

# Pharma & Biotech

Development & Valuation

# Introduction

Corporate investment and venture funding continues to play a pivotal role in the development of novel medical innovation -- from new pharmaceutical therapies to revolutionary medical devices. These innovations impact every American through improved patient outcomes.

The purpose of this study is to provide corporate finance professionals, managers, and investors, an overview of valuation fundamentals employed in today's pharmaceutical and biotech communities. These findings are relevant to understanding the values assigned by parties in negotiations for the acquisition or licensing of drug development programs and the approach in determining value.

The information presented in this report has been gathered with the utmost care from sources believed to be reliable, but is not guaranteed. This analysis has been prepared and is based on information available to it, including information derived from public sources that have not been independently verified.

This study was prepared by Tom Bird, an independent healthcare analyst. If you would like more information or would like to comment, please contact the author.



Gryphon Analytics

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# Executive Summary

Determining the monetary value of developmental pharma and biotech assets is vital to internal research prioritization, investor funding decisions, business development negotiations and equity analysis.

Complex science, long development times, the high risk of technical failure and changing regulatory and market conditions pose considerable challenges in forecasting cash flows and determining relative values of a drug development project.

A range of methods, each with differing computational complexities and limitations, can be used to determine the value of an individual drug, and as such, a pipeline as a whole. However, as market conditions evolve and uncertainties change – the precision of such valuation models are impacted.

This study examines:

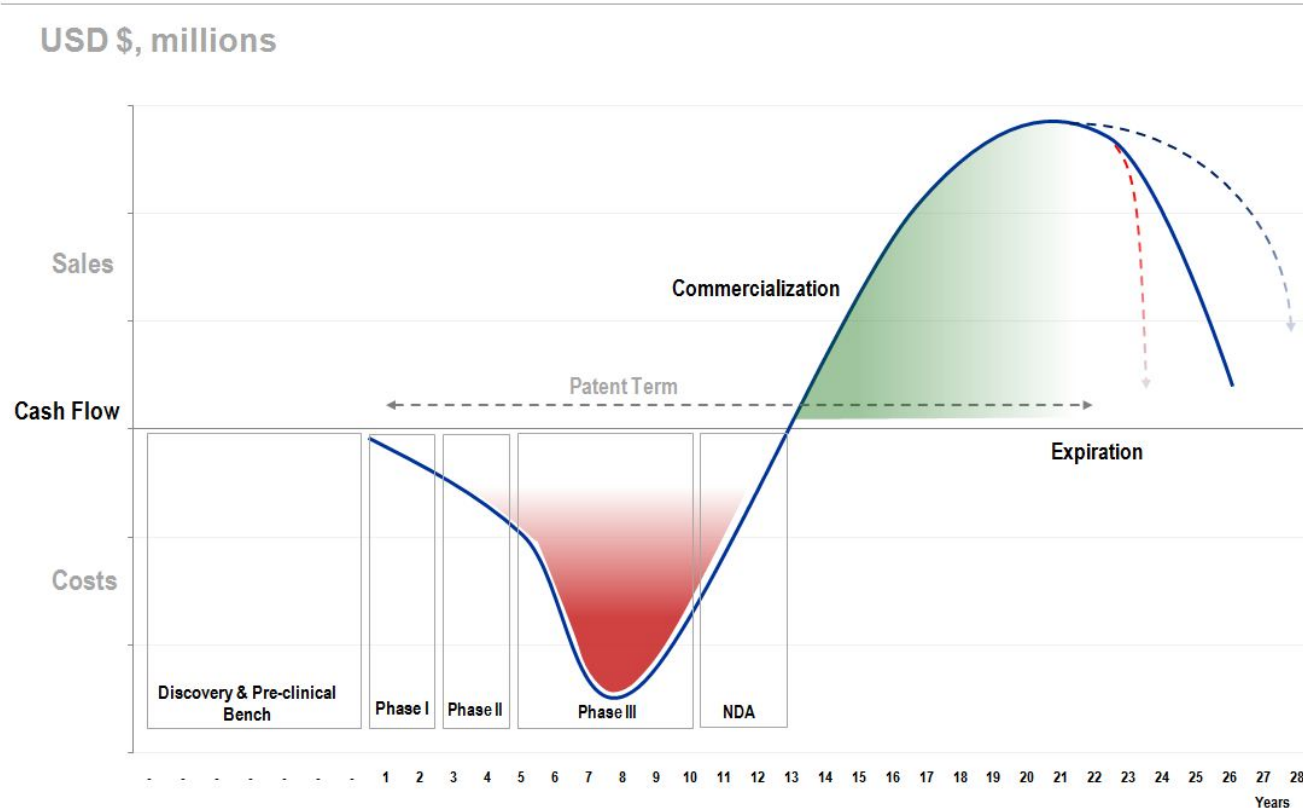
- General trends in the current pharma / biotech development process,
- Methods used to value drug development projects,
- The key challenges and limitations of each respective methodology; and
- Differences in how these methods are applied by various market participants.

# Drug Development Process



# Pharma & Biotech J-Curve

- The following diagram illustrates the typical pharma / biotech development profile



## Expiration Factors

- Generic competition can degrade 80% of sales over a period of weeks; alternatively
- A drug may operate in a niche category that is too small, or with a brand presence too strong, to attract competition on patent expiry
- A drug may be too complex to produce, particularly where the manufacturing processes are also protected; or
- In the case of competition from follow-on biologics, the current lack of clarity on regulatory requirements (especially in the US) poses a key challenge to new competitive entrants.

# Pharma Development Trends

Over the next five years, a broad range of pharmaceutical products are expected to drive industry revenue growth. Analysis of the 50 largest growth drivers – those products expected to deliver the most revenue expansion between 2013 and 2018 – provides a timely snapshot as to how manufacturers are hoping to both overcome the patent cliff and negotiate an increasingly complex global pharmaceutical market.

Today there are 5,000 medicines in clinical trials globally

The 15 largest growing products are expected to deliver over 50% in revenue expansion, with 5 products set to contribute an absolute increase in sales in excess of \$3 billion by 2017.

**The pharma industry's 50 largest growth products are expected to increase absolute sales by approximately \$80 billion.**

# Development – Top 50 Growth Products Gryphon Analytics

In 2012, oncology accounted for 13 products – or 26% of the 50 largest growth drivers. Combined, these drugs are expected to deliver absolute revenue growth of approximately \$18 billion over the next five years.

The rapidly growing market for diabetes therapies will account for 8 key growth driver products over the next 5 years, which are forecast by analysts to deliver combined absolute sales growth of around \$13 billion.

Immunology and inflammation disease products are forecast to deliver absolute annual sales growth of around \$9 billion by 2017.

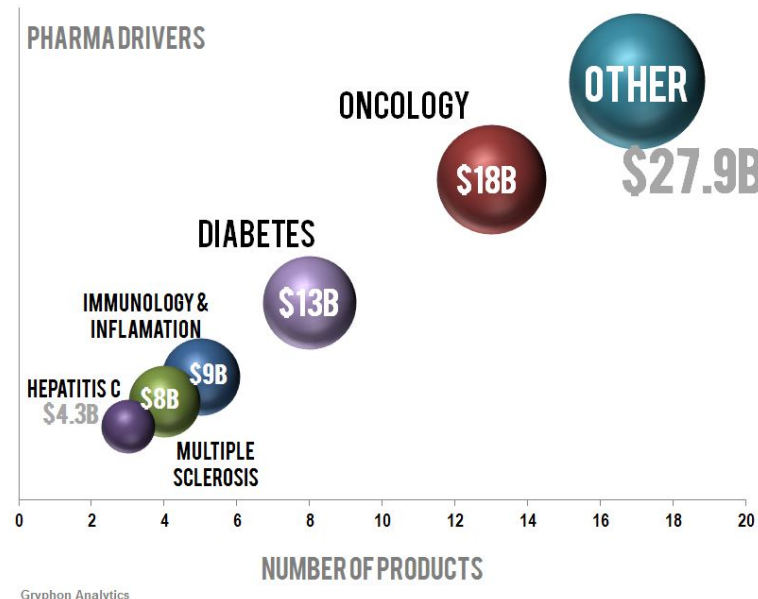
## Small Molecules

31 of the top 50 identified products in are small molecules and together are forecast to deliver combined absolute sales growth of \$50 billion (an average of \$1.6 billion per product).

## Biologics

There are 17 biologic products identified as key industry growth drivers with combined absolute annual sales growth of \$26.8 billion (averaging \$1.6 billion per product).

- within the biologic classification, 11 of the 50 products are monoclonal antibodies (combined absolute annual growth of \$19.3 billion, average growth of \$2.4 billion)
- with the remainder classed as therapeutic proteins (growth of \$7.5 billion, average growth of \$1.3 billion).



# Drug Valuation Methodologies

While numerous valuation methods exist, in practice industry participants most frequently rely on two common valuation methods:

- i) Comparable analysis and
- ii) Cash flow-based risk-adjusted net present value (rNPV).

Additionally, analysts possess alternative methodologies in weighing drug development, including:

- Monte Carlo Simulation and
- decision-tree analysis

This study examines a number of leading valuation methods:

- Comparable Pharma Analysis
- Quantitative Modeling: NPV & Risk-Adjusted NPV
- Monte Carlo Simulation



# Comparable Analysis

# Comparable Analysis

Comparable pharma analysis operates under the premise that similar drugs will possess similar values, respective of shared characteristics such as:

- i) remaining development costs,
- ii) stage of development,
- iii) market opportunity, and
- iv) likelihood of regulatory approval / commercialization, etc.

By using similar pharma comps, managers are enabled to determine value benchmarks and ranges.

In developing a project peer group, precision must be applied in assessing: stage of development, market size, growth characteristics, the novelty of the science, regulatory outlook, etc.

## **Limitations:**

- The primary shortcoming of relying on comparable analysis is the difficulty in identifying a large enough sized pool of suitable comps.
- Many transactions are undisclosed and limit full understanding of early stage and private deals.

It is important to note, pharma buyers commonly dismiss drug prices solely based on comparable analysis – as they simply would not have paid the same price and financial value is subjective.

Comparable analysis is less relevant in early-stage valuation,  
however it becomes increasingly important to late stage bidding / pricing.

# NPV & Risk-Adjusted NPV

# NPV Overview

Net Present Value compares the value of a dollar today to the value of that same dollar in the future, taking inflation and returns into account. If the NPV of a prospective project is positive, it should be accepted. In turn, if NPV is negative, the project should probably be rejected because cash flows will also be negative.

NPV when applied to a drug development project involves forecasting cash flows by projecting the cost of development and the revenues from commercialization. These cash flows are then discounted in accordance with finance theory to derive a net present value of the drug development project.

# NPV Mechanics Revisited

In calculating net present value, projected cash flows are discounted for time by multiplying by  $(1+k)^{-n}$ , where **k** is the discount rate and **n** is the number of years in the future the cash flow is projected to be realized.

Computationally, a lower discount rate yields a higher valuation, as such counterparties are likely to possess opposing views related to a suitable discount rate.

- As an example, market surveys suggest large in-licensors tend to use discount rates that are ~2% lower than those used by pre-commercial development companies.

NPV calculation illustrated:

Cash Flow												
Discount Rate	12.0%	(\$1,568.0)	\$428.4	\$553.4	\$580.1	\$587.3	\$589.1	\$578.3	\$276.7	\$153.5	\$53.6	\$17.9
Discount Period		-	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0
Discount Factor		1.00	0.89	0.80	0.71	0.64	0.57	0.51	0.45	0.40	0.36	0.32
Discounted Cash Flow		(1,568.0)	382.5	441.1	412.9	373.2	334.2	293.0	125.2	62.0	19.3	5.7
Example NPV		\$881.2										

$$NPV = -Principal + \sum_{i=1}^n \frac{payment_i}{(1 + rate)^i}$$

NPV is simply the summation of all cash Flows discounted to the present

viii) "An Introduction to Valuation," Aswath Damodaran, NYU Stern, 2012  
ix) "Discounted Cash Flow Valuation," Aswath Damodaran, NYU Stern

# Forecasting Cash Flows: Costs

Accurately forecasting the long-term commercialization of new pharma & life science products is an extraordinary challenge which involves a myriad of discrete assumptions.

## Development Costs

### Pre-clinical Development Costs

- Assessing pre-clinical costs for a specific development project is difficult as pre-clinical costs are usually incurred as part of broader R&D that involves multiple projects.
- Specific costs include: basic research, discovery, testing in assays, and testing in animal models.

### Clinical Development Costs

- Clinical development costs will vary wildly depending on therapeutic areas, with increased costs associated with chronic and degenerative diseases.
  - In addition to the varied scope and complexity of clinical trials, costs are driven by the number of patients needed for trials, the treatment costs per patient (e.g. outpatient versus intensive care treatment, cost of diagnostic procedures and co-medications, durations of treatment and requirements of follow-up) and the length of the clinical trial.
  - Specific costs include: trial design, patient recruitment, investigator and clinician costs, monitoring costs, data analysis, close-out and reporting results, actual clinical trial administration, and animal testing during the clinical period.

# Costs (contd)

## Regulatory Review Costs

- The costs of regulatory approval are dependent on the market, with most drugs at least aiming for approval in the major territories (United States, Japan and certain Europe countries).
- The specific costs of preparing submissions in connection with regulatory approvals will vary depending on the amount and quality of data.

## Manufacturing Costs

- Specific costs include: contract manufacturing, facilities, raw materials, equipment, personnel, processing, documentation, and on-going compliance.

## Launch, Marketing & Sales Costs

- Initial launch and marketing costs are usually projected utilizing conventional assumptions (e.g. the marketing expenses for year 1, 100% of the revenues, the marketing expenses for year 2, 50% of the revenues etc).
  - Generally, hospital products possess lower marketing/sales costs compared to products promoted to specialists or primary physicians.

# Forecasting Cash Flows: Revenue

Market opportunity and launch potential are frequently assessed via top-down and bottom-up analyses.

## *Top-down*

- Projecting the eventual revenues of a drug candidate once developed, involves determining the size of the target market, market share likely to be attained, and subsequent growth

## *Bottom-Up*

- Alternatively, a bottom-up approach focuses on the number of patients and estimates sales by evaluating the following parameters:

$\text{sales} = \text{number of patients} \times \text{market share} \times \text{monthly drug price} \times \text{months of treatment}$

## **Market Share**

Swing factors defining a new product's ability to gain share include:

- clinical evidence of improved efficacy and safety,
- competition from available treatments and products (as well as those in development),
- relative advantages compared with current treatments (i.e. pricing / benefit analysis),
- dosage and formulation of the candidate; and
- patient/physician product loyalty.



# Revenue (contd)

## Price Premium

- Novel products and/or higher efficacy tied to improved patient outcomes warrant a price premium.
  - However, this will be moderated by the number of patients / physicians who are willing to switch to a more expensive product.

## Exclusivity & Generics

- During the forecast period products will eventually lose patent protection and become subject to competition from generics.
- Pricing regulations, policies and defensive strategies to retain market share should be considered when projecting revenue related to cash flow analysis.

Accurately forecasting the long-term commercialization of new pharma & life science products is dependent on numerous critical inputs.

# Risk-Adjusted NPV - rNPV

***As an extension of NPV, Risk-Adjusted NPV (rNPV) is a common valuation tool in the life sciences industry.***

rNPV is different from NPV as it considers the of risk and the likelihood of cash flows.

- NPV accounts for all risk by the discount rate, while rNPV includes attrition risk by multiplying the cash flows with their probability before discounting them – while using a different discount rate than NPV.

The path of developmental drug projects is highly regulated and generally follows a common progression - projects go through specifically defined phases. As such, statistical analyses can be applied to determine which phases account for corresponding percentages of failure.

- These statistical results are referred to as attrition rates and often a bit loosely as success rates.

These success rates quantify the risk of drug development projects depending on their stage, type of molecule, and disease area. The success rates, while based on historical data, enable a more specific comparison of risk amongst different projects.

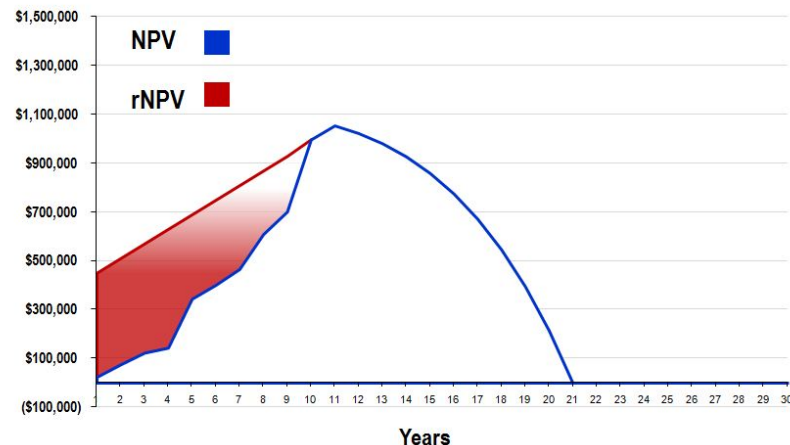
# rNPV Attrition

## Applied Attrition Rates

If a drug candidate is in a phase II trial, there is ~45% probability of reaching the subsequent phase III. If the phase II trial fails, the projected investment needed to fund phase III trials will never be spent.

- In the above example, the costs of phase III trials — and all of the future revenue and costs — should be adjusted down by approximately 45% in rNPV.

Comparison of Discounted Cash Flows



Gryphon Analytics

Importantly, risk estimates should be based on data from the relevant therapeutic area. Success rates amongst therapeutic classes vary considerably. As an example oncology possesses lower clinical success rates than do other areas (eg anti-infectives).

It is understood that in the rNPV method, all cash flows get adjusted by the probability that they occur. As such, a large portion of the risk is already included in this risk-adjustment.

- Consequently, the discount rate used in rNPV will be lower than that used in NPV.

xi) Jefferey Steward, Peter Allison, Ronald Johnson, "Putting a price on biotechnology," Nature Biotechnology 813-817, (Sep 2011)

# NPV Discount Rates

In cash flow valuation methods, the discount rate takes into account the time value of money and the risk or uncertainty of the anticipated future cash flows.

Historically, the discount rate used is often determined from a Capital Assets Pricing Model (CAPM) or Weighted Average Cost of Capital (WACC) whereby a premium is added to the risk free interest rate related to financial instruments with very low, or non existent financial risk; eg the 10 year government bond rate.

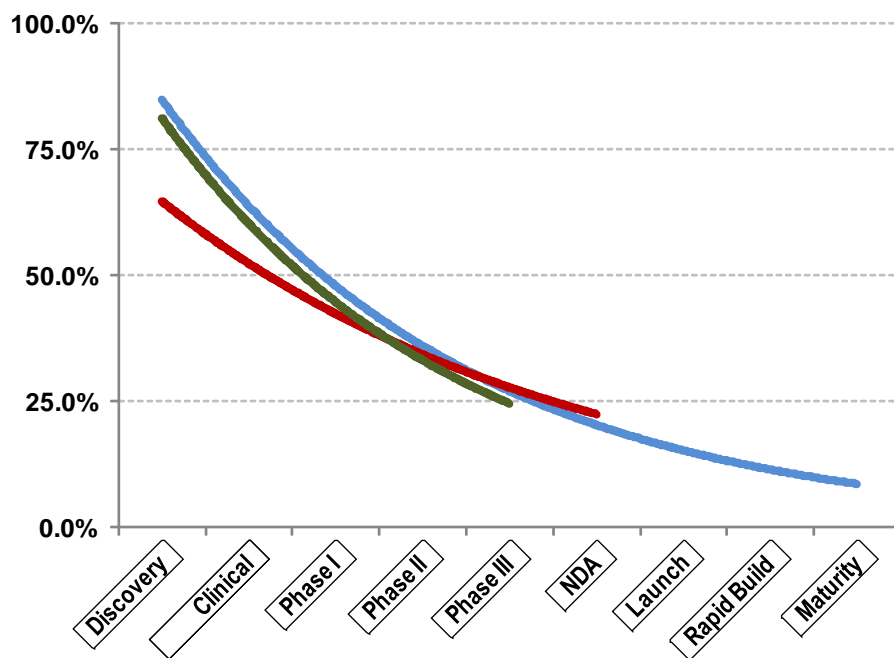
Over the years, this method of risk adjusting has become distorted as the NPV technique has become a tool of adjusting for both risk and time.

However, when ambiguous technical, scientific, market, or regulatory risk exists, corporate finance professionals commonly apply higher rates as a means to compensate for uncertainty. As a consequence, higher risk, long-term R&D projects have become unfairly disadvantaged.

# Discount Rates

The following table illustrates leading research in identifying appropriate discount rates through the separate stages of development.

Discount Rates



Stage of Development

	Proposed Stage Specific Discount Rates		
	Hambrecht & Quist	Lehman Brothers	Frei/Leleux
Discovery	80.0%	>60%	70%-100
Pre-Clinical	60.0%	>50%	50%-70%
Phase I	50.0%	45.0%	40.0%
Phase II	40.0%	40.0%	35.0%
Phase III	25.0%	30.0%	25.0%
NDA	22.5%	18%-20%	NA
Launch	17.5% - 15.0%	NA	NA
Rapid Build	12.5% - 10.0%	NA	NA
Maturity	7.5%	NA	NA

# rNPV Illustrated

The following chart illustrates the risk adjusted cash flows related to rNPV valuation

## Illustrated rNPV

USD \$, millions

Year	Projection Period										
	0	1	2	3	4	5	6	7	8	9	10
<b>Revenue</b>											
Projected Sales	-	\$1,200.0	\$1,550.0	\$1,625.0	\$1,645.0	\$1,650.0	\$1,620.0	\$775.0	\$430.0	\$150.0	\$50.0
<b>Expenses</b>											
Discovery & Pre-Clinical	\$564.0	-	-	-	-	-	-	-	-	-	-
Phase I & II	273.0	-	-	-	-	-	-	-	-	-	-
Phase III	633.0	-	-	-	-	-	-	-	-	-	-
Regulatory Fees	48.0	-	-	-	-	-	-	-	-	-	-
G&A	10.0	280.8	362.7	380.3	384.9	386.1	379.1	181.4	100.6	35.1	11.7
Manufacturing	5.0	259.2	334.8	351.0	355.3	356.4	349.9	167.4	92.9	32.4	10.8
Marketing & Sales	35.0	231.6	299.2	313.6	317.5	318.5	312.7	149.6	83.0	29.0	9.7
Total Expenses	1,568.0	771.6	996.7	1,044.9	1,057.7	1,061.0	1,041.7	498.3	276.5	96.5	32.2
<b>Net Cash Flow</b>	<b>(\$1,568.0)</b>	<b>\$428.4</b>	<b>\$553.4</b>	<b>\$580.1</b>	<b>\$587.3</b>	<b>\$589.1</b>	<b>\$578.3</b>	<b>\$276.7</b>	<b>\$153.5</b>	<b>\$53.6</b>	<b>\$17.9</b>
		35.7%	35.7%	35.7%	35.7%	35.7%	35.7%	35.7%	35.7%	35.7%	35.7%

### Cash Flow

Discount Rate	12.0%	(\$1,568.0)	\$428.4	\$553.4	\$580.1	\$587.3	\$589.1	\$578.3	\$276.7	\$153.5	\$53.6	\$17.9
Discount Period	-	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0	
Discount Factor	1.00	0.89	0.80	0.71	0.64	0.57	0.51	0.45	0.40	0.36	0.32	
Discounted Cash Flow		(1,568.0)	382.5	441.1	412.9	373.2	334.2	293.0	125.2	62.0	19.3	5.7

**Example NPV** **\$881.2**

### rNPV

rNPV Attrition Rate	100.0%	65.0%	70.0%	75.0%	85.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
<b>Risk-added Cash Flow</b>	(1,568.0)	278.5	387.3	435.1	499.2	589.1	578.3	276.7	153.5	53.6	17.9	
Discount Rate	6.9%											
Discount Period	-	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0	
Discount Factor	1.00	0.94	0.88	0.82	0.77	0.72	0.67	0.63	0.59	0.55	0.51	
Discounted Cash Flow	(1,568.0)	260.5	338.9	356.2	382.2	421.9	387.5	173.4	90.0	29.4	9.2	
<b>rNPV</b>												<b>\$881.2</b>

# NPV & rNPV Considerations

As previously discussed, the accuracy of NPV valuation is dependent on the quality of the assumptions regarding free cash flow, terminal value, and the discount rate.

In consideration volatility and the reliance on base assumptions:

- NPV valuations are usually expressed as a range of values rather than a single value.
- It is also common to run the NPV analysis for different scenarios, such as a base case, an optimistic case, and a pessimistic case to gauge sensitivity to various operating assumptions.

## Terminal Value

The terminal value often represents a large percentage of the total DCF valuation. In such cases, value is largely dependent on terminal value assumptions rather than operating assumptions for the business or the asset.

- Drug projections commonly eliminate the use of a terminal value by extending the forecast period.

While NPV / rNPV remain the most accepted valuation methods, corporate finance professionals should be reminded of its limitations, including:

- Cash flow analysis generally only starts at the beginning of Phase I— as such NPV excludes the true sum of time and investment.
- If only a single-valued answer is provided, managers can only make decisions whether to accept or decline a project – NPV omits scenario analysis or decision tree functionality

While the inputs come from a variety of sources, they must be evaluated objectively in the aggregate before finalizing the NPV valuation.

# Monte Carlo Simulation



# Monte Carlo Simulation

Monte Carlo simulation is a statistical valuation technique of randomly selecting numbers based on probabilities of distribution.

Monte Carlo simulates adjustments to multiple variables (e.g. market size, expenditures, pricing and time to market) to produce an overall distribution of possible outcomes. This is achieved by defining the statistical probability distribution of each variable. Software simulation is then used to repeatedly sample values from the probability distributions of each input. Each simulation generates a single NPV estimate. The end result of the repeated simulation is a range of possible NPVs and their respective probabilities of occurrence.

This provides an assessment of the risk associated with a set of decisions that analytical methods generally cannot capture.

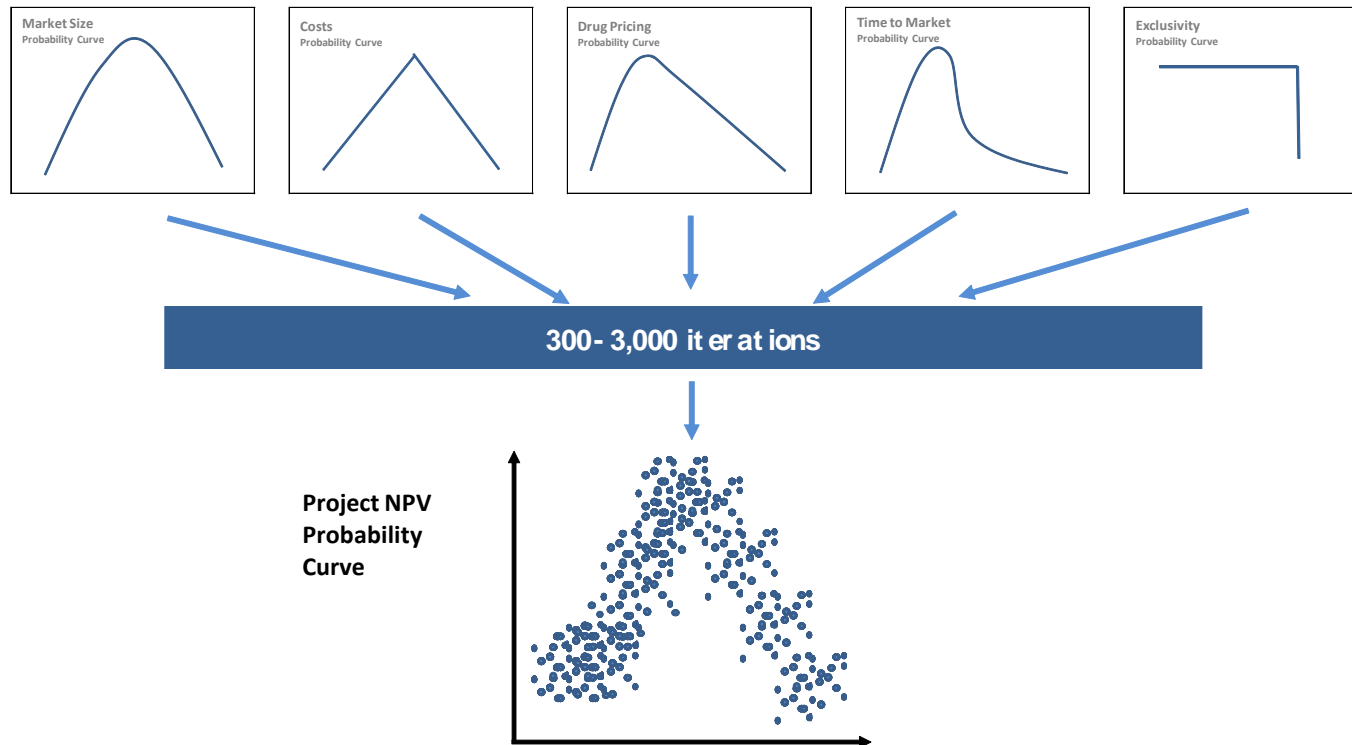
## *Limitations*

- A Monte Carlo simulation value depends on the choices of scenarios and the associated probabilities of occurrence – while useful for identifying a range of values for a project – it still does not yield a more reliable single value.

If the distribution of probabilities is available to managers - they possess competitive advantages in determining whether to accept a project and can more accurately compare projects while adjusting for individual forecast variables.

# Monte Carlo Simulation

Instead of just a single value estimate, Monte Carlo produces a range of values and the probability that different value levels will occur.



# Application

# Application – early Stage

## A Venture Capitalists Perspective

While risk adjusted NPV remains the predominant tool used to value drug development projects, the values yielded for early-stage projects have long been considered unreliable because of the high level of guess-work involved in forecasting early-stage cash flows.

During these early phases, forecasting cash flows remain dependent on incomplete information, guess-work and challenging risk assessment. As such, venture capitalists generally rely less on NPV modeling when valuing early-stage projects.

Venture capitalists instead focus on “business plan” type factors and what the potential value will be to an acquirer.

This fundamentally different approach weighs:

- i. Qualitative business plan factors – science novelty, drug segment, market size, management team, clinical issues, and regulatory hurdles,
- ii. Remaining costs & time to develop the candidate; and
- iii. Exit Strategy & horizon - potential exit value, likelihood, and complementary fit within portfolios
  - A key opportunity lies in positioning the drug with other products and technologies that are compatible.

Venture capitalist will rely less on cash flow based modeling techniques

# Application - Late Stage

## Equity Markets

Corporate finance professionals and investment banking firms generally rely on values derived from NPV modeling, however practice a bias towards later stage projects.

- As a consequence, analysts overweigh late stage value by focusing on the impact of near-term candidate launches and their immediate commercialization.

## Strategic Buyers

Conversely, if an early stage project is of strategic interest to an acquirer - then the acquirer will place a positive value on the project for which equity analysts may have given no value.

There remains a fundamental disconnect between early-stage and late-stage valuation.

Equity analysts frequently excessively discount pharma pipelines by assigning nominal credit to early stage development projects - Overlooking Trillions of Value

The value derived through cash flow modeling assumes that a developmental project possesses an intrinsic value; while in practice, most deal values are basically determined on the basis of which buyer wants/needs the asset more.

Key sources of value discrepancy continues to depend on qualitative factors and subjective criteria specific to each prospective investor/buyer/owner.

- Additionally bidders must not overlook the incalculable impact of non-intrinsic pricing inputs, such as dissimilar negotiating leverage.

Pharma Participants: For a pharma buyer, key factors include strategic factors (e.g. whether the project fills an important strategic gap in a product portfolio) and the synergies that a buyer can exploit (e.g. whether the buyer can leverage its existing sales force to market the new product).

- Additionally, pharma buyers heavily weigh pending expirations and the patent cliff.

Venture Capitalists: Factors relevant to determining what the project will be worth to venture investors focus on prospects of exit, funding requirements, and the general climate of capital markets.

Subjective and qualitative factors, distinct to the buyer, continue to drive real values.

# Conclusion

A myriad of valuation methods maybe used in determining the worth of pharma / biotech assets - the correct solution will likely be a composite largely influenced by the stage of development.

Fundamentally, pharma development entities possess pricing leverage over other investors, as they benefit from access to additional information related to discrete development costs, risks and internal development tendencies.

- Discontinued pharma projects are not widely reported, as such, pharma companies may hold additional information regarding the success rates and timing.

While pharma and biotech assets possess intrinsic value, a firm's ability to develop and maximize value will be unique, as such, market pricing and valuation remains dependent on a mix of both quantitative and qualitative factors.

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