調査報告書 23－10

An Overview of Innovative Activities in the Chinese Pharmaceutical Industry: Market Trends, Firm Financial Capacity, and Regulatory Environment

令和 6（2024）年 3 月

公益財団法人　アジア成長研究所

An Overview of Innovative Activities in the Chinese Pharmaceutical Industry: Market Trends, Firm Financial Capacity, and Regulatory Environment

Ying Yao

Abstract

This report examines the factors driving drug innovation in the Chinese pharmaceutical industry by analyzing market trends, firm financial capacity, and the regulatory environment spanning from 1990–2022. The descriptive analysis reveals that drugs targeting noncommunicable diseases such as oncology, immunology, and endocrinology have seen a surge in drug development, and that R&D investment decisions of Chinese pharmaceutical companies are influenced more by asset accumulation than by debt and profit margins, in contrast to other contexts. The report also highlights the role of government regulations in incentivizing and shaping pharmaceutical R&D, with regulatory instruments encouraging the development of treatments for rare diseases. However, price pressures linked to government regulations raise concerns about their potential impact on innovation. The findings underscore the challenges in assessing the impact of government regulations on innovative activities and the need for comprehensive data integration across corporate and disease dimensions to better understand the drivers of drug innovation in China's pharmaceutical industry.

List of Abbreviations

CDE Center for Drug Evaluation

DWPI Derwent World Patent Index

EBITDA Earnings Before Interest Taxes, Depreciation and Amortization

GICS Global Industrial Classification Standard

IND Investigational New Drug

NACE Nomenclature of Economic Activities

NCD Non-communicable Disease

NDA New Drug Application

NHSA National Healthcare Security Administration

NME New Molecular Entity

NMPA National Medical Products Administration

NRDL National Reimbursement Drug List

OECD Organisation for Economic Co-operation and Development

R&D Research and Development

ROA Return on Assets

WHO World Health Organization

Acknowledgment

This report has greatly benefited from access to the OSIRIS database provided by the Faculty of Economics at Kyushu University.

1. Introduction

Globally, approximately two billion people lack access to essential medicines, particularly in lower- and middle-income countries (The World Health Organization, 2017). Achieving equitable drug access requires collaborative actions to ensure that medicines are available, affordable, and appropriate for those in need. The development of medicines represents the first step towards closing persistent treatment gaps and attaining the highest possible standard of health, as outlined in the Sustainable Development Goals.

However, the high costs and risks associated with drug development pose significant challenges in addressing these treatment gaps. From drug discovery to clinical trials, regulatory approvals, and market launch, bringing a new drug to market is expensive and uncertain. The overall success rate from Phase I trials to approval stands at about 13.8 percent, with oncology drugs having the lowest success rate, at 3.4 percent (Wong et al., 2018). When including the cost of failed trials, introducing a new drug to the market often costs $1.1 billion (Wouters et al., 2020). These high costs are due, in part, to the extensive testing required to ensure the safety and efficacy of new drugs.

The challenges are even greater when it comes to rare diseases, also known as orphan diseases, which have particularly low prevalence. These conditions attract less attention and funding for research, and the profit expectations are low (Iizuka and Uchida, 2017). The lack of treatment options in these areas suggests that corporate investment in R&D does not always align with the clinical needs of the population. This inconsistency highlights a critical treatment gap that may persist without governmental intervention to stimulate innovation in these specialized areas (Finkelstein, 2004; Lichtenberg and Waldfogel, 2009).

To incentivize innovation, governments typically offer direct benefits such as tax credits, subsidies, and streamlined drug approval applications. However, these initiatives aimed at promoting R&D do not necessarily lead to affordable prices for patients. Pharmaceutical companies often set their prices based on the maximum amount consumers are willing to pay, aiming to recover their investments for profit maximization and ongoing R&D efforts. This pricing strategy can restrict patient access to these drugs. To mitigate this issue, governments frequently include such innovative drugs on insurance lists, aiming to alleviate the burden of diseases while also supporting corporate R&D endeavors. Yet, the inclusion of high-cost drugs can challenge the financial sustainability of healthcare systems (OECD, 2024).

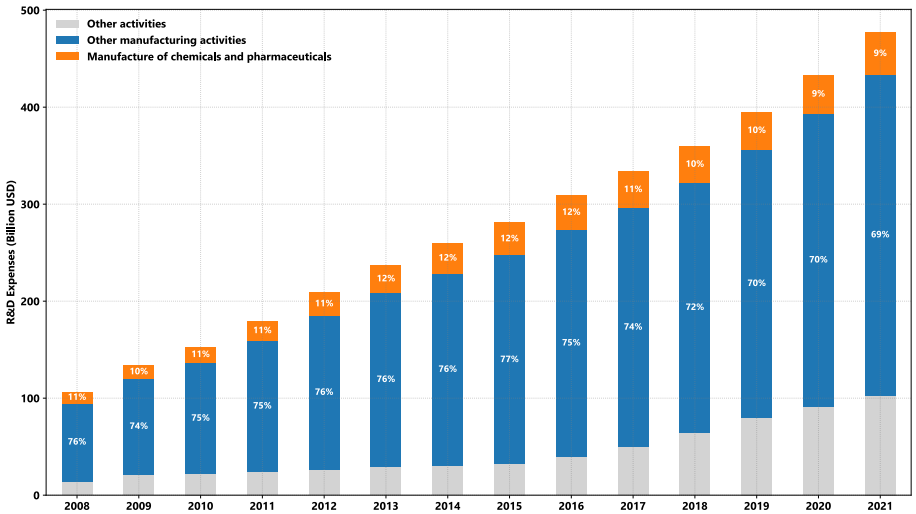
The decisions regarding which drugs to cover and at what price are of public concern. However, there is a clear lack of a cohesive strategy within healthcare policies that simultaneously promotes patient access to medicines and incentivizes drug innovation. This challenge is especially pronounced in developed countries. In developing nations, where

innovative firms are less common, there exists a pronounced gap in understanding both the factors influencing firms' investments in innovation and the impact of healthcare policies on stimulating drug innovation and improving access.

This report focuses on China, which, despite being the world's second-largest pharmaceutical market, is relatively nascent in its R&D endeavors. However, its R&D performance has gained global attention (Kong et al., 2022). In 2008, business enterprise expenditure on R&D was $106.4 billion (Exhibit 1), representing only 33 percent of the R&D investment in the United States pharmaceutical industry. By 2021, this investment had increased fivefold, driven primarily by the manufacturing sector, which consistently accounts for 80 percent of R&D expenditures. Moreover, the investment gap with the United States is closing, with corporate research investment reaching 80 percent of R&D investment in the United States pharmaceutical industry. Within the manufacturing sector, the chemical and pharmaceutical manufacturers contributed approximately ten percent of the total R&D investment.

The surge in R&D investment is closely linked to the growing demand for healthcare services in China, driven by lifestyle changes and a shift in disease burdens from infectious to chronic diseases such as diabetes, heart disease, and cancer (The World Bank, 2011). This substantial demand has attracted international companies to enter the market by establishing R&D centers and fostering collaborations. Concurrently, domestic companies are also embarking on the development of innovative and high-quality medicines, although these initiatives are still in their early stages.

Exhibit 1. Business Enterprise Expenditure on R&D in China: By Sector, 2008–2021



Notes: The graph extracts data from the ANBERD database of OCED's data explorer (https://data-explorer.oecd.org/). The R&D expenses are measured in US dollars and converted using PPP (Purchasing Power Parity) based on 2015 values.

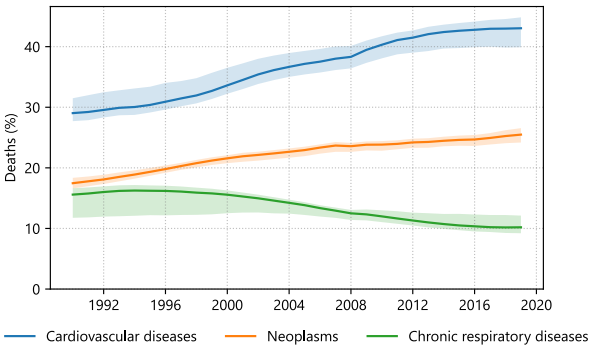
Despite observed progress, it remains unclear which factors determine the innovative activities in the Chinese pharmaceutical sectors. Before formally analyzing these factors, we provide an overview of the market trends, firm financial capacity, and regulatory environment of the Chinese pharmaceutical industry. First, we will review the demand and innovation investment trends, including disease burdens and market trends, with a particular focus on the development status across different disease categories and the availability of innovative drugs. Next, we will investigate the internal factors driving R&D, concentrating on firm-level financial capacities. Furthermore, we will present a descriptive analysis of external factors, emphasizing the regulatory environment, such as the drug approval process and patent filings. Finally, we will discuss the limitations of the preliminary results and identify potential avenues for future research.

2. Disease Burden and Pharmaceutical Market Trends

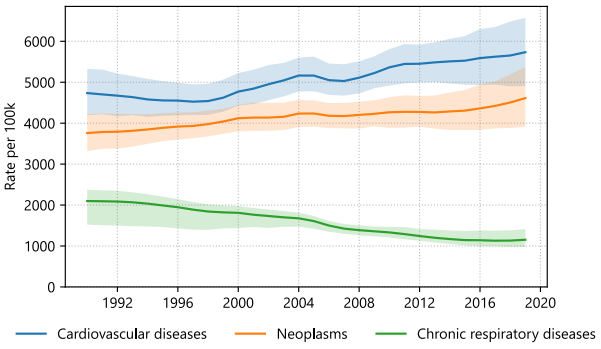
Over the past three decades, China has seen a notable increase in life expectancy, from 68 years in 1990 to 78 years in 2021 (The United Nations, 2022). This improvement can largely be attributed to the reduction in infectious diseases, such as respiratory infections and tuberculosis, with the mortality rate dropping from 16 percent in 1990 to three percent in 2019. Despite these advancements, China faces ongoing challenges with the rise of non-communicable diseases (NCDs), which accounted for 73 percent of total deaths in 1990 and increased to 90 percent by 2019.

The increasing trend in NCDs is associated with several major risk factors, including high blood pressure, smoking, and exposure to ambient particulate pollution (Zhou et al., 2019). Additionally, sedentary lifestyles, combined with unhealthy diets, have significantly driven the growing prevalence of NCDs. As a result, cardiovascular diseases (including heart attack, stroke, and heart failure), neoplasms (also known as tumors), and chronic respiratory diseases (including asthma and chronic obstructive pulmonary disease) have emerged as major contributors to the burden of disease, accounting for nearly 70 percent of NCD-related deaths as shown in Exhibit 2 (a). Moreover, the years of life lost due to early death from cardiovascular diseases and neoplasms have seen a continuous rise. As of 2019, the Years of Lost Life (YLLs) rates for these conditions climbed to 5,733 and 4,611 years per 100,000 people, respectively (see Exhibit 2 (b)). The economic cost of these diseases, reflected in early retirement and reduced labor supply and productivity, is estimated to reach $11.0 trillion (in 2010 US dollars) between 2012 and 2030 (Bloom. et al., 2014).

Exhibit 2. Top Causes of Deaths and Burden of Diseases in China Over the Years, 1990-2019



(a) % Deaths attributable to diseases



(b) YLLs (Years of Life Lost), rate per 100k

Note: The figures use data from the results of the Global Burden of Disease Study 2019 (GBD 2019).

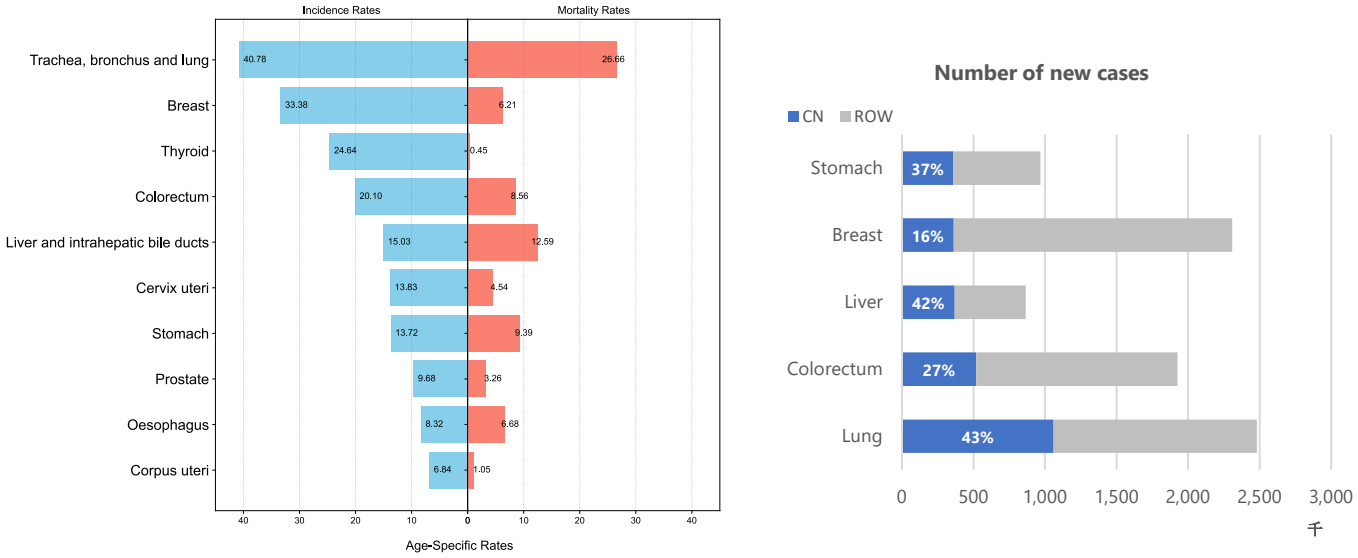
The prevalence of NCDs presents a growing market and fuels innovation and utilization in the pharmaceutical sector (Acemoglu and Linn, 2004; Dubois et al., 2015). Drug development in immunology, endocrinology, and oncology has seen a considerable surge. Since 2018, the Asian market, led by China and India, has significantly boosted the demand for oncology medicines (IQVIA, 2023). China, in particular, has a significant share in the global oncology market, with 43 percent of lung cancer, 42 percent of liver cancer, and 37 percent of stomach cancer patients globally (see Exhibit 3). In response, major multinational corporations, such as AstraZeneca and Novartis, have taken initiatives for a sustained presence in China's pharmaceutical and biotech sector through the establishment of R&D centers and greenfield investments (fDi Intelligence, 2019; ESCAP, 2022).

In addition to these initiatives, multinational companies are proactively entering the market following the global launches of their medicines. Two pioneering studies by Shao et al. (2016) and Ge et al. (2023) have documented 143 new molecular entities (NMEs) approved in both the United States and China across 19 therapeutic areas between 2004 and 2022. The NMEs were categorized according to their active ingredients and dosage forms. Areas receiving the most approvals include oncology, infection, endocrinology (hormone disorders), cardiovascular, and neurology (kidney diseases). Notably, 13 of the 35 molecules were developed in the oncology segment for lung cancer treatment, highlighting the industry's commitment to addressing this prevalent disease.

It is also noted that the yearly approval rate for oncology treatments was typically low, averaging one or two per year, but witnessed a spike to seven approvals in 2021 (Exhibit 4). Due to disparities in the drug approval process, there is an average delay of 2.4 years between the United States and China. Specifically, nephrology drugs were the most delayed, taking 7.3 years, followed by hematology (blood diseases) and ophthalmology (eye disorders) drugs, which took 4.5 years each. Oncology drugs, on average, faced a 2.8-year delay. The only exception was gastroenterology (digestive disorders), where approvals in China were 2.4

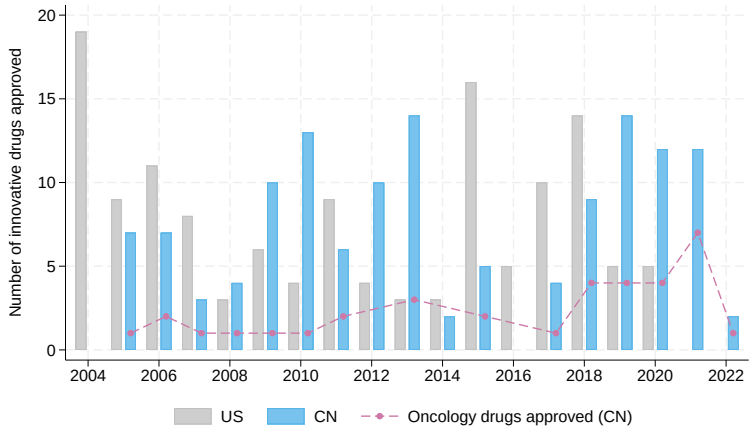
years ahead of those in the United States, as detailed in Exhibit A1 in the Appendix. The entry of innovative drugs has facilitated medicine use but has also contributed to increased drug expenditures. Over the next five years, spending on oncology treatments is estimated to surge by 104 percent, leading to an increase of $224 billion in spending by 2028 (IQVIA, 2023). Due to the promising market prospects, the development in this area is expected to experience significant growth.

Exhibit 3. Incidence and mortality rates in 2022: By cancer types



Notes: The figures use data from the International Agency for Research on Cancer's GLOBOCAN estimates. These estimates include incidence, mortality, and prevalence data for 36 types of cancer across 185 countries, segmented by sex and age group. Available from https://gco.iarc.fr/en.

Exhibit 4. Availability of new drugs in China, 2004-2022



Cancer type	#NMEs
Lung	13
Breast	8
Thyroid	2
Colorectum	5
Liver	3

Notes: The figure and table use data compiled by Shao et al. (2016) and Ge et al. (2023). Available from the supplementary materials of https://doi.org/10.1038/nrd.2016.200 and https://doi.org/10.1038/d41573-023-00058-0.

3. R&D Intensity in the Chinese Pharmaceutical Sector

In the Chinese pharmaceutical market, multinational companies have been the primary developers of innovative drugs. Despite China accounting for 40 percent of the global pharmaceutical market (Kong et al., 2022), the Chinese pharmaceutical sector remains fragmented, with 7,477 manufacturers (National Medical and Products Administration; NMPA, 2022). The vast majority of these manufacturers primarily produce generic drugs, with only a few possessing the resources necessary to invest in R&D and successfully launch products domestically and internationally.

Given the limited discussion on the R&D activities of Chinese pharmaceutical companies, we examine both the internal factors, with a specific focus on their financial capacity, and the output of their R&D investment, as reflected in the progress made across different stages of drug development.

3.1 Financial Capacity and R&D Investment

Previous studies have demonstrated that R&D investment decisions can be constrained by financial indicators such as firm size, age, leverage, and dividend payments (Himmelberg and Petersen, 1994; Brown et al., 2012; Campello et al., 2010; Zhang, 2015). It has been noted that large companies with more capital and better management capabilities are more likely to allocate resources to R&D (Fishman and Rob, 1999; Galende and González, 1999). The impact of a company's revenue or profitability on R&D investment is also significant. This connection is further reinforced by sales growth and the firm's operation scale, as indicated by the number of employees (Park et al., 2010). Furthermore, the health of a company's balance sheet, as reflected in leverage and debt service ratios, has been identified as a crucial determinant of firm investment (Gebauer et al., 2018; Arregui and Shi, 2023).

Despite the evidence, Chinese pharmaceutical companies may face different resource constraints and react differently to these constraints when making decisions. To investigate companies' internal determinants of R&D intensity, we employ a comprehensive OSIRIS database, a resource provided by Bureau van Dijk (BvD), a Moody's subsidiary. This database encompasses detailed business information on 68,940 publicly listed companies worldwide. Although our analysis may be constrained by the lack of data on smaller and unlisted firms, China's mandatory disclosure for listed companies provides us access to reliable R&D information (Li and Zhou, 2024).

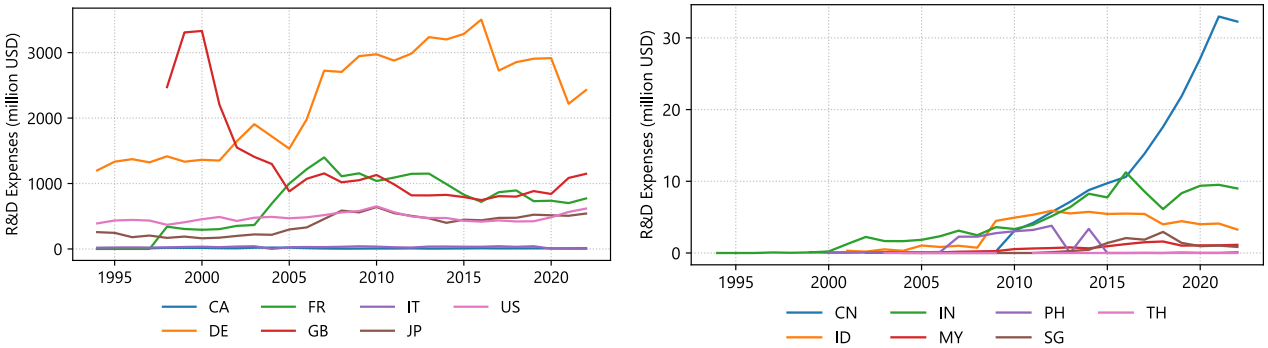
We use a two-step process to identify pertinent companies in the pharmaceutical sector. Initially, we apply a filter for companies under the "pharmaceuticals" industry based on the Global Industrial Classification Standard (GICS). Next, we refine our search to target companies whose core industry falls under "manufacture of basic pharmaceutical products and pharmaceutical preparations," in line with the NACE Rev. 2 code. This refinement helps us exclude companies involved in pharmaceutical products and services from various sectors.

These two steps finally generate a dataset of 1,109 pharmaceutical companies from 67 countries from 1994–2022, with 188 companies based in China.

First, we look at the R&D trends and gaps between developed and developing economies. Globally, major Advanced Economies such as Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States have dominated the innovation activity and sales of the pharmaceutical business. In 2022, the average R&D expenditure for companies in these countries reached $466 million. In terms of R&D intensity, calculated as the ratio of R&D expenses to net sales, the United States is in the lead with a range of 15–27 percent. In contrast, rapid growth in this sector has been observed in Asia, including Indonesia, Malaysia, the Philippines, Singapore, and Thailand, as well as emerging economies such as India and China. However, their investment in R&D is approximately one percent of the R&D investment observed in advanced economies.

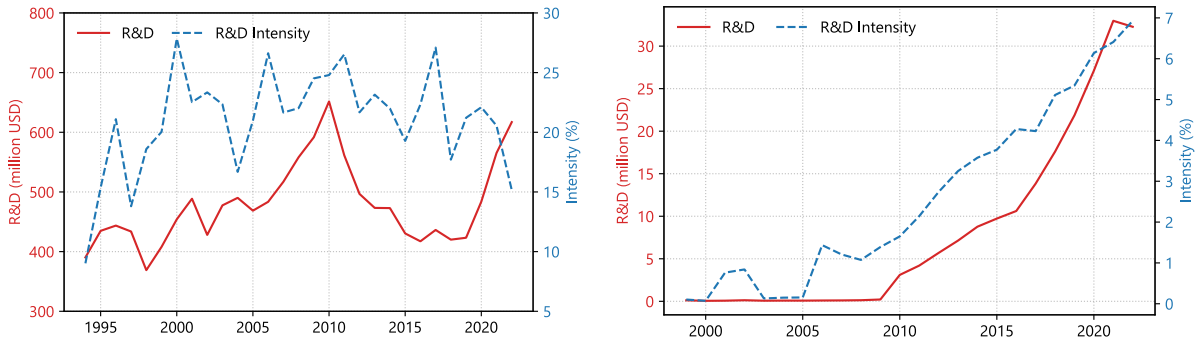
Exhibit 5. R&D Trends in the Pharmaceutical Sector: By Country, 1994–2022.

Panel A. Global R&D trends in the pharmaceutical sector



(a) Advanced Economies (b) ASEAN-5 plus India and China

Panel B. R&D trends in the leading pharmaceutical market



(c) The United States (d) China

Notes: The figures produced use data from the OSIRIS database. In panel A(a), the country codes are as follows: CA for Canada, FR for France, IT for Italy, US for the United States, DE for Germany, GB for the United Kingdom, and JP for Japan. In panel A(b), the country codes are CN for China, IN for India, PH for the Philippines, TH for Thailand, ID for Indonesia, MY for Malaysia, and SG for Singapore. Each cell representing a country-year combination reflects the average R&D expenses of publicly listed pharmaceutical companies documented in the database.

The gaps in R&D investment between developed and developing countries may reveal different approaches to fostering innovation. As the initial phase of our analysis, we explore the influence of internal financial capacity on investment decisions, as suggested by existing literature. Following the methods proposed by Gebauer et al. (2018), we look into the relationship between essential financial indicators and R&D spending. To conduct the analysis, we employ a fixed effect model accounting for unobserved heterogeneity across firms that could influence R&D spending. The specification used for analysis is expressed as follows:

$$RD_{it} = \beta_0 + \beta_1 Leverage_{it-1} + \gamma X_{it-1} + \alpha_i + \varepsilon_{it}$$

where subscripts i and t denote the company and year, respectively. The dependent variable, RD_{it}, denotes the logarithm of the company's R&D investments over the years. The key variable, $Leverage_{it-1}$, calculated debt-to-asset ratio, reflects the financial constraints faced by the firm. We also include a set of control variables X that determine R&D investments. These variables consist of the lagged values of debt service ratio (calculated as Earnings Before Interest Taxes Depreciation and Amortization (EBITDA) over debt), profitability (measured by profit margin as net profit over total revenue), sales growth, and tangibility (defined as the proportion of tangible assets in total assets). We also account for firm characteristics, including firm size (expressed as the natural logarithm of total assets) and firm age, along with firm- and year-fixed effects to adjust for unobserved heterogeneity across firms and time.

Exhibit 6 reports the preliminary results by gradually adding covariates to the analysis. Exhibit A2 in the Appendix presents the summary of statistics for each covariate. The results shown in columns (1) and (2) demonstrate that current R&D investment is constrained by past debt levels, as indicated by the lagged values of leverage. Column (4) identifies a negative relationship between asset tangibility and R&D investment. This finding is consistent with the idea that financial constraints on corporate investment are stronger for firms with low asset tangibility (Himmerlberg and Petersen, 1994; Almeida and Campello, 2007). R&D-intensive firms often lack the tangible assets necessary to secure external financing, as their assets are primarily intangible, such as intellectual property, human capital, and knowledge. Consequently, these firms may face higher borrowing costs or limited access to debt financing, which can affect their investment decisions and capital structure. On the contrary, profit margin exhibits a constantly positive association with R&D investment, with a one percentage point increase in profit margin resulting in a 0.31 percent increase in investment. These findings are consistent with results observed in other studies (e.g., Gebauer et al., 2018). However, when these factors are controlled for, as shown in column (6), the R&D investment decisions of Chinese pharmaceutical companies appear to be influenced by a company's asset accumulation, as indicated by its age and size. This contrasts with existing evidence that emphasizes the role of debt and profit margins in other contexts (e.g., Lim et al., 2020).

Exhibit 6. The Effect of Financial Constraints on R&D Investments

	(1)	(2)	(3)	(4)	(5)	(6)
L.leverage	-0.30*	-0.33**	-0.095	0.029	-0.022	-0.059
	(0.15)	(0.16)	(0.18)	(0.20)	(0.21)	(0.18)
L.debt service		-0.022	-0.029	-0.028	-0.040	-0.012
		(0.031)	(0.040)	(0.039)	(0.039)	(0.031)
L.profit margin			0.0036***	0.0031**	0.0032**	0.00049
			(0.0014)	(0.0014)	(0.0014)	(0.0014)
L.tangibility				-0.81*	-0.81	-0.49
				(0.48)	(0.50)	(0.52)
L.salesgrowth					0.0014	0.00093
					(0.0035)	(0.0026)
Age						0.097***
						(0.0097)
Size						0.60***
						(0.086)
Observations	1,982	1,982	1,956	1,956	1,884	1,884
Adjusted R^2	0.55	0.55	0.55	0.55	0.55	0.59

Notes: Each model accounts for year and firm fixed effects. Standard errors are presented in parentheses. Significance levels are indicated as follows: * p<0.10, ** p<0.05, *** p<0.01.

3.2 The Output of R&D Investment

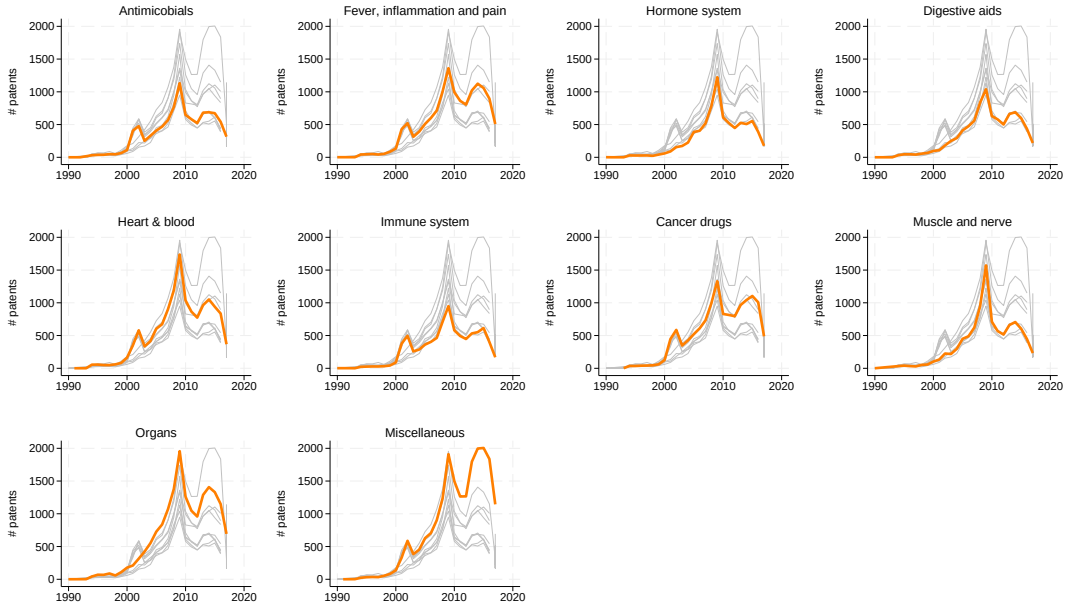
Drug development requires ongoing R&D investment and usually takes 10 to 20 years from the initial drug discovery to market launch. To gain insight into the investment trends in this industry, we examine the outputs at various stages of drug development, including patent filings, regulatory reviews, and drug approvals and launches.

We begin by examining patent filings across different disease categories using data constructed by Vorreuther and Warin (2021). The dataset aggregates information on China's top 20 Derwent World Patent Index (DWPI) patent categories from 1990 to 2017. Exhibit 7 reveals that all disease categories experienced a substantial decline in patent filings after reaching a peak in 2009. Although there was a brief rally around 2014 or 2015, the numbers decreased again in the following years. Patent applications within organ-related, cardiovascular and blood, muscle and nerve systems, and cancer treatments rank among the highest, reflecting prevalent disease trends. This pattern in patent filings could be attributed to factors such as changes in research priorities and funding availability. The decline in patent filings after 2009 may also reflect the long-term impact of the global financial crisis on R&D investments in the pharmaceutical industry.

Next, we turn our attention to the regulatory review and launch stages. We examine a dataset of 12,298 oncology products that underwent clinical trial and production approval filings by Chinese pharmaceutical firms between 2006 and 2023. Among these applications, 256 were

for novel drugs (Class 1.1), which are innovative drugs that have not been launched either internationally or domestically. However, 25 of these novel drug applications were rejected or withdrawn, and only four companies successfully navigated this process to achieve market launch. Exhibit 8 illustrates the time required for a company to progress from filing for clinical trials to obtaining production approval and launching a product on the market. The data reveal that clinical trials typically span approximately ten years, with an additional one or two years needed to secure a production license for market release.

Exhibit 7. Number of Chinese Pharmaceutical Patents: By Disease Category, 1990–2017.



Source: The graphs use data from Vorreuther and Warin (2021). The details on dataset construction are explained in https://doi.org/10.1016/j.dib.2021.106814.

Exhibit 8. Timeline from application to marketization for novel oncology drugs, 2006-2023

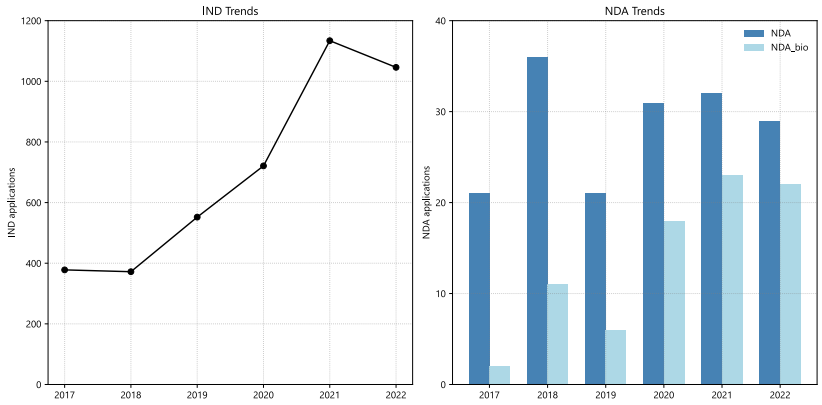
Product	Application for Clinical Trials	Application for Production	Approval for production	Market Launch	Total Years
Pyrotinib Maleate Tablets	2011	2017	2018	2023	12
Apatinib Mesylate Tablets	2006	2011	2014	2019	13
Savolitinib Tablets	2009	2020	2021	2021	12
Surufatinib Capsules	2009	2019	2020	2021	11
Anlotinib Hydrochloride Capsules	2010	2017	2018	2023	13
Fluzoparib Capsules	2012	2019	2020	2020	8
Flumatinib Mesylate Tablets	2006	2018	2019	2019	13

Source: Center for Drug Evaluation (CDE), NMPA. Available from https://www.cde.org.cn.

Despite the lengthy approval timeline, the Center for Drug Evaluation (CDE) of the NMPA has made efforts to streamline the approval process. As a result, there has been a significant increase in Investigational New Drug (IND) applications from 2017 to 2022, rising from 378 to 1,046 cases, as shown in Exhibit 9. An IND application is filed for authorization to conduct clinical trials in humans. In addition, New Drug Applications (NDAs) for chemical and biological products have also experienced a surge, with 20 to 30 cases filed annually. An NDA is a formal request for approval of a new pharmaceutical.

Companies may face rejections throughout the regulatory review process due to insufficient data or safety concerns. In some cases, companies may withdraw their applications if they encounter significant obstacles or determine that the drug is not marketable.

Exhibit 9. Trends in novel drug applications



Note: The data are compiled from the NMPA's 2022 Annual Drug Review Report.

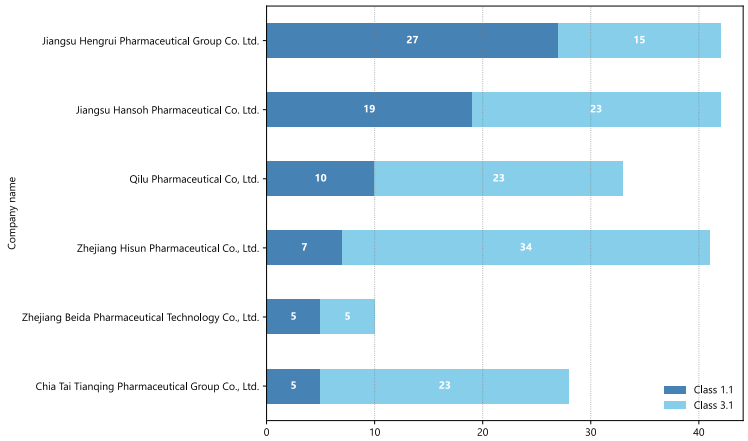
In addition to novel drugs, an emerging class of "new" drugs has been gaining considerable attention in the Chinese pharmaceutical industry. These drugs, classified as Class 3.1, are generic versions of products already marketed overseas but not yet in China. Unlike novel drugs (Class 1.1), which require extensive clinical trials to demonstrate safety and efficacy, generic versions usually undergo smaller-scale clinical trials that are less time-consuming and less expensive. Due to the high risks associated with developing novel drugs, companies are also increasingly investing in this drug class.

One unique feature of Class 3.1 drugs is that they receive a four-year monitoring period from the CDE. During this period, no registration applications for similar imported and domestic drugs are accepted, providing a competitive advantage to the companies that successfully bring these drugs to the market. Furthermore, the average approval timeline for these drugs is much shorter than for Class 1.1 drugs, and the average timeline for Class 3.1 drugs is much shorter than that for Class 1.1 drugs, typically around six years compared to the 10-12 years required for novel drugs. This regulatory environment has led to a surge in Class 3.1

applications. In stark contrast to the scarcity of novel drug applications, the competition for these drugs is intense.

From 2003 to 2015, applications for oncology drugs in this category jumped from 14 to 301, reaching a cumulative total of 1,392 cases. Exhibit 10 presents the clinical trial and production approval applications for Classes 1.1 and 3.1 drugs, filed by five leading companies in oncology drug development from 2003 to 2017. The share of Class 3.1 applications out of their total new drug applications ranges from 36 percent to 82 percent, reflecting the strategic advantages gained by early adopters in the market. These drugs provide an opportunity for companies to expand their product portfolios and gain market share, which may encourage companies to increase their R&D investments to enhance their product pipelines further.

Exhibit 10. New Drug Applications for Oncology Drugs by Leading Domestic Companies, 2003-2017



Note: The figure uses data on the registration status provided by the Center for Drug Evaluation (CDE), NMPA.

4. Regulatory Environment

The trends in drug development and approval demonstrate the role of the regulatory environment in shaping R&D. As shown in Exhibit 7, the peaks and downturns of patent filings may be attributed not only to the financial capabilities of firms but also to the incentives provided by policy measures. These policy incentives can be categorized into “push” and “pull” mechanisms. The “push” approach directly supports pharmaceutical firms to reduce R&D costs. Such support can be in the form of direct research funding to research institutes and companies for early-stage research, tax credits and subsidies, and expedited approval processes. On the other hand, the “pull” approach uses mechanisms such as patent protection, pricing, and reimbursement coverage to secure returns on investment following the drug launch (Kyle, 2020). In contrast to other developed economies, China’s regulatory landscape is uniquely tailored to its own context. Since 2008, China has introduced a series of incentive policies and funding initiatives to promote drug R&D, covering areas such as national strategy,

expedited approval, and data protection. Exhibit 11 summarizes the push and pull strategies employed between 2008 and 2023.

The push strategies in China's pharmaceutical sector are characterized by direct funding support, guidance on potential R&D directions, and expedited drug review processes. While the primary financing in this sector mainly comes from corporate sources and venture capital, government funding has significantly contributed to advancing research, especially for rare diseases. Such initiatives involve the National Key New Drug Creation Program and the Key Technologies R&D Program.

The National Natural Science Foundation of China (NSFC), in particular, has been a steady funding source for rare disease-related projects. From 2012 to 2021, the NSFC funded 784 projects targeting 78 of the 121 rare diseases identified in the National List of Rare Diseases, disbursing a total of $53.36 million. The year 2020 witnessed a peak in both the amount of funding provided and the number of projects supported. Furthermore, the competence of Chinese pharmaceutical firms in orphan drug innovation has been on the rise. Between 2016 and 2022, 86 products developed by 73 Chinese companies received orphan drug designations from the US FDA. Notably, the financial backing for orphan drug R&D in China mainly comes from government grants, marking a distinct approach from the US and Japan. In these countries, substantial tax credits are offered to alleviate some of the R&D expenses, a benefit China currently does not extend (Zhao et al., 2023).

Like in other advanced economies, the improved drug registration and approval system facilitates the market availability of innovative drugs. The number of drugs approved for marketing and drug candidates entering clinical studies is increasing. Specifically, the share of approved orphan drugs among all drugs granted priority review and approval designation increased from 3.6% in 2018 to 20.4% in 2021. By the end of 2021, China has approved 30 orphan drugs for marketing through this expedited regulatory route. This progress presents a notable departure from the situation before 2015, when the approval of new drugs in China was hindered by the substantial backlog of applications and delays in approval. In 2015, the waiting list for application review exceeded 21,000, overwhelming the capabilities of the CDE staff, with the average wait time for initiating a clinical trial for an innovative drug reaching 14 months.

Although there has been notable progress, delays remain apparent compared to the US. For instance, within the G20 nations, the average waiting period from the first global launch of a new drug to its availability in the local market spans 27 months, with an additional 19 months before inclusion in public reimbursement programs. In comparison, the total wait time for drug

access is four months in the United States, 17 months in Japan, 63 months in China, and 81 months in India, as reported by PhRMA (2023).

While these policy interventions have effectively improved access to innovative drugs, they have also sparked concerns among pharmaceutical companies about price pressures linked to regulatory stipulations. These pressures are connected to pricing strategies and insurance coverage. Since 2015, the National Healthcare Security Administration (NHSA) has been advocating for the inclusion of innovative drugs in the National Reimbursement Drug List (NRDL), handling adjustments to the NRDL, and setting drug prices through negotiation. Remarkably, seven orphan drugs were incorporated into the NRDL during the 2019, 2021, and 2022 updates. A significant leap occurred in 2023, with 25 orphan drugs clearing the preliminary NRDL assessment, of which 15 were eventually cataloged. From 2019 to 2023, drugs subjected to price negotiations were cut by between 50% and 61.7% (NHSA, 2023). Medicines that are shown to offer high clinical value have the option to request a price renegotiation should the initial price cut be deemed unsatisfactory.

The regulatory framework outlined above illustrates the government's effort to balance the affordability of treatment and support for ongoing R&D. To secure a place on the NRDL, pharmaceutical companies have to reduce prices, aiming for long-term profitability. Moreover, innovative drugs face challenges of generic competition upon market entry, which can diminish their first-entry advantage and affect their profitability and capacity to invest in R&D. For example, when a generic version of a branded drug enters the market, it can quickly capture a significant market share due to its lower price, eroding the sales and revenues of the innovative drug manufacturers (Berndt and Aitken, 2011).

Given these challenges, a pertinent question arises: Do government pricing strategies dampen the drive for R&D that regulatory incentives aim to boost? While some studies have begun to explore the relationship between pricing strategies and R&D incentives in the pharmaceutical industry (e.g., Danzon and Epstein, 2012; Eger and Mahlich, 2014), there remains a noticeable gap in understanding how pharmaceutical companies adapt to this complex regulatory environment. This inquiry highlights a potential area for further exploration in this area.

Exhibit 11. Regulatory Framework of China's Pharmaceutical Industry

Policy	Year of introduction	Objectives
Push Strategies		
National Key New Drug Creation Program	2008	To establish state-owned innovative drug companies and foster research institute-company alliances. - Invest in innovative drug R&D projects to complete clinical trials for 30 drugs by 2010. - Fund R&D for existing market-leading products, focusing on efficacy, safety, and quality. - Establish technology platforms for safety and efficacy appraisals on new drugs. - Provide subsidies to companies to set up new drug development platforms.
Key Technologies R&D Program	2014	National funding programs that support R&D in areas of social welfare and people's livelihood, including agriculture, energy and resources, environmental protection, and healthcare.
Accelerated Drug Approval	2013, 2016 (expansion of drug categories)	To encourage needs-based innovation in the pharmaceutical sector. - Improve the efficiency of market approval for drugs with patents or addressing clinical needs - Enhance access to drugs for critical diseases (e.g., HIV/AIDS, cancer, etc.), pediatrics, and rare diseases.
Rare Disease List	2018, 2023	To incentivize orphan drug development. - The 2018 list covers 121 rare diseases, and the list covers an additional 86 drugs in 2023. - Medicines targeted at rare diseases in the catalog are eligible for priority review, facilitating faster marketing authorization approval.
Pull Strategies		
Evidence-based Coverage Decisions	2009, 2016, 2019	- Introduce health technological assessment (HTA) to assess the cost and effect of innovative drugs. - HTA-assisted selection of innovative drugs into the National Reimbursement Drug List (NRDL). In 2018, 17 anticancer drugs were included in NRDL, and 70 additional drugs have been selected in 2019.
Intellectual Property Protection	2018	Provide data protection for innovative chemical drugs. - Innovative chemical drugs can enjoy a maximum 6-year data protection period during which no similar generic drug(s) will be reviewed or approved
Price Regulations		
Price Reform	2015	Shift from price-capped pricing system to classified pricing strategies. - For patent drugs and drugs provided by a single manufacturer, NHSA determines their inclusion on the NRDL and the prices to be reimbursed based on negotiation
NRDL Adjustments	2019	Drugs targeting cancer and rare diseases were included in the reimbursement list, with prices determined through negotiations. - Allowing pharmaceutical firms to seek renegotiation if the standard price cut is unsatisfactory.

5. Concluding Remarks

This report provides an overview of the internal and external factors influencing drug innovation activities within the rapidly growing Chinese pharmaceutical industry. Similar to innovation trends in other advanced markets such as the US and Japan, the expansion of the Chinese pharmaceutical industry is driven by demographic changes and a shift in disease

burden from infectious to chronic diseases. In contrast to other advanced markets, the industry remains highly fragmented, with most companies competing in the generics market. Only a few allocate substantial resources to R&D activities, given the lengthy and high-risk nature of the R&D process, from drug discovery through to approval.

Government regulations play a crucial role in incentivizing and shaping the direction of pharmaceutical R&D in China. Regulatory instruments such as fast-track drug review and approval processes are used to encourage the development of treatments for rare diseases over those for more common conditions, such as cardiovascular diseases. These incentives have increased pharmaceutical investment for high-risk, low-demand conditions, yet companies face price pressures. For example, securing a spot on government insurance lists guarantees sustained market presence but necessitates compulsory price cuts. While this approach enhances drug affordability for the public and reduces fiscal strain on the government, it raises concerns among pharmaceutical companies that price reductions could stifle innovation. The net impact of these compound policies on R&D investment remains unclear.

Empirically assessing the impact of government regulations can be challenging due to the difficulty in identifying the main drivers of innovative activities from multiple regulations. Furthermore, the task of evaluation is compounded by the availability of data and the intricacies involved in data compilation. In our next evaluation steps, we aim to encompass corporate and disease dimensions. This process requires integrating datasets sourced from various origins and lacking uniformity in product or corporate naming. The analyses will focus on pharmaceutical products and manufacturing firms organized by disease category or company.

Reference

Acemoğlu, D., & Linn, J. (2004). Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry. The Quarterly Journal of Economics, 119(3), 1049–1090.

Almeida, H., & Campello, M. (2007). Financial constraints, asset tangibility, and corporate investment. The Review of Financial Studies, 20(5), 1429–1460.

Arregui, N., & Shi, Y. (2023). Labor Productivity Dynamics in Spain: A Firm-Level Perspective: Spain. Selected Issues Paper No. 2023/002, International Monetary Fund.

Berndt, E. R., & Aitken, M. (2011). Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century after the 1984 Waxman-Hatch Legislation. International Journal of the Economics of Business, 18(2), 177–201.

Bloom, D. E., Cafiero, E., McGovern, M. E., Prettner, K., Stanciole, A., Weiss, J. A., Bakkila, S., & Rosenberg, L. (2014). The macroeconomic impact of non-communicable diseases in China and India: Estimates, projections, and comparisons. The Journal of the Economics of Ageing, 4, 100–111.

Blume-Kohout M.E., Sood N. (2013) Market size and innovation: Effects of Medicare Part D on pharmaceutical research and development. Journal Public Economics. 97, 327–336.

Brown, J. R., Martinsson, G., & Petersen, B. C. (2012). Do financing constraints matter for R&D? European Economic Review, 56(8), 1512–1529.

Campello, M., Graham, J. R., & Harvey, C. R. (2010). The real effects of financial constraints: Evidence from a financial crisis. Journal of Financial Economics, 97(3), 470–487.

Chen, Z., Liu, Z., Serrato, J. C. S., & Xu, D. Y. (2021). Notching R&D Investment with Corporate Income Tax Cuts in China. The American Economic Review, 111(7), 2065–2100.

Danzon, P. M., & Epstein, A. J. (2012). Effects of regulation on drug launch and pricing in interdependent markets. In Advances in health economics and health services research (pp. 35–71).

Dechezleprêtre, A., Einiö, E., Martin, R., Nguyen, K., & Van Reenen, J. (2023). Do Tax Incentives Increase Firm Innovation? An RD Design for R&D, Patents, and Spillovers. American Economic Journal: Economic Policy, 15(4), 486–521.

Dranove, D., Garthwaite, C., & Hermosilla, M. (2014). Pharmaceutical profits and the social value of innovation. NBER Working Papers 20212.

Dranove, D., Garthwaite, C., & Hermosilla, M. (2020). Expected profits and the scientific novelty of innovation. NBER Working Papers 27093.

Dubois, P., De Mouzon, O., Scott-Morton, F. M., & Seabright, P. (2015). Market size and pharmaceutical innovation. The RAND Journal of Economics, 46(4), 844–871.

Eger, S., & Mahlich, J. (2014). Pharmaceutical regulation in Europe and its impact on corporate R&D. Health Economics Review, 4(1).

Economic and Social Commission for Asia and the Pacific (ESCAP). (2023). Foreign direct investment and policies in the health sector in Aasia and the Pacific 2022/2023. United Nations, Bangkok.

fDi Intelligence (2019). AstraZeneca expands further into China's biotech sector. https://www.fdiintelligence.com/content/news/astrazeneca-expands-further-into-chinas-biotech-sector-76304

Finkelstein, A. (2004). Static and Dynamic Effects of Health Policy: Evidence from the Vaccine Industry. The Quarterly Journal of Economics, 119(2), 527–564.

Fishman, A., & Rob, R. (1999). The Size of Firms and R&D Investment. International Economic Review, 40(4), 915–931.

Galende, J., & González, I. S. (1999). A resource-based analysis of the factors determining a firm's R&D activities. Research Policy, 28(8), 891–905.

Ge, Q., Xu, L., DiMasi, J. A., Kaitin, K. I., & Shao, L. (2023). Impact of regulatory system changes on the availability of innovative drugs in China. Nature Reviews Drug Discovery, 22(5), 344–345.

Gebauer, S., Setzer, R., & Westphal, A. (2018). Corporate debt and investment: A firm-level analysis for stressed euro area countries. Journal of International Money and Finance, 86, 112–130.

Himmelberg, C. P., & Petersen, B. C. (1994). R&D and Internal Finance: A Panel Study of Small Firms in High-Tech Industries. The Review of Economics and Statistics, 76(1), 38.

Iizuka, T., & Uchida, G. (2017). Promoting innovation in small markets: Evidence from the market for rare and intractable diseases. Journal of Health Economics, 54, 56–65.

IQVIA. (2023). The Global Use of Medicines 2023: Outlook to 2027. Report. https://www.iqvia.com/insights/the-iqvia-institute/reports/global-medicine-spending-and-usage-trends-outlook-to-2025

Kong, L., Li, Q., Kaitin, K. I., & Shao, L. (2022). Innovation in the Chinese pharmaceutical industry. Nature Reviews Drug Discovery, 22(1), 12–13.

Kyle, M. (2020). The Alignment of Innovation Policy and Social Welfare: Evidence from Pharmaceuticals. Innovation Policy and the Economy, 20, 95–123.

Lichtenberg, F. R., & Waldfogel, J. (2003). Does Misery Love Company? Evidence from pharmaceutical markets before and after the Orphan Drug Act. NBER Working Papers 9750.

Li, X., & Zhang, L. (2024). Does mandating narrative disclosure of innovation help unveil the curtain of R&D expenditure? Evidence from regulation change in China. International Review of Financial Analysis, 91, 103000.

Lim, S. C., Macias, A. J., & Moeller, T. (2020). Intangible assets and capital structure. Journal of Banking and Finance, 118, 105873.

National Healthcare Security Administration (NHSA). (2023). 2023 National Drug Catalogue for Basic Medical Insurance, Work Injury Insurance and Maternity Insurance. Beijing: National Healthcare Security Administration.

National Medical Products Administration (NMPA) (2022). 2021 Annual statistics on drug supervision and management. Beijing: National Medical Products Administration.

OECD (2018), Pharmaceutical Innovation and Access to Medicines, OECD Health Policy Studies, OECD Publishing, Paris.

OECD (2024), Fiscal Sustainability of Health Systems: How to Finance More Resilient Health Systems When Money Is Tight?, OECD Publishing, Paris.

Park, Y., Shin, J. & Kim, T. (2010). Firm size, age, industrial networking, and growth: a case of the Korean manufacturing industry. Small Business Economics, 35, 153–168.

PhRMA (2023). Global Access to New Medicines Report., Pharmaceutical Research and Manufacturers of America, Washington.

Shao, L., Xu, L., Li, Q., Chakravarthy, R., Yang, Z., & Kaitin, K. I. (2016). Innovative drug availability in China. Nature Reviews Drug Discovery, 15(11), 739–740.

The United Nation (UN) (2022). World Population Prospects 2022: The 2022 Revision. United Nations Department of Economic and Social Affairs. https://population.un.org/wpp.

Vorreuther, C. M., & Warin, T. (2021). Patent relatedness and velocity in the Chinese pharmaceutical industry: A dataset of Jaccard similarity indices. Data in Brief, 35, 106814.

Wouters, O. J., McKee, M., & Luyten, J. (2020). Estimated research and development investment needed to bring a new medicine to market, 2009-2018. JAMA, 323(9), 844.

Wong, C. H., Siah, K. W., & Lo, A. W. (2018). Estimation of clinical trial success rates and related parameters. Biostatistics, 20(2), 273–286.

World Bank. (2011). Toward a Healthy and Harmonious Life in China: Stemming the Rising Tide of Non-Communicable Diseases. World Bank: Washington, DC.

World Health Organization (WHO). (2017). Ten years in public health, 2007–2017. World Health Organization: Geneva.

Zhang, W. (2015). R&D investment and distress risk. Journal of Empirical Finance, 32, 94–114.

Zhang, X., & Nie, H. (2021). Public health insurance and pharmaceutical innovation: Evidence from China. Journal of Development Economics, 148, 102578.

Zhou, M., Wang, H., Zeng, X., Yin, P., Zhu, J., Chen, W., Li, X., Wang, L., Wang, L., Liu, Y., Liu, J., Zhang, M., Qi, J., Yu, S., Afshin, A., Gakidou, E., Glenn, S., Krish, V., Miller-Petrie, M. K., . . . Liang, X. (2019). Mortality, morbidity, and risk factors in China and its provinces, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet, 394(10204), 1145–1158.

Appendix

Exhibit A1. Drugs approved both in the US and China, 2004-2022.

Therapeutic area	# Trade name	Average of Approval delay in years (US versus China)
Oncology	35	2.8
Infection	27	2.5
Endocrinology/ Metabolism	12	3.4
Cardiovascular	11	1.0
Neurology	9	2.1
Diagnostic Agent	7	0.0
Hematology	4	4.5
Rheumatology	4	2.4
Endocrinology and metabolism	3	2.4
Haematology	3	2.5
Psychiatry	3	2.1
Pulmonology	3	1.6
Urology	3	3.9
Analgesic	2	0.7
Gastroenterology	2	-2.4
Ophthalmology	2	4.5
Respiratory	2	3.6
Dermatology	1	3.7
Nephrology	1	7.3
Grand Total	**134**	**2.4**

Exhibit A2. Key Financial indicators for listed pharmaceutical companies in China, 2000-2022.

Year	Sample size	Has R&D spending (%)	Age (from the year of incorporation)	Total Assets (mil. USD)	Operating Revenue (mil. USD)	Number of employees (th)	Return on Asset (ROA)	Profit margin (%)
2000	36	0.06	27.10	169.29	92.62	2.60	6.44	17.18
2001	46	0.07	27.00	194.88	99.05	1.98	2.21	12.94
2002	59	0.07	26.38	173.36	100.98	2.62	5.83	12.87
2003	64	0.06	26.21	196.13	118.28	2.37	4.54	11.07
2004	67	0.07	26.17	208.21	125.41	2.89	3.61	9.37
2005	69	0.06	25.99	224.06	143.35	2.97	3.81	8.49
2006	80	0.06	25.58	219.60	147.39	2.63	4.57	8.57
2007	100	0.07	25.02	223.80	152.12	2.56	8.54	15.38
2008	112	0.09	24.49	227.47	174.99	2.53	9.41	14.40
2009	114	0.12	24.51	272.63	197.69	2.59	10.00	16.50
2010	116	0.55	24.48	358.82	245.79	2.63	8.68	17.47
2011	126	0.72	24.26	430.87	290.88	2.77	8.30	17.59
2012	144	0.72	23.84	451.42	300.06	3.28	8.16	16.84
2013	155	0.84	23.51	509.44	341.02	3.24	7.96	16.74
2014	176	0.92	23.06	547.25	339.70	2.89	8.64	17.53
2015	178	0.93	22.99	621.59	349.98	3.01	7.67	17.65
2016	181	0.93	22.97	670.58	357.92	3.03	7.50	18.65
2017	184	0.95	22.95	824.72	428.14	3.13	6.92	17.59
2018	187	0.99	22.95	860.44	461.81	3.24	5.76	12.91
2019	188	1.00	22.96	875.46	488.91	3.36	4.45	13.11
2020	188	1.00	22.91	982.14	514.09	3.26	4.04	10.06
2021	188	1.00	22.93	1076.03	574.77	3.42	5.06	10.86
2022	188	0.99	22.96	1055.63	542.15	3.35	3.82	8.91

An Overview of Innovative Activities in the Chinese Pharmaceutical Industry: Market Trends, Firm Financial Capacity, and Regulatory Environment

令和 6 年 3 月発行

発行所　公益財団法人アジア成長研究所
〒803-0814　北九州市小倉北区大手町 11 番 4 号
Tel：093-583-6202／Fax：093-583-6576
URL：https://www.agi.or.jp
E-mail：office@agi.or.jp