

The challenge of drug development

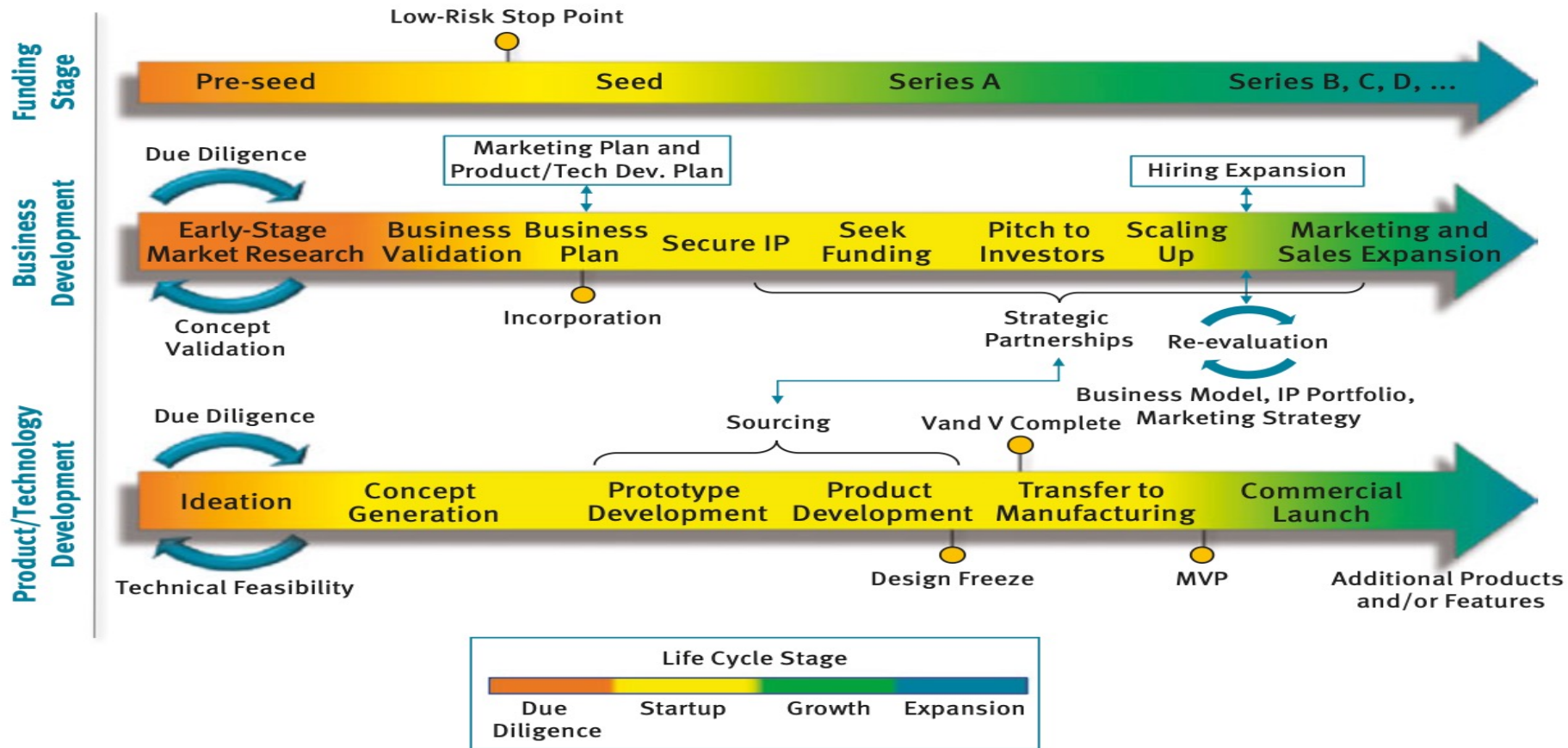


Figure A: Graphic representation of the various processes involved in simultaneously developing a business and bringing a product/technology to market.

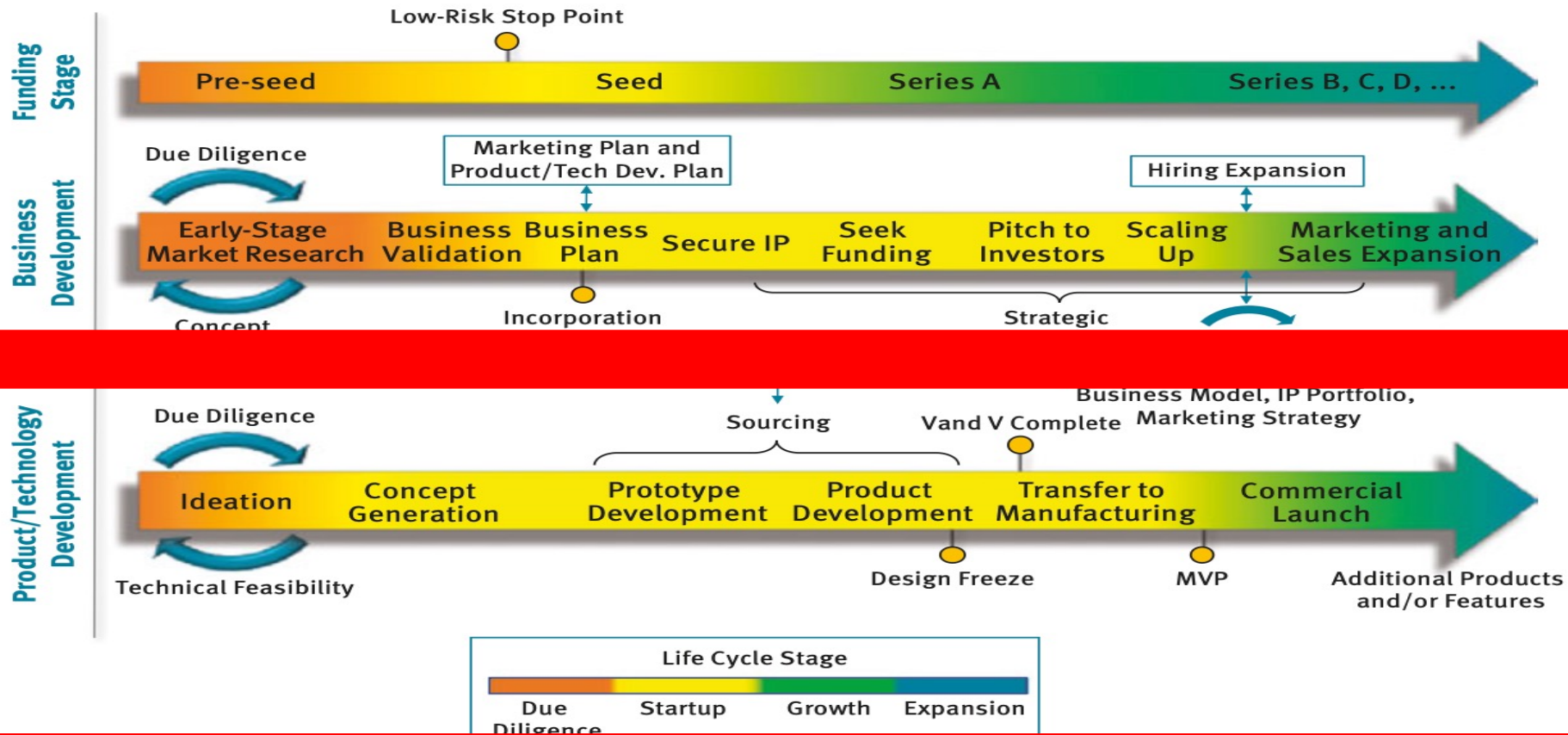


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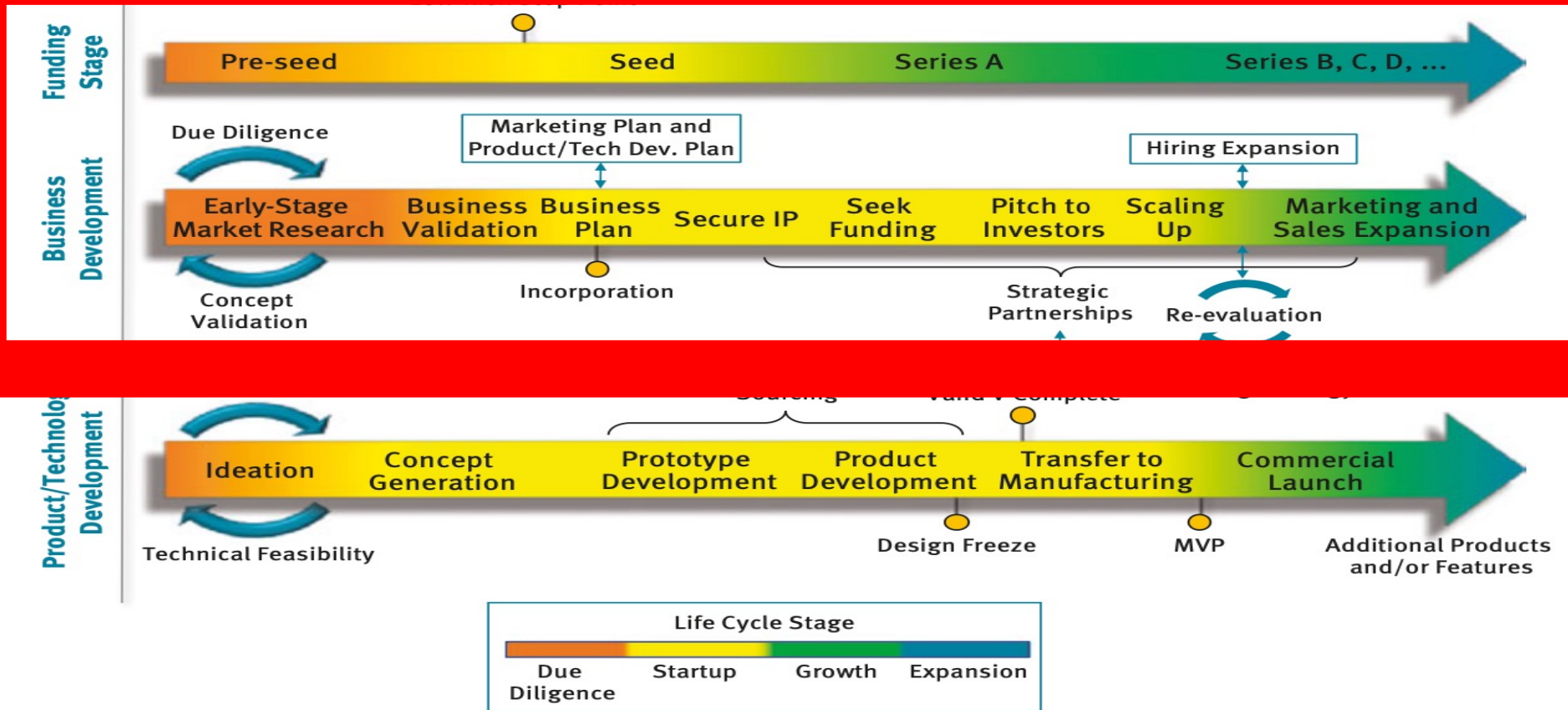


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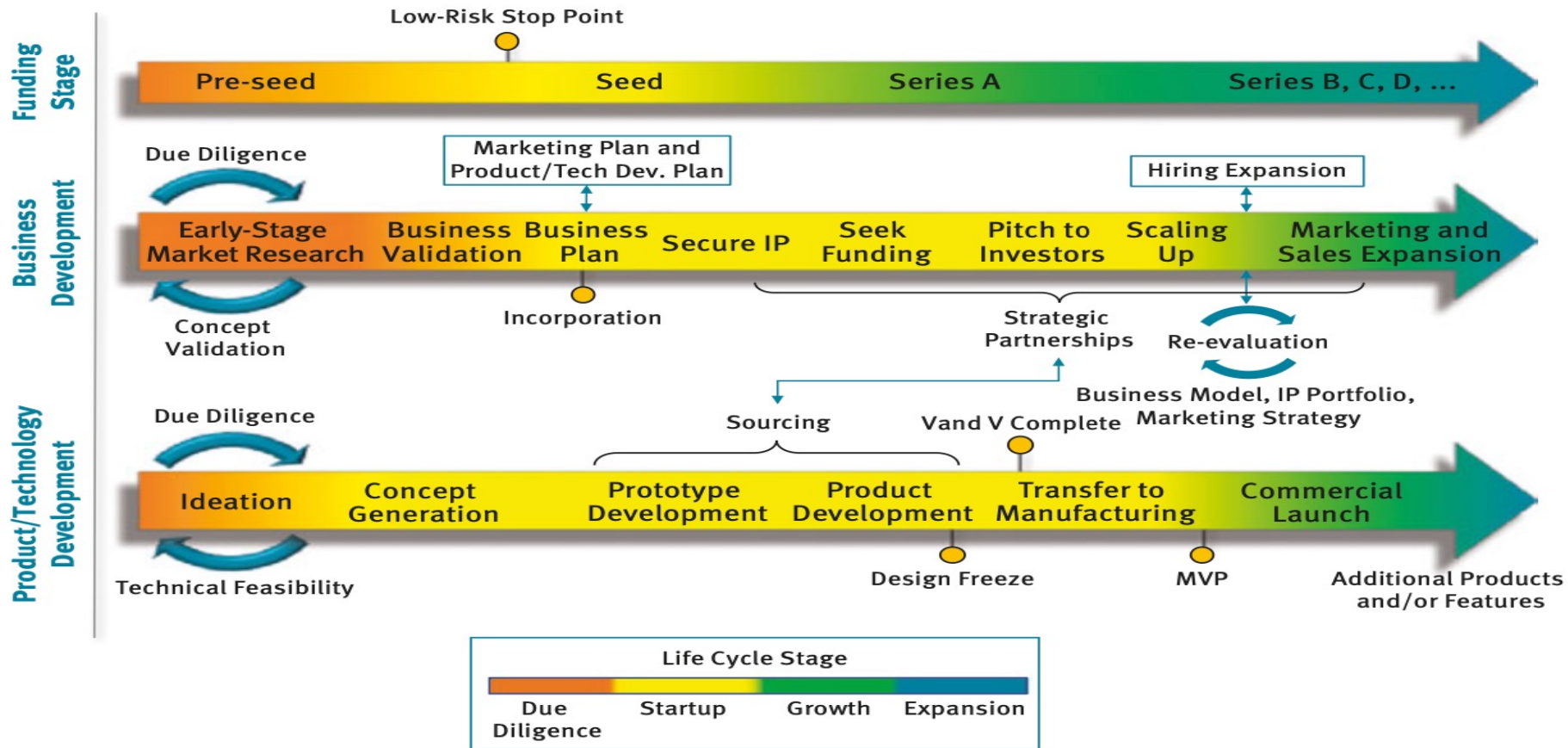


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Thai tech startup ecosystem map

by techsauce.co (Aug 2015)

Notable Startups

Event

Education

Incubators/ Accelerators

Government

Tech Media

Coworking Space

Startup Association

Venture Capital

Angel Groups / Clubs

Venture builders

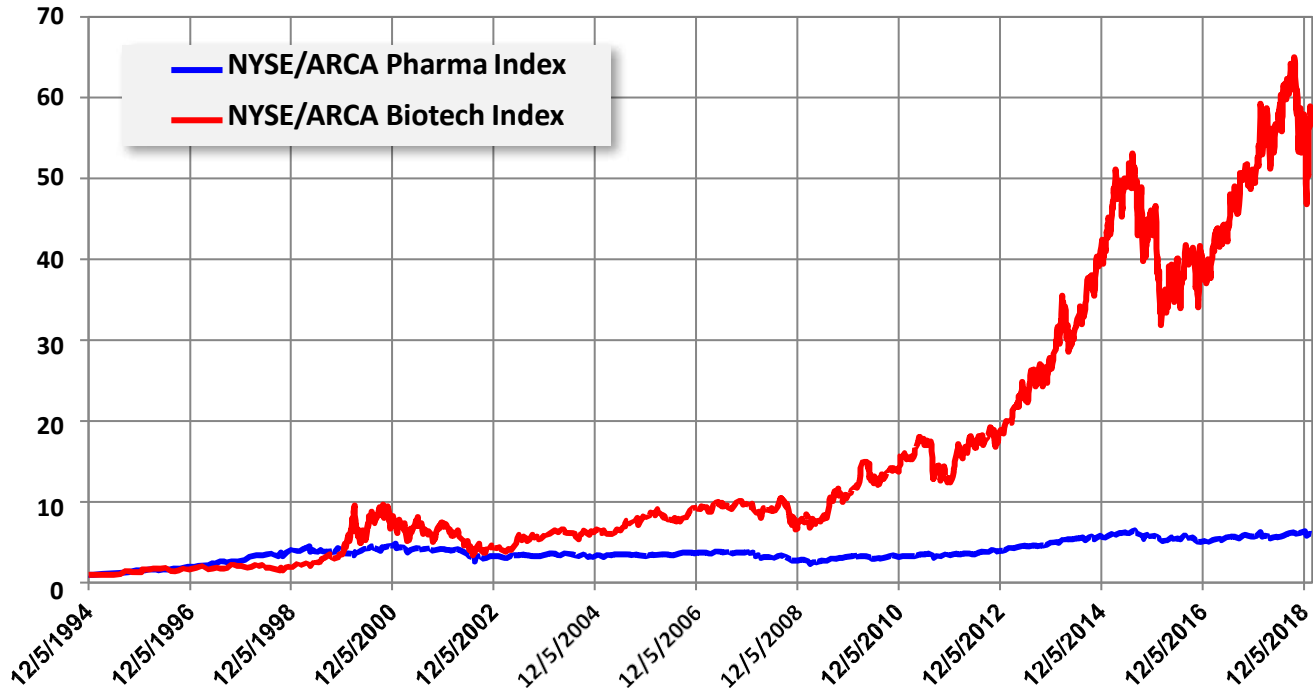
Alpha Founders
Ardent Lab
HUBBA X
Inspire

Companies (IPO or M&A)

Biotech breakthrough on the Stock Market

Pharma vs. Biotech

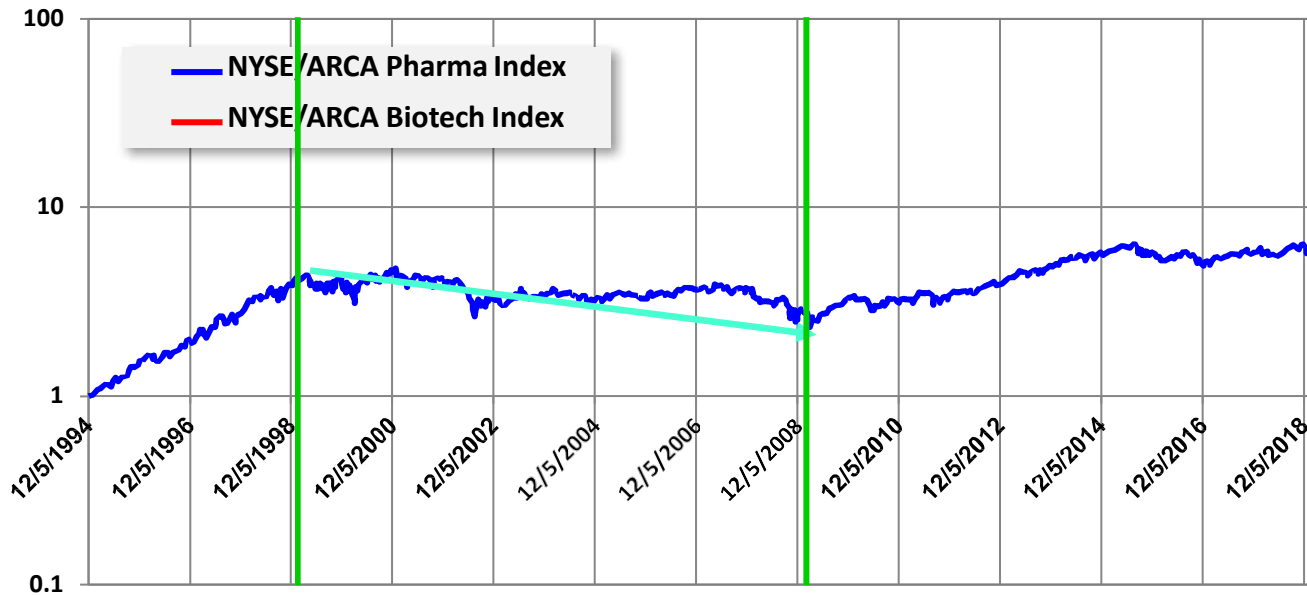
December 5, 1994 to February 1, 2019



Biotech breakthrough on the Stock Market

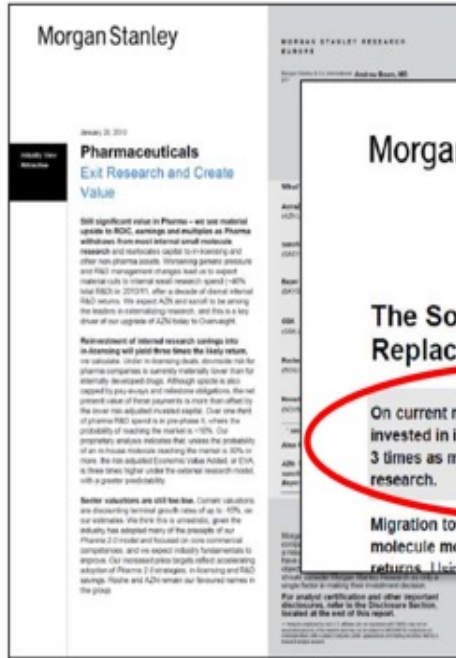
Pharma vs. Biotech

December 5, 1994 to February 1, 2019



Pharma industry

- The pharma industry is composed of **publicly traded companies** and shared value went down during the decade between the late 1990s and early 2000s.
- **Wall Street told the pharma industry you should get out of the research business and focus instead on the M&A business:** acquire companies or deals, do joint ventures, licensing deals, and bring it in-house as opposed to trying to do it yourself.



Morgan Stanley

MORGAN STANLEY RESEARCH
January 20, 2010
Pharmaceuticals

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

Exhibit 16
Cumulative risk-adjusted Economic Value Added of in-licensed phase IIIB drug...

Value Added
1,500
2,000
2,500

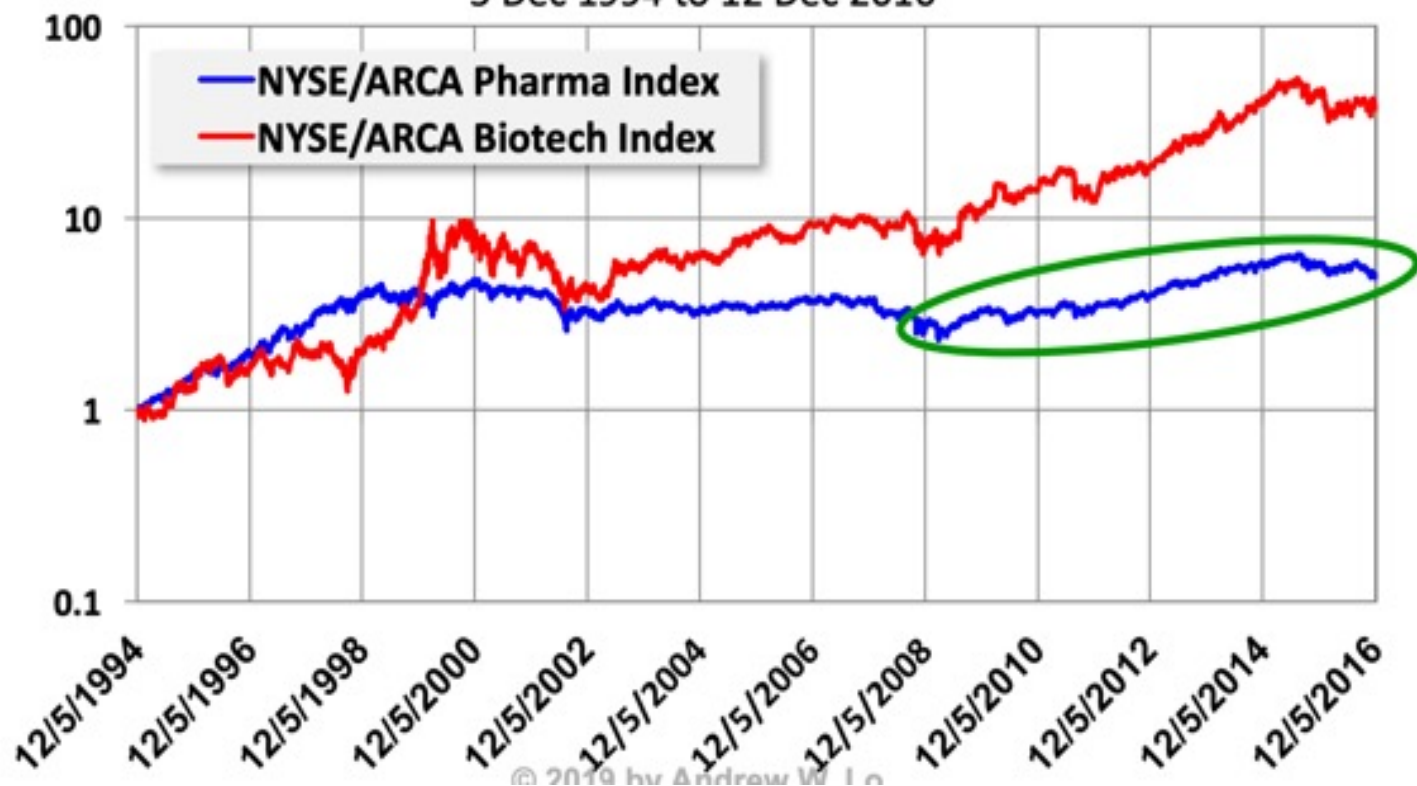
\$1 invested in in-license compounds-- licensed from other companies in to your company-- will, on average, deliver three times as much value as \$1 invested in in-house research.

Pharma industry listened to Wall Street

- From 2008 to 2013 the pharma industry **fired about 150,000 people, most of whom were in R&D.**
- Cutting costs, reducing risk, increasing their Sharpe ratio is working.
- **Share value went up during the last decade but this has also created the valley of death** because we now have less money in the early stages of R&D.

Pharma vs. Biotech

5 Dec 1994 to 12 Dec 2016



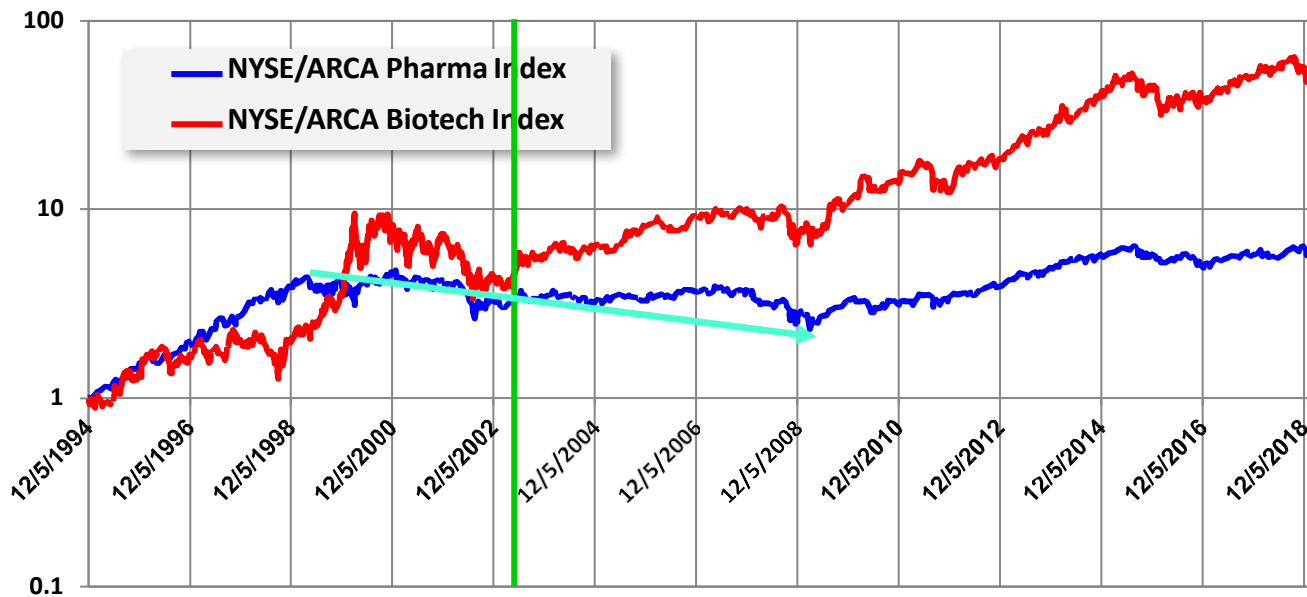
Amgen

- *Ex. pharma company, Amgen in 2016 third quarter had about \$38 billion of cash sitting on its balance sheets.*
- *Amgen financed the vast majority of that by issuing bonds. So \$30 billion of that \$38 billion of cash is long-term debt.*
- *Amgen is not investing it in early stage projects but keeps cash on hand to go shopping for other companies. They are looking for is high Sharpe ratio investments, meaning good return, low risk.*
- *If you look at Amgen's growth over time, you can see all of the different acquisitions that they've made.*

April 14, 2003

Pharma vs. Biotech

December 5, 1994 to February 1, 2019



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.

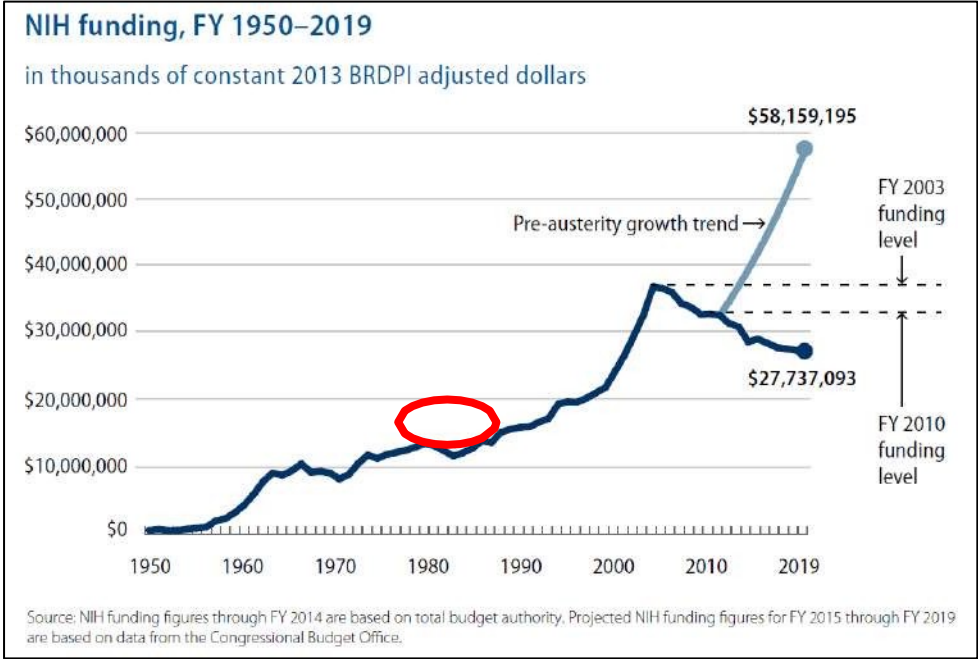
Is private sector investing in
biotechnology?

Increasing Risk and Uncertainty

Why??



Funding Declining



Funding Declining

Table 2 Number of active VC firms

Region	2008	2009	2010	2011	2012	2013	2014
Canada	10	5	10	16	9	7	5
China	2	4	5	4	3	4	11
Europe	105	106	111	74	76	76	81
India	1	3	1	5	8	5	
Israel	12	6	5	5	7	3	5
United States	201	163	143	128	141	147	138
Global total ^a	309	256	252	204	202	211	208

^aThe global total is not a sum of all regions, as an investor that invested in many regions counts only once in the global total. Source: Dow Jones VentureSource

Source: Huggett, NBT May 2015

So Why Is Funding
Declining?

So the question is, why?

- At the very early stages of drug discovery-- funding for preclinical phase 1 or phase 2, has been going down.
- It's gotten so bad that people now call this the "**valley of death**" **because it's very hard to raise money from that preclinical period**

Increasing risk and
uncertainty

The Consequences of Risk and Uncertainty 15.480

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
Biotech VC	Higher startup costs, longer time to milestones, increasing complexity, 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	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 institutions with “proven” track records, shorter time-to-delivery, less speculative research
Academia	Less grant money, fewer job opportunities, uncertain career paths	Study finance 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
- Gene therapy to **cure** Alzheimer’s

Hollywood film industry

Five big movie studios

- There are still today five big movie studios as they were 30 years ago. But the five big movie studios have a very **different business model** today than 30 years ago.
- The movie industry is about **two different kinds of businesses**:
 - one business is making movies and making movies is really hard. Nobody knows how to predict a winner or loser.
 - the second business is in licensing and distributing films. That is a great business, high margin, high return, low volatility business. (example, striking a deal between Sony Pictures and Netflix in order to make a few movies and then have Netflix distribute them).

Distribution business

- distribution business is a very **profitable** business
- The probability of a blockbuster movie in Hollywood is about 5%...bout the probability of producing a cancer drug.

DreamWorks SKG

- *DreamWorks SKG started up in 1994 by three film veterans, Steven Spielberg, Jeff Katzenberg, and David Geffen. And they decided to partner together with Paul Allen, one of the co-founders of Microsoft, to create a new film studio, and they produced lots of movies from 1994 on.*
- *In 2002, they raised \$1 and 1/2 billion of money, and they raised it not in the form of equity, but in the form of debt (bonds) and pledged as collateral a slate of movies, the next, say 25 movies. They borrowed money from investors to make those films....*
- *What happens if they do not pay back?*

They borrowed money from investors to make those films with the obligation that if they don't pay back the promised interest, investors get to take the pot.

This is called slate financing

Gun Hill Road

- *In 2005, Gun Hill Road, a company that was formed as a joint venture between Sony and Universal, they raised \$600 million for a slate of 17 pictures from hedge funds. Hedge funds invested in that.*

Slate financing is growing

- Billion dollar transactions happen routinely in financing Hollywood movies...despite the fact that nobody knows anything, despite the fact that it's a **5% probability of success**.
- The point is that if you have the right portfolio, you can finance it.

Can we do the same for
biotech?