UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER
PURSUANT TO RULE 13A-16 OR 15D-16
OF THE SECURITIES EXCHANGE ACT OF 1934

For the month of September 2020

Commission Filing Number: 001-38205

ZAI LAB LIMITED

(Translation of registrant's name into English)

4560 Jinke Road, Bldg. 1, 4F, Pudong, Shanghai, China 201210
(Address of principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover Form 20-F or Form 40-F: Form 20-F x Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): ☐

EXHIBIT INDEX

Exhibit No.	Description
99.1	Zai Lab Limited Supplemental and Updated Disclosures

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ZAI LAB LIMITED

By: /s/ Billy Cho
Name: Billy Cho
Title: Chief Financial Officer

Date: September 11, 2020

Exhibit 99.1

Zai Lab Limited Supplemental and Updated Disclosures

We recently filed a listing application with The Stock Exchange of Hong Kong Limited, or the Hong Kong Stock Exchange, in connection with a proposed secondary listing, or the Listing, of our ordinary shares, par value US$0.00006 per share, or the Shares, on the Main Board of the Hong Kong Stock Exchange together with a Hong Kong initial public offering and a global offering, or the Global Offering, of the Shares.

The listing application contains supplemental and additional descriptions of certain aspects of our business and financial information as required by the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited, or the Hong Kong Listing Rules, as well as updated disclosure of certain information previously disclosed in our annual report on Form 20-F for the year ended December 31, 2019, or our 2019 Annual Report. This exhibit sets forth such new, supplemental and updated information and disclosures as described below. The disclosure herein supplements and should be read in conjunction with the disclosure in our 2019 Annual Report and other disclosures furnished on Form 6-K.

As we have applied for a secondary listing on the Hong Kong Stock Exchange, the Nasdaq Global Market, or the Nasdaq, will continue to be our primary listing venue. We have also applied for a number of waivers and/or exemptions from strict compliance with the relevant provisions of the Hong Kong Listing Rules, the Securities and Futures Ordinance (Chapter 571 of the Laws of Hong Kong), or the SFO and the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Chapter 32 of the Laws of Hong Kong), or the Companies (WUMP) Ordinance, and a ruling in relation to the Codes on Takeovers and Mergers and Share Buy-backs issued by the Securities and Futures Commission of Hong Kong, or the Takeovers Codes. If these applications are approved, we would be exempted from certain requirements to which other companies listed on the Hong Kong Stock Exchange are normally subject to without such waivers and exemptions, as discussed in greater detail below. We do not expect the Listing to result in significant additional compliance or disclosure obligations for our company.

Unless otherwise stated, all translations of Renminbi and Hong Kong dollars into U.S. dollars and from U.S. dollars into Renminbi in this document were made at a rate of RMB7.0651 to US$1.00 and HKD7.7501 to US$1.00, the respective exchange rate on June 30, 2020 set forth in the H.10 statistical release of the Federal Reserve Board.

There is no assurance as to if or when the Listing will take place. This communication is neither an offer to sell nor a solicitation of an offer to buy, nor shall there be any offer, solicitation or sale of our securities in any jurisdiction in which such offer, solicitation or sale would be unlawful.

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RISK FACTORS

The following sets forth certain risk factors that have been updated and/or supplemented to reflect changes since the filing of our 2019 Annual Report as well as additional new risk factors relating to the Listing.

RISKS RELATED TO OUR FINANCIAL POSITION AND NEED FOR ADDITIONAL CAPITAL

We have incurred significant losses since our inception and anticipate that we will continue to incur losses in the future and may never achieve or maintain profitability.

The Hong Kong Department of Health approved ZEJULA in October 2018 and we launched ZEJULA in Hong Kong in December 2018. In June 2019, we received marketing authorization to commercialize ZEJULA in Macau for women with relapsed ovarian cancer. The China National Medical Products Administration, or NMPA, approved ZEJULA in December 2019 as a maintenance therapy for adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy and we launched ZEJULA in the People's Republic of China, or PRC or China, in January 2020. In December 2018, we announced the launch of Optune for the treatment of glioblastoma multiforme, or GBM, in Hong Kong.

In May 2020, we obtained the NMPA MAA approvals for Optune in combination with TMZ for the treatment of patients with newly diagnosed GBM, and also as a monotherapy for the treatment of patients with recurrent GBM. Although we launched ZEJULA in China in January 2020 for recurrent ovarian cancer, in Macau in June 2019 for recurrent ovarian cancer, and in Hong Kong in December 2018 for adult patients with platinum-sensitive relapsed high grade serous epithelial ovarian cancer who are in a complete response or partial response to platinum-based chemotherapy and we launched Optune in Hong Kong in December 2018 and in China in May 2020, it will take some time to attain profitability and we may never do so. We have also obtained the rights to commercialize many clinical-stage drug candidates. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a drug candidate will fail to gain regulatory approval or become commercially viable. To date, we have financed our activities primarily through private placements, our initial public offering on Nasdaq in September 2017 and multiple follow-on offerings. For the year ended December 31, 2018 and 2019 and for the six months ended June 30, 2020, we generated revenue of US$0.1 million, US$13.0 million and US$19.2 million from product sales, respectively, and we continue to incur significant development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception in 2013. For the years ended December 31, 2018 and 2019 and for the six months ended June 30, 2020, we reported a net loss of US$139.1 million, US$195.1 million and US$128.6 million, respectively.

We expect to continue to incur losses in the foreseeable future, and we expect these losses to increase as we:

- continue to commercialize ZEJULA, Optune and any other products for which we may obtain regulatory approval;
- maintain and expand sales, marketing and commercialization infrastructure for ZEJULA, Optune and any other products for which we may obtain regulatory approval;
- maintain and expand regulatory approvals for our products and drug candidates that successfully complete clinical trials;
- continue our development and commence clinical trials of our drug candidates;

- maintain our manufacturing facilities;
- hire additional clinical, operational, financial, quality control and scientific personnel;
- seek to identify additional drug candidates;
- obtain, maintain, expand and protect our intellectual property portfolio;
- enforce and defend intellectual property-related claims; and
- acquire or in-license other intellectual property, drug candidates and technologies.

To become and remain profitable, we must continue commercialization efforts of ZEJULA and Optune and develop and eventually commercialize other drug candidates with significant market potential. This will require us to be successful in a range of challenging activities, including manufacturing, marketing and selling commercialized products such as ZEJULA, Optune and other products for which we may obtain marketing approval as well as completing pre-clinical testing and clinical trials of and obtaining marketing approval for our clinical and pre-clinical stage drug candidates. We will also need to be successful in satisfying any post-marketing requirements with respect to all of our products and drug candidates. We may not succeed in any or all of these activities and, even if we do, we may never generate product revenues that are significant or large enough to achieve profitability. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts and commercialization efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

We had net operating cash outflow during the Track Record Period.

Our operations have consumed substantial amounts of cash since inception. The net cash used in our operating activities was US$97.5 million, US$191.0 million and US$92.3 million for the years ended December 31, 2018 and 2019 and the six months ended June 30, 2020, respectively. We expect our expenses to increase significantly in connection with our ongoing activities, particularly as we continue to commercialize ZEJULA and Optune, research and develop our pre-clinical-stage drug candidates and initiate additional clinical trials of, and seek and/or expand regulatory approval for, ZEJULA, Tumor Treating Fields and our other drug assets. In addition, if we obtain regulatory approval for any additional drug candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. In particular, if more of our drug candidates are approved, additional costs may be substantial as we may have to modify or increase the production capacity at our current manufacturing facilities or contract with third-party manufacturers. We have, and may continue to, incur expenses as we create additional infrastructure to support our operations. Our liquidity and financial condition may be materially and adversely affected by the negative net cash flows, and we cannot assure you that we will have sufficient cash from other sources to fund our operations.

We will continue to require substantial additional funding for our drug development programs and for our commercialization efforts for ZEJULA, Optune and other products for which we may obtain regulatory approval, which may not be available on acceptable terms, or at all. If we are unable to raise capital on acceptable terms when needed, we could incur losses or be forced to delay, reduce or terminate such efforts.

To date, we have financed our activities primarily through private placements, our initial public offering on Nasdaq in September 2017 and multiple follow-on offerings. As of June 30, 2020, through these offerings, we have raised US$958.6 million. We will likely need to obtain substantial additional funding in connection with our continuing operations through public or private equity offerings, debt financing, collaborations or licensing arrangements or other sources. If we are unable to raise capital when needed or on acceptable terms, we could incur losses and be forced to delay, reduce or terminate our research and development programs or any future commercialization efforts.

We believe our cash and cash equivalents and short-term investments as of June 30, 2020 will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the cost and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution for ZEJULA, Optune and any other products for which we receive regulatory approval;
- the cash received, if any, from future commercial sales of ZEJULA, Optune and any other products for which we receive regulatory approval;
- the number and development requirements of the drug candidates we pursue;
- the scope, progress, timing, results and costs of researching and developing our drug candidates, and conducting pre-clinical and clinical trials;
- the number and characteristics of other drug candidates that we may pursue;
- the cost, timing and outcome of seeking, obtaining, maintaining and expanding regulatory approval of our products and drug candidates;
- our ability to establish and maintain strategic partnerships, collaboration, licensing or other arrangement and the financial terms of such arrangements;
- the cost, timing and outcome of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property related claims;
- the extent to which we acquire or in-license other drug candidates and technologies;
- resources required to develop and implement policies and processes to promote ongoing compliance with applicable healthcare laws and regulations;
- costs required to ensure that our and our partners' business arrangements with third parties comply with applicable healthcare laws and regulations;
- our headcount growth and associated costs; and
- the costs of operating as a public company in both the United States and Hong Kong.

RISKS RELATED TO OUR DEPENDENCE ON THIRD PARTIES

We rely on supplies from our licensors, which may severely harm our business and results of operations.

We currently source key materials from third parties, either directly through agreements with suppliers or indirectly through our manufacturers who have agreements with suppliers, as well as through our licensors. Any significant disruption in our potential supplier relationships, whether due to price hikes, manufacturing or supply related issues, could harm our business. We anticipate that, in the near term, all key materials will be sourced through third parties. There are a small number of suppliers for certain capital equipment and key materials that are used to manufacture some of our drugs. Such suppliers may not sell these key materials to us or our manufacturers at the times we need them or on commercially reasonable terms. We currently do not have any agreements for the commercial production of these key materials. Any significant delay in the supply of a product or drug candidate or its key materials for an ongoing clinical study could considerably delay completion of our clinical studies, product or drug testing and potential regulatory approval of our products or drug candidates. If we or our manufacturers are unable to purchase these key materials after regulatory approval has been obtained for our drug candidates, the commercialization of our products or the commercial launch of our drug candidates could be delayed or there could be a shortage in supply, which would impair our ability to generate revenues from the sale of our products and drug candidates.

During the Track Record Period, we relied on a limited number of customers for a substantial portion of our revenue.

During the Track Record Period, a substantial amount of our revenue was derived from sales to a limited number of customers, which are distributors as consistent with industry norm. In 2018, 2019 and the first half of 2020 (the "**Track Record Period**"), the aggregate amount of revenue generated from our five largest customers accounted for approximately 89.6%, 85.0% and 44.5% of our total revenue, respectively. Revenue generated from our largest customer for the same periods accounted for approximately 39.6%, 41.6% and 16.8% of our total revenue, respectively. Please refer to the section headed "Business — Customers" for more details. While we are rapidly expanding our customer base upon our successful launch of ZEJULA and Optune in China, we may continue to rely on such major customers in ramping up the sales of our commercialized products. There is no assurance that our five largest customers will continue to purchase from us at the current levels or at all in the future. If any of our five largest customers significantly reduces its purchase volume or ceases to purchase from us, and we are not able to identify new customers in a timely manner, our business, financial condition and results of operation may be materially and adversely affected. In addition, there is no assurance that our major customers will not negotiate for more favorable terms for them in the future. Under such circumstances, we may have to agree to less favorable terms so as to maintain the ongoing cooperative relationships with our major customers. If we are unable to reduce our production cost accordingly, our profitability, results of operations and financial condition may be materially and adversely affected. Therefore, any risks which could have a negative impact on our major customers could in turn have a negative impact on our business.

If we fail to maintain an effective distribution channel for our products, our business and sales of the relevant products could be adversely affected.

We rely on third-party distributors to distribute our commercialized products. We also expect to rely on third-party distributors to distribute our other products and internally discovered products, if approved. Our ability to maintain and grow our business will depend on our ability to maintain an effective distribution channel that ensures the timely delivery of our products to the relevant markets where we generate market demand through our sales and marketing activities. However, we have relatively limited control over our distributors, who may fail to distribute our products in the manner we contemplate. If price controls or other factors substantially reduce the margins our distributors can obtain through the resale of our products to hospitals, medical institutions and sub-distributors, they may terminate their relationship with us. While we believe alternative distributors are readily available, there is a risk that, if the distribution of our products is interrupted, our sales volumes and business prospects could be adversely affected.

RISKS RELATED TO OUR BUSINESS AND INDUSTRY

Even though we have launched ZEJULA and Optune in China, Hong Kong and Macau, we may never obtain approval of ZEJULA and Tumor Treating Fields for other indications or jurisdictions outside of the regulatory approvals we have already obtained, which would limit our ability to realize their full market potential.

In order to market products in any given jurisdiction, we must comply with numerous and varying regulatory requirements of such jurisdiction regarding safety, efficacy and quality. The Hong Kong Department of Health approved ZEJULA in October 2018 and we launched ZEJULA in Hong Kong in December 2018. In June 2019, we received marketing authorization to commercialize ZEJULA in Macau for women with relapsed ovarian cancer. The NMPA approved ZEJULA in December 2019 as a maintenance therapy for adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy and we launched ZEJULA in China in January 2020. In December 2018, we announced the launch of Optune for the treatment of GBM in Hong Kong. In May 2020, we obtained the NMPA MAA approvals for Optune in combination with TMZ for the treatment of patients with newly diagnosed GBM, and also as a monotherapy for the treatment of patients with recurrent GBM. The approval of ZEJULA and Optune for certain indications does not mean that the NMPA will approve ZEJULA and Tumor Treating Fields for other indications. Approval procedures vary among jurisdictions and clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other jurisdiction.

We face risks related to health epidemics, including the recent COVID-19 pandemic, which could have a material adverse effect on our business and results of operations.

In December 2019 a respiratory illness caused by a novel strain of coronavirus, SARS-CoV-2, causing the Coronavirus Disease 2019, also known as COVID-19 or coronavirus emerged. Global health concerns relating to the COVID-19 pandemic have been weighing on the macroeconomic environment, and the pandemic has significantly increased economic volatility and uncertainty. The pandemic has resulted in government authorities implementing numerous measures to try to contain the virus, such as travel bans and restrictions, quarantines, shelter-in-place or stay-at-home orders, and business shutdowns. The extent to which the coronavirus impacts our operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the outbreak and travel bans and restrictions, quarantines, shelter-in-place or stay-at-home orders, and business shutdowns. The continued COVID-19 pandemic could adversely impact our operations, given the impact it may have on the manufacturing and supply chain, sales and marketing and clinical trial operations of us and our business partners, and the ability to advance our research and development activities and pursue development of any of our pipeline products, each of which could have an adverse impact on our business and our financial results.

For example, due to business interruptions to hospitals and treatment centers in China arising in connection with the outbreak of COVID-19, some patients have experienced difficulties in accessing hospital care and, as a result, our commercialization team has had fewer opportunities to reach patients who could benefit from ZEJULA or Optune. In addition, we have experienced delays in the enrollment of patients in our clinical trials due to the outbreak of COVID-19. Our commercial partners and licensors also have similarly experienced delays in enrollment of patients to their clinical trials due to the outbreak of COVID-19 in their respective territories. None of our NDA submission and acceptance nor CTA approvals are delayed, however.

However, as the outbreak of COVID-19 has largely been contained in China, we believe we have experienced only minimal disruption to our commercialization of ZEJULA and Optune and our planned clinical trials since the outbreak. Nevertheless, outbreaks may occur again and may result in similar business interruptions in the future. Additionally, although we have not experienced material supply disruptions due to the outbreak of COVID-19, we cannot guarantee that we will not experience supply disruptions in the future due to COVID-19 or any other pandemic, epidemic or other public health crises, natural catastrophe or other disasters.

There are no comparable recent events that provide guidance as to the effect the COVID-19 outbreak as a global pandemic may have, and, as a result, the ultimate impact of the pandemic is highly uncertain and subject to change. To the extent the outbreak of COVID-19 results in delay and interruptions to our or our commercial partners' and licensors' clinical trials in the future, such delays may result in increased development costs for our products and drug candidates, which could cause the value of our company to decline and limit our ability to obtain additional financing.

The pharmaceutical industry in China is highly regulated and such regulations are subject to change, which may affect the approval and commercialization of our drugs and drug candidates.

The pharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, manufacturing, distribution, and marketing of new drugs. In recent years, the pharmaceutical laws and regulations in China has undergone significant changes, including but not limited to the adoption of some exploratory programs in pilot regions, and we expect that the transformation will continue. Any changes or amendments with respect to government regulation and supervision of the pharmaceutical industry in China may result in uncertainties with respect to the interpretation and implementation of the relevant laws and regulations or adversely impact the development or commercialization of our drugs and drug candidates in China. For instance, in March 2020, Medical Products Administration of Hainan Province promulgated the Interim Measures for the Administration of Taking Away the Imported Urgently Needed Drug from the Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province (《海南博鰲樂城國際醫療旅遊先行區臨床急需進口藥品帶離先行區使用管理暫行辦法》), which allows that a patient may apply for taking away a small amount of the legally imported drugs that is not yet registered domestically but is on urgent medical need from the Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province following his therapeutic schedule, which is also known as the special Named Patient Program (NPP). However, as NPP is newly adopted, any change in future policies or implementing measures, which we may not be able to predict or control, could create uncertainties affecting our development and commercialization of our drugs candidates.For further information regarding government regulation in China, see "Regulatory Environment — PRC Regulation of Pharmaceutical Product Development and Approval."

If safety, efficacy, manufacturing or supply issues arise with any therapeutic that we use in combination with our products and drug candidates, we may be unable to market such products or drug candidate or may experience significant regulatory delays or supply shortages, and our business could be materially harmed.

We plan to develop certain of our products and drug candidates for use as a combination therapy. However, we did not develop or obtain regulatory approval for, and we do not manufacture or sell any therapeutic we use in combination with our products or drug candidates. If the NMPA, FDA or another regulatory agency revokes its approval of any therapeutic we use in combination with our products and drug candidates, we will not be able to market our products and drug candidates in combination with such revoked therapeutic. If safety or efficacy issues arise with the therapeutics that we seek to combine with our products and drug candidates in the future, we may experience significant regulatory delays, and we may be required to redesign or terminate the applicable clinical trials. In addition, if manufacturing or other issues result in a supply shortage of any combination therapeutic, we may not be able to successfully commercialize our products or drug candidates on our current timeline or at all.

Even after obtaining regulatory approval for use in combination with any therapeutic, we would continue to be subject to the risk that the NMPA, FDA or another regulatory agency could revoke its approval of the combination therapeutic, or that safety, efficacy, manufacturing or supply issues could arise with any of our combination therapeutic. This could result in our products being removed from the market or being less successful commercially.

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

There is a risk of failure for each of our drug candidates. It is difficult to predict when or if any of our drug candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining regulatory approval from regulatory authorities for the sale of any drug candidate, our drug candidates must complete pre-clinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive, difficult to design and implement, and can take many years to complete.

The outcomes of pre-clinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain regulatory approval of their drug candidates. Future clinical trials of our drug candidates may not be successful. For example, brivanib (ZL-2301) failed to meet its primary endpoint of overall survival, or OS, noninferiority for brivanib (ZL-2301) versus sorafenib in Phase III trials in patients with HCC conducted by Bristol-Myers Squibb Company, or BMS, before we licensed the development rights from them. In addition, brivanib (ZL-2301) showed no difference when compared to placebo in the primary efficacy endpoint. We believe that brivanib (ZL-2301) has the potential to be an effective treatment for Chinese patients and merits further clinical trials patients. We are currently developing ZL-2301 as a combination therapy where ZL-2301 is currently at Phase I dose escalation for the Phase I/II combination trial. We, however, cannot guarantee that our future clinical trials of brivanib (ZL-2301) in Chinese patients will be successful. In early 2018, we terminated ZL-1204, an in-house early-stage candidate, after evaluating the relevant competitive landscape and potential market opportunity.

Commencement of clinical trials is subject to finalizing the trial design based on ongoing discussions with the NMPA, FDA and/or other regulatory authorities. The NMPA, FDA and other regulatory authorities could change their position on the acceptability of trial designs or clinical endpoints, which could require us to complete additional clinical trials or impose approval conditions that we do not currently expect. Successful completion of our clinical trials is a prerequisite to submitting an NDA (or equivalent filing) to the NMPA, FDA and/or other regulatory authorities for each drug candidate and, consequently, the ultimate approval and commercial marketing of our drug candidates. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. There are inherent uncertainties associated with development of our drug candidates. We do not know whether the clinical trials for our drug candidates will begin or be completed on schedule, if at all. Our future clinical trial results may not be favorable.

We may incur additional costs or experience delays in completing pre-clinical or clinical trials, or ultimately be unable to complete the development and commercialization of our products and drug candidates. You may lose all or part of your investment if we are unable to successfully complete clinical development, obtain regulatory approval and successfully commercialize our products and drug candidates.

We may experience delays in completing our pre-clinical or clinical trials, and numerous unforeseen events could arise during, or as a result of, future clinical trials, which could delay or prevent us from receiving regulatory approval, including:

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

We could encounter regulatory delays if a clinical trial is suspended or terminated by us or, as applicable, the IRBs or the ethics committee of the institutions in which such trials are being conducted, by the data safety monitoring board, which is an independent group of experts that is formed to monitor clinical trials while ongoing, or by the NMPA, FDA or other regulatory authorities. Such authorities may impose a suspension or termination due to a number of factors, including: a failure to conduct the clinical trial in accordance with regulatory requirements or the applicable clinical protocols, a failure to obtain the regulatory approval and/or complete record filings with respect to the collection, preservation, use and export of China's human genetic resources, inspection of the clinical trial operations or trial site by the NMPA, FDA or other regulatory authorities that results in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates. Further, the NMPA, FDA or other regulatory authorities may disagree with our clinical trial design or our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials. You may lose all or part of your investment if we are unable to successfully complete clinical development, obtain regulatory approval and successfully commercialize our products and drug candidates.

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

- be delayed in obtaining regulatory approval for our products and drug candidates;
- not obtain regulatory approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- be subject to post-marketing testing requirements;
- encounter difficulties obtaining or be unable to obtain reimbursement for use of our products and drug candidates;
- be subject to restrictions on the distribution and/or commercialization of our products and drug candidates; or
- have our products and drug candidates removed from the market after obtaining regulatory approval.

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

If we are unable to obtain NMPA approval for our products and drug candidates to be eligible for an expedited registration pathway, the time and cost we incur to obtain regulatory approvals may increase. Even if we receive Category 1 drug designation, it may not lead to a faster development, review or approval process.

The NMPA categorizes innovative drug applications as Category 1, provided such drug has a new and clearly defined structure, pharmacological property and apparent clinical value and has not been marketed anywhere in the world. Such innovative drugs will be attributed to Category 1 for their clinical trial application, or CTA, and NDA applications. Our CTAs for ZEJULA and omadacycline (ZL-2401) were approved as Category 1 drugs by the NMPA. A Category 1 designation by the NMPA may not be granted for any of our other drug candidates that will not be first approved in China or, if granted, such designation may not lead to faster development or regulatory review or approval process. Moreover, a Category 1 designation does not increase the likelihood that our product or drug candidates will receive regulatory approval. Optune is a medical device and does not follow the NMPA drug categorization.

Furthermore, despite positive regulatory changes introduced since 2015 which significantly accelerated time to market for innovative drugs, the regulatory process in China is still relatively ambiguous and unpredictable. The NMPA might require us to change our planned clinical study design or otherwise spend additional resources and effort to obtain approval of our drug candidates. In addition, policy changes may contain significant limitations related to use restrictions for certain age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. If we are unable to obtain regulatory approval for our drug candidates in one or more jurisdictions, or any approval contains significant limitations, we may not be able to obtain sufficient funding or generate sufficient revenue to continue the development of our drug candidates or any other drug candidate that we may in-license, acquire or develop in the future.

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

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

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

In addition to in-licensing or acquiring drug candidates, we may engage in future business acquisitions that could disrupt our business, cause dilution to the holders of our Shares and/or ADSs and harm our financial condition and operating results.

We have, from time to time, evaluated partnership opportunities or investments and may, in the future, make acquisitions of, or investments in, companies that we believe have products or capabilities that are a strategic or commercial fit with our current drug candidates and business or otherwise offer opportunities for our company. In connection with these acquisitions or investments, we may:

- issue stock that would dilute the percentage of ownership of the holders of our Shares and/or ADSs;
- incur debt and assume liabilities; and
- incur amortization expenses related to intangible assets or incur large and immediate write-offs.

We also may be unable to find suitable acquisition candidates and we may not be able to complete partnership opportunities or investments on favorable terms, if at all. If we do enter into partnership opportunities or investments, we cannot assure you that it will ultimately strengthen our competitive position or that it will not be viewed negatively by customers, financial markets or investors. Further, future partnership opportunities or investments could also pose numerous additional risks to our operations, including:

- problems integrating the purchased business, products or technologies;
- increases to our expenses;
- the failure to have discovered undisclosed liabilities of the acquired asset or company;
- diversion of management's attention from their day-to-day responsibilities;
- harm to our operating results or financial condition;
- entrance into markets in which we have limited or no prior experience; and
- potential loss of key employees, particularly those of the acquired entity.

We may not be able to complete one or more partnership opportunities or investments or effectively integrate the operations, products or personnel gained through any such partnership opportunities or investments without a material adverse effect on our business, financial condition and results of operations.

We may become involved in lawsuits to protect or enforce our intellectual property.

Competitors may infringe our patent rights or misappropriate or otherwise violate our intellectual property rights. If we are unable to protect our intellectual property, our competitors could use our intellectual property to market offerings similar to ours and we may not be able to compete effectively. Moreover, others may independently develop technologies that are competitive to ours or infringe on our intellectual property. To counter infringement or unauthorized use, litigation may be necessary in the future to enforce or defend our intellectual property rights, to protect our trade secrets or to determine the validity and scope of our own intellectual property rights or the proprietary rights of others. This can be expensive and time consuming. Any claims that we assert against perceived infringers could also provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property rights. We may not be able to prevent third parties from infringing upon or misappropriating our intellectual property, particularly in countries where the laws may not protect intellectual property rights as fully as in the United States. An adverse result in any litigation proceeding could put our patent, as well as any patents that may issue in the future from our pending patent applications, at risk of being invalidated, held unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

We are subject to laws and government regulations relating to privacy and data protection that have required us to modify certain of our policies and procedures with respect to the collection and processing of personal data, and future laws and regulations may cause us to incur additional expenses or otherwise limit our ability to collect and process personal data.

We may be subject to data privacy and security laws in the various jurisdictions in which we operate, obtain or store personally identifiable information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business.

Within the United States, there are numerous federal and state laws and regulations related to the privacy and security of personal information. For example, at the federal level, our operations may be affected by the Health Insurance Portability and Accountability Act of 1996 as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, collectively, HIPAA, which impose obligations on certain "covered entities" and their "business associates" with respect to the privacy and security and transmission of individually identifiable health information. Although we believe that we are not currently directly subject to HIPAA, HIPAA affects the ability of health care providers and other entities with which we may interact to disclose patient health information to us. As another example, at the state level, we are subject to the California Consumer Privacy Act, or CCPA, that became effective on January 1, 2020 and has been enforced by the California Attorney General since July 1, 2020. The CCPA gives California consumers (defined to include all California residents) certain rights, including the right to ask companies to disclose details about the personal information they collect, as well as other rights such as the right to ask companies to delete a consumer's personal information and opt out of the sale of personal information.

Numerous other jurisdictions regulate the privacy and security of personally identifiable data. For example, the General Data Protection Regulation, or GDPR, imposes obligations on companies that operate in our industry with respect to the processing of personal data collected in relation to an establishment located in the European Economic Area (EEA) or in connection with the offering goods and services to individuals located in the EEA or monitoring the behavior of individuals located in the EEA. GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If we or our service providers fail to comply with any applicable GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill. GDPR additionally places restrictions on the cross-border transfer of personal data from the EEA to countries that have not been found by the European Commission to offer adequate data protection legislation, such as the People's Republic of China and the United States. In July 2020, the Court of Justice of the European Union ("CJEU") invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the U.S. This CJEU decision may lead to increased scrutiny on data transfers from the EEA to the U.S. generally and increase our costs of compliance with data privacy legislation. For further information regarding data privacy regulations in China, see "Regulatory Environment — PRC Regulation of Pharmaceutical Product Development and Approval — Data Privacy and Data Protection".

We could be subject to regulatory actions and/or claims made by individuals and groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims under the laws described, as well as for alleged unfair or deceptive practices. If our operations are found to be in violation of any of the privacy laws, rules or regulations that apply to us, we could be subject to penalties, including civil penalties, damages, injunctive relief, and other penalties, which could adversely affect our ability to operate our business and our financial results. We will continue to review these and all future privacy and other laws and regulations to assess whether additional procedural safeguards are warranted, which may cause us to incur additional expenses or otherwise limit our ability to collect and process personal data.

RISKS RELATED TO DOING BUSINESS IN CHINA

Restrictions on currency exchange may limit our ability to receive and use financing in foreign currencies effectively.

Our PRC subsidiaries' ability to obtain foreign exchange is subject to significant foreign exchange controls and, in the case of transactions under the capital account, requires the approval of and/or registration with PRC government authorities, including the state administration of foreign exchange, or SAFE. In particular, if we finance our PRC subsidiaries by means of foreign debt from us or other foreign lenders, the amount is not allowed to, among other things, exceed the statutory limits and such loans must be registered with the local counterpart of the SAFE. If we finance our PRC subsidiaries by means of additional capital contributions, these capital contributions are subject to registration with the State Administration for Market Regulation or its local branch, reporting of foreign investment information with the PRC Ministry of Commerce, or registration with other governmental authorities in China.

In the light of the various requirements imposed by PRC regulations on loans to, and direct investment in, PRC entities by offshore holding companies, we cannot assure you that we will be able to complete the necessary government formalities or obtain the necessary government approvals on timely basis, if at all, with respect to future loans or capital contributions by us to our PRC subsidiaries. If we fail to complete such registrations or obtain such approval, our ability to capitalize or otherwise fund our PRC operations may be negatively affected, which could materially and adversely affect our liquidity and our ability to fund and expand our business.

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

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

Our auditor, like other independent registered public accounting firms operating in China, is not inspected by the U.S. Public Company Accounting Oversight Board, or the PCAOB, and consequently you are deprived of the benefits of such inspection.

Auditors of companies that are registered with the SEC and traded publicly in the United States, including the independent registered public accounting firm of our company, must be registered with the PCAOB, and are required by the laws of the United States to undergo regular inspections by the PCAOB to assess their compliance with the laws of the United States and professional standards. Because substantially all of our operations are within China, a jurisdiction where the PCAOB is currently unable to conduct inspections without the approval of the Chinese authorities, our auditor is not currently inspected by the PCAOB.

In May 2013, the PCAOB entered into a Memorandum of Understanding on Enforcement Cooperation with the China Securities Regulatory Commission, or CSRC, and the Ministry of Finance, to establish a cooperative framework between the parties for the production and exchange of audit documents relevant to investigations undertaken by the PCAOB in the United States or the CSRC or the Ministry of Finance in the PRC. The PCAOB has announced that, since May 2013, cooperation has not been sufficient to enable the PCAOB to obtain timely access to relevant documents and testimony necessary to carry out its mission. The PCAOB continues to address these issues with Chinese regulators, and whether the PCAOB will obtain equivalent access remains an open issue.

In December 2018, the SEC and the PCAOB issued a joint statement highlighting continued challenges faced by the U.S. regulators in their oversight of financial statement audits of U.S.-listed companies with significant operations in China. In April 2020, the SEC and the PCAOB issued another joint statement reiterating the greater risk that disclosures will be insufficient in many emerging markets, including China, compared to those made by U.S. domestic companies. In discussing the specific issues related to the greater risk, the statement again highlights the PCAOB's inability to inspect audit work paper and practices of accounting firms in China, with respect to their audit work of U.S. reporting companies. However, it remains unclear what further actions, if any, the SEC and PCAOB will take to address the problem.

This lack of PCAOB inspections in China prevents the PCAOB from evaluating audits and quality control procedures of any auditors operating in China, including our auditor. As a result, investors may be deprived of the benefits of PCAOB inspections. The inability of the PCAOB to conduct inspections of auditors in China makes it more difficult to evaluate the effectiveness of our auditor 's audit procedures or quality control procedures as compared to auditors outside of China that are subject to PCAOB inspections. Additionally, the SEC, the U.S. Department of Justice and other authorities often have substantial difficulties in bringing and enforcing actions against non-U.S. persons and companies, including those based in China. Investors should understand the attendant risks. Further, as a result, investors may lose confidence in our reported financial information and procedures and the quality of our financial statements as a result thereof.

As part of a continued regulatory focus in the United States on access to audit and other information currently protected by national law, in particular China's, in June 2019, a bipartisan group of lawmakers introduced bills in both houses of Congress that would require the SEC to maintain a list of issuers for which the PCAOB is not able to inspect or investigate an auditor report issued by a foreign public accounting firm. The Ensuring Quality Information and Transparency for Abroad-Based Listings on our Exchanges (EQUITABLE) Act prescribes increased disclosure requirements for such issuers and, beginning in 2025, the delisting from national securities exchanges such as Nasdaq of issuers included for three consecutive years on the SEC's list. In May 2020, the U.S. Senate passed S. 945, the Holding Foreign Companies Accountable Act (the "Kennedy Bill"). If passed by the U.S. House of Representatives and signed by the U.S. President, the Kennedy Bill would amend the Sarbanes-Oxley Act of 2002 to direct the SEC to prohibit securities of any registrant from being listed on any of the U.S. securities exchanges or traded "over-the-counter" if the auditor of the registrant's financial statements is not subject to PCAOB inspection for three consecutive years. Enactment of any of such legislations or other efforts to increase U.S. regulatory access to audit information could cause uncertainty for affected issuers, including us. The market price of our Shares and/or ADSs could be adversely affected, and we could be delisted if we are unable to cure the situation to meet the PCAOB inspection requirement in time. It is unclear if and when any of such proposed legislations will be enacted. Furthermore, there have been recent media reports on deliberations within the U.S. government regarding potentially limiting or restricting China-based companies from accessing U.S. capital markets. On June 4, 2020, the U.S. President issued a memorandum ordering the President's Working Group on Financial Markets, or the PWG, to submit a report to the President that includes recommendations for actions that can be taken by the executive branch and by the SEC or PCAOB on Chinese companies listed on U.S. stock exchanges and their audit firms, in an effort to protect investors in the United States. On August 6, 2020, the PWG released a report recommending that the SEC take steps to implement the five recommendations outlined in the report. In particular, to address companies from non-cooperating jurisdictions, or NCJs, that do not provide the PCAOB with sufficient access to fulfill its statutory mandate, the PWG recommends enhanced listing standards on U.S. stock exchanges. This would require, as a condition to initial and continued exchange listing, PCAOB access to work papers of the principal audit firm for the audit of the listed company. Companies unable to satisfy this condition as a result of governmental restrictions on access to audit work papers in NCJs may satisfy this condition by providing a co-audit from an audit firm with comparable resources and experience where the PCAOB determines it has sufficient access to audit work papers and practices to conduct an appropriate inspection of the co-audit firm. The report permits the listing standards to provide for a transition period until January 1, 2022 for listed companies, but would apply immediately to new listings once the necessary rulemakings and/or standard-setting are effective. If we fail to meet the listing standards, if adopted, before the deadline specified thereunder due to factors beyond our control, we could face possible de-listing from the Nasdaq, deregistration from the SEC and/or other risks, which may materially and adversely affect, or effectively terminate, our ADS trading in the United States.

Changes in U.S. and international trade policies and relations, particularly with regard to China, may adversely impact our business and operating results.

The U.S. government has recently made statements and taken certain actions that led to changes to U.S. and international trade policies and relations, including imposing several rounds of tariffs affecting certain products manufactured in China, as well as imposing certain sanctions and restrictions in relation to China. In March 2018, U.S. President Donald J. Trump announced the imposition of tariffs on steel and aluminum entering the United States and in June 2018 announced further tariffs targeting goods imported from China. Recently both China and the United States have each imposed further tariffs as well as certain sanctions and restrictions on each other, indicating the potential for further fallout between the two countries. It is unknown whether and to what extent new tariffs or other new executive orders, laws or regulations will be adopted, or the effect that any such actions would have on us or our industry. We conduct preclinical and clinical activities and have business operations both in the U.S. and China, any unfavorable government policies on international trade, such as capital controls or tariffs, may affect the demand for our drug products, the competitive position of our drug products, the hiring of scientists and other research and development personnel, and import or export of raw materials in relation to drug development, or prevent us from selling our drug products in certain countries. If any new tariffs, legislation, executive orders and/or regulations are implemented, or if existing trade agreements are renegotiated or, in particular, if the U.S. or PRC governments takes retaliatory actions due to the recent U.S. — China tension, such changes could have an adverse effect on our business, financial condition and results of operations.

It may be difficult to enforce against us or our management in China any judgments obtained from foreign courts.

On July 14, 2006, Hong Kong and China entered into the Arrangement on Reciprocal Recognition and Enforcement of Judgments in Civil and Commercial Matters by the Courts of the Mainland and of the Hong Kong Special Administrative Region Pursuant to Choice of Court Agreements Between Parties Concerned (《關於內地與香港特別行政區法院相互認可和執行當事人協議管轄的民商事案件判決的安排》), or the Arrangement, pursuant to which a party with a final court judgment rendered by a Hong Kong court requiring payment of money in a civil and commercial case according to a choice of court agreement in writing may apply for recognition and enforcement of the judgment in China. Similarly, a party with a final judgment rendered by a Chinese court requiring payment of money in a civil and commercial case pursuant to a choice of court agreement in writing may apply for recognition and enforcement of such judgment in Hong Kong. On January 18, 2019, the Supreme People's Court and the Hong Kong Government signed the Arrangement on Reciprocal Recognition and Enforcement of Judgments in Civil and Commercial Matters by the Courts of the Mainland and of the Hong Kong Special Administrative Region (關於內地與香港特別行政區法院相互認可和執行民商事案件判決的安排), or the New Arrangement, which seeks to establish a mechanism with greater clarity and certainty for recognition and enforcement of judgments in wider range of civil and commercial matters between Hong Kong and the Mainland. The New Arrangement discontinued the requirement for a choice of court agreement for bilateral recognition and enforcement. The New Arrangement will only take effect after the promulgation of a judicial interpretation by the Supreme People's Court and the completion of the relevant legislative procedures in the Hong Kong. The New Arrangement will, upon its effectiveness, supersedes the Arrangement. Therefore, before the New Arrangement becomes effective it may be difficult or impossible to enforce a judgment rendered by a Hong Kong court in China if the parties in the dispute do not agree to enter into a choice of court agreement in writing.

Furthermore, China does not have treaties or agreements providing for the reciprocal recognition and enforcement of judgments awarded by courts of the United States, the United Kingdom, most other western countries or Japan. Hence, the recognition and enforcement in China of judgments of a court in any of these jurisdictions in relation to any matter not subject to a binding arbitration provision may be difficult or even impossible.

We may be subject to fines due to the lack of registration of our leases.

Pursuant to the Measures for Administration of Lease of Commodity Properties (《商品房屋租賃管理辦法》), which was promulgated by the Ministry of Housing and Urban-Rural Development of the PRC (中華人民共和國住房和城鄉建設部) on December 1, 2010 and became effective on February 1, 2011, both lessors and lessees are required to file the lease agreements for registration and obtain property leasing filing certificates for their leases. As of the September 7, 2020 (the "**Latest Practicable Date**"), we leased certain properties primarily as office space in China and did not register all of our lease agreements as tenant. We may be required by relevant governmental authorities to file these lease agreements for registration within a time limit, and may be subject to a fine for non-registration exceeding such time limit, which may range from RMB1,000 to RMB10,000 for each lease agreement. As of the Latest Practicable Date, we were not aware of any action, claim or investigation being conducted or threatened by the competent governmental authorities with respect to such defects in our leased properties.

Failure to renew our current leases or locate desirable alternatives for our leased properties could materially and adversely affect our business.

We lease properties for our offices and manufacturing facilities. We may not be able to successfully extend or renew such leases upon expiration of the current term on commercially reasonable terms or at all, and may therefore be forced to relocate our affected operations. This could disrupt our operations and result in significant relocation expenses, which could adversely affect our business, financial condition and results of operations. In addition, we compete with other businesses for premises at certain locations or of desirable sizes. As a result, even though we could extend or renew our leases, rental payments may significantly increase as a result of the high demand for the leased properties. In addition, we may not be able to locate desirable alternative sites for our current leased properties as our business continues to grow and failure in relocating our affected operations could adversely affect our business and operations.

RISKS RELATED TO INTELLECTUAL PROPERTY

If we or our licensors or collaboration partners do not obtain patent term extension and data exclusivity for our products or their products or any drug candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of our products or any drug candidates we may develop, one or more of our owned or in-licensed U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch Waxman Amendments. The Hatch Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. The PRC has not established a patent term extension system, but the government proposed to grant patent term extension to new drugs for up to 5 years.

In China, there is currently no effective law or regulation providing for patent term extension, patent linkage, or data exclusivity. Therefore, a lower-cost generic or biosimilar drug can emerge onto the market more quickly. Chinese regulators have set forth a framework for integrating patent linkage and data exclusivity into the Chinese regulatory regime and for establishing a pilot program for patent term extension. To be implemented, this framework will require promulgation of laws, regulations and detailed implementation measures. To date, no laws, regulations or implementation measures have been promulgated and become effective. Consequently, the absence of currently effective laws and regulations on patent linkage, patent term extension and data exclusivity or the cancellation of the previous five-year administrative exclusivity for domestically manufactured new drugs could result in much weaker protection for us against generic competition in China. For instance, the patents we have in China are not yet eligible to be extended for patent term lost during clinical trials and the regulatory review process. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

RISKS RELATED TO OUR SHARES, THE ADSS, THE LISTING AND THE GLOBAL OFFERING

As a company applying for listing under Chapter 19C and Chapter 18A, we adopt different practices as to certain matters as compared with many other companies listed on the Hong Kong Stock Exchange.

As we are applying for listing under Chapter 19C and Chapter 18A of the Listing Rules, we will not be subject to certain provisions of the Listing Rules pursuant to Rule 19C.11, including, among others, rules on notifiable transactions, connected transactions, share option schemes, content of financial statements as well as certain other continuing obligations. In addition, in connection with the Listing, we have applied for a number of waivers and/or exemptions from strict compliance with the Listing Rules, the Companies (WUMP) Ordinance, the Takeovers Codes and the SFO. As a result, we will adopt different practices as to those matters as compared with other companies listed on the Hong Kong Stock Exchange that do not enjoy those exemptions or waivers.

Furthermore, if 55% or more of the total worldwide trading volume, by dollar value, of our Shares and ADSs over our most recent fiscal year takes place on the Hong Kong Stock Exchange, the Hong Kong Stock Exchange will regard us as having a dual primary listing in Hong Kong and we will no longer enjoy certain exemptions or waivers from strict compliance with the requirements under the Listing Rules, the Companies (WUMP) Ordinance, the Takeovers Codes and the SFO, which could result in our incurring of incremental compliance costs.

The trading prices of our Shares and/or ADSs can be volatile, which could result in substantial losses to you.

The trading price of our Shares and/or ADSs can be volatile and fluctuate widely in response to a variety of factors, many of which are beyond our control. For example, from September 19, 2017 to the Latest Practicable Date, the closing price of our ADSs ranged from a high of US$89.48 to a low of US$14.29 per ADS. In addition, the performance and fluctuation of the market prices of other companies with business operations located mainly in the PRC that have listed their securities in Hong Kong or the United States may affect the volatility in the price of and trading volumes for our Shares and/or ADSs. The securities of some of these companies have experienced significant volatility since their initial public offerings, including, in some cases, substantial price declines in the trading prices of their securities. The trading performances of these PRC companies' securities may affect the overall investor sentiment towards other PRC companies listed in Hong Kong or the United States and consequently may impact the trading performance of our Shares and/or ADSs, regardless of our actual operating performance. In addition, any negative news or perceptions about inadequate corporate governance practices or fraudulent accounting, corporate structure or matters of other Chinese companies may also negatively affect the attitudes of investors towards Chinese companies in general, including us, regardless of whether we have conducted any inappropriate activities.

In addition to market and industry factors, the price and trading volume for our Shares and/or ADSs may be highly volatile for specific business reasons, including:

- announcements of regulatory approval or a complete response letter, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- announcements of therapeutic innovations, new products, acquisitions, strategic relationships, joint ventures or capital commitments by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;

- any adverse changes to our relationship with manufacturers or suppliers; the results of our testing and clinical trials;
- the results of our efforts to acquire or license additional drug candidates; variations in the level of expenses related to our existing products and drug candidates or preclinical, clinical development and commercialization programs;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general; fluctuations in product revenue, sales and marketing expenses and profitability; manufacture, supply or distribution shortages;
- variations in our results of operations; announcements about our results of operations that are not in line with analyst expectations, the risk of which is enhanced because it is our policy not to give guidance on results of operations;
- publication of operating or industry metrics by third parties, including government statistical agencies, that differ from expectations of industry or financial analysts;
- changes in financial estimates by securities research analysts; media reports, whether or not true, about our business;
- additions to or departures of our management; fluctuations of exchange rates between the RMB, the U.S. dollar and Hong Kong dollar;
- release or expiry of lock-up or other transfer restrictions on our outstanding Shares or ADSs;
- sales or perceived potential sales of additional Shares or ADSs by us, our executive officers and directors or our Shareholders; general economic and market conditions and overall fluctuations in the U.S. or Hong Kong equity markets; changes in accounting principles; and
- changes or developments in the PRC or global regulatory environment.

Furthermore, the stock market, in general, and pharmaceutical and biotechnology companies have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our Shares and/or ADSs, regardless of our actual operating performance. Further, the current volatility in the financial markets and related factors beyond our control may cause the ordinary share and/or ADS price to decline rapidly and unexpectedly.

In addition, our directors and employees may face additional exposure to claims and lawsuits as a result of their position in other public companies. The existence of litigation, claims, investigations and proceedings against our directors and employees, even if they do not involve our company, may harm our reputation and adversely affect the trading price of our Shares and/or ADSs.

We may be at an increased risk of securities class action litigation.

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

If we fail to establish and maintain proper internal financial reporting controls, our ability to produce accurate financial statements or comply with applicable regulations could be impaired.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to file a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. The presence of material weaknesses in internal control over financial reporting could result in financial statement errors which, in turn, could lead to errors in our financial reports and/or delays in our financial reporting, which could require us to restate our operating results. We might not identify one or more material weaknesses in our internal controls in connection with evaluating our compliance with Section 404 of the Sarbanes-Oxley Act. In order to maintain and improve the effectiveness of our disclosure controls and procedures and internal controls over financial reporting, we will need to expend significant resources and provide significant management oversight. Implementing any appropriate changes to our internal controls may require specific compliance training of our directors and employees, entail substantial costs in order to modify our existing accounting systems, take a significant period of time to complete and divert management's attention from other business concerns. These changes may not, however, be effective in maintaining the adequacy of our internal control.

If we fail to maintain effective internal control over financial reporting in the future, our management and our independent registered public accounting firm may not be able to conclude that we have effective internal controls over financial reporting, investors may lose confidence in our operating results, the price of our Shares and/or ADSs could decline and we may be subject to litigation or regulatory enforcement actions. In addition, if we are unable to meet the requirements of Section 404 of the Sarbanes-Oxley Act, the ADSs may not be able to remain listed on Nasdaq.

While we currently enjoy exemptions afforded to a foreign private issuer, we will be subject to U.S. domestic issuer disclosure requirements beginning on January 1, 2021, which could result in significant additional costs and expenses.

We currently still enjoy certain exemptions afforded to a foreign private issuer for the year of 2020, during which period we are not required to comply with all of the periodic disclosure and current reporting requirements of the U.S. Exchange Act and therefore there may be less publicly available information about us than if we were a U.S. domestic issuer. For example, we are currently not subject to the proxy rules in the United States and disclosure with respect to our annual general meetings will be governed by the Cayman Islands requirements. In addition, our officers, directors and principal Shareholders are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the U.S. Exchange Act and the rules thereunder. Therefore, our Shareholders may not know on a timely basis when our officers, directors and principal Shareholders purchase or sell our Shares or ADSs.

In addition, as a foreign private issuer, we are currently permitted to take advantage of certain provisions in Nasdaq rules that allow us to follow Cayman Islands law for certain governance matters. Certain corporate governance practices in the Cayman Islands may differ significantly from corporate governance listing standards as, except for general fiduciary duties and duties of care, Cayman Islands law has no corporate governance regime which prescribes specific corporate governance standards. We currently follow Cayman Islands corporate governance practices in lieu of the corporate governance requirements of Nasdaq in respect of the following: (i) the majority independent director requirement under Section 5605(b)(1) of Nasdaq rules, (ii) the requirement under Section 5605(d) of Nasdaq rules that a compensation committee comprised solely of independent directors governed by a compensation committee charter oversee executive compensation, (iii) the requirement under Section 5605(e) of Nasdaq rules that director nominees be selected or recommended for selection by either a majority of the independent directors or a nominations committee comprised solely of independent directors and (iv) the requirement under Section 5605(b)(2) of Nasdaq rules that our independent directors hold regularly scheduled executive sessions. Therefore, our Shareholders may be afforded less protection than they otherwise would have under corporate governance listing standards applicable to U.S. domestic issuers.

However, the determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter and, in our case, June 30, 2020. We have determined that, as of July 1, 2020, more than 50% of our Shares were directly or indirectly held by residents of the U.S. and, therefore, we will file with the SEC periodic reports and registration statements on U.S. domestic issuer forms beginning on January 1, 2021, which are more detailed and extensive than the forms available to a foreign private issuer. We will also have to mandatorily comply with U.S. federal proxy requirements, and our officers, directors and principal Shareholders will become subject to the short-swing profit disclosure and recovery provisions of Section 16 of the U.S. Exchange Act beginning on January 1, 2021. In addition, we will lose our ability to rely upon exemptions from certain corporate governance requirements under Nasdaq rules described above beginning on January 1, 2021. As a U.S. listed public company that is not a foreign private issuer, we will incur significant additional legal, accounting and other expenses that we will not incur as a foreign private issuer, and accounting, reporting and other expenses in order to maintain a listing on a U.S. securities exchange.

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

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

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

The value of the renminbi against the U.S. dollar and other currencies may fluctuate and is affected by, among other things, changes in political and economic conditions. On July 21, 2005, China government changed its decade-old policy of pegging the value of the renminbi to the U.S. dollar, and the renminbi appreciated more than 20% against the U.S. dollar over the following three years. Between July 2008 and June 2010, this appreciation halted, and the exchange rate between the renminbi and U.S. dollar remained within a narrow band. In June 2010, the PBOC announced that China government would increase the flexibility of the exchange rate, and thereafter allowed the renminbi to appreciate slowly against the U.S. dollar within the narrow band fixed by the PBOC. However, more recently, on August 11, 12 and 13, 2015, the PBOC significantly devalued the renminbi by fixing its price against the U.S. dollar 1.9%, 1.6%, and 1.1% lower than the previous day's value, respectively. On October 1, 2016, the renminbi joined the International Monetary Fund's basket of currencies that make up the Special Drawing Right, or SDR, along with the U.S. dollar, the Euro, the Japanese yen and the British pound. In the fourth quarter of 2016, the renminbi depreciated significantly while the U.S. dollar surged and China experienced persistent capital outflows. With the development of the foreign exchange market and progress towards interest rate liberalization and renminbi internationalization, the Chinese government may in the future announce further changes to the exchange rate system. There is no guarantee that the renminbi will not appreciate or depreciate significantly in value against the U.S. dollar in the future. It is difficult to predict how market forces or PRC or U.S. government policy may impact the exchange rate between the renminbi and the U.S. dollar in the future.

Significant revaluation of the renminbi may have a material adverse effect on your investment. For example, to the extent that we need to convert U.S. dollars into renminbi for our operations, appreciation of the renminbi against the U.S. dollar would have an adverse effect on the renminbi amount we would receive from the conversion. Conversely, if we decide to convert our renminbi into U.S. dollars for the purpose of making payments for dividends on our Shares or ADSs or for other business purposes, appreciation of the U.S. dollar against the renminbi would have a negative effect on the U.S. dollar amount available to us. In addition, appreciation or depreciation in the value of the renminbi relative to U.S. dollars would affect our financial results reported in U.S. dollar terms regardless of any underlying change in our business or results of operations.

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

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

Holders of our ADSs do not have the same rights as our Shareholders and may only exercise the voting rights with respect to the underlying Shares in accordance with the provisions of the deposit agreement. Under our Articles of Association, an annual general meeting and any extraordinary general meeting may be called with not less than seven days' notice. When a general meeting is convened, the holders of ADSs may not receive sufficient notice of a Shareholders' meeting to permit them to withdraw the Shares underlying their ADSs to allow them to vote with respect to any specific matter. If we ask for the instructions of the holders of ADSs, we will give the depositary notice of any such meeting and details concerning the matters to be voted upon at least 30 days in advance of the meeting date and the depositary will send a notice to the holders of ADSs about the upcoming vote and will arrange to deliver our voting materials to them. The depositary and its agents, however, may not be able to send voting instructions to the holders of ADSs or carry out their voting instructions in a timely manner. We will make all commercially reasonable efforts to cause the depositary to extend voting rights to the holders of ADSs in a timely manner, but there can be no guarantee that the holders of ADSs will receive the voting materials in time to ensure that the holders of ADSs can instruct the depositary to vote the Shares underlying their ADSs. Furthermore, the depositary will not be liable for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. A holder or beneficial owner of ADSs may have limited recourse if we or the depositary fail to meet our respective obligations under the deposit agreement or if they wish us or the depositary to participate in legal proceedings. As a result, the holders of ADSs may not be able to exercise their right to vote and they may lack recourse if their ADSs are not voted as they request. In addition, in their capacity as an ADS holder, the holders of ADSs will not be able to call a Shareholders' meeting.

In addition, under the deposit agreement, if you do not vote, the depositary may give us a discretionary proxy to vote the ordinary shares underlying the ADSs at shareholders' meetings if we have timely provided the depositary with notice of meeting and related voting materials and with a brief statement as to the manner and timing in which voting instructions may be deemed to have been given in accordance with the depositary agreement if no instructions are received prior to the deadline set for such purposes to the depositary to give a discretionary proxy to a person designated by us. The effect of this discretionary proxy is that you cannot prevent our Shares underlying your ADSs from being voted, except under the circumstances described above. This may adversely affect your interests and make it more difficult for ADS holders to influence the management of our company. Holders of our Shares are not subject to this discretionary proxy.

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

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

The right of the holders of ADSs to participate in any future rights offerings may be limited, which may cause dilution to your holdings.

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

We are a Cayman Islands company. Because judicial precedent regarding the rights of Shareholders is more limited under Cayman Islands law than under Hong Kong law or U.S. law, Shareholders may have fewer Shareholder rights than they would have under Hong Kong law or U.S. law and may face difficulties in protecting your interests.

We are an exempted company with limited liability incorporated in the Cayman Islands. Our corporate affairs are governed by our Articles of Association (as may be further amended from time to time), the Companies Law (as amended) of the Cayman Islands and the common law of the Cayman Islands. The rights of Shareholders to take action against the directors, actions by minority Shareholders and the fiduciary responsibilities of our directors are to a large extent governed by the common law of the Cayman Islands. This common law is derived in part from comparatively limited judicial precedent in the Cayman Islands as well as from English common law, which has persuasive, but not binding, authority on a court in the Cayman Islands. The rights of our Shareholders and the fiduciary responsibilities of our directors under Cayman Islands law are not as clearly established as they would be under statutes or judicial precedent in some jurisdictions in Hong Kong and the United States. In particular, the Cayman Islands has a less developed body of securities law than the Hong Kong or United States In addition, some states in the United States, such as Delaware, have more fully developed and judicially interpreted bodies of corporate law than the Cayman Islands.

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

Some of our directors and executive officers reside outside of Hong Kong and the United States and a substantial portion of their assets are located outside of Hong Kong and the United States. As a result, it may be difficult or impossible for you to bring an action against us or against these individuals in the Cayman Islands or in China in the event that you believe that your rights have been infringed under the securities laws of Hong Kong, the United States or otherwise. In addition, some of our operating subsidiaries are incorporated in China. To the extent our directors and executive officers reside in China or their assets are located in China, it may not be possible for investors to effect service of process upon us or our management inside China. Even if you are successful in bringing an action, the laws of the Cayman Islands and China may render you unable to enforce a judgment against our assets or the assets of our directors and officers. There is no statutory recognition in the Cayman Islands of judgments obtained in the United States, Hong Kong or China, although the courts of the Cayman Islands will generally recognize and enforce a non-penal judgment of a foreign court of competent jurisdiction without retrial on the merits.

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

Taxing authorities could reallocate our taxable income among our subsidiaries, which could increase our overall tax liability.

We are incorporated under the laws of the Cayman Islands and currently have subsidiaries in China, Hong Kong, the Cayman Islands, the United States, Australia and the British Virgin Islands. If we succeed in growing our business we expect to conduct increased operations through our subsidiaries in various tax jurisdictions pursuant to transfer pricing arrangements between us, our parent company and our subsidiaries. If two or more affiliated companies are located in different countries, the tax laws or regulations of each country generally will require that transfer prices be the same as those between unrelated companies dealing at arms' length and that appropriate documentation is maintained to support the transfer prices. While we believe that we operate in compliance with applicable transfer pricing laws and intend to continue to do so, our transfer pricing procedures are not binding on applicable tax authorities.

If tax authorities in any of these countries were to successfully challenge our transfer prices as not reflecting arms' length transactions they could require us to adjust our transfer prices and thereby reallocate our income to reflect these revised transfer prices, which could result in a higher tax liability to us. In addition, if the country from which the income is reallocated does not agree with the reallocation, both countries could tax the same income, resulting in double taxation. If tax authorities were to allocate income to a higher tax jurisdiction, subject our income to double taxation or assess interest and penalties, it would increase our consolidated tax liability, which could adversely affect our financial condition, results of operations and cash flows.

A tax authority could asset that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Holders of our Shares and/or ADSs may have difficulty enforcing judgments obtained against us.

We are a company incorporated under the laws of the Cayman Islands, and substantially all of our assets are located outside the United States. Substantially all of our current operations are conducted in the PRC. In addition, some of our directors and officers are nationals and residents of countries or regions other than the United States or Hong Kong. A substantial portion of the assets of these persons are located outside the United States. As a result, it may be difficult for investors to effect service of process within the United States or Hong Kong upon these persons, or to bring an action against us or against these individuals in the United States or Hong Kong in the event that they believe that their rights have been infringed under the U.S. federal securities laws, Hong Kong laws or otherwise. Even if shareholders are successful in bringing an action of this kind, the laws of the Cayman Islands and China may render them unable to enforce a judgment against our assets or the assets of our directors and officers. There is uncertainty as to whether the courts of the Cayman Islands or China would recognize or enforce judgments of U.S. courts against us or such persons predicated upon the civil liability provisions of the securities laws of the United States or any state.

The recognition and enforcement of foreign judgments are provided for under China Civil Procedures Law. PRC courts may recognize and enforce foreign judgments in accordance with the requirements of China Civil Procedures Law based either on treaties between China and the country where the judgment is made or on principles of reciprocity between jurisdictions. China does not have any treaties or other forms of reciprocity with the United States that provide for the reciprocal recognition and enforcement of foreign judgments. In addition, according to China Civil Procedures Law, China courts will not enforce a foreign judgment against us or our directors and officers if they decide that the judgment violates the basic principles of PRC laws or national sovereignty, security or public interest. As a result, it is uncertain whether and on what basis a PRC court would enforce a judgment rendered by a court in the United States.

Holders of ADSs may be subject to limitations on transfers of their ADSs.

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

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

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

Divestiture in the future of our Shares and/or ADSs by Shareholders, the announcement of any plan to divest our Shares and/or ADS, or hedging activity by third-party financial institutions in connection with similar derivative or other financing arrangements entered into by Shareholders, could cause the price of our Shares and/or ADSs to decline. Furthermore, although all of our directors and executive officers have agreed to a lock-up of their Shares, any major disposal of our Shares and/or ADSs by any of them upon expiration of the relevant lock-up periods (or the perception that these disposals may occur upon the expiration of the lock-up period) may cause the prevailing market price of our Shares and/or ADSs to fall which could negatively impact our ability to raise equity capital in the future.

The different characteristics of the capital markets in Hong Kong and the U.S. may negatively affect the trading prices of our Shares and/or ADSs.

Upon the Listing, we will be subject to Hong Kong and Nasdaq listing and regulatory requirements concurrently. The Hong Kong Stock Exchange and Nasdaq have different trading hours, trading characteristics (including trading volume and liquidity), trading and listing rules, and investor bases (including different levels of retail and institutional participation). As a result of these differences, the trading prices of our Shares and our ADSs may not be the same, even allowing for currency differences. Fluctuations in the price of our ADSs due to circumstances peculiar to the U.S. capital markets could materially and adversely affect the price of our Shares, or vice versa. Certain events having significant negative impact specifically on the U.S. capital markets may result in a decline in the trading price of our Shares notwithstanding that such event may not impact the trading prices of securities listed in Hong Kong generally or to the same extent, or vice versa. Because of the different characteristics of the U.S. and Hong Kong capital markets, the historical market prices of our ADSs may not be indicative of the trading performance of our Shares after the Global Offering.

Exchange between our Shares and our ADSs may adversely affect the liquidity and/or trading price of each other.

Our ADSs are currently traded on Nasdaq. Subject to compliance with U.S. securities law and the terms of the Deposit Agreement, holders of our Shares may deposit Shares with the depositary in exchange for the issuance of our ADSs. Any holder of ADSs may also withdraw the underlying Shares represented by the ADSs pursuant to the terms of the Deposit Agreement for trading on the Hong Kong Stock Exchange. In the event that a substantial number of Shares are deposited with the depositary in exchange for ADSs or vice versa, the liquidity and trading price of our Shares on the Hong Kong Stock Exchange and our ADSs on Nasdaq may be adversely affected.

The time required for the exchange between our Shares and ADSs might be longer than expected and investors might not be able to settle or effect any sale of their securities during this period, and the exchange of Shares into ADSs involves costs.

There is no direct trading or settlement between Nasdaq and the Hong Kong Stock Exchange on which our ADSs and our Shares are respectively traded. In addition, the time differences between Hong Kong and New York and unforeseen market circumstances or other factors may delay the deposit of Shares in exchange of ADSs or the withdrawal of Shares underlying the ADSs. Investors will be prevented from settling or effecting the sale of their securities during such periods of delay. In addition, there is no assurance that any exchange of Shares into ADSs (and vice versa) will be completed in accordance with the timelines investors may anticipate.

Furthermore, the depositary for the ADSs is entitled to charge holders fees for various services including for the issuance of ADSs upon deposit of Shares, cancelation of ADSs, distributions of cash dividends or other cash distributions, distributions of ADSs pursuant to share dividends or other free share distributions, distributions of securities other than ADSs and annual service fees. As a result, Shareholders who exchange Shares into ADSs, and vice versa, may not achieve the level of economic return the Shareholders may anticipate.

If securities or industry analysts do not continue to publish research or publish inaccurate or unfavorable research about our business, the market price for our Shares and/or ADSs and trading volume could decline.

The trading market for our Shares and/or ADSs relies in part on the research and reports that equity research analysts publish about us or our business. We do not control these analysts. If research analysts do not maintain adequate research coverage or if one or more of the analysts who covers us downgrades our Shares and/or ADSs or publishes inaccurate or unfavorable research about our business, the market price for our Shares and/or ADSs would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, we could lose visibility in the financial markets, which, in turn, could cause the market price or trading volume for the Shares and/or ADSs to decline significantly. As the public offering price is higher than our net tangible book value per ordinary share, you will incur immediate and substantial dilution.

If you purchase Shares in the Global Offering, you will pay more for your Shares than the amount paid by existing holders for their Shares or ADSs on a per ordinary share basis. As a result, you will experience immediate and substantial dilution after giving effect to the Global Offering. In addition, you will experience further dilution to the extent that our Shares are issued upon the exercise of share options or vesting of restricted share units. All of the Shares issuable upon the exercise of currently outstanding share options will be issued at a purchase price on a per ordinary share basis that is less than the public offering price per ordinary share in the Global Offering.

An active trading market for our Shares on the Hong Kong Stock Exchange might not develop or be sustained and trading prices of our Shares might fluctuate significantly.

Following the completion of the Global Offering, we cannot assure you that an active trading market for our Shares on the Hong Kong Stock Exchange will develop or be sustained. The trading price or liquidity for our ADSs on Nasdaq might not be indicative of those of our Shares on the Hong Kong Stock Exchange following the completion of the Global Offering. If an active trading market of our Shares on the Hong Kong Stock Exchange does not develop or is not sustained after the Global Offering, the market price and liquidity of our Shares could be materially and adversely affected.

In 2014, the Hong Kong, Shanghai and Shenzhen Stock Exchanges collaborated to create an inter-exchange trading mechanism called Stock Connect that allows international and mainland Chinese investors to trade eligible equity securities listed in each other's markets through the trading and clearing facilities of their home exchange. Stock Connect currently covers over 2,000 equity securities trading in the Hong Kong, Shanghai and Shenzhen markets. Stock Connect allows mainland Chinese investors to trade directly in eligible equity securities listed on the Hong Kong Stock Exchange, known as Southbound Trading; without Stock Connect, mainland Chinese investors would not otherwise have a direct and established means of engaging in Southbound Trading. The ineligibility or any delay of our Shares for trading through Stock Connect will affect mainland Chinese investors' ability to trade our Shares and therefore may limit the liquidity of the trading of our Shares on the Hong Kong Stock Exchange.

Since there will be a gap of several days between pricing and trading of our Shares, the price of our ADSs traded on Nasdaq may fall during this period and could result in a fall in the price of our Shares to be traded on the Hong Kong Stock Exchange. The pricing of the Offer Shares will be determined on the Price Determination Date.

However, our Shares will not commence trading on the Hong Kong Stock Exchange until they are delivered, which is expected to be about four Hong Kong business days after the Price Determination Date. As a result, investors may not be able to sell or otherwise deal in our Shares during that period. Accordingly, holders of our Shares are subject to the risk that the trading price of our Shares could fall when trading commences as a result of adverse market conditions or other adverse developments that could occur between the Price Determination Date and the time trading begins. In particular, as our ADSs will continue to be traded on Nasdaq and their price can be volatile, any fall in the price of our ADSs may result in a fall in the price of our Shares to be traded on the Hong Kong Stock Exchange.

There is uncertainty as to whether Hong Kong stamp duty will apply to the trading or conversion of our ADSs following our initial public offering in Hong Kong and Listing of our Shares on the Hong Kong Stock Exchange.

In connection with our initial public offering of Shares in Hong Kong, or the Hong Kong IPO, we will establish a branch register of members in Hong Kong, or the Hong Kong share register. Our Shares that are traded on the Hong Kong Stock Exchange, including those to be issued in the Hong Kong IPO and those that may be converted from ADSs, will be registered on the Hong Kong share register, and the trading of these Shares on the Hong Kong Stock Exchange will be subject to the Hong Kong stamp duty. To facilitate ADS-ordinary share conversion and trading between Nasdaq and the Hong Kong Stock Exchange, we also intend to move a portion of our issued Shares from our register of members maintained in the Cayman Islands to our Hong Kong share register.

Under the Hong Kong Stamp Duty Ordinance, any person who effects any sale or purchase of Hong Kong stock, defined as stock the transfer of which is required to be registered in Hong Kong, is required to pay Hong Kong stamp duty. The stamp duty is currently set at a total rate of 0.2% of the greater of the consideration for, or the value of, shares transferred, with 0.1% payable by each of the buyer and the seller. To the best of our knowledge, Hong Kong stamp duty has not been levied in practice on the trading or conversion of ADSs of companies that are listed in both the United States and Hong Kong and that have maintained all or a portion of their ordinary shares, including ordinary shares underlying ADSs, in their Hong Kong share registers. However, it is unclear whether, as a matter of Hong Kong law, the trading or conversion of ADSs of these dual-listed companies constitutes a sale or purchase of the underlying Hong Kong-registered ordinary shares that is subject to Hong Kong stamp duty. We advise investors to consult their own tax advisors on this matter. If Hong Kong stamp duty is determined by the competent authority to apply to the trading or conversion of our ADSs, the trading price and the value of your investment in our Shares and/or ADSs may be affected.

There can be no assurance of the accuracy or completeness of certain facts, forecasts and other statistics obtained from various independent third party sources, including the industry expert reports, contained in this document.

This document, particularly the sections headed "Business" and "Industry Overview," contains information and statistics relating to the global and China oncology drug markets. Such information and statistics have been derived from a third-party report commissioned by us and publicly available sources. We believe that the sources of the information are appropriate sources for such information, and we have taken reasonable care in extracting and reproducing such information. However, we cannot guarantee the quality or reliability of such source materials. The information has not been independently verified by us, the Joint Sponsors, the Joint Representatives, the Joint Global Coordinators, the Joint Bookrunners, the Joint Lead Managers, or any other party involved in the Global Offering, and no representation is given as to its accuracy. Collection methods of such information may be flawed or ineffective, or there may be discrepancies between published information and market practice, which may result in the statistics included in this document being inaccurate or not comparable to statistics produced for other economies. You should therefore not place undue reliance on such information. In addition, we cannot assure you that such information is stated or compiled on the same basis or with the same degree of accuracy as similar statistics presented elsewhere. You should consider carefully the importance placed on such information or statistics.

You should read the entire document carefully and should not rely on any information contained in press articles or other media regarding us and the Global Offering. We strongly caution you not to rely on any information contained in press articles or other media regarding us and the Global Offering. Prior to the publication of this document, there has been press and media coverage regarding us and the Global Offering. Such press and media coverage may include references to certain information that does not appear in this document, including certain operating and financial information and projections, valuations and other information. We have not authorized the disclosure of any such information in the press or media and do not accept any responsibility for any such press or media coverage or the accuracy or completeness of any such information or publication. We make no representation as to the appropriateness, accuracy, completeness or reliability of any such information or publication. To the extent that any such information is inconsistent or conflicts with the information contained in this document, we disclaim responsibility for it and you should not rely on such information.

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The following section sets forth new information relating to the Global Offering, including information concerning stamp duty and the establishment of a Hong Kong Share Registrar, the conversion between our ADSs listed on the Nasdaq and our Shares proposed to be listed on the Main Board of the Hong Kong Stock Exchange.

Register of Members and Stamp Duty

Our principal register of members will be maintained by our principal share registrar in the Cayman Islands, and our Hong Kong register of members will be maintained by the Hong Kong Share Registrar, Computershare Hong Kong Investor Services Limited, in Hong Kong.

Dealings in our Shares registered on our Hong Kong share register will be subject to Hong Kong stamp duty. The stamp duty is charged to each of the seller and purchaser at the ad valorem rate of 0.1% of the consideration for, or (if greater) the value of, our Shares transferred. In other words, a total of 0.2% is currently payable on a typical sale and purchase transaction of our Shares. In addition, a fixed duty of HK$5.00 is charged on each instrument of transfer (if required).

To facilitate deposits of Shares to and withdrawals of Shares from the ADS facility, we also intend to move a portion of our issued Shares, including all of the Shares deposited in our ADS program, from our Cayman share register to our Hong Kong share register. It is unclear whether, as a matter of Hong Kong law, the trading of ADSs representing Shares constitutes a sale or purchase of the underlying Hong Kong-registered Shares that is subject to Hong Kong stamp duty. We advise investors to consult their own tax advisors on this matter. See "Risk Factors — Risks related to our Shares, the ADSs, the Listing and the Global Offering — There is uncertainty as to whether Hong Kong stamp duty will apply to the trading or conversion of our ADSs following our initial public offering in Hong Kong and Listing of our Shares on the Hong Kong Stock Exchange."

Dealings and Settlement of Shares in Hong Kong

Our Shares will trade on the Hong Kong Stock Exchange in board lots of 50 Shares. Dealings in our Shares on the Hong Kong Stock Exchange will be conducted in Hong Kong dollars.

The transaction costs of dealings in our Shares on the Hong Kong Stock Exchange include:

(a) Hong Kong Stock Exchange trading fee of 0.005% of the consideration of the transaction, charged to each of the buyer and seller;

(b) SFC transaction levy of 0.0027% of the consideration of the transaction, charged to each of the buyer and seller;

(c) trading tariff of HK$0.50 on each and every purchase or sale transaction. The decision on whether or not to pass the trading tariff onto investors is at the discretion of brokers;

(d) transfer deed stamp duty of HK$5.00 per transfer deed (if applicable), payable by the seller;

(e) ad valorem stamp duty at a total rate of 0.2% of the value of the transaction, with 0.1% payable by each of the buyer and the seller;

(f) stock settlement fee, which is currently 0.002% of the gross transaction value, subject to a minimum fee of HK$2.00 and a maximum fee of HK$100.00 per side per trade;

(g) brokerage commission, which is freely negotiable with the broker (other than brokerage commissions for IPO transactions which are currently set at 1% of the subscription or purchase price and will be payable by the person subscribing for or purchasing the securities); and

(h) the Hong Kong share registrar will charge between HK$2.50 to HK$20, depending on the speed of service (or such higher fee as may from time to time be permitted under the Listing Rules), for each transfer of Shares from one registered owner to another, each share certificate canceled or issued by it and any applicable fee as stated in the share transfer forms used in Hong Kong.

Investors must settle their trades executed on the Hong Kong Stock Exchange through their brokers directly or through custodians. For an investor who has deposited his/her Shares in his/her stock account or in his/her designated CCASS participant's stock account maintained with CCASS, settlement will be effected in CCASS in accordance with the General Rules of CCASS and CCASS Operational Procedures in effect from time to time. For an investor who holds the physical certificates, settlement certificates and the duly executed transfer forms must be delivered to his/her broker or custodian before the settlement date.

Exchanges Between Shares Trading in Hong Kong and ADSs

In connection with the initial public offering of our Shares in Hong Kong, or the Hong Kong Public Offering, we have established a branch register of members in Hong Kong, or the Hong Kong share register, which will be maintained by our Hong Kong Share Registrar, Computershare Hong Kong Investor Services Limited. Our principal register of members, or the Cayman share register, will continue to be maintained by our Principal Share Registrar, International Corporation Services Ltd.

All Shares offered in the Hong Kong Public Offering will be registered on the Hong Kong share register in order to be listed and traded on the Hong Kong Stock Exchange. Holders of Shares registered on the Hong Kong share register will be able to exchange those Shares for ADSs and vice versa.

The following section sets forth new information and statistics relating to the industry in which we operate. Such information and statistics were extracted from different official government publications, available sources from public market research and other sources from independent suppliers. In addition, we engaged Frost & Sullivan for preparing the Frost & Sullivan Report, an independent industry report in respect of the Global Offering.

OVERVIEW OF THE GLOBAL AND CHINA PHARMACEUTICAL MARKETS

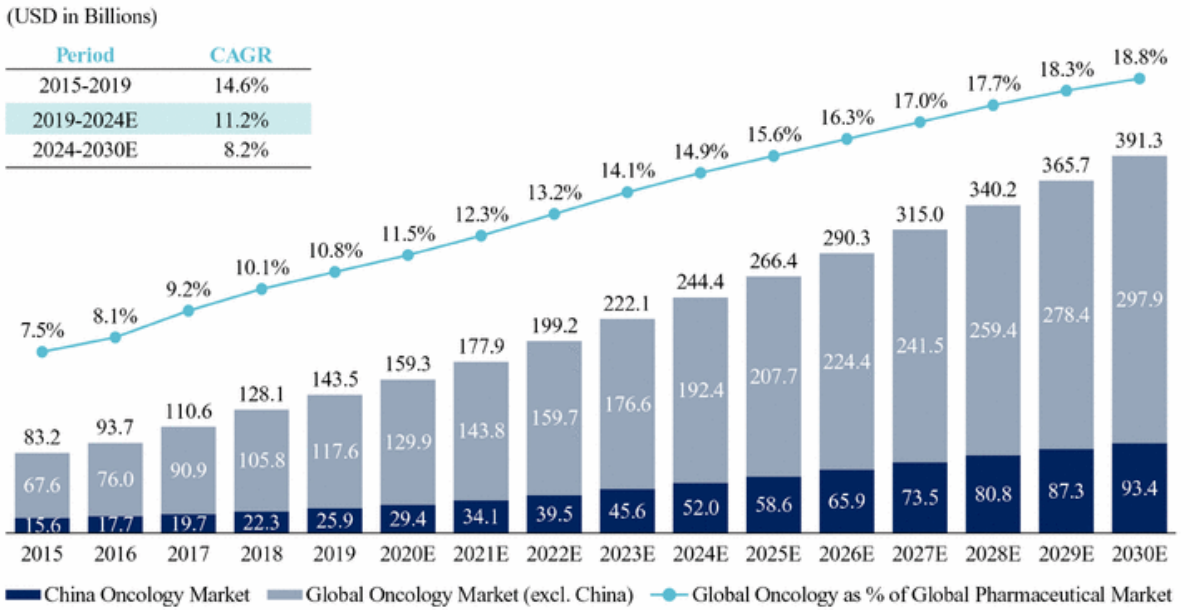
The global pharmaceutical market grew from US$1,105.0 billion in 2015 to US$1,324.5 billion in 2019, representing a CAGR of 4.6% from 2015 to 2019. The market is expected to further grow to US$1,639.5 billion in 2024, at a CAGR of 4.4% from 2019 to 2024, and to US$2,078.5 billion in 2030, at a CAGR of 4.0% from 2024 to 2030. Such growth will be primarily driven by an aging population, increasing prevalence of chronic diseases, increasing affordability, rising public health awareness, as well as continuous innovation and product launches as the result of increasing capital investment into the pharmaceutical industry.

China's pharmaceutical market, the second largest in the world, has benefited from strong momentum in healthcare demand, having increased in size from RMB1,220.7 billion in 2015 to RMB1,633.0 billion in 2019, representing a CAGR of 7.5% from 2015 to 2019. The market is expected to grow to RMB2,228.8 billion in 2024, representing a CAGR of 6.4% from 2019 to 2024. By 2030, China's pharmaceutical market is estimated to reach RMB3,194.5 billion in sales. This growth rate, surpassing the expected growth rate of the global pharmaceutical market during the same period, is driven by growing demand for effective treatments as well as by regulatory tailwinds and expanding reimbursement coverage for innovative drugs, which are expected to improve the population's access to more effective therapeutics while reducing the innovation gap between China and more developed pharmaceutical markets.

OVERVIEW OF THE GLOBAL ONCOLOGY DRUG MARKET

The global oncology drug market has demonstrated strong growth momentum, having increased from US$83.2 billion in 2015 to US$143.5 billion in 2019, representing a CAGR of 14.6% between 2015 and 2019. According to the Frost & Sullivan Report, the market is expected to further grow to US$244.4 billion in 2024 at a CAGR of 11.2% from 2019 to 2024. By 2030, the global oncology market is estimated to reach US$391.3 billion in sales, representing a 2024-2030 CAGR of 8.2%. This growth is mainly driven by the aging global population and growing incidence of cancer, as well as by scientific progress and the launch of new therapies.

Global Oncology Drug Market

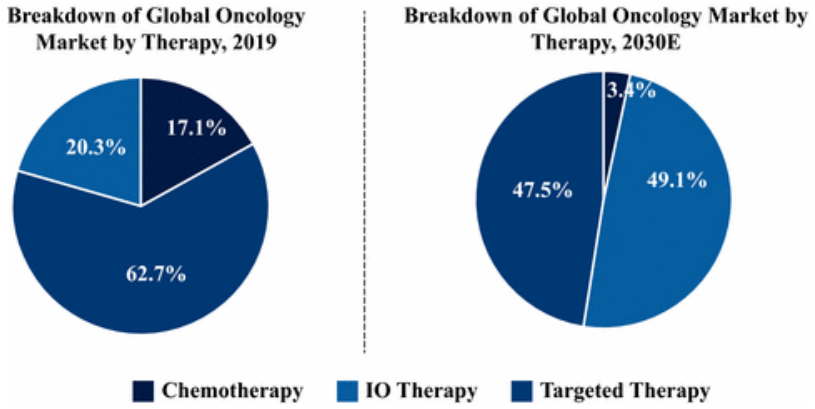


Note:

The translation of renminbi into U.S. Dollars was made at a rate of RMB7.0651 to US$1.00, being the exchange rate on June 30, 2020 set forth in the H.10 statistical release of the Federal Reserve Board.

Source: Frost & Sullivan

The field of cancer treatment has developed significantly in the past decades. Main treatment methods today include surgery, radiotherapy, chemotherapy, targeted therapy, and immuno-oncology therapy ("IO Therapy"). Targeted therapy and immuno-oncology therapy have revolutionized cancer treatment and are expected to further drive the growth of global oncology drug market.



Source: Frost & Sullivan Analysis

Key Growth Drivers of the Global Oncology Market

According to the Frost & Sullivan Report, the global oncology market will be primarily driven by an aging population and rising incidence of cancer, scientific progress, the emergence of combination therapies and the launch of new therapies:

- *Aging Population and Rising Incidence of Cancer* — The probability of developing cancer increases with age. It is projected that the total global population aged over 65 years old will exceed 800 million by 2025. As the result of the aging of the world's population, it is expected that cancer will have a higher incidence in the future and result in increasing demand for effective therapies.

- *Scientific Progress* — Over the past decade, there has been a rapid evolution in the treatment of cancer, driven by advances in personalized medicine and immuno- oncology therapies. From 2015 through 2019, 57 novel therapies were approved by the FDA for the treatment of cancer. These developments and novel treatments have led to improved outcomes for patients and an increased number of patients receiving treatment.

- *Emergence of Combination Therapies* — An increasing trend in the oncology area is the emergence of combination therapies, which offer low toxicity and robust efficacy associated with molecularly-targeted and immuno-oncology therapies. There is a wide academic and industry understanding that these combination therapies have the potential to improve efficacy, treatment response rates and durability as compared to single-agent therapies.

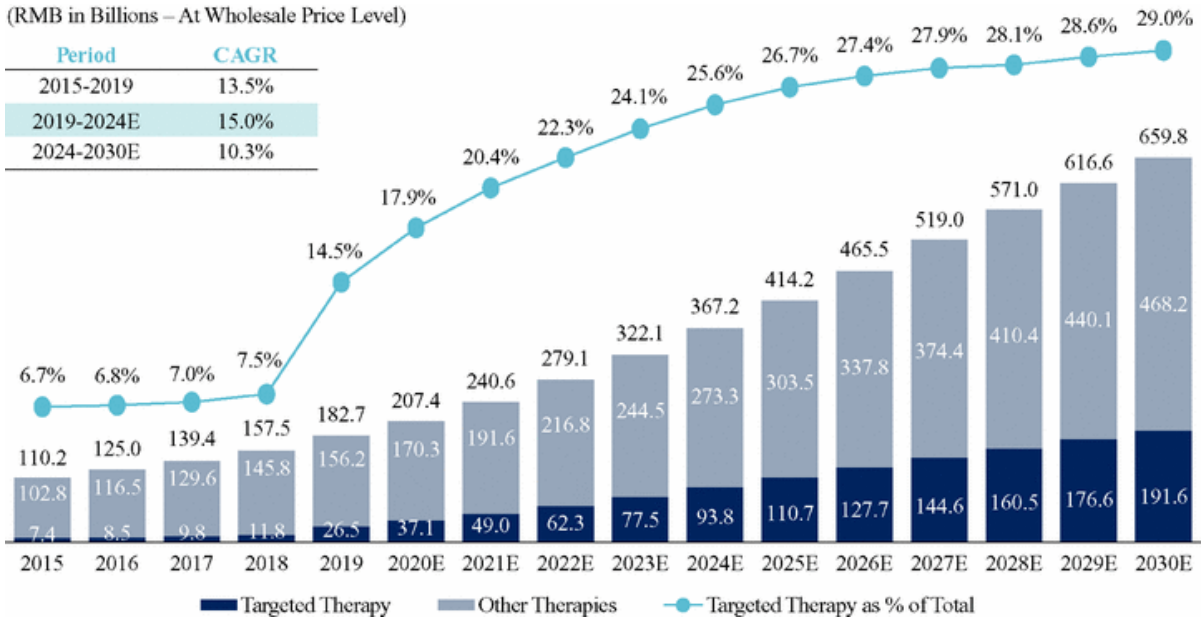
- *Launch of New Therapies* — The pipeline of oncology drugs in clinical development has expanded by 77% over the past ten years and remains robust, with over 800 molecules in late stage development. The pharmaceutical industry's focus on oncology will remain high over the next decade, driven by ongoing investment in research and development seeking to address unmet medical needs.

OVERVIEW OF CHINA'S ONCOLOGY DRUG MARKET

Historical and Estimated Size of China's Oncology Drug Market

China's oncology drug market has grown rapidly in recent years. The total sales of oncology drugs in China grew from RMB110.2 billion in 2015 to RMB182.7 billion in 2019, representing a CAGR of 13.5% between 2015 and 2019, according to the Frost & Sullivan Report. The market is expected to further grow to RMB367.2 billion in 2024 at a CAGR of 15.0% from 2019 to 2024, and to RMB659.8 billion in 2030 at a CAGR of 10.3% from 2024 to 2030. Compared to other therapeutic areas, oncology has the highest growth rate in healthcare expenditures. The strong growth prospects of China's oncology drug market are increasingly driving the growth of the global oncology market in general.

China Oncology Market (2015-2030E)



Source: Frost & Sullivan

Key Growth Drivers for the Oncology Market in China

According to the Frost & Sullivan Report, China's oncology market is largely driven by the following key growth drivers.

- *Large and Increasing Patient Base* — Cancer incidence in China has increased steadily in the past five years, climbing from 4.0 million in 2015 to 4.4 million in 2019. The incidence is expected to grow at an accelerated pace, and is projected to reach 5.0 million by 2024 and 5.7 million in 2030, which is primarily attributable to changes in life style, diet, and the aging population in China. The large and growing cancer patient base in China not only generates substantial market demand for cancer treatments, but also provides a favourable clinical trial environment for the rapid development of new therapeutics.

- *Increasing Healthcare Expenditure and Affordability* — Healthcare expenditure in China is expected to grow due to rising incomes, continued urbanization and strong governmental support. The expansion of the National Reimbursement Drug List ("NRDL") is expected to make oncology treatments more accessible, contributing to an increasing market size of oncology drugs. The 5th NRDL was adjusted in the negotiation that occurred in November 2019 to add 97 drugs, which mainly consist of oncology, chronic disease, and rare disease drugs.

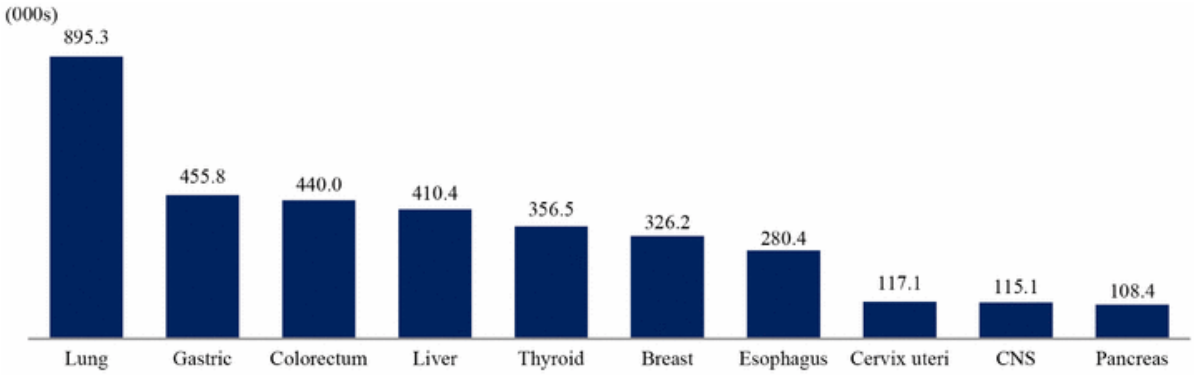
- *Transformation of the Drug Approval Process in China* — On October 8, 2017, the General Office of the State Council released the Opinions on Reform of the Drug and Medical Device Review and Approval (the "Opinions"), which has shifted the regulatory landscape of China's pharmaceutical market. The Opinions aim to accelerate the drug development and approval process in China, and to encourage greater innovation in drug and medical devices by 1) reforming clinical trial management; 2) accelerating review and approval; 3) improving China's participation in global clinical trials and acceptance of foreign clinical data; and 4) protecting innovators.

- *Accelerated Penetration of Innovative Therapies* — According to Frost & Sullivan, the market share of chemotherapy as a percentage of the total oncology market in China was above 70% in 2019, which is more than four times that of the total global oncology market. The lower penetration rate of targeted therapies and immunotherapies in China indicates that oncology treatment in China is lagging behind the advancement of oncology treatment globally. The growth of targeted therapies and immunotherapies in China are expected to outpace those of the global market. China's small molecule targeted therapy grew from RMB7.4 billion in 2015 to RMB26.5 billion in 2019, representing a CAGR of 37.6% from 2015 to 2019. It is expected to further grow to RMB93.8 billion in 2024 at a CAGR of 28.7% from 2019 to 2024, and to RMB191.6 billion in 2030 at a CAGR of 12.6% from 2024 to 2030. The penetration rate of targeted therapy in China oncology market reached 14.5% in 2019 and is expected to rise further to 29.0% by 2030.

Epidemiology by Cancer Type in China

Cancer incidence and mortality have been increasing in China, making cancer the leading cause of death (accounting for more than 25% of all causes of death) in 2019 and a major public health problem in the country. The increasing incidence of cancer is mainly attributable to population growth and aging, as well as socio-demographic changes such as pollution, changing lifestyles and dietary patterns, such as increasing consumption of tobacco and alcohol. The following chart shows the top 10 cancers by incidence in China in 2019:

New Cases for Top 10 Cancers in China, 2019



Source: Frost & Sullivan

In China, the top 5 most commonly diagnosed cancers are lung, gastric, colorectum, liver and thyroid cancers, which in aggregate accounted for approximately 60% of all cancer incidence. According to Frost & Sullivan, China has the highest number of cancer-related deaths in the world in 2019, and a higher mortality rate of 187 per 100,000 individuals, compared to the global average of 128 per 100,000 individuals.

China has a differentiated epidemiology profile than the rest of the world. In the rest of the world, top 5 cancer types in terms of annual incidence are lung, breast, colorectum, skin and prostate cancer. Only lung cancer and colorectum cancer are top 5 cancers, in terms of annual incidence, both around the globe and in China.

Overview of Selected Cancer Disease Areas

We have established our broad oncology portfolio and oncology strategy with a focus on specific diseases areas. At the moment, we are targeting the leading prevalent tumor disease areas in China, namely gynecologic cancer, breast cancer, gastro-intestinal cancer, brain cancer, lung cancer and hematological malignancies.

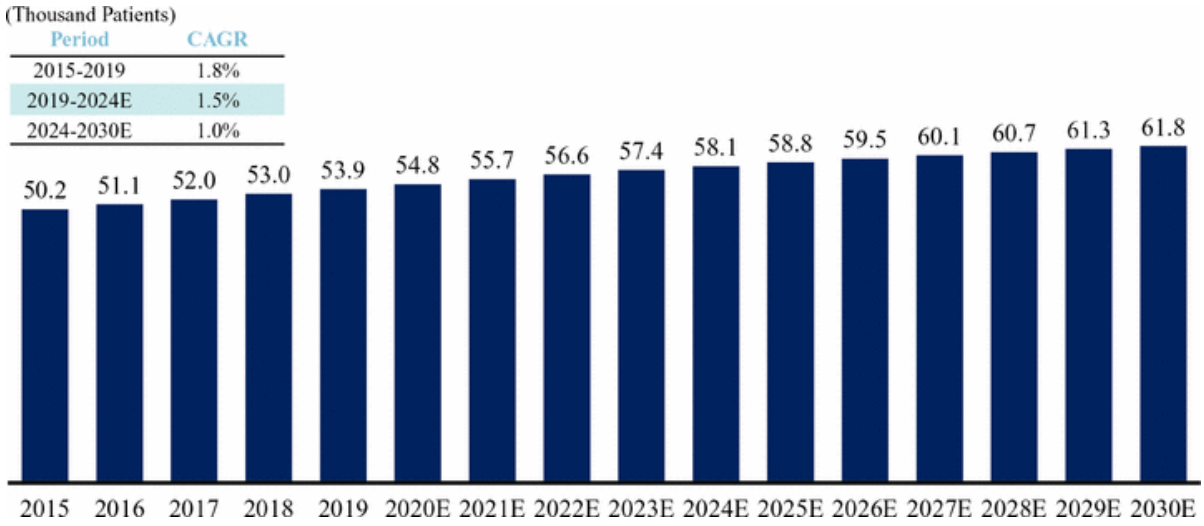
According to the Frost & Sullivan report, novel therapies will demonstrate significant market potential in all these disease areas given the large patient incidence and tremendous unmet needs as the result of limited treatment options, lack of satisfactory or durable efficacy of current treatments, poor prognosis and others.

Women's cancer

Ovarian Cancer

In 2015, the incidence of ovarian cancer in China reached 50.2 thousand, which increased to 53.9 thousand in 2019 with a CAGR of 1.8% from 2015 to 2019. According to the Frost & Sullivan Report, it is estimated that the incidence of ovarian cancer will continue to grow and reach 58.1 thousand by 2024 with a CAGR of 1.5% from 2019 to 2024, and 61.8 thousand by the year of 2030 with a CAGR of 1.0% from 2024 to 2030.

Incidence of Ovarian Cancer in China (2015-2030E)



Source: Frost & Sullivan

Globally, 70% of patients with ovarian cancer are in advanced stage when they are first diagnosed, according to the Frost & Sullivan Report. The previous standard of care in China mainly consists of radical surgery and platinum-based chemotherapy. Although platinum-based chemotherapy is effective at inducing an initial response, an estimated 85% of patients with epithelial ovarian cancer who achieve a full remission following first-line therapy will develop recurrent disease. According to the Frost & Sullivan Report, the 5-year survival rate of ovarian cancer is less than 40%. Historically, there have been limited treatment options for relapsed ovarian cancer patients. Moreover, the interval between recurrences decreases with the increase in the number of recurrences.

According to the Frost & Sullivan Report, the current ovarian cancer treatment paradigm is facing multiple significant challenges including:

- *Limited Clinical Efficacy of First-Line Maintenance Treatment with Chemotherapy* — The standard first-line maintenance treatment which is typically chemotherapy, has shown limited efficacy, with approximately 85% of first-line patients eventually relapsing.

- *Limited Treatment Options for Relapsed Patients* — While the time interval of recurrence becomes shorter after each relapse, effective treatment options for subsequent lines of treatments are limited.

According to the Frost & Sullivan Report, clinical evidence shows that PARP inhibitors, a novel drug class, can significantly delay the recurrence time and prolong PFS of patients when used in the maintenance of ovarian cancer. This has resulted in a series of new therapy approvals globally which have transformed the standard of care in the ovarian maintenance treatment setting. Indeed, PARP inhibitors have now been included in the clinical guidelines (2020 Guidelines for Clinical Application of PARP Inhibitors in Ovarian Cancer) for treatment of ovarian cancer, according to the Frost & Sullivan Report. Main adverse events associated with PARP inhibitors include nausea, thrombocytopenia, anemia, fatigue, decreased appetite, headache, neutropenia, leukopenia etc.

The below table set forth maintenance and treatment options for ovarian cancer under the clinical guidelines as referenced in China:

Stage	Treatment
First-line treatment	· Postoperative adjuvant chemotherapy
First-line maintenance treatment	· BRCA1/2 mutation:
	· Olaparib ± Bevacizumab
	· Niraparib
	· Wild type BRCA1/2, HRD positive:
	· Olaparib ± Bevacizumab
	· Niraparib
	· Wild type BRCA1/2, HRD negative:
	· Niraparib
Second-line treatment	· Chemotherapy
Maintenance treatment after second-line treatment	· Platinum-sensitive relapse
	· Olaparib
	· Niraparib
	· Rucaparib[(1)]
Subsequent line treatment	· Platinum-sensitive relapse
	· BRCA1/2 mutation:
	· Olaparib
	· Rucaparib
	· HRD positive:
	· Niraparib
	· Platinum-resistant relapse
	· BRCA1/2 mutation:
	· Olaparib
	· Niraparib ± Pembrolizumab
	· Rucaparib[(1)]

Note:

(1) Rucaparib is a PARP inhibitor from Clovis, which has not begun clinical trial or been approved in China as of the Latest Practicable Date.

2018 Guideline for Diagnosis and Treatment of Ovarian Cancer

2020 Guidelines for Clinical Application of PARP Inhibitors in Ovarian Cancer

Source: Frost & Sullivan Report

Hong Kong and Macau follow the NCCN Guidelines with respect to the standard of care and treatment guidelines for ovarian cancer, which is largely consistent with the standard of care and treatment guidelines recognized in China described above, according to the Frost & Sullivan Report.

As of July 2020, there were only two marketed PARP inhibitors in China, one is LYNPARZA (olaparib) from AstraZeneca, which was approved in 2018; the other one is ZEJULA (niraparib), which was approved in 2019, according to the Frost & Sullivan Report.

ZEJULA is a potential best-in-class PARP inhibitor, given it is the only PARP inhibitor approved as monotherapy for all-comer patients in the first-line and recurrent maintenance treatment settings, according to Frost & Sullivan. We believe that our early entrant status as one of the first PARP inhibitors in the China market, coupled with the global recognition, differentiated profile and availability of global and China clinical evidence for ZEJULA, position us favourably in China's PARP inhibitor market.

The main competitive drug, LYNPARZA of AstraZeneca, was (i) approved by the FDA in December 2018 in first-line maintenance therapy but only for BReast CAncer gene ("BRCA")-positive patients, and (ii) approved by the FDA in May 2020 for patients whose cancer is associated with homologous recombination deficiency (HRD) positive status, which represent 50% of the advanced ovarian cancer patients, but only in combination with Avastin (bevacizumab). On the other hand, ZEJULA was approved (i) for all advanced ovarian cancer patients regardless of biomarker status, and (ii) as a monotherapy.

Four additional PARP inhibitors are in phase III clinical development or at NDA stage in China, comprising both China developed and global drug candidates. Three of these PARP inhibitors' lead indications focus on late-stage ovarian cancer while one focuses on metastatic prostate cancer. In the late stage ovarian cancer indications, one of the products is targeting BRCA+ patients only. We believe that, pending on the NMPA's approval of our supplemental new drug application (sNDA) for ZEJULA as a maintenance in first-line ovarian cancer, ZEJULA would target the broadest patient population.

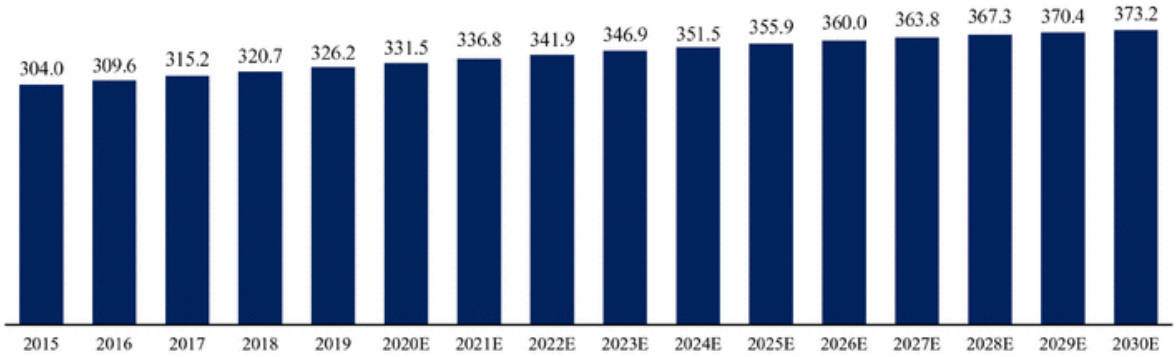
Breast Cancer

According to the Frost & Sullivan Report, breast cancer is the most common cancer in women.

Incidence of Breast Cancer in China (2015-2030E)

(Thousand Patients)

Period	CAGR
2015-2019	1.8%
2019-2024E	1.5%
2024-2030E	1.0%



Source: Frost & Sullivan

The incidence of breast cancer in China grow from 304.0 thousand in 2015 to 326.2 thousand in 2019 with a CAGR of 1.8% from 2015 to 2019, according to the Frost & Sullivan Report. It is estimated that the number will continue to grow and will reach 351.5 thousand by the year of 2024 and 373.2 thousand by the year of 2030, representing a CAGR of 1.5% from 2019 to 2024 and 1.0% from 2024 to 2030, respectively, according to the Frost & Sullivan Report. According to the Frost & Sullivan Report, the 5-year survival rate for breast cancer in China is 82.0%.

Globally, HER2+ represents 25% of breast cancer cases. According to Frost & Sullivan, the current HER2+ breast cancer treatment is facing multiple significant challenges including:

- *Limited Treatment Options in the Late-Stage Setting* — The HER2 oncoprotein drives the aggressive behavior of HER2+ breast and other cancers and has proven to be a good target for cancer therapeutics. However, after treatment failure or disease progression after second-line anti-HER2 treatment, there is no approved effective treatment in late-stage setting in China and globally. There is a significant need for new and effective HER2 targeted therapeutics that can be administered to patients with HER2+ metastatic breast cancer who have previously been treated with other anti-HER2-targeted therapies.

- *Recurrence and Metastases for HER2+ Patients* — Even with treatment, breast cancer patients sometimes have recurrence or even brain metastases since most of the therapies do not penetrate the blood-brain barrier. A study published on the Oncologist has shown that more than 35% of patients with HER2+ metastatic breast cancer (MBC) treated with trastuzumab (Herceptin)-based therapy developed breast cancer brain metastases. The aims of this observational study were to evaluate the incidence of CNS metastases in HER-2-positive MBC patients, to define the outcome of patients with CNS metastases, and to identify the risk factors for CNS relapse. At a median follow-up of 28 months from the occurrence of metastatic disease, 43 patients (35.2%) developed CNS metastases. See "Central Nervous System Metastases in HER-2Positive Metastatic Breast Cancer Patients Treated with Trastuzumab: Incidence, Survival, and Risk Factors." in The Oncologist, 12: 766-773. doi:10.1634/theoncologist.12-7-766.

The below table set forth maintenance and treatment options for HER2+ metastatic breast cancer under the clinical guidelines as referenced:

Stage	Treatment
First-line treatment	· Chemotherapy + trastuzumab + pertuzumab
	· Chemotherapy + trastuzumab/pertuzumab
Second-line treatment	· T-DM1
	· Lapatinib/pyrotinib + chemotherapy
	· Trastuzumab + chemotherapy (other chemotherapy drugs that have not been used before)
	· Trastuzumab + lapatinib

2019 Guidelines and Norms for Diagnosis and Treatment of Breast Cancer by Chinese Anti-Cancer Association

Source: Frost & Sullivan Report

Gastrointestinal Cancer

Gastrointestinal cancer refers to malignant conditions of the gastrointestinal (GI) tract and other organs involved in digestion, including the oesophagus, stomach, biliary system, pancreas, small intestine, large intestine, rectum and anus. The following table illustrates the incidence of major gastrointestinal cancer types in China for the periods indicated.

Incidence of Major Gastrointestinal Cancer Types in China (2015-2030E)

(Thousand Patients)	2015	2016	2017	2018	2019	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2015-2019	2019-2024E	2024E-2030E
Gastric Cancer	403.0	415.9	429.0	442.3	455.8	469.5	483.3	497.3	511.5	525.8	540.3	554.9	569.6	584.4	599.2	613.8	3.1%	2.9%	2.6%
Colorectum Cancer	388.0	400.7	413.6	426.7	440.0	453.5	467.3	481.2	495.3	509.6	524.1	538.8	553.6	568.6	583.6	598.8	3.2%	3.0%	2.7%
Liver Cancer	370.0	380.0	390.1	400.2	410.4	420.7	431.1	441.6	452.1	462.8	473.4	484.1	494.7	505.2	515.6	526.0	2.6%	2.4%	2.2%
Esophageal Cancer	246.0	254.4	262.9	271.6	280.4	289.4	298.5	307.7	317.1	326.6	336.2	345.9	355.5	365.1	374.6	383.9	3.3%	3.1%	2.7%
Pancreatic Cancer	95.0	98.2	101.5	104.9	108.4	112.0	115.6	119.4	123.2	127.1	131.1	135.2	139.4	143.6	147.9	152.2	3.4%	3.2%	3.0%
GIST	28.1	29.0	30.0	31.0	31.9	32.7	33.6	34.6	35.6	36.6	37.6	38.6	39.6	40.9	42.1	43.3	3.2%	2.8%	2.8%

According to the Frost & Sullivan Report, gastric cancer is the largest type of gastrointestinal cancer and also one of the most frequently occurring cancers in China. Gastric cancer includes certain cancer types of the gastroesophageal junction or GEJ, while esophageal cancer also includes other types, as GEJ lies in between the two organs. The incidence of gastric cancer in China was 455.8 thousand in 2019, and it is expected to increase to 525.8 thousand in 2024 and to 613.8 thousand in 2030, according to the Frost & Sullivan Report. The 5-year survival rate for gastric cancer in China is 35.1%, according to the Frost & Sullivan Report.

According to Frost & Sullivan, the current gastric cancer treatment options are limited:

- *Chemotherapy being Only First-Line Treatment* — Gastric cancer has very poor prognosis and is often diagnosed at an advanced stage, which leads to a low 5-year survival rate of 35.1%. Chemotherapy is the standard of care for first-line therapy and may be combined with trastuzumab for the approximately 20% of patients whose tumors are HER2+. For HER2- gastric cancer, there is no currently available targeted drug for first-line treatment other than chemotherapy.

- *Limited Availability of Targeted Therapies* — Despite an incidence of approximately 455.8 thousand in gastric cancer, there are only three targeted treatment options for advanced gastric cancer: trastuzumab, apatinib, and nivolumab. For HER2+ advanced gastric cancer, trastuzumab is the only HER2-targeted antibody. There has been a strong demand for new reliable and affordable treatment options for advanced gastric cancer.

The below table set forth maintenance and treatment options for gastric cancer under the clinical guidelines as referenced:

Stage	Treatment
First-line treatment	· Chemotherapy (with trastuzumab if patients are HER2-positive advanced metastatic gastric cancer)
Second-line treatment	· Chemotherapy (with trastuzumab if patients are HER2-positive advanced metastatic gastric cancer)
Third-line treatment	· Apatinib
	· Single agent chemotherapy
	· Anti-PD-1 monoclonal antibody

2019 CSCO Guidelines for Diagnosis and Treatment of Gastric Cancer

Source: Frost & Sullivan Report

GIST is another type of gastrointestinal cancer and the most common mesenchymal tumor of the gastrointestinal tract. GIST are believed to arise from the interstitial cells of Cajal or their precursors and are heterogeneous histologically, showing spindle cells, epitheloid cells and mixed cells. KIT mutations and PDGFRα mutations drive 80% and 8% of GIST, respectively. Estimates for 5-year survival range from 48% to 90% depending upon the stage of the disease at diagnosis. In China, there was an incidence of 31.9 thousand in 2019.

According to Frost & Sullivan, the currently available GIST treatment standard in China has faced various limitations:

- *Limited Treatment Modalities* — GIST are generally resistant to conventional chemotherapy and radiotherapy treatments. Surgery and Tyrosine Kinase Inhibitors (TKIs) are the only two main treatment modalities to treat GIST. Only 3 TKI therapies have been approved for treating GIST currently, namely Glivec (imatinib) from Novartis, Sutent (sunitinib) from Pfizer and Stivarga (regorafenib) from Bayer. Limited treatment modalities restrict treatment options for patients.

- *Most Responding Patients Acquire Drug Resistance* — Although TKIs are initially effective in treating advanced GIST, patients eventually develop drug resistance resulting in disease progression. Genomic alterations contribute to tumorigenic progression in GIST such as secondary KIT mutations. Available TKIs can only target a limited spectrum of primary/secondary KIT and PDGFRα mutations. New therapies which could target a broader spectrum of primary/secondary KIT mutations and PDGFRα mutations are needed.

- *No Approved Treatment Option for Fourth-Line Therapy or Beyond* — TKIs were approved in the first-line, second-line and third line therapies to provide significant survival benefits for the patients. However, there is no available treatment if patients have a recurrence after third-line therapy. While ripretinib and avapritinib are recommended as fourth-line therapies in the guidelines, they are still awaiting for approval in China.

The below table set forth maintenance and treatment options for GISTs that are unresectable, recurrent, or metastatic under the clinical guidelines as referenced:

Stage	Treatment
First-line treatment	· GISTs with unknown genotype
	· Imatinib
	· Dasatinib
	· GISTs with C-kit exon 9 mutation
	· Imatinib
	· GISTs with PDGFRα D842V
	· Avapritinib (recommended for PDGFRα mutation only with Level 2A evidence)
	· GISTs with mutation except for C-kit exon 9 mutation and PDGFRα D842V
	· Imatinib
	· GISTs with PDFGRα exon 18 mutation
	· Imatinib
	· Avapritinib (recommended for PDGFRα mutation only with Level 2A evidence)
Second-line treatment	· Limited progression
	· Resection if feasible
	· Sunitinib
	· Imatinib
	· TACE/RFA for GISTs with liver metastases
	· Radiotherapy
	· Widespread progression
	· Sunitinib
	· Imatinib
	· Dasatinib
Third-line treatment	· Regorafenib
Fourth-line treatment	· Ripretinib (recommended with Level 1 evidence)
	· Avapritinib
	· Imatinib[(1)]

Note:

(1) Although imatinib is recommended as fourth-line treatment with Level 3 recommendation, in clinical practice patients may not be able to re-use imatinib again as it has been highly recommended in previous lines of the treatment.

2017 Consensus on Diagnosis and Treatment of Gastrointestinal Stromal Tumors

2020 CSCO Guidelines for Diagnosis and Treatment of Gastrointestinal Stromal Tumors, or 2020 CSCO Guidelines

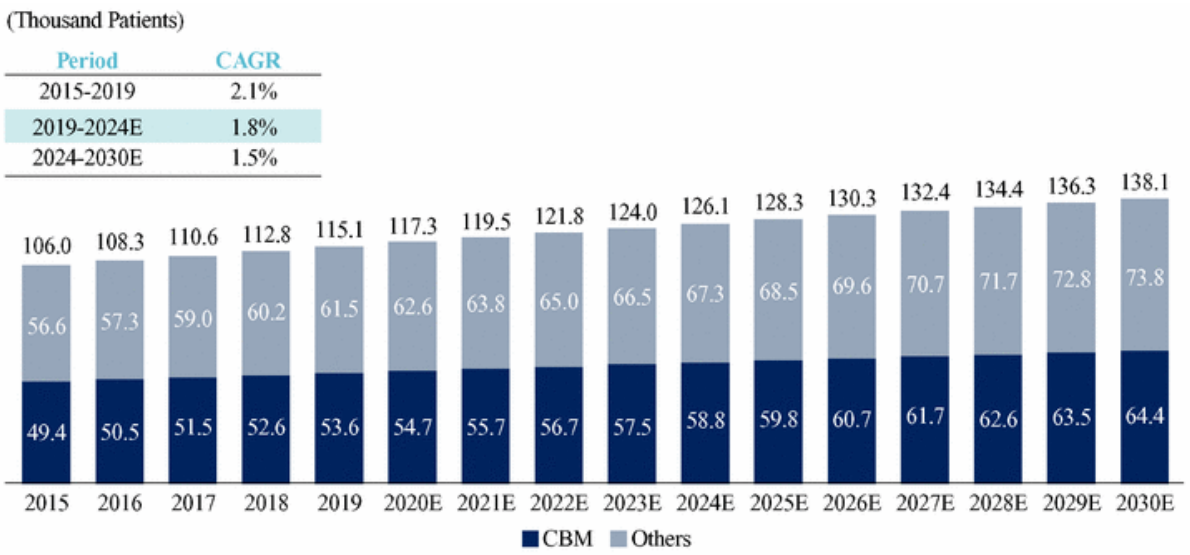
Source: Frost & Sullivan Report

According to the Frost & Sullivan, in the newly published 2020 CSCO Guidelines, for fourth-line treatment, ripretinib gets Level 1 recommendation, whereas avapritinib gets Level

Brain cancer

Malignant gliomas are the most common brain cancers. They originate in the glial cells of the central nervous system (CNS). Gliomas can be divided into 3 main types: astrocytomas, oligodendrogliomas, and ependymomas. Glioblastoma multiforme (GBM) is the most common and aggressive type of primary brain tumor. About 50% of gliomas are GBM, which is classified as Grade IV (most serious) astrocytoma. According to Frost & Sullivan, the incidence of brain cancer in China has reached 115.1 thousand in 2019 with a CAGR of 2.1% from 2015 to 2019. It is estimated that the incidence will further reach 126.1 thousand in 2024 and 138.1 thousand in 2030, according to the Frost & Sullivan Report.

Incidence of Brain Cancer in China (2015-2030E)



Source: Frost & Sullivan

GBM grows rapidly and is the most invasive type of glioma. There are multiple challenges in treating GBM, such as tumor heterogeneity, the blood brain barrier, glioma stem cells, drug efflux pumps and DNA damage repair mechanisms. In 2019, GBM had 53.6 thousands incidences in China, representing 46.6% of all brain cancer incidence in China, according to the Frost & Sullivan Report. GBM's 5 year survival rate in China is less than 5%, according to the Frost & Sullivan Report.

According to the Frost & Sullivan Report, there are two treatments approved for GBM globally in the past fifteen years, namely TMZ and Optune (Tumor Treating Fields). TMZ is a chemotherapy drug approved in 2007 in China and is the only currently available drug approved to treat newly diagnosed GBM cases in China, according to the Frost & Sullivan Report. Optune (Tumor Treating Fields) is a novel cancer therapy that uses electric fields to inhibit tumor growth, which was approved in May 2020 in China. In addition, there are also generics of two drugs, which were approved globally over 40 years ago, available in China, namely carmustine and lomustine; however, their respective recommendation level is not as high as TMZ and they are recommended for recurrent cases only. Developing drugs for GBM is particularly challenging as the result of the blood-brain barrier, which hinders small molecule transport. Factors such as drug resistance mechanisms also need to be resolved.

The below table set forth maintenance and treatment options for GBM under the clinical guidelines as referenced in China:

Stage	Treatment
Treatment for newly diagnosed GMB	· Radiation ± TMZ ± Tumor Treatment Fields
Subsequent treatment after relapse	· Bevacizumab ± Chemotherapy
	· TMZ
	· Lomustine/Carmustine
	· PCV
	· Cyclophosphamide
	· Chemotherapy

2018 Guidelines for Diagnosis and Treatment of Glioma

Source: Frost & Sullivan Report

Hong Kong, Macau and Taiwan follow the NCCN Guidelines with respect to the standard of care and treatment guidelines for GBM, which is largely consistent with the standard of care and treatment guidelines recognized in China described above, according to the Frost & Sullivan Report.

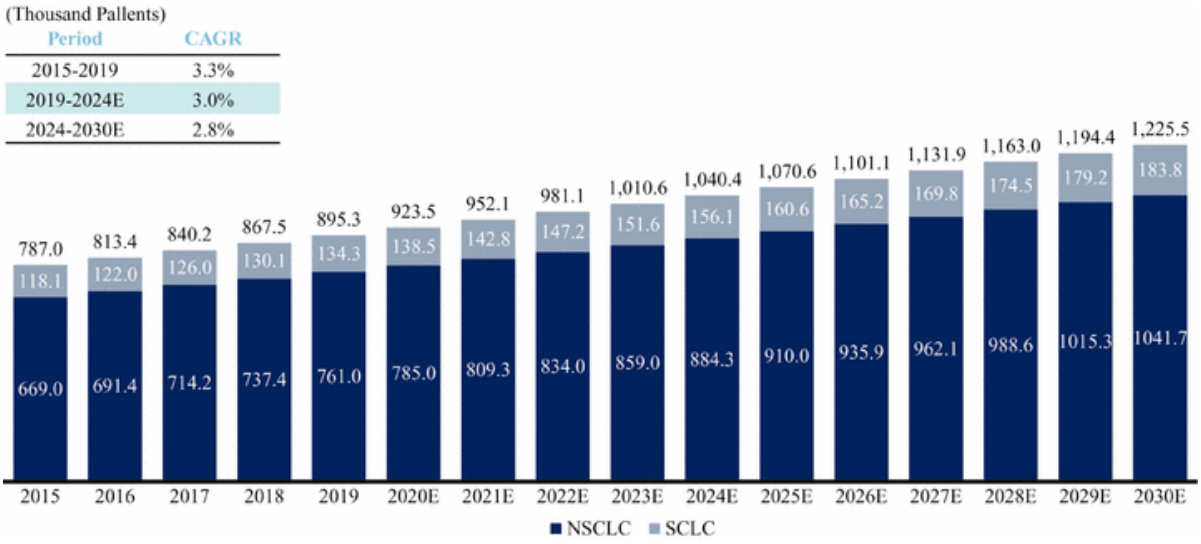
Optune (Tumor Treating Fields) is recommended in the national treatment guideline in the U.S. with category 1 recommendation for newly diagnosed GBM. Tumor Treating Fields was recommended with Level 1 evidence as a treatment for newly diagnosed GBM patients in the first Glioma Treatment Guideline (2018 Version) (腦膠質瘤診療規範(2018年版) published by the National Health Commission of China. In addition, Optune is the first innovative treatment approved for GBM treatment since 2007 in China. Major adverse events associated with Tumor Treating Fields include thrombocytopenia, nausea, constipation, vomiting, fatigue, medical device site reaction, such as treatment related skin toxicity, allergic reaction to the plaster or to the gel, electrode overheating leading to pain and/or local skin burns, infection at the sites of electrode contact with the skin, headache, convulsions, and depression.

Optune is indicated for the treatment of adult patients (22 years of age or older) with histologically-confirmed recurrence in the supra-tentorial region of GBM. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. Optune with TMZ is indicated for the treatment of adult patients with newly diagnosed, supratentorial GBM following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy.

Lung cancer

According to the Frost & Sullivan Report, the incidence of lung cancer in China is estimated at 895.3 thousand in 2019 and is expected to reach 1,040.4 thousand in 2024 and 1,225.5 thousand in 2030. Lung cancer can be categorized into non-small-cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC is any type of epithelial lung cancer other than SCLC. The most common types of NSCLC are squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. All types can occur in unusual histologic variants and developed as mixed cell-type combinations. NSCLC accounts for approximately 85% of total lung cancer patients in China. The incidence of NSCLC in China reached 761.0 thousand in 2019, with a CAGR of 3.3% from the year of 2015 to the year of 2019; such number is expected to reach 884.3 thousand in 2024 representing a CAGR of 3.0% from 2019 to 2024, and 1.0 million in 2030 with a CAGR of 2.8% from 2024 to 2030, according to the Frost & Sullivan Report. The 5-year survival rate for lung cancer in China is 19.7% according to the Frost & Sullivan Report.

Incidence of Lung Cancer in China (2015-2030E)



Source: Frost & Sullivan

With the successful identification of activating oncogenic mutations found in NSCLC, molecularly targeted therapy has been used to treat NSCLC and has provided significant survival benefits for NSCLC patients. However, almost all patients ultimately develop acquired resistance, limiting the duration of the clinical benefits and reducing the mean Progression Free Survival (PFS) range to 9.2—13.1 months. Thus, it is important to find effective therapies for patients with acquired resistance.

According to Frost & Sullivan, currently available NSCLC treatment options have shown clinical limitations:

- *Poor Survival Rate* — The 5-year survival rate of lung cancer in China stands only at 19.7% and the rate is also comparable to the U.S. level. The significantly low survival rate is also due to the lack of early detection tools and to the recognition of the symptoms at late stage. In China, the majority of non-small cell lung cancer patients are diagnosed when their disease is already at late stage, with approximately 17.0% patients at stage III and 50.0% at stage IV, resulting in low chance of survival, given current treatment options.

- *Drug Resistance* — Drug resistance is a major cause for therapeutic failure in NSCLC, leading to tumor recurrence and disease progression. For early treatment of NSCLC, there are multiple established predictive biomarkers for target therapy include ALK rearrangements, ROS1 rearrangements, sensitizing EGFR mutations, BRAF V600E point mutations, and PD-L1 expression levels. Unfortunately, despite disease control in the initial stage of treatment, targeted therapy fails to prolong the Overall Survival (OS) of these patients, since almost all patients develop acquired resistance limiting the duration of the clinical benefits and reducing the mean PFS range to 9.2-13.1 months.

As of July 2020, there were three ROS1/NTRK/ALK targeted drugs marketed in China, of which there is only one approved targeted therapy for patients with advanced ROS1-positive lung cancer and despite its efficacy, most patients eventually acquire resistance. The unmet need in the ROS1-positive lung cancer patient population is significant. The preliminary clinical activity and safety data generated to date for repotrectinib represent a promising clinical profile. ROS1 rearrangement is estimated to be an oncogenic driver in approximately 3 percent of patients with advanced NSCLC in China, while NTRK is estimated to be an oncogenic driver in approximately 0.5-1 percent of patients with wide range of solid tumors in China, according to the Frost & Sullivan Report.

The below table set forth maintenance and treatment options for NSCLC under the clinical guidelines as referenced:

	Treatment					
Stage	**EGFR mutations**	**ALK Rearrangement**	**ROS1 Rearrangement+**	**BRAF V600E mutation**	**NTRK Rearrangement**	**Driver Gene-/Unknown Genotype**
First-line treatment	– Gefitinib ± Chemotherapy – Erlotinib ± Chemotherapy/ Bevacizumab – Icotinib – Afatinib – Osimertinib – Chemotherapy ± Bevacizumab (Nonsquamous carcinoma)	– Alectinib – Crizotinib – Chemotherapy ± Bevacizumab (Nonsquamous carcinoma) – Brigatinib[1]	– Crizotinib – Chemotherapy ± Bevacizumab (Nonsquamous carcinoma) – Entrectinib[1]	– Dabrafenib ± Trametinib – Refer to the fist-line treatment of NSCLC with Driver Gene-/Unknown Genotype	– Larotrectinib[1] – Entrectinib[1] – Refer to the fist-line treatment of NSCLC with Driver Gene-/Unknown Genotype	– Chemotherapy – Bevacizumab ± Chemotherapy – Pembrolizumab ± Chemotherapy – Camrelizumab+ Chemotherapy – Atezolizumab+ Chemotherapy ± Bevacizumab – Recombinan human endostatin ± Chemotherapy
Second-line treatment	– T790M positive: Osimertinib – T790M negative: Chemotherapy ± Bevacizumab (Non - squamous carcinoma) – Almonertinib	– Continued EGFR-TKI Therapy – Alectinib/ Ceritinib – Chemotherapy ± Bevacizumab (Non- squamous carcinoma) – Brigatinib(1) – Lorlatinib(1	– Continued EGFR-TKI Therapy – Alectinib/ Ceritinib – Chemotherapy ± Bevacizumab (Non- squamous carcinoma) – Brigatinib[1] – Lorlatinib[1]	– Refer to the subsequent line treatment of NSCLC with Driver Gene+/-.	– Refer to the subsequent line treatment of NSCLC with Driver Gene+/-.	– Chemotherapy – Nivolumab – Pembrolizumab – Atezolizumab
Third-line treatment	– Single agent chemotherapy ± Bevacizumab (Non-squamous carcinoma) – Anlotinib	– Single agent chemotherapy ± Bevacizumab (Non- squamous carcinoma) – Anlotinib	– Single agent chemotherapy ± Bevacizumab (Non- squamous carcinoma)	– Refer to the subsequent line treatment of NSCLC with Driver Gene+/-.	– Refer to the subsequent line treatment of NSCLC with Driver Gene+/-.	– Nivolumab – Chemotherapy – Anlotinib

Notes:

(1) Larotrectinib, brigatinib, lorlatinib and entrectinib have not been approved in China as of the Latest Practicable Date.

(2) Crizotinib is only recommended for CNS metastasis or oligometastases patients in the second-line treatment.

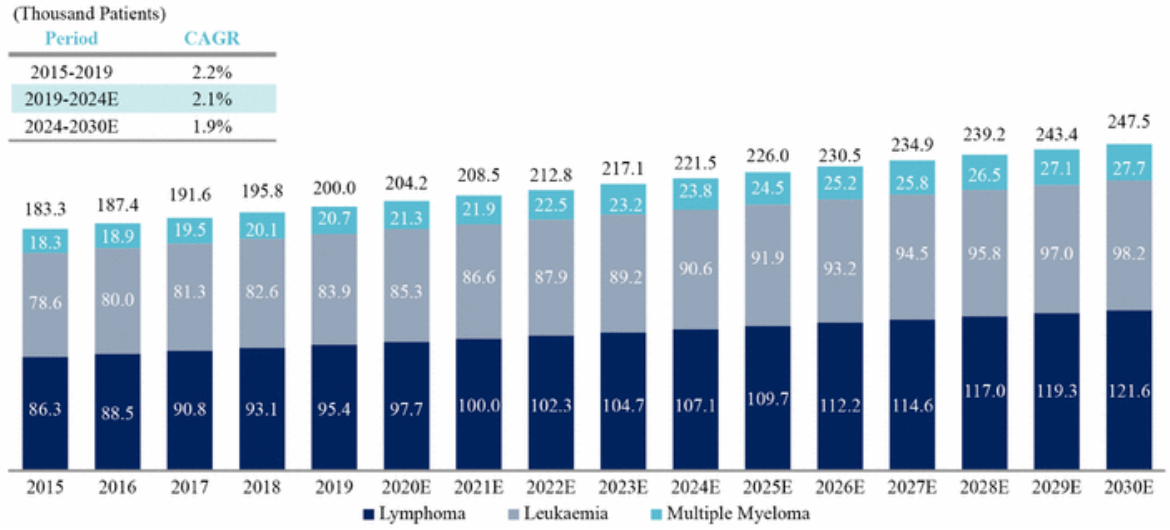
2020 CSCO Guidelines for Diagnosis and Treatment of NSCLC

Source: Frost & Sullivan Report

Hematological Malignancy

Hematological malignancy, also called blood cancer, is cancer that begins in blood- forming tissue, such as the bone marrow, or in the cells of the immune system. According to Frost & Sullivan, hematological malignancy had an incidence of 200.0 thousand in China in 2019, and the biggest sub-type of hematological malignancy was lymphoma, with an incidence of 95.4 thousand in 2019. The two main categories of lymphomas are Hodgkin's lymphomas (HL) and the non-Hodgkin lymphomas (NHL). NHL accounts for approximately 90% of lymphoma and has a variety of subtypes, which are categorized by the characteristics of the lymphoma cells, including their appearance, the presence of proteins on the surface of the cells and their genetic features.

Incidence of Hematological Malignancy in China (2015-2030E)



Source: Frost & Sullivan

NHL originating in B-cells (B-NHL) makes up 85% of all NHL cases, with the three most common subtypes in China being DLBCL (Diffuse large B-cell lymphoma), MZL (Marginal zone lymphoma) and FL (Follicular lymphoma), according to the Frost & Sullivan Report. DLBCL alone accounts for about 41% of all NHL cases while MZL and FL accounts for 8% and 6%, respectively in China, according to Frost & Sullivan. DLBCL is an aggressive or fast-growing NHL that affects B-lymphocytes. MZL is a group of indolent or slow growing NHL B-cell lymphomas, FL is typically a slow-growing or indolent form of NHL that arises from B-lymphocytes, making it a B-cell lymphoma.

According to Frost & Sullivan, there are multiple critical obstacles in NHL treatment:

- *Limited Efficacy* — In China, the prevalence of NHL reached 485.0 thousand patients in 2019, with an overall 5-year survival rate of NHL of 37.0%, lower than that of cancer in general in China. Some aggressive types of NHL, such as DLBCL, can involve organs other than the lymph nodes, progressing rapidly and becoming fatal due to invasion across all areas of the body if treatment is not administered at an early stage. Only early-stage detection and treatment can lead to a higher chance of survival. On the other hand, indolent subtypes of NHL, such as FL, despite slow progression, can be long-standing over years and are less likely to be cured with current treatment methods. The current treatment paradigm and survival rate have demonstrated the difficult nature of NHL, indicating significant unmet clinical needs.

- *Drug Resistance* — Anti-CD20 antibodies in combination with chemotherapy (or R-CHOP) are the standard of care for the treatment of B-NHLs; however, despite initial responses, about 50% of NHL patients will eventually experience disease progression due to drug resistance, indicating a need for new treatment options. In particular, around 15% of DLBCL (the most common subtype of NHL) patients are characterized as primary refractory towards first-line R-CHOP therapy. For these refractory patients, treatments options with new modalities are highly necessary. According to the Frost & Sullivan Report, there are currently no marketed bispecific antibody drugs for hematological malignancy in China as of July 2020.

The below table set forth maintenance and treatment options for DLBCL under the clinical guidelines as referenced:

Stage	Treatment
First-line treatment	· Monoclonal antibody + Chemotherapy
	– R-CHOP
	– R-miniCHOP
	– R-CHOEP
	– R-DAEPOCH
Second-line treatment	· Monoclonal antibody + Chemotherapy
	– R-DHAP
	– R-ICE
	– R-GDP
	– R-ESHAP
	– R-GD
	– R-DAEPOCH
	– R-GemOx
	– R-MINE
	· Small molecule targeted therapy
	– Ibrutinib (BTK inhibitor)[1]
Third-line treatment	· Monoclonal antibody + Chemotherapy
	– R-DHAP
	– R-ICE
	– R-GDP
	– R-ESHAP
	– R-DAEPOCH
	– R-GemOx
	– R-MINE
	· Small molecule targeted therapy
	– Ibrutinib (BTK inhibitor)(1)
	· Monoclonal antibody + Small molecule targeted therapy
	– R2

Note: R-CHOP(rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone); R-CHOEP (rituximab, cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone); R-DAEPOCH(rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin); R-miniCHOP (rituximab, lower dosage of CHOP); R-DHAP(rituximab, dexamethasone, cisplatin, cytarabine); R-ESHAP (rituximab, etoposide, methylprednisolone, cytarabine, cisplatin); R-GemOx (rituximab, gemcitabine, oxaliplatin); RICE (irituximab, fosfamide, carboplatin, etoposide); RMINE (rituximab, mesna, ifosfamide, mitoxantrone, etoposide);R2 (rituximab, lenalidomide); R-GD (rituximab, gemcitabine, dexamethasone); R2 (rituximab, revlimid)(2); R-GDP(rituximab, gemcitabine, dexamethasone, cisplatin).

(1) BTK is only approved for relapsed or refractory MCL and chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), although it has been recommended in the guidelines of NHL for the treatment of refractory or relapsed DLBCL (>=2) who are not eligible for haematopoietic stem cell transplant, and with Level 3 recommendation.

(2) Revlimid has not been approved for treatment of DLBCL in China as of the Latest Practicable Date.

2019 CSCO Guidelines for Diagnosis and Treatment of Lymphoma

Source: Frost & Sullivan Report

Stage	Treatment
First-line treatment	· Monoclonal antibody
	– Rituximab
	– Obinutuzumab
	· Chemotherapy
	– Chlorambucil
	– Cyclophosphamide
	· Monoclonal antibody + Chemotherapy
	– R-CHOP
	– R-CVP
	– R-Bendamustine
	– R-Alkylating agent
	· Monoclonal antibody + Small molecule targeted therapy
	– R-Lenalidomide
Second-line treatment	· Monoclonal
	– Rituximab
	· Chemotherapy
	– Chlorambucil
	– Cyclophosphamide
	· Monoclonal antibody + Chemotherapy
	– R-CHOP
	– R-CVP
	– R-Bendamustine
	– Alkylating agent + Rituximab
	· Monoclonal antibody + Small molecule targeted therapy
	– R-Lenalidomide
	· Small molecule targeted therapy
	– Idelalisib
	– Copanlisib (PI3K inhibitors)

Note: R(rituximab); R-CHOP(rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone); R-CVP (rituximab, cyclophosphamide, vincristine, prednisone); Alkylating agent (Chlorambucil or Cyclophosphamide);

2019 CSCO Guidelines for Diagnosis and Treatment of Lymphoma

Source: Frost & Sullivan Report

The below table set forth maintenance and treatment options for MCL under the guidelines as referenced:

Stage	Treatment
First-line treatment	· Monoclonal antibody
	– Rituximab
	· Monoclonal antibody + Chemotherapy
	– -R-CHOP
	– R-DHAP
	– R-HyperCAVD
	– R-Bendamustine
	– VR-CAP
	– RBAC
	· Monoclonal antibody + Small molecule targeted therapy
	– R-Lenalidomide
Second-line treatment	· Small molecule targeted therapy
	– Lenalidomide
	– Bortezomib
	– Ibrutinib (BTK inhibitor)
	· Monoclonal antibody + Small molecule targeted therapy
	– R-Lenalidomide
	– R-Bortezomib
	– R-Ibrutinib
	– R-Ibrutinib-Lenalidomide
	· Monoclonal antibody + Chemotherapy
	– R-Bendamustine
	· Monoclonal antibody + Chemotherapy + Small molecule targeted therapy
	– R-Bendamustine-Bortezomib

Note: R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone); R-CHOEP (rituximab, cyclophosphamide, doxorubicin, vincristine,etoposide, prednisone); R-DAEPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin); R-miniCHOP (rituximab, lower dosage of CHOP); R-DHAP(rituximab, dexamethasone, cisplatin, cytarabine); R-ESHAP(rituximab, etoposide, methylprednisolone, cytarabine, cisplatin); R-HyperCVAD(Regimen A: rituximab, cyclophosphamide, mesna, doxorubicin, dexamethasone, vincristine; Regimen B: rituximab, methotrexate, cytarabine); VR-CAP(bortezomib, rituximab, vincristine, doxorubicin, prednison); RBAC(rituximab, bendamustine, cytarabine)

2019 CSCO Guidelines for Diagnosis and Treatment of Lymphoma

Source: Frost & Sullivan Report

OVERVIEW OF CHINA'S ANTI-INFECTIOUS DISEASE DRUG MARKET

The market size of anti-infective drugs in China amounted to RMB225.5 billion in 2019, accounting for 13.8% of the entire pharmaceutical market in China, and is expected to increase to RMB260.7 billion by 2024, growing at a CAGR of 2.9% from 2019 to 2024, according to the Frost & Sullivan Report. The recent slowdown of the overall anti-infective market growth is the result of improved health conditions together with the government restriction on use of antibiotics. Over the past ten years, there were eight novel antibiotics approved in China, namely Tigecycline (替加環素) from Pfizer, Morinidazole (嗎啉硝唑) from Hansoh, Nemonoxacin (奈諾沙星) from Zhejiang Medicine, Carrimycin (可利黴素) from Shanghai Tonglian, Tedizolid (特地唑胺) from Merck Sharp & Dohme B.V., Sitafloxacin (西他沙星) from Daiichi Sankyo, Garenoxacin (加諾沙星) from Toyama Chemical and Ceftazidime/Avibactam (頭孢他啶/阿維巴坦) from Pfizer, according to the Frost & Sullivan Report.

Multi-Drug Resistance (MDR) is defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories. MDR is are increasingly problematic in healthcare settings, primarily because of the small availability of effective antimicrobial agents that are available to treat infections with these organisms. The growth rate of China MDR antibiotics market, on the other hand, remained stable in the past 5 years, increasing from RMB15.4 billion in 2015 to RMB24.6 billion in 2019 at a CAGR of 12.4%, according to the Frost & Sullivan Report. The market will further grow to RMB39.6 billion from 2019 to 2024, representing a CAGR of 10.0%, and is estimated to reach RMB58.4 billion in 2030.

China MDR Antibiotics Market (2015—2030E)

Source: Frost & Sullivan

The evolving resistance to anti-infective drugs of has become a pressing public health issue, which has to be addressed through the prudent use of such drugs and the replacement with new anti-infective drugs. As a result, the growth rate of anti-infective drugs treating multi-drug resistant bacteria is expected to be much higher than that of the anti-infective drug market as a whole.

According to the Frost & Sullivan Report, for multi-drug resistant bacteria infections, the major recommended antibiotics include Vancomycin, Tigecycline, Linezolid, Teicoplanin, Daptomycin, Carbapenem, Polymxin and BL/BLI combinations (Cefoperazone/Sulbactam, Piperacilin/Tazobactam), which are recommended to treat infections caused by MDR bacteria such as Methicillin-resistant Staphylococcus aureus (MRSA), Vancomycin-resistant Enterococci (VRE) and Multidrug-resistant Acinetobacter, etc. Zai Lab's omadacycline is a type of tetracycline, a category that tigecycline also falls in. However, compared to tigecycline, omadacycline has both IV and oral formulation which rendering more flexibility for clinical use.

Key Growth Drivers of China's MDR Antibiotic Drug Market

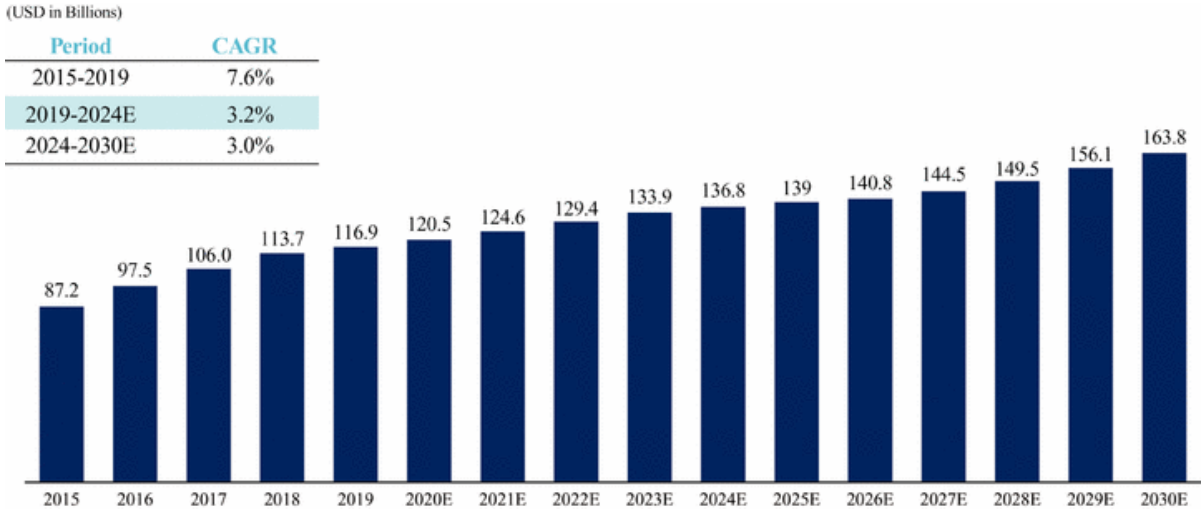
According to Frost & Sullivan, the growth of MDR is driven by the following key factors:

- *Increasing in Health Awareness and Patient Pool* — The disposable income and health awareness are increasing in China; whereas, the number of patients suffering from infections is increasing as well.
- *Growing Drug Resistance* — Bacterial resistance to commonly used antibiotics is still on the rise in China. For example, in 2018, the drug resistance rate of Streptococcus pneumoniae to erythromycin was as high as 95.4%; meanwhile, the resistance of Escherichia coli to third generation cephalosporins was 53%, and the resistence of A. baumannii to carbapenems was 56.1%.
- *The Need for Reliable Treatments* — Both G+ bacteria and G-bacteria experience high drug resistance rates, while antibiotics to treat resistant organisms are very limited. Despite high demand from China's patient population and medical community, China has approved only eight novel antibiotics in the last ten years. Besides, many currently approved drugs have significant safety issues, including allergic reactions, renal toxicity, bone marrow toxicity, vomiting, nausea and diarrhea.
- *Favourable Policies* — The government has introduced various policies to encourage and support research and development of the next-generation antibiotics.
- *Improving Affordability* — In the 2019 NRDL update, 200 anti-infective drugs were included, which achieved a large coverage in this therapeutic area. In addition, in the NRDL negotiation in 2019, 11 new therapies were successfully included. Since the government implements a dynamic adjustment mechanism for NRDL, there is a possibility that more new anti-infective drugs will be included in the future.

OVERVIEW OF THE GLOBAL AUTOIMMUNE DISEASES MARKET

Autoimmune diseases are conditions in which the human body's immune system mistakenly attacks the body and can be associated with over-activity of the immune system. According to the Frost & Sullivan Report, the global autoimmune disease market was US$87.2 billion in 2015 and reached US$116.9 billion in 2019 at a CAGR of 7.6% from 2015 to 2019. The market is expected to grow to US$136.8 billion in 2024 and US$163.8 billion in 2030, representing a CAGR of 3.2% from 2019 to 2024 and a CAGR of 3.0% from 2024 to 2030, according to the Frost & Sullivan Report. The chart below illustrates the historical and forecast size of the global autoimmune diseases market.

Global Autoimmune Diseases Market



Source: Frost & Sullivan

Autoimmune disease remains a major burden on health systems around the world and significantly impacting the patients' quality of life. With few exceptions, autoimmune diseases have proven very challenging to treat, and impossible to cure. Although much progress has been made in understanding the mechanism of autoimmune disease, effective and highly targeted treatments have proven elusive. Most current therapeutic agents broadly suppress the body's immune system, require continued and sometimes life-long therapy, and result in an increased risk of malignancy and infection. Biologics have established themselves as a new effective drug class used when older systemic treatments, such as methotrexate and cyclosporine, fail to control the disease. As a result, biologics such as monoclonal antibodies have become an increasingly important contributor to the growth of the global autoimmune market, and represent a key areas of focus for the research and development of novel therapies that would provide more treatment options to patients. However, there remain limitations associated with current biologics. For example, TNFα inhibitors are recommended for a number of autoimmune disease types, however they fail to obtain sufficient response in other types. Furthermore, some patients who initially responded tend to lose response over time due to the development of anti-drug antibodies. Some TNFα inhibitors are also associated with several shortcomings as a life-long therapy, including inconvenient intravenous or subcutaneous formulation and an FDA black-box warning of potential serious infections and malignancy. Similarly, while IL-17 blockers are used in psoriasis with unprecedented efficacy, they can nevertheless result in certain safety issues due to immunosuppression, are restricted to more severely affected patient populations, and have to be administered by IV or SC injection. There is therefore significant unmet need for novel therapies with better safety profiles and better efficacy, as well as more convenient dosing, which can expand the market, providing additional options to patients.

The following section sets forth updated and supplemental information relating to selected regulations to reflect changes and updates subsequent to the filing of our 2019 Annual Report.

PRC REGULATION OF PHARMACEUTICAL PRODUCT DEVELOPMENT AND APPROVAL

Regulatory Authorities

In the PRC, the newly formed NMPA is the authority under the State Administration for Market Regulation that monitors and supervises the administration of pharmaceutical products, medical appliances and equipment, and cosmetics. The NMPA was established in March 2018 as part of the institutional reform of the State Council. Predecessors of the NMPA include the former China Food and Drug Administration, or the CFDA, that was established in March 2013, the State Food and Drug Administration, or the SFDA, that was established in March 2003 and the previous State Drug Administration, that was established in August 1998.

The primary responsibilities of the NMPA include:

- monitoring and supervising the administration of pharmaceutical products, medical appliances and equipment, as well as cosmetics in the PRC;
- formulating administrative rules and policies concerning the supervision and administration of the pharmaceutical, medical device, and cosmetics industry;
- evaluating, registering and approving of chemical drugs, biological products and traditional Chinese medicine, or TCM;
- approving and issuing permits for the manufacture and export/import of pharmaceutical products; and
- examining and evaluating the safety of pharmaceutical products, medical devices, and cosmetics and handling significant accidents involving these products.

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》), promulgated by the CFDA in March 2017 and came into effect in May 2017, the approval of clinical trial application should be issued by the Center for Drug Evaluation (the "CDE") in the name of the CFDA.

The National Health and Family Planning Commission, or NHFPC, is rebranded as the National Health Commission, or NHC. The NHC is an authority at the ministerial level under the State Council and is primarily responsible for national public health. The NHC combines the responsibilities of the former NHFPC, the Leading Group Overseeing Medical and Healthcare Reform under the State Council, the China National Working Commission on Aging, partial responsibilities of the Ministry of Industry and Information Technology in relation to tobacco control, and partial responsibilities from the State Administration of Work Safety in relation to occupational safety. The predecessor of NHFPC is the Ministry of Health, or MOH. Following the establishment of the former SFDA in 2003, the MOH was put in charge of the overall administration of the national health in the PRC excluding the pharmaceutical industry. The NHC performs a variety of tasks in relation to the health industry such as establishing and overseeing the operation of medical institutes, which also serve as clinical trial sites, regulating the licensure of hospitals and producing professional codes of ethics for public medical personnel. The NHC plays a significant role in drug reimbursement. The NHC and its local counterparts at or below provincial-level local governments also oversee and organize public medical institutions' centralized bidding and procurement process for pharmaceutical products, which is the chief means through which public hospitals and their internal pharmacies acquire drugs. The NHC is also responsible for overseas affairs, such as dealings with overseas companies and governments.

Drug Administration Laws and Regulations

The Drug Administration Law of the PRC (《中華人民共和國藥品管理法》), or the Drug Administration Law, was promulgated by the Standing Committee of the NPC, in September 1984. The last two amendments to the Drug Administration Law were the amendment promulgated in April 2015 and in August 2019. The Regulations for the Implementation of the Drug Administration Law (《藥品管理法實施條例》) was promulgated by the State Council in August 2002, and was last amended in March 2019. The Drug Administration Law and the Regulations for the Implementation of the Drug Administration Law have jointly laid down the legal framework for administration of pharmaceutical products in China, including the research, development and manufacturing of drugs. The Drug Administration Law applies to entities and individuals engaged in the development, production, trade, application, supervision and administration of pharmaceutical products, which regulates and provides for a framework for the administration of pharmaceutical manufacturers, pharmaceutical trading companies and medicinal preparations of medical institutions, and the development, research, manufacturing, distribution, packaging, pricing and advertisements of pharmaceutical products. The Regulations for the Implementation of the Drug Administration Law, at the same time, provide the detailed implementation regulations for the Drug Administration Law.

In August 2019, the Standing Committee of the NPC promulgated the new Drug Administration Law (the "2019 Amendment"), which came into effect in December 2019. The 2019 Amendment contains many of the major reform initiatives implemented by the Chinese government since 2015, including but not limited to the marketing authorization holder system (the "MAH System"), conditional approvals of drugs, traceability system of drugs, and the cancellation of relevant certification according to the Good Manufacturing Practice and the Good Supply Practice. To further implement the 2019 Amendment, the amended Administrative Measures for Drug Registration (《藥品註冊管理辦法》), the amended Good Clinical Trial Practice for Drugs (《藥物臨床試驗質量管理規範》) and the amended Measures on the Supervision and Administration of the Manufacture of Drugs (《藥品生產監督管理辦法》) etc. have been promulgated and come into effect in July 2020. See "— PRC Regulation of Pharmaceutical Product Development and Approval — Administrative Measures for Drug Registration", "— PRC Regulation of Pharmaceutical Product Development and Approval — Regulations on the Clinical Trials and Registration — Compliance with GCP and Drug Clinical Institutions", "— Permits and Licenses for Manufacturing and Distributing of Drugs — Pharmaceutical Manufacturing Permit and GMP Requirements".

Data Privacy and Data Protection

The Cyber Security Law of the PRC (《中華人民共和國網絡安全法》) was promulgated by the Standing Committee of the NPC in November, 2016, which regulates network operators, a broad category that covers all organizations in China that own, operate or manage computer networks, and requires them to take certain technical measures and other necessary measures to ensure the security of their networks and data stored on their networks. In addition, network operators shall obtain the prior consent of an individual before collecting and use his or her personal information or providing his or her personal information to others and shall adopt measures to prevent the personal information they have collected from being divulged, damaged or lost. Additional regulations, guidelines and other measures under the framework of the Cyber Security Law of the PRC or personal information protection are expected to be published or adopted, including the Measures for Security Assessment for Cross-border Transfer of Personal Information and Important Data (Draft for Comment) (《個人信息和重要數據出境安全評估辦法(徵求意見稿)》), published in 2017, and the Measures for Security Assessment for Cross-border Transfer of Personal Information (Draft for Comment) (《個人信息出境安全評估辦法(徵求意見稿)》), published in 2019, which indicate a trend of more stringent compliance requirement, and if adopted, may require security assessment and review before transferring personal health information out of China.

Administrative Measures for Drug Registration

The Administrative Measures for Drug Registration ("Registration Measures") was promulgated by SFDA in July 2007 and then amended by the SAMR in January 2020, which became effective in July 2020. The Registration Measures mainly cover: (1) definitions of drug marketing registration applications and regulatory responsibilities of the drug administration; (2) general requirements for drug marketing registration; (3) clinical trials; (4) application, examination and approval of drugs; (5) supplemental applications and re-registrations of drugs; (6) inspections; (7) registration standards and specifications; (8) time limit; (9) associated review of drugs, excipients and packaging materials; (10) expedited registration of drugs; and (11) liabilities and other supplementary provisions.

Drug Categorization

According to the Registration Measures, 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.

In March 2016, the CFDA issued the Reform Plan for Registration Category of Chemical Medicine (《化學藥品註冊分類改革工作方案》), which aims to reclassify the registration application of chemical drugs stipulated by the Registration Measures promulgated in 2007. According to the Reform Plan for Registration Category of Chemical Medicine, Category 1 drugs refer to innovative chemical drugs that have not been marketed anywhere in the world. Improved new chemical drugs that are not marketed anywhere in the world fall into Category 2 drugs, among which, chemical drugs contain new indications with known active ingredients would be classified as Category 2.4 drugs. Generic chemical drugs, that have equivalent quality and efficacy to the originator's drugs have been marketed abroad but not yet in China, can be classified as Category 3 drugs. Generic drugs, that have equivalent quality and efficacy to the originator's drugs and have been marketed in China, fall into Category 4 drugs. Category 5 drugs are drugs which have already been marketed abroad, but are not yet approved in China.

As a support policy and implementing rule of the Registration Measures newly amended in 2020, the NMPA issued the Chemical Drug Registration Classification and Application Data Requirements (《化學藥品註冊分類及申報資料要求》) in June 2020, effective in July 2020, which reaffirmed the principles of the classification of chemical drugs set forth by the Reform Plan for Registration Category of Chemical Medicine, and made minor adjustments to the subclassifications of Category 5. According to such rule, Category 5.1 are innovative chemical drugs and improved new chemical drugs while Category 5.2 are generic chemical drugs, all of which shall have been already marketed abroad but not yet approved in China.

Accelerated Approval for Clinical Trial and Registration

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

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

The CFDA promulgated the Opinions on Encouraging the Priority Review and Approval for Drug Innovations (《關於鼓勵藥品創新實行優先審評審批的意見》) in December 2017, which further clarified that a fast track clinical trial approval or drug marketing registration pathway will be available to innovative drugs. Particularly, concurrent applications for new drug clinical trials which are already approved in the United States or the European Union are also eligible for fast track clinical trial approval.

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

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

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

- Procedures for conditional approval: during the drug clinical trials, for drugs which fall under the following circumstances, an application for conditional approval of marketing registration may be submitted (i) for drugs for treatment of life- threatening illnesses for which there is no effective treatment approach, the clinical trial of drugs already has data to prove efficacy and is able to forecast the clinical value; (ii) for drugs urgently needed for public health, the clinical trial of drugs already has data to prove efficacy and is able to forecast the clinical value; and (iii) for other vaccines urgently needed for major public health emergencies or deemed by the NHC to be urgently needed, its benefits outweigh the risks according to the evaluation.

- Procedures for prioritized reviews and approval: at the time of the drug marketing registration, drugs have obvious clinical value may apply for application of procedures for prioritized review and approval, including (i) clinically and urgently needed but insufficient drug, innovative drugs and improved new drugs for prevention and treatment of major contagious diseases and rare diseases; (ii) new pharmaceutical product types, dosage form and specifications of pediatric drugs which comply with pediatric physiological characteristics; (iii) vaccines and innovative vaccines urgently needed for prevention and control of diseases; (iv) drug included in the procedures for ground-breaking therapeutic drug; (v) drug which comply with conditional approval criteria; and (vi) other circumstances of prioritized review stipulated by the NMPA.

- Procedures for special examination and approval: at the time of a threat or occurrence of public health emergency, the NMPA may, in accordance with law, decide to implement special examination and approval for urgently needed drug required for the prevention and treatment during the public health emergency. Drug included in the special examination and approval procedures may, based on special needs of disease prevention and control, be restricted for use within a certain period and scope.

Regulations on the Clinical Trials and Registration of Drugs

Four Phases of Clinical Trials

According to the Registration Measures, a clinical development program consists of Phases I, II, III and IV clinical trial as well as bioequivalence trial. Based on the characteristics of drugs and research objective, the research contents shall include clinical pharmacology research, exploratory clinical trial, confirmatory clinical trial and post-marketing research.

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 SFDA in May 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 SFDA.

Approval Authority and Process for Clinical Trial Applications

According to the Registration Measures, upon the completion of the pharmaceutical, pharmacological and toxicological research of the drug clinical trial, the applicant may submit relevant research materials to CDE for applying of a Clinical Trial Application, or the CTA, to conduct drug clinical trial. The CDE will organize pharmaceutical, medical and other technicians to review the application and to decide whether to approve the drug clinical trial within 60 days of the date of acceptance of the application. Once the decision is made, the result will be notified to the applicant through the website of the CDE and if no notice of decision is issued within the aforementioned time limit, the application of clinical trial shall be deemed as approval. The Registration Measures further requires that the applicant shall, prior to conducting the drug clinical trial, register the information of the drug clinical trial plan, etc. on the Drug Clinical Trial Information Platform. During the drug clinical trials, the applicant shall update registration information continuously, and register information of the outcome of the drug clinical trial upon completion. The applicant shall be responsible for the authenticity of the drug clinical trial information published on the platform. Pursuant to the Notice on the Drug Clinical Trial Information Platform (《關於藥物臨床試驗信息平台的公告》) promulgated by SFDA in September 2013, the applicant shall complete the trial pre-registration within one month after obtaining the approval of the clinical trial application 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, the applicant shall submit an explanation, and if the first submission is not completed within three years, the approval of the clinical trial application shall automatically expire.

Compliance with GCP and Drug Clinical Institutions

The conduct of clinical trials must adhere to the Good Clinical Trial Practice for Drugs (the "GCP Rules") which was promulgated by the SFDA in August 2003 and further amended in April 2020 and came into effect in July 2020. According to the GCP Rules, clinical trial means systematical investigation of drugs conducted on human subjects (patients or healthy volunteers) to prove or reveal the clinical, pharmacological and other pharmacodynamic effects, adverse reactions or absorption, distribution, metabolism and excretion of the drug being investigated. In order to ensure the quality of clinical trials and the safety of human subjects, the GCP Rules provides comprehensive and substantive requirements on the design and conduct of clinical trials in China. In particular, the GCP Rules enhances the protection for study subjects and tightens the control over bio-samples collected under clinical trials.

The GCP Rules stipulated that the sponsor shall bear the expenses for medical treatment and the corresponding compensation for any human subject who is harmed or dies due to reasons connected with the clinical trial. The sponsor and investigator shall pay the human subject the compensation or indemnification in a timely manner. However, the GCP Rules promulgated in 2020 abolishes the compulsory insurance the sponsor provides to human subjects participating in a clinical trial compared with the GCP Rules promulgated in 2003.

The GCP Rules also set out the qualifications and requirements for the investigators and drug clinical trial institutions, including: (i) professional certification at a drug clinical trial institutions, professional knowledge, training experience and capability of clinical trial, and being able to provide the latest resume and relevant qualification documents per request; (ii) being familiar with the trial protocol, investigator's brochure and relevant information of the trial drug provided by the applicant; (iii) being familiar with and comply with the Revised GCP Rules and relevant laws and regulations relating to clinical trials; (iv) keeping a copy of the authorization form on work allocation signed by investigators; (v) investigators and drug clinical trial institutions shall accept supervision and inspection organized by the applicant and inspection by the drug regulatory authorities; and (vi) in the case of investigators and drug clinical trial institutions authorizing other individual or institution to undertake certain responsibilities and functions relating to clinical trial, they shall ensure such individual or institution are qualified and establish complete procedures to ensure the responsibilities and functions are fully performed and generate reliable data.

The GCP Rules also summarizes the role of ethic committee in clinical trial process. An ethic committee shall consist of experts working in the medical, pharmaceutical and other fields. The clinical trial protocol may not be executed unless approved by the ethic committee. In November 2019, the NMPA and the NHC jointly promulgated the Notice on Issuing the Administration Rules of Drug Clinical Trial Institution (《關於發布藥物臨床試驗機構管理規定的公告》), which stipulates that each drug clinical trial institution shall maintain an ethic committee responsible for the ethical review of drug clinical trial.

According to the Notice on Issuing the Administration Rules of Drug Clinical Trial Institution, drug clinical trial institutions refer to institutions eligible to undertake the drug clinical trials and shall have been duly recorded with the online platform designated by NMPA. These rules have specified the requirements for drug clinical trial institutions and require that a clinical trial institution should evaluate or engage a third party to evaluate whether it has met such requirements before applying for recordal. A drug clinical trial applicant should only engage a duly recorded clinical trial institution to carry out a drug clinical trial and the clinical trial institution engaged must, during the conduct of clinical trials, comply with the GCP Rules and other technical guidelines for drug clinical trials.

Drug Marketing Registration

According to the Registration Measures, the applicant may submit an application for drug marketing registration to CDE upon completion of relevant research on pharmacy, pharmacology, toxicology and drug clinical trials, determination the quality standards of the drug, validation of commercial-scale production processes and preparation for acceptance of verification and inspection conducted by professional technical institution designated by competent NMPA. The CDE will organize pharmaceutical, medical and other technicians to conduct comprehensive review of the safety, efficacy and quality controllability, among others, of the drug according to the application materials submitted by the applicant, the results of the verification and inspection conducted by professional technical institution, etc. If the comprehensive review conclusion is affirmative, the drug shall be approved for marketing and a drug registration certificate will be issued containing the information of the drug approval number, the MAH and the manufacturer.

Marketing Authorization Holder System

The MAH System was formally established by the 2019 Amendment and symbolized the general application of the MAH System throughout the country. According to which: (i) an MAH refers to enterprise or drug research and development institute which has obtained a drug registration certificate; (ii) an MAH shall be responsible for managing the whole manufacturing and marketing chain and the whole life cycle of drugs and assumes the full legal liability for non-clinical study, clinical trial, manufacturing and operation, post-market launch study, monitoring, reporting and handling of adverse reactions of the drugs; (iii) the legal representative and the key person-in-charge of a drug MAH shall be fully responsible for the quality of drugs; (iv) an MAH shall establish a drug quality assurance system and be equipped with special personnel to take charge of quality management on drugs independently; and (v) an MAH shall regularly review the quality management system of the drug manufacturer and the drug distributor, and supervise its continuous quality assurance and control capabilities. As a part of the healthcare reform in China in recent years, the MAH System is embedded with favorable governmental policies in terms of drug manufacturing, distribution and transfer, etc. MAH may either engage in drug manufacturing on its own or may engage licensed contract manufacturers for manufacturing. An MAH may either engage in drug sales on its own or may engage licensed contract distributor for drug sales. Upon approval by the drug administrative department of the State Council, an MAH may transfer the drug registration certificate for a certain drug obtained by it to a qualified transferee and upon the completion of the transfer, such transferee will be the new MAH for that drug.

Acceptance of Foreign Clinical Trial Studies

The NMPA issued the Technical Guidance Principles on Accepting Foreign Drug Clinical Trial Data (《接受藥品境外臨床試驗數據的技術指導原則》) in July 2018, as one of the implementing rules for the Innovation Opinions, which provides that overseas clinical data can be submitted for the drug marketing registration applications in China. Such applications can be in the form of waivers to China-based clinical trials, bridging trials and direct drug marketing registration. According to the Technical Guidance Principles on Accepting Foreign Drug Clinical Trial Data, sponsors may use the data of foreign clinical trials to support drug marketing registration in China, provided that sponsors must ensure the authenticity, integrity, accuracy and traceability of foreign clinical trial data and such data must be obtained consistent with the relevant requirements under the Good Clinical Trial Practice of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (the "ICH"). Moreover, sponsors shall ensure the scientific design of overseas clinical trials, the compliance of clinical trial quality management system requirements, and the accuracy and integrity of statistical analysis of data. 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 sponsors may, prior to implementing pivotal clinical trials, contact the CDE to ensure the compliance of pivotal clinical trials' design with the essential technical requirements for drug registration in China. Sponsors must also comply with other relevant sections of the Registration Measures when applying for drug marketing registrations in China using foreign clinical trial data.

The NMPA now officially permits, and its predecessor agencies have permitted on a case-by-case basis in the past, drugs approved outside of China to be approved in China on a conditional basis without pre-approval clinical trials being conducted in China. Specifically, the NMPA and the NHC released the Procedures for Reviewing and Approval of Clinical Urgently Needed Overseas New Drugs (《關於臨床急需境外新藥審評審批相關事宜的公告》) in October 2018, permitting drugs that have been approved within the last ten years in the United States, the European Union or Japan and that prevent or treat orphan diseases or prevent, or treat serious life-threatening illnesses for which there is either no effective therapy in China, or for which the foreign-approved drug would have clear clinical advantages. Applicants will be required to establish a risk mitigation plan and may be required to complete trials in China after the drug has been marketed. The CDE has developed a list of qualifying drugs that meet the foregoing criteria.

Import of Urgently Needed Drug in Boao Pilot Zone

According to the Drug Administration Law, based on urgent medical need by medical institution of certain drug that is not yet registered domestically (the "Urgently Needed Drug"), subject to the approval of NMPA or competent provincial government, a small amount of such Urgently Needed Drug may be imported but shall be solely applied for specific medical purpose at the designated medical institution.

The State Council issued the Official Reply of the State Council to Approve the Establishment of Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province (《國務院關於同意設立海南博鰲樂城國際醫療旅遊先行區的批復》) in February 2013, according to which, Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province (the "Boao Pilot Zone") shall be established as a pilot zone where accelerated approval of the import of the Urgently Needed Drug is available. The State Council further issued the Decision on Temporarily Adjusting the Implementation of the Relevant Provisions of the Implementing Measures of the Drug Administration Law in the Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province (《國務院關於在海南博鰲樂城國際醫療旅遊先行區暫時調整實施<中華人民共和國藥品管理法實施條例>有關規定的決定》) in December 2018, according to which, the State Council empowers the People's Government of Hainan Province (the "Hainan Government") to approve the import of the Urgently Needed Drug (excluding vaccines).

The Hainan Government promulgated the Interim Provisions on the Administration of Imported Drugs of Urgent Need in Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province (《海南博鰲樂城國際醫療旅遊先行區臨床急需進口藥品管理暫行規定》) in April 2019, according to which, a qualified medical institution in the Boao Pilot Zone may apply for the import of certain Urgently Needed Drug (excluding vaccines and other drugs under special management) and apply to patient on case by case basis. Such application shall be subject to the evaluation and approval of Hainan Provincial Health Commission and the Medical Products Administration of Hainan Province, as well as the customs formalities with Haikou Customs.

Medical Products Administration of Hainan Province promulgated the Interim Measures for the Administration of Taking Away the Imported Urgently Needed Drug from the Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province (《海南博鰲樂城國際醫療旅遊先行區臨床急需進口藥品帶離先行區使用管理暫行辦法》) in March 2020, according to which, a patient may apply for taking away a small amount of the legally imported Urgently Needed Drug from the Boao Pilot Zone following his therapeutic schedule issued by a medical institution. Such application shall be subject to the evaluation and approval of Hainan Provincial Health Commission and the Medical Products Administration of Hainan Province.

PERMITS AND LICENSES FOR MANUFACTURING AND DISTRIBUTING OF DRUGS

Pharmaceutical Manufacturing Permit and GMP Requirements

According to the Drug Administration Law and the Implementing Regulations of the Drug Administration Law, to manufacture pharmaceutical products in the PRC, a pharmaceutical manufacturing enterprise must first obtain a Pharmaceutical Manufacturing Permit issued by the relevant pharmaceutical administrative authorities at the provincial level where the enterprise is located. Among other things, such a permit must set forth the scope of production and effective period. The grant of such license is subject to an inspection of the manufacturing facilities, and an inspection to determine whether the sanitary condition, quality assurance systems, management structure and equipment meet the required standards.

According to the Regulations of Implementation of the Drug Administration Law and the Measures on the Supervision and Administration of the Manufacture of Drugs (the "GMP Rules"), promulgated in August 2004 and amended in November 2017 and January 2020, respectively, each Pharmaceutical Manufacturing Permit issued to a pharmaceutical manufacturing enterprise is effective for a period of five years. Any enterprise holding a Pharmaceutical Manufacturing Permit is subject to review by the relevant regulatory authorities on an annual basis. The enterprise is required to apply for renewal of such permit within six months prior to its expiry and will be subject to reassessment by the issuing authorities in accordance with then prevailing legal and regulatory requirements for the purposes of such renewal.

The World Health Organization encourages the adoption of good manufacturing practice, or GMP, standards in pharmaceutical production in order to minimize the risks involved in any pharmaceutical production that cannot be eliminated through testing the final products.

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

Pharmaceutical Operation Permit and GSP Requirements

The Administration of Pharmaceutical Operation Permit (《藥品經營許可證管理辦法》) promulgated in February 2004 and amended in November 2017 by the CFDA provides the application procedures and requirements for Pharmaceutical Operation Permit. According to which, a Pharmaceutical Operation Permit is valid for five years. Each holder of the Pharmaceutical Operation Permit must apply for an extension of its permit six months prior to expiration. The establishment of a wholesale pharmaceutical distribution company requires the approval of the provincial medicine administrative authorities. Upon approval, the authority will grant a Pharmaceutical Operation Permit in respect of the wholesale pharmaceutical product distribution company. The establishment of a retail pharmacy store requires the approval of the local medicine administrative authorities at or above the county level. Upon approval, the authority will grant a Pharmaceutical Operation Permit in respect of the retail pharmacy store.

According to the Drug Administration Law and its implementing regulations and the Measures for the Supervision and Administration of Circulation of Pharmaceuticals (《藥品流通監督管理辦法》), which was promulgated by the SFDA in January 2007 and came into effect in May 2007, a pharmaceutical enterprise shall be responsible for the quality of pharmaceuticals they manufacture, operate or use, purchase, sale, transportation, storage, including activities carried out by its staff on its behalf, and it shall not store or sell, pharmaceuticals at a place other than the address approved by the pharmaceutical regulatory authority. Where a pharmaceutical enterprise knows or ought to know that any person operates pharmaceutical business without the Pharmaceutical Operation Permit but still supplies such person with pharmaceutical products, the pharmaceutical regulatory authority may give a disciplinary warning to the pharmaceutical enterprise, order such enterprise to rectify the non-compliance and impose a fine of no more than RMB10,000. In the case of a serious violation, such enterprise may be fined in an amount ranging from RMB10,000 to RMB30,000.

The Good Supply Practice for Drugs (《藥品經營質量管理規範》) was promulgated in April 2000 and was amended respectively in November 2012, May 2015 and June 2016. The Good Supply Practice for Drugs is laid down as the basic rules for drug operation and quality control, sets forth the requirements for enterprises throughout the process of drug purchase, storage, sales and transportation.

U.S. REGULATION OF PHARMACEUTICAL PRODUCT DEVELOPMENT AND APPROVAL

Clinical Studies

The clinical stage of development involves the administration of the drug product to human subjects or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which establish standards for conducting, recording data from, and reporting the results of, clinical trials, and are intended to assure that the data and reported results are accurate, and that the rights, safety, and well-being of study participants are protected. GCPs also include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also reviews and approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. For example, information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

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

- Phase I: The drug is initially introduced into a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the drug candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing may be conducted in patients with the target diseases.

- Phase II: The drug is administered to a limited patient population to determine dose tolerance and optimal dosage required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy.

- Phase III: The drug is administered to an expanded number of patients, generally at multiple sites that are geographically dispersed, in well-controlled clinical trials to generate enough data to demonstrate the efficacy of the drug for its intended use, its safety profile, and to establish the overall benefit/risk profile of the drug and provide an adequate basis for drug approval and labeling of the drug product. Phase III clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a drug during marketing. Generally, two adequate and well-controlled Phase III clinical trials are required by the FDA for approval of an NDA. A pivotal study is a clinical study that adequately meets regulatory agency requirements for the evaluation of a drug candidate's efficacy and safety such that it can be used to justify the approval of the drug. Generally, pivotal studies are also Phase III studies but may be Phase II studies if the trial design provides a well-controlled and reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need. Post-approval trials, sometimes referred to as Phase IV clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of Phase IV clinical trials.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA, and more frequently if serious adverse events occur. Written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk to human subjects. The FDA, the IRB, or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, cGMPs impose extensive procedural, substantive and recordkeeping requirements to ensure and preserve the long term stability and quality of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Other U.S. Regulatory Matters

Manufacturing, sales, promotion and other activities following drug approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Drug Enforcement Administration for controlled substances, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the United States, sales, marketing and scientific/educational programs must also comply with state and federal fraud and abuse laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Health Care Reform Law, as amended by the Health Care and Education Affordability Reconciliation Act, or ACA. If drugs are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Drugs must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical drugs is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical drugs.

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of drugs, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

COVERAGE AND REIMBURSEMENT

PRC Coverage and Reimbursement

Reimbursement under the National Medical Insurance Program

The national medical insurance program was adopted pursuant 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 in December 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. The State Council promulgated 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》) in July 2007, under which urban residents of the pilot district, rather than urban employees, may voluntarily join Urban Resident Basic Medical Insurance. According to the Social Insurance Law of Peoples' Republic of China (《中華人民共和國社會保險法》) which was promulgated by the Standing Committee of the NPC in October 2010 and amended in December 2018, all employees are required to enroll in the basic medical insurance program and the insurance premium is jointly contributed by the employers and employees as required by the state.

The Opinions on Deepening the Reform of the Healthcare Security System (《中共中央、國務院關於深化醫療保障制度改革的意見》) was promulgated jointly by Central Committee of the PRC Communist Party and the State Council in February 2020. which envisages that a higher level healthcare system should be established by 2030, which centers on basic medical insurance, is underpinned by medical aid and pursues the common development of supplementary medical insurance, commercial health insurance, charitable donations and medial mutual assistance. To this end, such opinions map out tasks in several respects, including making the mechanism of medical insurance benefits guarantee more impartial and appropriate, improving the robust and sustainable operating mechanism for funds raised, establishing more effective and efficient healthcare payment mechanism and enhancing the supervision and administration on medical security fund and etc.

The Interim Measures for the Administration of Use of Drugs Covered by the Basic Medical Insurance (《基本醫療保險用藥管理暫行辦法》) was promulgated by NHSA in April 2020 and came into effect in September 2020. According to which, expenses of drugs listed in the Basic Medical Insurance Catalog will be paid in full or part from the basic medical insurance fund in accordance with applicable provisions, and the drugs with the same generic names as those specified in the Basic Medical Insurance Catalog will be automatically regulated by the Basic Medical Insurance Catalog and shall also be eligible for the reimbursement by the basic medical insurance fund. These measures further clarify that the Basic Medical Insurance Catalog shall be promulgated by the healthcare security department under the State Council and adjusted on an annual basis. Provinces shall have the right to add eligible ethnic drugs, preparations of medical institutions, and traditional Chinese medicine decoction pieces into the provincial medical insurance-based payment scope, which shall be implemented after being filed with the healthcare security department under the State Council for record.

The PRC Ministry of Human Resources and Social Security, together with other government authorities, has the power to determine the medicines included in the National Reimbursement Drug List, or the NRDL. In August 2019, the PRC Ministry of Human Resources and Social Security released the National Drug Catalogue for Basic Medical Insurance, Work-Related Injury Insurance and Maternity Insurance (《關於印發國家基本醫療保險、工傷保險和生育保險藥品目錄的通知》), or the 2019 NRDL. In November 2019, NHSA organized another round of price negotiation with drug companies for 119 new drugs that had not been included in the NRDL at the time of the negotiation, which resulted in an average price reduction by over 60% for 70 of the 119 drugs that passed the negotiation; subsequently, the NRDL was expanded to include the 70 new drugs.

Medicines included in the NRDL are divided into two parts, Part A and Part B.

Patients purchasing medicines included in Part A of the NRDL are entitled to reimbursement of the entire amount of the purchase price. Patients purchasing medicines included in Part B of the NRDL are required to pay a certain percentage of the purchase price and obtain reimbursement for the remainder of the purchase price. The percentage of reimbursement for Part B medicines differs from region to region in the PRC.

According to 2019 NRDL, all provinces shall implement the 2019 NRDL in a strict manner, and shall not have the discretion to formulate the catalogue or increase the drugs of Part B in any form, or adjust the scope of limited payment, except for eligible ethnic drugs, preparations of medical institutions, and traditional Chinese medicine decoction pieces. For those drugs that were already added to Part B of the provincial catalogue in accordance with the previous NRDL, the drugs shall be gradually removed within 3 years.

The total amount of reimbursement for the cost of medicines, in addition to other medical expenses, for an individual participant under the national medical insurance program in a calendar year is capped at the amounts in such participant's individual account under such program. The amount in a participant's account varies, depending on the amount of contributions from the participant and his or her employer.

In August 2020, the NHSA promulgated the Work Plan for the Adjustment of 2020 National Medical Insurance Catalog (《2020年國家醫保藥品目錄調整工作方案》) (the "2020 Work Plan"), according to which, drugs listed in the Urgently Needed Overseas New Drugs List (臨床急需境外新藥名單) promulgated by the CDE which have been granted the approval for drug marketing registration by the NMPA on and before August 17, 2020 may be considered as candidates to be included into the 2020 NRDL. The 2020 Work Plan further provides that the price negotiation with drug companies for 2020 NRDL will be arranged between October and November 2020 and the 2020 NRDL will be finalized and published between November and December 2020.

Supplementary Insurance

The Circular of Ministry of Finance, Ministry of Labor and Social Security on Issues Related to the Supplementary Medical Insurance Established by Enterprises (《財政部、勞動保障部關於企業補充醫療保險有關問題的通知》) was promulgated jointly by the Ministry of Finance and Ministry of Labor and Social Security in May 2002. According to which, enterprises may, on the basis of participation in basic medical insurance program, at their own discretion whether or not to establish the supplementary medical insurance to contribute reasonable allowance for the medical fees borne by their employees other than those paid by the basic medical insurance program for urban employees, so as to reduce the burden of medical expenses of the employees participating in the insurance. The Opinions on Deepening the Reform of the Healthcare Security System (《中共中央、國務院關於深化醫療保障制度改革的意見》) was promulgated jointly by Central Committee of the PRC Communist Party and the State Council in February 2020, which envisages that a higher level healthcare system should be established by 2030, which centers on basic medical insurance, is underpinned by medical aid and pursues the joint development of supplementary medical insurance, commercial health insurance, charitable donations and medical mutual assistance.

Price Controls and Two-invoice System

Instead of direct price controls which were historically used in China, the government regulates prices mainly by establishing a consolidated procurement mechanism, revising medical insurance reimbursement standards and strengthening regulation of medical and pricing practices.

According to the Notice on Issuing Certain Regulations on the Trial Implementation of Centralised Tender Procurement of Drugs by Medical Institutions (《醫療機構藥品集中招標採購試點工作若幹規定》) promulgated in July 2000 and the Notice on Further Improvement on the Implementation of Centralised Tender Procurement of Drugs by Medical Institutions (《國家藥品監督管理局關於進壹步做好醫療機構藥品集中招標採購工作的通知》) promulgated in August 2001, not-for-profit medical institutions established by county or higher level government are required to implement centralised tender procurement of drugs.

The MOH promulgated the Working Regulations of Medical Institutions for Procurement of Drugs by Centralised Tender and Price Negotiations (for Trial Implementation) (《醫療機構藥品集中招標採購和集中議價採購工作規範(試行)》) in March 2002, which provides rules for the tender process and negotiations of the prices of drugs, operational procedures, a code of conduct and standards or measures of evaluating bids and negotiating prices. The Notice of the Financial Planning Department of Ministry of Health on Issue of Opinions on Further Regulating Centralised Procurement of Drugs by Medical Institutions (《衛生部財務規劃司關於印發<進一步規範醫療機構藥品集中採購工作的意見>的通知》) was promulgated in January 2009. According to the notice, not-for-profit medical institutions owned by the government at the county level or higher or owned by state-owned enterprises (including state-controlled enterprises) shall purchase pharmaceutical products by online centralised procurement. Each provincial government shall formulate its catalogue of drugs subject to centralised procurement. Except for drugs in the National List of Essential Drugs (the procurement of which shall comply with the relevant rules on National List of Essential Drugs), certain pharmaceutical products which are under the national government's special control, such as toxic, radioactive and narcotic drugs and traditional Chinese medicines, in principle, all drugs used by not-for-profit medical institutions shall be covered by the catalogue of drugs subject to centralised procurement. The Opinions of the General Office of the State Council on Improvement of the Policy of Production, Circulation and Use of Drugs (《國務院辦公廳關於進一步改革完善藥品生產流通使用政策的若干意見》) promulgated in January 2017 by the General Office of the State Council aims to deepen the reform of medicine health system, improve the quality of the drug and regulate the distribution and use of the drug. The Notice of the General Office of the State Council on Issuing Pilot Plan of Centralised Procurement and Use of the Drug Organised by the State (《國務院辦公廳關於印發國家組織藥品集中採購和使用試點方案的通知》) promulgated in January 2019 aims to improve the pricing mechanism of the drug, which also further regulates the scope and mode of centralised procurement.

The centralized tender process takes the form of public tender operated and organised by provincial or municipal government agencies. The centralised tender process is in principle conducted once every year in the relevant province or city in China. The bids are assessed by a committee composed of pharmaceutical and medical experts who will be randomly selected from a database of experts approved by the relevant government authorities. The committee members assess the bids based on a number of factors, including but not limited to, bid price, product quality, clinical effectiveness, product safety, qualifications and reputation of the manufacturer, after-sale services and innovation. Only pharmaceuticals that have won in the centralised tender process may be purchased by public medical institutions funded by the governmental or state-owned enterprise (including state-controlled enterprises) in the relevant region.

In order to further optimize the order of purchasing and selling pharmaceutical products and reduce circulation steps, under the 2016 List of Major Tasks in Furtherance of the Healthcare and Pharmaceutical Reforms (《深化醫藥衛生體制改革2016年重點工作任務》) issued by the General Office of the State Council in April 2016, the ''two-invoice System'' (兩票制) will be fully implemented in the PRC. According to the Circular on Issuing the Implementing Opinions on Carrying out the Two-invoice System for Drug Procurement among Public Medical Institutions (for Trial Implementation) 《印發〈關於在公立醫療機構藥品採購中推行「兩票制」的實施意見(試行)〉的通知》), which came into effect in December 2016, the two-invoice system means one invoice between the pharmaceutical manufacturer and the pharmaceutical distributor, and one invoice between the pharmaceutical distributor and the hospital, and thereby only allows a single level of distributor for the sale of pharmaceutical products from the pharmaceutical manufacturer to the hospital.

Insurance Reform

In January 2016, the State Council issued the Opinions on Integrating the Basic Medical Insurance Systems for Urban and Rural Residents (《關於整合城鄉居民基本醫療保險制度的意見》), which call for 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 arrangement who participate in the basic medical insurance for urban employees.

In August 2018, the General Office of the State Council issued the Notice on the Main Tasks of Strengthening the Reform of Healthcare System in second half of 2018 (《關於印發深化醫藥衛生體制改革2018年下半年重點工作任務的通知》). Highlights of these healthcare reform policies and regulations include (1) establishing a basic healthcare system to cover both urban and rural residents and providing the Chinese people with safe, effective, convenient and affordable healthcare services, (2) improving the healthcare system through the reform and development of a graded hierarchical healthcare system, modern hospital management, basic medical insurance, drug supply support and comprehensive supervision, and (3) improving the efficiency and quality of the healthcare system to meet the various medical needs of the Chinese population.

In May 2019, the General Office of the State Council issued the Main Tasks of Healthcare System Reform in 2019 (《深化醫藥衛生體制改革2019年重點工作任務》), highlighting the following policies and regulations (1) reinforcing the degree of cancer prevention and treatment, accelerating the registration and approval of anti-cancer new drugs at home and abroad and remaining the temporary channel of imperative anti-cancer drugs importation open, (2) consolidating and improving the basic medicine system and establishing an inventive and restrictive mechanism for preferential use. Improving the dynamic adjusting mechanism of the NRDL and incorporating the eligible therapeutic drugs listing in the National List of Essential Drugs into the NRDL first in accordance with the procedure.

In July 2020, the General Office of the State Council issued the Main Tasks of Healthcare System Reform in the Second Half of 2020 (《深化醫藥衛生體制改革2020下半年重點工作任務》), which set forth six major tasks covering 26 concrete measures, including but not limited to boosting the reform of medical insurance payment methods, strengthening the management of medical insurance funds, and accelerating the development of commercial health insurance.

In December 2019, the Standing Committee of the NPC promulgated the Law of the People's Republic of China on Promotion of Basic Medical and Health Care (《中華人民共和國基本醫療衛生與健康促進法》), which established the legal framework for the administration of basic medical and health services for citizens in China, including the administration of basic medical care services, medical care institutions, medical staff, guarantee of drug supply, health promotion and guarantee of medical funds.

The Opinions on Deepening the Reform of the Healthcare Security System envisages that a higher level healthcare system should be established by 2030, which centers on basic medical insurance, is underpinned by medical aid and pursues the joint development of supplementary medical insurance, commercial health insurance, charitable donations and medial mutual assistance. To this end, such opinions map out tasks in several respects, including making the mechanism of medical insurance benefits guarantee more impartial and appropriate, improving the robust and sustainable operating mechanism for funds raised, establishing more effective and efficient healthcare payment mechanism and enhancing the supervision and administration on medical security fund and etc.

U.S. Coverage and Reimbursement

Successful sales of our products or drug candidates in the U.S. market, if approved, will depend, in part, on the extent to which our drugs will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. Patients who are provided with prescriptions as part of their medical treatment generally rely on such third-party payors to reimburse all or part of the costs associated with their prescriptions and therefore adequate coverage and reimbursement from such third-party payors are critical to new product acceptance. These third-party payors are increasingly reducing reimbursements for medical drugs and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic drugs. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Inadequate third-party reimbursement for our drug candidates, if approved, or a decision by a third-party payor to not cover our drug candidates could reduce physician usage of such drugs and have a material adverse effect on our sales, results of operations and financial condition.

Healthcare reform initiatives have resulted in significant changes to the coverage, reimbursement and delivery of health care, including drugs. Health care reform efforts are likely to continue and such efforts have included, and may include in the future, attempts to repeal or otherwise challenge prior healthcare reform. The spread of COVID-19 has resulted in widespread federal and state legislative and administrative action to impose new or revise existing health care regulation, sometimes on a temporary basis, to limit the spread of the disease, ensure access to necessary health care and address adverse financial impacts.

General legislative cost control measures may also affect reimbursement for our products. The Budget Control Act of 2011, as amended, resulted in the imposition of 2% reductions in Medicare (but not Medicaid) payments to providers in 2013 and, except for a suspension from May 1, 2020 through December 31, 2020, will remain in effect through 2030 unless additional Congressional action is taken. If we obtain approval to market a drug candidate in the United States, any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and/or any significant taxes or fees that may be imposed on us could have an adverse impact on our results of operations.

OTHER SIGNIFICANT PRC REGULATION AFFECTING OUR BUSINESS ACTIVITIES IN CHINA

PRC Regulation of Product Liability

In addition to the strict new drug approval process, certain PRC laws have been promulgated to protect the rights of consumers and to strengthen the control of medical products in the PRC. Under current PRC law, manufacturers and vendors of defective products in the PRC may incur liability for loss and injury caused by such products. Pursuant to the General Principles of the Civil Law of the PRC (《中華人民共和國民法通則》), or the PRC Civil Law, promulgated in April 1986 and amended on August 27, 2009, a defective product which causes property damage or physical injury to any person may subject the manufacturer or vendor of such product to civil liability for such damage or injury. The Civil Code of the PRC (《中華人民共和國民法典》), which was promulgated in May 2020 and will become effective on 1 January 2021, will amalgamate and replace a series of specialized laws in civil law area, including the PRC Civil Law. The rules on product liability in the Civil Code of the PRC remain consistent with the rules in the PRC Civil Law.

In February 1993, the Product Quality Law of the PRC (《中華人民共和國產品質量法》), or the Product Quality Law, was promulgated to supplement the PRC Civil Law aiming to protect the legitimate rights and interests of the end-users and consumers and to strengthen the supervision and control of the quality of products. The Product Quality Law was last revised in December 2018. Pursuant to the revised Product Quality Law, manufacturers who produce defective products may be subject to civil or criminal liability and have their business licenses revoked.

The Law of the PRC on the Protection of the Rights and Interests of Consumers (《中華人民共和國消費者權益保護法》) was promulgated in October 1993 and was amended in August 2009 and October 2013 to protect consumers' rights when they purchase or use goods and accept services. According to which, all business operators must comply with this law when they manufacture or sell goods and/or provide services to customers. Under the latest amendment, all business operators shall pay high attention to protect the customers' privacy and strictly keep it confidential any consumer information they obtain during the business operation. In addition, in extreme situations, pharmaceutical product manufacturers and operators may be subject to criminal liability if their goods or services lead to the death or injuries of customers or other third parties.

PRC Tort Law

Under the Tort Law of the PRC (《中華人民共和國侵權責任法》) promulgated by the Standing Committee of the NPC in December 2009, if damages to other persons are caused by defective products due to the fault of a third party, such as the parties providing transportation or warehousing, the producers and the sellers of the products have the right to recover their respective losses from such third parties. If defective products are identified after they have been put into circulation, the producers or the sellers shall take remedial measures such as issuance of a warning, recall of products, etc. in a timely manner. The producers or the sellers shall be liable under tort if they fail to take remedial measures in a timely manner or have not made efforts to take remedial measures, thus causing damages. If the products are produced or sold with known defects, causing deaths or severe adverse health issues, the infringed party has the right to claim punitive damages in addition to compensatory damages. Civil Code of the PRC will amalgamate and replace the Tort Law from 1 January 2021. The rules on tort in the Civil Code of the PRC are generally consistent with the Tort Law.

PRC Regulation of Intellectual Property Rights

Trade Secrets

According to the PRC Anti-Unfair Competition Law (《反不正當競爭法》) promulgated by the Standing Committee of the NPC in September 1993, as amended in November 2017 and in April 2019 respectively, the term "trade secrets" refers to technical and business information that is unknown to the public that has utility and 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 (1) above; (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; or (4) instigating, inducing or assisting others to violate confidentiality obligation or to violate a rights holder's requirements on keeping confidentiality of trade secrets, disclosing, using or permitting others to use the trade secrets of the rights holder. If a third party knows or should have known of the abovementioned 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.

HONG KONG REGULATIONS

Our Company has commercialized ZEJULA and launched Optune in Hong Kong, and is subject to the following Hong Kong laws and regulations which may be material to our operations in Hong Kong.

Registration of Pharmaceutical Products

The Department of Health in Hong Kong is responsible for overseeing the safety, efficacy and quality of all medicines and pharmaceutical products marketed in Hong Kong. Non-Chinese medicines such as ZEJULA are regulated under the Pharmacy and Poisons Ordinance (Chapter 138 of the Laws of Hong Kong) (the "Pharmacy and Poisons Ordinance"). Pursuant to the Pharmacy and Poisons Ordinance, all pharmaceutical products and medicine must be registered with the Pharmacy and Poisons Board of Hong Kong (the "Pharmacy and Poisons Board") before they can be sold, offered for sale, distributed or possessed for the purposes of sale, distribution or other use in Hong Kong. Any person who engages in the sale of unregistered pharmaceutical products commits an offense and is liable to a maximum fine of HK$100,000 and imprisonment for 2 years.

Under the Pharmacy and Poisons Ordinance, "pharmaceutical product" and "medicine" mean any substance or combination of substances:

- presented as having properties for treating or preventing disease in human beings or animals; or
- that may be used in, or administered to, human beings or animals, either with a view to (i) restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action; or (ii) making a medical diagnosis.

A pharmaceutical product or medicine will only be approved for registration if it meets the criteria of safety, efficacy and quality relevant to it. The applicant has to provide a set of information including production formula, product specification, laboratory report and manufacturer licence in its application for registration for the approval of the Pharmacy and Poisons Board. Upon registration, the pharmaceutical product or medicine will be given a registration number by the Pharmacy and Poisons Board, which is required to be printed on the label of the pharmaceutical product or medicine.

ZEJULA is a registered pharmaceutical product in Hong Kong with registration number HK65945.

Poisons List

In Hong Kong, the Poisons List (the "Poisons List") under the Tenth Schedule of the Pharmacy and Poisons Regulations (Chapter 138A of the Laws of Hong Kong) (the "Pharmacy and Poisons Regulations") lists out certain ingredients classified as poisons. Some poisons are further categorized under different parts of the Poisons List and other different schedules under the Pharmacy and Poisons Regulations according to their potency, toxicity and potential side-effects. Such categorization determines the different levels of control over their sale. For instance, pharmaceutical products that do not contain any poisons or contain poisons listed under Part 2 of the Poisons List ("Part 2 poisons") are referred to as over-the-counter medicines. Pharmaceutical products that do not contain any poisons can be sold in any retail shops, while pharmaceutical products that contain Part 2 poisons can be sold in authorized sellers of poisons ("ASP," usually known as pharmacies or dispensaries) and listed sellers of poisons (usually known as medicine stores), both regulated by the Department of Health in Hong Kong. Pharmaceutical products containing poisons listed under Part 1 of the Poisons List ("Part 1 poisons") can only be sold in pharmacies (ASPs) in the presence and under the supervision of registered pharmacists.

Certain Part 1 poisons are further listed in the First Schedule and the Third Schedule of the Pharmacy and Poisons Regulations, which impose additional restrictions on the sale of pharmaceutical products containing such poisons at the retailers. For example, retailers of pharmaceutical products containing poisons listed in the First Schedule of the Pharmacy and Poisons Regulations are required to keep sales records which include the date of sale, the name, number of identity card, address and signature of the purchaser, the name and quantity of the medicine as well as the purpose for which it is required. The sale of pharmaceutical products containing poisons listed in the Third Schedule of the Pharmacy and Poisons Regulations must be authorized by a prescription from a registered medical practitioner, a registered dentist or a registered veterinary surgeon.

ZEJULA contains poisons that are listed under the First Schedule and the Third Schedule of the Pharmacy and Poisons Regulations. Therefore, ZEJULA can only be sold with prescription and the sales records of ZEJULA, which should include the required particulars as summarized above, must be kept in accordance with the Pharmacy and Poisons Regulations.

Emission of Radio Frequency

In Hong Kong, telecommunications equipment ("TE") and industrial, scientific and medical ("ISM") equipment emitting radio frequency energy intentionally are subject to requirements on technical specifications prescribed by the Communications Authority of Hong Kong. The technical specifications are mainly set for the purposes of electrical safety, prevention of interference, network compatibility and network interoperability. Under the Hong Kong Telecommunications Equipment Evaluation and Certification Scheme (the "HKTEC Scheme") regulated by the Communications Authority of Hong Kong, certain TE and ISM equipment which falls under the "Compulsory Certification Scheme" must be certified by a local certification body accredited under section 32E of the Telecommunications Ordinance (Chapter 106 of the Laws of Hong Kong) (a "Certification Body") before it can be used or marketed in Hong Kong. Such TE or ISM equipment may be granted a certificate by a Certification Body once it has been evaluated to be in compliance with the relevant technical specification. Given Optune, an ISM equipment which emits radio frequency, falls under the Compulsory Certification Scheme under the HKTEC Scheme, it must be approved by the Office of the Communications Authority ("OFCA"), the executive arm of the Communications Authority, and be granted a certificate by a Certification Body before it can be used or offered for sale in Hong Kong. With respect to Optune, we have obtained the approval from OFCA and a certificate from a Certification Body with certificate numbers HK0011801953 and HK0012002185.

The following section sets forth updated and supplemental information relating to selected aspects of our business and operations to reflect changes subsequent to the filing of our 2019 Annual Report.

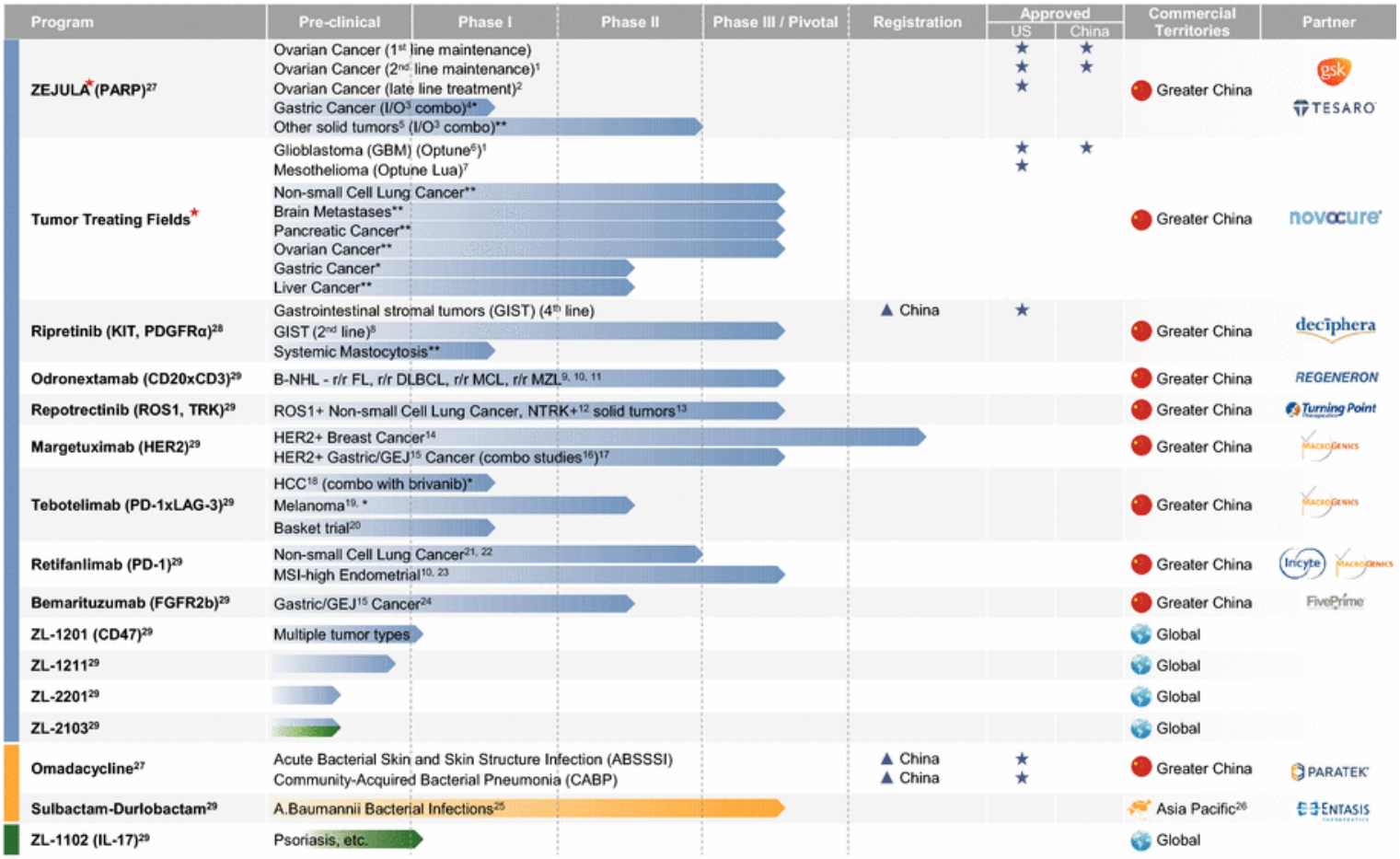
OVERVIEW

We are an innovative, research-based, commercial-stage biopharmaceutical company with a focus on discovering, licensing, developing and commercializing therapies that address areas of large unmet medical need in the China and global markets, including the fields of oncology, infectious and autoimmune diseases. By effectively executing our plan and closely following our strategy, we have built an integrated platform to bring both in-licensed and internally-discovered novel therapeutics to patients globally. We believe we are one of the first biopharmaceutical companies in China to scale, allowing us to further capitalize on the latest innovation and business opportunities globally.

Since our inception, we have executed our strategic approach of in-licensing promising biopharmaceutical products via global collaboration and investing in internal discovery and development efforts. Our robust portfolio consists of 16 products and drug candidates, including two commercialized products in China, Hong Kong and Macau and seven assets in pivotal or potentially registration-enabling trials in oncology and infectious diseases, which are therapeutic areas with a large unmet needs and lack of innovative treatment options in Greater China. Although we have limited experience in manufacturing and commercializing our products and drug candidates, we are nevertheless at the inflection point of commercialization with recent launches of ZEJULA and Optune (Tumor Treating Fields) in multiple regions, empowered by our commercialization team with a proven track record and heritage from top-selling MNCs and innovative oncology brands. We believe that we remain the trusted partner in our areas of focus for the biopharmaceutical industry as we provide a differentiated approach for our collaborators to achieve success while also conducting timely trials and achieving eventual commercialization of promising therapies, accelerating access to the large patient population.

We founded Zai Lab with the intent to build a highly differentiated biopharmaceutical company delivering transformative therapies to patients. We have assembled a leadership team of industry veterans with global experience in the biopharmaceutical sector who have been at the frontier of framing the Chinese biopharma industry for more than two decades. Led by our management team, we have developed into a leading biopharmaceutical company with products approved in Greater China, broad pipeline with differentiated innovative assets from collaboration and in-house development and state-of-art capabilities across research and development, clinical development, manufacturing and commercialization.

We have assembled a deep, clinically-validated and innovative portfolio through collaborations and partnerships with global biopharmaceutical companies as well as in-house discovery and development, targeting large markets and characterized by high unmet medical need. We believe our product portfolio is one of the most robust and differentiated portfolios in the biopharmaceutical sector, in China with therapeutics that aim to treat serious diseases such as gynecologic cancer, gastric cancer, brain cancer, lung cancer and multidrug-resistant bacterial infections. The following table summarizes the global development status of our portfolio of commercialized products and drug candidates and programs.



Note:*denotes our core product; * denotes China-only trials; ** Greater China trial in preparation or under planning

(1) Also launched in Hong Kong and Macau; (2) Bridging study initiated in China; (3) Immuno-oncology; (4) Phase Ib proof-of-concept combo trial with tebotelimab; (5) Including non-small cell lung cancer; (6) Class III medical device by NMPA; (7) Under preparation for MAA submission in China; (8) Bridging trial application approved in China; (9) B-NHL, B-cell non-Hodgkin lymphoma; r/r, relapsed or refractory; FL, follicular lymphoma; DLBCL, diffuse large B-cell lymphoma; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; (10) Global potentially registration-enabling trial; (11) Phase II pivotal trial application submitted in China; (12) Neurotrophic tropomyosin receptor kinase; (13) Phase II registrational trial application submitted in China; (14) Bridging study initiated in Greater China; (15) Gastroesophageal junction cancer; (16) Global Phase II/III study and registration path in first-line gastric & GEJ cancer; combo with retifanlimab and tebotelimab, respectively; (17) Phase II/III trial application approved in Greater China; (18) Hepatocellular Carcinoma; Phase I proof-of-concept trial; (19) Phase II proof-of-concept trial; (20) Phase I trial application approved in Greater China; (21) Global Phase III study in preparation; (22) Phase III trial application approved in China; (23) Phase II trial application accepted in China; (24) Phase II trial initiated in Greater China; (25) Phase III trial initiated in Greater China; (26) Including China, Hong Kong, Macau, Taiwan, South Korea, Vietnam, Thailand, Cambodia, Laos, Malaysia, Indonesia, the Philippines, Singapore, Australia, New Zealand and Japan; (27) Class 1 drug by NMPA; (28) Class 5.1 drug by NMPA; (29) The drug class will be designated upon the NDA submission.

Our team has successfully advanced each of the programs above on timelines that have met or exceeded our expectations. For example, it took us less than three years from ZEJULA's FDA approval to commercial launch in China. It took us less than three months from obtaining the exclusive license for Optune to commercial launch in Hong Kong, and an additional 20 months further to commercial launch in China, without the need of clinical trial. In less than six years since our founding, we have successfully transformed into a fully-integrated commercial enterprise. Beyond ZEJULA and Optune, we have submitted two NDAs with respect to omadacycline and ripretinib, respectively, which are under priority review. On September 8, 2020, the NMPA also approved our sNDA for ZEJULA as a maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy.

To implement our commercialization strategy, we have built our own commercial team to execute the successful launches of ZEJULA and Optune in China, Hong Kong and Macau. We launched ZEJULA in China in January 2020, and as of August 31, 2020, ZEJULA has been successfully enrolled into the regional reimbursement program that complements China's basic medical insurance scheme in one province and six cities. As of August 31, 2020, ZEJULA has also been listed in 17 commercial health insurances and 12 supplemental insurances guided by municipal governments (城市定制險); in addition, since we launched Optune in China in June 2020, Optune has been listed in four supplemental insurances guided by provincial or municipal governments, as of August 31, 2020, both of which underscores our execution capability in bringing important therapies to patients.

In addition to our development stage products, we have seen similar success in building comprehensive in-house research and development capabilities in China and the U.S. We have assembled an integrated drug discovery and development team with nearly 400 dedicated personnel who have extensive experience from discovery, translational medicine to late stage development and have been directly involved in the discovery and development of several innovative drug candidates. Through these efforts over the past few years, we have advanced two of our in-house discovery candidates, namely ZL-1102 and ZL-1201, with global intellectual property into global clinical development and we plan to have multiple innovative and differentiated assets move into clinical development over the next few years. We believe our discovery initiatives along with our collaborations with leading academic institutions will enable us to achieve our long-term goal of generating a sustainable, internally discovered product pipeline of new products and drug candidates for patients around the world.

To supplement our discovery, research and development and commercialization efforts, we have also efficiently established both large and small molecule drug manufacturing capabilities, capable of supporting clinical and commercial production of our drug candidates. These facilities would allow us to produce both large and small molecule therapeutics under global standards, such as current good manufacturing practices, or cGMP. Our small molecule manufacturing facility supports the commercial production of ZEJULA. The production capacity of our small molecule manufacturing facility is up to 50 million units per year for both commercial oral tablets and capsules. During the Track Record Period, less than 10 percent of the total production capacity of our small molecule manufacturing facility was utilized. Our large molecule manufacturing facility supports the clinical production of ZL-1201. The annual production capacity of our large molecule manufacturing capacity is up to 12 to 18 200L or 1000L clinical batches, respectively. During the Track Record Period, approximately 40% of the production capacity of our large molecule manufacturing facility was utilized. We intend to expand our manufacturing capacity in a manner that will provide us with tangible and intangible benefits, including cost advantages, better control over quality and enhanced compliance capabilities and better ability to plan logistics for commercialization of drug candidates.

We aim to stay at the forefront of innovation in our industry by quickly and efficiently adopting technologies to further enhance our capabilities across research and development, manufacturing and commercialization. Together with our unique and strengthening platform and commitment to global standards, we believe we will contribute significantly to the improvement of the well-being of the patients globally.

OUR STRENGTHS

We believe the following strengths have contributed to our success and differentiate us from our competitors:

Proprietary platform committed to bring innovative and differentiated therapies to patients

Since our inception, we have been committed to pursuing global innovation through our proprietary, science-driven approach. Under the leadership of our management team led by Dr. Samantha Du, who has been pioneering China-based global biopharmaceutical innovation for over two decades, we have assembled an experienced execution team with in-depth knowledge and capabilities spanning research and development, regulatory approval process and commercialization. Our team is further supported by the expertise of our advisory board, academic collaborations and key opinion leader relationships. We believe that our disciplined approach in building a science-driven platform have allowed us to successfully identify and build strategic relationship to leverage the latest innovation with a truly global perspective, and to pursue a multi-source strategy for innovation. Through in-licensing, strategic co- development partnerships as well as our internal discovery efforts, we have assembled a robust portfolio of 16 potential best-in-class/first-in-class products and drug candidates, establishing a proven track record for open innovation while also gaining significant operational scale. Research and development of innovative therapies is high risk in nature, characterized by high failure rates, long timelines and increasingly high costs. By integrating both internal and external knowledge and technologies, our proprietary innovation model and expanding know-how enable us to source suitable potentially global best-in-class/first-in-class therapies and efficiently commercialize them for patient use with lowered development risk at reduced research and development costs. This model also shortens our in-house discovery and development cycle and improves overall success rates.

The recognition of our company as a preferred partner of choice in China is evidenced by our partnerships with leading global biopharmaceutical companies, including GSK, Novocure, Deciphera, Regeneron, Turning Point, MacroGenics, Incyte, Five Prime, Paratek, and Entasis, which have out-licensed select clinical products to us, many of which were their respective lead assets.

In addition to entrusting us with exclusive regional development and commercialization rights, some of our global partners have selected us to be their global co-development strategic partner in charge of managing the China portion of global trials and recruiting patients from China to these studies. Since 2018, we have successfully secured seven deals with six out of the seven being global co-development arrangements. Given the strategic importance of China to the development and commercialization of these drugs, we believe our strategic co- development model is sustainable and scalable. We believe our experienced leadership team with proven execution capabilities and our established expertise and network will facilitate China patient recruitment and clinical development, thereby accelerating development and approval of such drugs both in China and globally, while attracting more opportunities in the future.

To drive our long-term vision, we have also built a highly experienced in-house research and development team which was previously involved in the discovery and development of several innovative drug candidates at leading global biopharmaceutical companies. Our in-house research and development team focuses on the development of innovative therapeutics for the treatment of oncology, infectious diseases and autoimmune diseases. Our discovery efforts have resulted in the identification of a number of proprietary candidates against targets in our focus areas with high scientific validation including immuno-oncology, synthetic lethality and oncogenic signaling. As of the Latest Practicable Date, we have achieved FPIs for our internally generated drug candidates (ZL-1102 in autoimmune diseases and ZL-1201 in oncology) with multiple other compounds are in the candidate selection stage, in addition to other multiple discovery stage programs, which are synergistic with our clinical pipeline. We believe our internal research team and our in-house discovery and development capabilities will enable us to achieve our long-term goal of commercializing internally discovered innovative medicine with global rights for patients worldwide.

Highly differentiated and validated portfolio of innovative assets with significant commercial opportunities

We are committed to bring in suitable potential best-in-class/first-in-class therapies and have assembled a broad and highly differentiated innovative portfolio of 16 products and drug candidates, with potentially global best-in-class/first-in-class potential, addressing huge unmet medical needs for oncology, autoimmune and infectious diseases to patients in China and around the world. Our innovative portfolio offers patients access to a novel and significantly improved treatment paradigm over existing standards of care for their targeted indications, especially for patients in China where there is a lack of innovative treatment options. We have two approved, commercial stage products with significant market opportunity and seven assets in pivotal or potentially registration-enabling trials, two of which have had their NDA successfully submitted to China's NMPA.

We believe the success of our commercialised and late-stage oncology drug candidates with greater China rights will be driven by their differentiated clinical profiles, efficacy in patients and ability to provide clinical benefits over existing standards of care in a market where innovative therapies are often unavailable or less utilized relative to more developed potentially registration-enabling trials, two of which are already approved by the US FDA. We believe these assets represent a significant commercial opportunity.

- **ZEJULA (Niraparib)**. ZEJULA is a potentially global best-in-class PARP inhibitor for ovarian cancer based on its clinical data to date, once-daily dosing and PK properties. ZEJULA is currently the only PARP inhibitor to have received a broad approval by FDA to treat all advanced ovarian cancer patients regardless of biomarker status as a monotherapy in both first-line and recurrent maintenance treatment settings. ZEJULA was also recommended in the NCCN Clinical Practice Guidelines in Oncology as monotherapy for first-line maintenance treatment for women with ovarian cancer.

    - ZEJULA was the first and only approved Category 1 PARP inhibitor in China, supported by local patient data from the first fully-powered randomized, controlled Phase III trial ever done in ovarian cancer in China. Moreover, ZEJULA is recommended in the national treatment guideline in China.

    - We licensed ZEJULA from Tesaro (now GSK) in September 2016 and successfully commercialized it in Hong Kong in October 2018, Macau in June 2019 and China in January 2020. On September 8, 2020, the NMPA also approved our sNDA for ZEJULA as a maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy.

- **Optune (Tumor Treating Fields)** is an only-in-class innovative cancer therapy which has demonstrated overall survival benefits in patients with newly diagnosed GBM. Tumor Treating Fields uses electric fields tuned to specific frequencies to disrupt cell division, inhibiting tumor growth and causing affected cancer cells to die. Under this unique MoA, the anti-mitotic effect of Tumor Treating Fields has also demonstrated clinical proof of concept in multiple other tumor types and has ongoing global Phase III studies in brain metastases, non-small cell lung cancer (NSCLC), pancreatic cancer and ovarian cancer, which represent significant commercial opportunities in China. In addition, Optune (Tumor Treating Fields) was recommended with Level 1 evidence as a treatment for newly diagnosed GBM patients in the first Glioma Treatment Guideline in China and was included in the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology with Category 1 recommendation, contributing to the establishment of a new and improved standard of care for newly diagnosed GBM patients in China.

Optune was granted "Innovative Medical Device Designation" from the NMPA in August 2019, and its Marketing Authorization Application (MAA) was approved by the NMPA in May 2020, making it the first innovative treatment approved for the treatment of GBM in China since 2007.

- ***Ripretinib*** is a potential best-in-class treatment for advanced GIST. It is the only drug approved by the FDA for the treatment of Fourth-Line GIST in the all-comer setting according to Frost & Sullivan. Although GIST patients may experience periods of disease control with approved first-to third-line treatments, due to the heterogeneous nature of the mutations that drive the disease, many patients continue to progress and ultimately fail all lines of treatment. Ripretinib was specifically designed to improve the treatment of GIST patients by inhibiting a broader spectrum of mutations in KIT and PDGFRα than approved first-to third-line treatments of GIST which inhibit only a limited subset of KIT and PDGFRα mutations known to occur in GIST patients.

- ***Odronextamab*** is an innovative, potential first-in-class CD20xCD3 bispecific antibody in Greater China. Odronextamab is the most advanced investigational fully human bispecific antibody invented by Regeneron's proprietary VelocImmune® technology and Veloci-Bi® bispecific platform and is designed to trigger tumor killing by binding to both a protein expressed on B-cell cancers (CD20) and a component of the T-cell receptor ("TCR") complex (CD3). Odronextamab was granted orphan drug designation by the FDA for the treatment of diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL), which have limited existing treatment options and relatively poor prognosis globally.

- ***Repotrectinib*** is an investigational next-generation TKI designed to effectively target ROS1 and TRK A/B/C with potential to treat TKI-naïve or-pretreated patients. ROS1 rearrangement is estimated to be an oncogenic driver in approximately 3 percent of patients with advanced NSCLC in China, and NTRK is estimated to be an oncogenic driver in approximately 0.5-1 percent of patients with other advanced solid tumors in China, according to Frost & Sullivan. Utilizing a July 22, 2019 data cut-off, data from the Phase 1 portion of TRIDENT-1 demonstrated the potential for repotrectinib to be best-in-class for the treatment of ROS1-positive advanced NSCLC in patients who were not previously treated with a TKI.

Other oncology drug candidates include retifanlimab, bemarituzumab, tebotelimab and margetuximab. In July 2019, we received the rights to develop and exclusively commercialize retifanlimab, an investigational monoclonal antibody that inhibits PD-1, in haematology and oncology in Greater China from Incyte. In May 2018, we received CTA approval from the NMPA to enroll Chinese patients in the bemarituzumab (a humanized monoclonal antibody, IgG1 isotype, specific to FGFR2b) global registrational study, and we will manage the China portion of this global Phase III study and contribute patients from China. We obtained an exclusive license to develop and commercialize tebotelimab in Greater China from MacroGenics in November 2018. We also hold exclusive rights to develop and commercialize Margetuximab in Greater China.

In addition to these oncology-focused products, we believe that our two novel antibiotics, NUZYRA (omadacycline) and sulbactam-durlobactam, will address significant unmet patient and market needs. Over the past ten years, there were only eight novel antibiotics approved in China, according to Frost & Sullivan. The prevalent overuse of antibiotics, evolution of resistant bacteria and state of current treatment practices are expected to lead to an increase in drug-resistant infection rates.

- ***ZL-2401/NUZYRA (Omadacycline)*** is a novel tetracycline, specifically designed to overcome tetracycline resistance and improve activity across a broad spectrum of bacterial infections. NUZYRA is designed to overcome the two major mechanisms of tetracycline resistance, known as pump efflux and ribosome protection. In April 2017, we licensed omadacycline from Paratek, which in October 2018 received FDA marketing approval and omadacycline was launched as NUZYRA in the United States in February 2019. There are limited treatment options against drug-resistant bacteria in China and NUZYRA is particularly well positioned for the China market due to its broad activity covering a wide spectrum of pathogens. In addition, drugs competing with omadacycline in the same class are only available in IV formulation. In contrast, omadacycline is available in both IV and oral once-daily formulations, which makes treatment more convenient for care givers and patients. In February 2020, the NMPA accepted our NDA with Category 1 new drug designation for NUZYRA for the treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infection (ABSSSI). The recent COVID-19 outbreak further evidenced the unmet medical demand for effective antibiotics such as NUZYRA as CABP is the most common secondary infection and respiratory complication resulting from the COVID-19 infection. We also believe that omadacycline has the potential to help physicians combat the growing antibiotic resistance problem in China.

- ***ZL-2402 (Sulbactam-Durlobactam)*** is a novel beta-lactamase inhibitor for the treatment of carbapenem-resistant Acinetobacter baumannii infections including penem-resistant A. baumannii. Acinetobacter infections occur predominantly in the hospital setting; the pathogen is often multi-drug resistant (MDR), and has become extremely difficult to treat. With over 200,000 occurrences estimated each year, China ranks among the countries with the highest incidence of A. baumannii infections in the world. We have licensed durlobactam from Entasis as part of a global strategic collaboration. The FDA has granted SUL-DUR Qualified Infectious Disease Product (QIDP) status, which is established by the FDA to incentivize the development of new antibiotics to treat serious or life-threatening infections caused by pathogens. Such QIDP status makes SUL-DUR eligible for the FDA's Fast Track and Priority Review designations. Entasis has initiated a pivotal Phase III study in MDR Acinetobacter pneumonia and bloodstream infections in 2019, which will serve as a global registrational study. In May 2020, first Chinese patient was enrolled into the global Phase 3 ATTACK trial of durlobactam for Acinetobacter infections.

Established disease area strongholds within oncology driving scale and operational synergies

Through our consistent focus on world class innovation and global oncology partnerships, we have thoughtfully constructed our broad oncology portfolio targeting prevalent tumor disease areas in China, namely gynecologic cancer, breast cancer, gastro-intestinal cancer, brain cancer, lung cancer and hematological malignancies. Combining this focused oncology portfolio with dedicated expertise in each core business function across our fully-integrated platform, we are able to realize significant scientific, clinical development and commercial synergies in our operations. For example, through our continued efforts in advancing drug candidates within the same disease area into different stages of development, we are able to significantly enhance our understanding of disease biology. Such build-up in expertise and knowhow will allow us to more successfully identify attractive candidates that we would want to in-license and acquire the China or regional rights of in order to expand our portfolio and potential combination therapies between products. This expertise will also accelerate our internal discovery progress and enable us to prioritize resources on moving pre-clinical candidates into clinic. We also leverage the expertise of our scientific advisory board, academic collaborations and key opinion leader relationships to expand our insights.

From a clinical development perspective, as our pipeline expands, we accumulate increasing execution experience in each disease area and expect to benefit from significant synergies in clinical operations when conducting multiple trials with different lines and biomarkers in the same disease area. On the commercialization side, our dedicated oncology sales team will be able to promote multiple products to the same physician pool, while building stronger relationships with key opinion leaders. The combined impact of these synergies can bring significant efficiencies from an operating cost perspective, while allowing us to more rapidly scale our oncology business and effectively build our internal capabilities to support our global mission by leveraging China's large patient population. We believe we are well positioned to explore expansion of our disease strongholds to other indications.

We also believe that our rich oncology portfolio allows us to develop innovative combination-therapies and expand the commercial potential of our pipeline in each disease area. We managed to assemble innovative assets to treat cancers with diversified MoAs and modalities targeting key pathways and checkpoints of the tumor cell proliferation. Our various MoAs and modalities include, but are not limited to, synthetic lethality, Tumor Treating Fields, targeted therapy, immune-oncology therapy, small molecule, mAb and bispecific antibody. We also believe that our rich oncology portfolio has both the scale and mix to enable significant combination-therapy synergies and to develop innovative combination-therapies.

Distinguished world-class leadership team and deep talent pool

We have assembled a world-class leadership team with in-depth knowledge and extensive execution capabilities spanning pharmaceutical research, development and commercialization experience in both global and Chinese biopharmaceutical companies. Our leadership team led by Dr. Samantha Du has been pioneering China-based global biopharmaceutical innovation for decades, and we believe that we are leading the China biotech industry by successfully translating scientific visions into tangible drug candidates, solving complex issues in clinical development, progressing drug candidates through regulatory approval and commercializing innovative therapies.

Our Founder, Chairwoman and Chief Executive Officer, Samantha Du, Ph.D., is widely recognized as a leading figure in the China biopharmaceutical industry. Prior to founding our company, Dr. Du was Managing Director of healthcare investments at Sequoia Capital China, founder and CEO of Hutchison Medi-Pharma and co-founder and Chief Scientific Officer of Hutchison China MediTech Limited, where she pioneered China-based global biopharmaceutical innovation by bringing five internally-discovered innovative drug candidates into clinical trials, including two global Phase III ready drug candidates. Our other key management team members are also leaders in their respective areas globally or in China, heading clinical, medical, business development, commercial or corporate functions in globally renowned biopharmaceutical companies and MNCs before joining us.

Our visionary management team, together with the high-caliber talent pool we have established in both China and overseas, is key to propelling our company ahead of our peers in the Chinese biopharmaceutical industry. We have also assembled a scientific advisory board of respected academic leaders in their respective fields with a deep connection with scientific communities around the globe. Such a high-caliber talent pool has strengthened our capacity to discover potentially global best-in-class/first-in-class therapies through in-licensing and in-house discovery efforts, and these superior development opportunities in turn attract additional high-caliber talents to our platform, thereby forming a virtuous cycle. In particular, as a leading biotech company, attracting top talent globally has been, and will continue to be, an important driver of our organic growth. We have established and maintained a stable, growing team with 913 full-time employees as of the Latest Practicable Date, including nearly 400 employees in research and development.

We believe that the global academic resources and industry expertise of our leadership team, as well as our extensive and growing high-caliber talent pool will empower us to become a world-renowned biopharmaceutical company.

Proven institutionalized execution capabilities and track record of success

We believe that the execution capabilities of our management team, our scale of operation and unique resources, our commitment to excellence as well as our accumulated knowledge base and proprietary insights into the pharmaceutical industry, clinical development pathway and regulatory system in China have enabled us to institutionalize strong execution capabilities across our organization. This has been proven by our extensive execution track records to identify and license in clinical assets with potential best-in-class/first-in-class potential, efficiently navigate through the clinical and regulatory approval process as well as quickly commercialize our products in Greater China.

- *Selectively screened and identified potentially global first- and/or best-in-class assets.* As a preferred partner of choice for global biopharma companies, we have accumulated proprietary know-how and insights, with extensive experience in selecting the clinical assets that are complementary to our existing portfolio. We managed to screen, identify and license in innovative and differentiated products in oncology, including DNA damage response (ZEJULA), targeted kinase inhibitors (ripretinib), novel HER-2 targeted antibody (margetuximab), fully human bispecifics antibody (odronextamab), investigational next-generation targeted kinase inhibitors (repotrectinib) and several immuno-oncology assets including retifanlimab, tebotelimab and ZL-1201.

- *Efficiently brought innovative clinical assets to the market*. Our experienced in-house clinical operations team has efficiently brought potential best-in-class/first-in-class assets to the China market, which is evidenced by the fact that it took us less than three years from ZEJULA's FDA approval to commercial launch in China. It took us less than three months from obtaining the exclusive license for Optune to commercial launch in Hong Kong, and an additional 20 months further to commercial launch in China, without the need of a clinical trial.

- *Successfully established commercialisation track record and manufacture infrastructure.* We have successfully brought two of our clinical assets to commercialization and quickly penetrated the market, as evidenced by ZEJULA's majority market share in Hong Kong. We have also commercially launched ZEJULA in China in January 2020, and ZEJULA has been successfully enrolled into the regional reimbursement program that complements China's basic medical insurance scheme in one province and six cities. As of August 31, 2020, ZEJULA has also been listed in 17 commercial health insurances and 12 supplemental insurances guided by municipal governments (城市定制險). We later built up our own commercialization team consisting of 401 employees as of the Latest Practicable Date to launch our drug products under global standards. In addition, we have efficiently established both small and large molecule drug manufacturing capabilities in 2017 and 2018.

Fully-integrated global biopharmaceutical platform with end-to-end capabilities

By focusing on developing, commercializing and manufacturing our late-stage in- licensed drug candidates and expanding our earlier-stage internal research and discovery capabilities, we have grown to a fully-integrated biopharmaceutical company with end-to-end capabilities and 913 employees encompassing all key disciplines including 377 and 401 employees in R&D and commercial. We have an established global operation with dual headquarters in China and the US, allowing us to capitalize on the latest innovation and business opportunities on a global scale.

- **Research**. With extensive research track records in both global and Chinese biopharmaceutical companies, our leadership team has assembled an in-house discovery team dedicated to the research and discovery of novel therapeutics in the areas of oncology and autoimmune diseases, with a focus on large market opportunities with unmet clinical needs. Our scientific advisory board is also comprised of world-renowned experts with valuable expertise in oncology and immunology. In addition, we have collaborations with academic institutions in China, including Tsinghua University, Shanghai Institute of Materia Medica and Shanghai Institute of Organic Chemistry, the Chinese Academy of Sciences, to expand our in-house research projects.

- **Clinical development**. We believe our experienced in-house clinical operations team with proven execution capabilities distinguishes us from other biopharmaceutical companies in China. As of the Latest Practicable Date, we had 244 clinical development staff. As of the same date, we had more than over 25 ongoing or planned clinical trials in China and Australia across over 20 indications. We believe our strong regulatory affairs team also enables us to keep up with the evolving regulatory environment for drug development and steer our drug registration practice towards the most efficient pathway to approval.

- **Commercialization**. To support our commercial launch of ZEJULA in Hong Kong, Macau and China, we have built and are expanding our nimble and science-driven commercialization team of 401 staff as of the Latest Practicable Date to cover major medical centers in Greater China. Our in-house sales and marketing team includes experienced personnel from MNCs such as AstraZeneca, Roche, Novartis and BMS. We have also established and continued to maintain strong working relationships with leading hospitals and medical professionals, including KOLs, in oncology and infectious diseases through our research and clinical development efforts. We believe we will continue to be well-positioned for the planned commercial launches of our late-stage products covering multiple therapeutic areas.

- **Manufacturing**. We currently operate two manufacturing facilities in Suzhou. In early 2017, we built a cGMP-compliant small molecule facility in Suzhou capable of supporting clinical and commercial production. In 2018, we completed construction of a large molecule facility in Suzhou capable of supporting the clinical production of our drug candidates. We believe that possessing manufacturing capabilities presents tangible benefits, which include maintaining better control over the quality and compliance of our operations given increasingly stringent industry regulations.

OUR STRATEGIES

Since our inception in 2013, our mission has been to leverage our expertise and insight to address the increasing needs of patients in China and to utilize our China-based competencies to improve the lives of patients worldwide. We believe that we have created substantial value for our shareholders and various other stakeholders through our proprietary and science-driven approach which has resulted in two successful commercial launches and multiple drug candidates advanced into late-stage clinical trials. With our proven track record and integrated capabilities, we believe we are uniquely positioned to take advantage of a once-in-a-generation opportunity to build a significant market leader on the back of China's rapid emergence and technological advances in the global biopharmaceutical space. We believe we are one of the first biotech companies in China to scale. We are committed to elevating Zai to the next level to become a leading global biopharmaceutical company, leveraging our capabilities and global network to help drive the next wave of innovation in the biopharmaceutical sector. Over the next three years, we expect to have a steady stream of approvals and commercial product launches in Greater China across multiple therapeutic areas, establish transformative partnerships, expand our global footprint, and advance our internally discovered global pipeline into the pivotal stage.

Rapidly ramp up the sales of our commercialized products and establish a strong commercial presence in Greater China

We plan to focus our resources on rapidly delivering ZEJULA and Optune to patients. We intend to leverage the momentum from the successful China launch of ZEJULA to penetrate more cities, leveraging our commercialization team dedicated to promoting ZEJULA. We will continue to leverage our strong momentum in commercial insurance coverage and aim for near-term NRDL so as to improve patient affordability, which drives the demand for healthcare products and services. With over 800 hospitals covered at the time of launch in China, we will strengthen commercialization efforts for ZEJULA through our established relationships with leading hospitals and medical professionals, including KOLs. We also plan to replicate the successful commercial launch of Optune in Hong Kong and rapidly drive the sales of Optune in China. We view our initial commercial success in Hong Kong as an encouraging sign for Optune and the unmet need Optune can address in China, based on its inclusion in the National Treatment Guidelines. We believe our experience successfully launching ZEJULA in China, as well as strong physician endorsement, will provide important lessons for the launch of Optune.

We also plan to expand our commercialization team in China in anticipation of the increased market demand for ZEJULA and the launch of Optune. We further aim to develop our commercialization team to be highly specialized and efficient through recruiting key talents in relevant indications to drive future product launch and bring innovative cancer therapies to our target markets. We believe our key commercialization leadership members, who have substantial experience and a strong track record relevant to our pipeline drug candidates, can leverage their experience launching innovative oncology products in China to strengthen our competitive position in the market.

Further expand our drug pipeline through our proprietary platform

We plan to further expand our drug pipeline through our proprietary platform to continue developing potentially global best-in-class/first-in-class assets around our disease strongholds within oncology, as well as in infectious and autoimmune diseases. We will further solidify our position as a partner of choice for global biopharmaceutical companies looking for access into China for either its vast commercial market potential or the opportunity to accelerate global development, while also developing our own pipeline candidates.

We will also seek bolt-on and transformational business development opportunities by leveraging our relationship with existing in-licensing partners and expertise in our focused therapeutic areas. In particular, we will focus on drug candidates complementary to our current drug pipeline with demonstrated promising data in early clinical studies and global market potential. We will also expand beyond existing areas leveraging our platform. We seek to utilize the advantages of drug development in China, including relatively fast patient enrollment and low clinical costs, to rapidly establish proof of concept for such candidates prior to pursuing further global multi-center trials for the global market with a focus on China-prevalent diseases, such as gastro-intestinal, brain and lung cancers. We believe that this unique approach, coupled with our global network and partnerships with major global biopharmaceutical companies, will make us an increasingly important contributor to the next wave of global innovation in biopharmaceuticals and allow us to access new areas of cutting-edge research for our future pipeline candidates, as well as to utilize our broad portfolio to identify unique combination therapies.

In addition, as part of our global development strategy, we continue to evaluate partnership opportunities and may invest in companies that offer a strategic or commercial fit with our current drug candidates and business.

Seek expedited approval on our late-stage clinical assets and advance other clinical or IND stage candidates through development stages

We plan to seek rapid indication expansion for our two commercialized products and to expedite approval of our other two NDA-stage clinical compounds to broaden our commercial portfolio and fully utilize our commercial infrastructure.

- **ZEJULA**. We intend to pursue expedited registration and expect to commercialize ZEJULA as a maintenance treatment of adult patients with ovarian cancer who are in a complete or partial response to first-line platinum-based chemotherapy, with our sNDA under priority review by the NMPA. Meanwhile, we will continue to explore the combination potential of ZEJULA with immuno-oncology therapy, targeted therapy and chemotherapy in the other clinically relevant indications.

- **Tumor Treating Fields**. We plan to submit MAA for MPM in China in the first half of 2021, and expect to leverage our experience in launching Optune in Hong Kong as well as China with a strong network of leading hospitals and medical professionals to explore incremental commercialization opportunities with additional coverage of MPM patients. In addition, we are conducting clinical trials of Tumor Treating Fields in Chinese patients with gastric cancer and plan to join global Phase III pivotal trials in non-small cell lung cancer, locally advanced pancreatic cancer and brain metastases in Greater China.

- **Ripretinib**. In July 2020, our NDA submission of ripretinib for advanced GIST was accepted by the NMPA. The NMPA granted priority review to our NDA for ripretinib for the treatment of adult patients with advanced GIST in August 2020. In July 2020, we also received the Clinical Trial Authorization (CTA) approval for the registrational bridging study of ripretinib in patients with second-line GIST. As the only product with all comer label in late lines, we believe Ripretinib will be able to address significant unmet medical needs in advanced GIST setting.

- **Omadacycline**. We received acceptance from the NMPA for our NDA for Omadacycline (ZL-2401) under priority review for CABP and ABSSSI in February 2020, and entered into a contract sales agreement with Hanhui, a local pharmaceutical company with a strong commercial presence in antibiotics. We plan to leverage Hanhui's existing infrastructure to optimize a potential future commercial launch of omadacycline in China given that omadacycline is a broad spectrum antibiotic in both the hospital and community settings.

We also plan to continue our efforts in rapidly developing other drug candidates in our pipeline.

- **Odronextamab**. We will continue to explore regulatory approval pathways for odronextamab in R/R B-NHL in China by joining the global Phase II program with multiple, potentially registrational cohorts of different subtypes of R/R B-NHL plan to enroll first Chinese patient into the potentially registrational global Phase 2 program by early 2021.

- **Repotrectinib**. We plan to open additional sites for the TRIDENT-1 Phase 2 registrational clinical study of repotrectinib. The ongoing study is currently active in 11 countries globally and enrolling patients with ROS1-positive advanced NSCLC and NTRK-positive solid tumors.

- **Other Oncology Drug Candidates**. We plan to participate in the upcoming global studies in the second half of 2020 of margetuximab (MAHOGANY) in combination with retifanlimab or tebotelimab in gastric cancer sponsored by MacroGenics in HER2+ first-line treatment of gastric cancer. In addition, with respect to retifanlimab, we plan to initiate pivotal trial in second-line MSI-high endometrial cancer in China in the second half of 2020 and enroll China patients to global Phase III study in first-line NSCLC in the second half of 2020. Furthermore, for tebotelimab, we intend to enroll the first Chinese patient in the second half of 2020 for this bispecific PD-1 x LAG-3 DART molecule in its global Phase I basket trial.

In addition to our oncology compounds, we also plan to rapidly advance the development of sulbactam-durlobactam so that we can introduce into China new and effective broad- spectrum antibiotics. Indeed, the first Chinese patient was enrolled into the global Phase III ATTACK trial of sulbactam-durlobactam for Acinetobacter infections.

With respect to the above late-stage clinical drug candidates with China rights, in addition to China, we intend to seek registration and commercialization in all geographies where we have applicable rights.

Enhance our internal research platform and discovery efforts

We believe internal research capabilities are a critical part of our platform. We have assembled an internal research and development team with extensive capabilities that we will leverage to discover, develop and commercialize innovative drug candidates that can address significant unmet medical needs globally. We have prioritized specific areas of cancer biology with clinical validation, synergistic with our clinical pipeline and aligned to our growing in-house expertise, including immune-oncology, DNA damage response and repair as well as oncogenic signaling.

Our discovery operations in Shanghai, China and San Francisco, California established in 2015 and 2018, respectively, have been focusing on generating small and large molecule therapeutics. We will continue to invest in and expand our internal research and discovery programs and expand our presence in both China and the United States to enhance internal drug discovery efforts. We continue to expand our U.S. presence to enhance internal drug discovery, clinical development and business development, with the opening of a new 20,000 sq.ft research facility in Menlo Park, California and the expansion of our Boston office.

We intend to continue to grow our internal pipeline and continue to progress assets with global rights into the clinic. We believe our discovery efforts will enable us to achieve our long-term goal of generating a sustainable, internally discovered pipeline of new products and drug candidates for patients around the world.

Efficiently grow our world-class organization and invest in our capabilities to support our global aspirations

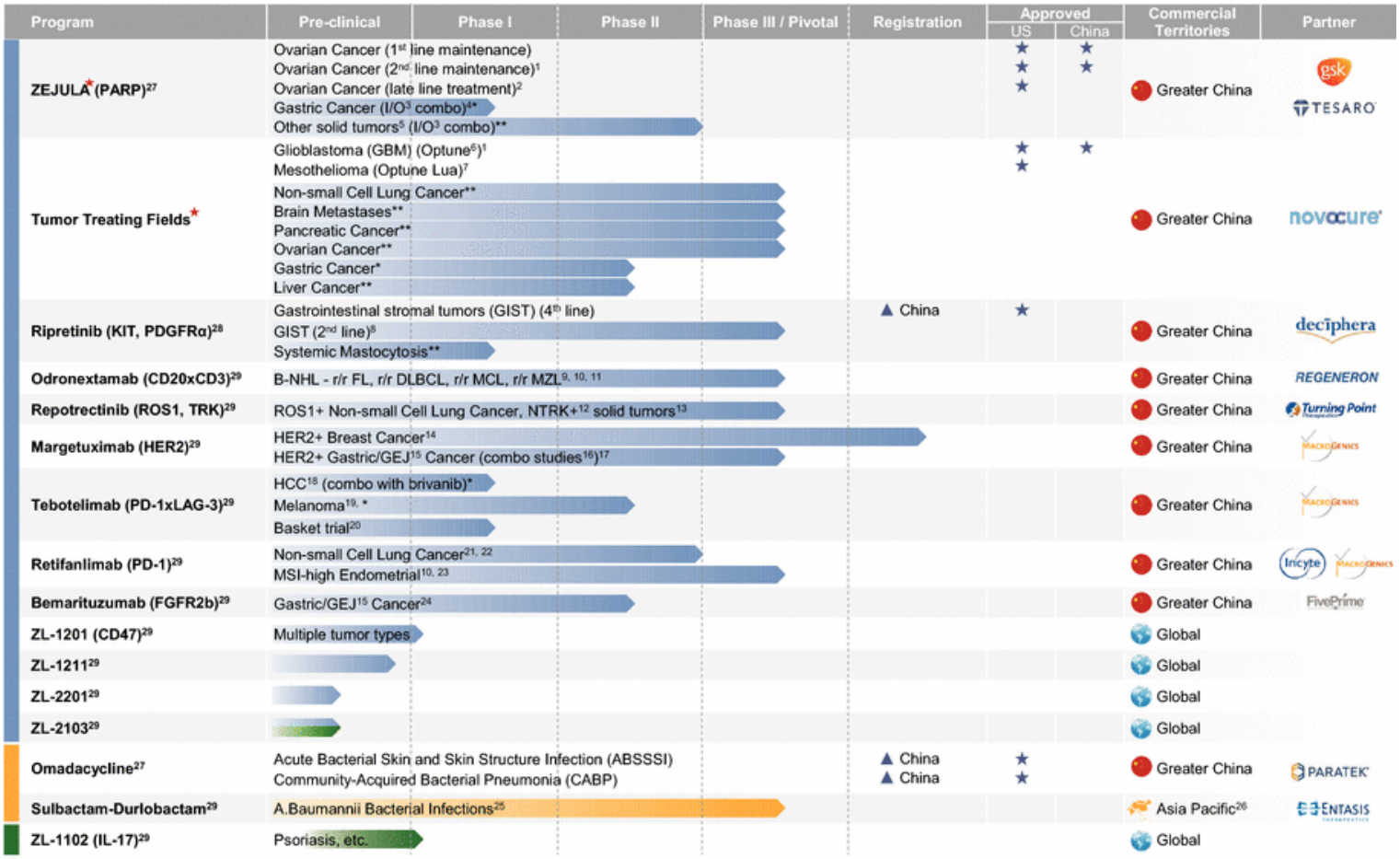
With our significant integrated capabilities in R&D, manufacturing and commercialization, we plan to strengthen and expand our platform and develop into a world-class organization with continued capital efficiency. In addition to expanding our product portfolio, we are committed to being innovative in our business model by identifying transformative deals and concepts globally, utilizing global clinical trial data, strengthening translational research and leveraging technologies. We also plan to expand the scale of our commercial organization and the breadth of our market coverage.

To support our efforts to grow our world-class organization, we will continue to recruit and train high-caliber talent globally to maintain our competitiveness in a rapidly evolving industry, in particular talent with expertise and experience in R&D and commercialization. By the end of 2020, we expect to have more than 1,000 employees. We expect vast majority of the new hires in the second half of 2020 will be for our sales and marketing team with our continued effort to expand our commercial capabilities in the preparation of launching of drug candidates and drugs with new indications, if approved. We expect by end of 2020, approximately 90% of our sales and marketing team will be based in municipalities (namely Beijing, Tianjin, Shanghai, and Chongqing) and provincial capitals to reinforce our commercial penetration primarily into Class III Hospitals in these regions. We are looking for talents with clinical medicine or life science background and business development, product management or portfolio management experience in a pharmaceutical or biotech/life science industry. We will strengthen our high-caliber and highly-skilled talent pool through the integration of external recruitment and internal training and enhance our incentive schemes to provide qualified employees with equity participation and promotion opportunities.

In addition, as our commercial-stage portfolio grows, we intend to expand our manufacturing capacity in-line with market demand for our products, whether by building new production facilities or expanding current production facilities, engaging contract manufacturing organizations (CMOs) and optimizing third-party manufacturer structure. Through both expanded in-house manufacturing capacities and diversified CMO cooperation, we believe our manufacturing capabilities will continue to support our validated portfolio in both clinical and commercial development.

OUR PRODUCTS AND DRUG CANDIDATES PIPELINE

We have a broad portfolio of proprietary products and drug candidates that range from discovery stage to late-stage clinical to commercial-stage programs. Our portfolio consists of 16 potential best-in-class/first-in-class products and drug candidates, including two commercialized products in China, Hong Kong and Macau and seven assets in pivotal or potentially registration-enabling trials in oncology, infectious and autoimmune diseases, which are therapeutic areas where there is a large unmet need and lack of innovative treatment options in China. The following table summarizes the global development status of our portfolio of commercialized products and drug candidates and programs.



Note:*denotes our core product; * denotes China-only trials; ** Greater China trial in preparation or under planning

(1) Also launched in Hong Kong and Macau; (2) Bridging study initiated in China; (3) Immuno-oncology; (4) Phase Ib proof-of-concept combo trial with tebotelimab; (5) Including non-small cell lung cancer; (6) Class III medical device by NMPA; (7) Under preparation for MAA submission in China; (8) Bridging trial application approved in China; (9) B-NHL, B-cell non-Hodgkin lymphoma; r/r, relapsed or refractory; FL, follicular lymphoma; DLBCL, diffuse large B-cell lymphoma; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; (10) Global potentially registration-enabling trial; (11) Phase II pivotal trial application submitted in China; (12) Neurotrophic tropomyosin receptor kinase; (13) Phase II registrational trial application submitted in China; (14) Bridging study initiated in Greater China; (15) Gastroesophageal junction cancer; (16) Global Phase II/III study and registration path in first-line gastric & GEJ cancer; combo with retifanlimab and tebotelimab, respectively; (17) Phase II/III trial application approved in Greater China; (18) Hepatocellular Carcinoma; Phase I proof-of-concept trial; (19) Phase II proof-of-concept trial; (20) Phase I trial application approved in Greater China; (21) Global Phase III study in preparation; (22) Phase III trial application approved in China; (23) Phase II trial application accepted in China; (24) Phase II trial initiated in Greater China; (25) Phase III trial initiated in Greater China; (26) Including China, Hong Kong, Macau, Taiwan, South Korea, Vietnam, Thailand, Cambodia, Laos, Malaysia, Indonesia, the Philippines, Singapore, Australia, New Zealand and Japan; (27) Class 1 drug by NMPA; (28) Class 5.1 drug by NMPA; (29) The drug class will be designated upon the NDA submission.

Our drug candidates are subject to approval by the relevant authorities, such as the FDA and the NMPA, before commercialization in each jurisdiction. See "Regulatory Environment" for details. As of the Latest Practicable Date, we had not received any material comments or concerns raised by the relevant authorities regarding, among others, our products, drug candidates or programs that we are not able to satisfactorily address in a timely manner.

Our Marketed Core Products

ZEJULA

Overview

ZEJULA (niraparib), one of our Core Products, is an once-daily small molecule poly (ADP-ribose) polymerase 1/2, or PARP 1/2, inhibitor approved by the NMPA as Category 1 drug for treatment across multiple solid tumor types in China. ZEJULA was approved in March 2017 by the FDA and in November 2017 by the EMA, as a maintenance treatment for women with recurrent platinum-sensitive ovarian cancer. Maintenance therapy is for those women who have had prior treatment but are expected to see their cancer return, with the purpose of avoiding or slowing a recurrence if the cancer is in remission after the prior treatment. A platinum-sensitive cancer is one that responded to initial platinum-based chemotherapy and remained in remission post-chemotherapy for more than six months.

ZEJULA is the first PARP inhibitor approved by the FDA for ovarian cancer that does not require BRCA mutation or other biomarker testing. This makes ZEJULA suitable for a wide patient population and significantly more accessible to patients in China where BRCA biomarker diagnostic tests are not widely accessible.

We obtained an exclusive license for the development and commercialization of ZEJULA in China, Hong Kong and Macau in 2016 from Tesaro (now GSK). For further details of the exclusive license, see "— Overview of Our License and Strategic Collaboration Agreements." In October 2018, the Hong Kong Department of Health approved our application for ZEJULA in Hong Kong for adult patients with platinum-sensitive relapsed high grade serous epithelial ovarian cancer who are in a complete response or partial response to platinum-based chemotherapy and we began commercializing ZEJULA in Hong Kong in the fourth quarter of 2018. In June 2019, we received the marketing authorization to commercialize ZEJULA in Macau for women with relapsed ovarian cancer. In December 2019, ZEJULA was approved by the NMPA in China as a Category 1 maintenance therapy for adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy. ZEJULA was the first and, as of the date of this document, the only approved Category 1 PARP inhibitor in China, supported by local patient data from the first fully-powered randomized, controlled Phase III trial ever done in ovarian cancer in China. Moreover, ZEJULA is recommended in the national treatment guidelines in China. Since the commercial launch in China in January 2020, ZEJULA has been successfully enrolled into the regional reimbursement program that complements China's basic medical insurance scheme in one province and six cities. It has also been listed in 17 commercial health insurances and 12 supplemental insurances guided by municipal governments (城市定制險) as of August 31, 2020.

In 2019, ZEJULA was designated as a "National Sciences and Technology Major Project" by the Chinese government as part of a key initiative to strengthen local innovation. On September 8, 2020, the NMPA also approved our sNDA for ZEJULA as a maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy. Such sNDA was previously under the NMPA's priority review. Priority review was established in China to facilitate drug registration and accelerate the development of new drugs with clinical value under the guidance of the Opinions on Encouraging the Priority Review and Approval for Drug Innovations (《關於鼓勵藥品創新實行優先審評審批的意見》) issued by the former CFDA in December 2017. According to the guidelines, the regulatory authority will prioritize the review process and evaluation resources for applications under priority review, which should expect reduced review and approval timelines. Since the date of issue of the relevant regulatory approvals and as of the Latest Practicable Date, no material unexpected or adverse changes had occurred. We had not received any material comments or concerns raised by the relevant authorities regarding the completed or ongoing clinical trials of ZEJULA that we are not able to satisfactorily address in a timely manner as of the Latest Practicable Date.

We continue to explore ZEJULA in patients with breast cancer and non-small cell lung cancer in China. In February 2020, we dosed the first patient in the Phase Ib study of ZEJULA with tebotelimab, a potential first-in-class PD1/LAG-3 bispecific antibody, in advanced or metastatic gastric cancer. We are also exploring the combination potential of ZEJULA with immuno- oncology therapy, targeted therapy and chemotherapy in the clinically relevant indications.

Background on PARP Inhibitors

PARP inhibition has become an important part of cancer therapy, given its role in blocking DNA repair, which is a well-studied area of PARP activity. DNA contains genetic instructions used in the development and functioning of most known living organisms. DNA can be damaged by many types of mutagens, including oxidizing agents, alkylating agents, ultraviolet light and X-rays. An important property of DNA is that it can replicate, or make copies of itself. This is critical when cells divide because each new cell needs to have an exact copy of the DNA present in the old cell. It is also critical to the integrity and survival of cells that DNA damage can be repaired. Cells have evolved multiple mechanisms to enable such DNA repair, and these mechanisms are complementary to each other, each driving repair of specific types of DNA damage. If a cell's DNA damage repair system is overpowered, then the cell is programmed to die.

Radiation and certain chemotherapies such as alkylating agents and topoisomerase inhibitors induce significant damage to tumor cells, which results in programmed cell death. DNA repair mechanisms may reduce the activity of these anti-cancer therapies and, conversely, inhibition of DNA repair processes may enhance the effects of DNA-damaging anti-cancer therapy. For example, cancer cells can maintain viability despite disruption of the key DNA repair pathway known as the homologous recombination pathway, but they become particularly vulnerable to chemotherapy if an alternative DNA repair pathway is disrupted. This is known as "synthetic lethality"-a situation where the individual loss of either repair pathway is compatible with cell viability, but the simultaneous loss of both pathways results in cancer cell deaths.

Clinical studies have shown that PARP inhibitors are effective as a monotherapy in patients with certain types of cancer, including those with gene mutations as discussed below. PARP inhibitors have also been explored in numerous clinical trials to enhance chemotherapy treatments, including in combination with TMZ, cisplatin, carboplatin, gemcitabine and topotecan.

Mechanism of Action

Many DNA repair processes involve PARP-1 and PARP-2, which are zinc-finger DNA-binding enzymes that sense DNA damage and convert it into intracellular signals to promote DNA repair. PARP inhibitors block DNA repair by the base excision repair pathway. PARP inhibitors appear most effective when used to treat tumors with underlying defects in DNA repair or when combined with another DNA-damaging agent. This is because, in normal cells, the homologous recombination pathway compensates for PARP-mediated inhibition of the base excision repair pathway and maintains the fidelity of DNA repair. In cells with a deficiency in the homologous recombination pathway, such as those with BRCA-1 and BRCA-2 mutations, PARP inhibition leads to irreparable double-strand breaks, collapsed replication forks, and an increased use of the less effective nonhomologous end joining pathway. These disruptions ultimately result in synthetic lethality, and, in this manner, treatment with PARP inhibitors represents an opportunity to selectively kill cancer cells with deficiencies in homologous recombination and other DNA repair mechanisms. PARP inhibitors also have an additional mechanism of action known as "PARP trapping." The effect of PARP trapping is to poison DNA by stabilizing PARP-1 and PARP-2 at sites of DNA damage, generating complexes that may be even more toxic than the unrepaired single-strand breaks which result from PARP inhibition.

ZEJULA is designed to be a highly potent, selective inhibitor of PARP-1 and PARP-2. In an ovarian cancer patient-derived xenograft model, where tumor models are established from transplantation of a human tumor specimen from a cancer patient directly into a mouse, ZEJULA has been shown to have greater tumor concentration, allowing it to deliver sustained anti-tumor activity as compared to olaparib, an FDA-approved PARP inhibitor marketed by AstraZenaca for gBRCA+ ovarian cancer patients who have received at least three prior lines of chemotherapy.

Market Opportunity and Competition

We believe that ZEJULA represents a significant market opportunity in China, given its differentiated clinical profile, demonstrated clinical relevance to multiple solid tumor types, potential to provide a notable improvement to existing standards of care, and prospects to be utilized in multiple combination and monotherapy treatment options. We have the right to all indications in greater China (except prostate cancer), and we intend to pursue the approval and registration of ZEJULA as a Category 1 drug for treatment across multiple solid tumor types in China.

ZEJULA is the first PARP inhibitor approved by the FDA for all ovarian cancer patients regardless of biomarker status. With a potentially global best-in-class profile, it was approved by the FDA in both first-line and recurrent maintenance treatment settings. ZEJULA is recommended in national treatment guideline in the United States. ZEJULA has unique suitability for patients in China where biomarker diagnostic tests are still not widely accessible. As the first and only approved Category 1 PARP inhibitor in China, ZEJULA is supported by local patient data from the first fully-powered, randomized, controlled Phase III trial ever done in ovarian cancer in China. Similar to its status in the U.S., ZEJULA is also recommended in the national treatment guideline in China. In addition, ZEJULA obtained recognition and funding support from the Chinese government.

As of July 2020, there were only two marketed PARP inhibitors in China, one is LYNPARZA (olaparib) from AstraZeneca, which was approved in 2018; the other one is ZEJULA (niraparib), which was approved in 2019, according to the Frost & Sullivan Report.

The main competitive drug, LYNPARZA of AstraZeneca, was (i) approved by the FDA in December 2018 in first-line maintenance therapy but only for BReast CAncer gene (“BRCA”)-positive patients, and (ii) approved by the FDA in May 2020 for patients whose cancer is associated with homologous recombination deficiency (HRD) positive status, which represent 50% of the advanced ovarian cancer patients, but only in combination with Avastin (bevacizumab). On the other hand, ZEJULA was approved (i) for all advanced ovarian cancer patients regardless of biomarker status, and (ii) as a monotherapy.

An additional four PARP inhibitors are in phase III clinical development or at NDA stage in China, comprising both China developed and global drug candidates. Three of these PARP inhibitors’ lead indications focus on late-stage ovarian cancer while one focuses on metastatic prostate cancer. In the late stage ovarian cancer indications, one of the products is targeting BRCA+ patients only. We believe that, pending on the NMPA’s approval of our supplemental new drug application (sNDA) for ZEJULA as a maintenance in first-line ovarian cancer, ZEJULA would target the broadest patient population.

ZEJULA is a potential best-in-class PARP inhibitor, given it is the only PARP inhibitor approved in the US as monotherapy for all-comer patients in the first-line and recurrent maintenance treatment settings, according to Frost & Sullivan. We believe that our early entrant status as one of the first PARP inhibitors in the China market, coupled with the global recognition, differentiated profile and availability of global and China clinical evidence for ZEJULA, position us favourably in China's PARP inhibitor market.

Our currently targeted indications for ZEJULA include the following:

Ovarian Cancer

Ovarian cancer had an estimated annual incidence of 53,900 patients in China in 2019, which is more than double that of the 22,500 patients in the United States, and has seen increasing mortality rates, according to NCCR and ACS. Since early symptoms of ovarian cancer are non-specific and difficult to detect, approximately 70% of women with ovarian cancer are diagnosed when the disease is at an advanced stage, when prognosis is poor. Finding effective therapeutic approaches for advanced ovarian cancer patients represents a large unmet medical need.

The previous standard of care in China consists of radical surgery and platinum-based chemotherapy. Although platinum-based chemotherapy is effective at inducing an initial response, ovarian cancer will recur in approximately 85% of patients. Many patients continue to respond to second-line platinum based chemotherapy, and following a response, the guideline-recommended approach for many patients is surveillance, monitoring patients for disease progression and managing their symptoms. However, during the surveillance period, ovarian cancer survivors report anxiety about cancer antigen testing and fear of recurrence, many experiencing symptoms associated with post-traumatic stress disorder. After relapse, patients respond moderately or poorly to subsequent chemotherapy, with later lines of therapy leading to progressively shorter treatment-free intervals. We believe effective maintenance therapies that address a broad patient population are needed to prolong the duration of response following platinum-based treatment. ZEJULA was recommended as a monotherapy first-line maintenance treatment for women with platinum-responsive advanced ovarian cancer in the Ovarian Cancer PARP Inhibitor Clinical Guidelines (卵巢癌PARP抑制劑臨床應用指南) published by Gynecological Oncology, Chinese Medical Association (中華醫學會婦科腫瘤學分會) in May 2020. This shows that ZEJULA is regarded as the standard of care in first-line maintenance treatment for women with advanced ovarian cancer in China.

Given the broad applicability of ZEJULA across all patient populations, regardless of gBRCA mutation status, we are currently targeting the entire platinum sensitive ovarian cancer patient population. This represents a significant advantage for patient convenience and access, given that there is no need for patients to utilize diagnostic tests to determine their gBRCA mutation status, particularly in China where such tests are not widely accessible.

Lung Cancer

Lung cancer has the highest total incidence as well as the highest mortality rate of any cancer in China. Annual incidence was estimated at 895.3 thousand patients in China in 2019, according to Frost & Sullivan.

Lung cancer can be categorized into non-small-cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC is any type of epithelial lung cancer other than (SCLC). The most common types of NSCLC are squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. All types can occur in unusual histologic variants and developed as mixed cell-type combinations. NSCLC accounts for approximately 85% of total lung cancer patients in China. The incidence of NSCLC in China reached 761.0 thousands in 2019, with a CAGR of 3.3% between 2015 and 2019; in the future, the incidence is expected to reach 884.3 thousand in 2024 representing a CAGR of 3.0% from 2019 to 2024, and 1.0 million in 2030 with a CAGR of 2.8% from 2024 to 2030, according to the Frost & Sullivan Report. The 5-year survival rate of lung cancer in China is 19.7%, according to the Frost & Sullivan Report.

We intend to explore ZEJULA's efficacy in patients with NSCLC based on the large unmet need for effective treatment for such patients in China. The relatively limited therapy options for Chinese physicians and patients make us believe that a small molecule PARP inhibitor will offer an attractive addition to the standard of care.

Gastric Cancer

Cancer of the stomach, also called gastric cancer (GC), and cancer of the gastroesophageal junction (GEJ), which is where the esophagus joins the stomach, are collectively referred to as gastroesophageal adenocarcinoma, which is the third leading cause of cancer death worldwide according to the World Health Organization in 2018. Both GC and GEJ cancer are often diagnosed at an advanced stage and therefore have very poor prognosis, with a 5-year survival of 20-35%.

Gastric cancer is the second most common cancer in China and the third leading cause of death in China. The incidence of gastric cancer in China has reached 455.8 thousand in 2019, and it is expected to be 525.8 thousand in 2024, representing a CAGR of 2.9% from 2019 to 2024, and 613.8 thousand in 2030, with a CAGR of 2.6% from 2024 to 2030, according to the Frost & Sullivan Report. Current therapies of gastric cancer include surgery, chemotherapy, radiotherapy and targeted therapy. However, there are limited effective treatment options in China or globally for patients with advanced or metastatic gastric cancer who have failed prior treatment.

In February 2020, we initiated a Phase Ib study of ZEJULA in combination with tebotelimab in advanced or metastatic gastric cancer in China for the treatment of patients with advanced or metastatic gastric adenocarcinoma or gastroesophageal junction adenocarcinoma (collectively as gastric cancer) who failed prior treatment.

Clinical Development Plan and Strategy for ZEJULA in the China Market

Ovarian Cancer

In July 2018, we completed our open-label study evaluating the pharmacokinetic, or PK, profile of our China-produced formulation of ZEJULA in Chinese ovarian cancer patients. Results from the study show a comparable PK profile of the Chinese patients administered ZEJULA to that of patients evaluated in GSK's global PK study. The study demonstrated that the drug exposure increased proportionally from 100mg to 300mg, with a Tmax of approximately three hours. Systemic exposure to ZEJULA, as measured by Cmax and AUC, increased approximately proportionally with increased dose. There were no unexpected safety issues noted during the trial. All key PK and safety parameters were comparable to those in global studies. The study results and population PK data did not identify ethnicity differences between Chinese and non-Chinese patients.

In January 2019, we completed patient enrollment of our Phase III NORA trial evaluating ZEJULA as a second-line maintenance therapy in patients with recurrent platinum-sensitive ovarian cancer. NORA is a Zai Lab self-sponsored Phase III randomized, double-blind, placebo-controlled, study of ZEJULA conducted by us as a second-line maintenance therapy in Chinese patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer (collectively termed as ovarian cancer) who are in a complete or partial response to platinum-based chemotherapy. NORA randomized 265 patients at 2:1 to receive ZEJULA or placebo until disease progression. The study evaluated the efficacy of ZEJULA as a maintenance treatment, with the primary endpoint being progression-free survival (PFS) as assessed by blinded independent central review.

The starting dose was individualized at 200 mg except for those with a baseline body weight >77kg and a platelet count >150K/μL in which case the starting dose is 300 mg. Such individualized starting dose regimen was shown to be effective with improved safety profile in Chinese patients, with lower rates of anemia and thrombocytopenia. The study met its primary endpoint of a statistically significant improvement in progression free survival for patients with ovarian cancer regardless of their biomarker status. The safety profile was consistent with what was observed from the global NOVA study with lower rates of anemia and thrombocytopenia. NORA is a first fully powered, randomized, controlled (RCT) Phase III trial ever completed in ovarian cancer in China, excluding Chinese traditional medicines studies.

In November 2019, we completed patient enrollment of our Phase III PRIME trial evaluating ZEJULA as a first-line maintenance therapy in ovarian cancer patients who are in a complete or partial response to first-line platinum-based chemotherapy. PRIME is our self-sponsored Phase III randomized, double-blind, placebo-controlled study of ZEJULA as a maintenance therapy in Chinese patients with advanced ovarian cancer who are in a complete or partial response to first-line platinum-based chemotherapy. Advanced ovarian cancer patients were randomized 2:1 to receive ZEJULA or placebo as maintenance therapy. Randomization was stratified by use of neoadjuvant chemotherapy (yes or no), best response to platinum therapy (CR or PR), and homologous recombination deficiency (HRD) status (positive or negative/not determined). The primary end point was progression-free survival (PFS) in patients who had tumors with HRD+ve and in those in the overall population, as determined on hierarchical testing.

In China, ZEJULA has been approved as a Category 1 drug by the NMPA in December 2019 as maintenance therapy for adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy. The NMPA accepted and granted priority review to our sNDA for ZEJULA as a Category 2.4 first-line maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy in March 2020 and April 2020, respectively.

In May 2020, we announced positive top-line results from the NORA Phase III study of ZEJULA as maintenance therapy for Chinese patients with platinum-sensitive, recurrent ovarian cancer. In July 2020, we completed NORA Trial, at which time we completed the study report. The NORA trial met all primary and secondary endpoints with improved safety profile in Chinese patients. The full results from the NORA study will be presented at European Society for Medical Oncology (ESMO) 2020 Virtual Congress on September 19, 2020.

We dosed the first patient in registrational bridging trial for late-line ovarian cancer treatment in August 2020.

On September 8, 2020, the NMPA also approved our sNDA for ZEJULA as a maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy.

Lung Cancer

We initiated a Phase III study in patients with platinum responsive small cell lung cancer as maintenance therapy in August 2018. Given the rapidly changing landscape in the management of small cell lung cancer, particularly with the introduction of PD1/PD-L1 antibodies in the first-line treatment of small cell lung cancer, we terminated this study to prioritize our resources to other opportunities including exploring potential combination regimen for ZEJULA and immuno-oncology agents in the maintenance setting for non-small cell lung cancer.

Gastric Cancer

In February 2020, we dosed the first patient in the Phase Ib dose escalation and expansion clinical study of ZEJULA in China, in combination with tebotelimab, for the treatment of patients with advanced or metastatic gastric adenocarcinoma or gastroesophageal junction adenocarcinoma (collectively as gastric cancer) who failed prior treatment.

The primary endpoint of the study is assessing the safety of ZEJULA in combination with tebotelimab in patients with advanced gastric cancer and determining the recommended phase 2 dose. Secondary endpoints include objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS).

We continue to explore the combination potential of ZEJULA with immuno-oncology therapy, targeted therapy and chemotherapy in the other clinically relevant indications.

Summary of Clinical Trial Results

The following clinical trials were conducted by our business partner, GSK.

NOVA, a Phase III maintenance study of ZEJULA versus placebo in patients with recurrent platinum-sensitive ovarian cancer

In March 2017, the FDA approved ZEJULA as a maintenance treatment for women with recurrent platinum-sensitive ovarian cancer, regardless of BRCA mutation or biomarker status, three months ahead of the FDA's scheduled decision date (PDUFA date). ZEJULA's FDA approval followed the release of successful results from GSK NOVA trial in which ZEJULA demonstrated a clinically meaningful increase in progression-free survival in women with recurrent ovarian cancer, regardless of gBRCA mutation or biomarker status. Treatment with ZEJULA reduced the risk of disease progression or death by 73% in gBRCA mutation positive patients (hazard ratio = 0.27) and by 55% in patients without gBRCA mutations (hazard ratio = 0.45). Hazard ratio is the probability of an event (such as disease progression or death) occurring in the treatment arm divided by the probability of the event occurring in the control arm of a study, with a ratio of less than one indicating a lower probability of an event occurring for patients in the treatment arm. P-value is a measure of the probability of obtaining the observed sample results, with a lower value indicating a higher degree of statistical confidence in these studies. The magnitude of benefit was similar for patients entering the trial with a partial response or a complete response to platinum treatment.

The NOVA trial was a Phase III randomized double-blind trial that assessed the effectiveness of ZEJULA compared with placebo to delay tumor progression following a platinum containing chemotherapy regimen. Patients enrolled into one of two independent cohorts based on gBRCA mutation status. A total of 553 patients were enrolled in the NOVA study at 107 centers worldwide. The study population has 203 patients assigned to the gBRCA mutation positive cohort and 350 patients assigned to the gBRCA mutation negative cohort. Among the patients in the gBRCA mutation negative cohort, 162 had tumors that were tumors deficient in homologous recombination, or HRDpos, and 134 had tumors did not have a homologous recombination deficiency, or HRDneg. The homologous recombination deficiency status was not determined for 54 patients. The gBRCA mutation negative cohort analyses included all patients randomized, regardless of homologous recombination deficiency status.

Within each cohort, patients were randomized 2:1 to receive ZEJULA or placebo, and were continuously treated with placebo or ZEJULA until progression. The primary endpoint of this study was progression free survival. Secondary endpoints included patient-reported outcomes, chemotherapy free interval length, and OS. This trial successfully achieved its primary endpoint in both cohorts, showing that ZEJULA treatment significantly prolonged progression free survival, compared to control in patients who were gBRCA mutation positive and in patients who were gBRCA mutation negative. In addition, within the gBRCA mutation negative cohort, ZEJULA treatment significantly prolonged progression free survival compared to placebo for the prospectively defined patient population with HRDpos tumors. A high proportion of patients in both treatment groups in both cohorts had received three or more prior lines of chemotherapy. The most common treatment-emergent grade 3/4 adverse events in the ZEJULA arm of the NOVA study, based on the National Cancer Institute's Common Terminology Criteria for Adverse Event, or CTC, which is a set of criteria for the standardized classification of adverse effects of drugs used in cancer therapy (with one and two being relatively mild and higher numbers up to five being more severe), were thrombocytopenia, anemia, and neutropenia.

The figures below present the results for the primary endpoint of progression free survival for the three primary efficacy populations.

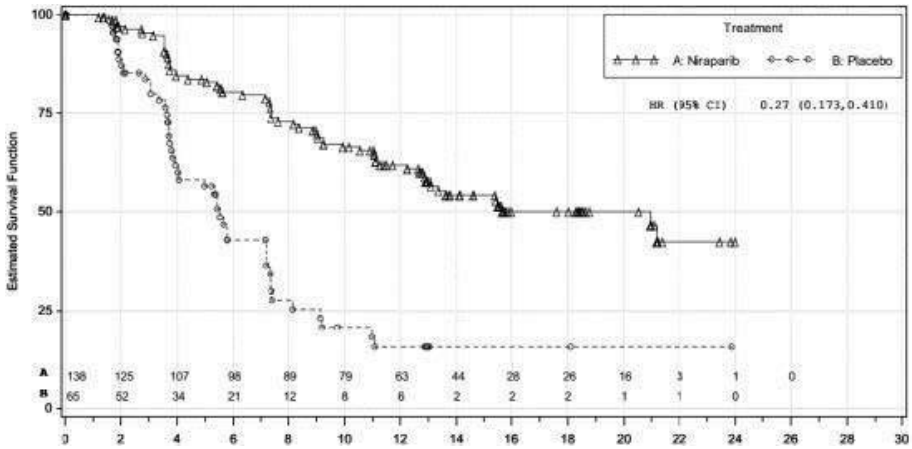
Figure 1: Progression free survival was significantly longer for patients who received ZEJULA compared to those who received placebo for all primary efficacy populations.

Treatment	Median PFS (95% CI) (Months)	Hazard Ratio (95% CI) p Value	Disease Progression Free (%) 6 Months	12 Months	18 Months
gBRCAmut Cohort					
ZEJULA (N = 138)	21.0(12.9, NE)	0.27(0.173, 0.410)	80%	62%	50%
Placebo (N = 65)	5.5(3.8, 7.2)	p<0.0001	43%	16%	16%
HRDpos Subgroup					
ZEJULA (N = 106)	12.9(8.1, 15.9)		69%	51%	37%
Placebo (N = 56)	3.8(3.5, 5.7)		35%	13%	9%
Non-gBRCAmut Cohort					
ZEJULA (N = 234)	9.3(7.2, 11.2)	0.45(0.338, 0.607)	61%	41%	30%
Placebo (N = 116)	3.9(3.7, 5.5)	p <0.0001	36%	14%	12%

Source: GSK.

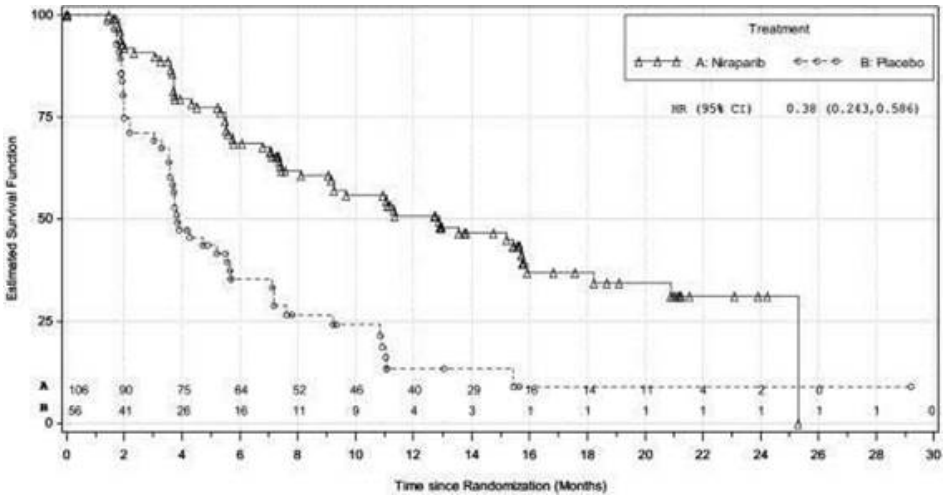
Notes: gBRCAmut = gBRCA mutation positive; non-gBRCAmut = gBRCA mutation negative

Figure 2: Progression free survival in the gBRCA mutation positive cohort of patients treated with ZEJULA versus placebo



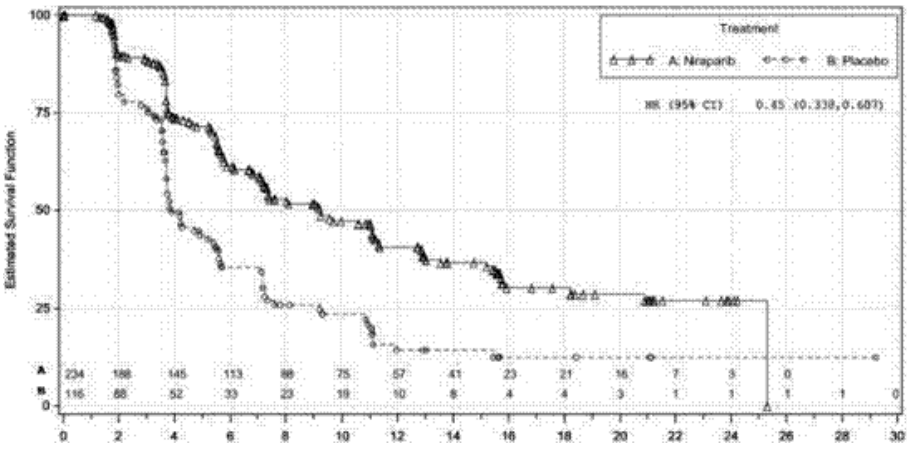
Source: GSK.

Figure 3: Progression free survival in the HRDpos group of the gBRCA mutation negative cohort of patients treated with ZEJULA versus placebo


Treatment
A: Niraparib
B: Placebo
HR (95% CI) 0.38 (0.243,0.586)
Estimated Survival Function
100
75
50
25
0
A 106 90 75 64 52 46 40 29 16 14 11 4 2 0
B 56 41 26 16 11 9 4 3 1 1 1 1 1 1 1 0
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30
Time since Randomization (Months)

Source: GSK.

Figure 4: Progression free survival in the overall gBRCA mutation negative cohort of patients treated with ZEJULA versus placebo



Source: GSK.

Within the gBRCA mutation positive cohort, the median progression free survival was 21.0 months on ZEJULA versus 5.5 months on placebo (hazard ratio=0.27; p<0.0001). As shown in the chart above, ZEJULA's treatment effect started very early during treatment as seen by the two curves being separated at first efficacy assessment. Progression free survival was also significantly longer with ZEJULA in the HRDpos group of the gBRCA mutation negative cohort (median, 12.9 months versus 3.8 months; hazard ratio=0.38; p<0.0001) and in the overall gBRCA mutation negative cohort (median, 9.3 months versus 3.9 months; hazard ratio = 0.45; p<0.0001). Additionally, in an exploratory pooled analysis that evaluated all patients in both cohorts combined, progression free survival was longer with ZEJULA (median 11.3 months versus 4.7 months, hazard ratio = 0.38, 95% confidence interval: 0.303, 0.488; p<0.0001).

As it is maintenance therapy, quality of life is important to patients receiving treatment. Patient-reported outcome data from validated survey tools indicated that ZEJULA-treated patients reported no significant difference from placebo in measures associated with symptom specific and general quality of life.

Furthermore, ZEJULA treatment did not reduce the effectiveness of subsequent therapies, and continued to show carry-over of the beneficial treatment effect in the secondary efficacy measure of second objective disease progression, which is time from randomization to objective tumor progression on next-line treatment or death from any cause. OS data, while immature, showed no negative impact of ZEJULA treatment.

The incidences of CTC grade 3/4 treatment emergent adverse events (74% vs 23%), serious adverse events (30% vs 15%), treatment-emergent adverse events leading to treatment interruption (67% vs 15%), treatment-emergent adverse events leading to dose reduction (69% vs 5%), and treatment-emergent adverse events leading to treatment discontinuation (15% vs 2%) were higher for ZEJULA versus placebo. There were no on-treatment deaths reported.

The most commonly observed hematological treatment-emergent adverse events (all CTC grades) related to ZEJULA were thrombocytopenia (61%), anemia (50%) and neutropenia (30%). Although CTC grade 3/4 hematological laboratory events were common at the initiation of treatment, no severe clinical sequelae were observed and relatively few patients discontinued due to these adverse events. Dose adjustment based on individual tolerability during the first cycles substantially reduced the incidence of these events beyond the third 28-day treatment cycle, indicating the overall effectiveness of the approach to dose modification. Overall the treatment-emergent adverse events were manageable, with no negative impact on quality of life.

PRIMA, a Phase III maintenance study of ZEJULA versus placebo in patients with advanced ovarian cancer following response on front-line platinum-based chemotherapy PRIMA is a randomized, double-blind, Phase III trial evaluating ZEJULA versus placebo as maintenance therapy in patients with advanced ovarian cancer following response on front-line platinum-based chemotherapy. The study was designed to enroll subjects with Stage III or IV ovarian cancer (including fallopian and peritoneal cancers) who had previously completed front-line platinum-based therapy with a physician-assessed response of CR or PR. Randomization was stratified by use of neoadjuvant chemotherapy (yes or no), best response to platinum therapy (CR or PR), and homologous recombination deficiency (HRD) status (positive or negative/not determined). The primary end point was progression-free survival (PFS) in patients who had tumors with HRD+ve and in those in the overall population, as determined on hierarchical testing.

From July 2016 through June 2018 and across 220 sites worldwide, a total of 733 patients were randomized at 2:1 to receive ZEJULA or placebo as maintenance therapy, of whom 373 (50.9%) had tumors with HRD. Among the patients in this category, the median PFS was significantly longer in the ZEJULA group than in the placebo group (21.9 months vs. 10.4 months; hazard ratio for disease progression or death, 0.43; 95% confidence interval [CI], 0.31 to 0.59; P<0.001). In the overall population, the corresponding progression-free survival was 13.8 months and 8.2 months (hazard ratio, 0.62; 95% CI, 0.50 to 0.76; P<0.001) (Table 1, Figure 5 and 6). At the 24-month interim analysis, the rate of overall survival was 84% in the ZEJULA group and 77% in the placebo group (hazard ratio, 0.70; 95% CI, 0.44 to 1.11).

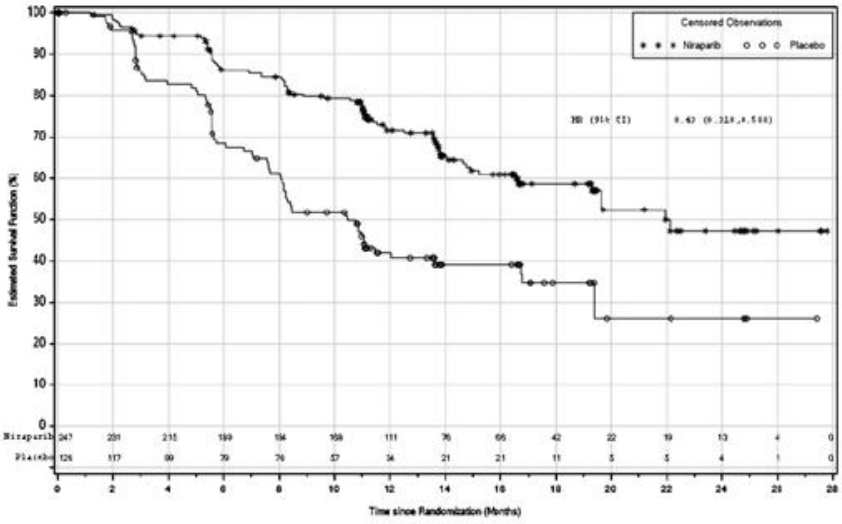
The safety profile observed in the PRIMA study was consistent with the known safety profile of ZEJULA seen in previous clinical studies and other PARP inhibitors, including gastrointestinal and hematological events. In the safety population, for the ZEJULA versus placebo treatment arms, the incidences of CTCAE Grade >3 TEAEs (70.5% versus 18.9%), SAEs (32.2% versus 13.1%), TEAEs leading to treatment interruption (79.5% versus 18.0%), TEAEs leading to dose reduction (70.9% versus 8.2%), and of TEAEs leading to treatment discontinuation (12.0% versus 2.5%) were higher for those receiving ZEJULA vs placebo. There were no on-treatment deaths reported during the study. The incidence of the most commonly reported events (overall and Grade ≥3) was higher for subjects who received a fixed starting dose of ZEJULA (300mg) compared with those who received an individualized starting dose based on baseline body weight and platelet count (300mg or 200mg).

Table 1: Primary efficacy endpoint of PFS based on blinded independent central review (BICR) (ITT Population)

	HRDpos		Overall	
Parameters	**ZEJULA (N=247)**	**placebo (N=126)**	**ZEJULA (N=487)**	**placebo (N=246)**
PFS (months) median (95%CI)	21.9 (19.3, N)	10.4 (8.1,12.1)	13.8 (11.5,14.9)	8.2 (7.3,8.5)
Survival distribution function (95% CI)				
6-month	0.86 (0.81,0.90)	0.68 (0.59,0.76)	0.73 (0.69,0.77)	0.60 (0.53,0.66)
12-month	0.72 (0.65,0.77)	0.42 (0.33,0.51)	0.53 (0.48,0.58)	0.35 (0.29,0.42)
18-month	0.59 (0.50,0.66)	0.35 (0.25,0.45)	0.42 (0.36,0.47)	0.28 (0.21,0.35)
24-month	0.47 (0.36,0.58)	0.26 (0.14,0.39)	0.32 (0.25,0.39)	0.23 (0.14,0.32)
30-month	0.47 (0.36,0.58)	0.26 (0.14,0.39)	0.32 (0.25,0.39)	0.23 (0.14,0.32)
P value	<0.0001		<0.0001	
HR (95%CI)	0.43 (0.310,0.588)		0.62 (0.502,0.755)	

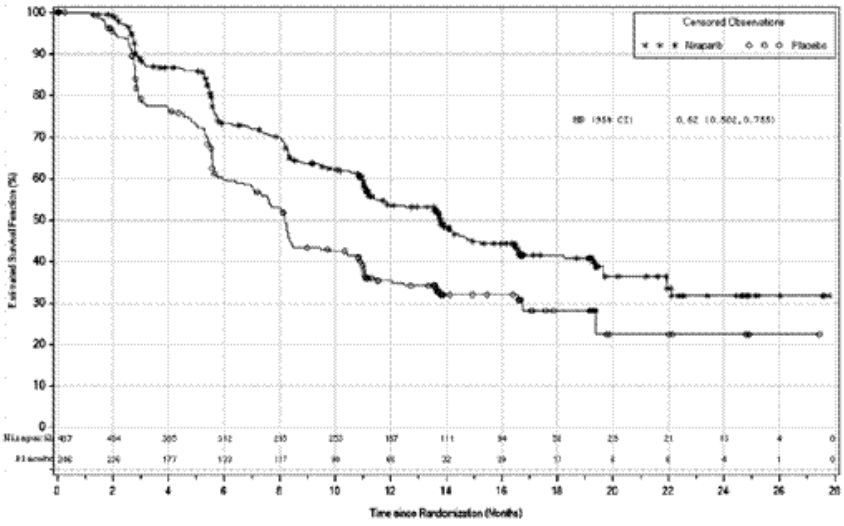
Source: GSK.

Figure 5: Kaplan-Meier plot of PFS by BICR assessment in subjects with HRD tumors (ITT Population)



Source: GSK.

Figure 6: Kaplan-Meier plot of PFS by BICR assessment in overall population (ITT Population)



Source: GSK.

Based on PRIMA results, sNDA application for ZEJULA for first-line maintenance treatment for women with platinum-responsive advanced ovarian cancer has been submitted to FDA. On April 29, 2020, the FDA approved ZEJULA for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy.

Licenses, Rights and Obligations

In September 2016, we entered into a collaboration, development and license agreement with Tesaro (now GSK) under which we obtained an exclusive sublicense under certain patents and know-how that Tesaro (now GSK) licensed from Merck Corp. and AstraZeneca UK Limited to develop, manufacture, use, sell, import and commercialize GSK's proprietary PARP inhibitor, ZEJULA, in China, Hong Kong and Macau, or licensed territory, in the licensed field of treatment, diagnosis and prevention of any human diseases or conditions (other than prostate cancer). For more information, see "— Overview of Our License and Strategic Collaboration Agreements — GSK."

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET ZEJULA IN OTHER CLINICALLY RELEVANT INDICATIONS SUCCESSFULLY.

Optune and Tumor Treating Fields

Optune (Tumor Treating Fields)

Optune (Tumor Treating Fields), one of our Core Products, is a portable battery or power supply operated device which act by delivering low intensity (1-3 V/cm), intermediate frequency (100-300 kHz), alternating Tumor Treating Fields to the patient's shaved head by means of electrically insulated surface transducer arrays. Tumor Treating Fields is a cancer therapy that uses electric fields tuned to specific frequencies to disrupt cell division, inhibiting tumor growth and causing affected cancer cells to die. Optune is approved by the FDA under the Premarket Approval ("PMA") pathway for the treatment of adult patients with newly diagnosed GBM in combination with TMZ, a chemotherapy drug, and for adult patients with GBM following confirmed recurrence after chemotherapy as monotherapy treatment. It also has approval or a CE certificate to market Optune for the treatment of GBM in the European Union, Japan and certain other countries.

In September 2018, we announced a global strategic development collaboration with Novocure, under which we obtained an exclusive license to develop and commercialize Optune (Tumor Treating Fields) in China, Hong Kong and Macau and will also support enrollment of Chinese patients to accelerate the development of Tumor Treating Fields in multiple solid tumor cancer indications. For further details of the exclusive license, see "— Overview of Our License and Strategic Collaboration Agreements." In December 2018, within three months of signing the partnership deal with Novocure, we launched Optune in Hong Kong and treated its first patient with newly diagnosed GBM.

In May 2019, our partner Novocure received the U.S. FDA approval of a Humanitarian Use Device (HUD) for Optune Lua ™in combination with chemotherapy for the first-line treatment of adult patients with unresectable, locally advanced or metastatic malignant pleural mesothelioma (MPM), which is anticipated to be our next MAA filing with the NMPA. A device designated as a HUD is intended to benefit patients by treating or diagnosing a disease that affects, or is manifested in, not more than 8,000 individuals in the U.S. per year. The application submitted to the FDA for market approval of a HUD is an Humanitarian Device Exemption (HDE), that is similar in both form and content to a traditional premarket approval application (PMA) for non-HUD devices, in that the HDE applicant must demonstrate a reasonable assurance of safety, but in an HDE application, the applicant seeks an exemption from the PMA requirement of demonstrating a reasonable assurance of effectiveness. The HDE pathway provides an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting smaller patient populations. Optune Lua ™, the first treatment for MPM approved by the U.S. FDA since 2007, is a non-invasive, antimitotic cancer treatment that delivers Tumor Treating Fields within the torso.

In August 2019, the NMPA granted Innovative Medical Device Designation for Optune, which allowed us to take advantage of an expedited approval process for Optune that offered opportunities for pre-consultation with and input from the NMPA throughout the approval process. In May 2020, the NMPA approved the Marketing Authorization Application (MAA) for Optune without the need of a clinical trial in combination with TMZ for the treatment of patients with newly diagnosed GBM, and also as a monotherapy for the treatment of patients with recurrent GBM, which makes Optune the first treatment for glioblastoma approved in China since 2007. In August 2020, Optune Lua™ was launched for the treatment of MPM in Hong Kong. Since the date of issue of the relevant regulatory approvals and as of the Latest Practicable Date, no material unexpected or adverse changes had occurred.

Background of Tumor Treating Fields

Tumor Treating Fields were invented in 2000 by Professor Emeritus Yoram Palti of the Technion Institute of Technology in Israel, who founded Novocure (Israel) in 2000, conducted pre-clinical studies of Tumor Treating Fields, developed a medical device capable of delivering Tumor Treating Fields to patients, and finally brought Tumor Treating Fields into clinical use through clinical testing in patients with recurrent glioblastoma. Today, after more than 15 years of pre-clinical research, it is known that Tumor Treating Fields are an electric field based loco-regional, antimitotic treatment modality, which inhibits the growth of cancerous tumors in vitro and in vivo. As intermediate frequency (200 kHz) and low intensity (1-3 V/cm) alternating electric fields, Tumor Treating Fields act predominantly during two phases of mitosis: 1) during metaphase, by disrupting the formation of the mitotic spindle, and 2) during cytokinesis, by dielectrophoretic dislocation of intracellular constituents resulting in apoptosis. Tumor Treating Fields cannot stimulate nerves or muscles, nor do they lead to heating of the tumor or surrounding tissues. Since Tumor Treating Fields are generated using electrically insulated electrodes (transducer arrays), there is no direct current flow into the tissue so that electrolysis and tissue damage do not occur over time. Since most normal adult brain cells proliferate very slowly, if at all, they are minimally affected by the Tumor Treating Fields.

The efficacy of Tumor Treating Fields is frequency dependent on specific cell types. The anti-mitotic effect of Tumor Treating Fields has been shown in multiple cell lines when the appropriate frequency was utilized. This includes but not limited to the following tumor models: glioblastoma at 200 kHz, NSCLC at 150kHz; breast carcinoma at 120kHz; mouse melanoma at 100kHz.

Four Phase III trials of Tumor Treating Fields in a variety of solid tumors are ongoing. PANOVA-3 is Tumor Treating Fields combined with chemotherapy for newly-diagnosed pancreatic cancer. LUNAR is targeting advanced NSCLC with disease progression on or after prior platinum-based treatment, to evaluate Tumor Treating Fields combined with chemotherapy versus chemotherapy alone, METIS trial is intended for patients who have recently been diagnosed with brain metastases from NSCLC, and ENGOT-ov50/INNOVATE-3 trial is intended for patients who have recently been diagnosed with ovarian cancer that progressed and became resistant to chemotherapy containing platinum (platinum resistant ovarian cancer).

Market Opportunity and Competition

Novocure currently has global Phase III studies evaluating the safety and efficacy of Tumor Treating Fields in brain metastases, non-small cell lung cancer, or NSCLC, pancreatic cancer and ovarian cancer, which are large commercial opportunities in China.

Glioblastoma Multiforme (GBM)

GBM, a malignant form of astrocytoma, is the most common primary intracranial neoplasm. Incidence of GBM represents 46.6% of all brain cancer incidence in China, according to the Frost & Sullivan Report, and in 2019, GBM had 53.6 thousand incidences in China. GBM is treated mainly by surgery, radiotherapy combined with TMZ chemotherapy and other methods. However, as a primary malignant central nervous system tumor, despite numerous attempts to improve the outcome of patients with GBM, long-term survival remains poor. The global five-year survival rate of GBM patients is still at a mid-single digits, ranging from 5% to 6%, and in China, the rate is less than 5%, according to Frost & Sullivan. Optune (Tumor Treating Fields) was approved in 2020 in China as a new treatment for glioblastoma.

- Optune is indicated for the treatment of adult patients (22 years of age or older) with histologically-confirmed recurrence in the supra-tentorial region of GBM. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted.

- Optune with TMZ is indicated for the treatment of adult patients with newly diagnosed, supratentorial GBM following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy.

As of July 2020, there are two main treatment choices in China — one is TMZ, a chemotherapy drug which was approved in 2007 (original version was approved in 2007, whereas the generic was approved in 2004); and the other one is Optune (Tumor Treating Fields) from Zai Lab, a novel cancer therapy that uses electric fields to inhibit tumor growth, which was approved in May 2020. Tumor Treating Fields was recommended with Level 1 evidence as a treatment for newly diagnosed GBM patients in the first Glioma Treatment Guideline (2018 Version) (腦膠質瘤診療規範(2018年版) published by the National Health Commission of China.

Optune has an "only-in-class" profile which more than doubles survival benefit in GBM patients. It is recommended in the national treatment guideline in the U.S. with category 1 recommendation for newly diagnosed GBM. In China, Optune is the first innovative treatment approved for GBM treatment since 2007.

Mesothelioma

The incidence of mesothelioma in China reached 3.1 thousand in 2019, with a CAGR of 2.7% from the year of 2015, according to Frost & Sullivan.

Gastric Cancer

For market opportunity and competition information with respect to gastric cancer, please see "— ZEJULA — Market Opportunity and Competition — Gastric Cancer".

Lung Cancer

For market opportunity and competition information with respect to lung cancer, please see "— ZEJULA — Market Opportunity and Competition — Lung Cancer".

Pancreatic Cancer

The incidence of pancreatic cancer in China has grown rapidly in recent years. From 2015 to 2019, the incidence of pancreatic cancer in China has increased from 95.0 thousand to 108.4 thousand, representing a CAGR of 3.3%. The incidence is estimated to reach 127.1 thousand by 2024, representing a CAGR of 3.2% from 2019 to 2024. By 2030, it is anticipated to reach 152.2 thousand.

The treatment of pancreatic cancer mainly includes surgical treatment, radiotherapy, chemotherapy, interventional therapy, ERCP related treatment and TCM treatment. Currently, the option of targeted therapies is quite limited. Several targeted therapies besides erlotinib have been assessed in combination with emcitabine, but none has been shown to significantly impact outcomes.

Ovarian Cancer

For market opportunity and competition information with respect to ovarian cancer, please see "— ZEJULA — Market Opportunity and Competition — Ovarian Cancer".

Liver Cancer

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer, accounting for approximately 90% of all liver cancer, and is the most common cause of death in people with cirrhosis. HCC incidence increased to 369.4 thousand in 2019 at a CAGR of 2.6% from 2015 to 2019, and is expected to reach 473.4 thousand in 2030, representing a CAGR of 2.2%. The 5-year survival rate of HCC in China is 12.1%, according to the Frost & Sullivan Report. Current treatment of HCC include surgery, localized treatments, hepatic artery chemoembolization, radiation therapy and drug therapy. Overall, chemotherapy remains the main drug treatment method for HCC in China. There is only a low level of usage of targeted therapy with agents such as sorafenib. There is, therefore, a large unmet medical need to develop new treatments for advanced HCC treatment in China which presents better efficacy and tolerability for Chinese patients. This is especially relevant since chemotherapy drugs are generally less effective in HCC, compared to other cancers.

Summary of Clinical Trial Results

The following clinical trials were conducted by our business partner, Novocure.

Pivotal Study of Tumor Treating Fields for Recurrent GBM Subjects

In a prospective, randomized, open label, active parallel control trial (EF-11) was conducted to compare the effectiveness and safety. A total of 237 patients (120 Tumor Treating Fields; 117 best supportive care, BSC) with progressive or recurrent GBM were enrolled in the study. Baseline characteristics were similar between treatment groups. In the ITT population which included all randomized subjects, overall survival in subjects treated with Tumor Treating Fields was comparable to that observed in subjects treated with BSC (median OS=6.3 vs. 6.4 months; p=0.98). The pivotal study data establish that Tumor Treating Fields therapy is comparable to BSC therapy in extending OS.

The one-year survival is similar in the Tumor Treating Fields and BSC groups in the ITT population (21.9% vs. 22.1%). Progression free survival at 6 months (PFS6) is the same in the ITT population (21.4% vs. 15.2%). Radiological response rates from the subset of patients evaluated were reported as 14% for the Tumor Treating Fields group compared to 9.6% for the BSC group in the ITT population. Median time to progression, or TTP, was 9.3 weeks for Tumor Treating Fields vs. 9.6 weeks for BSC.

Tumor Treating Fields subjects experienced fewer adverse events in general, significantly fewer treatment related adverse events, and significantly lower gastrointestinal, hematological and infectious adverse events compared to BSC controls. The only device- related adverse event seen was a mild to moderate skin irritation beneath the device transducer arrays, which was easily treated with topical ointments. Finally, certain quality of life measures were better in Tumor Treating Fields subjects as a group when compared to subjects receiving effective BSC chemotherapy.

Pivotal Study of Tumor Treating Fields for Newly Diagnosed GBM

An international Phase III trial (EF-14) in newly diagnosed GBM, evaluating the role of Tumor Treating Fields in combination with TMZ maintenance after surgery and chemoradiation versus TMZ alone was conducted between July 2009 and September 2014 to evaluate efficacy and safety.

A total of 695 patients were randomized, the median number of maintenance TMZ cycles was 6 and 5 cycles, for Tumor Treating Fields/TMZ and TMZ alone, respectively. The median progression-free survival was 6.7 months for the patients treated with Tumor Treating Fields/TMZ versus 4.0 months for TMZ alone (HR 0.63;95% CI 0.52-0.76; p<0.001). Median overall survival from randomization was 20.9 months versus 16 months for the Tumor Treating Fields/TMZ and TMZ alone, respectively, with a hazard ratio of 0.63 (95% CI 0.53-0.76), p<0.001. The most common adverse events in the Tumor Treating Fields /TMZ arm, defined as occurring in >10% of patients, were thrombocytopenia, nausea, constipation, vomiting, fatigue, medical device site reaction, headache, convulsions, and depression. Grade 3 to 4 adverse events were well balanced between the 2 treatment arms. None of the systemic grade 3 to 4 adverse events were considered related to Tumor Treating Fields by any of the investigators. Mild to moderate skin toxicity underneath the transducer arrays occurred in 52% of patients who received Tumor Treating Fields-TMZ vs no patients who received TMZ alone.

Based on the data, FDA expanded approval of Optune in combination with TMZ for the treatment of adult patients with newly diagnosed GBM.

Our Clinical Trial Designs and Strategy for Tumor Treating Fields in the China Market

In August 2019, the NMPA granted Innovative Medical Device Designation for Optune, which allowed us to take advantage of an expedited approval process for Optune that offered opportunities for pre-consultation with and input from the NMPA throughout the approval process. In May 2020, the NMPA approved the Marketing Authorization Application (MAA) for Optune without the need of a clinical trial in combination with TMZ for the treatment of patients with newly diagnosed GBM, and also as a monotherapy for the treatment of patients with recurrent GBM, which makes Optune the first treatment for glioblastoma approved in China since 2007. As recommended by the NMPA, we are currently collecting efficacy and safety data from GBM patients treated with Optune. We believe that the collection of data in Chinese patients will facilitate our registration certificate renewal for Optune in five years as well as market promotion.

In January 2020, we began patient enrollment for a Phase II pilot trial of Tumor Treating Fields in gastric cancer in Greater China. The First-Patient-In (FPI) occurred in January 2020 in Hong Kong and as of the Latest Practicable Date, four patients had been enrolled. The initiation of enrollment in China is expected by the end of 2020. The National Institutes for Food and Drug Control under the NMPA is currently conducting a technical testing on Tumor Treating Fields. We must pass the technical testing prior to the ethics committee approval and the initiation of patient enrollment in China.This trial is single arm, open-label, multi-center study designed to investigate the safety and efficacy of Tumor Treating Fields in combination with chemotherapy as the first-line treatment of unresectable gastric adenocarcinoma, or gastroesophageal junction adenocarcinoma. If the results of such ongoing Phase II pilot trials are positive, we contemplate to participate in the larger-in-scale pivotal or potentially registration-enabling trials that will be initiated by Novocure.

We are preparing to join global Phase III pivotal trials in non-small cell lung cancer, locally advanced pancreatic cancer and brain metastases in Greater China by early 2021.

We are in the planning phase for clinical trials in liver cancer and ovarian cancer in Greater China.

Licenses, Rights and Obligations

In September 2018, we entered into a license and collaboration agreement with Novocure. Under the terms of the agreement, Novocure exclusively licensed to us the rights to perform clinical studies, sublicensable to affiliates and third parties (subject to Novocure's consent), sell, offer for sale and import Tumor Treating Fields products in the field of oncology, each, a licensed product and collectively, the licensed products, in China, Hong Kong, Macau and Taiwan, or the territory. For more information, see "— Overview of Our License and Strategic Collaboration Agreements — Novocure."

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET TUMOR TREATING FIELDS IN OTHER CLINICALLY RELEVANT INDICATIONS SUCCESSFULLY.

Our Oncology Pipeline

Ripretinib

Overview

Ripretinib is an investigational KIT and PDGFRα kinase switch control inhibitor in clinical development for the treatment of KIT and/or PDGFRα-driven cancers, including GIST, systemic mastocytosis, or SM, and other cancers. Ripretinib was specifically designed to improve the treatment of GIST patients by inhibiting a broad spectrum of mutations in KIT and PDGFRα. Ripretinib is a KIT and PDGFRα inhibitor that blocks initiating and secondary KIT mutations in exons 9, 11, 13, 14, 17, and 18, involved in GIST as well as the primary D816V exon 17 mutation involved in SM. Ripretinib also inhibits primary PDGFRα mutations in exons 12, 14 and 18, including the exon 18 D842V mutation, involved in a subset of GIST.

We obtained an exclusive license to develop and commercialize ripretinib in China, Hong Kong, Macau and Taiwan in June 2019 from Deciphera. For further details of the exclusive license, see "— Overview of Our License and Strategic Collaboration Agreements — Deciphera."

In December 2019, an NDA was submitted to the FDA for ripretinib in the treatment of patients with advanced GIST who have received prior treatment with imatinib, sunitinib, and regorafenib. The NDA submission is based on positive results from first Phase III study, INVICTUS, in fourth-line and fourth-line plus GIST patients, for whom there are currently no approved therapies other than avapritinib in the U.S. which is approved for GIST patients with PDGFRα exon 18 mutations only (estimated approximately 6% of all patients with newly- diagnosed GIST). In August 2019, the top-line results from INVICTUS was published, including that the study achieved its primary endpoint of improved PFS compared to placebo as determined by blinded independent central radiologic review using modified RECIST. In February 2020, the FDA accepted the NDA for ripretinib for the treatment of patients with fourth-line and fourth-line plus GIST, granted priority review and set an action date of August 13, 2020 under the PDUFA. On May 15, 2020, the FDA approved ripretinib for adult patients with advanced GIST who have received prior treatment with three or more kinase inhibitors, including imatinib. In July 2020, we received the CTA approval for the registrational bridging study of ripretinib in patients with second-line GIST. The NMPA accepted and granted priority review to our NDA for ripretinib for the treatment of adult patients with advanced GIST who have received prior treatment with three or more kinase inhibitors, including imatinib in July 2020 and August 2020, respectively. Ripretinib has been approved by Health Commission and Medical Products Administration of Hainan Province as the first Urgently Needed Drug that can be taken out from the Boao Pilot Zone by a designated patient, which is also known as the special Named Patient Program (NPP). Under the NPP, patients may apply for taking away a small amount of the legally imported drugs that is not yet registered domestically (neither inside or outside the Boao Pilot Zone) but is on urgent medical need from the Boao Pilot Zone following his therapeutic schedule. See "Regulatory Environment — PRC Regulations of Pharmaceutical Product Development and Approval — Import of Urgently Needed Drug in Boao Pilot Zone".

Mechanism of Action

KIT and PDGFRα are dual switch kinases, each containing i) an auxiliary inhibitory switch encoded by KIT exon 11 or PDGFRα exon 12 and ii) a main activation loop switch within the kinase domain encoded by KIT exons 17 and 18 or PDGFRα exons 18 and 19. This dual switch mechanism carefully regulates cellular kinase activity by controlling kinase conformation in either an "on" or "off" position. Oncogenic kinase mutations predominantly function by disrupting one or more regulatory switch mechanisms, leading to dysregulated switch function and loss of normal, physiologic conformational control. Ripretinib is a novel switch-control tyrosine kinase inhibitor (TKI) specifically designed to broadly inhibit KIT and PDGFRα kinase signaling through a dual mechanism of action that locks the kinase into an inactive conformation, resulting in inhibition of downstream signaling and cell proliferation.

Ripretinib precisely and durably binds to both the switch pocket region and the activation loop to lock the kinase in the inactive "off" state. Portions of ripretinib mimic the inhibitory loop and occupy the switch pocket, thereby preventing the activation loop's entry. Other residues on ripretinib bind to the activation loop, stabilizing it out of the switch pocket and covering the adenosine triphosphate (ATP) binding site, so kinase activation cannot occur.

This dual mechanism of action secures KIT and PDGFRα kinases in their inactive conformations providing broad in vitro inhibition of KIT and PDGFRα kinase activity, including wild type and multiple primary and secondary mutations. Ripretinib also inhibits other kinases in vitro, such as PDGFRb, TIE2, VEGFR2, and BRAF.

The dual MoA of ripretinib provided broad-spectrum inhibition of KIT and PDGFRα kinase signaling in vitro, including multiple primary and secondary mutations and wild type GIST.

Market Opportunity and Competition

Gastrointestinal Stromal Tumor (GIST)

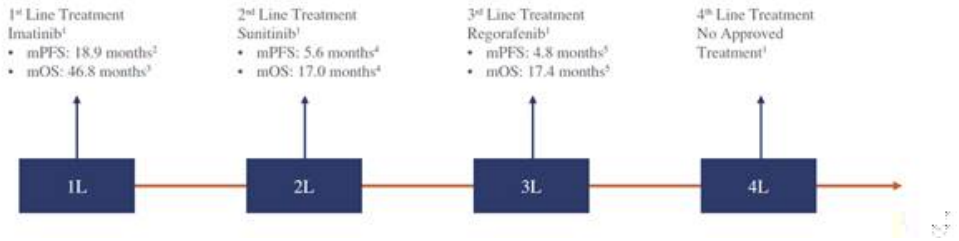
GIST are the most common sarcoma of the gastrointestinal tract and present most often in the stomach or small intestine. The typical patient is over 50 years old. Estimates for 5-year survival range from 48% to 90% depending upon the stage of the disease at diagnosis. GIST has 31.9 thousand incidences in China in 2019, according to the Frost & Sullivan Report.

GIST is a disease driven initially by primary mutations in KIT kinase in approximately 75% to 80% of cases or in PDGFRα kinase in approximately 5% to 10% of cases. In approximately 12% of all GIST patients, the disease is not driven by KIT or PDGFRα but by other genetic mutations or alterations.

Metastatic KIT-driven GIST is a disease characterized by many mutations in KIT, with over 90% of individual KIT-driven GIST patients harboring multiple mutations that drive progression of their disease. Multiple secondary mutations can arise within an individual patient and/or tumor in different areas or sites of tumor growth.

The complex heterogeneity of KIT mutations within individual tumors and individual patients is a major cause of resistance to existing therapies, which individually only address a subset of the mutations driving disease progression. A kinase inhibitor that could inhibit a broad spectrum of clinically relevant KIT mutations could be of high therapeutic value in the treatment of KIT-driven GIST in patients who are unresponsive to treatment or have grown resistant to treatment. In PDGFRα-driven GIST, there are no approved therapies other than avapritinib. The primary PDGFRα mutations are mostly insensitive to imatinib and other drugs approved for GIST. The design of ripretinib as a PDGFRα switch control inhibitor may make the appearance of secondary mutations less likely after treatment than with a traditional kinase inhibitor.

The following table shows reported PFS or TTP (as applicable), ORR, overall survival, all as per RECIST, for imatinib, sunitinib, and regorafenib in first-line, second-line, and third-line GIST, respectively, based upon the published results of registrational trials that were presented to the FDA for approval of these drugs. This treatment paradigm is also applicable in China.



Notes: mPFS=median progression free survival; mOS=median overall survival.

1 As of January 9, 2020, avapritinib is approved in the U.S. for GIST patients with PDGFRα exon 18 mutations only, which mutations are harbored by an estimated ~6% of patients with newly diagnosed GIST;

2. Gleevec. Stein, Switzerland: Novartis; 2008;

3. Casali PG, et al. J Clin Oncol. 2017;35:1713-1720;

4. Sutent. New York, NY: Pfizer; 2011, mPFS and mOS converted from weeks to months;

5. Stivarga. Germany: Bayer Healthcare; 2013.

While imatinib, sunitinib, and regorafenib inhibit certain clinically relevant initiating and drug resistance-causing mutations in KIT, these approved drugs, in addition to avapritinib, each inhibit only a limited subset of KIT and PDGFRα mutations known to occur in GIST patients. Although GIST patients may experience periods of disease control with these treatments, due to the heterogeneous nature of the mutations that drive the disease, many patients continue to progress and ultimately fail all lines of treatment.

According to Frost & Sullivan, only three TKI therapies have been approved for treating GIST currently, namely Glivec (imatinib) from Novartis, Sutent (sunitinib) from Pfizer and Stivarga (regorafenib) from Bayer, and a vast majority of advanced and metastatic GIST patients will eventually relapse after first-line and subsequent lines of treatment. This creates a significant opportunity for new drugs that can help overcome the problem of patient lack of responsiveness or who have developed resistance to existing treatments.

Summary of Clinical Trial Results

INVICTUS: Completed Phase III Study in Fourth-Line and Fourth-Line Plus GIST

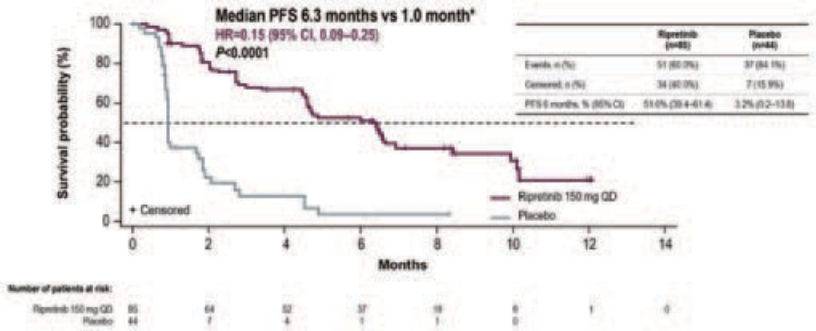
The INVICTUS Phase III study was a randomized, double-blind, placebo-controlled, global, multicenter trial conducted by Deciphera to evaluate the safety, tolerability, and efficacy of ripretinib compared to placebo in patients with advanced GIST whose previous therapies have included at least imatinib, sunitinib, and regorafenib. The trial enrolled 129 patients who had a confirmed diagnosis of GIST and had previously received at least three different kinase inhibitors including imatinib, sunitinib, and regorafenib. Patients were treated with ripretinib or placebo, in accordance with their randomization, until they developed disease progression, experienced unacceptable toxicity, or withdrew consent. Placebo patients had the opportunity to cross over to ripretinib treatment upon disease progression with placebo. Patients on ripretinib had the opportunity to remain on their current dose or escalate to 150 mg twice daily (BID) upon disease progression.

Patients were randomized 2:1 to either 150 mg of ripretinib or placebo once daily (QD) in repeated 28-day cycles with best supportive care. Patients were evaluated for PFS based upon independent radiologic review of CT scans, as assessed by modified RECIST. Tumor response assessments per modified RECIST were conducted every cycle for the first three cycles and then every two cycles thereafter beginning with the fourth cycle. The primary efficacy endpoint was PFS as determined by independent radiologic review using modified RECIST. Secondary endpoints as determined by independent radiologic review using modified RECIST included ORR, overall survival (OS), and TTP.

In 2019, the top-line results from INVICTUS is published, including that the study achieved its primary endpoint of improved PFS compared to placebo.

In the INVICTUS study, ripretinib demonstrated a median PFS of 6.3 months (27.6 weeks) compared to 1.0 month (4.1 weeks) in the placebo arm and significantly reduced the risk of disease progression or death by 85% (Hazard Ratio (HR) of 0.15, 95% Confidence Interval (0.09,0.25), p-value <0.0001) compared to placebo. This PFS benefit was consistent across all assessed patient subgroups. The following graph shows the estimated PFS probability at each time point for the ripretinib and placebo arms in INVICTUS:

INVICTUS: Estimated PFS Probability for Ripretinib and Placebo Arms



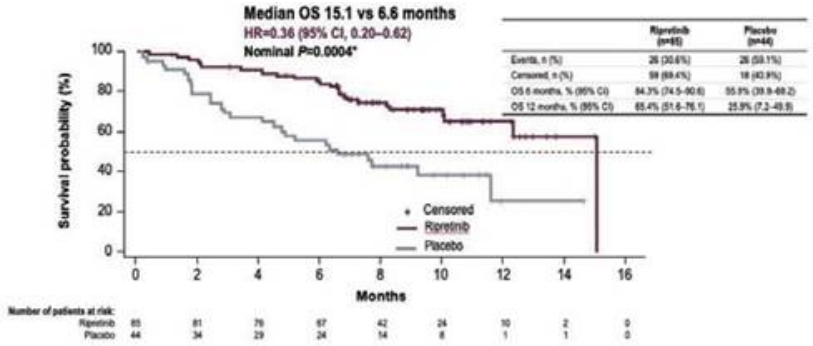
** Double-blind period*

Source: Deciphera

For the key secondary endpoint of ORR as determined by blinded independent radiologic review using modified RECIST, ripretinib demonstrated an ORR of 9.4% compared with 0% for placebo (p-value=0.0504), which was not statistically significant. As of the cutoff date of May 31, 2019, the median duration of response had not been reached with seven of the eight patients still responding to treatment. All responders had partial responses.

Ripretinib also showed a clinically meaningful improvement over placebo in terms of the secondary endpoint of OS (median OS 15.1 months with ripretinib compared to 6.6 months with placebo, HR = 0.36, 95% Confidence Interval (0.20, 0.62), nominal p-value=0.0004). The OS data for the placebo arm includes patients taking placebo who, following progression, were crossed-over to ripretinib treatment. The following graph shows the estimated OS probability at each time point for the ripretinib and placebo arms in INVICTUS:

INVICTUS: Estimated OS Probability for Ripretinib and Placebo Arms



* Due to hierarchical testing procedures of the endpoints, the OS endpoint could not be formally tested because the ORR was not statistically significant. Data includes all time periods, including dose escalations. Placebo arm includes patients taking placebo who, following progression, were crossed- over to ripretinib treatment.

Source: Deciphera

Ripretinib was generally well tolerated and the adverse events reported in the INVICTUS study were consistent with data from previously presented Phase I study results. Grade 3 or 4 treatment-emergent adverse events (TEAEs) occurred in 42 patients (49%) on the ripretinib arm compared to 19 patients (44%) on the placebo arm. Grade 3 or 4 TEAEs in greater than 5% of patients in the ripretinib arm were anemia (9%; n=8), abdominal pain (7%; n=6), and hypertension (7%; n=6). Grade 3 or 4 TEAEs in greater than 5% of patients in the placebo arm were anemia (14%; n=6).

The below table lists all TEAEs (and corresponding grade 3 and 4 TEAEs) in greater than 10% of patients in the ripretinib arm compared to the placebo arm in INVICTUS.

INVICTUS: TEAEs in >10% of Patients (and Corresponding Grade 3 and 4 TEAEs)

Treatment Emergent Adverse event	Ripretinib any grade (n=85)	Ripretinib grade 3 amd 4 (n=85))1	Placebo any grade (n=43))2	Placebo grade 3 and 4 (n=43))1,2
Any TEAE or grade 3/4 TEAE3	**84(98.8)%**	**42(49.4)%**	**42(97.7)%**	**19(44.2)%**
Alopecia	44(51.8)%	0	2(4.7)%	0
Fatigue	36(42.4)%	3(3.5)%	10(23.3)%	1(2.3)%
Nausea	33(38.8)%	3(3.5)%	5(11.6)%	0
Abdominal pain	31(36.5)%	6(7.1)%	13(30.2)%	2(4.7)%
Constipation	29(34.1)%	1(1.2)%	8(18.6)%	0
Myalgia	27(31.8)%	1(1.2)%	5(11.6)%	0
Diarrhea	24(28.2)%	1(1.2)%	6(14)%	1(2.3)%
Decreased appetite	23(27.1)%	1(1.2)%	9(20.9)%	1(2.3)%
Palmar-plantar erythrodysesthesia syndrome	18(21.2)%	0	0	0
Vomiting	18(21.2)%	3(3.5)%	3(7)%	0
Headache	16(18.8)%	0	2(4.7)%	0
Weight decreased	16(18.8)%	0	5(11.6)%	0
Arthralgia	15(17.6)%	0	2(4.7)%	0
Blood bilirubin increased	14(16.5)%	1(1.2)%	0	0
Edema peripheral	14(16.5)%	1(1.2)%	3(7)%	0
Muscle spasms	13(15.3)%	0	2(4.7)%	0
Anemia	12(14.1)%	8(9.4)%	8(18.6)%	6(14)%
Hypertension	12(14.1)%	6(7.1)%	2(4.7)%	0
Asthenia	11(12.9)%	1(1.2)%	6(14)%	2(4.7)%
Dry skin	11(12.9)%	0	3(7)%	0
Dyspnea	11(12.9)%	0	0	0
Hypophosphatemia	9(10.6)%	4(4.7)%	0	0
Lipase increased	9(10.6)%	4(4.7)%	0	0
Pruritus	9(10.6)%	0	2(4.7)%	0
Stomatitis	9(10.6)%	0	0	0

Notes:

1 Corresponding grade 3 and 4 TEAEs to TEAEs in >10% of patients receiving ripretinib
2 44 patients were randomized to placebo, but 1 did not receive treatment
3 Regardless of causality

Source: Deciphera

TEAEs leading to dose reduction occurred in 7% of patients on the ripretinib arm compared to 2% on the placebo arm. TEAEs leading to dose interruption occurred in 24% of patients on the ripretinib arm compared to 21% on the placebo arm. TEAEs leading to study treatment discontinuation occurred in 8% of patients on the ripretinib arm compared to 12% of patients on the placebo arm. TEAEs leading to death occurred in 6% of patients on the ripretinib arm compared to 23% on the placebo arm.

INTRIGUE: Ongoing Phase III Study in Second-Line GIST

The INTRIGUE Phase III study is an interventional, randomized, global, multicenter, open-label study conducted by Deciphera to evaluate the safety, tolerability, and efficacy of ripretinib compared to sunitinib in approximately 358 patients with GIST previously treated with imatinib. Patients are randomized 1:1 to either 150 mg of ripretinib once daily or 50 mg of sunitinib once daily for four weeks followed by two weeks without sunitinib. The primary efficacy endpoint is PFS as determined by independent radiologic review using modified RECIST. Secondary endpoints as determined by independent radiologic review using modified RECIST include ORR and OS.

Our Clinical Trial Designs and Strategy for Ripretinib in the China Market

We will seek regulatory approval for ripretinib in China using data from global studies and China bridging studies. In November 2019, we received the NMPA approval to conduct the bridging study in fourth-line GIST. In July 2020, we received the CTA approval for the registrational bridging study of ripretinib in patients with second-line GIST. The NMPA accepted and granted priority review to our NDA for ripretinib for the treatment of adult patients with advanced GIST who have received prior treatment with three or more kinase inhibitors, including imatinib in July 2020 and August 2020, respectively.

We are in the planning phase for clinical trials in systemic mastocytosis in China.

Odronextamab

Overview

Odronextamab is an investigational bispecific monoclonal antibody that is designed to trigger tumor killing by linking and activating a cytotoxic T-cell (binding to CD3) to a lymphoma cell (binding to CD20). Odronextamab is currently being evaluated as a treatment for late stages of follicular lymphoma (FL) and diffuse large B-cell lymphoma (DLBCL) and other lymphomas in a Phase I trial as well as a potentially registrational Phase II trial odronextamab was granted orphan drug designation by the FDA for the treatment of FL and DLBCL and was invented by Regeneron using the company's proprietary *VelocImmune*® technology and proprietary *Veloci-Bi*® bispecific platform. *Veloci-Bi*® allows for the generation of full-length bispecific antibodies similar to native antibodies that are amenable to production by standard antibody manufacturing techniques, and likely to have favorable antibody-like pharmaco-kinetic properties.

Odronextamab has demonstrated clinical activity in heavily pre-treated patients with Relapsed/Refractory (R/R) B-NHL in a Phase I trial and is currently being investigated in a potentially registrational Phase II program.

In April 2020, we entered into a strategic collaboration with Regeneron for the development and exclusive commercialization of odronextamab in oncology in mainland China, Hong Kong, Taiwan and Macau. For further details of the exclusive license, see "— Overview of Our License and Strategic Collaboration Agreements — Regeneron."

Mechanism of Action

Bispecific antibodies are an emerging class of therapeutic molecules which have been engineered to engage more than one target. When targeted to CD3, a component of the T-cell receptor (TCR), and a tumor target antigen, these molecules can direct cytotoxic effector T-cells to kill tumor cells in an antigen-specific manner that is independent of the specificity of the TCR. In the case of odronextamab, that binds to CD3 and CD20 (a B-cell surface antigen present on normal B cells and several B-cell lineage malignancies), this binding directs T-cells to specifically kill CD20 expressing target cells.

Market Opportunity and Competition

Non-Hodgkin lymphomas (NHL) is the most common hematological malignancy in the world. It comprises a heterogeneous group of malignancies with lymphoid characteristics that arise from hematopoietic progenitor cells. In China, there were an estimated 90,300 new cases and 52,900 deaths due to NHL in 2019.

Among the heterogeneous group of NHLs, 85% are of B-cell origin (B-NHL), which includes FL, DLBCL, mantle cell lymphoma (MCL), marginal zone lymphoma (MZL), and several other subtypes of B-NHLs. DLBCL and MZL are the two most common subtypes of B-NHL, accounting for approximately 41.0% and 8.0% of NHL in China. Anti-CD20 antibodies in combination with chemotherapy (or R-CHOP) are the standard of care for the treatment of B-NHLs; however, despite initial responses, about 50% of NHL patients will eventually experience disease progression due to drug resistance, indicating a need for new treatment options. In particular, around 15% of DLBCL (the most common subtype of NHL) patients are characterized as primary refractory towards first-line R-CHOP therapy. For these refractory patients, treatments options with new modalities are highly necessary. According to the Frost & Sullivan Report, there are currently no marketed bispecific antibody drugs for hematological malignancy in China as of July 2020.

Preclinical and Clinical Development

Pre-clinical Pharmacology

In vitro assays were performed to examine the ability of odronextamab to bind to target cells and to activate T-cells to specifically kill CD20-expressing target cells. Odronextamab was shown to bind to both Raji cells, a CD20+ B-cell lymphoma line, and Jurkat cells, an immortalized CD3+ T-cell line, as well as to primary human B and T-cells. In cellular cytotoxicity assays, odronextamab was able to engage T-cells to kill CD20-expressing cells in a target dependent manner. In these cytotoxicity assays, odronextamab also induced the expression of T-cell activation markers, T-cell proliferation, and cytokine release.

In vivo experiments utilizing murine tumor models were performed to evaluate the anti-tumor efficacy of odronextamab. In a model where Raji (B) lymphoma cells were grown in mice and human PBMC were added as effector cells, odronextamab treatment resulted in significant tumor growth suppression.

Nonclinical pharmacokinetics

The PK profile of odronextamab was evaluated in cynomolgus monkeys during a single-dose PK study. In general, the PK of total odronextamab in the monkey is described by non-linear, target-mediated elimination. Following a single IV infusion, mean total odronextamab serum maximum concentration (Cmax) values in monkeys increased in an approximately dose-proportional manner. The concentration-time profile of total odronextamab was characterized by a short distribution phase, followed by a saturating beta elimination phase at higher doses and an accelerated target mediated elimination phase at low doses (and corresponding low serum concentrations). Target mediated elimination (presumably due to binding of odronextamab to the CD20 target on B cells) was observed in the distribution phase and correlated with the nearly complete depletion of B cells observed 24 hours post infusion. The duration of peripheral B cell depletion increased with the odronextamab dose and in general, the rate of B cell repletion was positively correlated with the rate of clearance of total odronextamab.

Nonclinical Toxicology

The toxicity profile of odronextamab was evaluated in an exploratory, non-GLP, single-dose intravenous (IV) infusion toxicology study (dose level 1mg/kg) and a 4-week repeat dose GLP-toxicology study (dose levels 0.01, 0.1, and 1 mg/kg). The no-observed- adverse-effect-level (NOAEL) for each of the toxicology studies conducted is considered to be 1.0 mg/kg, the highest dosage administered. Odronextamab resulted in B cell depletion at all doses tested, with earlier recovery at the lower doses. This depletion extended into deep tissues including lymph nodes and spleen. A transient release of cytokines was observed whose magnitude correlated with the strength of the dose, and at the highest dose several animals also displayed some vomiting with the first dose. Neither cytokine release nor symptoms occurred upon second or subsequent dosing. An ex vivo tissue cross-reactivity study also was conducted to assess the binding specificity of odronextamab in a panel of human and cynomolgus monkey tissues. All staining in this study was consistent with expected reactivity with the target antigens, and no unanticipated cross-reactivity of odronextamab was observed.

Clinical Background

In an ongoing Phase I study (NCT02290951) of odronextamab in patients with B-cell malignancies, a total of 110 patients (61 with DLBCL; 31 with grade 1 to 3a FL; 9 with MCL; 6 with MZL; and 3 with other B-cell malignancies) were treated with odronextamab ranging from 0.03-320 mg as of 3rd September 2019. Patients had a median of 3 prior lines of therapy (range 1-11).

Among the 22 patients with R/R FL who were treated with ≥5 mg of odronextamab, the overall response rate (ORR) was 95.5% and the complete response (CR) rate was 77.3%. Patients with R/R FL who were treated with ≥80 mg of odronextamab had an ORR of 100%. The median progression-free survival for R/R FL patients treated with ≥5mg of odronextamab was 11.4 months (95% CI, 6.7-not evaluable). In the DLBCL cohort, the objective response rate (ORR) was 57.9% (11/19), and the CR rate was 42.1% (8/19) with treatment at ≥80 mg of odronextamab. At this dosage, the ORR was 71.4% in those patients not treated with prior chimeric antigen receptor (CAR) T-cell therapy (n = 7), which included all CRs. In those who received prior CAR T-cell therapy, the ORR and CR rate were 50% and 25%, respectively. The response rate was higher in patients who had not previously received CAR T-cell therapy (Figure 7). Survival rates and ongoing response rates are shown in Figure 8 by diagnosis, dose of odronextamab, and prior CAR T therapy.

Figure 7. Efficacy results by diagnosis and dose of odronextamab

Diagnosis	FL, n (%)	DLBCL N (%)	DLBCL with prior CART T therapy, n (%)	DLBCL without prior CAR T therapy n (%)
Dose of odronextamab	≥5mg	≥80mg	≥80mg	≥80mg
N	22	19	12	7
ORR	21(95.5)	11(57.9)	6(50.0)	5(71.4)
CR	17(77.3)	8(42.1)	3(25.0)	5(71.4)
PR	4(18.2)	3(15.8)	3(25.0)	0
SD	1(4.5)	2(10.5)	1(8.3)	1(14.3)
PD	0	3(15.8)	2(16.7)	1(14.3)
Not available	0	3(15.8)	3(25.0)	0

Source: Regeneron

CAR, chimeric antigen receptor; CR, complete response; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease

Figure 8. Median survival and responses by diagnosis, prior CAR T therapy and odronextamab dosing

Diagnosis	Patients with FL,	DLBCL with prior CAR T therapy	DLBCL without prior CAR T therapy
Dose of odronextamab	≥5mg	≥80mg	≥80mg
N	22	12	7
Median PFS, months (95% CI)	11.4 (6.7 – not available)	NR	NR
Median duration of follow-up months (range)	6.8 (1.0 – 22.1)	2.6 (0.4-9.9)	5.3 (1.2-11.8)
Number of patients with ongoing response at last assessment	14/21	4/6	5/5
Number of patients with ongoing CRs at last tumor assessment	12/17	3/3	5/5

Source: Regeneron

CAR, chimeric antigen receptor; CR, complete response; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; NR, not reported; PFS, progression-free survival

No dose limiting toxicities (DLTs) were observed during dose escalation. The most common treatment-emergent adverse events (TEAEs) of any grade were pyrexia (80%) and cytokine release syndrome (CRS, 59.1%). Grade 3-4 TEAEs that occurred in 10% or more of patients are anemia (21.8%), hypophosphatemia (19.1%), neutropenia (19.1%), lymphopenia (19.1%), thrombocytopenia (13.6%), and leukopenia (10.0%). CRS grade >3 occurred in 6.4% of patients and no seizures or grade 4-5 neurologic events were observed.

Preliminary data from the Phase I study showed broad antitumor activity with odronextamab in heavily pretreated R/R B-NHL patients, including some with progression after prior chimeric antigen receptor T (CAR T)-cell therapy. Odronextamab has been tolerated at doses up to 320 mg weekly, with no observed dose limiting toxicities.

Odronextamab is currently evaluated in a potentially pivotal Phase II program. This open-label, multi-center, Phase II program (NCT03888105) is evaluating the efficacy and safety of odronextamab in different disease-specific cohorts, including patients with R/R FL, DLBCL, MCL, MZL and other B-NHL subtypes. Recruitment of this study is ongoing.

Our Clinical Trial Designs and Strategy for Odronextamab in the China Market

We are exploring regulatory approval pathways for odronextamab in R/R B-NHL in China by joining the global Phase II program with multiple, potentially registrational cohorts of different subtypes of R/R B-NHL. We have submitted Phase II pivotal CTA to the NMPA and plan to enroll the first Chinese patient into the potentially registrational global Phase II study by early 2021.

Repotrectinib

Overview

Repotrectinib is an investigational next-generation tyrosine kinase inhibitor (TKI) designed to effectively target ROS1 and TRK A/B/C with potential to treat TKI-naïve or-pretreated cancer patients. Repotrectinib is currently being evaluated in an ongoing Phase I/II trial called TRIDENT-1 for the treatment of patients with ROS1+ advanced NSCLC and patients with NTRK+ advanced solid tumors.

Turning Point Therapeutics (“Turning Point”) initiated the multi-cohort Phase II registrational portion of TRIDENT-1 in June 2019 and plans to conduct the Phase II portion of the trial in approximately 120 sites in North America, Europe and Asia-Pacific regions, and to enroll a total of approximately 320 patients. The Phase II portion of TRIDENT-1 is a registrational trial for potential approval in ROS1+ advanced NSCLC and NTRK+ advanced solid tumors. The FDA has granted orphan drug designations for the development of repotrectinib in NSCLC with adenocarcinoma histology and fast track designations for the treatment of ROS1+ advanced NSCLC patients who have been previously treated with one prior line of platinum-based chemotherapy and one prior line of a ROS1 TKI, and for the treatment of ROS1+ advanced NSCLC patients who have not been previously treated with a ROS1 TKI.

We obtained an exclusive license from Turning Point to develop and commercialize repotrectinib in China, Hong Kong, Macau and Taiwan in July 2020. For further details of the exclusive license, see “— Overview of Our License and Strategic Collaboration Agreements — Turning Point.”

Mechanism of Action

Repotrectinib is a small (low molecular weight), macrocyclic TKI of ROS1, TRK, and ALK. Repotrectinib was designed to efficiently bind with the active kinase conformation and avoid steric interference from a variety of clinically resistant mutations, especially the solvent front and gatekeeper mutations of the ROS1 and TRK kinases. Repotrectinib has a rigid, three-dimensional structure and is smaller than currently approved or investigational ROS1, TRK and ALK inhibitors. The rigid, three-dimensional structure enables repotrectinib to precisely and efficiently bind to its oncogenic targets with a desirable selectivity profile. Turning Point has screened repotrectinib against approximately 400 kinases which indicated repotrectinib is a selective multi-targeted kinase inhibitor that is highly potent against ROS1, TRK, and ALK, and inhibits JAK2, SRC and FAK.

The selectivity index (SI) is defined as the kinase IC50 value divided by the lowest IC50 value (0.071 nM) from the inhibition against the ROS1 kinase. SI for ROS1 is 1, followed by kinases with 1< SI <10 (TRKA, TRKB and TRKC), 10< SI <20 (ALK, JAK2, and SRC family member FYN), and 20< SI <250 (SRC family members LYN, YES1, FGR and SRC; TXK, ARK5, DDR1 and FAK). Based on the selectivity profile, Turning Point believes repotrectinib will be able to target ROS1 and TRK family members with high potency, and target JAK2, some SRC family members and FAK with moderate potency. According to a 2015 review article, selective multi-targeted kinase inhibitors with a favorable safety profile may be more suitable for cancer treatment, which Turning Point believes is due to their activity against redundant signaling pathways mediated by different kinases. Repotrectinib inhibits JAK2, SRC and FAK leading to the modulation of STAT3 signaling, one of the major signaling pathways that is common for both intrinsic and acquired resistance. Turning Point believes the inhibition of JAK2, SRC and FAK may lead to a longer duration of response for patients treated with repotrectinib.

Market Opportunity and Competition

For market opportunity and competition information with respect to lung cancer, please see "— ZEJULA — Market Opportunity and Competition — Lung Cancer".

Specifically in relation to repotrectinib, ROS1 rearrangement is estimated to be an oncogenic driver in approximately 3 percent of patients with advanced NSCLC in China, while NTRK is estimated to be an oncogenic driver in approximately 0.5-1 percent of patients with wide range of solid tumors in China, according to the Frost & Sullivan Report. As of July 2020, there were three ROS1/NTRK/ALK targeted drugs marketed in China, of which there is only one approved targeted therapy for patients with advanced ROS1-positive lung cancer and despite its efficacy, most patients eventually acquire resistance. The unmet need in the ROS1-positive lung cancer patient population is significant. The preliminary clinical activity and safety data generated to date for repotrectinib represent a promising clinical profile.

Clinical Development by Turning Point

In the Phase I portion of TRIDENT-1, as of the July 22, 2019 data cut-off, a total of 93 patients had been dosed, 23 patients were still on treatment, and the MTD had not been reached. Of the 93 patients, 40 of 52 with ROS1+ advanced NSCLC and five of 10 with NTRK+ advanced solid tumors were evaluable by blinded independent central review (BICR). All patients received at least one dose of repotrectinib across nine dose cohorts ranging from 40 mg QD to 200 mg BID.

Utilizing the July 22, 2019 data cut-off, with a median follow-up of 20.1 months (range: 5.3 to 24.9+), repotrectinib demonstrated a confirmed overall response rate (ORR) by BICR of 91 percent (N=11, 95% CI: 59-100) in patients with ROS1+ advanced NSCLC who are ROS1 TKI-naïve and repotrectinib demonstrated a median duration of response (DOR) of 23.1 months (95% CI: 5.6-NR) (based on Kaplan-Meier estimation). The probability of patients with a DOR $\geq$ 9 months, $\geq$ 12 months and $\geq$ 18 months was 78%, 65%, and 65%, respectively. Also, repotrectinib showed a median progression-free survival (PFS) of 24.6 months (95% CI: 7.2-NR). With an additional 8.5 months of follow-up as of April 6, 2020, 4 of the 5 responding patients remained in a PR (partial response) per physician assessment data since the July 22, 2019 data cutoff and the duration of treatment ranged from 9.2 to 34.2+ months with 7 of the total 11 (64%) patients remaining on repotrectinib. All 7 (64%) remained on treatment for more than 17 months, 6 (55%) on treatment for more than 24 months, and 3 (27%) on treatment for more than 30 months at the time of the analysis. Repotrectinib has demonstrated CNS activity among patients with ROS1+ advanced NSCLC who are ROS1 TKI-naïve, with an intracranial objective response rate (IC-ORR) of 100% (3 of 3 patients, 95% CI: 29-100) with durations of response, as of the July 22, 2019 data cut-off, of 14.8+, 17.6+ and 23.1 months. All three of these patients remained on treatment, as of April 6, 2020, for 26.0+, 28.5+ and 34.2+ months.

In the ROS1+ advanced NSCLC patients who had received one prior TKI, the confirmed ORR by BICR was 39 percent (N=18, 95% CI: 17-64). Repotrectinib has demonstrated CNS activity among patients with ROS1+ advanced NSCLC who have received one prior TKI, with an intracranial objective response rate (IC-ORR) of 75% (N=4, 95% CI: 19-99). As of April 6, 2020, 6 of 29 (21%) TKI pre-treated ROS1+ advanced NSCLC patients remained on repotrectinib. All 6 patients remained on treatment for more than 12 months, 2 on treatment for more than 24 months and 1 patient on treatment for more than 30 months.

Turning Point anticipates reporting preliminary physician assessed safety and efficacy data from approximately 30 to 40 patients across multiple Phase II cohorts of TRIDENT-1, including both registrational and exploratory cohorts, in the third quarter of 2020. Turning Point also commenced a Phase I/II study of repotrectinib in pediatric and young adult patients with ALK+, ROS1+ or TRK+ advanced solid tumors in November 2019.

Turning Point is currently evaluating potential combination regimens for repotrectinib based on preclinical data Turning Point presented at the 2020 AACR virtual Annual Meeting in late June. In preclinical models, repotrectinib synergized with a proxy molecule for the KRAS G12C inhibitor AMG510 and inhibited KRAS G12C tumor cell proliferation, increased apoptosis, and reduced KRAS G12C tumor cell cytokine release. Repotrectinib also enhanced the efficacy of AMG510 in KRAS G12C xenograft models. Turning Point's preclinical studies also showed that repotrectinib, in combination with the MEK inhibitor trametinib, was synergistic in KRAS mutant NSCLC, colorectal cancer, and pancreatic cancer tumor cell lines and enhanced efficacy in mutant KRAS xenograft models in vivo, highlighting the potential for repotrectinib to enhance the effectiveness of MEK inhibitors targeting KRAS mutant cancer when used in combination.

Our Clinical Trial Designs and Strategy for Repotrectinib in the China Market

We have submitted Phase II registrational CTA and anticipate opening additional sites for the TRIDENT-1 Phase II registrational clinical study of repotrectinib in China.

Margetuximab

Overview

Margetuximab is a human/mouse chimeric IgG1 anti-HER2 antibody with an optimized Fc domain designed to outperform trastuzumab whose mechanism of action involves not only the inhibition of the signal transduction pathway from HER2, but also the antibody-dependent cytotoxicity (ADCC) mediated by the binding of the Fc domain of the antibody with CD16A (Fcg receptor IIIA or FcgRIIIA) expressed on the surface of the natural killer (NK) cells and macrophages. Both 158V and 131H variants bind the Fc of IgG1 with higher affinity than their respective allelic counterparts. With optimized Fc domain, margetuximab binds different CD16 variants with similar affinity, leading to stronger ADCC than trastuzumab. A Phase III trial known as SOPHIA compared margetuximab in combination with chemotherapy with trastuzumab in combination with chemotherapy in HER2+ breast cancer after 2 or more lines of treatment with other HER2-targeting agents including trastuzumab and pertuzumab. The study reported positive outcome indicating that margetuximab is superior to trastuzumab in a heavily pretreated HER2+ metastatic breast cancer. Additional clinical trials are being planned to evaluate margetuximab in HER2+ breast and gastric cancer.

We obtained an exclusive license to develop and commercialize margetuximab in China, Hong Kong, Macau and Taiwan from MacroGenics in November 2018. For further details of the exclusive license, see "— Overview of Our License and Strategic Collaboration Agreements — MacroGenics."

Mechanism of Action

HER2 oncoprotein drive the aggressive behavior of HER2+ breast and other cancer and it proves to be a good target for cancer therapeutics exemplified by the clinical success of the monoclonal antibody trastuzumab. Margetuximab is believed to mediate its therapeutic activity against HER2+ tumors by a combination of mechanisms that are initiated by binding of margetuximab to HER2 expressed on the cell surface, including the following:

- Direct impact on HER2 receptor leading to reduced HER receptor dimerization and subsequent activation, induction of endocytosis of the HER2 receptor, and prevention of shedding of the extracellular domain of the HER2 receptor (thereby preventing formation of a constitutively active truncated intracellular receptor);

- Induction of apoptosis; and

- Antibody-mediated cellular cytotoxicity, or ADCC, and presentation of the antigenic determinants of opsonized cells to antigen-presenting cells.

Fcγ-receptor (FcγR)-mediated mechanisms, such as ADCC, play a critical part in the action of many antibodies including trastuzumab. Optimization of the Fc component of margetuximab enhances binding to the V/F heterozygous subtype and the F/F homozygous subtype of FcγR compared to trastuzumab, potentially leading to enhanced ADCC activity in a broader patient population. Margetuximab significantly increased the level of ADCC activity mediated by Fc domain optimization, and the enhanced ADCC was observed in a range of breast, gastric, bladder and colorectal cancer cell lines. Margetuximab maintains the same direct anti-proliferative activity as trastuzumab, but, in contrast to trastuzumab, margetuximab interacts efficiently with both 158F and 158V allotypes of CD16A due to specific mutations introduced into its Fc region. Consistent with its enhanced binding to CD16A, margetuximab exhibits enhanced in vitro antitumor activity against HER2-expressing tumor cell lines, including against lines expressing low HER2 levels, and in xenograft models in human CD16A+ transgenic mice. The data from the nonclinical pharmacology studies support the hypothesis that margetuximab can be active against HER2-expressing tumors.

Market Opportunity

HER2-expressing tumors

HER2 is a protein found on the surface of some cancer cells that promotes growth and is associated with aggressive disease and poor prognosis. HER2-expressing tumors represent approximately 25% of breast cancer and approximately 20% of gastric cancer. The HER2 positive rate may be lower for gastric cancer in China. HER2-targeting agents have had significant impact on the behavior of HER2+ breast and gastric cancers. Monoclonal antibody-based therapies targeting HER2 have greatly improved outcomes of patients with HER2+ breast cancer and are now standard of care in both early-and late-stage disease. Ongoing HER2 blockade is recommended for patients who have relapsed or refractory HER2+ disease; after progression occurs during treatment with other HER2-directed therapies, the need for additional agents in later lines remains. In the metastatic setting, trastuzumab in combination with pertuzumab and chemotherapy has become the standard of care (SOC) in the first line treatment of HER2+ breast cancer, while trastuzumab in combination with chemotherapy is the SOC in the first line treatment of HER2+ gastric cancer. Trastuzumab has been demonstrated to improve PFS of patients with gastric and GEJ tumors that overexpress HER-2 from 5.5 months to 6.7 months and OS from 11.1 months to 13.8 months when added to chemotherapy compared to chemotherapy alone. The addition of a targeted mAb to chemotherapy has also demonstrated improved PFS and OS in the second line setting. Ramucirumab (a mAb targeting the vascular endothelial growth factor pathway) improved median OS to 9.6 months when added to paclitaxel chemotherapy compared to 7.4 months with paclitaxel chemotherapy alone.

Breast cancer

Approximately 25% of breast tumors overexpress the HER2 protein which is a member of the ErbB receptor tyrosine kinase family and plays an important role in the growth and proliferation of HER2-expressing cancer cells. HER2 expression is associated with aggressive metastatic cancers with a poor prognosis. The incidence of breast cancer in China grew from

304.0 thousand in 2015 to 326.2 thousand in 2019 with a CAGR of 1.8% from 2015 to 2019, according to the Frost & Sullivan Report. Many HER2-targeting agents have been developed and marketed with trastuzumab (Herceptin) as one of the most important treatments for HER2+ breast cancer.

There are different types of treatment for patients with breast cancer. Six types of standard treatment are used, including surgery, radiation therapy, chemotherapy, hormone therapy, targeted therapy and immunotherapy. As of July 2020, there were three HER2-targeted mAbs marketed in China. However, after treatment failure or disease progression after second-line anti-HER2 treatment, there is no approved effective treatment in late-stage setting in China and globally. There would be a significant need for new and effective HER2 targeted therapies that can be administered to patients with HER2+ metastatic breast cancer who have previously been treated with other anti-HER2-targeted therapies. Zai Lab's margetuximab is at Phase I clinical trial stage.

Gastric cancer

For market opportunity and competition information with respect to gastric cancer, please see "— ZEJULA — Market Opportunity and Competition — Gastric Cancer."

For patients with advanced metastatic gastric cancer, systemic treatment has been adopted clinically at present. Chemotherapy and targeted therapy are the main treatments for advanced metastatic gastric cancer. For HER2+ advanced gastric cancer, trastuzumab is the only HER2-targeted antibody, according to Frost & Sullivan; thus, there has been a strong demand for reliable and affordable treatment options for advanced gastric cancer.

Preclinical and Clinical Development

Nonclinical Pharmacology

In ligand binding studies, compared to the wild-type Fc domain, margetuximab imparts enhanced binding to both the CD16A-158F and CD16A-158V alleles. Binding to human CD32A is unchanged (131H allele) or decreased (131R allele), and there is a substantial decrease in binding to the human inhibitory receptor, CD32B. In the monkey, the optimized Fc domain of margetuximab imparts increased binding to all three cynomolgus FcγRs (CD16A, CD32A and CD32B) compared to the wild type Fc domain.

Consistent with its enhanced binding to CD16A, margetuximab exhibits enhanced anti-tumor activity against HER2-expressing tumor cell lines in vitro and in xenograft models in human CD16A-transgenic mice. Margetuximab, as a single agent, is active against HER2-expressing breast, ovarian or pancreatic tumors in a manner consistent with that of trastuzumab. In general, HER2 3+ tumors (breast BT474 and ovarian SKOV3 cell lines) were highly sensitive to treatment with either margetuximab or a trastuzumab analogue, RES120, with maximal effects observed at the lowest dose tested. Margetuximab showed enhanced activity against JIMT-1 xenografts compared to RES120 in mCD16-/-hCD16A+ transgenic mouse lines. JIMT-1 is a HER2+ (2+ by HercepTest) cell line derived from a metastatic breast cancer patient that progressed on trastuzumab therapy and is insensitive to trastuzumab anti-proliferative activity. Margetuximab was also active as a single agent against HER2- expressing gastric cancer xenografts and when combined with a chemotherapy agent (taxane or irinotecan). The anti-tumor effects of the combinations were enhanced compared to that of the individual agents.

Based on in vitro secondary pharmacology studies conducted with human PBMC and anti-HER2 monoclonal antibodies in the absence or presence of immobilized HER2 antigen, the optimized Fc domain of margetuximab does not contribute to enhanced cytokine release in vitro. These data suggest that margetuximab is not likely to induce cytokine release in human patients to levels any higher than those induced by trastuzumab.

Margetuximab exhibited anti-tumor activity equal to or better than that of RES120, its WT Fc domain counterpart, in all models tested and increased potency compared with RES120 in a selected system where the contribution of the optimized Fc domain can be ascertained. These data support the hypothesis that margetuximab is more potent than trastuzumab. In addition, margetuximab exhibited enhanced tumor activity when combined with chemotherapy agents. For patients with HER2-expressing tumors, margetuximab has the potential to expand the benefit to the whole patient population, irrespective of the CD16A genotype. Thus, these data support the use of margetuximab, in combination with chemotherapy, to treat HER2+ breast cancer.

Nonclinical pharmacokinetics

In the single dose toxicology study, intravenous infusion of margetuximab at 50 mg/kg led to a mean Cmax of 1.62 mg/mL for males and 1.70 mg/mL for females. The terminal phase half-life was estimated to be 223.9 hours in males and 233.9 hours in females, while serum clearance was 0.434 mL/hr and 0.400 mL/hr in males and females, respectively. The volume of distribution at steady state (Vss) was estimated to be 132.4 mL in males and 127.2 mL in females, which is similar to the plasma volume. No gender related differences were apparent in the pharmacokinetic profile. The pharmacokinetic properties for RES120, an antibody identical to margetuximab except for the presence of a wild type human IgG1 Fc domain, were similar to those for margetuximab. In the multi-dose toxicology study, margetuximab was administered weekly for 6 weeks at doses of 15, 50 or 150 mg/kg. Toxicokinetic measurements showed an increase in exposure to margetuximab with increasing dose. Cmax appeared to increase linearly with dose following the first dose on Day 1; however, increases in Cmax were not dose proportional following the sixth dose on Day 36. Similar trends were observed with respect to AUC0-∞. Terminal serum half-life ranged from 133 to 189 hours on Day 1 and 176 to 222 hours on Day 36. Serum clearance ranged from 0.55 to 1.09 mL/hr on Day 1 and 0.20 to 0.36 mL/hr on Day 36. The volume of distribution approximated to the blood volume. No substantial gender differences were observed. The more rapid clearance following the first dose on Day 1 as compared to Day 36 was probably due to binding to the target receptor and saturation of this binding following multiple doses. Taken together, these data indicate that the pharmacokinetic profile of margetuximab in monkeys is comparable to that of other anti-HER2IgG1 monoclonal antibodies.

Nonclinical Toxicology

Margetuximab has been investigated in single and repeat dose toxicity studies in the cynomolgus monkey and in a battery of in vitro tissue cross-reactivity studies in human and cynomolgus monkey tissues. Cynomolgus monkeys (Macaca fascicularis) express both the target antigen and FcγRs that are relevant for modeling margetuximab. A direct comparison of margetuximab and trastuzumab revealed similar staining patterns in human and cynomolgus monkey tissues. A second (rodent) species was not used in repeat dose toxicity studies because margetuximab, which retains the HER2-binding properties of 4D5, the original precursor to the trastuzumab antibody, does not cross react with rodent HER2/neu.

In a pilot toxicology study in cynomolgus monkeys margetuximab or RES120 was well tolerated when administered by IV infusion at a single dose of 50 mg/kg. There were no test article-related mortalities and no test article-related changes with regard to clinical signs, food consumption, body weights, haematology, coagulation, or urinalysis parameters. There were also no macroscopic, organ weight or microscopic findings related to the administration of RES120 or margetuximab. Mild increases in alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactate dehydrogenase (LD), with both margetuximab and RES120, were consistent with a nonhepatic source and can be observed following 1-hour infusions and frequent blood sampling for toxicokinetic analysis. In the repeat dose study, margetuximab, administered weekly via 1-hour intravenous infusion for six weeks at 15, 50 and 150 mg/kg, was well tolerated in male and female cynomolgus monkeys. There were no margetuximab-related mortalities or clinical signs and no test article-related changes in food consumption, body weights, ECG, troponin I or ophthalmic examinations, physical examinations, blood pressure or heart rate, haematology, coagulation, or urinalysis parameters. No margetuximab-related changes were observed in natural killer (NK) cell cytolytic activity during the dosing or recovery intervals. There were no gross findings observed at necropsy, no organ weight or organ weight ratio alterations, and no microscopic findings attributed to the administration of margetuximab (including no findings in heart tissue).

Clinical Development — Breast Cancer

In December 2019, MacroGenics submitted a Biologics License Application (BLA) to the FDA for margetuximab for the treatment of patients with metastatic HER2+ breast cancer in combination with chemotherapy. The BLA submission was based primarily on data from SOPHIA, the Phase III clinical trial comparing margetuximab plus chemotherapy versus trastuzumab plus chemotherapy in patients with HER2+ metastatic breast cancer who have previously been treated with anti-HER2-targeted therapies. In February 2020, the BLA was accepted for review by the FDA.

The SOPHIA study enrolled 536 patients at approximately 200 trial sites across North America, Europe and Asia. Patients were treated with either margetuximab or trastuzumab in combination with one of four chemotherapy agents (capecitabine, eribulin, gemcitabine or vinorelbine). All study patients had previously received trastuzumab and pertuzumab, and approximately 90% had previously received ado-trastuzumab emtansine. Primary endpoints are sequentially-assessed progression-free survival (PFS), determined by centrally-blinded radiological review, and overall survival (OS). A pre-specified exploratory objective of the study was to evaluate the effect of CD16A Fcγ receptor) allelic variation on margetuximab activity; approximately 85% of the overall human population, as well as patients enrolled in the SOPHIA study, carry the CD16A 158F allele, which has been previously associated with diminished clinical response to trastuzumab and other antibodies.

In June 2019, at a medical conference, the data from SOPHIA as of the aforementioned October 2018 data cut-off that showed a statistically significant improvement in PFS in patients treated with margetuximab plus chemotherapy compared to trastuzumab plus chemotherapy in the intention-to-treat (ITT) population after 265 PFS events (median PFS=5.8 months versus 4.9 months; hazard ratio [HR]=0.76; 95% confidence interval [CI]: 0.59-0.98; P=0.033). In the pre-specified, exploratory subpopulation of patients carrying the CD16A 158F allele, PFS was prolonged by 1.8 months in the margetuximab arm compared to the trastuzumab arm (median PFS=6.9 months versus 5.1 months; HR=0.68; 95% CI: 0.52-0.90; P=0.005). The data from the planned first interim analysis of OS based on 158 OS events. This interim analysis was not expected to and did not reach statistical significance. In the ITT population, median OS was 18.9 months in the margetuximab arm versus 17.2 months in the trastuzumab arm (HR=0.95; 95% CI: 0.69-1.31). In the pre-specified, exploratory subpopulation of patients carrying the CD16A 158F allele, median OS was 23.6 months in the margetuximab arm versus 16.9 months in the trastuzumab arm (HR=0.82; 95% CI: 0.58-1.17). As a secondary outcome measure in the SOPHIA study, the objective response rate (ORR) in the ITT population was 22% in the margetuximab arm (95% CI: 17.3-27.7%) compared to 16% in the trastuzumab arm (95% CI: 11.8-21.0%).

At a medical conference in December 2019, the data from the planned second interim analysis of OS as of a September 2019 cut-off after 270 OS events showed that, OS favored margetuximab plus chemotherapy compared with trastuzumab plus chemotherapy in the ITT population; however, these data were not expected to and did not reach statistical significance (median OS=21.6 months versus 19.8 months; HR=0.89; 95% CI: 0.69-1.13; nominal P=0.326). The final pre-specified OS analysis is planned after 385 OS events have accrued, which is projected to occur in the second half of 2020, at which point the results may or may not reach statistical significance. Among the genetically defined exploratory subpopulation of patients carrying a CD16A 158F allele, the median OS at the second interim analysis was prolonged by 4.3 months in the margetuximab arm compared to the trastuzumab arm (23.7 months versus 19.4 months; HR=0.79; 95% CI: 0.61-1.04; nominal P=0.087). Among the approximately 15% of patients who were homozygous for the CD16A 158V allele, the trastuzumab arm performed better than the margetuximab arm.

As of the April 2019 data cut-off for safety, Grade 3 or greater adverse events occurred in 142 (54%) patients on the margetuximab arm compared to 140 (53%) patients on the trastuzumab arm. Serious adverse events occurred in 43 (16%) patients on the margetuximab arm compared to 49 (18%) patients on the trastuzumab arm. Infusion-related reactions (IRR) were more common with margetuximab treatment than with trastuzumab (13% versus 3%) and were mostly Grade 1 or 2 and associated with the first dose. A substudy evaluating shorter, 30-minute infusions of margetuximab in Cycle 2 and beyond showed no effect on safety outcomes, including risk or severity of IRR.

Clinical Development — Gastric Cancer

In September 2019, an ongoing Phase II, open-label, dose escalation and expansion study of margetuximab plus pembrolizumab, an anti-PD-1 monoclonal antibody, in patients with advanced HER2+ GC or GEJ cancer who have previously been treated with chemotherapy and trastuzumab in the metastatic setting were presented. In this study, 92 patients, including 61 patients with GC and 31 patients with GEJ, who had HER2+ disease, were treated at the recommended Phase II dose of 15 mg/kg margetuximab and 200 mg pembrolizumab, both administered every three weeks, and were included in the analysis. HER2 positivity was characterized by a score of 3+ by immunohistochemistry (IHC), or IHC3-positve, or a score of 2+ by IHC and detection by fluorescence in situ hybridization (FISH), or IHC2-positive/FISH-positive. Patients in the study were enrolled irrespective of programmed death-ligand 1 (PD-L1) expression status. MacroGenics reported data as of July 10, 2019. As of this data cut-off date, the study was ongoing with eight patients remaining on therapy. Acceptable tolerability was observed in this study in patients treated with margetuximab and pembrolizumab. Grade 3 or higher treatment-related adverse events (TRAE) occurred in 19.6% of patients. Response rates, median PFS and OS observed in the ongoing study are summarized in the following table:

	Gastroesophageal Adenocarcinoma (GEA = GC + GEJ)				**Gastric Cancer (GC)**			
	ORR	**DCR**	**Median PFS (months)**	**Median OS (months)**	**ORR**	**DCR**	**Median PFS (months)**	**Median OS (months)**
All Patients	20*/92 (21.7%)	50/92 (54.4%)	2.7	12.5	18*/61 (29.5%)	40/61 (65.6%)	4.1 4.7	13.9 14.6
HER2 1HC3+	20*/71 (28.2%)	45/71 (63.4%)	4.3	13.9	18*/55 (32.7%)	38/55 (69.1%)		
HER2 1HC3+/PD-L1+	12/25 (48.0%)	19/25 (76.0%)	4.8	20.5	12/23 (52.2%)	19/23 (82.6%)	5.5	20.5

* Three unconfirmed responses; ORR includes complete responses (CR) and partial responses (PR); DCR=disease control rate and includes CR, PR and stable disease (SD).

Source: MacroGenics

Based on these results, in September 2019, MacroGenics initiated the MAHOGANY study, a Phase II/III registration-directed clinical trial to evaluate, in Module A, margetuximab in combination with MGA012, an anti-PD-1 monoclonal antibody, in patients with tumors that are both HER2+ and PD-L1 positive. This approach is designed as a chemotherapy-free regimen that engages both innate and adaptive immunity for the treatment of patients with GC or GEJ cancer in the first-line setting. The primary outcome measure for efficacy in Module A is ORR per Response Evaluation Criteria in Solid Tumors (RECIST) v 1.1. In Module B, is to evaluate margetuximab with chemotherapy and tebotelimab, a PD-1 x LAG-3 bispecific DART molecule, compared to standard of care therapy of trastuzumab with chemotherapy in MAHOGANY study. In this portion of the randomized, controlled study, patients are planned to be enrolled irrespective of PD-L1 expression. The primary outcome measure for efficacy in Module B is planned to be OS.

Our Clinical Trial Designs and Strategy for Margetuximab in the China Market

We are exploring regulatory approval pathways for margetuximab in HER2+ breast cancer in China using a bridging approach which may require a PK study and a bridging trial. In February 2020, the first patient was dosed in the registrational bridging study of margetuximab in combination with chemotherapy for the treatment of patients with metastatic HER2+ breast cancer. Data from the positive SOPHIA study and the bridging study data will be used to support potential regulatory filing and approval in China. In addition, we plan to we plan to enroll the first Chinese patient in second half of 2020 in MacroGenics sponsored Phase II/III global studies of margetuximab (MAHOGANY) in combination with a PD-1 antibody or a PD-1 x LAG-3 bispecific DART molecule in the first line treatment of HER2+ gastric cancer.

Retifanlimab

Overview

Retifanlimab (PD-1) is an investigational monoclonal antibody that inhibits PD-1. retifanlimab (PD-1) is currently being evaluated as monotherapy in registration-directed trials for patients with MSI-high endometrial cancer, Merkel cell carcinoma and anal cancer. Incyte is currently developing retifanlimab (PD-1) in Phase II/III clinical trials for the gastric cancer and oesophageal cancer; Phase II clinical trials for anal cancer; endometrial cancer; merkel cell carcinoma; solid tumors; Phase I/II clinical trials for colorectal cancer; and Phase I clinical trials for acute myeloid leukaemia, among other indications.

We obtained an exclusive license from Incyte to develop and commercialize retifanlimab (PD-1) in haematology and oncology in China, Hong Kong, Macau and Taiwan in July 2019. For further details of the exclusive license, see "— Overview of Our License and Strategic Collaboration Agreements — Incyte."

Mechanism of Action

PD-1 is expressed on T-cells (CD4+ and CD8+), B-cells, NK cells, and myeloid-derived cells. The interaction of PD-1 with its ligands, PD-L1 and PD-L2, forms a negative signaling axis in T-cells to suppress T-cell function which is the mechanism utilized by the immune system to help maintain self-tolerance and modulate the duration and amplitude of physiological immune responses.

PD-L1 and PD-L2 have also been found to be abnormally expressed by tumor cells in the tumor microenvironment. Extensive research has shown that cancer cells co-opt certain immune checkpoint pathways, including the PD-1 pathway, as a major mechanism of immune evasion/resistance, particularly against T-cells that are specific for tumor antigens. Disruptors of this pathway using antibodies that inhibit PD-1 receptor-ligand interactions have been shown to inhibit tumor growth in murine models through enhancing T-cell proliferation and restore immune responses. Moreover, blocking the PD-1-PD-L1/L2 pathway has been clinically validated as an effective cancer treatment in multiple clinical settings.

Clinical Development

Pharmacology

Preliminary PK data from the 167 participants in the dose expansion cohorts receiving weight-based or flat doses of retifanlimab suggested that first dose retifanlimab exposure increased in a dose-proportional manner, consistent with the observations in participants receiving weight-based doses. A population PK analysis demonstrated that the concentrations of retifanlimab can be adequately described by a 2-compartment model, and body weight dependence of clearance was characterized by a power relationship with an exponent of 0.911.

Simulations demonstrated that the median steady-state concentration of retifanlimab 500mg Q4W was approximately 21.1 µg/mL, which is the median trough concentration for pembrolizumab 200 mg Q3W.

Safety

Adverse events in participants treated with retifanlimab monotherapy included fatigue, diarrhea, nausea, and pyrexia (very common), ALT increased, colitis, dysgeusia, hyperthyroidism, hypothyroidism, influenza-like illness, infusion-related reaction, lipase increased, myalgia, pruritus, and rash (includes terms of rash, maculopapular rash, and macular rash) (common), and pneumonitis (uncommon). These AEs are similar to those observed with other anti-PD-1 antibodies.

The 375 mg Q3W and 500 mg Q4W doses were selected for further development based on favorable safety and PK profiles.

Efficacy

Preliminary efficacy data demonstrate clinical activity of retifanlimab based on durable RECIST responses in multiple tumor types. Preliminary efficacy in terms of RECIST response has been shown in previously treated NSCLC, cervical, and endometrial cancers. Based on the available data, the preliminary efficacy profile of retifanlimab is consistent with that of other anti-PD-1 antibodies.

Retifanlimab is currently in development as a single agent or in combinations in multiple tumor types including endometrial cancer, anal cancer, NSCLC, and others.

Our Clinical Trial Designs and Strategy for Retifanlimab in the China Market

Our CTA application for Phase II confirmatory study has been accepted for second-line MSI-high endometrial cancer. We plan to enroll the first Chinese patient into the Incytesponsored global Phase I/II potentially registration-enabling study in second half of 2020. In addition, we have obtained Phase III CTA approval and plan to enroll the first Chinese patient into the Incyte-sponsored global Phase 3 study of retifanlimab with platinum-based chemotherapy in first-line metastatic squamous and non-squamous non-small cell lung cancer in second half of 2020.

Tebotelimab

Overview

Tebotelimab is a bispecific monoclonal antibody designed to block the interaction of PD-1 or LAG-3 with their respective ligands, thereby contributing to sustain or restore the function of exhausted T-cells. Tebotelimab is an Fc-bearing bispecific tetravalent (bivalent for each antigen) DART protein engineered as a hinge stabilized IgG4 molecule designed to concomitantly bind PD-1 and LAG-3, 2 checkpoint molecules expressed by T lymphocytes following antigen-induced activation. Tebotelimab is under development as a therapeutic candidate for the treatment of cancer. We obtained an exclusive license to develop and commercialize Tebotelimab in China, Hong Kong, Macau and Taiwan from MacroGenics in November 2018. For further details of the exclusive license, see "— Overview of Our License and Strategic Collaboration Agreements — MacroGenics."

Mechanism of Action

PD-1 and LAG-3 protein play an important role in immune response regulation. PD-1 is expressed on T (CD4+ and CD8+) cells, B cells, natural killer cells, and myeloid-derived cells. LAG-3 is a membrane protein that belongs to the Ig superfamily and binds to MHC-II. It enhances T regulatory cell activity and negatively regulates T-cell proliferation and differentiation. LAG-3 has been shown to be expressed on dysfunctional T-cells and is a marker for T regulatory cells. Upon interaction with their respective ligands, PD-1 and LAG-3 act as negative regulators of T-cell function. The combined PD-1 and LAG-3 expression on tumor-infiltrating lymphocytes (TILs) or chronically viral-infected T-cells have been correlated with immune dysfunction, also known as "T-cell exhaustion." LAG-3 appears to negatively regulate CD4+ and CD8+ T-cell proliferation, function, and homeostasis in a manner that is distinct from that of PD-1.

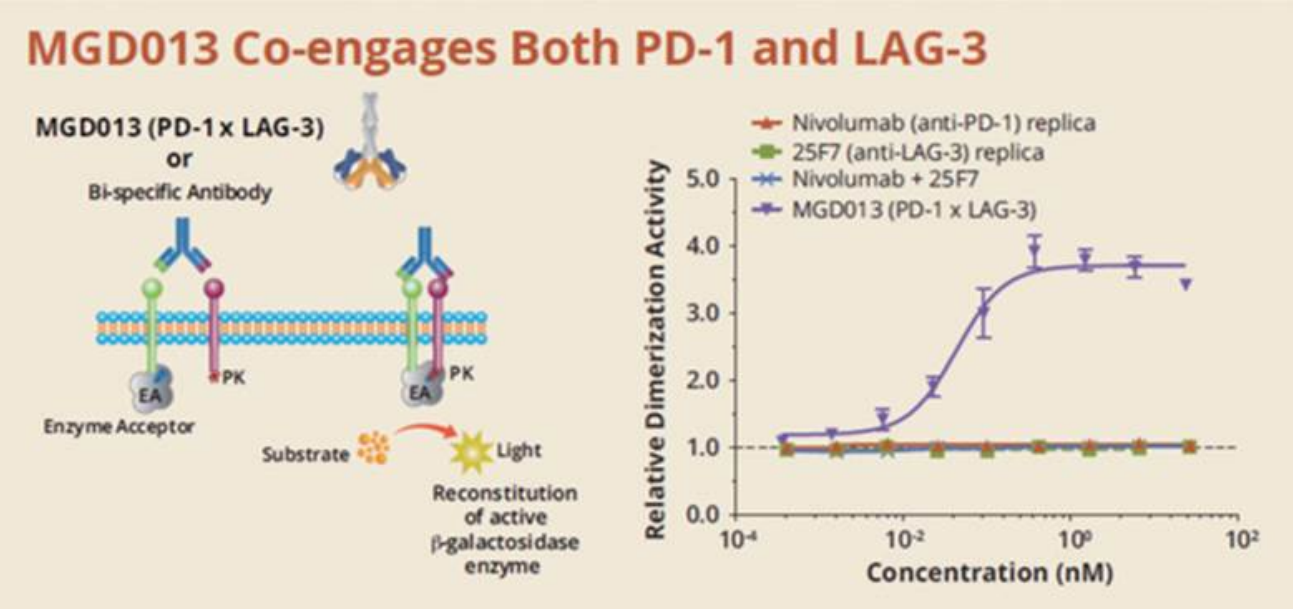
Cancer cells can co-opt certain immune-checkpoint pathways, including the PD-1 pathway, as a major mechanism of immune evasion/resistance, particularly against T-cells that are specific for tumor antigens (seen in the figure below). Blockade of PD-1 provides clinical benefit in patients with certain advanced tumors. Furthermore, combined blockade of 2 inhibitory receptors on T-cells may exert greater efficacy than monotherapy. Studies in mouse tumor models have indicated that PD-1 and LAG-3 blockade can synergize to generate potent tumor eradicating immunity. Furthermore, translational studies using TILs from patients with ovarian cancer showed that NY-ESO-1 antigen-specific LAG-3+/PD-1+ CD8+ T-cells were impaired in their ability to respond to antigen stimulation, but following combined LAG-3 and PD-1 blockade, T-cell responsiveness could be restored to a greater extent than a single-agent blockade. Together, these data suggest that, in tumors in which PD-1 and/or LAG-3 are expressed on TILs, dual therapy may increase response rates and/or effectiveness of immunotherapy. Currently, several anti-LAG-3 mAbs are under investigation in clinical trials, either as a monotherapy or in combination with anti-PD-1.

Competition

There is no marketed PD-(L)1-based bispecific monoclonal antibody in China, according to the Frost & Sullivan Report.

Pre-Clinical and Clinical Background

In vitro studies were performed to evaluate the ability of tebotelimab to co-engage PD-1 and LAG-3 receptors within an enzyme dimerization assay. Briefly, serial equal molar dilutions of tebotelimab, nivolumab replica, and/or relatlimab replica (negative control antibodies) were incubated with the DiscoverX PathHunter® U2OS PD1/LAG-3 dimerization cell line. PathHunter cells are genetically engineered to over-express the two proteins, whereby one protein is fused to Prolink and the second protein is fused to the enzyme acceptor (EA) of the β-galactosidase enzyme. As shown in the figure below, co-engagement of two proteins by tebotelimab, but not anti-PD-1 and/or anti-LAG-3 mAbs, drives complementation between PK and EA, resulting in the reconstitution of an active β-galactosidase enzyme that cleaves a substrate to generate chemiluminescent signal.



Sadhna Shankar, et al. Abstract No. P244, SITC 2017

Tebotelimab is currently in Phase I development in a basket trial of multiple tumor types. The specific indication for tebotelimab has not been defined and data from the basket trial may inform on the selection of specific indications for further development.

Our Clinical Trial Designs and Strategy for Tebotelimab in the China Market

Our global partner, MacroGenics, is conducting a Phase I, open-label, dose escalation and cohort expansion study designed to characterize the safety, tolerability, PK, pharmacodynamics, immunogenicity, and preliminary antitumor activity of tebotelimab administered by IV infusion on a Q2W or Q3W schedule. The study consists of a Dose Escalation Phase to determine the MTD or MAD (if no MTD is defined) of tebotelimab, followed by a Cohort Expansion Phase to further define the safety and initial antitumor activity of tebotelimab with the dose established in the Dose Escalation Phase. To date, the RP2D of tebotelimab on a Q2W or Q3W had been selected and the Cohort Expansion is ongoing in multiple tumor types.

In February 2020, we dosed the first patient in an open-label, single-arm, multicenter, Phase Ib dose escalation and expansion clinical study to assess the safety and antitumor activity of ZEJULA, in combination with tebotelimab, in patients with advanced or metastatic gastric cancer who failed prior treatment. In April 2020, we initiated a tebotelimab monotherapy and in combination with brivanib dose escalation and expansion study in advanced liver cancer patients. The study consists of a dose escalation phase to determine the Recommended Phase II Dose (RP2D) of tebotelimab monotherapy and that of tebotelimab when in combination with brivanib in subjects with advanced liver cancer, followed by a dose expansion phase. The part 1 of the dose expansion study is to assess the safety and efficacy of tebotelimab monotherapy and tebotelimab in combination with brivanib in subjects with advanced hepatocellular carcinoma (HCC). In the part 2 of the dose expansion study, a therapeutic method (tebotelimab monotherapy or tebotelimab in combination with brivanib, determined by the sponsor according to the obtained data) will be selected for dose expansion study in HCC subjects who have previously failed immune checkpoint inhibitor treatment, to further evaluate the safety and efficacy of the study treatments in the specific group of subjects.

In addition, we plan to enroll Chinese patients in Phase II/III global MAHOGANY study of margetuximab in combination with retifanlimab or tebotelimab in gastric cancer sponsored by MacroGenics in HER2+ first line treatment of gastric cancer and to initiate MAHOGANY Cohort B in China, Hong Kong, Macau and Taiwan in the second half of 2020. We also have obtained Phase I CTA approval in January 2020 and intend to enroll the first Chinese patient in the second half of 2020 for tebotelimab into its global Phase I basket trial sponsored by MacroGenics. Further, we have obtained CTA approval in June 2020 and are conducting a Phase I (proof of concept) clinical trial for second-line melanoma in Greater China.

Bemarituzumab

Overview

Bemarituzumab is a humanized monoclonal antibody (IgG1 isotype) specific to the human FGFR2b receptor in clinical development as a targeted immuno-therapy for tumors that overexpress FGFR2b, including gastric and gastroesophageal cancer. Gastric cancer, including gastroesophageal junction (GEJ) cancer, carries a poor prognosis, with five year overall survival (OS) rates below 30% for advanced stage disease (Stage III and IV) in the United States. China has one of the highest incidence rates of gastric cancer in the world, with approximately 680,000 new cases annually.

We obtained an exclusive license from Five Prime to develop and commercialize bemarituzumab in China, Hong Kong, Macau and Taiwan in December 2017. For further details of the exclusive license, see "— Overview of Our License and Strategic Collaboration Agreements — Five Prime."

In December 2017, Five Prime initiated dosing in a Phase I safety lead-in portion of its Phase I/III clinical trial of bemarituzumab in combination with the mFOLFOX6 chemotherapy regimen in patients with previously untreated, advanced gastric or gastroesophageal cancer. The randomized, controlled Phase III portion of the trial evaluating bemarituzumab plus chemotherapy, the FIGHT trial, was initiated in the second half of 2018 and we enrolled the 1st patient in September 2018 in this global registrational study for the treatment of front-line gastric and gastroesophageal cancers. We and Five Prime intend to use the proposed global pivotal Phase III study and additional supportive data from clinical and nonclinical development to form the basis of an eventual marketing application for bemarituzumab both within and outside of China.

Five Prime has paused enrollment in the FIGHT trial pending the occurrence of a sufficient number of events to trigger a futility analysis that is expected to occur in mid-2020. Approximately 150 patients with newly diagnosed advanced stage gastric cancer were enrolled into the FIGHT trial before Five Prime paused enrollment in the fourth quarter of 2019. Five Prime expects that it will only resume enrollment in the FIGHT trial if the trial passes the futility analysis and Five Prime will look to enter into a collaboration or license agreement that will pay for all or substantially all of any future development and commercialization costs for bemarituzumab.

In March 2020, Five Prime announced the publication of results from the Phase I escalation and expansion study of bemarituzumab in patients with advanced solid tumors and FGFR2b-selected gastroesophageal adenocarcinoma in the digital edition of the Journal of Clinical Oncology. The purpose of the Phase I trial was to evaluate the safety, pharmacokinetics, and preliminary activity of single-agent bemarituzumab in patients with FGFR2b-overexpressing GEA. Seventy-nine patients were enrolled in the trial and no dose-limiting toxicities were reported. Bemarituzumab was well tolerated and the most frequent treatment-related adverse events (TRAEs) were fatigue, nausea, and dry eye. The overall response rate observed in this study of advanced-stage patients with high FGFR2b- overexpressing GEA was 17.9% (95% CI 6.1% to 36.9%) with five of 28 patients achieving a confirmed partial response.

In May 2020, Five Prime announced that the FIGHT trial is being converted from a Phase III to a randomized, double-blind, Phase II trial based on the approximately 150 patients enrolled. The Phase II FIGHT study is expected to have a sufficient number of progression-free survival (PFS) and overall survival (OS) events to generate clinically meaningful data by the end of 2020 or early 2021. Five Prime believes that converting to a Phase II trial is the fastest path to generating informative data about bemarituzumab: the first agent to target FGFR2b overexpressing gastric and gastroesophageal junction cancer (GEJ).

Mechanism of Action

Bemarituzumab is a humanized monoclonal antibody (IgG1 isotype) specific to the human FGFR2b receptor (National Center for Biotechnology Information; NCBI; reference sequence ID NP_001138385.1) that blocks FGF ligand binding to the receptor. Bemarituzumab is directed against the third Ig region of the FGFR2b receptor isoform, the region that is alternatively spliced and regulates ligand specificity. This antibody is glycosylated, but is produced in a Chinese hamster ovary (CHO) cell line that lacks the FUT8 gene (α1,6-Fucosyltransferase) and therefore lacks a core fucose in the polysaccharide portion of the antibody. The absence of the core fucose results in higher affinity for the Fc receptor FcγRIIIa compared to the fucosylated molecule and potentially enhances immune cell-mediated tumor cell killing. The antibody has thus been glycoengineered for enhanced antibody-dependent cell-mediated cytotoxicity (ADCC). Bemarituzumab inhibits FGF ligand-stimulated FGFR2b phosphorylation and cell proliferation in cell culture in FGFR2b overexpressing gastric and breast cancer cell lines. Bemarituzumab also inhibits tumor growth in FGFR2b overexpressing gastric and breast xenograft models. The 3 potential mechanisms of action of bemarituzumab thus include blocking ligand binding and downstream signaling, decreasing expression of the FGFR2b driver protein, and enhancing ADCC.

Bemarituzumab can produce complete and durable tumor growth inhibition in FGFR2b- overexpressing and FGFR2 gene-amplified gastric cancer xenografts in immune-compromised mice where FGFR2b is considered a driver of tumor growth. In addition, bemarituzumab demonstrates recruitment of natural killer (NK) cells and concomitant tumor growth inhibition in the 4T1 syngeneic tumor model with modest expression of FGFR2b. These data suggest that ADCC may be efficacious in patients without FGFR2 gene amplification with moderate FGFR2b overexpression, and that ADCC activity may be a major contributor to the mechanism of action in these patients.

Additionally, since bemarituzumab is specific for the FGFR2b receptor, it does not interfere with signaling of the other FGFs/FGFRs, including FGFR2c. In contrast to the FGFR tyrosine kinase inhibitors (TKIs), bemarituzumab does not inhibit FGF23 signaling. FGF23 is a ligand involved in calcium/phosphate metabolism. Thus, treatment with bemarituzumab is not expected to cause the dose-limiting hyperphosphatemia associated with the FGFR TKIs.

Market Opportunity

Gastric cancer, including a portion of gastroesophageal junction (GEJ) cancer, carries a poor prognosis, with five year OS rates below 30% for advanced stage disease (Stage III and IV) in the United States and China. Intensive multimodal therapy fails to cure the majority of patients with locoregional disease and for advanced stage disease, standard chemotherapy provides only short-term benefits. First-line chemotherapy used in metastatic or recurrent disease consists of a fluoropyrimidine (5FU, capecitabine, or S-1) with a platinum agent (usually oxaliplatin or cisplatin). This combination chemotherapy treatment prolongs survival by 6 months compared to best supportive care but still only provides short-term benefit, with a progression free survival (PFS) of five to six months and a median OS of nine to 10 months. FGFR2 amplification in gastric cancer results in high levels of FGFR2b expression, which is correlated with poor prognosis for OS when compared to patients without FGFR2b overexpression. FGFR2 is amplified in approximately 3% to 9% of tumors from patients with gastric cancer, with similar rates being observed across Japan, Korea, China, and the United Kingdom, and across platforms used to assess gene amplification (including reverse transcription polymerase chain reaction; RT-PCR; fluorescence in situ hybridization; FISH; and single nucleotide polymorphism; SNP; arrays). Using a validated immunohistochemistry (IHC) assay to specifically detect FGFR2b expression in solid tumors, approximately 12% of gastric cancers from China express a range of FGFR2b protein. To date, no drug has been approved for the FGFR2b-overexpressing molecular subset of patients with gastric cancer including cancer of the GEJ.

Bemarituzumab is a recombinant, afucosylated, humanized immunoglobulin G1 (IgG1) kappa monoclonal antibody directed against FGFR2b. Bemarituzumab is glycoengineered for enhanced antibody-dependent cell-mediated cytotoxicity (ADCC). Pre-clinically, bemarituzumab blocks ligand binding and acts as a targeted immunotherapy that drives NK cells and recruits T-cells into targeted tumors. As well as driving NK cells into tumors, in vivo pre-clinical studies have shown that bemarituzumab creates an "inflamed" tumor microenvironment consisting of recruited T-cells and elevated levels of programmed death- ligand 1 (PD-L1). The three potential mechanisms of action of bemarituzumab include blocking ligand binding and downstream signaling, decreasing expression of the FGFR2b driver protein, and ADCC.

There is currently no marketed FGFR2-targeted drug for gastric cancer in China, according to the Frost & Sullivan Report. Among the pipelines in this category, bemarituzumab, anlotinib and erdafitinib are in late clinical stage for gastric cancer.

Clinical Background

Bemarituzumab (FPA144) is being developed in combination with chemotherapy for the treatment of patients with unresectable, locally advanced, or metastatic gastric cancer including cancer of the GEJ whose tumors overexpress FGFR2b, as determined by an investigational device(s) being developed as a companion diagnostic test(s). Evaluation of this agent in patients with gastric cancer whose tumors have alterations of FGFR2 is an important strategy to improve the outcome for these patients.

A Phase I study, bemarituzumab-001, entitled "A Phase I Open-Label, Dose-Finding Study Evaluating Safety and Pharmacokinetics of bemarituzumab in Patients with Advanced Solid Tumors" is ongoing in the United States, South Korea, and Taiwan. Safety and efficacy data in 74 patients, including preliminary data from an expansion cohort of 24 gastric cancer patients with high FGFR2b overexpression (IHC 3+ intensity in ≥ 10% of tumor cells as determined in a laboratory developed test), support further clinical investigation of bemarituzumab in patients with FGFR2b-selected tumors. Based on an August 7, 2017 data cut, treatment with bemarituzumab resulted in no dose-limiting toxicities (DLTs) reported at doses up to 15 mg/kg administered every two weeks. Of the 74 patients who have received at least one dose of bemarituzumab, 50 patients had gastric cancer, of whom 24 had gastric cancer with high FGFR2b overexpression and were evaluable for response. Of these 24 patients, four, or 16.7% (95% CI 4.7-37.4%), reported a radiographically confirmed partial response (PR) per Response Evaluation Criteria in Solid Tumors (RECIST) criteria (version 1.1). The median duration of response (DoR) in these four patients was 15.4 weeks (95% CI 9.1 to 19.1 weeks). Conversely, no responses were reported in the 25 patients with gastric cancer who either had low or moderate FGFR2b overexpression, were IHC negative, or who had unknown FGFR2b status. One patient with gastric cancer did not have measurable disease and was inevaluable for response.

To address the unmet medical need of patients with unresectable, locally advanced, or metastatic gastric cancers and based on the preliminary Phase I data, Five Prime is proposing bemarituzumab-004 (FIGHT), a double-blind, randomized, controlled, global Phase III study of bemarituzumab in combination with modified FOLFOX6 (mFOLFOX6) chemotherapy, preceded by a Phase I safety run-in. The Phase I safety run-in will be conducted in the United States and will assess safety and tolerability and identify the recommended dose (RD) of bemarituzumab as an add-on therapy to fluorouracil, leucovorin, and oxaliplatin (mFOLFOX6, a combination that is used globally) for patients with gastrointestinal (GI) tumors.

The global Phase III portion of the study will evaluate the efficacy and safety of bemarituzumab in combination with mFOLFOX6 versus placebo in combination with mFOLFOX6 in patients with unresectable, locally advanced, or metastatic gastric cancers whose tumors have FGFR2b overexpression, as determined by an IHC assay, and/or FGFR2 amplification, as determined by a circulating tumor DNA (ctDNA) assay. The proposed Phase III study will enroll a majority of Asian patients, from countries including Japan, South Korea, Taiwan, Thailand, and China. The primary endpoint for the proposed Phase III study will be OS, supported by a principle secondary endpoint of investigator-assessed PFS. Other secondary and exploratory endpoints include overall response rate (ORR), DoR, and physical function, as measured by EQ-5D-5L and EORTC QLQ-C30. Additional development of bemarituzumab for the treatment of gastric cancer includes bemarituzumab-002, a Phase I pharmacokinetic (PK) safety study in Japan. This dose escalation study is designed to assess the PK and safety of single agent bemarituzumab and will identify the RD for single agent bemarituzumab in Japanese patients. The first cohort of three patients treated on bemarituzumab-002 had no DLTs reported at doses of 10 mg/kg administered every two weeks.

Our Clinical Trial Designs and Strategy for Bemarituzumab in the China Market

As bemarituzumab is a targeted biologic, the clinical development of bemarituzumab will ultimately be in selected patients with alterations in the fibroblast growth factor receptor 2, or FGFR2, pathway that are most likely to respond to this novel agent. The tumor types most relevant to date include gastric, bladder, and possibly cholangiocarcinoma. Each of these cancers needs new therapeutic options. The FIGHT (bemarituzumab-004) study is designed to evaluate the efficacy, safety, and PK of bemarituzumab in combination with modified FOLFOX (infusional 5-FU, leucovorin, and oxaliplatin) (mFOLFOX6) chemotherapy treatment. Patients with gastrointestinal (GI) tumors will be enrolled in a Phase I safety run in. The primary endpoint for Phase I part is the incidence of Grade 2 or higher AEs assessed as related to bemarituzumab by the Investigator and the incidence of clinical laboratory abnormalities defined as DLTs.

Our partner, Five Prime, announced the FIGHT trial has been converted to a Phase II randomized, double-blind trial, based on the approximately 150 patients enrolled. The Phase II FIGHT study is expected to generate clinical data to inform the further development strategy of bemarituzumab by the end of the year or early 2021. We have halted the enrollment in China, and will wait for our partner to provide further guidance.

Our Infectious Disease Pipeline

Omadacycline

Overview

Omadacycline (ZL-2401) is a broad-spectrum antibiotic in a new class of tetracycline derivatives, known as aminomethylcyclines. Omadacycline is primarily being developed for ABSSSI, CABP and UTI in both the hospital and community settings and is designed to overcome the two major mechanisms of tetracycline resistance, known as pump efflux and ribosome protection. Omadacycline has been granted QIDP and Fast Track status by the FDA. The drug has been administered to over 1,500 patients and has an established safety and tolerability profile. In October 2018, following priority review, Omadacycline was approved by FDA for both indications and for both the IV and oral once-daily formulations.

In June 2016, Paratek announced positive top-line efficacy data in a Phase III registration study in ABSSSI which demonstrated the efficacy and safety of IV to oral once-daily omadacycline compared to linezolid. In April 2017, Paratek announced positive top-line results from a global, pivotal Phase III clinical study in CABP which demonstrated the efficacy, general safety and tolerability of IV to oral omadacycline compared to moxifloxacin. In July 2017, Paratek also announced positive top-line results from a Phase III study comparing oral-only administration of omadacycline in ABSSSI compared to oral-only linezolid, which met all of its primary endpoints.

Omadacycline was approved by the FDA in October 2018 for both indications. It was launched as NUZYRA in the United States in February 2019. It is labeled for once-daily oral or intravenous administration for the treatment of adults with CABP and ABSSSI. The European Marketing Authorization Application for oral and IV omadacycline was submitted in October 2018.

In October 2019, Paratek announced that it is withdrawing its application in Europe for Nuzyra for business reasons. While approvable by EMA for skin infections, EMA requested a second study in CABP to meet current European regulatory standards of two Phase III studies in the indication. Paratek plans to re-submit application to EMA following completion of the planned Post-Marketing Approval CABP study already agreed with the FDA. Paratek conducted two exploratory studies in UTI for dose-finding purposes, one in women with acute cystitis (cUTI) and another in patients with pyelonephritis (cUTI). As per a press release in October 2019, Paratek plans to conduct additional analyses and investigations for these UTI indications.

We obtained the exclusive license from Paratek to develop, manufacture and commercialize omadacycline in the field of all human therapeutic and preventative uses (other than biodefense) in China, Hong Kong, Macau and Taiwan in April 2017. For further details of the exclusive license, see "— Overview of Our License and Strategic Collaboration Agreements — Paratek." In March 2020, we entered into a contract sales agreement with Hanhui, a local pharmaceutical company with a strong commercial presence in antibiotics. The agreement allows us to leverage Hanhui's existing infrastructure to optimize a potential future commercial launch of omadacycline in China given that omadacycline is a broad spectrum antibiotic in both the hospital and community setting.

Competition

In China, there is currently only one marketed tetracycline derivative antibiotic, which was approved in 2010. Omadacycline is expected to be the second approved drug in this category.

Summary of Clinical Results

Background on Tetracycline Antibiotics

The tetracycline class of antibiotics was introduced into the clinic in the 1960s and found considerable use in the treatment of respiratory and gastrointestinal infections. They are mostly bacteriostatic drugs interfering with protein synthesis by binding selectively to the bacterial 30S ribosomal subunit.

Tetracyclines provide excellent broad-spectrum coverage of Gram-positive, Gram- negative, anaerobes and special pathogens (e.g., malaria, anthrax, Lyme borrelia, nocardia). Resistance is due to efflux mechanisms and ribosomal mutations, but despite the gradual and inevitable increase in resistance over many decades of continued use, doxycycline is still an effective and commonly used drug today.

Omadacycline — Pharmacokinetics

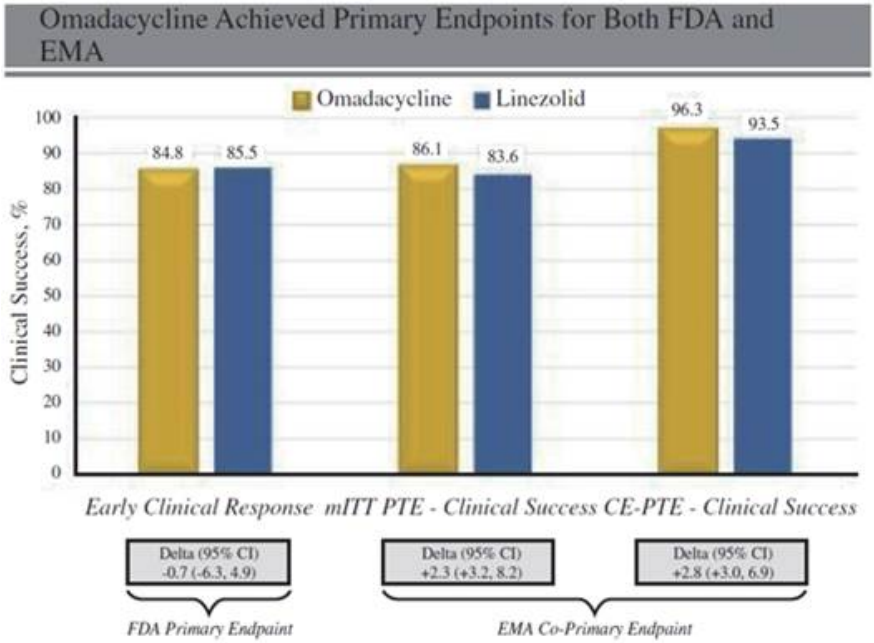
Studies showed that oral doses of 300 mg provide bioequivalent exposure with the therapeutic IV dose of 100 mg. Like with other tetracyclines, absorption is affected by food and divalent cations. The drug has a long half-life (approximately 17 hours) and excellent penetration into tissues, including alveolar and epithelial lining fluid. In contrast to other tetracyclines, plasma protein binding is low (20%) and not dose-related. The drug is not metabolized and excretion is predominantly via the biliary route. There is no need for dose adjustment in hepatic or renal impairment.

Phase III Pivotal Trial-ABSSSI/OASIS-ABSI 1108

Omadacycline was statistically non-inferior to linezolid IV/PO in a direct comparison study following a protocol established under an SPA agreed to with the FDA as well as the criteria outlined by the EMA. In this trial, patients with wound infections, major abscesses, and erysipelas/cellulitis were enrolled in equal numbers. On average, patients received IV omadacycline for 4.4 days, and oral omadacycline for 5.5 days.

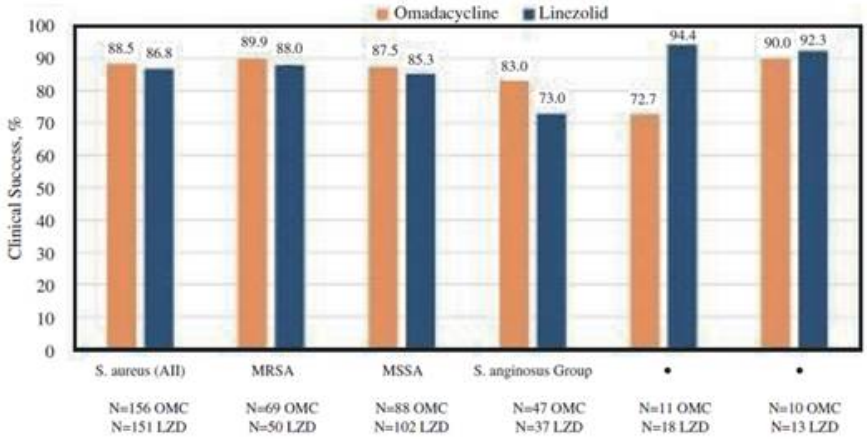
S. aureus (both MSSA and MRSA) was the predominant pathogen isolated from patients followed by streptococci. Clinical response and bacterial eradication rates showed the high efficacy of omadacycline against skin pathogens including MRSA.

Figure 9: Omadacycline vs Linezolid-ABSSSI Trial-Primary Efficacy Outcomes



Source: Rodrigo, Keith. Infection and Drug Resistance; 2019:12 1895-1915

Figure 10: Early Clinical Success by Pathogen-micro-mITT Population



Source: Omadacycline - Antimicrobial Drugs Advisory Committee (AMDAC) Briefing Book. Paratek Pharmaceuticals; 2018

The safety/tolerability profile was very similar between the treatment arms with only a slightly higher rate of gastrointestinal side effects and infusion site reactions in omadacycline recipients. There was no significant imbalance in treatment emergent adverse events, or TEAEs, serious TEAEs, premature discontinuations or deaths.

This study was recently published in the New England Journal of Medicine (W O'Riordan et al. Omadacycline for Acute Bacterial Skin and Skin-Structure Infections, N Engl J Med 2019; 380:528-538).

Figure 11: Study ABSI-1108: Most Frequent TEAEs (> 3%)-Safety Population

	Omadacycline N = 323 %	Linezolid N = 322 %
Subjects with Any TEAE	48.3	45.7
Nausea	12.4	9.9
Infusion Site Extravasation	8.7	5.9
Subcutaneous Abscess	5.3	5.9
Vomiting	5.3	5.0
Cellulitis	4.6	4.7
Headache	3.1	4.0
ALT Increased	2.8	4.3
AST Increased	2.5	3.7
Diarrhea	2.2	3.1

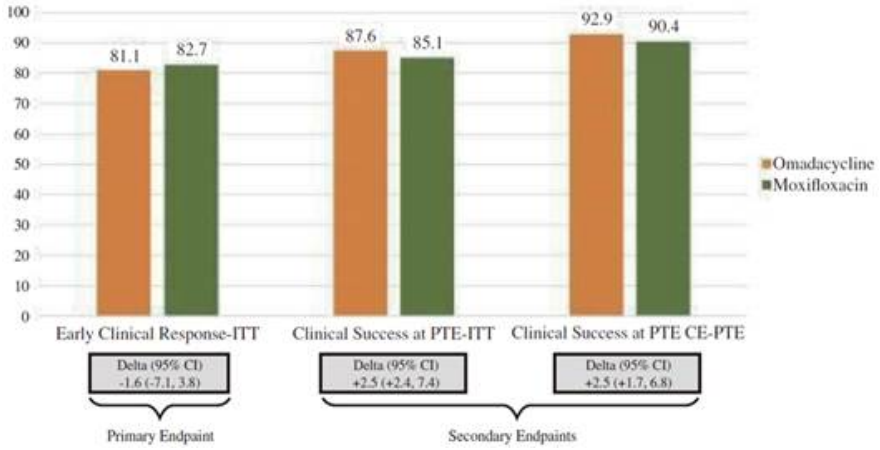
Source: William O'Riordan, et al. The New England Journal of Medicine; 2019

Phase III Pivotal Trial-CABP/OPTIC-CABP1200

Omadacycline was non-inferior to moxifloxacin IV/oral in this direct comparison study following a protocol established under an SPA agreed with the FDA as well as the criteria outlined by the EMA. In this trial, patients with PORT Class II-IV were recruited; less than 25% of patients had received non-study antibiotics before enrollment.

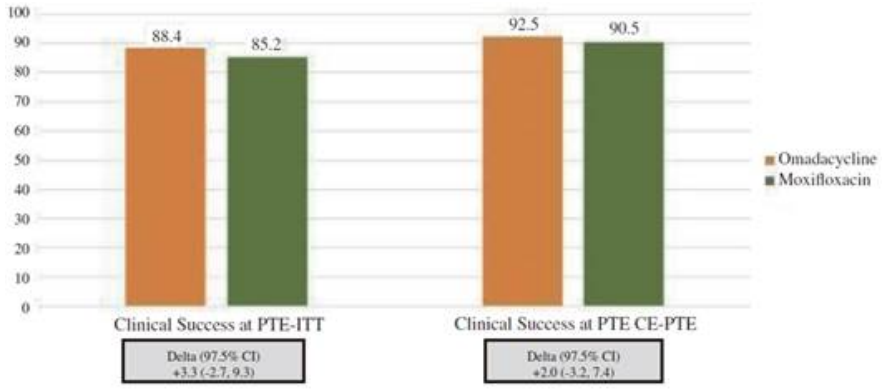
Streptococcus pneumoniae and Mycoplasma pneumoniae were the predominant pathogens isolated, followed by H. influenzae, H. parainfluenzae, Legionella and Chlamydophila. The clinical response rates were high for all respiratory pathogens isolated at entry and very similar between omadacycline and moxifloxacin, a powerful respiratory fluoroquinolone.

Figure 12: CABP Study — OPTIC: Primary Efficacy Results — FDA Analysis



Source: Roman Stets et al. The New England Journal of Medicine; 2019

Figure 13: CABP Study — OPTIC: Primary Efficacy Results — EMA Analysis



Source: EMA assessment report

Figure 14: CABP Study-OPTIC: Clinical Success at PTE by Baseline Pathogen

	Omadacycline (N = 204)		Moxifloxacin (N = 182)	
Baseline Pathogen	**N**	**Clinical Success n (%)**	**N1**	**Clinical Success n (%)**
Atypical Pathogens	118	109 (92.4)	106	97 (91.5)
Mycoplasma Pneumoniae	70	66 (94.3)	57	50 (87.7)
Chlamydophila Pneumoniae	28	25 (89.3)	28	25 (89.3)
Legionella Pneumophila	37	35 (94.6)	37	36 (97.3)
Gram-Negative Bacteria (aerobes)	79	67 (84.8)	68	55 (80.9)
Haemophilus Influenzae	32	26 (81.3)	16	16 (100.0)
Haemophilus Parainfluenzae	18	15 (83.3)	17	13 (76.5)
Klebsiella Pneumoniae	13	10 (76.9)	13	11 (84.6)
Gram-Positive Bacteria (aerobes)	61	52 (85.2)	56	49 (87.5)
Steptococcus Pnemoniae	43	37 (86.0)	34	31 (91.2)
PSSP	26	23 (88.5)	22	21 (95.5)
Macrolide Resistant	10	10 (100.0)	5	5 (100.0)
Stephylococcus Aereus	11	8 (72.7)	11	9 (81.8)

* 10 or More Isolates for Omadacycline

Source: Roman Stets et al. The New England Journal of Medicine; 2019

Neither gastrointestinal side effects nor IV infusion reactions occurred more frequently in the omadacycline arm than in the comparator arm. Cardiovascular signs and symptoms and liver function test abnormalities occurred in both study arms with similar frequency.

This study was recently published in the New England Journal of Medicine (R Stets et al.. Omadacycline for Community-Acquired Bacterial Pneumonia, N Engl J Med 2019; 380:517-527).

Figure 15: TEAEs in CABP Trial

	Omadacycline (N = 382) N (%)	Linezolid (N = 388) N (%)
Subjects with at Least One TEAE	157 (41.1)	188 (48.5)
ALT Increased	14 (3.7)	18 (4.6)
Hypertension	13 (3.4)	11 (2.8)
GGT Increased	10 (2.6)	8 (2.1)
Insomnia	10 (2.6)	8 (2.1)
Vomiting	10 (2.6)	6 (1.5)
Constipation	9 (2.4)	6 (1.5)
Nausea	9 (2.4)	21 (5.4)
AST Increased	8 (2.1)	14 (3.6)
Headache	8 (2.1)	5 (1.3)

Source: Roman Stets et al. The New England Journal of Medicine; 2019

Phase III trial — ABSSSI/OASIS-2

Paratek's third Phase III clinical study (OASIS-2) was an oral-only administration of omadacycline in ABSSSI compared to oral-only linezolid. Oral, once daily omadacycline met the FDA-specified primary efficacy endpoint of statistical non-inferiority in the modified intent-to-treat, or mITT, population (10% non-inferiority margin, 95% confidence interval) compared to oral, twice daily linezolid at the early clinical response, or ECR, 48-72 hours after initiation of therapy. The ECR rates for the omadacycline and linezolid treatment arms were 87.5% and 82.5%, respectively. In addition, omadacycline met specified co-primary endpoints for the EMA, which are key secondary endpoints for the FDA. For these endpoints, non-inferiority in the mITT and clinically evaluable populations in at the post treatment evaluation, seven to 14 days after end of treatment, omadacycline demonstrated a high response rate and met statistical non-inferiority to linezolid for both populations using a pre-specified 95% confidence interval. High success rates were observed with response rates of 84.2% (omadacycline) vs. 80.8% (linezolid) and 97.9% (omadacycline) vs. 95.5% (linezolid), respectively.

The most common TEAEs in omadacycline-treated patients (occurring in > 3% of patients) were gastrointestinal adverse events of omadacycline vs. linezolid included: vomiting (16.8% vs. 3.0%), nausea (30.2% vs. 7.6%), diarrhea (4.1% vs. 2.7%). In addition, alanine aminotransferase, or ALT, increase (5.2% with omadacycline vs. 3.0% with linezolid), aspartate aminotransferase increases (4.6% with omadacycline vs. 3.3% for linezolid) and headache (3.5% with omadacycline vs. 2.2% with linezolid). Drug-related TEAEs were 37.8% for omadacycline vs. 14.2% for linezolid (including gastrointestinal events). Discontinuation for TEAEs was uncommon, 1.6% for omadacycline vs. 0.8% for linezolid. Serious TEAEs occurred in 1.4% of omadacycline patients and 1.4% of linezolid patients; only one serious TEAE was considered related to the study drug and the event occurred in a linezolid patient.

Phase II studies

In a small study (N=111) conducted in cSSSI patients omadacycline showed comparable efficacy and safety to linezolid IV/PO ± aztreonam. However, the design of the Phase II study (and a truncated Phase III study with 68 patients) was no longer consistent with newer FDA guidance issued for ABSSSI in 2008 which required, among other changes, an early efficacy read-out at 48-72 hours.

In addition, this early omadacycline program used a 200 mg oral step-down dose that proved to not be bioequivalent to the 100 mg IV dose. Hence, these data are now considered supportive and cannot be merged easily with the larger pivotal program trials in ABSSSI and CABP that were conducted with FDA guidance and bioequivalent IV to oral step-down dosing.

A Phase II study (IV and oral) in patients with acute pyelonephritis was initiated by Paratek in 2018.

Phase I studies

Omadacycline has been evaluated in multiple Phase I studies, including food-effect, age and gender, and renal/hepatic insufficiency studies.

Omadacycline has a very favorable PK profile. It was absorbed well; its plasma T 1/ of 14-20 hours permitted once-daily dosing. The drug was not metabolized and drug-drug interactions were minimal. In contrast to other tetracyclines, which paradoxically display dose-dependent increases in protein binding, 80% of omadacycline remained available as free drug. Excretion was via biliary and urinary routes. Data from hepatic and renal impairment studies showed that dose adjustments are not needed for patients with either condition.

In bioequivalence studies, the 300 mg oral dose was found to match the area under the curve of the 100 mg IV dose.

Omadacycline was negative on hERG testing and had no appreciable effect on cardiac conduction in a Thorough QT trial at supra-therapeutic doses. However, in animal tests and during Phase I, a dose-dependent elevation of blood pressure (systolic and diastolic) and heart rate were observed. Omadacycline was found to be an acetylcholine antagonist for muscarinic receptor subtype M2, essentially acting as a vagolytic agent. In subsequent patient studies, these effects were less pronounced or absent and clinically asymptomatic. All Phase II and III studies included systematic cardiovascular pre-and post-dose monitoring of blood pressure and heart rate to further characterize these effects both qualitatively and quantitatively.

An ELF study showed excellent penetration of omadacycline into bronchoalveolar lavage fluid and into alveolar macrophages.

A cystitis (uUTI) study was conducted by Paratek to obtain PK information for different oral dosing regimens of omadacycline.

Our Clinical Trial Designs and Strategy for Omadacycline in the China Market

We have completed the technology transfer stage and discussed with key opinion leaders our planned China development activities in preparation for NMPA interactions. We have submitted documents and filed for an investigational new drug application, or IND, with Chinese medical regulatory authorities in December 2017 and submitted our NDA in December 2019. In May 2020, the NMPA has granted priority review status to our NDA for omadacycline for the treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI).

We have actively engaged key opinion leaders in discussions on our planned China development strategy, on our study design in China, and the interpretation or data from the program. We have also completed a bioequivalence study for the oral tablet, which is required by the authority to compare the PK exposures of the locally-manufactured formulation to the formulation used by the licensor. The study has showed that the formulation locally manufactured in China has comparable PK exposures compared to that used by Paratek.

We have completed a microbiology study investigating the activity of omadacycline against pathogens obtained from Chinese and other Asian patients. In this trial of 3,832 isolates, omadacycline activity was essentially identical to the susceptibility results obtained in a larger 2016 surveillance study of 21,000 isolates conducted outside China (mainly in the United States and the European Union). These data have been published in an article titled "Antimicrobial Activity of Omadacycline Tested against Clinical Bacterial Isolates from Hospitals in China, Hong Kong and Taiwan: Results from the SENTRY Antimicrobial Surveillance Program (2013 to 2016)" in Antimicrobial Agents and Chemotherapy 2019 63 (3): e02262-18. doi: 10.1128/AAC.02262-18]. We have also completed a microbiology study against 1,041 more recent patient isolates from China. This study further confirmed the undiminished activity of omadacycline against ABSSSI and CABP pathogens; publication of this data is pending.

We have also conducted a PK study in Chinese patients with both the IV and oral formulation. This study showed similar exposure to Caucasians with the selected dosing regimens for the IV formulation and somewhat higher but well tolerated exposures with the PO formulation. PK/PD analysis suggest that omadacycline IV and PO at standard doses will provide excellent coverage against pathogens from Chinese sources.

We have enrolled 125 patients in an ABSSSI in our clinical efficacy study with linezolid as comparator. Results showed equal clinical efficacy in both treatment arms. Likewise, the safety/tolerability of omadacycline in Chinese patients was excellent. These studies were part of our bridging plan for regulatory approval in China as discussed with regulators. They also were designed, conducted and analyzed in collaboration with Chinese KOLs in PK, microbiology and infectious disease.

We have completed a Phase III study in China to evaluate the efficacy and safety of omadacycline for the treatment of ABSSSI and CABP. In May 2020, the NMPA has granted priority review status to our NDA for omadacycline for the treatment of CABP and ABSSSI.

Durlobactam

Overview

Durlobactam (ZL-2402) is a novel β-lactamase inhibitor of class A, C, and D beta-lactamases. As such it is active against multiple members of the β-lactamases commonly found in Acinetobacter baumannii. In particular, it is a potent inhibitor of several Class D enzymes which confer MDR to many β-lactam antibiotics. In combination with sulbactam, durlobactam reduces the minimum inhibitory concentration, or MIC, against this organism and restores susceptibility to sulbactam. It is being developed by Entasis as SUL-DUR, a combination of durlobactam and sulbactam. The microbiologic efficacy of this combination was demonstrated in large studies of well-characterized MDR Acinetobacter isolates from diverse regions, including Asia. SUL-DUR was bactericidal and active against penem-resistant Acinetobacter organisms. SUL-DUR was synergistic with imipenem, further lowering MICs on in-vitro testing. The FDA has granted SUL-DUR QIDP, Fast Track and Priority Review status.

Durlobactam without sulbactam but in combination with other β-lactams lowered the MICs for E. coli, K. pneumoniae and P. aeruginosa compared to the partner β-lactam antibiotic alone. Entasis has conducted a comprehensive Phase I safety and PK program for durlobactam. Single ascending dose and multiple ascending dose studies showed that durlobactam alone and in combination with sulbactam or imipenem is well tolerated and safe. There were no noticeable drug-drug interactions.

Entasis plans to develop SUL-DUR for the treatment of severe A. baumannii infections. Entasis has finished a Phase II cUTI trial in 2018, reviewed clinical Phase III plans with FDA and started enrollment in the pivotal Phase III trial in MDR Acinetobacter infections in the second half of 2019.

We obtained the exclusive license from Entasis to develop and commercialize durlobactam in China, Hong Kong, Macau, Taiwan, Korea, Vietnam, Thailand, Cambodia, Laos, Malaysia, Indonesia, the Philippines, Singapore, Australia, New Zealand and Japan in April 2018. For further details of the exclusive license, see "— Overview of Our License and Strategic Collaboration Agreements — Entasis."

Market Opportunity

Background on Acinetobacters

Acinetobacter is one of the most resistant pathogens encountered in clinical practice. It is one of the ESKAPE pathogens, a leading cause of nosocomial infections throughout the world, for which new treatment options are needed as these organisms are MDR to most antibiotics currently available. Approximately 60% of Acinetobacter isolates are carbapenem resistant (so-called CRAB pathogens) and can only be treated with polymyxin, a rather toxic drug, or tigecycline which is often ineffective.

Of great concern, colistin resistance has been reported in recent years, especially from Asia, in E. coli and in K. pneumoniae. So far, there is only scattered report of mcr-1 resistance in Acinetobacter have been reported but the risk is high that chromosomal and — more ominously — plasmid mediated resistance may spread to other bacteria, especially in an environment with high veterinary colistin use like in China. Recent case reports of successful treatment with experimental phage therapy as a last resort when available antibiotics fail. Severe Acinetobacter infections are associated with mortality rates of 50-60% despite intensive medical care. These infections usually present as blood-stream infections or hospital-acquired pneumonia. Less severe infections of the skin and urinary tract are not uncommon.

The frequency of Acinetobacter infections is on the rise world-wide. In the United States and the European Union, the incidence of infection is between 80,000 and 120,000 patients per year in each region. The incidence is higher in the Asia Pacific region and especially in China where the organism ranks among the most frequent isolates in intensive care unit patients. In 2015, over 180,000 infections were reported from China alone. In Japan, over 30,000 cases were reported for 2015, which is an increase of approximately 50% since 2012.

Background on Sulbactam

Sulbactam, a β-lactam derivative, has been in use since the 1980s. It is a IV BLI used in combination with ampicillin, known in the United States as Unasyn and widely used since 1987. It is a β-lactam with a proven safety record. Sulbactam has antibiotic activity of its own, notably against Acinetobacter. However, β-lactamase-mediated resistance to sulbactam has developed and is now common in Acinetobacter.

Durlobactam is a non-β-lactam BLI of the DBO class. It has structural similarities to avibactam, a BLI approved in combination with ceftazidime (Avycaz). However, durlobactam has demonstrated much greater potency against many β-lactamases, especially the Class D OXA enzymes prevalent in Acinetobacter.

Our Clinical Trial Designs and Strategy for Durlobactam in the China Market

We and our partner, Entasis Therapeutics, will cooperate in conducting the trial in China with us taking the operational lead by conducting the screening, enrollment and treatment of patients and coordinating development, registration and commercialization of SUL-DUR in specified countries in the Asia-Pacific region including Japan. In May 2020, the first Chinese patient was enrolled into the global Phase III ATTACK trail of durlobactam for Acinetobacter infections.

Set forth below is a table summarizing the clinical trials disclosed in the following sections headed “Our Marketed Products”, “Our Oncology Pipeline” and “Our Infectious Disease Pipeline”.

Study Guide	Official Title	NCT number	Study initiation date
NORA	A Randomized, Double-Blind Placebo-Controlled, Multi-Center, Phase III Clinical Trial Evaluating the Efficacy and Safety of ZL-2306 (Niraparib) for Maintenance Treatment in Patients With Platinum-sensitive Relapsed Ovarian Cancer, Fallopian Tube Carcinoma or Primary Peritoneal Cancer (Collectively Referred to as Ovarian Cancer)	NCT03705156	June 2017
NOVA	A Phase 3 Randomized Double-blind Trial of Maintenance With Niraparib Versus Placebo in Patients With Platinum Sensitive Ovarian Cancer	NCT0184727	June 2013
PRIME	A Randomized, Double-Blind Placebo-Controlled, Multi-Center, Phase III Clinical Trial Evaluating the Efficacy and Safety of ZL-2306 (Niraparib) for Maintenance Treatment in Patients With Advanced Ovarian Cancer, Fallopian Tube Carcinoma or Primary Peritoneal Cancer (Collectively Referred to as Ovarian Cancer) Who Have Achieved Effective Response After First-line Platinum-containing Chemotherapy	NCT03709316	June 2018

Study Guide	Official Title	NCT number	Study initiation date
PRIMA	A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of Niraparib Maintenance Treatment in Patients With Advanced Ovarian Cancer Following Response on Front-Line Platinum-Based Chemotherapy	NCT02655016	July 2016
EF-11	A Prospective, Multi-center Trial of NovoTTF-100A Compared to Best Standard of Care in Patients With Progressive or Recurrent GBM	NCT00379470	September 2006
EF-14	A Prospective, Multi-center Trial of NovoTTF-100A Together With Temozolomide Compared to Temozolomide Alone in Patients With Newly Diagnosed GBM	NCT00916409	June 2009
INVICTUS	A Phase 3, Interventional Double-Blind, Placebo-Controlled Study to Assess the Safety and Efficacy of Ripretinib In Patients With Advanced Gastrointestinal Stromal Tumors Who Have Received Treatment With Prior Anticancer Therapies	NCT03353753	February 2018
INTRIGUE	A Phase 3, Interventional Randomized, Multicenter, Open-Label Study of DCC-2618 vs Sunitinib in Patients With Advanced Gastrointestinal Stromal Tumors After Treatment With Imatinib	NCT03673501	February 2019

Study Guide	Official Title	NCT number	Study initiation date
TRIDENT-1	A Phase 1/2, Open-Label, Multi-Center, First-in-Human Study of the Safety, Tolerability, Pharmacokinetics, and Anti-Tumor Activity of TPX-0005 in Patients With Advanced Solid Tumors Harboring ALK, ROS1, or NTRK1-3 Rearrangements	NCT03093116	February 2017
SOPHIA	A Phase 3, Randomized Study of Margetuximab Plus Chemotherapy vs Trastuzumab Plus Chemotherapy in the Treatment of Patients With HER2+ Metastatic Breast Cancer Who Have Received Prior Anti-HER2 Therapies and Require Systemic Treatment	NCT02492711	August 2015
MAHOGANY	Phase 2/3 Trial to Evaluate Margetuximab in Combination With INCMGA00012 and Chemotherapy or MGD013 and Chemotherapy in Patients With Metastatic or Locally Advanced, Treatment-naïve, HER2-Positive Gastric or Gastroesophageal Junction Cancer	NCT04082364	September 2019
FIGHT	A Phase 2 Randomized, Double Blind, Controlled Study Evaluating Bemarituzumab (FPA144) and Modified FOLFOX6 in Patients With Previously Untreated Advanced Gastric and Gastroesophageal Junction Cancer: Phase 2 Preceded by Dose-Finding in Phase 1	NCT03694522	September 2018
ATTACK	A Randomized, Active-Controlled Study to Evaluate the Efficacy and Safety of Intravenous Sulbactam-ETX2514 in the Treatment of Patients With Infections Caused by Acinetobacter Baumannii-calcoaceticus Complex	NCT03894046	April 2019

Internal Clinical Programs with Global Rights

ZL-1201

ZL-1201 is a humanized, IgG4 monoclonal antibody engineered to reduce effector function, that specifically targets CD47. The emerging clinical data for agents targeting the CD47-SIRPalpha axis continues to look promising. We made modifications to the antibody which may reduce the incidence of hemolysis seen with other agents in the class based on pre-clinical data. CD47 has recently emerged as a novel macrophage immune checkpoint and a promising target for therapeutic intervention. Our pipeline includes several assets, including a novel bi-specific T cell engager and checkpoint inhibitors, that lend themselves to rational combinations with a CD47-targeted therapeutic. The therapeutic potential of these ZL-1201 combinations will be assessed in both solid tumors and hematological malignancies. First-inhuman was achieved in June 2020 in the US.

ZL-1102

ZL-1102 is a human nanobody targeting IL-17 with high affinity and avidity. ZL-1102 is being developed for the topical treatment of chronic plaque psoriasis. The role of IL-17 in psoriasis has been confirmed. IL-17 blockers have consistently demonstrated lesion clearance relative to older therapeutics. Despite their unprecedented efficacy, therapy with IL-17 antibodies can result in certain safety issues due to immunosuppression. Labeling therefore restricts their use to more severely affected patient populations. Like other full-size monoclonal antibodies, therapy with IL-17 antibodies have to be administered by IV or SC injection. In contrast, ZL-1102 is smaller molecule designed to be administered topically, thus avoiding significant systemic exposure. As a result of these distinguishing properties, ZL-1102 may have an improved safety and tolerability profile over available biologics targeting IL-17. If confirmed in clinical trials, ZL-1102 could potentially enable treatment of the majority of psoriasis patients, including those with milder disease, and for whom currently available IL-17 inhibitors are not indicated. In July 2020, we achieved first-in-human dosing in the global Phase I study in Australia.

Our Discovery Pipeline

Our in-house discovery team, nearly all of whom hold a PhD degree, is dedicated to the research and discovery of novel therapeutics in the areas of oncology and autoimmune diseases, with a focus on large market opportunities with unmet clinical needs. Our Shanghai research facility was established in 2015 with a focus on internal development of small and large molecule therapeutics and San Francisco, California research facility, established in 2018, focuses on internal discovery. We continue to expand our U.S. presence to enhance internal drug discovery and clinical development, with the opening of a new 20,000 sq.ft research facility in Menlo Park, California. Our current San Francisco-based discovery operations team will move into the Menlo Park research facility and commence operations in second half of 2020. We have collaborations with leading academic institutions in China, Tsinghua University and Shanghai Institute of Organic Chemistry under the Chinese Academy of Sciences, to support our in-house research projects. We aim to submit up to two global INDs in 2020. We believe our discovery efforts will enable us to achieve our long-term goal of generating a sustainable, internally discovered product pipeline of new products and drug candidates for patients around the world.

Our discovery efforts have resulted in the identification of a number of proprietary candidates against targets in our focus areas with high scientific validation including immuno-oncology, DNA damage response/repair and oncogenic signaling. We identify pre-clinical assets through both internal-discovery efforts and co-development collaboration with our business partners. Both ZL-1102 and ZL-1201 are internally-developed drug candidates. As of the Latest Practicable Date, we had achieved FPIs for our internally generated drug candidates, including ZL-1102 in autoimmune diseases and ZL-1201 in oncology. Depending on the Phase I clinical trial results, we may proceed with Phase II clinical trial with promising indications. Our discovery pipeline also includes ZL-1211, ZL-2201 and ZL-2103, which will be potentially developed for the treatment of oncology and/or autoimmune diseases.

Overview of Regulatory Status

The following table summarizes the details of the PRC regulatory status of our products and drug candidates as of the Latest Practicable Date.

Program	Type of Regulatory Application	Status	Date for Obtaining the Current Status	Application Number
ZEJULA	NDA	Approved	2019-12-26 2020-01-20	Original Number (原始編號): 31160076 Acceptance Number (受理號): CXHS180043國 Approval Number (批件號): 2019S00731
	sNDA	Approved	2020-09-08	Acceptance Number (受理號): CXHS2000009
Ripretinib	NDA	Accepted	Accepted: 2020-7-20	JXHS2000121國
Omadacycline	CTA	Approved	2018-07-03	Original Number (原始編號): 31170071 Acceptance Number (受理號): CXHL1700339 Approval Number (批件號): 2018L02776
	CTA	Approved	2018-07-03	Original Number (原始編號): 31170070 Acceptance Number (受理號): CXHL1700338 Approval Number (批件號): 2018L02775
	NDA — Priority Review	Accepted	2020-02-07	Acceptance Number (受理號): CXHS2000003國
		Accepted	2020-02-07	Acceptance Number (受理號): CXHS2000002國

Program	Type of Regulatory Application	Status	Date for Obtaining the Current Status	Application Number
Tebotelimab	CTA	Approved	2020-1-20	JXSL1900114
	CTA	Approved	2020-2-10	JXSL1900116
	CTA	Approved	2020-2-10	JXSL1900134
	CTA	Approved	2020-2-10	JXSL1900135
	CTA	Approved	2020-5-6	JXSB2000090
	CTA	Approved	2020-6-2	JXSL2000031
Optune		Approved	2020-5-11	國械注進20203090269
Repotrectinib	CTA	Submitted	2020-8-31	TBD
Odronextamab	CTA	Approved	2020-6-3	JXSL2000105 JXSL2000106
		Currently under review		JXSL2000107 JXSL2000108 JXSL2000109
Margetuximab	CTA	Approved	2020-2-10	JXSL1900113
	CTA	Approved	2020-2-3	JXSL1900115
		Approved	2020-6-3	JYSB2000178
Retifanlimab	CTA	Approved	2020-2-10	JXSL1900119
	CTA	Approved	2020-2-10	JXSL1900118
	CTA	Approved	2020-2-12	JXSL1900140
	CTA	Approved	2020-9-4	JXSL2000083
	CTA	Approved	2020-9-8	JXSL2000087
Bemarituzumab	CTA	Approved	2018-5-18	JXSL1800003
Durlobactam	CTA	Approved	2019-7-26	JXHL1900112
ZL-1201	CTA	Approved	2020-7-16	CXSL2000096
ZL-1102*	NA	NA	NA	NA

Note:

*We have not yet started regulatory application process in China.

OVERVIEW OF OUR LICENSE AND STRATEGIC COLLABORATION AGREEMENTS

GSK

In September 2016, we entered into a collaboration, development and license agreement with Tesaro (now GSK) under which we obtained an exclusive sublicense under certain patents and know-how that Tesaro (now GSK) licensed from Merck, Sharp & Dohme Corp. ("Merck") and AstraZeneca UK Limited to develop, manufacture, use, sell, import and commercialize GSK's proprietary PARP inhibitor, ZEJULA, in China, Hong Kong and Macau in the licensed field of treatment, diagnosis and prevention of any human diseases or conditions (other than prostate cancer). Janssen Biotech, Inc. entered a worldwide collaboration and license agreement with Tesaro (GSK) for exclusive rights to the investigational compound niraparib (ZEJULA) in prostate cancer in April 2016 before we entered the license agreement with Tesaro. We also obtained the right of first negotiation to obtain a license to develop and commercialize certain follow-on compounds of ZEJULA being developed by GSK in our licensed field and licensed territory. Under the agreement, we agreed not to research, develop or commercialize certain competing products and we also granted GSK the right of first refusal to license certain immuno-oncology assets developed by us.

We are obligated to use commercially reasonable efforts to develop and commercialize the licensed products in our licensed field and licensed territory. We are also responsible for funding all development and commercialization of the licensed products in our licensed territory.

We also agree to take any action or omission reasonably requested by GSK that is necessary or advisable to maintain compliance with the terms of the license agreements between GSK and each of Merck and AstraZeneca UK Limited.

Under the terms of the agreement, we made an upfront payment of US$15.0 million and accrued two development milestone payments in total of US$4.5 million to Tesaro (now GSK). On top of those, if we achieve other specified regulatory, development and commercialization milestones, we may be additionally required to pay further milestone payments of up to US$36.0 million to GSK. In addition, if we successfully develop and commercialize the licensed products, we will pay GSK tiered royalties at percentage rates in the mid-to high-teens on the net sales of the licensed products, until the later of the expiration of the last-to-expire licensed patent covering the licensed product, the expiration of regulatory exclusivity for the licensed product, or the tenth anniversary of the first commercial sale of the licensed product, in each case on a product-by-product and region-by-region basis. In February 2018, we entered into an amendment with GSK to eliminate GSK's option to co-market ZEJULA in the licensed territory.

The agreement with GSK will remain in effect until the expiration of the royalty term and may be earlier terminated by either party for the other party's uncured material breach, bankruptcy or insolvency or by mutual agreement of the parties. In addition, we have the right to terminate the agreement for convenience at any time upon advance notice to GSK. Upon early termination of the agreement, we must grant to GSK an exclusive license under certain of our intellectual property to develop and commercialize the licensed products outside the licensed territory

Novocure

In September 2018, we entered into a license and collaboration agreement with Novocure. Under the terms of the agreement, Novocure exclusively licensed to us the rights to perform clinical studies, sublicensable to affiliates and third parties (subject to Novocure's consent), sell, offer for sale and import Tumor Treating Fields products in the field of oncology, each, a licensed product and collectively, the licensed products, in China, Hong Kong, Macau and Taiwan, or the territory. In partial consideration for the license grant to us for the territory, we paid Novocure a non-refundable, upfront license fee in the amount of US$15.0 million and a milestone payment of US$2.0 million. In addition, we accrued a milestone payment of US$8.0 million. We also agreed to pay certain development, regulatory and commercial milestone payments in total of up to an aggregate of US$68.0 million, and tiered royalties at percentage rates from ten up to the mid-teens on the net sales of the licensed products in the Territory.

We will purchase licensed products exclusively from Novocure at Novocure's fully burdened manufacturing cost. The agreement continues, on a region-by-region and licensed product-by-licensed product basis, in effect until the expiration of and payment by us of all of our royalty payment obligations applicable to such licensed product and such region as specified in the agreement. Each party may terminate the agreement upon the material breach of the agreement by the other party, subject to certain cure periods. In addition, we may terminate the agreement for convenience on twelve months' prior notice prior to commercializing a licensed product and on eighteen months' prior notice after commercializing a licensed product, and Novocure may terminate the agreement due to our diligence failure or material FCPA violation, subject to certain cure periods and dispute resolution mechanisms if disputes arise with respect to such failure or material violation, each as defined in the agreement.

Deciphera

In June 2019, we entered into a license agreement with Deciphera. Under the terms of the agreement, Deciphera exclusively licensed to us the rights to perform clinical studies, sublicenseable to affiliates without Deciphera's consent and third parties (subject to Deciphera's consent), sell, offer for sale and import ripretinib, a licensed product, in the field of the prevention, prophylaxis, treatment, cure or amelioration of any disease or medical condition in humans in China, Hong Kong, Macau and Taiwan. In partial consideration for the license grant to us for the territory, we paid Deciphera a non-refundable, upfront license fee in the amount of US$20.0 million and one milestone payment of US$5.0 million. In addition, we accrued a milestone payment of US$2.0 million. We also agreed to pay certain additional development, regulatory and commercial milestone payments up to an aggregate of US$178.0 million, and tiered royalties at percentage rates from low-to high-teens on the net sales of the licensed products in the territory.

We will purchase the licensed products exclusively from Deciphera at a certain mark up of Deciphera's fully burdened manufacturing cost. The agreement continues, on a region-by- region and licensed product-by-licensed product basis, in effect until the expiration of and payment by us of all of our royalty payment obligations applicable to such licensed product and such region as specified in the agreement. Each party may terminate the agreement upon the material breach of a material term of the agreement by the other party, subject to the ability to cure. In addition, we may terminate the agreement for convenience on 180 days' prior notice, and Deciphera may terminate the agreement due to our patent challenge against certain Deciphera's patents, subject to the ability to cure and dispute resolution mechanisms if disputes arise with respect to such failure or material violation, each as defined in the agreement. In January 2020, we entered into an amendment with Deciphera to clarify several operational matters.

Regeneron

In April 2020, we entered into a strategic collaboration with Regeneron for the development and exclusive commercialization of odronextamab in oncology in mainland China, Hong Kong, Taiwan and Macau, or the territory. We can also sublicense such rights to affiliates and third parties (subject to Regeneron's consent). In partial consideration for the rights grant to us for the territory, we paid Regeneron a non-refundable, upfront fee in the amount of US$30 million. We also agreed to pay certain regulatory and commercial milestone payments of up to US$160 million, as well as royalties based on a percentage of net sales of odronextamab in the territory.

We will purchase odronextamab exclusively from Regeneron at Regeneron's fully burdened manufacturing cost. The agreement continues in effect after the date of the agreement and until, unless earlier terminated, such time when we have ceased development and commercialization activities on odronextamab for six consecutive months (other than due to a delay by Regeneron or a regulatory authority).

Turning Point

In July 2020, we entered into an exclusive license agreement with Turning Point Therapeutics, Inc., or Turning Point. Under the terms of the exclusive license agreement, Turning Point exclusively licensed to us the rights to develop and commercialize products containing repotrectinib (licensed products), in China, Hong Kong, Macau and Taiwan, or the territory. In partial consideration for the license grant to us for the territory, we will pay Turning Point an upfront licensee fee in the amount of US$25 million, with potential for Turning Point to receive up to an additional US$151 million in development, regulatory and sales-based milestone payments. We also agreed to pay mid-to-high teen royalties based on annual net sales of licensed products in the territory.

Under the exclusive license agreement, we are responsible for funding all development and commercialization activities related to the products in our licensed territory, subject to certain exceptions pursuant to which Turning Point may be responsible for the cost. Turning Point will be responsible for funding global clinical studies of the licensed products. The agreement continues in effect until expiration of the last royalty term for a licensed product in any region in the licensed territory, where the royalty term for a licensed product in a region continues until the later of (i) the date of the last-to-expire valid claim within Turning Point's patent rights that covers the licensed product in such region in the licensed territory; (ii) the expiry of the regulatory exclusivity for such licensed product in such region; or (iii) the close of business of the day that is exactly 10 years after the date of the first commercial sale of such licensed product in such region. In addition, we may terminate the agreement for convenience by providing written notice to Turning Point, which termination will be effective following a prescribed notice period. Turning Point may terminate the agreement under specified circumstances if we or certain other parties challenge its patent rights. Either party may terminate the agreement for the other party's uncured material breach of the agreement, with a customary notice and cure period, for the other party's insolvency or if the other party is acquired in a change of control transaction and the acquirer is engaged in activities with a competing product that is not divested or discontinued within a specified period.

MacroGenics

In November 2018, we entered into a collaboration agreement with MacroGenics. Under the terms of the collaboration agreement, MacroGenics exclusively licensed to us regional development and commercialization rights to margetuximab, tebotelimab and an undisclosed multi-specific TRIDENT molecule in pre-clinical development, or the TRIDENT molecule, and, together with margetuximab and tebotelimab, each, a licensed product, in China, Hong Kong, Macau and Taiwan, or the territory. In partial consideration for the license grant to us for the territory, we paid MacroGenics a non-refundable, upfront license fee in the amount of US$25.0 million and two milestone payments in total of US$4.0 million. We also agreed to pay certain development and regulatory-based milestone payments up to an aggregate of US$136.0 million, and tiered royalties at percentage rates of mid-teens to 20% for net sales of Margetuximab in the territory, mid-teens for net sales of tebotelimab in the territory and 10% for net sales of TRIDENT molecule in the territory.

As part of the collaborative clinical development effort, we and MacroGenics intend to initiate a global study using combination regimens containing margetuximab in order to maximize potential clinical benefit in gastric cancer, the fifth most common cancer in the world and the second most common in China.

The collaboration agreement continues, on a region-by-region and licensed product-by- licensed product basis, in effect until the expiration of and payment by us of all of our payment obligations applicable to such licensed product and such region as specified in the collaboration agreement. Each party may terminate the collaboration agreement upon the material breach of the collaboration agreement by the other party, subject to certain cure periods. In addition, at any time after November 29, 2020, we may terminate the collaboration agreement for convenience with prior notice to MacroGenics. MacroGenics may terminate the collaboration agreement in its entirety or on a licensed product-by-licensed product basis with prior notice if one or more major safety issues have occurred with respect to such licensed product prior to the first commercial sale of such licensed product in the territory and MacroGenics has discontinued the global development, manufacturing and commercialization activities with respect to such licensed product.

Incyte

In July 2019, we entered into a collaboration and license Agreement with Incyte. Under the terms of the agreement, Incyte exclusively licensed to us the rights to perform clinical studies, sublicenseable to affiliates in China, Hong Kong, Macau and Taiwan without Incyte's consent and other affiliates and third parties (subject to Incyte's consent), sell, offer for sale and import retifanlimab (PD-1) in the field of the treatment, palliation, diagnosis or prevention of diseases in the fields of hematology or oncology in humans in China, Hong Kong, Macau and Taiwan. In partial consideration for the license grant to us for the territory, we paid Incyte a non-refundable, upfront license fee in the amount of US$17.5 million. We also agreed to pay certain development, regulatory and commercial milestone payments of up to an aggregate of US$60.0 million, and tiered royalties at percentage rates from low-to high-twenties on the net sales of retifanlimab (PD-1) in China, Hong Kong, Macau and Taiwan.

We will purchase licensed products exclusively from Incyte at Incyte's fully burdened manufacturing cost. The agreement continues, on a region-by-region and Licensed Product- by-Licensed Product basis, in effect until the expiration of and payment by us of all of our royalty payment obligations applicable to such Licensed Product and such region as specified in the agreement. Each party may terminate the agreement upon the material breach of a material term of the agreement by the other party, subject to the ability to cure. In addition, we may terminate the agreement for convenience on 60 days' prior notice, and Incyte may terminate the agreement due to our development or commercialization diligence failures, subject to the ability to cure and dispute resolution mechanisms if disputes arise with respect to such failure or material violation, each as defined in the agreement.

Five Prime

In December 2017, we entered into a license and collaboration agreement with Five Prime, under which we obtained exclusive rights to develop and commercialize Five Prime's proprietary afucosylated FGFR2b antibody known as bemarituzumab (FPA144), and all fragments, conjugates, derivatives and modifications thereof in China, Hong Kong, Macau and Taiwan, or the licensed territory.

We are responsible for (i) developing and commercializing licensed products under a territory development plan (ii) performing certain development activities to support Five Prime's global development and registration of licensed products, including Five Prime's global Phase III registrational trial of bemarituzumab (FPA144) in combination with FOLFOX in front-line gastric and gastroesophageal cancer, or the bemarituzumab (FPA144)-004 Study, in the licensed territory under a global development plan.

Under the terms of the agreement, we made an upfront payment of US$5.0 million and a milestone payment of US$2.0 million to Five Prime. Additionally, we may be required to pay further development and regulatory milestone payments of up to an aggregate of US$37.0 million to Five Prime.

We are also be obligated to pay Five Prime a royalty, on a licensed product-by-licensed product and region-by-region basis, in the high teens or low twenties, depending on the number of patients we enroll in the bemarituzumab (FPA144)-004 study, subject to reduction in certain circumstances, on net sales of each licensed product in the licensed territory until the latest of (i) the 11th anniversary of the first commercial sale of such licensed product in such region, (ii) the expiration of certain patents covering such licensed product in such region, and (iii) the date on which any applicable regulatory, pediatric, orphan drug or data exclusivity with respect to such licensed product expires in such region.

Under the terms of the agreement, provided that we enroll and treat a specified number of patients in the bemarituzumab (FPA144)-004 study in China, we are eligible to receive a low single-digit percentage royalty, on a licensed product-by-licensed product basis on net sales of a licensed product outside the licensed territory until the 10th anniversary of the first commercial sale of each such licensed product outside the licensed territory.

Unless earlier terminated by either party, the agreement will expire on a licensed product-by-licensed product and region-by-region basis upon the expiration of our payment obligations with respect to each licensed product under the agreement. We may terminate the agreement in its entirety at any time with advance written notice. Either party may terminate the agreement in its entirety with written notice for the other party's material breach if such party fails to cure the breach. Five Prime may terminate the agreement in its entirety with written notice for the material breach of our diligence obligations with respect to development and obtaining marketing approval, and may terminate the agreement on a region-by-region basis for the breach of our diligence obligations with respect to timely commercialization of a licensed product in a region following marketing approval. Five Prime may terminate the agreement in its entirety if we or one of our affiliates or sublicensees commences a legal action challenging the validity, enforceability or scope of any of Five Prime's patents in the licensed territory. Either party also may terminate the agreement in its entirety upon certain insolvency events involving the other party.

Paratek

In April 2017, we entered into a license and collaboration agreement with Paratek Bermuda, Ltd., a subsidiary of Paratek, under which we obtained both an exclusive license under certain patents and know-how of Paratek Bermuda Ltd. and an exclusive sub-license under certain intellectual property that Paratek Bermuda Ltd. licensed from Tufts University to develop, manufacture, use, sell, import and commercialize omadacycline (ZL-2401) in China, Hong Kong, Macau and Taiwan, or licensed territory, in the field of all human therapeutic and preventative uses other than biodefense, or the licensed field. Under certain circumstances, our exclusive sub-license to certain intellectual property Paratek Bermuda Ltd. licensed from Tufts University may be converted to a non-exclusive license if Paratek Bermuda Ltd.'s exclusive license from Tufts University is converted to a non-exclusive license under the Tufts Agreement. We also obtained the right of first negotiation to be Paratek Bermuda Ltd.'s partner to develop certain derivatives or modifications of omadacycline in our licensed territory. Paratek Bermuda Ltd. retains the right to manufacture the licensed product in our licensed territory for use outside our licensed territory. We also granted to Paratek Bermuda Ltd. a non-exclusive license to certain of our intellectual property for Paratek Bermuda Ltd. to develop and commercialize licensed products outside of our licensed territory. Under the agreement, we agreed not to commercialize certain competing products in our licensed territory. We are obligated to use commercially reasonable efforts to develop and commercialize the licensed products in our licensed field and licensed territory, including making certain regulatory filings within a specified period of time.

Under the terms of the agreement, we made an upfront payment of US$7.5 million and two milestone payments in total of US$8.0 million to Paratek Bermuda Ltd. and we may be required to pay further milestone payments of up to an aggregate of US$46.5 million to Paratek Bermuda Ltd. for the achievement of certain development and sales milestone events. In addition, we will pay to Paratek Bermuda Ltd. tiered royalties at percentage rates in the range of low-to mid-teens on the net sales of licensed products, until the later of the abandonment, expiration or invalidation of the last-to-expire licensed patent covering the licensed product, or the eleventh anniversary of the first commercial sale of the licensed product, in each case on a product-by-product and region-by-region basis.

The agreement with Paratek Bermuda Ltd. will remain in effect until the expiration of the royalty term and may be earlier terminated by either party for the other party's uncured material breach, bankruptcy or insolvency. In addition, we have the right to terminate the agreement for convenience at any time upon advance notice to Paratek Bermuda Ltd. Paratek Bermuda Ltd. has the right to terminate the agreement if we challenge its patents. Upon termination of the agreement, our license of certain intellectual property to Paratek Bermuda Ltd. will continue for Paratek Bermuda Ltd. to develop and commercialize licensed products worldwide.

Entasis

In April 2018, we entered into a collaboration and license agreement with Entasis under which we obtained exclusive rights to develop and commercialize Entasis' proprietary compounds known as durlobactam and SUL-DUR, with the possibility of developing and commercializing a combination of such compounds with Imipenem, in China, Hong Kong, Macau, Taiwan, Korea, Vietnam, Thailand, Cambodia, Laos, Malaysia, Indonesia, the Philippines, Singapore, Australia, New Zealand and Japan, or the territory. Our rights to develop and commercialize the licensed products are limited to the lead product (SUL-DUR) until such product receives FDA approval in the U.S.

Under the terms of the agreement, we are responsible for (i) developing and commercializing the licensed products in the territory under a mutually agreed development plan and (ii) providing Entasis (or its CRO) with clinical and financial support in the territory for the global pivotal Phase III clinical trial of SUL-DUR as set forth in mutually agreed development plans.

We made an upfront payment of US$5.0 million and two development milestone payments of US$7.0 million to Entasis. Additionally, we may be required to pay Entasis development, regulatory and research milestone payments (other than existing ones) and commercial milestone payments of up to an aggregate of US$91.6 million. We are also responsible for a portion of the costs of the global pivotal Phase III clinical trial of SUL-DUR outside of the territory.

We are also obligated to pay Entasis a royalty based on a percentage of net sales of licensed products ranging from the high single digits to low teens, depending on the amount of net sales of licensed products in the territory, subject to reduction in certain circumstances, until, with respect to a licensed product in a region in the territory, the latest of (i) the 10th anniversary of the first commercial sale of such licensed product in such region, (ii) the expiration of certain patents covering such licensed product in such region, and (iii) the date on which any applicable regulatory, pediatric, orphan drug or data exclusivity with respect to such licensed product expires in such region.

Unless earlier terminated by either party, the agreement will expire on a country-by- country basis upon the expiration of our payment obligations applicable to such country under the agreement. We may terminate the agreement in its entirety at any time with advance written notice. Either party may terminate the agreement in its entirety with written notice for the other party's material breach if such party fails to cure the breach. Entasis may terminate the agreement on a country-by-country basis if we cease to commercialize the licensed products in such country for a certain period of time. Entasis may terminate the agreement in its entirety if we or one of our affiliates or sublicensees commences a legal action challenging the validity, enforceability or scope of any of Entasis's patents in the licensed territory. Either party also may terminate the agreement in its entirety upon certain insolvency events involving the other party.

Bristol-Myers Squibb

In March 2015, we entered into a license agreement with BMS, under which we obtained an exclusive license under certain patents and know-how of BMS to develop, manufacture, use, sell, import and commercialize BMS's proprietary multi-targeted kinase inhibitor, brivanib in China, Hong Kong and Macau, or the licensed territory, in the field of diagnosis, prevention, treatment or control of oncology indications, or licensed field, with the exclusive right to expand our licensed territory to include Taiwan and Korea under certain conditions. BMS retains the non-exclusive right to use the licensed compounds to conduct internal research and the exclusive right to use the licensed compounds to manufacture compounds that are not brivanib. Under the agreement, we agreed not to develop and commercialize certain competing products for specified time periods.

We are obligated to use commercially reasonable efforts to develop and commercialize the licensed products in our licensed field and licensed territory. BMS has the option to elect to co-promote the licensed products in our licensed territory. If BMS exercises its co-promotion option, BMS will pay us an option exercise fee and we will share equally with BMS the operating profits and losses of the licensed products in our licensed territory.

If BMS does not exercise its co-promotion option, we may be required to pay BMS milestone payments for the achievement of certain development and sales milestone events of up to an aggregate of US$114.5 million, and also tiered royalties at percentage rates in the mid-to high-teens on the net sales of the licensed products in our licensed territory, until the later of the expiration of the last-to-expire licensed patent covering the licensed product, the expiration of regulatory exclusivity for the licensed product, or the twelfth anniversary of the first commercial sale of the licensed product, in each case on a product-by-product and region-by-region basis.

We also have the right to opt-out of the commercialization of the licensed products in our licensed territory under certain conditions. If we elect to opt-out, BMS will have the right to commercialize the licensed products in our licensed territory and will pay us royalties on the net sales of the licensed products in our licensed territory.

BMS has the option to use the data generated by us from our development of the licensed products to seek regulatory approval of the licensed products outside our licensed territory, and if BMS exercises such option, BMS will be obligated to make certain payments to us, including upfront, milestone and royalty payments.

The agreement with BMS will remain in effect until the expiration of all payment obligations, and may be earlier terminated by either party for the other party's uncured material breach, safety reasons or failure of the development of the licensed products. In addition, we have the right to terminate the agreement for convenience after a certain specified time period upon advance notice to BMS. BMS may also terminate the agreement for our bankruptcy or insolvency.

INTELLECTUAL PROPERTY

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our drug candidates and our core technologies and other know-how to operate without infringing, misappropriating or otherwise violating on the proprietary rights of others and to prevent others from infringing, misappropriating or otherwise violating our proprietary or intellectual property rights. We expect that we will seek to protect our proprietary and intellectual property position by, among other methods, licensing or filing our own U.S., international and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position, which we generally seek to protect through contractual obligations with third parties. As of the Latest Practicable Date, we were not involved in any proceedings in respect of, and we had not received notice of any claims of infringement of, any intellectual property rights that may be threatened or pending, in which we may be a claimant or a respondent.

Patents

Patents, patent applications and other intellectual property rights are important in the sector in which we operate. We consider on a case-by-case basis filing patent applications with a view to protecting certain innovative products, processes, and methods of treatment. We may also license or acquire rights to patents, patent applications or other intellectual property rights owned by third parties, academic partners or commercial companies which are of interest to us. For the internally developed drug candidates, we identify patents through both self-development effort and joint-development through collaboration with business partners such as academic institutions. We have global rights with respect to the patents identified through self-development effort, and we will be automatically granted with global rights with respect to the patents identified through joint-development efforts upon business partners' transfer of such patents to us under the terms of collaboration agreement.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our drug candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our pending patent applications, and any patent applications that we may in the future file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Any issued patents that we may receive or license in the future may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority of our patents and patent applications over third-party patents and patent applications. In addition, because of the extensive time required for clinical development and regulatory review of a drug candidate we may develop, it is possible that, before any of our drug candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting protection such patent would afford the respective product and any competitive advantage such patent may provide. For more information regarding the risks related to our intellectual property, please see "Risk Factors — Risks Related to Intellectual Property."

ZEJULA

As of June 30, 2020, we exclusively licensed two issued patents in China directed to ZEJULA's free base compound, and salts thereof, and analogues of ZEJULA. These issued patents are projected to expire between 2027 and 2028. We also exclusively licensed one pending patent application in China directed to a salt that covers 4-methylbenzenesulfonate monohydrate, the API of ZEJULA. If this patent application issues as a patent, such patent will be projected to expire in 2029. Besides, we also exclusively licensed one pending patent application in China directed to methods of treating ovarian cancer. If this patent application issues as a patent, such patent will be projected to expire in 2037. We have filed an application in China and a PCT application that cover intermediate synthesis process. The claims in the Chinese application had been allowed, and the PCT application has entered into the United States, the European Union, Israel, Japan, Korea and India. We own this PRC application and the PCT application.

Tumor Treating Fields

As of June 30, 2020, we licensed eight issued patents in China and one issued patent in Hong Kong that relate to Tumor Treating Fields. Additional patent applications that relate to Tumor Treating Fields are pending, including five in China and in Hong Kong. We are pursuing patent rights to protect our rights in these technologies and has continued our efforts to secure patent rights in China for our devices and technologies for applying electric fields to a patient for treating a disease or condition, especially diseases that promote tumor growth.

Ripretinib

As of June 30, 2020, we exclusively licensed one issued patent and two pending patent applications in China as well as one issued in Hong Kong directed to dihydronaphthyridines, the API of ripretinib. These issued patent and pending patent applications are projected to expire by 2032. We do not own or have an exclusive license to any patents or patent applications in any jurisdictions outside of China, Hong Kong, Macau or Taiwan.

Odronextamab

As of June 30, 2020, we exclusively licensed two issued patents in China, one issued patent in Hong Kong, five issued patents in Taiwan. These issued patents are directed to CD3/CD20 bispecific antibody odronextamab, and are projected to expire between 2030 and 2034. We have also exclusively licensed four pending patent applications in China, three pending patent applications in Hong Kong and two pending patent applications in Taiwan that relate to methods of tumor treatment using CD3/CD20 bispecific antibody and related combination therapy. If issued, claims of these patent applications are projected to expire between 2035 and 2037. We do not own or have an exclusive license to any patents or patent applications in any jurisdictions outside of China, Hong Kong, Macau and Taiwan.

Repotrectinib

As of June 30, 2020, we exclusively licensed one issued patent and two pending patent applications in China, one issued patent and two pending patent applications in Hong Kong, one issued patent and one pending patent application in Taiwan. These issued patents or pending applications are directed to Repotrectinib, and are projected to expire in 2025. We have also exclusively licensed three pending patent applications in China, three pending patent applications in Hong Kong and one pending patent application in Taiwan, that relate to chiral diaryl macrocycles, diaryl macrocycles polymorph, the use thereof and combination therapy involving diaryl macrocyclic compounds. If issued, claims of these patent applications are projected to expire between 2037 and 2038. We do not own or have an exclusive license to any patents or patent applications in any jurisdictions outside of China, Hong Kong, Macau or Taiwan.

Margetuximab

As of June 30, 2020, we exclusively licensed two pending patent applications in China and one issued patent in Hong Kong. The pending patent applications in this portfolio cover antibody sequences and therapeutic uses of margetuximab. The issued patent in Hong Kong that we exclusively licensed is projected to expire in 2029.

Retifanlimab

As of June 30, 2020, we exclusively licensed two pending patent applications in China, one issued patent and one pending patent application in Taiwan and one pending patent application in Hong Kong directed to the API of retifanlimab (PD-1). If these patent applications issue as patents, such patents will be projected to expire in 2036 to 2039. We do not own or have an exclusive license to any patents or patent applications in any jurisdictions outside of China, Hong Kong, Macau or Taiwan.

Tebotelimab

As of June 30, 2020, we exclusively licensed four pending patent applications in China, three pending patents in Hong Kong, and two issued patents and one pending patent application in Taiwan. The pending patent applications in this portfolio cover antibody sequences and therapeutic uses of tebotelimab. The issued patents that we exclusively licensed are projected to expire between 2035 and 2036.

Bemarituzumab

As of June 30, 2020, we exclusively licensed one issued patent in China and two issued patents in Hong Kong. These issued patents are directed to certain anti-FGFR2b antibodies, and are projected to expire in 2029. We have also exclusively licensed one pending patent application in China, two issued patents in Taiwan, one issued patent in Hong Kong. The issued patents that we exclusively licensed are projected to expire in 2034. Besides, we also exclusively licensed one pending patent applications in China and one pending patent applications in Taiwan directed to anti-FGFR2b antibodies in combination with immune stimulating agents in cancer treatment. We do not own or have an exclusive license to any patents or patent applications in any jurisdictions outside of China, Hong Kong, Macau and Taiwan.

Omadacycline

As of June 30, 2020, we exclusively licensed four issued patents in China directed to omadacycline's compound, formulations and crystal form and two pending patent applications in China directed to other crystalline forms of omadacycline. The issued composition of matter patent covering omadacycline is projected to expire in 2021 and the other three issued patents are projected to expire in 2029. We have also exclusively licensed one issued patent in Hong Kong and two issued patents in Taiwan, respectively that cover a crystalline salt form of omadacycline, which expire in 2029. We have also exclusively licensed four pending patent applications in China, three pending patent applications in Hong Kong and three pending patent applications in Taiwan, respectively that relate to different methods of treatment related to omadacycline. We do not own or have an exclusive license to any patents or patent applications in any jurisdictions outside of China, Hong Kong, Macau and Taiwan.

Durlobactam

As of June 30, 2020, we exclusively licensed one issued patent in China, one issued patent in Japan, and one corresponding issued patent or pending patent application in each of several additional jurisdictions in the territory covered by our agreement with Entasis, including Hong Kong, Taiwan and Korea. These issued patents or pending applications are directed to certain beta-lactamase inhibitor compounds, and are projected to expire in 2033. We have also exclusively licensed a second family of patent applications with three issued applications in China, Hong Kong and Australia and two pending patent applications in Taiwan and Korea. If issued, claims of these patent applications are projected to expire in 2035. We do not own or have an exclusive license to any patents or patent applications in any jurisdictions outside of the territory of the Entasis Agreement.

Brivanib

As of June 30, 2020, we exclusively licensed four issued patents in China and one issued patent in Hong Kong that relate to brivanib. Of these issued patents, two patent in China are composition-of-matter patents that cover the brivanib compound and its analogues, and are projected to expire in 2023. Our exclusively licensed patents also include a patent in China that covers a manufacturing process for intermediates useful in the synthesis of brivanib's API. This patent is projected to expire in 2027. In addition, one patent we exclusively licensed in China covers a crystal form of brivanib alaninate and is projected to expire in 2026. The issued patent in Hong Kong that we exclusively licensed is projected to expire in 2023. We do not own or have an exclusive license to any patents or patent applications in any jurisdictions other than China, Hong Kong and Macau.

The following table summarizes the details of the granted material patents and filed material patent applications in connection with our products and drug candidates.

Summary of granted material patents and filed material patent applications of our products and drug candidates

Product/Drug Candidate	Scope of Patent Protection	Jurisdiction (Country/Region)	Status	Commercial Rights of Zai Lab
ZEJULA	Directed to structure and its use	China and Hong Kong	Granted	Exclusive license to develop and commercialize in China, Hong Kong and Macau
	Directed to salts and their use	China	Pending	
	Directed to preparation process	United States, Japan, Europe, India, Israel and Korea	Pending	Owned by Zai Lab
		China	Granted	
Tumor Treating Fields	Directed to device and its use	China and Hong Kong	Granted	Exclusive license to develop and commercialize in China, Hong Kong, Macau and Taiwan
	Directed to detection method		Pending	
Ripretinib	Directed to structure and its use	China and Hong Kong	Granted	License to develop and commercialize in China, Hong Kong, Macau and Taiwan
Odronextamab	Directed to structure and its use	Taiwan	Granted	Exclusive license to develop and commercialize in China, Hong Kong, Macau and Taiwan
		China and Hong Kong	Pending	
	Directed to combination therapy	China	Pending	

Product/Drug Candidate	Scope of Patent Protection	Jurisdiction (Country/Region)	Status	Commercial Rights of Zai Lab
Repotrectinib	Directed to structure and its use	China, Hong Kong and Taiwan	Granted	Exclusive license to develop and commercialize in China, Hong Kong, Macau and Taiwan
		Macau	Pending	
	Directed to polymorph and its use	China and Hong Kong	Pending	
	Directed to combination therapy	China and Hong Kong and Taiwan	Pending	
Margetuximab	Directed to structure and its use	Hong Kong	Granted	Exclusive license to develop and commercialize in China, Hong Kong, Macau and Taiwan
		China	Pending	
Retifanlimab	Directed to structure and its use	Taiwan	Granted	Exclusive license to develop and commercialize in China, Hong Kong, Macau and Taiwan
		China and Hong Kong	Pending	
Tebotelimab	Directed to structure and its use	Taiwan	Granted	Exclusive license to develop and commercialize in China, Hong Kong, Macau and Taiwan
		China and Hong Kong	Pending	
Bemarituzumab	Directed to structure and its use	China and Hong Kong	Granted	Exclusive license to develop and commercialize in China, Hong Kong, Macau and Taiwan
Omadacycline	Directed to structure and its use	China and Hong Kong and Taiwan	Granted	Exclusive license to develop and commercialize in China, Hong Kong, Macau and Taiwan
	Directed to formulation and its use	China	Granted	
	Directed to salts and polymorphs and their use	China, Hong Kong and Taiwan	Granted	
	Directed to preparation process	China	Pending	
		Hong Kong	Granted	

Product/Drug Candidate	Scope of Patent Protection	Jurisdiction (Country/Region)	Status	Commercial Rights of Zai Lab
Durlobactam	Directed to structure and its use	New Zealand and Singapore	Pending	Exclusive license to develop and commercialize in China, Hong Kong, Macau, Taiwan, South Korea, Vietnam, Thailand, Cambodia, Laos, Malaysia, Indonesia, the Phillippines, Singapore, Australia, New Zealand and Japan
		China, Hong Kong, South Korea and Taiwan	Granted	
	Directed to combination therapy	China, South Korea, Japan, Taiwan, the Philippines and Singapore	Pending	
		Hong Kong and Australia	Granted	
Brivanib	Directed to structure and its use	China and Hong Kong	Granted	Exclusive license to develop and commercialize in China, Hong and Macau
	Directed to crystalline forms and its use	China	Granted	
	Directed to preparation process	China	Granted	

The term of a patent depends upon the laws of the country in which it is issued. In most jurisdictions that we principally operate in, a patent term is 20 years from the earliest filing date of a non-provisional patent application. Under China Patent Law, the term of patent protection starts from the date of application. Patents relating to inventions are effective for twenty years, and utility models and designs are effective for ten years from the date of application.

The laws of each jurisdiction vary, and patent term adjustment or patent term extension may not be available in any or all jurisdictions in which we own or license patents. For example, there are currently no patent term adjustments or patent term extensions available for issued patents in China. However, the government recently announced a proposal which is under consideration to allow a five-year patent term extension for innovative drugs if they will be concurrently reviewed for marketing authorizations in and outside China.

As of the Latest Practicable Date, we were not involved in any proceedings in respect of, and we had not received notice of any claims of infringement of, any intellectual property rights that may be threatened or pending, in which we may be a claimant or a respondent.

Trade Secrets

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and know-how can be difficult to protect. We seek to protect our proprietary information, in part, by executing confidentiality agreements with our partners, collaborators, scientific advisors, employees, consultants and other third parties, and invention assignment agreements with our consultants and employees. We have also executed agreements requiring assignment of inventions with selected scientific advisors and collaborators. The confidentiality agreements we enter into are designed to protect our proprietary information and the agreements or clauses requiring assignment of inventions to us are designed to grant us ownership of technologies that are developed through our relationship with the respective counterparty. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes or that these agreements will afford us adequate protection of our intellectual property and proprietary information rights. If any of the partners, collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements or otherwise discloses our proprietary information, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result.

Trademarks and domain names

We conduct our business using trademarks with various forms of the "ZAI LAB" and "再鼎醫藥" brands, as well as domain names incorporating some or all of these trademarks.

RESEARCH AND DEVELOPMENT

We believe research and development is critical to our future growth and our ability to remain competitive in the biopharmaceutical market in China. We are dedicated to discover or license, develop and commercialize proprietary therapeutics that address areas of large unmet medical need in the China and global markets, including in the fields of oncology, infectious and autoimmune diseases.

We have built an integrated drug discovery and development platform that aims to bring both in-licensed and internally-discovered medicines to patients in China and globally. We have assembled an in-house research and development team with nearly 400 dedicated personnel who have extensive experience from discovery, translational medicine to late stage development. Our in-house research and development team had previously been directly involved in the discovery and development of several innovative drug candidates at Hutchison Medi-Pharma, including fruquintinib and savolitinib. Our in-house research and development team focuses on the development of innovative therapeutics for the treatment of oncology and autoimmune diseases. We believe our discovery efforts will enable us to achieve our long-term goal of generating a sustainable, internally discovered product pipeline of new products and drug candidates for patients around the world. This effort has resulted in the identification of a number of proprietary candidates against targets in our focus areas that include immuno- oncology, DNA damage response/repair and oncogenic signaling that we are moving into pre-clinical development. Our company has a leadership team with extensive pharmaceutical research, development and commercialization track records in both global and Chinese biopharmaceutical companies. We believe this team and our in-house discovery and development capabilities will enable us to achieve our long-term goal of commercializing our internally discovered innovative medicine for patients worldwide. In addition, we collaborate with external research partners, such as leading CROs, academic institutions and commercial partners. We contract with these parties for execution of our pre-clinical and clinical trials. For details, see "— Suppliers."

For the years ended December 31, 2018 and 2019 and the six months ended June 30, 2020, our research and development expenses were US$120.3 million, US$142.2 million and US$102.0 million, respectively.

Clinical Development

We believe clinical development capabilities are critical to success in our industry. We have built internal clinical development capabilities, which we believe provide a competitive advantage over other biopharmaceutical companies in China. As of the Latest Practicable Date, we had 244 clinical development staff. Led by our experienced in-house clinical development team, we had more than over 25 ongoing or planned clinical trials in China, the United States and Australia across over 20 indications, as of the Latest Practicable Date. We believe that the global experience and local expertise of our clinical development team enables us to take advantage of significant regulatory reforms in China by integrating China and global clinical development.

Highlights of Our Research Efforts

The scope of research that we are permitted to conduct with respect to the in-licensed drug candidates is subject to the terms of respective license agreement. For example, with respect to ZEJULA, we have the right to develop ZEJULA for treatment, diagnosis and prevention of any human diseases or conditions (other than prostate cancer) in China, Hong Kong and Macau, which allows us to conduct a combination trial with tebotelimab in patients with advanced or metastatic gastric cancer who failed prior treatment. Janssen Biotech, Inc. entered a worldwide collaboration and license agreement with Tesaro (GSK) for exclusive rights to the investigational compound niraparib (ZEJULA) in prostate cancer in April 2016 before we entered the license agreement with Tesaro (GSK).To the extent further research and/or development is permitted under respective license agreement, we typically evaluate academic and/or industry research, pre-clinical and clinical results and rationale for clinical pharmacology to explore the possibility of treatment for diseases or conditions other than those that are being studied, or conducting combination trials with or among our drug candidates. For instance, we believe tebotelimab together with brivanib has the potential to treat HCC patients in China, given the relative high prevalence of HCC in China, and merits further clinical trials.

As our late-stage drug candidates had been in clinical development outside of China at the time when we in-licensed from our business partners, we have primarily focused our R&D on the clinical development of these drug candidates since the in-licensing. Typically, we formulate clinical development plans and clinical protocols that consider the characteristics of the Chinese population and clinical practices in China. We also investigate candidate hospitals to evaluate their suitability as potential clinical sites. To ensure consistency in clinical trial operations, we organize training sessions to educate potential investigators about clinical protocols. Below are select highlights of our research and/or clinical studies that we are conducting with respect to our late-stage drug candidates.

ZEJULA

- In May 2018, we completed enrollment ahead of schedule for our Phase I pharmacokinetics, or PK, study for Chinese patients with platinum-sensitive ovarian cancer. In August 2018, we completed our PK study for Chinese patients with platinum-sensitive ovarian cancer, which demonstrated a comparable efficacy profile to studies in non-Chinese patients.

- We initiated the Phase III study of ZEJULA (NORA Trial) in patients with recurrent platinum-sensitive ovarian cancer as a second-line maintenance therapy in September 2017 and completed NORA Trial in July 2020, at which time we completed the study report. The NORA trial met all primary and secondary endpoints with improved safety profile in Chinese patients. The full results from the NORA study will be presented at European Society for Medical Oncology (ESMO) 2020 Virtual Congress on September 19, 2020. We have obtained the NMPA approval for ZEJULA as treatment for patients with recurrent platinum-sensitive ovarian cancer as a second-line maintenance therapy.

- We dosed the first patient in registrational bridging trial for late-line ovarian cancer treatment in August 2020.

- On September 8, 2020, the NMPA approved our sNDA for ZEJULA as a maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy.

- In February 2020, we dosed the first patient in the Phase Ib dose escalation and expansion clinical study of ZEJULA in China, in combination with tebotelimab, for the treatment of patients with advanced or metastatic gastric adenocarcinoma or gastroesophageal junction adenocarcinoma (collectively as gastric cancer) who failed prior treatment.

- We plan to initiate additional indications and combinations for niraparib in collaboration with our partner GSK.

Tumor Treating Fields

- We have obtained MAA approval from NMPA for GBM without the need of a clinical trial.

- We plan to file MAA for mesothelioma in China in first half of 2021.

- We are collaborating with Novocure in a pilot Phase II study aimed to evaluate the efficacy and safety of Tumor Treating Fields concomitant with chemotherapy as first-line treatment of unresectable gastroesophageal junction or gastric adenocarcinoma initiated in Greater China.

- We are preparing to join global Phase III pivotal trials in non-small cell lung cancer, brian metastases and locally advanced pancreatic cancer in Greater China by early 2021.

- We are in the planning phase for clinical trials in liver cancer and ovarian cancer in Greater China.

Ripretinib

- We have completed patient enrollment for a bridging study to evaluate the safety, tolerability, and efficacy of ripretinib in patients with fourth-line GIST (i.e. with GIST who have received at least three prior lines of treatment) in China. We have submitted NDA to the NMPA based on the study results, which is under priority review.

- We have commenced a bridging study of ripretinib to assess efficacy, safety and pharmacokinetics in patients with second-line GIST (i.e. with GIST who was treated with imatinib) in China. Our CTA for the China bridging study has been approved by the NMPA.

- We are in the planning phase for clinical trials in systemic mastocytosis in China.

Odronextamab

- We are exploring regulatory approval pathways for odronextamab in R/R B-NHL in China by joining the global Phase II program with multiple, potentially registrational cohorts of different subtypes of R/R B-NHL.

- We have submitted Phase II pivotal CTA to the NMPA and plan to enroll the first Chinese patient into the potentially registrational global Phase II study by early 2021.

Repotrectinib

- We have submitted Phase II registrational CTA and anticipate opening additional sites in China to join the global TRIDENT-1 Phase II registrational clinical study of repotrectinib. TRIDENT-1 is an ongoing Phase I/II trial for the treatment of patients with ROS1+ advanced NSCLC and patients with NTRK+ advanced solid tumors.

Margetuximab

- We are conducting and dosed the first patient in a potentially registration enabling Phase II bridging trial study to evaluate the efficacy and safety of margetuximab plus chemotherapy head-to-head compared with trastuzumab plus chemotherapy in Chinese patients (Mainland China, Hong Kong and Taiwan) with advanced HER2+ breast cancer who have received at least two prior lines of anti-HER2 directed therapy in the metastatic setting and such prior lines of therapy must include trastuzumab (Herceptin) treatment.

- We expect to enroll the first Chinese patient in second half of 2020 in MacroGenics sponsored Phase II/III global studies of margetuximab (MAHOGANY) in combination with retifanlimab (PD-1) or tebotelimab (PD-1 x LAG-3) in the front-line treatment of HER2+ gastric cancer.

Tebotelimab

- In February 2020, we dosed the first patient in an open-label, single-arm, multicenter, Phase Ib dose escalation and expansion clinical study to assess the safety and antitumor activity of ZEJULA, in combination with tebotelimab, in patients with advanced or metastatic gastric cancer who failed prior treatment.

- We are conducting a Phase I/II dose escalation and expansion clinical study in China to evaluate the safety and efficacy of tebotelimab as monotherapy and in combination with brivanib in patients with advanced liver cancer.

- We expect to enroll Chinese patients in second half of 2020 in Phase II/III global MAHOGANY study of margetuximab in combination with retifanlimab or tebotelimab in gastric cancer sponsored by MacroGenics in HER2+ first line treatment of gastric cancer and to initiate MAHOGANY Cohort B in Greater China.

- We have obtained CTA in June 2020 and are conducting a Phase I (proof of concept) clinical trial for second-line melanoma in Greater China.

- We have obtained Phase I CTA approval in January 2020 and intend to enroll the first Chinese patient in the second half of 2020 for tebotelimab into its global Phase I basket trial sponsored by MacroGenics.

Retifanlimab

- We have also obtained Phase III CTA approval and plan to enroll the first Chinese patient into the Incyte-sponsored global Phase III study of retifanlimab with platinumbased chemotherapy in first-line metastatic squamous and nonsquamous non-small cell lung cancer in second half of 2020.

- Our CTA application for Phase II confirmatory study has been accepted for second-line MSI-high endometrial cancer. We plan to enroll the first Chinese patient into the Incyte-sponsored global Phase I/II potentially registration-enabling study in second half of 2020.

Bemarituzumab

- Our partner, Five Prime, announced the FIGHT trial has been converted to a Phase II randomized, double-blind trial, based on the approximately 150 patients enrolled. The Phase II FIGHT study is expected to generate clinical data to inform the further development strategy of bemarituzumab by the end of the year or early 2021. We have halted the enrollment in China, and will wait for our partner to provide further guidance.

Omadacycline

- We have completed a Phase III bridging study in China to evaluate the efficacy and safety of omadacycline for the treatment of ABSSSI and CABP, evidenced by the completion of the study reports. The NMPA granted priority review to the NDA for omadacycline for the treatment of ABSSSI and CABP in May 2020.

Sulbactam-Durlobactam

- In May 2020, we enrolled the first Chinese patient into the global Phase III ATTACK trial of durlobactam for Acinetobacter infections.

- We and our partner, Entasis Therapeutics, will cooperate in conducting the trial in China with us taking the operational lead by conducting the screening, enrollment and treatment of patients and coordinating development, registration and commercialization of SUL-DUR in specified countries in the Asia-Pacific region including Japan.

ZL-1201

- We are conducting a Phase I study of anti-CD47 antibody in subjects with advanced cancer in the US. The major aims of the study are to define the safety, tolerability and preliminary antitumor activity of this new drug, and to determine a recommended dose and schedule for potential additional trials.

ZL-1102

- We are conducting a Phase I study in Australia to investigate the safety, tolerability, efficacy and pharmacokinetics of ZL-1102 in subjects with mild-to-moderate chronic plaque psoriasis.

Our Scientific Advisory Board

Our research and development capabilities are supplemented by support from our Scientific Advisory Board, which currently comprises of five globally renowned biophysicists and key opinion leaders, including Lieping Chen, M.D., Ph.D., Richard A. Flavell, Ph.D., Neal Rosen, M.D., Ph.D., Timothy Yap, M.D., Ph.D. and Alex A. Adjei, M.D., Ph.D., FACP.

Lieping Chen, M.D., Ph.D. has served on our Scientific Advisory Board since 2018. Dr. Chen is the scientific founder and Chair of the Scientific Advisory Board of NextCure (NASDAQ ticker: NXTC), a clinical-stage biopharmaceutical company focused on discover and developing novel immunomedicines to treat cancer. Dr. Chen is the United Technologies Corporation Professor in Cancer Research, Co-Director of the Cancer Immunology Program at the Yale Cancer Center and a Professor of Immunobiology, Dermatology and Medicine (Medical Oncology) at the Yale University School of Medicine.

Richard A. Flavell, Ph.D., FRS has served on our Scientific Advisory Board since 2017. Since 2002, Dr. Flavell has been the Sterling Professor of Immunobiology at Yale University School of Medicine.

Neal Rosen, M.D., Ph.D. has served on our Scientific Advisory Board since 2016. Dr. Rosen is the scientific advisor of the following companies: Ribon Therapeutics, a clinical-stage biotechnology company focused on the discovery and development of molecular inhibitors to block the fundamental ability of cancer cells to survive under stress; BeiGene (NASDAQ ticker: BGNE), a commercial-stage biopharmaceutical company focused on the discovery, development and commercialization of molecularly targeted and immune-oncology drugs for the treatment of cancer; and Kura Oncology Inc., (NASDAQ ticker: KURA) a clinical-stage biopharmaceutical company focuses on the discovery and development of personalized therapeutics for the treatment of tumors and blood cancers. Dr. Rosen is a Member of the Department of Medicine and a Member of the Molecular Pharmacology and Chemistry Program at Memorial Sloan Kettering Cancer Center, where he serves as Head of Developmental Therapeutics.

Timothy Yap, M.D., Ph.D. has served on our Scientific Advisory Board since 2019. Dr. Yap is the scientific advisor of the following companies: I-MAB (NASDAQ ticker: IMAB), a clinical stage biopharmaceutical company focuses on the discovery, development and commercialization of novel biologics to treat diseases with significant unmet medical needs, particularly cancers and autoimmune disorders; and Cybrexa Therapeutics (also known as Cybrexa Inc.), an oncology-focused biotechnology company. Dr. Yap is an Associate Professor in the Department of Investigational Cancer Therapeutics and Medical Director of The Institute for Applied Cancer Science at The University of Texas MD Anderson Cancer Center, Houston, TX.

Alex A. Adjei, M.D., Ph.D., FACP has served on our Scientific Advisory Board since 2019. Dr. Adjei is a Consultant in Oncology, Professor of Oncology and Professor of Pharmacology at Mayo Clinic and Mayo College of Medicine, in Rochester, MN.

We believe by virtue of the valuable and unique expertise and insights of the members of our Scientific Advisory Board in various disciplines, we are able to further enhance our research and development capabilities. As of the Latest Practicable Date, we are not aware of any conflict of interest of between any member of our Scientific Advisory Board and us.

SALES AND MARKETING

Commercialization

As we believe the scale and sophistication of our commercial operation are crucial to our business, we have invested, and will continue to invest, substantial financial and management resources to build out our commercial infrastructure and to recruit and train sufficient additional qualified marketing, sales and other personnel in support of the sales of our commercialized products. We successfully launched ZEJULA in Hong Kong in the fourth quarter of 2018 and achieved over majority market share in the PARP inhibitor category with in terms of sales in 2019. Leveraging the valuable marketing experience and strong physician endorsement we accumulated from the successful commercial launch of ZEJULA, we launched Optune in Hong Kong in December 2018. As of the Latest Practicable Date, we have commercialized ZEJULA in Hong Kong, Macau and China, and Optune in Hong Kong and China. We believe our initial commercial success in Hong Kong allows us to establish our commercial presence in Greater China.

As of the Latest Practicable Date, our commercialization team consisted of 401 sales and marketing staff, covering major medical centers across Greater China. Our commercialization team has a proven track record and experience from top-selling oncology multinational pharmaceutical companies including AstraZeneca, Roche, Novartis and BMS in China. In anticipation of the increased market demand for ZEJULA and Optune in China, and more late-stage drug candidates becoming available for sale, if approved, we plan to further expand our sales and marketing force in the next few years to scale up the precedence of our ZEJULA and Optune in China and ramp up the sales of our commercialized products in the target markets.

Our commercial team has capabilities that cover the product sales cycle, including medical affairs, market access, and distributor management. We tailor our commercialization strategies according to our individual products and their different market potential to drive product launch and ensure post-launch success. For ZEJULA, we plan to increase market penetration in China and substantially increase our hospital coverage in China by 2021. To implement this commercial strategy, we plan to increase the number of sales in our ZEJULA sales team to facilitate greater product access for more patients. For Optune, we plan to increase brand awareness in China and provide more post-launch product support services to patients in China. To implement this commercial strategy, we plan to increase the number of device support staff to build up our Optune product service team.

We consider many factors in determining our pricing strategies and we continuously monitor market prices as development and clinical and regulatory progress of other similar drug candidates. As of the Latest Practicable Date, ZEJULA in China is priced at RMB24,990 per box with 2 boxes per month, which leads to monthly end-patient price of RMB49,980. In China, we have collaborated with charitable foundations to provide patient assistance program (PAP) to patients who meet certain medical and socioeconomic criteria. Under the PAP, eligible patients are able to receive one box of ZEJULA free for every box purchased. After being treated with a total of 24 boxes, they are also entitled to receive free boxes of ZEJULA until disease progression.

With respect to the pricing details of LYNPARZA, according to Frost & Sullivan, after reimbursement under the NRDL (which is only available for second-line treatment), as of the Latest Practicable Date, it is priced at RMB9,464 per box with 2 boxes per month, which leads to monthly end-patient price being RMB18,928. Patient will self-pay 5% to 30% of the total cost, depending on the regional reimbursement policies, according to the Frost & Sullivan Report.

As of the Latest Practicable Date, monthly end-patient price for Optune in China is RMB132,998 per month. Similar to ZEJULA, for Optune, we have also collaborated with charitable foundations to provide PAP to patients who meet certain medical and socioeconomic criteria. Under the PAP, eligible patients can buy one month's supply of Optune transducer array (an accessory component of Optune) and get one month's supply for free. After this initial one-month supply period, patients can qualify for further assistance under the PAP.

With respect to the patient cost of TMZ, a chemotherapy used for the treatment of GBM, the total monthly cost is in the range of RMB13,000 to RMB33,000; and after reimbursement under the NRDL, depending on whether it is generic or original, patients are estimated to pay in the range of RMB2,600 to RMB6,000 on a monthly basis, according to the Frost & Sullivan Report.

As of the Latest Practicable Date, neither of ZEJULA nor Optune was subject to the bulk procurement program in China.

Our Distribution Channel

We rely on our independent third party distributors in China to sell our commercialized products, which is consistent with the pharmaceutical industry norm. We believe our distributors help us effectively execute our marketing strategies specifically tailored to each geographical location and the hospitals located within their locations across China. We started to engage distributors in China in 2020 after we launched ZEJULA and Optune in China to rapidly ramp up sales of these two commercialized products. As of the Latest Practicable Date, we had collaborated with 48 such distributors in China, which are independent third parties, and have not terminated the relationship with any of our distributors. The relationship between our distributors and us constitutes a seller and buyer relationship. Accordingly, we recognize revenue when our products are delivered to and accepted by the distributors.

We selected our distributors based on their business qualifications and distribution capabilities, such as distribution network coverage, quality, number of personnel, cash flow conditions, creditworthiness, logistics, compliance standard and past performance, and its capacities in customer management. As of the Latest Practicable Date, we were not aware of any potential abuses or improper use of our name by our distributor which could adversely affect our reputation, business operation or financial condition.

Set forth below are the key contractual terms of our agreements with our distributors in the PRC:

- *Duration and termination*. The distribution agreement typically has a term of one year, subject to early termination by us upon at least 90 days' prior written notice or under certain conditions provided in the agreement. The term of agreement can be renewed by mutual agreement.

- *Geographic exclusivity*. Our distributors shall not sell or otherwise distribute the products outside the PRC, unless otherwise agreed by us in writing.

- *Rights and obligations of parties involved*. We offer rebates to our distributors, consistent with pharmaceutical industry practice. We retain no ownership control over the products sold to our distributors, and all significant risks (including inventory risks) and rewards associated with the products are generally transferred to the distributors upon delivery to and acceptance by the distributors.

- *Sales and pricing policies*. We sell our products to our distributors at a fixed price provided in the agreement, which is subject to change upon a 30 days' prior notice by us. Our distributors retain the discretion to determine the retail prices with reference to local market conditions, competition and customer demand in the regions where they operate, whether greater or lesser than any prices charged by us.

- *Obsolete stock arrangements*. There is no obsolete stock arrangements condition.

- *Return and exchange policy*. We have in place a return and exchange policy that is in line with industry practice. Our distributors may submit return or exchange applications to us, which shall provide the details of the products to be returned or exchanged. Upon inspection and approval by us, we fully or partially refund the returned products and we typically allow exchange for the same type of products. We had not experienced any material product return during the Track Record Period.

- *Sales and inventory reports and estimates*. Our distributors shall provide to us monthly reports containing full details about the sales, products sold, inventory and forecasts of the products.

- *Minimum sales target and purchase amounts*. We do not require our distributors to meet any minimum sales target and purchase amounts. Our distributors may from time to time place orders for our products depending on their own demands.

- *Payment and credit terms*. Credit term is generally 40 days following the invoice date.

- *Use of confidential information*. Our distributors shall have a non-sublicensable, non-transferable, non-assignable and non-exclusive right to use our confidential information, including trademark, in connection with selling our products during the contract term.

We started to engage distributors in China in 2020 after we launched ZEJULA and Optune in China to rapidly ramp up sales of these two commercialized products. Four of our five largest customers in the six months ended June 30, 2020 are also major distributors for the same period. For their background information, please see "— Customers".

MANUFACTURING

We currently operate two manufacturing facilities in Suzhou, China, which support clinical and commercialized production of certain of our products and drug candidates, including ZEJULA, one of our Core Products. We do not manufacture Optune, one of our Core Products; instead, we source Optune from our licensor, Novocure.In early 2017, we built a cGMP-compliant small molecule facility in Suzhou capable of supporting clinical and commercialized production. In 2018, we completed construction of a large molecule facility in Suzhou using GE Healthcare FlexFactory platform technology capable of supporting the clinical production of our drug candidates. We are investing in the expansion of the manufacturing site to anticipate the increased sales of our current commercialized products and the launch of our clinical drug candidates. We believe that possessing manufacturing and commercialization capabilities presents benefits, which include maintaining better control over the quality and compliance of our operations with increasingly stringent industry regulations. As of the Latest Practicable Date, our manufacturing team consisted of 60 employees.

Our two manufacturing facilities feature an oral solid dosage and a biological processing/formulation production lines and are designed to comply with both the PRC and PIC/S drug manufacturing standards. The facilities cover the entire production process from mixing, roller compression, tableting to bottling. We procure our manufacturing equipment from leading domestic and international suppliers. We have acquired manufacturing licenses for both oral solid dosage and biological facilities, and are in the process of applying MAH manufacturing license. We have passed an onsite inspection by NMPA for ZEJULA, our first commercialized product. We expect our two manufacturing facilities to be able to satisfy the commercial as well as clinical needs and support the growth of our business in the near future.

Our small molecule manufacturing facility mainly supports the commercial production of ZEJULA. The production capacity of our small molecule manufacturing facility is up to 50 million units per year for both commercial oral tablets and capsules. During the Track Record Period, less than 10 percent of the total production capacity of our small molecule manufacturing facility was utilized. Our large molecule manufacturing facility supports the clinical production of ZL-1201. The annual production capacity of our large molecule manufacturing capacity is up to eighteen 1,000 liter clinical batches of large molecule drug substance. During the Track Record Period, approximately 40% of the production capacity of our large molecule manufacturing facility was utilized.

In addition, we outsource to a limited number of external CMOs the production of some drug substances and drug products, and we expect to continue to do so to meet the preclinical, clinical and commercial requirements of our drug products and candidates. By outsourcing a portion of our manufacturing activities, we can increase our focus on core areas of competence such as drug candidate development, commercialization and research. We have adopted procedures to ensure that the production qualifications, facilities and processes of our third-party CMOs comply with the relevant regulatory requirements and our internal guidelines. We select our CMOs carefully by taking into account a number of factors, including their qualifications, relevant expertise, production capacity, geographic proximity, reputation, track record, product quality, reliability in meeting delivery schedules, and terms offered by such CMOs. As of the Latest Practicable Date, we had engaged approximately six CMOs, who are independent third parties. Under the respective licensing and/or collaboration agreements, we have the right to manufacture ZEJULA and omadacycline.We use Asymchem Laboratories as the API (chemical) MAH for ZEJULA and omadacycline. We also use Zhejiang Hisun Pharmaceutical and Haimen Pharma as the formulation (manufacturing) MAH for omadacycline. We believe we have readily accessible alternative suppliers to provide the raw materials necessary to manufacture ZEJULA and omadacycline. In light of the current situations and the peculiarities of the biopharmaceutical industry, we are of the view that the U.S. — China tension has not had any material impact on our business operations and manufacturing, including our collaborations with business partners. Please refer to "Risk Factors — Changes in U.S. and international trade policies and relations, particularly with regard to China, may adversely impact our business and operating results."

We enter into agreements with our CMOs, under which they generally provide services to us on a short-term and project-by-project basis. Agreements with our CMOs typically set out terms, including but not limited to product quality or service details, technical standards or methods, delivery terms, agreed price and payment, and product inspection and acceptance criteria. Our CMOs procure raw materials themselves. We are required to make payments to the CMOs in accordance with the payments schedule set forth in the agreement. We may terminate the agreements by serving a 30 days' prior notice to the CMO.

CUSTOMERS

We commercially launched ZEJULA in Hong Kong in the fourth quarter of 2018 and started to generate revenue from the sales of ZEJULA to our customers. As we continued to expand our footprint across China with our successful launch of ZEJULA and Optune in China in January 2020 and May 2020, respectively, we have been rapidly broadening our customer base and deriving substantial revenue from our distributors in China. For details of the commercial arrangements with our distributors in China, see "— Sales and Marketing — Our Distribution Channel."

During the Track Record Period, our top five customers accounted for 89.6%, 85.0% and 44.5% of our total revenues for the years ended December 31, 2018 and 2019 and the six months ended June 30, 2020, respectively. During the same period, revenues from our largest customer accounted for approximately 39.6%, 41.6% and 16.8% of our total revenues, respectively.

Please see below a summary of the sales to our five largest customers for the periods indicated:

Five Largest Customers for the year ended December 31, 2018	Customer Background	Covered Region	Our Products	Sales Amount	Percentage of Total Revenue
				US$'000	
Customer A	A private medical center	Hong Kong	ZEJULA	51.3	39.6%
Customer B	A private oncology center	Hong Kong	ZEJULA	34.2	26.4%
Customer C	A private clinic specializing internal medicine oncology	Hong Kong	ZEJULA	13.7	10.6%
Customer D	Aprivate clinical oncologycenter	Hong Kong	ZEJULA	10.0	7.7%
Customer E	A private clinic specializing clinical oncology	Hong Kong	ZEJULA	6.8	5.3%
Total				116.0	89.6%

Five Largest Customers for the year ended December 31, 2019	Customer Background	Covered Region	Our Products	Sales Amount	Percentage of Total Revenue
				US$'000	
Customer A	A private medical center offering medical services in general medicine, specialist areas as well as out-patient surgeries, diagnostic screening, etc.	Hong Kong	ZEJULA	5,397.2	41.6%
Customer F	A private oncology center	Hong Kong	Optune	4,682.4	36.1%
Customer G	A private medical group	Hong Kong	ZEJULA and Optune	541.8	4.2%
Customer H	A private general hospital	Hong Kong	ZEJULA	223.4	1.7%
Customer I	A public district general hospital	Hong Kong	ZEJULA	186.1	1.4%
Total				11,030.9	85.0%

Five Largest Customers for the six months ended June 30, 2020	Customer Background	Covered Region	Our Products	Sales Amount	Percentage of Total Revenue
				US$'000	
Customer J	A pharmaceutical distributor	China	ZEJULA and Optune	3,236.2	16.8%
Customer F	A private oncology center	Hong Kong	Optune	1,815.1	9.5%
Customer K	A pharmaceutical distributor	China	ZEJULA	1,774.5	9.2%
Customer L	A pharmaceutical distributor	China	ZEJULA	961.1	5.0%
Customer M	A pharmaceutical distributor	China	ZEJULA	769.5	4.0%
Total				8,556.3	44.5%

As of the Latest Practicable Date, none of our directors or any shareholder, who, to the knowledge of our directors, owns more than 5% of our issued share capital immediately following completion of the Global Offering (but without taking into account the exercise of the over-allotment option) nor any of their respective associates had any interest in any of our five largest customers.

SUPPLIERS

During the Track Record Period, our suppliers consisted primarily of (i) third party licensors from which we obtained license rights in respect of our in-licensed products and drug candidates; (ii) selected CROs; and (iii) suppliers of other raw materials for our clinical trial activities. For details of the agreements with our licensors, see "— Overview of Our License and Strategic Collaboration Agreements."

We engage a limited number of highly reputable third-party CROs to monitor, manage data and execute for some of our ongoing pre-clinical and clinical programs. We select our CROs by considering their track record, industry reputation, compliance with relevant regulatory agencies and cost competitiveness.

We obtain raw materials for our clinical trial activities from multiple suppliers who we believe have sufficient capacity to meet our demands. In addition, we believe that adequate alternative sources for such supplies exist. However, a risk exists that an interruption to supplies would materially harm our business. We typically order raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements. While we do experience price fluctuations associated with our raw materials, we have not experienced any material disruptions in the supply of these raw materials in the past. In addition, we have suppliers across the world and do not rely exclusively on the imports from the suppliers in the U.S. In particular,

- with respect to our ZEJULA, we have been using Asymchem Laboratories, a PRC-based company, as the API (chemical) MAH. In addition, we operate a small molecule manufacturing facility, mainly supporting the commercial production of ZEJULA. During the Track Record Period, we have not experienced any material disruptions to the supplies or manufacturing of ZEJULA. We believe reasonable alternatives to Asymchem Laboratories are readily accessible. Furthermore, we plan to source domestically manufactured drug substances if the supply from overseas are not available; and

- with respect to Optune and our other late-stage drug candidates, we primarily rely on the supplies from our licensors who have global manufacturing capabilities. During the Track Record Period, we have not experienced any material disruptions to the supplies or manufacturing of such late-stage candidates and we expect to be able to maintain adequate sources of quality supplies in the foreseeable future. However, we cannot guarantee that we will always have access to such supplies at reasonable price or at all. See "Risk Factors — We rely on supplies from our licensors, which may severely harm our business and results of operations."

For the years ended December 31, 2018 and 2019 and the six months ended June 30, 2020, purchases from our five largest suppliers accounted for approximately 52.0%, 44.3% and 50.3% of our total purchases, respectively. During the same period, purchases from our largest supplier accounted for approximately 21.2%, 19.7% and 28.9% of our total purchases, respectively.

The table below sets forth the details of our five largest suppliers during the Track Record Period.

Five Largest Supplier for the Year ended December 31, 2018	Supplier Background	Type of Products/Services Provided	Purchase Amount	Percentage of Total Purchase
			US$'000	
Supplier A*	A biopharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and clinical supplies and manufacturing related activities	25,515.2	21.2%
Supplier B*	An oncology company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and purchase of inventory	14,664.4	12.2%
Supplier C*	A biopharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and development and research services	11,124.4	9.3%
Supplier D	A private company providing R&D and one-stop production services	Manufacturing of active pharmaceutical ingredients	6,147.0	4.9%
Supplier E*	A biopharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates	5,307.1	4.4%
Total			62,758.0	52.0%

*Note: * a US publicly listed company*

Five Largest Supplier for the Year ended December 31, 2019	Supplier Background	Type of Products/Services Provided	Purchase Amount	Percentage of Total Purchase
			US$'000	
Supplier F*	A biopharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and development and research services	27,965.8	19.7%
Supplier G*	A pharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and development and research services	18,362.3	12.9%
Supplier H*	A pharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and development and research services	8,918.8	4.8%
Supplier D	A private company providing R&D and one-stop production services	Manufacturing of active pharmaceutical ingredients	7,862.7	3.8%
Supplier C*	A biopharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and development and research services	4,588.9	3.2%
Total			67,698.5	44.3%

*Note: * a US publicly listed company*

Five Largest Supplier for the Six Months ended June 30, 2020	Supplier Background	Type of Products/Services Provided	Purchase Amount	Percentage of Total Purchase
			US$'000	
Supplier I*	A biopharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and development and research services	31,022.0	28.9%
Supplier B*	An oncology company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and purchase of inventory	12,312.8	11.5%
Supplier A*	A biopharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and clinical supplies and manufacturing related activities	5,204.5	4.9%
Supplier E*	A biopharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates	3,018.6	2.8%
Supplier F*	A biopharmaceutical company	Licensor from which we obtained intellectual property rights in respect of our in-licensed drug candidates and development and research services	2,428.5	2.3%
Total			53,986.4	50.3%

*Note: * a US publicly listed company*

As of the Latest Practicable Date, none of our directors or any dhareholder, who to the knowledge of our directors, owns more than 5% of our issued share capital immediately following completion of the Global Offering (but without taking into account the exercise of the over-allotment option) nor any of their respective associates had any interest in any of our five largest suppliers.

PROPERTIES

We are headquartered in Shanghai where we have our main administrative and laboratory offices, which is 3,632 square meters in size. The lease for this facility expires in 2023. We also have a 2,475 square meter commercial office for in Shanghai, the lease for which expires in 2022, and a 493 square meter office in Beijing, the lease for which expires in 2020. We have a 445 square meter commercial office in Hong Kong, the leases for which expire in 2022. We lease an administrative office in Guangzhou from a third party.We also have a 2,652 square feet administrative office and an 18,707 square feet laboratory office in San Francisco, the leases for which expire in 2021 and 2026, respectively. We also lease from a third party an administrative office in Boston. In early 2017, we built a small molecule drug product facility in Suzhou, China, capable of supporting clinical and commercialized production, which is 4,223 square meters. The lease for this facility expires in 2023. In 2018, we built a large molecule facility in Suzhou, China, using GE Healthcare FlexFactory platform technology capable of supporting clinical production of our drug candidates, which is 4,223 square meters. The lease for this facility expires in 2021 and we do not expect difficulties in renewing such lease. The cost to complete the small molecule facility was approximately US$6.7 million and was paid with cash on hand. The construction of the large molecule facility was completed in 2018, which cost approximately US$12.9 million and was financed with cash. We believe our current facilities are sufficient to meet our near-term needs. In 2019, we acquired land use rights of 50,851 square meters in Suzhou for the purpose of constructing and operating the research center and biologics manufacturing facility in Suzhou. The terms of the land use rights are 30 years.

COMPETITION

Our industry is highly competitive and subject to rapid and significant change. While we believe that our management's research, development and commercialization experience provide us with competitive advantages, we face competition from global and China-based biopharmaceutical companies, including specialty pharmaceutical companies, generic and biosimilar drug companies, biologics drug companies, academic institutions, government agencies and research institutions.

For our global drug candidates, we expect to face competition from a broad range of global and local pharmaceutical companies. Many of our competitors have significantly greater financial, technical and human resources than we have, and mergers and acquisitions in the biopharmaceutical industry may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop or market products or other novel therapies that are more effective, safer or less costly than our current or future drug candidates, or obtain regulatory approval for their products more rapidly than we may obtain approval for our drug candidates.

INSURANCE

We maintain insurance policies that are required under PRC laws and regulations as well as based on our assessment of our operational needs and industry practice. We maintain liability insurance for certain clinical trials, which covers the patient human clinical trial liabilities such as bodily injury, product liability insurance to cover our product liability claims and general insurance policies covering property loss due to accidents or natural disasters. We do not maintain insurance to cover intellectual property infringement, misappropriation or violation. We do not maintain "key person" insurance for any of our executives or other employees. We believe the coverage of the insurance obtained by us is adequate and consistent with industry norm for our business and operations.

EMPLOYEES

As of the Latest Practicable Date, we had 913 full-time employees, 886 of which were located in Greater China and 27 were located abroad. Of the total of 913 full-time employees, 377 employees are in R&D department. The number of employees by function as of Latest Practicable Date was as follows:

By Function	Number of employees
Research and Development	377
Commercial	401
Manufacturing	64
General and Administrative	71
Total	913

We provide formal and comprehensive company-level and department-level training to our new employees followed by on-the-job training. We also provide training and development programs to our employees from time to time to ensure their awareness and compliance with our various policies and procedures. Given our emphasis on operating a seamless, fully- integrated platform for our drug development processes, some of the training is conducted jointly by different groups and departments serving different functions but working with or supporting each other in our day-to-day operations.

As required under PRC regulations, we participate in housing fund and various employee social security plans that are organized by applicable local municipal and provincial governments, including housing, pension, medical, work-related injury and unemployment benefit plans, under which we make contributions at specified percentages of the salaries of our employees. As advised by our PRC Legal Advisor, we had complied with all statutory social security plans and housing fund payment obligations in all material respects.

None of our employees is represented by a labor union or covered by a collective bargaining agreement. We believe that we maintain good working relationship with our employees and we have not experienced any material labor disputes or any difficulty in recruiting staff for our operations during the Track Record Period and up to the Latest Practicable Date.

Employment Agreements with Key Management and Research Staff

We enter into standard confidentiality and employment agreements with our research staff and each of our executive officers and our directors (other than our non-employee directors). The contracts with our key personnel generally include a standard non-compete clause that prohibits the employee from competing with us, directly or indirectly, during his or her employment and for generally two years after the termination of his or her employment. As advised by our PRC Legal Advisor, to the extent such contracts governed by PRC laws, the non-compete clause set forth therein is legally enforceable.The contracts also typically include undertakings regarding assignment of inventions and discoveries made during the course of his or her employment. For further details regarding the terms of confidentiality and employment agreements with our key management, please refer to the section headed “Directors and Senior Management”.

Dr. Du is employed by Zai Lab Limited, pursuant to an employment agreement that became effective December 1, 2018 and Dr. Du is also a party to an employment agreement with Zai Lab (Shanghai) Co., Ltd. (In addition, Dr. Du has entered into an agreement with our U.S. subsidiary, Zai Lab (US) LLC, pursuant to which a portion of her base salary will be paid by Zai Lab (US) LLC based on the level of services that she provides this entity). Dr. Fu, Dr. Reinhart and Mr. Edmondson are each employed by Zai Lab (US) LLC pursuant to employment agreements and amended and restated employment agreements that became effective on January 25, 2019, December 1, 2018 and August 15, 2020, respectively. Dr. Hei is employed by Zai Lab (US) LLC and also party to an employment agreement with Zai Lab (Shanghai) Co., Ltd. Mr. Cho is employed by Zai Lab (Hong Kong) Limited. Mr. Liang is employed by Zai Lab (Shanghai) Co. Ltd.

QUALITY CONTROL AND ASSURANCE

We have our own independent quality control system and devote significant attention to quality control for the designing, manufacturing and testing of our drug candidates. We have established a strict quality control system in accordance with NMPA regulations. Our laboratories are staffed with highly educated and skilled technicians to ensure quality of all batches of products released. We monitor our operations in real time throughout the entire production process, from inspection of raw and auxiliary materials, to manufacture and delivery of finished products to clinical testing at hospitals. Our quality assurance team is also responsible for ensuring that we are in compliance with all applicable regulations, standards and internal policies. Our senior management team is actively involved in setting quality policies and managing the internal and external quality performance of the Company.

LEGAL PROCEEDINGS AND COMPLIANCE

As of the Latest Practicable Date, we were currently not a party to any actual or threatened material legal or administrative proceedings. We are committed to maintaining the highest standards of compliance with the laws and regulations applicable to our business. However, we may from time to time be subject to various legal or administrative claims and proceedings arising in the ordinary course of business.

ENVIRONMENT MATTERS AND WORKPLACE SAFETY

We strive to operate our facilities in a manner that protects the environment and the health and safety of our employees, patients and communities. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. We have implemented company-wide environmental, health and safety (EHS) manuals, policies and standard operating procedures.

We have not had any significant workplace accidents in the history of our Company.

During the Track Record Period and up to the Latest Practicable Date, we had not been subject to any fines or other penalties due to non-compliance with environment and workplace safety regulations.

PERMITS, LICENSES AND OTHER APPROVALS

As of the Latest Practicable Date, we had obtained all requisite licenses, approvals and permits from relevant authorities that are material to our operations.

RISK MANAGEMENT AND INTERNAL CONTROL

Risk Management

We have adopted a consolidated risk management methodology and program which set out a risk management framework to identify, assess, evaluate and monitor key risks associated with our strategic objectives on an on-going basis. Our audit committee, and ultimately our directors supervise the implementation of our risk management programs. Risks identified by management will be analyzed on the basis of likelihood and impact, and will be properly followed up and mitigated and rectified by our Group and reported to our directors.

The following key principles outline our Group’s approach to risk management and internal control:

- Our audit committee oversees and manages the overall risks associated with our business operations, including (i) reviewing and approving our risk management programs and procedures to ensure that it is consistent with our corporate objectives; (ii) monitoring the most significant risks associated with our business operation and our management's handling of such risks; (iii) reviewing our corporate risk matrix in the light of our corporate risk tolerance; (iv) reviewing the significant residual risks and the needs to set up mitigating controls; and (v) monitoring and ensuring the appropriate application of our risk management framework across our Group.

- Our chief financial officer, Mr. Billy Cho, is responsible for (i) formulating and updating our risk management program and target; (ii) reviewing and approving major risk management issues of our Company; (iii) promulgating risk management measures; (iv) providing guidance on our risk management approach to the relevant departments in our Company; (v) reviewing the relevant departments' reporting on key risks and providing feedbacks; (vi) supervising the implementation of our risk management measures by the relevant departments; (vii) ensuring that the appropriate structure, processes and competences are in place across our Group; and (viii) reporting to our audit committee on our material risks

- The relevant departments in our Company, including the finance department, the legal and compliance department, and the human resources department, are responsible for implementing our risk management program and carrying out our day-to-day risk management practice. In order to formalize risk management across our Group and set a common level of transparency and risk management performance, the relevant departments will (i) gather information about the risks relating to their operation or function; (ii) conduct risk assessments, which include the identification, prioritization, measurement and categorization of all key risks that could potentially affect their objectives; (iii) continuously monitor the key risks relating to their operation or function; (iv) implement appropriate risk responses where necessary; and (v) develop and maintain an appropriate mechanism to facilitate the application of our risk management framework.

Internal Control

Our Board is responsible for establishing our internal control system and reviewing its effectiveness. We have engaged an internal control consulting firm (the "Internal Control Consultant") to perform certain agreed-upon procedures (the "Internal Control Review") in connection with the internal control of our Company and our major operating subsidiaries and to report factual findings on our Group's entity-level controls and internal controls of various processes, including financial reporting and disclosure controls, sales accounts receivable and collection, procurement and vendor management, accounts payable and payment, fixed assets and assets under construction, human resources and payroll management, cash and treasury management, inventory management, general controls of IT system, taxation management, production and costing, insurance management, research and development and intangible assets. The Internal Control Consultant performed the Internal Control Review in August 2019 and a follow-up review in January 2020. As of the Latest Practicable Date, there were no material outstanding issues relating to our Group's internal control.

We regularly reviewed and enhanced our internal control system. Below is a summary of the internal control policies, measures and procedures we have implemented or plan to implement:

- We have adopted various measures and procedures regarding each aspect of our business operation, such as financial controlling, protection of intellectual property, information security, adverse event reporting, quality control, environmental protection and occupational health and safety, etc. We provide periodic training about these measures and procedures to our employees as part of our employee training program. We also constantly monitor the implementation of those measures and procedures through our on-site internal control teams for each stage of the biologics development process.

- Our senior management team and our directors (who are responsible for monitoring the corporate governance of our Group) with help from our legal advisors, will also periodically review our compliance status with all relevant laws and regulations. We have internally established a set of compliance policies to provide guidance to our employees on expected business practices and ethical and moral behaviors, such as Code of Conduct and Ethics Policy and Anti-Bribery and Corruption Policy. We strictly require our employees to comply with anti-corruption laws in every countries and regions that we operate or are listed e.g., the PRC, Hong Kong or the U.S. Specifically, we require our employees to comply with applicable anti-corruption laws including, but are not limited to: (i) the Criminal Law of the PRC, the Anti-Unfair Competition Law of the PRC and the related regulations and judicial interpretations, (ii) the Foreign Corrupt Practices Act of the U.S,, and (iii) other applicable anti-corruption laws or regulations. Such anti corruption laws generally prohibit the offer, promise, payment or receipt of anything of value to obtain, retain or grant business opportunities or to exchange in an improper advantage. Any employee that violates the Anti-Bribery and Corruption Policy can be subject to disciplinary actions, up to and including termination of employment. We also prohibit employees from engaging in any illegal or unethical economic behavior and seeking benefits from it, and implement strict management and audit procedures to prevent lack of transparency and corruption during the sale or procurement process.

- We have established an audit committee in August 2017, which (i) makes recommendations to our directors on the appointment and removal of external auditors; (ii) reviews the financial statements and render advice in respect of financial reporting and internal controls; and (iii) as well as oversee internal control procedures and any significant risks of our Group.

We maintain strict anti-corruption policies among our sales personnel and distributors in our sales and marketing activities and we believe we will therefore be less affected by the increasingly stringent measures taken by the PRC government to correct corruptive practices in the pharmaceutical industry.

Investment Risk Management

We engage in short-term investments with surplus cash on hand. Our investment portfolio primarily consists of time deposits. Our primary objective of short-term investment is to preserve principal, and increase liquidity without significantly increasing risks. Under the supervision of our Chief Financial Officer, our finance department is responsible for managing our short-term investment activities. Before making any investment proposal, our finance department will assess our cash flow levels, operational needs and capital expenditures. We operate under our investment policy, which provides the guidelines and specific instructions on the investment of our funds.

Our investment strategy aims to minimize risks by reasonably and conservatively matching the maturities of the portfolio to anticipated operating cash needs. We make our investment decisions on a case-by-case basis after thoroughly considering a number of factors, including but not limited to macro-economic environment, general market conditions and the expected profit or potential loss of the investment. Our portfolio to date have been required to hold only instruments with an effective final maturity of 12 months or less, with effective final maturity being defined as the obligation of the issuer to repay principal and interest. Under our investment policy, we are prohibited from investing in high risk products and the proposed investment must not interfere with our business operation or capital expenditure. As of the Latest Practicable Date, our investment decisions did not deviate from our investment policy.

We believe that our internal investment policies and the related risk management mechanism are adequate. We may invest in time deposits in consistency with our investment policy where we believe it is prudent to do so after the Listing.

The following section sets forth supplemental financial information for the years ended December 31, 2019 and 2018 and as of December 31, 2019 and the six months ended June 30, 2020 and 2019 and as of June 30, 2020, including certain new disclosures made in connection with the Listing.

The following consolidated financial data for the periods and as of the dates indicated are qualified by reference to and should be read in conjunction with our consolidated financial statements and related notes and Item 5. "Operating and Financial Review and Prospects" in our 2019 Annual Report as well as our consolidated financial statements as of June 30, 2020 and for the six months ended June 30, 2019 (unaudited) and 2020 included as Exhibit 99.1 of our report on Form 6-K furnished to the SEC on September 11, 2020 and the related disclosures contained herein and therein.

OVERVIEW

We are an innovative, research-based, commercial-stage biopharmaceutical company with a focus on discovering, licensing, developing and commercializing potentially global best-in-class/first- in-class therapies that address areas of large unmet medical need in the China and global markets, including the fields of oncology, infectious and autoimmune diseases. By effectively executing our plan and closely following our strategy, we have built an integrated platform to bring both in-licensed and internally-discovered novel therapeutics to patients globally. We believe we are one of the first biopharmaceutical companies in China to scale, allowing us to further capitalize on the latest innovation and business opportunities globally.

Since our inception, we have executed our strategic approach of in-licensing promising biopharmaceutical products via global collaboration and investing in internal discovery and development efforts. Our portfolio consists of 16 potential best-in-class/first-in-class products and drug candidates, including two commercialized products in China, Hong Kong and Macau and seven assets in pivotal or potentially registration-enabling trials in oncology and infectious diseases, which are therapeutic areas where there is a large unmet need and lack of innovative treatment options in Greater China. We are at the inflection point of commercialization with recent launches of ZEJULA and Optune in multiple regions, empowered by our commercialization team with a proven track record and heritage from top-selling MNCs and innovative oncology brands. We believe that we remain the preferred partner of choice in our areas of focus for the biopharmaceutical industry as we provide a differentiated approach for our collaborators to achieve success while also conducting timely trials and achieving eventual commercialization of promising therapies, accelerating access to the large patient population.

Our consolidated net loss attributable to ordinary shareholders for the year ended December 31, 2018 and 2019 and for the six months ended June 30, 2019 and 2020 was US$139.1 million, US$195.1 million, US$83.3 million and US$128.6 million, respectively.

BASIS OF PRESENTATION

Our consolidated statement of operations data for the years ended December 31, 2018 and 2019 and for the six months ended June 30, 2019 and 2020 and our consolidated statement of financial position data as of December 31, 2018 and 2019 and June 30, 2020 have been derived from our audited consolidated financial statements. Our consolidated financial statements appearing elsewhere in this document have been prepared in accordance with U.S. GAAP.

MAJOR FACTORS AFFECTING OUR RESULTS OF OPERATIONS

Our results of operations, financial condition and the period-to-period comparability of our financial results have been, and are expected to continue to be, principally affected by a number of factors, many of which may be beyond our control. A discussion of the key factors is set out below:

Our Ability to Increase the Sales of Our Commercialized Products

We started to generate revenue from sales of our commercialized products since 2018 and have since achieved significant revenue growth. Our revenue increased from US$0.1 million in 2018 to US$13.0 million in 2019, and from US$3.4 million for the six months ended June 30, 2019 to US$19.2 million for the six months ended June 30, 2020. As we generate revenue solely from product sales, sales volume of our commercialized products, currently being ZEJULA and Optune, has a significant impact on our results of operation. Our ability to increase the sales of our commercialized products depends on whether we are able to effectively implement our marketing strategies. We intend to focus our resources on promoting ZEJULA and Optune in China. With respect to ZEJULA, we intend to leverage our dedicated commercialization team to penetrate more cities in China, thereby ramping up the sales. We will continue to leverage strong momentum in commercial insurance coverage and aim for near-term NRDL inclusion to reach more patients. With respect to Optune, we plan to rapidly drive the sales of Optune in China. We believe that our strong commercialization team and well-established sales network will enable us to execute our sales and marketing strategies and increase the sales of our commercialized products.

Research and Development Expenses

We believe our ability to successfully develop drug candidates will be the primary factor affecting our long-term competitiveness, as well as our future growth and development. Developing high quality drug candidates requires a significant investment of resources over a prolonged period of time, and a core part of our strategy is to continue making sustained investments in this area. As a result of this commitment, our pipeline of drug candidates has been steadily advancing and expanding, with seven assets in pivotal or potentially registration- enabling trials being investigated. For more information on the nature of the efforts and steps necessary to develop our drug candidates, see “Business” and “Regulatory Environment.”

To date, we have financed our activities primarily through private placements, our initial public offering in September 2017 and multiple follow-on offerings. Through June 30, 2020, we have raised approximately US$164.6 million in private equity financing and approximately US$794.0 million in net proceeds after deducting underwriting commissions and the offering expenses payable by us in our initial public offering and our subsequent follow-on offerings. Our operations have consumed substantial amounts of cash since inception. The net cash used in our operating activities was US$97.5 million and US$191.0 million, for the years ended December 31, 2018 and 2019, respectively, and was US$83.2 million and US$92.3 million for the six months ended June 30, 2019 and 2020, respectively. We expect our expenditures to increase significantly in connection with our ongoing activities, particularly as we advance the clinical development of our clinical assets and continue research and development of our pre-clinical assets and initiate additional clinical trials of, and seek regulatory approval for, these and other future drug candidates. These expenditures include:

- expenses incurred for payments to CROs, investigators and clinical trial sites that conduct our clinical studies;
- employee compensation related expenses, including salaries, benefits and equity compensation expense;
- expenses for licensors;
- the cost of acquiring, developing, and manufacturing clinical study materials;
- facilities, depreciation, and other expenses, which include office leases and other overhead expenses;

- costs associated with pre-clinical activities and regulatory operations;
- expenses associated with the construction and maintenance of our manufacturing facilities; and
- costs associated with operating as a public company.

For more information on the research and development expenses incurred for the development of our drug candidates, see "— Discussion of Selected Components of Statements of Operations and Other Comprehensive Loss Items — Research and Development Expenses."

Selling, General and Administrative Expenses

Our selling, general and administrative expenses consist primarily of personnel compensation and related costs, including share-based compensation for commercial and administrative personnel. Other selling, general and administrative expenses include product distribution and promotion costs, professional service fees for legal, intellectual property, consulting, auditing and tax services as well as other direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies used in selling, general and administrative activities. We anticipate that our selling, general and administrative expenses will increase in future periods to support our increasing commercial and research and development activities and as we continue to commercialize, develop, and manufacture our products and product assets. These increases will likely include increased headcount, increased share compensation charges, increased product distribution and promotion costs, expanded infrastructure and increased costs for insurance. We also incur increased legal, compliance, accounting and investor and public relations expenses associated with being a public company.

Our Ability to Commercialize Our Products and Drug Candidates

All of our products and drug candidates are still in development in China (including, with respect to ZEJULA and Optune, for indications not yet approved in China). As of June 30, 2020, 14 of such products and drug candidates are in clinical development and various others are in pre-clinical development in China. Our ability to generate revenue from our products and drug candidates is dependent on their receipt of regulatory approval for and successful commercialization of such products, which may never occur. Certain of our products and drug candidates may require additional pre-clinical and/or clinical development, regulatory approval in multiple jurisdictions, manufacturing supply, substantial investment and significant marketing efforts before we generate any revenue from product sales.

Our License Arrangements

Our results of operations have been, and we expect them to continue to be, affected by our licensing, collaboration and development agreements. We are required to make upfront payments upon our entry into such agreements and milestone payments upon the achievement of certain development, regulatory and commercial milestones for the relevant assets under these agreements as well as tiered royalties based on the net sales of the licensed products. These expenses have been recorded in research and development expense in our consolidated financial statements and totaled US$59.2 million and US$58.7 million for the years ended December 31, 2018 and 2019, respectively, and US$22.7 million and US$51.7 million for the six months ended June 30, 2019 and 2020, respectively.

DISCUSSION OF SELECTED COMPONENTS OF STATEMENTS OF OPERATIONS AND OTHER COMPREHENSIVE LOSS ITEMS

Revenue

We started to generate revenue from sales of our commercialized products since 2018. We recognize revenue from product sales when we deliver the prescribed products to our customers. In 2018, our revenue was primarily generated from the sales of ZEJULA in Hong Kong. In 2019, our revenue was primarily generated from the sales of ZEJULA and Optune in Hong Kong. In the six months ended June 30, 2020, we generated revenue primarily from the sales of both ZEJULA and Optune in Hong Kong and China. Our revenue was US$0.1 million and US$13.0 million for the years ended December 31, 2018 and 2019, respectively, and US$3.4 million and US$19.2 million for the six months ended June 30, 2019 and 2020, respectively.

Cost of Sales

Cost of sales primarily consists of the purchase cost of products and royalty fees. During the Track Record Period, our cost of sales was US$43.3 thousand and US$3.7 million for the years ended December 31, 2018 and 2019, respectively, and US$0.9 million and US$5.0 million for the six months ended June 30, 2019 and 2020, respectively.

Research and Development Expenses

Our research and development expenses consist of (i) personnel compensations and related costs, relating to our personnel engaged in research and development activities, (ii) licensing fees, primarily including upfront and research and development ("**R&D**") milestone fees related to our in-licensed products and drug candidates, (iii) payment to CROs, CMOs and investigators, representing the expenses related to our external research and development activities (excluding licensing fees), and (iv) other costs, which include lab consumables, professional service expenses, depreciation and amortization. The following table sets forth the components of our research and development expenses for the periods indicated.

	Year Ended December 31,				Six Months Ended June 30,			
	2018	%	2019	%	2019	%	2020	%
					(Unaudited)			
	(US dollars in thousands, except percentage)							
Research and development expenses:								
Personnel compensations and related costs	16,755	13.9	30,820	21.6	15,095	25.6	21,600	21.2
Licensing fees	59,152	49.2	58,682	41.3	22,700	38.5	51,720	50.7
Payment to CROs/CMOs/Investigators	32,282	26.8	36,814	25.9	14,647	24.9	19,812	19.4
Other costs	12,089	10.1	15,905	11.2	6,486	11.0	8,917	8.7
Total	120,278	100.0	142,221	100.0	58,928	100.0	102,049	100.0

The following table summarizes our research and development expenses by program for the periods indicated.

	Year Ended December 31,				Six Months Ended June 30,			
	2018	%	2019	%	2019	%	2020	%
					(Unaudited)			
	(US dollars in thousands, except percentage)							
Research and development expenses:								
Clinical programs	89,556	74.5	96,442	67.8	37,230	63.2	72,335	70.9
Pre-clinical programs	8,102	6.7	8,268	5.8	3,763	6.4	2,915	2.9
Unallocated research and development expenses	22,620	18.8	37,511	26.4	17,935	30.4	26,799	26.2
Total	120,278	100.0	142,221	100.0	58,928	100.0	102,049	100.0

We manage our external research and development expenses by program; however, we do not allocate our internal research and development expenses by program because our employees and internal resources may be engaged in projects for multiple programs at any time.

Selling, General and Administrative Expenses

Our selling, general and administrative expenses consist primarily of (i) personnel compensation and related costs, including share-based compensation for commercial and administrative personnel, (ii) professional service fee, representing legal, intellectual property, consulting, auditing and tax services, and (iii) other costs, mainly including product distribution and promotion costs, depreciation and amortization and other direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies used in selling, general and administrative activities. The following table sets forth the components of our selling, general and administrative expenses for the periods indicated.

	Year Ended December 31,				Six Months Ended June 30,			
	2018	%	2019	%	2019	%	2020	%
					(Unaudited)			
	(US dollars in thousands, except percentage)							
Selling, General and Administrative Expenses:								
Personnel compensation and related costs	13,410	62.2	43,572	62.1	19,352	65.6	27,082	63.8
Professional service fee	3,266	15.1	2,887	4.1	1,607	5.5	4,570	10.8
Other costs	4,900	22.7	23,752	33.8	8,530	28.9	10,820	25.4
Total	21,576	100.0	70,211	100.0	29,489	100.0	42,472	100.0

Interest Income

Interest income consists primarily of interest generated from cash and our short-term investments, which primarily comprise of the time deposits with original maturities between three months and one year. We generated interest income of US$3.3 million and US$8.2 million in 2018 and 2019, respectively, and US$3.4 million and US$2.9 million for the six months ended June 30, 2019 and 2020, respectively.

Other Income (Expense), Net

Other income (expense), net consists primarily of government subsidies received from local governments in China and foreign exchange income or loss. We generated other income, net of US$0.1 million and US$0.9 million in 2018 and 2019, and other expense, net of US$0.3 million and US$0.7 million for the six months ended June 30, 2019 and 2020, respectively.

Share of Loss from Equity Method Investment

In June 2017, we entered into an agreement with three third-parties to launch JING Medicine Technology (Shanghai) Ltd., or JING, an entity that will provide services for drug discovery and development, consultation and transfer of pharmaceutical technology. We account for our investment using the equity method of accounting because we do not control the investee but have the ability to exercise significant influence over the operating and financial policies of the investee. An investment loss of US$0.6 million and US$0.8 million related to this investment was recorded in 2018 and 2019, respectively, and an investment loss of US$0.3 million and US$0.4 million related to this investment was recorded for the six months ended June 30, 2019 and 2020, respectively.

Income Tax Expense

We are subject to various rates of income tax under different jurisdictions. The following summarizes major factors affecting our applicable tax rates in the Cayman Islands, the PRC and Hong Kong.

Cayman Islands

Zai Lab Limited is incorporated in the Cayman Islands. The Cayman Islands currently levies no taxes on profits, income, gains or appreciation earned by individuals or corporations. In addition, our payment of dividends, if any, is not subject to withholding tax in the Cayman Islands.

People's Republic of China

Our subsidiaries incorporated in China are governed by the EIT Law and regulations. Under the EIT Law, the standard EIT rate is 25% on taxable profits as reduced by available tax losses. Tax losses may be carried forward to offset any taxable profits for following five or ten years.

Hong Kong

Our subsidiaries incorporated in Hong Kong are subject to two-tiered tax rates during the Track Record Period on assessable profits earned in Hong Kong where the profits tax rate for the first HK$2 million of assessable profits is subject to profits tax rate of 8.25% and the assessable profits above HK$2 million is subject to profits tax rate of 16.5%. Our subsidiaries incorporated in Hong Kong did not have assessable profit during the Track Record Period.

RESULTS OF OPERATIONS

The following table sets forth a summary of our consolidated results of operations for the periods indicated. This information should be read together with our consolidated financial statements and related notes included elsewhere in this document. Our operating results in any period are not necessarily indicative of the results that may be expected for any future period.

	Year Ended December 31,		Six Months Ended June 30,	
	2018	2019	2019	2020
			(Unaudited)	
	(US dollars in thousands, except share and per share data)			
Comprehensive Loss Data:				
Revenue	129	12,985	3,420	19,213
Expenses:				
Cost of sales	(43)	(3,749)	(882)	(4,980)
Research and development	(120,278)	(142,221)	(58,928)	(102,049)
Selling, general and administrative	(21,576)	(70,211)	(29,489)	(42,472)
Loss from operations	(141,768)	(203,196)	(85,879)	(130,288)
Interest income	3,261	8,232	3,365	2,882
Interest expense	(40)	(293)	(137)	(114)
Other income (expense), net	59	938	(307)	(691)
Loss before income tax and share of loss from equity method investment	(138,488)	(194,319)	(82,958)	(128,211)
Income tax expenses	—	—	—	—
Share of loss from equity method investment	(587)	(752)	(316)	(406)
Net loss attributable to ordinary shareholders	(139,075)	(195,071)	(83,274)	(128,617)
Weighted-average shares used in calculating net loss	52,609,810	64,369,490	60,919,842	73,847,551
Net loss per share, basic and diluted	(2.64)	(3.03)	(1.37)	(1.74)

Six Months Ended June 30, 2020 Compared to Six Months Ended June 30, 2019

Revenue

The following table sets forth the revenue breakdown by product for the periods indicated.

	Six Months Ended June 30,			
	2019	%	2020	%
	(Unaudited)			
	(US dollars in thousands, except percentage)			
ZEJULA	1,925	56.3	13,791	71.8
Optune	1,495	43.7	5,422	28.2
Total	3,420	100.0	19,213	100.0

Revenue increased significantly by US$15.8 million to US$19.2 million for the six months ended June 30, 2020 from US$3.4 million for the six months ended June 30, 2019, primarily due to the increase in revenue generated from both ZEJULA and Optune as a result of our commercial launch of these two commercialized products in China during the first half of 2020.

Cost of Sales

Cost of sales increased by US$4.1 million to US$5.0 million for the six months ended June 30, 2020 from US$0.9 million for the six months ended June 30, 2019, primarily attributable to the increased cost and royalty fees in connection with the sales of ZEJULA and Optune in China for the six months ended June 30, 2020.

Research and Development Expenses

The following table sets forth the components of our research and development expenses for the periods indicated.

	Six Months Ended June 30,			
	2019	%	2020	%
	(Unaudited)			
	(US dollars in thousands, except percentage)			
Research and development expenses:				
Personnel compensations and related costs	15,095	25.6	21,600	21.2
Licensing fees	22,700	38.5	51,720	50.7
Payment to CROs/CMOs/Investigators	14,647	24.9	19,812	19.4
Other costs	6,486	11.0	8,917	8.7
Total	58,928	100.0	102,049	100.0

Research and development expense increased by US$43.1 million to US$102.0 million for the six months ended June 30, 2020 from US$58.9 million for the six months ended June 30, 2019. The increase in research and development expense included the following:

- US$6.5 million for increased personnel compensation and related costs which was primarily attributable to increased employee compensation costs, due to hiring of more R&D personnel and increase of compensation levels for our R&D personnel during the six months ended June 30, 2020;
- US$29.0 million for increased licensing fees which was primarily attributable to the upfront fee we paid to Regeneron under our collaboration agreement that we entered into in April 2020 and milestone payments for our existing projects;
- US$5.2 million for increased payment to CROs/CMOs/Investigators as we advanced our drug candidate pipeline; and
- US$2.4 million for increased other costs, including professional service expenses and rental expenses.

The following table summarizes our research and development expenses by program for the periods indicated.

	Six Months Ended June 30,			
	2019	%	2020	%
	(Unaudited)			
	(US dollars in thousands, except percentage)			
Research and development expenses:				
Clinical programs	37,230	63.2	72,335	70.9
Pre-clinical programs	3,763	6.4	2,915	2.9
Unallocated research and development expenses	17,935	30.4	26,799	26.2
Total	58,928	100.0	102,049	100.0

During the six months ended June 30, 2020, 70.9% and 2.9% of our total research and development expenses were attributable to clinical programs and pre-clinical programs, respectively. During the six months ended June 30, 2019, 63.2% and 6.4% of our total research and development expenses were attributable to clinical programs and pre-clinical programs, respectively.

Selling, General and Administrative Expenses

	Six Months Ended June 30,			
	2019	%	2020	%
	(Unaudited) (US dollars in thousands, except percentage)			
Selling, General and Administrative Expenses:				
Personnel compensation and related costs	19,352	65.6	27,082	63.8
Professional service fee	1,607	5.5	4,570	10.8
Other costs	8,530	28.9	10,820	25.4
Total	29,489	100.0	42,472	100.0

Selling, general and administrative expenses increased by US$13.0 million to US$42.5 million for the six months ended June 30, 2020 from US$29.5 million for the six months ended June 30, 2019. The increase in general and administrative expenses included the following:

- US$7.7 million for increased personnel compensation and related costs which was primarily attributable to increased commercial and administrative personnel costs, due to hiring of more personnel as we continued to ramp up the sales of ZEJULA and Optune, and increase of compensation levels for our commercial and administrative personnel during the six months ended June 30, 2020;

- US$3.0 million for increased professional service fee in connection with the sales of ZEJULA and Optune in China after our commercial launch of these two commercialized products during the six months ended June 30, 2020; and

- US$2.3 million for increased other costs, mainly including selling, rental, and administrative expenses primary attributable to the commercial operation in Hong Kong and PRC.

Interest Income

Interest income decreased by US$0.5 million to US$2.9 million for the six months ended June 30, 2020 from US$3.4 million for the six months ended June 30, 2019, primarily due to the decrease of our short-term investment balance and interest rates associated with our USD-denominated investments.

Interest Expense

Interest expense decreased by US$23.0 thousand to US$114.0 thousand for the six months ended June 30, 2020 from US$137.0 thousand for the six months ended June 30, 2019 due to the decrease of our bank loan balance.

Share of Loss from Equity Method Investment

We incurred an investment loss of US$0.4 million and US$0.3 million related to our investment in JING for the six months ended June 30, 2020 and 2019, respectively.

Other Income (Expense), Net

Other expense, net increased by US$0.4 million to US$0.7 million for the six months ended June 30, 2020 from US$0.3 million for the six months ended June 30, 2019 due to foreign exchange loss.

Net Loss Attributable to Ordinary Shareholders

As a result of the foregoing, we had net loss attributable to ordinary shareholders of US$128.6 million for the six months ended June 30, 2020 compared to net loss attributable to ordinary shareholders of US$83.3 million for the six months ended June 30, 2019.

Year Ended December 31, 2019 Compared with the Year Ended December 31, 2018

Revenue

The following table sets forth the revenue breakdown by product for the periods indicated.

	Year Ended December 31,			
	2018	%	2019	%
	(US dollars in thousands, except percentage)			
ZEJULA	129	100.0	6,625	51.0
Optune	—	—	6,360	49.0
Total	129	100.0	12,985	100.0

Revenue increased significantly by US$12.9 million to US$13.0 million for the year ended December 31, 2019 from US$0.1 million for the year ended December 31, 2018, primarily due to the increase in revenue generated from both ZEJULA and Optune as a result of the increase in sales of ZEJULA and our commercial launch of Optune in Hong Kong in 2019.

Cost of Sales

Cost of sales increased to US$3.7 million for the year ended December 31, 2019 from US$43.0 thousand for the year ended December 31, 2018, primarily attributable to the increased cost and royalty fees in connection with the sales of ZEJULA and Optune in Hong Kong in 2019.

Research and Development Expenses

The following table sets forth the components of our research and development expenses for the periods indicated.

	Year Ended December 31,			
	2018	%	2019	%
	(US dollars in thousands, except percentage)			
Research and development expenses:				
Personnel compensations and related costs	16,755	13.9	30,820	21.6
Licensing fees	59,152	49.2	58,682	41.3
Payment to CROs/CMOs/Investigators	32,282	26.8	36,814	25.9
Other costs	12,089	10.1	15,905	11.2
Total	120,278	100.0	142,221	100.0

Research and development expenses increased by US$21.9 million to US$142.2 million for year ended December 31, 2019 from US$120.3 million for year ended December 31, 2018. The increase in research and development expenses included the following:

- US$14.1 million for increased personnel compensation and related costs which was primarily attributable to increased employee compensation costs, due to hiring of more personnel during the year ended December 31, 2019 and the grants of new share options and vesting of restricted shares to certain employees;

- US$4.5 million for increased payment to CROs/CMOs/Investigators in fiscal year 2019 as we advanced our pipeline; and

- US$3.8 million for increased other costs, including lab consumables and professional service expenses.

The following table summarizes our research and development expenses by program for the periods indicated.

	Year Ended December 31,			
	2018	%	2019	%
	(US dollars in thousands, except percentage)			
Research and development expenses:				
Clinical programs	89,556	74.5	96,442	67.8
Pre-clinical programs	8,102	6.7	8,268	5.8
Unallocated research and development expenses	22,620	18.8	37,511	26.4
Total	120,278	100.0	142,221	100.0

During the year ended December 31, 2019, 67.8% and 5.8% of our total research and development expenses were attributable to clinical programs and pre-clinical programs, respectively. During the year ended December 31, 2018, 74.5% and 6.7% of our total research and development expenses were attributable to clinical programs and pre-clinical programs, respectively.

Selling, General and Administrative Expenses

	Year Ended December 31,			
	2018	%	2019	%
	(US dollars in thousands, except percentage)			
Selling, General and Administrative Expenses:				
Personnel compensation and related costs	13,410	62.2	43,572	62.1
Professional service fee	3,266	15.1	2,887	4.1
Other costs	4,900	22.7	23,752	33.8
Total	21,576	100.0	70,211	100.0

Selling, general and administrative expenses increased by US$48.6 million to US$70.2 million for year ended December 31, 2019 from US$21.6 million for year ended December 31, 2018. The increase in general and administrative expenses included the following:

- US$30.2 million for increased personnel compensation and related costs which was primarily attributable to increased commercial and administrative personnel costs, due to hiring of more personnel during year ended December 31, 2019 and the grants of new share options and vesting of restricted shares to certain employees; and

- US$18.9 million for increased other costs, including selling, rental, and travel expenses primary attributable to the commercial operation in Hong Kong and PRC for the year ended December 31, 2019.

Interest Income

Interest income increased by US$5.0 million for year ended December 31, 2019 primary attributable to interest income on higher cash and short-term investments balance in 2019.

Interest Expense

Interest expense increased by US$0.3 million for year ended December 31, 2019 primary attributable to increased balance of short-term borrowings in 2019.

Share of Loss from Equity Method Investment

We incurred an investment loss of US$0.8 million and US$0.6 million related to our investment in JING for the year ended December 31, 2019 and 2018, respectively.

Other Income (Expense), Net

Other income, net increased by US$0.9 million for year ended December 31, 2019 primarily due to the increase in governmental subsidies.

Net Loss Attributable to Ordinary Shareholders

As a result of the foregoing, we had net loss attributable to ordinary shareholders of US$195.1 million for the year ended December 31, 2019 compared to net loss attributable to ordinary shareholders of US$139.1 million for the year ended December 31, 2018.

LIQUIDITY AND CAPITAL RESOURCES

Since our inception, we have incurred net losses and negative cash flows from our operations. Substantially all of our losses have resulted from funding our research and development programs and selling, general and administrative costs associated with our operations. We incurred net losses of US$139.1 million, US$195.1 million and US$128.6 million for the years ended December 31, 2018 and 2019 and for the six months ended June 30, 2020, respectively. As of December 31, 2019 and June 30, 2020, we had an accumulated deficit of US$444.7 million and US$573.3 million, respectively. Our primary use of cash is to fund research and development costs. Our operating activities used US$97.5 million and US$191.0 million of cash flows during the years ended December 31, 2018 and December 31, 2019, respectively, and US$92.3 million for the six months ended June 30, 2020. Historically, we have financed our operations principally through proceeds from private placements as well as proceeds from our initial public offering and subsequent follow-on offerings. As of December 31, 2019 and June 30, 2020, we had cash and cash equivalents and short-term investments of US$275.9 million and US$463.6 million, respectively. In January 2020, we raised US$280.6 million in net proceeds from our subsequent follow-on offering of 6,300,000 ADSs. Our expenditures as a company principally focused on research and development, are largely discretionary and as such our current losses and cash used in operations do not present immediate going concern issues. Based on our current operating plan, we expect that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditures requirements for at least the next 12 months after the date of this document. However, in order to bring to fruition our research and development objectives the company will ultimately need additional funding sources and there can be no assurances that they will be made available.

Our ability to pay dividends may depend on receiving distributions of funds from our PRC subsidiaries. Relevant PRC statutory laws and regulations permit payments of dividends by our PRC subsidiaries only out of their retained earnings, if any, as determined in accordance with PRC accounting standards and regulations. The results of operations reflected in the consolidated financial statements prepared in accordance with U.S. GAAP differ from those reflected in the statutory financial statements of our PRC subsidiaries. In accordance with the relevant applicable PRC laws and regulations, a domestic enterprise is required to provide statutory reserves of at least 10% of its annual after-tax profit until such reserve has reached 50% of its respective registered capital based on the enterprise's PRC statutory accounts. A domestic enterprise is also required to provide discretionary surplus reserve, at the discretion of the board of directors, from the profits determined in accordance with the enterprise's PRC statutory accounts. The aforementioned reserves can only be used for specific purposes and are not distributable as cash dividends. Our PRC subsidiaries were established as domestic enterprises and therefore are subject to the above mentioned restrictions on distributable profits.

During the years ended December 31, 2018 and 2019 and during the six months ended June 30, 2020, no appropriation to statutory reserves was made because our PRC subsidiaries had substantial losses during such periods. As a result of relevant applicable PRC laws and regulations subject to the limit discussed above that require annual appropriations of 10% of after-tax income to be set aside, prior to payment of dividends, as a general reserve fund, our PRC subsidiaries are restricted in their ability to transfer a portion of its net assets. Foreign exchange and other regulations in China may further restrict our PRC subsidiaries from transferring funds to us in the form of dividends, loans and advances. As of December 31, 2019 and June 30, 2020, amounts restricted are the paid-in capital of our PRC subsidiaries, which amounted to US$155.9 million and US$205.9 million, respectively.

Cash Flows

The following table provides information regarding our cash flows for the periods indicated:

	Year Ended December 31,		Six Months Ended June 30,	
	2018	2019	2019	2020
			(Unaudited)	
	(US dollars in thousands)			
Operating cash flows before changes in operating assets and liabilities	(124,920)	(167,728)	(71,210)	(110,709)
Changes in operating assets and liabilities	27,382	(23,283)	(11,974)	18,390
Net cash (used in) operating activities	(97,538)	(191,011)	(83,184)	(92,319)
Net cash (used in) investing activities	(212,554)	(14,892)	(106,017)	(6,521)
Net cash provided by financing activities	144,147	219,302	217,880	281,500
Effect of foreign exchange rate changes	(763)	91	(28)	12
Net (decrease) increases in cash and cash equivalents	(166,708)	13,490	28,651	182,672

Net cash used in operating activities

We had net cash outflows in operating activities during the Track Record Period. Our primary uses of cash are to fund the development of both our in-licensed and internally developed drug candidates, our clinical trials, our payment for the construction of research and manufacturing facilities and for the purchase of equipment, selling and administrative expenses and other recurring expenses. Our operating cash flow will continue to be affected by our research and development expenses. During the Track Record Period and up to the Latest Practicable Date, we primarily funded our working capital requirements from proceeds from our initial public offering and subsequent follow-on offerings. As our business develops and expands, we expect to generate cash flow from operations including but not limited to the selling of our commercial products. We shall continue to advance our late stage clinical assets into NDA stage and commercialization which will bring incremental cash flow to fund our operation in the foreseeable future.

During the six months ended June 30, 2020, our operating activities used US$92.3 million of cash, which resulted principally from our net loss of US$128.6 million, adjusted for non-cash charges of US$17.9 million, and by cash provided by our operating assets and liabilities of US$18.4 million. Our net non-cash charges during the year ended June 30, 2020 primarily consisted of US$2.1 million depreciation expense, US$13.4 million share-based compensation expense and US$2.1 million non-cash lease expense.

During the six months ended June 30, 2019, our operating activities used US$83.2 million of cash, which resulted principally from our net loss of US$83.3 million, adjusted for non-cash charges of US$12.1 million, and by cash used in our operating assets and liabilities of US$12.0 million. Our net non-cash charges during the year ended June 30, 2019 primarily consisted of US$1.6 million depreciation expense, US$9.3 million share-based compensation expense and US$1.0 million non-cash lease expense.

During the year ended December 31, 2019, our operating activities used US$191.0 million of cash, which resulted principally from our net loss of US$195.1 million, adjusted for non-cash charges of US$27.3 million, and by cash used in our operating assets and liabilities of US$23.2 million. Our net non-cash charges during the year ended December 31, 2019 primarily consisted of US$3.8 million depreciation expense, US$20.3 million share-based compensation expense and US$2.8 million noncash lease expense.

During the year ended December 31, 2018, our operating activities used US$97.5 million of cash, which resulted principally from our net loss of US$139.1 million, adjusted for non-cash charges of US$14.2 million, and by cash provided by our operating assets and liabilities of US$27.4 million. Our net non-cash charges during the year ended December 31, 2018 primarily consisted of US$1.6 million depreciation expense, US$12.2 million share-based compensation expense and a US$0.6 million share of loss from equity method investment and offset by a US$0.3 million amortization of deferred income.

Net cash used in investing activities

Net cash used in investing activities was US$6.5 million for the six months ended June 30, 2020 compared to US$106.0 million for the six months ended June 30, 2019. The decrease in cash used in investing activities was primary due to the proceeds from maturity of short-term investments, net of purchases of short-term investments.

Net cash used in investing activities was US$14.9 million for the year ended December 31, 2019 compared to US$212.6 million for the year ended December 31, 2018. The decrease in cash used in investing activities was primary due to the proceeds from maturity of short-term investments, net of purchases of short-term investments.

Net cash provided by financing activities

Net cash provided by financing activities was US$281.5 million for the six months ended June 30, 2020 compared to US$217.9 million for the six months ended June 30, 2019. The net cash provided by financing activities was mainly attributable to the issuance of ADSs in our subsequent follow-on offering in January 2020.

Net cash provided by financing activities was US$219.3 million for the year ended December 31, 2019 compared to US$144.1 million for the year ended December 31, 2018. The net cash provided by financing activities was mainly attributable to the issuance of ADSs in our subsequent follow-on offering in 2019.

CASH OPERATING COSTS

The following table provides information regarding our cash operating costs for the relevant periods:

	Year Ended December 31		Six Months Ended June 30,	
	2018	2019	2019	2020
	(US dollars in thousands)			
Research and Development Costs for Core Products	28,427	15,809	6,712	6,848
Research and Development Costs for Other Products and Drug Candidates	40,785	104,172	44,254	61,219
Unallocated research and development costs	5,865	6,691	2,840	5,199
Workforce Employment Cost (including Research and Development Workforce Employment Cost of Core Products and Other Products and Drug Candidates)	15,845	48,210	23,071	37,324
Direct Production Cost	25	2,326	418	4,980
Non-income Taxes, Royalties and Other Governmental Charges	6	949	—	449
Contingency Allowances	—	—	—	—
Product Marketing	2,234	19,057	6,762	10,045
Other Significant Costs	—	—	—	—

CAPITAL EXPENDITURES

Our cash payment for property and equipment, intangible assets and land use right totaled US$10.1 million and US$15.2 million in 2018 and 2019, respectively, and US$4.8 million and US$1.5 million for the six months ended June 30, 2019 and 2020, respectively. We funded our capital expenditure requirements during the Track Record Period mainly from equity financing and cash at bank. We expect that our capital expenditure in 2020 and 2021 will focus on plant, laboratory equipment and leasehold improvement. We plan to fund our planned capital expenditure mainly using our cash at bank and the estimated net proceeds received from the Global Offering. We may reallocate the fund to be utilized on capital expenditure based on our ongoing business needs.

CONTRACTUAL OBLIGATIONS

The following table sets forth our contractual obligations as of June 30, 2020. Amounts we pay in future periods may vary from those reflected in the table.

	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
	(US dollars in thousands)				
Contractual Obligations					
Purchase Obligations	3,971	3,971	—	—	—
Operating Lease Obligations	15,437	4,580	6,442	2,975	1,440

We also have obligations to make future payments to third party licensors that become due and payable on the achievement of certain development, regulatory and commercial milestones as well as tiered royalties on net sales. We have not included these commitments on our balance sheet or in the table above because the commitments are cancellable if the milestones are not completed and achievement and timing of these obligations are not fixed or determinable.

As of June 30, 2020, we had outstanding principal amounts of short-term borrowings of US$4.2 million, which were unsecured and guaranteed by Zai Lab Shanghai. As of June 30, 2020, we also had operating lease liabilities amounting to US$14.6 million, certain of which were secured by the rental deposits and all of which were unguaranteed.

As of June 30, 2020, save as disclosed in our audited consolidated financial statements, we did not have significant contingent liabilities.

Save as disclosed above, since June 30, 2020 and up to the date of this document, there has not been any material and adverse change in our indebtedness and contingent liabilities. Our directors do not foresee any potential difficulty in obtaining bank facilities should the need arise.

WORKING CAPITAL

We recorded net current assets of US$220.3 million, US$245.8 million, and US$428.3 million, respectively, as of December 31, 2018 and 2019 and June 30, 2020. The following table sets forth a breakdown of our current assets and liabilities as of the dates indicated.

The table below sets forth our current assets, current liabilities and net current assets as of the dates indicated:

	As of December 31,		As of June 30,
	2018	2019	2020
	(US dollars in thousands)		
Current assets:			
Cash and cash equivalents	62,952	75,932	258,604
Short-term investments	200,350	200,000	205,000
Accounts receivable (net of allowance of nil, nil, and US$2 as of December 31, 2018 and 2019 and June 30, 2020, respectively)	90	3,791	7,024
Inventories	4	6,005	6,569
Prepayments and other current assets	5,749	6,736	7,684
Total current assets	**269,145**	**292,464**	**484,881**
Current liabilities:			
Short-term borrowings	3,643	6,450	4,238
Accounts payable	37,432	22,660	32,392
Current operating lease liabilities	—	4,351	4,175
Other current liabilities	7,767	13,174	15,750
Total current liabilities	**48,842**	**46,635**	**56,555**
Net current assets	**220,303**	**245,829**	**428,326**

For a detailed discussion on our cash position, being the balance sheet item that has material impact on our liquidity, as well as material changes in the various working capital items, see "— Liquidity and Capital Resources."

Working Capital Confirmation

Taking into account the financial resources available to us including our cash and cash equivalents on hand and the estimated net proceeds from the Global Offering, our directors are of the view that we have sufficient working capital to cover at least 125% of our costs, including selling, general, administrative and operating costs (including any production costs) and research and development costs for the next 12 months from the date of this document.

KEY FINANCIAL RATIOS

The following table sets forth our key financial ratios for the periods indicated:

	As of December 31,		As of June 30,
	2018	2019	2020
Gross margin(1)	66.7%	71.1%	74.1%
Current ratio(2)	5.5	6.3	8.6
Gearing ratio(3)	1.5%	2.2%	0.9%

Notes:

(1) Gross margin equals gross profit divided by revenue for the period.

(2) Current ratio equals current assets divided by current liabilities as of the end of the period.

(3) Gearing ratio equals total interest-bearing loans divided by total equity as of the end of the period.

Our gross margin increased from 66.7% as of December 31, 2018 to 77.1% as of December 31, 2019, primarily because we started generating revenue only from the last quarter of 2018. Gross margin increased further to 74.1% as of June 30, 2020, mainly due to the launch of ZEJULA in China and the decrease in cost of sales resulting from the local manufacturing.

Our current ratio increased from 5.5 as of December 31, 2018 to 6.3 as of December 31, 2019, mainly due to (i) the increase in cash and cash equivalents as a result of our public offering of ADSs in May 2019 and (ii) a higher level of accounts receivable and inventories. Current ratio increased further to 8.6 as of June 30, 2020, mainly due to the increase of cash and cash equivalents resulting from the issuance of ADSs in our subsequent follow-on offering in January 2020.

Our gearing ratio increased from 1.5% as of December 31, 2018 to 2.2% as of December 31, 2019, mainly due to the increase of short-term borrowings from commercial banks and partially offset by the increase in additional paid-in capital as a result of our public offering of ADSs in May 2019. Gearing ratio decreased from 2.2% as of December 31, 2019 to 0.9% as of June 30, 2020, mainly due to the increase in additional paid-in capital as a result of our follow-on offering of ADSs in January 2020.

See sections headed "— Results of Operations — Six Months Ended June 30, 2020 Compared to Six Months Ended June 30, 2019" and "— Results of Operations — Year Ended December 31, 2019 Compared with the Year Ended December 31, 2018" in this section for a discussion of the factors affecting our results of operations during the respective periods.

OFF-BALANCE SHEET COMMITMENTS AND ARRANGEMENTS

We currently do not engage in trading activities involving non-exchange traded contracts or interest rate swap transactions or foreign currency forward contracts. In the ordinary course of our business, we do not enter into transactions involving, or otherwise form relationships with, unconsolidated entities or financial partnerships that are established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes.

QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risk including foreign exchange risk, credit risk, cash flow interest rate risk and liquidity risk.

Foreign Exchange Risk

Renminbi, or RMB, is not a freely convertible currency. The State Administration of Foreign Exchange, under the authority of the People's Bank of China, controls the conversion of RMB into foreign currencies. The value of RMB is subject to changes in central government policies and to international economic and political developments affecting supply and demand in the China Foreign Exchange Trading System market. The cash and cash equivalents of our company included aggregated amounts of RMB26.9 million, RMB47.2 million and RMB165.5 million, which were denominated in RMB, as of December 31, 2018 and 2019 and June 30, 2020, respectively, representing 6%, 9% and 9% of the cash and cash equivalents as of December 31, 2018 and 2019 and June 30, 2020.

Our business mainly operates in China with a significant portion of our transactions settled in RMB, and our financial statements are presented in U.S. dollars. We do not believe that we currently have any significant direct foreign exchange risk and have not used any derivative financial instruments to hedge our exposure to such risk. Although, in general, our exposure to foreign exchange risks should be limited, the value of your investment in our ADSs will be affected by the exchange rate between the U.S. dollar and the RMB because the value of our business is effectively denominated in RMB, while the ADSs will be traded in U.S. dollars.

The value of the RMB against the U.S. dollar and other currencies may fluctuate and is affected by, among other things, changes in China's political and economic conditions. The conversion of RMB into foreign currencies, including U.S. dollars, has been based on rates set by the PBOC. On July 21, 2005, China government changed its decade-old policy of pegging the value of the RMB to the U.S. dollar. Under the revised policy, the RMB is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. This change in policy resulted in a more than 20% appreciation of the RMB against the U.S. dollar in the following three years. Between July 2008 and June 2010, this appreciation halted, and the exchange rate between the RMB and U.S. dollar remained within a narrow band. In June 2010, the PBOC announced that China government would increase the flexibility of the exchange rate, and thereafter allowed the RMB to appreciate slowly against the U.S. dollar within the narrow band fixed by the PBOC. However, more recently, on August 11, 12 and 13, 2015, the PBOC significantly devalued the RMB by fixing its price against the U.S. dollar 1.9%, 1.6%, and 1.1% lower than the previous day's value, respectively.

To the extent that we need to convert U.S. dollars into RMB for our operations or if any of our arrangements with other parties are denominated in U.S. dollars and need to be converted into RMB, appreciation of the RMB against the U.S. dollar would have an adverse effect on the RMB amount we receive from the conversion. Conversely, if we decide to convert RMB into U.S. dollars for the purpose of making payments for dividends on our ordinary shares or ADSs or for other business purposes, appreciation of the U.S. dollar against the RMB would have a negative effect on the U.S. dollar amounts available to us.

Credit Risk

Our credit risk is primarily attributable to the carrying amounts of cash and cash equivalents, short-term investment. The carrying amounts of cash and cash equivalents and short-term investment represent the maximum amount of loss due to credit risk. As of December 31, 2019 and 2018, and June 30, 2020, all of our cash and cash equivalents and short-term investments were held by major financial institutions located in China and international financial institutions outside of China which we believe are of high credit quality, and we will continually monitor the credit worthiness of these financial institutions.

Inflation

In recent years, China has not experienced significant inflation, and thus inflation has not had a material impact on our results of operations. According to the National Bureau of Statistics of China, the Consumer Price Index in China increased by 2.9% and 2.1% in 2019 and 2018, respectively. Although we have not been materially affected by inflation in the past, we can provide no assurance that we will not be affected in the future by higher rates of inflation in China.

Critical Accounting Policies and Significant Judgments and Estimates

We prepare our financial statements in conformity with U.S. GAAP, which requires us to make judgments, estimates and assumptions. We continually evaluate these estimates and assumptions based on the most recently available information, our own historical experiences and various other assumptions that we believe to be reasonable under the circumstances. Since the use of estimates is an integral component of the financial reporting process, actual results could differ from our expectations as a result of changes in our estimates. Some of our accounting policies require a higher degree of judgment than others in their application and require us to make significant accounting estimates.

The selection of critical accounting policies, the judgments and other uncertainties affecting application of those policies and the sensitivity of reported results to changes in conditions and assumptions are factors that should be considered when reviewing our financial statements. We believe the following accounting policies involve the most significant judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

In May 2014, the Financial Accounting Standards Board, or FASB, issued a comprehensive new standard which amends revenue recognition principles. In 2018, we adopted of ASC Topic 606, or ASC 606, *Revenue from Contracts with Customers*, in recognition of revenue. Under ASC 606, we recognize revenue when a customer obtains control of promised goods or services, in an amount that reflects the consideration expected to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services we transfer to the customer. Once a contract is determined to be within the scope of ASC 606 at contract inception, we review the contract to determine which performance obligations we must deliver and which of these performance obligations are distinct. We recognize as revenue the amount of the transaction price that is allocated to each performance obligation when that performance obligation is satisfied or as it is satisfied.

Our revenue is all from product sales. We recognize revenue from product sales when we have satisfied the performance obligation by transferring control of the product to the customers. Control of the product generally transfers to the customers when the delivery is made and when title and risk of loss transfers to the consumers. Cost of sales mainly consists of the purchase cost of products and royalty fee.

We have applied the practical expedients under ASC 606 with regard to assessment of financing component and concluded that there is no significant financing component given that the period between delivery of goods and payment is generally one year or less.

We started to generate product sales revenue since 2018. For the year ended December 31, 2018, our product revenues were generated from the sale of ZEJULA to customers. For the year ended December 31, 2019 and six months ended June 30, 2020, our product revenues were generated from the sale of ZEJULA and Optune to customers.

In China, we sell the products to distributors, who ultimately sell the products to health care providers. Based on the nature of the arrangements, the performance obligations are satisfied upon the products delivery to distributors. Rebates are offered to distributors, consistent with pharmaceutical industry practices. The estimated amount of unpaid or unbilled rebates are recorded as a reduction of revenue if any. Estimated rebates are determined based on contracted rates, sales volumes and distributor inventories. We regularly review the information related to these estimates and adjusts the amount accordingly.

In Hong Kong, we sell the products to customers, which are typically healthcare providers such as oncology centers. We utilize a third party for warehousing services. We are a principal in the transaction since we are primarily responsible for fulfilling the promise to provide the products to the customers, maintain inventory risk until delivery to the customers and have latitude in establishing the price. Revenue was recognized at the amount to which we expected to be entitled in exchange for the sale of the products, which is the sales price agreed with the customers. Consideration paid to the third party is recognized in operating expenses.

We didn't recognize any contract assets and contract liabilities as of December 31, 2018 and 2019, and June 30, 2020.

Share-Based Compensation

We grant share options to eligible employees, management and directors and account for these share-based awards in accordance with ASC Topic 718, *Compensation-Stock Compensation*, or ASC 718.

Share-based awards are measured at the grant date fair value and recognized as an expense (i) immediately at grant date if no vesting conditions are required or (ii) using a graded vesting method over the requisite service period, which is the vesting period.

All transactions in which goods or services are received in exchange for equity instruments are accounted for based on the fair value of the consideration received or the fair value of the equity instrument issued, whichever is more reliably measurable.

To the extent the required vesting conditions are not met resulting in the forfeiture of the share-based awards, previously recognized compensation expense relating to those awards are reversed.

We determine the fair value of the stock options granted to employees. Before 2018, the binomial option pricing model was applied in determining the estimated fair value of the options granted to employees. In 2018, we changed to use the Black-Scholes option valuation model. A change in the valuation technique is a change in accounting estimate for purposes of applying ASC 250, and has been applied prospectively to new awards.

Before January 2019, we have accounted for equity instruments issued to non-employees in accordance with the provisions of ASC 505, *Equity-Based Payments to Non-Employees*. All transactions in which goods or services are received in exchange for equity instruments are accounted for based on the fair value of the consideration received or the fair value of the equity instrument issued, whichever is more reliably measurable. The measurement date of the fair value of the equity instrument issued is the date on which the counterparty's performance is completed as there is no associated performance commitment.

The expense is recognized in the same manner as if we had paid cash for the services provided by the nonemployees.

From January 2019, we grant share options to eligible non-employees and accounts for these share based awards in accordance with ASC 718, *Compensation-Stock Compensation*. Non-employees' share-based awards are measured at the grant date fair value of the awards and recognized as expenses (1) immediately at grant date if no vesting conditions are required; or (2) using graded vesting method over the requisite service period, which is the vesting period. All transactions in which goods or services are received in exchange for equity instruments are accounted for based on the fair value of the consideration received or the fair value of the equity instrument issued, whichever is more reliably measurable. To the extent the required vesting conditions are not met resulting in the forfeiture of the share-based awards, previously recognized compensation expense relating to those awards are reversed. We determine the fair value of the stock options granted to non-employees using the Black-Scholes option valuation model.

Income Taxes

Current income taxes are provided on the basis of net income for financial reporting purposes, adjusted for income and expense items which are not assessable or deductible for income tax purposes, in accordance with the regulations of the relevant tax jurisdictions. We follow the liability method of accounting for income taxes.

Under this method, deferred tax assets and liabilities are determined based on the temporary differences between the financial statements carrying amounts and tax bases of assets and liabilities by applying enacted statutory tax rates that will be in effect in the period in which the temporary differences are expected to reverse. We record a valuation allowance to offset deferred tax assets if based on the weight of available evidence, it is more likely than not that some portion, or all, of the deferred tax assets will not be realized. The effect on deferred taxes of a change in tax rate is recognized in our consolidated financial statements in the period of change.

In accordance with the provisions of ASC 740, *Income Taxes*, we recognize in our financial statements the benefit of a tax position if the tax position is "more likely than not" to prevail based on the facts and technical merits of the position. Tax positions that meet the "more likely than not" recognition threshold are measured at the largest amount of tax benefit that has a greater than fifty percent likelihood of being realized upon settlement. We estimate our liability for unrecognized tax benefits which are periodically assessed and may be affected by changing interpretations of laws, rulings by tax authorities, changes and/or developments with respect to tax audits, and expiration of the statute of limitations. The ultimate outcome for a particular tax position may not be determined with certainty prior to the conclusion of a tax audit and, in some cases, appeal or litigation process.

We consider positive and negative evidence when determining whether some portion or all of our deferred tax assets will not be realized. This assessment considers, among other matters, the nature, frequency and severity of current and cumulative losses, forecasts of future profitability, the duration of statutory carry-forward periods, our historical results of operations, and our tax planning strategies. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. Based upon the level of our historical taxable income and projections for future taxable income over the periods in which the deferred tax assets are deductible, we believe it is more likely than not that we will not realize the deferred tax assets resulted from the tax loss carried forward in the future periods.

The actual benefits ultimately realized may differ from our estimates. As each audit is concluded, adjustments, if any, are recorded in our financial statements in the period in which the audit is concluded. Additionally, in future periods, changes in facts, circumstances and new information may require us to adjust the recognition and measurement estimates with regard to individual tax positions. Changes in recognition and measurement estimates are recognized in the period in which the changes occur. As of December 31, 2018 and 2019, and June 30, 2020, we did not have any significant unrecognized uncertain tax positions.

RECENTLY ISSUED ACCOUNTING STANDARDS

For a summary of recently issued accounting standards, see our audited consolidated financial statements.

DIVIDEND POLICY

We have never declared or paid dividends on our ordinary shares. We currently expect to retain all future earnings for use in the operation and expansion of our business and do not have any present plan to pay any dividends. The declaration and payment of any dividends in the future will be determined by our board of directors in its discretion, and will depend on a number of factors, including our earnings, capital requirements, overall financial condition, and contractual restrictions. Our shareholders in a general meeting may approve any declaration of dividends, which must not exceed the amount recommended by our Board. As advised by our Cayman counsel, under the Companies Law a Cayman Islands company may pay a dividend out of either profits or share premium account, provided that in no circumstances may a dividend be paid if this would result in the company being unable to pay its debts as they fall due in the ordinary course of business. In light of our accumulated losses as disclosed in this document, it is unlikely that we will be eligible to pay a dividend out of our profits in the foreseeable future. We may, however, pay a dividend out of our share premium account unless the payment of such a dividend would result in our Company being unable to pay our debts as they fall due in the ordinary course of business. There is no assurance that dividends of any amount will be declared to be distributed in any year. If we pay dividends in the future, in order for us to distribute dividends to our shareholders, we will rely to some extent on any dividends distributed by our PRC subsidiaries.

Any dividend distributions from our PRC subsidiaries to us will be subject to PRC withholding tax. In addition, regulations in the PRC currently permit payment of dividends of a PRC company only out of accumulated distributable after-tax profits as determined in accordance with its articles of association and the accounting standards and regulations in China. See “Risk Factors — Risks Relating to Doing Business in China”.

MAJOR SHAREHOLDERS

The following section sets forth updated information concerning certain of our major shareholders subsequent to the filing of our 2019 Annual Report.

We had 75,375,511 Shares outstanding as of the Latest Practicable Date. The following table and accompanying footnotes set forth information relating to the beneficial ownership of our Shares as of the Latest Practicable Date by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding Shares;
- each of our directors;
- each of our executive officers; and
- all of our executive officers and directors as a group.

Our major shareholders do not have voting rights that are different from our shareholders in general. Beneficial ownership is determined in accordance with the rules and regulations of the SEC. In computing the number of shares beneficially owned by a person and the percentage ownership of that person, we have included shares that the person has the right to acquire within 60 days, including through the exercise of any option, warrant or other right or the conversion of any other security. These shares, however, are not included in the computation of the percentage ownership of any other person.

	Shares Beneficially Owned	
Name of beneficial owner†	**Number**	**Percent**
Executive Officers and Directors:		
Samantha Du[(1)]	6,083,054	7.8%
Billy Cho	*	*
F. Ty Edmondson	—	—
Tao Fu	*	*
Yongjiang Hei	*	*
William Liang	*	*
Harald Reinhart	*	*
Kai-Xian Chen	*	*
John Diekman	*	*
Nisa Leung	—	—
William Lis	*	*
Leon O. Moulder, Jr	*	*
Peter Wirth	*	*
All Executive Officers and Directors as a Group	7,604,401	9.6%
Beneficial Owners of 5% or More of our Shares:		
QM 11 Limited[(2)]	9,072,932	12.0%
FMR, LLC[(3)]	7,075,122	9.4%
Capital Group[(4)]	5,923,328	7.9%
Investment funds affiliated with Advantech Capital[(5)]	4,551,772	6.0%

* The person beneficially owns less than 1% of our outstanding Shares.

† The business address of all directors and officers is 4560 Jinke Road, Bldg. 1, 4F, Pudong, Shanghai, China 201210.

(1) Includes 3,087,076 Shares issuable to Dr. Du upon exercise of vested options and options exercisable within 60 days of the Latest Practicable Date and 36,820 ADSs purchased by Dr. Du in multiple open market transactions. Includes 1,959,325 Shares held by certain holders of Shares, including Zai management and their affiliates. Although Dr. Du does not have any pecuniary interest in these Shares, these shareholders have granted Dr. Du the right to vote their shares and, therefore, she may be deemed to be the beneficial owner of the Shares held by these shareholders.

(2) Based on a Schedule 13G/A filed on February 14, 2020, which is the most updated information published on the SEC as at the Latest Practicable Date. The address for QM 11 Limited is Units 4205-06 Gloucester Tower, The Landmark, Central, Hong Kong.

(3) As of June 30, 2020 based on a Form 13F filed on August 14, 2020, which is the most updated information published on the SEC as at the Latest Practicable Date. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act ("Fidelity Funds") advised by Fidelity Management & Research Company ("FMR Co"), a wholly-owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. FMR Co carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. The address for FMR LLC is 245 Summer Street, Boston, Massachusetts 02110.

(4) As of June 30, 2020 based on a Form 13F filed on August 14, 2020. The address for Capital Group is 333 South Hope Street, Los Angeles, CA 90071

(5) Based on a Schedule 13G/A filed on February 11, 2020, which is the most updated information published on the SEC as at the Latest Practicable Date. Consists of (i) 4,246,791 Shares held by Maxway Investment Limited and (ii) 304,981 Shares held by Harbor Front Investment Limited. The address for Maxway Investment Limited and Harbor Front Investment Limited is c/o DMS House, 20 Genesis Close, George Town, Grand Cayman, KY1-1103, Cayman Islands.

The following section sets forth updates to our directors and management subsequent to the filing of our 2019 Annual Report.

Name	Age	Position(s)	Date of Appointment as Director or Senior Management	Year of Joining our Group
Executive Officers				
F. Ty Edmondson	54	Chief Legal Officer	August 2020	2020

F. Ty Edmondson joined our Company as Chief Legal Officer in August 2020. Mr. Edmondson has served in various legal and compliance roles during his tenure at Biogen Inc., a leading global biotech company where he has been from June 2014 through August 2020. Most recently, Mr. Edmondson served as Senior Vice President, Chief Corporation Counsel and Assistant Secretary. During his time at Biogen, he also served as the Chief Compliance Officer and Chief Commercial Counsel of the company. Prior to Biogen, Mr. Edmondson served as Vice President, Associate General Counsel and Corporate Secretary for Sepracor Inc. as well as in various senior legal and compliance positions in Japan and China after Sepracor's acquisition by Sumitomo Dainippon Pharma Co., Ltd. Before Sumitomo, Mr. Edmondson served in various roles with life sciences companies with a focus on international and U.S. FDA work, including Eisai, Inc., Boston Scientific and Bristol-Myers Squibb, with a focus on international and U.S. FDA work. Before his work in the life sciences industry, he was an associate with the admiralty law firm, Royston Rayzor in Houston, Texas. Mr. Edmondson received a BA degree in British Imperial and Commonwealth History from Washington & Lee University in June 1988 and received a J.D. from the Widener University School of Law in May 1993.