

REGULATORY OVERVIEW

1. REGULATIONS RELATING TO DRUGS IN CHINA

Drug Administration Laws and Regulations

The PRC Drug Administration Law (《中華人民共和國藥品管理法》) (the “**Drug Administration Law**”) promulgated by the Standing Committee of the National People’s Congress (the “SCNPC”) on September 20, 1984, and last amended on August 26, 2019, and the Implementing Measures of the PRC Drug Administration Law (《中華人民共和國藥品管理法實施條例》) (the “**Drug Administration Law Implementing Measures**”) issued by the State Council on August 4, 2002, and last amended on December 6, 2024 have together laid down the legal framework for the administration of drugs. The primary regulation governing clinical trial applications, marketing authorization, and post-approval amendment and re-registration is the Administrative Measures for Drug Registration (《藥品註冊管理辦法》). Its latest version was promulgated by the State Administration for Market Regulation of the PRC on January 22, 2020, and became effective on July 1, 2020.

Non-Clinical Research and Animal Testing

The SAMR requires preclinical data to support registration applications for imported and domestic drugs. According to the Administrative Measures for Drug Registration, non-clinical drug safety studies shall comply with the Good Laboratory Practice for Non-clinical Laboratory Studies (《藥物非臨床研究質量管理規範》) (the “GLP”). The GLP was initially issued by the CFDA on August 6, 2003 to improve the quality of non-clinical research, and the good laboratory practice. Its latest version was promulgated on July 27, 2017, and has been implemented since September 1, 2017. Pursuant to the Measures for Administration of Certification of the Good Laboratory Practice for Nonclinical Laboratory Studies (《藥物非臨床研究質量管理規範認證管理辦法》) promulgated by the National Medical Products Administration (“NMPA”) on January 19, 2023, the NMPA is responsible for the certification of non-clinical research institutions nationwide, while the local provincial medical products administrative authorities is in charge of the daily supervision of non-clinical research institution.

Pursuant to the Administrative Regulations on Experimental Animals (《實驗動物管理條例》) issued by the State Science and Technology Commission on November 14, 1988, and latest amended on March 1, 2017 by the State Council, the Administrative Measures on Good Practice of Experimental Animals (《實驗動物質量管理辦法》) jointly issued by the State Science and Technology Commission and the State Bureau of Quality and Technical Supervision on December 11, 1997, and the Administrative Measures on the Certificate for Experimental Animals (Trial) (《實驗動物許可證管理辦法(試行)》) issued by the Ministry of Science and Technology and other regulatory authorities on December 5, 2001, using and breeding experimental animals shall be subject to certain rules, and performing experiments on animals requires a Certificate for Use of Experimental Animals.

Approval and Reform for Clinical Trials of New Drugs

Pursuant to the Drug Administration Law, the Drug Administration Law Implementing Measures and the Administrative Measures for Drug Registration, new drug registration applications are subject to clinical trials. The Center for Drug Evaluation (the “CDE”), an institution under the NMPA, is responsible for the applications for clinical trials of new drugs.

The NMPA has taken certain measures to improve the efficiency for approving clinical trial applications, and enhanced the extent of supervising and implementation of the Good Clinical Practice for Drug Trials (《藥物臨床試驗質量管理規範》) (the “PRC GCP”), to ensure the completeness of the data. The PRC GCP was initially issued by the CFDA on August 6, 2003. Its latest version was issued by the NMPA and the National Health Commission (“NHC”), which took effect from July 1, 2020.

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The Opinions of the State Council on the Reform of Evaluation and Approval System for Drugs and Medical Devices (《國務院關於改革藥品醫療器械審評審批制度的意見》) issued by the State Council on August 9, 2015, established a reform framework of the evaluation and approval system for drugs and medical devices, and indicated the tasks of enhancing the standards of approval for, among others, drug registration, accelerating the evaluation and approval process for innovative drugs, and improving the approval for clinical trials of drugs.

The Announcement of the CFDA on Several Policies on the Evaluation and Approval of Drug Registration (《國家食品藥品監督管理總局關於藥品註冊審評審批若干政策的公告》) issued by the CFDA on November 11, 2015, further simplified the approval process of drugs that the IND of new drugs are subject to one-off umbrella approval instead of declaration, evaluation and approval by stages.

According to the Announcement of the NMPA on Adjusting the Evaluation and Approval Procedures for Clinical Trials of Drugs (《國家藥品監督管理局關於調整藥物臨床試驗審評審批程序的公告》) issued by the NMPA on July 24, 2018, which took effect therefrom, within 60 days from the acceptance of the IND and relevant fees paid up, if the applicant has not received any negative or questioning opinion from the CDE, the applicant may conduct the clinical trials for drugs pursuant to the protocol submitted.

Clinical Trial Registration of Drugs

According to the Administrative Measures for Drug Registration, upon obtaining the approval of IND, the applicant shall, prior to conducting the clinical trials of the drugs, register the information in relation to the clinical trial protocol on the registration and information publication platform for clinical trials of drugs.

Pursuant to the Announcement on the Drug Clinical Trial Information Platform (《關於藥物臨床試驗信息平台的公告》) issued by the CFDA on September 6, 2013, for all the clinical trials approved by the CFDA and conducted in the PRC, the applicants shall log in the registration and information publication platform for clinical trials of drugs to register, and publish the information of, the clinical trials.

Phases of Clinical Trials and Communication with the CDE

According to the Administrative Measures for Drug Registration, based on the drug's characteristics and the purpose of research, clinical trials of drugs consist of Phase I, II, III and IV clinical trials, as well as the bioequivalence trials, which include clinical pharmacological research, exploratory clinical trials, confirmatory clinical trials and post-marketing research.

Clinical Trials shall be conducted in accordance with the provisions of the PRC GCP, including the preparation for clinical trials, clinical trial protocols, responsibilities of sponsors and investigators, and protection of subjects.

According to the Announcement of the NMPA on Adjusting the Evaluation and Approval Procedures for Clinical Trials of Drugs (《關於調整藥物臨床試驗審評審批程序的公告》), where the clinical trials of a new drug has been approved, upon the completion of Phase I and II clinical trials and prior to Phase III clinical trials, the applicant shall apply to the CDE for a communication session, to discuss with the CDE the key technical issues including the design of Phase III clinical trials.

Pursuant to the Administrative Measures for Communication on Drug Development and Technical Reviews (《藥物研發與技術審評溝通交流管理辦法》) issued by the CDE on December 10, 2020 and effective therefrom, during the research and development, and application for registration stages of innovative drugs, the applicants may propose communication sessions with the CDE. The forms of communication can be face-to-face conference, video conference, telephone conference or written reply. The communication sessions are classified into three types. Type I sessions are held to address the key safety issues in the clinical trials of drugs and the key technical issues in the research and development of breakthrough therapeutic drugs. Type II sessions are

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held during the key research and development stages of drugs, mainly including the sessions held prior to the application of IND, the sessions held upon completion of Phase II clinical trials and prior to commencement of Phase III clinical trials of new drugs, the sessions held prior to application for marketing approvals of new drugs, and the risk evaluation and control sessions. Type III sessions are those sessions not falling into the categories of Type I or II sessions.

Filings and Approvals for Human genetic Resources International Cooperation

To effectively protect and rationally utilize the human genetic resources in the PRC, the Ministry of Science and Technology and the Ministry of Health (the “MOH”) jointly issued the Interim Administrative Measures on Human Genetic Resources (《人類遺傳資源管理暫行辦法》) on June 10, 1998, which was replaced by Administrative Regulations of the PRC on Human Genetic Resources (《中華人民共和國人類遺傳資源管理條例》) issued by the State Council on May 28, 2019 and amended on March 10, 2024. According to the Administrative Regulations of the PRC on Human Genetic Resources and the Service Guidance, Scope and Procedures of Filing and Prior Reporting for Human Genetic Resources Administrative Licensing Items (人類遺傳資源行政許可事項服務指南、備案以及事先報告範圍和程序) issued by the NHC on March 20, 2025, any research using human genetic resources of China that involves a foreign entity sponsor shall fall within the scope of international cooperation. The cooperating PRC organization must submit an application for approval to the NHC via the official online system.

Pursuant to the Administrative Regulations on Human Genetic Resources of the PRC (《中華人民共和國人類遺傳資源管理條例》) issued by the State Council on May 28, 2019 and revised on March 10, 2024 which became effective on May 1, 2024, in order to obtain marketing approvals for the relevant drugs and medical devices in the PRC, no approval is required in the event international cooperating clinical trials are conducted at clinical institutions using the human genetic resources of the PRC but not involving the exit of human genetic resource materials. However, the cooperating parties shall file with the competent health department of the State Council the type, quantity and purpose of the human genetic resources intended to be used prior to conducting clinical trials.

On October 17, 2020, the SCNPC promulgated the Biosecurity Law of the PRC (《中華人民共和國生物安全法》) (the “**Biosecurity Law**”) which was later amended on April 26, 2024 and effective since then, establishing a comprehensive legislative framework on the current regulations in the areas including epidemic control of human, animal and plant infectious diseases, security of biotechnology research, development and application, biosafety management of pathogenic microbiology laboratories, security management of human genetic resources and biological resources, countermeasures against microbial resistance and prevention of bioterrorism and threat of biological weapons.

On May 26, 2023, the Ministry of Science and Technology issued the Implementing Rules of the Administrative Regulations on Human Genetic Resources (《人類遺傳資源管理條例實施細則》) (the “**Human Genetic Resources Implementing Rules**”), which became effective on July 1, 2023, further clarifying the requirements for administrative licensing, record-filing and security review in respect of the collection, preservation, use, and outbound supply of Chinese human genetic resources, and detail the issues concerning relevant supervision, inspection and administrative penalties.

New Drug Application, Approval and Registration

According to the Administrative Measures for Drug Registration, upon completion of pharmacological and toxicological studies, clinical trials and other research supporting the marketing registration of drugs, determination of quality standards, completion of validation of commercial-scale production processes, and preparation for acceptance of verification and inspection for drug registration, the applicant may apply for the New Drug Approval (the “NDA”). The NMPA shall

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evaluate the application pursuant to applicable laws and regulations. The applicant must obtain the NDA before the drugs can be manufactured and sold in the PRC. If (i) a drug is used for the treatment of severe life-threatening diseases currently lacking effective treatment and the data of clinical trials of the drug can prove the efficacy and forecast the clinical value of the drug; (ii) a drug which is urgently needed for public health and the data of clinical trials of the drug can show the efficacy and forecast the clinical value of the drug; or (iii) a vaccine which is urgently needed to deal with major public health emergencies or deemed to be urgently needed by the NHC, and by assessment the benefit of the vaccine outweighs the risk, the applicant may apply for the conditional NDA during the clinical trials of the drug or vaccine.

According to the Administrative Provisions on Special Examination and Approval of New Drug Registration (《新藥註冊特殊審批管理規定》) issued by the CFDA on January 7, 2009 and effective therefrom, the special examination and approval by the CFDA for new drug registration applications applies when (i) the effective constituent extracted from, among others, plants, animals or minerals or the preparations thereof have never been marketed in the PRC, or the medicinal materials are newly discovered or the preparations thereof; (ii) the chemical raw medicines or the preparations thereof, or the biological products have not been approved for marketing either in the PRC or abroad; (iii) the new drugs are for the treatment of such diseases as AIDS, malignant tumors or rare diseases with distinctive clinical treatment advantages; or (iv) the new drugs are for the treatment of the diseases currently lacking effective treatment. Under the circumstances of (i) or (ii), the drug registration applicant (the "Applicant") may apply for the special examination and approval when submitting the application for clinical trials of the new drug; while, under the circumstances of (iii) or (iv), the Applicant may only apply for the special examination and approval when applying for production.

On November 11, 2015, the CFDA issued the Circular on Several Policies of the Review and Approval of Drug Registrations (《關於藥品註冊審評審批若干政策的公告》), which provided fast-track clinical trial approvals and drug registration pathways for the following new drug applications: (i) registration of innovative drugs for the prevention or treatment of HIV, malignant tumors (cancers), severe infectious diseases and rare diseases; (ii) registration of pediatric drugs; (iii) registration of geriatric drugs for the treatment of diseases specially or commonly contracted by the senior population; (iv) registration of drugs listed in national major science and technology projects or national key research and development plan; (v) registration of innovative drugs using advanced technology or innovative treatment methods, or having distinctive clinical benefits; (vi) registration of foreign innovative drugs to be manufactured locally in China; (vii) concurrent applications for the clinical trials of new drugs which have been already approved in the United States or the European Union, or concurrent drug registration applications for drugs which are in the process of applying for marketing approvals and have passed onsite inspections by the competent review and approval authorities of drugs of the United States or the European Union, and are manufactured with the same production line in the PRC; and (viii) clinical trial applications for drugs with urgent clinical need and patent expiry within three years, and applications for manufacturing approvals of drugs with urgent clinical need and patent expiry within one year.

Drug Manufacturing License

Pursuant to the Drug Administration Law, a drug manufacturer must obtain a drug manufacturing license from the provincial medical products administration authority before manufacturing drugs. Prior to granting drug manufacturing licenses, the relevant governmental authorities shall inspect the applicant's production facilities and decide whether the sanitary conditions, quality assurance system, management structure and equipment of such facilities have met the required standards. Each drug manufacturing license will be valid for five years and the manufacturer is required to apply for renewal of the license within six months prior to the expiration date and the authorities shall reassess such application of renewal in accordance with the current legal and regulatory requirements.

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Drug Operation

According to the Drug Administration Law, a drug operator shall obtain a drug operation license from the provincial drug administration department before conducting the drug wholesaling or from the county’s drug administration department before conducting the drug sale. On November 17, 2017, the CFDA issued the Administrative Measures for Drug Operation Licenses (《藥品經營許可證管理辦法》), which was repealed by Measures for Quality Supervision and Management of Drug Operation and Use (《藥品經營和使用質量監督管理辦法》), issued by the SAMR on September 27, 2023 and effective on January 1, 2024, which further clarify the procedure, renewal, supervision and inspection of the drug operation licenses.

Good Manufacturing Practice (“GMP”)

The World Health Organization encourages the adoption of GMP standards in the drug production, in order to minimize the risks of failure to pass the finished product tests in the drug production.

The MOH first issued the Guidelines on Good Manufacturing Practices (《藥品生產質量管理規範》) on March 17, 1988, which was later revised on December 28, 1992. After its establishment, the NMPA revised the Guidelines on Good Manufacturing Practices on June 18, 1999, which became effective from August 1, 1999. The Guidelines on Good Manufacturing Practices revised by the MOH on January 17, 2011, which took effect on March 1, 2011 provided the basic standards for drug production, including production facilities, qualification of management personnel, production plant and facilities, documentation, material packaging and labeling, testing, production management, sales and return of products, and complaints of customers.

On December 30, 2015, the CFDA issued the Notice on Effectively Implementing the Good Manufacturing Practice (《關於切實做好實施藥品生產質量管理規範有關工作的通知》), which provided that those drug manufacturers that failed to obtain the GMP certificates shall not be granted the drug manufacturing license.

On November 29, 2019, the NMPA issued the Announcement on Matters relating to the Implementation of the Drug Administration Law of the PRC (《關於貫徹實施〈中華人民共和國藥品管理法〉有關事項的公告》), which confirmed that the GMP certification would be canceled from December 1, 2019, and no application for GMP certification would be accepted and no GMP certificate would be granted. However, according to the Drug Administrative Law, drug manufacturers shall still comply with the GMP, establish and improve the GMP system, and ensure the whole drug production process consistently in compliance with statutory requirements.

On May 24, 2021, the NMPA issued the Administrative Measures for Drug Inspection(Trial) (《藥品檢查管理辦法(試行)》) which became effective on the same day, and was amended on July 19, 2023 by the NMPA, which repealed the Administrative Measures for the Certification of Good Manufacturing Practice. The Administrative Measures for Drug Inspection (Trial) provided that onsite inspections shall be conducted pursuant to the GMP on a drug manufacturer applying for the drug manufacturing license for the first time, while for the drug manufacturers applying for the renewal of drug manufacturing licenses, the review shall be conducted based on the risk management principles, in combination with the drug manufacturers’ compliance with the laws and regulations of drug administration, and the operation of the GMP and quality management system, and inspections on the drug manufacturers’ conformity to the GMP may be conducted where necessary.

Administrative Protection and Monitoring Periods for New Drugs

According to the Drug Administration Law Implementing Measures, to protect public health, the NMPA may provide for administrative monitoring periods of up to five years for new drugs approved to be manufactured, to consistently monitor the safety of such new drugs.

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During the monitoring period of a new drug, the NMPA will not approve any other enterprises’ applications to manufacture or import a similar new drug.

2. REGULATIONS RELATING TO PRODUCT LIABILITY

Pursuant to the PRC Civil Code (《中華人民共和國民法典》) promulgated by the NPC on May 28, 2020 and coming into effect on January 1, 2021, where a patient suffers damage due to defects in drugs, he may seek compensation from the drug marketing authorization holder or also from the medical institution. Where the patient seeks compensation from the medical institution, the medical institution, after it has made the compensation, shall have the right to recover the compensation from the liable drug marketing authorization holder.

3. REGULATIONS ON INTELLECTUAL PROPERTY RIGHTS

Trademarks

Trademarks are protected by the Trademark Law of the PRC (《中華人民共和國商標法》) which was promulgated on August 23, 1982 and subsequently amended on February 22, 1993, October 27, 2001, August 30, 2013, April 23, 2019 and took effect on November 1, 2019 as well as the Implementation Regulation of the PRC Trademark Law (《中華人民共和國商標法實施條例》) adopted by the State Council on August 3, 2002 and revised on April 29, 2014. In the PRC, registered trademarks include commodity trademarks, service trademarks, collective marks and certification marks. The Trademark Office of National Intellectual Property Administration handles trademark registrations and grants a term of 10 years to registered trademarks, renewable every 10 years where a registered trademark needs to be used after the expiration of its validity term.

Patents

According to the Patent Law of the PRC (《中華人民共和國專利法》) (the “**Patent Law**”), promulgated by the SCNPC on March 12, 1984 and further amended on September 4, 1992, August 25, 2000, December 27, 2008, October 17, 2020 and came into effect on June 1, 2021 and the Implementing Rules of the Patent Law of the PRC (《中華人民共和國專利法實施細則》), promulgated by the China Patent Bureau Council on January 19, 1985, and latest amended on December 11, 2023 by the State Council and came into effect on January 20, 2024, the term “invention-creations” refers to inventions, utility models and designs. The duration of patent right for inventions shall be twenty years, the duration of patent right for utility models shall be ten years and the duration of patent right for designs shall be fifteen years, counted from the date of filing. In the event that a dispute arises due to a patent being exploited without the prior authorization of the patentee, that is to say an infringement upon the patent right of the patentee.

Internet Domain Names

The Administrative Measures for Internet Domain Names (《互聯網域名管理辦法》), which was promulgated by the Ministry of Industry and Information Technology of the PRC (the “**MIIT**”) on August 24, 2017 and became effective on November 1, 2017, regulates the “.CN” and the “.zhongguo (in Chinese character)” shall be China’s national top-level domains. Any party that engages in internet information services shall use its domain name in compliance with laws and regulations and in line with relevant provisions of the telecommunications authority but shall not use its domain name to commit any violation.

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4. REGULATIONS ON EMPLOYMENT AND SOCIAL SECURITY

Labor Laws

The Labor Law of the PRC (《中華人民共和國勞動法》), which was promulgated by the SCNPC on July 5, 1994, came into effect on January 1, 1995, and was amended on August 27, 2009 and December 29, 2018, provides that an employer shall develop and improve its rules and regulations to safeguard the rights of its workers. Labor safety and health facilities must comply with relevant national standards. Workers engaged in special operations shall have received specialized training and obtained the pertinent qualifications.

The Labor Contract Law of the PRC (《中華人民共和國勞動合同法》), which was promulgated by the SCNPC on June 29, 2007, came into effect on January 1, 2008, and was amended on December 28, 2012, and came into effect on July 1, 2013, and the Implementation Regulations on Labor Contract Law (《中華人民共和國勞動合同法實施條例》) which was promulgated and came into effect on September 18, 2008 by the State Council, regulate the relations of employer and the employee, and contain specific provisions involving the terms of the labor contract.

Social Security and Housing Funds

According to the Provisional Regulations on the Collection and Payment of Social Insurance Premium (《社會保險費徵繳暫行條例》), the Regulations on Work Injury Insurance (《工傷保險條例》), the Regulations on Unemployment Insurance (《失業保險條例》) and the Trial Measures on Employee Maternity Insurance of Enterprises (《企業職工生育保險試行辦法》), enterprises in China must provide benefit plans for their employees, which include basic pension insurance, unemployment insurance, maternity insurance, work injury insurance and medical insurance. An enterprise must provide social insurance by processing social insurance registration with local social insurance agencies and must pay or withhold relevant social insurance premiums for or on behalf of employees.

The PRC Law on Social Insurance (《中華人民共和國社會保險法》), which was promulgated by the SCNPC on October 28, 2010 and came into effect on July 1, 2011, and was amended on December 29, 2018 regulates basic pension insurance, unemployment insurance, maternity insurance, work injury insurance and medical insurance, and has elaborated in detail the legal obligations and liabilities of employers who do not comply with relevant laws and regulations on social insurance.

The Regulations on the Administration of Housing Provident Fund (《住房公積金管理條例》), which was promulgated on April 3, 1999 and came into effective on the same date, and was amended on March 24, 2002 and March 24, 2019, stipulates that housing provident fund contributions paid by an individual employee and housing provident fund contributions paid by his or her employer shall all belong to the individual employee.

5. REGULATIONS ON TAXATION

Enterprise Income Tax

According to the Enterprise Income Tax Law of the PRC (《中華人民共和國企業所得稅法》) (the “EIT Law”), which was promulgated by the NPC on March 16, 2007, came into effect on January 1, 2008 and amended by the SCNPC on February 24, 2017 and December 29, 2018, and the Implementation Regulations on the EIT Law (《中華人民共和國企業所得稅法實施條例》), which was promulgated by the State Council on December 6, 2007 and came into effect on January 1, 2008, and last amended by the State Council on December 6, 2024 and came into effect on January 20, 2025, a uniform income tax rate of 25% will be applied to domestic enterprises, foreign-invested enterprises and foreign enterprises that have established production and operation

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facilities in China. These enterprises are classified as either resident enterprises or non-resident enterprises. Resident enterprises refer to enterprises that are established in accordance with PRC laws, or that are established in accordance with the laws of foreign countries but whose actual or de facto control is administered from within the PRC. Non-resident enterprises refer to enterprises that are set up in accordance with the laws of foreign countries and whose actual administration is conducted outside the PRC, but who (whether or not through the establishment of institutions in the PRC) derive income from the PRC. Under the EIT Law and relevant implementing regulations, a uniform corporate income tax rate of 25% is applicable. However, if non-resident enterprises have not established institutions or places in the PRC, or if they have established institutions or places in the PRC but there is no actual relationship between the relevant income derived in the PRC and the institutions or places set up by them, enterprise income tax is set at the rate of 10%.

6. REGULATIONS ON FOREIGN EXCHANGE

Foreign Exchange Regulation

On January 29, 1996, the State Council promulgated the Administrative Regulations on Foreign Exchange of the PRC (《中華人民共和國外匯管理條例》) which became effective on April 1, 1996 and was amended on January 14, 1997 and August 5, 2008. Foreign exchange payments under current account items shall, pursuant to the administrative provisions of the foreign exchange control department of the State Council on payments of foreign currencies and purchase of foreign currencies, be made using self-owned foreign currency or foreign currency purchased from financial institutions engaging in conversion and sale of foreign currencies by presenting the valid document. Domestic entities and domestic individuals making overseas direct investments or engaging in issuance and trading of overseas securities and derivatives shall process registration formalities pursuant to the provisions of the foreign exchange control department of the State Council.

According to the Notice of the State Administration of Foreign Exchange on Reforming the Management Mode of Foreign Exchange Capital Settlement of Foreign Investment Enterprises (《國家外匯管理局關於改革外商投資企業外匯資本結匯管理方式的通知》), or the SAFE Circular 19 promulgated on March 30, 2015, coming effective on June 1, 2015 and partially abolished on December 30, 2019 and March 23, 2023, foreign-invested enterprises could settle their foreign exchange capital on a discretionary basis according to the actual needs of their business operations. Whilst, foreign-invested enterprises are prohibited to use the foreign exchange capital settled in RMB (a) for any expenditures beyond the business scope of the foreign-invested enterprises or forbidden by laws and regulations; (b) for direct or indirect securities investment; (c) to provide entrusted loans (unless permitted in the business scope), repay loans between enterprises (including advances by third parties) or repay RMB bank loans that have been on-lent to a third party; and (d) to purchase real estates not for self-use purposes (save for real estate enterprises).

On June 9, 2016, SAFE issued the Notice of the State Administration of Foreign Exchange on Reforming and Standardizing the Foreign Exchange Settlement Management Policy of Capital Account (《國家外匯管理局關於改革和規範資本項目結匯管理政策的通知》), or the SAFE Circular 16, which came into effect on the same day and partially amended on December 4, 2023 and effective since then. The SAFE Circular 16 provides that discretionary foreign exchange settlement applies to foreign exchange capital, foreign debt offering proceeds and remitted foreign listing proceeds, and the corresponding RMB capital converted from foreign exchange may be used to extend loans to related parties or repay inter-company loans (including advances by third parties).

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7. REGULATIONS ON THE COMPANIES AND FOREIGN INVESTMENT IN CHINA

The Company Law of the PRC (《中華人民共和國公司法》) (the “**Company Law**”), which was last amended by the SCNPC on December 29, 2023 and became effective on July 1, 2024, provides for the establishment, corporate structure and corporate management of companies, which also applies to foreign-invested enterprises in PRC.

On March 15, 2019, the NPC promulgated the Foreign Investment Law of the PRC (《中華人民共和國外商投資法》) (the “**Foreign Investment Law**”), which took effect on January 1, 2020 and repealed the Sino-foreign Equity Joint Ventures Law of the PRC (《中華人民共和國中外合資經營企業法》), the Wholly Foreign-owned Enterprise Law of the PRC (《中華人民共和國外資企業法》) and the Sino-foreign Cooperative Joint Ventures Law of the PRC (《中華人民共和國中外合作經營企業法》). Since then, the Foreign Investment Law has become the fundamental law regulating foreign-invested enterprises wholly or partially invested by foreign investors. According to the Foreign Investment Law and the Implementation Regulations for the Foreign Investment Law of the PRC (《中華人民共和國外商投資法實施條例》) issued by the State Council on December 26, 2019 and effective from January 1, 2020, foreign investment refers to any investment activity directly or indirectly carried out by foreign natural persons, enterprises or other organizations (the “**foreign investors**”) within the territory of the PRC, including the following circumstances: (i) a foreign investor establishes a foreign-funded enterprise within the territory of the PRC, either alone or together with any other investor; (ii) a foreign investor acquires shares, equities, property shares or any other similar rights and interests of a PRC enterprise; (iii) a foreign investor invests in any new project within the territory of the PRC, either alone or together with any other investor; or (iv) a foreign investor invests in any other way as stipulated under the laws or administrative regulations or provided by the State Council. The organization form and structure, and the operating rules of foreign-funded enterprises are subject to the provisions of the Company Law, the Partnership Enterprise Law of the PRC and other applicable laws.

8. REGULATIONS RELATING TO THE ACCESS OF FOREIGN INVESTMENT

On October 26, 2022, the MOFCOM and the National Development and Reform Commission of the PRC (“**NDRC**”) jointly released the Catalog of Industries for Encouraging Foreign Investment (2022 Version) (《鼓勵外商投資產業目錄》(2022年版)), which became effective on January 1, 2023 and replace the previous version. This Catalog aims to encourage and guide foreign investors to invest in specific industries and fields, including manufacturing of new types of drugs by employing bioengineering technology.

The Special Administrative Measures for Access of Foreign Investment (Negative List) (《外商投資准入特別管理措施(負面清單)》), the “**Negative List**”) was firstly issued by the NDRC and the MOFCOM on June 28, 2018, and latest amended and promulgated on September 6, 2024. The Negative List sets forth the prohibited or restricted industries or economic activities for foreign investment in China, including that the investment in the development and application of human stem cells, genetic diagnosis and treatment technologies are prohibited.

Issued jointly by the MOFCOM, NHC and NMPA on September 7, 2024 (Shangzi Han [2024] No. 568) (商資函[2024]568號文), the Circular on Carrying out Pilot Work for Expanding Opening-up in the Medical-related Field aims to promote high-quality development of China’s medical sector and meet public health needs. It permits foreign-invested enterprises in designated pilot areas (Beijing, Shanghai, Guangdong Pilot Free Trade Zones and Hainan Free Trade Port) to engage in human stem cell, gene diagnosis and treatment technology development and application for product registration, marketing and production, with approved products available nationwide. Foreign-invested enterprises must comply with relevant laws on human genetic resources, clinical trials and ethical reviews, and complete required regulatory procedures.

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9. REGULATIONS ON OVERSEAS LISTING

The CSRC promulgated the Overseas Listing Trial Measures and five relevant guidelines on February 17, 2023, which took effect on March 31, 2023. The Overseas Listing Trial Measures comprehensively reform the regulatory regime for overseas offering and listing of PRC domestic companies’ securities, either directly or indirectly, into a filing-based system. According to the Overseas Listing Trial Measures, the PRC domestic companies that seek to offer and list securities in overseas markets, either in direct or indirect means, are required to fulfill the filing procedure with the CSRC and report relevant information. The Overseas Listing Trial Measures provide that an overseas listing or offering is explicitly prohibited, if any of the following applies: (i) such securities offering or listing is explicitly prohibited by provisions in PRC laws, administrative regulations or relevant state rules; (ii) the proposed securities offering or listing may endanger national security as reviewed and determined by competent authorities under the State Council in accordance with laws; (iii) the domestic company intending to be listed or offer securities in overseas markets, or its controlling shareholder(s) and the actual controller, have committed crimes such as corruption, bribery, embezzlement, misappropriation of property or undermining the order of the socialist market economy during the latest three years; (iv) the domestic company intending to be listed or offer securities in overseas markets is currently under investigations for suspicion of criminal offenses or major violations of laws and regulations, and no conclusion has yet been made thereof; or (v) there are material ownership disputes over equity held by the domestic company’s controlling shareholder(s) or by other shareholder(s) that are controlled by the controlling shareholder(s) and/or actual controller. According to the Overseas Listing Trial Measures, initial public offerings or listings in overseas markets shall be filed with the CSRC within three working days after the relevant application is submitted overseas.

On February 24, 2023, the CSRC and other relevant government authorities promulgated the Provisions on Strengthening the Confidentiality and Archives Administration of Overseas Securities Issuance and Listing by Domestic Enterprises (《關於加強境內企業境外發行證券和上市相關保密和檔案管理工作的規定》) (the “**Provision on Confidentiality**”), which took effect on March 31, 2023. Pursuant to the Provision on Confidentiality, where a domestic enterprise provides or publicly discloses to the relevant securities companies, securities service institutions, overseas regulatory authorities and other entities and individuals, or provides or publicly discloses through its overseas listing subjects, documents and materials involving state secrets and working secrets of state organs, it shall report the same to the competent department with the examination and approval authority for approval in accordance with the law, and submit the same to the secrecy administration department of the same level for filing. Domestic enterprises providing accounting archives or copies thereof to entities and individuals concerned such as securities companies, securities service institutions and overseas regulatory authorities shall perform the corresponding procedures pursuant to the relevant provisions of the State. The working papers formed within the territory of the PRC by the securities companies and securities service institutions that provide corresponding services for the overseas issuance and listing of domestic enterprises shall be kept within the territory of the PRC, and those that need to leave the PRC shall go through the examination and approval formalities in accordance with the relevant provisions of the State.

10. REGULATIONS ON CYBERSECURITY AND DATA EXPORTATION SECURITY

On December 28, 2021, the Cyberspace Administration of China (“CAC”), jointly with 12 other governmental authorities, promulgated the Measures for Cybersecurity Review (《網絡安全審查辦法》) (the “**Measures for Cybersecurity Review**”), which became effective on February 15, 2022, provides that critical information infrastructure operators that purchase network products and services and data processing operators engaging in data processing activities that affect or may affect national security must be subject to the cybersecurity review.

On July 7, 2022, the CAC issued the Measures on the Security Assessment of Cross-border Data Transfer (《數據出境安全評估辦法》) (the “**Security Assessment Measures**”), which took effect on September 1, 2022. The Security Assessment Measures generally apply to data processors that provide abroad important data or personal

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information that was collected or produced through operations within the PRC. Companies that are subject to the Security Assessment Measures need to conduct data mapping on cross-border data transfers, prepare the self-assessment and submission, as well as implement data classification and apply controls on cross-border data transfers.

In March 2024, the CAC issued the Provisions on Promoting and Regulating Cross-border Data Flows (《促進和規範數據跨境流動規定》), which required security assessment for the following types of cross-border data transfers, (i) for critical information infrastructure operators, the outbound transfer of personal information or important data, and (ii) for data processors that are not critical information infrastructure operators, the outbound transfer of important data or the cumulative outbound transfer within one calendar year of the personal information of over one million people or the sensitive personal information of over 10,000 people. These provisions also stipulated that, when data processors that are not critical information infrastructure operators engage in the cumulative outbound transfer within one calendar year of the personal information of over 100,000 people but less than one million people or the sensitive personal information of less than 10,000 people, the data processors must enter into a standard contract for cross-border transfer of personal information with the data recipient or obtain a certification for the protection of personal information. Furthermore, these provisions clarified that data processors do not need to treat any data as “important data” the outbound transfer of which requires security assessments, if government authorities have not declared or notified them that the data are “important data”.

11. REGULATIONS ON STOCK INCENTIVE PLANS

On February 15, 2012, SAFE promulgated the Notice on Foreign Exchange Administration of PRC Residents Participating in Share Incentive Plans of Offshore Listed Companies (《國家外匯管理局關於境內個人參與境外上市公司股權激勵計劃外匯管理有關問題的通知》), or the Stock Option Rules. According to the Stock Option Rules, individuals participating in any stock incentive plan of any overseas publicly listed company who are Chinese citizens or foreign citizens who reside in mainland China for a continuous period of not less than one year, subject to a few exceptions, are required to register with SAFE or its local branches and complete certain other procedures through a domestic qualified agent, which could be a Chinese subsidiary of such overseas listed company. The participants must also retain an overseas entrusted institution to handle matters in connection with their exercise of stock options, the purchase, and sale of corresponding stocks or interests, and fund transfers.

Under the Circular of the State Administration of Taxation on Issues Concerning Individual Income Tax concerning Equity Incentives (《國家稅務總局關於股權激勵有關個人所得稅問題的通知》) promulgated by the STA and effective on August 24, 2009, and was partially abolished on May 1, 2011. Listed companies and their domestic organizations shall, according to the individual income tax calculation methods for “wage and salary income” and stock option income, lawfully withhold and pay individual income tax on such income.

12. REGULATIONS ON CLINICAL TRIALS IN THE UNITED STATES AND ORPHAN DRUG DESIGNATION

The FDA and other regulatory authorities at federal, state, and local levels, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drugs and biologics such as those we are developing. FDA’s regulatory requirements are frequently changing and evolving. For instance, over the last few years, FDA has been developing its policy around the use of artificial intelligence and machine learning in drug development and clinical trial programs. This is likely to be an evolving area of FDA regulation. We, along with third-party contractors and our customers, will be required to navigate the various preclinical, clinical and commercial approval requirements to conduct studies or seek approval or licensure of product candidates.

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Our product candidates are subject to regulation by the FDA and may be regulated as drugs or biologics. Our customers are also subject to FDA regulation and, as such, our services for our customers may be directly or indirectly regulated. Prior to marketing in the United States, drugs require the submission and approval of a New Drug Application, or NDA, and biologics require the submission and approval of a Biologics License Application, or BLA. Although drugs and biologics require different applications and are subject to certain different regulatory requirements, biologics are also considered a kind of drug. Failure to comply with applicable FDA or other requirements at any time during product development, clinical testing, the NDA/BLA approval process or after NDA/BLA approval may result in administrative or judicial actions, including the FDA’s refusal to approve pending applications, suspension or revocation of approved applications, warning letters, product recalls, product seizures, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

The process required by the FDA before drug product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA’s Good Laboratory Practices, or GLP, regulations;
- submission to the FDA of an Investigational New Drug application, or IND, which must become effective before clinical trials may begin and must be reported on annually and amended when significant changes are made;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety and effectiveness of the proposed product candidate for its intended indications;
- preparation of and submission to the FDA of an NDA/BLA when adequate data are obtained from pivotal clinical trials;
- registration of the manufacturing facility or facilities at which the proposed product will be manufactured, packaged or labeled;
- a determination by the FDA within 60 days of its receipt of an NDA/BLA to accept the application for review;
- satisfactory completion of a potential FDA Advisory Committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection, either remotely or in person, of the manufacturing facility or facilities at which the proposed product is manufactured to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the drug’s continued safety and efficacy or the biological product’s continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with Good Clinical Practices, or GCP regulations;
- potential FDA audit, remotely or in person, of the nonclinical study and clinical trial sites that generated the data in support of the NDA/BLA, if applicable; and
- FDA review and approval of the NDA/BLA to permit commercial distribution and marketing of the product for approved indications for use in the United States.

IND Application and Clinical Development

Prior to initiating the first clinical trial with a product candidate in the United States, sponsors must submit an IND application to the FDA. An IND application is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND application is on the general investigational plan and the protocol(s) for clinical trials. The IND application also includes results of animal and *in vitro*

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pre-clinical studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the investigational product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product.

Preclinical studies must generally be conducted in accordance with the FDA's GLPs, which set forth the minimum basic requirements for the conduct of preclinical research, as well as the requirements of other U.S. agencies regarding the conduct of animal research. Notably, FDA is currently working to phase out animal testing requirements for certain drugs, and replace them with validated new approach methodologies, which include in vitro human-based systems, computer-based modeling, and other innovative platforms.

An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. If the IND sponsor is not able to address the FDA's concerns satisfactorily within the 30-day time frame, the IND may be placed on clinical hold. The IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical hold is removed by the FDA and the clinical trial can begin.

Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial. Clinical holds may also be imposed by the FDA at any time before or during trials due to safety concerns or non-compliance.

If a clinical trial involves the use of an investigational device, including an in vitro diagnostic device or delivery device, the sponsor may also need to comply with FDA's investigational device regulations and obtain an investigational device exemption from the FDA. Drugs and biologics that require the use of a medical device may also be considered combination products. In such cases, the use of the two products together must be shown to be safe and effective for the proposed intended use and the labeling of the two products must reflect their combined use. In some cases, the device component may require a separate premarket submission. Once approved or cleared, the sponsor of the device component submission (or the combination product submission, if both components are covered by one premarket submission) would need to comply with FDA's post-market device requirements.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Generally, a separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives.

Additionally, some clinical trials are overseen by an independent group of experts organized by the sponsor, which may be called data monitoring committees or data safety monitoring boards. This group may review data and advise the sponsor on the trial (including modifications or discontinuation) and product safety.

A number of other requirements also apply to FDA regulated clinical trials. For instance, FDA seeks to ensure that clinical trial data is meaningful for and applicable to a U.S. population and medical practice, which may impact FDA's acceptance of data from foreign clinical studies. Additionally, information about certain clinical trials must be timely submitted to clinicaltrials.gov, for public posting. Sponsors or distributors of investigational products for the diagnosis, monitoring, or treatment of one or more serious disease or conditions must also have a public policy on expanded access. Sponsors must further make certain disclosure statements to FDA with respect to investigator conflicts of interest.

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Additionally, the manufacture of investigational drugs and biologics for clinical trials is subject to cGMP requirements. Investigational drugs/biologics and active ingredients/substances that are imported into the United States must also comply with FDA and other regulatory requirements. Further, the export of investigational products from the United States is subject to regulatory requirements of the receiving country as well as U.S. export requirements.

A sponsor may choose, but is not required, to conduct a clinical trial at sites outside the United States under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval or licensing. In particular, such studies must be conducted in accordance with GCP, including review and approval by an IRB or independent ethics committee, or IEC, and informed consent from volunteers. The FDA must be able to validate the data through an onsite inspection or remote regulatory assessment, if deemed necessary by the FDA.

For purposes of NDA/BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap. Phase 1 clinical trials may be conducted in patients or healthy volunteers to evaluate the product's safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism distribution, excretion, and pharmacokinetics and, if possible, seek to gain an early indication of its effectiveness. Phase 2 clinical trials usually involve controlled trials in a larger but still relatively small number of subjects from the relevant patient population to evaluate dosage tolerance and appropriate dosage; identify possible short-term adverse effects and safety risks; and provide a preliminary evaluation of the efficacy of the drug or biologic product for specific indications. Phase 3 clinical trials evaluate clinical efficacy and safety in a larger, geographically dispersed patient population. These trials typically compare the product candidate to placebo, standard treatments, or other active comparators to provide statistically significant evidence for approval. The goal is to establish the overall risk-benefit profile and provide an adequate basis for physician labeling. Phase 3 trials are larger, more complex, and more costly than Phase 1 and Phase 2 trials. The FDA typically requires data from two adequate and well-controlled trials for approval, but in certain circumstances, a single trial plus confirmatory evidence or a single large multicenter trial may suffice.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the NDA/BLA. These clinical trials are typically used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, and to the clinical investigators, regarding serious and unexpected adverse events, as well as any findings from other studies, tests in laboratory animals or *in vitro* testing that suggest either a significant risk for human patients or a clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. In addition, concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Additionally, NDAs or BLAs or supplements to NDAs or BLAs for a new active ingredient, dosage form, dosage regimen, or route of administration must contain data to assess the safety and effectiveness of the product for pediatric patients and to support

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pediatric dosing and administration. The FDA may, on its own initiative or at the request of the applicant, grant deferrals or partial waivers. This requirement does not generally apply to orphan designated products, but pediatric studies may be required if approval is sought for indications for which the product has not received orphan designation. Further, for product candidates intended for the treatment of adult cancer which are directed at molecular targets that the FDA determines to be substantially relevant to the growth or progression of pediatric cancer, with the application, sponsors must submit reports from molecularly targeted pediatric cancer investigations designed to yield clinically meaningful pediatric study data, gathered using appropriate formulations for each applicable age group, to inform potential pediatric labeling. The FDA may, on its own initiative or at the request of the applicant, grant deferrals or waivers of some or all of this data. Orphan products are not exempt from this requirement.

Premarket Submission and Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials are submitted to the FDA as part of an NDA/BLA requesting approval to market the product for one or more indications. The NDA/BLA must include all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. The submission of an NDA/BLA requires payment of a substantial application user fee to the FDA unless a waiver or exemption applies.

Once an original NDA/BLA has been submitted, the FDA has 60 days to determine whether the application can be filed. If the FDA determines that an application is deficient on its face in a way that precludes a complete review, the FDA may not accept the application for review and may issue a refuse-to-file letter to the sponsor. If the FDA determines the application is fileable, the FDA's goal is to review standard applications within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews an NDA/BLA to determine whether a drug is safe and effective for its intended uses. The FDA also reviews the applications to determine whether the facilities in which products are manufactured, processed, packed, or held meet standards designed to assure the product's continued safety and efficacy. The FDA may convene an advisory committee to provide insight on application review questions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully. Before approving an NDA/BLA, the FDA will typically inspect, either remotely or in person, the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to ensure consistent production of the product within required specifications. Additionally, before approving an NDA/BLA, the FDA will typically inspect, either remotely or in person, one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it may request additional testing or information.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the NDA/BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than the company interprets the same data. If the FDA decides not to approve an NDA/BLA in its present form, the FDA will issue a complete response letter that describes all of the specific deficiencies in the application identified by the FDA. The complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA/BLA, addressing all of the deficiencies identified in the letter, request a hearing or withdraw the application.

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If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the drug subject to a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and 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. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates that FDA may grant upon a sponsor's application. Designations, however, may be revoked if a product candidate no longer meets the applicable qualifying criteria.

The Fast Track program is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and nonclinical or clinical data demonstrate the potential to address an unmet medical need for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a Fast Track product has opportunities for frequent interactions with the review team during product development and, once an NDA/BLA is submitted, the product may be eligible for priority review. A Fast Track product may also be eligible for rolling review, in which case the FDA may consider for review sections of the NDA/BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA/BLA, the FDA agrees to accept sections of the NDA/BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA/BLA.

A product intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product can receive breakthrough therapy designation if it is intended to treat a serious or life threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product, including involvement of senior managers.

Any marketing application for a drug or biologic submitted to the FDA for approval, including a product with a Fast Track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition compared to marketed products. For products containing new molecular entities, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (compared with ten months under standard review).

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Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. To receive accelerated approval, the product must generally provide a meaningful advantage over available therapies. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In fact, by the date of approval of an accelerated approval product, FDA must specify the conditions for the required post approval studies, including enrollment targets, the study protocol, milestones, and target completion dates. FDA may also, and frequently does, require that the confirmatory Phase 4 studies be commenced prior to FDA granting a product accelerated approval. In addition, the FDA currently requires as a condition for accelerated approval pre-submission of promotional materials, which could adversely impact the timing of the commercial launch of the product. Reports on the progress of the required Phase 4 confirmatory studies must be submitted to the FDA every 180 days after approval. If the trials fail to verify the clinical benefit of the drug or biologic product, the FDA may withdraw approval of the application through a statutorily defined streamlined process. Failure to conduct the required Phase 4 confirmatory studies or to conduct such studies with due diligence, as well as failure to submit the required update reports can subject a sponsor to penalties.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant the orphan drug designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or to a drug intended to treat a disease or condition affecting more than 200,000 individuals in the United States if there is no reasonable expectation that the cost of developing and making available the drug to treat that disease or condition will be recovered from sales in the United States for that drug. Sponsors must also provide a medically plausible basis for the use of the drug for the rare disease or condition. Additionally, sponsors must present a plausible hypothesis for clinical superiority to obtain orphan designation if there is a product already approved by the FDA that that is considered by the FDA to be the same as the already approved product and is intended for the same indication. This hypothesis must be demonstrated to obtain orphan exclusivity. Orphan drug designation must be requested before submitting an application for marketing approval. After the FDA grants the orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

If a product that has the orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusive approval (or exclusivity), which means that the FDA may not approve any other applications, including a full NDA/BLA, to market the same drug for the same indication for seven years, except in certain circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the disease or condition for which the drug was designated.

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Additional U.S. Research Requirements

Depending on the scope of our specific activities, we may be subject to additional U.S. laws and regulations related to research activities, including those with respect to laboratory biosecurity, licensing (with associated compliance obligations), and the regulation of certain chemicals and other biological substances, specimens, and materials.

We may also be subject to regulation by other agencies, including the U.S. Environmental Protection Agency and agencies that regulate workplace safety.