Decision Analysis Application and Patterns at Boehringer Ingelheim Pharmaceuticals

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at DAAG Meeting

in Las Vegas, NV

What is Boehringer Ingelheim?

- One of the world's 20 leading pharmaceutical corporations
- Largest privately held pharmaceutical company
- Human pharmaceutical business produces 95% of sales
- 2000 revenues more than EUR 6 billion
- 16% was re-invested in R&D
- Employs almost 27,400 people worldwide

R&D in BI

- Seven R&D centers: 3,100 scientists in Germany, USA, Canada, Austria, Japan, Italy & Argentina
- 1,500 people working in clinical development in 16 countries
- Therapeutic areas: cardiovascular, respiratory, central nervous system, oncology, immune system, virology

All else being equal...

- We should expend the least amount of resources necessary
- We should discover, develop & launch new products as quickly as possible
- We should take the least risky path ...

...to meet our goals.

However, our decisions involve complex trade-offs of cost, speed & risk

For decisions where only modest resources must be committed before the outcome is clear, we do not need a complex decision process.

However for important decisions about discovery & development of new products, the outcome is not clear until:

- we have expended large resources
- taken substantial risks, and
- it is too late to change the decision and recycle

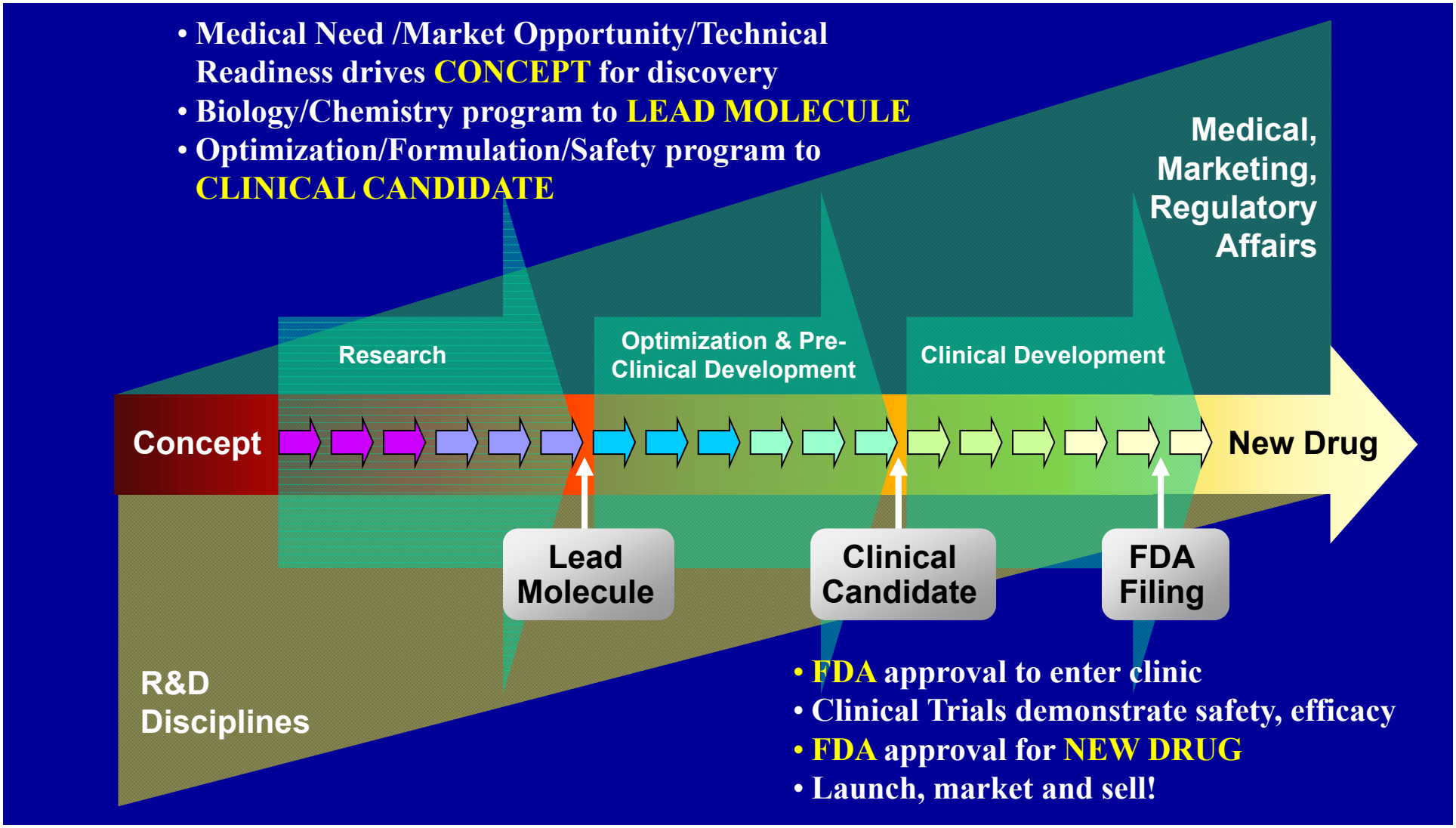
Decision Making at BI

- Well developed system of milestone decisions (like Stage Gates)
- Matrix organization
  - Project Management is responsible for timelines
  - Discipline-based departments are responsible for resources
- Decisions made by Senior Management
  - committees meet approx. every 2 months
  - control the passage of projects through the gates

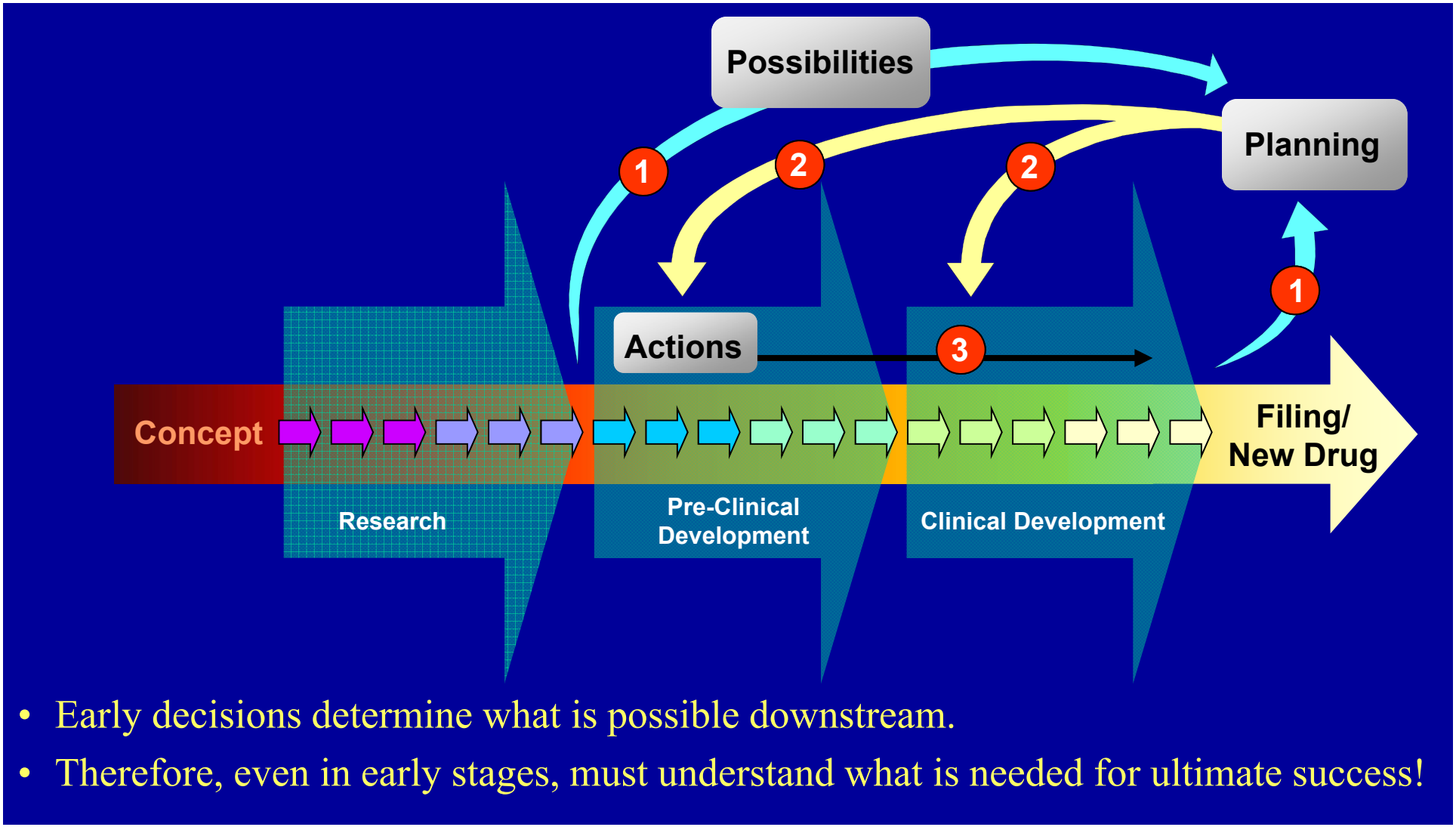
Decision Making at BI (2)

- In the past...
  - The organization was very decentralized
  - Autonomous units made recommendations for Development
- A new focus for R&D is evolving...
  - R&D is proactively seeking expertise from other functional areas to help guide better decision-making
  - Commercial issues are being brought into focus much earlier

Drug Development Process

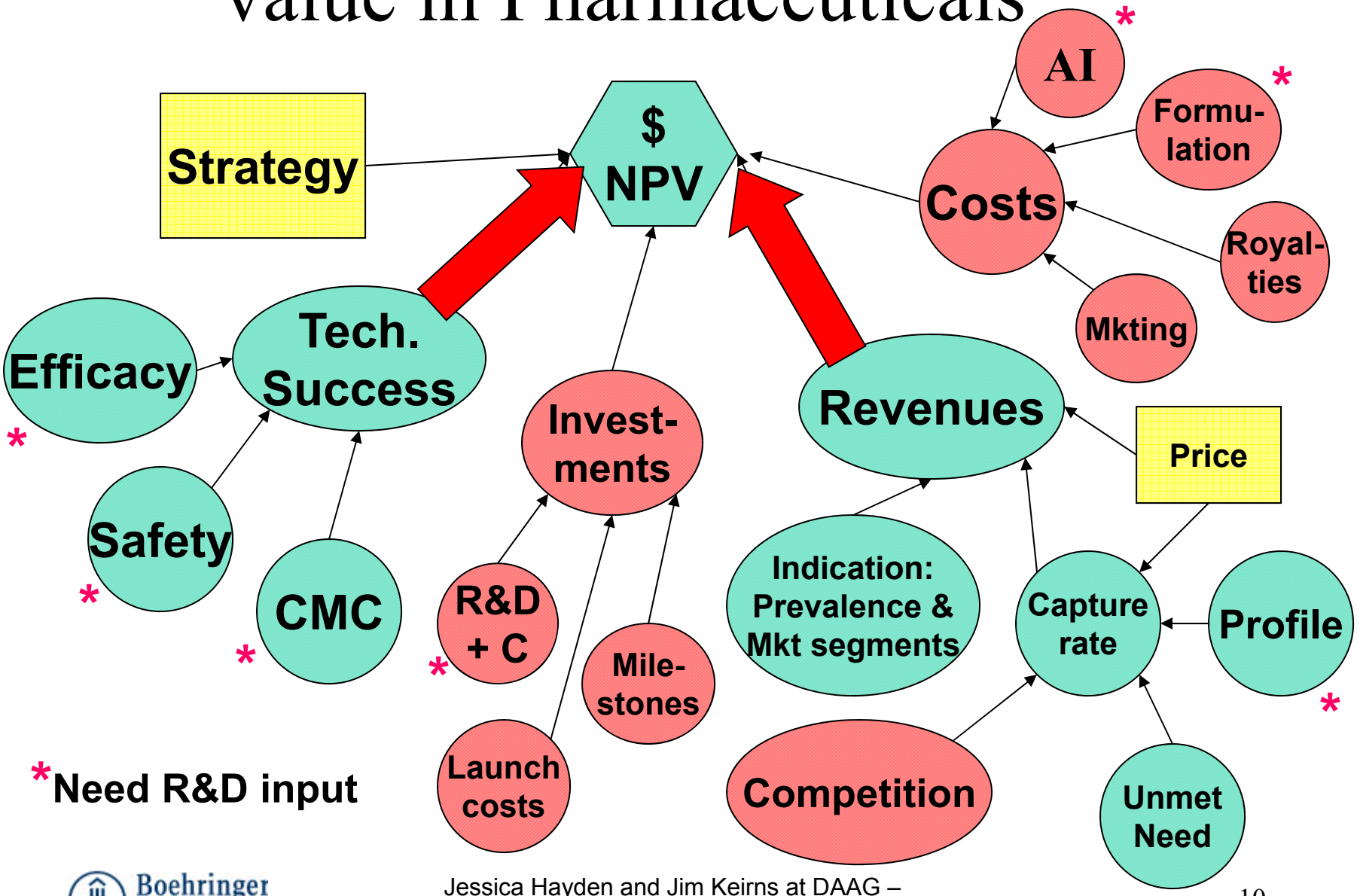


"The Process" is *Not* as Linear as it Looks



- Early decisions determine what is possible downstream.
- Therefore, even in early stages, must understand what is needed for ultimate success!

Major factors that drive shareholder value in Pharmaceuticals



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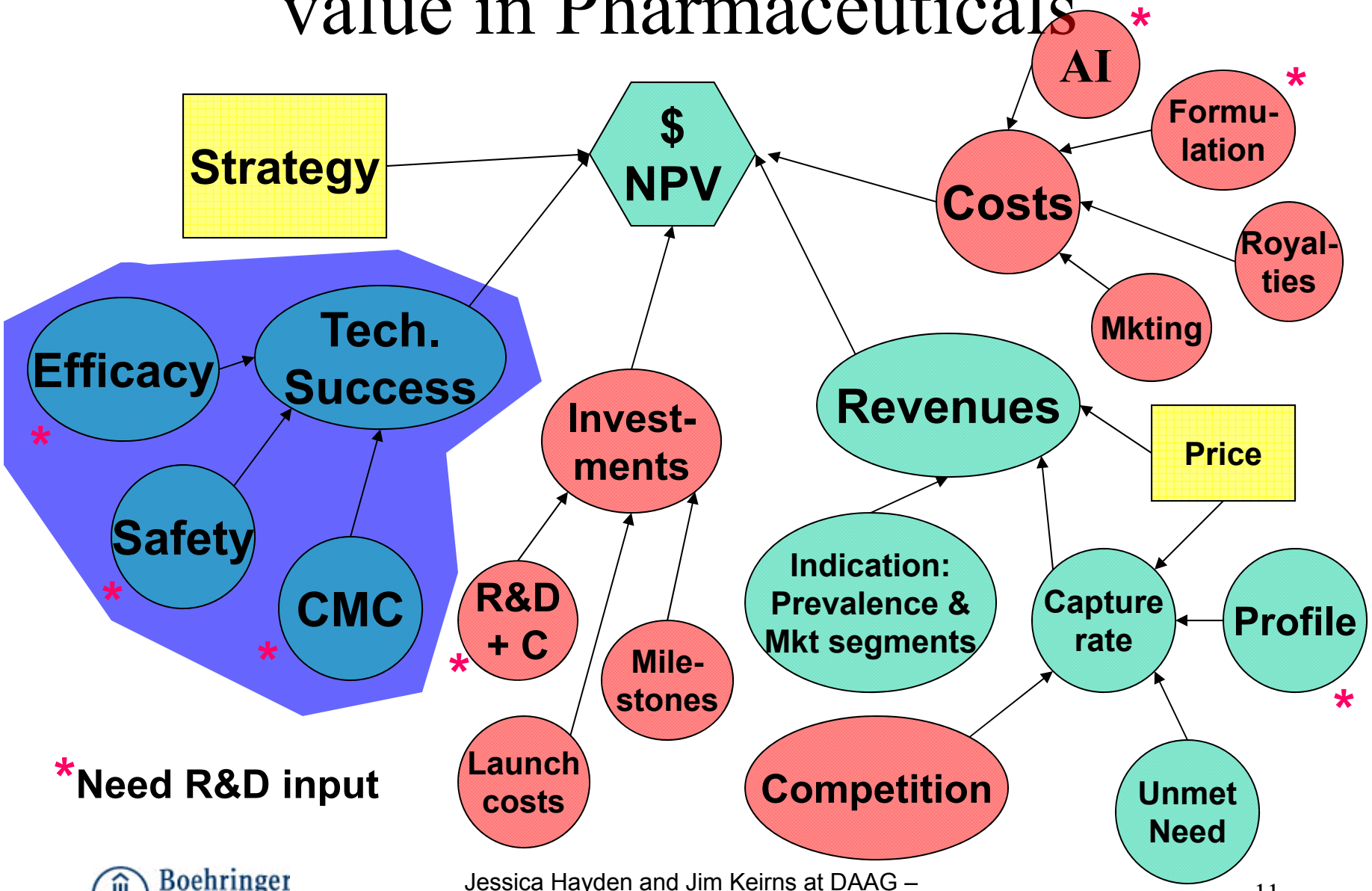
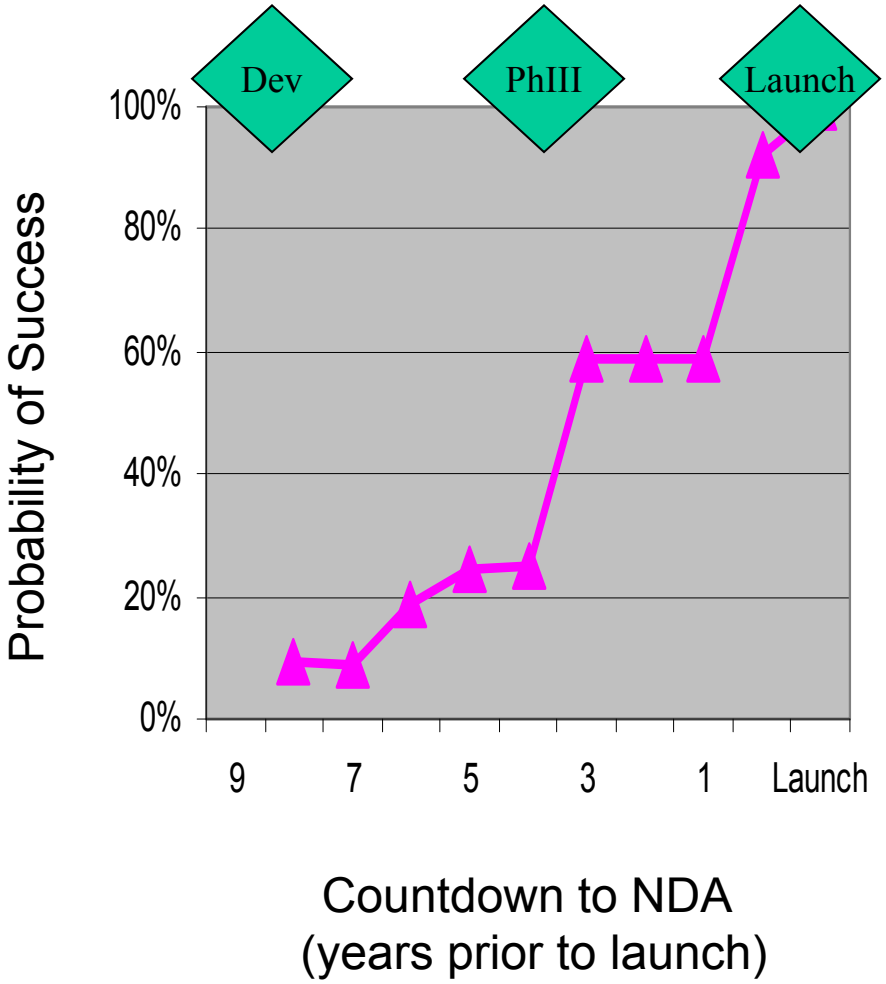


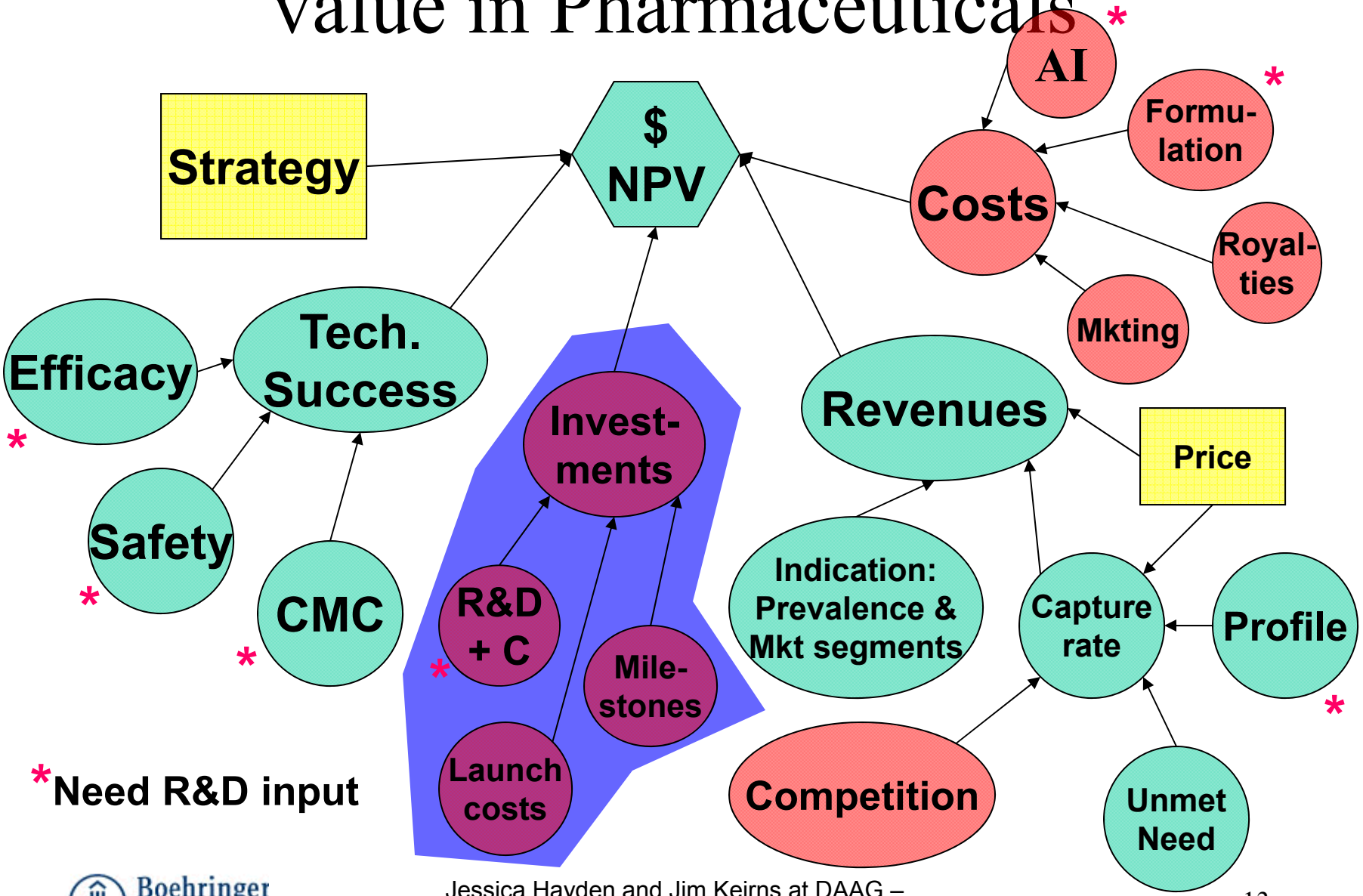
Cumulative Probability of a Successful NCE Launch



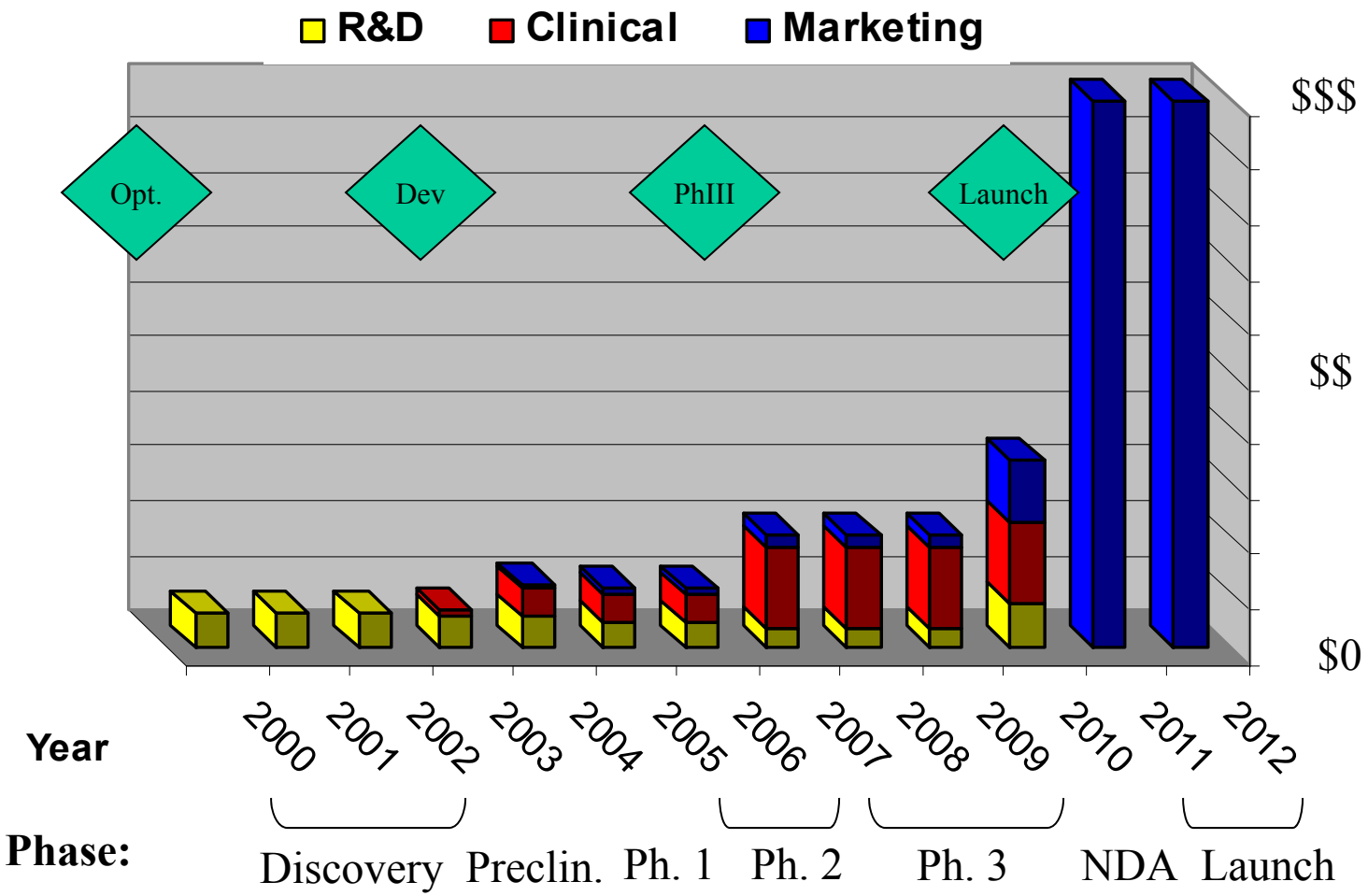
Stage	Duration (in Years)	Success in Phase
Preclinical	1.5	50%
Phase I	1	75%
Phase II	2	42%
Phase III	3	64%
NDA	1	92%
TOTAL	**8**	**9%**

Data from Tufts

Major factors that drive shareholder value in Pharmaceuticals



Investments for an NCE (1 Indication)



Case 1: Exclusive vs non-exclusive license for an enabling technology

Issue:

- A non-exclusive license was 10-fold less than exclusive one
- R&D budget limits constrained perspective
- The incremental expense seemed cost prohibitive

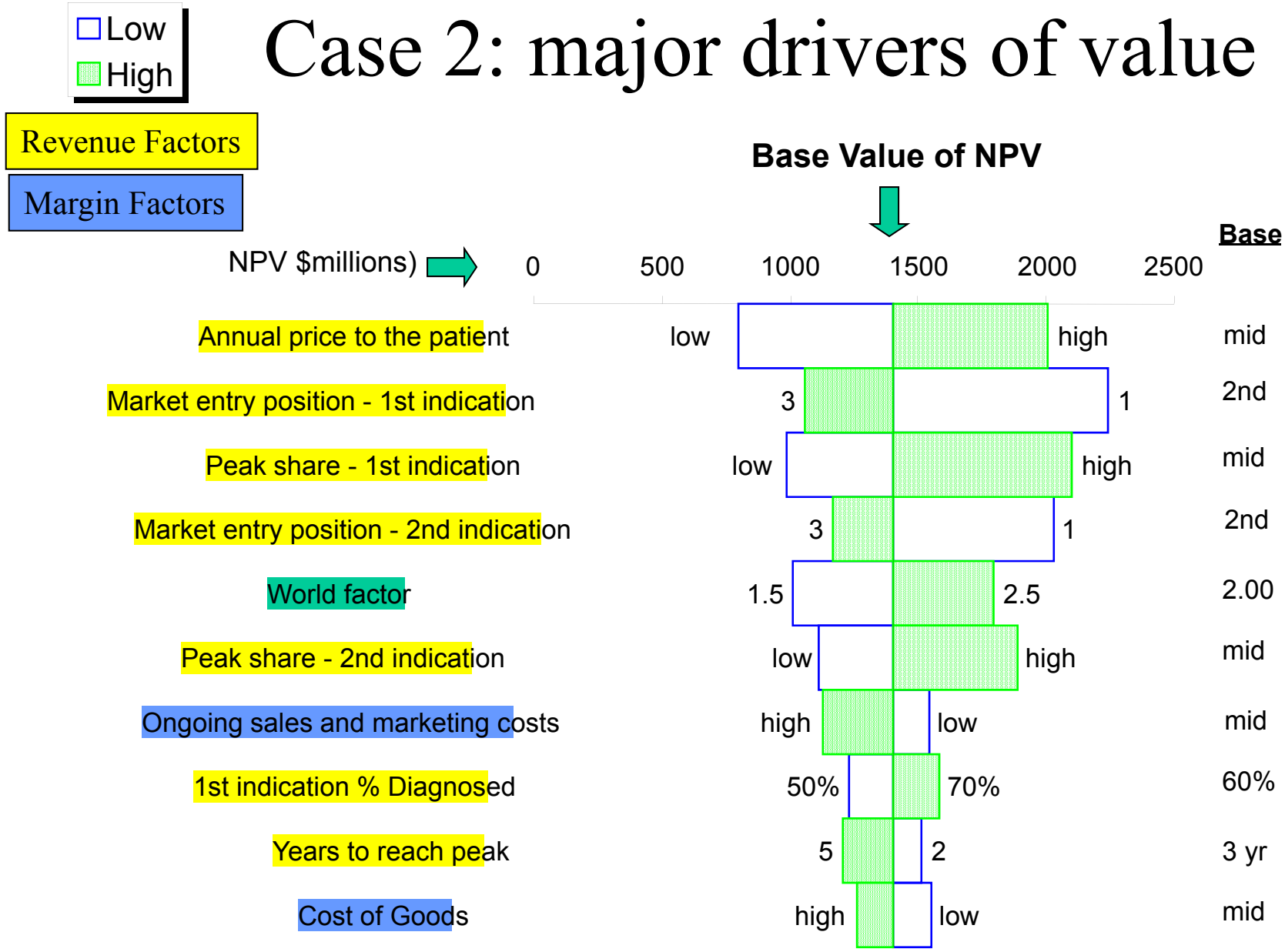
Decision Analysis:

- In the long-term the net difference in investment would be trivial
- The market share impact of exclusivity was 10-15%--worth a 50-fold return on investment!

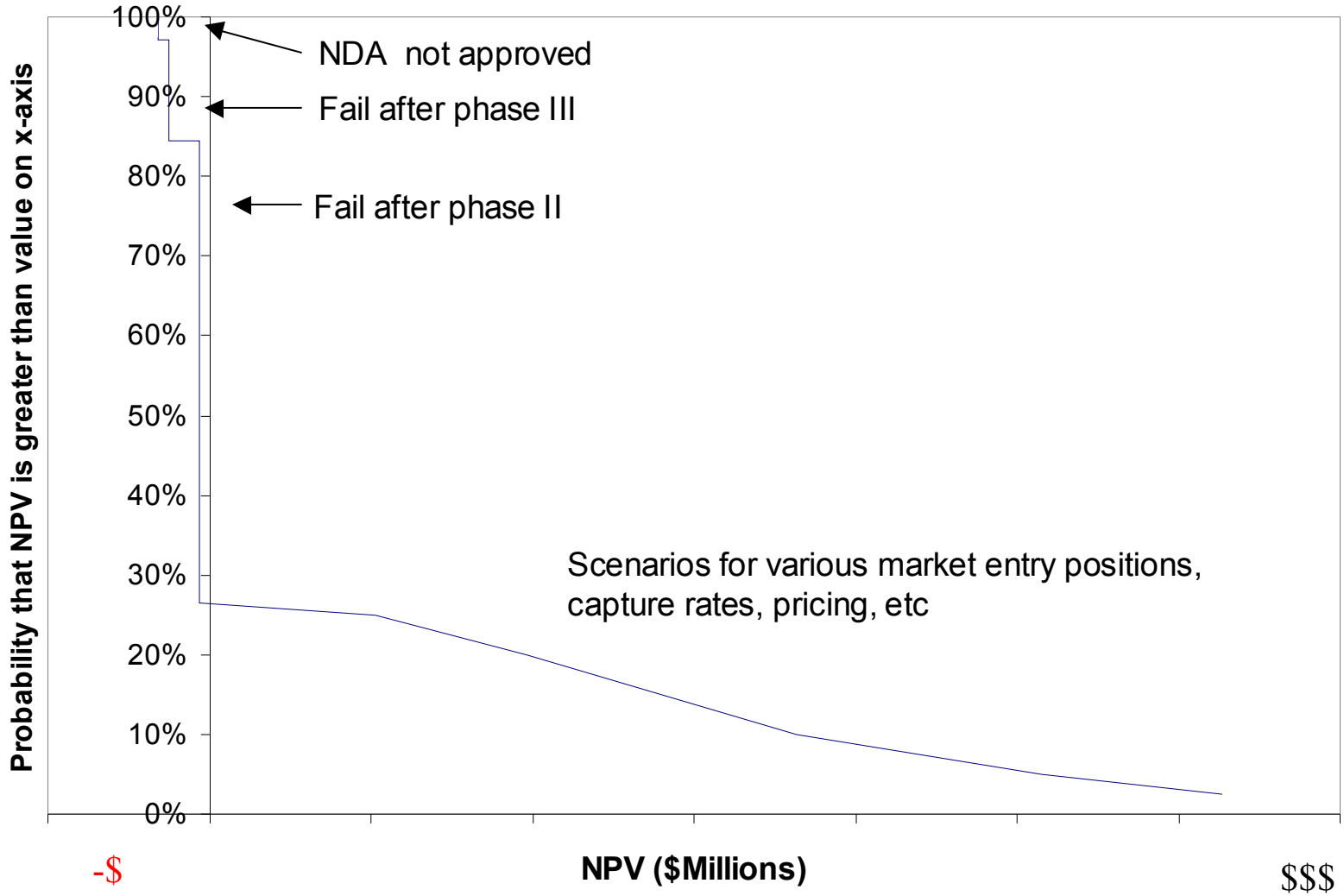
Case 2

- Pharmacodynamic agent (e.g. blood pressure drug)
- Indications:
  - two with large patient populations (initial DA)
  - one with small patient population (subsequent DA)
- Status: entering phase II

Case 2: major drivers of value



Case 2: Probability of NPV



Blockbuster

What about the small indication for Case 2?

- Modeling the added value of the the small 3rd indication, the NPV was near zero.
- In the sensitivity analysis the cost of phase III clinical was at the top of the tornado, even though for most projects it is not in the top 10 at all.
- Provoked a discussion in the project team which led to a hybrid strategy: Do phase II but not III for the 3rd indication, and expect that if the product is approved for one of the two larger indications, then may be able to negotiate with FDA to allow smaller study

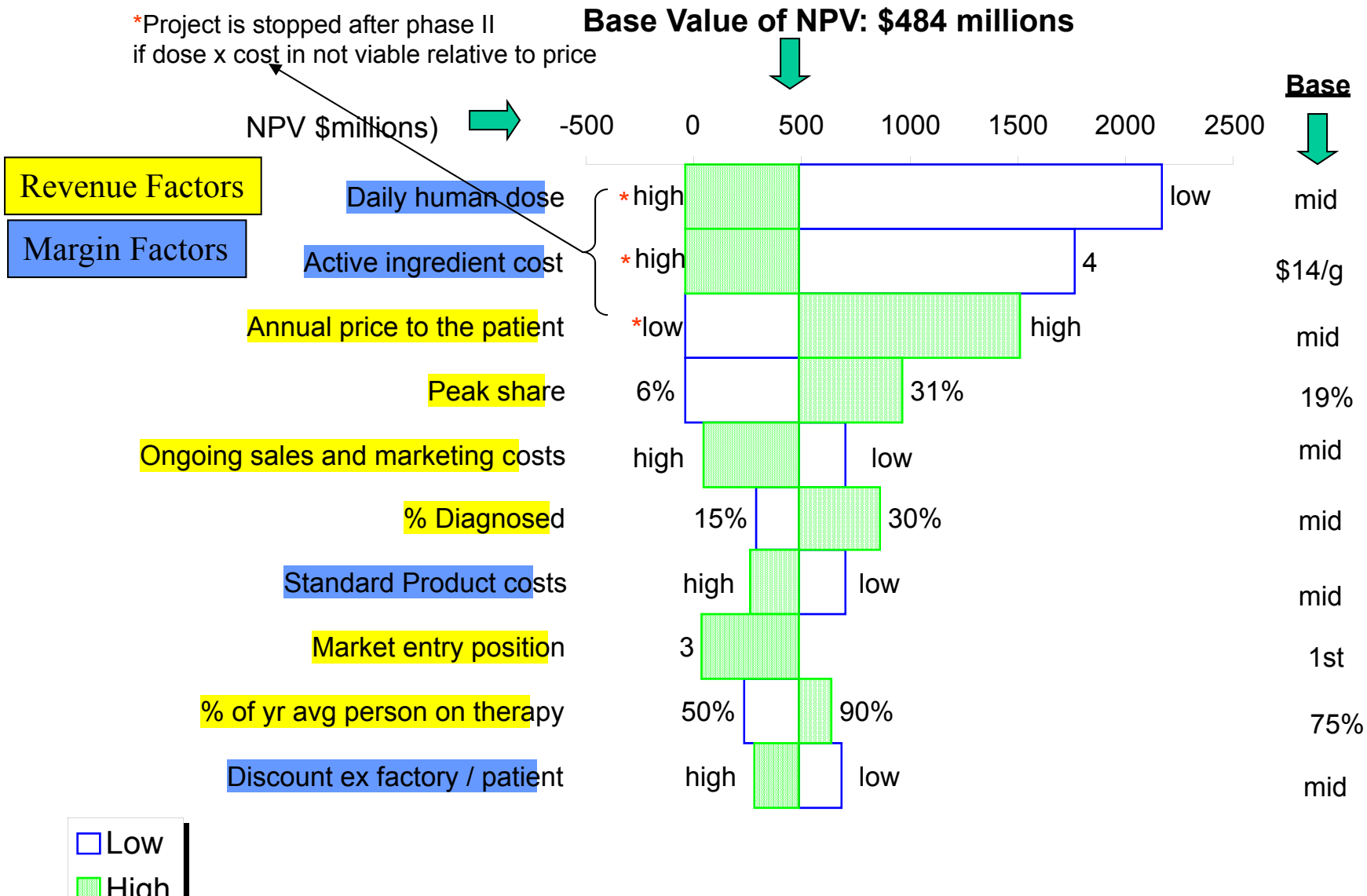
Case 3

- Chemotherapeutic agent (e.g. antimicrobial-high dose)
- Status: entering phase I
- Opportunity to be first in the market with an orally active compound for an indication with a high prevalence of in the major market countries **and** a large unmet need
- Opportunity for accelerated approval after phase II

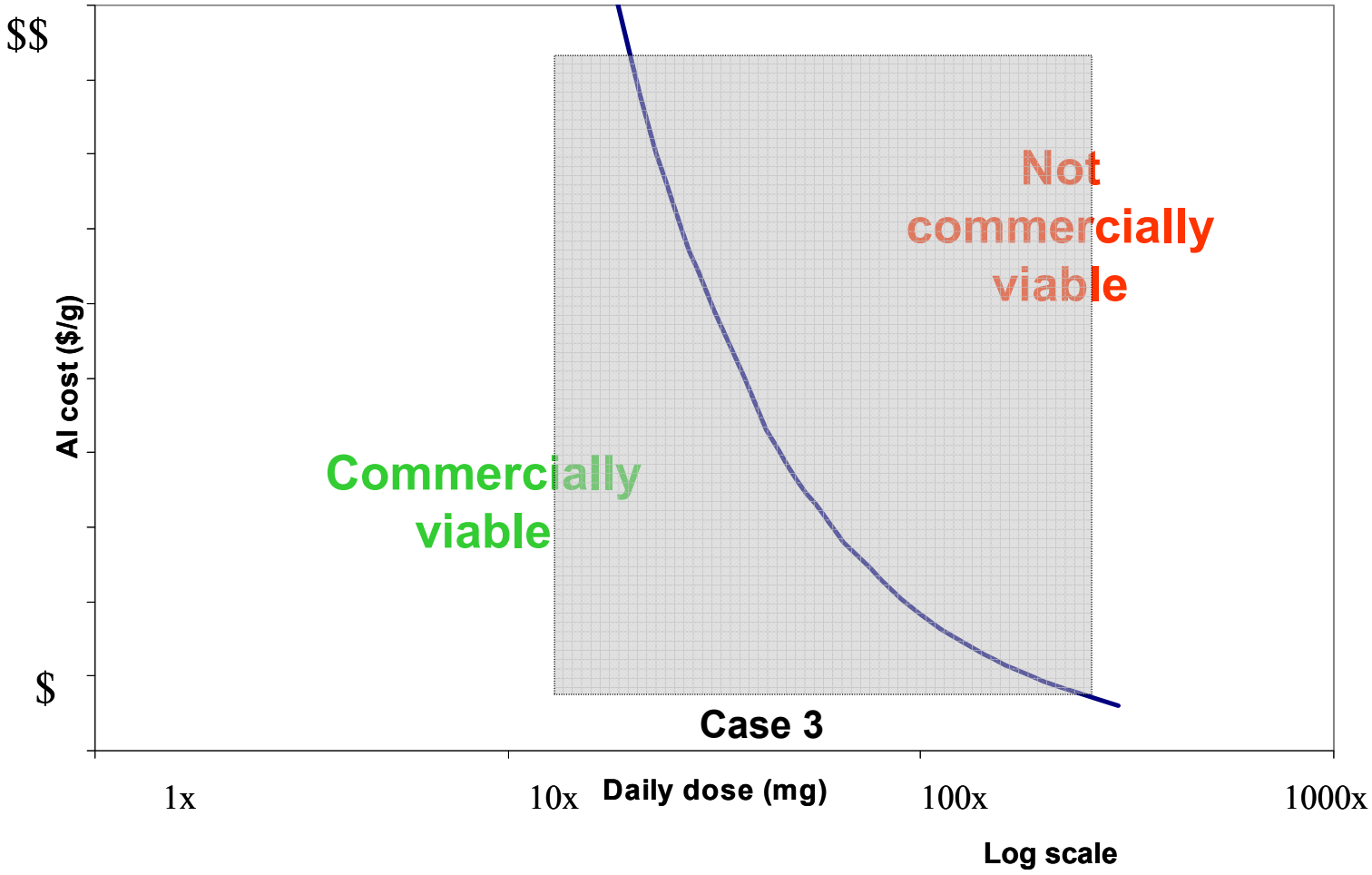
Case 3: most critical issue

- Complex compound requiring many steps to synthesize, leading to high cost of active ingredient.

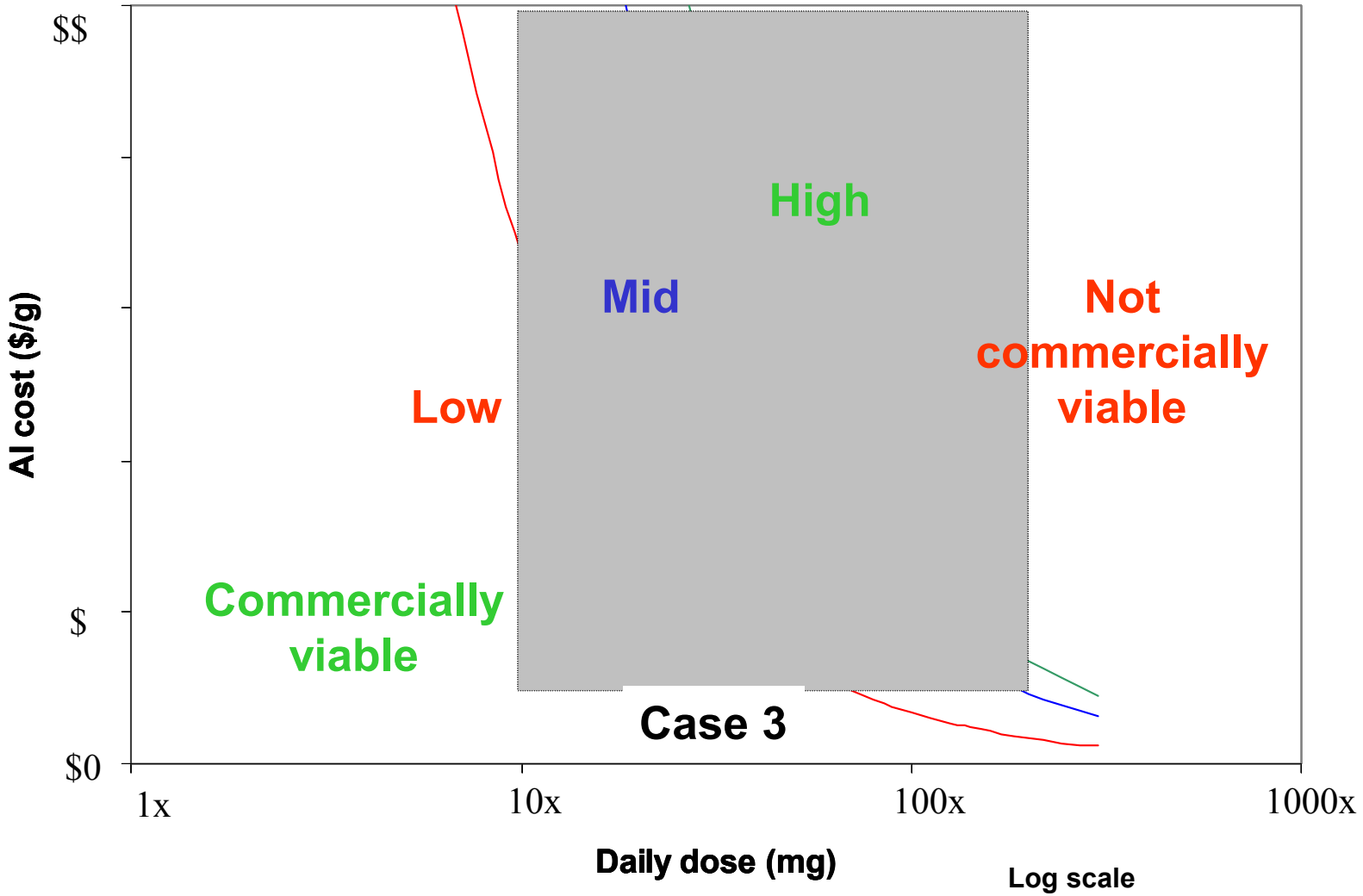
Case 3: major drivers of value



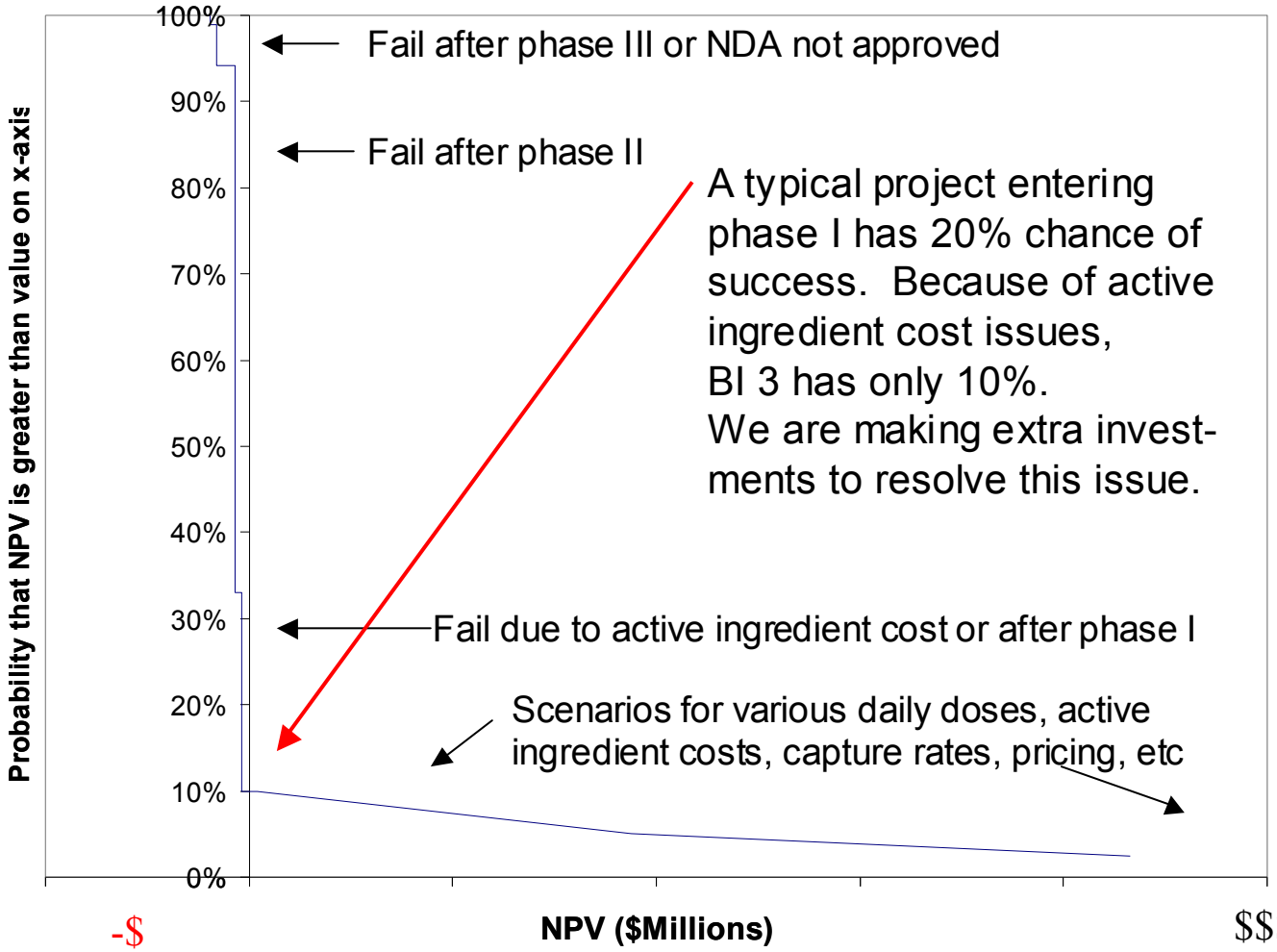
Relationship of Dose & Active Ingredient (AI) Cost at Mid-range Price to the Patient



Relationship of Dose & Active Ingredient (AI) Cost at Different Annual Prices to the Patient



Case 3: Probability of NPV



Case 4

- Another chemotherapeutic agent
- Status: preclinical.
- Opportunity: superior profile for well established mechanism of action

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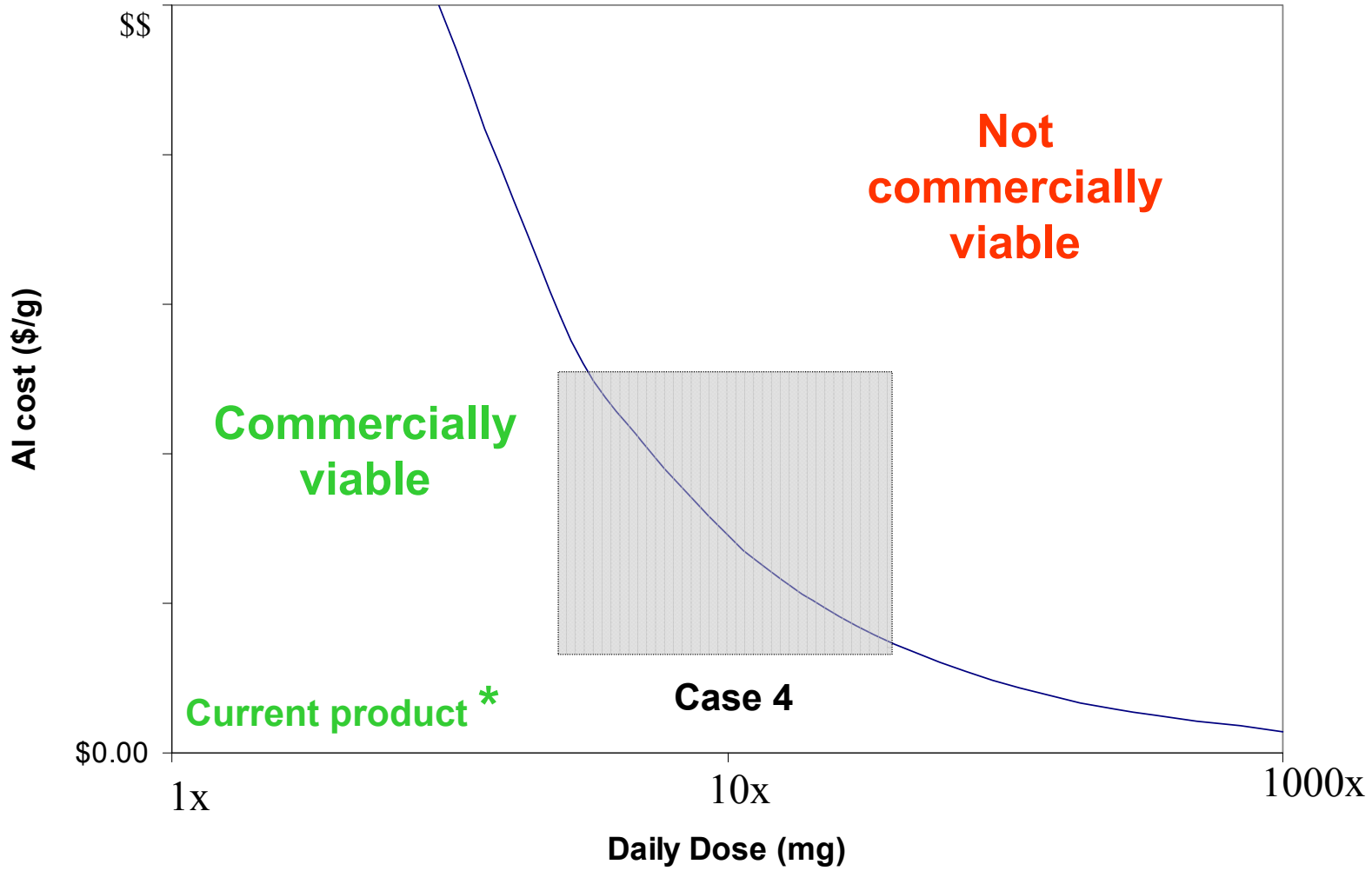
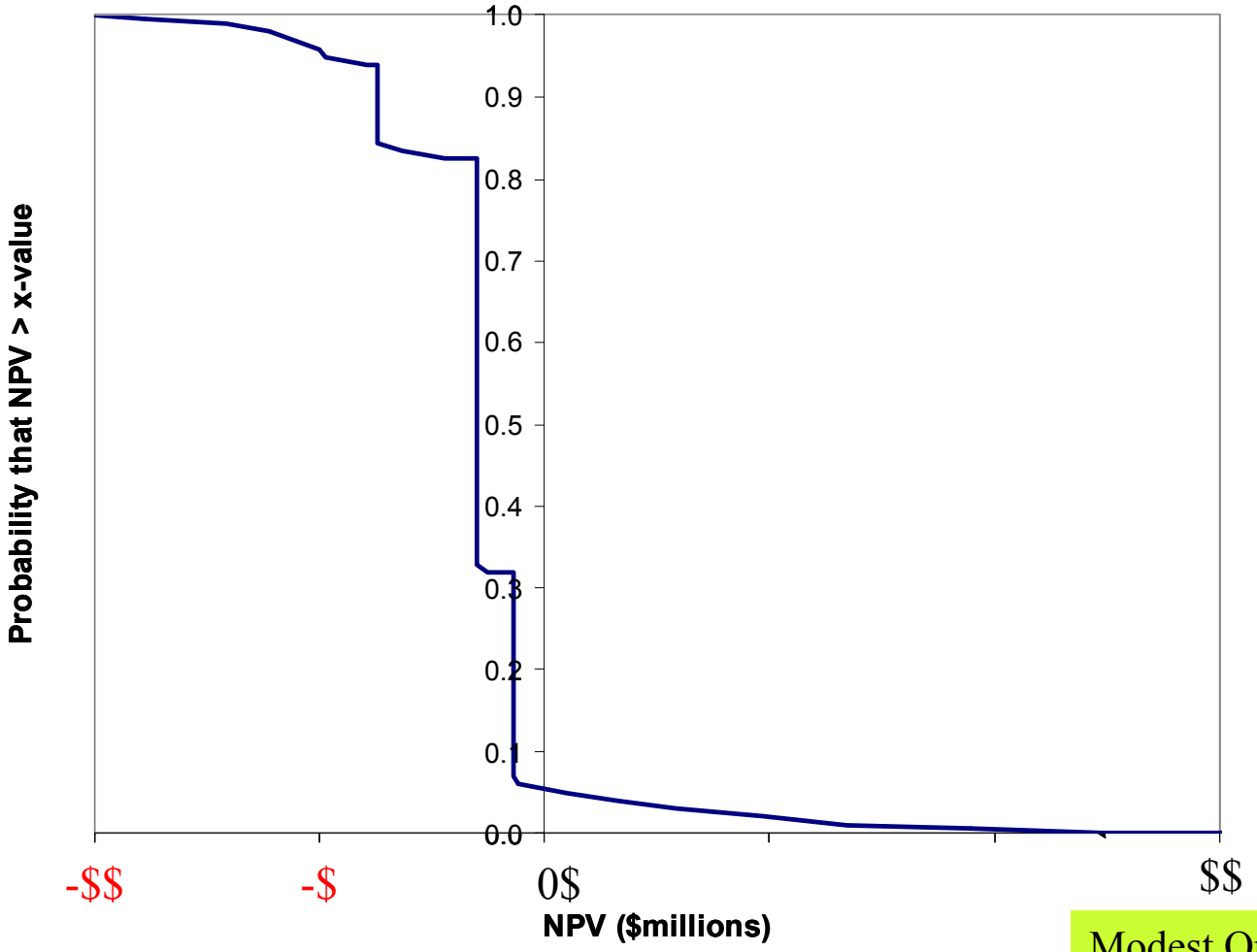


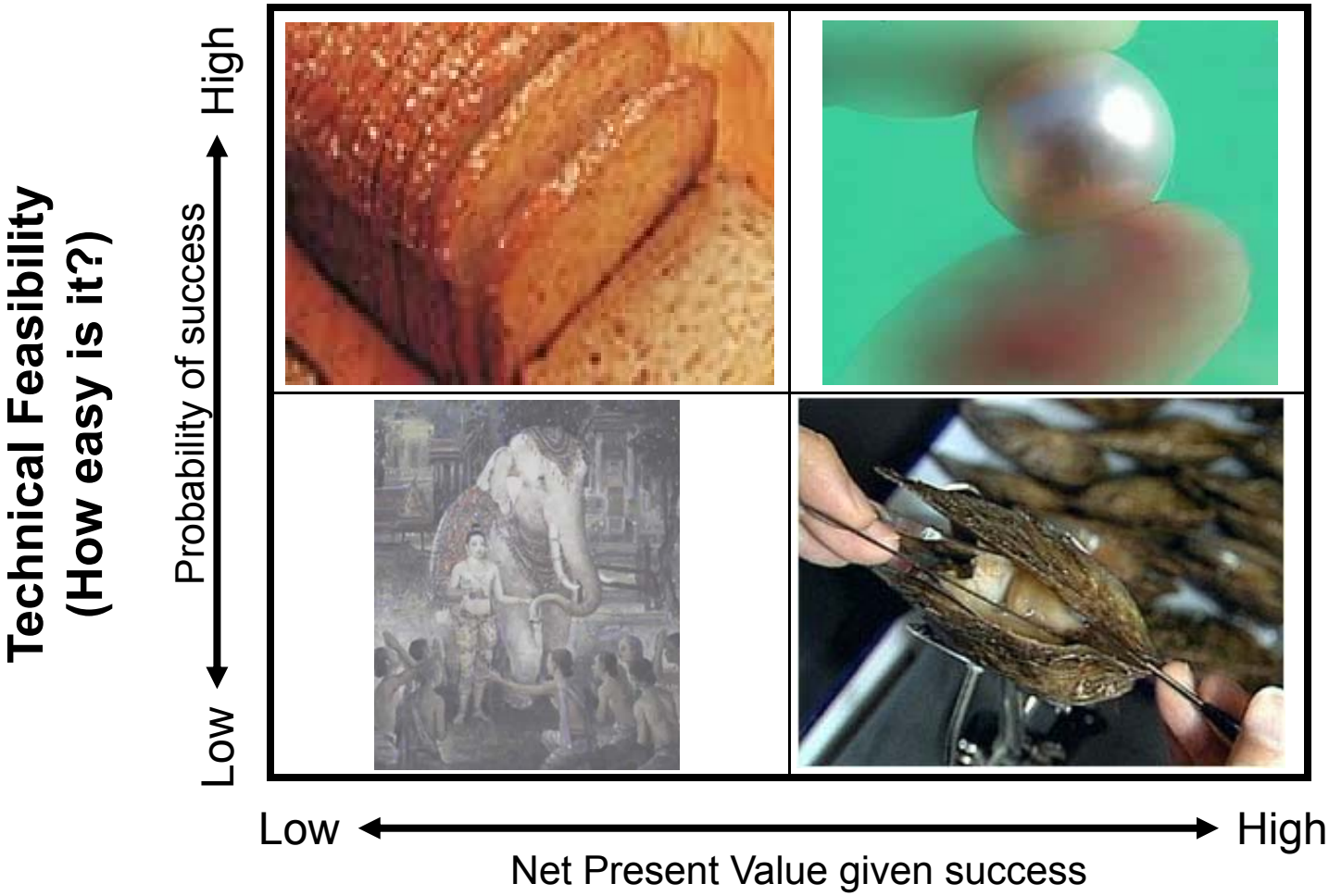
Case 4: Probability of NPV



NOTE: Range of x-axis scale is smaller than for BI3

Modest Opportunity

Project Portfolio Matrix



Maintain Competitiveness

Commercial Potential (Why do it?)

Gain strategic advantage

Ref: David & James Matheson, The Smart Organization

Conclusions

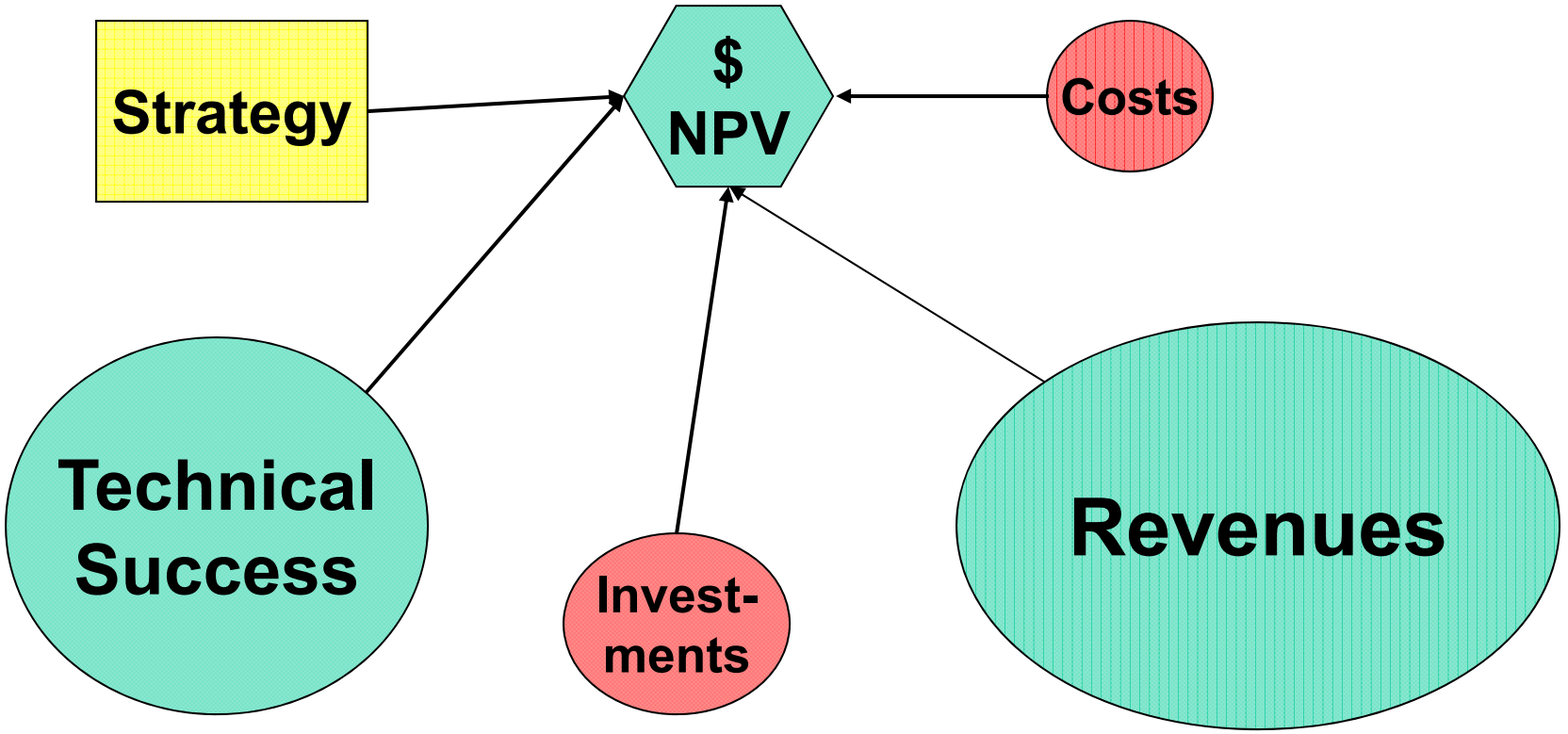
- Patterns:
  - Most of BI's early to mid-stage projects are Oysters (low probability of success, high value given success)
- DA reveals exceptions
  - Case 2 typical
  - Cases 3&4 were examples of how factors that are normally unimportant can become important
- Patterns can be misleading

Back-up slides

How can we make the best decision?

- Check our frame to assure that we are asking the most important question.
- Generate creative, doable alternatives
- Focus on long-term shareholder value, **e**xpected **N**et **P**resent **V**alue
- Have our most knowledgeable & experienced people assess the various key inputs that drive value
- Use logically correct reasoning to infer the eNPV of the alternatives in the face of uncertainties
- Build-in commitment of the organization to implement the decision

Major factors that drive value of a project



Phase Transition Probabilities

	Phase I to II	Phase II to III	Phase III to approval	Overall
All NCEs	75%	42%	64%	20%
anti-infect	78%	50%	77%	30%
CNS	90%	44%	50%	20%
rDNA proteins	88%	72%	50%	32%

presented by Kenneth Kaitin, Center for Study of Drug Development, Tufts University

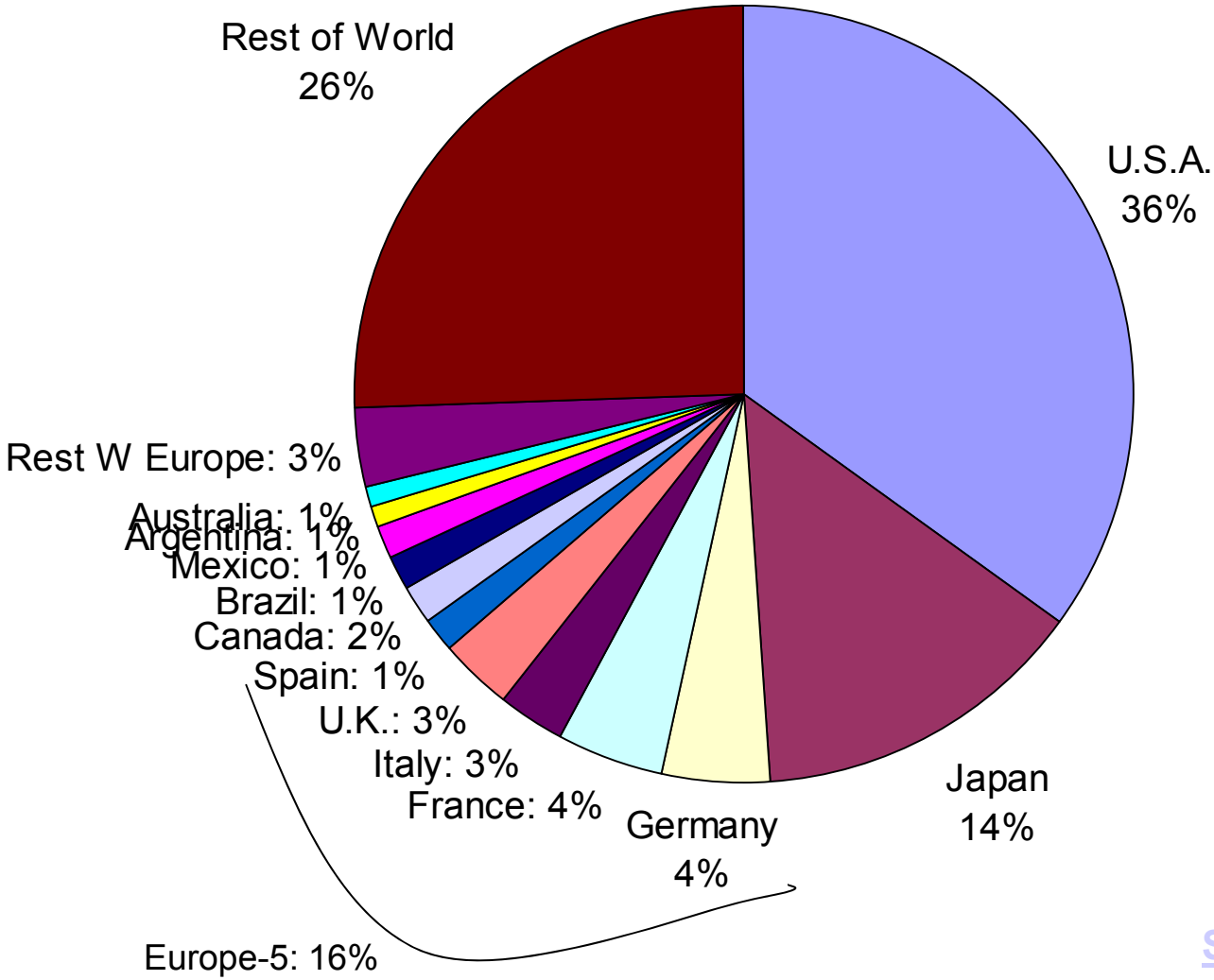
references: DiMasi, PharmacoEcon, **7**: 152-69, 1995;
Gross, Clin. Pharm. Ther., **60**: 608-18, 1996

World Pharma Market in 2000

COUNTRY	2000 Pharma sales (billion)	GDP (billions)	Population (millions)	GDP per head	Pharma Sales as % of GDP	Pharma Sales per head	% of World Pharma Sales	BI share of total market
U.S.A.	$131.11	$9,333	274.9	$33,951	1.40%	$477	35.1%	1.07%
JAPAN	$51.46	$3,913	127.4	$30,717	1.32%	$404	13.8%	1.27%
GERMANY	$16.77	$2,260	82.7	$27,333	0.74%	$203	4.5%	2.70%
FRANCE	$16.69	$1,465	58.7	$24,956	1.14%	$284	4.5%	0.93%
ITALY	$10.84	$1,237	57.8	$21,400	0.88%	$188	2.9%	1.59%
U.K.	$11.05	$1,424	59.5	$23,929	0.78%	$186	3.0%	1.53%
SPAIN	$5.29	$577	39.4	$14,640	0.92%	$134	1.4%	2.11%
CANADA	$6.16	$692	30.9	$22,395	0.89%	$199	1.6%	0.95%
BRAZIL	$5.15	$536	163.4	$3,279	0.96%	$32	1.4%	3.02%
MEXICO	$4.90	$497	98.4	$5,046	0.99%	$50	1.3%	4.72%
ARGENTINA	$3.43	$326	37.0	$8,816	1.05%	$93	0.9%	2.53%
AUSTRALIA	$3.04	$416	19.1	$21,801	0.73%	$159	0.8%	1.43%
Rest of W Europe	$12.89	$2,247	89.7	$25,052	0.57%	$144	3.4%	1.79%
Sub-total	$278.79	$24,923	1138.9				74.5%	
Rest of World	$95.21	$5,778	4872.1	$1,186	1.65%	$20	25.5%	
Whole world	$374.00	$30,701	6011.0	$5,107	1.22%	$62	100.0%	1.38%

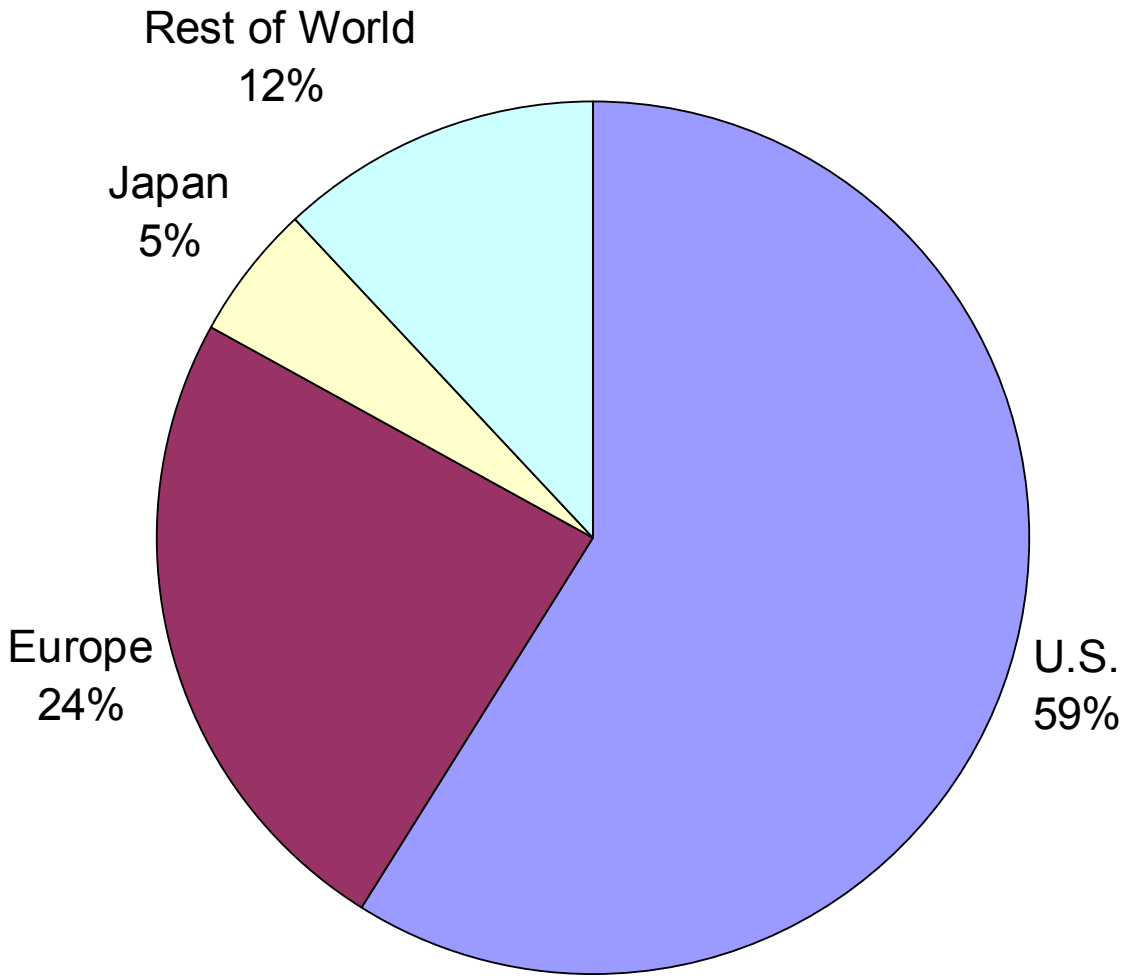
Sources: Pharma sales from IMS. GDP & population from the Economist

2000 Pharmaceutical Sales



Source: IMS

1999 Sales of drugs launched since 1995



Source IMS Health, cited in Wall St Journal, March 20, 2000

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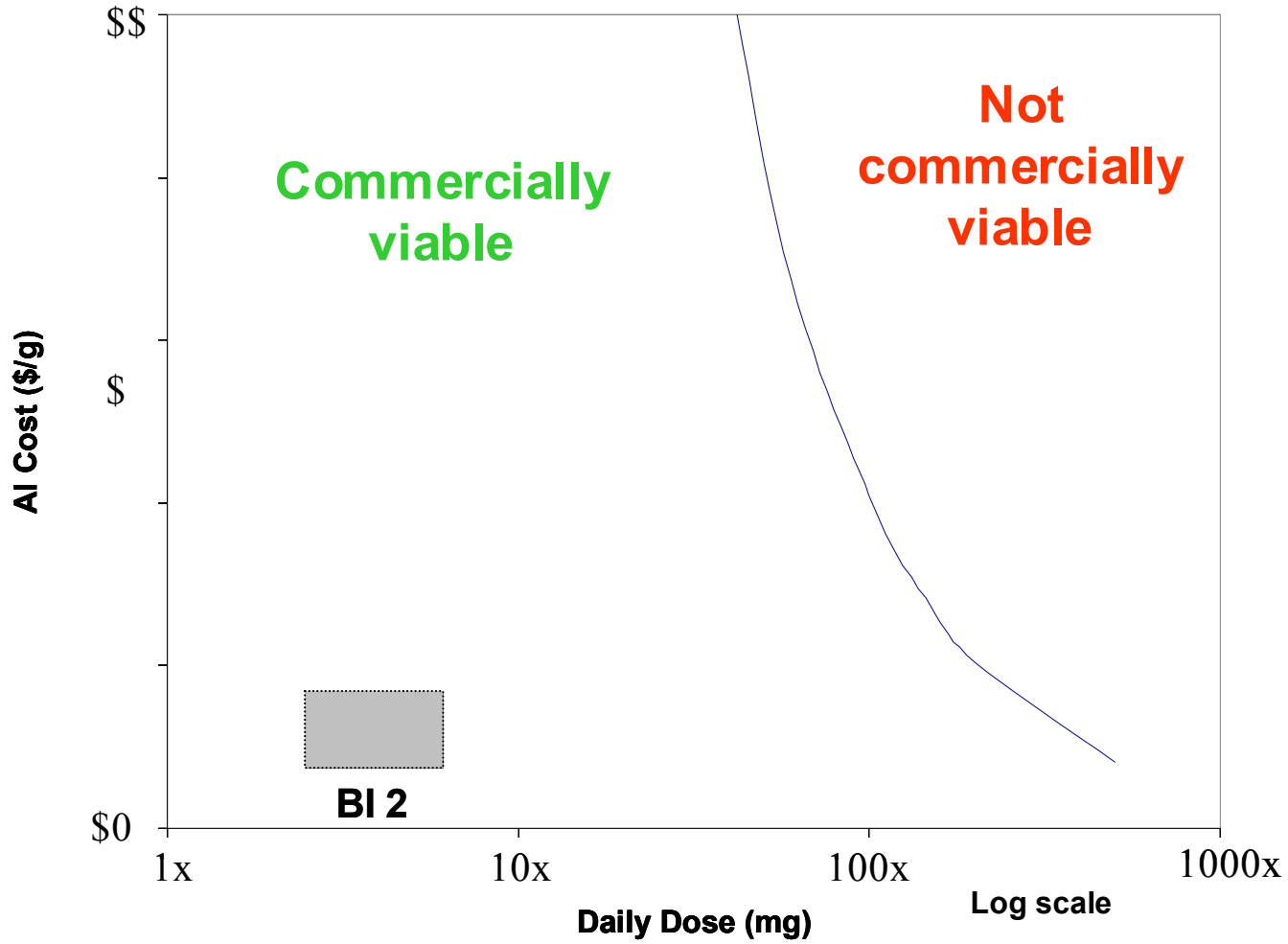

Dose-Response