Valuation of investments in medical devices and pharmaceutical products using real options analysis

Prepared for the Licensing Executives Society
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Agenda

- Concepts
  - The relationship between value of intellectual property and value of the device or drug
  - The difference between risks and options
  - Valuation in practice
    - Typical implementation via a scenario and its limitations
    - Transparent valuation using a binomial tree to account for options and risks
- Quantitative example
  - Three stage R&D with abandonment option

Concepts

Concept 1: Value of IP versus value of the drug or device

- Difference between value of the device or drug & the value of the patent, trademark or trade secrets that represent the intellectual property (IP) behind the device or drug.
- Value of the device or drug represents the present value of the expected cash flows that will flow from commercialization.
  - Total value will be allocated amongst the holder of the IP & the entity that can commercially exploit the IP.
  - The commercial entity is responsible for manufacturing, distribution & marketing & the holder of the IP is responsible for the idea & the science.
  - One entity can perform both roles – development & commercialization – but it is easiest to think of two entities with specialized roles.
- How total value of the device or drug is allocated amongst the R&D firm & the commercial firm depends upon their capabilities & market power.
  - If we have a blockbuster drug that could halve obesity rates or increase cancer survival by 10 per cent, the value allocation will shift towards the R&D firm. The importance of manufacturing efficiency & marketing capability is diminished because the drug will sell itself.
  - In contrast, some devices could be thought of as better mousetraps – they are better than alternatives, but the large medical device companies have the power to determine which devices are pushed through a distribution pipeline.
- This seminar relates to the total valuation of the investment in the device or drug.
  - Is it worthwhile for an R&D firm to invest in clinical trials at a reasonably early stage?
  - How can we handle the valuation problem for a product in which there are multiple stages, the payoffs are highly uncertain but which are very large if we are ultimately successful?

Concept 2: Risk versus options (1) – Pathways create options

- Devices & drugs have pathways to market that differ from other consumer products, largely because of consumer risk.
  - For a risky medical device to be sold to consumers it has to receive premarket approval (PMA) by the FDA or receive clearance because it is substantially equivalent to a device that is already allowed (a “predicate device”).
  - For a drug to be sold to consumers the FDA needs to attest that it is safe and effective.
- Cars, toys & food do not need to meet the same hurdles.
- This means that we have well-defined, staged pathways for devices and drugs to reach the market. We can’t simply run a pilot program.
- Options for abandonment or change in direction generated by those pathways
  - The existence of these multi-stage pathways for development is the first plank underpinning the use of real options for valuation. As the development of a device or drug proceeds from one stage to the next, the R&D firm has the option to abandon the project or change direction in response to new information about safety, efficacy or alternative uses.
  - This means that we can think of an investment in a device or drug as an investment in a package of options to proceed to the next stage of development, & this leads to the use of the valuation technique known as real options analysis.

Concept 2: Risk versus options (2) – Risk lowers value, options increase value

- Characteristics supporting real options analysis
  - Multi-stage investments.
  - High dispersion of payoffs depending upon ultimate success or failure.
  - Investment plan can be altered as new information comes to light which resolves uncertainty.
    - This information relates to technical performance, concerns of the FDA and insurance companies, and the size of the market and the potential benefits to consumers.
    - This characteristic is the one that makes the difference between the negative impact on value associated with risk, versus the positive impact on value associated with real options.
- There are other investments in different industries that meet these three criteria.
  - Oil exploration
  - Information technology
  - In fact, all investments can be valued using real options analysis. But the option value increases along with multiple stages, dispersion of payoffs and flexibility in decision-making

Concept 2: Risk versus options (3) – Irreversible investment

Type of investment	Irreversible investment
What does variation in outcomes mean?	**Risk** that leads to **lower valuations**
Example	Toll bridge or tunnel
Description	The investment is irreversible and cannot be altered as new information resolves uncertainty about volumes. Prior to the first month of traffic this is a risky investment: • Brisbane’s Clem7 tunnel cost A$3 b to build and was sold to Queensland Motorways for A$618 m • Sydney’s Cross City tunnel cost A$1 b to build and was sold to Transurban for A$475 m • Sydney’s Lane Cove tunnel cost A$1 b to build and was sold to Transurban for A$630 m After the first month traffic volumes are predictable and this is a safe investment.
Key characteristic	**Huge amounts of capital are sunk before any data comes to hand about whether earnings expectations will be met.**
Implication	If a new toll road is priced using the same metrics as existing toll roads (discount rate or valuation multiples) then the risk will be understated and hence value will be overstated. The **more variation in outcomes the riskier the project** and the variation does not create option value.

Concept 2: Risk versus options (4) – Investment with options

Type of investment	Projects that can be altered as new information is received
What does variation in outcomes mean?	**Options** that **increase project value**
Example	Drug development
Description	Development of a new drug involves early stage research, 3 stages of clinical trials & regulatory approval. This is a risky bet because the ultimate odds of success are low. The odds of success at each stage might be just: Stage 1 success (small sample, toxicity) ~30% Stage 2 success (small sample, efficacy) ~40% Stage 3 success (large sample, efficacy) ~60% Regulatory approval ~90% So the cumulative odds of success are low at 6.5% (0.3 × 0.4 × 0.6 × 0.9 = 6.5%) but the payoffs are high in the event of success (potentially > $1 billion annual revenue) But … the risk is not as great as many people think because large amounts of capital are spent after the project has been de-risked (when the odds of success are higher) Representative capital expenditure assumptions are $20 m for stage 1, $80 m for stage 2, $100 m for stage 3 & $20 m for FDA approval. (Note that projected investment spending on a blockbuster drug exceeds $1 billion if we include all the spending on drugs which fail.)
Key characteristic	Total capital spend of $220 million occurs in **4 stages & incremental spend only occurs upon good results are revealed.**
Implication	The new drug project is still riskier than a proven drug, but it is less risky than an equivalent project in which there is a commitment to make the capital investments over time. **The more variation in outcomes the more option value.** Intuitively, executives in pharmaceutical companies understand this but surveys suggest that almost no-one properly prices risk and options in multi-stage investments

Concept 3: Valuation in practice

- Our fundamental valuation principle is that the value of any asset is the present value of expected cash flows
  - Investors care about three things – the timing, magnitude & risk of expected cash flows.
  - All else equal …
    - cash sooner is better than cash later;
    - more cash is better than less cash; &
    - a lower risk payoff is better than a higher risk payoff.
- The expectation has its statistical meaning: the probability weighted average of all possible cash flows
- But for practical purposes we almost always use one scenario as the proxy for the expectation (for example, produce *x* widgets at *y* variable cost per widget & *z* fixed costs)
- That works fine for projects in which there are few options to change direction. Sure, outcomes could be better or worse than projected but a well-specified scenario will be close to the expected outcome.
- But for projects with options the use of a scenario based model fails, because there are many paths the project could take & a single scenario based model cannot handle this
- It can't be fixed by simply running more scenarios because the scenarios need to reflect the exercise of management discretion at each point in time
- Real options analysis can be implemented in two phases, with the first phase being most important.
  - Recall that in valuation we care about the timing, magnitude & risk of expected cash flows.
  - Phase 1 is to use a binomial tree to correctly work out the timing & magnitude of expected cash flows, & convert them to present value using a risk-adjusted discount rate. This ensures that we correctly estimate the expected cash flows.
  - Phase 2 is to extend the analysis to incorporate the risk reduction that comes from embedded options.
  - The valuation performed at Phase 2 should always be higher than the valuation performed in Phase 1 & is the more accurate valuation.

Application

Description

- Representative drug R&D after 1st stage success.
- Odds of ultimate success from now are 21.6%.
- Total investment over 3 stages is $ 200 m
- Potential payoff in 5 years is $1,167 m.
- What is the R&D worth today?

Valuation assumptions			
Investment, odds of success and timing:			
Stage	Cost	Odds	Years
2 (small sample, efficacy)	$ 80 m	40%	2
3 (large sample, efficacy)	$100 m	60%	2
FDA & ins.	$ 20 m	90%	1
Payoff if you have success	$1,167 m (Present value of expected cash flows upon receiving FDA approval & insurance acceptance in 5 years. From $432 m revenue growing at 2% per year & 30% margin over 15 years at a discount rate of 9%.)		
Government bond yield	3%		
Inflation	2%		
Risk-adjusted discount rate	12%		

Results preview

Decision-tree analysis: No change to discount rate to reflect risk reduction	
Value without options	-29.4
Estimate of option value without proper adjustment to discount rate to reflect risk reduction	+ 57.5
Value of options without proper adjustment to discount rate to reflect risk reduction	= 28.1
Nominal discount rate	12.00%
Real discount rate	9.80%

Real options analysis: Valuation reflects risk reduction from options	
Value without options	-29.4
Estimate of option value without proper adjustment to discount rate to reflect risk reduction	+ 71.2
Value of options without proper adjustment to discount rate to reflect risk reduction	= 41.9
Nominal discount rate	9.74%
Real discount rate	7.59%

Valuation steps: Overview

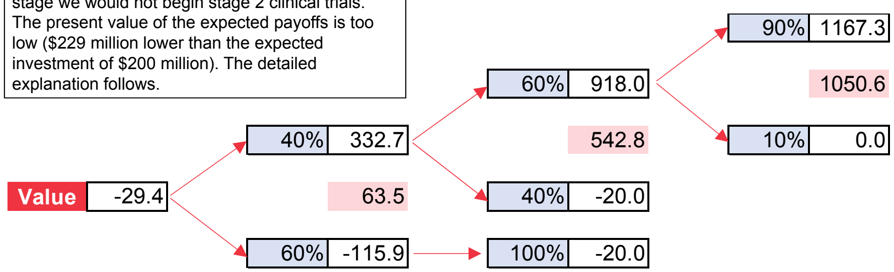
1. Value the project as if you were **fully committed** to seeing the project to completion by working backwards
   - Why work backwards? Value today depends upon what something is expected to sell for later, and a discount to reflect risk and the time value of money
   - Why consider the fully committed project? We want a framework for comparing projects with options, and without options, to see how much extra value we get from flexibility in decision-making.
2. Value the project as if you were **not fully committed** to seeing the project to completion by working backwards
   - What is the valuation difference between step 1 and step 2? Higher *expected* cash flows. Expected cash flows are the probability weighted average cash flows from the possible outcomes. The expected cash flows increase because you re-assess the project at each stage and only exercise valuable options.
3. Account for **the lower risk of a project with options by using risk-neutral probabilities**
   - What are risk-neutral probabilities? A clever computational technique (which contributed to a Nobel prize) accounting for the upside potential of options but no downside. A project with options, compared to the same project without options, has higher expected cash flows and lower risk. Step 2 accounts for the cash flow increase and step 3 accounts for the risk adjustment.

Valuation steps: Detail (1) – Valuation of R&D without options

1. Value the project as if you were **fully committed** to seeing the project to completion by working backwards
   a) Ask, what is the project value at the end of stage 3?
      i. Go to the final stage (FDA approval and insurance co. acceptance) and estimate payoffs for approval versus rejection
      ii. Compute the expected payoff (the weighted average of the possible payoffs)
      iii. Discount the expected payoff to the end of the stage 3 trials
      iv. Subtract the cost of seeking FDA approval and lobbying insurers
   b) Ask, what is the project value at the end of stage 2?
      i. Go the end of stage 2 and estimate payoffs for success versus failure in stage 3
      ii. Compute the expected payoff from success or failure
      iii. Discount the expected payoff to the end of stage 2 trials
      iv. Subtract the cost of stage 3 clinical trials
   c) Ask, what is the project value at the end of stage 1?
      i. Go the end of stage 1 (today) and estimate payoffs for success versus failure in stage 2
      ii. Compute the expected payoff from success or failure
      iii. Discount the expected payoff to today
      iv. Subtract the cost of stage 2 clinical trials

What would be the value of the project without options? (1)

If we were fully committed to investing at each stage we would not begin stage 2 clinical trials. The present value of the expected payoffs is too low ($229 million lower than the expected investment of $200 million). The detailed explanation follows.



Expected future payoff (a weighted average of the possible payoffs)

Odds of success and failure at each stage

Valuation at each stage after making the decision to either (a) invest in the next stage or (b) abandon

What would be the value of the project without options? (2)

Suppose you had success at stage 3, what is the R&D worth?

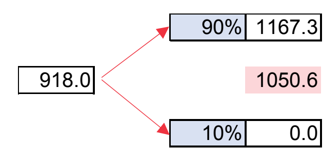
There is a 90% chance of FDA approval and insurance coverage, and if that happens the payoff is $1,167 million.

There is a 10% chance that your application is rejected and the R&D is worth nothing.

So the *expected* payoff, in one year's time, is $1,051 million.

We discount the expected payoff to $938 million ($1,051 ÷ 1.12^1 = $938).

We still need to spend $20 million on FDA approval and lobbying insurers, so after spending this money the R&D is worth $918 million.



Expected future payoff (a weighted average of the possible payoffs)

Odds of success and failure at each stage

Valuation at each stage after making the decision to either (a) invest in the next stage or (b) abandon

What would be the value of the project without options? (3)

Suppose you had success at stage 2, what is the R&D worth?

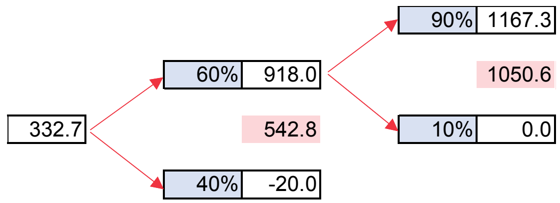
There is a 60% chance that the project is worth $918 m in another 2 years.

There is a 40% chance that the project is worthless but we are committed to spending $20 m on approvals.

So the *expected* payoff, in one year's time, is $543 million.

We discount the expected payoff to $433 million ($543 ÷ 1.12^2 = $433).

We still need to spend $100 million on stage 3 trials so the R&D is worth $333 million.



Expected future payoff (a weighted average of the possible payoffs)

Odds of success and failure at each stage

Valuation at each stage after making the decision to either (a) invest in the next stage or (b) abandon

What would be the value of the project without options? (4)

Suppose you had success at stage 1, what is the R&D worth?

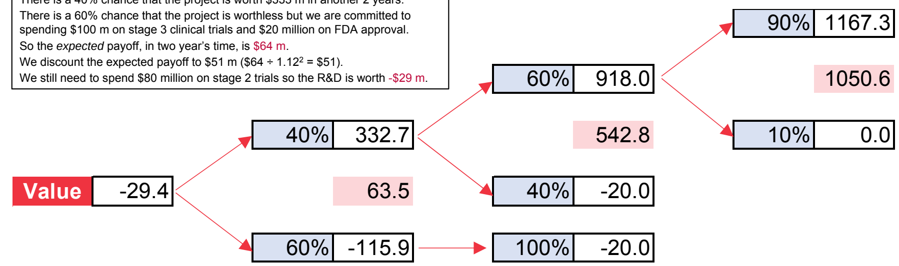
There is a 40% chance that the project is worth $333 m in another 2 years.

There is a 60% chance that the project is worthless but we are committed to spending $100 m on stage 3 clinical trials and $20 million on FDA approval.

So the *expected* payoff, in two year's time, is $64 m.

We discount the expected payoff to $51 m ($64 ÷ 1.12^2 = $51).

We still need to spend $80 million on stage 2 trials so the R&D is worth -$29 m.



Expected future payoff (a weighted average of the possible payoffs)

Odds of success and failure at each stage

Valuation at each stage after making the decision to either (a) invest in the next stage or (b) abandon

Valuation steps: Detail (2) – Valuation of R&D with options

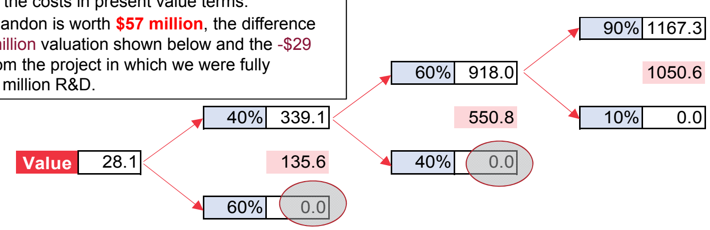
2. Value the project as if you were **not fully committed** to seeing the project to completion by working backwards
   a) Ask, what is the project value at the end of stage 3?
      i. Go to the final stage (FDA approval and insurance co. acceptance) and estimate payoffs for approval versus rejection
      ii. Compute the expected payoff (the weighted average of the possible payoffs)
      iii. Discount the expected payoff to the end of the stage 3 trials
      iv. Subtract the cost of seeking FDA approval and lobbying insurers
      v. **Ask, what is the maximum value associated with all possible options? In this case, seek FDA approval or abandon.**
   b) Ask, what is the project value at the end of stage 2?
      i. Go the end of stage 2 and estimate payoffs for success versus failure in stage 3
      ii. Compute the expected payoff from success or failure
      iii. Discount the expected payoff to the end of stage 2 trials
      iv. Subtract the cost of stage 3 clinical trials
      v. **Ask, what is the maximum value associated with all possible options? In this case, invest in stage 3 trials or abandon.**
   c) Ask, what is the project value at the end of stage 1?
      i. Go the end of stage 1 (today) and estimate payoffs for success versus failure in stage 2
      ii. Compute the expected payoff from success or failure
      iii. Discount the expected payoff to today
      iv. Subtract the cost of stage 2 clinical trials
      v. **Ask, what is the maximum value associated with all possible options? In this case, invest in stage 2 or abandon.**

What would be the value of the project **with options** if we do not account for risk reduction? **$28 million**

No longer committed to spending $200 million on trials, FDA approval and lobbying.

Only make incremental investments if the benefits of the spending outweigh the costs in present value terms.

So the option to abandon is worth **$57 million**, the difference between the $28 million valuation shown below and the -$29 million valuation from the project in which we were fully committed to $200 million R&D.



Expected future payoff (a weighted average of the possible payoffs)

Odds of success and failure at each stage

Valuation at each stage after making the decision to either (a) invest in the next stage or (b) abandon

Valuation steps: Detail (3) – Accounting for risk reduction

3. Account for **the lower risk of a project with options by using risk-neutral probabilities**

The R&D with the abandonment option is less risky than the equivalent project with full commitment. But we used the same 12% discount rate for both projects. We should reduce the discount rate to account for lower risk, but there are two problems.

- We don't know what the discount rate is for the lower risk project
- The risk changes throughout the tree, and so there is not one constant rate

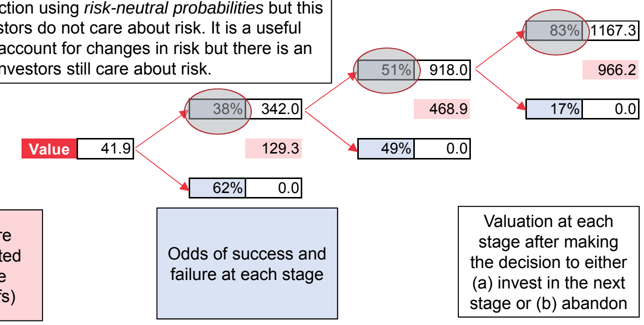
Thankfully, the clever researchers Black, Scholes and Merton worked out a way to address this problem and won a Nobel prize. The answer is to use risk-neutral probabilities and discount at the risk-free rate.

This approach does not mean we have assumed investors are risk neutral – they are still risk averse.

a) From the analysis of the project without options, estimate risk-neutral probabilities
b) For the project with options, repeat the analysis but use risk-neutral probabilities and discount at the risk-free rate of interest
c) For presentation purposes, show what discount rate would give the same valuation if we use the real-world probabilities in the analysis. The difference between the risk-adjusted discount rate used in step 1 and this computation of the discount rate provides the reader with a reference point for the risk reduction associated with options.

What would be the value of the project **with options** if we account for risk reduction? **$42 million**

The valuation is now **$42 million,** up from **$28 million,** because we have accounted for lower risk.
Compared to the project without options we have the same upside but less downside. So we have higher expected cash flows but also less risk.
We account for risk reduction using *risk-neutral probabilities* but this does not mean that investors do not care about risk. It is a useful computational device to account for changes in risk but there is an in-built assumption that investors still care about risk.



Summary

Decision-tree analysis: No change to discount rate to reflect risk reduction	
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