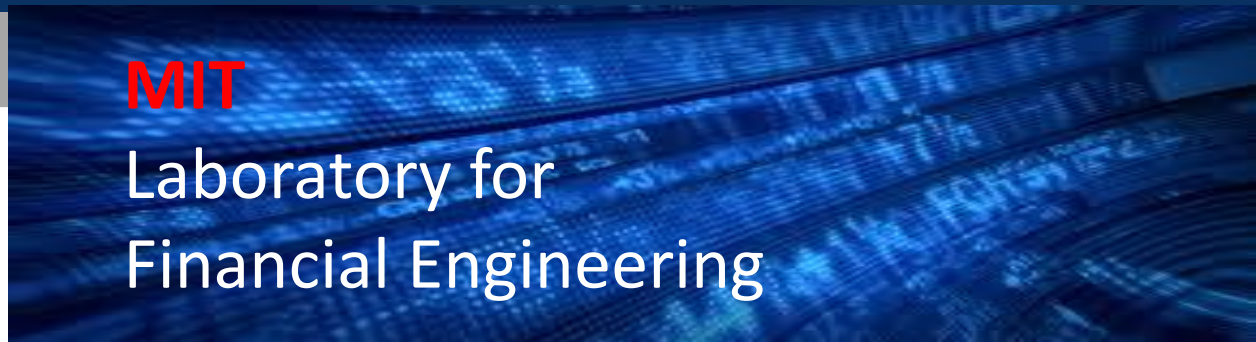
Can Financial Economics Help Cure Cancer?

Andrew W. Lo, MIT

October 17, 2020

90th International Atlantic Economic Society Conference



Biomedicine Is At An Inflection Point

REUTERS

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

Jimmy Carter says he no longer needs cancer treatments

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.

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

U.S. President Jimmy Carter

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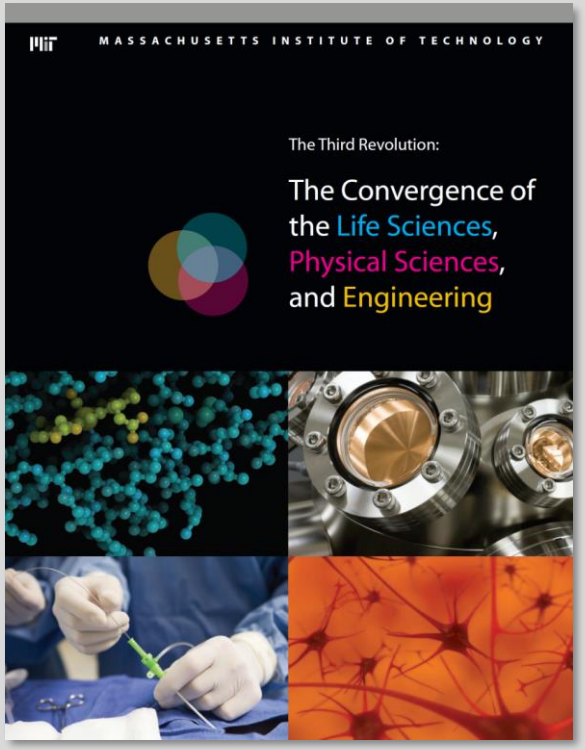
Biomedicine Is At An Inflection Point



The "omics" Revolution:

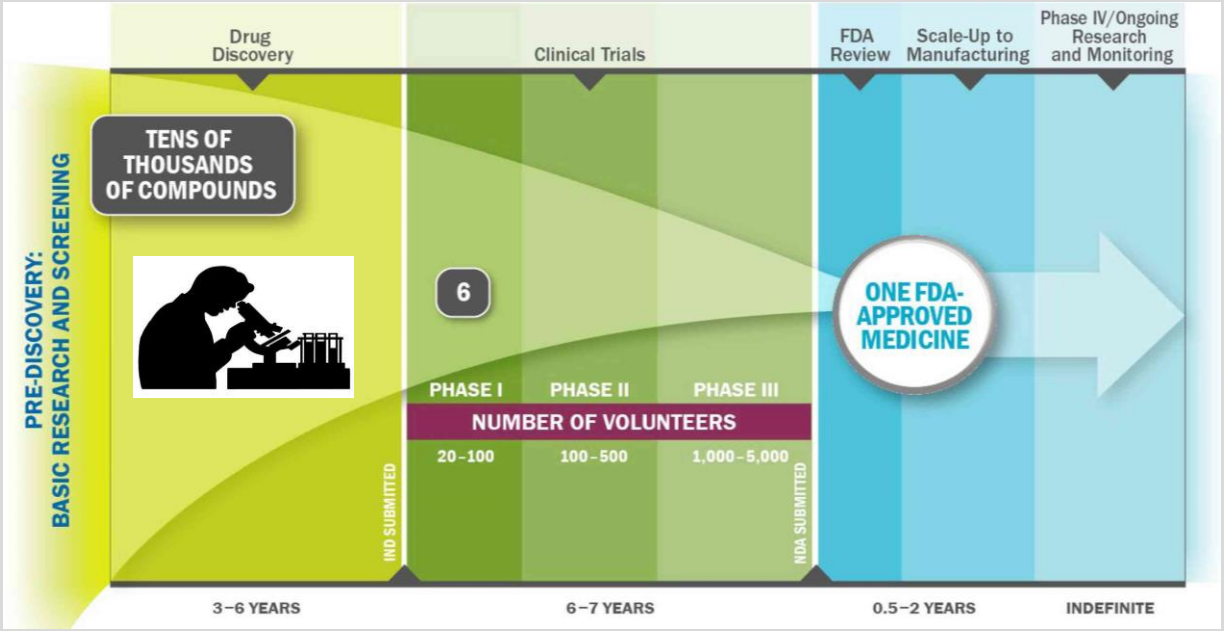
- Gen**omics**
- Epigen**omics**
- Transcript**omics**
- Prote**omics**
- Metabol**omics**
- Microbi**omics**

What About Economics**??**

Increasing Risk and Uncertainty

Why??

The Challenge of Drug Development



3 Features:

1. Costly
2. Low PoS
3. Long duration

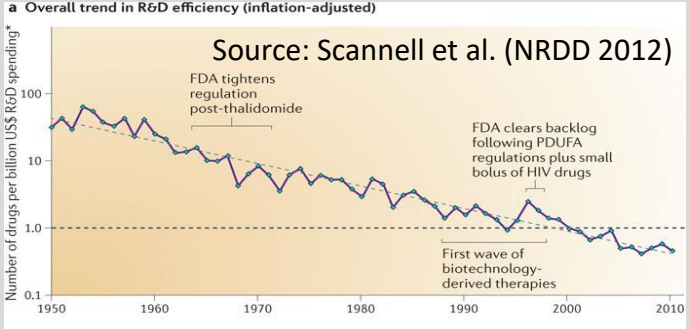
The Challenge of Drug Development

MIT LFE

Example: Combination Therapies

- 2,800 approved drugs
- 3,918,600 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.

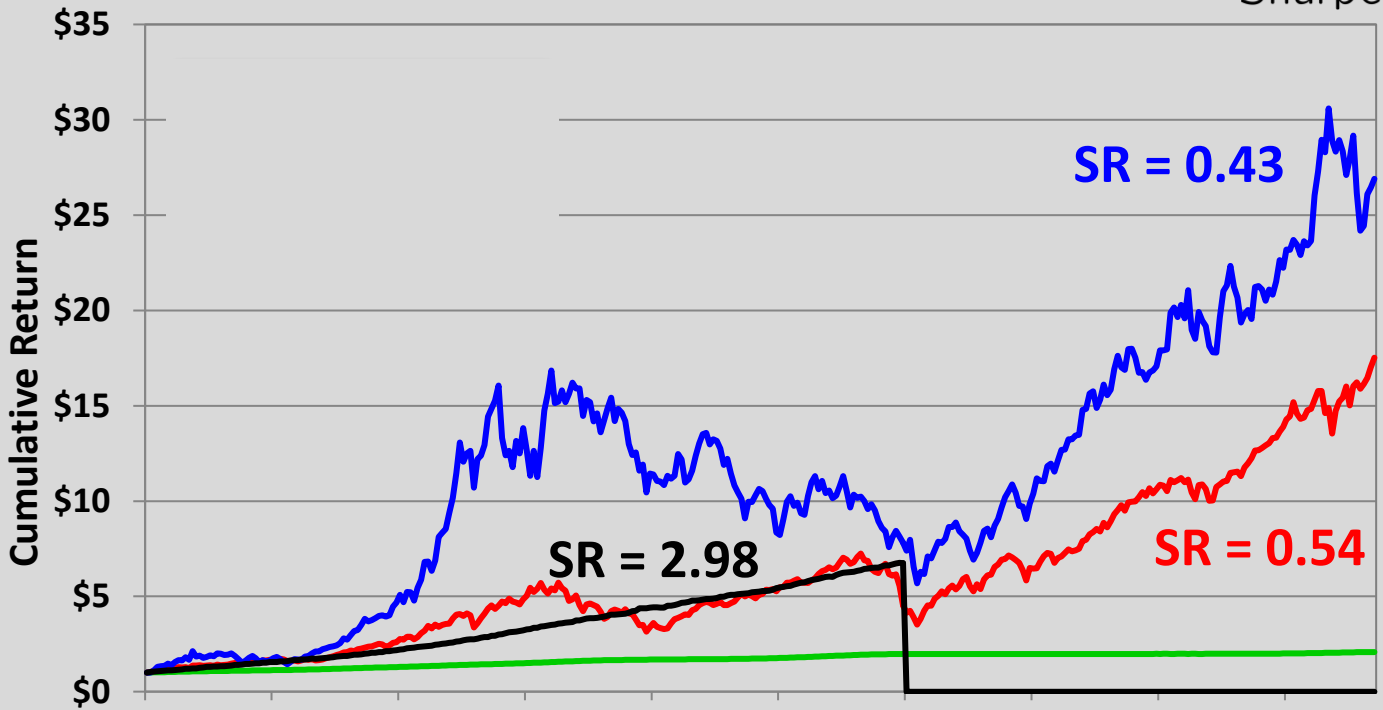
Eroom's Law



Investment Pop Quiz #1

MIT LFE

$$\text{Sharpe Ratio} \equiv \frac{\mathrm{E}[R] - R_f}{\mathrm{SD}[R]}$$



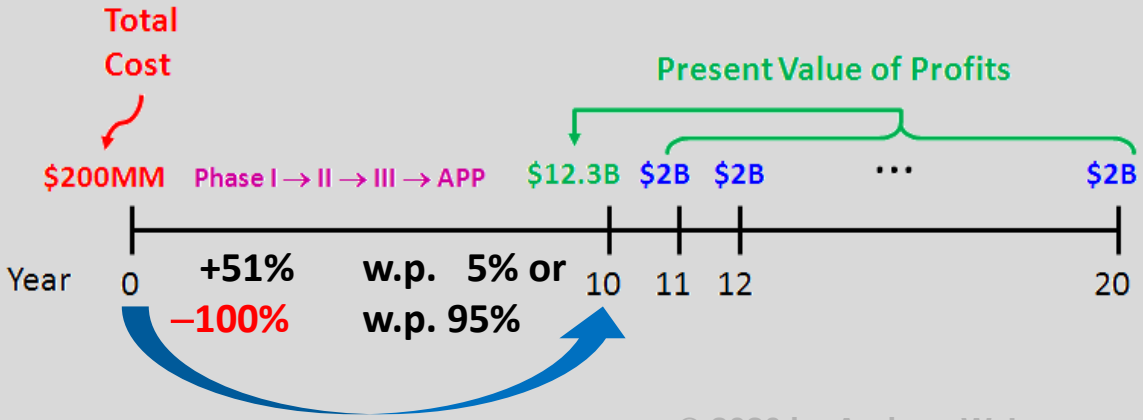
Investment Pop Quiz #2

MIT LFE

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%
SR = 0.02



Financial Engineering Can Help

MIT LFE

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:

$$\begin{aligned} \mathrm{E}[R] &= 11.9\% \\ \mathrm{SD}[R] &= 423.5\%/\sqrt{150} = 34.6\% \end{aligned}$$

- But can we raise $30B?? → **SR = 0.34**
- It depends on the portfolio's risk/reward profile (correlations?)

Financial Engineering Can Help

MIT LFE

What If We Invest In 150 Programs Simultaneously?:

- With reduced risk, debt-financing is feasible!

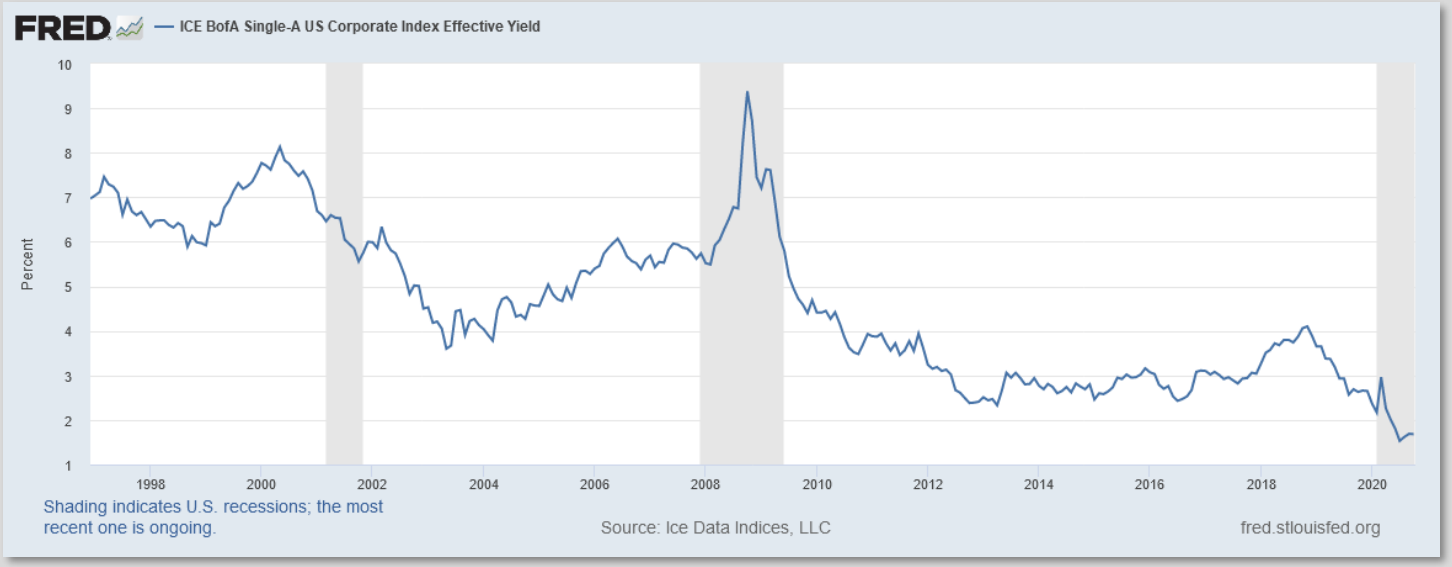
Event	Probability	Minimum Year-10 NPV	Maximum Year-0 Proceeds at 1.53% (BofAML AA 10-Yr as of 10/12/20)	Maximum Year-0 Proceeds at 1.68% (BofAML A 10-Yr as of 10/12/20)	Maximum Year-0 Proceeds at 2.41% (BofAML BBB 10-Yr as of 10/12/20)
At least 1 hit:	99.95%	$12,289	$10,558	$10,403	$8,321
At least 2 hits:	99.59%	$24,578	$21,116	$20,806	$16,641
At least 3 hits:	98.18%	$36,867	$31,674	$31,210	$24,962
At least 4 hits:	94.52%	$49,157	$42,232	$41,613	$33,282
At least 5 hits:	87.44%	$61,446	$52,789	$52,016	$41,603

Financial Engineering Can Help

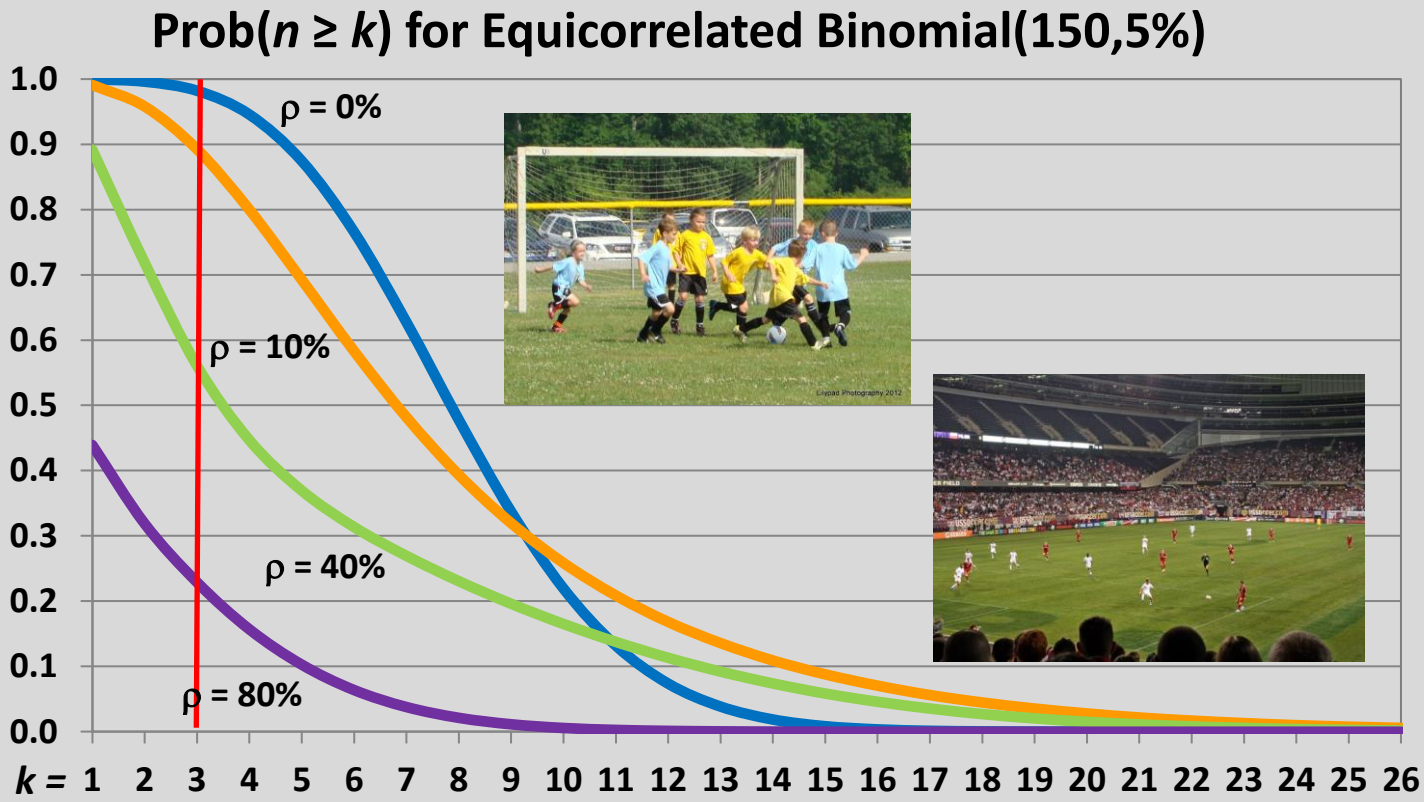
MIT LFE

ICE Bank of America Single-A U.S. Corporate Index Effective Yield

Dec 31, 1996 to Oct 12, 2020



Financial Engineering Can Help

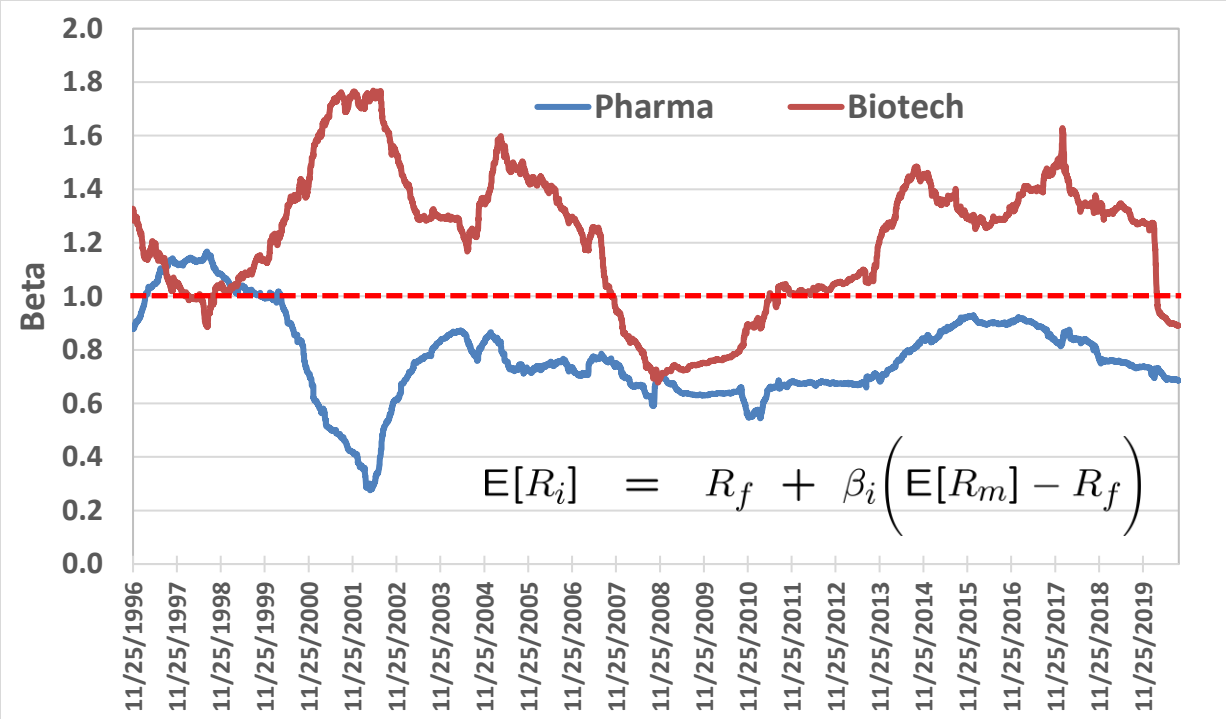


Diversification can lower the cost of capital

Investment Pop Quiz #3

500-Day Rolling-Window Betas

25 Nov 1996 to 17 Sep 2020



Why Do Biotechs Have Such High Betas??

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

Short Answer

Short Answer

Long Answer

- **Cancer**: Fernandez, Stein, Lo (2012), Das and Lo (2017), Das, Rousseau, Adamson, Lo (2018), Chaudhuri, Cheng, Pepke, Rinaudo, Roman, Spencer, Lo (2019), Alexander et al. (2019), Wong, Siah, Lo (2019)
- **Alzheimers**: Lo, Ho, Cummings, Kosik (2014)
- **Vaccines and Anti-Infectives**: Vu, Chaudhuri, Kaplan, Mansoura, Lo (2019), Wong, Siah, Lo (2020)
- **Guarantees**: Fagnan, Stein, Fernandez, Lo (2013)
- **Rare diseases, NCATS**: Fagnan, Gromatzky, Stein, Lo (2014), Fagnan, Yang, McKew, Lo (2015), Kim and Lo (2016), Das, Huang, Lo (2019),
- **Dynamic leverage**: Montazerhodjat, Frishkopf, Lo (2015)
- **Drug mortgages**: Montazerhodjat, Weinstock, Lo (2016)
- **Clinical trial design**: Montazerhodjat, Chaudhuri, Sargent, Lo (2017), Chaudhuri, Sheldon, Irony, Ho (2018), Isakov, Lo, Montazerhodjat (2019), Chaudhuri and Lo (2020), Xu, Chaudhuri, Xiao, Lo (2020)
- **Estimating and forecasting clinical trial outcomes**: Wong, Siah, Lo (2019, 2020a,b), Siah, Wong, Lo (2019,2020)

How Much Capital Do We Need?

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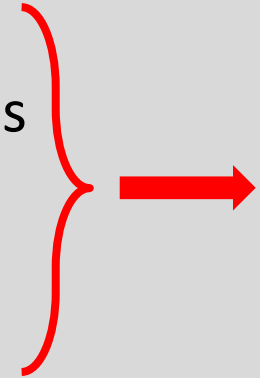
The Amount of Capital Needed Depends On:

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



Siah and Lo (2020)
https://bit.ly/33Fpqdh
Sourcecode:
https://projectalpha.mit.edu

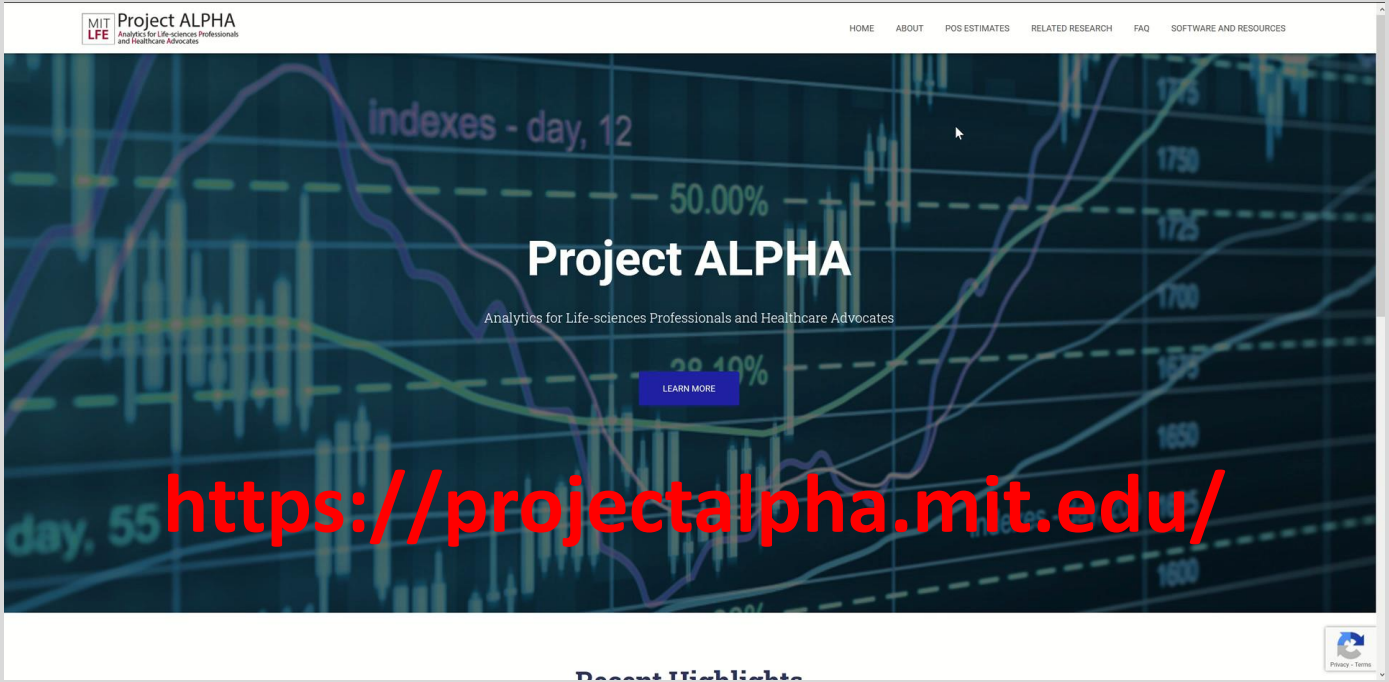
Finance and Biomedical Experts Must Collaborate

Fundamental Law of Healthcare Finance

$$\mathrm{E[NPV]} = \mathrm{PV[Profits]} \times \mathrm{PoS} - \mathrm{Costs}$$

Fundamental Law of Healthcare Finance

Analytics for Lifesciences Professionals and Healthcare Advocates

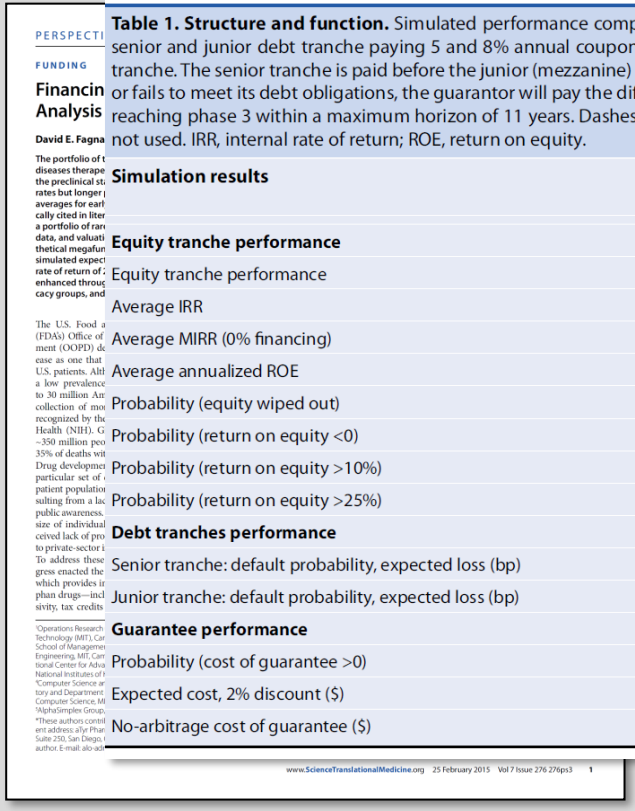


Orphan Diseases

- Often due to mutation in a single gene, e.g, hemophilia, cystic fibrosis, ALS, Gaucher, paroxysmal nocturnal hemoglobinuria
- 30 million Americans suffer from over 7,000 rare diseases
- Smaller population, urgent need, higher prices, lower development costs, higher success rates (25%), faster approvals (3–7 years), 1983 Orphan Drug Act, etc.
- $400–$500 million of capital and 10–20 projects are sufficient

Lack of Correlation Is Critical!

Fagnan, Yang, McKew, Lo (2015)


PERSPECTI

FUNDING

Financin
Analysis

David E. Fagna

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www.ScienceTranslationalMedicine.org 25 February 2015 Vol 7 Issue 276 276ps3 1

Table 1. Structure and function. Simulated performance comparing an all-equity structure (using no debt financing); an RBO structure using a senior and junior debt tranche paying 5 and 8% annual coupon rates, respectively; and a second RBO structure with a single guaranteed senior tranche. The senior tranche is paid before the junior (mezzanine) tranche, which is paid before the equity holder. In the event that the fund defaults or fails to meet its debt obligations, the guarantor will pay the difference. Each structure acquires only preclinical compounds, with a target goal of reaching phase 3 within a maximum horizon of 11 years. Dashes indicate cases in which the corresponding type of financing and/or guarantee is not used. IRR, internal rate of return; ROE, return on equity.

Simulation results	All equity (similar equity)	Research-backed obligation (RBO)	RBO with guarantee (no mezzanine)
Equity tranche performance			
Equity tranche performance	3.25	5.14	5.32
Average IRR	26.7%	N/A	N/A
Average MIRR (0% financing)	18.3%	21.6%	22.7%
Average annualized ROE	11.6%	[illegible]	15.4%
Probability (equity wiped out)	1.3 bp	0.52%	0.34%
Probability (return on equity <0)	8.0%	6.2%	5.1%
Probability (return on equity >10%)	61.9%	76.8%	78.6%
Probability (return on equity >25%)	2.2%	10.4%	11.0%
Debt tranches performance			
Senior tranche: default probability, expected loss (bp)	—	0.1, <0.1	<0.1, <0.1
Junior tranche: default probability, expected loss (bp)	—	50, 15	—
Guarantee performance			
Probability (cost of guarantee >0)	—	—	0.3%
Expected cost, 2% discount ($)	—	—	65,000
No-arbitrage cost of guarantee ($)	—	—	110,000

Example: AADC Deficiency

New Business Models Are Emerging

ENDPOINTS NEWS

KKR backs monster $300M raise to build up a new-model biotech --

BridgeBio Pharma, Inc. (BBIO)
NasdaqGS - NasdaqGS Real Time Price. Currency in USD

Add to watchlist | Visitors trend 2W ↑ 10W ↑ 9M ↑

39.73 -0.14 (-0.35%)
At close: 4:00PM EDT

39.73 0.00 (0.00%)
After hours: 4:01PM EDT

Summary | Company Outlook | Chart | Conversations | Statistics | Historical Data | Profile | Financials | Analysis | Options

Previous Close	39.87	Market Cap	4.861B
Open	39.82	Beta (5Y Monthly)	N/A
Bid	38.50 x 1800	PE Ratio (TTM)	N/A
Ask	39.75 x 1200	EPS (TTM)	-4.73
Day's Range	38.46 - 40.74	Earnings Date	Nov 09, 2020 - Nov 13, 2020
52 Week Range	14.23 - 48.36	Forward Dividend & Yield	N/A (N/A)
Volume	728,684	Ex-Dividend Date	N/A
Avg. Volume	617,836	1y Target Est	46.78

1D 5D 1M 6M YTD 1Y 5Y Max | Full screen

Trade prices are not sourced from all markets

June 27, 2019 06:55 AM EDT *Updated July 3, 07:14 AM* | Natalie Grover | IPOs

BridgeBio takes crown for biggest h IPO of 2019, as fellow unicorn ive raises offering size and price

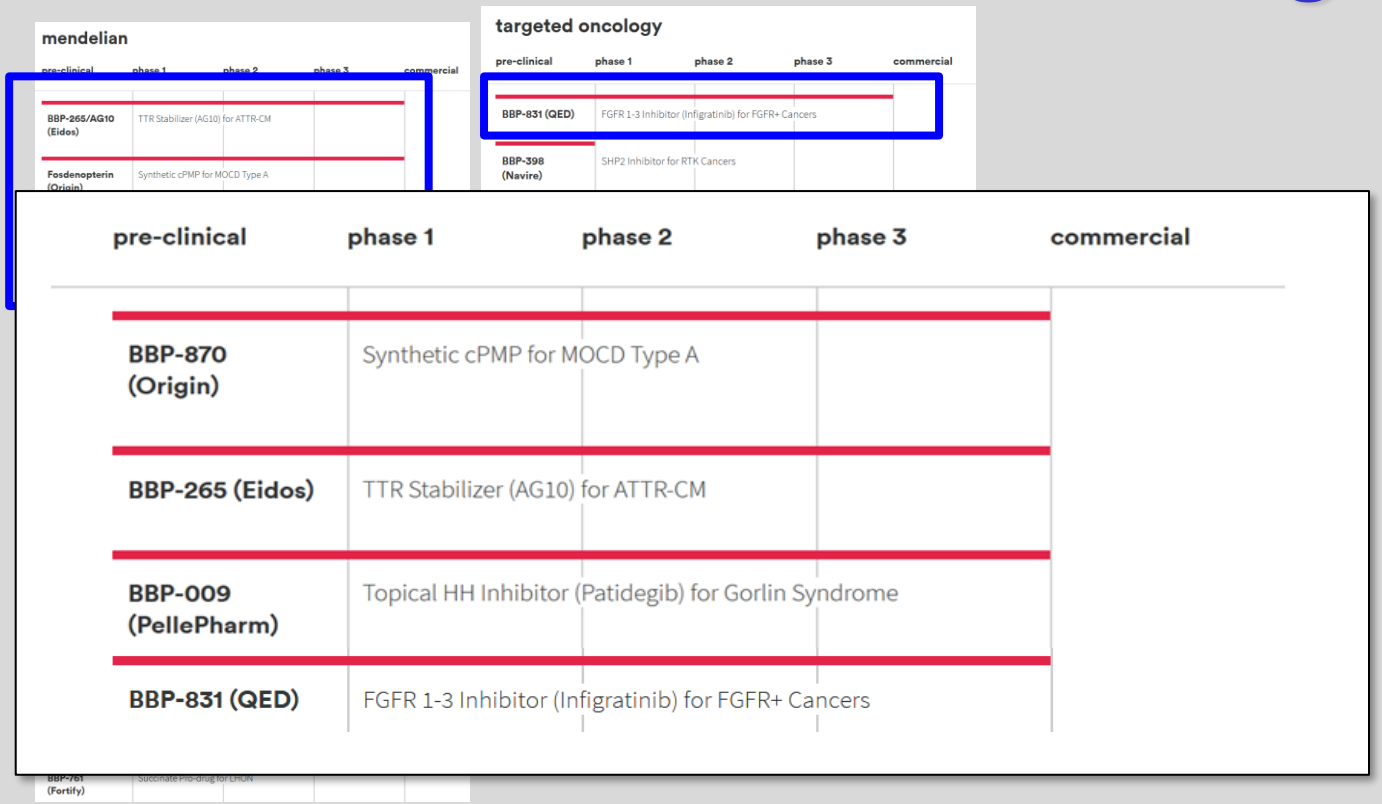
arma and Adaptive Biotechnologies have not just upsized IPO offerings unicorns have also raised their offering prices above the range, hauling d $648.5 million.

BridgeBio Pharma, founded in 2015, has a panies focused on diseases that are driven a single gene — encompassing dermatology, eurology, endocrinology, renal disease, and gy — and cancers with clear genetic drivers. nill birthed a plethora of firms such as Ei- QED Therapeutics and PellePharm, which s subsidiaries.

Neil Kumar *Endpoints*

, California-based company now has 16 which 4 are in or approaching late-stage de- he company, in which KKR owns a 10% stake, raised about $299 million in a fresh round of financing in January.

New Business Models Are Emerging

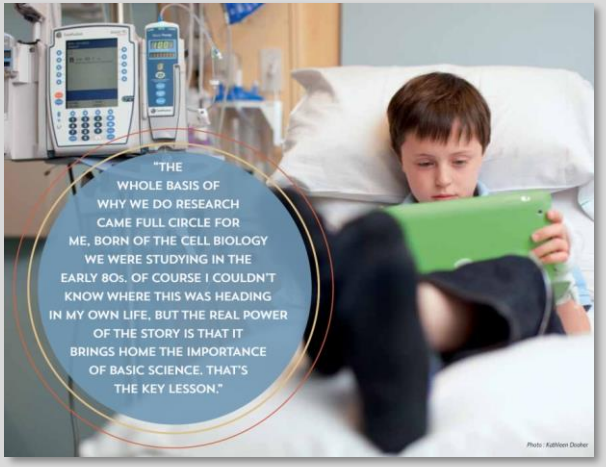


New Business Models Are Emerging

BioBonds in 2021??

Conclusion

I Want To Be Harvey Lodish!



With the right kind of financing and at the right scale, we can do well by doing good!

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

Thank You!