Real Options in the Pharmaceutical Industry

Alain Bensoussan, Lama Moussawi

ICDRiA

Contents

- Challenges in the Pharmaceutical industry
- The drug development pipeline
- Valuation of Pharmaceutical Real Options
- Examples from the industry

Challenges in the Pharmaceutical Industry

- Managed care organizations controlling costs
  - ✓ use of lower cost generic drugs
- Regulations
  - ✓ increased marketing expenditures
- The period for a patent has been reduced significantly
  - ✓ barriers to entry have diminished
- Drug development process: complex, costly, highly risky, and spans over a long period of time.
- Failure rate
  - ✓ Once in market, seven out of ten fail to return the cost of the company's capital
- Technology and Market risks

Considerable Resources Spent on Pharmaceutical R&D Projects

- Total cost of bringing a new drug to market is between $350 and 500 million (Jacob et al. 2002)
- A project may fail at any time
  - ✓ Usually, around 50 projects are run in parallel
  - ✓ High failure rates due to scientific failures
- A drug research project takes10-15 years (Jacob et al. 2002, Nichols 1994)
- Pharmaceutical firms spend 15-20% of revenues on R&D, in comparison to only 10% on production (Ulrich et al., 2005)

ICDRiA
INTERNATIONAL CENTER FOR DECISION AND RISK ANALYSIS

Significant Federal R&D Funding at NIH

While the overall NIH 2006 budget will increase only 0.5%, the Roadmap for Biomedial Research is targeted to increase 41% to boost clinical research, high-risk basic research, and collaborative research

Federal Research Funding

Research Funding by Agency (basic + applied, in billions of dollars)	**FY2005** estimate	**FY2006** budget
Health and Human Services	$28.7	$28.9
National Institutes of Health	***27.5***	***27.8***
Defense (military)	6.8	5.6
NASA	4.8	5.4
Energy	5.6	5.4
National Science Foundation	3.7	3.7
Agriculture	1.9	1.7
Commerce	0.9	0.8
All Other	3.4	3.5
Total Research	**$56.0**	**$55.2**

Source: American Association for the Advancement of Science, Analysis of R&D in the FY 2006 Budget

Source: Report on The Drug Development Pipeline, The Massachussetts Technology Roadmap and Strategic Alliances Study, 2005.

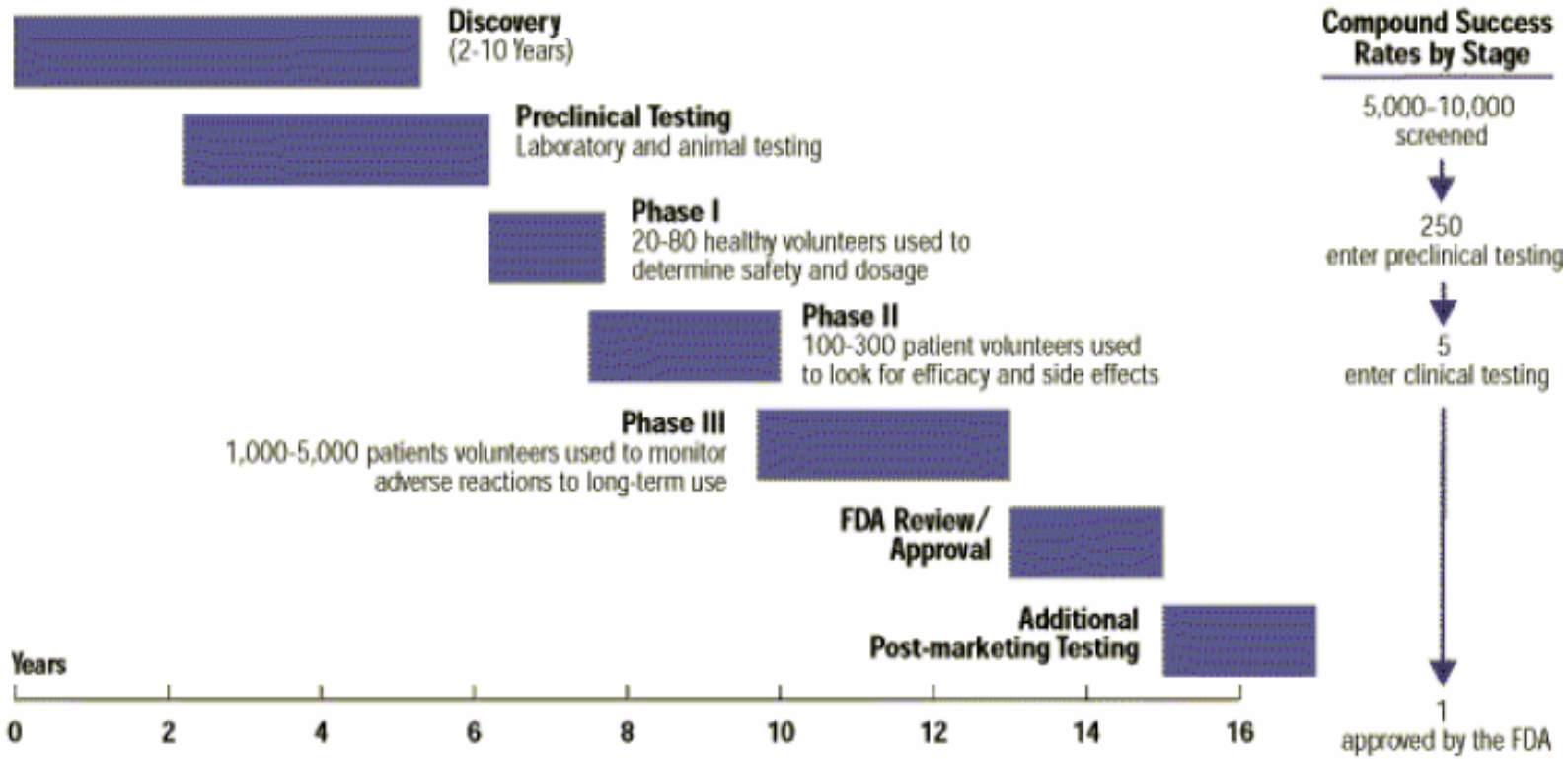
ICDRIA
INTERNATIONAL CENTER FOR DECISION AND RISK ANALYSIS

Concerns in the Pharmaceutical Industry

- Decrease in productivity in terms of number of drugs launched per year

- Emphasis on the development of project management techniques and methodologies
  - ✓ develop a drug quickly and efficiently
  - ✓ maintain the flexibility to react to different types of uncertainties

The Drug Development Pipeline



Source: PhRMA, based on data from Center for the Study of Drug Development, Tufts University, 1995.

ICDRIA
INTERNATIONAL CENTER FOR DECISION AND RISK ANALYSIS

The Drug Development Pipeline

- *Drug discovery:* (2-10 years)
  - ✓ A specific target is identified
  - ✓ Thousand of compounds or molecules are screened to get around hundred of potential drugs
- *Preclinical testing: (*3-6 years)
  - ✓ Animal studies to evaluate drug safety and show that it has a biological activity against the disease target.
- *Investigational New Drug Application (IND):*
  - ✓ This application shows results of the preclinical experiments.

The Drug Development Pipeline

- *Clinical Trials:*
  - ✓ **Phase I** (6months-1year):
    - medicine tested in a small group of healthy volunteers (20-100)
  - ✓ **Phase II** (6monts-1year):
    - 100-500 volunteer patients
    - The goal: demonstrate medicine effectively treats the disease.
  - ✓ **Phase III** (1-4years):
    - medicine tested in large, with 1000-5000 patients in hospitals, and clinics
    - Researchers closely monitor patients to confirm that drug is effective and identify the side effects.
- Company files a *New Drug Application (NDA)* with the FDA (16.9 months for approval)

Need to Accommodate Complexity and Dynamics of Pharmaceutical R&D Projects

- Actual market is characterized by change, uncertainty, and competitive interactions.
- As new information arrives and uncertainty gradually resolved, management needs flexibility
  - ✓ Alter the operating strategy
  - ✓ Seize valuable opportunities and mitigate losses
- For a good project evaluation, sources of risks need to be identified, and decision points defined.

ICDRiA
INTERNATIONAL CENTER FOR DECISION AND RISK ANALYSIS

Valuation
using Traditional Discounted Cash Flow

- A traditional approach using NPV
- NPV method is static
  - ✓ Ignores managers flexibility
  - ✓ Ignores changing market conditions
- NPV methods undervalue the projects in the presence of high uncertainty
- Traditional NPV rule yields same results as real options analysis when:
  - ✓ Market and technology uncertainties are very small (tend to zero)
  - ✓ Investment required for the product development is reversible

ICDRiA
INTERNATIONAL CENTER FOR DECISION AND RISK ANALYSIS

Introducing Real Options

- An option is the right but not obligation to take an action in the future
- Bridges the gap between strategic thinking and finance
  - ✓ A way of thinking
  - ✓ Similar to contingent decisions: depending on conditions, management takes decisions to create highest value
- The real options approach is an extension of the financial option theory to real (non-financial) assets
  - ✓ A new financial project evaluation tool superior to DCF

Real Options as a Managerial Flexibility

- Higher uncertainty in a project payoffs increases the real option value of the managerial flexibility or the value of the real option
  - ✓ with higher payoff uncertainty, flexibility has a higher potential of enhancing the upside while limiting the downside.
- Management has the flexibility to alter the initial strategy
- This flexibility enhances the investment value relative to the initial expectations

Real Options Thinking

- To support management ask the right questions when evaluating a project:
  - ✓ How can decisions be defined in order to reduce uncertainty?
  - ✓ What are the project goals?
  - ✓ What are the possible alternative strategies, and which will create the highest value?
  - ✓ What are the possible outcomes and how can management react?

Real Options as Solution

- Myers (1984), and Dixit and Pindyck (1994) realized that DCF methods inadequately value the R&D projects.
- “DCF techniques may have been misused and consequently not accepted in strategic applications”- Myers (1984)
- R&D investment opportunities are real options
- “I believe the most promising line of research is to try to use options pricing theory to model the time-series interaction between investments.” - Myers (1984)

Analogies between Real Options & Financial Options

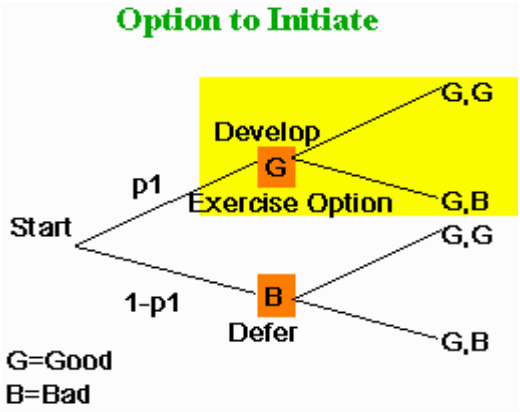
- Investing in an R&D project creates an option in investing in forthcoming development phases
- Follow-up investments are made only when the results of the initial projects are satisfactory and market conditions favorable
- Management has the right but not obligation to invest in the next R&D phase
- The downside risk is limited by the flexibility to react to new information
- The upside potential is increased

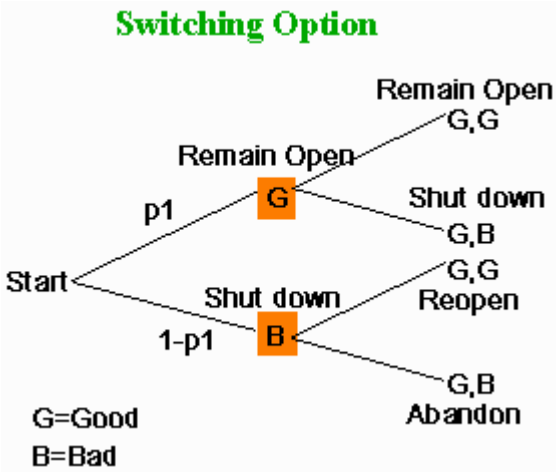
Types of Real Options

- In a staged project, each stage is an option

- *Initiate / Defer option*:
  waiting until more information becomes available

- *Switching option*:
  changing the mode of operation of an asset

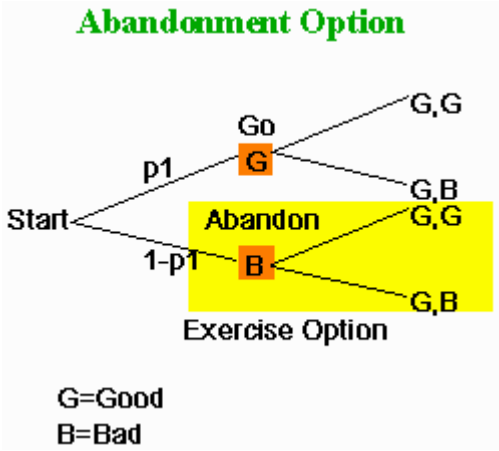


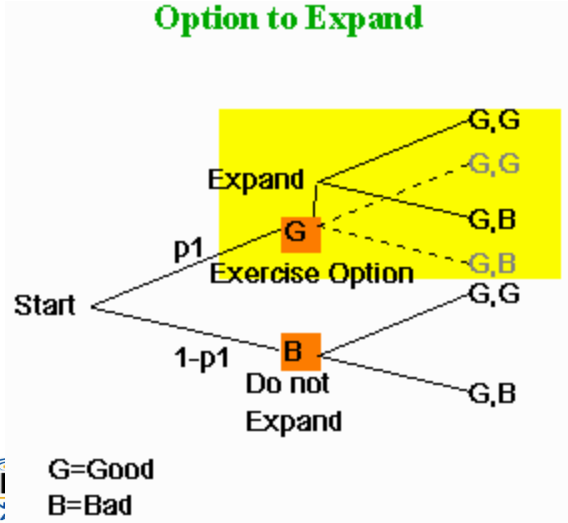


ICDRiA
INTERNATIONAL CENTER FOR DECISION AND RISK ANALYSIS

Types of Real Options

- *Abandonment option*:
  - making the investment in stages
  - deciding at each stage whether to stop or continue
- *Expansion/contraction option*:
  - possibility to adjust the scale of the investment depending on the market conditions





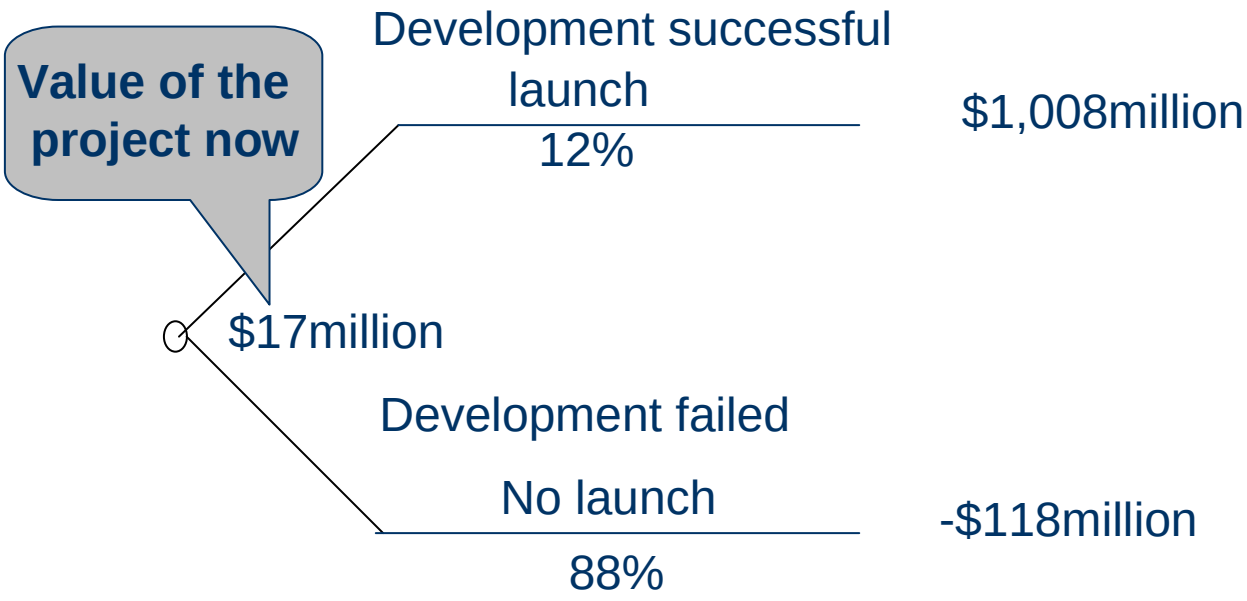
Valuation
of Real Options using Decision Tree Analysis

- NPV analysis extended to account for uncertainty through the Decision Tree Analysis (DTA) framework
- Excellent tool to model subsequent activities, possible outcomes, and uncertainties
- NPV estimates obtained through moving backward in the decision tree and applying the discounted cash flow methodology
- DTA is inferred from Cox, Ross, Rubinstein (1979) “Option Pricing: A Simplified Approach” developed a binomial model to value american options using decision trees

ICDRiA
INTERNATIONAL CENTER FOR DECISION AND RISK ANALYSIS

Example 1: Traditional NPV inappropriate

Value of option is missed

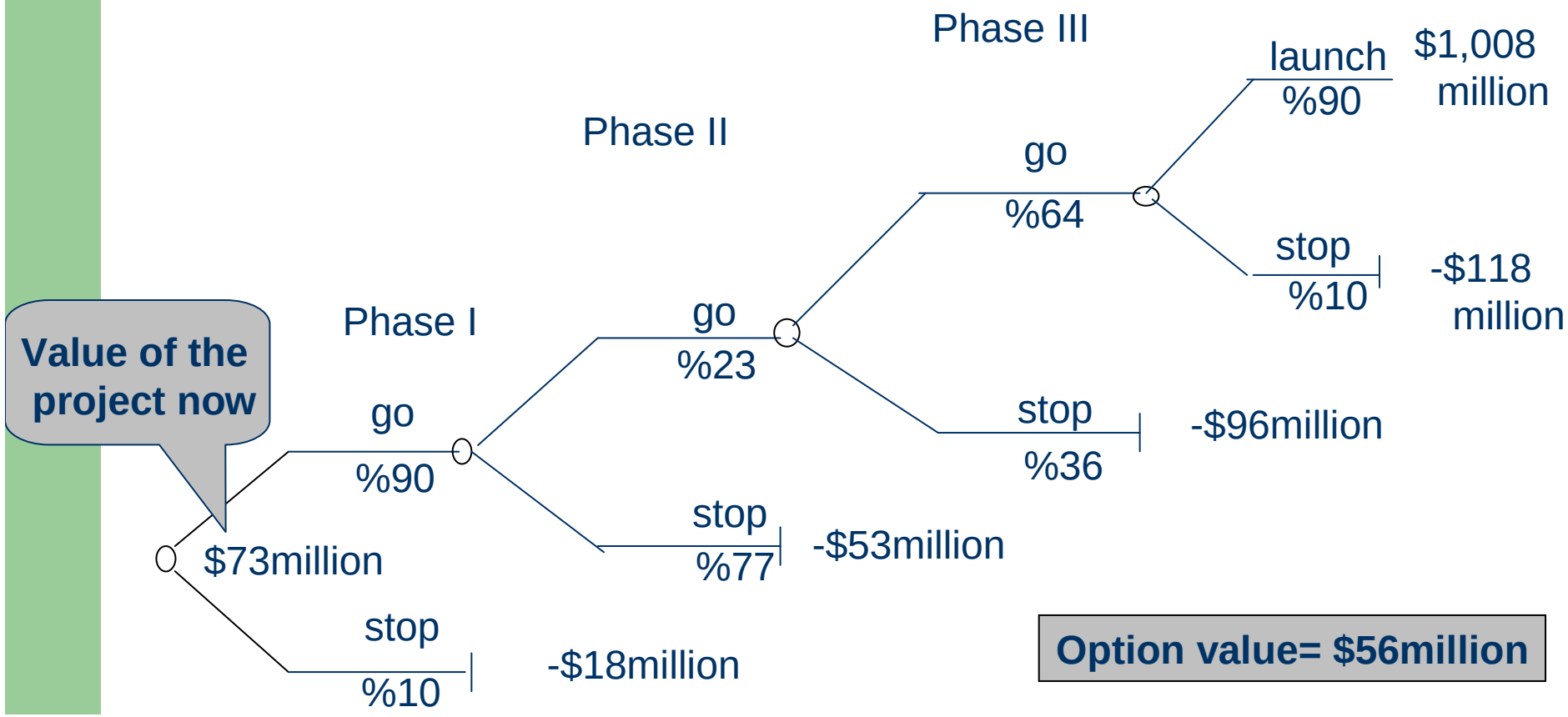


However, in reality, many more scenarios are possible, and further milestones at which decisions can be made on whether to continue or stop investing.

ICDRiA
INTERNATIONAL CENTER FOR DECISION AND RISK ANALYSIS

Example 2: Typical Abandonment Option for Pharmaceutical Projects (Scrip Reports-2000)

Including abandonment option increases the project's value:



ICDRIA
INTERNATIONAL CENTER FOR DECISION AND RISK ANALYSIS

Disadvantages of DTA

- The sequence of research activities in projects in innovative areas may be difficult to define
  - ✓ Decision points are hard to define
- In large companies, many projects run in parallel
  - ✓ Diversification reduces technical risks
- Time-consuming
  - ✓ In the pharmaceutical case, the problem requires very large decision trees to adequately capture the options and the uncertainties.
- Use options pricing techniques for valuing R&D investment is suggested by many researchers

Valuation of Real Options using Black-Scholes Model

- Most common is Black-Scholes (1973) model for option pricing
  - ✓ Derives option value from five variables
  - ✓ Assumes value of the underlying asset changes continuously and is lognormally distributed
  - ✓ Volatility of underlying asset is continuous and increases linearly with time
  - ✓ Reasonable to describe volatility of stock prices, but not for that of R&D investments
  - ✓ Technical risks of the project are not within the scope of the analysis

Disadvantages of Black-Scholes Model

- Can be applied for certain cases in the pharmaceutical industry
  - ✓ when the parameters can be reliably identified by referring to similar publicly traded assets
  - ✓ Ex: a particular research project may have a similar risk structure as a project undertaken in a biotech company
- The expert's assumptions regarding probabilities of success at each step are not reflected
- The Black-Scholes model should be reserved to special situations

Example 3: The Case of Merck (Nichols 1994)

- Merck applies the Black-Scholes formula:

$$C = S * N(d_1) - E * e^{-Rt} N(d_2)$$

with $d_1 = [\ln(S/E) + (R+\sigma^2/2) * t] / \sigma * \sqrt{t}$

$d_2 = d_1 - \sigma * \sqrt{t}$;

σ is the standard deviation of the rate of return on underlying asset.

- Pharmaceutical companies enters into business relationships with small biotechnology companies or universities to gain access to research projects.
  - ✓ up-front payment followed by a series of payments
  - ✓ payments give the pharmaceutical company the right but not obligation to make further investments

- Option to terminate the project any time if dissatisfied with the progress of the research

Option Analysis at Merck (Nichols 1994)

- Five variables affect the project's value:
  - ✓ *Exercise Price:*
    - *Is the capital investment to be made at end of the project's life*
  - ✓ *Stock Price:*
    - *Or value of the underlying asset, is the PV of the cash flows from the project*
  - ✓ *Time to expiration:*
    - *Merck determines the time of expiration with respect to market conditions*
  - ✓ *Project's Volatility:*
    - *Using a sample of typical biotechnology stocks to measure project's volatility, a range was set at 40% to 60%*
  - ✓ *Risk-free rate of interest: 4.5% assumed*

Conclusion

- Real Options are the best framework within which pharmaceutical R&D projects can be valued
- Research on methods using Real Options for risky staged R&D projects is still not well developed
- Need for Tools designed specifically for staged R&D investments