OVERVIEWS OF LAWS AND REGULATIONS IN THE PRC

The section summarizes the principal PRC laws, rules and regulations that are relevant to our business.

Drug Regulatory Regime

Primary Regulatory Authorities

Drug regulatory regime in China consists of the Standing Committee of the National People's Congress (全國人民代表大會常務委員會, the "**SCNPC**"), the State Council and several ministries and agencies under its authority including, among others, the National Medical Product Administration (國家藥品監督管理局, the "**NMPA**"), the predecessor of which is China Food and Drug Administration (國家食品藥品監督管理總局, the "**CFDA**"), the National Health Commission (國家衛生健康委員會, the "**NHC**"), the predecessor of which is the National Health and Family Planning Commission of the PRC (國家衛生和計劃生育委員會), and the National Healthcare Security Administration (國家醫療保障局).

The NMPA, which inherits the drug supervision function from its predecessors, the CFDA, is the primary drug regulatory authority. The NMPA is responsible for drug registration and supervision, including non-clinical research, clinical trial, marketing approval, production, circulation, etc. under the supervision of State Administration for Market Regulation (the "**SAMR**," the predecessors of which is State Administration of Industry and Commerce, an institution for supervising and administrating the market in China).

The NHC is the chief healthcare regulator of the PRC, which is primarily responsible for drafting national healthcare policies and regulating public health, medical services and health contingency system, coordinating the healthcare reform and supervising the operation of medical institutions and practicing of medical personnel.

The National Healthcare Security Administration (a new authority established in May, 2018 in accordance with *the Institutional Reform Program of the State Council* (國務院機構改革方案)) is responsible for drafting and implementing policies, plans and standards on medical insurance, maternity insurance and medical assistance; administering healthcare fund; formulating a uniform medical insurance catalogue and payment standards on drugs, medical disposables and healthcare services; formulating and administering the bidding and tendering policies for drugs and medical disposables.

Laws and Regulations Relating to Drugs

Drug Administration Laws and Regulations

The PRC Drug Administration Law (中華人民共和國藥品管理法) (the "***Drug Administration Law***") promulgated by the SCNPC on September 20, 1984, and amended on February 28, 2001, December 28, 2013, April 24, 2015 and August 26, 2019, and *the Implementing Measures of the PRC Drug Administration Law* (中華人民共和國藥品管理法實施條例) (the "***Drug Administration Law Implementing Measures***") issued by the State Council on August 4, 2002, and amended on February 6, 2016 and March 2, 2019 have together laid down the legal framework for the administration of drugs, including the research, development, manufacturing and business operation of new drugs, and administer the pharmaceutical manufacturing enterprises, pharmaceutical trading enterprises, and medicinal preparations of medical institutions, and the development, research, manufacturing, distribution, packaging, pricing and advertisements of drugs.

Non-Clinical Research and Animal Testing

The SAMR requires preclinical data to support registration applications for imported and domestic drugs. According to *the Administrative Measures for Drug Registration* (藥品註冊管理辦法), non-clinical drug safety studies shall comply with *the Good Laboratory Practice for Non-clinical Laboratory Studies* (藥物非臨床研究質量管理規範) (the "**GLP**"). The GLP was issued by the CFDA on August 6, 2003 and latest revised on July 27, 2017 to improve the quality of non-clinical research, and the good laboratory practice has been implemented since September 1, 2017. Pursuant to *the Circular on Administrative Measures for Certification of Good Laboratory Practice for Non-clinical Laboratory Studies* (關於印發藥物非臨床研究質量管理規範認證管理辦法的通知) issued by the CFDA on April 16, 2007, the NMPA is responsible for the certification of non-clinical research institutions nationwide, while the local provincial medical products administrative authorities is in charge of the daily supervision of non-clinical research institution. The NMPA decides whether an institution is qualified for undertaking non-clinical pharmaceutical research by evaluating such institution's organizational administration, research personnel, equipment and facilities, and the operation and administration of non-clinical pharmaceutical projects. A GLP Certificate will be issued by the NMPA if all the relevant requirements are satisfied, which will also be published on the NMPA's website. Any entity without such certification must engage a qualified third party to conduct such non-clinical activities regulated under relevant laws and regulations.

Pursuant to *the Administrative Regulations on Experimental Animals* (實驗動物管理條例) issued by the State Science and Technology Commission on November 14, 1988, and latest amended on March 1, 2017 by the State Council, *the Administrative Measures on Good Practice of Experimental Animals* (實驗動物質量管理辦法) jointly issued by the State Science and Technology Commission and the State Bureau of Quality and Technical Supervision on December 11, 1997, and *the Administrative Measures on the Certificate for Experimental Animals (Trial)* (實驗動物許可證管理辦法(試行)) issued by the Ministry of Science and Technology and other regulatory authorities on December 5, 2001, using and breeding experimental animals shall be subject to certain rules, and performing experiments on animals requires a Certificate for Use of Experimental Animals. Any entity without such certification must engage a qualified third party to conduct such non-clinical activities regulated under relevant laws and regulations.

Approval and Reform for Clinical Trials of New Drugs

Pursuant to *the Drug Administration Law*, *the Drug Administration Law Implementing Measures* and *the Administrative Measures for Drug Registration* issued by the SAMR on January 22, 2020 which became effective on July 1, 2020, new drug registration applications are subject to clinical trials. The Center for Drug Evaluation (the "**CDE**"), an institution under the NMPA, is responsible for the applications for clinical trials of new drugs.

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

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

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

On October 8, 2017, the General Office of the Central Committee of the Communist Party of China and the General Office of the State Council jointly issued *the Opinions on Deepening the Reform of the Evaluation and Approval System and Encouraging Innovation of 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), aiming to simplify the clinical trial procedures and shorten the time. For new drugs and medical devices urgently needed in clinical practice and drugs and medical devices used for the treatment of rare diseases, the evaluation and approval procedures for marketing shall be accelerated.

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

The Priority Evaluation and Approval Procedures for Marketing Approvals of Drugs (Trial) (藥品上市許可優先審評審批工作程序(試行)) issued by the NMPA on July 7, 2020, further indicated that a fast track IND or drug registration pathway will be available to the innovative drugs.

International Multi-Center Clinical Trials

Pursuant to *the International Multi-Center Clinical Trial Guidelines (Trial)* (國際多中心藥物臨床試驗指南(試行)) issued by the CFDA on January 30, 2015 and effective from March 1, 2015, applicants may simultaneously conduct clinical trials in different centers of multiple regions using the same clinical trial protocol, or conduct regional clinical trials simultaneously in multiple centers in different countries within a certain region using the same protocol. Where the data derived from the international multi-center clinical trials are to be used for application for a drug registration in the PRC, it shall satisfy the requirements for clinical trials set forth in *the Administrative Measures for Drug Registration*. Where the applicants plan to conduct the international multi-center clinical trials in the PRC, it shall comply with *the Drug Administration Law*, *the Drug Administration Law Implementing Measures* and *the Administrative Measures for Drug Registration* and other relevant laws and regulations, to carry out the PRC GCP with reference to international recognized principles such as the ICH-GCP, and to meet the requirements of the laws and regulations of the relevant countries at the same time.

The NMPA issued *the Technical Guiding Principles for the Acceptance of Overseas Clinical Trial Data of Drugs* (接受藥品境外臨床試驗數據的技術指導原則) on July 6, 2018, to guide work related to the acceptance of overseas clinical trial data as clinical evaluation reference by the applicants applying for the registration of drugs in the PRC.

Clinical Trial Registration of Drugs

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

Pursuant to *the Announcement on the Drug Clinical Trial Information Platform* (關於藥物臨床試驗信息平台的公告) issued by the NMPA on September 6, 2013, for all the clinical trials approved by the NMPA and conducted in the PRC, the applicants shall log in the registration and information publication platform for clinical trials of drugs to register, and publish the information of, the clinical trials. The applicant shall complete the pre-registration of the trials within one month after obtaining the approval for the IND, so as to obtain the unique registration number for the trial, and complete the registration of follow-up information before the enrollment of the first subject. If the applicant fails to complete the first submission and publication within one year after obtaining the approval for the IND, the applicant shall submit an explanation; if the applicant fails to complete the first submission and publication within three year after obtaining the approval for the IND, the approval for the IND will expire automatically.

Phases of Clinical Trials and Communication with the CDE

According to *the Technical Guiding Principles for Clinical Trials of Antineoplastic Drugs* (抗腫瘤藥物臨床試驗技術指導原則) issued by the CFDA on May 15, 2012, the clinical study of antineoplastic drugs usually consists of Phases I, II and III clinical trials. The primary objectives of Phase I clinical trials are the preliminary study of drug tolerance and pharmacokinetics, so as to provide data support for the design of dosage regimen in later-stage research. Phase II clinical trials are mainly exploratory studies, such as the exploration of drug administration dose, medication scheme and efficacy on tumors, as well as the observation of safety. Phase III clinical trials are intended to further confirm the clinical benefits for tumor patients on the basis of Phase II study, so as to provide sufficient evidence for obtaining the marketing approval.

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

On November 19, 2021, the CDE issued *the Clinical Value-oriented Guiding Principles on the Clinical Study for Antineoplastic Drugs* (以臨床價值為導向的抗腫瘤藥物臨床研發指導原則), which offered suggestions on the clinical study of antineoplastic drugs from the perspective of patients' demands, in order to instruct the applicants to implement the clinical value-oriented and patient-centered study concepts during the clinical study, and provided references for the promotion of the scientific and orderly development of antineoplastic drugs.

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

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

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

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

Filings for Gathering and Collecting Human Genetic Resources

To effectively protect and rationally utilize the human genetic resources in the PRC, the Ministry of Science and Technology and the Ministry of Health (the "**MOH**") jointly issued *the Interim Administrative Measures on Human Genetic Resources* (人類遺傳資源管理暫行辦法) on June 10, 1998. According to *the Service Guidance for the Administrative Licensing Items of Collection, Gathering, Trading, Export or Exit of Human Genetic Resources* (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) issued by the Ministry of Science and Technology on July 2, 2015 and effective therefrom, and *the Notice on Implementing the Administrative Licensing for Collection, Gathering, Trading, Export and Exit of Human Genetic Resources* (關於實施人類遺傳資源採集、收集、買賣、出口、出境行政許可的通知) issued by the Ministry of Science and Technology on August 24, 2015 and effective therefrom, the collection, gathering or research activities of human genetic resources participated by a foreign-invested sponsor falls within the scope of international cooperation, and the cooperating PRC organization shall apply for the approval of the China Human Genetic Resources Management Office via the online system. On October 26, 2017, the Ministry of Science and Technology issued *the Circular on Optimizing the Procedures for 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 became effective on December 1, 2017, simplifying the procedures for the examination and approval for collection and gathering of human genetic resources for marketing a drug in the PRC.

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

On October 17, 2020, the SCNPC promulgated *the Biosecurity Law of the PRC* (中華人民共和國生物安全法) (the "***Biosecurity Law***") which became effective on April 15, 2021, establishing a comprehensive legislative framework on the current regulations in the areas including epidemic control of human, animal and plant infectious diseases, security of biotechnology research, development and application, biosafety management of pathogenic microbiology laboratories, security management of human genetic resources and biological resources, countermeasures against microbial resistance and prevention of bioterrorism and threat of biological weapons. According to *the Biosecurity Law*, the high-risk and medium-risk biotechnology research and development activities shall be carried out by legal entities lawfully established in the PRC, and shall be approved or filed; the establishment of a pathogenic microbiology laboratory shall be lawfully approved or filed; (i) collecting human genetic resources of important genetic families or specific areas in the PRC, or collecting human genetic resources of which the types and quantities are subject to provisions of the competent department of science and technology under the State Council, (ii) preserving human genetic resources of the PRC, (iii) using human genetic resources of the PRC to carry out international scientific research cooperation, or (iv) transporting, mailing or exiting human genetic resource materials of the PRC, shall be approved by the competent department of science and technology.

On March 21, 2022, the Ministry of Science and Technology issued *the Implementing Rules of the Administrative Regulations on Human Genetic Resources (for Public Comments)* (人類遺傳資源管理條例實施細則(徵求意見稿)) (the "***Human Genetic Resources Implementing Rules***") for public comments, which provided specific provisions on the collection, preservation, utilization and external provision of human genetic resources of the PRC. As of the Latest Practicable Date, *the Human Genetic Resources Implementing Rules* has not been officially issued and implemented.

Regulations relating to New Drug Approval

According to *the Administrative Measures for Drug Registration*, upon completion of pharmacological and toxicological studies, clinical trials and other research supporting the marketing registration of drugs, determination of quality standards, completion of validation of commercial-scale production processes, and preparation for acceptance of verification and inspection for drug registration, the applicant may apply for the New Drug Approval (the "**NDA**"). The NMPA shall evaluate the application pursuant to applicable laws and regulations. The applicant must obtain the NDA before the drugs can be manufactured and sold in the PRC. If (i) a drug is used for the treatment of severe life-threatening diseases currently lacking effective treatment and the data of clinical trials of the drug can prove the efficacy and forecast the clinical value of the drug; (ii) a drug which is urgently needed for public health and the data of clinical trials of the drug can show the efficacy and forecast the clinical value of the drug; or (iii) a vaccine which is urgently needed to deal with major public health emergencies or deemed to be urgently needed by the NHC, and by assessment the benefit of the vaccine outweighs the risk, the applicant may apply for the conditional NDA during the clinical trials of the drug or vaccine.

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

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

competent review and approval authorities of drugs of the United States or the European Union, and are manufactured with the same production line in the PRC; and (8) clinical trial applications for drugs with urgent clinical need and patent expiry within three years, and applications for manufacturing approvals of drugs with urgent clinical need and patent expiry within one year.

In addition, on May 17, 2018, the NMPA and the NHC jointly issued *the Circular on Issues Concerning Optimizing the Review and Approval of Drug Registrations* (關於優化藥品註冊審評審批有關事宜的公告), which further simplified and accelerated the drug review and approval process.

On July 7, 2020, the NMPA issued *the Working Procedures for Priority Review and Approval of Drug Marketing Approvals (Trial)* (藥品上市許可優先審評審批工作程序(試行)), which provided that during the clinical trials of drugs, for innovative drugs or improved new drugs for the prevention or treatment of severe life-threatening or life-quality-affecting diseases currently lacking effective prevention or treatment method or having obvious clinical advantages compared to the existing treatment method shown by sufficient evidence, the applicant may apply for the application of the procedures for breakthrough therapeutics during Phase I or II clinical trials, and usually no later than the Phase III clinical trials.

Drug Manufacturing License

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

GMP

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

The MOH first issued *the Guidelines on Good Manufacturing Practices* (藥品生產質量管理規範) on March 17, 1988, which was later revised on December 28, 1992. After its establishment, the NMPA revised *the Guidelines on Good Manufacturing Practices* on June 18, 1999, which became effective from August 1, 1999. *The Guidelines on Good Manufacturing Practices* revised by the MOH on October 19, 2010, which took effect on March 1, 2011 provided the basic standards for drug production, including production facilities, qualification of management personnel, production plant and facilities, documentation, material packaging and labeling, testing, production management, sales and return of products, complaints of customers, etc.

On August 2, 2011, the CFDA issued *the Circular on Printing and Distributing the Administrative Measures for the Certification of Good Manufacturing Practice* (關於印發藥品生產質量管理規範認證管理辦法的通知), which provided that newly established drug manufacturers, or existing drug manufacturers that wish to expand manufacturing scope or build new workshops shall apply for the GMP certification in accordance with *the Drug Administration Law Implementing Measures*. Those drug manufacturers that have already obtained the GMP certificates shall re-apply for the GMP certification within six months prior to the expiration date of the GMP certificates. On December 30, 2015, the CFDA issued *the Notice on Effectively Implementing the*

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

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

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

Administrative Protection and Monitoring Periods for New Drugs

According to *the Drug Administration Law Implementing Measures*, to protect public health, the NMPA may provide for administrative monitoring periods of up to five years for new drugs approved to be manufactured, to consistently monitor the safety of such new drugs. During the monitoring period of a new drug, the NMPA will not approve any other enterprises' applications to manufacture or import a similar new drug.

Other PRC Regulations relating to the Pharmaceutical Industry

Coverage of the National Medical Insurance Program

The national medical insurance program was first adopted according to *the Decision of the State Council on Establishing the Urban Employees' Basic Medical Insurance System* (國務院關於建立城鎮職工基本醫療保險制度的決定) issued by the State Council on December 14, 1998, under which all employers and their employees in urban cities are required to enroll in the basic medical insurance program and the insurance premium is jointly contributed by the employers and employees. On July 10, 2007, the State Council issued *the Guiding Opinions of the State Council on the Pilot Urban Resident Basic Medical Insurance* (國務院關於開展城鎮居民基本醫療保險試點的指導意見), which further expanded the coverage of the basic medical insurance program, and accordingly the urban non-employed residents of the pilot districts may voluntarily enroll in the Urban Resident Basic Medical Insurance. In addition, on January 3, 2016, *the Opinions of the State Council on Integrating the Basic Medical Insurance Systems for Urban and Rural Residents* (國務院關於整合城鄉居民基本醫療保險制度的意見) issued by the State Council required the integration of the urban resident basic medical insurance and the new rural cooperative medical care system and the establishment of a unified basic medical insurance system, which will cover all urban and rural residents other than rural migrant workers and persons in flexible employment arrangements who participate in the basic medical insurance for urban employees. The participants of the medical insurance programs are eligible for full or partial reimbursement of the cost of the medicines included in the national medical insurance catalogue.

Pursuant to *the Notice of the Tentative Administrative Measures of the Scope of Basic Medical Insurance Coverage for Pharmaceutical Products for Urban Employees* (關於印發城鎮職工基本醫療保險用藥範圍管理暫行辦法的通知) jointly issued by the Ministry of Labor and Social Security, the Ministry of Finance and other authorities on May 12, 1999, a pharmaceutical product listed in the medical insurance catalogue must be clinically necessary, safe, effective, reasonably priced, easy to use, available in sufficient quantity, and must meet any of the following requirements: (i) being included in the pharmacopoeia of the PRC, (ii) satisfying the standards as set out by the NMPA, or (iii) having been approved by the NMPA for imported.

According to *the Tentative Administrative Measures of the Scope of Basic Medical Insurance Coverage for Pharmaceutical Products for Urban Employees*, the Ministry of Labor and Social Security and other relevant governmental authorities have the power to determine the medicines to be included in the national medical insurance catalogue, which is divided into two parts of Part A and Part B. Provincial governments are required to include all Part A medicines listed in the national medical insurance catalogue in their provincial medical insurance catalogue, but have the discretion to adjust upwards or downwards by no more than 15% from the total number of Part B medicines listed in the national medical insurance catalogue. As a result, the contents of Part B of the provincial medical insurance catalogues may differ from region to region in the PRC. Patients purchasing medicines included in Part A of the medical insurance catalogue are entitled to reimbursement in accordance with the regulations in respect of basic medical insurance. Patients purchasing medicines included in Part B of the medical insurance catalogue are required to pay a certain percentage of the purchase price and the remainder shall be reimbursed in accordance with the regulations in respect of basic medical insurance. The percentage of reimbursement for Part B medicines is decided by local authorities and as a result may differ from region to region.

National Essential Drug List

According to *the Opinions of the General Office of the State Council on Improving the National Essential Drugs System* (國務院辦公廳關於完善國家基本藥物制度的意見) issued on September 13, 2018 and effective therefrom, *the Circular on the Printing and Distribution of the Administrative Measures for the National Essential Drug List* (關於印發國家基本藥物目錄管理辦法的通知) issued on February 13, 2015 and effective therefrom, and *the National Essential Drug List (2018 version)* (國家基本藥物目錄(2018年版)) (the "***National Essential Drug List***") issued by the NHC on September 30, 2018 and effective from November 1, 2018, basic healthcare institutions funded by the government, which primarily include county-level hospitals, county-level Chinese medicine hospitals, rural clinics and community clinics, shall store up and use drugs listed in the *National Essential Drug List*. The drugs listed in the *National Essential Drug List* shall be purchased by centralized tender process and shall be subject to the price control by the National Development and Reform Commission (the "**NDRC**"). Remedial drugs listed in the *National Essential Drug List* are all listed in the medical insurance catalogue and the entire amount of the purchase price of such drugs is entitled to reimbursement.

Medical Insurance Reimbursement Standards

According to *the Decision of the State Council on Establishing the Urban Employees' Basic Medical Insurance System*, *the Opinions on the Establishment of the New Rural Cooperative Medical System* (關於建立新型農村合作醫療制度意見的通知) issued by the General Office of the State Council on January 16, 2003, *the Guiding Opinions of the State Council on the Pilot Urban Resident Basic Medical Insurance* and *the Opinions of the State Council on Integrating the Basic Medical Insurance Systems for Urban and Rural Residents*, medical insurance shall be available to all employees and residents in both rural and urban areas.

According to *the Notice on Printing and Distribution of the Opinion on the Management of Diagnosis and Treatment Items, Scope and Payment Standards of Medical Service Facilities Covered by the Urban Employees Basic Medical Insurance Program* (關於印發〈城鎮職工基本醫

療保險診療項目管理、醫療服務設施範圍和支付標準意見〉的通知) issued on June 30, 1999, the basic medical insurance program may cover a portion of the costs of diagnostic and treatment devices and diagnostic testing. The scope and rate of reimbursement shall be decided by provincial policies.

On June 20, 2017, the General Office of the State Council issued *the Guidance on Further Deepening the Reform of the Payment Method of Basic Medical Insurance* (關於進一步深化基本醫療保險支付方式改革的指導意見), which aimed to implement a diverse medical insurance payment mechanism that includes diagnosis-related groups, per-capita caps, and per-bed-day caps. By 2020, such new reimbursement mechanism will be implemented across the country, replacing the current reimbursement method based on service category and product price. Local medical insurance authorities shall implement the total budget control for their respective administrative regions and determine the amount of reimbursement to public hospitals based on their performance and the expenditure targets of the individual basic medical insurance funds.

Other Significant PRC Regulations Affecting Our Business in the PRC

Regulations relating to the Company Law and Foreign Investment

The establishment, operation and management of corporate entities in the PRC are governed by *the Company Law of the PRC* (中華人民共和國公司法) (the "***Company Law***"), which was promulgated by the SCNPC on December 29, 1993 and became effective on July 1, 1994, and was amended on December 25, 1999, August 28, 2004, October 27, 2005, December 28, 2013 and October 26, 2018 respectively. Pursuant to *the Company Law*, companies are classified into 2 categories, namely limited liability companies and limited companies by shares. *The Company Law* also applies to foreign-invested limited liability companies and companies limited by shares. According to *the Company Law*, the provisions otherwise prescribed by the laws on foreign investment shall prevail.

According to *the Company Law*, companies shall contribute 10% of the profits into their statutory capital reserve upon distribution of their post-tax profits of the current year. A company may discontinue the contribution when the aggregate sum of the statutory capital reserve is more than 50% of its registered capital. Where the balance of the statutory capital reserve of a company is insufficient to make up its losses in the previous year, the company shall make up such losses using its profits of the current year before making contribution to the statutory capital reserve. Upon contribution to the statutory capital reserve with its post-tax profits, a company may make further contribution to the capital reserve with its post-tax profits. After making up its losses and accrued reserves, a company may distribute post-tax profits to its shareholders.

Furthermore, *the Company Law of the PRC (Revised Draft)* (中華人民共和國公司法(修訂草案)) and *the Company Law of the PRC (Revised Draft for Second Review)* (中華人民共和國公司法(修訂草案二次審議稿)) (together, the "***Draft Company Law***") were released for public comments on December 24, 2021 and December 30, 2022, respectively. The major revisions made by *the Draft Company Law* included improvement of the system for the establishment and exit of companies, optimization of organizational structures of companies, improvement of capital system of companies, strengthening the responsibilities of the controlling shareholder and management staff, enhancing the social responsibilities of companies, etc. As of the Latest Practicable Date, *the Draft Company Law* has not been formally adopted.

On March 15, 2019, the National People's Congress (the "**NPC**") promulgated *the Foreign Investment Law of the PRC* (中華人民共和國外商投資法) (the "***Foreign Investment Law***"), which took effect on January 1, 2020 and repealed *the Sino-foreign Equity Joint Ventures Law of the PRC* (中華人民共和國中外合資經營企業法), *the Wholly Foreign-owned Enterprise Law of the PRC* (中華人民共和國外資企業法) and *the Sino-foreign Cooperative Joint Ventures Law of the PRC* (中華人民共和國中外合作經營企業法). Since then, *the Foreign Investment Law* has become the

fundamental law regulating foreign-invested enterprises wholly or partially invested by foreign investors. According to *the Foreign Investment Law* and *the Implementation Regulations for the Foreign Investment Law of the PRC* issued by the State Council on December 26, 2019 and effective from January 1, 2020, foreign investment refers to any investment activity directly or indirectly carried out by foreign natural persons, enterprises or other organizations (the "**foreign investors**") within the territory of the PRC, including the following circumstances: (i) a foreign investor establishes a foreign-funded enterprise within the territory of the PRC, either alone or together with any other investor; (ii) a foreign investor acquires shares, equities, property shares or any other similar rights and interests of a PRC enterprise; (iii) a foreign investor invests in any new project within the territory of the PRC, either alone or together with any other investor; or (iv) a foreign investor invests in any other way as stipulated under the laws or administrative regulations or provided by the State Council. The organization form and structure, and the operating rules of foreign-funded enterprises are subject to the provisions of *the Company Law*, *the Partnership Enterprise Law of the PRC* and other applicable laws.

The administrative system for foreign investment is pre-entry national treatment and negative list in the PRC. Pre-entry national treatment refers to the treatment accorded to foreign investors and their investments at the stage of the entry of investments which shall be no less favorable than that accorded to domestic investors and their investments. Negative list refers to the special administrative measures taken for the entry of foreign investment in the specific sectors stipulated by the PRC government. National treatment will be accorded by the PRC government to the foreign investments not included in the negative list.

The NDRC and the Ministry of Commerce (the "**MOFCOM**") jointly issued *the Catalogue of Encouraged Industries for Foreign Investment (2022 version)* (鼓勵外商投資產業目錄(2022年版)) on October 26, 2022, which became effective from January 1, 2023 and *the Special Administrative Measures (Negative List) for the Entry of Foreign Investment (2021 version)* (外商投資准入特別管理措施(負面清單) (2021年版)) (the "***Negative List***") on December 27, 2021, which became effective on January 1, 2022, which together constitute the catalogue of encouraged industries for foreign investment and the special administrative measures for the entry of foreign investment in the restricted or prohibited industries for foreign investment. The *Negative List* provided the special administrative measures for the entry of foreign investment, such as the requirements on equity and senior management personnel. Any industry not included in the *Negative List* shall be administered under the principle of equal treatment to domestic and foreign investment. Domestic enterprises engaged in businesses in the prohibited industries for foreign investment as listed in the *Negative List* shall be subject to the review and approval by the relevant competent authorities for the issuance of shares and listing on the foreign stock markets. Foreign investors shall not participate in the operation and management of the enterprises, and their equity ratio shall be governed with reference to the relevant regulations on the management of overseas investors investing in domestic securities.

The Measures on Reporting of Foreign Investment Information (外商投資信息報告辦法) was jointly issued by the MOFCOM and the SAMR on December 30, 2019, which became effective on January 1, 2020. According to *the Measures on Reporting of Foreign Investment Information*, if a foreign investor carries out investment activities directly or indirectly within the territory of the PRC, the foreign investors or the foreign-invested enterprise shall report to the competent authorities of commerce the investment information pursuant to such measures. When a foreign-invested enterprise submits the annual report, it shall report the basic information of the enterprise, information of investors and the actual controller, and operation, assets and liabilities information of the enterprise, and where the special administrative measures for the entry of foreign investment are involved, it shall as well report the information of the relevant industry approvals obtained.

Regulations Relating to Intellectual Property Rights

Patents

Pursuant to the *Patent Law of the PRC* (中華人民共和國專利法) promulgated by the SCNPC on March 12, 1984 and amended on September 4, 1992, August 25, 2000, December 27, 2008 and October 17, 2020 respectively and effective from June 1, 2021, and *the Implementation Rules of the Patent Law of the PRC* (中華人民共和國專利法實施細則) issued by the State Council on June 15, 2001 and last amended on January 9, 2010 and effective from February 1, 2010, an invention-creation shall refer to an invention, utility model or design. Inventions and utility models for which patent rights are granted shall possess novelty, creativity and practicality. The Patent Office under the State Intellectual Property Office is responsible for the acceptance, examination and approval of patent applications. The protection period is 20 years for an invention patent, 10 years for a utility model patent and 15 years for a design patent, commencing from their respective application dates.

The Patent Law of the PRC, for the first time, introduced the patent term compensation and patent linkage system. Pursuant to *the Patent Law of the PRC*, for the purpose of compensating for the time taken to examine and approve a new drug to be marketed, the patent administrative department under the State Council shall grant compensation to the validity period of patent rights for the invention patents of new drugs approved to be marketed in the PRC upon request of the patentee. The compensation period shall not exceed five years, and the total validity period of patent rights after a new drug is approved to be marketed shall not exceed 14 years. The Patent Law of the PRC also introduced a system for the early resolution of patent disputes concerning generic drug applications.

Trademarks

Pursuant to *the Trademark Law of the PRC* (中華人民共和國商標法) promulgated by the SCNPC on August 23, 1982 and amended on February 22, 1993, October 27, 2001 and August 30, 2013, and last amended on April 23, 2019 and effective from November 1, 2019 and *the Implementation Regulations of the Trademark Law of the PRC* (中華人民共和國商標法實施條例) issued by the State Council on August 3, 2002 which became effective on September 15, 2002, and revised on April 29, 2014 which became effective on May 1, 2014, the validity period of registered trademarks is 10 years, commencing from the date of approval of registration. A trademark registrant intending to continue to use the registered trademark upon expiry of its validity period shall go through the formalities of renewal within 12 months before the expiry according to the relevant provisions. If failing to do so, the trademark registrant may be granted a six-month grace period. The validity period of each renewal is 10 years, commencing from the day after the expiry date of the last validity period of the registered trademark. If the formalities of renewal are not undergone within the grace period, the registration of the trademark will be cancelled.

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

Domain names are protected by *the Administrative Measures of Internet Domain Names* (互聯網域名管理辦法) issued by the Ministry of Industry and Information Technology (the "**MIIT**") on August 24, 2017 and effective from November 1, 2017 and *the Implementing Rules on Registration of China Country Code Top-level Domain Names* (國家頂級域名註冊實施細則) issued by China Internet Network Information Center on June 18, 2019 and effective therefrom. The MIIT is the regulatory body responsible for the administration of PRC internet domain names. The China Internet Network Information Center is responsible for the administration of registration of China country code top-level domain names. Domain name registrations are processed by the domain name registration service agencies established pursuant to the relevant provisions. The applicants become domain name holders upon successful registration.

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, 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.

Regulations relating to Foreign Exchange

The principal law governing the foreign currency exchange in the PRC is *the Foreign Exchange Administration Regulations of the PRC* (中華人民共和國外匯管理條例) (the "***Foreign Exchange Administration Regulations***"), which was issued by the State Council on January 29, 1996 and became effective on April 1, 1996, and amended on January 14, 1997 and August 5, 2008 respectively. Pursuant to *the Foreign Exchange Administration Regulations*, international payments in foreign currencies and transfer of foreign currencies under the current account are not restricted by the government. However, foreign currency transactions under the capital account are still subject to limitations and require approvals from, or registration with, the State Administration of Foreign Exchange of the PRC (中華人民共和國外匯管理總局) (the "**SAFE**") or its local counterparts and other relevant PRC governmental authorities.

Pursuant to *the Regulation of Settlement, Sale and Payment of Foreign Exchange* (結匯、售匯及付匯管理規定) issued by the People's Bank of China on June 20, 1996 which became effective on July 1, 1996, foreign-invested enterprises may only buy, sell or remit foreign currencies at banks authorized to conduct foreign exchange business after providing valid commercial supporting documents and, in the case of transactions under the capital account, obtaining approvals from the SAFE or its local counterpart.

On March 30, 2015, the SAFE issued *the Circular on Reforming the Management Approach regarding the Settlement of Foreign Exchange Capital of Foreign-invested Enterprises* (國家外匯管理局關於改革外商投資企業外匯資本金結匯管理方式的通知) (the "***SAFE Circular 19***"), which became effective on June 1, 2015. Pursuant to *the SAFE Circular 19*, the foreign exchange capital, for which the monetary contribution has been confirmed by the foreign exchange authorities (or for which the monetary contribution has been credited into account by banks) in the capital account of a foreign-invested enterprise may be settled at banks under the actual operation needs of enterprise. Meanwhile, the use of such Renminbi shall be subject to the restrictions as set out in *the SAFE Circular 19*, such that it cannot be directly or indirectly used for payment beyond the business scope of the enterprises or as prohibited by the laws and regulations, for securities investments unless otherwise provided by the laws and regulations, for offering Renminbi entrusted loans (unless permitted by the business scope), repaying inter-enterprise borrowings (including advances by a third party) or repaying the Renminbi bank loans that have been sub-lent to a third party, or paying the expenses related to the purchase of real estate not for self-use, except for the foreign-invested real estate enterprises.

On June 9, 2016, the SAFE issued *the Circular on Reforming and Regulating Policies on the Control over Foreign Exchange Settlement of Capital Accounts* (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) (the "***SAFE Circular 16***") which became effective therefrom. Where the previous provisions, such as *the SAFE Circular 19*, are not consistent with *the SAFE Circular 16*, *the SAFE Circular 16* shall prevail. *The SAFE Circular 16* unified the discretional foreign exchange settlement for all the domestic institutions. Furthermore, the foreign exchange proceeds under the capital account of a domestic institution shall be used within the business scope of the domestic institution and under the principles of authenticity and self-use. *The SAFE Circular 16* reaffirmed that the foreign exchange proceeds under the capital account of and the Renminbi funds obtained from foreign exchange settlement by a domestic institution may be used for expenditures under the current account within its business scope or the expenditures under the capital account permitted by the laws and regulations. The foreign exchange proceeds under the capital account of and the Renminbi funds obtained from foreign exchange settlement by a domestic institution (i) shall not be used directly or indirectly for expenditures beyond the business scope of the domestic institution or as prohibited by the laws and regulations, (ii) unless otherwise provided, shall not be used directly or indirectly for securities investments or other investments than principal-secured products of banks, (iii) shall not be used for offering loans to non-affiliated enterprises, unless expressly permitted by the business scope or (iv) shall not be used for the construction or purchase of real estate not for self-use (except for real estate enterprises).

According to *the Circular on Optimizing Foreign Exchange Administration to Support the Development of Foreign-related Business* (國家外匯管理局關於優化外匯管理支持涉外業務發展的通知) issued by the SAFE on April 10, 2020 which took effect therefrom, the reform to facilitate the payments of proceeds under the capital accounts shall be promoted nationwide by the SAFE. Provided that the use of funds is true and compliant, and in compliance with the current administrative provisions on the use of the proceeds under the capital accounts, enterprises satisfying the requirements are not required to provide the banks with supporting documents to prove authenticity for each transaction beforehand when making domestic payments with the proceeds under the capital accounts, such as the capital funds and the proceeds of foreign debt or overseas listing.

Distribution of Dividends

On January 26, 2017, the SAFE issued *the Notice on Promoting the Reform of Foreign Exchange Administration and Improving the Review of Authenticity and Compliance* (關於進一步推進外匯管理改革完善真實合規性審核的通知) which provided that when processing the outward remittance of profits of a domestic institution equivalent to more than 50,000 US dollars, the bank shall, in light of the principle of genuine transaction, review the profit distribution resolution made by the board of directors (or by the partners), original tax filing form and audited financial statements relating to the outward remittance of profits, and chop on the original tax filing form to endorse the amount and date of the outward remittance. The domestic institution shall make up for its losses in the previous years according to the laws before remitting the profits.

Regulations relating to Outbound Investment

Pursuant to *the Administrative Measures on Outbound Investments* (境外投資管理辦法) issued by the MOFCOM on March 16, 2009 and amended on September 6, 2014, the MOFCOM and the provincial competent departments of commerce shall subject the outbound investments of enterprises to filing or approval, depending on the actual circumstances of such investments. Outbound investments of enterprises involving sensitive country or region, or sensitive industry shall be subject to approval. Other outbound investments of enterprises shall be subject to filing.

Pursuant to *the Administrative Measures for the Outbound Investments of Enterprises* (企業境外投資管理辦法) issued by the NDRC on December 26, 2017 and effective from March 1, 2018, if an enterprise in the territory of the PRC (the "**Investor**") intends to make outbound investments, it shall go through the formalities, such as approval or filing, for the outbound investment project (the "**Project**"), report relevant information and cooperate in the supervisory inspections. The sensitive Projects invested directly by the Investor or through the foreign enterprises controlled by the Investor shall be subject to approval. The non-sensitive Projects invested directly by the Investor, which involve the direct contribution of assets, rights and interests, or provision of financing or guarantee by the Investor, shall be subject to filing. The aforementioned sensitive Projects include the Projects involving sensitive country of region, or sensitive industry. *The Catalogue of Sensitive Sectors for Outbound Investment (2018 Edition)* (境外投資敏感行業目錄(2018年版)) issued by the NDRC on January 31, 2018 and effective from March 1, 2018 listed in detail the sensitive sectors.

Regulations relating to Enterprise Income Tax

Pursuant to *the Enterprise Income Tax Law of the PRC* (中華人民共和國企業所得税法) (the "***EIT Law***") promulgated by the SCNPC on March, 16 2007, which became effective from January 1, 2008, and last amended on December 29, 2018, enterprises shall be classified into resident enterprises and non-resident enterprises. The income tax rate of resident enterprises is 25%, while the income tax rate of non-resident enterprises is 20%. According to *the EIT Law* and *the Implementation Regulations for the Enterprise Income Tax Law of the PRC* (中華人民共和國企業所得税法實施條例) (the "***Implementation Regulations for EIT Law***") issued by the State Council on December 6, 2007, which became effective from January 1, 2008, and last amended on April 23, 2019, enterprise income tax shall be payable by a resident enterprise for the income derived from or accruing in or outside the PRC. Enterprise income tax shall be payable by a non-resident enterprise with office or premises within the territory of the PRC for the income derived from or accruing in the PRC by its office or premises, and the income derived from or accruing outside the PRC for which its office or premises has a de facto relationship. Where the non-resident enterprise has no office or premises within the territory of the PRC or the income derived or accrued has no de facto relationship with its office or premises, enterprise income tax shall be payable by the non-resident enterprise for the income derived from or accruing in the PRC at a reduced rate of 10%.

According to *the EIT Law* and *the Implementation Regulations for EIT Law*, dividends, premium and other gains from equity investments between the qualified resident enterprises shall be tax-exempted.

Pursuant to *the Arrangement between the Mainland and the Hong Kong Special Administrative Region for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with respect to Taxes on Income* (內地和香港特別行政區關於對所得避免雙重徵税和防止偷漏税的安排) issued by the State Administration of Taxation (the "**SAT**") on August 21, 2006, last amended and executed through the Protocol V on July 19, 2019 and effective from December 6, 2019, dividends paid by PRC resident enterprises to Hong Kong residents may be taxed in Hong Kong or taxed pursuant to the PRC laws. However, if the beneficial owner of dividends is a Hong Kong resident, the tax charged shall not exceed (i) 5% of the total amount of the dividends if the Hong Kong resident is a company directly holding at least 25% capital of the PRC resident enterprise, or (ii) 10% of the total amount of the dividends in any other case. *The Announcement on Issues Relating to "Beneficial Owner" in Tax Treaties* (關於税收協定中"受益所有人"有關問題的公告) issued by the SAT on February 3, 2018 and effective from April 1, 2018 further clarified the issues concerning the determination of "beneficial owners" under the articles with respect to dividends, interests and royalties in the tax treaties.

In addition, pursuant to *the Notice on Issues Relating to the Implementation of the Dividend Clauses in the Tax Treaties* (關於執行税收協定股息條款有關問題的通知) issued by the SAT on February 20, 2009 and effective therefrom, where a PRC resident company pays dividends to a Hong Kong tax resident and the Hong Kong tax resident (or the dividends receiver) is the beneficial owner of the dividends, then the dividends received by the Hong Kong tax resident is entitled to the treatment under the tax treaties and to calculate the income tax payable in the PRC at the tax rate as prescribed in the tax treaties. If the tax rate prescribed in the tax treaties is higher than that provided in the tax laws of the PRC, the taxpayer may pay taxes in accordance with the tax laws of the PRC. A taxpayer who intends to enjoy the treatment prescribed in the preceding paragraph under the tax treaties shall satisfy all the following conditions: (i) a taxpayer eligible for the treatment under the tax treaties shall be a Hong Kong tax resident; (ii) a taxpayer eligible for the treatment under the tax treaties shall be the beneficial owner of the relevant dividends; (iii) dividends eligible for the treatment under the tax treaties shall be dividends, premium and other gains from equity investments recognized in accordance with the tax laws of the PRC; and (iv) any other conditions as prescribed by the SAT. Where a Hong Kong tax resident directly holds a certain proportion or more of capital of the PRC resident company which pays the dividends, the dividends received by the Hong Kong tax resident may be entitled to the tax rate prescribed in the tax treaties. A Hong Kong tax resident intending to enjoy the treatment under the tax treaties shall satisfy all the following conditions: (i) the Hong Kong tax resident who receives dividends shall be a company in accordance with the tax treaties; (ii) both the proportion of the total owners' equity and the proportion of the shares with voting rights in the PRC resident company directly held by the Hong Kong tax resident satisfy the proportion requirements as prescribed in the relevant provisions; and (iii) the proportion of the capital of the PRC resident company directly held by the Hong Kong tax resident shall, at any time within the consecutive 12 months before receiving the dividends, satisfy the proportion requirements as prescribed in the tax treaties.

Product Liability

Pursuant to *the Product Quality Law of the PRC* (中華人民共和國產品質量法) promulgated by the SCNPC on February 22, 1993 and last amended on December 29, 2018 and effective therefrom, manufacturers shall be liable for the quality of products produced by them and guarantee that the product quality satisfies the requirements stipulated by laws, and shall not mix impurities or imitations into products, or to pass fake goods off as genuine ones, or shoddy products off as good ones or sub-standard products off as standard ones. Sellers shall take measures to ensure the quality of the products sold by them. A manufacturer shall be liable to compensate for any bodily injuries or damage to property other than the defective product itself

resulting from the defects in the product, unless the manufacturer is able to prove that (i) the product has never been circulated; (ii) the defects causing injuries or damage did not exist at the time when the product was circulated; or (iii) the science and technology at the time when the product was circulated were at a level incapable of detecting the defects. A seller shall be liable to compensate for any bodily injuries or damage to property of others caused by the defects in the product if such defects are attributable to the seller. And a seller shall pay compensation if it fails to indicate neither the manufacturer nor the supplier of the defective product. A person who is injured or whose property is damaged caused by the defects in the product may claim for compensation from the manufacturer or the seller of the product. Where the compensation is made by the manufacturer or seller of the product, the manufacturer or seller of the product shall have the right of recovery against the liable party of the product.

According to *the Civil Code of the PRC* (中華人民共和國民法典) promulgated by the NPC on May 28, 2020 and effective from January 1, 2021, where a patient suffers damage due to defects in a drug, the patient may claim for compensation from the holder of the marketing approval for the drug, manufacturer or the medical institution. Where the patient claims for compensation from the medical institution, the medical institution, after making compensation, shall have the right of recovery against the liable holder of the marketing approval for the drug or manufacturer.

Equity Incentive Plans

On February 15, 2012, the SAFE issued *the Circular on Issues concerning the Foreign Exchange Administration for Domestic Individuals Participating in Equity Incentive Plans of Overseas Listed Companies* (關於境內個人參與境外上市公司股權激勵計劃外匯管理有關問題的通知) (the "***Equity Incentive Rules***"). Pursuant to *the Equity Incentive Rules*, all individuals (including PRC citizens and the foreigners who have continuously resided within the territory of the PRC for one year, except the foreign diplomatic personnel and representatives of international organizations stationed in the PRC) participating in the same equity incentive plan of an overseas listed company shall collectively entrust a domestic agency (the "**Domestic Agency**") to deal with the relevant matters, such as foreign exchange registration, account opening, and transfer, remittance and exchange of funds, through their domestic company. The Domestic Agency shall open a special domestic account for foreign exchange at a bank with the foreign exchange registration certificate for the equity incentive plan. The incomes of the account include the foreign exchange funds transferred from individual's foreign exchange deposit accounts, the foreign exchange funds obtained from the purchase of foreign exchange by the Domestic Agency for the individuals, principals and proceeds repatriated after the sale of the shares or equities under the equity incentive plan by the individuals, the dividend funds repatriated, and other incomes approved by the local branch of the SAFE. The payments of the account include the outbound payments of the funds required for the participation in the equity incentive plan, foreign exchange settlement of the funds repatriated, the funds transferred into the individual's foreign exchange deposit accounts, and other payments approved by the local branch of the SAFE. The Domestic Agency shall, upon the significant changes or the termination of the equity incentive plan of the overseas listed company, carry out the registration of change of deregistration with the local branch of the SAFE.

Labor and Social Insurance

The Labor Law of the PRC (中華人民共和國勞動法) promulgated on July 5, 1994 and last amended on December 29, 2018 and *the Labor Contract Law of the PRC* (中華人民共和國勞動合同法) promulgated on June 29, 2007, effective from January 1, 2008, and amended on December 28, 2012 and effective from July 1, 2013, by the SCNPC, together provided the relationship between the employers and the employees as well as specific provisions on the terms and conditions of the labor contracts.

Pursuant to *the Social Insurance Law of the PRC* (中華人民共和國社會保險法) promulgated by the SCNPC on October 28, 2010, effective from July 1, 2011, and amended on December 29, 2018 and effective therefrom, *the Provisional Regulations for 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 last amended on March 24, 2019, and *the Regulations on the Administration of Housing Accumulation Fund* (住房公積金管理條例) issued by the State Council on April 3, 1994, and amended on March 24, 2002 and March 24, 2019, respectively, employers and/or employees are required to contribute to social insurance premiums, including basic endowment insurance, unemployment insurance, basic medical insurance, employment injury insurance and maternity insurance, and to housing accumulation funds.

Regulations relating to Environmental Impact Assessment of Construction Projects

According to *the Environmental Protection Law of the PRC* (中華人民共和國環境保護法) promulgated by the SCNPC on December 26, 1989 and amended on April 24, 2014 and effective from January 1, 2015, *the Administrative Regulations on the Environmental Protection of Construction Projects* (建設項目環境保護管理條例) issued by the State Council on November 29, 1998, and amended on July 16, 2017 and effective from October 1, 2017, *the Environmental Impact Assessment Law of the PRC* (中華人民共和國環境影響評價法) promulgated by the SCNPC on October 28, 2002 and amended on July 2, 2016 and December 29, 2018 respectively, and *the Interim Measures on the Inspection and Acceptance of Environmental Protection of Completed Construction Projects* (建設項目竣工環境保護驗收暫行辦法) issued by the Ministry of Environmental Protection. on November 20, 2017 and effective therefrom, where the completion of a construction project may have impact on the environment, the construction enterprise shall submit a report (form) of environmental impact or a registration form of environmental impact to the relevant authorities of environmental protection. The environmental impact assessment documents of construction projects required by the relevant laws to prepare reports (forms) of environmental impact shall be approved by the authorities of environmental protection before the commencement of construction. Upon completion of construction projects, the construction enterprises shall conduct the inspection and acceptance of environmental protection and prepare the reports of inspection and acceptance pursuant to the standards and procedures as stipulated by the competent authorities of environmental protection.

Precursor Chemicals

According to *the Administrative Regulations on Precursor Chemicals* (易製毒化學品管理條例) issued by the State Council on August 26, 2005 and effective from November 1, 2005, and amended on July 29, 2014, February 6, 2016 and September 18, 2018 respectively, the production, distribution, purchase, transportation, import and export of precursor chemicals are governed by the government. If an entity intends to purchase Class II or Class III precursor chemicals, it shall file with the public security authorities of the local people's government at the county level the type and quantity of precursor chemicals in demand prior to the purchase.

Fire Control

Pursuant to *the Fire Protection Law of the PRC* (中華人民共和國消防法) promulgated by the SCNPC on April 29, 1998, and last amended on April 29, 2021 and effective therefrom, the Department of Emergency Management under the State Council and the local people's governments at or above county level shall supervise and administer the matters of fire protection, while the fire control and rescue institutions of such people's governments shall be responsible for implementation. The design of fire control of the construction projects must comply with the national technical standards of fire control. If the design of fire control of a construction project has not been examined pursuant to the relevant laws or failed to pass the examination, the

construction of such project is not allowed. If a completed construction project has not gone through the fire safety inspection or failed to satisfy the requirements of fire safety upon inspection, such project is not allowed to be put to use or business.

Regulations relating to Information Security and Data Privacy

On June 10, 2021, the SCNPC promulgated *the Data Security Law of the PRC* (中華人民共和國數據安全法) (the "***Data Security Law***"), which became effective from September 1, 2021. According to *the Data Security Law*, a data classification protection system shall be established to protect data by classification. Entities engaged in data processing activities shall, in accordance with the laws and regulations, establish a sound whole-process data security management system, organize data security education and training, and take corresponding technical measures and other necessary measures to ensure data security.

According to *the Civil Code*, personal information of natural persons is protected by law. Any organization or individual that needs to obtain personal information of others shall obtain legally and ensure the information security, and shall not illegally collect, use, process, transmit, trade, provide or disclose personal information of others. *The Personal Information Protection Law of the PRC* (中國人民共和國個人信息保護法) promulgated by the SCNPC on August 20, 2021 and effective from November 1, 2021 further emphasized the duties and responsibilities of the processing personnel for the protection of personal information, and provided stricter protection measures for processing sensitive personal information.

On November 7, 2016, the SCNPC promulgated *the Cybersecurity Law of the PRC* (中華人民共和國網絡安全法) (the "***Cybersecurity Law***"), which became effective from June 1, 2017. According to *the Cybersecurity Law*, network operators shall abide by the principles of legality, legitimacy and necessity when collecting and using personal information. Network operators shall disclose the rules for collection and use, specify the purpose, methods and scope of collection and use of information, and obtain consent from the persons whose personal information is collected, when collecting and using personal information. Network operators shall not collect the personal information irrelevant to the services they provide, nor disclose, tamper with or damage the personal information they collect, and shall not provide relevant personal information to others without the prior consent of the persons whose personal information is collected, except for the personal information that cannot be identified and restored after processing.

On July 7, 2022, the CAC issued *the Measures on Security Assessment of Cross-border Data Transfer* (數據出境安全評估辦法) (the "***Cross-border Data Transfer Measures***") which became effective on September 1, 2022. Pursuant to the *Cross-border Data Transfer Measures*, the security assessment of outbound data transfer shall adhere to the integration of prior assessment and continuous supervision and the integration of risk self-assessment and security assessment, so as to prevent security risks arising from outbound data transfer and ensure the orderly and free flow of data in accordance with the law. A data processor shall expressly agree on the data security protection responsibilities and obligations in the legal documents concluded with the overseas recipient.

On July 12, 2018, the NHC issued *the Administrative Measures on National Health and Medical Care Big Data Standards, Security and Services (Trial)* (國家健康醫療大數據標準、安全和服務管理辦法(試行)) (the "***Measures on Health and Medical Care Big Data***"), which became effective on the same day. *The Measures on Health and Medical Care Big Data* provided the guidelines and principles of health and medical big data standard management, security management and service management. According to *the Measures on Health and Medical Care Big Data*, the NHC, together with other relevant departments, is responsible for the management of national health and medical care big data, while the authorities of health above the county level, together with other relevant departments, are responsible for the management of health and medical care big data within their respective administrative regions. Medical institutions and

relevant enterprises, including those engaged by medical institutions to store or operate health and medical care big data, shall take measures, such as data classification, important data backup and encryption, to ensure the security of health and medical care big data, and provide secured channels for the query and replication of information. The responsible parties shall, pursuant to *the Cybersecurity Law*, strictly control the authorization to users at different levels to access and use data, and ensure the use of data within the scope of authorization. Without authorization, no unit or individual shall use or disseminate any health and medical care big data or data beyond the scope of authorization, nor obtain any data in illegal ways. The responsible parties shall abide by the relevant regulations when disclosing health and medical care big data, shall not divulge state secrets, trade secrets or personal privacy, shall not infringe upon the interests of the state or the public, and shall not infringe upon the legitimate rights and interests of citizens, enterprise entities or other organizations.

Regulations relating to Overseas Listing

On February 17, 2023, the CSRC promulgated *the Trial Administrative Measures of the 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 "***Overseas Listing Trial Measures***") and relevant five guidelines, which will become effective on March 31, 2023. The *Overseas Listing Trial Measures* will comprehensively improve and reform the existing regulatory regime for overseas offering and listing of PRC domestic companies' securities and will regulate both direct and indirect overseas offering and listing of PRC domestic companies' securities by adopting a filing-based regulatory regime.

According to the *Overseas Listing Trial Measures*, a domestic company seeking direct overseas offering and listing shall file with the CSRC, submit the filing report, legal opinions and other relevant materials as required under the *Overseas Listing Trial Measures*, and state the shareholders' information and other matters in a truthful, accurate and complete manner. Where a domestic company submits an application for initial public offering to the competent overseas regulators, such domestic company shall file with the CSRC within three business days after such application is submitted. The *Overseas Listing Trial Measures* also require subsequent reports to be filed with the CSRC on material events, such as a change-of-control event, or voluntary or forced delisting of the issuer who has completed the overseas offering and listing. If the issuer fails to complete the filing procedure or conceals any material fact or falsifies any major content in its filing documents, it may be subject to administrative penalties, such as order to rectify, warnings, fines, and its controlling shareholders, actual controllers, the person directly in charge and other directly liable persons may also be subject to administrative penalties, such as warnings and fines.

On the same day, the CSRC also held a press conference for the release of the *Overseas Listing Trial Measures* and issued *the Notice on Administration for the Filing of Overseas Offering and Listing by Domestic Companies* (關於境內企業境外發行上市備案管理安排的通知), which, among others, clarified that, a domestic company that has already obtained the approval document from the CSRC for overseas public offering and listing may proceed with the overseas listing within the validity period of the approval document. Where the overseas listing has not been completed upon the expiration of the approval document, filing procedures specified in the *Overseas Listing Trial Measures* shall be made as required.

Regulations relating to H Share Full Circulation

"Full circulation" refers to the listing and circulation of the domestic unlisted shares of an H-share listed company on the Stock Exchange of Hong Kong Limited, 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 China Securities Regulatory Commission issued *the Guidelines on the Application of "Full Circulation" of Domestic Unlisted Shares by H-share Companies*

(Announcement of the CSRC [2019] No. 22) (H股公司境內未上市股份申請"全流通"業務指引) (the "***Guidelines on 'Full Circulation'***"). According to *the Guidelines on "Full Circulation,"* provided that the requirements set out in the relevant laws and regulations and in the policies for state-owned assets management, foreign investments and industry regulation are satisfied, the shareholders of domestic unlisted shares may decide at their own discretion through negotiation the amount and proportion of shares applying for circulation, and entrust the H-share Listed Company to submit the application for "full circulation." The H-share Listed Company shall apply to the CSRC for "full circulation" in accordance with the administrative licensing procedures required for the "examination and approval of overseas public offering and listing of shares (including additional issuance) by joint stock companies." Upon approval of the application for "full circulation" by the CSRC, the H-share Listed Company shall submit a report to the CSRC within 15 days after completion of the registration of shares involved in the application with the China Securities Depository and Clearing Co., Ltd. (the "**CSDC**"). Pursuant to the *Overseas Listing Trial Measures* which will become effective on March 31, 2023, for a domestic company seeking direct overseas listing, the shareholders holding the domestic unlisted shares of such domestic company who apply for the conversion of the domestic unlisted shares into overseas listed shares shall comply with the relevant provisions of the CSRC and entrust such domestic company to file with the CSRC.

On December 31, 2019, the CSDC and Shenzhen Stock Exchange jointly issued *the Implementation Measures for H-share "Full Circulation" Business* (H股"全流通"業務實施細則), which applied to the cross-border transfer registration, maintenance of deposit and holding details, transaction entrustment and instruction transmission, settlement, management of settlement participants, services of nominee holders and other businesses in relation to H-share "full circulation" business.

In order to fully promote the reform of H-share "full circulation" and specify the business arrangements and procedures for registration, custody, settlement and delivery of relevant shares, the CSDC issued the Circular on Issuing *the Guidance for H-share "Full Circulation"* (關於發布《H股"全流通"業務指南》的通知) on February 7, 2020, which specified the business preparation, account arrangements, cross-border share transfer registration and overseas centralized custody, etc. In February 2020, the China Securities Depository and Clearing (Hong Kong) Co., Ltd. (the "**CSDC (Hong Kong)**") issued *the Guidance of the China Securities Depository and Clearing (Hong Kong) Co., Ltd. For H-share "Full Circulation"* (中國證券登記結算(香港)有限公司H股"全流通"業務指南), which specified the custody, deposit, agent services, settlement and delivery arrangements by the CSDC (Hong Kong) and other relevant matters.

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 preclinical testing, which includes laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as animal studies. Preclinical testing is conducted in accordance with FDA's Good Laboratory Practice regulations. A sponsor of an IND must submit the results of the preclinical 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.

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 FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than 7 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 current Good Manufacturing Practice ("**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.

U.S. Review and Approval Processes

The results of product development, preclinical 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, or 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.

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 unmet 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 an unmet medical need for the disease or condition. Under the fast track program, the sponsor of a drug candidate may request 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 FDA, 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 FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, 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 FDA if FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

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.

Accelerated Approval

Under 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 ("**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 preclinical 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.

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 preclinical 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.

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 have driven healthcare reform in the United States by extending health insurance coverage and substantially changing the way healthcare 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 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 enacted by the Congress in 2017 which 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 eliminates, 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 eliminates 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.