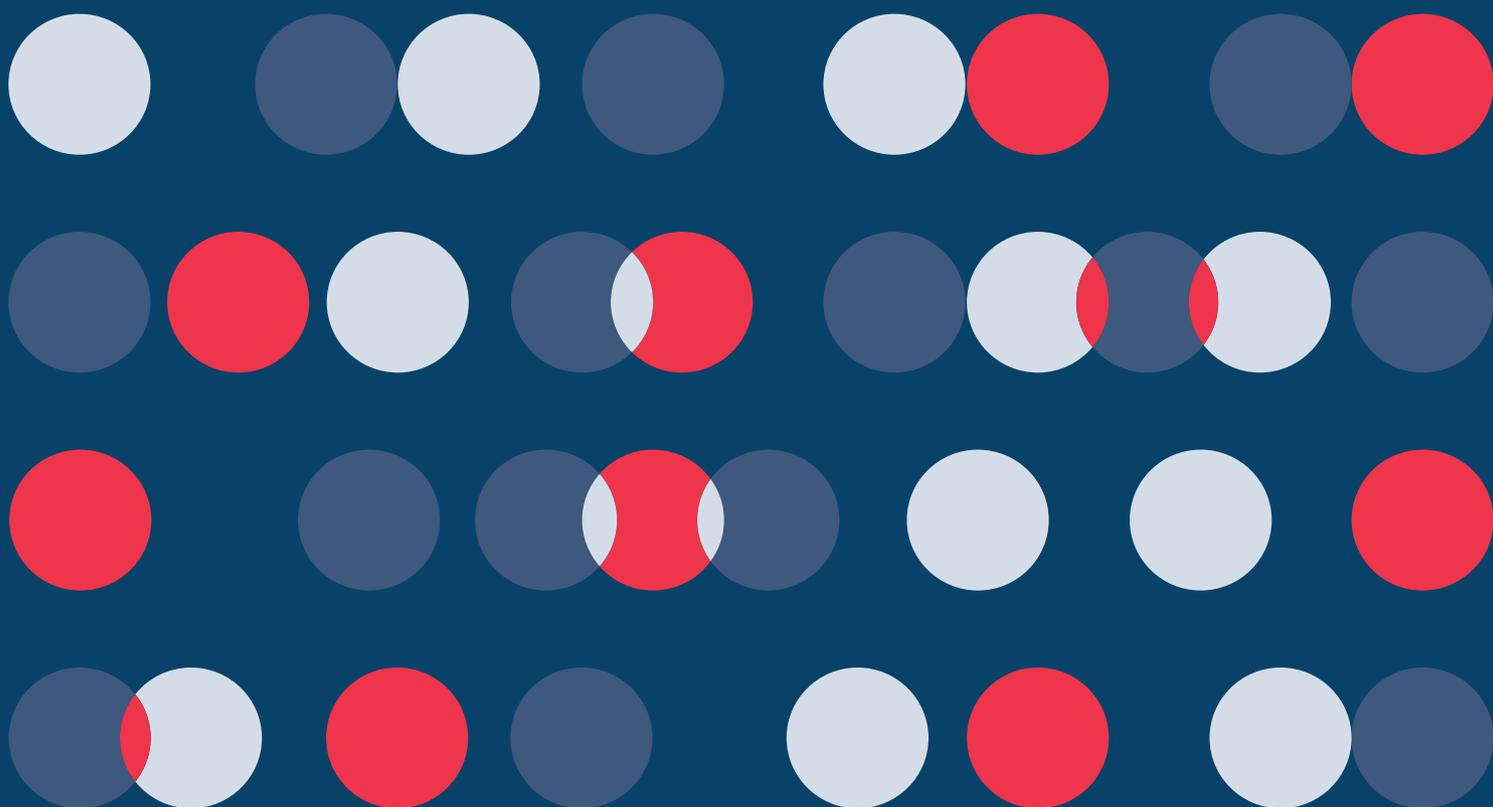


May 2019

RESEARCH REPORT

INVESTMENT BENCHMARK FOR
ASIA'S BIOTECHNOLOGY SECTOR:
CES HK BIOTECHNOLOGY INDEX



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SUMMARY

Global economic development, population growth and an aging society have given new impetus to the biomedical industry. Compared to traditional sectors, biomedical companies are characterised by having substantial investment, high-value outputs and high risks, and being technology-intensive. They usually adopt equity financing rather than debt financing as an important source of financing during their growth period. Financing by different methods at different stages of development of a biomedical company according to development characteristics provide strong financial support for the sector's development. Major global stock markets have in recent years developed new listing rules specifically for the biotechnology (biotech) sector to facilitate effective allocation of venture capitals and private equity funds, completing the "input-output" cycle of capital deployment and optimise resources allocation.

The Mainland's biomedical industry thrives largely because of policy support, increasing capital inputs, accelerating industry consolidation and other favourable factors. In April 2018, HKEX amended its Listing Rules and opened up a new listing channel for pre-revenue or pre-profit biotech companies in Asia, creating a sound environment for the financing of, and investment in, this dynamic and promising sector.

Relevant indices and financial products have been rolled out across major global capital markets to broaden investor access to the biomedical sector. The most representative ones are the NASDAQ Biotechnology Index and the S&P Biotechnology Select Industry Index, and a series of exchange traded funds (ETFs) based on these indices. In the Asian market, the CES HK Biotechnology Index ("CES HK Biotech" for short) tracks biotech companies listed according to Hong Kong's new listing rules and Hong Kong-listed biomedical companies which are in relatively mature development stage. The index gives a comprehensive picture of the performance of Hong Kong's biomedical sector and serves as an industry investment benchmark.

The launch of CES HK Biotech will further increase the diversity of the Hong Kong capital market. The use of biotechnology by index constituent stocks in therapies for human illnesses represents the future development direction of biotechnology in Asia. This is of high significance for China to strengthen its competitiveness in biomedical innovation.

1. THE CAPITAL MARKET AS THE BOOSTER OF BIOTECH MEDICAL INDUSTRY

1.1 The recent rapid growth of biotech medical industry

Global economic development, population growth and an aging society have given new impetus to the biomedical industry. The global pharmaceutical market exhibited much stronger growth than the overall economic growth. Genetics, molecular biology and biochemistry continue to make technological breakthroughs. Given technological advancement and the increasing demand, the biomedical sector enters into a golden age of development. According to the EvaluatePharma 2017 report, the global prescription drug market will see a compound annual growth rate (CAGR) of 6.5% in five years and be expected to reach US\$1.06 trillion in 2022. The biologics segment, in particular, will develop most rapidly. By 2022, 52% of the top 100 best-selling pharmaceutical products would be biotech products. The share of biomedical industry in the entire pharmaceutical market would increase from 17% in 2008 to 30% (US\$326 billion) in 2022¹.

The biomedical sector, due to its speedy growth, has gradually become the new engine of economic growth. In the US, the powerhouse for the biomedical industry, the industry's total production accounts for about 17% of the gross domestic product (GDP) and biomedical clusters have emerged in cities like Boston and Los Angeles. In developed countries like Japan and Germany, the share of the healthcare industry in GDP also exceeds 10%, making the industry a key engine of social and economic growth². Strong growth was also seen in China's medical industry. The Mainland's pharmaceutical market expanded at a CAGR of 15% between 2011 and 2016³. In the Outline of the Healthy China 2030 Plan released in 2016, the development of China with a healthy population has become a national strategy. Mainland healthcare service is estimated to reach RMB 16 trillion by 2030⁴. With the wide application of frontier biotechnology (or biotech for short) in the medical field, it is foreseeable that biomedicine will gradually become the fastest growing and most technology-intensive involved sub-sector in the healthcare industry, and that some remarkably innovative companies will emerge in this field to become a new driver for national economic growth and industry innovation.

1.2 Equity financing providing the necessary financial resources to biomedical companies

Firstly, equity financing (rather than debt financing) is an important mode of financing for biomedical companies in their growth stage.

Compared to traditional sectors, biomedical companies are characterised by having substantial investment, high-value outputs and high risks, and being technology-intensive. A new drug has to go through clinical trials at multiple stages in its production cycle before launch, where it is tested for safety, curative effects, hazards and adverse reactions. It also needs to be approved by regulators before it is released to the market. According to a report on clinical drug development success rates issued by the Biotechnology Innovation Organisation (BIO) in the US⁵, the likelihood of a drug candidate in Phase I clinical trials receiving final approval by the US FDA⁶ is merely 10%. Most candidates fail to advance from Phase II to Phase III, rendering a failure in the entire research and development (R&D)

¹ Source: EvaluatePharma, *World Preview 2017*, June 2017.

² Source: 〈發展健康產業是引領我國經濟增長的重要動力〉(“Healthcare industry is key engine of national economic growth”), *Xinhuanet*, 20 July 2017.

³ Source: McKinsey, *CPA-McKinsey China Hospital Pharmaceuticals Report: An In-depth Perspective*, August 2017.

⁴ See the State Council's “Outline of the Healthy China 2030 Plan” (《健康中國 2030 規劃綱要》), October 2016.

⁵ BIO, *Clinical Development Success Rates 2006-2015*, May 2016.

⁶ US Food and Drug Administration (FDA) is the highest law enforcement agency authorised by the US Congress that specialises in food and drug management.

process. Therefore, according to the experience of some large overseas biomedical companies, investing in a biomedical company has been long-term, costly and high risky. It required an average funding of US\$250 million, but a product took about eight to ten years from concept to launch, with an average annual loss of US\$30 million⁷.

The huge uncertainties facing drug development imply that the biomedical industry has very high entry barriers, and that venture capital and equity financing would be the key channels for meeting the financing needs of these companies. Different modes of financing may be adopted by a biomedical company at its different stages of development according to its development characteristics, thereby providing strong financial support for the sector's development. In recent years, new listing regimes have been developed in the capital market specifically for the listing of biomedical companies to facilitate effective allocation of venture capitals and private equity funds, thereby completing the "input-output" cycle of capital deployment and optimise resources allocation.

Secondly, as a result of intensive competition in drug research and development, the global biomedical industry has become more concentrated. Major pharmaceutical companies need to acquire massive capital from the capital market in order to maintain their market dominance.

Examples are Pfizer's acquisition of Warner Lambert in 2000 and Pharmacia in 2003 and Aventis's merger with Sanofi in 2004. In 2017, there were more than 400 mergers and acquisitions (M&As) in the global biomedical industry, involving more than US\$180 billion. Most of the deals were acquisitions of small and medium-sized enterprises (SMEs) by large enterprises to obtain emerging technologies for market expansion⁸. Companies can use funds obtained through venture capital financing and equity financing to industrialise their products, promote R&D innovation among peers, and speed up growth. Table 1 presents the list of major pharmaceutical companies in the world and their businesses.

Table 1. The world's top 10 pharmaceutical companies and their major biologics products

Company	Pharmaceutical business revenue in 2017 (USD mil)	R&D expenses (USD mil)	Principal business
Pfizer	52,540	7,657	A research-based pharmaceutical company dedicated to a wide range of therapeutic fields for health purposes and the prevention and treatment of diseases, providing medicine in the fields of cardiology, oncology and immunology.
Roche	44,368	10,392	A R&D-focused healthcare company that develops, manufactures and delivers innovative therapies as well as diagnostic instruments and tests. Pharmaceutical products cover oncology, diabetes, ophthalmology, neuroscience, immunology, infectious diseases, etc.
Sanofi	36,663	6,697	French pharmaceutical company providing prescription and over-the-counter drugs for the central nervous system, cardiovascular diseases, oncology and diabetes, general medicine and vaccines.
Johnson & Johnson	36,256	10,554	Providing drugs for hepatitis C (HCV), HIV/AIDS, and digestive ailments.

⁷ Source: R&D-based Pharmaceutical Association Committee under the China Association of Enterprises with Foreign Investment, et. al. 〈推動臨床研究體系設計與實施·深化醫藥創新生態系統構建〉("Facilitating the design and implementation of the clinical research framework, deepening the formation of the medical innovation ecosystem"), December 2017.

⁸ Source: hsmap (《火石創造》) ed. (2018) 《中國生物醫藥產業發展藍皮書 2017》(Blue Book on the Development of Biomedical Industry in China (2017)), August 2018.

Company	Pharmaceutical business revenue in 2017 (USD mil)	R&D expenses (USD mil)	Principal business
MSD	35,390	10,000	Research-based pharmaceutical company offering drugs for oncology, fertility, neurodegenerative diseases and endocrinology.
Novartis	33,000	8,972	Innovative biotherapies and drugs in a variety of therapeutic areas such as oncology, cardiology, neuroscience, immunology, ophthalmic care, generics and biosimilar.
AbbVie	28,216	4,982	Research-based biopharmaceutical company that mainly develops and markets drugs for rheumatism, gastroenterology, dermatology, oncology, virology, neurological diseases, metabolic diseases, etc.
Gilead	25,662	3,374	Research-based biopharmaceutical company that specialises in virology, hepatology, hematology, oncology, cardiovascular diseases, inflammation, respiratory diseases, etc.
GSK	24,038	6,235	Research-based biopharmaceutical company that provides drugs for cardiovascular diseases, gynecology, diabetes, anti-infection, skin diseases, respiratory diseases etc.
Amgen	22,849	3,562	Pharmaceutical company headquartered in California, US, specialising in the discovery and development of innovative biologics and small molecular drugs.

Source: Igeahub, *Top 10 Pharmaceutical Companies in 2018*.

Thirdly, cancer immunotherapy is a major field where biotechnology is applied in the pharmaceutical industry. Most of the innovative biomedical companies in this area raised capital through listing on the exchange market to support drug development for cancer immunotherapy.

Representative drugs for immunotherapy are PD-1 and PD-L1 antibodies. There are five types of antibody drug in the world, including Bristol-Myers Squibb's Opdivo and MSD's Keytruda. Opdivo's global revenue increased from US\$20 million in 2014 to US\$5,753 million in 2017, with a CAGR exceeding 560%. Keytruda's global revenue increased from US\$55 million in 2014 to US\$3,809 million in 2017, with a CAGR exceeding 310%⁹. These became the best-selling drugs in the biomedical sector. The sales performance encourages biomedical companies to increase their R&D in this segment and offers a safeguard for biomedical companies' profit after listing on the exchange market. Effective support offered by the capital market to biotech companies would boost the emergence of more cancer treatment drugs.

1.3 Recent reforms in the global capital market driving further development of the biomedical industry

Biotech companies which had been barred from traditional capital markets are attracted to list on major securities markets which have undertaken market rules reforms in recent years targeting the listing of biotech companies. NASDAQ in US is the key market for the listing of global biomedical companies. It has a flexible listing regime under which companies may list on various boards according to their financial performance in terms of profits, net assets, total assets and market size. In April 2012, the US promulgated the Jumpstart Our Business Startups Act (JOBS Act) to support the equity financing and listing of start-ups and innovative

⁹ Source: Frost & Sullivan.

SMEs, especially biotech companies. It facilitates the refinancing and supports the development and industrialisation of innovative biomedical products. As of February 2019, about 745 health-related companies were listed on NASDAQ, of which 171 were biomedical companies with a total market capitalisation of US\$490.7 billion¹⁰. Several Chinese medical companies have also listed in the US (see Table 2).

Table 2. Chinese biomedical enterprises listed on NASDAQ in recent years

Company	Listing year	Company profile
BeiGene	2016	Specialised in innovative molecular targeted drugs and immune pharmaceuticals for cancer treatment, listed on NASDAQ in February 2016.
Hutchison MediPharma	2016	Specialised in the discovery and development of innovative therapies for cancer and auto-immune diseases; listed on AIM of London Stock Exchange in the UK in May 2006 and obtained a secondary listing on NASDAQ in March 2016.
Zai Lab	2017	Mainly engaged in R&D for drugs that treat cancer, auto-immune and infectious diseases; listed on NASDAQ in September 2017.

Source: Compiled according to public information.

Amendments of main board listing rules have been continued in other stock exchanges as well to promote biotech industry development. Since 1993, the London Stock Exchange (LSE) in the UK undertook a series of institutional reforms to its main board and launched the Alternative Investment Market (AIM) in 1995 to speed up the growth of the UK biotech industry. In 2014, the UK topped other countries in Europe in terms of the number and value of new venture capital investments in the biotech industry. In 2016, a total of 11 health-related companies were newly listed on the main board and AIM of the LSE. Among them was the biomedical company, ConvaTec, which raised GBP 1,465 million of funds — the largest case of initial public offer (IPO) by a European medical company in nearly two decades¹¹.

In an attempt to solve the financing needs of high-growth technology companies, the Frankfurt Stock Exchange (FWB) had established outside its main board a new market (Neuer Markt). In 2003, the FWB sought to reshape its stock market into segments that adopt different disclosure standards¹²; and in 2005, it set up a junior board for SMEs. Such innovative moves facilitated biotech R&D and corporate developments, and accelerated Germany's biotech industry development. Germany now leads other European countries in new drug R&D, accounting for over 40% of drugs produced in Europe¹³. In January 2018, the FWB listed its first Mainland biotech company¹⁴.

2. NEW GROWTH IMPETUS FOR ASIAN BIOMEDICAL INDUSTRY

2.1 Policy support for Mainland biomedical sector and industry consolidation

The biomedical industry in the Mainland thrives owing largely to the support of favourable policy reforms that have created new development opportunities for the industry. The speedy implementation of national strategies such as the “13th Five-Year Plan” and “Healthy China

¹⁰ Source: NASDAQ's website, as of 25 February 2019.

¹¹ Source: Beyond Laboratory.

¹² This included splitting the market into two independent boards (Prime Standard and General Standard) and creating new industry sector indices. Only issuers listed on Prime Standard are eligible for admission into FWB indices; enterprises of high market capitalisation and turnover value are included in DAX; SMEs of traditional industries are included in MDAX and SDAX; SMEs of technology industries are included in TecDAX.

¹³ Source: 〈2017-2022 年中國醫藥工業行業市場行情動態與投資戰略研究報告〉 (“Research Report on China's Medical Industry Development and Investment Strategy 2017-2022”), Zhiyan.org website.

¹⁴ The company is Beroni Group Ltd.

2030 Plan”, the acceleration of reforms undertaken by the State Food and Drug Administration (SFDA) and other regulatory authorities, and the reforms in launching new version of the medical insurance catalogue, standardised evaluation, priority review, and fast-track approval of innovative drugs. The government continues to increase support for autonomous innovation with the focus moving from generic drugs during the 11th Five-Year Plan period and autonomous innovation during the 12th Five-Year Plan period to the current national blueprint for technological innovation in the 13th Five-Year Plan. The strong government support has promoted the rapid growth of Chinese biomedical companies and provided critical support for nourishing innovative capabilities conducive to the establishment of a healthy nation.

With increasing capital inputs, there has been accelerated consolidation within the Mainland biomedical industry. Biomedical industry clusters formed around the Yangtze River Delta, the Pearl River Delta and Bohai Bay gradually generate industry agglomeration effect. Shenzhen's biomedical industry had a value exceeding RMB 200 billion in 2016. There are now key innovative companies in the city, such as BGI, Mindray and Beike Biotech¹⁵. In the first 10 months of 2018, 357 M&As valued at more than RMB 120 billion were completed among Mainland medical and healthcare companies, a year-on-year increase of almost 20% (see examples in Table 3). Among them, biomedical M&As accounted for three fifths of the total in number terms. More than 240 cases (or 49%) were related to biopharmaceutical investment¹⁶. In particular, increasing industry consolidation was seen in the areas of cancer treatments and drugs, products and services for gene diagnosis and treatment, and implanted interventionist medical products. This further improves the R&D capabilities for innovative biomedical products.

Table 3. Certain M&A cases of Mainland biomedical companies

Year	Acquirer	Company acquired	Amount / Equity holding	Field
2014	MicroPort	Wright	US\$290 million	Joint implant
2014	PW MedTech	TianXinFu	RMB 800 million / 100%	Orthopedic implanted device
2015	Anke Biotechnology	AGCU ScieTech	RMB 450 million / 100%	Genetic testing
2015	Shanghai Yiliao	Zhonggu Shengwu	RMB 270 million / 67.5%	Anti-cancer intermediate drug
2016	Nanjing Cenbest	Sinocord	RMB 3.4 billion / 76%	Hematopoietic stem cells
2016	Bai Hua Cun	Huawei Medicine	RMB 1,954 million / 100%	Anti-cancer drug R&D
2017	SanPower Group	Findgene	RMB 680 million	Genetic testing
2018	Huaxi Holdings, Hicin Pharmaceutical	NMS	US\$369 million	Anti-cancer drug R&D
2018	Huadong Medicine	UK Sinclair	GBP 169 million / 100%	Biotechnology

Source: 《中國生物醫藥產業發展藍皮書 2017》(China Biomedical Industry Development Blue Paper 2017); GBI SOURCE Database.

¹⁵ Source: 〈深圳生物產業規模超 2000 億元〉(“Shenzhen's biotech industry value exceeds RMB 200 billion”), *China Economic Daily*, 31 March 2017.

¹⁶ Source: zyghan.com.

2.2 Better supports from the Hong Kong capital market for the development of biomedical companies in the region

In April 2018, HKEX amended its Listing Rules to open up a new listing channel for pre-revenue or pre-profit biotech companies. After the implementation of the new listing rules, in addition to the listing of companies with revenue and profit pursuant to the pre-existing listing rules, companies without operating income are now able to access the Hong Kong capital market upon satisfying the requirements under the new listing rules.

The Hong Kong new Listing Rules in 2018 recognise China Food and Drug Administration (CFDA) as a regulator qualified to assess biotech products — putting it on par with the US' FDA and the European Medicine Agency (EMA). This is conducive to the application and promotion of Chinese standards in the international market.

The exit channel provided by the listing platform of HKEX may help attract more venture capital to the high-risk and high-return biotech field. Compared to investors in overseas markets, investors in the Hong Kong market would have a better understanding of Mainland regulations and market conditions, allowing them to better evaluate the investment risks in Mainland biotech companies. On the other hand, Mainland investors can buy biotech stocks listed in Hong Kong through Stock Connect, thereby helping create a sound investor base for biotech companies and a good environment for financing of, and investment in, these companies.

3. BIOTECH INDICES AND RELATED PRODUCTS IN THE CAPITAL MARKET

3.1 Major biotech indices in the US capital market

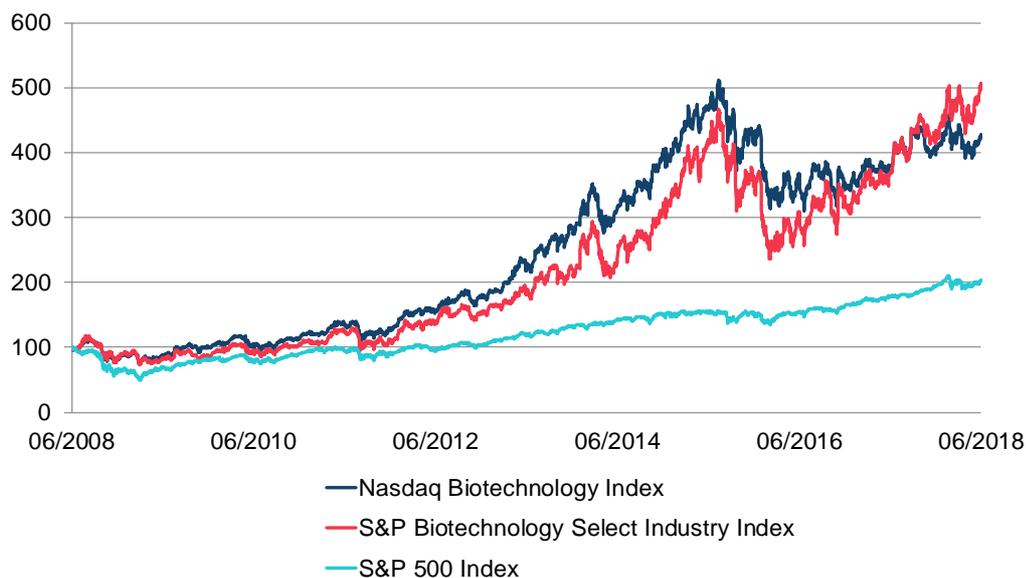
Being in the most dynamic and the most promising industry sub-sector, biomedical companies have attracted much attention from the market. In order to facilitate investor participation in this market, related indices and financial products have been launched in major capital markets in the world. The most representative ones are: the S&P Biotechnology Select Industry Index launched by Standard & Poor's (S&P) in January 2006, which has 119 constituent stocks and a total market capitalisation of US\$7,078 million¹⁷; and the Nasdaq Biotechnology Index (NBI) launched in 1993, which has 221 constituent stocks¹⁸ and is now a major sector index that covers Nasdaq-listed companies specialised in biotech and gene pharmaceuticals. Over the past decade, both indices had a total return two to three times that of the S&P 500 index (see Figure 1 and Table 4)¹⁹.

¹⁷ Source: S&P's website, as of 31 January 2019.

¹⁸ Source: NASDAQ's website, as of 25 February 2019.

¹⁹ Past performance is not an indicator of future performance.

Figure 1. Comparison of daily movements of major US biotech indices with S&P 500 (6 Jun 2008 — 8 Jun 2018) (Rebased on 6 Jun 2008)



Source: Bloomberg.

Table 4. Performance comparison of major US biotech indices with S&P 500

Index	3-year return	5-year return	10-year return	PE (times)
Nasdaq Biotechnology Index	34.75%	85.17%	325.96%	48.03
S&P Biotechnology Select Industry Index	110.81%	162.50%	398.97%	-13.02
S&P 500 Index	42.56%	69.10%	104.24%	20.28

Source: Bloomberg. Data for returns were as of 6 June 2018 and data for PE were as of 29 January 2019.

3.2 ETF products based on biotechnology indices

The US has the world's largest market of biotechnology exchange-traded funds (ETFs), having a total of 18 biotech ETFs available with the total assets under management (AUM) amounted to about US\$19 billion (see Table 5). All of the underlying stocks of these ETFs are listed in the US. These ETFs mainly track three major US biomedical indices: the Nasdaq Biotechnology Index, the S&P Biotechnology Select Industry Index and the New York Stock Exchange's biotechnology index. Among them, iShares Nasdaq Biotechnology ETF had the largest AUM (US\$9.6 billion), tracking the Nasdaq Biotechnology Index. There are also six leveraged and inverse biotech ETFs which further broaden the range of US biotech index products. In Europe, two biotech ETFs are listed respectively in London and Frankfurt, the larger (AUM of US\$490 million) of which was launched by Invesco and tracks the Nasdaq Biotechnology Index.

In the Mainland, there are six biotechnology index funds but no biotech ETFs. Four of these funds track Mainland A-share biotechnology indices and two track US biotechnology indices. Three of the six funds are structured funds. There are currently no biotechnology index futures or other related derivatives available for trading in the Mainland. (See Table 6.)

Table 5. Major biotechnology index ETF products listed in the US and Europe					
Stock code	Product name	Product nature	Issuer	Underlying index	Total asset value* (USD mil)
US-listed					
IBB	iShares Nasdaq Biotechnology ETF	Traditional	BlackRock iShares	NASDAQ Biotechnology Index	9,563.22
XBI	SPDR S&P Biotech ETF	Traditional	State Street Global Advisor	S&P Biotechnology Select Industry Index	5,386.64
FBT	First Trust Amex Biotechnology Index ETF	Traditional	First Trust	NYSE Arca Biotechnology Index	1,728.72
BBH	VanEck Vectors Biotech ETF	Traditional	VanEck	MVIS US Listed Biotech 25 Index	430.79
LABU	Direxion Daily S&P Biotech Bull 3x Shares	Leveraged (300%)	Direxion	S&P Biotechnology Select Industry Index	411.66
BIB	ProShares Ultra Nasdaq Biotechnology ETF	Leveraged (200%)	ProShares	NASDAQ Biotechnology Index	363.94
PBE	Invesco Dynamic Biotechnology & Genome ETF	Traditional	Invesco	Dynamic Biotechnology & Genome Intellidex Index	280.12
ARKG	ARK Genomic Revolution Multi-Sector ETF	Traditional	ARK Investment Management	Nil	226.11
SBIO	ALPS Medical Breakthroughs ETF	Traditional	ALPS	Poliwogg Medical Breakthroughs Index	224.71
BBC	Virtus LifeSci Biotech Clinical Trials ETF	Traditional	Virtus	LifeSci Biotechnology Clinical Trials Index	79.18
LABD	Direxion Daily S&P Biotech Bear 3x Shares	Inverse (-300%)	Direxion	S&P Biotechnology Select Industry Index	77.47
CNCR	Loncar Cancer Immunotherapy ETF	Traditional	Exchange Traded Concepts	Loncar Cancer Immunotherapy Index	59.67
BTEC	Principal Healthcare Innovators Index ETF	Traditional	Principal Financial Group	NASDAQ U.S. Health Care Innovators Index	54.62
UBIO	ProShares UltraPro Nasdaq Biotechnology ETF	Leveraged (300%)	ProShares	NASDAQ Biotechnology Index	37.64
BBP	Virtus LifeSci Biotech Products ETF	Traditional	Virtus	LifeSci Biotechnology Clinical Trials Index	34.36
BIS	ProShares UltraShort Nasdaq Biotechnology ETF	Inverse (-200%)	ProShares	NASDAQ Biotechnology Index	28.97
IEIH	iShares Evolved U.S. Innovative Healthcare ETF	Traditional	BlackRock iShares	Nil	5.15

Table 5. Major biotechnology index ETF products listed in the US and Europe

Stock code	Product name	Product nature	Issuer	Underlying index	Total asset value* (USD mil)
ZBIO	ProShares UltraPro Short Nasdaq Biotechnology ETF	Inverse (-300%)	ProShares	NASDAQ Biotechnology Index	2.99
Europe-listed					
SBIO	Invesco Nasdaq Biotech UCITS ETF	Traditional	Invesco	NASDAQ Biotechnology Index	490.65
A2DWA	iShares NASDAQ US Biotechnology UCITS ETF	Traditional	BlackRock iShares	NASDAQ Biotechnology Index	14.36

* As of 10 July 2018.

Source: Bloomberg and websites of issuers.

Table 6. Biotechnology index funds in China

Product name	Underlying index	Total asset value* (RMB mil)
SWSMU CSI SWS Health Care Index Structured Fund	CSI SWS Health Care Index	853.53
China Merchants CNI Biomedicine Index Leverage Fund	CNI Biomedicine Index	394.56
GF NASDAQ Biotechnology Index Launched Type Securities Investment Fund	NASDAQ Biotechnology Index	359.15
E Fund Biotech Index Graded Securities Investment Fund	CSI WIND Biotechnology Index	210.00
E Fund's S&P Biotech Index Securities Investment Fund	S&P Biotechnology Select Industry Index	78.50
China Universal CSI Biotechnology Theme Index Launched Fund	CSI Biotechnology Thematic Index	77.50

* As of 10 July 2018.

Source: Bloomberg and websites of issuers.

3.3 Asia-based CES HK Biotechnology Index

Unlike in the US and Europe, the biotech industry in Asia is in its infancy. There are few large biopharmaceutical companies in the region while the world's top 10 medical companies, such as Roche and Novartis (see Table 1 above), are in Europe and the US. Neither does Asia have world class biotech R&D centres such as the Sanger Institute in Cambridge in the UK, which can commercialise biomedical findings. Hence, biotech R&D clusters cannot easily be formed in Asia to attract knowledge and talents. Asian investors and analysts also lack adequate experience and expertise to assess pharmaceutical companies. Hong Kong's new listing rules will no doubt attract more quality biotech companies to the region and instill new energy into the region's biomedical industry.

Increasing demand will be seen in the capital market for benchmarks that track and reflect developments of the biotechnology sector. Biotech stocks are prone to be volatile as most of the products of biomedical companies are still at R&D stage and their stock prices are to a

large extent subject to the progress of clinical trials. Therefore, there is a need for an industry benchmark to help investors diversify the risk of investment in individual biotech stocks.

For this purpose, China Exchanges Services Company Limited (CESC), a joint venture of the three stock exchanges in Shanghai, Shenzhen and Hong Kong, launched the CES HK Biotechnology Index ("CES HK Biotech" with the index code of CESHKB) on 14 November 2018 as the benchmark that measures the performance of Hong Kong-listed biotech stocks. The methodology and performance of the index are described below.

(1) Selection of constituents

The base date of the index is 12 December 2014. The base point is 2000. The index universe for CES HK Biotech is comprised of common stocks with primary or secondary listing on the Main Board of the SEHK. On 11 April 2019, the index had 17 constituents.

The constituents are selected according to the following selection criteria:

- To be eligible for inclusion, a company must be classified as either "Biotechnology Company" according to the Industry Classification, or "Biotechnology Company" listed under Chapter 18A of the SEHK Main Board Listing Rules; and
- The stock must attain a daily average total market capitalisation of at least HK\$1.5 billion in the most recent year.

In order to include as many suitable biotech stocks as possible, the fast entry rule will be applied to a newly listed stock which meets the selection criteria after the close of its 10th trading day if the number of constituents falls below 20. For newly listed stocks, the daily average total market capitalisation is derived from the data between the 4th trading day and the review cut-off date for assessing the stock's eligibility.

(2) Index calculation

The index value of CES HK Biotech is calculated based on the free float-adjusted weighted market capitalisation of the constituents. The bigger the free float market capitalisation, the greater the impact of the constituent is on the index. Changes in the share price of a constituent will be directly reflected in the movement of the index. When the share price of a constituent rises, the market capitalisation of the constituent also rises and so does the weight of the constituent. Conversely, the constituent's market capitalisation as well as the weight of the constituent fall when the share price of a constituent falls. The calculation is as follows:

Calculation formula

$$\text{Current index} = \frac{\text{current adjusted market capitalisation of constituents}}{\text{divisor}} \times 2000$$

Where adjusted market capitalisation = $\sum(\text{price} \times \text{adjusted number of shares} \times \text{weight factor})$

Determination of the divisor

The initial value of the divisor is the total market capitalisation of the constituents on 12 December 2014. To ensure the continuity of the index, when the list of constituents or their share structure changes, or when there is a change in the market capitalisation of the constituents due to non-trading factors, the divisor will be revised according to the index maintenance rule.

$$\frac{\text{adjusted market capitalisation before revision}}{\text{old divisor}} = \frac{\text{adjusted market capitalisation after revision}}{\text{new divisor}}$$

Where adjusted market capitalisation after revision = adjusted market capitalisation before revision +/- the increase/decrease in adjusted market capitalisation.

Determination of the share price

The share price (X) of each constituent is determined according to the following principle²⁰:

If there is no transaction that day, X = reference opening price;
otherwise X = the last traded price

Adjusted number of shares

$$\text{Adjusted number of shares} = \text{Total number of issued shares} \times \text{weight ratio} / \text{inclusion factor}$$

The weight ratio is a ratio applied to the total number of issued shares based on the ratio of the free-float shares to the total issued share capital (free float ratio²¹). To reflect the change in the actual number of free-float shares in the market, restricted shares and non-tradable shares held for strategic and other reasons are excluded from index calculation. The remaining shares are the free-float shares or simply called free float. The weight ratio of each constituent is calculated based on the free float ratio to ensure the number of shares of each constituent is relatively stable for calculating the index.

Weight adjustment

When calculating CES HK Biotech, the weight factor is set between 0 and 1 so that no constituent accounts for more than 10%. However, if the number of constituents is less than 20, a 15% cap will be applied to their weights. When the number of constituents is less than 8, a 25% cap will be applied. When the number of constituents is less than 5, the constituents will be equally weighted. Weight factors will be adjusted along with changes to the list of constituents at periodic reviews, with the same implementation date. The weight factor generally remains the same until the next periodic review²².

(3) Index performance and outlook

Based on data as of 6 March 2019, WuXi Biologics had the highest weight (16.30%) among constituents of CES HK Biotech; Innovent Biologics had a weight of 13.46%; Sino Biopharmaceutical, 3SBio and Genscript Biotech each had a weight of over 10%²³. The index consists of biotech companies listed under the new listing rules as well as relatively more developed companies in the industry, providing a comprehensive picture of the whole sector to investors. Derivative products on the index would also facilitate investors to diversify the investment risk stemmed from individual biotech stocks.

The annualised volatility of CES HK Biotech was close to that of the NASDAQ Biotechnology Index and higher than that of the NASDAQ Composite Index. Its

²⁰ Real-time stock prices of index constituents are obtained from the trading data disseminated by HKEX via various channels. The real-time index is calculated during the trading hours of HKEX.

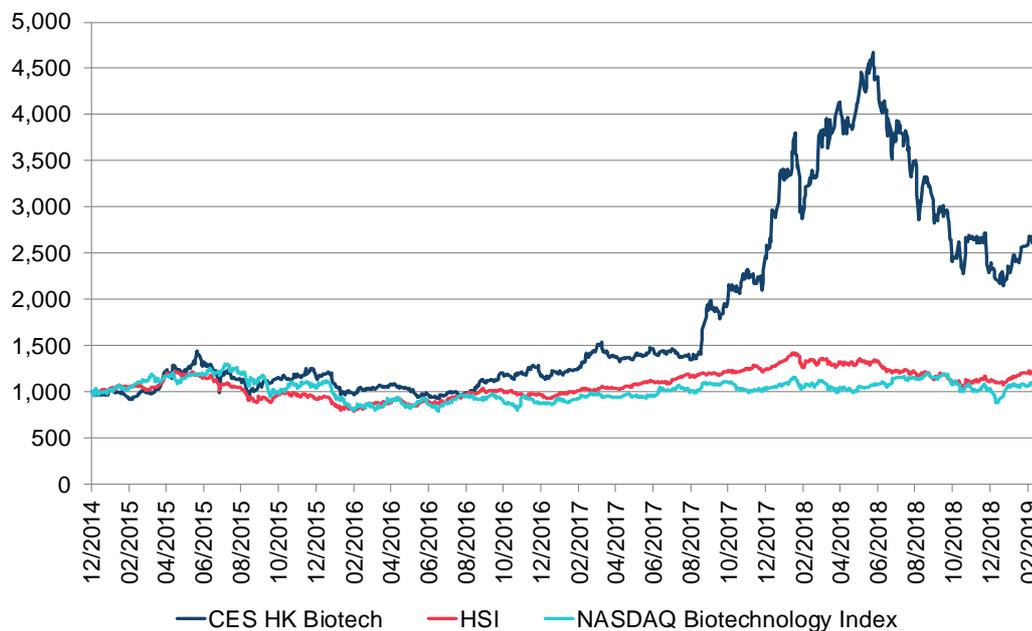
²¹ Free float ratio = free float shares / total number of issued shares.

²² For the index calculation methodology, see "Calculation and Maintenance Methodology" (<https://www.cesc.com/en/Index/Hong-Kong-Overseas/Ces-Hk-Biotech.html>)

²³ Source: CESC.

annualised return was 42.41% in the past three years, surpassing the performance of the Hang Seng Index and the NASDAQ Biotechnology Index in the same period (see Figure 2 and Table 7).

Figure 2. Comparison of CES HK Biotech with Hang Seng Index and NASDAQ Biotechnology Index (12 Dec 2014 — 6 Mar 2019) (Rebased on 12 Dec 2012)



Source: Bloomberg.

Table 7. Performance comparison of CES HK Biotech with Hang Seng Index and NASDAQ Biotechnology Index

Index	Annualised return			Annualised volatility			Risk-adjusted return*		
	2019 up to 6 Mar	1-year	3-year	2019 up to 6 Mar	1-year	3-year	2019 up to 6 Mar	1-year	3-year
CES HK Biotech	30.00%	-10.03%	42.41%	28.52%	41.84%	35.43%	1.05	-0.24	1.20
HSI	12.35%	-2.84%	12.90%	15.48%	18.64%	15.97%	0.80	-0.15	0.81
NASDAQ Biotechnology Index	13.51%	-0.93%	7.85%	24.09%	24.69%	31.10%	0.56	-0.04	0.25

* Risk-adjusted return is calculated by dividing the annualised return by the annualised volatility.

Source: Calculation based on daily closing data from Bloomberg, as of 6 March 2019.

4. CONCLUSION

China's biotechnology sector has entered a stage of growth with a projected long period of development. HKEX introduced new listing rules that suits the special financial characteristics and investment risks of these companies in their start-up stage (no profit or revenue for a long time before and after listing) will help channel more venture capital and private equity funds into the industry and companies. This will be conducive to the emergence of large innovative biotech companies, thereby stimulating the development of such core industries in the region and facilitating the upgrade of the regional economy.

The launch of CES HK Biotech will further increase the diversity of the Hong Kong capital market. The use of biotechnology by index constituent stocks in therapies for human illnesses represents the future direction of biotechnology in Asia. This is of high significance for China to strengthen its competitiveness in biomedical innovation.

APPENDIX. CES HK BIOTECHNOLOGY INDEX CONSTITUENTS AND THEIR PROFILE

Stock code	Company name	Listing date	Return on assets in 2018 (%)	Return on equity in 2018 (%)	Earnings per share in 2018		Income growth in 2018 (%)	Debt to equity ratio in 2018 (%)
					Annual growth (%)	Value (HKD)		
775	CK Life Sciences	16/07/2002	2.50	5.92	1.86	0.03	11.50	108.98
1035	BBI Life Sciences	30/12/2014	8.24	10.82	22.88	0.17	25.78	0.86
1061	Essex Bio-Technology	27/06/2001	17.71	27.70	36.13	0.41	30.78	5.92
1177	Sino Bio-pharmaceutical	29/09/2000	25.59	47.09	274.67	0.87	40.96	9.09
1530	3SBio	11/06/2015	9.26	15.95	35.14	0.59	22.75	36.99
1548	Genscript Biotech	30/12/2015	2.99	6.09	-22.37	0.09	51.34	2.13
1672	Asclepis Pharma	01/08/2018	-0.32	-0.36	86.54	-0.01	212.63	0.00
1801	Innovent Biologics	31/10/2018	-134.69	-512.60	-926.38	-20.44	-48.88	18.88
1877	Junshi Biosciences	24/12/2018	-26.16	-28.56	-123.29	-1.41	-18.64	0.00
2269	Wuxi Biologics	13/06/2017	8.86	10.49	116.67	0.62	56.56	0.00
2359	WuXi AppTec	13/12/2018	12.83	18.81	70.23	2.64	23.85	0.85
2552	Hua Medicine	14/09/2018	-415.05	-1602.61	-1221.06	-11.94	274.07	0.00
2616	CStone Pharmaceuticals	26/02/2019	-158.92	-370.68	N/A	-12.28	N/A	0.00
6118	Austar Lifesciences	07/11/2014	0.01	0.02	-175.00	0.00	49.30	4.16
6160	BeiGene	08/08/2018	-41.03	-56.00	-416.67	-7.29	-22.17	2.82
6185	Cansino Biologics	28/03/2019	-16.64	-24.92	N/A	N/A	N/A	29.86
6826	Shanghai Haohai Biological Technology	30/04/2015	9.74	12.17	11.16	3.07	14.94	0.96

N/A: Not applicable.

Note: Constituent list is as of 11 April 2019.

Source: CESC website for constituent list; Bloomberg and Wind for stock data, retrieved on 4 April 2019.

Disclaimer

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