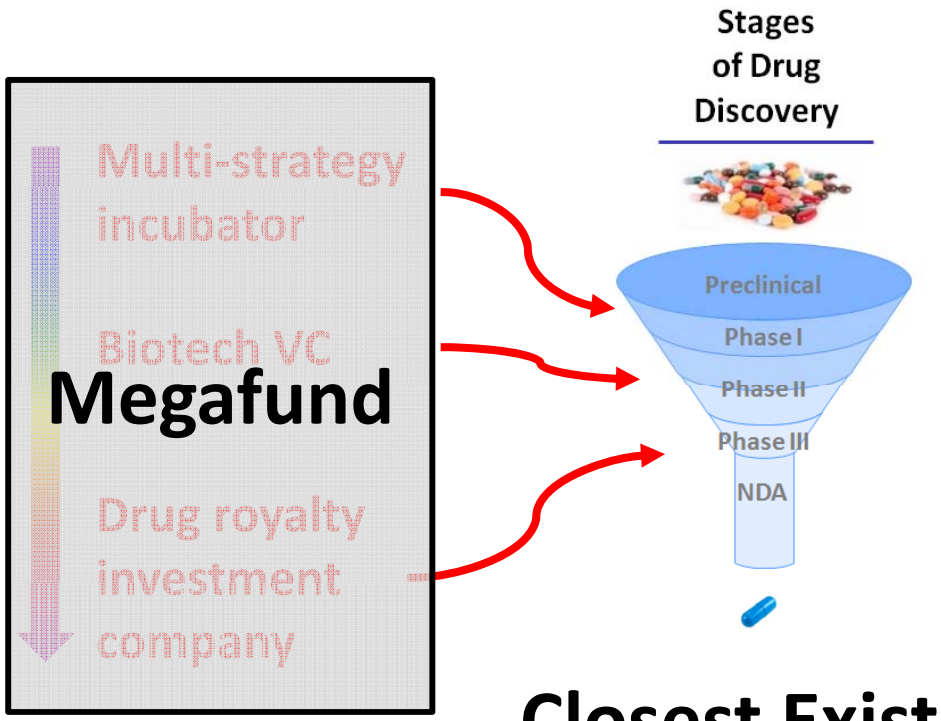
- Given the reduction in risk, debt-financing is possible!

Event	Probability	Minimum Year-10 NPV	Maximum Year-0 Proceeds at 3.44% (10-Yr Aa as of 1/31/14)	Maximum Year-0 Proceeds at 3.66% (10-Yr A as of 1/31/14)
At least 1 hit:	99.95%	$12,289	$8,763	$8,578
At least 2 hits:	99.59%	$24,578	$17,525	$17,157
At least 3 hits:	98.18%	$36,867	$26,288	$25,735
At least 4 hits:	94.52%	$49,157	$35,051	$34,314
At least 5 hits:	87.44%	$61,446	$43,813	$42,892

- $17.5B of high-quality debt can be issued
- With securitization, debt capacity is even larger
- See Fernandez, Stein, Lo, *Nature Biotech* 30(2012)

Megafund Business Model

- A new business model is required
  - Not a pharma company; not a biotech VC; not a mutual fund



Closest Existing Model ⇒ Royalty Pharma

Simulating A Cancer Megafund

Simulation Results: Matlab and R Software Available

Variable or Summary Statistic	Simulation A		Simulation B	
	All-Equity	RBOs	All-Equity	RBOs
Number of Compounds				
Preclinical	60	100	—	—
Phase I	60	100	—	—
Phase II	—	—	50	100
Phase III	—	—	—	—
Research Impact				
Number of compounds to reach Phase II	63.4	103.1	—	—
Number of compounds sold in Phase III and NDA	1.1	2.2	7.4	20.7
Number of compounds sold once APP	0.8	1.1	6.4	8.1
Liabilities				
Capital ($ million)	3,000	5,000	7,500	15,000
Senior Tranche ($ million)	—	1,250	—	6,500
Junior Tranche ($ million)	—	750	—	1,000
Equity Tranche ($ million)	3,000	3,000	7,500	7,500
Equity Tranche Performance				
Average annualized return on equity	7.9%	9.1%	7.7%	10.6%
Prob (return on equity < 0)	15%	19%	13%	12%
Prob(return on equity > 5%)	65%	69%	67%	76%
Prob (return on equity > 15%)	18%	34%	14%	35%
Debt Tranches Performance				
Senior Tranche: default prob., expected loss (bp)	—	1 , < 1	—	3 , < 1
Junior Tranche: default prob., expected loss (bp)	—	35 , 10	—	20 , 12

Do We Really Need $30 Billion?

It Depends…

- Fagnan, Gromatzky, Fernandez, Stein, and Lo (2014)
- **Orphan Diseases**: smaller population, urgent need, higher prices, lower development costs, higher success rates (20%), faster time to approval (3–7 years)

Phase	Clinical Trial Cost ($MM)	Clinical Trial Success Rate	Clinical Trial Duration (years)	Valuation ($MM)
Preclinical	5	69%	1.00	7.1
Phase 1	5	84%	1.66	27.6
Phase 2	8	53%	2.09	75.6
Phase 3	43	74%	2.15	321.5
NDA	—	96%	0.80	701.9
APP	—	—	—	817.6

Do We Really Need $30 Billion?

Orphan Drug Fund Simulation

- $575 million fund yields attractive returns!

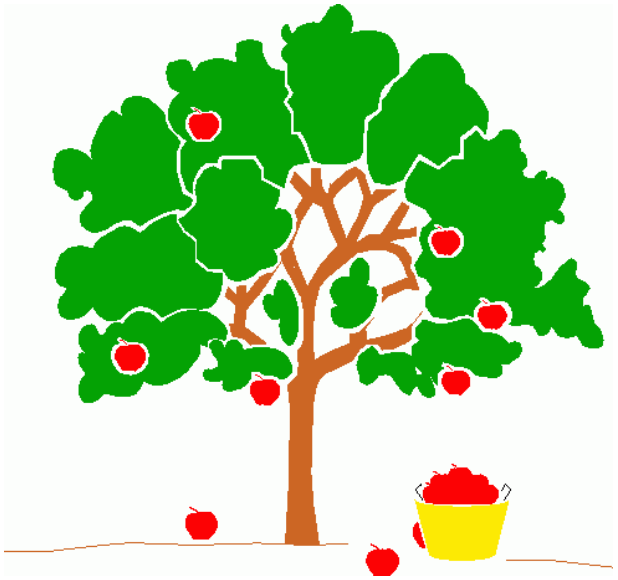
	All Equity (Same Equity)	RBO	All Equity (Same Capital)
Number of Compounds			
Preclinical	3	8	8
Phase 1	3	8	8
Research Impact			
Number sold in Phase 2	0.7	2.3	1.7
Number sold in Phase 3	1.8	4.6	5.0
Liabilities			
Capital ($ millions)	230	575	575
Senior tranche ($ millions)	—	115	—
Junior tranche ($millions)	—	230	—
Equity tranche ($millions)	230	230	575
Equity tranche performance			
Average annualized ROE	19.6%	33.8%	23.2%
Prob. (equity wiped out)	2bp	81bp	<0.1 bp
Prob. (return on equity < 0)	10.4%	2.5%	14bp
Prob. (return on equity > 10%)	79.1%	95.4%	93.7%
Prob. (return on equity > 25%)	40.5%	82.9%	45.7%
Debt tranches performance			
Senior tranche: default prob., expected loss (bp)	—	1.2, <0.1	—
Junior tranche: default prob., expected loss (bp)	—	80, 27	—

Do We Really Need $30 Billion?

But For Alzheimer's, $30 Billion Is Not Enough!

- 13-year development time, not 10
- $500 million 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
- Number of new cancer drugs in 2013?:
- Number of new Alzheimer's drugs in last decade?:

Investing in Basic Science



National Cancer Act of 1971 + Human Genome Project

Orphan Drug Act of 1983 + Human Genome Project

National Alzheimer's Project Act of 2011 + BRAIN Initiative

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 Disease…

Put A Price Tag On Its Head Instead!

With Sufficient Scale, We Can Do Well By Doing Good

- Finance does not always have to be a zero-sum game

Thank You!