

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A. Reserved.

B. Capitalization and Indebtedness.

Not applicable.

C. Reasons for the Offer and Use of Proceeds.

Not applicable.

D. Risk Factors.

HUTCHMED (China) Limited is a Cayman Islands holding company which conducts its operations in China through its PRC subsidiaries (our corporate group does not utilize any variable interest entities). We face various legal and operational risks and uncertainties as a company with substantial operations in China. The PRC government has significant authority to exert influence on the ability of a company with substantial operations in China, like us, to conduct its business, accept foreign investments or be listed on a U.S. stock exchange. For example, we face risks associated with PRC regulatory approvals of offshore offerings, anti-monopoly regulatory actions, cybersecurity, data privacy and from U.S. regulators if there is a lack of inspection from the U.S. Public Company Accounting Oversight Board, or PCAOB, on our auditors, which is further discussed below under “Holding Foreign Companies Accountable Act” and in various risk factors in this section. The PRC government may also intervene with or influence our operations as the government deems appropriate to further regulatory, political and societal goals. The PRC government publishes from time to time new policies that can significantly affect our industry and we cannot rule out the possibility that it will in the future further release regulations or policies regarding our industry that could adversely affect our business, financial condition and results of operations. Any such action, once taken by the PRC government, could cause the value of our ADSs and ordinary shares to significantly decline or in extreme cases, become worthless.

Holding Foreign Companies Accountable Act

Pursuant to the Holding Foreign Companies Accountable Act, or the HFCAA, if the SEC determines that we have filed audit reports issued by a registered public accounting firm that has not been subject to inspections by the PCAOB for two consecutive years, the SEC will prohibit our shares or the ADSs from being traded on a national securities exchange or in the over-the-counter trading market in the United States. On December 16, 2021, the PCAOB issued a report to notify the SEC of its determination that the PCAOB was unable to inspect or investigate completely registered public accounting firms headquartered in mainland China and Hong Kong, including our auditor. In March 2022, the SEC conclusively listed us as a Commission-Identified Issuer under the HFCAA following the filing of our annual report on Form 20-F for the fiscal year ended December 31, 2021. On December 15, 2022, the PCAOB issued a report that vacated its December 16, 2021 determination and removed mainland China and Hong Kong from the list of jurisdictions where it is unable to inspect or investigate completely registered public accounting firms. As a result, the SEC will not provisionally or conclusively identify an issuer as a Commission-Identified Issuer if it files an annual report with an audit report issued by a registered public accounting firm headquartered in mainland China or Hong Kong on or after December 15, 2022, until such time as the PCAOB issues a new determination. Whether the PCAOB will continue to be able to satisfactorily conduct inspections of PCAOB-registered public accounting firms headquartered in mainland China and Hong Kong in the future is subject to uncertainty and depends on a number of factors out of our, and our auditor's, control, including the uncertainties surrounding the relationship between China and the United States. If PCAOB determines in the future that it no longer has full access to inspect and investigate completely accounting firms in mainland China and Hong Kong and we continue to use an accounting firm headquartered in one of these jurisdictions to issue an audit report on our financial statements filed with the Securities and Exchange Commission, we would be identified as a Commission-Identified Issuer following the filing of the annual report on Form 20-F for the relevant fiscal year. There can be no assurance that we would not be identified as a Commission-Identified Issuer for any future fiscal year, and if we were so identified for two consecutive years, we would become subject to the prohibition on trading under the HFCAA. See Item 3.D. "Risk Factors—Risks Relating to our ADSs—The PCAOB had historically been unable to inspect our auditor in relation to their audit work performed for our financial statements and the inability of the PCAOB to conduct inspections of our auditor in the past has deprived our investors with the benefits of such inspections." and Item 3.D. "Risk Factors—Risks Relating to our ADSs—Our ADSs may be prohibited from trading in the United States under the HFCAA in the future if the PCAOB is unable to inspect or investigate completely auditors located in China. The delisting of the ADSs, or the threat of their being delisted, may materially and adversely affect the value of your investment."

Permissions, Approvals, Licenses and Permits Required from the PRC Authorities for Our Operations and for the Offering of Our Securities

We conduct our business primarily through our subsidiaries and joint ventures in China. Our operations in China are governed by PRC laws and regulations. As of the date of this annual report, we and our non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals, have obtained the requisite permissions, approvals, licenses and permits from the PRC government authorities that are material for the business operations of our subsidiaries and our joint ventures in China, including, among others, pharmaceutical manufacturing permits, business licenses, drug registration certificates and pharmaceutical distribution permits and no such material permission or approval has been denied. For a detailed discussion on the licenses and permits we and our non-consolidated joint venture are required to obtain as a pharmaceutical company operating in China, see Item 4.B. "Business Overview—Certificates and Permits", "Business Overview—Regulations—Government Regulation of Pharmaceutical Product Development and Approval," "Business Overview—Regulations—Coverage and Reimbursement" and "Business Overview—Regulations—Other Healthcare Laws." Given the uncertainties of interpretation and implementation of relevant laws and regulations and the enforcement practice by relevant government authorities, we may be required to obtain additional requisite permissions, approvals, licenses, permits and filings for the operation of our business in the future. See also "Risks Relating to Sales of Our Internally Developed Drugs and Other Drugs—Pharmaceutical companies in China are required to comply with extensive regulations and hold a number of permits and licenses to carry on their business. Our and our joint ventures' ability to obtain and maintain these regulatory approvals is uncertain, and future government regulation may impose additional burdens on our operations."

Furthermore, the PRC government has recently indicated an intent to exert more oversight and control over offerings that are conducted overseas and/or foreign investment in China-based issuers. For example, the CSRC published the Trial Measures and Listing Guidelines (defined below) on February 17, 2023 and became effective on March 31, 2023, designed to regulate overseas securities offerings by PRC domestic companies. Given the recent nature of the introduction of the Trial Measures and Listing Guidelines, there remains significant uncertainty as to the interpretation and implementation of regulatory requirements related to overseas securities offerings and other capital markets activities. As of the date of this annual report, in connection with our historical issuance of securities to foreign investors, we are not aware of any currently effective PRC laws, regulations and regulatory rules that would require us or our non-consolidated joint venture to obtain permissions from the China Securities Regulatory Commission (the “CSRC”), and we have not received any formal notice from any PRC authority indicating that we should apply for such permission or are subject to cybersecurity review or security assessment. If (i) we mistakenly conclude that certain regulatory filings, permissions and approvals are not required or (ii) applicable laws, regulations, or interpretations change and (iii) we are required to obtain such filings, permissions or approvals in the future, but fail to receive or maintain such filings, permissions or approvals, we may face sanctions by the CSRC, the Cyberspace Administration of China (the “CAC”) or other PRC regulatory agencies. In addition, rules and regulations in China can change with little advance notice. These regulatory agencies may impose fines and penalties on our operations in China, limit our operations in China, limit our ability to pay dividends outside of China, limit our ability to list on stock exchanges outside of China or offer our securities to foreign investors or take other actions that could have a material adverse effect on our business, financial condition, results of operations and prospects, as well as the trading price of our securities. Our non-consolidated joint venture faces the same risks as well. See also “Other Risks and Risks Relating to Doing Business in China—The PRC government exerts substantial influence over the manner in which we conduct our business activities. Its oversight and discretion over our business could result in a material adverse change in our operations and the value of our ordinary shares and ADSs. Changes in laws, regulations and policies in China and uncertainties with respect to the PRC legal system could materially and adversely affect us.” and “—The PRC government has increasingly strengthened oversight in offerings conducted overseas or on foreign investment in China-based issuers, which could result in a material change in our operations and our ordinary shares and ADSs could decline in value or become worthless.”

Cash Flows Through Our Organization

HUTCHMED (China) Limited is a Cayman Islands incorporated holding company with no material operations of its own. We conduct our operations primarily in China through our PRC subsidiaries and non-consolidated joint ventures, collectively referred to as the Onshore Entities below. HUTCHMED (China) Limited has an indirect equity ownership interest in all Onshore Entities through offshore Hong Kong-incorporated holding companies, and it has received funding through various capital markets transactions. We also fund our operations through cash flows generated and dividend payments from our Oncology/Immunology and Other Ventures operations (substantially all of which have been generated in China), service and milestone and upfront payments from our collaboration partners to our PRC subsidiaries, and bank loans to our subsidiaries.

We utilize a portion of our funds outside of China to support the operations of our subsidiaries in China through capital contributions and/or shareholder loans, which are the only methods by which we can fund our subsidiaries under PRC laws and regulations. Such capital contributions and shareholder loans are subject to the satisfaction of applicable government registration and approval requirements in China and limitations on the amount of shareholder loans relative to the amount of total capital contributions. If such subsidiaries generate sufficient income, they may repay shareholder loans or distribute retained earnings through cash dividends as determined by their respective board of directors. Our PRC subsidiaries are permitted to pay dividends only out of their retained earnings, if any, as determined in accordance with PRC accounting standards and regulations. Furthermore, our PRC subsidiaries are required to make appropriations to certain statutory reserve funds or may make appropriations to certain discretionary funds, which are not distributable as cash dividends except in the event of a solvent liquidation of the companies. The amount of any repayment of shareholder loans or dividend payments can be distributed to our various offshore subsidiaries through our offshore Hong Kong-incorporated holding companies. For more information, see Item 3.D. “Risk Factors—Other Risks and Risks Relating to Doing Business in China—Restrictions on currency exchange may limit our ability to receive and use our revenue effectively.” and Item 4.B. “Business Overview—Regulations—PRC Regulation of Foreign Currency Exchange, Offshore Investment and State-Owned Assets—Regulation on Investment in Foreign Invested Enterprises.” Our joint ventures in China do not require intra-group funding as they have been profitable. Service and milestone and upfront payments from our collaboration partners are received directly by our PRC subsidiaries and reinvested into their operations.

For the years ended December 31, 2023, 2022 and 2021, HUTCHMED provided funds to its PRC subsidiaries of \$20.0 million, \$310.0 million and \$230.0 million, respectively, of which \$20.0 million, \$100.0 million and \$100.0 million, respectively, were in the form of capital contributions and nil, \$210.0 million and \$130.0 million, respectively, were in the form of shareholder loans. Additionally, during the years ended December 31, 2023 and 2022, shareholder loans of approximately \$2.6 million and \$3.4 million were repaid by a PRC subsidiary, respectively. There were no transfers of assets other than transfers of cash to/from PRC subsidiaries in 2023, 2022 and 2021.

For the years ended December 31, 2023, 2022 and 2021, the Hong Kong immediate holding company of our onshore non-consolidated joint venture, Shanghai Hutchison Pharmaceuticals, received dividends totaling approximately \$42.3 million, \$43.7 million and \$49.9 million, respectively. These dividends were subject to a 5% withholding tax upon distribution from Shanghai Hutchison Pharmaceuticals to its Hong Kong immediate holding company.

HUTCHMED also conducts operations outside of China through subsidiaries in the U.S. and E.U. Such subsidiaries in the U.S. and E.U. have entered into service agreements with our PRC subsidiaries pursuant to which cash is transferred by our PRC subsidiaries to them to support their operations via the settlement of service invoices based on actual activities.

We have comprehensive cash management policies in place, including specific policies with respect to fund transfers through our organization. Our management regularly monitors the liquidity position and funding requirements of our subsidiaries and joint ventures. When funding is required by our operations in China, a thorough assessment is performed on the purpose of the funding (e.g., R&D investment, capital expenditures, etc.), the amount of funding and the form of injection (i.e., shareholder loans or capital contributions). Conversely, when a dividend distribution is to be made by an onshore joint venture, a similar assessment is performed on the cash flow forecast, sufficiency of funds and related factors. All necessary approvals are obtained at the chairman and chief executive officer levels and the board of directors for the relevant entities prior to any transfer. All such transfers and distributions are reviewed and approved by the relevant authorities where necessary, including the State Administration of Foreign Exchange, or SAFE, and the State Administration for Market Regulations, or SAMR. Our cash management policies and procedures also govern the management of any funds that are not yet required by our operations. Such funds are retained by our subsidiaries outside of China mainly in the form of short-term investments, such as time deposits with major banks in Hong Kong.

We have never declared or paid dividends on our ordinary shares. There have been no transfers, dividends or distributions made to U.S. investors to date. We currently expect to retain all future earnings for use in the operation and expansion of our business and do not have any present plan to pay any dividends. The declaration and payment of any dividends in the future will be determined by our board of directors in its discretion, and will depend on a number of factors, including our earnings, capital requirements, overall financial condition, and contractual restrictions. See Item 8. "Financial Information—A.8 Dividend Policy" and Item 3.D. "Risk Factors—Risks Relating to Our ADSs—We do not currently intend to pay dividends on our securities, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of the ADSs."

You should carefully consider all of the information in this annual report before making an investment in the ADSs. Below please find a summary of the principal risks and uncertainties we face, organized under relevant headings. In particular, as we are a China-based company incorporated in the Cayman Islands, you should pay special attention to subsections headed "Item 3. Key Information—3.D. Risk Factors—Other Risks and Risks Related to Doing Business in China."

The following summarizes some, but not all, of the risks provided below. Please carefully consider all of the information discussed in this Item 3.D. "Risk Factors" in this annual report for a more thorough description of these and other risks.

Risks Relating to Our Financial Position and Need for Capital

- Risks relating to our need for additional funding
- Risks relating to our existing and future indebtedness

Risks Relating to Our Oncology/Immunology Operations and Development of Our Drug Candidates

- Risks relating to our approach to the discovery and development of drug candidates and the lengthy, expensive and uncertain clinical development process

- Risks relating to expediting regulatory review, obtaining and maintaining regulatory approval and ongoing regulatory review for our drug candidates
- Risks relating to the commercialization of our drug candidates
- Risks relating to undesirable side effects of our drug candidates
- Risks relating to competition in discovering, developing and commercializing drugs
- Risks relating to our collaboration partners with respect to clinical trials, marketing and distribution
- Risks relating to our international operations

Risks Relating to Sales of Our Internally Developed Drugs and Other Drugs

- Risks relating to obtaining and maintaining permits and licenses for our and our joint ventures' pharmaceutical operations in China
- Risks relating to leveraging our Other Ventures' prescription drug business to commercialize our internally developed drug candidates
- Risks relating to competition in selling our approved, internally developed drugs and drugs of our Other Ventures
- Risks relating to maintaining and enhancing the brand recognition of our drugs
- Risks relating to the availability of reimbursement of our drugs, the lack of which could diminish our sales or profitability
- Risks relating to counterfeit products in China
- Risks relating to rapid changes in the pharmaceutical industry rendering our products obsolete
- Risks relating to cultivating or sourcing raw materials
- Risks relating to adverse publicity of us, our collaboration partners, our joint ventures or our products

Risks Relating to Our Dependence on Third Parties

- Risks relating to disagreements with current or future collaboration partners which we rely on for certain drug development activities including the conducting of clinical trials, manufacturing and commercialization of our medicines
- Risks relating to relying on third party suppliers for the active pharmaceutical ingredients in our drug candidate and drug products
- Risks relating to our collaboration partners or our CROs' failure to comply with regulatory requirements pertaining to clinical trials
- Risks relating to our collaboration partners, principal investigators, CROs and other third-party contractors and consultants engaging in misconduct or other improper activities
- Risks relating to relying on distributors for logistics and distributions services
- Risks relating to the availability of benefits currently enjoyed by virtue of our association with CK Hutchison

Other Risks and Risks Relating to Doing Business in China

- Risks relating to compliance with privacy and cybersecurity laws, information security policies and contractual obligations related to data privacy and security and any information technology or data security failures
- Risks relating to product liability claims or lawsuits
- Risks relating to liabilities under anti-corruption laws, environmental, health and safety laws and laws relating to equity incentive plans
- Risks relating to changes in laws, regulations and policies in China and uncertainties with respect to the PRC legal system, China's currency exchange limits and PRC government tax incentives or treatment

Risks Relating to Intellectual Property

- Risks relating to our, our joint ventures and our collaboration partners' abilities to protect and enforce intellectual property rights and maintain confidentiality of trade secrets
- Risks relating to infringing upon third parties' intellectual property rights

Risks Relating to our ADSs

- Risks relating to being delisted from the Nasdaq if the PCAOB is unable to inspect or investigate completely auditors located in China in the future
- Risks relating to our largest shareholder which may limit the ability of other shareholders to influence corporate matters

You should carefully consider the following risk factors in addition to the other information set forth in this annual report. If any of the following risks were actually to occur, our company's business, financial condition and results of operations prospects could be adversely affected and the value of our ADSs would likely suffer.

Risks Relating to Our Financial Position and Need for Capital

We may need substantial additional funding for our product development programs and commercialization efforts. If we are unable to raise capital on acceptable terms when needed, we could incur losses and be forced to delay, reduce or eliminate such efforts.

We expect to incur significant expenses in connection with our ongoing activities, particularly as we or our collaboration partners advance the clinical development of our clinical drug candidates which are currently in active or completed clinical studies in various countries. We will incur significant expenses as we continue research and development and initiate additional clinical trials of, and seek regulatory approval for, these and other future drug candidates. In addition, we have incurred and expect to continue to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution in China for surufatinib (marketed as Sulanda), our unpartnered drug product approved in China in December 2020, and any of our other unpartnered drug candidates that may be approved in the future. For example, the costs that may be required for the manufacture of any drug candidate that receives regulatory approval may be substantial as we may have to modify or increase the production capacity at our current manufacturing facilities or contract with third-party manufacturers. We may also incur expenses as we create additional infrastructure to support the research and development, commercialization and manufacturing of our drug products and candidates.

As a result, we have experienced negative cash flows from operations in the past. Our net cash used in operating activities was \$204.2 million and \$268.6 million for the years ended December 31, 2021 and 2022, respectively. Even though we generated significant amount of net cash of \$219.3 million from our operating activities in 2023, this may not continue in the future as it depends on a variety of factors, including but not limited to:

- the number and development requirements of the drug candidates we pursue;
- the scope, progress, timing, results and costs of researching and developing our drug candidates, and conducting pre-clinical and clinical trials;
- the cost, timing and outcome of regulatory review of our drug candidates;
- the cost and timing of commercialization activities, including product manufacturing, marketing, sales and distribution, for our drug candidates for which we have received regulatory approval;
- the amount and timing of any upfront milestone or royalty payments, service payments and reimbursement of manufacturing costs from our collaboration partners, with whom we cooperate with respect to the development and potential commercialization of certain of our drug candidates;
- the cash received from commercial sales of drug candidates for which we have received regulatory approval;
- our ability to establish and maintain strategic partnerships, collaboration, licensing or other arrangements and the financial terms of such agreements; and
- the cost, timing and outcome of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims.

Accordingly, we may need to obtain substantial funding in connection with our continuing operations through public or private equity offerings, debt financings, collaborations or licensing arrangements or other sources. If we are unable to raise capital when needed or on attractive terms to supplement the cash generated from operating activities to support our operations, we could incur losses and be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Raising capital may dilute our shareholders, restrict our operations or require us to relinquish rights to technologies or drug candidates.

We expect to finance our cash needs in part through cash flow from our operations, and we may also rely on raising capital through a combination of public or private equity offerings, debt financings and/or license and development agreements with collaboration partners. In addition, we may seek capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise capital through the sale of equity or convertible debt securities (including potential further listings on other stock exchanges), the ownership interest of our shareholders may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect the rights of our existing shareholders. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends. Additional debt financing would also result in increased fixed payment obligations.

In addition, if we raise funds through collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or drug candidates or grant licenses on terms that may not be favorable to us. We may also lose control of the development of drug candidates, such as the pace and scope of clinical trials, as a result of such third-party arrangements. If we are unable to raise funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

Our existing and any future indebtedness could adversely affect our ability to operate our business.

Our outstanding indebtedness combined with current and future financial obligations and contractual commitments, including any additional indebtedness beyond our current loan facilities could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, and prepayment and repayment fees and penalties, thereby reducing money available to fund working capital, capital expenditures, product development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents and short-term investments. Nevertheless, we may not have sufficient funds, and may be unable to arrange for financing, to pay the amounts due under our existing debt. Failure to make payments or comply with other covenants under our existing debt instruments could result in an event of default and acceleration of amounts due.

We have historically incurred significant net operating cash outflows, and may continue to experience net cash outflow from operating activities.

Investment in biopharmaceutical drug development is highly speculative. It entails substantial upfront expenditures and significant risk that a drug candidate might fail to gain regulatory approval or become commercially viable. Therefore, we expect to continue to incur significant expenses related to our ongoing operations, particularly research and development expenses, for the foreseeable future as we expand our development of, and seek regulatory approvals for, our drug candidates. We have historically generated net cash outflows from operations in 2021 and 2022. Although our net cash from operations turned positive in 2023, there is no guarantee that we will be able to continue to do so in the future as our operating cash flows depend on a number of variables that we may not be able to accurately predict or fully control, including the number and scope of our drug development programs and the associated cost of those programs, the cost of commercializing any approved products, our ability to generate revenue and the timing and amount of milestones and other payments we make or receive through arrangements with third parties. Our failure to generate positive cash flow from operations may adversely affect our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

We face risks with our short-term investments and in collecting our accounts receivables.

Our short-term investments are bank deposits with maturities of more than three months but less than one year. Our short-term investments were \$317.7 million and \$602.7 million as of December 31, 2022 and 2023, respectively, and are placed with major financial institutions. These investments may earn yields substantially lower than expected. Failure to realize the benefits we expected from these investments may materially and adversely affect our business and financial results. To date, we have experienced no loss or lack of access to our invested cash or cash equivalents; however, we can provide no assurance that access to our invested cash and cash equivalents will not be impacted by adverse conditions in the financial and credit markets.

Our accounts receivable balance, net of allowance for credit losses, totaled \$98.0 million and \$116.9 million as of December 31, 2022 and 2023, respectively. We have policies and procedures in place to ensure that sales are made to customers with an appropriate credit history. We perform periodic credit evaluations of our customers and monitor risk factors and forward-looking information, such as country risk, when determining credit limits for customers. However, there can be no assurance such policies and procedures will effectively limit our credit risk and enable us to avoid losses, which could adversely affect our financial condition and results of operations. In addition, amounts due to us are not covered by collateral or credit insurance. If we fail to collect all or part of such accounts receivable in a timely manner, or at all, our financial condition may be materially and adversely affected.

Risks Relating to Our Oncology/Immunology Operations and Development of Our Drug Candidates

Our Oncology/Immunology operations historically operated at a net loss, and our future profitability is dependent on the performance of our Oncology/Immunology operations which rely on the successful commercialization of our drug candidates.

To date, savolitinib, fruquintinib and surufatinib (marketed as Orpathys, Elunate and Sulanda, respectively in China and in the U.S. for fruquintinib as Fruzaqla) are our only internally developed drug candidates that have been approved for sale. We do not expect our Oncology/Immunology operations to be significantly profitable unless and until we consistently generate substantial revenue from them and can successfully commercialize our other drug products.

Successful commercialization of our drug candidates is subject to many risks. Savolitinib is marketed as Orpathys in collaboration with our partner, AstraZeneca. We have partnered with Eli Lilly and Takeda on the commercialization of fruquintinib. Surufatinib is marketed by us as Sulanda without the support of a collaboration partner. Savolitinib, fruquintinib and surufatinib are the first innovative oncology drugs we, as an organization, have commercialized, and there is no guarantee that we or our collaboration partners will be able to successfully commercialize them or any of our other drug candidates for their approved indications. There are numerous examples of failures to meet expectations of market potential, including by pharmaceutical companies with more experience and resources than us. There are many factors that could cause the commercialization of savolitinib, fruquintinib and surufatinib or our other drug products to be unsuccessful, including a number of factors that are outside our control. In the case of fruquintinib, for example, the third-line metastatic colorectal cancer, or mCRC, patient population in China may be smaller than we estimate or physicians may be unwilling to prescribe, or patients may be unwilling to take, fruquintinib for a variety of reasons. Additionally, any negative development for fruquintinib, surufatinib or savolitinib in clinical development in additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of savolitinib, fruquintinib and surufatinib in China and globally. For example, in April 2022, the FDA issued a Complete Response Letter regarding the NDA for surufatinib for the treatment of non-pancreatic neuroendocrine tumors (NETs) and pancreatic NETs and determined that the data package submitted did not support an approval in the U.S. at the time. We subsequently withdrew our submissions to the FDA and the EMA for surufatinib. Thus, significant uncertainty remains regarding the commercial potential of savolitinib, fruquintinib and surufatinib.

Although our operations were profitable in 2023, we may not continue to achieve profitability based on the revenue to be generated from savolitinib, fruquintinib and surufatinib and/or our other drug candidates, if ever. If the commercialization of savolitinib, fruquintinib, surufatinib and/or our other drug candidates is unsuccessful or perceived as disappointing, our stock price could decline significantly and the long-term success of the product and our company could be harmed.

All of our drug candidates are still in development. If we are unable to obtain regulatory approval and ultimately commercialize our drug candidates, or if we experience significant delays in doing so, our business will be materially harmed.

All of our drug candidates are still in development, including those that have already received approval for the treatment of certain indications in China and United States. Although we may receive payments from our collaboration partners, including upfront payments and payments for achieving development, regulatory or commercial milestones, for certain of our drug candidates, our ability to generate significant revenue from our drug candidates is dependent on their receipt of additional regulatory approval and successful commercialization, which may never occur. Each of our drug candidates in development will require additional pre-clinical and/or clinical trials, regulatory approval in multiple jurisdictions, and substantial investment in manufacturing and significant efforts before we generate significant revenue from product sales. The success of our drug candidates will depend on several factors, including the following:

- successful completion of additional pre-clinical and/or clinical trials;
- successful enrollment in, and completion of, additional clinical trials;
- receipt of additional regulatory approvals from applicable regulatory authorities for planned clinical trials, future clinical trials, drug registrations or post-approval trials;
- successful completion of all studies required to obtain regulatory approval and/or fulfillment of post-approval requirements in the United States, China, Europe, Japan and other jurisdictions for our drug candidates;
- adapting our commercial manufacturing capabilities to the specifications for our drug candidates for clinical supply and commercial manufacturing;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our drug candidates;
- launching commercial sales of our drug candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the drug candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- enforcing and defending intellectual property rights and claims; and
- maintaining a continued acceptable safety profile of the drug candidates following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our drug candidates, which would materially harm our business.

Our primary approach to the discovery and development of drug candidates focuses on the inhibition of kinases, some of which are unproven.

A primary focus of our research and development efforts is on identifying kinase targets for which drug compounds previously developed by others affecting those targets have been unsuccessful due to limited selectivity, off-target toxicity and other problems. We then work to engineer drug candidates which have the potential to have superior efficacy, safety and other features as compared to such prior drug compounds. We also focus on developing drug compounds with the potential to be global best-in-class/next-generation therapies for validated kinase targets.

Even if we are able to develop compounds that successfully target the relevant kinases in pre-clinical studies, we may not succeed in demonstrating safety and efficacy of the drug candidates in clinical trials. Even if we are able to demonstrate safety and efficacy of compounds in certain indications in certain jurisdictions, we may not succeed in demonstrating the same in other indications or in the same indications in other jurisdictions. As a result, our efforts may not result in the discovery or development of drugs that are commercially viable or superior to existing drugs or other therapies on the market. While the results of pre-clinical studies, early-stage clinical trials as well as clinical trials in certain indications have suggested that certain of our drug candidates may successfully inhibit kinases and may have significant utility in several cancer indications, potentially in combination with other cancer drugs, chemotherapy and immunotherapies, we have not yet demonstrated efficacy and safety for many of our drug candidates in later stage clinical trials.

We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we must limit our research programs to specific drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. In addition, if we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements when it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate.

The regulatory approval processes of the U.S. Food and Drug Administration, or FDA, National Medical Products Administration of China, or NMPA, EMA, PDMA and comparable authorities in other countries are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, our ability to generate revenue will be materially impaired.

Our drug candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export, are subject to comprehensive regulation by the FDA, NMPA, EMA, PDMA and other regulatory agencies in the United States, China, Europe, Japan and by comparable regulatory authorities in other countries. Securing regulatory approval requires the submission of extensive pre-clinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our drug candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use.

The process of obtaining regulatory approvals in the United States, China, Europe, Japan and other countries is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. Changes in regulatory approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted New Drug Application, or NDA, pre-market approval or equivalent application types, may cause delays in the approval or rejection of an application. The FDA, NMPA, EMA, PDMA and comparable regulatory authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional pre-clinical, clinical or other studies. Our drug candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA, NMPA, EMA, PDMA or comparable regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, NMPA, EMA, PDMA or comparable regulatory authorities that a drug candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, NMPA, EMA, PDMA or comparable regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;

- the FDA, NMPA, EMA, PDMA or comparable regulatory authorities may disagree with our interpretation of data from pre-clinical studies or clinical trials;
- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA, NMPA, EMA, PDMA or comparable regulatory authorities may fail to approve the manufacturing processes for our clinical and commercial supplies;
- the approval policies or regulations of the FDA, NMPA, EMA, PDMA or comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval;
- the FDA, NMPA, EMA, PDMA or comparable regulatory authority may prioritize treatments for emerging health crises, such as COVID-19, resulting in delays for our drug candidates;
- the FDA, NMPA, EMA, PDMA or comparable regulatory authorities may restrict the use of our products to a narrow population; and
- our collaboration partners or CROs that are retained to conduct the clinical trials of our drug candidates may take actions that materially and adversely impact the clinical trials.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our drugs, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

Furthermore, even though the NMPA has granted approval for fruquintinib and surufatinib for use in third-line mCRC and NET patients, respectively, and approval for savolitinib for lung cancer with MET exon 14 skipping alterations, we are still subject to substantial, ongoing regulatory requirements. See “—Even if we receive regulatory approval for our drug candidates, we are subject to ongoing obligations and continued regulatory review, which may result in significant additional expense.”

If the FDA, NMPA, EMA, PDMA or another regulatory agency revokes its approval of, or if safety, efficacy, manufacturing or supply issues arise with, any therapeutic that we use in combination with our drug candidates, we may be unable to market such drug candidate or may experience significant regulatory delays or supply shortages, and our business could be materially harmed.

We are currently developing combination therapies using our savolitinib, fruquintinib, surufatinib and other drug candidates with various immunotherapies, targeted therapies and/or other therapies. For example, we are currently developing savolitinib in combination with immunotherapy (Imfinzi) and targeted therapy (Tagrisso). However, we did not develop and we do not manufacture or sell Imfinzi, Tagrisso or any other therapeutic we use in combination with our drug candidates. We may also seek to develop our drug candidates in combination with other therapeutics in the future.

If the FDA, NMPA, EMA, PDMA or another regulatory agency revokes its approval, or does not grant approval, of any of these and other therapeutics we use in combination with our drug candidates, we will not be able to market our drug candidates in combination with such therapeutics. If safety or efficacy issues arise with these or other therapeutics that we seek to combine with our drug candidates in the future, we may experience significant regulatory delays, and we may be required to redesign or terminate the applicable clinical trials. In addition, if manufacturing or other issues result in a supply shortage of these or any other combination therapeutics, we may not be able to complete clinical development of savolitinib, fruquintinib, surufatinib and/or any other of our drug candidates on our current timeline or at all.

Even if one or more of our drug candidates were to receive regulatory approval for use in combination with a therapeutic, we would continue to be subject to the risk that the FDA, NMPA, EMA, PDMA or another regulatory agency could revoke its approval of the combination therapeutic, or that safety, efficacy, manufacturing or supply issues could arise with one of these combination therapeutics. This could result in savolitinib, fruquintinib, surufatinib or one of our other products being removed from the market or being less successful commercially.

We face substantial competition, and our competitors may discover, develop or commercialize drugs before or more successfully than we do.

The development and commercialization of new drugs is highly competitive. We face competition with respect to our current drug candidates, and will face competition with respect to any drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market drugs or are pursuing the development of therapies in the field of kinase inhibition for cancer and other diseases. Some of these competitive drugs and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Specifically, there are a large number of companies developing or marketing treatments for cancer and immunological diseases, including many major pharmaceutical and biotechnology companies.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we or our collaborators may develop. Our competitors also may obtain FDA, NMPA, EMA, PDMA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Clinical development involves a lengthy and expensive process with an uncertain outcome.

There is a risk of failure for each of our drug candidates. It is difficult to predict when or if any of our drug candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining regulatory approval from regulatory authorities for the sale of any drug candidate, we or our collaboration partners must complete pre-clinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive, difficult to design and implement and can take many years to complete. The outcomes of pre-clinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain regulatory approval of their drug candidates. Our current or future clinical trials may not be successful.

Commencing each of our clinical trials is subject to finalizing the trial design based on ongoing discussions with the FDA, NMPA, EMA, PDMA or other regulatory authorities. The FDA, NMPA, EMA, PDMA and other regulatory authorities could change their position on the acceptability of our trial designs or clinical endpoints, which could require us to complete additional clinical trials or impose approval conditions that we do not currently expect. Successful completion of our clinical trials is a prerequisite to submitting an NDA or analogous filing to the FDA, NMPA, EMA, PDMA or other regulatory authorities for each drug candidate and, consequently, the ultimate approval and commercial marketing of our drug candidates. We do not know whether any of our clinical trials will begin or be completed on schedule, if at all.

We and our collaboration partners may incur additional costs or experience delays in completing our pre-clinical or clinical trials, or ultimately be unable to complete the development and commercialization of our drug candidates.

We and our collaboration partners, including AstraZeneca, Eli Lilly, Takeda, BeiGene Ltd., or BeiGene, Inmagene, Innovent Biologics (Suzhou) Co., Inc., or Innovent, Genor Biopharma Co. Ltd., or Genor, Shanghai Junshi Biosciences Co. Ltd., or Junshi and Epizyme, Inc. (a subsidiary of Ipsen Pharma SAS), or Epizyme may experience delays in completing our pre-clinical or clinical trials, and numerous unforeseen events could arise during, or as a result of, future clinical trials, which could delay or prevent us from receiving regulatory approval, including:

- regulators, institutional review boards, or IRBs, ethics committees or the China Human Genetic Resources Administration Office may not authorize us or our investigators to commence or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or we may fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs, who conduct clinical trials on behalf of us and our collaboration partners, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials may produce negative or inconclusive results, and we or our collaboration partners may decide, or regulators may require us or them, to conduct additional clinical trials or we may decide to abandon drug development programs;
- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- third-party contractors used in our clinical trials may fail to comply with regulatory requirements or meet their contractual obligations in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we or our collaboration partners add new clinical trial sites or investigators;
- we or our collaboration partners may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research for various reasons, including non-compliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our drug candidates may be greater than we anticipate;
- the supply or quality of our drug candidates, companion diagnostics, if any, or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate; and
- our drug candidates may have undesirable side effects or unexpected characteristics, causing us or our investigators, regulators, IRBs or ethics committees to suspend or terminate the trials, or reports may arise from pre-clinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our drug candidates.

We could encounter regulatory delays if a clinical trial is suspended or terminated by us or our collaboration partners, by, as applicable, the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, which is an independent group of experts that is formed to monitor clinical trials while ongoing, or by the FDA, NMPA, EMA, PDMA or other regulatory authorities. Such authorities may impose a suspension or termination due to a number of factors, including: a failure to conduct the clinical trial in accordance with regulatory requirements or the applicable clinical protocols, inspection of the clinical trial operations or trial site by the FDA, NMPA, EMA, PDMA or other regulatory authorities that results in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates. Further, the FDA, NMPA, EMA, PDMA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

If we or our collaboration partners are required to conduct additional clinical trials or other testing of our drug candidates beyond those that are currently contemplated, if we or our collaboration partners are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining regulatory approval for our drug candidates;
- not obtain regulatory approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- be subject to post-marketing testing requirements; or
- have the drug removed from the market after obtaining regulatory approval.

Our drug development costs will also increase if we experience delays in testing or regulatory approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant pre-clinical study or clinical trial delays also could allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our drug candidates and may harm our business and results of operations. Any delays in our clinical development programs may significantly harm our business, financial condition and prospects.

If we or our collaboration partners experience delays or difficulties in the enrollment of patients in clinical trials, the progress of such clinical trials and our receipt of necessary regulatory approvals could be delayed or prevented.

We or our collaboration partners may not be able to initiate or continue clinical trials for our drug candidates if we or our collaboration partners are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, NMPA, EMA, PDMA or similar regulatory authorities. In particular, we and our collaboration partners have designed many of our clinical trials, and expect to design future trials, to include some patients with the applicable genomic alteration that causes the disease with a view to assessing possible early evidence of potential therapeutic effect. Genomically defined diseases, however, may have relatively low prevalence, and it may be difficult to identify patients with the applicable genomic alteration. In addition, for many of our trials, we focus on enrolling patients who have failed their first or second-line treatments, which limits the total size of the patient population available for such trials. The inability to enroll a sufficient number of patients with the applicable genomic alteration or that meet other applicable criteria for our clinical trials would result in significant delays and could require us or our collaboration partners to abandon one or more clinical trials altogether.

In addition, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates.

Patient enrollment may be affected by other factors including:

- the severity of the disease under investigation;
- the total size and nature of the relevant patient population;
- the design and eligibility criteria for the clinical trial in question;
- the availability of an appropriate genomic screening test/companion diagnostic;
- the perceived risks and benefits of the drug candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;

- the patient referral practices of physicians;
- the availability of competing therapies which are undergoing clinical trials;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients ; and
- the impact of the spread of infectious diseases, including but not limited to the duration and scope of related government orders and restrictions.

Enrollment delays in our clinical trials may result in increased development costs for our drug candidates, which could cause the value of our company to decline and limit our ability to obtain financing.

Our drug candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if any.

Undesirable side effects caused by our drug candidates could cause us or our collaboration partners to interrupt, delay or halt clinical trials or could cause regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, NMPA, EMA, PDMA or other regulatory authorities. In particular, as is the case with all oncology drugs, it is likely that there may be side effects associated with the use of certain of our drug candidates. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA, NMPA, EMA, PDMA or comparable regulatory authorities could order us to cease further development of or deny approval of our drug candidates for some or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, our drug candidates could cause undesirable side effects related to off-target toxicity. Many of the currently approved tyrosine kinase inhibitors or TKIs have been associated with off-target toxicities because they affect multiple kinases. While we believe that the kinase selectivity of our drug candidates has the potential to significantly improve the unfavorable adverse off-target toxicity issues, if patients were to experience off-target toxicity, we may not be able to achieve an effective dosage level, receive approval to market, or achieve the commercial success we anticipate with respect to any of our drug candidates, which could prevent us from ever generating revenue or achieving profitability. Many compounds that initially showed promise in early-stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound.

Clinical trials assess a sample of the potential patient population. With a limited number of patients and duration of exposure, rare and severe side effects of our drug candidates may only be uncovered with a significantly larger number of patients exposed to the drug candidate. If our drug candidates receive regulatory approval and we or others identify undesirable side effects caused by such drug candidates (or any other similar drugs) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such drug candidates;
- regulatory authorities may require the addition of labeling statements, such as a “boxed” warning or a contra-indication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way such drug candidates are distributed or administered, conduct additional clinical trials or change the labeling of the drug candidates;
- regulatory authorities may require a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;

- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such drug candidates from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our drug candidates; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected drug candidates and could substantially increase the cost of commercializing our drug candidates, if approved, and significantly impact our ability to successfully commercialize our drug candidates and generate revenue.

We and our collaboration partners have conducted and intend to conduct additional clinical trials for certain of our drug candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations or may require additional U.S.-based trials.

We and our collaboration partners have conducted, currently are conducting and intend in the future to conduct, clinical trials outside the United States, particularly in China where our Oncology/Immunology operations are headquartered as well as in other jurisdictions such as Australia, Japan, South Korea and various European countries.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted by qualified investigators in accordance with current good clinical practices, or GCPs, including review and approval by an independent ethics committee and receipt of informed consent from trial patients. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. Generally, the patient population for any clinical trial conducted outside of the United States must be representative of the population for which we intend to seek approval in the United States. In addition, while these clinical trials are subject to applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also comply with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from our clinical trials conducted outside the United States, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay or permanently halt our ability to develop and market these or other drug candidates in the United States. In April 2022, we received a Complete Response Letter from the FDA regarding the NDA for surufatinib for the treatment of pancreatic NETs and non-pancreatic NETs. The FDA determined that the data package submitted in the application, based on two successful Phase III trials in China and one bridging study in the U.S., were not sufficient to support approval in the U.S.. The Complete Response Letter indicated that a multi-regional clinical trial would be required for U.S. approval. We subsequently withdrew our submissions to the FDA and the EMA for surufatinib.

In addition, there are risks inherent in conducting clinical trials in jurisdictions outside the United States including:

- regulatory and administrative requirements of the jurisdiction where the trial is conducted that could burden or limit our ability to conduct our clinical trials;
- foreign exchange fluctuations;
- manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research; and
- the risk that patient populations in such trials are not considered representative as compared to patient populations in the United States and other markets.

If we are unable to obtain and/or maintain priority review by the NMPA, fast track designation by the FDA, or another expedited registration pathway for our drug candidates, the time and cost we incur to obtain regulatory approvals may increase. Even if we receive such approvals, they may not lead to a faster development, review or approval process.

Under the Breakthrough Therapy Drug Review Procedures (For Trial Implementation), the Review and Approval Procedures for Conditional Approval of Drug Marketing Applications (For Trial Implementation), and the Priority Review and Approval Procedures for Drug Marketing Authorization (For Trial Implementation), the NMPA (or, where applicable, the National Health Commission, or the NHC) may grant priority review approval (i) to innovative drugs or new improved drugs undergoing clinical trials that are used to prevent and treat diseases that are seriously life-threatening or which seriously affect quality of life for which there is no effective prevention or treatment, or for which there is sufficient evidence to show obvious clinical advantages compared with existing treatments, (ii) to drugs undergoing clinical trials which meet the conditions for conditional approval specified in the Technical Guidelines for Conditional Approval of Drugs, (iii) to innovative drugs and new improved drugs which are in shortage, prevent and treat major infectious diseases and rare diseases, (iv) to new varieties, dosage forms and specifications that meet the physiological characteristics of children, (v) to vaccines (including innovative vaccines) urgently needed for control and prevention of diseases, and (vi) under other circumstances stipulated by the NMPA. Priority review provides a fast track process for drug registration. In the past, we received priority review status for a number of our drug candidates, including for example fruquintinib for the treatment of advanced colorectal cancer, or CRC, savolitinib for the treatment of NSCLC and surufatinib for the treatment of advanced NET. We anticipate that we may seek priority review for certain of our other drug candidates in the future.

In the United States, if a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, we may apply for fast track designation by the FDA. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular drug candidate is eligible for this designation, we cannot be sure that the FDA would decide to grant it. We have sought and will likely continue to seek fast track designation for some of our drug candidates. Even if we receive fast track designation for a drug candidate, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

A failure to obtain and/or maintain priority review, fast track designation or any other form of expedited development, review or approval for our drug candidates would result in a longer time period to commercialization of such drug candidate, could increase the cost of development of such drug candidate and could harm our competitive position in the marketplace. In addition, even if we obtain priority review, there is no guarantee that we will experience a faster review or approval compared to non-accelerated registration pathways or that a drug candidate will ultimately be approved for sale.

Even if we or our collaboration partners receive regulatory approval for our drug candidates, we or our collaboration partners are subject to ongoing obligations and continued regulatory review, which may result in significant additional expense.

If the FDA, NMPA, EMA, PDMA or a comparable regulatory authority approves any of our drug candidates, we or our collaboration partners will continue to be subject to extensive and ongoing regulatory requirements. For example, even though the NMPA has granted approval of fruquintinib, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for fruquintinib continue to be subject to the NMPA's oversight. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing processes.

Any regulatory approvals that we or our collaboration partners receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including post-approval testing, sometimes referred to as Phase IV clinical trials, and surveillance to monitor the safety and efficacy of the drug. In addition, regulatory policies may change or additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we or our collaboration partners are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaboration partners are not able to maintain regulatory compliance, we or our collaboration partners may lose any regulatory approval that we or our collaboration partners may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with any of our drugs that receive regulatory approval.

Once a drug is approved by the FDA, NMPA, EMA, PDMA or a comparable regulatory authority for marketing, it is possible that there could be a subsequent discovery of previously unknown problems with the drug, including problems with third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements. If any of the foregoing occurs with respect to our drug products, it may result in, among other things:

- restrictions on the marketing or manufacturing of the drug, withdrawal of the drug from the market, or drug recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA, NMPA, EMA, PDMA or comparable regulatory authority to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of drug license approvals;
- drug seizure or detention, or refusal to permit the import or export of drugs; and
- injunctions or the imposition of civil or criminal penalties.

Any government investigation of alleged violations of law could require us to expend significant time and resources and could generate negative publicity. If we or our collaborators are not able to maintain regulatory compliance, regulatory approval that has been obtained may be lost and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

The incidence and prevalence for target patient populations of our drug candidates are based on estimates and third-party sources. If the market opportunities for our drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.

Periodically, we make estimates regarding the incidence and prevalence of target patient populations for particular diseases based on various third-party sources and internally generated analysis and use such estimates in making decisions regarding our drug development strategy, including determining indications on which to focus in pre-clinical or clinical trials. These estimates may be inaccurate or based on imprecise data. For example, the total addressable market opportunity will depend on, among other things, their acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients in the addressable markets may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drugs, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the expertise of the members of our research and development team, as well as the other principal members of our management, including Weiguo Su, Ph.D., our Chief Executive Officer, Chief Scientific Officer and director. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time with three months' prior written notice. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified management, scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

We have operations internationally and are subject to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects.

We have been involved in clinical and non-clinical development internationally for over a decade. Conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including, among other things:

- the increased complexity and costs inherent in managing international operations;
- diverse regulatory, financial and legal requirements, and any future changes to such requirements, in one or more countries where we are located or do business;
- country-specific tax, labor and employment laws and regulations;
- applicable trade laws, tariffs, export quotas, custom duties or other trade restrictions and any changes to them;
- challenges inherent in efficiently managing employees in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and other regulations;
- changes in currency rates; and
- regulations relating to data security and the unauthorized use of, or access to, commercial and personal information.

There can be no assurance that we will effectively manage the increased complexity without experiencing operating inefficiencies or control deficiencies. Such increased complexity may also lead to decisions to reposition our international operations to align them with our overall and evolving business strategy, including with our recent strategic change to focus on path to profitability. Significant management time and effort is required to effectively manage the increased complexity of our company, and our failure to successfully do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We may be restricted from transferring our scientific data abroad.

On March 17, 2018, the General Office of the State Council promulgated the Measures for the Management of Scientific Data, or the Scientific Data Measures, which provides a broad definition of scientific data and relevant rules for the management of scientific data. According to the Scientific Data Measures, enterprises in China must seek governmental approval before any scientific data involving a state secret may be transferred abroad or to foreign parties. Further, any researcher conducting research funded at least in part by the Chinese government is required to submit relevant scientific data for management by the entity to which such researcher is affiliated before such data may be published in any foreign academic journal. Given that the term state secret is not clearly defined in the Scientific Data Measures, if and to the extent our research and development of drug candidates will be subject to the Scientific Data Measures and any subsequent laws as required by the relevant government authorities, we cannot assure you that we can always obtain relevant approvals for sending scientific data (such as the results of our pre-clinical studies or clinical trials conducted within China) abroad or to our foreign partners in China. The PRC Personal Information Protection Law, effective November 2021, provides that where a personal information processor needs to provide personal information outside the territory of the PRC due to business or other needs, it shall meet any of the following conditions: (i) it shall pass the security evaluation organized by the Cyberspace Administration of China (“CAC”) in accordance with the provisions of Article 40 thereof, (ii) it shall have been certified by a specialized agency for protection of personal information in accordance with the provisions of the CAC, (iii) it shall enter into a contract with the overseas recipient under the standard contract formulated by the CAC, specifying the rights and obligations of both parties, or (iv) it shall meet other conditions prescribed by laws, administrative regulations or the CAC. If we are unable to obtain necessary approvals or meet the necessary requirements in a timely manner, or at all, our research and development of drug candidates may be hindered, which may materially and adversely affect our business, results of operations, financial conditions and prospects. If the relevant government authorities consider the transmission of our scientific data to be in violation of the requirements under the Scientific Data Measures, we may be subject to fines and other administrative penalties imposed by those government authorities.

Any adverse developments related to the administration of our drug candidates in compassionate use programs may affect our and/or our partners' ability to obtain regulatory approval or commercialize our drug candidates.

In many countries, physicians are permitted to administer unapproved drugs to patients who have life-threatening disease with no viable available therapy. From time to time, we and our partners participate in such programs and offer our drug candidates for patient treatment. Given that the patients receiving treatment under such programs often have very advanced diseases, there is an increased risk that they may experience more severe adverse events. If serious adverse events or other issues that call into question the potential efficacy and safety of our drug candidates occur when our drug candidates are administered through compassionate use programs, the NMPA, the FDA and other regulatory authorities may delay, limit, or deny approval of our drug candidates or require us and/or our partners to conduct additional clinical trials as a condition to marketing approval, which would increase drug development costs.

Risks Relating to Sales of Our Internally Developed Drugs and Other Drugs

Pharmaceutical companies in China are required to comply with extensive regulations and hold a number of permits and licenses to carry on their business. Our and our joint ventures' ability to obtain and maintain these regulatory approvals is uncertain, and future government regulation may impose additional burdens on our operations.

The pharmaceutical industry in China is subject to extensive government regulation and supervision. The regulatory framework addresses all aspects of operations in the pharmaceutical industry, including approval, production, distribution, advertising, licensing and certification requirements and procedures, periodic renewal and reassessment processes, registration of new drugs and environmental protection. Violation of applicable laws and regulations may materially and adversely affect our business. In order to manufacture and distribute pharmaceutical products in China, we and our joint ventures are required to, among other things:

- obtain a pharmaceutical manufacturing permit for each production facility from the NMPA;
- obtain a drug registration certificate, which includes a drug approval number, from the NMPA for each drug manufactured by us;
- obtain a pharmaceutical distribution permit from the NMPA; and
- renew the pharmaceutical manufacturing permits, the pharmaceutical distribution permits, drug registration certificates, among other requirements.

If we or our joint ventures are unable to obtain or renew such permits or any other permits or licenses required for our or their operations, we will not be able to engage in the manufacture and distribution of our products and our business may be adversely affected.

The regulatory framework regarding the pharmaceutical industry in China is subject to change and amendment from time to time. Any such change or amendment could materially and adversely impact our business, financial condition and results of operations. The PRC government has introduced various reforms to the Chinese healthcare system in recent years and may continue to do so, with an overall objective to expand basic medical insurance coverage and improve the quality and reliability of healthcare services. Specific upcoming regulatory and policy changes remain uncertain. The implementing measures to be issued may not be sufficiently effective to achieve the stated goals and, as a result, we may not be able to benefit from such reform to the level we expect, if at all. Moreover, the reform could give rise to regulatory developments, such as more burdensome administrative procedures, which may have an adverse effect on our business and prospects.

For further information regarding government regulation in China and other jurisdictions, see Item 4.B. "Business Overview—Regulations—Government Regulation of Pharmaceutical Product Development and Approval," "Business Overview—Regulations—Coverage and Reimbursement" and "Business Overview—Regulations—Other Healthcare Laws."

As a significant portion of the operations of our Other Ventures is conducted through joint ventures, we are dependent on the success of our joint ventures, our receipt of dividends or other payments from our joint ventures for cash to fund our operations, and our investments in our joint ventures are subject to liquidity risk.

We are party to a joint venture agreement with Shanghai Pharmaceuticals, relating to our non-consolidated joint venture namely, Shanghai Hutchison Pharmaceuticals, which forms part of the operations of our Other Ventures. Our equity in earnings of such non-consolidated joint venture, net of tax, was \$44.7 million, \$49.7 million and \$47.3 million for the years ended December 31, 2021, 2022 and 2023, respectively, as recorded in our consolidated financial statements. As such, our results of operations and financial performance have been, and will continue to be, affected by the financial performance of such joint venture as well as any other equity investees we have or may have in the future. We may also be required to recognize an impairment charge in our consolidated financial statements if there is a decline in the fair market value of our investments in such businesses below their carrying amounts for whatever reason that is determined to be other-than-temporary. Furthermore, we have consolidated joint ventures with Sinopharm which accounted for substantially all of our Other Ventures' consolidated revenue for the years ended December 31, 2021, 2022 and 2023.

As a result, our ability to fund our operations and pay our expenses or to make future dividend payments, if any, is partly dependent on the earnings of our joint ventures and the payment of those earnings to us in the form of dividends. Payments to us by our joint ventures will be contingent upon our joint ventures' earnings and other business considerations and may be subject to statutory or contractual restrictions. Each joint venture's ability to distribute dividends to us is subject to approval by their respective boards of directors, which in the case of Shanghai Hutchison Pharmaceuticals is comprised of an equal number of representatives from each party. Furthermore, our ability to promptly sell one or more of our interests in our joint ventures in response to changing corporate strategy or economic, financial and investment conditions is limited. The market for such investments can be affected by various factors, such as general economic and market conditions, availability of financing, interest rates and investor demand, many of which are beyond our control. If we determine to sell any of our joint venture investments, we cannot predict if we will be successful or whether any price or other terms offered by a prospective purchaser would be acceptable to us.

Operationally, our joint venture partners have certain responsibilities and/or certain rights to exercise control or influence over operations and decision-making under the joint venture arrangements. Therefore, the success of our joint ventures depends on the efforts and abilities of our joint venture parties. For example, we appoint the general managers of Hutchison Sinopharm and Shanghai Hutchison Pharmaceuticals pursuant to the respective joint venture agreements governing these entities and therefore oversee the day-to-day management of these joint ventures. However, we still rely on our joint venture partners Sinopharm and Shanghai Pharmaceuticals to provide certain distribution and logistics services. See "Risks Relating to Our Dependence on Third Parties—Joint ventures form an important part of our Other Ventures, and our ability to manage and develop the businesses conducted by these joint ventures depends in part on our relationship with our joint venture partners" for more information.

We may not be successful in building a commercial team to successfully manufacture, sell and market our approved drugs, and we may not be able to generate any revenue from such products.

We have leveraged our experience operating our prescription drugs business to commercialize certain of our approved, internally developed drug candidates in China. We must adapt our know-how to build a specific oncology and/or immunology focused sales and marketing team. As of December 31, 2023, we had an oncology commercial team with over 900 staff to support the commercialization of fruquintinib, surufatinib and our other drug candidates, if approved. There are risks involved in establishing an in-house oncology commercial team. For example, recruiting and/or training a sales force to detail our approved drug candidates is time consuming and could delay any drug launch. Factors that may inhibit our efforts to commercialize our drug candidates include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- our inability to effectively manage the expansion of our operations and train additional qualified personnel in the relevant areas of oncology and/or immunology;
- our failure to prevent inappropriate business conducts, including behaviors that may violate anti-bribery and anti-corruption laws and regulations;
- the inability of our sales personnel to obtain access to physicians or educate adequate numbers of physicians who then prescribe any future drugs; and

- the lack of complementary drugs to be offered by our sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines.

In such case, our business, results of operations, financial condition and prospects will be materially and adversely affected.

We face substantial competition in selling our approved, internally developed drugs and the drugs of our Other Ventures.

The marketed drugs developed and sold by our Oncology/Immunology operations and the prescription drugs business which is part of our Other Ventures' operations face substantial competition in the pharmaceutical industry in China, which is characterized by a number of established, large pharmaceutical companies, as well as smaller emerging pharmaceutical companies, engaged in the development, production, marketing or sales of prescription drugs, in particular cardiovascular drugs. The identities of the key competitors with respect to drugs sold by our Oncology/Immunology and Other Ventures operations vary by product and, in certain cases, competitors have greater financial resources than us and may elect to focus these resources on developing, importing or in-licensing and marketing products in the PRC that are substitutes for our products and may have broader sales and marketing infrastructure with which to do so.

Such drugs may compete against products that have lower prices, superior performance, greater ease of administration or other advantages compared to our products. In some circumstances, price competition may drive our competitors to conduct illegal manufacturing processes to lower their manufacturing costs. Increased competition may result in price reductions, reduced margins and loss of market share, whether achieved by either legal or illegal means, any of which could materially and adversely affect our profit margins. We and our joint ventures may not be able to compete effectively against current and future competitors.

If we are not able to maintain and enhance brand recognition of our drugs to maintain a competitive advantage, our reputation, business and operating results may be harmed.

We believe that market awareness of our products sold through our Oncology/Immunology and Other Ventures operations, which include our joint ventures' branded products, such as Shang Yao, and the brands of third-party products which are distributed through our joint ventures, has contributed significantly to our success. We also believe that maintaining and enhancing such brands is critical to maintaining our competitive advantage. Although the sales and marketing staff of such businesses will continue to further promote such brands to remain competitive, they may not be successful. If we or our joint ventures are unable to further enhance brand recognition and increase awareness of such products, or are compelled to incur excessive marketing and promotion expenses in order to maintain brand awareness, our business and results of operations may be materially and adversely affected. Furthermore, our results of operations could be adversely affected if the Shang Yao brand, or the brands of any other products, or our reputation, are impaired by certain actions taken by our joint venture partners, distributors, competitors or relevant regulatory authorities.

Reimbursement may not be available for the products currently sold through our Oncology/Immunology and Other Ventures operations or our drug candidates in China, the United States or other countries, which could diminish our sales or affect our profitability.

The regulations that govern pricing and reimbursement for pharmaceuticals vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after regulatory approval is granted. In some foreign markets, pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Furthermore, once marketed and sold, government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Adverse pricing reimbursement levels may hinder market acceptance of our drug candidates or other products sold by us.

In China, for example, the Ministry of Human Resources and Social Security of the PRC (the “MOHRSS”) or provincial or local human resources and social security authorities, together with other government authorities, review the inclusion or removal of drugs from the Medicines Catalogue for the National Basic Medical Insurance, Labor Injury Insurance and Childbirth System in China, or the National Reimbursement Drug List, or NRDL, or provincial or local medical insurance catalogues for the National Medical Insurance Program, and the category under which a drug will be classified, both of which affect the amounts reimbursable to program participants for their purchases of those medicines. These determinations are made based on a number of factors, including price and efficacy. Depending on the category under which a drug is classified in the provincial medicine catalogue, a National Medical Insurance Program participant residing in that province can be reimbursed for the full cost of Category A medicine and for the majority of the cost of a Category B medicine. In some instances, if the price range designated by the local or provincial government decreases, it may adversely affect our business and could reduce our total revenue, and if our revenue falls below production costs, we may stop manufacturing certain products. Since January 2020, January 2022 and March 2023, Elunate, Sulanda and Orpathys have been included in China’s NRDL as a Category B medicine, respectively.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs which may affect reimbursement rates of our drug candidates if approved. Various federal and state laws have been enacted to control drug pricing or require manufacturers to disclose information about drug pricing. For example, the Inflation Reduction Act of 2022, or IRA, was signed into law, and, among other provisions, mandates the negotiation of eligible Medicare Part B and Part D drugs; redesigns the Medicare Part D benefit; and imposes inflationary rebates for Medicare drugs that increase in price faster than the rate of inflation.

The IRA, or other federal or state laws, could affect the market conditions for, or pricing or reimbursement of, our products. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results. We expect that additional U.S. state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

Moreover, eligibility for reimbursement in the United States does not imply that any drug will be paid for in all cases, or by all payors, or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim U.S. reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by U.S. government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors in the United States often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition.

Sales of our generic prescription drugs sold through our Other Ventures rely on the ability to win tender bids for the medicine purchases of hospitals in China.

Our prescription drugs business markets to hospitals in China that may make bulk purchases of a medicine only if that medicine is selected under a government-administered tender process that was initiated in 2018 and aimed at driving consolidation in the fragmented generic prescription drug market in China. Pursuant to this process, major cities bulk-buy certain generic drugs together, forcing companies to bid for contracts and driving down prices. The process was later expanded nationwide to cover more cities and drugs. This process, which only applies to generic prescription drugs, may reduce our Other Ventures’ product portfolio as some of our third-party generic drug partners may fail to win bids.

Periodically, a bidding process is organized on a provincial or municipal basis. Whether a drug manufacturer is invited to participate in the tender depends on the level of interest that hospitals have in purchasing this drug. The interest of a hospital in a medicine is evidenced by:

- the inclusion of this medicine on the hospital’s formulary, which establishes the scope of drug physicians at this hospital may prescribe to their patients, and
- the willingness of physicians at this hospital to prescribe a particular drug to their patients.

We believe that effective marketing efforts are critical in making and keeping hospitals interested in purchasing the prescription drugs sold through our Other Ventures so that we and our joint ventures are invited to submit the products to the tender. Even if we and our joint ventures are invited to do so, competitors may be able to substantially reduce the price of their products or services. If competitors are able to offer lower prices, our and our joint ventures' ability to win tender bids during the hospital tender process will be materially affected, and could reduce our total revenue or decrease our profit.

Counterfeit products could negatively impact our revenue, brand reputation, business and results of operations.

Our products are subject to competition from counterfeit products, especially counterfeit pharmaceuticals which are manufactured without proper licenses or approvals and are fraudulently mislabeled with respect to their content and/or manufacturer. Counterfeiters may illegally manufacture and market products under our or our joint venture's brand names, the brand names of the third-party products we or they sell, or those of our or their competitors. Counterfeit pharmaceuticals are generally sold at lower prices than the authentic products due to their low production costs, and in some cases are very similar in appearance to the authentic products. Counterfeit pharmaceuticals may or may not have the same chemical content as their authentic counterparts. If counterfeit pharmaceuticals illegally sold under our or our joint ventures' brand names or the brand names of third-party products we or they sell result in adverse side effects to consumers, we or our joint ventures may be associated with any negative publicity resulting from such incidents. In addition, consumers may buy counterfeit pharmaceuticals that are in direct competition with products sold through our Oncology/Immunology and Other Ventures operations, which could have an adverse impact on our revenue, business and results of operations. The proliferation of counterfeit pharmaceuticals in China and globally may grow in the future. Any such increase in the sales and production of counterfeit pharmaceuticals in China, or the technological capabilities of the counterfeiters, could negatively impact our revenue, reputation, business and results of operations.

Rapid changes in the pharmaceutical industry may render our Other Ventures' products or our internally developed drugs and drug candidates obsolete.

Future technological improvements by our competitors and continual product developments in the pharmaceutical market may render our and our joint ventures' existing products, our or their third-party licensed products or our drug candidates obsolete or affect our viability and competitiveness. Therefore, our future success will largely depend on our and our joint ventures' ability to:

- improve existing products;
- develop innovative drug candidates;
- diversify the product and drug candidate portfolio;
- license diverse third-party products; and
- develop new and competitively priced products which meet the requirements of the constantly changing market.

If we or our joint ventures fail to respond to this environment by improving our existing products, licensing new third-party products or developing new drug candidates in a timely fashion, or if such new or improved products do not achieve adequate market acceptance, our business and profitability may be materially and adversely affected.

Certain of our joint ventures' principal products involve the cultivation or sourcing of key raw materials including botanical products, and any quality control or supply failure or price fluctuations could adversely affect our ability to manufacture our products and/or could materially and adversely affect our operating results.

The key raw materials used in the manufacturing process of certain of our joint ventures' principal products are medicinal herbs whose properties are related to the regions and climatic conditions in which they are grown. Access to quality raw materials and products necessary for the manufacture of our products is not guaranteed. We rely on materials sourced from third-party growers and suppliers. The availability, quality and prices of these raw materials are dependent on and closely affected by weather conditions and other seasonal factors which have an impact on the yields of the harvests each year. The quality, in some instances, also depends on the operations of third-party growers or suppliers. There is a risk that such growers or suppliers sell or attempt to sell us or our joint ventures raw materials which are not authentic. If there is any supply interruption for an indeterminate period of time, our joint ventures may not be able to identify and obtain alternative supplies that comply with our quality standards in a timely manner. Any supply disruption could adversely affect our ability to satisfy demand for our products, and materially and adversely affect our product sales and operating results. Moreover, any use by us or our joint ventures of unauthentic materials illegally sold to us by third-party growers or suppliers in our or our joint ventures' products may result in adverse side effects to the consumers, negative publicity, or product liability claims against us or our joint ventures, any of which may materially and adversely affect our operating results.

The prices of necessary raw materials and products may be subject to price fluctuations according to market conditions, and any sudden increases in demand in the case of a widespread illness such as COVID-19, SARS, MERS or avian flu may impact the cost of production. Raw material price fluctuations could increase the cost to manufacture our products and adversely affect our operating results.

Adverse publicity associated with our company or collaboration partners, our joint ventures or our or their products or third-party licensed products or similar products manufactured by our competitors could have a material adverse effect on our results of operations.

Sales of our and our joint ventures' products are highly dependent upon market perceptions of the safety and quality of such products, including proprietary products and third-party products we and they distribute. Concerns over the safety of biopharmaceutical products manufactured in China could have an adverse effect on the reputation of our industry and the sale of such products, including products manufactured or distributed by us, our collaboration partners and our joint ventures.

We and our joint ventures could be adversely affected if any of our or our joint ventures' products, third-party licensed products or any similar products manufactured by other companies prove to be, or are alleged to be, harmful to patients. Any negative publicity associated with severe adverse reactions or other adverse effects resulting from patients' use or misuse of our and our joint ventures' products or any similar products manufactured by other companies could also have a material adverse impact on our results of operations. We and our joint ventures have not, to date, experienced any significant quality control or safety problems. If in the future we or our joint ventures become involved in incidents of the type described above, such problems could severely and adversely impact our financial position and reputation.

We are dependent on our joint ventures' production facilities in Shanghai, China, our manufacturing facilities in Suzhou and Shanghai, China and third-party or our collaboration partners' manufacturing facilities for the manufacture of the principal products of our joint ventures and our own drug candidates and products.

The principal products sold by our Other Ventures are mainly produced or expected to be produced at our joint ventures' manufacturing facilities in Shanghai, China. Our commercial supplies of finished product for fruquintinib and surufatinib sold by our Oncology/Immunology operations are manufactured at our manufacturing facility in Suzhou, China. We outsourced the manufacture of active pharmaceutical ingredients and finished product of savolitinib to a third-party manufacturer based in Shanghai, China. We have also outsourced the manufacture of the active pharmaceutical ingredients to third-party manufacturers based in China for fruquintinib and surufatinib and we have engaged a back-up supplier for fruquintinib for China only. Until our new manufacturing facility in Shanghai is fully operational and it receives all the requisite government and other approvals, we have no back-up manufacturing facility for the finished product of savolitinib and surufatinib, and our ability to produce such drugs will be negatively impacted if we experience any significant production problems at our Suzhou facility or at our third party manufacturers' facilities. In relation to the U.S. market, finished product for fruquintinib can be supplied by either our facility in Suzhou or a third-party manufacturer in Switzerland and potentially this third-party manufacturer could supply finished product to us to be sold in China subject to relevant approvals. A significant disruption at our, our collaboration partners', our joint ventures' and/or our contract manufacturer's facilities, even on a short-term basis, could impair our, our collaboration partners' and/or our joint ventures' ability to timely produce and ship products, which could have a material adverse effect on our business, financial position and results of operations.

Our, our collaboration partners', our joint ventures' and our contract manufacturer's manufacturing operations are vulnerable to interruption and damage from natural and other types of disasters, including earthquake, fire, floods, environmental accidents, power loss, communications failures and similar events. If any disaster were to occur, our ability to operate our, our collaboration partners', our joint ventures' or our contract manufacturer's business at these facilities would be materially impaired. In addition, the nature of our production and research activities could cause significant delays in our programs and make it difficult for us to recover from a disaster or switch to other contract manufacturers. We and our joint ventures maintain insurance for business interruptions to cover some of our potential losses; however, such disasters could still disrupt our operations and thereby result in substantial costs and diversion of resources.

In addition, our, our collaboration partners', our joint ventures' and our contract manufacturer's production process requires a continuous supply of electricity. We and they have encountered power shortages historically due to restricted power supply to industrial users during summers when the usage of electricity is high and supply is limited or as a result of damage to the electricity supply network. Because the duration of those power shortages was brief, they had no material impact on our or their operations. Interruptions of electricity supply could result in lengthy production shutdowns, increased costs associated with restarting production and the loss of production in progress. Any major suspension or termination of electricity or other unexpected business interruptions could have a material adverse impact on our business, financial condition and results of operations.

Risks Relating to Our Dependence on Third Parties

Disagreements or disputes with our current or future collaboration partners, the amendment of any collaboration agreement or the termination of any collaboration arrangement, could cause delays in our product development and materially and adversely affect our business.

Our collaborations, including those with our oncology drug partners AstraZeneca, Eli Lilly and Takeda and our in-licensing arrangement with Epizyme, and any future collaborations that we enter into may not be successful. Disagreements or disputes between parties to a collaboration arrangement regarding issues such as clinical development and commercialization, intellectual property ownership and transfer, clinical supply of drug candidates or products, cost allocation and other matters can lead to delays in the development process or commercializing the applicable drug candidate and, in some cases, termination of the collaboration arrangement. In addition, we or our partners may seek to amend the terms of one or more our collaboration agreements to adjust, among other things, the respective roles of our company and our collaboration partners as circumstances change. Our interests may not always be aligned with those of our collaboration partners, for instance, we may be much smaller than our collaboration partners and because they or their affiliates may sell competing products. This may result in potential conflicts between our collaborators and us on matters that we may not be able to resolve on favorable terms or at all.

Collaborations with pharmaceutical or biotechnology companies and other third parties, including our existing agreements with AstraZeneca, Eli Lilly and Takeda, are often terminable by the other party for any reason with certain advance notice. Any such termination or expiration would adversely affect us financially and could harm our business reputation. For instance, in the event that one of the strategic alliances with a current collaborator is terminated, we may require significant time and resources to secure a new collaboration partner, if we are able to secure such an arrangement at all. As noted in the following risk factor, establishing new collaboration arrangements can be challenging and time-consuming. The loss of existing or future collaboration arrangements would not only delay or potentially terminate the possible development or commercialization of products we may derive from our technologies, but it may also delay or terminate our ability to test specific target candidates.

We rely on our collaborations with third parties for certain of our drug development activities, and, if we are unable to establish new collaborations when desired on commercially attractive terms or at all, we may have to alter our development and commercialization plans.

Certain of our drug development programs and the potential commercialization of certain drug candidates rely on collaborations, such as savolitinib with AstraZeneca and fruquintinib with Eli Lilly for China and with Takeda outside of China. In the future, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of our other drug candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, NMPA, EMA, PDMA or similar regulatory authorities outside the United States, China, Europe, Japan and the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative drug candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our drug candidate. The terms of any additional collaboration or other arrangements that we may establish may not be favorable to us. We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or eventually close the deal. If we are unable to do so, we may have to curtail the development of the drug candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate drug revenue.

The third-party vendors upon whom we rely for the supply of the active pharmaceutical ingredients used in some of our drug candidates and drug products are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.

The active pharmaceutical ingredients used in some of our drug candidates and products are supplied to us from third-party vendors. Our ability to successfully develop our drug candidates, and to supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the active pharmaceutical ingredients for these drugs in accordance with regulatory requirements and in sufficient quantities for commercialization and clinical testing. We currently obtain active pharmaceutical ingredients for each of our drug candidates from a limited number of suppliers. For example, a single supplier based in Shanghai manufactures and provides us active pharmaceutical ingredient for savolitinib. In the event any of our current suppliers of such active pharmaceutical ingredient cease operations for any reason, it may lead to an interruption in our production and supply of the product.

For all of our drug candidates and products, we aim to identify and qualify a manufacturer to provide such active pharmaceutical ingredient prior to submission of an NDA to the FDA and/or NMPA. We are not certain, however, that our current supply arrangements will be able to meet our demand, either because of the nature of our agreements with third party suppliers, our limited experience with third party suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess third party vendors' ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand on a timely basis in the past, they may subordinate our needs in the future to their other customers.

Establishing additional or replacement suppliers for the active pharmaceutical ingredients used in our drug candidates and products, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such alternative arrangements would need to be qualified and may require additional regulatory approval, which could result in further delay. While we seek to maintain adequate inventory of the active pharmaceutical ingredients used in our drug candidates and products, any interruption or delay in the supply of components or materials, or our inability to obtain such active pharmaceutical ingredient from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development and commercialization efforts, which could harm our business, results of operations, financial condition and prospects.

We and our collaboration partners rely, and expect to continue to rely, on third parties to conduct certain of our clinical trials for our drug candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be harmed.

We do not have the ability to independently conduct large-scale clinical trials. We and our collaboration partners rely, and expect to continue to rely, on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct or otherwise support certain clinical trials for our drug candidates. Nevertheless, we and our collaboration partners (as applicable) will be responsible for ensuring that each clinical trial is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of clinical trials for our drug candidates, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

Although we or our collaboration partners design the clinical trials for our drug candidates, CROs conduct most of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, are outside of our direct control. Our reliance on third parties to conduct clinical trials results in less control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially and adversely affect the willingness or ability of third parties to conduct our and our collaboration partners' clinical trials and may subject us or them to unexpected cost increases that are beyond our or their control.

If any of our and our collaboration partners' relationships with these third-party CROs terminate, we or they may not be able to enter into arrangements with alternative CROs on reasonable terms or at all. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, we believe that our financial results and the commercial prospects for our drug candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We, our collaboration partners or our CROs may fail to comply with the regulatory requirements pertaining to clinical trials, which could result in fines, adverse publicity and civil or criminal sanctions.

We, our collaboration partners and our CROs are required to comply with regulations for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the NMPA and comparable foreign regulatory authorities for any drugs in clinical development. In the United States, the FDA regulates GCP through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we, our collaboration partners or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require additional clinical trials before approving the marketing applications for the relevant drug candidate. We cannot assure you that, upon inspection, the FDA or other applicable regulatory authority will determine that any of the future clinical trials for our drug candidates will comply with GCPs. In addition, clinical trials must be conducted with drug candidates produced under applicable manufacturing regulations. Our failure or the failure of our collaboration partners or CROs to comply with these regulations may require us or them to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action. We are also required to register applicable clinical trials and post certain results of completed clinical trials on a U.S. government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil sanctions.

Our collaboration partners, principal investigators, CROs and other third-party contractor and consultants may engage in misconduct or other improper activities.

We are exposed to the risk that collaboration partners, principal investigators, CROs and other third-party contractor and consultants may engage in fraudulent or other illegal activity with respect to our business. Their misconduct could include intentional, reckless and/or negligent conduct or unauthorized activity that violates NMPA, FDA, EMA, PDMA or other regulations, including but not limited to those laws requiring the reporting of true, complete and accurate information. In addition, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of insurance, pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. We may not be able to identify and deter such misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, our collaboration partners, principal investigators, CROs and other third-party contractor and consultants, and we and/or such other parties are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, contractual damages, reputational harm, diminished profits and future earnings and disruption of our operations.

Joint ventures form an important part of our Other Ventures, and our ability to manage and develop the businesses conducted by these joint ventures depends in part on our relationship with our joint venture partners.

We are party to joint venture agreements with each of Shanghai Pharmaceuticals and Sinopharm, which together form a major portion of our Other Ventures. Under these arrangements, our joint venture partners have certain operational responsibilities and/or certain rights to exercise control or influence over operations and decision-making.

Our equity interests in these operating companies do not provide us with the unilateral ability to control actions which require shareholder approval. In addition, under the joint venture contracts for these entities, the consent of the directors nominated by our joint venture partners is required for the passing of resolutions in relation to certain matters concerning the operations of these companies. As a result, although we participate in the management and nominate the management and run the day-to-day operations of our joint ventures, Hutchison Sinopharm and Shanghai Hutchison Pharmaceuticals, we may not be able to secure the consent of our joint venture partners to pursue activities or strategic objectives that are beneficial to or that facilitate our overall business strategies. Furthermore, disagreements or disputes which arise between us and our joint venture partners may potentially require legal action to resolve and hinder the smooth operation of our Other Ventures or adversely affect our financial condition, results of operations and prospects.

We, our collaboration partners and our joint ventures rely on our distributors for logistics and distribution services.

We, our collaboration partners and our joint ventures rely on distributors to perform certain operational activities, including invoicing, logistics and delivery of the products we and they market to the end customers. Because we, our collaboration partners and our joint ventures rely on third-party distributors, we have less control than if we handled distribution logistics directly and can be adversely impacted by the actions of our distributors. Any disruption of our, our collaboration partners' and our joint ventures' distribution network, including failure to renew existing distribution agreements with desired distributors, could negatively affect product sales and materially and adversely affect our business, financial condition and results of operations.

There is no assurance that the benefits currently enjoyed by virtue of our association with CK Hutchison will continue to be available.

Historically, we have relied on the reputation and experience of, and support provided by, our founding shareholder, a wholly owned subsidiary of CK Hutchison, to advance our joint ventures and collaborations in China and elsewhere. CK Hutchison indirectly held approximately 38.2% of our total outstanding share capital as of February 15, 2024. We believe that CK Hutchison group's reputation in China has given us an advantage in negotiating collaborations and obtaining opportunities.

We also benefit from sharing certain services with the CK Hutchison group including, among others, legal and regulatory services, company secretarial support services, tax and internal audit services, participation in the CK Hutchison group's pension, medical and insurance plans, participation in the CK Hutchison group's procurement projects with third-party vendors/suppliers, other staff benefits and staff training services, company functions and activities and operation advisory and support services. We pay a management fee to an affiliate of CK Hutchison for the provision of such services. In each of the years ended December 31, 2021, 2022 and 2023, we paid a management fee of approximately \$1.0 million, \$1.0 million and \$1.0 million respectively. In addition, we benefit from the fact that two retail chains affiliated with the CK Hutchison group, PARKnSHOP and Watsons, sell certain of our Other Ventures' products in their stores throughout Hong Kong and in other Asian countries. For the years ended December 31, 2021, 2022 and 2023, sales of our products to members of the CK Hutchison group amounted to \$4.3 million, \$3.6 million and \$1.9 million, respectively.

Our business also depends on certain intellectual property rights licensed to us by the CK Hutchison group. See "—Risks Relating to Intellectual Property—We and our joint ventures are dependent on trademark and other intellectual property rights licensed from others. If we lose our licenses for any of our products, we or our joint ventures may not be able to continue developing such products or may be required to change the way we market such products" for more information on risks associated with such intellectual property licensed to us.

There can be no assurance the CK Hutchison group will continue to provide the same benefits or support that they have provided to our business historically. Such benefit or support may no longer be available to us, in particular, if CK Hutchison's ownership interest in our company significantly decreases in the future.

Other Risks and Risks Relating to Doing Business in China

We are subject to stringent privacy and cybersecurity laws, information security policies and contractual obligations related to data privacy and security, and we may be exposed to risks related to our management of the medical data of subjects enrolled in our clinical trials and other personal or sensitive information.

We routinely receive, collect, generate, store, process, transmit and maintain medical data, treatment records and other personal details of the subjects enrolled in our clinical trials, along with other personal or sensitive information. As such, we are subject to the relevant local, state, national and international data protection and privacy laws, directives regulations, and standards that apply to the collection, use, retention, protection, disclosure, transfer and other processing of personal data in the various jurisdictions in which we operate and conduct our clinical trials. We are also subject to contractual obligations regarding the processing of personal data. Legal requirements regarding data protection and privacy continue to evolve and may result in ever-increasing public scrutiny and escalating levels of enforcement and sanctions and increased cost of compliance. Failure to comply with any of these laws could result in enforcement action against us, including investigations, civil and criminal enforcement action, fines, imprisonment of company officers and public censure, claims for damages by customers and other affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

Data protection and privacy laws and regulations generally require clinical trial sponsors and operators and their personnel to protect the privacy of their enrolled subjects and prohibit unauthorized disclosure of personal information. We have established procedures to protect the confidentiality of medical records and personal data of subjects enrolled in our clinical trials. Access to clinical trial data has been strictly limited to authorized personnel only according to the relevant rules and regulations. External parties involved in clinical trials are also required to comply with all relevant data protection and confidentiality requirements. Data are to be used only for the intended use, as agreed by the patients and consistent with the patients' informed consent form. While we have adopted security policies and measures to protect our proprietary data and patients' privacy, personal patient information could be subject to leaks caused by hacking activities, human error, employee misconduct or negligence or system breakdown. We also cooperate with third parties including collaboration partners, principal investigators, hospitals, CROs and other third-party contractor and consultants for our clinical trials and operations. Any leakage or abuse of patient data by our third-party partners may be perceived by the patients as a result of our failure. Furthermore, any change in applicable laws and regulations could affect our ability to use medical data and subject us to liability for the use of such data for previously permitted purposes. For instance, we may be subject to additional regulations, laws and policies adopted by the PRC government to apply more stringent social and ethical standards in data privacy resulting from the increased global focus on this area. Any failure or perceived failure by us to prevent information security breaches or to comply with privacy policies or privacy-related legal obligations, or any compromise of information security that results in the unauthorized release or transfer of personally identifiable information or other patient data, could cause our customers to lose trust in us and could expose us to regulatory action and legal claims.

There are numerous U.S. federal and state laws and regulations relating to the privacy and security of personal information. In particular, regulations promulgated pursuant to the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended, establish privacy and security standards that limit the use and disclosure of individually identifiable health information (known as “protected health information”), require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information, and create breach reporting obligations in cases of certain unauthorized uses or disclosures. While we do not believe that we are directly subject to HIPAA as either a “covered entity” or “business associate,” U.S. sites at which we conduct clinical trials are likely to be covered entities and thus must ensure that they obtain adequate patient authorization or establish another basis under HIPAA to disclose a clinical trial subject’s individually identifiable health information to us and other entities participating in our clinical trials. In addition to federal regulation, many U.S. states have begun to focus on efforts to regulate privacy and data security. For example, in California, the California Consumer Protection Act, or CCPA, which went into effect on January 1, 2020 and was expanded by the California Consumer Privacy Rights Act, or CPRA, which went into effect on January 1, 2023, collectively establishes a privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. A separate law, the California Confidentiality of Medical Information Act, also applies to pharmaceutical companies, including requirements for written authorization to use and disclose medical information and restrictions on the circumstances under which medical information can be used for marketing purposes. Several other states have also recently enacted or are considering comprehensive data privacy and security laws. Furthermore, all fifty states, the District of Columbia, Puerto Rico, and U.S. territories have enacted data breach notification laws that require, among other things, notifications to state governments and/or the affected individuals in the event of a data breach. These various state laws differ from one another and impose significant compliance burden. Although we take measures to protect sensitive data from unauthorized access, use or disclosure, and whenever possible contractually require third-party partners to do the same, our information technology and infrastructure and those of our third-party partners may be vulnerable to attacks by hackers or viruses or breached due to employee error, malfeasance or other malicious or inadvertent disruptions. Any such breach or interruption could compromise those networks and the information stored there could be accessed by unauthorized parties, manipulated, publicly disclosed, lost or stolen. Any such access, breach, or other loss of information relating to our information technology and infrastructure or that of our third-party partners may subject us to reputation damage, increased scrutiny and liability including legal claims or proceedings and liability under federal or state laws that protect the privacy of personal information.

Regulatory authorities in China have implemented a number of legislative and regulatory proposals concerning data protection. The PRC Cyber Security Law, which became effective in June 2017, created China's first national-level data protection for "network operators," which may include all organizations in China that provide services over the internet or another information network. The PRC Data Security Law, which took effect in September 2021, provides for a security review procedure for the data activities that may affect national security. The PRC Personal Information Protection Law, which took effect from November 2021, provides the circumstances under which a personal information processor could process personal information and the requirements for such circumstances. The PRC Personal Information Protection Law clarifies the scope of application, the definition of personal information and sensitive personal information, the legal basis of personal information processing and the basic requirements of notice and consent. The Measures for Cybersecurity Review, which took effect on February 15, 2022, provides that critical information infrastructure operators that purchase network products and services and online platform operators engaging in data processing activities that affect or may affect national security shall be subject to the cybersecurity review, and elaborates the factors to be considered when assessing the national security risks of the relevant activities. The Measures for Cybersecurity Review further stipulates that online platform operators holding personal information of over one million users shall apply with the Cybersecurity Review Office for a cybersecurity review before any public listing in a foreign country. As of the date of this annual report, we have not received any formal notice from any PRC cybersecurity regulator that we should apply for or otherwise be subject to the cybersecurity review, or subject to any investigation or received any inquiry, notice or sanction on cybersecurity review. The exact scope of "critical information infrastructure operators" under the current regulatory regime remains unclear, and the PRC government authorities may have wide discretion in the interpretation and enforcement of the applicable laws. Therefore, it is uncertain whether we would be deemed to be a critical information infrastructure operator under PRC law. If we are deemed to be a critical information infrastructure operator under the PRC cybersecurity laws and regulations, we may be subject to obligations in addition to what we have fulfilled under the PRC cybersecurity laws and regulations. In addition, on November 14, 2021, the Data Security Management Measures (Draft for Comments) was published by the CAC for public comments, which provides that data processors conducting the following activities shall apply for cybersecurity review: (i) a merger, reorganization or division of online platform operators that have acquired a large number of data resources related to national security, economic development or public interests which affect or may affect national security; (ii) a listing abroad when the data processor processes over one million users' personal information; (iii) a listing in Hong Kong which affects or may affect national security; or (iv) other data processing activities that affect or may affect national security. It also requires data processors processing important data or listed outside China to carry out a data security assessment annually by itself or through a third party data security service provider and submit an assessment report to the local agency of the CAC. As there are still uncertainties regarding the further enactment of new laws and regulations as well as the revision, interpretation and implementation of those existing laws and regulations, we cannot assure you that we will be able to comply with such regulations in all respects.

The Measures on Security Assessment of Cross-border Data Transfer, or the Security Assessment Measures, were published on July 7, 2022, and became effective on September 1, 2022. The Security Assessment Measures specify that data controllers and/or critical information infrastructure operators will be subject to security assessment under the following circumstances: (i) data controllers exporting important data (which, under the Security Assessment Measures, is defined as data which if tampered with, damaged, leaked, or if obtained or used illegally may endanger national security, the economy, social stability, and public health and safety, etc.), (ii) critical information infrastructure operators or data controllers processing the personal information of one million people or more exporting personal information, (iii) data controllers who have exported the personal information of 100,000 people or the sensitive personal information of 10,000 people since January 1 of the previous year, or (iv) other situations provided for by the CAC that require a security assessment. As of the date of this annual report, we have not received any formal notice from any PRC cybersecurity regulator that the Company should apply for or otherwise be subject to security assessment, or subject to any investigation or received any inquiry, notice or sanction on security assessment. PRC government authorities may have wide discretion in the interpretation and enforcement of the Security Assessment Measures, including whether we have exported "important data" as defined thereunder, and thus there is uncertainty as to whether we may be subject to security assessment. Further, drafts of some of these measures have now been published, including the Measures on Security Assessment for Individual Information Cross-border Transfer (Draft for Comments) in June 2019, which may, upon enactment, require security review before transferring human health-related data out of China.

In addition, certain industry-specific laws and regulations affect the collection and transfer of personal data in China. For example, the Regulations of the PRC on the Administration of Human Genetic Resources, or HGR Regulations, which became effective and implemented on July 1, 2019, stipulates that use of Chinese human genetic resources, or HGR, for the purposes of carrying out collaborative international scientific research shall be approved by the administrative department of science and technology under the State Council. However, no approval is required for “international collaboration in clinical trials” that do not involve the export of HGR materials, provided that the two parties to the international collaboration shall file the type, quantity and usage of the HGR to be used with the administrative department of science and technology under the State Council before clinical trials. The PRC Biosecurity Law, which took effect on April 15, 2021, stipulates that foreign organizations and individuals, as well as institutions they establish or are the actual controllers of, must not collect or preserve HGR within the territory of China and must not provide China’s HGR to overseas. The Implementation Rules for the Administrative Regulation on Human Genetic Resources, or Implementation Rules for HGR, became effective on July 1, 2023, setting out circumstances under which the provision of or granting of access to human genetic resource information to overseas organizations, individuals or agencies controlled thereby affecting public health, national security or public interest in China would be subject to security review by the Ministry of Science and Technology, including where (i) human genetic resource information of important genetic families is involved; (ii) human genetic resource information of specific regions is involved, (iii) exome sequencing and genome sequencing information resources with of a sample exceeding 500 individuals is involved; and (iv) other circumstances that may affect the public health, national security and social public interest of China. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices, potentially resulting in confiscation of HGR samples and associated data and administrative fines, penalties and negative publicity.

Our clinical trial programs may implicate European data privacy laws, including the General Data Protection Regulation, or the GDPR, and local laws further implementing or supplementing the GDPR. The GDPR implements more stringent operational requirements for processors and controllers of personal data including requirements for such companies to be able to ensure and be able to demonstrate compliance with the GDPR. If our or our third-party partners’ privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or significant fines. In addition to statutory enforcement, non-compliance can lead to compensation claims by affected individuals, negative publicity and a potential loss of business. We are also subject to European laws on personal data export, as we may transfer personal data from the E.U. (or U.K.) to other jurisdictions which are not considered by the European Commission to offer “adequate” protection of personal data (such as Hong Kong or the United States). Following the Schrems II decision of the European Court of Justice in 2020, there has been intensified focus on exports of personal data which do not meet the high standards of protection expected by the E.U. Certain supervisory authorities in the E.U. have now begun to take enforcement action in this area, ordering restrictions on certain transfers of personal data to third countries such as the United States. These changes could require us to make operational changes and could increase costs and may lead to governmental enforcement actions, litigation, fines and penalties or adverse publicity that could have an adverse effect on our business.

We believe, to the best of our knowledge, our business operations do not violate any of the above laws and regulations currently in force in all material aspects. We have been taking and will continue to take reasonable measures to comply with applicable data privacy, data protection and cybersecurity laws. We cannot guarantee the effectiveness of the measures undertaken by us and business partners, and such measures may still be determined as insufficient, improper, or even as user-privacy invasive, by the relevant authorities, which may result in penalties against us. Complying with all applicable laws, regulations, standards and obligations relating to data privacy, security, and transfers may cause us to incur substantial operational costs or require us to modify our data processing practices and processes. To the extent that we need to alter our business model or practices to adapt to these announcement and provisions and future regulations, laws and policies, we could incur additional expenses. We cannot assure you we can adapt our operations to it in a timely manner. Non-compliance could result in proceedings against us by data protection authorities, governmental entities or others, including class action privacy litigation in certain jurisdictions, which would subject us to significant fines, penalties, judgments and negative publicity. In addition, if our practices are not consistent or viewed as not consistent with legal and regulatory requirements, including changes in laws, regulations and standards or new interpretations or applications of existing laws, regulations and standards, we may become subject to audits, inquiries, whistleblower complaints, adverse media coverage, investigations, loss of export privileges, severe criminal or civil sanctions and reputational damage. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Product liability claims or lawsuits could cause us, our collaboration partners or our joint ventures to incur substantial liabilities.

We, our collaboration partners and our joint ventures face an inherent risk of product liability exposure related to the use of our drug candidates in clinical trials, sales of our or our joint ventures' products or the products we or they license from third parties. If we, our collaborators and our joint ventures cannot successfully defend against claims that the use of such drug candidates in our clinical trials or any products sold by us or our joint ventures, including savolitinib, fruquintinib, surufatinib and/or any of our drug candidates which receive regulatory approval, caused injuries, we, our collaboration partners and our joint ventures could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our and our joint ventures' products;
- significant negative media attention and reputational damage;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any drug candidates that we may develop.

Our principal insurance policies cover product liability for savolitinib, fruquintinib, surufatinib, certain prescription drugs and health supplements, property loss due to accidents or natural disasters and adverse events in clinical trials. Existing PRC laws and regulations do not require us, our collaborators or our joint ventures to have, nor do we or they, maintain liability insurance to cover product liability claims except with respect to savolitinib, fruquintinib, surufatinib, certain prescription drugs and health supplements, and liability with respect to our oncology and immunology clinical trials. Any litigation might, result in substantial costs and diversion of resources. While we maintain liability insurance for clinical trials and products, this insurance may not fully cover our potential liabilities. Inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of products that we or our collaborators develop.

An occurrence of a widespread health epidemic or other outbreaks or natural disasters could have a material adverse effect on our business, financial condition and results of operations.

Our business could be materially and adversely affected by the outbreak of a widespread health epidemic, such as COVID-19, swine flu, avian influenza, severe acute respiratory syndrome, Ebola and Zika; natural disasters, such as earthquakes, snowstorms, storm surges, floods, fires, drought and other extreme weather events and other effects of climate change; or other events, such as wars, acts of terrorism, environmental accidents, power shortages or communication interruptions. The occurrence of a disaster or a prolonged outbreak of an epidemic illness or other adverse public health developments could materially disrupt our industry and our business and operations, and have a material adverse effect on our business, financial condition and results of operations. For example, these events could cause a temporary closure of the facilities we use for our operations, significantly disrupt manufacturing and supply chain, our sales and marketing and clinical trial operations and those of our collaboration partners, and the ability to advance our research and development activities and pursue development of any of our drug candidates. Our operations could also be disrupted if any of our employees or employees of our business partners are suspected of contracting an epidemic disease, since this could require us or our business partners to quarantine some or all of these employees or disinfect the facilities used for our operations.

We may engage in strategic transactions, including acquisitions, investments, joint ventures or divestitures. If unsuccessful, such transaction may have an adverse effect on our business.

From time to time, we may pursue strategic transactions, including acquisitions, investments, joint ventures and divestitures. For example, we are continuing to actively evaluate non-core assets divestment opportunities as part of our strategy to focus on our core businesses, which include the potential divestment of Shanghai Hutchison Pharmaceuticals. For more information, please refer to Item 4.A. "History and Development of the Company." Acquisitions and investments involve numerous risks such as difficulties in finding suitable partners or acquisition candidates, difficulties in obtaining financing on favorable terms, if at all, the assumption of certain known and unknown liabilities of acquired companies and difficulties in integrating operations, services, products and personnel. Joint ventures may result in issues such as conflicts in goals and corporate cultures, commercial disputes with joint venture partners as well as imbalanced contributions and benefits. Divestitures also involve numerous risks. Any divestiture could result in a dilutive impact to our future earnings and significant write-offs, including those related to goodwill and other intangible assets, which could have a material adverse effect on our results of operations and financial condition. Divestitures could also result in difficulties in the separation of operations, services, products and personnel, the diversion of management's attention from other business concerns, the disruption of our business and the potential loss of key employees. There is also no guarantee that we can complete strategic transactions in a timely manner, on a cost-effective basis, or at all, and we may not realize the expected benefits of any transaction. We may not be successful in managing these or any other significant risks that we encounter if we engage in a strategic transaction. If we are not successful in managing the risks, uncertainties and potential disruptions, a strategic transaction could have a negative impact on our business, results of operations or financial position.

We, our collaboration partners, our joint ventures and our third party contractors may be exposed to liabilities under the U.S. Foreign Corrupt Practices Act, or FCPA, U.S. healthcare fraud and abuse laws, the Bribery Act 2010 of the United Kingdom, or U.K. Bribery Act, and Chinese anti-corruption laws, and any determination that we or they have violated these laws could have a material adverse effect on our business or our reputation.

In the day-to-day conduct of our business, we, our collaboration partners, our joint ventures and our third party contractors are in frequent contact with persons who may be considered government officials under applicable anti-corruption, anti-bribery and anti-kickback laws, which include doctors at public hospitals in China and elsewhere. Therefore, we, our collaboration partners, our joint ventures and our third party contractors are subject to risk of violations under the FCPA, the U.K. Bribery Act, and other laws in the countries where we or they do business. We, our collaboration partners, our joint ventures and our third party contractors have operations in China, agreements with third parties in China, and we and our joint ventures make most of our sales in China. The PRC laws and regulations also strictly prohibit bribery of government officials. Our and our joint ventures' activities in China create the risk of unauthorized payments or offers of payments by the directors, employees, representatives, distributors, consultants or agents of our company, our collaboration partners, our joint ventures or our collaboration partners, even though they may not always be subject to our control. It is our policy to implement safeguards to discourage these practices by our, our collaboration partners', our joint ventures' and our collaboration partners' employees and third parties. We have implemented and adopted policies designed by the R&D-based Pharmaceutical Association Committee, an industry association representing approximately 40 global biopharmaceutical companies, to ensure compliance by us and our joint ventures and our and their directors, officers, employees, representatives, distributors, consultants and agents with the anti-corruption laws and regulations. We cannot assure you, however, that our existing safeguards are sufficient or that our, our collaboration partners', our joint ventures' or our third party contractors' directors, officers, employees, representatives, distributors, consultants and agents have not engaged and will not engage in conduct for which we may be held responsible, nor can we assure you that our business partners have not engaged and will not engage in conduct that could materially affect their ability to perform their contractual obligations to us or even result in our being held liable for such conduct. Violations of the FCPA, the U.K. Bribery Act or Chinese anti-corruption laws may result in severe criminal or civil sanctions, and we may be subject to other liabilities, which could have a material adverse effect on our business, reputation, financial condition, cash flows and results of operations.

When we or our collaboration partners begin to commercialize products in the United States and secure governmental reimbursement of our products, we and our collaboration partners also will be subject to the risk of violating U.S. federal and state healthcare fraud and abuse laws, including the Anti-Kickback Statute and the False Claims Act. These laws broadly prohibit providing or receiving kickbacks in connection with government-reimbursed healthcare items or services, as well submitting or causing the submission of false or fraudulent claims to government healthcare programs. Violations of these laws may result in severe criminal or civil sanctions and other administrative sanctions, which could have a material adverse effect on our business, reputation, financial condition, cash flows and results of operations.

Ensuring that our, our collaboration partners', our joint ventures' and our third party contractors' future business arrangements with third parties comply with applicable laws could also involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our or our joint ventures' operations were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment and exclusion from government funded healthcare programs, any of which could substantially disrupt our operations. If the physicians, hospitals or other providers or entities with whom we, our collaboration partners, our joint ventures, and our third party contractors do business are found not to be in compliance with applicable laws, they may also be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct by our employees. Misconduct by our employees could include intentional failures to comply with applicable regulations, provide accurate information to regulatory authorities or comply with healthcare fraud and abuse laws and regulations. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we have taken to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

If we or our joint ventures fail to comply with environmental, health and safety laws and regulations, we or they could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and our joint ventures are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemical materials. Our operations also produce hazardous waste products. We and our joint ventures are therefore subject to PRC laws and regulations concerning the discharge of waste water, gaseous waste and solid waste during our manufacturing processes. We and our joint ventures are required to establish and maintain facilities to dispose of waste and report the volume of waste to the relevant government authorities, which conduct scheduled or unscheduled inspections of our facilities and treatment of such discharge. We and our joint ventures may not at all times comply fully with environmental regulations. Any violation of these regulations may result in substantial fines, criminal sanctions, revocations of operating permits, shutdown of our facilities and obligation to take corrective measures. We and our joint ventures generally contract with third parties for the disposal of these materials and waste. We and our joint ventures cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from the use of hazardous materials, we and/or our joint ventures could be held liable for any resulting damages, and any liability could exceed our resources. We and/or our joint ventures also could incur significant costs associated with civil or criminal fines and penalties.

Although we and our joint ventures maintain workers' compensation insurance to cover costs and expenses incurred due to on-the-job injuries to our employees and third-party liability insurance for injuries caused by unexpected seepage, pollution or contamination, this insurance may not provide adequate coverage against potential liabilities. Furthermore, the PRC government may take steps towards the adoption of more stringent environmental regulations. Due to the possibility of unanticipated regulatory or other developments, the amount and timing of future environmental expenditures may vary substantially from those currently anticipated. If there is any unanticipated change in the environmental regulations, we and our joint ventures may need to incur substantial capital expenditures to install, replace, upgrade or supplement our equipment or make operational changes to limit any adverse impact or potential adverse impact on the environment in order to comply with new environmental protection laws and regulations. If such costs become prohibitively expensive, we may be forced to cease certain aspects of our or our joint ventures' business operations.

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively.

We are heavily dependent on critical, complex and interdependent information technology systems, including internet-based systems, to support our business processes. Our information technology system security is continuously reviewed, maintained and upgraded in response to possible security breach incidents. Despite the implementation of these measures, our information technology systems and those of third parties with which we contract are vulnerable to damage from external or internal security incidents, breakdowns, malicious intrusions, cybercrimes, including State-sponsored cybercrimes, malware, misplaced or lost data, programming or human errors or other similar events. System failures, accidents or security breaches could cause interruptions in our operations and could result in inappropriately accessed, tampered with, modified or stolen scientific data or a material disruption of our clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. Such event could significantly harm our Oncology/Immunology operations, including resulting in the loss of clinical trial data which could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Such events could also lead to the loss of important information such as trade secrets or other intellectual property and could accelerate the development or manufacturing of competing products by third parties. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our research and development programs and the development of our drug candidates could be delayed.

We have granted, and may continue to grant, options, long-term incentive scheme ("LTIP") awards and other types of awards under our Option Schemes and our LTIP, or collectively the Schemes, which may result in increased share-based compensation expenses and give rise to potential employment related disputes.

We have adopted the Options Schemes for the purpose of granting share-based compensation awards to certain management, directors, employees and other eligible grantees as a means to retain, incentivize, reward, remunerate, compensate and/or provide benefits to eligible grantees. We recognized share-based compensation expenses of \$42.0 million, \$30.6 million and \$36.6 million for the years ended December 31, 2021, 2022 and 2023, respectively, in our consolidated financial statements in accordance with U.S. GAAP.

We believe the granting of share-based compensation is of significant importance to our ability to attract and retain key personnel and employees, and we will continue to grant share-based compensation in the future. As a result, our expenses associated with share-based compensation may increase, which may have an adverse effect on our results of operations. We may re-evaluate the vesting schedules, exercise price or other key terms applicable to the grants under our currently effective Schemes from time to time, which may result in a substantial change in our share-based compensation expenses in the reporting periods. In addition, we could in the future become involved in disputes or legal proceedings with our employees or former employees on employment related matters (including disputes on the entitlement of options, awards and other share-based compensation or in connection with the employees' incentive or compensation arrangements). If such disputes or legal proceedings arise, there can be no assurance that we will prevail in them, and in any event defending against these disputes or legal proceedings could cause us to incur legal and other costs. Any adverse outcome of these disputes or legal proceedings could have a material adverse effect on our reputation, business and results of operations.

For more information on the Schemes, please refer to Item 6.B. "Compensation—Equity Compensation Schemes and Other Benefit Plans."

The PRC's economic, political and social conditions, as well as governmental policies, could affect the business environment and financial markets in China, our ability to operate our business, our liquidity and our access to capital.

Substantially all of our and our joint ventures' business operations are conducted in China. Accordingly, our results of operations, financial condition and prospects are subject to economic, political and legal developments in China to a significant degree. China's economy differs from the economies of developed countries in many respects, including with respect to the amount of government involvement, level of development, growth rate, control of foreign exchange and allocation of resources. If the business environment in China deteriorates from the perspective of domestic or international investors, our or our joint ventures' business in China may also be adversely affected.

Although the PRC government has implemented measures emphasizing the utilization of market forces for economic reform, the reduction of state ownership of productive assets, and the establishment of improved corporate governance in business enterprises, a substantial portion of productive assets in China is still owned by the government. In addition, the PRC government continues to play a significant role in regulating industry development by imposing industrial policies. The PRC government also exercises significant control over China's economic growth by allocating resources, controlling payment of foreign currency-denominated obligations, setting monetary policy, regulating financial services and institutions and providing preferential treatment to particular industries or companies. See also "The PRC government exerts substantial influence over the manner in which we conduct our business activities. Its oversight and discretion over our business could result in a material adverse change in our operations and the value of our ordinary shares and ADSs. Changes in laws, regulations and policies in China and uncertainties with respect to the PRC legal system could materially and adversely affect us. In addition, rules and regulations in China can change quickly with little advance notice."

While the PRC economy has experienced significant growth in the past 40 years, growth has been uneven across different regions and among various economic sectors of China. The PRC government has implemented various measures to encourage economic development and guide the allocation of resources. Some of these measures benefit the overall PRC economy, but may have a negative effect on us or our joint ventures. For example, our financial condition and results of operations may be adversely affected by government control over capital investments or changes in tax regulations that are applicable to us or our joint ventures.

The PRC government exerts substantial influence over the manner in which we conduct our business activities. Its oversight and discretion over our business could result in a material adverse change in our operations and the value of our ordinary shares and ADSs. Changes in laws, regulations and policies in China and uncertainties with respect to the PRC legal system could materially and adversely affect us. In addition, rules and regulations in China can change quickly with little advance notice.

We conduct a substantial portion of our business through our subsidiaries and joint ventures in China. PRC laws and regulations govern our and their operations in China. The Chinese government has exercised and continues to exercise substantial control over virtually every sector of the Chinese economy through regulation and state ownership. For example, the PRC government has recently published new policies that significantly affected certain industries such as the education and internet industries, and we cannot rule out the possibility that it will in the future release regulations or policies regarding our industry that could adversely affect our business, financial condition and results of operations. See also "The PRC's economic, political and social conditions, as well as governmental policies, could affect the business environment and financial markets in China, our ability to operate our business, our liquidity and our access to capital" and "The PRC government has increasingly strengthened oversight in offerings conducted overseas or on foreign investment in China-based issuers, which could result in a material change in our operations and our ordinary shares and ADSs could decline in value or become worthless."

Our ability to operate in China may be harmed by changes in its laws and regulations. The central or local governments may impose new, stricter regulations or interpretations of existing regulations that would require additional expenditures and efforts on our part to ensure our compliance with such regulations or interpretations. For instance, regulations introduced by the NMPA concerning drug inspection, investigation, evidence collection and disposal are relatively new, and because of the limited volume of published judicial decisions, which are non-binding in nature, the interpretation and enforcement of these laws and regulations are uncertain. In addition, the implementation of laws and regulations may be in part based on government policies and internal rules that are subject to the interpretation and discretion of different government agencies (some of which are not published on a timely basis or at all) that may have a retroactive effect. As a result, we may not be aware of our, our collaboration partners' or our joint ventures' violation of these policies and rules until sometime after the violation. The imposition of new regulations or interpretations of existing regulations can occur quickly with little advance notice. We may incur penalties for any failure to comply with PRC laws and regulations. In addition, any litigation in China, regardless of outcome, may be protracted and result in substantial costs and diversion of resources and management attention. Since PRC administrative and court authorities have significant discretion in interpreting and implementing statutory and contractual terms, it may be difficult to evaluate the outcome of administrative and court proceedings and the level of legal protection we enjoy.

For further information regarding government regulation in China and other jurisdictions, see Item 4.B. “Business Overview—Regulations—Government Regulation of Pharmaceutical Product Development and Approval—PRC Regulation of Pharmaceutical Product Development and Approval,” “Business Overview—Regulations—Coverage and Reimbursement—PRC Coverage and Reimbursement” and “Business Overview—Regulations—Other Healthcare Laws—Other PRC Healthcare Laws.”

The PRC government has increasingly strengthened oversight in offerings conducted overseas or on foreign investment in China-based issuers, which could result in a material change in our operations and our ordinary shares and ADSs could decline in value or become worthless.

The PRC government has indicated an intent to take actions to exert more oversight and control over offerings that are conducted overseas and/or foreign investment in China-based issuers. For example, on July 6, 2021, the relevant PRC government authorities made public the Opinions on Strictly Scrutinizing Illegal Securities Activities in Accordance with the Law, or the Opinions. These Opinions emphasized the need to strengthen the administration over illegal securities activities and the supervision of overseas listings by China-based companies and proposed to take effective measures, such as promoting the construction of relevant regulatory systems to deal with the risks and incidents faced by China-based overseas-listed companies.

On December 24, 2021, the CSRC issued the Provisions of the State Council on the Administration of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments) and the Administrative Measures for the Filing of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments), collectively the Draft Overseas Listing Regulations, for public comment until January 23, 2022.

Following issuance of the Draft Overseas Listing Regulations, on February 17, 2023, the CSRC issued the Notice on Filing Arrangements for Overseas Securities Offering and Listing by Domestic Companies (the “**CSRC Filing Notice**”), stating that the CSRC has published the Trial Administrative Measures of Overseas Securities Offering and Listing by Domestic Companies (the “**Trial Measures**”) and five supporting guidelines (the “**Listing Guidelines**”), collectively the Trial Measures and Listing Guidelines. Among others, the Trial Measures and Listing Guidelines provide that overseas offerings and listings by PRC domestic companies shall:

- (i) require submission of relevant materials that contain a filing report and a legal opinion, providing truthful, accurate and complete information on matters including but not limited to the shareholders of the issuer. Where the filing documents are complete and in compliance with stipulated requirements, the CSRC shall, within 20 working days after receipt of filing documents, conclude the filing procedure and publish filing results on the CSRC website. Where filing documents are incomplete or do not conform to stipulated requirements, the CSRC shall request supplementation and amendment thereto within five working days after receipt of the filing documents. The issuer should then complete supplementation and amendment within 30 working days;
- (ii) abide by laws, administrative regulations and relevant state rules concerning foreign investment in China, state-owned asset administration, industry regulation and outbound investment, and shall not disrupt the PRC domestic market order, harm state or public interests or undermine the lawful rights and interests of PRC domestic investors;
- (iii) abide by national secrecy laws and relevant provisions. Necessary measures shall be taken to fulfill confidentiality obligations. Divulgence of state secrets or working secrets of government agencies is strictly prohibited. Provision of personal information and important data, etc., to overseas parties in relation to overseas offering and listing of PRC domestic companies shall be in compliance with applicable laws, administrative regulations and relevant state rules; and
- (iv) be made in strict compliance with relevant laws, administrative regulations and rules concerning national security in the spheres of foreign investment, cybersecurity, data security, etc., and issuers shall duly fulfill their obligations to protect national security. If the intended overseas offering and listing necessitates a national security review, relevant security review procedures shall be completed according to the law before the application for such offering and listing is submitted to any overseas parties such as securities regulatory agencies and trading venues;

The Trial Measures came into effect on March 31, 2023. PRC domestic companies seeking to offer and list securities (which, for the purposes of the Trial Measures, are defined thereunder as equity shares, depository receipts, corporate bonds convertible to equity shares, and other equity securities that are offered and listed overseas, either directly or indirectly, by PRC domestic companies) in overseas markets, either via direct or indirect means, must file with the CSRC within three working days after their application for an overseas listing is submitted.

The Trial Measures provide that where a PRC domestic company seeks to indirectly offer and list securities in overseas markets, the issuer shall designate a major domestic operating entity, which shall, as the domestic entity responsible, file with the CSRC. The Trial Measures stipulate that an overseas listing will be determined as “indirect” if the issuer meets both of the following conditions: (1) 50% or more of any of the issuer’s operating revenue, total profit, total assets or net assets as documented in its audited consolidated financial statements for the most recent accounting year are accounted for by PRC domestic companies (“**Condition I**”), and (2) the main parts of the issuer’s business activities are conducted in the PRC, or its main places of business are located in the PRC, or the senior managers in charge of its business operations and management are mostly Chinese citizens or domiciled in the PRC (“**Condition II**”); whether Chinese citizens from Taiwan, Hong Kong, and Macau are included in the foregoing specification is not specified. The determination as to whether or not an overseas offering and listing by PRC domestic companies is indirect shall be made on a ‘substance over form’ basis. The Listing Guidelines further stipulate that if an issuer not satisfying Condition I submits an application for issuance and listing in overseas markets in accordance with relevant non-PRC issuance regulations requiring such issuer to disclose risk factors mainly related to the PRC, the securities firm(s) and the issuer’s PRC counsel should follow the principle of ‘substance over form’ in order to identify and argue whether the issuer should complete a filing under the Trial Measures.

Subsequent securities offerings of an issuer in (i) the same overseas market where it has previously offered and listed securities, and (ii) an overseas market other than one where the issuer has previously offered and listed securities shall be filed with the CSRC within three working days after offerings are completed. Additionally, the Trial Measures stipulate that after an issuer has offered and listed securities in an overseas market, the issuer shall submit a report to the CSRC within three working days after the occurrence and public disclosure of (i) a change of control thereof, (ii) investigations of or sanctions imposed on the issuer by overseas securities regulators or relevant competent authorities, (iii) changes of listing status or transfers of listing segment, and (iv) a voluntary or mandatory delisting.

The CSRC Filing Notice states that, beginning from March 31, 2023, PRC domestic enterprises which have already issued and listed securities overseas and fall within the scope of filing under the Trial Measures shall be considered “existing enterprises” (“**Existing Listed Enterprises**”). Existing Listed Enterprises are not required to complete filings immediately; rather, Existing Listed Enterprises should complete filings if they are subsequently involved in matters require filings, such as follow-on financing activities, in accordance with the Trial Measures.

There is a possibility that we may be deemed as an Existing Listed Enterprise as defined under the CSRC Filing Notice, and that future offerings of listed securities or listings outside China by us may be subject to CSRC filing requirements in accordance with the Trial Measures. Given that the Trial Measures and Listing Guidelines have been introduced recently, and that there remain substantial uncertainties surrounding the enforcement thereof, we cannot assure you that, if required, we would be able to complete the filings and fully comply with the relevant new rules on a timely basis, if at all.

In addition, the Measures for Cybersecurity Review, which took effect on February 15, 2022, requires, among others, prior cybersecurity review for online platform operators holding over one million users’ personal information before any public listing in a foreign country. The Measures on Security Assessment of Cross-border Data Transfer, effective on September 1, 2022, specify that data controllers and/or critical information infrastructure operators will be subject to security assessment. There remain uncertainties as to whether such measures are applicable to our business. See also “We are subject to stringent privacy and cybersecurity laws, information security policies and contractual obligations related to data privacy and security, and we may be exposed to risks related to our management of the medical data of subjects enrolled in our clinical trials and other personal or sensitive information.”

On February 24, 2023, the CSRC and other PRC governmental authorities jointly issued the Provisions on Strengthening Confidentiality and Archives Administration of Overseas Securities Offering and Listing by Domestic Companies (the “Confidentiality Provisions”), which came into effect on March 31, 2023. According to the Confidentiality Provisions, PRC domestic companies that directly or indirectly conduct overseas offerings and listings shall strictly abide by the laws and regulations on confidentiality when providing or publicly disclosing, whether directly or through their overseas listed entities, materials to securities services providers. In the event such materials contain state secrets or working secrets of government agencies, PRC domestic companies shall first obtain approval from authorities, and file with the secrecy administrative department at the same level with the approving authority; in the event that such materials, if divulged, will jeopardize national security or public interest, PRC domestic companies shall comply with procedures stipulated by national regulations. PRC domestic companies shall also provide a written statement of the specific sensitive information provided when providing materials to securities service providers, and such written statements shall be retained for inspection. As the Confidentiality Provisions were recently promulgated and are effective, their interpretation and implementation remain substantially uncertain.

If (i) we mistakenly conclude that certain regulatory filings, permissions and approvals are not required or (ii) applicable laws, regulations, or interpretations change and (iii) we are required to obtain such filings, permissions or approvals in the future, we may be unable to obtain them in a timely manner, or at all, and such filings, permissions or approvals may be denied or rescinded even if obtained. We may face adverse actions or sanctions by the CSRC or other PRC regulatory agencies if we are unable to comply with such requirements, which may result in fines and penalties, restrictions on our operations, having to delist from a stock exchange outside of China, the halting of securities offerings to foreign investors and other actions that could materially and adversely affect our operations and the interest of our investors and cause a significant depreciation in the price of our ordinary shares and ADSs.

Certain PRC regulations may make it more difficult for us to pursue growth through acquisitions. Any failure or perceived failure by us to comply with PRC anti-monopoly laws and regulations may result in governmental investigations or enforcement actions, litigation or claims against us and could have an adverse effect on our business, financial condition and results of operations.

We may pursue potential strategic acquisitions that are complementary to our business and operations. In doing so, we will be subject to a variety of PRC anti-monopoly laws. The Regulations on Mergers and Acquisitions of Domestic Enterprises by Foreign Investors, or the M&A Rules, adopted by six PRC regulatory agencies in 2006 and amended in 2009, established additional procedures and requirements that could make merger and acquisition activities by foreign investors more time-consuming and complex. For example, the M&A Rules require that the MOFCOM be notified in advance of any change-of-control transaction in which a foreign investor takes control of a PRC domestic enterprise if (i) any important industry is concerned, (ii) such transaction involves factors that have or may have impact on the national economic security or (iii) such transaction will lead to a change in control of a domestic enterprise which holds a famous trademark or PRC time-honored brand. The approval from the MOFCOM must be obtained in circumstances where overseas companies established or controlled by PRC enterprises or residents acquire affiliated domestic companies. Mergers, acquisitions or contractual arrangements that allow one market player to take control of or to exert decisive impact on another market player must also be notified in advance to the SAMR when the threshold under the Provisions on Thresholds for Prior Notification of Concentrations of Undertakings, or the Prior Notification Rules, issued by the State Council in 2008 and amended in 2018, is triggered. PRC national security review rules, which became effective in September 2011, require a strict review of (a) mergers and acquisitions by foreign investors that raise “national defense and security” concerns and (b) mergers and acquisitions through which foreign investors may acquire de facto control over domestic enterprises that raise “national security” concerns. The rules also prohibit any activities attempting to bypass a security review, including by structuring the transaction through a proxy or contractual control arrangement.

Further, the Measures for the Security Review of Foreign Investments promulgated by the NDRC and MOFCOM, which became effective from January 2021, require that a security review by relevant governmental authorities must be conducted for foreign investments that affect or may affect national security in accordance with the provisions thereunder.

The PRC anti-monopoly enforcement agencies have in recent years strengthened enforcement under the PRC Anti-Monopoly Law. In March 2018, the SAMR was formed as a new governmental agency to take over, among other things, the anti-monopoly enforcement functions from the relevant departments under the MOFCOM, the NDRC and SAMR. Since its inception, the SAMR has continued to strengthen anti-monopoly enforcement. In November 2021, the State Council inaugurated the National Anti-Monopoly Bureau, which aims to further implement fair competition policies and strengthen anti-monopoly supervision in the PRC, particularly to strengthen oversight and law enforcement in areas involving innovation, science and technology, information security and people's livelihoods.

SAMR issued the Provisions on Prohibition of the Abuse of Market Dominance on March 10, 2023, which came into effect on April 15, 2023, pursuant to which an abuse of market dominance determined by the SAMR shall satisfy all the following criteria: (i) the business operator is dominating the market; (ii) the business operator has eliminated or restricted competition; (iii) the business operator has no legitimate reason to carry out such acts; and (iv) such acts by the business operator have an impact on elimination or restriction of market competition. Pursuant to the Provisions on Prohibition of Monopoly Agreements issued by SAMR and effective from April 15, 2023, entering into monopolistic agreements, which means agreements or concerted practices to eliminate or restrict competition, is prohibited, unless such agreements satisfy the specific exemptions prescribed in the Anti-Monopoly Law, such as improving technologies or increasing the efficiency and competitiveness of small and medium-sized undertakings. If business operators fail to comply with the Anti-Monopoly Law or other relevant regulations, they may be ordered to cease business activities, unwind transactions, and be subject to confiscation of unlawful profits and fines.

Complying with the requirements of these regulations when pursuing acquisitive transactions could be time-consuming, and any required approval processes, including obtaining approval or clearance from the MOFCOM, may delay or inhibit our ability to complete such transactions, which could affect our ability to expand our business or maintain our market share. Due to the enhanced enforcement of the Anti-Monopoly Law, we may receive greater scrutiny and attention from regulators and more frequent and rigid investigations or review by regulators, which may increase our compliance costs and subject us to heightened risks and challenges. In addition, there are significant uncertainties on the evolving legislative activities and varied local implementation practices of anti-monopoly and competition laws and regulations in China. The amended Anti-Monopoly Law, published in October 2021 in draft form for public comment, became effective in August 2022. It imposes a higher regulatory requirement to complete an acquisitive transaction. Any failure or perceived failure by us to comply with the anti-monopoly laws and regulations may result in governmental investigations or enforcement actions, lawsuits or claims against us and could have an adverse effect on our business, financial condition and results of operations. See also “Risks Relating to Sales of Our Internally Developed Drugs and Other Drugs—We may engage in strategic transactions, including acquisitions, investments, joint ventures or divestitures that may have an adverse effect on our business. If we engage in a strategic transaction, there is no assurance that the transaction will be consummated.”

Restrictions on currency exchange may limit our ability to receive and use our revenue effectively.

Substantially all of our revenue is denominated in renminbi, which currently is not a freely convertible currency. A portion of our revenue may be converted into other currencies to meet our foreign currency obligations, including, among others, payments of dividends declared, if any, in respect of our ordinary shares or ADSs. Under China’s existing foreign exchange regulations, our subsidiaries and joint ventures are able to pay dividends in foreign currencies or convert renminbi into other currencies for use in operations without prior approval from the PRC State Administration of Foreign Exchange, or the SAFE, by complying with certain procedural requirements. However, we cannot assure you that the PRC government will not take future measures to restrict access to foreign currencies for current account transactions.

Our PRC subsidiaries’ and joint ventures’ ability to obtain foreign exchange is subject to significant foreign exchange controls and, in the case of amounts under the capital account, requires the approval of and/or registration with PRC government authorities, including the SAFE. In particular, if we finance our PRC subsidiaries or joint ventures by means of foreign debt from us or other foreign lenders, the amount is not allowed to exceed either the cross-border financing risk weighted balance calculated based on a formula by the PBOC or the difference between the amount of total investment and the amount of the registered capital. Further, such loans must be filed with and registered with the SAFE or their local branches and the National Development and Reform Commission (if applicable). If we finance our PRC subsidiaries or joint ventures by means of additional capital contributions, the amount of these capital contributions must first be filed with the relevant government approval authority. These limitations could affect the ability of our PRC subsidiaries and joint ventures to obtain foreign exchange through debt or equity financing.

Our business benefits from certain PRC government tax incentives. Any changes to, or our PRC subsidiaries/joint ventures failing to continuously meet the criteria for these incentives could have a material adverse effect on our operating results by significantly increasing our tax expenses.

Certain of our PRC subsidiaries and a joint venture have been granted High and New Technology Enterprise, or HNTE, status by the relevant PRC authorities. This status allows the relevant enterprise to enjoy a reduced Enterprise Income Tax, or EIT, rate at 15% on its taxable profits. For the duration of its HNTE grant, the relevant PRC enterprise must continue to meet the relevant HNTE criteria or else the 25% standard EIT rate will be applied from the beginning of the calendar year when the enterprise fails to meet the relevant criteria. If the rules for such incentives are amended, it would be uncertain whether any criteria as amended can be met, in which case the higher EIT rate may apply resulting in increased tax burden which will impact our business, financial condition, results of operations and growth prospects.

We may be treated as a resident enterprise for PRC Tax purposes under China's Enterprise Income Tax Law and Implementation Rules, or the EIT Law, and our global income may therefore be subject to PRC income tax.

China's EIT Law defines the term "de facto management bodies" as "bodies that substantially carry out comprehensive management and control on the business operation, employees, accounts and assets of enterprises." Under the EIT Law, an enterprise incorporated outside of China whose "de facto management bodies" are located in China is considered a "resident enterprise" and will be subject to a uniform 25% EIT rate on its global income. On April 22, 2009, China's State Administration of Taxation, or the SAT, in the Notice Regarding the Determination of Chinese-Controlled Offshore-Incorporated Enterprises as PRC Tax Resident Enterprises on the Basis of De Facto Management Bodies, or Circular 82, further specified certain criteria for the determination of what constitutes "de facto management bodies." If all of these criteria are met, the relevant foreign enterprise may be regarded to have its "de facto management bodies" located in China and therefore be considered a resident enterprise in China. These criteria include: (i) the enterprise's day-to-day operational management is primarily exercised in China; decisions relating to the enterprise's financial and human resource matters are made or subject to approval by organizations or personnel in China; (ii) the enterprise's primary assets, accounting books and records, company seals, and board and shareholders' meeting minutes are located or maintained in China; and (iii) 50% or more of voting board members or senior executives of the enterprise habitually reside in China. Although Circular 82 only applies to foreign enterprises that are majority-owned and controlled by PRC enterprises, not those owned and controlled by foreign enterprises or individuals, the determining criteria set forth in Circular 82 may be adopted by the PRC tax authorities as the test for determining whether the enterprises are PRC tax residents, regardless of whether they are majority-owned and controlled by PRC enterprises.

Except for our PRC subsidiaries and joint ventures incorporated in China, we believe that none of our entities incorporated outside of China is a PRC resident enterprise for PRC tax purposes. However, the tax resident status of an enterprise is subject to determination by the PRC tax authorities, and uncertainties remain with respect to the interpretation of the term "de facto management body."

If we are treated as a PRC tax resident, dividends distributed by us to our non-PRC shareholders and ADS holders or any gains realized by non-PRC shareholders and ADS holders from the transfer of our shares or ADSs may be subject to PRC tax.

Under the EIT Law, dividends payable by a PRC enterprise to its foreign investor who is (i) a non-PRC resident enterprise with no office or premises established in China, or (ii) a non-PRC resident enterprise with an office or premises established in China but whose income (i.e. dividends received) has no de facto relationship with said office or premises, as well as gains on transfers of shares of a PRC enterprise by such a foreign investor will generally be subject to a 10% withholding tax, unless such non-PRC resident enterprise's jurisdiction of tax residency has an applicable tax treaty with the PRC that provides for an exemption or a reduced rate of withholding tax.

If the PRC tax authorities determine that we should be considered a PRC resident enterprise for EIT purposes, any dividends payable by us to our non-PRC resident enterprise shareholders or ADS holders, as well as gains realized by such investors from the transfer of our shares or ADSs may be subject to a 10% withholding tax. Furthermore, if we are considered a PRC resident enterprise for EIT purposes, it is unclear whether our non-PRC individual shareholders (including our ADS holders) would be subject to any PRC tax on dividends or gains obtained by such non-PRC individual shareholders. If any PRC tax were to apply to dividends or gains realized by non-PRC individuals, it would generally apply at a rate of up to 20% (which in the case of dividends may be withheld at source). The foregoing rates may be reduced by an applicable tax treaty, but it is unclear if a non-PRC resident shareholder or ADS holder would be able to obtain in practice the benefits of any tax treaties between their country of tax residence and the PRC in the event that we are treated as a PRC resident enterprise. If dividends payable to our non-PRC resident shareholders, or gains from the transfer of our shares or ADSs by such shareholders are subject to PRC tax, the value of your investment in our shares or ADSs may decline significantly.

There is uncertainty regarding the PRC withholding tax rate that will be applied to distributions from our PRC subsidiaries and joint ventures to their respective Hong Kong immediate holding companies, which could have a negative impact on our business.

The EIT Law provides that a withholding tax at the rate of 10% is applicable to dividends payable by a PRC resident enterprise to investors who are “non-resident enterprises” (i.e., that do not have an establishment or place of business in the PRC or that have such establishment or place of business but the relevant dividend is not effectively connected with the establishment or place of business). However, pursuant to Article 10.2(1), or the Article, of the Arrangement between the Mainland of China and the Hong Kong Special Administrative Region for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with respect to Taxes on Income, or the Arrangement, withholding tax at a reduced rate of 5% may be applicable to dividends payable by PRC resident enterprises to beneficial owners of the dividends that are Hong Kong tax residents if certain requirements are met. There is uncertainty regarding whether the PRC tax authorities will consider us to be eligible to the reduced tax rate. If the Article is deemed not to apply to dividends payable by our PRC subsidiaries and joint ventures to their respective Hong Kong immediate holding companies that are ultimately owned by us, the withholding tax rate applicable to us will be the statutory rate of 10% instead of 5% which may potentially impact our business, financial condition, results of operations and growth prospects.

Any failure to comply with PRC regulations regarding our employee equity incentive plans may subject the PRC plan participants or us to fines and other legal or administrative sanctions, which could adversely affect our business, financial condition and results of operations.

In February 2012, the SAFE promulgated the Notices on Issues Concerning the Foreign Exchange Administration for Domestic Individuals Participating in Stock Incentive Plans of Overseas Publicly Listed Companies. Based on this regulation, PRC residents who are granted shares or share options by a company listed on an overseas stock market under its employee share option or share incentive plan are required to register with the SAFE or its local counterparts by following certain procedures. We and our employees who are PRC residents and individual beneficial owners who have been granted shares or share options have been subject to these rules due to our listing on the AIM market, Nasdaq and SEHK. We have registered the option schemes and the share incentive plan and will continue to assist our employees to register their share options or shares. However, any failure of our PRC individual beneficial owners and holders of share options or shares to comply with the SAFE registration requirements in the future may subject them to fines and legal sanctions and may, in rare instances, limit the ability of our PRC subsidiaries to distribute dividends to us.

In addition, the SAT has issued circulars concerning employee share options or restricted shares. Under these circulars, employees working in the PRC who exercise share options, or whose restricted shares vest, will be subject to PRC individual income tax. The PRC subsidiaries of an overseas listed company have obligations to file documents related to employee share options or restricted shares with relevant tax authorities and to withhold individual income tax of those employees related to their share options or restricted shares. Although the PRC subsidiaries currently withhold individual income tax from the PRC employees in connection with their exercise of share options, if they fail to report and pay the tax withheld according to relevant laws, rules and regulations, the PRC subsidiaries may face sanctions imposed by the tax authorities or other PRC government authorities.

We may be involved in litigation, legal disputes, claims or administrative proceedings which could be costly and time-consuming to resolve.

We may become subject, from time to time, to legal proceedings and claims that arise in the ordinary course of business or pursuant to governmental or regulatory enforcement activity. Any litigation or proceeding to which we become a party might result in substantial costs and divert management’s attention and resources. Furthermore, any litigation, legal disputes, claims or administrative proceedings which are initially not of material importance may escalate and become important to us due to a variety of factors, such as changes in the facts and circumstances of the cases, the likelihood of loss, the monetary amount at stake and the parties involved. Our insurance might not cover claims brought against us, provide sufficient payments to financially cover all of the costs to resolve such claims or continue to be available on terms acceptable to us.

The political relationships between China and other countries may affect our business operations.

We conduct our business primarily through our subsidiaries and joint ventures in China, but we also have clinical operations in the United States and other foreign jurisdictions. As a result, China's political relationships with the United States and other jurisdictions may affect our business operations. There can be no assurance that our clinical trial participants or customers will not alter their perception of us or their preferences as a result of adverse changes to the state of political relationships between China and the relevant foreign jurisdictions. Any tensions and political concerns between China and the relevant foreign jurisdictions may adversely affect our business, financial condition, results of operations, cash flows and prospects.

Risks Relating to Intellectual Property

If we, our joint ventures or our collaboration partners are unable to protect our or their products and drug candidates through intellectual property rights, our competitors may compete directly against us or them.

Our success depends, in part, on our, our joint venture partners' and our collaboration partners' ability to protect our and our joint ventures' and our collaboration partners' products and drug candidates from competition by establishing, maintaining and enforcing our or their intellectual property rights. We, our joint ventures and our collaboration partners seek to protect the products and technology that we and they consider commercially important by filing PRC and international patent applications, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. As of December 31, 2023, we had 274 issued patents, including 25 PRC patents, 24 U.S. patents and 13 European patents, 354 patent applications pending in major market jurisdictions, and 7 pending Patent Cooperation Treaty, or PCT, patent applications relating to the drug candidates of our Oncology/Immunology operations. For more details, see Item 4.B. "Business Overview—Patents and Other Intellectual Property." Patents may become invalid and patent applications may not be granted for a number of reasons, including known or unknown prior art, deficiencies in the patent application or the lack of originality of the technology. In addition, the PRC and the United States have adopted the "first-to-file" system under which whoever first files an invention patent application will be awarded the patent. Under the first-to-file system, third parties may be granted a patent relating to a technology which we invented. Furthermore, the terms of patents are finite. The patents we hold and patents to be issued from our currently pending patent applications generally have a twenty-year protection period starting from the date of application.

We, our joint ventures and/or our collaboration partners may become involved in patent litigation against third parties to enforce our or their patent rights, to invalidate patents held by such third parties, or to defend against such claims. A court may refuse to stop the other party from using the technology at issue on the grounds that our or our joint ventures' patents do not cover the third-party technology in question. Further, such third parties could counterclaim that we or our joint ventures infringe their intellectual property or that a patent we, our joint ventures or our collaboration partners have asserted against them is invalid or unenforceable. In patent litigation, defendant counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. In addition, third parties may initiate legal proceedings against us or our intellectual property to assert such challenges to our intellectual property rights.

The outcome of any such proceeding is generally unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information or made a misleading statement during prosecution. It is possible that prior art of which we, our joint ventures or our collaboration partners and the patent examiner were unaware during prosecution exists, which could render our or their patents invalid. Moreover, it is also possible that prior art may exist that we, our joint ventures or our collaboration partners are aware of but do not believe is relevant to our or their current or future patents, but that could nevertheless be determined to render our patents invalid. The cost to us or our joint ventures of any patent litigation or similar proceeding could be substantial, and it may consume significant management time. We and our joint ventures do not maintain insurance to cover intellectual property infringement.

An adverse result in any litigation proceeding could put one or more of our or our joint ventures' patents at risk of being invalidated or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering one of our or our joint ventures' products or our drug candidates, we could lose at least part, and perhaps all, of the patent protection covering such product or drug candidate. Competing drugs may also be sold in other countries in which our or our joint ventures' patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit, alleging our or our joint ventures' infringement of a competitor's patents, we could be prevented from marketing our drugs in one or more foreign countries. Any of these outcomes would have a materially adverse effect on our business.

Intellectual property and confidentiality legal regimes in China may not afford protection to the same extent as in the United States or other countries. Implementation and enforcement of PRC intellectual property laws may be deficient and ineffective. Policing unauthorized use of proprietary technology is difficult and expensive, and we or our joint ventures may need to resort to litigation to enforce or defend patents issued to us or them or to determine the enforceability, scope and validity of our proprietary rights or those of others. The experience and capabilities of PRC courts in handling intellectual property litigation varies, and outcomes are unpredictable. Further, such litigation may require a significant expenditure of cash and may divert management's attention from our or our joint ventures' operations, which could harm our business, financial condition and results of operations. An adverse determination in any such litigation could materially impair our or our joint ventures' intellectual property rights and may harm our business, prospects and reputation.

Developments in patent law could have a negative impact on our business.

From time to time, authorities in the United States, China, Europe and Japan and other government authorities may change the standards of patentability, and any such changes could have a negative impact on our business. For example, in the United States, the Leahy-Smith America Invents Act, or the America Invents Act, which was signed into law in 2011, includes a number of significant changes to U.S. patent law. These changes include a transition from a "first-to-invent" system to a "first-to-file" system, changes to the way issued patents are challenged, and changes to the way patent applications are disputed during the examination process. As a result of these changes, patent law in the United States may favor larger and more established companies that have greater resources to devote to patent application filing and prosecution. The U.S. Patent and Trademark Office, or USPTO, has developed regulations and procedures to govern the full implementation of the America Invents Act, and many of the substantive changes to patent law associated with the America Invents Act, and, in particular, the first-to-file provisions became effective on March 16, 2013. Substantive changes to patent law associated with the America Invents Act, including continually developing case law, may affect our ability to obtain patents, and if obtained, to enforce or defend them. Accordingly, it is not clear what, if any, impact the America Invents Act will have on the cost of prosecuting our or our joint ventures' patent applications and our or their ability to obtain patents based on our or our joint ventures' discoveries and to enforce or defend any patents that may issue from our or their patent applications, all of which could have a material adverse effect on our business.

If we are unable to maintain the confidentiality of our, our collaboration partners' and our joint ventures' trade secrets, the business and competitive position of ourselves and our joint ventures may be harmed.

In addition to the protection afforded by patents and the PRC's State Secret certification, we, our collaboration partners and our joint ventures rely upon unpatented trade secret protection, unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our, our collaboration partners' and our joint ventures' proprietary technology and processes, in part, by entering into confidentiality agreements with our and their collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our and their consultants and employees. We, our collaboration partners and our joint ventures may not be able to prevent the unauthorized disclosure or use of our or their technical know-how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we and our joint ventures may not have adequate remedies for any such breach or violation, and we, our collaboration partners could lose our trade secrets as a result. Enforcing a claim that a third-party illegally obtained and is using our or our joint ventures' trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts in China and other jurisdictions outside the United States are sometimes less prepared or willing to protect trade secrets.

The trade secrets of our company, our collaboration partners and our joint ventures could otherwise become known or be independently discovered by our or their competitors. For example, competitors could purchase our drugs and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our, our collaboration partners' or our joint ventures' trade secrets were to be lawfully obtained or independently developed by a competitor, we and our joint ventures would have no right to prevent them, or others to whom they communicate it, from using that technology or information to compete against us or our joint ventures. If our or our joint ventures' trade secrets are unable to adequately protect our business against competitors' drugs, our competitive position could be adversely affected, as could our business.

We, our collaboration partners and our joint ventures are dependent on trademark and other intellectual property rights licensed from others. If we lose our licenses for any of our products, we, our collaboration partners or our joint ventures may not be able to continue developing such products or may be required to change the way we market such products.

We, our collaboration partners and our joint ventures are parties to licenses that give us or them rights to third-party intellectual property that are necessary or useful for our, our collaboration partners' or our joint ventures' businesses. In particular, the "Hutchison", "Chi-Med", "Hutchison China MediTech" and "HUTCHMED" brands, among others, have been licensed to us by Hutchison Whampoa Enterprises Limited, an affiliate of our largest shareholder, Hutchison Healthcare Holdings Limited. Hutchison Whampoa Enterprises Limited grants us a royalty-free, worldwide license to such brands. For more details, please see "Item 7. Major Shareholders and Related Party Transactions—Related Party Transactions—Relationship with CK Hutchison—Intellectual property licensed by the CK Hutchison group." Under the terms of our brand license agreement, Hutchison Whampoa Enterprises Limited has the right to terminate the license if, among other things, we commit a material breach of the agreement, or within any twelve-month period the aggregate direct or indirect shareholding in our company held by CK Hutchison is reduced to less than 35%, 30% or 20%. Furthermore, the trademarks of Elunate and Orpathys are licensed to us in China by our collaboration partner Eli Lilly and AstraZeneca, respectively.

In some cases, our licensors have retained the right to prosecute and defend intellectual property rights licensed to us or our joint ventures. We depend in part on the ability of our licensors to obtain, maintain and enforce intellectual property protection for such licensed intellectual property. Such licensors may not successfully maintain their intellectual property, may determine not to pursue litigation against other companies that are infringing on such intellectual property, or may pursue litigation less aggressively than we or our joint ventures would. Without protection for the intellectual property we or our joint ventures license, other companies might be able to offer substantially identical products or branding, which could adversely affect our competitive business position and harm our business prospects.

If our, our collaboration partners' or our joint ventures' products or drug candidates infringe the intellectual property rights of third parties, we and they may incur substantial liabilities, and we and they may be unable to sell these products.

Our commercial success depends significantly on our, our collaboration partners and our joint ventures' ability to operate without infringing the patents and other proprietary rights of third parties. In the PRC, invention patent applications are generally maintained in confidence until their publication 18 months from the filing date. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made and invention patent applications are filed. Even after reasonable investigation, we may not know with certainty whether any third-party may have filed a patent application without our knowledge while we or our joint ventures are still developing or producing that product. While the success of pending patent applications and applicability of any of them to our or our joint ventures' programs are uncertain, if asserted against us or them, we could incur substantial costs and we or they may have to:

- obtain licenses, which may not be available on commercially reasonable terms, if at all;
- redesign products or processes to avoid infringement; and
- stop producing products using the patents held by others, which could cause us or them to lose the use of one or more of our or their products.

To date, we, our collaboration partners and our joint ventures have not received any material claims of infringement by any third parties. If a third-party claims that we, our collaboration partners or our joint ventures infringe its proprietary rights, any of the following may occur:

- we, our collaboration partners or our joint ventures may have to defend litigation or administrative proceedings that may be costly whether we or they win or lose, and which could result in a substantial diversion of management resources;
- we, our collaboration partners or our joint ventures may become liable for substantial damages for past infringement if a court decides that our technology infringes a third-party's intellectual property rights;
- a court may prohibit us, our collaboration partners or our joint ventures from producing and selling our or their product(s) without a license from the holder of the intellectual property rights, which may not be available on commercially acceptable terms, if at all; and

- we, our collaboration partners or our joint ventures may have to reformulate product(s) so that it does not infringe the intellectual property rights of others, which may not be possible or could be very expensive and time consuming.

Any costs incurred in connection with such events or the inability to sell our, our collaboration partners' or our joint ventures' products may have a material adverse effect on our business and results of operations.

We, our joint ventures and our collaboration partners may not be able to effectively enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our, our collaboration partners' or our joint venture's products or drug candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our, our joint ventures' or our collaboration partners' ability to protect and enforce our or their intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, the patent laws of some foreign countries do not afford intellectual property protection to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, may not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us or our joint ventures to stop the infringement of our or their patents or the misappropriation of our or their other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our or our joint ventures' inventions throughout the world. Competitors may use our or our joint ventures' technologies in jurisdictions where we or they have not obtained patent protection to develop their own drugs and, further, may export otherwise infringing drugs to territories where we or our joint ventures have patent protection, if our, our joint ventures' or our collaboration partners' ability to enforce our or their patents to stop infringing activities is inadequate. These drugs may compete with our drug candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our, our collaboration partners' or our joint ventures' patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our or their efforts and resources from other aspects of our and their businesses. While we intend to protect our intellectual property rights in the major markets for our drug candidates, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our drug candidates. Furthermore, some of our collaborators are responsible for enforcing our intellectual property rights, for example, AstraZeneca is responsible for enforcing our intellectual property rights with respect to savolitinib on our behalf, we may be unable to ensure that such rights are enforced or maintained in all jurisdictions. Accordingly, our efforts to protect the intellectual property rights of our drug candidates in such countries may be inadequate.

We, our collaboration partners and our joint ventures may be subject to damages resulting from claims that we or they, or our or their employees, have wrongfully used or disclosed alleged trade secrets of competitors or are in breach of non-competition or non-solicitation agreements with competitors.

We, our collaboration partners and our joint ventures could in the future be subject to claims that we or they, or our or their employees, have inadvertently or otherwise used or disclosed alleged trade secrets or other proprietary information of former employers or competitors. Although we try to ensure that our and our joint ventures' employees and consultants do not improperly use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us or our joint ventures, we or our joint ventures may in the future be subject to claims that we or they caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we, our collaboration partners, our joint ventures, or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor. Litigation may be necessary to defend against these claims. Even if we, our collaboration partners and our joint ventures are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our or our joint ventures' defenses to these claims fail, in addition to requiring us and them to pay monetary damages, a court could prohibit us or our joint ventures from using technologies or features that are essential to our or their products or our drug candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. An inability to incorporate such technologies or features would have a material adverse effect on our business, and may prevent us from successfully commercializing our drug candidates. In addition, we, our collaboration partners or our joint ventures may lose valuable intellectual property rights or personnel as a result of such claims. Moreover, any such litigation or the threat thereof may adversely affect our or our joint ventures' ability to hire employees or contract with independent sales representatives. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our drug candidates, which would have an adverse effect on our business, results of operations and financial condition.

Patent terms may be inadequate to protect the competitive position of our drug candidates for an adequate amount of time, and the absence of patent linkage, patent term extension and data and market exclusivity for NMPA-approved pharmaceutical products could increase the risk of early generic competition for our drug candidates in China.

In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984, generally referred to as the Hatch-Waxman Amendments, and similar legislation in the E.U. and certain other countries, provides the opportunity for limited patent term extension. The Hatch-Waxman Amendments permit a patent-term extension of up to five years to reflect patent term lost during certain portions of product development and the FDA regulatory review process. However, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of drug approval; only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. The application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. Depending upon the timing, duration and specifics of any FDA marketing approval process for any drug candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Amendments. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable period or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue patent term extension based on a patent that we in-license from a third party, we would need the cooperation of that third party. If we fail to obtain patent term extensions or if the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and thus our revenue could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and pre-clinical data and launch their product earlier than might otherwise be expected, and our competitive position, business, financial condition, results of operations and prospects could be materially adversely affected.

The Hatch-Waxman Amendments also include a process for patent linkage, pursuant to which the FDA will stay approval of certain follow-on applications during the pendency of litigation between the follow-on applicant and the patent holder or licensee, generally for a period of 30 months. Moreover, the Hatch-Waxman Amendments provide for statutory exclusivities that can prevent submission or approval of certain follow-on marketing applications. For example, federal law provides a five-year period of exclusivity within the United States to the first applicant to obtain approval of a new chemical entity and three years of exclusivity protecting certain innovations to previously approved active ingredients where the applicant was required to conduct new clinical investigations to obtain approval for the modification. Similarly, the U.S. Orphan Drug Act provides seven years of market exclusivity for certain drugs to treat rare diseases, where the FDA designates the drug candidate as an orphan drug and the drug is approved for the designated orphan indication.

Chinese regulators have set forth a framework for integrating patent linkage and data exclusivity into the China regulatory regime, as well as for establishing a pilot program for patent term extension. To be implemented, this framework will require adoption of regulations. On October 17, 2020, the Standing Committee of the National People's Congress published the Patent Law of PRC (Amended in 2020), which came into effect on June 1, 2021, or the Amended Patent Law. The Amended Patent Law provides that, among other things, the owner of the patent for an innovative new drug that has been granted the marketing authorization in China is entitled to request the Patent Administration Department under the State Council to grant a patent term extension of up to five years, in order to compensate the time required for the regulatory approval for the commercialization of such innovative new drug, provided that the patent term of such innovative new drug shall not exceed a total of 14 years. Furthermore, the PRC government entered into the Economic and Trade Agreement Between the Government of the People's Republic of China and the Government of the United States of America with the U.S. government in January 2020 which provides that the owner of the patent for an innovative new drug that has been granted the marketing authorization in China is entitled to request a patent term extension of up to five years, provided that the patent term of such innovative new drug shall not exceed a total of 14 years from the date of marketing approval in China. If we are unable to obtain patent term extension, or the term of any such extension is less than that we request, our competitors or other third parties may obtain approval of competing products following our patent expiration. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

Risks Relating to Our ADSs

The PCAOB had historically been unable to inspect our auditor in relation to their audit work performed for our financial statements and the inability of the PCAOB to conduct inspections of our auditor in the past has deprived our investors with the benefits of such inspections.

Our auditor, the independent registered public accounting firm that issues the audit report included elsewhere in this annual report, as an auditor of companies that are traded publicly in the United States and a firm registered with the PCAOB, is subject to laws in the United States pursuant to which the PCAOB conducts regular inspections to assess its compliance with the applicable professional standards. The auditor is located in mainland China, a jurisdiction where the PCAOB was historically unable to conduct inspections and investigations completely before 2022. As a result, we and investors in the ADSs were deprived of the benefits of such PCAOB inspections. The inability of the PCAOB to conduct inspections of auditors in China in the past has made it more difficult to evaluate the effectiveness of our independent registered public accounting firm's audit procedures or quality control procedures as compared to auditors outside of China that are subject to the PCAOB inspections. On December 15, 2022, the PCAOB issued a report that vacated its December 16, 2021 determination and removed mainland China and Hong Kong from the list of jurisdictions where it is unable to inspect or investigate completely registered public accounting firms. However, if the PCAOB determines in the future that it no longer has full access to inspect and investigate completely accounting firms in mainland China and Hong Kong, and we use an accounting firm headquartered in one of these jurisdictions to issue an audit report on our financial statements filed with the Securities and Exchange Commission, we and investors in our ADSs would be deprived of the benefits of such PCAOB inspections again, which could cause investors and potential investors in the ADSs to lose confidence in our audit procedures and reported financial information and the quality of our financial statements.

Our ADSs may be prohibited from trading in the United States under the HFCAA in the future if the PCAOB is unable to inspect or investigate completely auditors located in China. The delisting of the ADSs, or the threat of their being delisted, may materially and adversely affect the value of your investment.

Pursuant to the HFCAA, if the SEC determines that we have filed audit reports issued by a registered public accounting firm that has not been subject to inspections by the PCAOB for two consecutive years, the SEC will prohibit our shares or ADSs from being traded on a national securities exchange or in the over-the-counter trading market in the United States.

On December 16, 2021, the PCAOB issued a report to notify the SEC of its determination that the PCAOB was unable to inspect or investigate completely registered public accounting firms headquartered in mainland China and Hong Kong and our auditor was subject to that determination. In March 2022, the SEC conclusively listed us as a Commission-Identified Issuer under the HFCAA following the filing of our annual report on Form 20-F for the fiscal year ended December 31, 2021. On December 15, 2022, the PCAOB removed mainland China and Hong Kong from the list of jurisdictions where it is unable to inspect or investigate completely registered public accounting firms. For this reason, we do not expect to be identified as a Commission-Identified Issuer under the HFCAA after we file this annual report on Form 20-F for the fiscal year ended December 31, 2023.

Each year, the PCAOB will determine whether it can inspect and investigate completely audit firms in mainland China and Hong Kong, among other jurisdictions. If the PCAOB determines in the future that it no longer has full access to inspect and investigate completely accounting firms in mainland China and Hong Kong and we use an accounting firm headquartered in one of these jurisdictions to issue an audit report on our financial statements filed with the Securities and Exchange Commission, we would be identified as a Commission-Identified Issuer following the filing of the annual report on Form 20-F for the relevant fiscal year. In accordance with the HFCAA, our securities would be prohibited from being traded on a national securities exchange or in the over-the-counter trading market in the United States if we are identified as a Commission-Identified Issuer for two consecutive years in the future. Although our ordinary shares have been listed on the SEHK and AIM and the ADSs and ordinary shares are fully fungible, we cannot assure you that an active trading market for our ordinary shares on the Hong Kong Stock Exchange or AIM of the London Stock Exchange will be sustained or that the ADSs can be converted and traded with sufficient market recognition and liquidity, if our shares and ADSs are prohibited from trading in the United States. A prohibition of being able to trade in the United States would substantially impair your ability to sell or purchase our ADSs when you wish to do so, and the risk and uncertainty associated with delisting would have a negative impact on the price of our ADSs. Also, such a prohibition would significantly affect our ability to raise capital on terms acceptable to us, or at all, which would have a material adverse impact on our business, financial condition, and prospects.

The listings of our shares in multiple venues may adversely affect the liquidity and value of them.

Our ADSs continue to be listed on Nasdaq, and our shares continue to be admitted to trading on the AIM. Our shares were listed on the SEHK in June 2021. The listing of the shares on the AIM and the SEHK, and the ADSs on Nasdaq, may reduce the liquidity of these securities in one or each of these markets and may adversely affect the development of an active trading market for the shares in each of these markets. The price of the shares could also be adversely affected by trading on Nasdaq. Similarly, the price of the ADSs could also be adversely affected by trading on the AIM and the SEHK. We may also seek further listings on other stock exchanges such as the Shanghai Stock Exchange, which could further affect the liquidity and value of the shares and the ADSs. Furthermore, the shares trade on the SEHK largely in electronic book-entry form. However, the ADSs are backed by physical ordinary share certificates, and the depository for our ADS program is unable to accept book-entry interests into its custody in order to issue ADSs. As a result, if a holder of the shares wishes to deposit the shares into the ADS program and hold ADSs for trading on Nasdaq or vice versa, the issuance and cancellation process may be longer than if the depository could accept such book-entry interests.

Our largest shareholder owns a significant percentage of our ordinary shares, which may limit the ability of other shareholders to influence corporate matters.

As of February 15, 2024, Hutchison Healthcare Holdings Limited owned approximately 38.2% of our ordinary shares. Accordingly, Hutchison Healthcare Holdings Limited can influence the outcome of any corporate transaction or other matter submitted to shareholders for approval and the interests of Hutchison Healthcare Holdings Limited may differ from the interests of our other shareholders. Under our Articles of Association, certain matters, such as amendments to our amended and restated Memorandum and Articles of Association, require the approval of not less than three-fourths of votes cast by such shareholders as, being entitled so to do, vote in person (or, in the case of such shareholders as are corporations, by their respective duly authorized representative) or by proxy. Therefore, Hutchison Healthcare Holdings Limited's approval will be required to achieve any such threshold. In addition, Hutchison Healthcare Holdings Limited has and will continue to have a significant influence over the management and the strategic direction of our company.

Substantial future sales or perceived potential sales of our ADSs, ordinary shares or other equity or equity-linked securities in the public market could cause the price of our ADSs to decline significantly.

Sales of our ADSs, ordinary shares or other equity or equity-linked securities in the public market, or the perception that these sales could occur, could cause the market price of our ADSs to decline significantly. All of our ordinary shares represented by ADSs are freely transferable by persons other than our affiliates without restriction or additional registration under the Securities Act of 1933, or the Securities Act. The ordinary shares held by our affiliates are also available for sale, subject to volume and other restrictions as applicable under Rules 144 and 701 under the Securities Act, under sales plans adopted pursuant to Rule 10b5-1 or otherwise.

We have filed with the SEC registration statements on Form F-3, commonly referred to as a "shelf registration," that permit us to sell any number of ADSs in a registered offering at our discretion. We have completed registered offerings raising aggregate gross proceeds of approximately \$537.9 million under such shelf registration statements. Furthermore, our largest shareholder has completed registered secondary offerings raising aggregate gross proceeds of approximately \$310.4 million for it as a selling shareholder under a shelf registration statement. In addition, we completed our initial public offering in Hong Kong and global offering of our ordinary shares in 2021, raising aggregate gross proceeds of approximately \$614.9 million, including \$80.2 million through the fulfillment of the over-allotment. We may decide to conduct future offerings from time to time, and such sales could cause the price of our ADSs to decline significantly.

In connection with the issuance of ordinary shares in private placements in 2020 and 2021, we agreed to provide certain shareholders Form F-3 registration rights. Registration of the ordinary shares held by such shareholders may result in these shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. Sales of these shares, or the perception that such sales could occur, could cause the price of our ADSs to decline. In addition, any changes in the investment strategies or philosophies of our major shareholders may lead to the sale of our ADSs and other securities, which could cause the price of our ADSs to decline.

We may be at a risk of securities litigation.

Historically, securities litigation, particularly class action lawsuits brought in the United States, have often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant share price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our business, the price of our ADSs could decline.

The trading market for our ADSs will rely in part on the research and reports that industry or financial analysts publish about us or our business. We may not be able to maintain continuous research coverage by industry or financial analysts. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

As a foreign private issuer, we are not subject to certain U.S. securities law disclosure requirements that apply to a domestic U.S. issuer, which may limit the information publicly available to our shareholders.

As a foreign private issuer we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act and therefore there may be less publicly available information about us than if we were a U.S. domestic issuer. For example, we are not required to file quarterly reports on Form 10-Q. We are also not subject to the proxy rules in the United States, and we are not required to follow the related disclosure requirements with respect to our annual general meetings, including disclosing a compensation discussion and analysis. Our disclosure with respect to our annual general meetings will be governed by the AIM Rules for Companies, or the AIM Rules, listing rules in Hong Kong and Cayman Islands requirements. In addition, our officers, directors and principal shareholders are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and the rules thereunder. Therefore, our shareholders may not know on a timely basis when our officers, directors and principal shareholders purchase or sell our ordinary shares or ADSs.

As a foreign private issuer, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq corporate governance listing standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with corporate governance listing standards.

As a foreign private issuer, we are permitted to take advantage of certain provisions in the Nasdaq listing rules that allow us to follow Cayman Islands law for certain governance matters. Certain corporate governance practices in the Cayman Islands may differ significantly from corporate governance listing standards as, except for compliance with the obligations contained in the Companies Act and directors' general fiduciary duties and duties of care, Cayman Islands law has no corporate governance regime which prescribes specific corporate governance standards. We intend to continue to follow Cayman Islands corporate governance practices in lieu of the corporate governance requirements of the Nasdaq Global Select Market in respect of the following: (i) the majority independent director requirement under Section 5605(b)(1) of the Nasdaq listing rules, (ii) the requirement under Section 5605(d) of the Nasdaq listing rules that a remuneration committee comprised solely of independent directors governed by a remuneration committee charter oversee executive compensation and (iii) the requirement under Section 5605(e) of the Nasdaq listing rules that director nominees be selected or recommended for selection by either a majority of the independent directors or a nominations committee comprised solely of independent directors. Cayman Islands law does not impose a requirement that our board of directors consist of a majority of independent directors, nor does Cayman Islands law impose specific requirements on the establishment of a remuneration committee or nominating committee or nominating process. Therefore, our shareholders may be afforded less protection than they otherwise would have under corporate governance listing standards applicable to U.S. domestic issuers. We have voluntarily complied with the Corporate Governance Code contained in Appendix 14 of the Rules Governing the Listing of Securities on SEHK. See Item 6.C. "Board Practice-Hong Kong Corporate Governance Code" for more details.

We may in the future lose our foreign private issuer status under U.S. securities laws, which could result in significant additional costs and expenses.

We are a foreign private issuer as defined in the Securities Act, and therefore, we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act. The determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter, and, accordingly, the next determination will be made with respect to us on June 30, 2024. We would lose our foreign private issuer status if, for example, more than 50% of our ordinary shares are directly or indirectly held by residents of the United States on June 30, 2024 and we fail to meet additional requirements necessary to maintain our foreign private issuer status. If we lose our foreign private issuer status on this date, we will be required to file with the SEC periodic reports and registration statements on U.S. domestic issuer forms beginning on January 1, 2025, which are more detailed and extensive than the forms available to a foreign private issuer. We will also have to mandatorily comply with U.S. federal proxy requirements, and our officers, directors and principal shareholders will become subject to the short-swing profit disclosure and recovery provisions of Section 16 of the Exchange Act. In addition, we will lose our ability to rely upon exemptions from certain corporate governance requirements under the Nasdaq listing rules. As a U.S.-listed public company, should we lose our foreign private issuer status, we will incur significant additional legal, accounting and other expenses that we would not incur as a foreign private issuer.

Fluctuations in the value of the renminbi may have a material adverse effect on your investment.

The value of the renminbi against the U.S. dollar and other currencies fluctuates and is affected by, among other things, changes in China's and international political and economic conditions and the PRC government's fiscal and currency policies. Since 1994, the conversion of renminbi into foreign currencies, including U.S. dollars, has been based on rates set by the PBOC, which are set daily based on the previous business day's inter-bank foreign exchange market rates and current exchange rates on the world financial markets. It is expected that China may further reform its exchange rate system in the future.

Significant revaluation of the renminbi may have a material adverse effect on your investment. For example, to the extent that we need to convert U.S. dollars into renminbi for our operations, appreciation of the renminbi against the U.S. dollar would have an adverse effect on the renminbi amount we would receive from the conversion. Conversely, if we decide to convert our renminbi into U.S. dollars, appreciation of the U.S. dollar against the renminbi would have a negative effect on the U.S. dollar amount available to us. Appreciation or depreciation in the value of the renminbi relative to the U.S. dollar would affect our financial results reported in U.S. dollar terms regardless of any underlying change in our business or results of operations. In addition, our operating transactions and assets and liabilities in the PRC are mainly denominated in renminbi. Such amounts are translated into U.S. dollars for purpose of preparing our consolidated financial statements, with translation adjustments reflected in accumulated other comprehensive income/(loss) in shareholders' equity. We recorded a foreign currency translation gain of \$3.0 million, a foreign currency translation loss of \$8.5 million and a foreign currency translation loss of \$6.6 million for the years ended December 31, 2021, 2022 and 2023, respectively.

Very limited hedging options are available in China to reduce our exposure to exchange rate fluctuations. To date, we have not entered into any hedging transactions in an effort to reduce our exposure to foreign currency exchange risk. While we may decide to enter into hedging transactions in the future, the availability and effectiveness of these hedges may be limited and we may not be able to adequately hedge our exposure or at all. In addition, our currency exchange losses may be magnified by PRC exchange control regulations that restrict our ability to convert renminbi into foreign currency.

We do not currently intend to pay dividends on our securities, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of the ADSs.

We have never declared or paid any dividends on our ordinary shares. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your ADSs at least in the near term, and the success of an investment in ADSs will depend upon any future appreciation in its value. Consequently, investors may need to sell all or part of their holdings of ADSs after price appreciation, which may never occur, to realize any future gains on their investment. There is no guarantee that the ADSs will appreciate in value or even maintain the price at which our shareholders have purchased the ADSs.

The trading prices for our ADSs may be volatile which could result in substantial losses to you.

The market price of our ADSs has been volatile. From March 17, 2016 to February 15, 2024, the closing sale price of our ADSs ranged from a high of \$42.94 to a low of \$7.65 per ADS.

The market price for our ADSs is likely to be highly volatile and subject to wide fluctuations in response to factors, including the following:

- announcements of competitive developments;
- regulatory developments affecting us, our customers or our competitors;
- announcements regarding litigation or administrative proceedings involving us;
- actual or anticipated fluctuations in our period-to-period operating results;
- changes in financial estimates by securities research analysts;
- additions or departures of our executive officers;
- release or expiry of lock-up or other transfer restrictions on our outstanding ordinary shares or ADSs; and
- sales or perceived sales of additional ordinary shares or ADSs.

In addition, the securities markets have from time to time experienced significant price and volume fluctuations that are not related to the operating performance of particular companies. Prolonged global capital markets volatility may affect overall investor sentiment towards our ADSs, which would also negatively affect the trading prices for our ADSs.

The triple listing of our ordinary shares and the ADSs may adversely affect the liquidity and value of the ADSs.

Our ordinary shares are listed on the AIM market and on the SEHK. The triple listing of our ordinary shares and the ADSs may dilute the liquidity of these securities in one or more of these markets and may adversely affect the development of an active trading market for the ADSs in the United States or shares in Hong Kong and the United Kingdom. The price of the ADSs could also be adversely affected by trading in our ordinary shares on the AIM market and the SEHK.

Fluctuations in the exchange rate between the U.S. dollar, Hong Kong dollar and the pound sterling may increase the risk of holding the ADSs.

Our share price is quoted on the SEHK and AIM market in Hong Kong dollar and pence sterling, respectively, while the ADSs trade on Nasdaq in U.S. dollars. Fluctuations in the exchange rate between the U.S. dollar, Hong Kong dollar and the pound sterling may result in temporary differences between the value of the ADSs and the value of our ordinary shares, which may result in heavy trading by investors seeking to exploit such differences. In addition, as a result of fluctuations in the exchange rate between the U.S. dollar, Hong Kong dollar and the pound sterling, the U.S. dollar equivalent of the proceeds that a holder of the ADSs would receive upon the sale in Hong Kong of any ordinary shares or in the United Kingdom of any ordinary shares withdrawn from the depositary and the dollar equivalent of any cash dividends paid in Hong Kong dollar or pound sterling on our shares represented by the ADSs could also decline.

Securities traded on the AIM market or on the SEHK may carry or be perceived to carry a higher risk than shares traded on other exchanges and may impact the value of your investment.

Our ordinary shares are currently traded on the AIM market and on the SEHK. Investment in equities traded on AIM and the SEHK may be perceived by some to carry a higher risk than an investment in equities quoted on exchanges, such as the New York Stock Exchange or the Nasdaq. You should be aware that the value of our ordinary shares may be influenced by many factors, some of which may be specific to us and some of which may affect AIM-listed or Hong Kong-listed companies generally, including the depth and liquidity of the market, our performance, a large or small volume of trading in our ordinary shares, legislative changes and general economic, political or regulatory conditions, and that the prices may be volatile and subject to extensive fluctuations. Therefore, the market price of our ordinary shares underlying the ADSs may not reflect the underlying value of our company.

The depositary for our ADSs gives us a discretionary proxy to vote our ordinary shares underlying your ADSs if you do not vote at shareholders' meetings, except in limited circumstances, which could adversely affect your interests.

Under the deposit agreement for the ADSs, the depositary gives us a discretionary proxy to vote our ordinary shares underlying your ADSs at shareholders' meetings if you do not vote, unless:

- we do not wish a discretionary proxy to be given;
- we are aware or should reasonably be aware that there is substantial opposition as to a matter to be voted on at the meeting; or
- a matter to be voted on at the meeting would materially and adversely affect the rights of shareholders.

The effect of this discretionary proxy is that you cannot prevent our ordinary shares underlying your ADSs from being voted, absent the situations described above, and it may make it more difficult for shareholders to influence the management of our company. Holders of our ordinary shares are not subject to this discretionary proxy.

Holders of ADSs have fewer rights than shareholders and must act through the depositary to exercise their rights.

Holders of our ADSs do not have the same rights as our shareholders and may only exercise the voting rights with respect to the underlying ordinary shares in accordance with the provisions of the deposit agreement. Under our amended and restated Memorandum and Articles of Association, an annual general meeting shall be called by notice with not less than 21 clear days, and all other general meetings (including an extraordinary general meeting) shall be called by notice with not less than 14 clear days. When a general meeting is convened, you may not receive sufficient notice of a shareholders' meeting to permit you to withdraw the ordinary shares underlying your ADSs to allow you to vote with respect to any specific matter. If we ask for your instructions, we will give the depositary notice of any such meeting and details concerning the matters to be voted upon at least 30 days in advance of the meeting date and the depositary will send a notice to you about the upcoming vote and will arrange to deliver our voting materials to you. The depositary and its agents, however, may not be able to send voting instructions to you or carry out your voting instructions in a timely manner. We will make all reasonable efforts to cause the depositary to extend voting rights to you in a timely manner, but we cannot assure you that you will receive the voting materials in time to ensure that you can instruct the depositary to vote the ordinary shares underlying your ADSs. Furthermore, the depositary will not be liable for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, you may not be able to exercise your right to vote and you may lack recourse if your ADSs are not voted as you request. In addition, in your capacity as an ADS holder, you will not be able to call a shareholders' meeting.

You may not receive distributions on our ADSs or any value for them if such distribution is illegal or if any required government approval cannot be obtained in order to make such distribution available to you.

Although we do not have any present plan to pay any dividends, the depositary of our ADSs has agreed to pay to you the cash dividends or other distributions it or the custodian receives on ordinary shares or other deposited securities underlying our ADSs, after deducting its fees and expenses and any applicable taxes and governmental charges. You will receive these distributions in proportion to the number of ordinary shares your ADSs represent. However, the depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any holders of ADSs. For example, it would be unlawful to make a distribution to a holder of ADSs if it consists of securities whose offering would require registration under the Securities Act but is not so properly registered or distributed under an applicable exemption from registration. The depositary may also determine that it is not reasonably practicable to distribute certain property. In these cases, the depositary may determine not to distribute such property. We have no obligation to register under the U.S. securities laws any offering of ADSs, ordinary shares, rights or other securities received through such distributions. We also have no obligation to take any other action to permit the distribution of ADSs, ordinary shares, rights or anything else to holders of ADSs. This means that you may not receive distributions we make on our ordinary shares or any value for them if it is illegal or impractical for us to make them available to you. These restrictions may cause a material decline in the value of our ADSs.

Your right to participate in any future rights offerings may be limited, which may cause dilution to your holdings.

We may from time to time distribute rights to our shareholders, including rights to acquire our securities. However, we cannot make rights available to you in the United States unless we register the rights and the securities to which the rights relate under the Securities Act or an exemption from the registration requirements is available. Also, under the deposit agreement, the depositary bank will not make rights available to you unless either both the rights and any related securities are registered under the Securities Act, or the distribution of them to ADS holders is exempted from registration under the Securities Act. We are under no obligation to file a registration statement with respect to any such rights or securities or to endeavor to cause such a registration statement to be declared effective. Moreover, we may not be able to establish an exemption from registration under the Securities Act. If the depositary does not distribute the rights, it may, under the deposit agreement, either sell them, if possible, or allow them to lapse. Accordingly, you may be unable to participate in our rights offerings and may experience dilution in your holdings.

If we are a passive foreign investment company for any taxable year, U.S. investors could be subject to adverse U.S. federal income tax consequences.

The rules governing passive foreign investment companies, or PFICs, can have adverse U.S. federal income tax consequences for U.S. investors of non-U.S. corporations. The PFIC status of a non-U.S. corporation for any taxable year depends upon the composition of its income and assets, the value of its assets and the classification of items of its income and assets as active or passive under the PFIC rules, as discussed further in Item 10.E. "Taxation—U.S. Taxation—Material U.S. Federal Income Tax Considerations with Respect to Ordinary Shares and ADSs." Based on the composition of our income and assets and the estimated average value of our assets (including goodwill and other intangible assets), we believe that we were not a PFIC for our taxable year ended December 31, 2023. However, our PFIC status is a factual determination that is made on an annual basis and depends on particular facts and circumstances (such as the value of our assets, including goodwill and other intangible assets). We hold a substantial amount of cash and financial investments and while this continues to be the case, our PFIC status depends primarily on the average value of our goodwill and other intangible assets. The value of our goodwill and other intangible assets may be determined, in large part, by reference to our market capitalization, which has been, and may continue to be, volatile. Therefore, if our market capitalization declines we may be or become a PFIC. In addition, there is uncertainty as to how to apply the PFIC rules for purposes of classifying certain of our income and assets as active or passive. Furthermore, the proportionate value of our passive assets may increase over time if the value of our ownership stake in any other company in which we own less than 25% (by value) increases. In light of the foregoing, no assurance can be provided that we were not, or will not be, a PFIC for any taxable year.

If we are or become a PFIC, U.S. investors in our ordinary shares and ADSs generally will be subject to adverse U.S. federal income tax consequences, such as ineligibility for any preferential tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements under U.S. federal income tax laws and regulations. We do not expect to provide the information regarding our income that would be necessary in order for a U.S. investor to make a qualified electing fund, or QEF, election if we are a PFIC for any taxable year. U.S. investors in our ordinary shares or ADSs should consult their tax advisors regarding all aspects of the application of the PFIC rules to their ordinary shares and ADSs.

Under certain attribution rules, certain of our non-U.S. subsidiaries are expected to be treated as "controlled foreign corporations" for U.S. federal income tax purposes, and, as a result, there could be adverse U.S. federal income tax consequences to U.S. investors that own (directly or indirectly) our ordinary shares or ADSs and are treated as "Ten Percent Shareholders."

Certain "Ten Percent Shareholders" (as defined below) in a non-U.S. corporation that is a "controlled foreign corporation" (a "CFC") for U.S. federal income tax purposes generally are required to include in income for U.S. federal income tax purposes their pro rata share of the CFC's "Subpart F income," investment of earnings in U.S. property, and "global intangible low-taxed income," even if the CFC has made no distributions to its shareholders. A non-U.S. corporation generally will be a CFC for U.S. federal income tax purposes if Ten Percent Shareholders own, directly, indirectly or constructively (through attribution), more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the U.S. Internal Revenue Code of 1986, as amended) that owns directly or indirectly, or is considered to own constructively, 10% or more of the total combined voting power of all classes of stock entitled to vote of such corporation or 10% or more of the total value of the stock of such corporation. We are not expected to be a CFC. However, under certain "downward attribution" rules, certain of our non-U.S. subsidiaries are expected to be treated as CFCs by virtue of being constructively owned by our U.S. subsidiaries. As a non-U.S. company, we do not intend to take these U.S. tax rules into consideration in structuring its operations, nor do we intend to provide information to Ten Percent Shareholders that may be required in order for those shareholders to properly report their U.S. taxable income with respect to our operations. U.S. investors that are or may become Ten Percent Shareholders who directly or indirectly own our ordinary shares or ADSs should consult their tax advisors with respect to the application of the CFC rules to them.

We may be treated as a resident enterprise for U.K. corporate tax purposes, and our global income may therefore be subject to U.K. corporation tax.

U.K. resident companies are taxable in the United Kingdom on their worldwide profits. A company incorporated outside of the United Kingdom would be regarded as a resident if its central management and control resides in the United Kingdom. The place of central management and control generally means the place where the high-level strategic decisions of a company are made.

We are an investment holding company incorporated in the Cayman Islands and are admitted to trading on the AIM market of the London Stock Exchange or the AIM market. Our central management and control resides in Hong Kong, and therefore we believe that we are not a U.K. resident for corporate tax purposes. However, the tax resident status of a non-resident entity could be challenged by the U.K. tax authorities.

If the U.K. tax authorities determine that we are a U.K. tax resident, our profits will be subject to U.K. Corporation Tax rate at 19% for taxable profits below GBP 50,000 and 25% for taxable profits above GBP 250,000, subject to the potential availability of certain exemptions related to dividend income and capital gains. This may have a material adverse effect on our financial condition and results of operations.

You may have difficulty enforcing judgments obtained against us.

We are a company incorporated under the laws of the Cayman Islands, and substantially all of our assets are located outside the United States. Substantially all of our current operations are conducted in the PRC. In addition, most of our directors and officers are nationals and residents of countries other than the United States. A substantial portion of the assets of these persons are located outside the United States. As a result, it may be difficult for you to effect service of process within the United States upon these persons. It may also be difficult for you to enforce in U.S. courts judgments obtained in U.S. courts based on the civil liability provisions of the U.S. federal securities laws against us and our officers and directors, all of whom are not residents in the United States and whose assets are located outside the United States. In addition, there is uncertainty as to whether the courts of the Cayman Islands or the PRC would recognize or enforce judgments of U.S. courts against us or such persons predicated upon the civil liability provisions of the securities laws of the United States or any state.

You may be subject to limitations on transfers of your ADSs.

Your ADSs are transferable on the books of the depository. However, the depository may close its transfer books at any time or from time to time when it deems expedient in connection with the performance of its duties. In addition, the depository may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depository are closed, or at any time if we or the depository deems it advisable to do so because of any requirement of law or of any government or governmental body, or under any provision of the deposit agreement, or for any other reason.

It may be difficult for overseas regulators to conduct investigations or collect evidence within China.

Shareholder claims or regulatory investigation that are common in the United States generally are difficult to pursue as a matter of law or practicality in China. For example, in China, there are significant legal and other obstacles to providing information needed for regulatory investigations or litigation initiated outside China. Although the authorities in China may establish a regulatory cooperation mechanism with the securities regulatory authorities of another country or region to implement cross-border supervision and administration, such cooperation with the securities regulatory authorities in the United States may not be efficient in the absence of mutual and practical cooperation mechanisms. Furthermore, according to Article 177 of the PRC Securities Law, or Article 177, which became effective in March 2020, no overseas securities regulator is allowed to directly conduct investigations or evidence collection activities within the territory of the PRC. While detailed interpretations of or implementation rules under Article 177 have yet to be promulgated, the possible inability for an overseas securities regulator to directly conduct investigations or evidence collection activities within China may further increase difficulties you may face in protecting your interests.

We are a Cayman Islands company. As judicial precedent regarding the rights of shareholders under Cayman Islands law is different from U.S. law, English law or Hong Kong law, shareholders may have different shareholder rights than they would have under U.S. law, English law or Hong Kong law and may face difficulties in protecting your interests.

We are an exempted company with limited liability incorporated in the Cayman Islands. Our corporate affairs are governed by our Articles of Association (as may be further amended from time to time), the Companies Act (As Revised) of the Cayman Islands and the common law of the Cayman Islands. The rights of shareholders to take action against the directors, actions by minority shareholders and the fiduciary responsibilities of our directors are to a large extent governed by the common law of the Cayman Islands. This common law is derived in part from comparatively limited judicial precedent in the Cayman Islands as well as from English common law, which has persuasive, but not binding, authority on a court in the Cayman Islands. The laws of the Cayman Islands relating to the protection of the interests of minority shareholders differ in some aspects from those in the United States, the United Kingdom and Hong Kong. Such differences mean that the remedies available to our minority shareholders may be different from those they would have under the laws of United States, the United Kingdom, Hong Kong or other jurisdictions. In addition, some states in the United States, such as Delaware, have more fully developed and judicially interpreted bodies of corporate law than the Cayman Islands.

In addition, as a Cayman Islands exempted company, other than right to inspect and take copies of our register of members contained in our articles of association, our shareholders have no general rights under Cayman Islands law to inspect corporate records and accounts or to obtain copies of lists of shareholders of these companies with the exception that the shareholders may request a copy of the Articles of Association. Our directors have discretion under our Articles of Association to determine whether or not, and under what conditions, our corporate records may be inspected by our shareholders, but are not obliged to make them available to our shareholders. This may make it more difficult for you to obtain the information needed to establish any facts necessary for a shareholder motion or to solicit proxies from other shareholders in connection with a proxy contest. As a Cayman Islands company, we may not have standing to initiate a derivative action in U.S. federal courts, English courts or Hong Kong courts. As a result, you may be limited in your ability to protect your interests if you are harmed in a manner that would otherwise enable you to sue in U.S. federal courts, English courts or Hong Kong courts. In addition, shareholders of Cayman Islands companies may not have standing to initiate a shareholder derivative action in U.S. federal courts, English courts or Hong Kong courts.

Most of our directors and executive officers reside outside of the United States and a substantial portion of their assets are located outside of the United States. As a result, it may be difficult or impossible for you to bring an action against us or against these individuals in the United States in the event that you believe that your rights have been infringed under the securities laws of the United States or otherwise. In addition, some of our operating subsidiaries are incorporated in China. To the extent our directors and executive officers reside in China or their assets are located in China, it may not be possible for investors to effect service of process upon us or our management inside China. Even if you are successful in bringing an action, the laws of the Cayman Islands and China may render you unable to enforce a judgment against our assets or the assets of our directors and officers. Whilst there is no statutory recognition in the Cayman Islands of judgments obtained in the United States, Hong Kong or China, the courts of the Cayman Islands would recognize as a valid judgment, a final and conclusive judgment *in personam* obtained in such courts against the Company under which a sum of money is payable (other than a sum of money payable in respect of multiple damages, taxes or other charges of a like nature or in respect of a fine or other penalty) or, in certain circumstances, an *in personam* judgment for non-monetary relief, and would give a judgment based thereon provided that (a) such courts had proper jurisdiction over the parties subject to such judgment; (b) such courts did not contravene the rules of natural justice of the Cayman Islands; (c) such judgment was not obtained by fraud; (d) the enforcement of the judgment would not be contrary to the public policy of the Cayman Islands; (e) no new admissible evidence relevant to the action is submitted prior to the rendering of the judgment by the courts of the Cayman Islands; and (f) there is due compliance with the correct procedures under the laws of the Cayman Islands.

As a result of all of the above, public shareholders may have more difficulty in protecting their interests in the face of actions taken by management, members of the board of directors or controlling shareholders than they would as public shareholders of an English company, a U.S. company or a Hong Kong company.