Strategic Pharmaceutical Portfolio Decision Analysis

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Agenda

- Introduction
- Industry Portfolio Management challenges and common decision analysis methods
- Improvements using simulation techniques with @Risk
  - Excel Model demo
- Concluding remarks

Introduction

Introduction

- **Professional Background:**
  - 15 years in Biotech/Pharmaceutical industry in companies of varying sizes
  - **Current Position:**
    - Business Development Manager at Momenta Pharmaceuticals in Cambridge, MA.
    - Department responsibility includes
      - Obtaining development partnerships for existing projects
      - Modifications of existing collaborations
      - Member of Strategic Planning Team for key development projects

Objectives and Limitations

- To describe challenges in analyzing value and risk of project portfolio in support of strategic decisions
- To show how simulation techniques using @Risk can improve analysis and empower better decisions
- Briefly outline applicability to other industries
- Based on my limited experience!
- Get feedback from experts and learn.

Applications of @Risk in the pharmaceutical Industry

- Some of my past projects:
  - Strategic Portfolio Management
  - Market competition models and sales Forecasting
  - Project/Deal valuation (NPV, real options)
    - Optimization of milestone payments, profit share and value split.
  - Manufacturing optimization (capacity planning, process improvement options)
  - Hedging Derivatives (interest rates, forex)

Many other applications exist:
So much uncertainty, so little time!

Industry Portfolio Challenges and Common Decision Analysis Methods

Evidence that decision making process needs improvements?

- Only 1 out of 10 products selected to enter clinical trials succeed.
- 1 out of 3 marketed products have enough sales to recoup investments.
- The all-in costs (including failures) of a drug is increasing and estimated at about $1 Billion.
  - Rising clinical requirements and regulatory pressures have resulted in significant cost increases.
- Small companies often run out of cash and are forced to use dilutive financing.
- Larger companies are using M&A, followed by reduction of costs, as a strategy for growth.

Are these results of bad luck, odds that just can't be improved, or something else?

Typical Project Selection Process

- **Financial forecasting models are <u>often</u> used to make critical business decisions:**
  - Few companies do this early but thorough analysis is often done at Phase II-III
  - Calculate Net Present Value of discounted cash flows
  - Many individual and combined sources of uncertainty in the assumptions which may lead to downside or upside risks
  - Positive and high NPV are common decision criteria

- **But choices may be limited by:**
  - Intellectual property
  - Limitations on technology/skill sets
  - Industry issues (i.e. regulatory, economic, etc.)

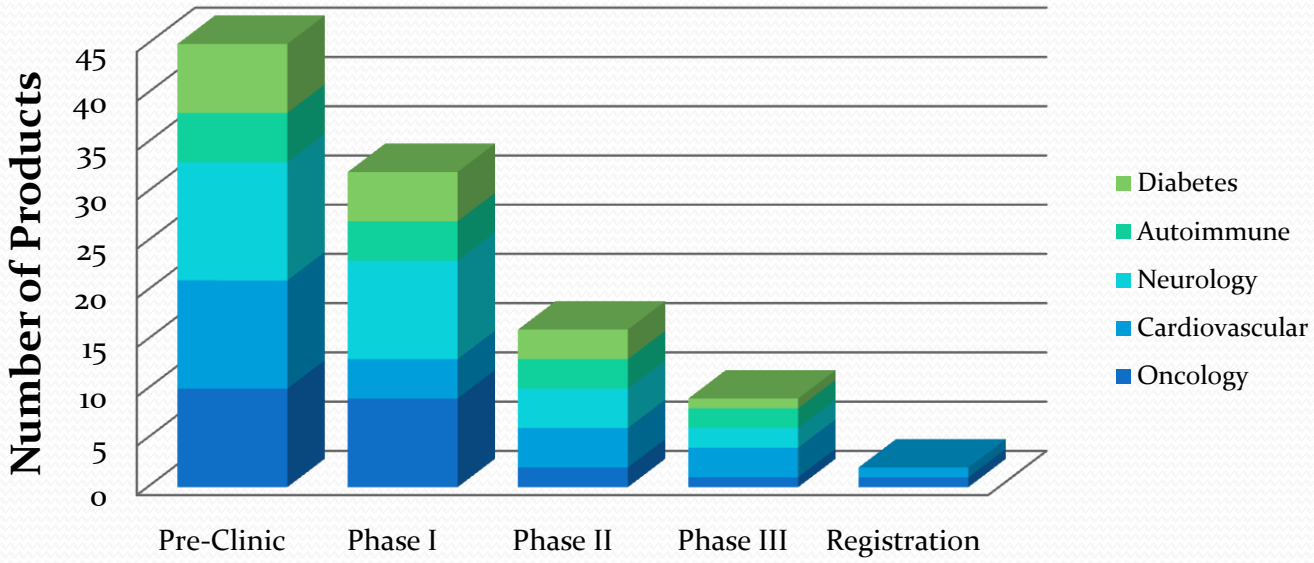
Improved Process Combines Value and Risks

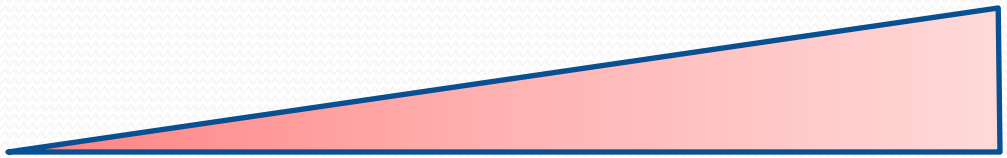
- How achievable is the value?
- In face of uncertainty, what is the margin for error in my decision?
- What are the limits of uncertainty in input assumptions that will lead to same decision?
- Should more time and resources be spent validate input assumptions?

Typical Big Pharma Portfolio of Products

Attributes: Existing large cash-flows used to fund R&D, experience and resources; can withstand high failure rates

Challenge: Productivity is far below levels needed for growth in face of patent expirations



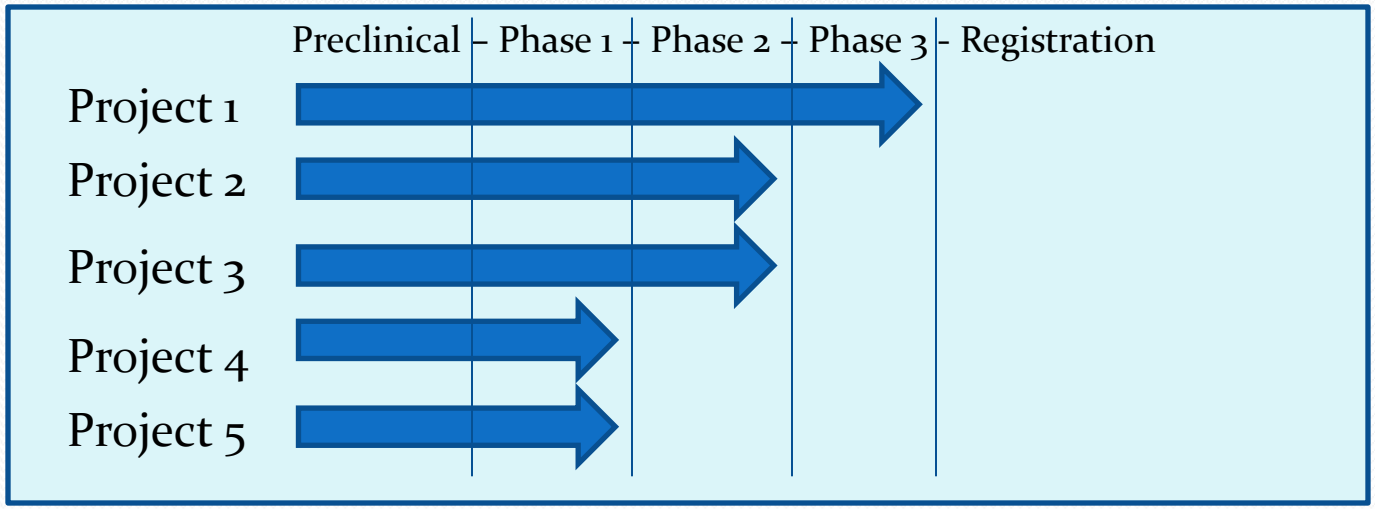


- Investment level
- probability of success

Small Pharma portfolio

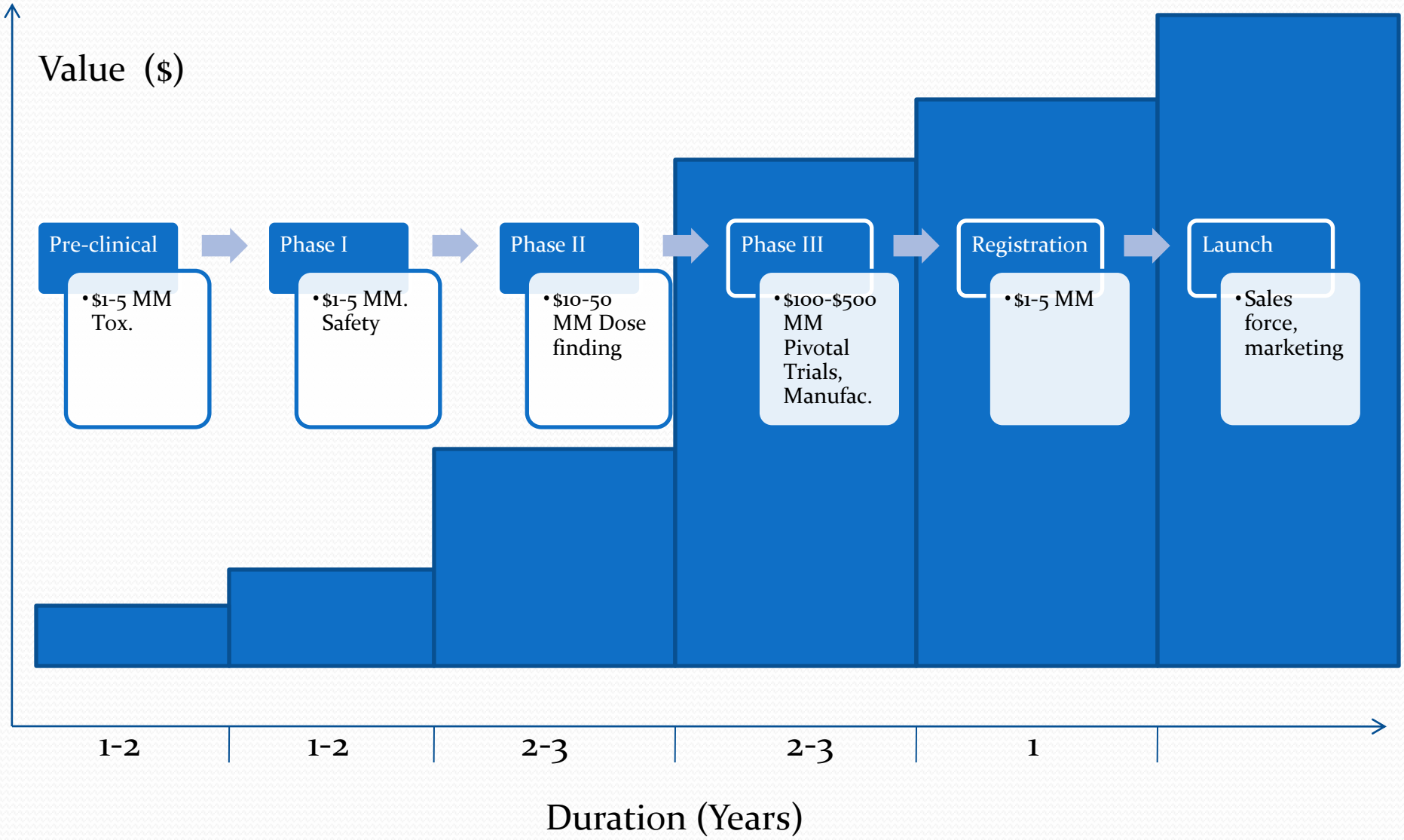
Attributes: Innovative intellectual property, negative-cash flows and limited capital

Challenge: Low margin of error (few shots on goal), partnering is necessary to diversify risks



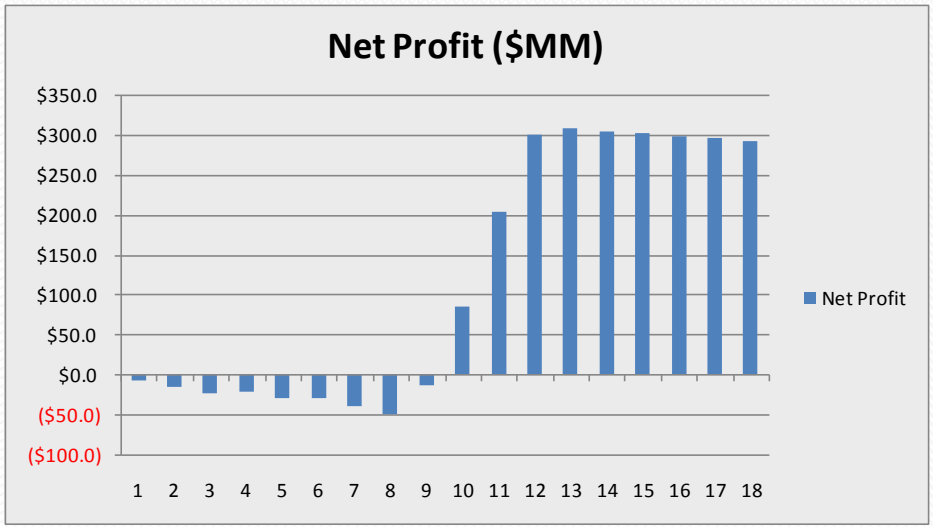
- Usually one technology is applied to few indications (high risks)
- Diversification is achieved through partnerships:
  - Cash upfront (invest new projects/technologies)
  - Milestone payments upon finishing each phase; option to invest in development
  - Commercial milestone payments and royalty on sales; profit share if investment option exercised
  - May split geographical location to increase value (i.e, US, EU, Japan and Rest of world)

Product Development Costs and Value creation



Project Valuation Methods: Discounted Cash Flows

- Cash flows are discounted to today's value based on company cost of capital (WACC)
- Higher WACC is often used to account for risks

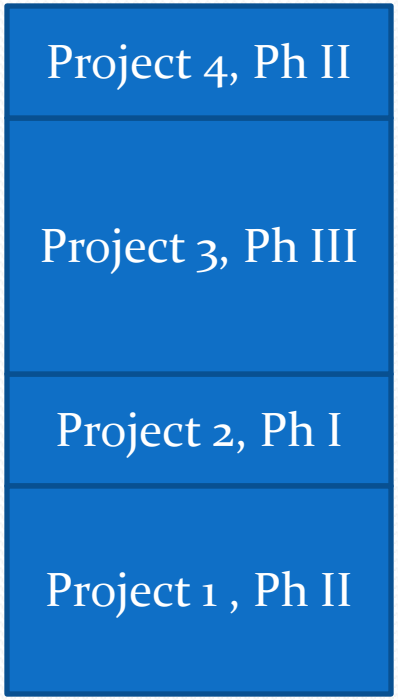


NPV Limitations:

- Different mix of costs, revenues and timing can lead to same NPV
- Vast majority of projects have positive NPV (does not match statistics)

$$\mathrm{NPV} = \sum_{t=0}^{n} \frac{C_t}{(1+r)^t}$$

Portfolio Value: Sum of Parts



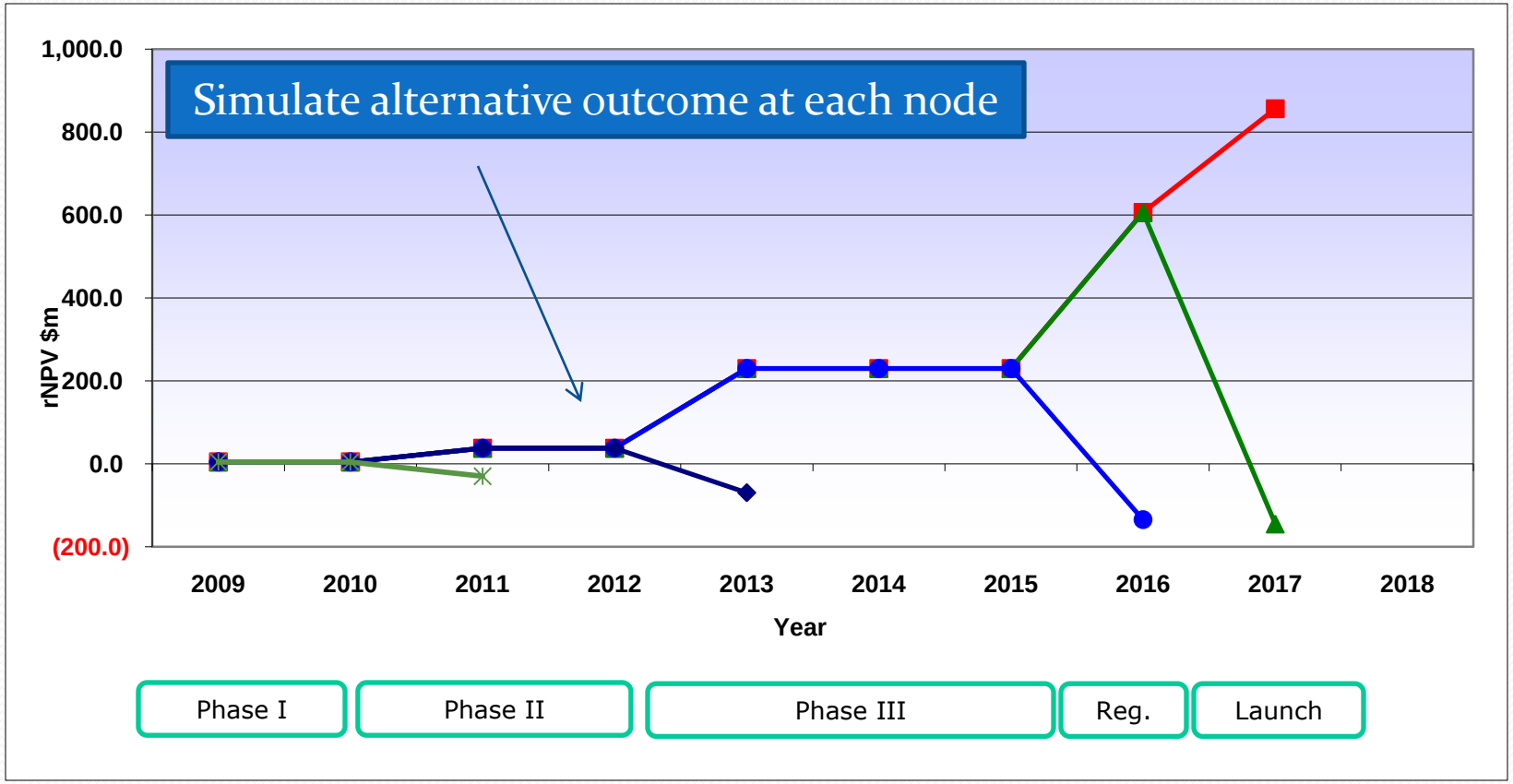
Sum of NPV = value of portfolio today
Best case and worse case are considered!

- **Unanswered questions:**
  - What is the risk of this plan?
  - What are the expected returns knowing that some projects will fail?
  - Do we have the optimum number of projects?
  - Raise money or partner?

Improvements using Simulation Techniques

Simulate Future Possibilities

- At each phase transition a project either fails or moves to next stage. Using a discrete probability distribution
- Sequential events lead to very low probability of achieving final goal



A Flexible Discrete Distribution

- Goal is to create the following distribution
  - Probability of Success = 60%
  - Probability of Failure = 40%

- Use Riskuniform function to create numbers from 0-100%.
- Use “IF” statement to make it a discrete event (=if(Distribution_Result>Target_Percent=True,False)
- Use multiple imbedded IF statements to combine scenarios
- The advantage of this method is flexibility in modeling variability in the distribution parameters

Probability of Success

- Use available industry statistics on phase transition probability to:
  - Risk adjust cash flow
  - Simulate all possible scenarios

	Phase I	Phase II	Phase III	Registration
Rate of success into next phase (used to simulate)	61%	44%	68%	84%

Source: DiMasi et al. (2001), Tufts University

Advantage:

• Creates standard methodology for evaluating all projects risk (comparing Apples to Apples)

• Project risk is assigned to its natural place, phase transition (as opposed to cost of capital ,WACC)

Hypothetical Portfolio of small Pharma company

- One scenario shown here

Legend
Phase I
Phase II
Phase III
Registration
Launch

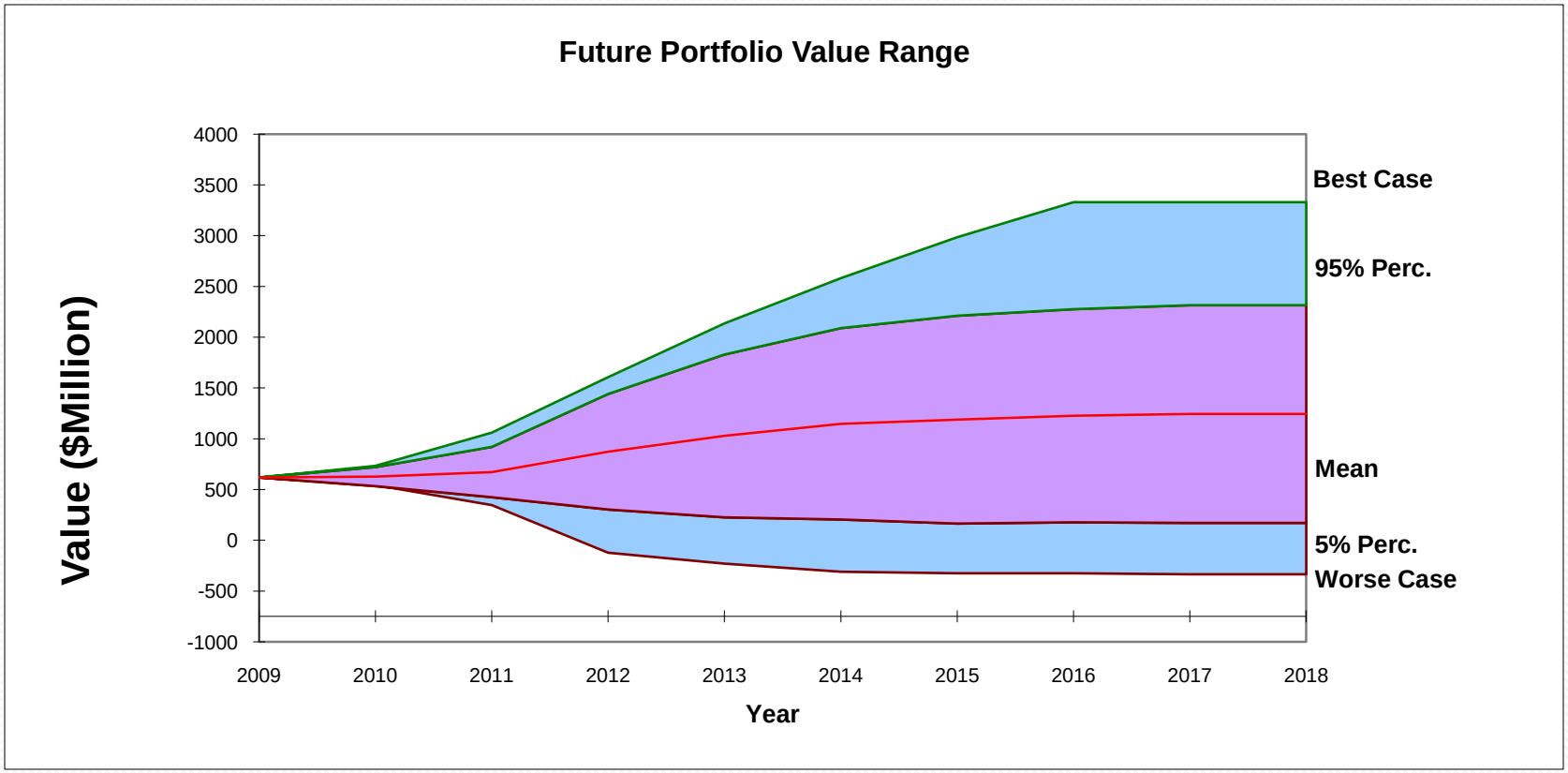
NPV $ Million	2009	2010	2011	2012	2013	2014	2015	2016	2017
Project 1	4	4	61% 37	37	44% 230	230	230	68% 606	84% 857
Project 2	113	113	44% 407	407	407	68% 1009	84% 1412	1412	1412
Project 3	50	44% 159	159	159	68% -110	84% -110	-110	-110	-110
Project 4	390	390	390	68% 933	84% 1,302	1,302	1,302	1,302	1,302
Portfolio Value	557	666	993	1,536	1,829	2,431	2,834	3,210	3,461

Lowest Potential Value in any year	557.2

Combining All Scenarios – using industry statistics

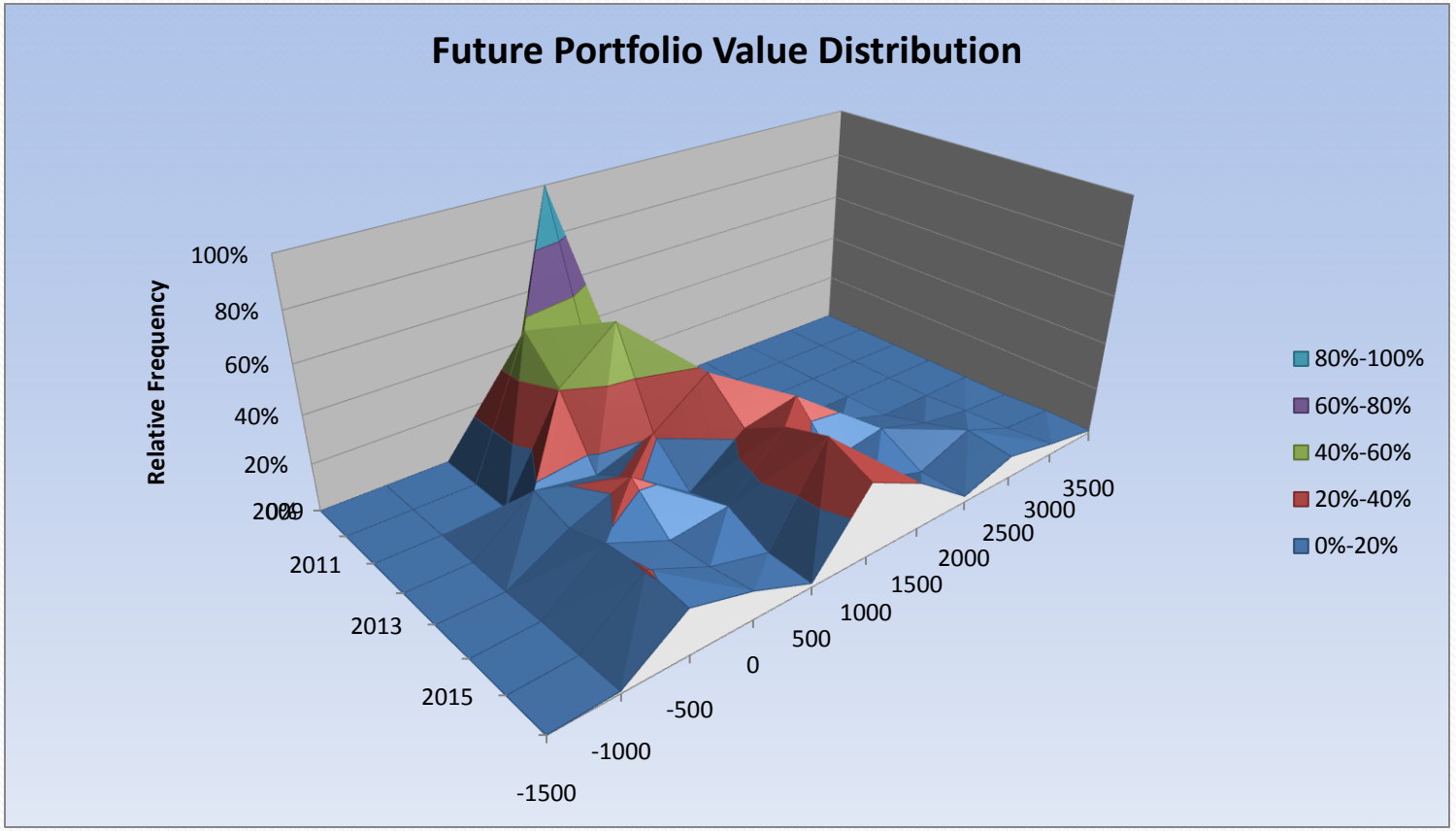
Results:

- Mean portfolio value over time (steep increase is desired)
- Distribution of the values (Shows upside potential and downside Risks)
- New Metric: Portfolio Variance (Mean/Std. Deviation)
- It can be used to compare different strategies (maximize mean or minimize deviation?)



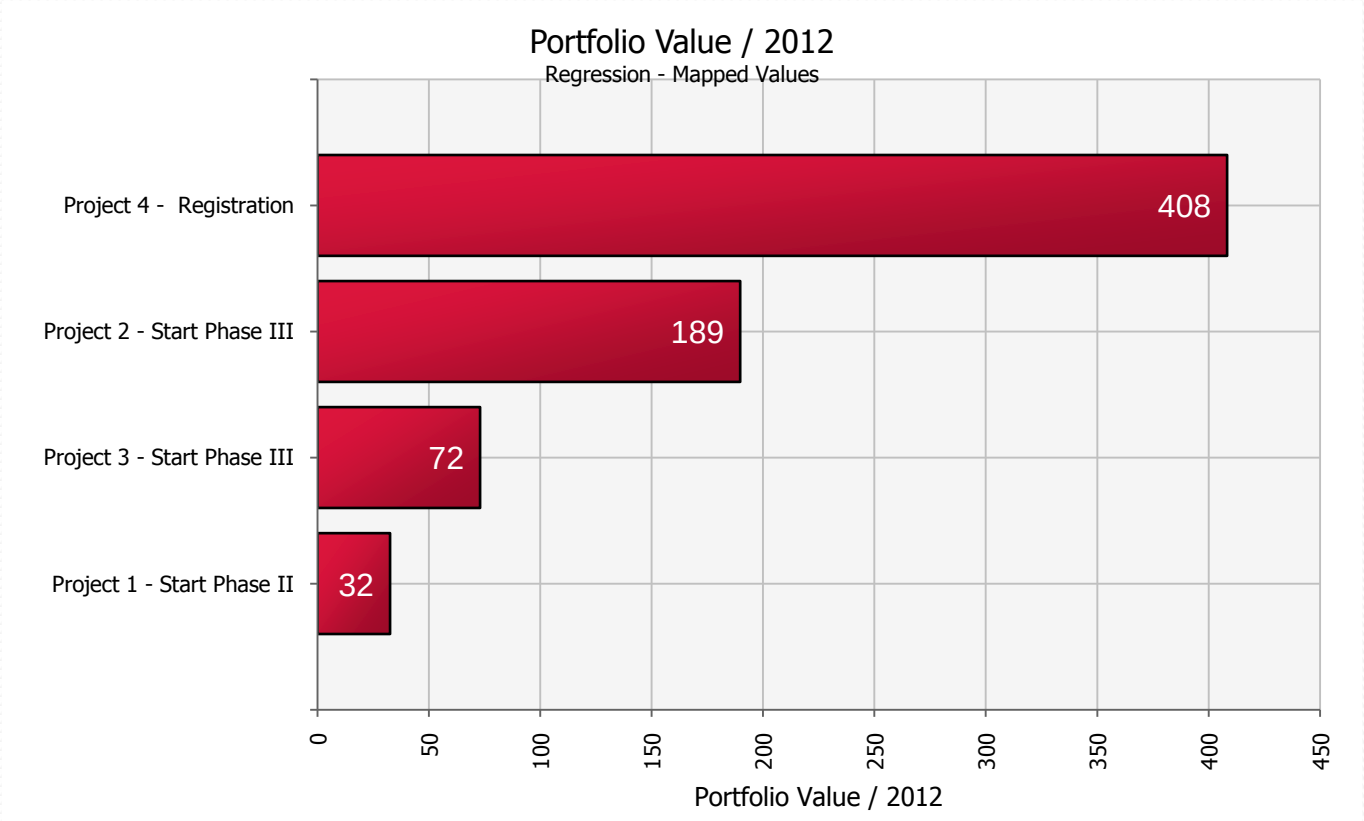
Results in 3D

- **In 2016, distribution suggests 2-3 values have highest probability (In this case: $1.2, $-0.5 or $2.5 Billion**
- **Conclusion: If you can beat the odds, upside potential is limited to two possible outcomes**



Project Impact on Value and Risk

- Example: Impact of variables on Year 2012 portfolio value
- Conclusions: Focus on getting the assumptions correct, prioritize resources to maximize success of important events



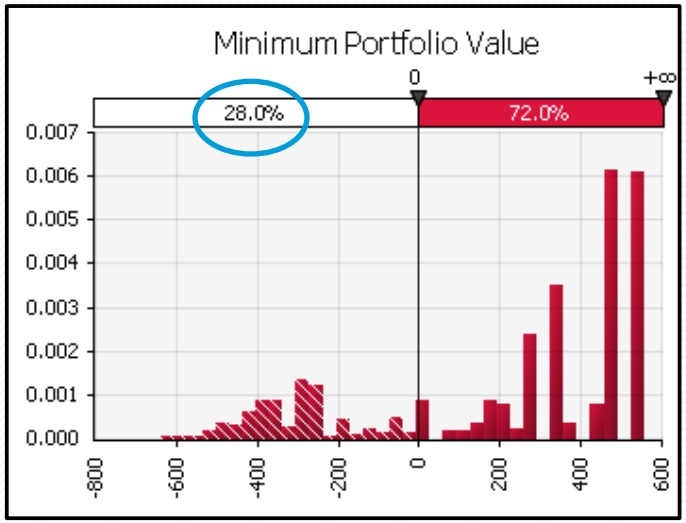
Additional Portfolio Decision Analyses

- The following additional analyses can be performed:
  1. Effect of partnering a project
     - Partnering causes loss of value in exchange for limiting downside risk…but to what extent?
  2. What are the combination of probabilities that will result in negative NPV or a target value?
  3. Portfolio prioritization using value created by investment at each phase

Effect of Partnership on Portfolio Risk

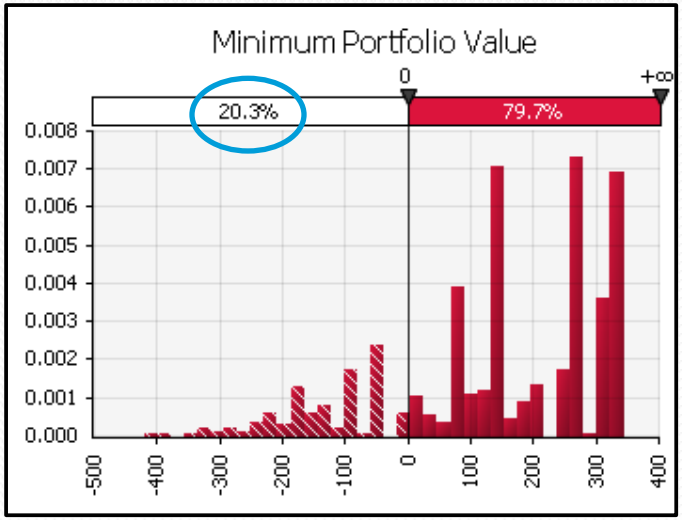
Potential Deal: $50 Million upfront cash payment, $120 Million in Milestone payments, 15% Royalty on sales, Partner responsible for all costs

Base Portfolio



Statistics	
Minimum	-635.0
Maximum	557.2
Mean	226.4
Std Dev	338.0

Project 4 Partnered



Statistics	
Minimum	-420.0
Maximum	344.6
Mean	147.1
Std Dev	171.0

Use @Risk Optimizer to Validate Inputs

- Question: What is the worse probability of success that would result in same decision?
- Where is breakeven?
- Solve NPV= zero in @Risk optimizer
- The results provide the lowest acceptable probability
- Challenge: There are many possible combinations.

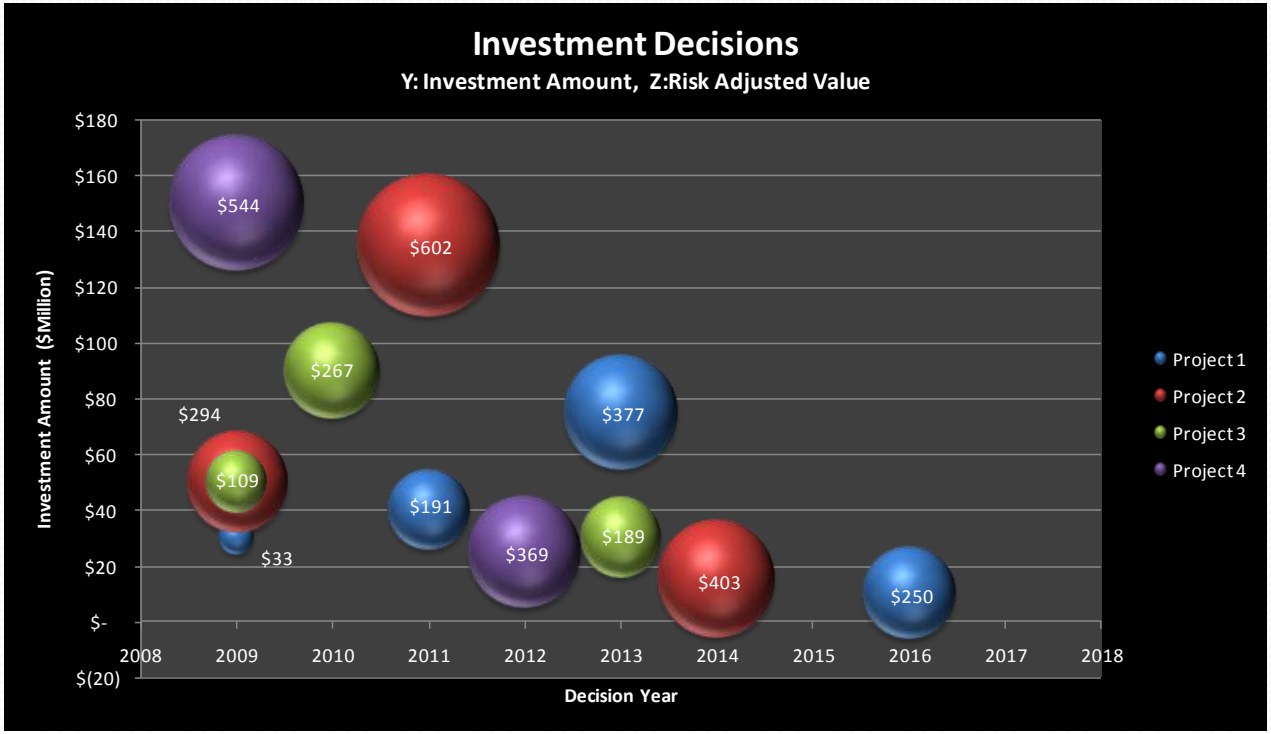
Results of Breakeven Analysis, NPV = zero

	Probability of success			
2012 Value (MM)	P3: Start Ph III	P2: Start Ph III	P1: Start Ph II	P4: File NDA
$900 (Mean NPV 2012)	**44%**	**44%**	**61%**	**68%**
$-3.7	**44%**	**12%**	**76%**	**58%**
$-3.7	**44%**	**44%**	**55%**	**27%**
$-3.7	**23%**	**44%**	**61%**	**55%**
…	**…**	**…**	**…**	**…**

This data suggests that portfolio is very sensitive to over estimation of only one variable!

Investment Prioritization

- Compare investment decisions, based on ROI, by breaking down the project into stages
- Optimum decisions have low investment requirement (lower on Y axis) and highest values (largest bubbles)



Applications in Other Industries

- Capital intensive projects with highly uncertain outcomes (Oil industry)
- Large difference in value between outcomes
- Sequential stages with varying required investments

Some Caveats

- Assumes no replacement of projects as they fail
- Assumes projects have a clean go/no-go and do not continue beyond original date and costs.
- Industry statistics could not be applicable:
  - Skewed by big pharma decisions (mergers, priorities, endless cash supply).
  - Assumes no correlation between projects
- This type of analysis only considers a financial assessment
  - Many other considerations including Legal and Technical.

Summary

- **This method creates a standard methodology for value and risk assessment across a portfolio of projects**
  - *Standardization of the decision making process*
  - *Applicable to Big and Small Pharmaceutical companies*
- **Portfolio Variance as a metric for evaluating decisions**
  - *Incorporates Value and Risk*
- **Comprehensive analysis of variables that impact the outcome:**
  - *Validate input assumptions using target optimization*
  - *The shape of the distribution of possible outcomes is important*
- **Analyze mix of projects and partnering options.**
  - *Optimize for highest Mean NPV vs. mitigate risk by lowering portfolio deviation*

Questions?