PRC LAWS AND REGULATIONS

We are subject to a variety of PRC laws, rules and regulations affecting many aspects of our business. This section summarizes the principal PRC laws, regulations and rules that are relevant to our business and operations.

Regulations on Company Establishment and Foreign Investment

The PRC Company Law (《中華人民共和國公司法》), which was promulgated by the Standing Committee of the National People's Congress (the "NPC") and further amended in December 1999, August 2004, October 2005, December 2013 and October 2018, applies to the establishment, operation and management of both PRC domestic companies and foreign-invested enterprises. According to the PRC Company Law, where there are otherwise provisions in the laws relating to foreign investment, such provisions shall prevail.

The Foreign Investment Law of the PRC (《中華人民共和國外商投資法》) (the "FIL"), which was promulgated by the NPC on March 15, 2019, and came into effect on January 1, 2020, provides that the "foreign investment" refers to the investment activities in China carried out directly or indirectly by foreign individuals, enterprises or other organizations ("Foreign Investors"), including the following: (1) Foreign Investors establishing foreign-invested enterprises in China alone or collectively with other investors; (2) Foreign Investors acquiring shares, equities, properties or other similar rights of Chinese domestic enterprises; (3) Foreign Investors investing in new projects in China alone or collectively with other investors; and (4) Foreign Investors investing through other ways prescribed by laws and regulations or the State Council. The FIL further adopts the management system of pre-establishment national treatment and negative list for foreign investment. The "pre-establishment national treatment" refers to granting to foreign investors and their investments, in the stage of investment access, the treatment no less favorable than that granted to domestic investors and their investments; the "negative list" refers to special administrative measures for access of foreign investment in specific fields as stipulated by the State. The FIL granted national treatment to foreign investments outside the negative list. The negative list will be released by or upon approval of the State Council.

In December 2019, the State Council promulgated the Regulations on Implementing the Foreign Investment Law of the PRC (《中華人民共和國外商投資法實施條例》) (the "Implementation Rules") which came into effect in January 2020. The Implementation Rules further clarified that the state shall encourage and promote foreign investment, protect the lawful rights and interests in foreign investments, regulate foreign investment administration, continue to optimize foreign investment environment, and advances a higher-level opening.

Investment activities in the PRC by foreign investors were principally governed by the Special Administrative Measures (Negative List) for Access 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"), and the Catalogue of Industries for Encouraging Foreign Investment (《鼓勵外商投資產業目錄(2020年版)》) (the "Encouraging List") promulgated by the MOFCOM and the NDRC in

December 2020. The Negative List, which came into effect on January 1, 2022, sets out special administrative measures (restricted or prohibited) in respect of the access of foreign investments in a centralized manner, and the Encouraging List, which came into effect on January 27, 2021, sets out the encouraged industries for foreign investment. The Negative Lists cover 11 industries, and any field not falling in the Negative Lists shall be administered under the principle of equal treatment for domestic and foreign investment. Our business as currently conducted does not fall within the confines of the Negative Lists and is not subject to special administrative measures.

The Measures on Reporting of Foreign Investment Information (《外商投資信息報告辦法》) was released by the MOFCOM and the State Administration for Market Regulation (the "SAMR") on December 30, 2019, and became effective on January 1, 2020. Foreign investors directly or indirectly conducting investment activities within the territory of China shall submit the investment information through submission of initial reports, change reports, deregistration reports, annual reports etc. to the competent commerce authorities in accordance with The Measures on Reporting of Foreign Investment Information. When submitting an annual report, a foreign-invested enterprise shall submit the basic information on the enterprise, the information on the investors and their actual controlling party, the enterprise's operation and asset and liabilities information etc, and where the foreign investment admission special administrative measures are involved, the foreign investment enterprise shall also submit the relevant industry licensing information.

Laws and Regulations on Pharmaceutical Product Development, Approval and Registration

Drug Regulatory Regime

We operate our business in China under a legal regime consisting of the SCNPC, the State Council and several ministries and agencies under its authority, including, among others, the National Medical Products Administration (the "NMPA"), the National Health Commission (the "NHC") and the SAMR. The NMPA's predecessor, the State Drug Administration, or the SDA, was replaced by the State Food and Drug Administration, the SFDA, which was later reorganized into the China Food and Drug Administration, or the CFDA, as part of the institutional reforms implemented by the State Council. The responsibilities of the National Health and Family Planning Commission (the "NHFPC") and certain other governmental authorities are consolidated into the NHC, and the CFDA had been replaced by the NMPA in accordance with the Institutional Reform Program of the State Council (《國務院機構改革方案》) promulgated by the NPC on March 18, 2018. The NMPA is a regulatory authority responsible for registration and supervision of pharmaceutical products, cosmetics and medical equipment under the supervision of the SAMR.

The NMPA has set up the Center for Drug Evaluation (the "CDE") conducting the technical evaluation of each drug and biologic application to assess safety and efficacy and other institutions. According to the Decision of the CFDA on Adjusting the Approval Procedures under the Administrative Approval Items for Certain Drugs (《國家食品藥品監督管理總局關於調整部分藥品行政審批事項審批程序的決定》) issued by the CFDA on March 17, 2017 and effective as of May 1, 2017, the approval for an investigational new drug application, or the IND, should be issued by the CDE in the name of the NMPA.

Pharmaceutical Product Development

In the PRC, the NMPA monitors and supervises the administration of pharmaceutical products, as well as medical devices and equipment. The local provincial medical products administrative authorities are responsible for supervision and administration of drugs within their respective administrative regions. The PRC Drug Administration Law (《中華人民共和國藥品管理法》) promulgated by the SCNPC in 1984, as amended in 2001, 2013, 2015, 2018 and 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》) promulgated by the State Council effective in September 2002 and amended on February 6, 2016 and March 2, 2019, have laid down the legal framework for the administration of pharmaceutical products, including the research, development and manufacturing of new drugs. The PRC Drug Administration Law applies to entities and individuals engaged in the research, production, trade, application, supervision and administration of pharmaceutical products. It regulates and prescribes a framework for the administration of pharmaceutical manufactures, pharmaceutical trading companies, and medicinal preparations of medical institutions and the development, research, manufacturing, distribution, packaging, pricing and advertisements of pharmaceutical products. The Implementing Measures of the PRC Drug Administration Law serves to provide detailed implementation regulation for the PRC Drug Administration Law.

Nonclinical Research

The NMPA promulgated the Administrative Measures for Good Laboratories Practice of Nonclinical Laboratory (2017) (《藥物非臨床研究質量管理規範》 (2017)) on July 27, 2017, and effective as from September 1, 2017, which replaced the Administrative Measures for Good Laboratories Practice of Nonclinical Laboratory issued in 2003. On April 16, 2007, the NMPA issued the Circular on Measures for Certification of Good Laboratory Practice and for Nonclinical Laboratory (《藥物非臨床研究質量管理規範認證管理辦法》), or NMPA Circular 214, which provides that the NMPA decides whether an institution is qualified for undertaking pharmaceutical nonclinical research upon the evaluation of the institution's organizational administration, its research personnel, its equipment and facilities and its operation and management of nonclinical pharmaceutical projects. If all the requirements are met, a Certification of Good Laboratory Practice will be issued by the NMPA and the result will be published on the NMPA's website.

Conduction of Clinical Trials

In addition, according to the Administration of Quality of Drug Clinical Practice (《藥物臨床試驗質量管理規範》) issued by the NMPA on April 23, 2020 and effective as of July 1, 2020, which replaced the Administration of Quality of Drug Clinical Practice issued on August 6, 2003 and effective as from September 1, 2003, and the Opinions on Deepening the Reform of the Evaluation and Approval System and Inspiring 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》) issued by the General Office of the CPC Central Committee and the General Office of the State Council on and effective as from October 8, 2017, the institutions for drug clinical trials should establish an independent ethics committee and the clinical trial schemes are subject to examination, approval and signing with approval opinions by the ethics committee before implementation, in order to protect the rights and interests of human subjects in clinical trials. For a multi-center clinical trial conducted in the PRC, after ethical review by the leader unit of the clinical trial, other member units should recognize the review results of the leader unit and should not conduct repeated reviews.

All clinical trials conducted in China for new drug registration purposes must be approved and conducted at pharmaceutical clinical trial institutions filed according to the Regulations on the Administration of Drug Clinical Trial Institutions (《藥物臨床試驗機構管理規定》) promulgated by NMPA and NHC on November 29, 2019, and took effect from December 1, 2019.

Clinical Trials Approval and Registration

According to the Administrative Measures for Drug Registration (《藥品註冊管理辦法》) promulgated by the NMPA in January 2020 and effective from July 1, 2020, which replaced the Administrative Measures for Drug Registration issued in 2007, the PRC Drug Administration Law and Implementing Measures of the PRC Drug Administration Law, new drug application is subject to clinical trials. Upon completion of nonclinical research, clinical trials must be conducted for the application of a new drug registration, and applicants must apply for approval of IND from the NMPA or the CDE before conducting clinical trials.

The Opinions on the Reform of Evaluation and Approval System for Drugs and Medical Devices and Equipment (《關於改革藥品醫療器械審評審批制度的意見》), or the Reform Opinions, promulgated by the State Council on August 9, 2015 established a framework for reforming the evaluation and approval system for drugs and medical devices. The Reform Opinions indicated enhancing the standard of approval for drug registration and accelerating the evaluation and approval process for innovative drugs as well as improving the approval of drug clinical trials.

The Circular Concerning Several Policies on Drug Registration Evaluation and Approval (《關於藥品註冊審評審批若干政策的公告》), or the Several Policies Circular, promulgated by the NMPA on November 11, 2015 further clarified the measures and policies regarding simplifying and accelerating the approval process of drugs on the basis of the Reform Opinions. The circular further provides that the IND of new drugs is subject to one-off umbrella approval, and the declaration review or approval by stages will no longer be adopted.

The Priority Review and Approval Procedures for Drug Marketing Authorizations (for Trial Implementation) (《藥品上市許可優先審評審批工作程序(試行)》) promulgated by the NMPA on July 7, 2020 further clarified that a fast track IND or drug registration pathway will be available to the innovative drugs.

According to the Circular on Adjusting Evaluation and Approval procedures for Clinical Trials for Drugs (《關於調整藥物臨床試驗審評審批程序的公告》) promulgated by the NMPA on July 24, 2018, within 60 days after the acceptance of and the fees paid for the IND, the applicant may conduct the clinical trials for the drug in accordance with the clinical trial protocol submitted, if the applicant has not received any negative or questioning opinion from the CDE.

According to the Administrative Measures for Drug Registration, upon obtaining the approval of its IND and before conducting a clinical trial, an applicant shall file a registration form with the NMPA containing various details, including the clinical study protocol, the name of the principal researcher of the leading institution, names of participating institutions and researchers, an approval letter from the ethics committee, and a sample of the Informed Consent Form, with a copy sent to the competent provincial administration departments where the trial institutions will be located. The Announcement on Drug Clinical Trial Information Platform (《關於藥物臨床試驗信息平台的公告》) announced by the NMPA on September 6, 2013, provides that, instead of the aforementioned registration field with the NMPA, all clinical trials approved by the NMPA and conducted in China shall complete a clinical trial registration and publish trial information through the Drug Clinical Trial Information Platform. The applicant shall complete the trial pre-registration within one month after obtaining the approval of the IND in order to obtain the trial's unique registration number and complete registration of certain follow-up information before the first subject's enrollment in the trial. If the registration is not completed within one year after the approval of the IND, the applicant shall submit an explanation, and if the first submission is not completed within three years, the approval of the IND shall automatically expire.

Phases of Clinical Trials and the Communication with the CDE

According to the Administrative Measures for Drug Registration, a clinical trial consists of Phases I, II, III, IV and bio-equivalence trial. Pursuant to the characteristics of a drug and the research purpose, the research contents shall include clinical pharmacological research, exploratory clinical trial, confirmatory clinical trial and post-marketing research.

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

According to the Circular on Adjusting Evaluation and Approval Procedures for Clinical Trials for Drugs, where the application for clinical trial of a new investigational drug has been approved, upon the completion of Phases I and II clinical trials and prior to Phase III clinical trial, the applicant shall submit the application for Communication Session to CDE to discuss with CDE the key technical questions including the design of Phase III clinical trial protocol.

According to the Guiding Principles for Clinical Research and Development of Anti-tumor Drugs Oriented by Clinical Value (《以臨床價值為導向的抗腫瘤藥物臨床研發指導原則》) issued by the CDE On November 19, 2021, the fundamental purpose of the drug market is to address the needs of patients, and drug research and development should be based on patient needs and clinical value.

Approval or Filing relating to Chinese Human Genetic Resources

On July 2, 2015, the MOST issued the Service Guide for Administrative Licensing Items concerning Examination and Approval of Sampling, Collecting, Trading or Exporting Human Genetic Resources, or Taking Such Resources out of the PRC (《人類遺傳資源採集、收集、買賣、出口、出境審批行政許可事項服務指南》), or the Service Guide, which became effective on October 1, 2015. According to the Service Guide, the sampling, collection or research activities of human genetic resources by a foreign-invested sponsor fall within the scope of international cooperation, and the cooperating organization of China shall apply for approval of the China Human Genetic Resources Management Office through the online system. On October 26, 2017, the MOST promulgated the Circular on Optimizing the Administrative Examination and Approval of Human Genetic Resources (《關於優化人類遺傳資源行政審批流程的通知》), simplifying the approval of sampling and collecting human genetic resources for the purpose of listing a drug in the PRC.

The Regulations of the PRC on the Administration of Human Genetic Resources (《中華人民共和國人類遺傳資源管理條例》) promulgated by the State Council on May 28, 2019 and implemented on July 1, 2019, further stipulates that using Chinese human genetic resources to carry out international scientific research cooperation shall meet certain conditions and subject to approval by the administrative department of MOST. It also provides that any providing or opening for use of Chinese human genetic resources information to foreign organizations, individuals or institutions established or actually controlled by foreign organizations and individuals shall make filing to the MOST and shall submit information backup.

The Implementation Rules of the Administration of Human Genetic Resources (《人類遺傳資源管理條例實施細則》) that is promulgated by the MOST on June 1, 2023 and will be effective from July 1, 2023 further clarify the requirements for administrative licensing, record-filing and security review in respect of the collection, preservation, use, and outbound supply of Chinese human genetic resources, and detail the issues concerning relevant supervision, inspection and administrative penalties.

According to the Bio-security Law of the PRC (《中華人民共和國生物安全法》) promulgated by the SCNPC on October 17, 2020 and implemented on April 15, 2021, where information on Chinese human genetic resources is to be provided or opened for use to foreign organizations, individuals or institutions established or actually controlled thereby foreign organizations and individuals, a report shall be filed in advance to the administrative department of the MOST and the information backup shall be submitted. It also provides that approvals are required to conduct international scientific research cooperation using Chinese biological resources. Furthermore, failure to comply with the requirement under the Bio-security Law of the PRC will result in the penalties, including fines, suspension of related activities and confiscation of related human genetic resources and gains generated from conducting these activities.

Regulations on International Multi-Center Clinical Trials and Acceptance of Overseas Clinical Trial Data

According to the Notice on Issuing the International Multi-Center Clinical Trial Guidelines (Trial) (《關於發佈國際多中心藥物臨床試驗指南(試行)的通告》), ("the Multi-Center Clinical Trial Guidelines"), promulgated by the NMPA on January 30, 2015 and effective from March 1, 2015, international multi-center clinical trial applicants may simultaneously perform clinical trials in different centers using the same clinical trial protocol. Where the applicants plan to implement the international multi-center clinical trials in the PRC, the applicants shall comply with relevant laws and regulations, such as the PRC Drug Administration Law, the Implementing Regulations of the PRC Drug Administration Law and the Administrative Measures for Drug Registration, execute the Good Clinical Practice (the "GCP"), make reference to universal international principles such as the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), and comply with the laws and regulations of the countries involved in the international multi-center clinical trials. Where the applicants plan to use the data derived from the international multi-center clinical trials for approval of a drug registration in the PRC, it shall involve at least two countries, including China, and shall satisfy the requirements for clinical trials set forth in the Multi-Center Clinical Trial Guidelines and other related laws and regulations.

According to the Opinions on Deepening the Reform of the Evaluation and Approval System and Inspiring Innovation of Drugs and Medical Devices, clinical trial data obtained in an international multi-center that conforms to China's requirements for registration of drugs and medical devices can be used for the application for registration in China.

According to 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》) promulgated by the NMPA on July 6, 2018, the basic principles for accepting overseas clinical trial data include: (1) applicants shall ensure the authenticity, integrity, accuracy and trace-ability of overseas clinical trial data; (2) the process of generating overseas clinical trial data shall comply with the relevant requirements of the ICH-GCP; (3) applicants shall ensure the scientific design of overseas clinical trials, the compliance of clinical trial quality management system with the requirements, and the accuracy and integrity of statistical analysis of data; and (4) to ensure that the clinical trial design and statistical analysis of the data are scientific and reasonable, for the drugs with simultaneous R&D at home and abroad and forthcoming clinical trials in China, the applicants may, prior to implementing registrational clinical trials, contact the CDE to ensure the compliance of registrational clinical trial's design with the essential technical requirements for drug registration in China. According to the Guiding Principles, the integrity of clinical trial data is the basic requirement for accepting registration applications. For overseas clinical trials used for drug registration applications in China, all overseas clinical trial data shall be fully provided but not selectively. For the subsequent clinical trials carried out in China after the clinical trials being carried out overseas, the drug registration applicants shall evaluate the existing overseas data first before the communication with the CDE.

Drug Application, Registration and Marketing Authorization

According to the Administrative Measures for Drug Registration, upon completion of clinical trials, 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 to the NMPA for approval of a new drug application. The NMPA then determines whether to approve the application according to the comprehensive evaluation opinion provided by the CDE of the NMPA.

An applicant shall complete studies in pharmacy, pharmacology, and toxicology, as well as clinical trials of pharmaceuticals, according to the Administrative Measures for Drug Registration. The applicant shall submit an application for drug marketing authorization and the relevant research materials in accordance with the submission requirements after determining quality standards, verifying commercial scale, manufacturing process, and preparing to undergo examination and inspection for drug registration. Pursuant to the Administrative Measures for Drug Registration, drug marketing registration applications shall be subject to three categories, namely traditional Chinese drugs, chemical drugs and biological products. Among them, the registration applications of chemical drugs shall be categorized by innovative chemical drugs, improved new chemical drugs, generic chemical drugs, etc.

CDE shall assemble pharmacists, medical professionals, and other technical specialists to analyze the application thoroughly, examining the drug's safety, effectiveness, and quality control. After the comprehensive review, the drug shall be approved for marketing and a drug registration certificate shall be issued.

Monitoring Periods for New Drugs

According to the Implementing Regulations of the Drug Administration Law and the Administrative Measures for Drug Registration, the NMPA may, for the purpose of protecting public health, provide for an administrative monitoring period of not more than five years for new drugs approved to be manufactured, commencing from the date of approval, to continually monitor the safety of such new drugs. During the monitoring period of a new drug, no approval shall be granted to any other manufacturer to produce or import the said drug. The only exception is that if, prior to the commencement of the monitoring period, the NMPA has already approved any other IND of the same drug, may proceed along with drug registration application, review and approval procedures. Where regulations are conformed to, the NMPA shall approve the production or import of the same drug, and the monitoring of such drug produced by the domestic manufacturers should be conducted together with the drug already in the monitoring period.

PRC Medical Insurance Coverage and Reimbursement Regulations

Coverage of the National Medical Insurance Program

The national medical insurance program was first adopted according to the Decision of the State Council on the Establishment of the Urban Employee Basic Medical Insurance Program (《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 in urban cities are required to enroll their employees 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 about 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》), further enlarging the coverage of the basic medical insurance program, under which urban residents of the pilot district, rather than urban employees, may voluntarily join Urban Resident Basic Medical Insurance. In addition, on January 3, 2016, the Opinions 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.

Medical Insurance Catalog

Program participants are eligible for full or partial reimbursement of the cost of medicines included in the medical insurance catalog. The Notice Regarding the Tentative Measures for the Administration of the Scope of Basic Medical Insurance Coverage for Pharmaceutical Products for Urban Employee (《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》), or the Medical Insurance Coverage Notice, jointly issued on May 12, 1999 by several authorities including, among others, the Ministry of Labour and Social Security and the

Ministry of Finance, provides that a pharmaceutical product listed in the medical insurance catalog must be clinically necessary, safe, effective, reasonably priced, easy to use, available in sufficient quantity, and must meet the following requirements: (1) be set forth in the pharmacopeia of the PRC, (2) satisfy the standards promulgated by the NMPA, and (3) be approved by the NMPA for imported pharmaceutical products.

The National Drug Catalog for Basic Medical Insurance, Work-related Injury Insurance and Maternity Insurance (《國家基本醫療保險、工傷保險和生育保險藥品目錄》), or the National Reimbursement Drug List, or the NRDL, sets forth the payment standard for pharmaceutical products under the basic medical insurance, work-related injury insurance and maternity insurance funds. The Ministry of Human Resources and Social Security, together with other government authorities, has the power to determine which medicines are listed in the NRDL. Medicines listed in the NRDL are divided into two parts, List A and List B. List A drugs are widely used clinical treatments with good efficacy and lower prices compared to similar drugs, while List B drugs are clinical treatments with good efficacy and slightly higher prices compared to List A drugs.

Medical Insurance Reimbursement Standards

According to the Notice of Opinion on the Diagnosis and Treatment Management, Scope and Payment Standards of Medical Service Facilities Covered by the National Urban Employees Basic Medical Insurance Scheme (《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》) promulgated on June 30, 1999, the basic medical insurance scheme would cover a portion of the costs of diagnostic and treatment devices, as well as diagnostic testing. The scope and rate of reimbursement are determined by provincial policies.

Intellectual Property Rights

Patents

According 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 most recently amended on October 17, 2020, the Implementation Rules of the Patent Law of the PRC (《中華人民共和國專利法實施細則》), promulgated by the State Council on June 15, 2001, last amended on January 9, 2010, and effective from February 1, 2010 and the Interim Measures on the Handling of Examination Operations in relation to the Implementation of the Amended Patent Law (《關於施行修改後專利法的相關審查業務處理暫行辦法》) issued by the China National Intellectual Property Administration on May 24, 2021, invention patents are valid for twenty years, utility model patents are valid for 10 years and design patents filed no later than May 31, 2021 are valid for 10 years while design patents filed on or after June 1, 2021 are valid for 15 years, from the date of application.

Trade Secrets

According to the PRC Anti-Unfair Competition Law (《中華人民共和國反不正當競爭法》), promulgated by the SCNPC in September 1993, as amended on November 4, 2017 and April 23, 2019 respectively, the term "trade secrets" refers to technical and business information that is unknown to the public, has utility, may create business interests or profits for its legal owners or holders, and is maintained as a secret by its legal owners or holders. Under the PRC Anti-Unfair Competition Law, business persons are prohibited from infringing others' trade secrets by: (1) obtaining the trade secrets from the legal owners or holders by any unfair methods such as theft, bribery, fraud, coercion, electronic intrusion, or any other illicit means; (2) disclosing, using or permitting others to use the trade secrets obtained illegally under item above; or (3) disclosing, using or permitting others to use the trade secrets, in violation of any contractual agreements or any requirements of the legal owners or holders to keep such trade secrets in confidence; (4) instigate, induce or assist others to violate confidentiality obligation or to violate a rights holder's requirements on keeping confidentiality of commercial secrets, so as to disclose, use or allow others to use the commercial secrets of the rights holder. If a third party knows or should have known of the above-mentioned illegal conduct but nevertheless obtains, uses or discloses trade secrets of others, the third party may be deemed to have committed a misappropriation of the others' trade secrets. The parties whose trade secrets are being misappropriated may petition for administrative corrections, and regulatory authorities may stop any illegal activities and fine infringing parties.

Trademarks

According 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, amended on February 22, 1993, October 27, 2001, August 30, 2013 and April 23, 2019 and effective from November 1, 2019, the period of validity for a registered trademark is 10 years, commencing from the date of registration. Upon expiry of the period of validity, the registrant shall go through the formalities for renewal within twelve months prior to the date of expiry, if intending to continue to use the trademark. Where the registrant fails to do so, a grace period of six months may be granted. The period of validity for each renewal of registration is 10 years, commencing from the day immediately after the expiry of the preceding period of validity for the trademark. In the absence of a renewal upon expiry, the registered trademark shall be canceled. Industrial and commercial administrative authorities have the authority to investigate any behavior in infringement of the exclusive right under a registered trademark in accordance with the law. In the case of a suspected criminal offense, the case shall be timely referred to a judicial authority and decided according to law.

Domain Names

Domain names are protected under the Administrative Measures on the Internet Domain Names (《互聯網域名管理辦法》) issued by the Ministry of Industry and Information Technology, or the MIIT, on August 24, 2017 and effective from November 1, 2017, and the Implementing Rules of China ccTLD Registration (《國家頂級域名註冊實施細則》) issued by

China Internet Network Information Center on June 18, 2019, which became effective on the same day. The MIIT is the main regulatory body responsible for the administration of the PRC internet domain names. Domain name registrations are handled through domain name service agencies established under the relevant regulations, and the applicants become domain name holders upon successful registration.

Regulations on Environmental Protection and Fire Prevention

Environment Protection

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, the Administrative Regulations on the Environmental Protection of Construction Project (《建設項目環境保護管理條例》) (the "Construction Environmental Protection Rule"), promulgated by the State Council on November 29, 1998 and amended on July 16, 2017, and other relevant environmental laws and regulations, enterprises which plan to construct projects shall provide the assessment reports, assessment form, or registration form on the environmental impact of such projects with relevant environmental protection administrative authority for approval or filing. Enterprises may entrust a technical entity to conduct an environmental impact assessment of its construction projects and prepare environmental impact reports and environmental impact statements on construction projects. If a construction entity has the technical capability of environmental impact assessment, it may carry out the above activities itself.

Inspection and Acceptance of Environmental Protection Facilities

The Construction Environmental Protection Rule also requires that upon completion of construction for which an environmental impact report or environmental impact statement is formulated, the constructor shall conduct an acceptance inspection of the environmental protection facilities pursuant to the standards and procedures stipulated by the environmental protection administrative authorities of the State Council, formulate the acceptance inspection report, and announce the acceptance inspection report pursuant to the law except for circumstances where there is a need to keep confidentiality pursuant to the provisions of the State. Where the environmental protection facilities have not undergone acceptance inspection or do not pass acceptance inspection, the construction project shall not be put into production or use.

Environmental Impact Assessment

According to 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, for any construction projects that have an impact on the environment, an entity is required to produce either a report, or a statement, or a registration form of such environmental impacts depending on the seriousness of effect that may be exerted on the environment.

Fire Protection Design Approval and Filing

The Fire Prevention Law of the PRC (《中華人民共和國消防法》) (the "Fire Prevention Law") was adopted on April 29, 1998 and latest amended on April 29, 2021. According to the Fire Prevention Law and other relevant laws and regulations of the PRC, the Emergency Management Authority of the State Council and its local counterparts at or above county level shall monitor and administer the fire prevention affairs. The Fire and Rescue Department of the People's Government are responsible for implementation. The Fire Prevention Law provides that the fire prevention design or construction of a construction project must conform to the national fire prevention technical standards (as the case may be). According to the Interim Provisions on the Administration of Fire Protection Design Review and Final Inspection of Construction Projects (《建設工程消防設計審查驗收管理暫行規定》), issued by the Ministry of Housing and Urban-Rural Development on April 1, 2020 and effective on June 1, 2020, special construction projects as defined under such Interim Provisions shall conduct fire protection design review and fire protection final inspection, construction projects other than such special construction projects shall fill protection design and acceptance of the project with competent authority.

Regulations on Construction and Leased Properties in the PRC

Approval or Record-filing for Projects

Pursuant to the Regulations on the Administration of Enterprise Investment Projects by Verification and Approval and Record-filing (《企業投資項目核准和備案管理條例》) promulgated by the State Council on November 30, 2016 and effective on February 1, 2017, fixed asset investment projects related to national security, layout of major production capacity across the country, strategic resources development and major public interests, etc. shall be subject to administration by verification and approval. Projects other than those prescribed above shall be subject to administration by record-filing.

Commodity House Leasing Filing

The Administrative Measures for Commodity House Leasing (《商品房屋租賃管理辦法》) was deliberated and adopted by the Ministry of Housing and Urban-Rural Development on December 1, 2010 and came into effect on February 1, 2011, within a prescribed time limit, the parties of such lease agreement shall conduct the house leasing filing with the competent authority. Any entity that fails to conduct such house leasing filing will be ordered to correct within the time limit and if such order of correction is ignored, such entity will be fined between RMB1,000 and RMB10,000.

Foreign Exchange Control

According to the PRC Regulation for the Foreign Exchange (《中華人民共和國外匯管理條例》), or the Foreign Exchange Regulations promulgated by the PRC State Council on January 29, 1996, which was amended on January 14, 1997 and August 5, 2008, and the Regulation on the Administration of the Foreign Exchange Settlement, Sales and Payment (《結匯、售匯及付匯管理規定》), or the Settlement Regulations promulgated by the People's Bank of China on June 20, 1996 and effective from July 1, 1996, foreign exchanges required for distribution of profits and payment of dividends may be purchased from designated foreign exchange banks in the PRC upon presentation of a board resolution authorizing distribution of profits or payment of dividends.

According to the Circular of the State Administration of Exchange Control on Further Improving and Adjusting the Foreign Exchange Policies on Direct Investment (《國家外匯管理局關於進一步改進和調整直接投資外匯管理政策的通知》) and its appendix, the Operating Rules for Foreign Exchange Issues with Regard to Direct Investment under Capital Account (《資本項目直接投資外匯業務操作規程》), promulgated on November 19, 2012 and amended on May 4, 2015 by the State Administration of Exchange Control (the "SAFE"), (1) the opening of and payment into foreign exchange accounts under direct investment accounts are no longer subject to approval by the SAFE; (2) reinvestment with legal income of foreign investors in China is no longer subject to approval by SAFE; (3) the procedures for capital verification and confirmation that foreign-funded enterprises need to go through are simplified; (4) purchase and external payment of foreign exchange under direct investment accounts are no longer subject to approval by SAFE; (5) domestic transfer of foreign exchange under direct investment account is no longer subject to approval by SAFE; and (6) the administration over the conversion of foreign exchange capital of foreign-invested enterprises is improved. Later, on February 13, 2015, the SAFE issued the Circular on Further Simplifying and Improving Foreign Exchange Administration Policies in Respect of Direct Investment (《關於進一步簡化和改進直接投資外匯管理政策的通知》), effective from June 1, 2015 and amended on December 30, 2019, which prescribed that the bank instead of SAFE can directly handle the foreign exchange registration and approval under foreign direct investment while SAFE and its branches indirectly supervise the foreign exchange registration and approval under foreign direct investment through the bank.

The Provisions on the Administration of Foreign Exchange in Foreign Direct Investments by Foreign Investors (《外國投資者境內直接投資外匯管理規定》), or the FDI Provisions, which were promulgated by the SAFE on May 11, 2013 and became effective on May 13, 2013, and as amended on October 10, 2018 and December 30, 2019, regulate and clarify the administration over foreign exchange administration in foreign direct investments.

According to the Circular on the Reform of the Management Method for 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》) promulgated by the SAFE on March 30, 2015, effective from June 1, 2015 and as amended on December 30, 2019, and the Circular on the Reform and Standardization of the Management Policy of the Settlement of Capital Projects

(《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》) promulgated by the SAFE on June 9, 2016, the settlement of foreign exchange by foreign invested enterprises shall be governed by the policy of foreign exchange settlement on a discretionary basis. However, the settlement of foreign exchange shall only be used for its own operation purposes within the business scope of the foreign invested enterprises and following the principles of authenticity.

The SAFE promulgated the Circular on Relevant Issues Concerning Foreign Exchange Control on Domestic Residents' Offshore Investment and Financing and Roundtrip Investment through Special Purpose Vehicles (《國家外匯管理局關於境內居民通過特殊目的公司境外投融資及返程投資外匯管理有關問題的通知》), or the SAFE Circular 37, on July 4, 2014. The SAFE Circular 37 requires PRC residents to register with the local branches of SAFE in connection with their direct establishment or indirect control of an offshore entity, for the purpose of overseas investment and financing, with such PRC residents' legally owned assets or equity interests in domestic enterprises or offshore assets or interests. Failure to comply with the SAFE registration requirements could result in liability under PRC law for evasion of foreign exchange controls. The Circular on Further Simplifying and Improving Foreign Exchange Administration Policies in Respect of Direct Investment provides that the bank instead of SAFE can directly handle the initial foreign exchange registration and amendment registration under SAFE Circular 37.

Labor and Social Security

According to the PRC Labor Law (《中華人民共和國勞動法》), which was promulgated by the SCNPC on July 5, 1994 and effective from January 1, 1995, and amended on August 27, 2009 and December 29, 2018 respectively, the PRC Labor Contract Law (《中華人民共和國勞動合同法》), which was promulgated by the SCNPC on June 29, 2007 and effective from January 1, 2008, and amended on December 28, 2012 and effective from July 1, 2013, and the Implementing Regulations of the Employment Contracts Law of the PRC (《中華人民共和國勞動合同法實施條例》), which was promulgated by the State Council on September 18, 2008, labor contracts in written form shall be executed to establish labor relationships between employers and employees. In addition, wages cannot be lower than the local minimum wage. The employers must establish a system for labor safety and sanitation, strictly abide by State rules and standards, provide education regarding labor safety and sanitation to its employees, provide employees with labor safety and sanitation conditions and necessary protection materials in compliance with State rules, and carry out regular health examinations for employees engaged in work involving occupational hazards.

According to the Social Insurance Law of PRC (《中華人民共和國社會保險法》), which was promulgated by the SCNPC on October 28, 2010 and effective from July 1, 2011, and amended on December 29, 2018, the Interim Regulations on the Collection and Payment of Social Security Funds (《社會保險費徵繳暫行條例》), which was promulgated by the State Council on January 22, 1999 and amended on March 24, 2019, and the Regulations on the Administration of Housing Provident Funds (《住房公積金管理條例》), which was promulgated by the State Council on April 3, 1999 and amended on March 24, 2002 and March 24, 2019, employers are required to open social insurance account and housing provident fund

account within 30 days from the date of establishment, and employers are also required to contribute, on behalf of their employees, to a number of social security funds, including funds for basic pension insurance, unemployment insurance, basic medical insurance, occupational injury insurance, maternity insurance and to housing provident funds. Any employer who fails to contribute may be fined and ordered to make good the deficit within a stipulated time limit.

Dividend Distribution

According to the FIL and its Implementation Rules (《中華人民共和國外商投資法實施條例》), which issued on December 26, 2019 and effective on January 1, 2020, foreign-invested enterprises in the PRC may pay dividends only out of their accumulated profits as determined in accordance with PRC accounting standards and regulations. Under the current regulatory regime in China, a foreign-invested enterprise is required to set aside at least 10% of its respective accumulated profits each year to fund certain reserve funds, until the accumulative amount of such fund reaches 50% of its registered capital. These wholly foreign-owned companies may also allocate a portion of their after-tax profits based on PRC accounting standards to staff welfare and bonus funds. Amounts allocated to these reserve funds and staff welfare and bonus funds reduce the amount distributable as cash dividends. Upon approval of the competent governmental authorities, foreign investors may utilize RMB dividends to invest or re-invest in enterprises established in China.

According to the Notice on Improving the Check of Authenticity and Compliance to Further Promote Foreign Exchange Control (《國家外匯管理局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》) promulgated by the SAFE on January 26, 2017, (1) under the principle of genuine transaction, banks shall check board resolutions regarding profit distribution, the original version of tax filing records and audited financial statements; and (2) Domestic entities must hold income to account for previous years' losses before remitting the profits. Moreover, domestic entities shall make detailed explanations of sources of capital and utilization arrangements, and provide board resolutions, contracts and other proof when completing the registration procedures in connection with an outbound investment.

Employee Stock Incentive Plan

On February 15, 2012, the SAFE promulgated the Notices on Issues Concerning the Foreign Exchange Administration for Domestic Individuals Participating in Stock Incentive Plans of Overseas Publicly Listed Companies (《國家外匯管理局關於境內個人參與境外上市公司股權激勵計劃外匯管理有關問題的通知》), or the Stock Option Rules, which prescribed that PRC citizens or non-PRC citizens residing in China for a continuous period of no less than one year (except for foreign diplomatic personnel in China and representatives of international organizations in China) who participate in any stock incentive plan of an overseas publicly listed company shall, through the domestic company to which the said company is affiliated, collectively entrust a domestic agency (may be the Chinese affiliate of the overseas publicly listed company which participates in stock incentive plan, or other domestic institutions qualified for asset trust business lawfully designated by such company) to handle foreign exchange registration, and entrust an overseas institution to handle issues like exercise of

options, purchase and sale of corresponding stocks or equity, and transfer of corresponding funds. In addition, the domestic agency is required to amend the SAFE registration with respect to the stock incentive plan if there is any material change to the stock incentive plan. Moreover, the SAFE Circular 37 provides that PRC residents who participate in a share incentive plan of an overseas unlisted special purpose company may register with local branches of SAFE before exercising rights.

Enterprise Income Tax

According to the Enterprise Income Tax Law of the PRC (《中華人民共和國企業所得税法》), or the EIT Law, promulgated by the NPC on March 16, 2007, which became effective on January 1, 2008 and was amended on February 24, 2017 and December 29, 2018, and the Implementation Rules of the EIT Law (《中華人民共和國企業所得税法實施條例》), promulgated by the State Council on December 6, 2007, which became effective on January 1, 2008, and amended on April 23, 2019, other than a few exceptions, the income tax rate for both domestic enterprises and foreign-invested enterprises is 25%. Enterprises are classified as either "resident enterprises" or "non-resident enterprises". Besides enterprises established within the PRC, enterprises established outside China whose "*de facto* management bodies" are located in China are considered "resident enterprises" and subject to the uniform 25% enterprise income tax rate for their global income. A non-resident enterprise refers to an entity established under foreign law whose "*de facto* management bodies" are not within the PRC but which have an establishment or place of business in the PRC, or which does not have an establishment or place of business in the PRC but have income sourced within the PRC. An income tax rate of 10% will normally be applicable to dividends declared to non-PRC resident enterprise investors that do not have an establishment or place of business in the PRC, or that have such establishment or place of business but the relevant income is not effectively connected with the establishment or place of business, to the extent such dividends are derived from sources within the PRC.

According to an Arrangement Between the mainland China and the Hong Kong Special Administrative Region for the Avoidance of Double Taxation and 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》), or the Double Tax Avoidance Arrangement issued on December 31, 2019 by the STA, and other applicable PRC laws, if a Hong Kong resident enterprise is determined by the competent PRC tax authority to have satisfied the relevant conditions and requirements under such Double Tax Avoidance Arrangement and other applicable laws, the 10% withholding tax on the dividends the Hong Kong resident enterprise receives from a PRC resident enterprise may be reduced to 5%. However, based on the Circular on Certain Issues with Respect to the Enforcement of Dividend Provisions in Tax Treaties (《關於執行税收協定股息條款有關問題的通知》) issued on February 20, 2009 by the STA, if the relevant PRC tax authorities determine, in their discretion, that a company benefits from such reduced income tax rate due to a structure or arrangement that is primarily tax-driven, such PRC tax authorities may adjust the preferential tax treatment; and based on the Announcement on Certain Issues with Respect to the "Beneficial Owner" in Tax Treaties (《國家税務總局關於税收協議中"受益所有人"有關問題的公告》) issued by the STA on February 3, 2018 and effective from April 1,

2018, if an applicant's business activities do not constitute substantive business activities, it could result in the negative determination of the applicant's status as a "beneficial owner", and consequently, the applicant could be precluded from enjoying the above-mentioned reduced income tax rate of 5% under the Double Tax Avoidance Arrangement.

Data Security, Cyber Security and Data Privacy Protection

Pursuant to the PRC Civil Code (《中華人民共和國民法典》) promulgated by the NPC on May 28, 2020 and effective from January 1, 2021, the personal information of a natural person shall be protected by the law. An information processor shall not disclose or tamper with any personal information collected or stored thereby; and without the consent of the natural person, no personal information shall be illegally provided to any other person.

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

The MCR was promulgated by the CAC and other twelve PRC regulatory authorities on December 28, 2021 and became effective on February 15, 2022. The Article 2 of the MCR provides that where a critical information infrastructure operator (the "**CIIO**") purchases network products and services, and an online platform operator carries out data processing activities, which affect or may affect national security, cybersecurity review shall be conducted. Article 7 of the MCR further provides that the online platform operators holding personal information of more than one million users shall file for cybersecurity review with the Cybersecurity Review Office if it is seeking a listing abroad. As of the Latest Practicable Date, (i) we had not been determined or identified as a CIIO by any governmental authorities; and (ii) the Directors believe that we are not online platform operators who carry out data processing activities that affect or may affect national security or possess personal information of more than one million users. Our PRC Legal Adviser is of the view that as long as there is no material change to the Group's current business, we have no obligation to proactively apply for cybersecurity review.

On November 14, 2021, the CAC promulgated the Draft Cyber Data Security Regulation, which proposes to provide more detailed guidelines on the current rules on various aspects of data processing, including the processors' announcement of data processing rules, obtaining consents and separate consents, security of important data and cross-border transfer of data, and further obligations of platform operators. Pursuant to Article 2 and Article 73 of the Draft Cyber Data Security Regulation, the Draft Cyber Data Security Regulation applies to data processing activities by utilizing internet as well as cyber date security supervision and management activities within the PRC. "Cyber data" refers to any information that is electronically recorded, whereas "data processing activities" refer to activities such as data collection, storage, usage, processing, transmission, provision, disclosure and deletion. In general, any company engages in data processing activities through internet within the PRC will be subject to the Draft Cyber Data Security Regulation. In addition, Article 13 of the Draft Cyber Data Security Regulation stipulates that data processors shall apply for cybersecurity review when carrying out activities including (i) seeking to be listed in Hong Kong that affects or may affect national security; and (ii) seeking to be listed abroad that processing the personal information of more than one million user.

Regulations relating to Overseas Securities Offering and Listing

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

Pursuant to the Overseas Listing Trial Measures, PRC domestic companies that seek to offer and list securities in overseas markets, either in direct or indirect means, are required to fulfil the filing procedure with the CSRC and report relevant information. The Overseas Listing Trial Measures provides that an overseas offering and listing is explicitly prohibited, if any of the following: (i) such securities offering and listing is explicitly prohibited by provisions in laws, administrative regulations and relevant state rules; (ii) the intended overseas securities offering and listing may endanger national security as reviewed and determined by competent authorities under the State Council in accordance with law; (iii) the domestic company intending to make the securities offering and listing, or its controlling shareholder(s) and the actual controller, have committed relevant crimes such as corruption, bribery, embezzlement, misappropriation of property or undermining the order of the socialist market economy during the latest three years; (iv) the domestic company intending to make the securities offering and listing is currently under investigations for suspicion of criminal offenses or major violations of laws and regulations, and no conclusion has yet been made thereof; or (v) there are material ownership disputes over equity held by the domestic company's controlling shareholder(s) or by other shareholder(s) that are controlled by the controlling shareholder(s) and/or actual controller.

The Overseas Listing Trial Measures also provides that if the issuer meets both the following criteria, the overseas securities offering and listing conducted by such issuer will be deemed as indirect overseas offering by PRC domestic companies: (i) 50% or more of any of the issuer's operating revenue, total profit, total assets or net assets as documented in its audited consolidated financial statements for the most recent fiscal year is accounted for by domestic companies; and (ii) the main parts of the issuer's business activities are conducted in mainland China, or its main place(s) of business are located in mainland China, or the majority of senior management staff in charge of its business operations and management are PRC citizens or have their usual place(s) of residence located in mainland China. The determination of the indirect overseas offering and listing of PRC domestic companies shall follow the principle of substance over form. Where an issuer submits an application for initial public offering to competent overseas regulators, such issuer must file with the CSRC within three business days after such application is submitted.

On the same day, the CSRC also held a press conference for the release of the Trial Measures and issued the Notice on Administration for the Filing of Overseas Offering and Listing by Domestic Companies, which, among others, clarifies that (1) on or prior to the effective date of the Overseas Listing Trial Measures, domestic companies that have already submitted valid applications for overseas securities offering and listing but have not obtained approval from overseas regulatory authorities or stock exchanges may reasonably arrange the timing for submitting their filing applications with the CSRC, and must complete the filing before the completion of their overseas securities offering and listing; (2) a six-month transition period will be granted to domestic companies which, prior to the effective date of the Overseas Listing Trial Measures, have already obtained and do not need to re-obtain the approval from overseas regulatory authorities or stock exchanges (such as the completion of hearing in the market of Hong Kong or the completion of registration in the market of the United States), but have not completed the indirect overseas listing; if domestic companies fail to complete the overseas listing within such six-month transition period, they shall file with the CSRC according to the requirements.

U.S. LAWS AND REGULATIONS

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

U.S. Government Regulation of Drug and Biological Products

In the U.S., the FDA regulates drugs under the FDCA, its implementing regulations and biologics 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. Any agency or judicial enforcement action could have a material adverse effect on our business, the market acceptance of our products and our reputation.

Once a product candidate is identified for development, it enters pre-clinical testing, which includes laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as animal studies. Pre-clinical testing is conducted in accordance with FDA's Good Laboratory Practice regulations. A sponsor of IND must submit the results of the pre-clinical testing, 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 ("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 reapprove 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 on 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 GMP 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, pre-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the product, proposed labeling and other relevant information, are submitted to the FDA as part of an NDA or BLA. Unless deferred or waived, NDAs or 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 an NDA or 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 NDA/BLA to ensure that it is sufficiently complete for substantive review before it accepts the NDA/BLA for filing. After accepting the NDA/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 GMP-compliant to assure the product's identity, strength, quality and purity. Before approving the NDA/BLA, the FDA typically will inspect whether the manufacturing processes and facilities are in compliance with GMP requirements and adequate to assure consistent production of the product within required specifications. The FDA may refer the NDA/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 NDA/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 NDA/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 NDA/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 NDA/BLA approval and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

In the U.S., products composed of components that would normally be regulated by different centers at the FDA are known as combination products. Typically, the FDA's Office of Combination Products assigns a combination product to a specific Agency Center as the lead reviewer. The FDA determines which Center will lead a product's review based upon the product's primary mode of action. Depending on the type of combination product, its approval, clearance or licensure may usually be obtained through the submission of a single marketing application. However, the FDA sometimes will require separate marketing applications for individual constituent parts of the combination product, which may require additional time, effort, and information. Even when a single marketing application is required for a combination product, the relevant Centers may participate in the review. An applicant will also need to discuss with the Agency how to apply certain premarket requirements and post-marketing regulatory requirements, including conduct of clinical trials, adverse event reporting and good manufacturing practices, to their combination product.

Expedited Development and Review Programs

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 IND, and the FDA must determine if the candidate qualifies for such designation within 60 days of receipt of the request. If so designated, the FDA shall act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather pre-clinical and clinical data is as efficient as practicable.