Portfolio Planning and Optimization

Outline

- Introduction and Rationale
- Portfolio Analysis Preparation
  - Using Forecasts as Inputs
- Portfolio Analysis Procedure
  - Decathlon Method
  - Sample Outputs
  - Sample One-Page Project Summary
- Results of Process

Portfolio Optimization Background

- Success equals picking the right portfolio to develop and then implementing well
  - The overall portfolio is more important than any one product
    - Total expenses, risk, and return comes from the overall portfolio
    - A balanced portfolio of “solid” products may be better than a portfolio with one or two “star” products
      - Barry Bonds was National League MVP four years in a row (2001-2004)
      - San Francisco Giants had best record in their division only once
    - Mike Trout has been rookie of the year, league MVP, and second in voting for MVP twice
      - Los Angeles Angels had best record in their division only once (2014)
    - Products should be picked by more sophisticated metrics than simply revenues or overall probability of success
- Portfolio planning determines future success
- Analysis is much cheaper than failure
- Select optimal portfolio of projects (product/indication) to develop
  - Maximize favorable metrics, minimize adverse metrics
  - Subject to constraints

Portfolio Analysis & Optimization

Portfolio Optimizer™

- Determines which combination of products are most promising
  - Accounts for uncertainties, costs, and timing involved
  - Compares all possible portfolio combinations both deterministically and probabilistically, subject to constraints applied
- Specify different portfolio objectives
  - Maximize profits
  - Minimize costs
  - Minimize risks
  - Maximum number of products launched
  - Maximize return on investment
  - Highest cash flow valley

Portfolio Optimization Overview

- Separate model for each marketed and developmental product (project)
  - Revenues, expenses, development steps (timing, costs, and probabilities)
  - Full P&L (income statement)
  - One-page summary for each project

- Specify different portfolio objectives:

Maximize profits	Maximize revenues
Maximize total NPV	Minimize risks
Minimize expenses	Maximum number of products launched
Maximize return on investment	Highest cash flow valley

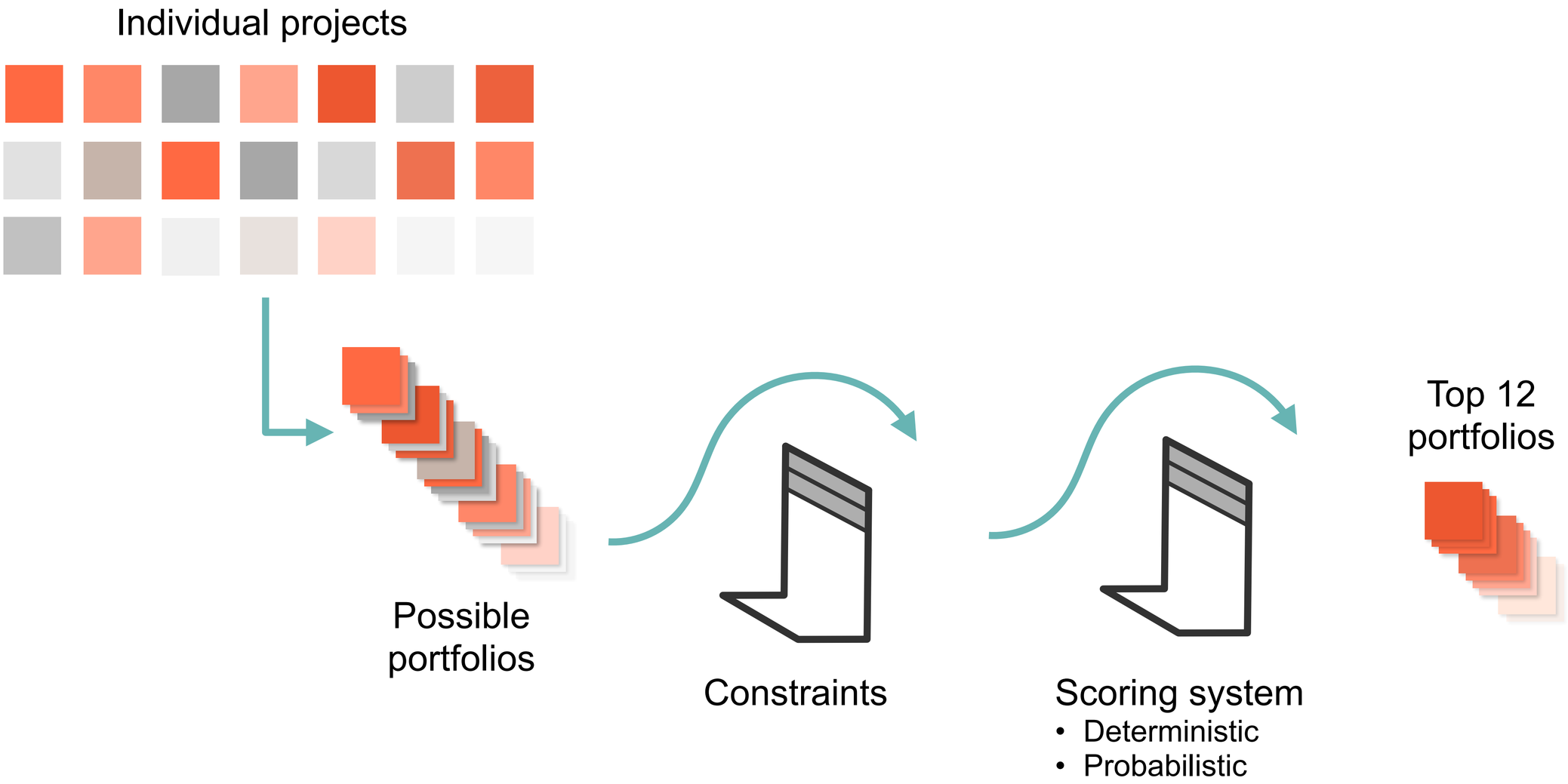
Portfolio Optimization Overview, cont.

- Compares all possible combinations both deterministically and probabilistically
  - Core projects (always included)
  - Optional projects (turned on or off)
  - Overhead costs in “overhead project”
- Logic constraints can be applied
- Select optimal portfolio of projects (product/indication) to develop
  - Maximize favorable metrics, minimize adverse metrics
  - Subject to constraints
- Display best dozen portfolios and rationale to management

Portfolio Analysis Steps

1. Identify projects (product/indication combinations)
   - Example: Idelalisib for frontline indolent NHL
   - Example: GS-5745 for COPD
   - Project A and Project A delayed are two separate projects
2. Create P&L (profit and loss) model for each project
   - Revenues
   - Expenses
   - Development steps (timing and probabilities)
3. Portfolio Analysis

Portfolio Analysis Process



Projects: Core, Optional, and Overhead

- Example of company with 27 projects
  - Core projects (9)
    - » Projects that are relatively certain to proceed due to corporate support
    - » Included in all portfolios
    - » The list can change as needed
  - Optional projects (18)
    - » 2^{18} = 262,144 possible combinations
    - » Some combination are included in each portfolio
      - 262,144 portfolios are “constructed”
  - Overhead costs in “overhead project”
    - » General and administrative, basic research, etc.
      - The CEO will still be needed with two or 27 projects
    - » Included to make absolute (as opposed to relative) assessments about portfolios

Example Projects

Portfolio Optimizer™

	Product	Indication	Type
Project 1	A	CLL	Core
Project 2	A	Refractory NHL	Optional
Project 3	A	Frontline NHL	Optional
Project 4	B	Myelofibrosis	Optional
Project 5	B	Pancreatic Cancer	Optional
Project 6	C	IPF	Core
Project 7	D	RA	Optional
Project 8	D	Crohn's	Optional
Overhead "Project"	N/A	N/A	N/A

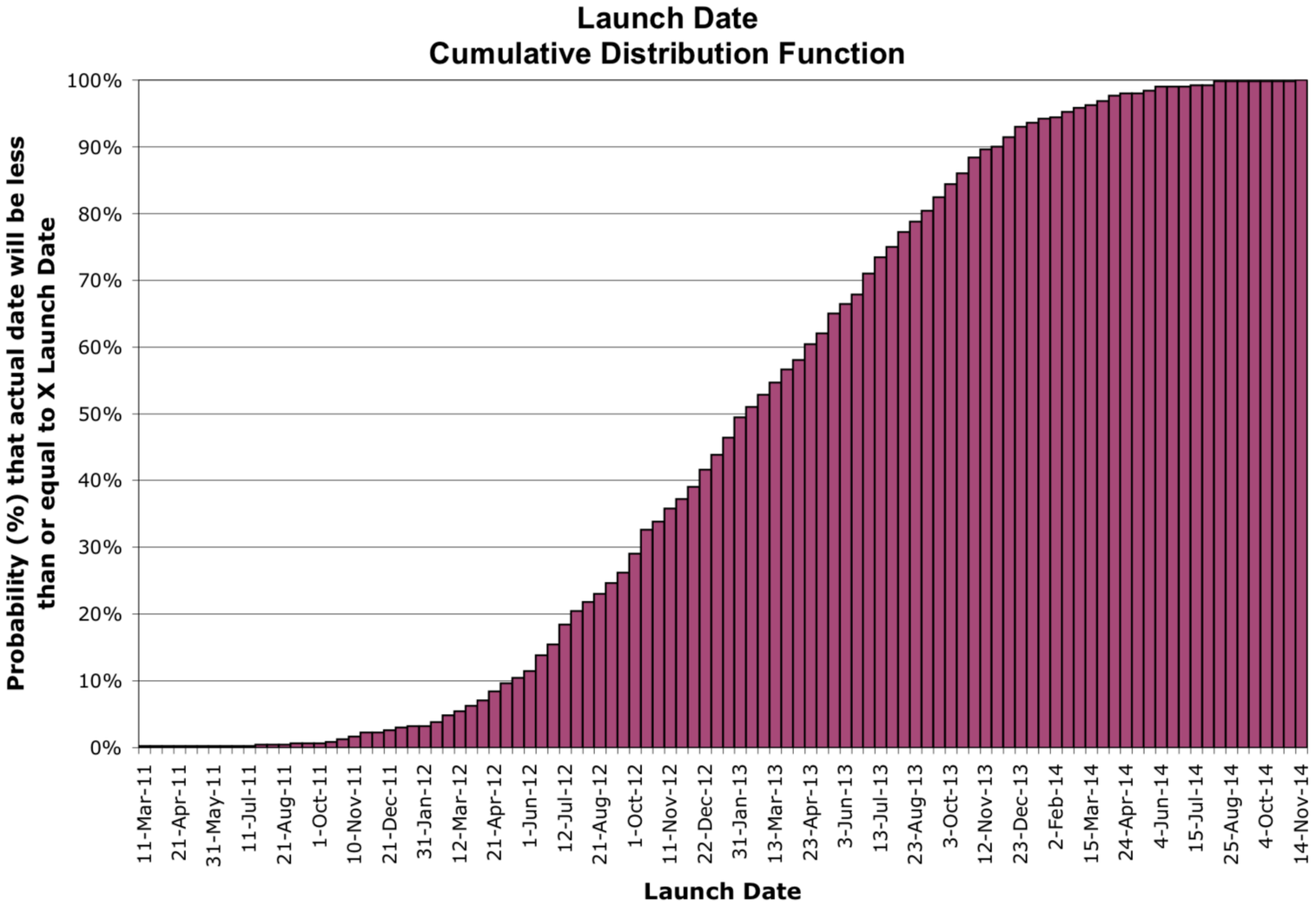
Long-Term ForecasterTM (LTF) Model Inputs

- Revenues
  – Forecast revenues for 20 years
- » Long enough for all projects to generate revenues
- – Directly enter into model from existing forecast or generate from LTF forecast structure
- Expenses
- Development steps
- – Probabilities – Timing
  – Costs
- Deal terms (in-license and/or out-license)
- Monte Carlo ranges for key variables

LTF Model Outputs

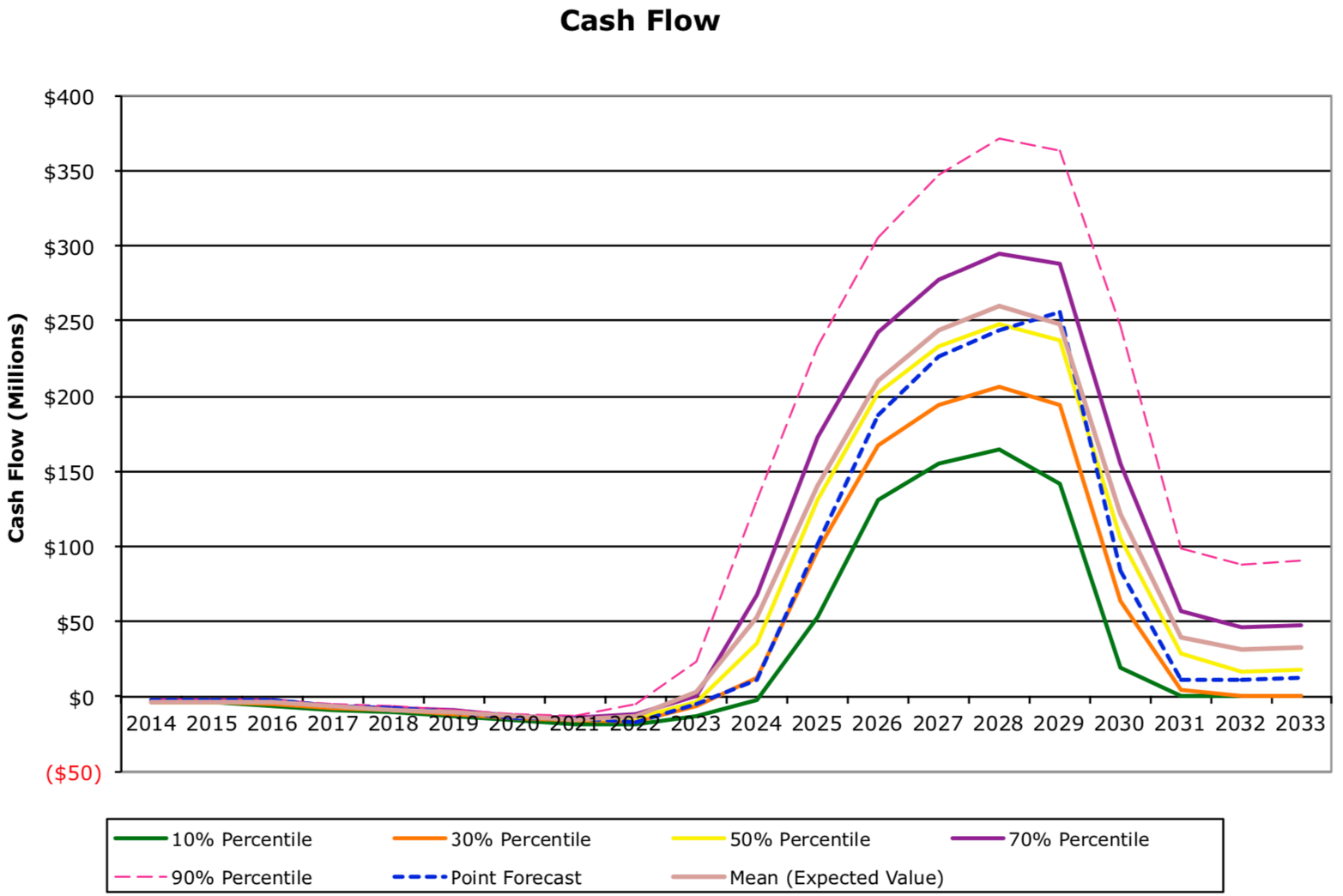
- Annual revenues, expenses, cash flow
- Cumulative cash flow
- Net-present value (NPV)
- Expected & risk-averse net-present value (EV or ENPV)
- Project value by development phase
- Overall probability of technical success
- Pearson Index

Sample Outputs: Launch Date

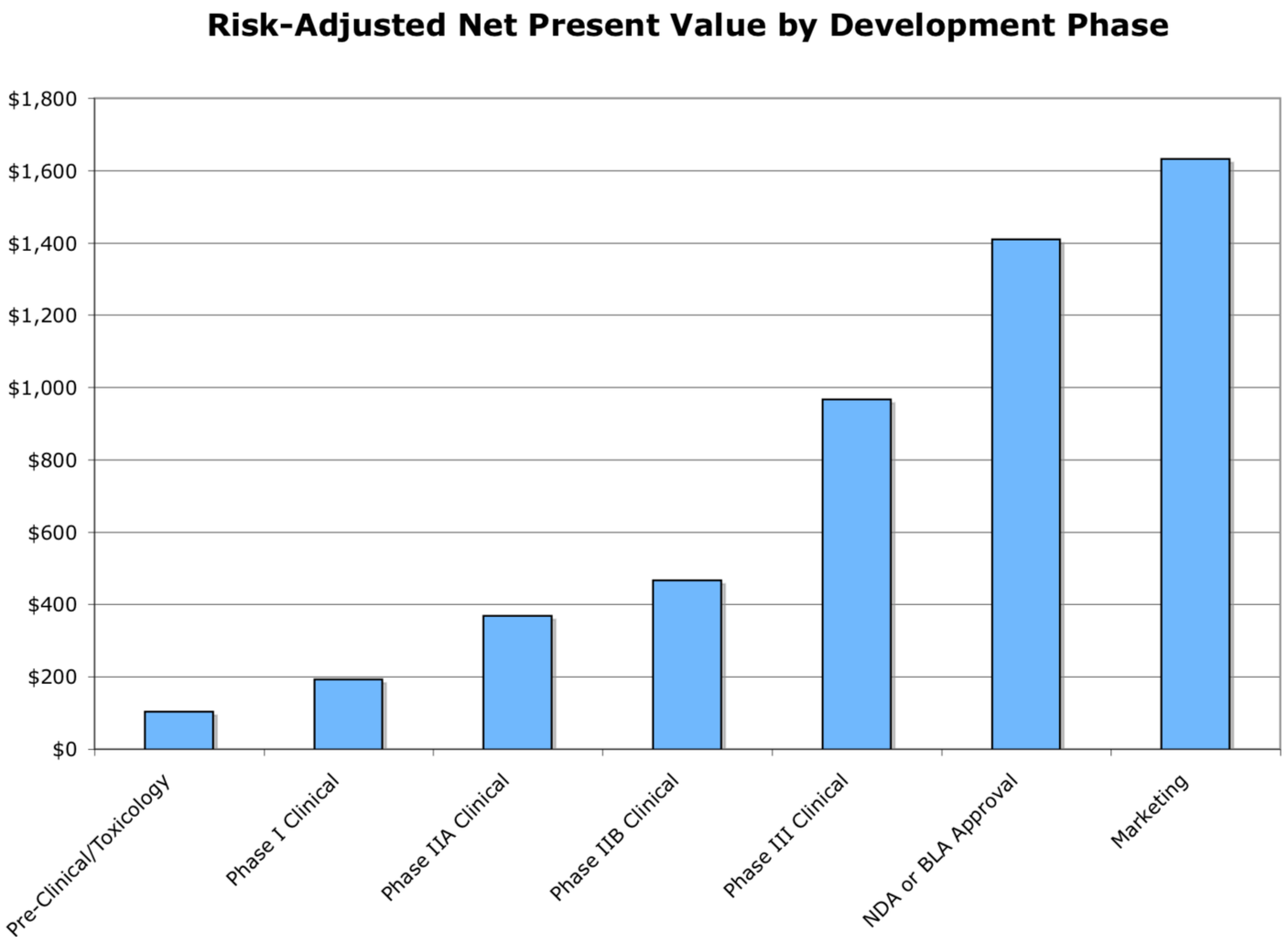


Sample Outputs: Project Value by Phase

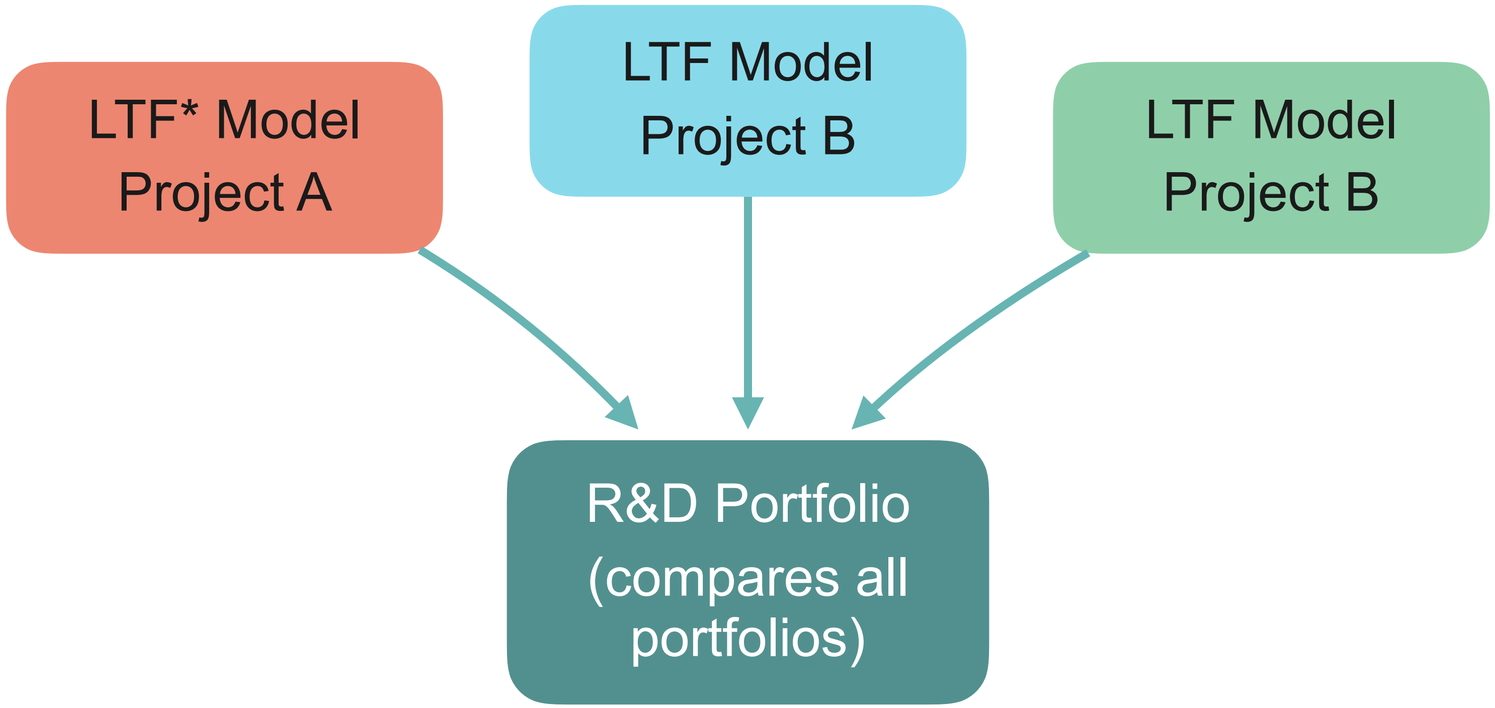
Portfolio Optimizer™



Sample Outputs: Cash Flow Deciles



Portfolio Model



Deterministic & Stochastic
(Monte Carlo simulation)

*Long-Term Forecaster™

Portfolio Analysis Procedure

- Example of company with 18 “optional” projects
  - All possible portfolio combinations (262,144)
- Apply logic constraints to limit number of possible combinations
  - Example: We will not develop more than two non-Hodgkin’s drugs
  - Example: We will develop at least one cholesterol-reducing drug
  - Example: We will develop at least three but not more than seven drugs at any time
- Pick 30 portfolios with the best deterministic (non-Stochastic) results
- “Build” each portfolio
- Run Monte Carlo simulations (probabilistic, Stochastic view)
- Pick best portfolios for final scrutiny
  - Some of the best deterministic portfolios
  - Some of the best probabilistic portfolios
  - Status quo or “teacher’s pet” = hand-selected portfolio
- Allow ad hoc analysis of any portfolio combinations

"Decathlon" Indices are Calculated

- Define favorable (good) metrics and adverse (bad) metrics
- Define a scoring system

Index Calculation Example

Index Weight	15%	10%	20%	30%	25%		
	Expected drug launches	Peak Revenues ($M)	Cash Flow Valley ($M)	EV ($M)	Year of Positive Cash Flow	Index Arithmetic Mean	Index Geometric Mean
Current Portfolio	2.3	$8,875	$121	$4,934	2009		
Index Value	0.38	0.64	0.52	0.56	0.92		
Weighted Index Value	0.28	0.32	0.52	0.84	1.15	0.62	0.54

Tabular Portfolio Results

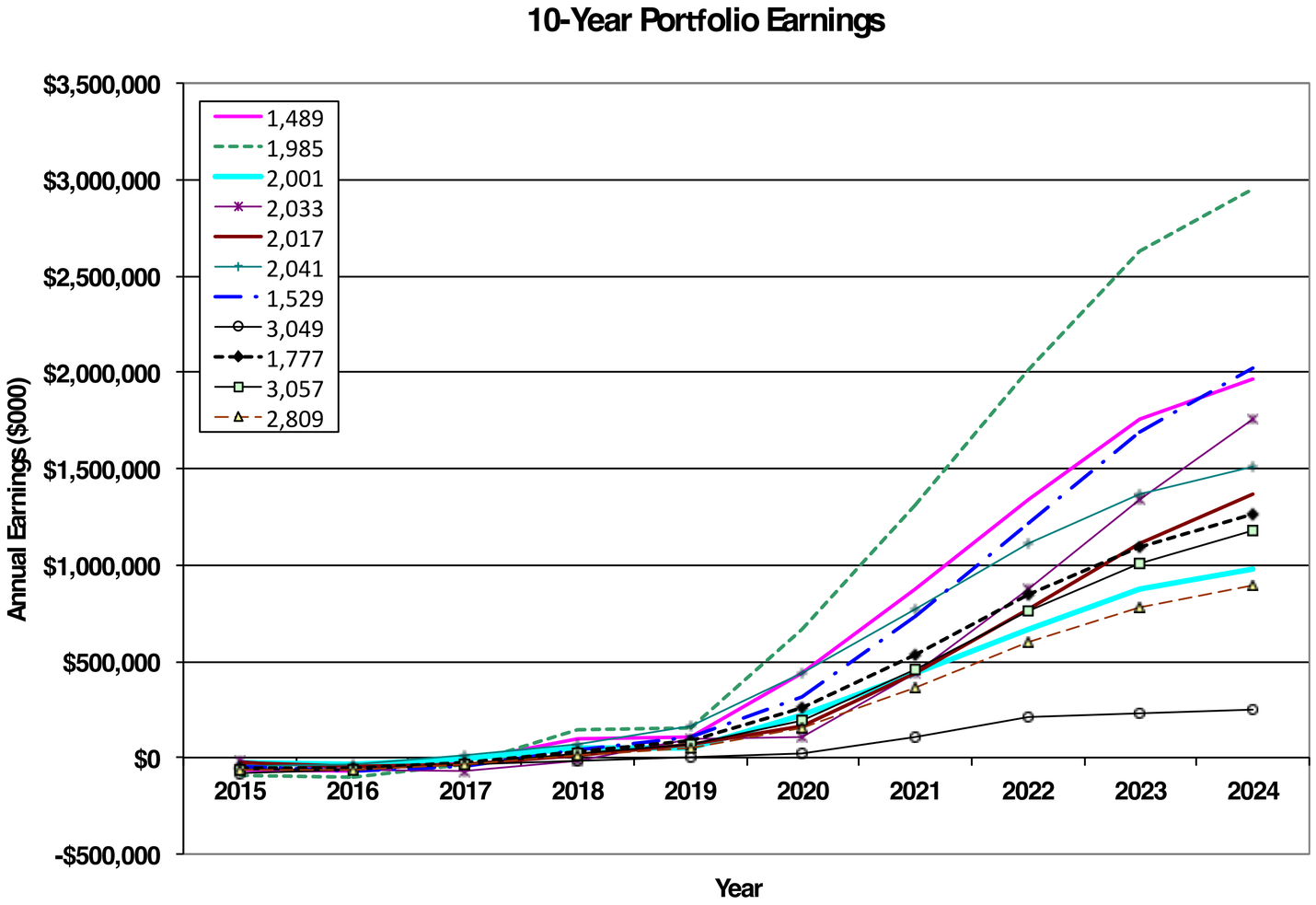
Portfolio Optimizer™

Result record	Project Combination	Probability at least one drug launches	Expected drug launches	Peak Revenues ($M)	Peak Annual Cash Outlay ($M)	Maximum Cash Exposure ($M)	NPV ($M)	EV ($M)	Year of Positive Cash Flow	Year of Positive Cumulative Cash Flow
1	5,505	99.9%	3.2	$8,906	$80.6	$79.0	$15,234	$5,043	2023	2023
2	4,993	99.9%	3.1	$7,999	$81.5	$72.0	$14,092	$4,661	2023	2023
3	4,481	99.8%	3.0	$7,604	$74.9	$59.0	$13,044	$4,575	2023	2023
4	385	99.6%	2.4	$7,023	$74.8	$40.9	$10,890	$3,299	2022	2025
5	6,273	99.8%	3.0	$8,079	$117.9	$41.6	$14,247	$5,670	2020	2021
6	6,529	100.0%	3.9	$8,137	$47.4	$39.4	$14,348	$5,762	2020	2020
7	8,129	100.0%	5.1	$9,947	$53.4	$44.0	$17,632	$6,359	2020	2022
8	385	99.6%	2.4	$7,023	$74.8	$40.9	$10,890	$3,299	2022	2025
9	5,421	97.0%	3.9	$10,002	$53.4	$44.0	$12,632	$6,508	2020	2023
10	6,100	95.6%	4.2	$11,088	$66.0	$118.0	$19,362	$7,019	2021	2022
11	199	98.0%	5.0	$7,992	$59.4	$51.8	$17,632	$7,208	2022	2021
12	9,999	98.6%	2.3	$8,875	$70.3	$120.8	$15,114	$4,934	2023	2023

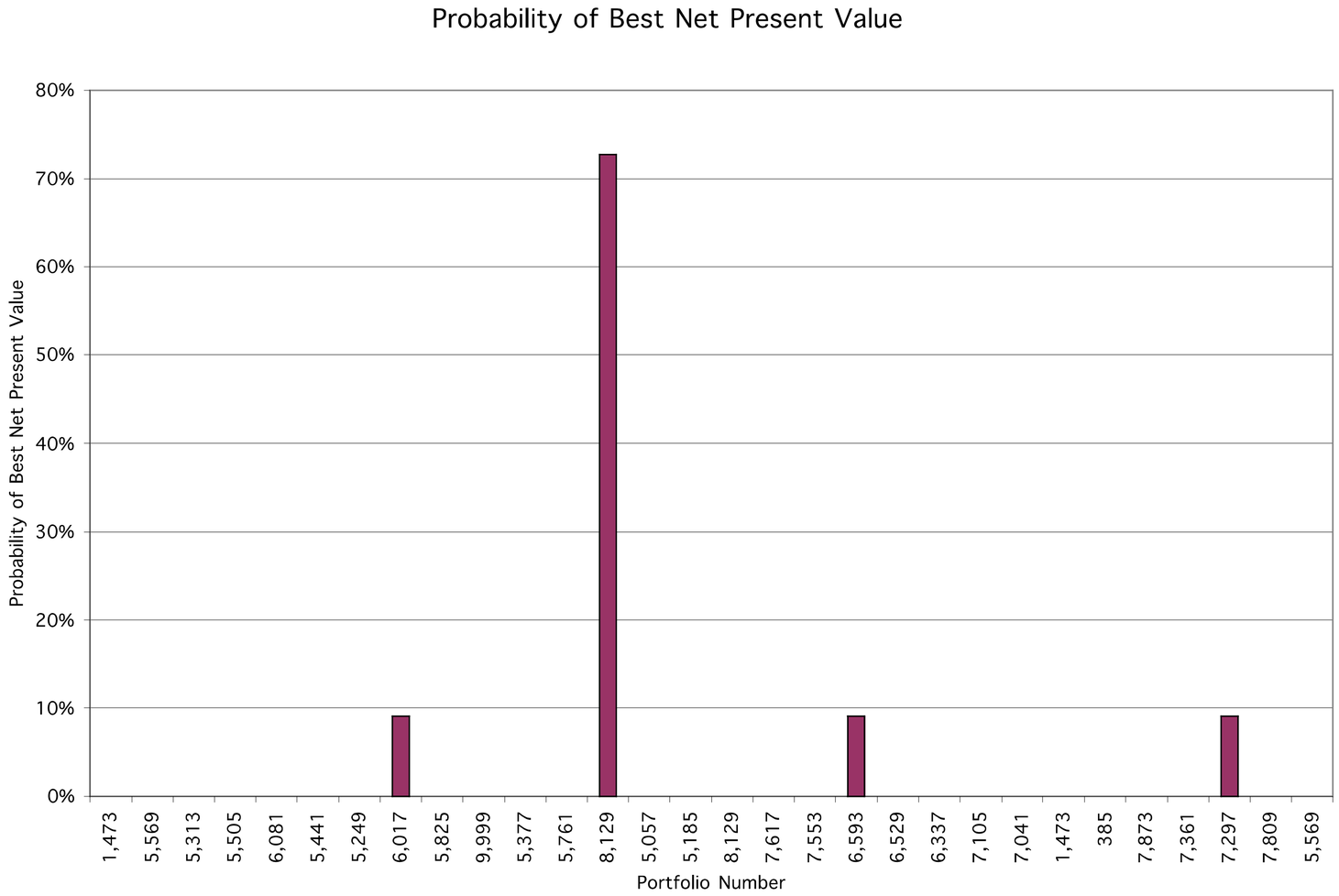
Acceptable values:	2023	2021	20%

Annual Cash Flow Growth	Pearson Index	Index Arithmetic Mean	Index Geometric Mean	Probability Best NPV	Probability Best CFV	Probability Acceptable Time to B.E.	Probability Acceptable Time to Profit	Probability Acceptable Cash Flow Growth
74.9%	58.68	0.4683	0.4086	1.1%	8.6%	0.0%	0.0%	59.1%
68.7%	60.84	0.4377	0.3717	6.6%	0.0%	0.0%	21.8%	5.0%
33.3%	68.22	0.4514	0.3626	0.0%	8.8%	22.2%	0.0%	0.0%
137.0%	72.09	0.4847	0.2506	21.8%	0.0%	0.0%	0.0%	98.7%
97.1%	84.55	0.4657	0.3346	5.0%	13.3%	0.0%	55.6%	0.0%
45.2%	83.44	0.5089	0.3431	11.1%	49.1%	100.0%	66.6%	11.1%
93.3%	63.59	0.5323	0.3806	9.0%	0.0%	100.0%	82.3%	0.0%
213.0%	72.09	0.4847	0.2506	2.5%	0.0%	0.0%	49.1%	100.0%
93.3%	51.40	0.5028	0.3806	15.9%	11.1%	100.0%	0.0%	0.0%
13.0%	44.00	0.5040	0.2408	23.1%	0.0%	100.0%	0.0%	50.8%
26.1%	63.59	0.5181	0.3333	0.0%	9.1%	100.0%	12.9%	22.2%
76.5%	58.43	0.4406	0.3821	3.9%	0.0%	0.0%	0.0%	0.0%

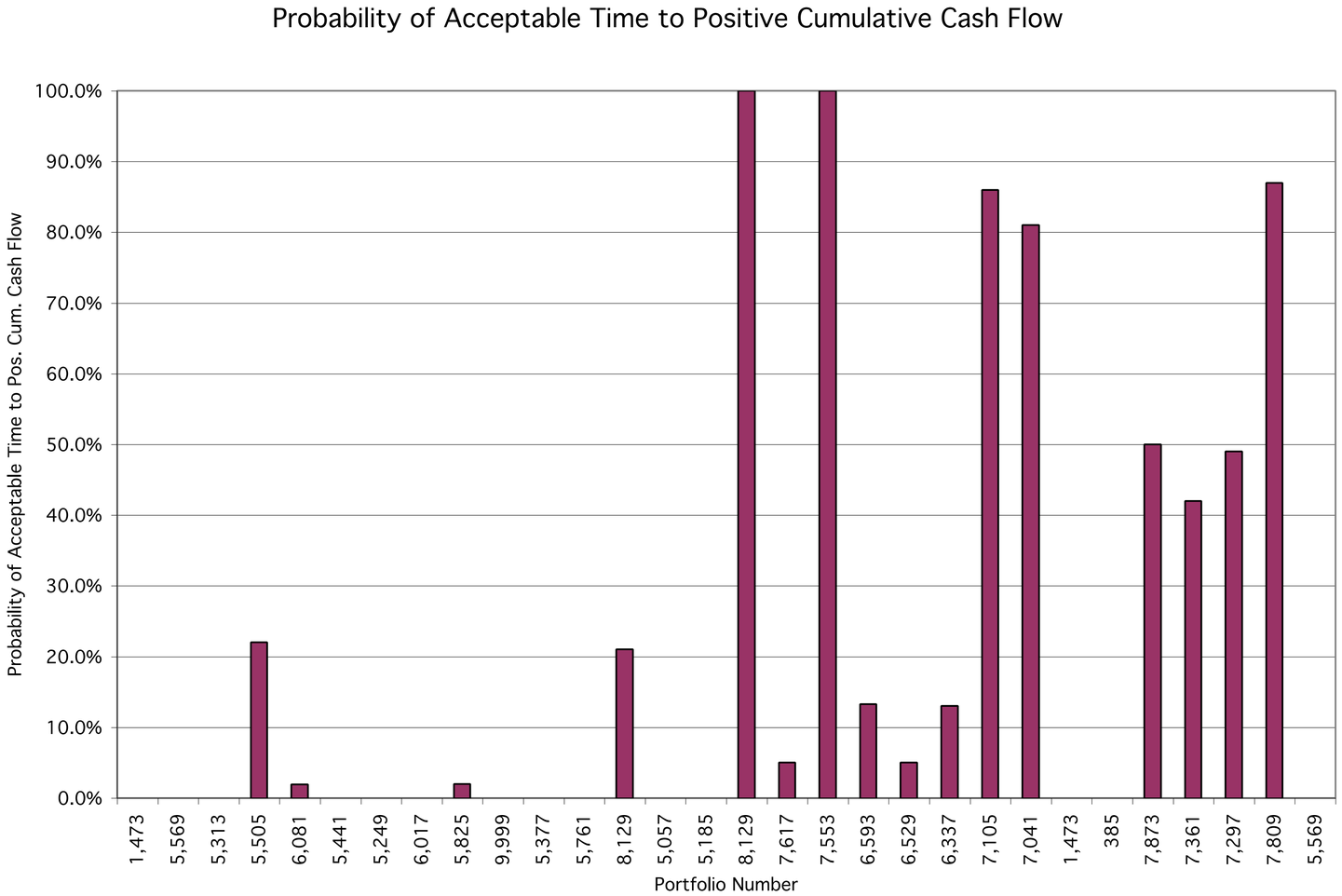
Earnings for Top Portfolios



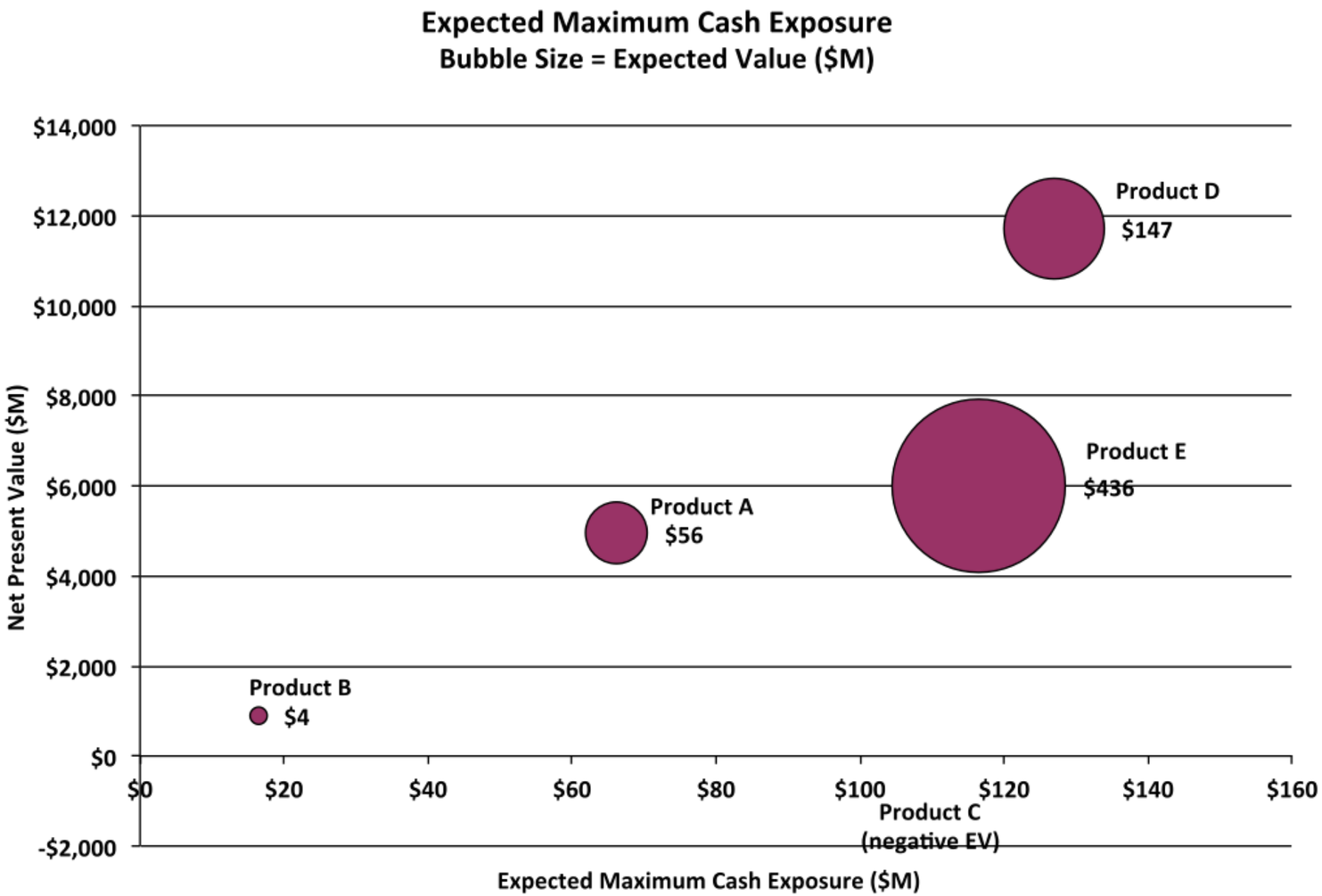
Stochastic Result: Best NPV



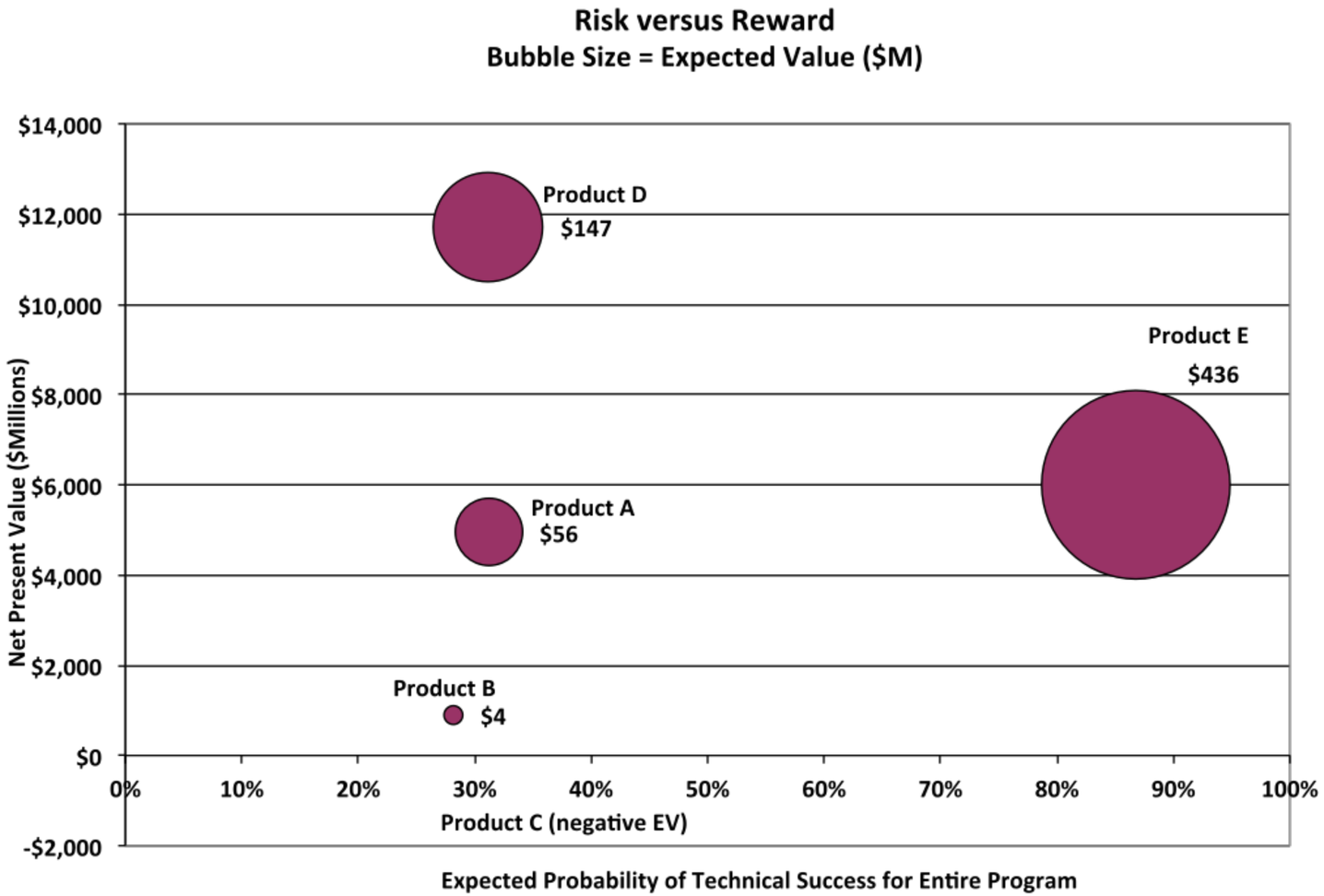
Stochastic Result: Acceptable Cash Flow



Cash Exposure Versus NPV



Risk Versus Reward



One-Page Project Summary

Project Summary for XX-53489 in Deep Vein Thrombosis

Product	XX-53489
Class	Anticoagulant
Market	Cardiovascular
Indication	Deep Vein Thrombosis
Launch	2Q2011
Version	Midyear Update
Date Prepared	31-Jul-03

Forecast Results ($ Millions)

NPV	$453.8
Risk-Adjusted NPV	$50.9
Monte Carlo Mean Revenue	$326.4
Monte Carlo Low Rev	$10.9
Monte Carlo High Rev	$384.1
Cash Flow Valley	($17.2)
Peak Year Cash Outflow	2007
Peak Year Outflow	($53.8)
Expected Cash Outflow	($68.1)

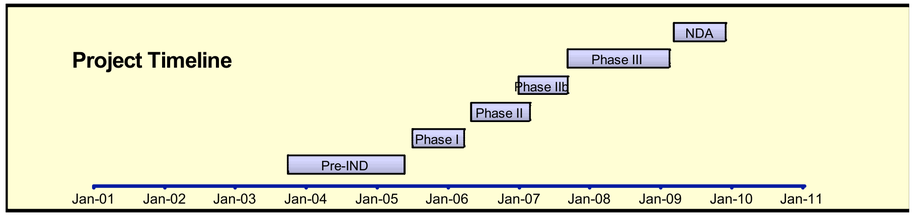
PTS	Project	Average
Pre IND	100%	65%
Phase I	40%	35%
Phase II	50%	50%
Phase IIb		
Phase III	85%	75%
NDA	90%	90%
Overall	15%	8%

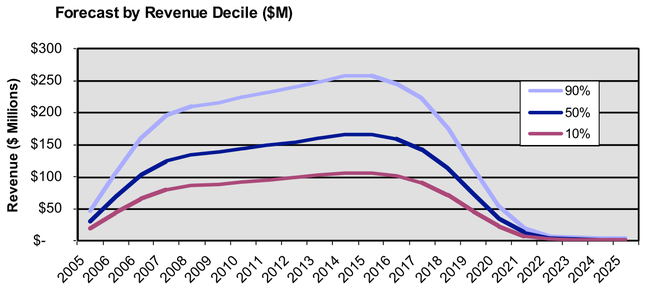
R&D ($ Million)	Project	Average
Pre IND		$3.1
Phase I	$7.3	$8.6
Phase II	$9.2	$11.6
Phase IIb		
Phase III	$25.4	$33.5
NDA	$2.4	$2.7
Overall	$44.3	$59.5

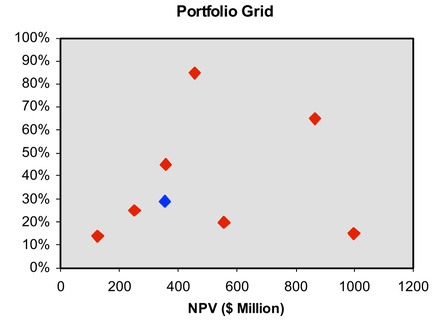
Forecast Variables	Most Likely	Low	High
Event Occurences (000)	2,500	1,200	4,500
% Eligible	85%	75%	90%
% Treated	50%	35%	55%
Market Share	20%	5%	30%
Revenue / Patient / Tx	$600	$200	$1,400

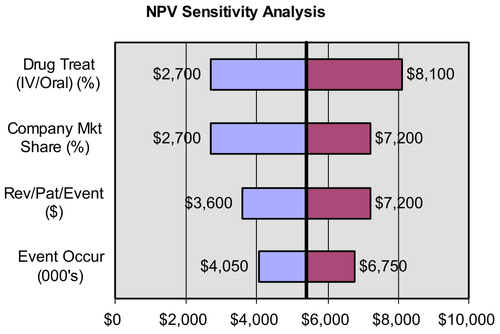
Project Rationale

1. List rationale here.









Portfolio Analysis Outcomes

- Determine the best of the best from the final list
- Present these dozen portfolios to the decision-makers
  - One page summary for each project
  - Graphs and tables for each project
  - Graphs and tables comparing the top portfolios
  - Rationale for selecting each portfolio
  - Rationale for selecting each project