Art & Science Of biotech investing

Art and Science of biotech valuations

Valuation and financial modelling
is a qualitative and numerical assessment of
risks and potential rewards

- Each biological target, product and company has a unique set of risks and potential rewards.
- Despite the uniqueness of each molecular entity and company, it is possible to establish a general valuation process in biotechnology

Where is valuation important?

- Investing
- Financing
- Partnering
- Selling

Who invests in Biopharma?

- Angel investors
- Venture capital
- Institutional funds
- Retail investors

Investors establish valuations

The value of a company is the price the next investor is willing to pay

- Private company – price set by the VC willing to lead the next round
- Public company:

  Daily basis – set by the next trade

  Financing – set by the lead investor

Why would you buy shares of a company ?

Mature Healthcare

- Capital gains from an increase in share price
- Income from dividends and distribution

Biotechnology

- Capital gains from an increase in share price

Investors also want liquidity

Exit Strategy

- IPO
- Sale or Acquisition of the company

What impacts daily buying & selling?

- Valuation
- Liquidity
- Some institutions may only buy deals
- News flow
- Clinical events which can impact share prices
- Development partners
- Competitive products
- Broad market performance
- Sector preferences
- Rising resource commodity prices attract high risk money

Investors in mature companies pay for growth

- Investors in mature companies pay for growth from:
- An increase in sales of products or services; and / or an increase in profitability (earnings per share or eps); and / or
- An increase in dividends or distributions.

Biotech investors also pay for growth

- Share prices in development stage biotechnology companies should be impacted by clinical, regulatory and financial events
- Investors pay for:

  Reduced risk; and / or

  Increased potential reward.

Valuations by stock analysts

- How do stock analysts value a biotechnology company that is several years from product approval and profitability?

- Discounted earnings / cash flow
- Comparative valuation
- Event-based stock movement

Models

- Now,

  the easy part - number crunching

The basics

The components of financial modelling in increasing order of importance are:

- The Excel spreadsheet
- The assumptions for the spreadsheet
- What you do with the numbers

Valuation Tools – Analysing the numbers

- Net Present Value (NPV)

  The preferred valuation tool
- Risk-Adjusted NPV

  Risk adjustments can be done here or at the portfolio level
- Internal Rate of Return (IRR)

  Uses the same spreadsheet and assumptions
- Payback Period

  Very useful in manufacturing projects
- Monte Carlo Simulation

  A structured sensitivity analysis

Net Present Value (NPV)

- A project or product cash flow analysis that takes into account the fact that $1 received or spent in 2010 is worth more than $1 received or spent in the future
- NPV = C 0 + C 1 /(1+R1)1 + C 2 /(1+R)2+ … Cn /(1+R)n
- C = cash flow in the specified financial period
- R = cost of capital (risk free or risk adjusted)

NPV – $100 received in the future

- What is the value today of $100 received in future years (risk-free discount rate of 5%)?

YEAR	NPV
2010	$100.00
2013	$86.38
2018	$67.68
2023	$53.03
2028	$41.55

NPV – effect of risk-adjusted discount rates

- What is the value today of $1 billion received in 8 years using risk-adjusted discount rates?

RATE	NPV
10%	$466.5 M
15%	$326.9 M
20%	$232.6 M
25%	$167.8 M
30%	$122.6 M
35%	$90.6 M

Financial model utilization

These models are usually based on little information and many assumptions

- The quality of your financial model will depend upon the quality of your assumptions
- Better assumptions result from asking the right questions

Financial model utilization

- They are generally not useful for absolute valuations, unless they are based on historical sales data
- What can you do with the financial models?

  Compare NPVs for different deal structures for the same product

  Compare NPVs and risk profiles for different products

The hard part

- assessing risks and potential rewards

Risks & Rewards

- Only about 10% of the drugs which enter human clinical trials will eventually be approved
- The development of novel healthcare products is a high risk business

Risks & Rewards

- Neither pharma nor stock analysts are good at picking winners
- Risk cannot be eliminated
- Risk can be mitigated by larger companies through portfolio management
- Risks can be assessed

Risks & Rewards : A Balancing Act

- Assessment of risks is much more important at the earlier stages of the development process
- Assessment of potential rewards, based on product sales, becomes more important as the product progresses through clinical development
- The only justification for taking these high risks is the potential large reward from successful product development
- Risks and potential rewards change with time and must be continuously assessed and balanced

Risks & Rewards: Three Stage Process

- Approval Risks

  What are the risks which could impact the approval of this product?
- Market Potential

  What is the market potential for this product?
- Market Risks

  What are the risks which could impact the market potential for this product?

Approval Risks

- Financial
- Clinical
- Regulatory
- Reimbursement
- Scientific

Financial Risks

- Money has been, and is likely to remain, the scarcest asset for Australian Biopharma companies
- Funding must be continuously obtained from two primary sources
- Capital markets
- Partners
- Supplementary funding is also available from other sources Governments & Disease associations

Show me the money

- Australian Biopharma companies have historically been able to get sufficient funding from private and public capital market sources, although limited when compared to USA &EEC
- Liquidity was also available from periodic IPO windows. In this context, companies preferred to periodically get financing in the public markets and continue development without a partner as long as possible

Show me the money, PLEASE!

- The markets and financing strategies changed dramatically starting in the fall of 2007
- Financing was more difficult
- Valuations plummeted
- IPOs were almost impossible
- Companies have been forced to consider all strategic and financing options
- For many small biotechnology companies, the focus became survival

Critical Questions

- Does the company have the financial resources to get to the next critical value-creation event, with a little breathing room?
- If the answer is no, can the company obtain that financing?
- If the answer is yes, and the event is positive, can the company then obtain additional funding either from the capital markets or a partner?

Partnering

- Big pharma:
- Has cash and infrastructure
- Needs products

- Small biotech:
- Needs cash and infrastructure
- Has products
- Partnerships will continue to be signed

Risks: Partnering Deal Hurdles

Buyer's perspective:

- Buyers see thousands of opportunities every year
- Buyers are risk averse
- NIH (not invented here) syndrome by internal R&D teams
- Detailed due diligence is expensive
- Valuation and deal terms

Seller's perspective:

- Loss of control
- Valuation and deal terms

Regulatory Risks: The Critical Question

- The critical event prior to generating revenues from sales is regulatory approval.
- “Is there a pathway to regulatory approval?”
- The starting point in assessing regulatory risk is the end of the process.

Basic Approval Requirements

- Two adequately controlled phase III clinical studies which have been designed to prove the safety and efficacy of the new drug for a specific therapeutic indication
- A single trial maybe acceptable for certain diseases

Regulatory Approval Risks (1)

- Therapeutic indication
- Is this the first product which the agency will assess for this therapeutic indication? If yes, is there a scientific or medical consensus on how to assess the product?
- If there have been unsuccessful pivotal studies, was it the product, therapeutic indication, intended population or the clinical design?
- Is the proposed indication a new monotherapy, an adjuvant to the current therapy or a rescue therapy to be used only when there is no response to current therapies?

Regulatory Approval Risks (2)

- Clinical Design
- Are there any differences in clinical design for this new entity versus clinical trials conducted for approved products?
- Are there any differences in clinical design for the Phase 3 study and the preceding Phase 2 study?
- If there are differences, what are the justifications for these changes?

Regulatory Approval Risks (3)

- Standard of Care
- Is there a single FDA-approved standard of care for the chosen therapeutic indication?
- Is there more than one FDA-approved standard of care for the chosen therapeutic indication?
- If there is not an FDA-approved standard of care, is there a standard of care accepted or approved by the relevant medical specialists?
- Are there products currently under regulatory review or in pivotal trials which, if approved, would result in a new standard of care?

Regulatory Approval Risks (4)

- Primary clinical endpoint
- Is there a clinical endpoint accepted by the FDA for proving efficacy in this therapeutic indication?
- If not, are there clinical endpoints accepted or approved by the relevant medical colleges?
- Are there any difficulties in attaining or interpreting these endpoints?
- Is the primary clinical objective a superior safety profile and non-inferior efficacy?

Regulatory Approval Risks (5)

- Statistical analysis
- What are the statistical assumptions used in the design of the clinical trial?
- How are patient trial withdrawals registered?
- Is there any history of accentuated placebo effects in this type of clinical trial?

Regulatory Approval Risks (6)

- Statistical versus clinical significance
- A result can be statistically significant but the clinical benefit can be so small that it may not be clinically significant
- For example, is a statistically significant 2-week increase in survival also clinically significant when survival on the current standard of care is about 6 months?
- This result may previously have only impacted potential sales but clinical significance is now being discussed at FDA advisory committee meetings

Regulatory Approval Risks (7)

- Safety profile
- The safety hurdle has been raised at the FDA
- The safety concern is highest for drugs which are intended for chronic use and for drugs to treat patients with medical conditions which are not immediately life-threatening but chronic

Manufacturing Approval Risk (1)

- Manufacturing is a critical regulatory component. The manufacturing process has to meet GMPs, The facility has to meet GMPs and be inspected
- Companies may face the following situation, If the process or facility used for Phase 3 / approval is not commercially viable, changes need to be made before significant sales can be developed.
- However, the cost of getting to a commercially viable process and facility prior to Phase 3 can require substantial scarce resources before knowing whether the product can be approved

Manufacturing Approval Risk (2)

- GMP processes must be reproducible and validated
- Chemical synthesis of small molecules is usually not a problem
- Isolation of natural products from a biomass can usually be controlled
- Recombinant manufacturing of proteins is complicated but controllable
- Upstream production
- Downstream purification
- Finished dosage form

Manufacturing Approval Risk (3)

- Manufacturing facilities are expensive
- Small molecules
- API – contract manufacturing
- Finished dose – contract manufacturing
- Biologics
- Capital cost of fermentation or cell culture facilities is enormous
- Contract manufacturing is available
- Changes in manufacturing scale and facilities can change the clinical activity of a biologic

Scientific Risk

- If the answers to the following five questions are yes, there is probably an acceptable level of scientific risk.
- Do we know how the drug works?
- Do we know what causes the disease and how the disease progresses?
- Is the drug's target a key factor in disease progression?
- Are the animal models predictive of human results?
- Does the preclinical data show that the drug is as effective as or superior to currently approved drugs or drugs currently in clinical development?

Manufacturing costs

- COGS (cost of goods sold) are an important component of due diligence conducted by potential partners and investors
- Rough guideline for COGS at commercial scale:
- COGS for biologics should be less than 10% of the selling price and preferably below 5%
- COGS for small molecule products should be less than 5% of the selling price and preferably less than 2%

Market Potential: Two Approaches

- There are two basic approaches to estimating the market potential for a new product
- The starting point for one approach is the number of patients with the medical condition, which is further refined by considering factors such as the number who are diagnosed, the number who are treated, success of current therapies and disease progression
- The starting point for another approach is the sales of drugs currently used to treat patients with this specific or similar medical conditions

Market Risks

- Approval Timing: First-In-Class
- Clinical Data: Best-In-Class
- Competition
- Reimbursement
- Patents

Market Risks: First-In-Class

- Where several new drugs are structurally related, have the same biological target and similar safety and efficacy profiles, first-in-class (first approved) should have a market advantage
- If the new drug is going to be a second or later market entrant, how is it going to take market share?

Market Risks: Best-In-Class

- Where several new drugs are structurally related and have the same biological target, best-in-class (superior safety and/or efficacy) would become the class sales leader even when it is not first-in-class
- If a new drug is not going to be best-in-class and it will reach the market after the superior product, should product development be terminated?

Market Risks: Three Levels of Competition

- There are three levels of competition:
- Currently approved drugs
- Drug candidates at the same stage of development
- Drug candidates at an earlier stage of development

Competition: Currently Approved Drugs (1)

- Currently approved drugs are competition only if the new drug is attempting to replace one of the currently approved drugs
- Currently approved drugs are not competition if the new drug is going to be used in combination with the currently approved drugs or will be used only after the currently approved drugs no longer provide the desired clinical benefit

Competition: Drug Candidates (2)

- Drug candidates at a similar stage of development can be categorized and the competitive threat assessed with respect to:
- The biological target
- Drug of the same chemical class, different chemical class or biologic
- Comparative safety and efficacy in similar clinical trials
- Drug candidates at an earlier stage of development are less important from a risk perspective but their development should be monitored
- Clinical trial patient recruitment competition

Market Risks: Reimbursement

- Obtaining reimbursement for new drugs and medical procedures used to be a simple case of submitting paperwork
- The pharmaceutical industry is fighting constantly to prevent restrictive formularies and comparative therapeutic testing
- Launching new medical devises and diagnostics is much easier if the new products can be covered by existing payment codes

Market Exclusivity: Patents

- The basic patent life is 20 years from date of filing. Patent life extension is available in the U.S. To account for regulatory delays and compensate for pediatric testing
- Data exclusivity now provides periods of exclusivity during which a generic product submission cannot be filed or approved if it relies in any way on the regulatory filings of the originator product

Patent Risks: Critical Questions

- Are there issued or filed patents which will provide a period of market exclusivity?
- Would the product infringe on other patents (freedom-to-operate)?
- Assuming product approval in year 20xy, how much market exclusivity is provided by both patents, patent extensions and data exclusivity?

Conclusion

- Valuation and financial modelling is qualitative and numerical assessment of risks and potential rewards
- Anybody can crunch the numbers
- Better assumptions lead to better numbers
- Better assumptions come from asking the right questions

iQnovate

- iQnovate asks the right questions
- validates the answers
- provides insight on expediting the time to market
- Prices the clinical development strategy
- Maps out the RRC strategy (registration-reimbursement-commercialization)
- iQnovate can work with your team to help you make an informed investment decision