Portfolio Planning and Optimization

2015
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 Rationale

- 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
  - 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
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 total NPV
  - Maximize return on investment
  - Maximize revenues
  - Minimize risks
  - Maximum number of products launched
  - Highest cash flow valley
- 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
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” (fewer with constraints)
- 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

<table>
<thead>
<tr>
<th>Project</th>
<th>Product</th>
<th>Indication</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
<td>CLL</td>
<td>Core</td>
</tr>
<tr>
<td>2</td>
<td>A</td>
<td>Refractory NHL</td>
<td>Optional</td>
</tr>
<tr>
<td>3</td>
<td>A</td>
<td>Frontline NHL</td>
<td>Optional</td>
</tr>
<tr>
<td>4</td>
<td>B</td>
<td>Myelofibrosis</td>
<td>Optional</td>
</tr>
<tr>
<td>5</td>
<td>B</td>
<td>Pancreatic Cancer</td>
<td>Optional</td>
</tr>
<tr>
<td>6</td>
<td>C</td>
<td>IPF</td>
<td>Core</td>
</tr>
<tr>
<td>7</td>
<td>D</td>
<td>RA</td>
<td>Optional</td>
</tr>
<tr>
<td>8</td>
<td>D</td>
<td>Crohn's</td>
<td>Optional</td>
</tr>
<tr>
<td>Overhead</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

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Long-Term Forecaster™ (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

Launch Date
Cumulative Distribution Function

Probability (%) that actual date will be less than or equal to X Launch Date

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Sample Outputs: Cash Flow Deciles
Sample Outputs: Project Value by Phase

Risk-Adjusted Net Present Value by Development Phase

- Pre-Clinical/Toxicology
- Phase I Clinical
- Phase IIA Clinical
- Phase IIB Clinical
- Phase III Clinical
- NDA or BLA Approval
- Marketing
Portfolio Model

LTF Model Project A

LTF Model Project B

LTF Model Project C

R&D Portfolio (compares all portfolios)

Deterministic & Stochastic (Monte Carlo simulation)
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 NHL drugs
  - Example: We will develop at least one RA drug
  - Example: We will develop at least X but not more than Y 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

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

<table>
<thead>
<tr>
<th>Result record</th>
<th>Project Combination</th>
<th>Probability at least one drug launches</th>
<th>Expected drug launches</th>
<th>Peak Revenues ($M)</th>
<th>Peak Annual Cash Outlay ($M)</th>
<th>Maximum Cash Exposure ($M)</th>
<th>NPV ($M)</th>
<th>EV ($M)</th>
<th>Year of Positive Cash Flow</th>
<th>Year of Cumulative Cash Flow</th>
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<tr>
<td>1</td>
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<td>99.9%</td>
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<td>$8,906</td>
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<td>$15,234</td>
<td>$5,043</td>
<td>2022</td>
<td>2022</td>
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<tr>
<td>2</td>
<td>4,993</td>
<td>99.9%</td>
<td>3.1</td>
<td>$7,999</td>
<td>$81.5</td>
<td>$72.0</td>
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<td>2022</td>
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<tr>
<td>4</td>
<td>385</td>
<td>99.6%</td>
<td>2.4</td>
<td>$7,023</td>
<td>$74.8</td>
<td>$40.9</td>
<td>$10,890</td>
<td>$3,299</td>
<td>2021</td>
<td>2024</td>
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<td>5</td>
<td>6,273</td>
<td>99.8%</td>
<td>3.0</td>
<td>$8,079</td>
<td>$117.9</td>
<td>$41.6</td>
<td>$14,247</td>
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<td>$39.4</td>
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<td>$9,947</td>
<td>$53.4</td>
<td>$44.0</td>
<td>$17,632</td>
<td>$6,359</td>
<td>2019</td>
<td>2021</td>
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<tr>
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<td>385</td>
<td>99.6%</td>
<td>2.4</td>
<td>$7,023</td>
<td>$74.8</td>
<td>$40.9</td>
<td>$10,890</td>
<td>$3,299</td>
<td>2024</td>
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<td>$10,002</td>
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<td>$11,086</td>
<td>$66.0</td>
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<td>$7,019</td>
<td>2020</td>
<td>2021</td>
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<td>11</td>
<td>199</td>
<td>98.0%</td>
<td>5.0</td>
<td>$7,992</td>
<td>$59.4</td>
<td>$51.8</td>
<td>$17,632</td>
<td>$7,208</td>
<td>2021</td>
<td>2020</td>
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<td>12</td>
<td>9,999</td>
<td>98.6%</td>
<td>2.3</td>
<td>$8,875</td>
<td>$70.3</td>
<td>$120.8</td>
<td>$15,114</td>
<td>$4,934</td>
<td>2022</td>
<td>2022</td>
</tr>
</tbody>
</table>

Acceptable values: 2021 2019 20%

<table>
<thead>
<tr>
<th>Annual Cash Flow Growth</th>
<th>Pearson Index</th>
<th>Index Arithmetic Mean</th>
<th>Index Geometric Mean</th>
<th>Probability Best NPV</th>
<th>Probability Best CFV</th>
<th>Probability Acceptable Time to B.E.</th>
<th>Probability Acceptable Time to Profit</th>
<th>Probability Acceptable Cash Flow Growth</th>
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<tbody>
<tr>
<td>74.9%</td>
<td>58.68</td>
<td>0.4683</td>
<td>0.4086</td>
<td>1.1%</td>
<td>8.6%</td>
<td>0.0%</td>
<td>0.0%</td>
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<tr>
<td>68.7%</td>
<td>60.84</td>
<td>0.4377</td>
<td>0.3717</td>
<td>6.6%</td>
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<td>0.0%</td>
<td>21.8%</td>
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<tr>
<td>33.3%</td>
<td>68.22</td>
<td>0.4514</td>
<td>0.3626</td>
<td>0.0%</td>
<td>8.8%</td>
<td>22.2%</td>
<td>0.0%</td>
<td>0.0%</td>
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<tr>
<td>137.0%</td>
<td>72.09</td>
<td>0.4947</td>
<td>0.2506</td>
<td>21.8%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>98.7%</td>
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<tr>
<td>97.1%</td>
<td>84.55</td>
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<td>0.3346</td>
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<td>13.3%</td>
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<tr>
<td>45.2%</td>
<td>83.44</td>
<td>0.5089</td>
<td>0.3431</td>
<td>11.1%</td>
<td>49.1%</td>
<td>100.0%</td>
<td>66.6%</td>
<td>11.1%</td>
</tr>
<tr>
<td>93.3%</td>
<td>63.59</td>
<td>0.5323</td>
<td>0.3806</td>
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<td>100.0%</td>
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<tr>
<td>213.0%</td>
<td>72.09</td>
<td>0.4847</td>
<td>0.2506</td>
<td>2.5%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>49.1%</td>
<td>100.0%</td>
</tr>
<tr>
<td>93.3%</td>
<td>51.40</td>
<td>0.5028</td>
<td>0.3806</td>
<td>15.9%</td>
<td>11.1%</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>13.0%</td>
<td>44.00</td>
<td>0.5040</td>
<td>0.2408</td>
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<td>0.0%</td>
<td>100.0%</td>
<td>0.0%</td>
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<tr>
<td>26.1%</td>
<td>63.59</td>
<td>0.5181</td>
<td>0.3333</td>
<td>0.0%</td>
<td>9.1%</td>
<td>100.0%</td>
<td>12.9%</td>
<td>22.2%</td>
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<tr>
<td>76.5%</td>
<td>58.43</td>
<td>0.4406</td>
<td>0.3821</td>
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<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>
Stochastic Result: Best NPV
Stochastic Result: Acceptable Cash Flow

Probability of Acceptable Time to Positive Cumulative Cash Flow

Portfolio Number

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Cash Exposure Versus NPV

Expected Maximum Cash Exposure
Bubble Size = Expected Value ($M)

Product A: $56
Product B: $4
Product C: (negative EV)
Product D: $147
Product E: $436
Risk Versus Reward

Risk versus Reward
Bubble Size = Expected Value ($M)

<table>
<thead>
<tr>
<th>Product</th>
<th>Expected Value ($M)</th>
<th>Net Present Value ($Millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product A</td>
<td>56</td>
<td>4</td>
</tr>
<tr>
<td>Product B</td>
<td>-2,000</td>
<td>0</td>
</tr>
<tr>
<td>Product C (negative EV)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Product D</td>
<td>147</td>
<td>$14,000</td>
</tr>
<tr>
<td>Product E</td>
<td>436</td>
<td>$12,000</td>
</tr>
</tbody>
</table>

Expected Probability of Technical Success for Entire Program
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