Incorporating ROI Into R&D Prioritization and Decision-Making

R&D Open Innovation and Portfolio Optimization
April 8, 2014

Katie MacFarlane, PharmD
Chief Commercial Officer
Agile Therapeutics
Managing Partner, SmartPharma LLC

Stacey Seltzer, MBA
Principal
Aisling Capital
Session Agenda

• Welcome
• ROI and the Changing Pharma Landscape
  – Impact of ROI on investment in pharmaceutical product development
  – Globalization and Health Policy Impact on ROI Analysis
• Break
• Modeling ROI – Elements of Decision-Making
• Decision Matrix Example
• Risks and Pitfalls
Introductions

• Session Speakers
  – Katie MacFarlane, PharmD
     Agile Therapeutics and SmartPharma LLC
  – Stacey Seltzer
     Aisling Capital
• Participants
• Interactive Session
The Challenge: How to Balance Innovation with ROI?

• Peak sales and asset value have declined

Source: Deloitte Center for Health Solutions and Thomson Reuters Life Sciences, Measuring the return from pharmaceutical innovation 2013. [http://thomsonreuters.com](http://thomsonreuters.com). Data based on 12 largest life science companies, products in Phase III or submitted for approval.
The Challenge: How to Balance Innovation with ROI?

- Average spend to bring a new product from discovery to market has risen to $1.3 Billion
- Late-stage trial failures have cost pharmaceutical firms $243 Billion since 2010

Source: Deloitte Center for Health Solutions and Thomson Reuters Life Sciences, Measuring the return from pharmaceutical innovation 2013. [http://thomsonreuters.com](http://thomsonreuters.com). Data based on 12 largest life science companies
The Challenge:
How to Balance Innovation with ROI?

• Expected ROI from the 12 biggest pharma firms late-stage pipelines has fallen

Venture Investing as a Driver of R&D Prioritization

- 64% of Pharma pipeline products come from outside the company (e.g. acquisitions)
- Corporate Pharma R&D continues to move towards an external innovation hub model
  - e.g. J&J Innovation Center, Sanofi’s Sunrise, Pfizer’s CTI
  - Big R&D megasites are shedding jobs
- There were 46 US Biotech IPOs in 2013
  - 32 of these were for VC-backed biotech companies
- ~ 3.5 Billion was raised into VC funds for life science investing in 2013

Data based on 12 largest life science companies
How Does the Current Environment Effect Investment in Biotech/Startups?

• What are the elements considered by venture investors?
  – Time to bring a new product to market?
  – Cost to bring a new product to market?
  – Potential revenue of new product?
  – Probability of success?
  – Opportunity for ‘exit’, either by IPO or acquisition?
What Types of Investments are VCs Making?

• Are there types of investments that are more or less attractive to venture investors today?
  – First financing / “seed” financing
  – Large biotech financings (e.g. >$50 Million)

• Do corporate venture funds invest differently than traditional venture funds?
What Markets Should be Considered for ROI?

Global pharma market is expected to expand to more than US $1 trillion by 2014, driven largely by Pharamerging markets.

- **US**
  - Size: US$360-390bn
  - CAGR 09-14: 3-6%

- **Japan**
  - Size: US$100-130bn
  - CAGR 09-14: 2-5%

- **Pharmerging” Markets**
  - Size: US$260-290bn
  - CAGR 09-14: 14-17%

  - China
  - Brazil
  - Russia
  - India
  - Mexico
  - Turkey
  - Venezuela
  - Poland
  - Argentina
  - Thailand
  - Romania
  - Indonesia
  - S. Africa
  - Egypt
  - Ukraine
  - Pakistan
  - Vietnam

- **Rest of World**
  - Size: US$180-210bn
  - CAGR 09-14: 4-7%

- **Global market**
  - 2014 Size: US$1,130-1,160bn
  - CAGR 09-14: 5-8%

Source: IMS Health Market Prognosis, Sep 2010, at www.asiahealthspace.com
The Pursuit of Improved R&D Returns

• Choose assets with higher commercial and therapeutic potential
• Fulfill genuine unmet needs
• Demonstrate value and cost-effectiveness

Source: Deloitte Center for Health Solutions and Thomson Reuters Life Sciences, Measuring the return from pharmaceutical innovation 2013. [http://thomsonreuters.com](http://thomsonreuters.com)
Unmet Market Needs

Breakthrough

Cure for Alzheimer's closer
by JAMES CHAPMAN, Daily Mail

Could an HIV injection
be on the horizon?

Hope for breakthrough on path
to Parkinson's cure

Drug Makers See Profit
Potential in Rare Diseases

Demonstrating Need for
Continued Improvement

Juxtapid And Kynamro: Race Of
Two Orphan Drugs To Market
March 6, 2013

Amgen's PCSK9 drug slashes
'bad' cholesterol in PhIII,
stoking blockbuster hopes
March 30, 2014

Source: Forecasting New Product Revenues, LEK Consulting Executive Insights, Volume IV, Issue 2, LEK.com
Health Policy Effects

• The ACA may bring the US closer to cost containment strategies in the rest of the developed world
• The ‘new buyers’ of healthcare are anticipated to increase influence on pricing and access
  – Payors (regional authorities, insurers, employers)
  – Patients
• Does Cost Effectiveness = ‘cost replacement’?

Questions from the New Buyers

• What outcomes will be achieved in my population?
• What is the clinical rationale for the product price point?

Incorporating ROI Into R&D Prioritization and Decision-Making

Break
Modeling ROI: Revenue Forecasts are an Integral Element

- Forecasting is not a perfect science…in fact, many would say it is not a science at all
Forecasts are Often Inaccurate

- More than 60% of consensus forecasts from sell-side analysts were over or under by at least 40%

- Forecast accuracy improves only marginally over time, after a drug is approved


Data set consists of more than 1,700 individual analyst forecasts on 260 launched drugs
Non-Big Pharma Drugs are More Likely to be Overestimated

Consensus average vs peak sales, by forecast year relative to launch year

Incorporating ROI into R&D Decision-Making

• Elements of Forecasting Revenue for R&D Products
  – Market sizing
  – Product uptake and usage
  – Pricing
  – Probability of success
  – Net Present Value (NPV)
Market Sizing Methodology

- **Rx-based**
  - Requires existing treatments / categories
  - May not reflect total potential – e.g. unmet need

- **Sales-based**
  - Requires existing treatments / categories
  - Need to adjust for price

- **Population based**
  - Relies on many estimates (prevalent population, etc)
  - May overstate the potential if data are not adjusted to reflect the true population for treatment
    - Age and sex
    - % diagnosed
    - % treated
    - compliance
Market Sizing: Population Size Hype and Reality

- Example: Alzheimer’s Disease Prevalence

**Hype**

5.2 Million
(Source: Alzheimer’s Association)

**Reality**

2.4 Million
(Source: ADAMS Study, NIH)

- Market Sizing Factors to Consider
  - Source of data – inherent bias
  - Surveillance data vs. diagnosed patients
  - Incidence and prevalence
    - Be careful when applying to population (e.g. including peds)
Market Sizing: Population Size Hype and Reality Example

• Example: IBS-C (constipation-predominant IBS)

Hype

10% prevalence = ~34 Million in US

Reality

4.5 Million
(Source: ADAMS Study, NIH)

• Remove pediatric population (92 million x 10% = 9.2 million)
• Remove male population (49%)
• Factor for IBS-C only (36%)
Product Uptake and Usage

• Potential sources of assumptions
  – Analysis of product characteristics compared to existing treatments
  – Model based on market analogs
    • Peak share
    • Time to peak share
  – Primary market research to estimate peak share
    • Qualitative vs. quantitative
    • Prescriber + consumer

Source: Forecasting New Product Revenues, LEK Consulting Executive Insights, Volume IV, Issue 2, LEK.com
Product Uptake and Usage

- Need to adjust estimates based upon
  - Physician stated intentions vs. actual prescribing behavior
    - Crude estimate (50%) vs. proprietary models
    - Adjustment may differ with degree of unmet market need
  - Changes in market environment over time, as compared to analogs, e.g.
    - Number of competitors
    - Reimbursement environment
    - Influence of consumer in choice
    - Expected level of promotional support

Source: Howie and Luby, MM&M August 2009, p.56-58 and LEK Consulting Executive Insights, Volume IV, Issue 2, LEK.com
### Summary of Published Literature on Probability of Success

<table>
<thead>
<tr>
<th>Source and Study Description</th>
<th>Phase I - Approval</th>
<th>Phase I - Phase II</th>
<th>Phase II – Phase III</th>
<th>Phase III - Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>DiMasi J, <em>J Health Economics</em> 2003 68 drugs, 1980-1999</td>
<td>22.2%</td>
<td>71.0%</td>
<td>44.2%</td>
<td>70.7%*</td>
</tr>
<tr>
<td>DiMasi J, <em>Clin Pharmacol Ther</em> 2010 1738 drugs, 1993-2004</td>
<td>19.0%</td>
<td>71.0%</td>
<td>45.0%</td>
<td>64.0%</td>
</tr>
<tr>
<td>Davis M, <em>Vaccine</em> 2011 4235 drugs, 132 vaccines, 1995-2011</td>
<td>26.2%*</td>
<td>74.0%</td>
<td>58.0%</td>
<td>61.0%</td>
</tr>
<tr>
<td>BIO BioMed Tracker Study, 2011 4275 drugs</td>
<td>9.0%</td>
<td>63.0%</td>
<td>33.0%</td>
<td>44.0%</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>19.1%</strong></td>
<td><strong>69.8%</strong></td>
<td><strong>45.1%</strong></td>
<td><strong>59.9%</strong></td>
</tr>
</tbody>
</table>

*calculated value

- Allows for adjustment for regulatory risk
- Should be employed at any point along the development path, including following NDA submission

Source: SmartPharma LLC analysis, 2013
## Example NPV (US Only)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Product X Gross Sales ($000)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rebates, Returns, Dist ($000)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Product X Net Sales ($000)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total A&amp;P Expenses ($000)</td>
<td>$ 2,000</td>
<td>$ 2,000</td>
<td>$ 2,000</td>
<td>$ 15,000</td>
<td>$ 25,000</td>
<td>$ 40,000</td>
<td>$ 50,000</td>
<td>$ 30,000</td>
</tr>
<tr>
<td>Annual US R&amp;D Expense ($000)</td>
<td>$ 2,000</td>
<td>$ 2,000</td>
<td>$ 2,000</td>
<td>$ 15,000</td>
<td>$ 25,000</td>
<td>$ 40,000</td>
<td>$ 50,000</td>
<td>$ 30,000</td>
</tr>
<tr>
<td>COGS ($000)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Product X Net Revenue ($000)</strong></td>
<td>$ (2,000)</td>
<td>$ (2,000)</td>
<td>$ (2,000)</td>
<td>$ (15,000)</td>
<td>$ (25,000)</td>
<td>$ (40,000)</td>
<td>$ (50,000)</td>
<td>$ (32,000)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>2022</th>
<th>2023</th>
<th>2024</th>
<th>2025</th>
<th>2026</th>
<th>2027</th>
<th>2028</th>
<th>2029</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product X Gross Sales ($000)</td>
<td>$ 2,623,979</td>
<td>$ 3,427,737</td>
<td>$ 3,517,571</td>
<td>$ 3,006,730</td>
<td>$ 2,611,564</td>
<td>$ 2,335,688</td>
<td>$ 2,431,919</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rebates, Returns, Dist ($000)</td>
<td>$ 393,597</td>
<td>$ 685,547</td>
<td>$ 879,393</td>
<td>$ 751,683</td>
<td>$ 652,891</td>
<td>$ 583,922</td>
<td>$ 607,980</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Product X Net Sales ($000)</strong></td>
<td>$ 2,230,383</td>
<td>$ 2,742,189</td>
<td>$ 2,638,178</td>
<td>$ 2,255,048</td>
<td>$ 1,958,673</td>
<td>$ 1,751,766</td>
<td>$ 1,823,939</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total A&amp;P Expenses ($000)</td>
<td>$ 3,500</td>
<td>$ 5,000</td>
<td>$ 100,000</td>
<td>$ 80,000</td>
<td>$ 80,000</td>
<td>$ 100,000</td>
<td>$ 100,000</td>
<td>$ 100,000</td>
<td>$ 100,000</td>
</tr>
<tr>
<td>Annual US R&amp;D Expense ($000)</td>
<td>$ 15,000</td>
<td>$ 5,000</td>
<td>$ 3,000</td>
<td>$ 2,000</td>
<td>$ 2,000</td>
<td>$ 2,000</td>
<td>$ 2,000</td>
<td>$ 2,000</td>
<td>$ 2,000</td>
</tr>
<tr>
<td>COGS ($000)</td>
<td>$ 131,199</td>
<td>$ 171,387</td>
<td>$ 175,879</td>
<td>$ 150,337</td>
<td>$ 130,578</td>
<td>$ 116,784</td>
<td>$ 121,596</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Product X Net Revenue ($000)</strong></td>
<td>$ (18,500)</td>
<td>$ (10,000)</td>
<td>$ 1,996,184</td>
<td>$ 2,488,803</td>
<td>$ 2,380,300</td>
<td>$ 2,002,711</td>
<td>$ 1,726,095</td>
<td>$ 1,532,982</td>
<td>$ 1,600,343</td>
</tr>
</tbody>
</table>

| Net Present Value ($000) | $ 1,131,849 |
| Discount Rate            | 20%         |
| Probability of Success   | 19%         |
| **Probability-Adjusted NPV ($000)** | $ 216,183 |
## Example R&D Decision Matrix

<table>
<thead>
<tr>
<th>Project</th>
<th>Unmet Need</th>
<th>Timing</th>
<th>Investment</th>
<th>Clinical Risk</th>
<th>Regulatory Risk</th>
<th>Commercial Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>XXX-0001</td>
<td>H / M / L</td>
<td>years</td>
<td>$Millions</td>
<td>H / M / L (Prob of Success)</td>
<td>H / M / L (Prob of Success)</td>
<td>NPV ($millions)</td>
</tr>
<tr>
<td>XXX-0002</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Risks and Pitfalls of Using ROI in Early R&D Decision-Making

• Many unknowns feeding into financials
  – Numbers can become very concrete
  – Try doing a qualitative analysis first
• High risk programs are most likely to have highest NPV, if they are fulfilling an unmet market need
  – Need to balance portfolio
  – Multiple ‘shots on goal’
  – Hedge for failure with multiple programs/indications
• Lower-risk programs may not look as desirable / may be difficult to get funded
  – Look for lifecycle opportunities
• ‘Not invented here’ syndrome
  – Give appropriate weight to external opportunities
Thank You