THE EVOLUTION OF CHINA'S BIOTECH INDUSTRY

January 2020

GLOBAL X
by **Mirae Asset**

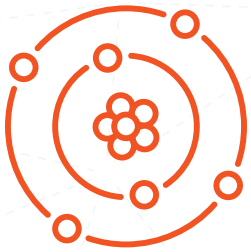
LEVEL 15, THREE PACIFIC PLACE, 1 QUEEN'S ROAD EAST, HONG KONG

+852 2295-1500
MIRAEHKETF@MIRAEASSET.COM

TABLE OF CONTENTS

LEVEL 15, THREE PACIFIC PLACE, 1 QUEEN'S ROAD EAST, HONG KONG

+852 2295-1500
MIRAEHKETF@MIRAEASSET.COM



1

THE EVOLUTION OF CHINA'S BIOTECH INDUSTRY

- China's strategic shift in focus to the creation of new biotech products
- Research and development strategies will evolve to accommodate this
- Demographics and greater access to capital will be critical drivers
- China to embrace a global approach as the biotech industry accelerates

Biotechnology is the science and business of using biological materials, such as proteins, antibodies, genes, and cells to develop new drugs and treatments. It is not a new concept. Humans have been harnessing the power of organisms for thousands of years – bread making is an early example.

That said, recent advances have revolutionized our understanding of biosciences and may present the first legitimate possibility of treating illnesses once thought incurable or fatal.

SIGNIFICANT IMPACTS

KEY TAKEAWAYS

- China's healthcare market is underpenetrated
- The National Medical Products Administration (NMPA) is attempting to forge a more transparent drug-approval system
- An increasing focus on clinical benefits and the establishment of a single-payer structure
- We should see an expansion in the domestic biotech industry

Healthcare in China remains relatively underpenetrated – more specifically, biotech-driven treatments account for only 12% of the country's total drug market. However, this is set to change with the emergence of several key catalysts which will have a significant impact on both companies and investors over the next decade. Most notably, these include the NMPA's attempt to build a more transparent and efficient drug-approval system based on global standards. We also have shifts in the prescription mix that have an increasing focus on clinical benefits, and the establishment of a more focused and dynamic, single-payer system.

This transformation is expected to alter the industry's strategic focus from the development of generic drugs to the creation of new products. In turn, it will drive consolidation among generic manufacturers and see the emergence of a new breed of innovative biotech companies that will potentially provide significant economic returns on investment. Further details on these drivers are noted below.

LEVEL 15, THREE PACIFIC PLACE, 1 QUEEN'S ROAD EAST, HONG KONG

+852 2295-1500
MIRAEHKETF@MIRAEASSET.COM

A GRADUAL EVOLUTION

KEY TAKEAWAYS

- Substantial investment in research and development (R&D) is required
- Risk-averse firms are playing safe with generic therapies
- There will be a gradual change, as R&D strategies improve
- Demographics and urbanization will be crucial drivers of the industry
- A rapid expansion in biotech-driven therapies

There are risks, of course. The biotech sector requires substantial investment in R&D, and this outlay is not guaranteed to result in commercially successful products. But it is important to note that a significant number of the Chinese biotech companies are seeking to mitigate research and development risks by developing so-called me-too drugs (which are closely related to existing products) or me-better offerings (these improve on existing treatments but can't be classed as 'new'). As a result, we see cancer and other therapeutic categories, in particular, being driven into a more crowded space. However, we do expect a gradual evolution of R&D strategies into a best-in-class or first-in-class approach. This move will potentially heighten innovation, ranging from contracted research and drug discovery to drug manufacturing, within the Chinese market.

We should also point out that a biotech firm's prospects are also vulnerable to changes in the regulatory environment as well as intensifying competition and the rapidly evolving nature of the technological progress. Intellectual property remains a concern, too. Furthermore, many companies are dependent on the ability to use and enforce intellectual property rights and patents, even if effective, the expiry of rights and licenses can have adverse financial consequences for those businesses.

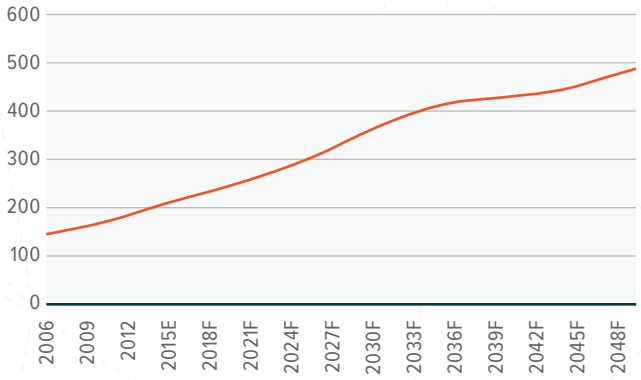
2

WHAT IS UNDERPINNING CHINA'S BIOTECH INDUSTRY?

The demand for quality healthcare in China will continue to be driven by its ageing society (over 400 million people will be 60 years or above by 2030), as well as the shift towards urbanization (over 56% of the population now live in towns and cities). It is also worth noting that people's ability to fund their healthcare costs is also increasing with the average disposable income of residents rising to Rmb28,228 in 2018 (or US$4,097) – this is 54% higher than five years earlier.

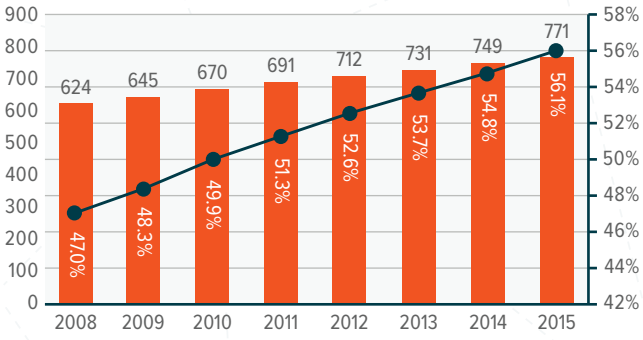
From a health perspective, the charts below show that incidence of cancer and the prevalence of diabetes will increase significantly beyond the age of 50–60 years.

PEOPLE AGED 60 YEARS OLD AND ABOVE, (PER MILLION)



Source: NHFPC, UBS estimates 2015.

URBANIZATION TREND IN CHINA (PER MILLION PEOPLE)

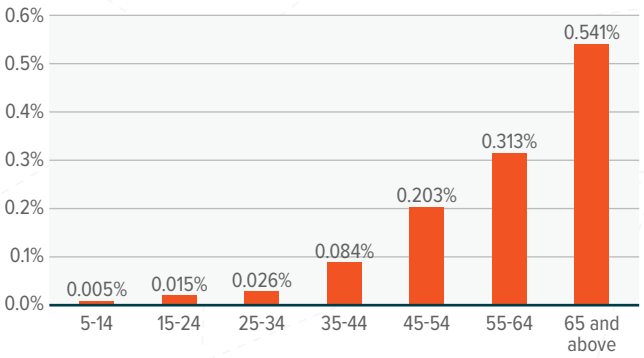


Source: NHFPC, UBS estimates 2015.

LEVEL 15, THREE PACIFIC PLACE, 1 QUEEN'S ROAD EAST, HONG KONG

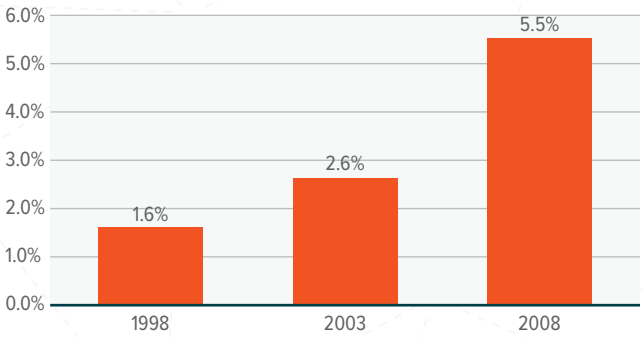
+852 2295-1500
MIRAEHKETF@MIRAEASSET.COM

CANCER INCIDENCE RATE



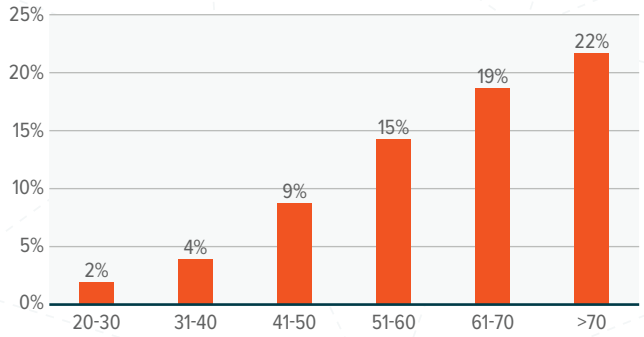
Source: NHFPC, UBS estimates 2015.

HYPERTENSION PREVALENCE IN CHINA



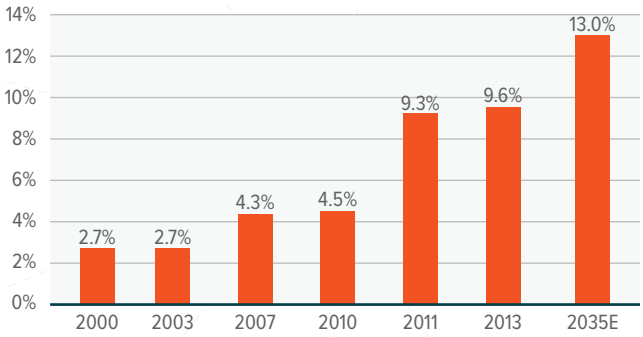
Source: CEIC, UBS, NHFPC, 2008 Diabetes prevalence survey, by the Chinese Medical Association, National Statistics Bureau, International Diabetes Federation, 6th edition

DIABETES INCIDENCE RATE



Source: CEIC, UBS, NHFPC, 2008 Diabetes prevalence survey, by the Chinese Medical Association, National Statistics Bureau, International Diabetes Federation, 6th edition

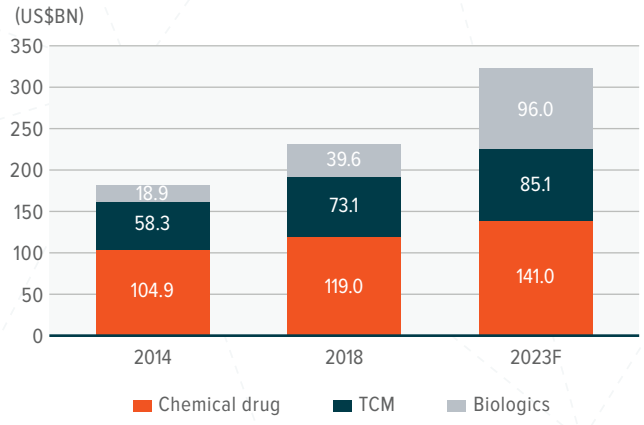
DIABETES PREVALENCE IN CHINA



Source: CEIC, UBS, NHFPC, 2008 Diabetes prevalence survey, by the Chinese Medical Association, National Statistics Bureau, International Diabetes Federation, 6th edition

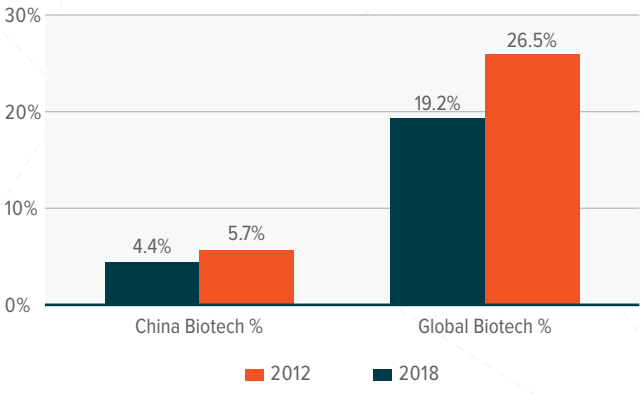
According to market analyst Frost & Sullivan, China's biotech market is expected to grow to US$96 billion by 2023, from US$40 billion in 2018, that is an annual growth rate of 19%.

CHINA'S PHARMACEUTICAL MARKET BREAKDOWN



Source: CLSA, Frost & Sullivan, PDB Database, Evaluate Pharma 2018.

BIOTECH ACCOUNTS FOR ONLY 5.7% OF THE CHINESE PHARMA MARKET



Source: CLSA, Frost & Sullivan, PDB Database, Evaluate Pharma 2018.

Several themes will drive the expansion of China's biotech industry:

- **ACCESSIBILITY:** As of April 2019, China's drug authority, the NMPA, licensed 33 antibody/fusion protein-based therapies, including 21 imported and 12 domestic drugs. This number is still below US levels, where approximately 100 treatments received the green light but is still a notable improvement on the 21 approvals as of May 2018.
- **REIMBURSEMENT COVERAGE IS IMPROVING:** In 2015–2017, a total of 18 monoclonal antibody (mAbs) and fusion proteins were added to the National Reimbursement Drug List (NRDL) for the first time. The NRDL is a catalog of treatments that qualify for reimbursement under government-supported health insurance schemes. In 2018, the NMPA then included 17 anti-cancer drugs in the NRDL. We expect this trend to continue as more therapies gain approval.
- **A SHIFT IN THE PRESCRIPTION MIX:** The growth of medical insurance funds is strictly controlled, but government initiatives aimed at reducing the amount spent on drugs that lack solid evidence of clinical benefits, such as traditional Chinese medicine (which still accounts for 30% of total market share), could create room for medical insurance spending on new therapies.
- **THE GROWING ADOPTION OF PHARMACOECONOMICS:** The government agencies that administer the medical insurance system in China have begun to recognize the value of pharmacoeconomics (an all-round measure of drug efficiency) in assessing the cost-benefits of new therapies. Since 2017, the Ministry of Human Resources and Social Security of the People's Republic of China (MOHRSS) has included pharmacoeconomic factors when deciding whether to bring the patent drugs into the NRDL catalog.
- **BIOSIMILARS DEVELOPMENT:** Biosimilars, which are drugs closely related to existing treatments, are currently being developed by Chinese companies. These are potentially cheaper alternatives to those already produced by the big multinationals. China approved its first biosimilar, (Henlius' Rituximab for the treatment of non-Hodgkin lymphoma) in February 2019. More launches will potentially follow this in the second half of 2019 and throughout 2020, as over 150 biosimilar candidates are at different stages of clinical development.

EXPANDING SALES

Globally, biotech-driven drugs have seen significant growth over the past few decades. In 2018, seven out of the top ten bestselling products globally were biologics, including two innovative PD-1 treatments.

LEVEL 15, THREE PACIFIC PLACE, 1 QUEEN'S ROAD EAST, HONG KONG

+852 2295-1500
MIRAEHKETF@MIRAEASSET.COM

TOP-10 GLOBAL DRUGS BY SALES IN 2018

Product name	Product name CN	Generic name	Generic name CN	Sales (US$bn)	Manufacturer	Indication	Drug type
Humira	修美樂	Adalimumab	阿達木單抗	19.936	AbbVie	Autoimmune diseases and moderate to severe active rheumatoid arthritis	Biological drug (antibody)
Eliquis	艾樂妥	Apixaban	阿哌沙班	9.872	BMS and Pfizer	Atrial fibrillation and Deep Vein Thrombosis (DVT)	Chemical drug
Revlimid	瑞復美	Lenalidomide	來那度胺	9.685	Celgene	Multiple myeloma	Chemical drug
Opdivo	歐狄沃	Nivolumed	納武單抗	7.570	BMS and One Pharma	Multiple cancers	Biological drug (antibody)
Keytruda	可瑞達	Pembrolizumab	帕博利珠單抗	7.171	Merck	Multiple cancers	Biological drug (antibody)
Enbrel	恩利	Etanercept	依那西普	7.126	Amgen and Pfizer	Autoimmune diseases including rheumatoid arthritis, psoriasis and other inflammatory conditions: RA; AS	Biological drug (fusion protein)
Herceptin	赫賽汀	Trastuzumab	曲妥珠單抗	6.981	Roche	Breast and gastric cancer	Biological drug (antibody)
Avastin	安維汀	Bevacizumab	貝伐珠單抗	6.847	Roche	Advanced colorectal, breast, lung, kidney, cervical and ovarian cancer, and relapsed glioblastoma	Biological drug (antibody)
Rituxan	美羅華	Rituximab	利妥昔單抗	6.750	Roche and Biogen	Multiple cancers	Biological drug (antibody)
Xarelto	拜利妥	Rivaroxaban	利伐沙班	6.589	Bayer and Johnson & Johnson	Stroke and systemic embolism; deep vein thrombosis (DVT) and pulmonary embolism (PE)	Chemical drug

Source: CLSA, Mirae Asset Research 2018.

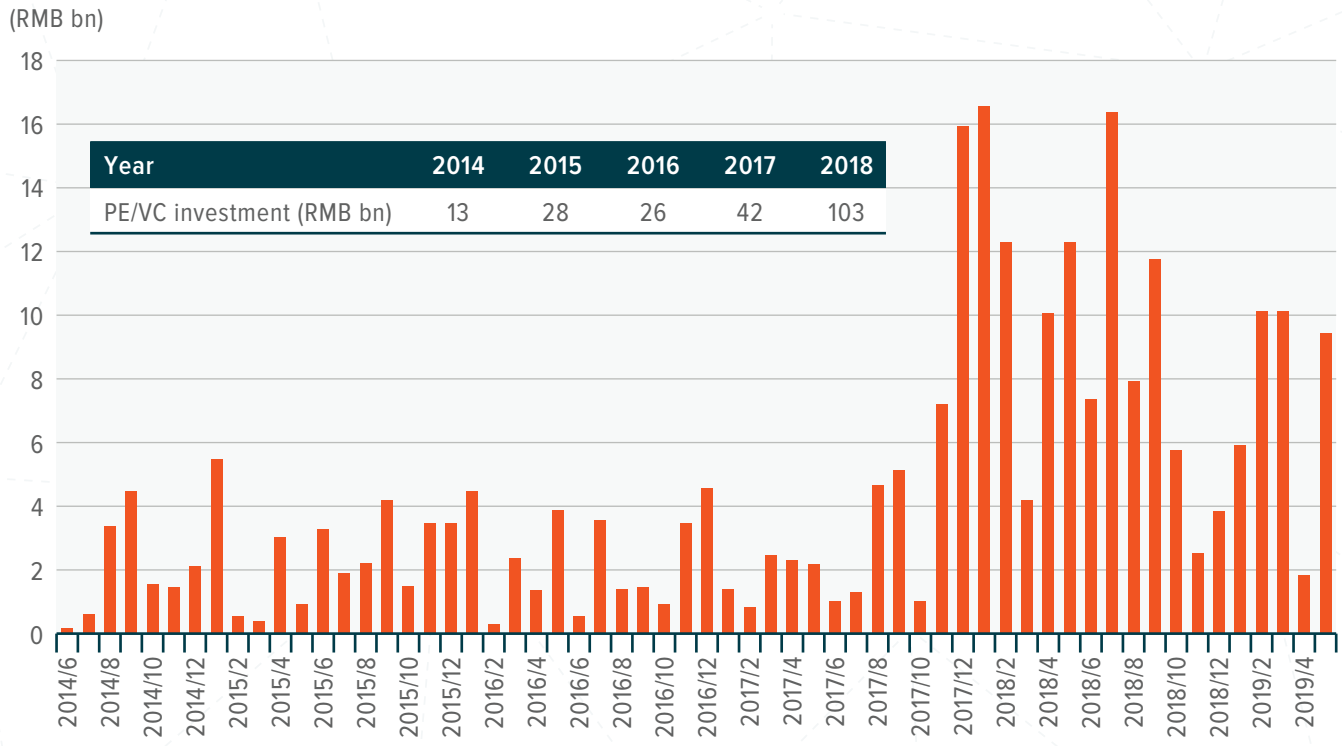
IMPROVING ACCESS TO CAPITAL

KEY TAKEAWAYS

- Changes to stock-exchange rules are accommodative for biotech firms
- China's Securities Regulatory Commission is fast-tracking the listing of 'high-tech' unicorns
- Growing investment in biotech from PE and the venture-capital sector

Key recent developments include (1) Changes to the Stock Exchange of Hong Kong's listing rules for pre-revenue biotech companies and the China Securities Regulatory Commission's new fast-track approval for the listing of high-tech 'unicorns', and 2) Growing private equity and venture capital investment in biotech.

PRIVATE INVESTMENT HAS RISEN SINCE 4Q17



Year	2014	2015	2016	2017	2018
PE/VC investment (RMB bn)	13	28	26	42	103

Source: Wind 2018.

LEVEL 15, THREE PACIFIC PLACE, 1 QUEEN'S ROAD EAST, HONG KONG

+852 2295-1500
MIRAEHKETF@MIRAEASSET.COM

3

IN THE FUTURE?

Over the longer term, China's biotech business has the potential to go global, either by out-licensing to overseas markets or by developing assets in the US, EU and elsewhere. According to industry analyst China Bio, Chinese biotech companies made 164 cross-border licensing deals in 2018, more than double the 2013 figure. Furthermore, China is pursuing trials for one-quarter of its innovative assets overseas.

The country's increasing dominance is also reflected in the numbers of biotechnology patents granted, rising from more than 1,000 (12% of the global total) in 2006 to more than 6,000 (27% of the world total) in 2016. In 2012, China even surpassed the US in this area.

Finally, China's government has listed biotechnology as one of the ten critical sectors for development under its Made in China 2025 industrial strategy. The authorities are improving the country's regulatory framework, reforming the drug-approval process and providing more explicit guidance for biosimilar developers.

4

FACT CHECK: WHAT ARE BIOLOGIC DRUGS?

Biological drugs refer to products derived from living organisms or parts of living organisms, such as proteins, vaccines, blood components and genes. A biologic drug differs from small single-molecule medicines – it is larger in terms of molecule size and more complex in structure.

This type of treatment has become more popular as new therapies in various diseases, such as cancer, autoimmune diseases and endocrine system diseases, have been developed. The manufacture of biologics is very different from chemical manufacturing: microorganisms are normally used, so a suitable environment for growing these is essential.

LEVEL 15, THREE PACIFIC PLACE, 1 QUEEN'S ROAD EAST, HONG KONG

+852 2295-1500
MIRAEHKETF@MIRAEASSET.COM

CHEMICAL DRUGS VS. BIOLOGICS; CHEMICAL GENERICS VS. BIOSIMILARS

	CHEMICAL DRUGS	BIOLOGICS
Molecule	Small molecules	Large and complex molecules, e.g. proteins / peptides
Size (molecular weight)	Lower molecular weight (e.g. Aspirin 180 Da; Lipitor 559 Da)	Higher molecular weight, could be as heavy as 150kDa
Immunogenicity	Mostly non-immunogenic	Immunogenic
Administration route	Multiple routes: oral, injectable and others	Mostly injectable
Thermostability	Relatively stable	Sensitive
Manufacturing	Chemically synthesized (made by following a chemical formula); less sensitive to minor changes in manufacturing process and environment; identical copy can be made	Grown in living cells (e.g. mammalian cell, *E.coli*, yeast, etc.); slight changes in manufacturing process could lead to notable change to product quality; impossible to produce identical copy (only "similar")

	CHEMICAL GENERICS	BIOSIMILAR
Interchangeable	Chemical generics are identical; in most cases, interchangeable with originator drug in clinical application	Biosimilar are not identical to the reference products, only highly similar; in most cases, not interchangeable in clinical setting unless approved by regulators
Development time	~ 2-3 years	5+ years or even longer, depending on the complexity of the targeted biologics
Development cost	~US$2-5mn	Could be over US$50mn or more

KEY TAKEAWAYS

- Biologic drugs are larger in terms of molecule size and more complex in structure
- Advances in the treatment of critical diseases is driving the expansion of the biotech sector
- Specialist manufacturing techniques are required

Disclaimer

This document contains the opinions of Mirae Asset Global Investments (HK) Limited ("MAGIHK") and is intended for your use only. It is not a solicitation, offer or recommendation to buy or sell any security or other financial instrument and shall not constitute any form of regulated financial advice, legal, tax or other regulated service. Information contained herein has been obtained from sources believed to be reliable, but is not guaranteed. MAGIHK makes no representation as to their accuracy or completeness and therefore do not accept any liability for a loss arising from the use of this document.

All Investments contain risks. Forecasts, past information and estimates have certain inherent limitations. Statements concerning financial market trends or portfolio strategies are based on current market conditions, which will fluctuate. There is no guarantee that these opinions are suitable for all investors and each investor should evaluate their ability to invest for the long term, especially during periods of downturn in the market. Outlook and strategies are subject to change without notice.

Past performance is not a guarantee or a reliable indicator of future results. Before making any investment decision, investors should read the applicable fund prospectus for details and the risk factors. Investors should ensure they fully understand the risks associated with the applicable investment and should also consider their own investment objective and risk tolerance level. Investors are advised to seek independent professional advice if in doubt.

This document is issued by MAGIHK (Licensed by the Securities and Futures Commission for Types 1, 4 and 9 regulated activities under the Securities and Futures Ordinance). This document has not been reviewed by the Securities and Futures Commission and no part of this publication may be reproduced in any form, or referred to in any other publication, without express written permission of MAGI HK. **Copyright 2020. All rights reserved.**

COM-2020-02-24-HK-R-MKT-ETFWEBSITE

LEVEL 15, THREE PACIFIC PLACE, 1 QUEEN'S ROAD EAST, HONG KONG

+852 2295-1500
MIRAEHKETF@MIRAEASSET.COM

GLOBAL X
by Mirae Asset

Beyond Ordinary ETFs™

600 LEXINGTON AVE
20TH FL
NEW YORK, NY 10022

1 (888) 493-8631
GLOBALXETFS.COM
@GLOBALXETFS