

Investing in Biotech — A Guide to Risk-Return Analysis with Valuation Techniques



The Opportunities of Venture Capitalists on Biotech Industry

Over the past decade, venture capital (“VC”) funds have been increasingly placing their attention on the Biotech industry, primarily due to the tremendous growth potential. According to BCIQ BioCentury Online Intelligence, the VC funds advanced more and more investments in the Biotech sector between 2010 and 2019, with a compound annual growth rate (“CAGR”) of 21%. In the early development stage, a Biotech company requires substantial capital to support research and development (“R&D”) and technical advancement. In the meantime, VC funds play a key role in the development of the Biotech company through their capital investments, professional experience and abundant business network. Initial Public Offering (“IPO”) is one of the typical “exit” events for the VC funds to recover their investments and generate a financial return.

In the market institutions, the Hong Kong Stock Exchange (“HKEx”) in 2018 issued and updated the Chapter 18A of the Main Board Listing Rules (“Chapter 18A”) to allow pre-revenue Biotech companies applying to list in Hong Kong. Until 30 Sep 2020, there had been cumulatively 44 Biotech companies to list in Hong Kong under Chapter 18A, with equity funds raised for HKD 53 billion.

We predict that the Biotech companies will be gaining more attention than ever from the investment community. The spread of Covid-19 has been elevating the expectation of innovative drugs, while the reform of capital market has also expanded the options of “exit” events for the VC funds to recover their investment.

A research finding (Kuckertz & Kollmann, 2010) indicated that the investment criteria employed by the VC funds included the experience of entrepreneurs, quality of products or services, market characteristics and financial characteristics. Nevertheless, the due diligence for the entrepreneurs and the products may not provide the quantitative analysis for investment decision-making. Accordingly, there is a need for investors to assess the market characteristics of the Biotech industry with a set of quantitative valuation methods, thereby complementing with the due diligence on entrepreneurs and products.

“3H” (High inputs in R&D, High Rewards, and High Risks) is characterised for the Biotech industry. In light of the pandemic and active financing activity from Biopharmaceutical companies in recent years, the market characteristics and corresponding valuation methods will be illustrated as follows on the basis of the Biopharmaceutical business.

Table 1: Biotech Companies Listed under Chapter 18A until 30 Sep 2020

Stock Code	Company	Listing Date	Category	Therapeutic Area	Funds Raised (HKD Billion)
9688	Zai Lab Ltd - SB	2020.09.28	Pharmaceutical	Oncology, infectious and autoimmune diseases (Gynecologic cancer, Gastric cancer, Brain cancer and Lung cancer)	6.61
1477	Ocumension Therapeutics - B	2020.07.10	Pharmaceutical	Ophthalmology	1.35
6978	Immunotech Biopharm Ltd - B	2020.07.10	Pharmaceutical	Cellular immunotherapy (Prevention of postsurgical recurrence of liver cancer)	1.00
9939	Kintor Pharmaceutical Ltd - B	2020.05.22	Pharmaceutical	Cancers and AR-related diseases (Prostate cancer)	1.64
9996	Peijia Medical Ltd - B	2020.05.15	Medical Devices	Transcatheter valve therapeutic medical device and neurointerventional procedural medical device	2.20
9926	Akeso Inc - B	2020.04.24	Pharmaceutical	Oncology and immunology	2.34
9969	InnoCare Pharma Ltd - B	2020.03.23	Pharmaceutical	Cancer and autoimmune diseases	2.00

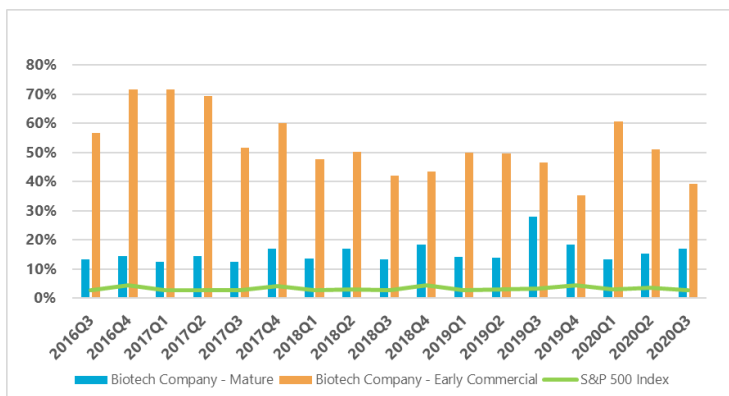
SOURCE: HKEx, Company Reports



Characteristic 1: High Input in R&D

Compared to other industries, the Biotech companies require considerable capital in R&D for their business success. The data combined from Bloomberg and S&P Capital IQ recognised the exceedingly higher R&D ratio in Biotech companies (Mature: 15-20%; Early Commercial: 50-70%) relative to the constituent companies of S&P 500 with only 3% of R&D ratio on average. The data represents the importance of R&D towards the business growth of a Biotech company, which needs to continuously invest in the professional labour force, raw materials and equipment for multiple R&D stages.

Figure 1: R&D as A Percentage of Revenue in Biotech Company



SOURCE: Bloomberg, S&P Capital IQ

With intensive inputs in R&D, the Biotech companies may not be able to generate positive cash flow, posing the challenge to the traditional valuation models. Even so, R&D is critical for whether a Biotech company can launch the leading and trustworthy products in the market. On the basis of this characteristic, the Price-to-research ratio ("PRR") is commonly used particularly for those pre-revenue Biotech companies.

Price-to-research ratio (PRR)

$$\text{Price-to-research ratio (PRR)} = \frac{\text{Market Capitalization}}{\text{Research \& Development (R\&D) Expense}}$$

Price-to-research ratio measures the relationship between the target company's market capitalisation and its R&D expense, by dividing the target company's market value by its previous 12 months of R&D expense.

Table 2: Price-to-research Ratio of Biotech Companies to Primary List in Hong Kong

Stock Code	Company	PRR*
1477.HK	Ocumension Therapeutics - B	97.90
6978.HK	Immunotech Biopharm Ltd - B	38.98
9939.HK	Kintor Pharmaceutical Ltd - B	12.63
9926.HK	Akeso Inc - B	48.06
9969.HK	InnoCare Pharma Ltd - B	35.79

*Based on the market value and financial data upon the companies' latest earnings announcement

SOURCE: S&P Capital IQ & AVISTA Research

The table above consolidates the PRR for those Biotech companies to primary list in Hong Kong in 2020, which reveals that the PRR is around 35-50x. In particular, it is relatively evident for Ocumension Therapeutics-B (1477.HK) with the PRR of 97.90x.

PRR provides a quantitative indicator for the investors to evaluate the capacity of the Biotech company in innovation and technology. Nonetheless, the accuracy of PRR is confined to the difference in clinical phases and therapeutic areas among the Biotech companies. In this sense, the accuracy and reliability of the investment decision merely relying on PRR would be challenged.

A research pointed out that R&D expense varies significantly across clinical phases and therapeutic areas of the drugs. The R&D expense required in phase I could be as low as USD 1.8 million, whereas that required in phase III could reach USD 25.2 million. Furthermore, the R&D expense in Phase III required for the clinical indication for Cardiovascular disease is significantly higher than that for Dermatology.

Table 3: R&D Costs by Clinical Trial Phase and Therapeutic Area (USD Million)

Therapeutic Area	Phase I	Phase II	Phase III
Dermatology	1.8	8.9	11.5
Gastrointestinal	2.4	15.8	14.5
Cardiovascular	2.2	7	25.2
Oncology	4.5	11.2	22.1

SOURCE: Eastern Research Group, Examination of Clinical Trial Costs and Barriers for Drug Development

Typically, the Biotech companies develop different drugs as multiple pipelines simultaneously, where each pipeline focuses on the distinct therapeutic area and clinical phase. The differences in the clinical cycle and therapeutic area among companies pose the difficulty to conduct comparable company analysis with mere PRR.

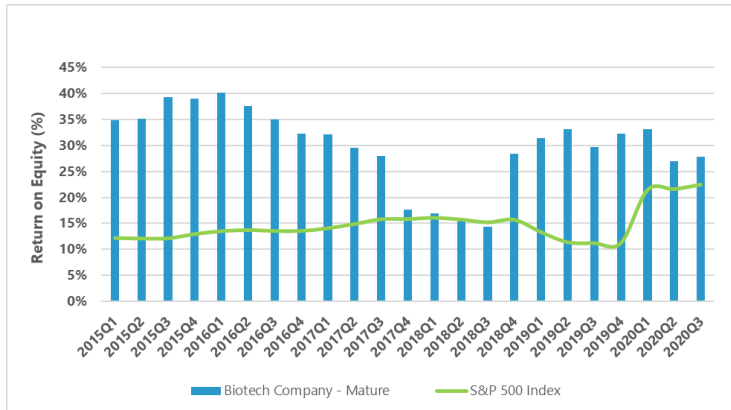
Accordingly, the investors need to further understand the characteristics of the Biotech industry, thereby concluding an appropriate investment decision with a set of valuation methods complementing with PRR.



Characteristic 2: High Rewards

According to Bloomberg, the Biotech company demonstrated superior returns over the past 5 years. Except few quarters, the return on equity ("ROE") of mature Biotech company was around 30-40%, which exceeded the 20-25% ROE of the constituent companies of S&P 500. The data revealed the great potential of the Biotech company to seize a leading and monopolistic market status with the approval of product registration and the upsurge in sales.

Figure 2: Return on Equity between 2015 and 2020 Q3



SOURCE: Bloomberg

Taking a reference from this characteristic, the investors could make use of P/Peak Sales method to assess the value of the target Biotech company with forecasting the peak sales of the drug candidates in the pipelines.

P/Peak Sales

$$\text{Value of Drug Candidate} = \frac{(\text{Peak Sales} \times \text{Peak Sales Multiple})}{(1 + \text{Weighted Average Cost of Capital})^T} \times \text{Probability of Success}$$

The P/Peak Sales method assesses the value of related drug candidates with reference to the comparable company or drug transactions for estimating the factors in the model above. With multiple pipelines typically developed as mentioned, the value of a Biotech company is aggregated by the values of all drug candidates.

Case Study

Biotech Company A focuses on the research of the clinical indications for autoimmune diseases, with drug 1, 2, and 3 as the main candidates in the pipelines. It is expected to reach the peak sales in 7-8 years.

Table 4: Demonstration of P/Peak Sales Valuation for Biotech Company A

Target: Biotech Company A with drug 1, 2, 3 as the main candidates in the pipelines

	Drug 1	Drug 2	Drug 3
Peak Sales Multiple	1.30	2.12	3.60
	<i>Estimated with reference to the transactions of comparable companies and drugs</i>		
Peak Sales (USD Thousand)	98,000	80,000	60,000
	<i>Considering the number of patients, annual fee, market share, etc.</i>		
Number of Patients	230,000	200,000	180,000
Annual Fee (USD)	2,130	2,666	1,333
Market Share (%)	20%	15%	25%
Probability of Success (From current stage to the approval of product registration)	25%	20%	30%
	<i>Estimated with reference to the data from comparable drugs for the probability of success to acquire registration approval from the current stage</i>		
Risk-adjusted Peak Sales x Peak Sales Multiple	31,850	33,920	64,800
	7	8	7
Time to reach peak sales (Year)	<i>Estimated with reference to the data from comparable drugs for the time to reach peak sales from the current stage</i>		
WACC	15%	15%	15%
Discount Factor	0.38	0.33	0.38
Value of Drug Candidate (USD Thousand)	11,974	11,089	24,361
Value of Biotech Company A	47,423		

SOURCE: AVISTA Research

The success of a Biotech company is heavily reliant on launching the products with an expectation to reach the peak sales in the future, by which the P/Peak Sales method measures the potential company value.

However, the objectivity of this valuation method is influenced by the experience of the investors and the management, as well as the availability of market information. Specifically, there may not be sufficient information of comparable company or drug transaction in the market, which requires the investors to have professional knowledge for the judgment of drug comparability. Moreover, the market share of the drugs also depends on the subjective forecast by the investors and management, which will further weaken the reliability of the valuation result.

Unlike PRR, this method may also overlook the value in the R&D clinical phases. Hence, it highlights the needs for the investors to consider the business cycle of the Biotech company, including the risk characteristic across clinical phases, to improve the deficiencies of the above methods and the accuracy of the valuation result.



Characteristic 3: High Risk

The risks facing the Biotech companies vary across different therapeutic areas and clinical phases. Overall, the probability of success in clinical phase I, II, and III are 66.4%, 48.6% and 59.0%, respectively. To take into account the entire process through the approval of product registration, the probability of success ("PoS") is only 13.8%, of which the PoS of the drugs for the indications of oncology is merely 3.4%. Under the context of intensive R&D inputs but a low probability of success, the investors are exposed to significant uncertainty and risks of R&D failures, which would pressure their investment return.

Table 5: Probability of Success by Clinical Phase and Therapeutic Area

Therapeutic Area	Phase I to Phase II	Phase II to Phase III	Phase III to Approval	Overall
Oncology	57.6%	32.7%	35.5%	3.4%
Cardiovascular	73.3%	65.7%	62.2%	25.5%
Central Nervous System	73.2%	51.9%	51.1%	15.0%
Autoimmune/inflammation	69.8%	45.7%	63.7%	15.1%
Vaccines (Infectious Disease)	76.8%	58.2%	85.4%	33.4%
Overall	66.4%	48.6%	59.0%	13.8%
Overall (Excluding Oncology)	73.0%	55.7%	63.6%	20.9%

SOURCE: American Council on Science and Health

Risk-adjusted Net Present Value ("rNPV"), therefore, is suggested for assessing the company value in the context of high uncertainty. Owing to the aforementioned limitations in the PRR and P/Peak Sales, rNPV is deemed to comprehensively incorporate the business cycle of the Biotech company including the R&D and commercialisation stage into the model.

Risk-adjusted Net Present Value (rNPV)

$$\text{Total Value} = \underbrace{\sum_{i=1}^T \frac{P \times C_i}{(1+r)^i}}_{\text{Present Value of Cash Flow from R\&D and Sales}} + \underbrace{\frac{EV_T}{(1+r)^T}}_{\text{Present Value of Terminal Value}}$$

P = Probability of Success in related clinical phases
C = Free Cash Flow in different phases
r = Discount rate, typically WACC
EV_T = Terminal Value

The rNPV enables the cash flow "C" in the projection period to reflect certain uncertainty with incorporating the probability of success "P" into the model. The company value is summed by the present value of the risk-adjusted cash flow and the terminal value, where it assumes the company to continuously grow indefinitely.

Case Study

Biotech Company B focuses on the research of the indications for cardiovascular diseases. In its pipelines, some investigational drugs were terminated for clinical trials owing to data issues while some have not entered the clinical phases. For simplicity, we will focus on the evaluation of drug 4 which demonstrates greater potential. Drug 4 has completed Phase II with preparation to initiate the Phase III clinical trial.

Table 6: Probability of Success for Drug Candidate in Biotech Company B

Target: Biotech Company B. For simplicity, the valuation of drug 4 will be focused

RMB Thousand (unless otherwise stated)

Probability of Success	Drug 4
Phase II to Phase III Clinical Trial	56%
Phase II to Product Registration	45%
Phase II to Commercialisation in the Market	25%

SOURCE: AVISTA Research



Case Study (cont.)

Table 7: Demonstration of rNPV Valuation for Biotech Company B

	FY20X0	FY20X1	FY20X2	FY20X3	FY20X4	FY20X5	FY20X6	FY20X7	FY20X8	FY20X9
Phase	Phase II	Phase III	Registra- tion	Market	Market	Market	Market	Market	Market	Market
Sales Revenue				200,000	1,200,000	3,500,000	6,000,000	7,500,000	8,800,000	9,500,000
Probability of Success (Cumulative)	100%	56%	45%	25%	25%	25%	25%	25%	25%	25%
Sales Revenue (Risk-adjusted)				50,000	300,000	875,000	1,500,000	1,875,000	2,200,000	2,375,000
Cost of Sales (Risk-adjusted)				(7,500)	(45,000)	(105,000)	(180,000)	(225,000)	(264,000)	(285,000)
Gross Profit				42,500	255,000	770,000	1,320,000	1,650,000	1,936,000	2,090,000
R&D Expense	(70,000)	(250,000)	(20,000)							
Probability of Success (Cumulative)	100%	56%	45%	25%	25%	25%	25%	25%	25%	25%
R&D Expense (Risk-adjusted)	(70,000)	(140,000)	(9,000)							
Operating Expense (Risk-adjusted)				(22,500)	(135,000)	(350,000)	(600,000)	(750,000)	(880,000)	(950,000)
Pre-tax Profit	(70,000)	(140,000)	(9,000)	20,000	120,000	420,000	720,000	900,000	1,056,000	1,140,000
Corporate Income Tax (25%)				(5,000)	(30,000)	(105,000)	(180,000)	(225,000)	(264,000)	(285,000)
Free Cash Flow	(70,000)	(140,000)	(9,000)	15,000	90,000	315,000	540,000	675,000	792,000	855,000
Discount factor (WACC = 15%)	0.87	0.76	0.66	0.57	0.50	0.43	0.38	0.33	0.28	0.25
Present Value of Free Cash Flow	(60,870)	(105,860)	(5,918)	8,576	44,746	136,183	203,006	220,659	225,136	211,343

SOURCE: AVISTA Research

Present Value of Free Cash Flow in the projection period	877,002
Add: Present Value of Terminal Value*	1,814,027
Company Value	<u>2,691,028</u>

SOURCE: AVISTA Research

Remarks: The Biotech company typically develops multiple pharmaceutical products for continuous growth. For simplicity, the above table focuses on the demonstration for the cash flow of drug 4 in the projection period and assumes the company can remain continuous growth after the achievement of drug 4's peak sales

Under the rNPV model above, the present value of risk-adjusted free cash flow of Biotech company B in the projection period is around RMB 900 million. The present value of terminal value is RMB 1.8 billion, assuming the company will be growing indefinitely after the projection period. As a result, the value of Biotech company B as of valuation date is RMB 2.7 billion.

It is undeniable that the rNPV valuation is also confined to the comparability of company and drugs, as well as the accuracy of the sales forecast. However, this model provides the investors a relative reliable and comprehensive analysis by deliberately taking into account the status at different stages (R&D stage and commercialisation stage) and the characteristics of Biotech industry (**H**igh input in R&D, **H**igh Rewards, and **H**igh Risks).

How AVISTA Can Help

Upon the study above, we could see the professional demand for the valuation of the Biotech company. The valuation for drugs relies heavily on professional industrial and pharmaceutical knowledge. Meanwhile, the intensive R&D inputs at the early stages and the varying risks of failures imply the uncertainty to the cash flow forecast, posing a challenge to the valuation.

As one of the leading independent professional valuation firms, AVISTA is experienced and knowledgeable in conducting valuation in the Biotech industry. Our valuation experts comprehend the industry characteristics and the limitations of traditional valuation models on the Biotech industry, as well as the investors' considerations. Our experience and knowledge will provide the reliable and professional valuation service to meet the needs of the Biotech company in terms of financing or acquisition.

Selected pre-IPO Clients in the Biotechnology Industry



Antengene Corporation Ltd. - B (6996.HK)



Gracell Biotechnologies Inc. (GRCL.US)



I-MAB (IMAB.US)



Kintor Pharmaceutical Ltd. - B (9939.HK)



Peijia Medical Ltd. - B (9996.HK)



SinoMab BioScience Ltd. - B (3681.HK)



Suzhou Basecare Medical Corporation Ltd. - B (2170.HK)

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