Pharmaceutical Portfolio Management

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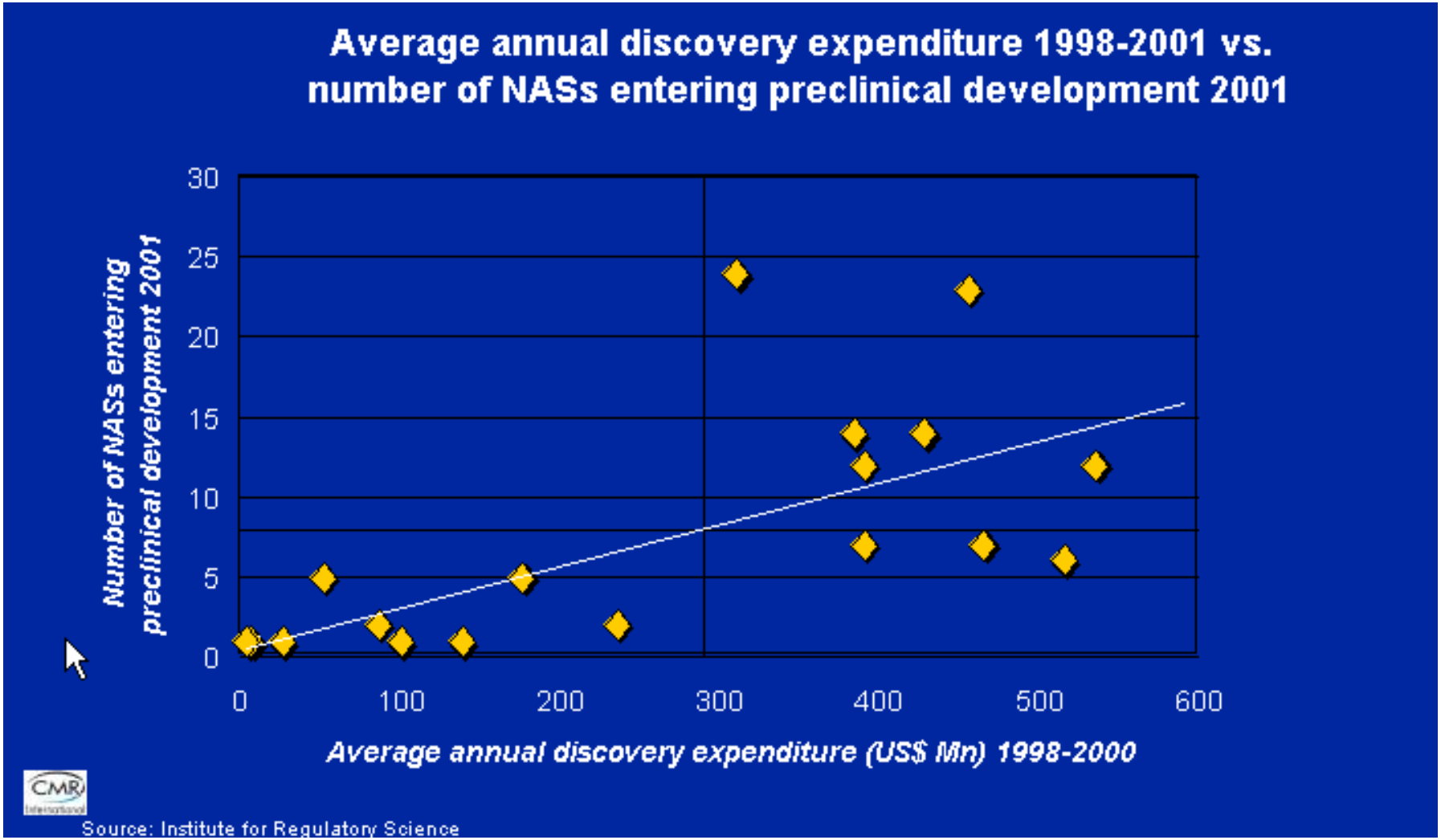
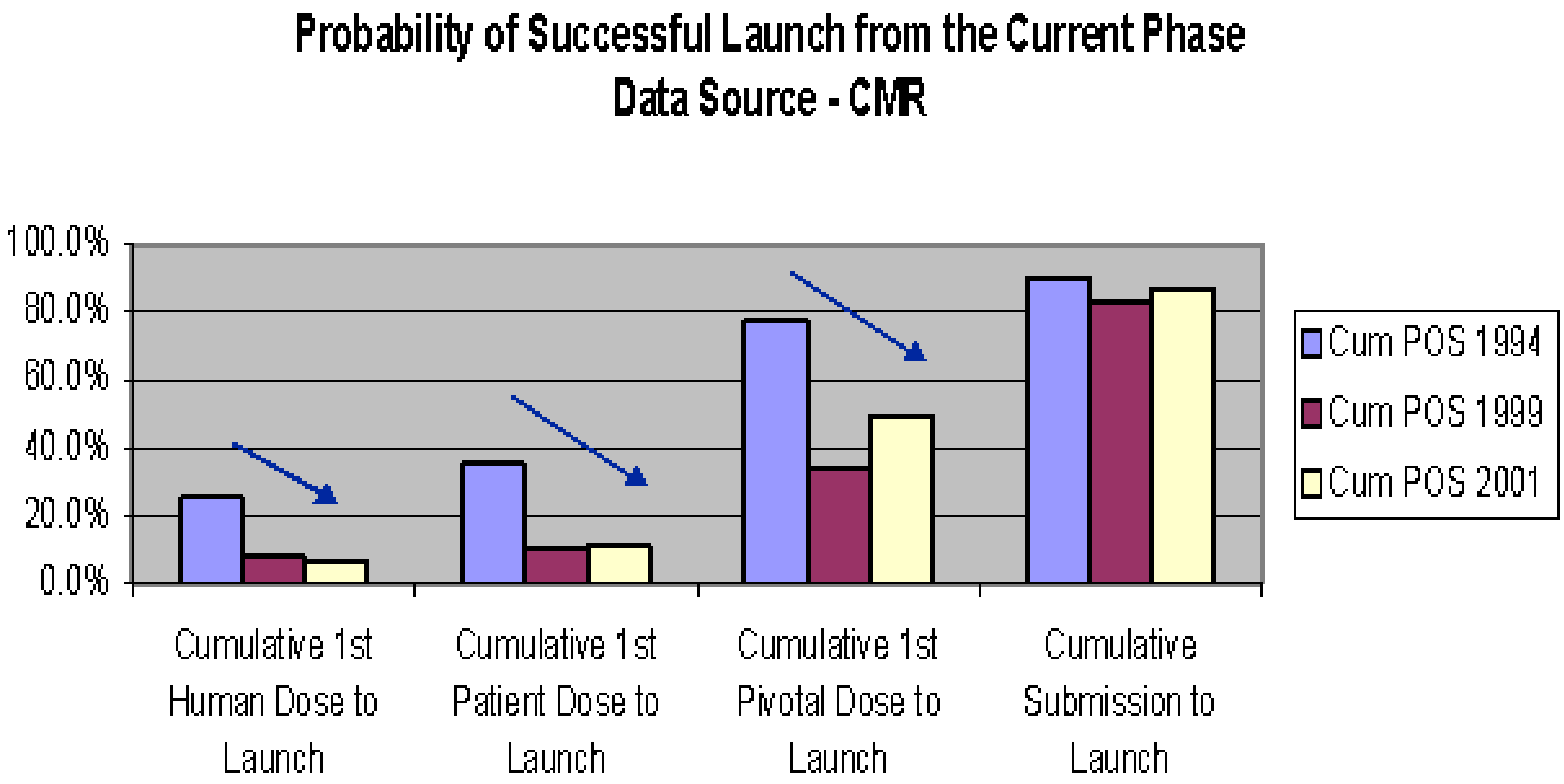
Outline

- Pharmaceutical Industry R&D Challenges
- Asset Evaluation - Application of Decision Analysis
- Portfolio Analysis & Management

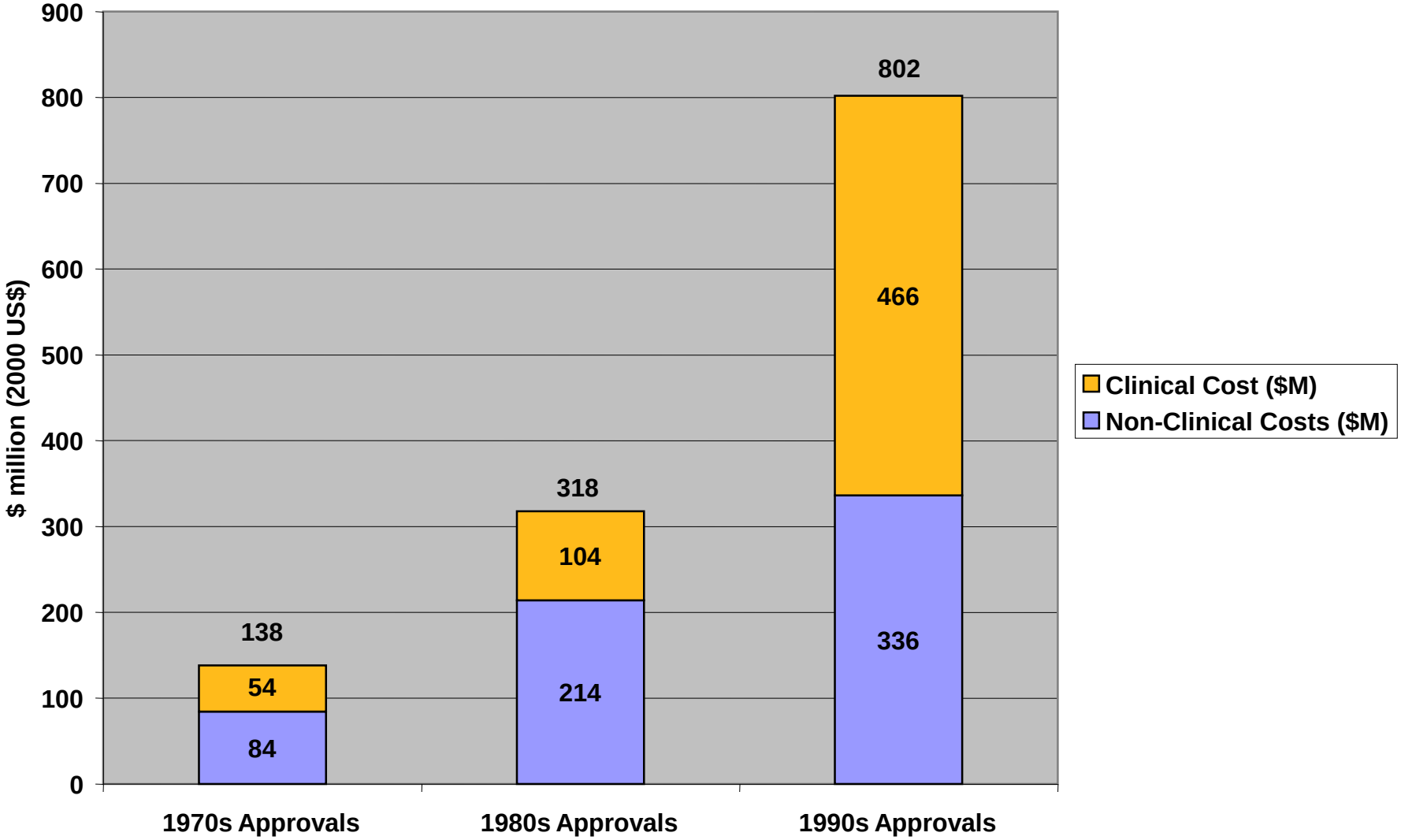
No economy of scale in drug discovery productivity



Overall probability of success has been declining over the last decade

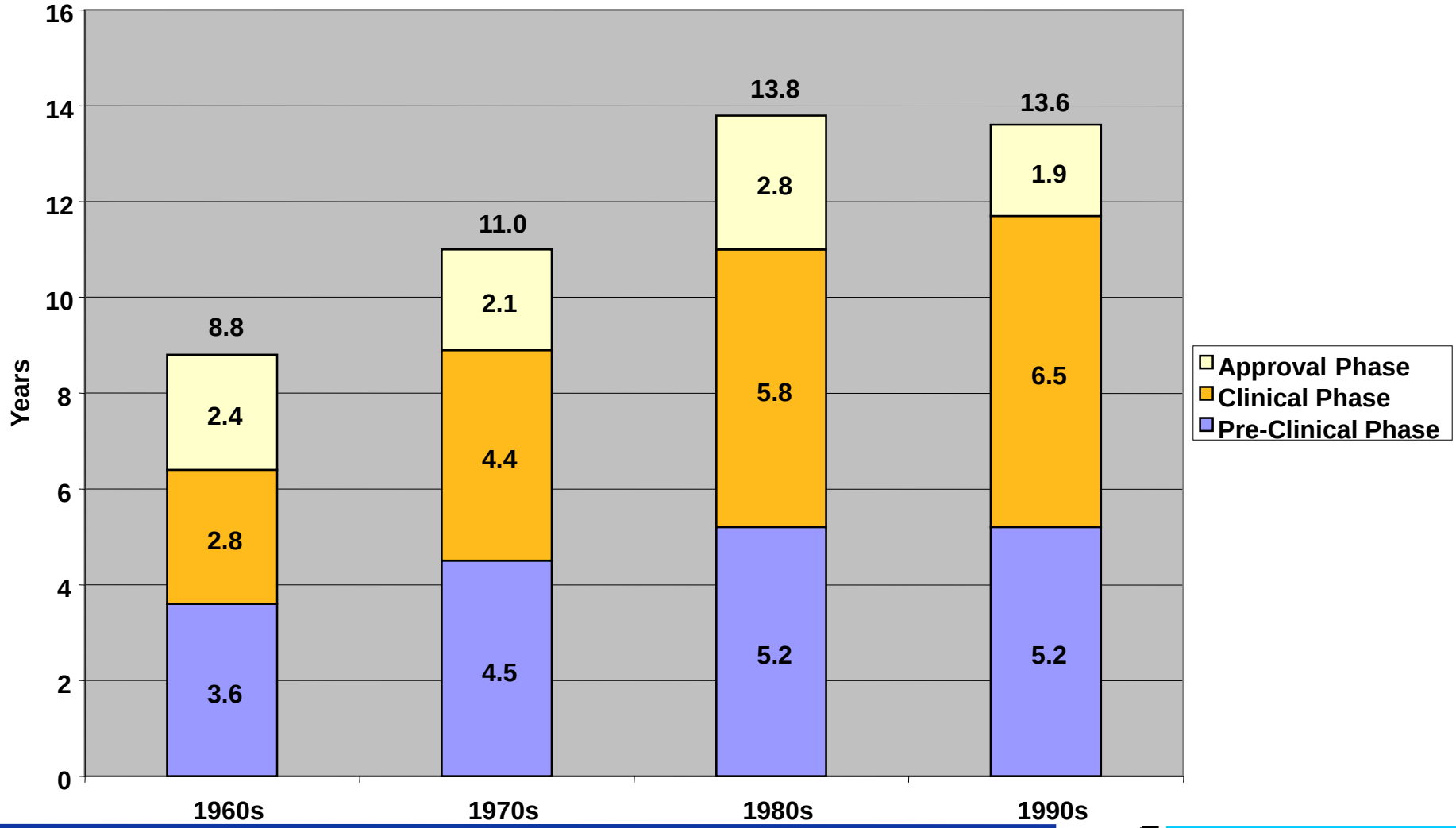


The drug discovery & development costs have been increasing significantly over the decades



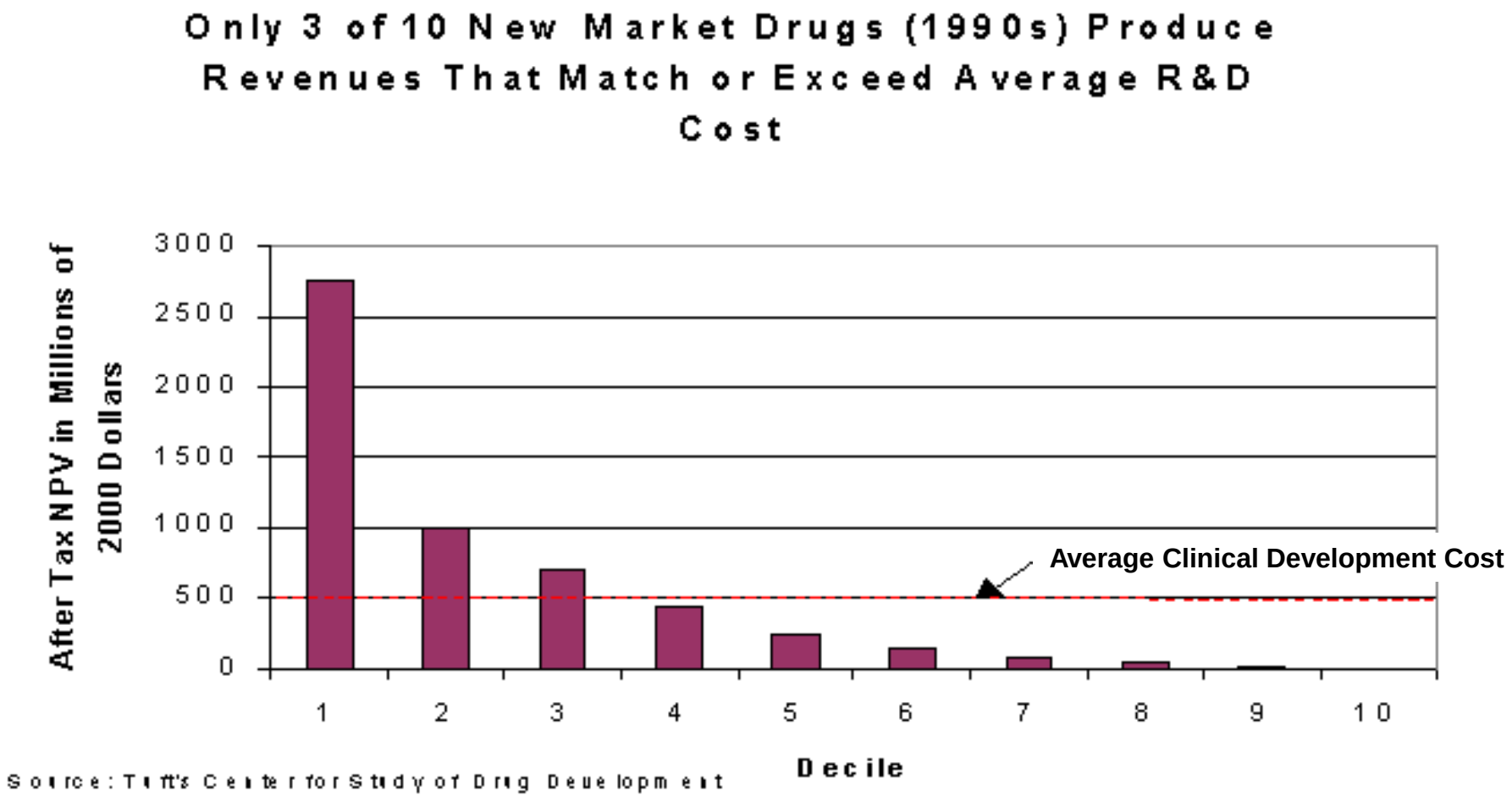
Source: Tufts CSDD 2002

It takes more than 10 years to develop a drug to market.



Source: Tufts CSDD 2002

Only limited number of drugs will have positive return on investment



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Asset Evaluation Process

Strategic Alternative Generation

Situation Assessment

- Define/confirm current plan
- Define project scope

Alternative Development

- Brainstorm options for each decision
- Define strategic alternatives for evaluation
- Create a rationale for each strategic alternative
- Develop Expected Target Profiles (ETPs)

ETP/Asset Valuation

Technical and Cost Analysis

- Define success criteria and assess probabilities
- Assess time to market
- Define development program assumptions
- Estimate development costs

Commercial Analysis

- Assess market size, share and price
- Assess competitor dynamics
- Assess commercial costs
- Identify key commercial value drivers

Final Valuation

- Calculate expected value and productivity for each alternative
- Develop analysis insights
- Draft recommendations for Steering Committee review

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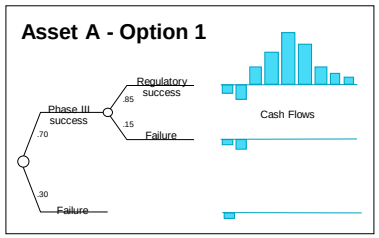
Portfolio Management Process



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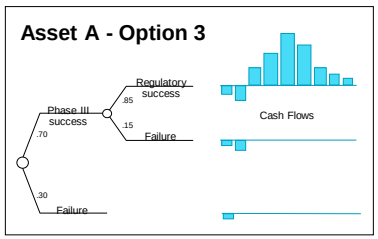

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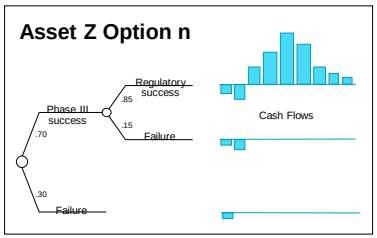

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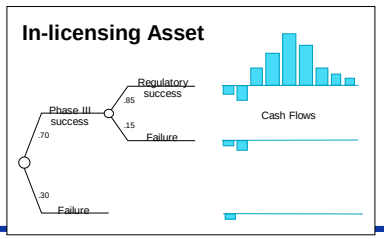


Multiple investment options per asset

Multi-year budget & resource constraints

Strategic considerations

Portfolio Management System

- Max ENPV given constraints, strategic choices & risk preferences
- Portfolio- level tradeoff analyses

Portfolio Decision Making

Partner commitments

Short vs. long-term tradeoffs

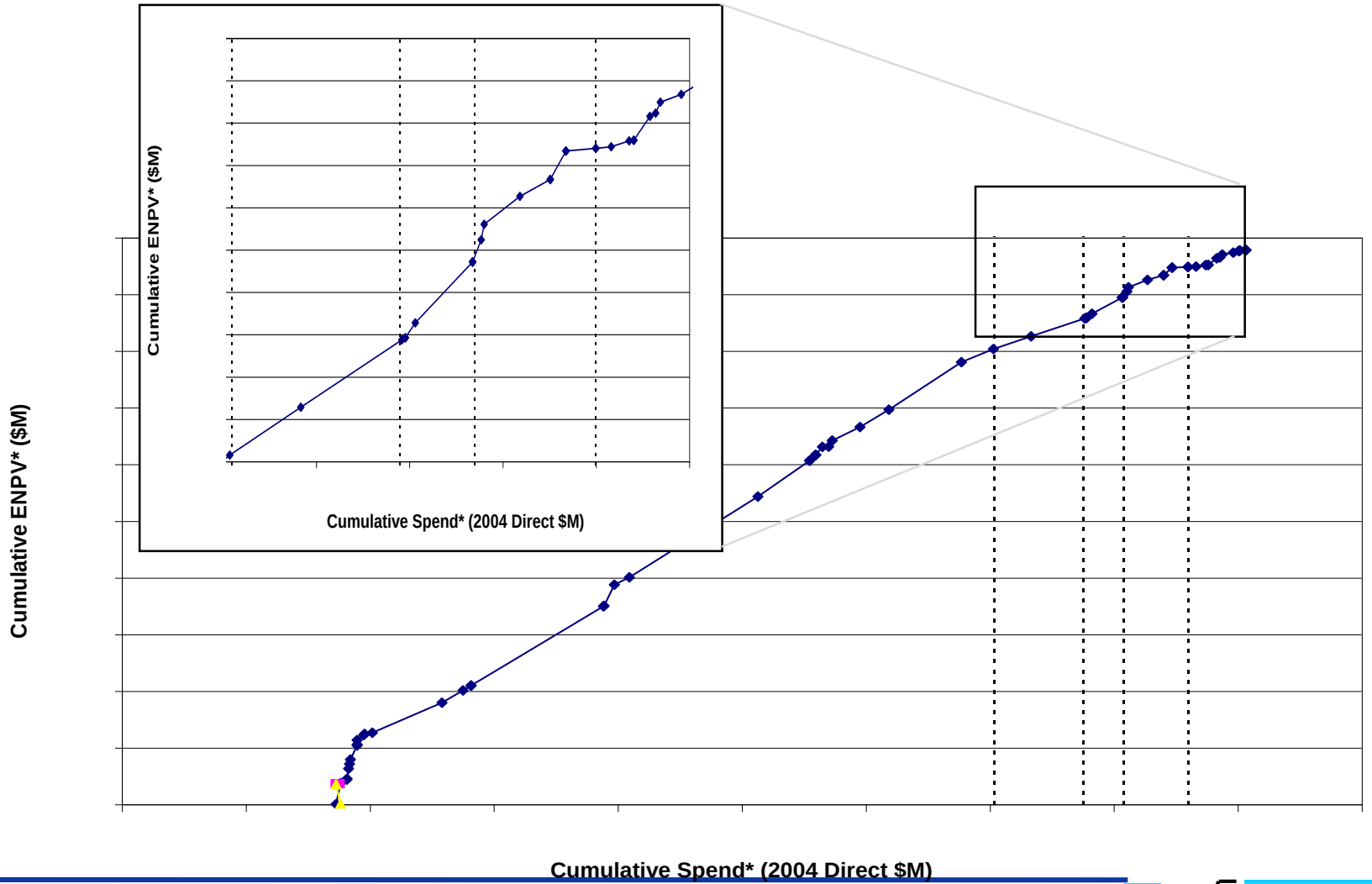
Improved analysis of near term constraints, long term requirements, and therapeutic area gaps

Asset Opportunity Ranking by Expected Internal Rate of Return (EIRR)

Assets Opportunity ID	PTRS	ENPV	EIRR	Assets Opportunity ID	PTRS	ENPV	EIRR
1	92%	370	535%	25	6%	3	29%
2	78%	120	345%	26	48%	411	29%
3	20%	250	318%	27	25%	129	27%
4	80%	182	301%	28	10%	71	27%
5	74%	80	230%	29	82%	837	26%
6	58%	80	230%	30	63%	288	26%
7	30%	250	210%	31	40%	12	26%
8	85%	80	90%	32	14%	116	24%
9	27%	90	83%	33	21%	137	24%
10	53%	18	83%	34	21%	132	24%
11	81%	23	76%	35	43%	183	24%
12	26%	214	59%	36	14%	80	23%
13	59%	582	58%	37	35%	151	22%
14	72%	87	54%	38	45%	12	20%
15	62%	1,400	48%	39	35%	8	19%
16	36%	77	42%	[illegible]	46%	230	19%
17	40%	27	[illegible]	[illegible]	19%	28	19%
18	24%	371	[illegible]	[illegible]	60%	3	19%
19	26%	102	[illegible]	[illegible]	42%	123	19%
20	89%	1,538	[illegible]	44	8%	15	18%
21	55%	633	[illegible]	45	31%	52	18%
22	7%	100	33%	46	7%	22	17%
23	24%	152	31%	47	18%	7	15%
24	64%	272	30%	48	38%	6	13%

ENPV: Expected Net Present Value
PTRS: Probability of Technical & Regulatory Success

Overall Portfolio Expected Net Present Value (ENPV) continues to increase given additional R&D spending (ranked by EIRR)



Portfolio Analysis -- Objective, Benefits, and Challenges

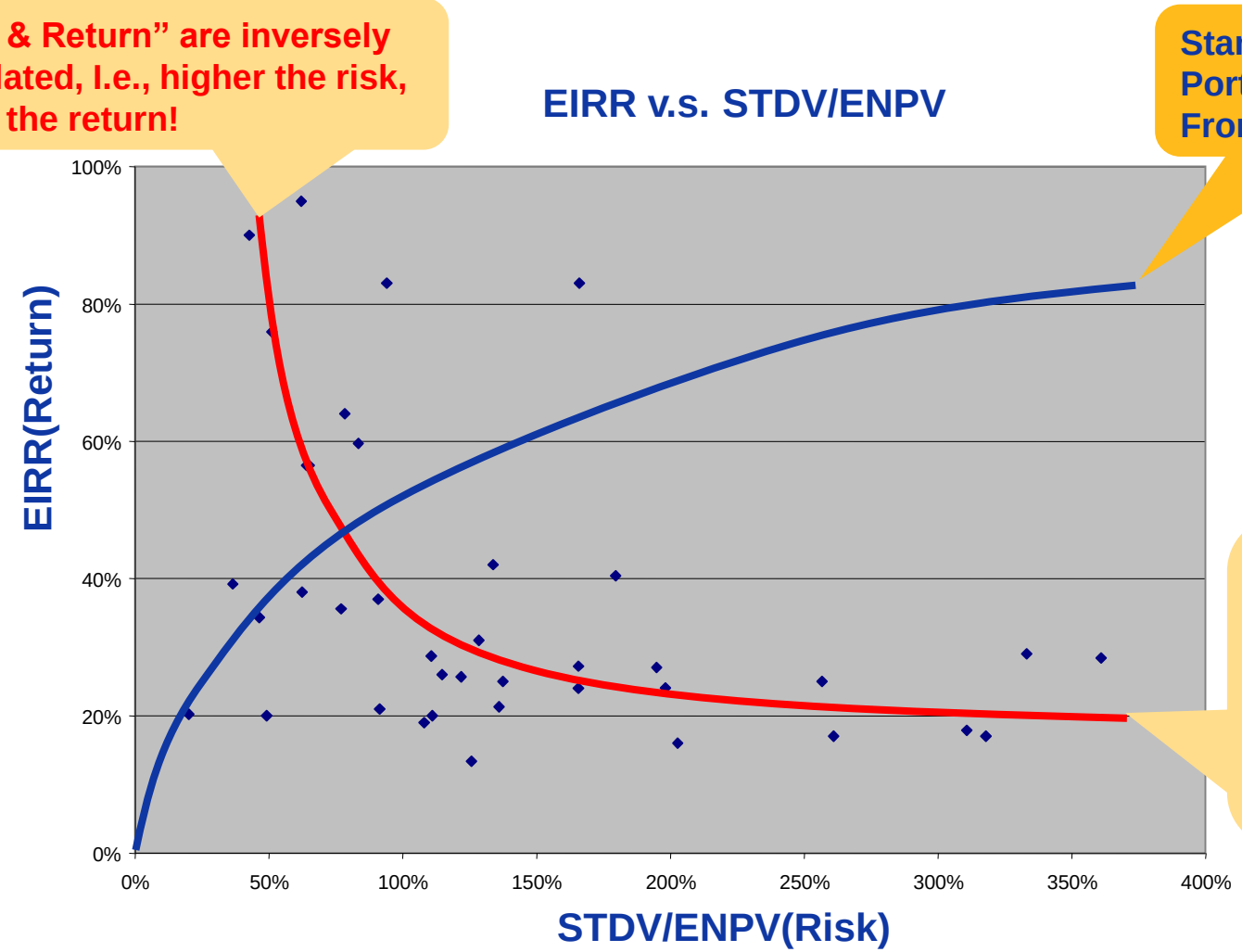
- Objective:
  - Find the “best” portfolio that meet short & long term strategic objectives of the company given coming year’s Budget & Resource Constraints
- Benefits:
  - Financial metric ranking (EIRR) or optimization (ENPV) provides clear prioritization of the assets.
  - Relatively simple to explain the recommendations
- Challenges:
  - Gross budget has a little relevance to actual spending - due to R&D spending uncertainty
  - Financial metric provides information related to “return”, but does not characterize the risk of portfolio sufficiently, (e.g., there is a systemic bias against early assets.)

Portfolio Analysis Challenges

- There are significant fundamental differences between the financial market portfolio and that of the pharmaceutical portfolio (Pipeline)
  - **Huge development uncertainty (high mortality rate as opposed to relatively stable financial assets)**
  - **Perishable nature of assets (limited patent life)**
  - **Maintenance of healthy pipeline is requirement for staying in business**
  - **Substantial lead time and transaction costs in modifying portfolio**
  - **Substantial cost in building and maintaining therapeutic area franchise**
  - **Shift in R&D/corporate strategy will have significant impact to the portfolio (e.g., potential attrition of assets, cost of acquiring new assets, rebuilding of portfolio and franchise)**
  - **Not all assets are tradable, nor available (inefficient market, arbitrage opportunity exists)**

Almost opposite relationship exists between risk and return from standard financial market relationship.

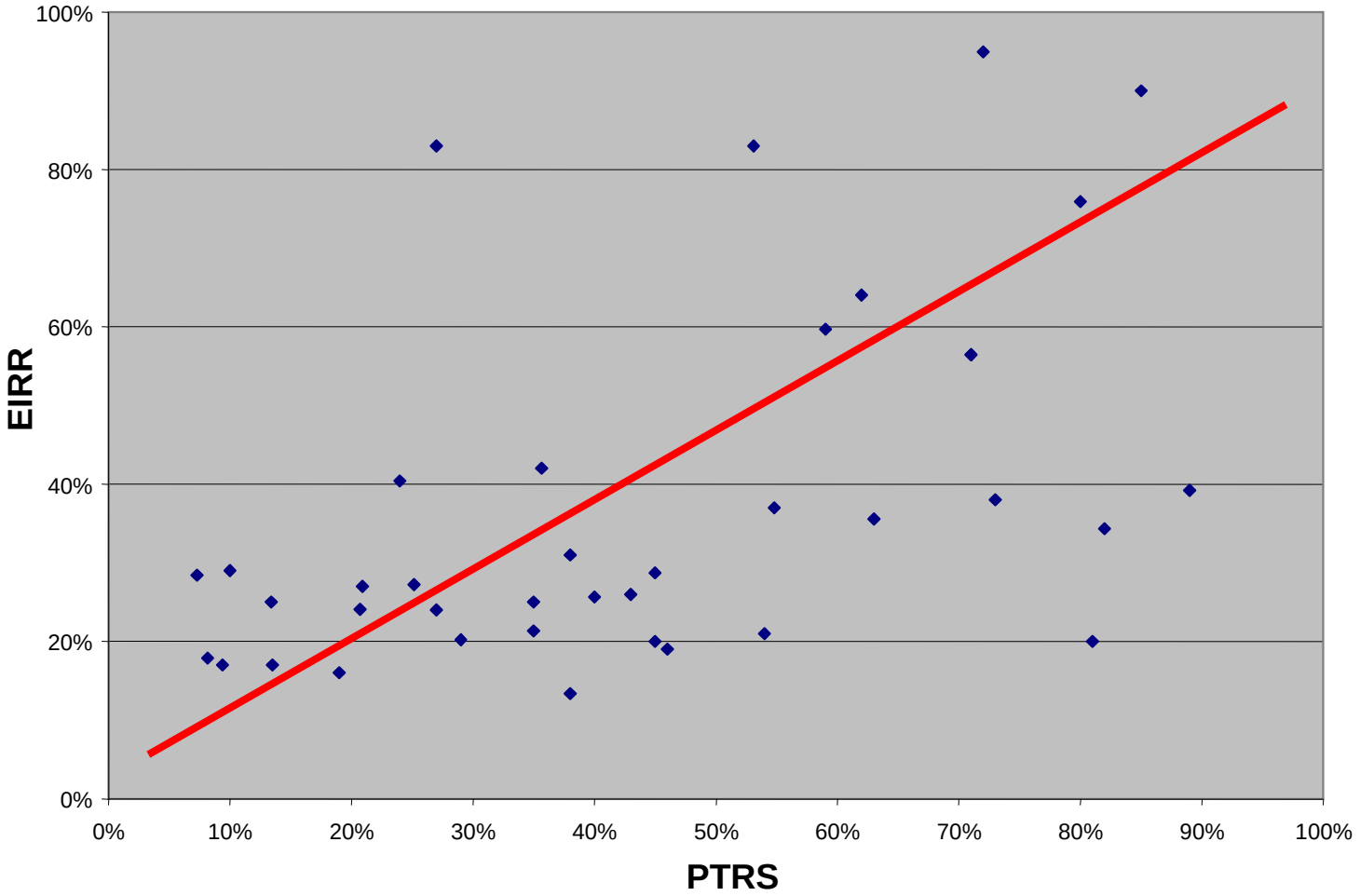
"Risk & Return" are inversely correlated, I.e., higher the risk, lower the return!



A successful asset moves along this line from right to left as it moves the development path.

EIRR: Expected Internal Rate of Return
PTRS: Probability of Technical & Regulatory Success

There is a positive correlation between the Expected Internal Rate of Return (EIRR) and the Probability of Technical and Regulatory Success (PTRS).



EIRR: Expected Internal Rate of Return
PTRS: Probability of Technical & Regulatory Success

KMR
1998-2002

The reasons for failure contain both decision outcomes and uncertain outcomes.

Reasons for Failure

	PC	Phase I	Phase II	Phase III	Registration
Clinical Safety	2%	24%	16%	18%	33%
Efficacy	8%	19%	49%	56%	44%
Formulation	4%	3%	1%	0%	0%
Market Potential	2%	5%	6%	5%	11%
PK/Bioavailability	4%	14%	4%	4%	0%
Strategic	10%	11%	14%	9%	11%
Resources	4%	0%	0%	0%	0%
Toxicology	56%	17%	3%	5%	0%
COGS	0%	1%	0%	0%	0%
Unknown	6%	4%	3%	4%	0%
Other	4%	3%	3%	0%	0%
TOTAL	100%	100%	100%	100%	100%
Subtotal excluded	16%	16%	20%	14%	22%

Treatment in benchmarks
exclude
include

KMR PTRS Benchmark Implications

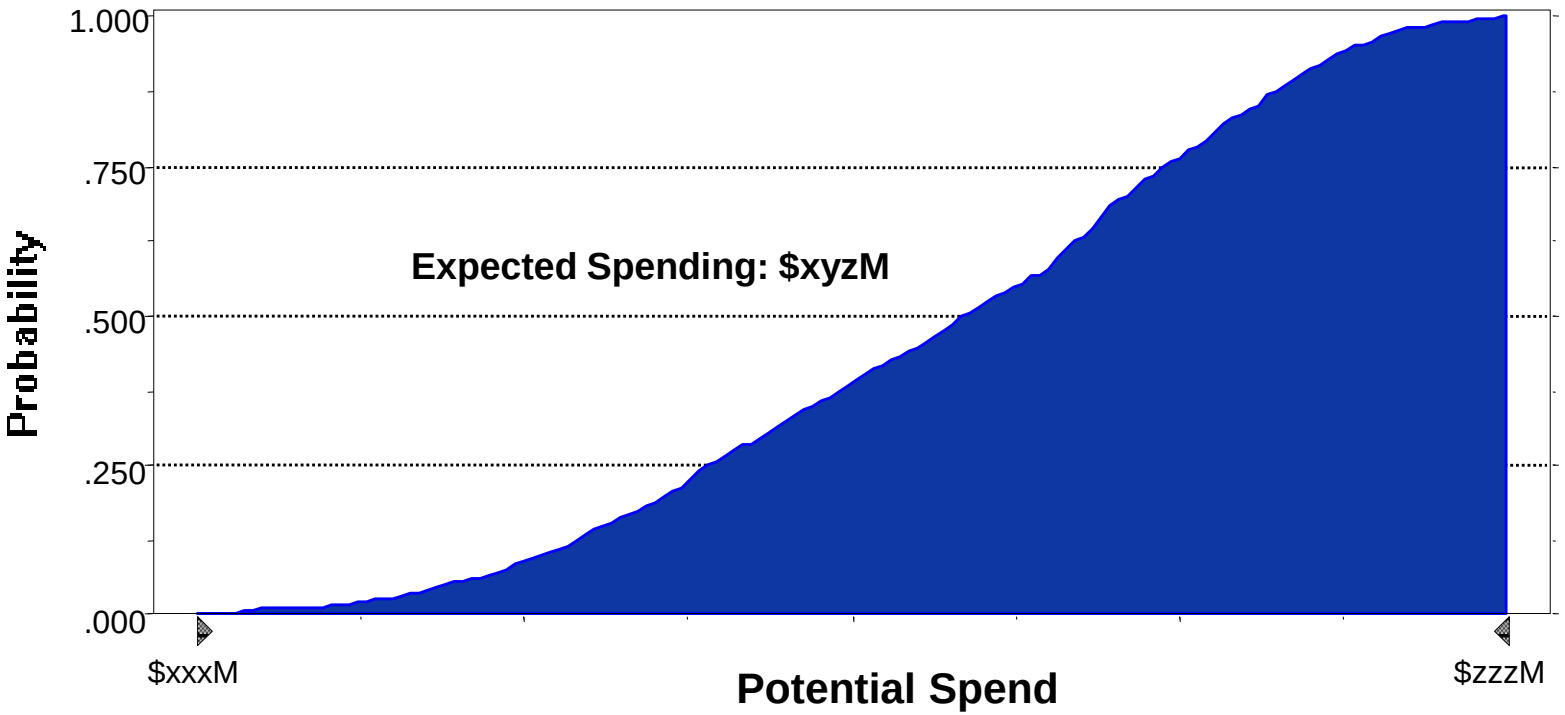
	PC	Phase I	Phase II	Phase III	Registration	Overall
Unadjusted	59%	49%	33%	56%	84%	4.5%
Adjusted	66%	57%	46%	62%	88%	9.5%

- **"Market Potential" has both decision and uncertainty elements, but included as the decision component.**

R&D spending uncertainty can be modeled to gain insights for operational and contingency planning

- Incorporate the uncertainty of Budget & Resource Constraints
  - Develop a Budget & Resource Estimation Model
    - **Explicit assessment of decision points of assets and their impact to the budget and resources**
    - **Explicit modeling of project delay / cost corrections for assets**
  - Perform Multi-year Portfolio Analysis
- Benefit
  - Better estimate & confidence to meet the budget & resource constraints targets
  - Better contingency plans for future challenges

Distribution of modeled year R&D spend



Protection of early assets is a critical issue as a part of portfolio allocation of assets in different stages of development.

- Rational:
  - Pure financial measures penalizes early assets due to huge technical and commercial uncertainty
  - There's no simple financial measure to directly address this issue.
- Solution:
  - Setting of optimization goals to maintain viable & healthy pharmaceutical portfolio (pipeline), e.g.,
    - **Set long term number of NCE launch targets (5th year & beyond)**
    - **Set long term cash flow and sales targets (around10th year)**

Concurrent Portfolio Management Tasks / Approaches

- **Diversification of Portfolio**
  - Diversify across therapeutic areas and target classes
  - Diversify across technologies and sources of innovation
- **Portfolio Risk Reduction via Strategic Alliances & Partnership**
  - Use alliances in discovery to
    - diversify across therapeutic areas, targets and technologies
    - maintain sufficient throughput of quality leads.
  - Use development alliances and partnering arrangements to
    - reduce risk of late stage failures
    - fill near and mid-term portfolio gaps
    - access key areas of expertise or alleviate resource bottlenecks
    - place some strategic, high risk, high return bets

Summary

- Pharmaceutical Industry has many challenges
- Portfolio management plays a critical role to maintain viable & healthy pharmaceutical pipeline portfolio
- Pharmaceutical pipeline portfolio requires innovative approaches to portfolio management in addition to the techniques available from the financial portfolio management.