Valuation of Biotech & Pharmaceutical Companies

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Biotech Therapeutics & Pharmaceuticals Sector

- U.S. spending on drugs $344 billion in 2018, of which $271 billion for branded products and $73 billion on generics
- > 700 public companies with market capitalization of $3.6 trillion
- > 40 IPOs in 2019
- > 3,500 private and public companies in the U.S.
- $17 billion in venture capital investments in 2019 with > 900 deals

Drug Development Process

Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6	Stage 7
Target Identification & Validation	Preclinical Development	IND Application	Clinical Trials	NDA Application	FDA Review	Post-Approval Studies
	<--- 3 to 5 years --->		Phase I Phase II Phase III Can be combined sometimes <------ 5 to 10 years ------>		1 to 2 years	Sometimes required

Median drug development cost estimated at $985 million (2007-2018)

Drug Development Success Probabilities

- The expected probability of developing a product from a Preclinical stage all the way through FDA approval is typically less than 10%
- Probabilities can vary significantly between different therapeutic (disease) areas
- Biologic (large molecule) products have higher success rates than traditional (small molecule) products
- Products aimed at rare diseases have higher success rates than those for chronic, common diseases

Example Drug Development Success Probabilities:

Stage	Success Probability	Compounded Probability
Preclinical	69%	69.0%
Phase I	60%	41.4%
Phase II	36%	14.9%
Phase III	62%	9.2%
FDA Approval	89%	8.2%

(average for all therapeutic areas based on 2 studies)

Intellectual Property & Marketing Exclusivity

- FDA provides exclusive marketing rights of 5 years for a “New Chemical Entity” (a drug that contains no active moiety that has been previously approved)
- Drugs for rare diseases classified as an “Orphan Drug” receive exclusive marketing rights for 7 years
- Exclusive marketing rights can extend beyond patent protection (20 years from filing date) and where patents have expired
- Successive patents can apply to a product which extend exclusivity period
- For some biologic products a natural monopoly can continue even after exclusivity ends due to difficulties in developing generic products, but potential alternative therapies need to be considered

Drug Market Size Estimation Considerations

- Prevalence (e.g. diabetes) or incidence (e.g. heart attacks) rate for a therapy
- Not all individuals with a therapy need may be aware of it
- Some individuals may not be able to afford a therapy or follow prescriptions
- Rare diseases can allow for very high pricing (>$100,000/year)
- Biologic products generally priced higher than small molecule products
- Pharmaceutical list prices do not reflect real pricing since rebates are often used
- Price assumptions generally based on estimated real prices for similar or competing products
- After end of product exclusivity a significant price or market share decline can often be assumed

Challenges in Valuing Biotech & Pharma Companies

- Companies may not have any revenues, or revenues may consist only of service revenues or research grants, and typically have negative cash flow
- Time to reach positive cash flow may be more than 10 years
- Projected cash flows are uncertain because probability of a product reaching the market can be very low
- Need to raise capital over many years can mean significant dilution effects which are difficult to incorporate in analysis
- Public comparables often do not have material revenues or positive earnings
- Royalty and milestone payment data availability is limited

rNPV (risk-adjusted Net Present Value) Analysis

- With rNPV analysis the expected future cash flows are calculated by first estimating the future cash flows without risk and then applying a probability to that cash flow
- If typical pharmaceutical development probabilities are applied the compound probability from Phase I to product approval will be ~12%
- Future net cash flows from a marketed product would be multiplied by this percentage to arrive at an expected net cash flow
- Cash flows are typically discounted to present value using an industry-based cost of capital representative of systematic risk (i.e. no company specific risk factor)

rNPV Analysis Example

rNPV Analysis Example															
(in $000)															
Stage	Phase 1	Phase 2	Phase 3		NDA	Marketing									
Year	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Projected Net Cash Flow	($10,000)	($20,000)	($25,000)	($25,000)	($5,000)	$10,000	$50,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000
Probability to Reach Next Stage	100.0%	60.0%	36.0%		62.0%	89.0%									
Compounded Probability	100.0%	60.0%	21.6%	21.6%	13.4%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%
Risk-Adjusted Net Cash Flow	($10,000)	($12,000)	($5,400)	($5,400)	($670)	$1,192	$5,959	$17,878	$17,878	$17,878	$17,878	$17,878	$17,878	$17,878	$17,878
Discount Factor	1.00	1.15	1.32	1.52	1.75	2.01	2.31	2.66	3.06	3.52	4.05	4.65	5.35	6.15	7.08
Present Value of Risk-Adjusted Net Cash Flow	($10,000)	($10,435)	($4,083)	($3,551)	($383)	$593	$2,576	$6,721	$5,844	$5,082	$4,419	$3,843	$3,342	$2,906	$2,527
Total Risk-Adjusted Present Value	$9,401														
WACC	15.0%														

Monte Carlo Simulation DCF Analysis

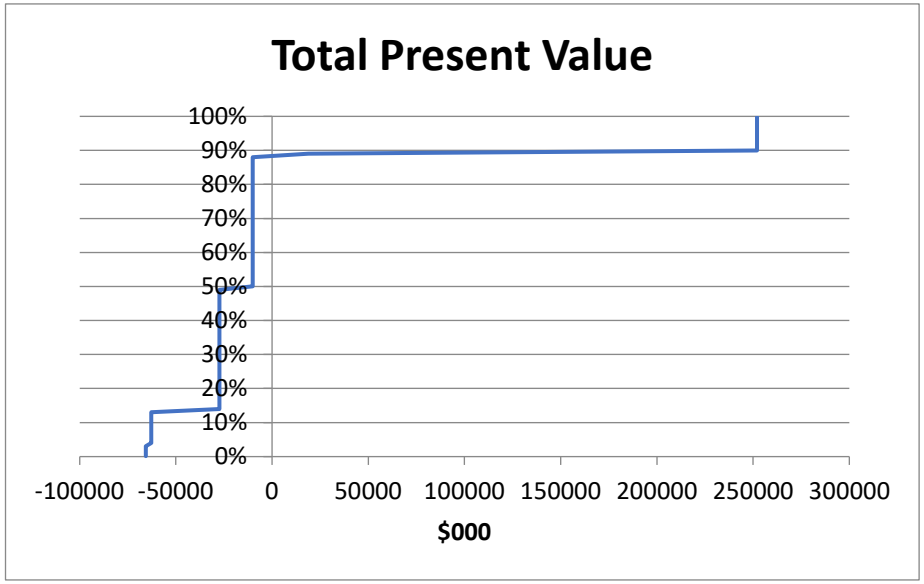
- The weakness of rNPV analysis is that it presents averages that will never occur in real life – a drug will never be 12% approved
- Monte Carlo Simulation DCF Analysis uses the same input assumptions as the rNPV analysis but each phase with an associated probability is treated as a binary outcome (fail/succeed) and analyzed over multiple trials
- Only cash flows associated with reached stages are included in calculation
- With Monte Carlo Simulation software thousands or millions of potential outcomes (trials) can be analyzed
- Results can be analyzed through average (expected) outcomes, graphical representations, and other statistical metrics

Monte Carlo Simulation DCF Analysis Example

MCS DCF Analysis Example															
(in $000)															
Stage	Phase 1	Phase 2	Phase 3		NDA	Marketing									
Year	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Projected Net Cash Flow	($10,000)	($20,000)	($25,000)	($25,000)	($5,000)	$10,000	$50,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000
Probability to Reach Next Stage	100.0%	60.0%	36.0%		62.0%	89.0%									
Simulation Outcome		73.3%	35.6%		32.5%	40.4%									
Success/Failure	100.0%	100.0%	0.0%		0.0%	0.0%									
Compounded Probability	100.0%	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Simulation Net Cash Flow	($10,000)	($20,000)	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Discount Factor	1.00	1.15	1.32	1.52	1.75	2.01	2.31	2.66	3.06	3.52	4.05	4.65	5.35	6.15	7.08
Present Value of Simulation Net Cash Flow	($10,000)	($17,391)	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Total Present Value for Simulation Trial	($27,391)														
Average Present Value for all Trials	$5,279														
WACC	15.0%														

Note: Red cells are simulation results from only <u>one</u> trial

Monte Carlo DCF Analysis Example (continued)

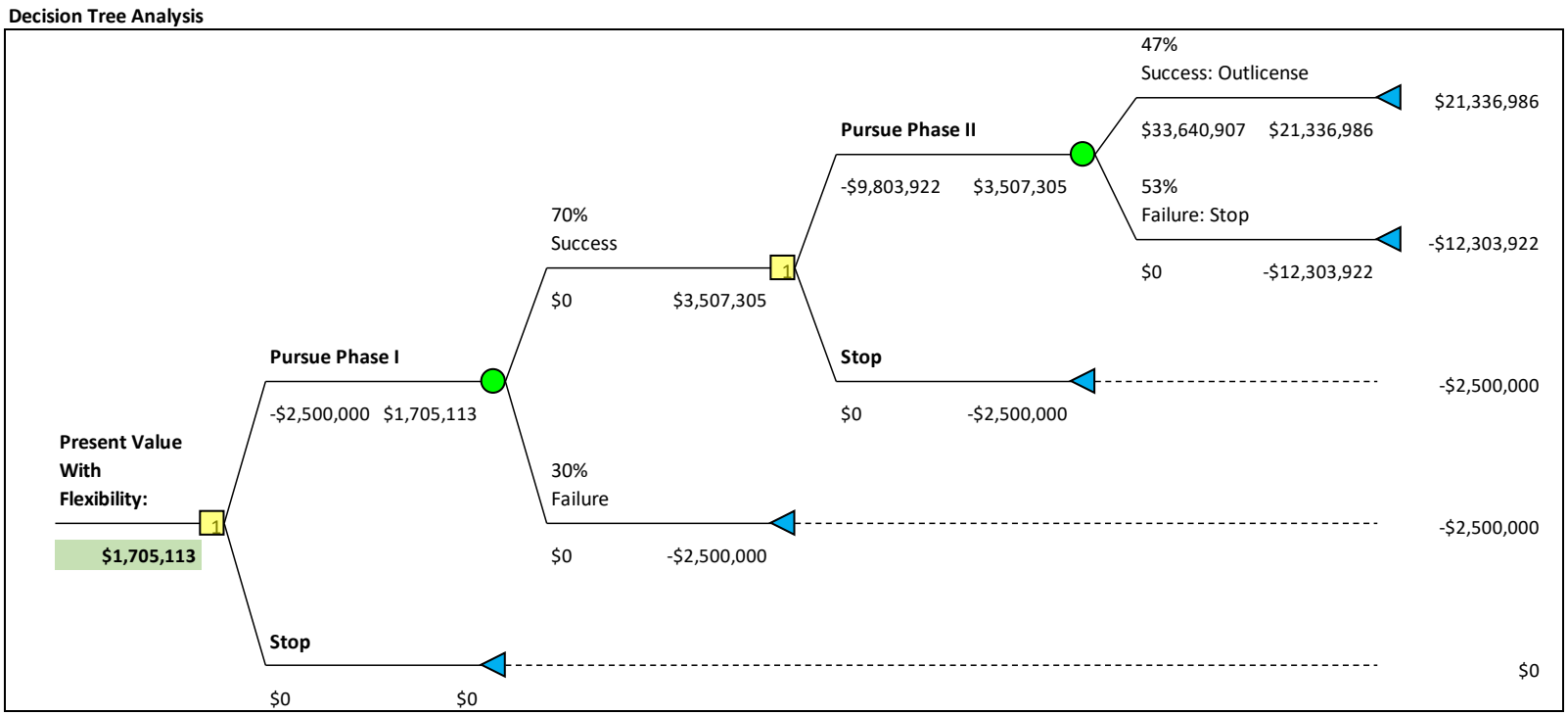


Trial #	Present Value	Comment
1	($27,391)	Failed in Phase 2
2	($27,391)	Failed in Phase 2
3	($10,000)	Failed in Phase 1
4	($27,391)	Failed in Phase 2
5	($10,000)	Failed in Phase 1
6	($27,391)	Failed in Phase 2
7	$251,996	Product approved
8	($27,391)	Failed in Phase 2
9	($27,391)	Failed in Phase 2
10	($27,391)	Failed in Phase 2
~	~	
1000	($27,391)	Failed in Phase 2
Average	$5,279	
High	$251,996	
Low	($65,592)	

Real Options Analysis

- Real Options analysis recognizes the inherent optionality in a development process, for example that a decision to take on costs for a Phase II trial does not need to be made until the results from a Phase I trial are known
- Projects that have a negative net present value in an rNPV analysis can have a positive net present value when analyzed with a Real Options methodology
- Often performed using a lattice options technique but can use Black-Scholes, Monte Carlo simulation, or decision trees
- Formulation of the analysis structure and setup can be challenging which has limited use of Real Options analysis
- Best suited for individual project valuation rather than overall company

Real Options Analysis Example



Real Options Analysis Example (continued)

NPV Analysis

Present Value Without Flexibility:	Year 1 Cash Flow (PV)	Year 2 Cash Flow (PV)	Year 3 Cash Flow (PV)
-$1,236,063	-$2,500,000	-$9,803,922	$11,067,859

Real Option Calculation

Value of Real Option:	
$1,705,113	a = Present Value With Flexibility
-$1,236,063	b = Present Value Without Flexibility
$2,941,176	= a - b

Biotech Company Valuation Case Study

- XRX Biotech (fictional) has 2 products in its pipeline:
  - XRX-101 is a biologic (large molecule) product which targets a rare disease in autoimmune area and is ready to enter Phase I clinical studies in 2021
  - XRX-102 is a biologic product which targets an oncology indication, is currently in Preclinical stage and expected to enter Phase I clinical studies in 2022
  - Company expects to out-license both products to a larger pharmaceutical group if Phase II trials are successful, in exchange for milestone payments and royalties on sales
  - Company has in-licensed intellectual property from a university for which it will pay royalties

General Assumptions for Case Study

- Analysis performed with both rNPV and Monte Carlo Simulation DCF (using 10,000 simulation runs)
- Patent protection effective until 2038 for both products
- Milestone payments are received from licensees after successful Phase II and FDA marketing approval
- Licensees will incur all R&D and regulatory costs for products after Phase II
- Company G&A expenses $2.0 million annually with modest growth
- General R&D is financed through research grants (no cash flow impact)
- WACC of 15.0%

Product Specific Assumptions

	XRX-101	XRX-102
Preclinical/IND		
Start Date	1/1/2019	6/30/2020
Months	18	20
End Date	6/24/2020	2/20/2022
Cost	$0	$1,500
Success Probability	100%	88%
Success Simulation	100%	79%
Success	100%	100%
Phase 1		
Start Date	1/1/2021	3/22/2022
Months	9	9
End Date	9/28/2021	12/17/2022
Cost	$4,000	$6,000
Success Probability	80%	70%
Simulation	23%	56%
Simulation Success	0%	100%
Phase 2		
Start Date	1/26/2022	4/16/2023
Months	12	12
End Date	1/21/2023	4/10/2024
Cost	$10,000	$15,000
Success Probability	45%	40%
Simulation	21%	36%
Simulation Success	0%	0%

Product Specific Assumptions (continued)

	XRX-101	XRX-102
Phase 3		
Start Date	5/21/2023	8/8/2024
Months	12	18
End Date	5/15/2024	1/30/2026
Cost	$0	$0
Success Probability	80%	70%
Simulation	33%	85%
Simulation Success	0%	100%
Marketing Approval		
Start Date	8/13/2024	4/30/2026
Months	12	12
End Date	8/8/2025	4/25/2027
Cost	$0	$0
Success Probability	95%	90%
Simulation	83%	87%
Simulation Success	100%	100%

Product Specific Assumptions (continued)

	XRX-101	XRX-102
Product Launch		
Start Date	11/6/2025	7/24/2027
Months	6	6
End Date	5/5/2026	1/20/2028
Cost	$0	$0
Success Probability	99%	99%
Simulation	82%	97%
Simulation Success	100%	100%
Milestone Income (Net)		
IND Filing	$0	$0
Phase I	$0	$0
Phase II	$5,000	$10,000
Phase III	$0	$0
Marketing Approval	$20,000	$40,000

Product Specific Assumptions (continued)

	XRX-101	XRX-102
Marketing		
Initial Penetration Projection - Most Likely	3.0%	2.0%
Initial Penetration Projection - 99th Percentile	5.0%	4.0%
Initial Penetration Simulation	3.5%	3.5%
Initial Penetration Forecast	3.5%	3.5%
Penetration Quarterly Growth	10.0%	10.0%
Max Penetration - Base Case	60.0%	30.0%
Max Penetration - Low	20.0%	10.0%
Max Penetration - High	70.0%	35.0%
Max Penetration - Simulation	57.0%	24.6%
Royalty Cost / Revenue Sharing %	20.0%	20.0%
Royalty Cost $000 per Year	$0	$0
Sales Costs %	0.0%	0.0%
Outlicense (Yes/No)	Yes	Yes
Outlicense Royalty % (Net)	15.0%	15.0%

Product Specific Assumptions (continued)

	XRX-101	XRX-102
Compounded Success Probability	27.1%	15.4%
Simulation Probability	1.1%	11.2%
Simulation Success	0.0%	0.0%
Launch Quarter	28	35
Exclusivity Expiration Year	2038	2038
Post-Exclusivity Annual Growth	-5%	-10%

Product Specific Assumptions (continued)

XRX-101 Market		
Annual Market Growth Rate		0.00%
Patient Population (m)	0.02	0.02
Average Treatments	1.0	1.0
Annual Treatments (m)	0.02	0.02
Price/Treatment ($)	$125,000	$125,000
Market Size	$ 2,500	$ 2,500
Accessible Market ($m)	$ -	$ 2,250
	0%	90%

XRX-102 Market		
Annual Market Growth Rate		0.00%
Patient Population (m)	0.50	0.50
Average Treatments	1.0	1.0
Annual Treatments (m)	0.50	0.50
Price/Treatment ($)	$25,000	$25,000
Market Size	$ 12,500	$ 12,500
Accessible Market ($m)	$ -	$ 8,750
	0%	70%

rNPV Analysis

	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039
WACC	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
Risk Adjusted Cash Flows											
Risk Adjusted Revenues											
XRX-101	$ 11.0	$ 16.1	$ 23.5	$ 34.5	$ 49.7	$ 54.8	$ 54.8	$ 54.8	$ 54.8	$ 54.8	$ 53.2
XRX-102	$ 8.3	$ 12.1	$ 17.8	$ 26.0	$ 38.1	$ 54.9	$ 60.5	$ 60.5	$ 60.5	$ 60.5	$ 56.8
	$ 19.3	$ 28.2	$ 41.3	$ 60.5	$ 87.8	$ 109.8	$ 115.4	$ 115.4	$ 115.4	$ 115.4	$ 110.0
S&M Expense											
General	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -
XRX-101	$ 2.2	$ 3.2	$ 4.7	$ 6.9	$ 9.9	$ 11.0	$ 11.0	$ 11.0	$ 11.0	$ 11.0	$ 10.6
XRX-102	$ 1.7	$ 2.4	$ 3.6	$ 5.2	$ 7.6	$ 11.0	$ 12.1	$ 12.1	$ 12.1	$ 12.1	$ 11.4
	$ 3.9	$ 5.6	$ 8.3	$ 12.1	$ 17.6	$ 22.0	$ 23.1	$ 23.1	$ 23.1	$ 23.1	$ 22.0
G&A Expense	$ 2.4	$ 2.4	$ 2.5	$ 2.5	$ 2.6	$ 2.6	$ 2.7	$ 2.7	$ 2.8	$ 2.9	$ 2.9
R&D Expense	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -
Total Operating Expenses	$ 6.2	$ 8.1	$ 10.8	$ 14.6	$ 20.1	$ 24.6	$ 25.8	$ 25.8	$ 25.9	$ 25.9	$ 24.9
EBITDA	$ 13.0	$ 20.1	$ 30.6	$ 45.9	$ 67.7	$ 85.2	$ 89.6	$ 89.5	$ 89.5	$ 89.4	$ 85.1
D&A	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -
Taxes	$ -	$ -	$ (3.0)	$ (11.5)	$ (16.9)	$ (21.3)	$ (22.4)	$ (22.4)	$ (22.4)	$ (22.4)	$ (21.3)
Net Cash Flow to Enterprise	$ 13.0	$ 20.1	$ 27.6	$ 34.4	$ 50.7	$ 63.9	$ 67.2	$ 67.2	$ 67.1	$ 67.1	$ 63.8

rNPV Analysis (continued)

rNPV Analysis Summary ($m)	
Present Value of Net Cash Flows	$45.1
Present Value of Terminal Value	$8.9
Total Enterprise Value	$54.0

Monte Carlo Simulation DCF Analysis

Discounted Cash Flow Analysis (Simulation)
(in $000)

Year	2020	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039
WACC	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
Net Cash Flow	$ (3,500.0)	$ (2,390.2)	$ (2,438.0)	$ (2,486.7)	$ (2,536.5)	$ (2,587.2)	$ (2,639.0)	$ (2,691.7)	$ (2,745.6)	$ (2,800.5)	$ (2,856.5)	$ (2,913.6)
Present Value of Cash Flow	$ (3,043.5)	$ (590.8)	$ (524.0)	$ (464.8)	$ (412.2)	$ (365.6)	$ (324.3)	$ (287.7)	$ (255.1)	$ (226.3)	$ (200.7)	**$ (178.0)**

Present Value of Cash Flows	$ (24,891.9)
Present Value of Terminal Value	$ (406.9)
Enterprise Value	**$ (25,298.8)**

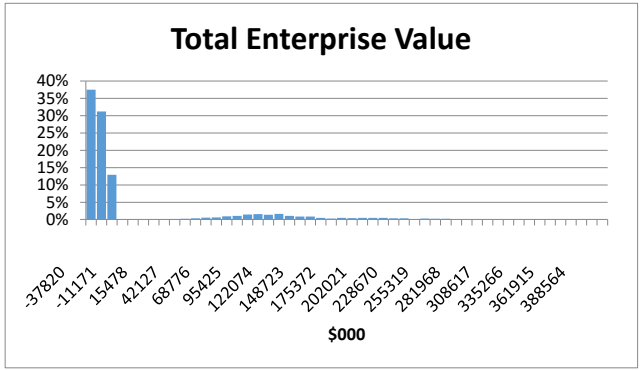
Expected (Average) Values

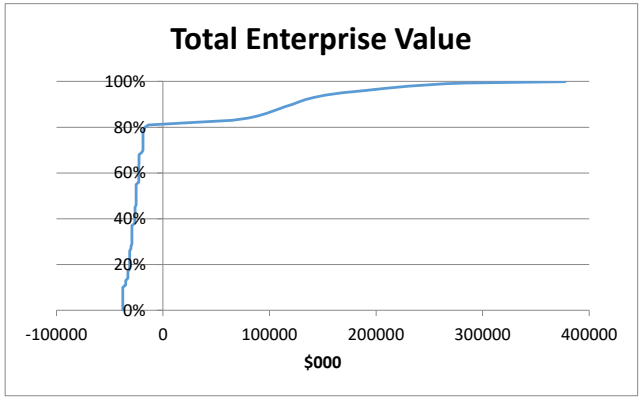
Present Value of Cash Flow	$ (3,043.5)	$ 735.2	$ 1,073.5	$ 1,526.6	$ 2,028.3	$ 2,408.1	$ 2,479.3	$ 2,329.7	$ 2,093.0	$ 1,845.3	$ 1,614.9	$ 1,330.6

Present Value of Cash Flows	$ 600.6
Present Value of Terminal Value	$ 3,041.3
Enterprise Value	$ 3,641.9

Monte Carlo Simulation DCF Analysis (continued)

Monte Carlo Simulation Discounted Cash Flow	
(in $ millions)	
Average Enterprise Value:	**$3.6**
95% Trimmed Expected Enterprise Value:	($2.3)
High Value:	$406.3
Low Value:	($37.8)
97.5th Percentile Value:	$218.7
2.5th Percentile Value:	($37.8)





Monte Carlo Simulation DCF Analysis (continued)

Comparing Results Based on Number of Trials

# Trials	Value ($m)
100	$3.0
500	$1.0
1,000	$4.2
2,500	$4.9
5,000	$4.1
7,500	$4.2
10,000	$3.6

Summary & Conclusions

- Sector specific experience is important for valuator
- Familiarity with advanced valuation methods is essential
- Close client collaboration is important in developing assumptions
- Range of value indications can be wide
- Indications and conclusions may require more explanations than with other sectors

Further Reading

- Forecasting for the Pharmaceutical Industry, Arthur G. Cook, ZS Associates
- Biotech Forecasting & Valuation, Frank S. David, Pharmagellan
- Biotechnology Valuation: An Introductory Guide, Karl Keegan
- Biotechnology Innovation Organization (BIO) – www.bio.org
- Probability Management / SIPmath – www.probabilitymanagement.org
- Real Options: A Practitioner's Guide, Tom Copeland and Vladimir Antikarov
- Decision Making with Insight, Sam Savage

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