
REGULATORY OVERVIEW

PRC LAWS AND REGULATIONS

This section sets forth a summary of the relevant significant PRC laws and regulations that affect our business and the industry in which we operate.

Regulatory Authorities

In the PRC, the National Medical Products Administration, or the NMPA, which was previously known as China Food and Drug Administration, is the primary regulatory agency for pharmaceutical products and businesses and regulates almost all of the key stages of the life-cycle of pharmaceutical products, including non-clinical studies, clinical trials, marketing approvals, manufacturing, advertising and promotion, distribution, and pharmacovigilance (i.e. post-marketing safety reporting obligations). The Center for Drug Evaluation, or the CDE, which is a subsidiary under the NMPA, conducts the technical evaluation on each drug and biologic application to assess the safety and efficacy of each candidate.

The National Health Commission, or the NHC (formerly known by names of the Ministry of Health and National Health and Family Planning Commission), is the primary healthcare regulatory agency in China. It is responsible for overseeing the operation of medical institutions, some of which also serve as clinical trial sites.

Also, the Ministry of Commerce, or the MOFCOM, and the State Administration for Market Regulation, or the SAMR, are the main regulatory authorities on our PRC subsidiaries with regard to the foreign investment activities and business supervision.

Laws and Regulations Related to Drugs

Introduction

In 2017, the drug regulatory system entered a new and significant period of reform. In October 2017, the General Office of the State Council and the General Office of the Central Committee of the China Communist Party jointly issued the Opinions on Deepening the Reform of the Evaluation and Approval System to Encourage Innovation in Drugs and Medical Devices (《關於深化審評審批制度改革鼓勵藥品醫療器械創新的意見》) (the “**Innovation Opinion**”) to encourage, among others, the reform of clinical trial management and acceleration of the review and approval for drugs and medical devices marketing.

To implement the regulatory reform introduced by the Innovation Opinion, the National People’s Congress (the “NPC”) and NMPA has been revising the fundamental laws, regulations and rules regulating pharmaceutical products and the industry, which include the framework law known as the PRC Drug Administration Law (《中華人民共和國藥品管理法》), or the Drug Administration Law. The Drug Administration Law was promulgated by the Standing Committee of the NPC (the “SCNPC”), on September 20, 1984 and latest amended on August 26, 2019 and took effect as of December 1, 2019. The State Council issued the Regulations for Implementation of the Drug Administration Law of the PRC (《中華人民共和國藥品管理法實

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施條例》), which was promulgated on August 4, 2002 and latest amended on March 2, 2019, to further implement the Drug Administration Law. The NMPA also has its own set of regulations for the Drug Administration Law, and the primary one governing clinical trial applications, marketing approval, and post-approval amendment and renewal is known as the Drug Registration Regulation (《藥品註冊管理辦法》) (the “**Drug Registration Regulation**”), which was latest amended by the SAMR on January 22, 2020 and effective from July 1, 2020.

Non-Clinical Research and Animal Testing

The NMPA promulgated the Administrative Measures for Good Laboratories Practice of Non-clinical Laboratory (《藥物非臨床研究質量管理規範》) (the “**GLP**”) in 2003, which were revised on July 27, 2017, and has conducted the Administrative Measures for Good Laboratories Practice of Non-clinical Laboratory, or GLP Certification since 2003. On April 16, 2007, the NMPA issued the Circular on Measures for Certification of Good Laboratory Practice and for Non-clinical Laboratory (《藥物非臨床研究質量管理規範認證管理辦法》), or the NMPA Circular 214, last amended on January 19, 2023 and will come into effect on July 1, 2023, which sets forth the requirements for an institution to apply for a Certification of Good Laboratory Practice to undertake non-clinical drug research.

The State Science and Technology Commission promulgated the Regulations for the Administration of Affairs Concerning Experimental Animals (《實驗動物管理條例》) in November, 1988, which were amended by the State Council in January 2011, July 2013 and March 2017. The State Science and Technology Commission and the State Bureau of Quality and Technical Supervision jointly promulgated the Administration Measures on Good Practice of Experimental Animals (《實驗動物質量管理辦法》) in December 1997. The State Science and Technology Commission and other regulatory authorities promulgated the Administrative Measures on the Certificate for Experimental Animals (for Trial implementation) (《實驗動物許可證管理辦法(試行)》) in December 2001. All of these laws and regulations require a Certificate for Use of Laboratory Animals for performing experimentation on animals.

Clinical Trials Approval

Before registering a new drug, a sponsor shall complete clinical trials according to the Drug Registration Regulation. To start the clinical trial, a sponsor needs to apply for clinical trial approval first, and the Administrative Regulations of Good Clinical Practice for Drug Trial (《藥物臨床試驗質量管理規範》) (the “**GCP**”), has been promulgated to further promote the research into good practice for clinical trials of drugs and enhance the quality thereof. The GCP was promulgated by NMPA on August 6, 2003 and latest amended by NMPA and NHC which came into effect on July 1, 2020. All clinical trials conducted in China for new drug registration purposes must be approved and conducted at pharmaceutical clinical trial institutions filed according to the Regulations on the Administration of Drug Clinical Trial Institutions (《藥物臨床試驗機構管理規定》) promulgated by NMPA and NHC on November 29, 2019.

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According to the Announcement of Several Policies on the Evaluation and Examination for Drug Registration (《關於藥品註冊審評審批若干政策的公告》) promulgated by NMPA on November 11, 2015, an umbrella approval would be issued by NMPA for all phases of a new drug clinical trial, instead of approvals phase by phase. Provided by the Announcement of the Adjustment of Procedures of the Evaluation and Examination for Drug Clinical Trial (《關於調整藥物臨床試驗審評審批程序的公告》) issued by NMPA on July 24, 2018, applicants could proceed with their clinical trials if they have not received any denial or query from the CDE within 60 business days after the application has been accepted and the relevant application fees have been paid. The newly revised Drug Administration Law further confirms that the CDE under the State Council shall, within 60 working days from the date on which the application for a clinical trial is accepted, decide on whether to approve it and then notify the clinical trial applicant. In the case of failure to notify the applicant within the prescribed time limit, it shall be deemed approved. On May 22, 2017, NMPA issued the Announcement of the Opinions on Handling Issues Related to Verification of Drug Clinical Trial Data (《關於藥物臨床試驗數據核查有關問題處理意見的公告》), according to which, if the clinical trial data is incomplete, ill-formed and insufficient to prove the safety and efficacy of the drug, the registration application of the drug will be rejected.

Drug Clinical Trial Registration

Pursuant to the Drug Registration Regulation, upon obtaining the clinical trial approval and before commencing a clinical trial, the sponsor shall register the scheme of the clinical trial and other information on the Drug Clinical Trial Registration and Information Platform for clinical trials of drugs. During the clinical trial of drugs, the sponsor shall update registration information continuously, and register information on the outcome of the clinical trial of drugs upon completion of the clinical trial of drugs. The registration information shall be published on the platform and the sponsor shall be responsible for the veracity of such information. More details are provided in the Announcement on Drug Clinical Trial Information Platform (《關於藥物臨床試驗信息平台的公告》) released by the NMPA on September 6, 2013, providing that for all clinical trials approved by the NMPA and conducted in China shall be published through the Drug Clinical Trial Registration and Information Platform. The applicant shall complete trial pre-registration within one month after obtaining the clinical trial approval to obtain the trial’s unique registration number and shall complete certain follow-up information and first submission for publication before the first subject’s enrollment in the trial. If the foregoing first time of publication has not been submitted within one year after obtaining the clinical trial approval, the applicant shall submit an explanation, and if the procedure is not completed within three years, the clinical trial approval shall automatically be annulled.

Clinical Trial Process and Good Clinical Practices

Typically, pursuant to the Drug Registration Regulation, drug clinical trials in China shall go through four phases – phase I clinical trial, phase II clinical trial, phase III clinical trial and phase IV clinical trial. Based on the characteristics of drugs and research objective, the research contents shall include clinical pharmacology research, exploratory clinical trial, confirmatory clinical trial and post-marketing research clinical. The NMPA requires that the different phases of clinical trials in China shall receive ethics committee approval respectively

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and comply with the relevant requirements of quality management standards for clinical trials of drugs in PRC. The sponsor shall submit safety update reports on the CDE website regularly during the research and development period. The sponsor shall promptly report to the CDE regarding suspicious and unexpected serious adverse reaction and other potential serious safety risks arising in the course of the clinical trial. Based on the severity of the safety risks, the sponsor may be required to adopt measures to strengthen risk control, and may be required to suspend or terminate the clinical trial of drugs where necessary.

However, according to the Technical Guiding Principles for Clinical Trials of Anti-tumor Drugs (《抗腫瘤藥物臨床試驗技術指導原則》) issued by the NMPA on May 15, 2012, the clinical study staging of anti-tumor drugs is not a fixed developmental sequence. The rapid development of anti-tumor drug research theories and technologies is likely to have an impact on future anti-cancer drug development models. Therefore, applicants can actively explore more scientific and rational research methods and promptly seek advice from the drug registration department under the NMPA.

On November 19, 2021, the CDE introduced the Guiding Principles for Clinical Research and Development of Anti-tumor Drugs Oriented by Clinical Value (《以臨床價值為導向的抗腫瘤藥物臨床研發指導原則》), or the Guiding Principle, for anti-tumor drugs, which states that the fundamental purpose of the drug market is to address the needs of patients, and emphasizes that drug research and development should be based on patient needs and clinical value. The Guiding Principle discourages repetitive research and development of “me-too drugs” (drugs with identical mechanisms of action) and excessive waste.

In terms of trial design for anti-tumor drugs, clinical trials for combination therapy should gather evidence of superior efficacy for a particular indication/tumor type relative to any monotherapies within that combination therapy for the same indication/tumor type. This implies that different monotherapies within a combination therapy should be designed for the treatment of the same indication. According to the GCP, the sponsor shall provide investigators and the clinical trial institution with legal and economic insurance or guarantee relating to the clinical trial, and ensure that such insurance or guarantee is appropriate to the nature and degree of risks of the clinical trial, excluding the damages caused by the negligence of investigators or the clinical trial institution. Pursuant to the Innovation Opinion, the accreditation of the institutions for drug clinical trials shall be subject to record-filing administration. The conduct of clinical trials must adhere to the GCP, and the protocols must be approved by the ethics committees. Pursuant to the newly amended Drug Administration Law and the Regulations on the Administration of Drug Clinical Trial Institution (《藥物臨床試驗機構管理規定》) jointly promulgated by NMPA and NHC on November 29, 2019 and effective from December 1, 2019, drug clinical trial institutions shall be subject to filing administration. Entities that only conduct analysis of biological samples related to clinical trials of drugs are not required to perform filing procedures.

Human Genetic Resources Approval and Registration

The Ministry of Science and Technology promulgated the Service Guide for Administrative Licensing Items concerning Examination and Approval of Sampling, Collecting, Trading or Exporting Human Genetic Resources, or Taking Such Resources out of the PRC (《人類遺傳資源採集、收集、買賣、出口、出境審批行政許可事項服務指南》) in July 2015, according to which, if the sampling, collection or research activities of human genetic resources by a foreign-invested sponsor fall within the scope of international cooperation, and the cooperating organization of China shall apply for approval of the China Human Genetic Resources Management Office through the online system. On October 26,

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2017, the Ministry of Science and Technology issued the Announcement on Optimizing the Administrative Examination and Approval of Human Genetic Resources (《關於優化人類遺傳資源行政審批流程的通知》), which simplified the approval for utilizing human genetic resources to obtain the marketing license of a drug in the PRC.

On May 28, 2019, the State Council of PRC issued the Administrative Regulations on Human Genetic Resources (《人類遺傳資源管理條例》) (the “**Human Genetic Resource Regulation**”), which became effective on July 1, 2019. According to the Human Genetic Resource Regulation, human genetic resource includes human genetic resource materials and information. Human genetic resource materials refer to organs, tissues, cells and other genetic materials containing human genome, genes and other genetic materials. Human genetic resource information refers to information, such as data, generated by human genetic resources materials. The Human Genetic Resource Regulation formalized the approval requirements pertinent to research collaborations between Chinese and foreign-owned entities, under which, a new filing system (as opposed to the advance approval approach originally in place) is put in place for clinical trials utilizing China’s human genetic resources in order to obtain market license at clinical institutions without involving the export of human genetic resources materials outside of China. Foreign organizations, individuals and institutions established or actually controlled by foreign organizations and individuals are not allowed to collect or preserve human genetic resources in China or provide human genetic resources abroad.

Overseas Clinical Trial

On January 30, 2015, the CFDA promulgated the International Multi-Center Clinical Trial Guidelines (for Trial implementation) (《國際多中心藥物臨床試驗指南(試行)》) (the “**IMCT Guidelines**”), to provide guidance for the regulation of application, implementation and administration of international multicenter clinical trials in China. Where the applicant intends to make use of the data derived from international multi-center clinical trials for application for approval of drug application, it is necessary to conduct an overall evaluation of global clinical trial data, and then conduct further trend analysis on clinical trial data in Asia and our country. The similarity of the patients selected for clinical trial and general patients shall also be considered. The samples from trials in China shall be sufficient to evaluate and conclude the safeness and effectiveness of the drug for trial to patients in China and shall satisfy the statistics and legal requirements. Furthermore, the institutions involved in the international multi-center clinical trial shall be subject to on-site inspections by our drug administrative authorities.

On October 8, 2017, the General Office of Chinese Communist Party’s Central Committee and the General Office of the State Council jointly issued the Opinion on Strengthening the Reform of the Drug and Medical Device Review and Approval Process to Encourage Drug and Medical Device Innovation (《關於深化審評審批制度改革鼓勵藥品醫療器械創新的意見》) which stipulates that overseas clinical trial results are acceptable in China. Data derived from overseas clinical trials can be used in application for registration of drugs and medical devices if the data satisfy the registration requirement for drugs and medical devices in China. For initial application for marketing of pharmaceutical products and medical devices in China, the applicants are required to provide clinical trial data to indicate whether there will be difference of trial results among different ethnic groups.

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According to the Notice on Technical Guiding Principles for the Acceptance of the Overseas Clinical Trial Data of Drugs (《關於發佈接受藥品境外臨床試驗數據的技術指導原則的通告》) issued by NMPA on July 6, 2018, if overseas clinical trial data is used in application for drug registration, all (and not some) overseas clinical trial data shall be submitted. If a clinical trial is initially conducted in overseas and subsequent clinical trial will be conducted in China, the applicant of drug registration application is required to evaluate the data from initial clinical trial and to compile a full report. The applicant shall negotiate with the Drug Evaluation Center for acceptance of the initial clinical trial data for subsequent clinical trials.

New Drug Application and Registration

According to the Drug Registration Regulation, an applicant shall, upon completion of studies including pharmacy, pharmacology and toxicology and clinical trial of drugs which support the registration of drug marketing, determination of quality standards, verification of commercial scale manufacturing process, and preparation to undergo examination and inspection for drug registration, submit an application for drug marketing authorization, and submit the relevant research materials in accordance with the submission requirements. The CDE shall organize pharmacist, medical and other technical personnel to comprehensively review the application regarding the safety, effectiveness and quality control of the drug. Where the application is cleared by the comprehensive review, the drug shall be approved for marketing and a drug registration certificate shall be issued. Under the Drug Registration Regulation, drugs are classified into Chinese medicine, chemical medicine, biological products and others. Biological products are further divided in 3 categories in the Registration Classification and Application Documents Requirements of Biological Products (《生物製品註冊分類及申報資料要求》) (the “**Registration Category**”), which was promulgated by the NMPA on June 29, 2020 and replaced the previous version issued in 2007. Pursuant to the Registration Category, Category I therapeutic biological products or vaccines refer to those have not been marketed in the PRC or abroad. Category II therapeutic biological products or vaccines refer to improved ones which, compared with the existing products marked in the PRC or abroad, could improve the safety, effectiveness and quality controllability, and have obvious advantages. Category III therapeutic biological products or vaccines refer to those have been marketed in the PRC or abroad.

Pursuant to the newly amended Drug Administration Law, an applicant who has obtained a drug registration certificate shall be recognized as a drug marketing authorization holder, responsible for non-clinical laboratory studies, clinical trials, production and distribution, post-market studies, and the monitoring, reporting, and handling of adverse reactions in connection with pharmaceuticals in accordance with the provisions of the Drug Administration Law. The drug marketing authorization holder may engage in manufacturing or distribution on its own or to entrust a licensed third party. At the time of application for drug marketing authorization, the applicant and the manufacturing enterprise shall have held the corresponding Pharmaceutical Manufacturing Permit.

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Accelerated Approval for Clinical Trial and Registration

The CFDA released the Circular Concerning Several Policies on Drug Registration Review and Approval (《關於藥品註冊審評審批若干政策的公告》) in November 2015, which clarified the measures and policies regarding simplifying and accelerating the approval process of clinical trials, including but not limited to a one-time umbrella approval procedure allowing the overall approval of all phases of a drug’s clinical trials, replacing the phase-by-phase application and approval procedure, will be adopted for drugs’ clinical trial applications.

The Innovation Opinions established a framework for reforming the evaluation and approval system for drugs, medical devices and equipment. The Innovation Opinions indicated enhancing the standard of approval for drug marketing registration and accelerating the evaluation and approval process for innovative drugs as well as improving the approval of drug clinical trials.

The CFDA promulgated the Opinions on Encouraging the Priority Review and Approval for Drug Innovations (《關於鼓勵藥品創新實行優先審評審批的意見》) in December 2017, which further clarified that a fast track clinical trial approval or drug marketing registration pathway will be available to innovative drugs. The Opinions on Implementing Priority Review and Approval to Encourage Drug Innovation was replaced by the Announcement of NMPA on Promulgating Three Documents including the Working Procedures for Evaluation of Breakthrough Therapy Designation Drugs (Trial) (《國家藥監局關於發佈〈突破性治療藥物審評工作程序(試行)〉等三個文件的公告》), which was issued and implemented on July 7, 2020, refined the requirements and scope of the fast track, and the Opinions on Implementing Priority Review and Approval to Encourage Drug Innovation was repealed simultaneously.

According to the Announcement on Matters Concerning the Optimization of Drug Registration Review and Approval (《關於優化藥品註冊審評審批有關事宜的公告》) jointly issued by the NMPA and the NHC in May 2018, the CDE will prioritize the allocation of resources for review, inspection, examination and approval of registration applications that have been included in the scope of fast track clinical trial approval.

The Drug Registration Regulation has incorporated the previous reform in respect of the accelerated approval for clinical trial and drug marketing registration and introduces four procedures for expedited marketing registration of drugs, which are procedures for groundbreaking therapeutic drugs, procedures for conditional approval, procedures for prioritized reviews and approval, and procedures for special examination and approval:

- Procedures for ground-breaking therapeutic drugs: during the drug clinical trials, for an innovative drug or improved new drug used for prevention and treatment of life-threatening illnesses or illnesses which have a serious impact on quality of life and for which there is no other effective prevention and treatment method or there is adequate evidence to prove that the said innovative drug or improved new drug has obvious clinical advantages over existing treatment approach, the applicant may request for application of procedures for ground-breaking therapeutic drugs.

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- Procedures for conditional approval: during the drug clinical trials, for drugs which fall under the following circumstances, an application for conditional approval of marketing registration may be submitted (i) for drugs for treatment of life-threatening illnesses for which there is no effective treatment approach, the clinical trial of drugs already has data to prove efficacy and is able to forecast the clinical value; (ii) for drugs urgently needed for public health, the clinical trial of drugs already has data to prove efficacy and is able to forecast the clinical value; and (iii) for other vaccines urgently needed for major public health emergencies or deemed by the NHC to be urgently needed, its benefits outweigh the risks according to the evaluation.
- Procedures for prioritized reviews and approval: at the time of the drug marketing registration, drugs have obvious clinical value may apply for application of procedures for prioritized review and approval, including (i) clinically and urgently needed but insufficient drug, innovative drugs and improved new drugs for prevention and treatment of major contagious diseases and rare diseases; (ii) new pharmaceutical product types, dosage form and specifications of pediatric drugs which comply with pediatric physiological characteristics; (iii) vaccines and innovative vaccines urgently needed for prevention and control of diseases; (iv) drug included in the procedures for ground-breaking therapeutic drug; (v) drug which comply with conditional approval criteria; and (vi) other circumstances of prioritized review stipulated by the NMPA.
- Procedures for special examination and approval: at the time of a threat or occurrence of public health emergency, the NMPA may, in accordance with law, decide to implement special examination and approval for urgently needed drug required for the prevention and treatment during the public health emergency. Drug included in the special examination and approval procedures may, based on special needs of disease prevention and control, be restricted for use within a certain period and scope.

Communication with the CDE

According to the Circular on Adjusting Evaluation and Approval Procedures for Clinical Trials for Drugs (《關於調整藥物臨床試驗審評審批程序的公告》) promulgated by the NMPA in July 2018, where the application for clinical trial of new investigational drug has been approved, upon the completion of Phases I and II clinical trials and prior to Phase III clinical trial, the applicant shall submit the application for Communication Session to CDE to discuss with CDE the key technical questions including the design of Phase III clinical trial protocol. Within 60 business days after the acceptance of and the fees paid for the clinical trial applications, the applicant may conduct the clinical trials for the drug in accordance with the clinical trial protocol submitted, if the applicant has not received any negative or questioning opinion from the CDE.

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According to the Registration Measures, applicants could communicate with the CDE the key issues before applying for drug clinical trials, through the clinical trials, before applying for marketing authorization, or during other key stages. According to the Administrative Measures for Communication on the Research, Development and Technical Evaluation of Drugs (《藥物研發與技術審評溝通交流管理辦法》), promulgated by the CDE on December 10, 2020, during the research and development periods and in the registration applications of drugs, the applicants may propose to conduct the communication session with the CDE. The communication session can be classified into three types. Type 1 meetings are convened to address key safety issues in clinical trials of drugs and key technical issues in the research and development of breakthrough therapeutic drugs. Type 2 meetings are held during the key research and development periods of drugs, mainly including meetings before the IND application, meetings upon the completion of Phase II trials and before the commencement of Phase III trials, meetings before submitting a marketing application for a new drug, and meetings for risk evaluation and control. Type 3 meetings refer to meetings not classified as Type 1 or Type 2.

Drug Manufacturing

According to the Drug Administration Law and the Regulations for Implementation of the Drug Administration Law of the PRC, a drug manufacturing enterprise is required to obtain a drug manufacturing license from the relevant provincial drug administration authority of the PRC. The grant of such license is subject to an inspection of the manufacturing facilities, and an inspection to determine whether the sanitary condition, quality assurance systems, management structure and equipment meet the required standards. According to the Regulations of Implementation of the Drug Administration Law and the Measures on the Supervision and Administration of the Manufacture of Drugs (《藥品生產監督管理辦法》) (the “**GMP Rules**”), promulgated in August 2004 and amended in November 2017 and January 2020, respectively, the drug manufacturing license is valid for five years and shall be renewed at least six months prior to its expiration date upon a re-examination by the relevant authority. In addition, the name, legal representative, registered address and unified social credit code specified in the drug manufacturing certificate shall be identical to that set forth in the business license as approved and issued by the industrial and commercial administrative department. According to such measures, to the extent the MAH does not manufacture the drug but through contract manufacturing organization, the MAH shall apply for drug manufacturing license with the provincial counterpart of the NMPA, subject itself to inspections and other regulatory oversight by the agency.

The Good Manufacturing Practice for Drugs (《藥品生產質量管理規範》) was promulgated in March 1988 and was amended in December 1992, June 1999 and January 2011. The Good Manufacturing Practice for Drugs comprises a set of detailed standard guidelines governing the manufacture of drugs, which includes institution and staff qualifications, production premises and facilities, equipment, hygiene conditions, production management, quality controls, product operation, raw material management, maintenance of sales records and management of customer complaints and adverse event reports.

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Laws and Regulations Related to Vaccines

Vaccine Policies

The Laws on Prevention and Treatment of Infectious Diseases (《中華人民共和國傳染病防治法》), issued in February 1989 and amended in August 2004 and June 2013, stipulates that a planned prophylactic vaccination system is performed in the PRC. The health administration department under the State Council and such departments under the people’s governments of provinces, autonomous regions, and municipalities directly under the central government shall, in accordance with the requirements of prevention and control of infectious diseases, draw up plans for prophylactic vaccination against infectious diseases and coordinate efforts for their implementation. Vaccines used for prophylactic vaccination shall conform to the quality standards of the PRC.

According to the Vaccine Administration Law of the PRC (《中華人民共和國疫苗管理法》) (the “**Vaccine Administration Law**”), which was promulgated by the SCNPC on June 29, 2019 and came into effect on December 1, 2019, the State applies the most stringent management system for vaccines, and adheres to the principles of safety first, risk management, whole-process control, scientific supervision and social co-governance. Also, a National Immunization Program system is applied in the PRC, under which the government would provide vaccines under the immunization program to the residents free of charge.

According to Biosecurity Law of the PRC (《中華人民共和國生物安全法》) (the “**Biosecurity Law**”), which was promulgated by the SCNPC on October 17, 2020 and came into effective on April 15, 2021, organizations engaged in biotechnology research and development shall comply with the national safety administration norms for biotechnology research and development. The high- or medium-risk biotechnology research and development activities shall be carried out by corporate bodies lawfully established within the territory of China and shall be approved or filed for record in accordance with the law. The corporate bodies engaged in high- or medium-risk biotechnology research and development activities shall conduct risk assessment, formulate risk prevention and control plans and emergency plans for biosafety incidents, and reduce the risks in the implementation of the research and development activities. The clinical research of new biomedical technologies shall pass the ethical review and be conducted in the medical institutions with corresponding qualifications; the operation of human clinical research shall be conducted by the professional medical workers with corresponding qualifications.

Vaccine Administration

On January 15, 2017, the General Office of State Council issued Opinions on Further Enhancing Administration of Circulation and Vaccination of Vaccines (《關於進一步加強疫苗流通和預防接種管理工作的意見》) (the “**Vaccine Opinion**”) among others, to improve the mechanism for the management of vaccines and promote the independent R&D and quality improvement of vaccines. On June 29, 2019, the SCNPC released the Vaccine Administration Law, which requires the most stringent management system for vaccines, and at the same time,

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supports the basic research and applied research on vaccines and promotes the development and innovation of vaccines, including the development, production and reserve of vaccines for the prevention and control of serious diseases in the national strategy. Entities and individuals engaged in vaccine development, production, circulation and vaccination shall abide by the laws, regulations, rules, standards and specifications, ensure that the information during the whole process is true, accurate, complete and traceable, assume responsibilities in accordance with the law and accept social supervision.

Development and Registration of Vaccines

On October 14, 2005, the NMPA promulgated the Notice on Issuing Six Technical Guidelines including the Technical Guidelines on Preclinical Study of Preventive Vaccines (《關於印發<預防用疫苗臨床前研究技術指導原則>等6個技術指導原則的通知》), which specified the requirements on preclinical research, change of production process, quality control in clinical stages of vaccine to ensure its safety and efficacy.

According to the Vaccine Administration Law, clinical trials of vaccines shall not be conducted without obtaining the approval of the drug administrative department under the State Council. Clinical trials of vaccines shall be conducted or organized for implementation by Grade III medical institutions that meet the conditions prescribed by the drug administrative department under the State Council and the competent health department under the State Council, or by disease prevention and control institutions at or above the provincial level.

A vaccine to be marketed within the territory of China shall be approved by the drug administrative department under the State Council and obtain a drug registration certificate; when applying for registration of a vaccine, an applicant shall provide true, sufficient and reliable data, information and samples.

According to the Vaccine Administration Law, for vaccines urgently needed for disease prevention and control as well as the innovative vaccines, the NMPA shall prioritize the evaluation and approval work. With respect to a vaccine urgently needed for responding to a major public health emergency or any other vaccines urgently needed as determined by the health department under the State Council, if the benefits outweigh the risks upon assessment, the drug administrative department under the State Council may conditionally approve the vaccine registration application.

According to the Drug Registration Regulation, before the applicant submits an application for drug marketing authorization, it shall communicate with the CDE and, upon communication and confirmation, submit the application for drug marketing authorization and simultaneously submit an application for prioritized review and approval. Upon included in the procedures for prioritized review and approval, the sponsors could enjoy, among others, a shortened review period for drug marketing authorization within 130 days.

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Long Term Efficacy and Safety of Vaccines and Biological Products

On March 20, 2003, the CFDA promulgated the Notice on Issuing Nine Technical Guidelines (《關於印發<預防用以病毒為載體的活疫苗製劑的技術指導原則>等9個技術指導原則的通知》), including the Technical Guidelines on Preclinical Study of Preventive DNA Vaccines (《預防用DNA疫苗臨床前研究技術指導原則》), the Technical Guidelines on the Quality Control of Recombinant DNA Products (《人用重組DNA製品質量控制技術指導原則》), the Technical Guidelines on Gene Therapy and the Quality Control of Preparation. (《人基因治療研究和製劑質量控制技術指導原則》). On October 14, 2005, the CFDA promulgated the Notice on Issuing Six Technical Guidelines (《關於印發<預防用疫苗臨床前研究技術指導原則>等6個技術指導原則的通知》), including the Technical Guidelines on Preclinical Study of Preventive Vaccines (《預防用疫苗臨床前研究技術指導原則》), which is revised on April 12, 2010, the Technical Guidelines on the Management on the Change of Production Process of Biological Products (《生物製品生產工藝過程變更管理技術指導原則》), the Technical Guidelines on the Preclinical and Clinical Studies of Combined Vaccines (《聯合疫苗臨床前和臨床研究技術指導原則》), the Technical Guidelines on the Production and Quality Control of Polypeptide Vaccines (《多肽疫苗生產及質控技術指導原則》), the Technical Guidelines on the Quality Control and Clinical Research of Combined Vaccines (《結合疫苗質量控制和臨床研究技術指導原則》), the Guiding Principles on the Grading Standard for Adverse Reactions in Clinical Trials of Preventive Vaccines (《預防用疫苗臨床試驗不良反應分級標準指導原則》), which is revised on December 26, 2019. These Guidelines specify the requirements on preclinical research, change of production process, quality control in clinical stages of vaccine to ensure its safety and efficacy.

On August 14, 2020, the CDE promulgated the Notice on Issuing Five Technical Guidelines for the Research and Development of COVID-19 Prophylactic Vaccines (for Trial Implementation) (《關於發布<新型冠狀病毒預防用疫苗研發技術指導原則(試行)>等5個指導原則的通知》), including the Technical Guidelines on research of COVID-19 Prophylactic Vaccines (for Trial Implementation) (《新型冠狀病毒預防用疫苗研發技術指導原則(試行)》), the Technical Guidelines on Pharmaceutical Research of COVID-19 Prophylactic mRNA Vaccines (for Trial Implementation) (《新型冠狀病毒預防用mRNA疫苗藥學研究技術指導原則(試行)》), the Technical Note for Non-clinical Validation Studies and Assessment of COVID-19 Prophylactic Vaccines (for Trial Implementation) (《新型冠狀病毒預防用疫苗非臨床有效性研究與評價技術要點(試行)》), the Technical Guidelines on Clinical Research of COVID-19 Prophylactic Vaccines (for Trial Implementation) (《新型冠狀病毒預防用疫苗臨床研究技術指導原則(試行)》), the Technical Guidelines on Clinical Assessment of COVID-19 Prophylactic Vaccines (for Trial Implementation) (《新型冠狀病毒預防用疫苗臨床評價指導原則(試行)》). These guidelines provide guidance, and referable technical standards for the clinical research and development of China’s COVID-19 vaccines.

REGULATORY OVERVIEW

Laws and Regulations Related to Oversea Listing

Foreign Investment

Since January 1, 2020, the Foreign Investment Law of the People’s Republic of China (《中華人民共和國外商投資法》) (the “**Foreign Investment Law**”) promulgated by the National People’s Congress has come into effect. The Law of the People’s Republic of China on Sino-Foreign Equity Joint Ventures and the Law of the People’s Republic of China on Wholly Foreign-Owned and Law of the People’s Republic of China on Sino-Foreign Cooperative Joint Ventures were abolished at the same time. Since then, the Foreign Investment Law has become the basic law regulating foreign-invested enterprises wholly or partially invested by foreign investors. While the organization form, institutional framework and standard of conduct of foreign-invested enterprises shall be subject to the provisions of the Company Law of the PRC and other laws. The PRC government will implement the management system of pre-entry national treatment and the Negative List for foreign investment abolished the original approval and filing administration system for the establishment and change of foreign-invested enterprises. Pre-entry national treatment refers to the treatment accorded to foreign investors and their investments at the stage of investment entry which is no less favorable than the treatment accorded to domestic investors and their investments. Negative List refers to a special administrative measure for the entry of foreign investment in specific sectors as imposed by the PRC. The PRC accords national treatment to foreign investment outside of the Negative List. The current Negative List is the Special Management Measures (the “**Negative List**”) for the Access of Foreign Investment (2021 Revision) (《外商投資准入特別管理措施(負面清單)(2021年版)》) issued by the NDRC and MOFCOM on December 27, 2021, and came into effect on January 1, 2022 which lists the special management measures for foreign investment access for industries regulated by the Negative List, such as equity requirements and senior management requirements.

While strengthening investment promotion and protection, the Foreign Investment Law further regulates foreign investment management and proposes the establishment of a foreign investment information reporting system that replaces the original foreign investment enterprise approval and filing system of the Ministry of Commerce. The foreign investment information reporting is subject to the Foreign Investment Information Reporting Method (《外商投資信息報告辦法》) jointly developed by the MOFCOM and the SAMR, which came into effect on January 1, 2020. According to the Foreign Investment Information Reporting Method, foreign investors who directly or indirectly carry out investment activities in China shall submit investment information to the competent commercial department through the enterprise registration system and the National Enterprise Credit Information Publicity System and the reporting methods include initial reports, change reports, cancelation reports, and annual reports.

Overseas Securities Offering and Listing by Domestic Enterprises

On December 24, 2021, the CSRC promulgated the Provisions of the State Council on the Administration of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments) (《國務院關於境內企業境外發行證券和上市的管理規定(草案徵求意見稿)》), and the Administrative Measures for the Filing of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments) (《境內企業境外發行證券和上市備案管理辦法(徵求意見稿)》) (the “**Draft Listing Measures**”, together with the Draft Listing Administrative Provisions, the “**New Draft Overseas Listing Rules**”), both of which had a comment period that expired on January 23, 2022.

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On February 17, 2023, after a year-long market consultation of the New Draft Overseas Listing Rules, the CSRC released the Trial Administrative Measures for Overseas Securities Offering and Listing by Domestic Companies (《境內企業境外發行證券和上市管理試行辦法》) (the “**Trial Measures**”), together with five interpretative guidelines thereof, which became effective on March 31, 2023 (the “**Implementation Date**”). The Trial Measures comprehensively improve and reform the existing regulatory regime for overseas offering and listing of PRC domestic companies’ securities, and regulate both direct and indirect overseas offering and listing of PRC domestic companies’ securities by adopting a filing-based regulatory regime. According to the Trial Measures, 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 within three (3) working days after submitting the listing application documents to the overseas supervisory authorities and report relevant information.

On the same date, the CSRC also released the Notice on the Arrangements for the Filing Management of Overseas Listing of Domestic Companies (《關於境內企業境外發行上市備案管理安排的通知》), which stipulated that prior to the Implementation Date, the CSRC would carry on its works on a normal basis pursuant to relevant regulations for the accepted applications for administrative approval for the overseas securities listing, under which circumstance if such companies could not obtain administrative approval prior to the Implementation Date, these companies shall complete the filing procedures with the CSRC.

H-share Full Circulation

“Full circulation” means listing and circulating on the stock exchange of the domestic unlisted shares of an H-share listed company, including unlisted domestic shares held by domestic shareholders prior to overseas listing, unlisted domestic shares additionally issued after overseas listing, and unlisted shares held by foreign shareholders. On November 14, 2019, the CSRC issued the Guidelines for the “Full Circulation” Program for Domestic Unlisted Shares of H-share Listed Companies (《H股公司境內未上市股份申請“全流通”業務指引》) (the “**Guidelines for the Full Circulation**”).

According to the Guidelines for the Full Circulation, shareholders of domestic unlisted shares may determine by themselves through consultation the amount and proportion of shares, for which an application will be filed for circulation, provided that the requirements laid down in the relevant laws and regulations and set out in the policies for state-owned asset administration, foreign investment and industry regulation are met, and the corresponding H-share listed company may be entrusted to file the said application for full circulation. To apply for full circulation, an H-share listed company shall file the application with the CSRC according to the administrative licensing procedures necessary for the “examination and approval of public issuance and listing (including additional issuance) of shares overseas by a joint stock company”. After the application for full circulation has been approved by the CSRC, the H-share listed company shall submit a report on the relevant situation to the CSRC within 15 days after the registration with CSDC of the shares related to the application has been completed.

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On December 31, 2019, CSDC and the Shenzhen Stock Exchange (“SZSE”) jointly announced the Measures for Implementation of H-share Full Circulation Business (《H股“全流通”業務實施細則》) (the “**Measures for Implementation**”). The businesses in relation to the H-share full circulation business, such as cross-border transfer registration, maintenance of deposit and holding details, transaction entrustment and instruction transmission, settlement, management of settlement participants, services of nominal holders, etc. are subject to the Measures for Implementation.

In order to fully promote the reform of H-share full circulation and clarify the business arrangement and procedures for the relevant shares’ registration, custody, settlement and delivery, CSDC promulgated the Circular on Issuing the Guide to the Program for Full Circulation of H-shares (《H股“全流通”業務指南》) on February 7, 2020, which specifies the business preparation, account arrangement, cross-border share transfer registration and overseas centralized custody, and other relevant matters. In February 2020, China Securities Depository and Clearing (Hong Kong) Limited also promulgated the Guide of China Securities Depository and Clearing (Hong Kong) Limited to the Program for Full Circulation of H-shares to specify the relevant escrow, custody, agent service, arrangement for settlement and delivery, risk management measures and other relevant matters.

According to the Measures for Implementation and the Guide to the Program for Full Circulation of H-shares, shareholders who apply for H Share Full Circulation (“**Participating Shareholders**”) shall complete the cross-border transfer registration for conversion of relevant domestic unlisted shares into H Shares before dealing in the shares, i.e., CSDC as the nominal shareholder, deposits the relevant securities held by Participating Shareholders at China Securities Depository and Clearing (Hong Kong) Limited (“**CSDC (Hong Kong)**”), and CSDC (Hong Kong) will then deposit the securities at HKSCC in its own name, and exercise the rights to the securities issuer through HKSCC, while HKSCC Nominees as the ultimate nominal shareholder is listed on the register of shareholders of H-share listed companies.

According to the Guide to the Program for Full Circulation of H-shares, H-share listed companies shall be authorized by Participating Shareholders to designate the only domestic securities company (“**Domestic Securities Company**”) to participate in the transaction of converted H shares. The specific procedure is as follows:

Participating Shareholders submit trading orders of the converted H Shares through the Domestic Securities Company, which transmits the orders to the Hong Kong Securities Company designated by the Domestic Securities Company through Shenzhen Securities Communications Co., Ltd.; and Hong Kong Securities Company conducts corresponding securities transactions in the Hong Kong market in accordance with the aforementioned trading orders and the rules of the Hong Kong Stock Exchange.

According to the Guide to the Program for Full Circulation of H-shares, upon the completion of the transaction, settlements between each of the Hong Kong Securities Company and CSDC (Hong Kong), CSDC (Hong Kong) and CSDC, CSDC and the Domestic Securities Company, and the Domestic Securities Company and the Participating Shareholders, will all be conducted separately.

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Laws and Regulations Related to Product Liability

Pursuant to the Product Quality Law (《中華人民共和國產品質量法》) promulgated on February 22, 1993 and amended on July 8, 2000, August 27, 2009 and December 29, 2018 respectively by SCNPC, Seller shall be responsible for the repair, replacement or return of the product sold if (1) the product sold does not possess the properties for use that it should possess, and no prior and clear indication is given of such a situation; (2) the product sold does not conform to the applied product standard as carried on the product or its packaging; or (3) the product sold does not conform to the quality indicated by such means as a product description or physical sample. If a consumer incurs losses as a result of purchased product, the seller shall compensate for such losses.

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.

The Law of the PRC on the Protection of the Rights and Interests of Consumers (《中華人民共和國消費者權益保護法》) was promulgated on October 31, 1993 and was amended on August 27, 2009 and October 25, 2013 to protect consumers' rights when they purchase or use goods and accept services. All business operators must comply with this law when they manufacture or sell goods and/or provide services to customers. Under the amendments made on October 25, 2013, all business operators must pay high attention to protecting customers' personal information and must strictly keep confidential any consumer information they obtain during their business operations.

Laws and Regulations Related to Environmental Protection and Fire Prevention

Environment Protection

The Environmental Protection Law of the PRC (《中華人民共和國環境保護法》), which was promulgated by the SCNPC on December 26, 1989, came into effect on the same day and last amended on April 24, 2014, outlines the authorities and duties of various environmental protection regulatory agencies. The Ministry of Environmental Protection is authorized to issue national standards for environmental quality and emissions, and to monitor the environmental protection scheme of the PRC. Meanwhile, local environment protection authorities may formulate local standards which are more rigorous than the national standards, in which case, the concerned enterprises must comply with both the national standards and the local standards.

REGULATORY OVERVIEW

Environmental Impact Appraisal

According to the Administration Rules on Environmental Protection of Construction Projects (《建設項目環境保護管理條例》), which was promulgated by the State Council on November 29, 1998, amended on July 16, 2017 and became effective on October 1, 2017, depending on the impact of the construction project on the environment, a construction employer shall submit an environmental impact report or an environmental impact statement, or file a registration form. As to a construction project, for which an environmental impact report or the environmental impact statement is required, the construction employer shall, before the commencement of construction, submit the environmental impact report or the environmental impact statement to the relevant authority at the environmental protection administrative department for approval. If the environmental impact assessment documents of the construction project have not been examined or approved upon examination by the approval authority in accordance with the law, the construction employer shall not commence the construction.

According to the Environmental Impact Appraisal Law of PRC (《中華人民共和國環境影響評價法》), which was promulgated by the SCNPC on October 28, 2002, amended on July 2, 2016 and December 29, 2018, for any construction projects that have an impact on the environment, an entity is required to produce either a report, or a statement, or a registration form of such environmental impacts depending on the seriousness of effect that may be exerted on the environment.

Pollutant Discharge Licensing

Pursuant to the Administrative Measures for Pollutant Discharge Licensing (for Trial Implementation) (《排污許可管理辦法(試行)》) promulgated on January 10, 2018 and partially revised on August 22, 2019 by the Ministry of Ecology and Environment, or the MEE, enterprises and public institutions as well as other producers and operators included in the Catalog of Classified Administration of Pollutant Discharge License for Stationary Pollution Sources shall apply for and obtain a pollutant discharge license within a prescribed time limit. Any enterprise that fails to obtain a pollutant discharge license as required shall not discharge pollutants.

According to the Catalog of Classified Administration of Pollutant Discharge License for Stationary Pollution Sources (2019 Version) (《固定污染源排污許可分類管理名錄(2019年版)》) issued by the MEE on December 20, 2019, key management, simplified management and registration management of pollutant discharge permits are implemented according to factors such as the amount of pollutants generated, the amount of emissions, the degree of impact on the environment, etc., and only pollutant discharge entities that implement registration management do not need to apply for a pollutant discharge permit.

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The State Council issued the Regulation on Pollutant Discharge Permit Administration (《排污許管理條例》) on January 24, 2021 to further enhance the pollutant discharge administration. The administration on pollutant discharge units are divided into key management and simplified management pursuant to the amount of pollutant caused and discharged and the impact on the environment. The review, decision and information disclosure of pollutant discharge licenses shall be handled through the national pollutant discharge license management information platform. The pollutant discharge license is valid for 5 years and the discharging units should apply for renewal 60 days before the expiry for continues pollutant discharge.

Acceptance Inspection on Environmental Protection Facilities

Interim Measures for Acceptance inspection of Environmental Protection upon Completion of Construction Projects (《建設項目竣工環境保護驗收暫行辦法》) also requires that upon completion of construction for which an environment impact report or environment impact statement is formulated, the constructor shall conduct acceptance inspection of the environmental protection facilities pursuant to the standards and procedures stipulated by the environmental protection administrative authorities of the State Council, formulate the acceptance inspection report, and announce the acceptance inspection report pursuant to the law except for circumstances where there is a need to keep confidentiality pursuant to the provisions of the State. Where the environmental protection facilities have not undergone acceptance inspection or do not pass acceptance inspection, the construction project shall not be put into production or use.

Fire Prevention Design and Acceptance

The Fire Prevention Law of the PRC (《中華人民共和國消防法》) (the “**Fire Prevention Law**”), was issued on April 29, 1998, then became effective on September 1, 1998 and latest amended on April 29, 2021. According to the Fire Prevention Law, for special construction projects stipulated by the housing and urban-rural development authority of the State Council, the developer shall submit the fire safety design documents to the housing and urban-rural development authority for examination, while for construction projects other than those stipulated as special development projects, the developer shall, at the time of applying for the construction permit or approval for work commencement report, provide the fire safety design drawings and technical materials which satisfy the construction needs. According to Interim Regulations on Administration of Examination and Acceptance of Fire Control Design of Construction Projects (《建設工程消防設計審查驗收管理暫行規定》) issued by the Ministry of Housing and Urban-Rural Development of the PRC on April 1, 2020, an examination system for fire prevention design and acceptance only applies to special construction projects, and for other projects, a record-filing and spot check system would be applied.

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Laws and Regulations Related to Intellectual Property

Patent

The Patent Law of the People’s Republic of China (《中華人民共和國專利法》) (the “**Patent Law**”) is revised by the SCNPC on October 17, 2020 and came into effect on June 1, 2021. According to the current Patent Law, when the invention or utility model patent is granted, unless otherwise stipulated in the Patent Law, without the approval of the patent owner, no entity or person shall implement the relevant patent, that is, manufacture, use, offer to sell, sell or import the patented products for business purpose, or use the patented method and use, offer to sell, sell or import the products directly obtained with the patented method. Implementing the patent without the approval of the patent owner constitutes the infringement of patent rights. Any dispute in connection with this shall be resolved by the relevant parties through negotiation. If the relevant parties refuse to negotiate or the negotiation fails, the patent owner or the relevant stakeholders may file a lawsuit in the people’s court or turn to the patent administration authorities for handling.

Pursuant to the Rules for Implementation of the Patent Law of the People’s Republic of China (《中華人民共和國專利法實施細則》), which was amended by the State Council on 9 January 2010 and became effective on 1 February 2010, where the entity to which a patent right is granted fails to agree with the inventor or the designer on, or to specify in its legitimately enacted company rules the way and amount of reward and remuneration specified in its rules and regulations established by law, the entity shall reward to the inventor or designer within 3 months after the announcement of granting the patent. The minimum reward for one invention patent shall not be less than RMB3,000; and the minimum reward for one utility model or design patent shall not be less than RMB1,000. The entity shall, after exploiting the patent for invention-creation within the term of the patent right, pay the inventor or designer remuneration at a percentage of not less than 2% each year from the profits generated from the exploitation of the invention or utility model patent, or at a percentage of not less than 0.2% from the profits gained from the exploitation of the design, or pay the inventor or creator a lump sum of remuneration by reference to the above percentages; where the entity to which a patent right is granted authorize other entity or individual to exploit its patent, it shall reward the inventor or designer at a percentage no less than 10% from the license and royalty fee.

Trademark

According to the Trademark Law of the People’s Republic of China (《中華人民共和國商標法》) revised by the SCNPC on April 23, 2019 and taking effect on November 1, 2019 (the “**Trademark Law**”), the registered trademark has a validity period of 10 years starting from the registration date. The trademark registrant enjoys the exclusive right to use the trademark. Any dispute in connection with the activities the infringe the exclusive right to use a registered trademark set out in Article 57 of the Trademark Law shall be resolved by the relevant parties through negotiation. If the relevant parties refuse to negotiate or the negotiation fails, the trademark registrant or the relevant stakeholders may file a lawsuit in the people’s court or turn to the industrial and commercial administrative department for handling.

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Copyright

Copyright is protected by the Copyright Law of the PRC (《中華人民共和國著作權法》) promulgated by the SCNPC on September 7, 1990 and last amended on November 11, 2020 and effective from June 1, 2021 and the Implementation Regulations of the Copyright Law of PRC (《中華人民共和國著作權法實施條例》) issued by the State Council on August 2, 2002 and last amended on January 30, 2013, which provided provisions on the classification of works and the obtaining and protection of copyright and the related rights.

Domain Names

In accordance with the Measures for the Administration of Internet Domain Names (《互聯網域名管理辦法》) which was issued by the Ministry of Information Industry on August 24, 2017 and came into effect on November 1, 2017, the Ministry of Information Industry is responsible for supervision and administration of domain name services in the PRC. Communication administrative bureaus at provincial levels shall conduct supervision and administration of the domain name services within their respective administrative jurisdictions. Domain name registration services shall, in principle, be subject to the principle of “first apply, first register”. A domain name registrar shall, in the process of providing domain name registration services, ask the applicant for which the registration is made to provide authentic, accurate and complete identity information on the holder of the domain name and other domain name registration related information.

Trade Secrets

According to the Anti-Unfair Competition Law of the PRC (《中華人民共和國反不正當競爭法》) promulgated by the SCNPC on September 2, 1993 and amended on November 4, 2017 and April 23, 2019 respectively and the Provisions of the Supreme People’s Court on Several Issues Concerning the Application of Law in the Trial of Civil Cases Involving Trade Secret Infringement (《最高人民法院關於審理侵犯商業秘密民事案件適用法律若干問題的規定》) issued by the Supreme People’s Court on September 10, 2020 and effective from September 12, 2020, the term “trade secrets” refers to technical, operational and other business information that is unknown to the public, has business value, may create business interests or profits for its legal owners or holders, and is maintained as a secret with relevant security measures taken by its right holders. According to the Anti-Unfair Competition Law of the PRC, business operators are prohibited from infringing others’ trade secrets by (i) acquiring a trade secret from the right holder by theft, bribery, fraud, coercion, electronic intrusion or any other illicit means; (ii) disclosing, using or allowing other person to use a trade secret acquired from the right holder by any means as specified in the preceding subparagraph; (iii) disclosing, using or allowing other person to use a trade secret in its possession in violation of its confidentiality obligation or the requirements of the right holder for keeping the trade secret confidential; (iv) abetting, tempting or aiding a person into or in acquiring, disclosing, using or allowing other person to use the trade secret of the right holder in violation of its confidentiality obligation or the requirements of the right holder for keeping the trade secret confidential. If a third party knows or should have known the abovementioned illegal conducts but nevertheless acquires,

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uses or allows other persons to use such trade secrets, the third party shall be deemed to have infringed others’ trade secrets. The right holders whose trade secrets are infringed may apply for administrative corrections, and the regulatory authorities shall order to stop any illegal activities and impose fine penalties on the infringers.

Information Security and Data Privacy

Pursuant to the PRC Civil Code (《中華人民共和國民法典》), the personal information of a natural person shall be protected by the law. An information processor shall not disclose or tamper with any personal information collected or stored thereby; and without the consent of the natural person, no personal information shall be illegally provided to any other person, excluding the information through which the specific individual cannot be identified after processing and which cannot be restored. An information processor shall take technical measures and other necessary measures to ensure the security of the personal information collected and stored thereby and prevent information leakage, tampering, and loss.

On May 8, 2017, the Supreme People’s Court and the Supreme People’s Procuratorate jointly released the Interpretations of the Supreme People’s Court and the Supreme People’s Procuratorate on Several Issues Concerning the Application of Law in the Handling of Criminal Cases Involving Infringement of Citizens’ Personal Information (《最高人民法院、最高人民檢察院關於辦理侵犯公民個人信息刑事案件適用法律若干問題的解釋》) (the “**Interpretations**”), which came into effect on June 1, 2017, clarifies several concepts regarding the crime of “infringement of citizens’ personal information” stipulated by Article 253A of the Criminal Law of the PRC (《中華人民共和國刑法》), including the “provision of citizens’ personal information” and “illegally obtaining any citizen’s personal information by other methods”. In addition, the Interpretations specify the standards for determining “serious circumstances” and “particularly serious circumstances” of this crime.

The Data Security Law of the PRC (《中華人民共和國數據安全法》), which was promulgated by the SCNPC on June 10, 2021 and took effect on September 1, 2021, provides that China shall establish a data classification and grading protection system, formulate the important data catalogs to enhance the protection of important data. Processors of important data shall specify the person responsible for data security and management agencies to implement data security protection responsibilities. Relevant authorities will establish the measures for the cross-border transfer of important data. If any company violates the Data Security Law of the PRC to provide important data outside China, such company may be punished by administration sanctions, including penalties, fines, and/or suspension of relevant business or revocation of the business license.

The Opinions on Strictly Cracking Down on Illegal Securities Activities in Accordance with the Law (《關於依法從嚴打擊證券違法活動的意見》), which were issued by the General Office of the State Council and another authority on July 6, 2021, require to speed up the revision of legislation on strengthening the confidentiality and archives coordination between regulators related to overseas issuance and listing of securities, and improvement to the legislation on data security, cross-border data flow, and management of confidential information.

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The Personal Information Protection Law of the PRC (《中華人民共和國個人信息保護法》) (the “**Personal Information Protection Law**”) was promulgated by the SCNPC on August 20, 2021 and came into effect on November 1, 2021. The Personal Information Protection Law reiterates the circumstances under which a personal information processor could process personal information and the requirements for such circumstances, such as when (1) the individual’s consent has been obtained; (2) the processing is necessary for the conclusion or performance of a contract to which the individual is a party; (3) the processing is necessary to fulfill statutory duties and statutory obligations; (4) the processing is necessary to respond to public health emergencies or protect natural persons’ life, health and property safety under emergency circumstances; (5) the personal information that has been made public is processed within a reasonable scope in accordance with this Law; (6) personal information is processed within a reasonable scope to conduct news reporting, public opinion-based supervision, and other activities in the public interest; or (7) under any other circumstance as provided by any law or regulation. It also stipulates the obligations of a personal information processor. Any violation of the provisions and requirements under the Personal Information Protection Law may subject a personal information processor to rectifications, warnings, fines, suspension of the related business, revocation of licenses, being entered into the relevant credit record or even criminal liabilities.

Laws and Regulations Related to Employment and Social Securities

Employment

According to the Labor Law of the People’s Republic of China (《中華人民共和國勞動法》) taking effect on January 1, 1995 and revised on December 29, 2018 and the Labor Contract Law of the People’s Republic of China (《中華人民共和國勞動合同法》) taking effect on January 1, 2008 and revised on December 28, 2012, a labor contract shall be signed when the employer establishes labor relationship with the worker. The labor contracts shall be signed in written. When agreement is reached after negotiation, labor contracts, including fixed term labor contract, open term labor contract or labor contract based on the completion of work, shall be signed, and the salary shall be no less than the local minimum wage standard. The employer and the worker shall each fully perform its/his obligations in accordance with the labor contract.

Social Securities

According to the Social Insurance Law of PRC (《中華人民共和國社會保險法》), which issued by the SCNPC on October 28, 2010 and came into effect on July 1, 2011 and was newly revised on December 29, 2018, enterprises and institutions in the PRC shall provide their employees with welfare schemes covering basic pension insurance, unemployment insurance, maternity insurance, work-related injury insurance and basic medical insurance. The employer shall apply to the local social insurance agency for social insurance registration within 30 days from the date of its formation. And it shall, within 30 days from the date of employment, apply to the social insurance agency for social insurance registration for the employee. Any employer who violates the regulations above shall be ordered to make correction within a prescribed time

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limit; if the employer fails to rectify within the time limit, the employer and its directly liable person will be fined. If the employer fails to pay social insurance contributions on time and in full, the social insurance agency shall place an order with the employer demanding full payment within a prescribed period, and an overdue payment fine at the rate of 0.5‰ shall be levied as of the date of indebtedness. When the payment is not made at the expiry of the prescribed period, a fine above the overdue amount but less than its triple shall be demanded by the authoritative administrative department.

Meanwhile, the Interim Regulation on the Collection and Payment of Social Insurance Premiums (《社會保險費徵繳暫行條例》) (issued by the State Council on January 22, 1999 and came into effect on the same day and was recently revised on March 24, 2019) prescribes the details concerning the social securities.

Housing Provident Fund

According to Regulations on Management of Housing Provident Fund (《住房公積金管理條例》) issued by the State Council on April 3, 1999 and revised and implemented on March 24, 2019, the enterprises shall fully pay the housing provident fund contribution for the employees on time, with the contribution ratio no less than 5% of the average monthly salary of the relevant employee in the previous year. The housing provident fund contribution paid by the employees and the employers shall be owned by the employees.

Laws and Regulations Related to Tax

Enterprise Income Tax

According to the Corporate Income Tax Law of the People's Republic of China (《中華人民共和國企業所得稅法》), which was promulgated 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 Implementation Regulations for the Corporate Income Tax Law of the People's Republic of China (《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 amended by the State Council on April 23, 2019 and came into effect on the same date, all the domestic enterprises in China (including foreign-invested enterprises) shall be subject to enterprise income tax at the uniform tax rate of 25%, except for the high-tech enterprises certificated by the state, which will be subject to enterprise income tax at the reduced rate of 15%, or the qualified small low-profit enterprises, which will enjoy the reduced enterprise income tax rate of 20%.

Value-added Tax

The Provisional Regulations on Value-added Tax of the People's Republic of China (《中華人民共和國增值稅暫行條例》), which was promulgated on December 13, 1993, came into effect on January 1, 1994, and last amended on November 19, 2017, and the Detailed Implementing Rules of the Provisional Regulations on Value-added Tax of the People's Republic of China (《中華人民共和國增值稅暫行條例實施細則》), which was promulgated

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on December 25, 1993 and came into effective on the same date, and was amended on December 15, 2008 and October 28, 2011, came into effect on November 1, 2011 set out that all taxpayers selling goods or providing processing, repairing or replacement services, sales of services, intangible assets and immovable assets and importing goods in China shall pay a value-added tax. A tax rate of 17% shall be levied on general taxpayers selling goods and services, leasing of tangible movable assets or importing goods whereas the applicable rate for the export of goods by taxpayers shall be nil, unless otherwise stipulated. According to the Notice of the Ministry of Finance and the SAT on Adjusting Value added Tax Rates (《財政部、國家稅務總局關於調整增值稅稅率的通知》) issued on April 4, 2018 and became effective on May 1, 2018, the deduction rates of 17% and 11% applicable to the taxpayers who have VAT taxable sales activities or imported goods are adjusted to 16% and 10%, respectively. According to the Notice of the Ministry of Finance, the SAT and the General Administration of Customs on Relevant Policies for Deepening Value Added Tax Reform (《關於深化增值稅改革有關政策的公告》) issued on March 20, 2019 and became effective on April 1, 2019, the VAT rate was reduced to 13% and 9%, respectively.

Laws and Regulations Related to Foreign Exchange

The Regulations on Foreign Exchange Control of the PRC (《中華人民共和國外匯管理條例》) issued by the State Council on January 29, 1996 and implemented on April 1, 1996, which was revised on January 14, 1997 and August 5, 2008 respectively, is the key foreign exchange control regulation in force, applicable to the foreign exchange income and payment and foreign exchange operation activities of the domestic institutions and domestic individuals in China and the foreign exchange payment and collection and foreign exchange operation activities of the overseas institutions and overseas individuals in China.

The Regulations on Foreign Exchange Settlement, Sale and Payment (《結匯、售匯及付匯管理規定》) issued by PBOC on June 20, 1996 and implemented on July 1, 1996 set out requirements on the foreign exchange settlement, purchase, payment, opening of foreign exchange account and external payment by the domestic institutions, individual citizens, foreign institutions in China and foreigners in China.

According to the Decision of the State Council on Canceling and Adjusting A Batch of Items Requiring Administrative Approval (《國務院關於取消和調整一批行政審批項目等事項的決定》) issued by the State Council on October 23, 2014, SAFE and its branches canceled the review and approval on the foreign exchange settlement for the repatriation of funds raised abroad under the overseas listed foreign capital stock account.

In addition, according to the Notice of SAFE on Relevant Issue Concerning the Administration of Foreign Exchange for Overseas Listing (《國家外匯管理局關於境外上市外匯管理有關問題的通知》) issued by the SAFE on December 26, 2014, the domestic companies shall register the overseas listing with the foreign exchange control bureau located at its registered address in 15 working days after the completion of the overseas listing and issuance. The funds raised by the domestic companies through overseas listing may be repatriated to China or deposited overseas, provided that the intended use of the fund shall be consistent with the contents of the document and other public disclosure documents.

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According to the Notice of SAFE on Reforming and Standardizing Capital Account Foreign Exchange Settlement Administration Policies (《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》) issued by SAFE on June 9, 2016, it has been specified clearly in the relevant policies that, for the capital account foreign exchange income subject to voluntary foreign exchange settlement (including the repatriation of the proceeds from overseas listing), the domestic institutions may conduct the foreign exchange settlement at the banks according to their operation needs. The proportion of the capital account foreign exchange income subject to voluntary foreign exchange settlement was tentatively set as 100%, provided that SAFE may adjust the aforesaid proportion according to the international payment balance status in good time.

LAWS AND REGULATIONS IN THE UNITED STATES

This section summarizes the principal laws and regulations in the United States that are relevant to our business.

U.S. Government Regulation of Drug and Biological Products

In the United States, the FDA regulates drugs under the Federal Food Drug and Cosmetic Act (the “FDCA”), its implementing regulations, and biologics implemented under the FDCA and the Public Health Service Act (the “PHSA”) and their implementing regulations. Both drugs and biologics also are subject to other federal, state and local statutes and regulations, such as those related to competition. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or following approval may subject an applicant to administrative actions or judicial sanctions. These actions and sanctions could include, among other actions, the FDA’s refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, untitled or warning letters, voluntary or mandatory product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal fines or penalties.

Once a product candidate is identified for development, it enters pre-clinical testing, which includes laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as animal studies. Pre-clinical testing is conducted in accordance with FDA’s Good Laboratory Practice regulations. A sponsor of an IND must submit the results of the pre-clinical tests, manufacturing information, analytical data, the clinical trial protocol, and any available clinical data or literature to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions and places the trial on a clinical hold within that 30-day period. FDA may also impose clinical holds or partial clinical holds at any time during clinical trials due to safety concerns or non-compliance.

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All clinical trials, which involve the administration of the investigational product to humans, must be conducted under the supervision of one or more qualified investigators in accordance with Good Clinical Practice regulations, including the requirement that all research subjects provide informed consent in writing before their participation in any clinical trial. Further, an Institutional Review Board (the “IRB”), must review and approve the plan for any clinical trial before it commences at any institution, and the IRB must conduct continuing review and re-approve the study at least annually. Each new clinical protocol and any amendments to the protocol must be submitted for FDA review, and to the IRBs for approval. An IRB can suspend or terminate approval of a clinical trial at its institution if the trial is not being conducted in accordance with the IRB’s requirements or if the product has been associated with unexpected serious harm to subjects.

Clinical trials generally are conducted in three sequential phases, known as Phase I, Phase II and Phase III, and may overlap.

- Phase I clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the product candidate.
- Phase II clinical trials involve studies in disease-affected patients to evaluate proof of concept and/or determine the dose required to produce the desired benefits. At the same time, safety and further PK and PD information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.
- Phase III clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product labeling.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA. Safety reports must be submitted to the FDA and the investigators 15 calendar days after the trial sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor’s initial receipt of the information. Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov.

Concurrent with clinical trials, companies usually complete additional animal studies and must also finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The process of obtaining regulatory approvals and compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements may subject an applicant to administrative or judicial sanctions.

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U.S. Review and Approval Processes

The results of product development, pre-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the product, proposed labeling and other relevant information, are submitted to the FDA as part of a BLA. Unless deferred or waived, BLAs, or supplements must contain data adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The submission of a BLA is subject to the payment of a substantial user fee and an annual prescription drug product program fee.

Within 60 days of its receipt, the FDA reviews the BLA to ensure that it is sufficiently complete for substantive review before it accepts the BLA for filing. After accepting the BLA filing, the FDA begins an in-depth substantive review to determine, among other things, whether a product is safe and effective for its intended use. The FDA also evaluates whether the product's manufacturing is cGMP-compliant to assure the product's identity, strength, quality and purity. Before approving the BLA, the FDA typically will inspect whether the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA may refer the BLA to an advisory committee, a panel of experts, for review whether the application should be approved and under what conditions and considers such recommendations when making decisions.

The FDA may refuse to approve the BLA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. The FDA will issue a complete response letter describing all of the specific deficiencies that the FDA identified in the BLA that must be satisfactorily addressed before it can be approved. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. The applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, withdraw the application or request an opportunity for a hearing.

The regulatory approval may be limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product-labeling. In addition, the FDA may require post-approval studies, including phase IV clinical trials, to further assess a product's safety and effectiveness after BLA approval and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

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Expedited Development and Review Programs

The FDA has various programs that are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

Fast Track Designation

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a drug is intended to treat a serious or life-threatening disease or condition for which there is no effective treatment and demonstrates the potential to address medical needs for the disease or condition. Under the fast track program, the sponsor of a drug candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the drug candidate. The FDA must make a fast track designation determination within 60 days after receipt of the sponsor’s request.

In addition to other benefits, such as the ability to use surrogate endpoints and have greater interactions with the FDA, the FDA may initiate review of sections of a fast track product’s NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA’s time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

As of the Latest Practicable Date, none of our drug candidates had obtained the fast track designation.

Priority Review

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under the Prescription Drug User Fee Act (the “PDUFA”) guidelines. These six- and ten- month review periods are measured from the “filing” date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

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Accelerated Approval

Under the FDA’s accelerated approval regulations, the FDA may approve a drug or biologic candidate for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments and demonstrates an effect on either 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 (the “IMM”), that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the disease or condition and the availability or lack of alternative treatments. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of post-approval clinical trial to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Breakthrough Designation

Another program available for sponsors is the breakthrough therapy designation. A drug or biologic may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A sponsor may request that a product be designated as a breakthrough therapy concurrently with, or at any time after, the submission of an IND, and the FDA must determine if the candidate qualifies for such designation within 60 days of receipt of the request. If so designated, the FDA shall act to expedite the development and review of the product’s marketing application, including by meeting with the sponsor throughout the product’s development, providing timely advice to the sponsor to ensure that the development program to gather pre-clinical and clinical data is as efficient as practicable.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs or biologic candidates intended to treat a rare disease or condition generally affecting fewer than 200,000 individuals in the U.S. The first applicant to receive FDA approval for the disease or indication for which it has orphan drug designation is entitled to a seven-year exclusive marketing period. During the exclusivity period, the FDA may not approve any other applications to market the same product for the same disease or condition except in limited circumstance.

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Post-Marketing Requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping activities, reporting of adverse experiences, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations, known as “off-label use,” and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the drug or biologic, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new BLA or BLA supplement, which may require the development of additional data or pre-clinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for a risk evaluation and mitigation strategy (the “REMS”), to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS. The FDA will not approve the BLA without an approved REMS, if required. A REMS 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. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for noncompliance with regulatory standards or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP regulations. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP.

Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP regulations, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved BLA, including recall.

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Once an approval is granted, the FDA may issue enforcement letters or withdraw the approval of the product if compliance with regulatory requirements and standards is not maintained or if problems occur after the drug or biologic reaches the market. Corrective action could delay drug or biologic distribution and require significant time and financial expenditures. Later discovery of previously unknown problems with a drug or biologic, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the drug or biologic, suspension of the approval, complete withdrawal of the drug from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of drug or biologic approvals; drug or biologic seizure or detention, or refusal to permit the import or export of drugs; or
- injunctions or the imposition of civil or criminal penalties.

Patient Protection and Affordable Health Care Act

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, the “ACA”), became law in the United States in March 2010, and has driven healthcare reform in the United States by extending health insurance coverage and substantially changing the way healthcare is financed by both governmental and private insurers in the United States. With regard to pharmaceutical products specifically, the ACA expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare prescription drug benefit. Among other things, the ACA contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, and mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on the pharmaceutical companies’ share of sales to federal health care programs.

Since its enactment, there have been judicial and congressional challenges to certain aspects of the ACA, and there may be additional challenges and amendments to the ACA in the future. Since January 2017, former President Trump has signed Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the ACA have passed, for example, the Tax Act

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enacted by the Congress in 2017 that eliminated the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate.” In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated “Cadillac” tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. There may be other efforts to challenge, repeal or replace the ACA.

Patent Term Restoration and Marketing Exclusivity

After approval, owners of relevant drug or biological product patents may apply for up to a five-year patent extension to restore a portion of patent term lost during product development and FDA review of a BLA if approval of the application is the first permitted commercial marketing or use of a biologic containing the active ingredient under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The allowable patent term extension is calculated as one-half of the product’s testing phase, which is the time between IND and BLA submission, and all of the review phase, which is the time between BLA submission and approval, up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed more than 14 years from the date of FDA approval of the product. Only one patent claiming each approved product is eligible for restoration, only those claims covering the approved product, a method for using it, or a method for manufacturing it may be extended, and the patent holder must apply for restoration within 60 days of approval. The United States Patent and Trademark Office (the “USPTO”), in consultation with the FDA, reviews and approves the application for patent term restoration. For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the USPTO must determine that approval of the drug candidate covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug candidate for which a BLA has not been submitted.