2018 Annual Report

Included in the 2018 Annual Report:
Form 10-K filed with the U.S. Securities and Exchange Commission on March 11, 2019

To Our Shareholders

2018 was a transformative year for Athenex. We completed enrollment of two pivotal Phase 3 studies of KX2-391 ointment in actinic keratosis and presented topline positive efficacy and safety data in early 2019. We also achieved several key milestones for the Oraxol program, including a second interim analysis conducted for the Phase 3 study in metastatic breast cancer. We continued to expand our clinical programs, with another Orascovery drug candidate receiving an IND allowance and the initiation of additional studies to evaluate combinations or new indications. The company's pipeline was further expanded with two new oncology technologies. We believe our commercial infrastructure is falling into place for our proprietary product launch.

The year didn't come without its challenges, but we are ready to face them head on. At Athenex, our mission is to improve the lives of cancer patients by creating more effective, safer and tolerable treatments. We remain committed to delivering stellar execution and positive clinical outcomes from our growing and value-generating pipeline. We believe this will keep us on the path towards realizing the true fundamental value of the company.

I am very pleased with our achievements in 2018 and I am confident that 2019 will be another landmark year.

YOUNG COMPANY WITH A UNIQUE STORY

To look at what the future will bring, let us first look back at our history and evolution. Athenex (formerly known as Kinex) started out as a small company in Buffalo, New York developing Kinase inhibitors. 15 years later, our pipeline has expanded to include four oncology-focused technologies with eight drug candidates in the clinic, which we soon expect to be ten. Of these, two drug candidates are in Phase 3 and the remaining are in either Phase 1 or 2. Our operations are spread across the globe, from the U.S. all the way to Asia. We are now eyeing Europe, bringing diversity and growth opportunities from all over the world. We have developed a number of valuable and trusted collaborative partnerships, including good relationships with two local governments. Our team is 500-strong and growing.

We could not do all of this without tremendous support from our shareholders, many of whom have believed in and stayed by Athenex since early in the company's history. In June 2017, we took the company public on the Nasdaq, a milestone that signified our increasing maturity and continuing growth. Since then, we completed a secondary offering and secured a strategic financial investment from a highly reputable US-based healthcare investor. We are committed to delivering value to reward our shareholders and believe we have come a long way in a short period of time.

Our company story has many layers but the mission remains the same. There is a lot that we want to achieve, and we are doing it with strategic focus and clarity, mindful of our experience in the laboratory while leveraging our corporate experience, and by utilizing our resources efficiently. By focusing on execution and staying true to our vision, we believe we will create more and more value for all of our stakeholders over the long run. There are so many possibilities and it is only the beginning of an exciting and fruitful journey.

THE YEAR AHEAD

We believe 2019 will be a defining year for Athenex in terms of the clinical pipeline. Two Phase 3 studies are nearing completion and we have commercialization and marketing plans ready for these products, if approved for commercialization. The number of clinical studies has only continued to grow, and the development of two new technologies is well underway.

With our lead drug candidate, Oraxol (HM30181A and oral paclitaxel), completing target enrollment in January 2019 for the Phase 3 study in metastatic breast cancer and anticipating topline results later this year, we believe we have real potential to change the tide of chemotherapy and establish our leadership in the oral taxane market. A similar Phase 2 study in metastatic breast cancer, conducted in Taiwan, has already shown encouraging response rates and safety results.

With the positive progress seen in the Oraxol program, we are extremely excited about what this means for the Orascovery Platform. To capture the immense opportunity we believe is available, we are pursuing clinical studies in other indications as well as advancing the clinical programs for other Orascovery drug candidates in the pipeline.

Our study evaluating Oraxol in combination with Eli Lilly's ramucirumab for the treatment of gastric cancer is in a Phase 1b study, now in a third cohort after seeing positive preliminary results from the first and second cohorts. We initiated a Phase 1/2 study to evaluate Oraxol in combination with an anti-PD1 antibody (pembrolizumab) in patients with advanced solid malignancies. The U.S. FDA also granted Oraxol an Orphan Drug Designation for the treatment of angiosarcomas and we have initiated a pilot study for Oraxol. We are committed to product life cycle management and we are seeing the potential benefits of Oraxol to treat a broad range of cancers.

We believe that our Orascovery technology works for other commonly used chemotherapeutic drugs that are P-glycoprotein substrates and have seen encouraging results confirming our belief. For instance, Oradoxel (HM30181A and oral docetaxel) and Oratecan (HM30181A and oral irinotecan) are ready to advance to Phase 2 studies, with preliminary results showing the potential for improved efficacy and/or mitigation of certain major side effects seen with the intravenous drugs. We are also delighted to have received an IND allowance for Eribulin ORA (HM30181A and oral eribulin) in October 2018, as eribulin is a compound that targets paclitaxel-resistant tumors. Overall, we believe the commercial opportunity for our Orascovery products could be very significant.

Our other lead drug candidate, KX2-391 (also known as KX-01) ointment for actinic keratosis (AK), is part of our Src Kinase Inhibition Platform. AK are very common, precancerous lesions caused by UV exposure. We announced topline Phase 3 results at the American Academy of Dermatology Annual Meeting in March 2019 in a late breaker session, and the efficacy and safety results were very positive. KX2-391 ointment has the potential to be a valuable treatment option for AK patients and we are working closely with our partner, Almirall, towards regulatory approval and commercialization in the U.S. and Europe. We are also exploring other markets, which could provide additional financial growth drivers.

KX2-391 is positioned for continued growth as we consider additional AK developments and other skin conditions for the ointment, as well as opportunities to treat skin-related diseases and cancers under other formulations. Also from the Src Kinase Inhibition Platform is KX2-361 (also known as KX-02), which has received an Orphan Drug Designation from the U.S. FDA for the treatment of glioblastoma multiforme. The ability of the compound to cross the blood-brain-barrier is potentially groundbreaking and could open up new treatment possibilities for these aggressive tumors.

In addition to the two Platforms above, we are making progress in the Cancer Immunotherapy and Arginine Deprivation Therapy Platforms, which we in-licensed in mid-2018. For the cancer immunotherapy product, we have seen encouraging preliminary results from investigator-initiated pilot studies in China. The program in China is led by our partner, Xiangxue Life Sciences, which recently received IND allowance from China's healthcare regulatory agency. Pegtomarginase has shown proof of concept in preclinical studies and is the first biologic drug we are developing. We expect to submit IND applications to the U.S. FDA for both drug candidates this year and look forward to initiating clinical studies in the U.S. soon.

All in all, we have two pivotal Phase 3 clinical candidates, and six other clinical candidates in either Phase 2 or 1 studies, demonstrating our breadth in R&D capabilities and commitment to our platforms.

LONGER TERM OUTLOOK

Oncology remains the largest therapeutic area in the world. The oncology field is constantly evolving, which is why we need to innovate. We expect chemotherapy to continue to be one of the most widely used approaches for cancer

treatment, while we also anticipate competing innovations, like immunotherapy, which has shown promising development and advancement in recent years, to compete for the oncology market share. There is also growing evidence that manipulating the tumor microenvironment to optimize the effects of cancer therapies will be a critical addition to this therapeutic area. We have learned that most cancer patients do not just take one therapy and a number of them unfortunately see the disease metastasize. We believe that combination therapies will be the core to the future of oncology, and maintenance therapy, a largely untapped area, will be increasingly relevant as it would give patients the chance to take long-term control of an ever-evolving disease.

While our current pipeline is expected to capture nearly 80% of all cancer-related mortality, we are already thinking about the second generation for Orascovery, namely the dual inhibition platform, and our preclinical efforts remain active. The Cancer Immunotherapy and Arginine Deprivation Therapy Platforms form an important part of our efforts to replenish our pipeline and demonstrate a unique foresight to address evolving and major unmet medical needs. These are all great examples of the continuous pursuit of our mission and the longer-term vision of capitalizing on the synergies in our pipeline. We are constantly innovating and, on the lookout, to evaluate and establish new technologies that complement our product portfolio and ultimately augment the cancer therapies available for patients.

We remain focused on strong execution, which we have demonstrated to date by meeting the milestones we set out during the IPO. Unlike many small-to-mid-sized biotechnology companies, we believe our commercial infrastructure is falling into place, with marketing plans for Oraxol and KX2-391 ointment ready and relationships with the healthcare community in the U.S. established, if and when the drugs get approved.

With the fundamental building blocks in place, we believe we are on the path to becoming a truly global oncology organization.

OUR PEOPLE, PARTNERS AND PATIENTS

We would like to express our gratitude to our people, partners and patients, who have been instrumental in getting the company to where it is today.

People

Our team is a diverse and hard-working group spread around the world but united by a passion to find the cure to a deadly disease and significantly improve the lives of cancer patients. In 2018 we hired several key leaders in clinical, commercial and operations to join our top-notch team. I am extremely fortunate to be able to work with seasoned professionals who possess strong experience, knowledge and intuition, and share in the company's vision. We will continue to add to our Athenex family by recruiting talent to support our continued growth and development.

Partners

Collaborations in development and commercialization are an important aspect for biotechnology companies. Since our inception, we have developed strong relationships with partner companies and public and private institutions globally that have allowed us to expand our portfolio, continually innovate and ensure the broadest commercial reach of our proprietary drugs once they are approved. Our partnership strategy is designed to create the most value for patients, the company and our shareholders, and we thank our partners for their trust in us.

Patients

We strive to develop and deliver life-changing medicines to cancer patients. We would like to thank the patients who have participated and are currently participating in our clinical trials, which will help us achieve our goals and give us valuable perspective as we continue to innovate.

CONCLUSION

We believe Athenex is well-positioned for long-term growth and to capture the maximum economic opportunity from the entire biopharmaceutical value chain. We are focused on excellent execution and developing next generation

cancer therapies. I am extremely proud of our Athenex family and what we have achieved over the past 15 years together. I am also extremely grateful to our Board of Directors for their guidance and support.

I look forward to 2019 and the years to come, as we continue to deliver results for patients and create increasing value for our shareholders.

Sincerely,

Johnson Y.N. Lau

Chief Executive Officer and Chairman of the Board of Directors

FORWARD-LOOKING STATEMENTS AND CERTAIN FACTORS MAY AFFECT OUR BUSINESS

We have included in this letter "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 relating to our results of operations and financial position, business strategy, potential growth opportunities, clinical development activities, the timing and results of clinical trials and potential regulatory approval and commercialization of product candidates. In some cases, these forward-looking statements may be identified by terminology such as "believe," "may," "will," "should," "predict," "goal," "strategy," "potentially," "estimate," "continue," "anticipate," "intend," "indicate," "could," "would," "project," "plan," "expect," "seek" and similar expressions. These statements are not guarantees of future performance. Actual outcomes and results may differ materially from our expectations and what is expressed in these forward-looking statements, based on risks, uncertainties and other factors discussed in the "Risk Factors" section of our Annual Report on Form 10-K and in other reports we file with the U.S. Securities and Exchange Commission, which are available through the Investor Relations section of our website at ir.athenex.com. Our forward-looking statements speak only as of the date of this letter or as of the date they are made, and we undertake no obligation to update them.

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2018

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to
Commission file number 001-38112

ATHENEX, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	43-1985966
State or other jurisdiction of incorporation or organization	**(I.R.S. Employer Identification No.)**
1001 Main Street, Suite 600 **Buffalo, NY** **United States**	**14203**
(Address of principal executive offices)	**(Zip Code)**

(716) 427-2950
Registrant's telephone number, including area code
Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Exchange on Which Registered
Common Stock, par value $0.001 per share	**The Nasdaq Global Select Market**

Securities registered pursuant to section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See the definitions of "large accelerated filer", "accelerated filer", "smaller reporting company", and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐ (Do not check if a smaller reporting company)	Smaller reporting company	☐
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of common equity held by non-affiliates of the registrant calculated based on the closing price of $18.66 of the registrant's common stock as reported on The Nasdaq Global Market on June 30, 2018, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $692.6 million.

As of March 1, 2019, 67,023,498 shares of common stock of the registrant were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2019 annual meeting of stockholders currently scheduled to be held June 11, 2019 are incorporated by reference into Part III hereof.

SPECIAL NOTE ABOUT FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (Annual Report) contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act), and section 27A of the Securities Act of 1933, as amended (Securities Act). All statements other than statements of historical fact are "forward-looking statements" for purposes of this Annual Report. These forward-looking statements may include, but are not limited to, statements regarding our future results of operations and financial position, business strategy, market size, potential growth opportunities, clinical development activities, the timing and results of clinical trials and potential regulatory approval and commercialization of product candidates. In some cases, forward-looking statements may be identified by terminology such as "believe," "may," "will," "should," "predict," "goal," "strategy," "potentially," "estimate," "continue," "anticipate," "intend," "indicate," "could," "would," "project," "plan," "expect," "seek," "strategy," "mission" and similar expressions and variations thereof. These words are intended to identify forward-looking statements.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in the "Risk Factors" section and elsewhere in this Annual Report on Form 10-K. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this report to conform these statements to actual results or to changes in our expectations, except as required by law.

Unless the context indicates otherwise, as used in this Annual Report, the terms "Athenex," "the Company," "we," "us," and "our" refer to Athenex, Inc., a Delaware corporation, and its subsidiaries taken as a whole, unless otherwise noted.

PART I

Item 1. Business.

Overview

We are a global clinical stage biopharmaceutical company dedicated to becoming a leader in the discovery and development of next generation drugs for the treatment of cancer. Athenex is organized around three platforms, including an Oncology Innovation Platform, a Commercial Platform and a Global Supply Chain Platform. The Company's current clinical pipeline is derived from four different platform technologies: (1) Orascovery, based on non-absorbed P-glycoprotein inhibitor, (2) Src kinase inhibition, (3) T-cell receptor-engineered T-cells (TCR-T), and (4) Arginine deprivation therapy. We have assembled a leadership team and have established operations in the U.S. and China across the pharmaceutical value chain to execute our mission to become a global leader in bringing innovative cancer treatments to the market and improve health outcomes.

Orascovery platform

Common treatments for cancer include surgery, radiation therapy, chemotherapy and such newer methods as targeted therapy; however, chemotherapy remains one of the key treatment options for cancer patients and is traditionally administrated intravenously. A major part of cancer treatment consists of IV chemotherapy. The limitations of IV chemotherapy involve repeated painful IV line insertions, potential anaphylactic reactions, expensive hospital visits, toxic side effects and poor quality of life for cancer patients. To address this unmet medical need, development of oral chemotherapy that is more effective and more tolerable, can be taken easily orally at home, avoiding weekly IV infusions and hospital visits (e.g. paclitaxel) is urgently needed. Oral administration of many IV chemotherapy drugs has been unsuccessful because human intestinal cells have a P-gp pump that pumps out chemotherapy drugs (e.g. paclitaxel, doxetaxel, irinotecan, etc.) before they can be absorbed. Many attempts at new drug development of P-gp inhibitors failed clinically because of lack of clinical efficacy or significant toxicities.

We believe that oral administration can overcome key limitations and challenges around IV administration of certain cytotoxic chemotherapies and that our Orascovery platform will establish a new paradigm in the use of oral anti-cancer drugs for cancer treatments. Our Orascovery platform is based on the novel P-gp pump inhibitor molecule HM30181A, which we in-licensed in 2011 from Hanmi Pharmaceutical Co., Ltd. ("Hanmi"), a major Korean pharmaceutical company focusing on research and development. The P-gp pump is a plasma membrane protein on the cells of the gut which forms a localized drug transport system and prevents oral absorption at therapeutic levels of many well-known, widely used P-gp substrate cancer chemotherapeutic drugs such as paclitaxel, irinotecan and docetaxel, limiting their current delivery to IV. These chemotherapy agents are widely used to treat multiple types of cancer. A cancer patient's inability to tolerate IV chemotherapies has limited the effectiveness of IV anti-cancer therapies. Co-administration of HM30181A with oral chemotherapies, like paclitaxel, facilitates the oral absorption of paclitaxel by blocking P-gp in intestinal cells and enables oral dosing at therapeutic blood levels which have not been successfully and safely achieved to date without the use of HM30181A. We have learned through clinical studies that this technology allows for certain active chemotherapeutic agents to be absorbed into the blood orally as compared to IV and may enable some patients to tolerate many cycles of treatment. Oraxol, our leading Orascovery drug candidate is composed of HM30181A co-administered with an oral dosage form of paclitaxel. We have four other major clinical product candidates in this platform, Oratecan, Oradoxel, Oratopo and Eribulin ORA, which include HM30181A co-administered with an oral formulation of the widely used IV-administered chemotherapeutic agents, irinotecan, docetaxel, topotecan and eribulin, respectively.

We believe our Orascovery platform will establish a new paradigm in the use of oral anti-cancer drugs for cancer treatments in at least three ways. First, with the use of HM30181A, clinicians may be able to consistently deliver oral doses of certain chemotherapeutic drugs over a greater number of cycles and duration of time. Second, we believe active drug exposure of chemotherapeutic agents in the patient over time is a critical element in determining efficacy, and we believe we can achieve greater tolerability with administration of HM30181A in combination with chemotherapeutic drugs as compared to the current IV standards of care. Third, in light of better tolerability of standard chemotherapies delivered orally, combination with immuno-oncology and targeted anti-cancer treatments can be potentially optimized compared to current treatment paradigms.

We are rapidly advancing our lead Orascovery drug candidate, Oraxol. In January 2018, we received positive feedback from the United States Food and Drug Administration (FDA) on the design of the ongoing Phase 3 trial, which indicated that if the study meets the primary endpoint with an acceptable benefit to risk profile, it could be adequate as a single comparative trial to support registration of Oraxol in the United States (U.S.) for the indication of metastatic breast cancer. Also, in January 2018, the National Medical Products Administration (NMPA, formerly the China Food & Drug Administration or CFDA) allowed the Investigational New Drug (IND) application for Oraxol. Acceptance of the Oraxol IND by the NMPA allowed us to commence a clinical trial program for Oraxol in China in 2018. In February 2018, we enrolled patients for a second interim analysis in the Oraxol KX-ORAX-001 Phase 3 clinical trial in the third quarter of 2018. In April 2018, the FDA granted orphan drug status to Oraxol for the treatment of angiosarcomas. In September 2018, we received a positive recommendation by the Data and Safety Monitoring Board (DSMB) of the

second interim analysis of the Oraxol Phase 3 Clinical Trial, a randomized controlled clinical trial comparing Oraxol monotherapy against IV paclitaxel monotherapy in patients with metastatic breast cancer. The DSMB reviewed the efficacy and safety data of this clinical trial, noted that more than 320 patients had been recruited and unanimously recommended that the Company continue the Oraxol Phase 3 Clinical Trial and complete the recruitment of the patients. In October 2018, we presented encouraging efficacy and safety data of Oraxol in the treatment of metastatic breast cancer patients obtained from a Phase 2 clinical trial conducted in Taiwan at the European Society for Medical Oncology (ESMO) Congress. Results from twenty-four patients with metastatic breast cancer were reported. Eleven patients (45.8%) achieved partial remission (PR), ten patients (41.7%) had stable disease (SD) (two patients with SD had their last computed tomography (CT) scans conducted in early November), and three patients had progressive disease (PD). Drug-related serious adverse events consisting of grade 4 neutropenia were observed in three patients and all recovered completely. There was no dose limiting neuropathy observed. The Oraxol pharmacokinetic (PK) profiles at week 1 were reproducible at week 4, and the plasma area under the curve (AUC) exposure is similar to those reported for IV paclitaxel at 80 mg/m^2 weekly. In November 2018, we initiated a Phase 1/2 clinical study to assess the safety, tolerability and activity of Oraxol in combination with an anti-PD1 antibody (pembrolizumab) in patients with advanced solid malignancies. The study, KX-ORAX-011, is a Phase 1/2 study being conducted in patients with urothelial, gastric/gastroesophageal or non-small cell lung cancer that have previously failed treatment with a checkpoint inhibitor. The primary outcome measures are tumor response rate and determination of maximum tolerated dose (MTD), while the secondary outcome measures include progression free survival, overall survival, duration of response and pharmacokinetics. In December 2018, our global Phase 1b clinical trial of Oraxol (oral paclitaxel plus HM30181A) plus ramucirumab (monoclonal antibody to VEGF-R2) in gastric cancer patients who failed previous chemotherapies completed the second cohort of patients. The results indicated strong positive signals of efficacy and the treatment was well tolerated. In January 2019, the target enrollment of 360 patients in the Oraxol Phase 3 clinical trial in metastatic breast cancer was achieved on schedule. We reaffirmed that top line data from the study is expected to be available in mid-2019.

Src Kinase Inhibition platform

We have also developed novel small molecule compounds through our Src Kinase Inhibition platform. The Src Kinase inhibition platform refers to novel small molecule compounds that have differentiated multiple-mechanisms of actions including: (1) the inhibition of the activity of Src Kinase and (2) the inhibition of tubulin polymerization. We believe the combination of the two mechanisms of action (MOAs) provides a broader range of anti-cancer activity compared to either MOA alone. Our three key clinical product candidates in this platform are KX2-391 (or KX-01) ointments for actinic keratosis, skin cancers and psoriasis; KX-01 oral for solid and liquid tumors; and KX2-361 (or KX-02) for glioblastoma multiforme, or GBM.

We are rapidly advancing our lead candidate in the Src Kinase Inhibition platform, KX2-391 ointment, for actinic keratosis, or AK. AK has an estimated prevalence of over 58 million patients and was found in approximately 14% of patients visiting dermatologists in the U.S. while GBM has an incidence of 2 to 3 per 100,000 adults per year and accounts for 52% of all primary brain tumors according to satistics published by National Cancer Institue. If left untreated, 10-15% of AK lesions will develop into skin cancers. Our Phase 1 clinical study and data from our Phase 2 clinical study demonstrated a complete response rate of up to 43% among subjects who received treatment on their faces, with few severe local skin reactions, or LSRs, reported with the dosing regimen studied. Currently available treatments are limited by severe LSRs such as vesiculation, pustulation, erosion and ulceration, with low patient compliance. We believe physicians and patients have avoided topical treatments because of the pronounced side effects of the current treatments such as ingenol mebutate, imiquimod, fluorouracil, and that an ointment product with good clinical activity and a favorable side effect profile could capture substantial new market share for treatment of this condition. Patient enrollment in two Phase 3 studies commenced in September 2017, and the enrollment was completed in February 2018. In July 2018, we announced that both of our Phase 3 pivotal efficacy studies achieved their primary endpoint of 100% clearance of AK lesions at Day 57 within the face or scalp treatment areas with each study achieving statistical significance ($p<0.0001$). Statistical significance ($p<0.001$) was achieved for both face and scalp subgroups as well. These two double-blind, randomized, vehicle-controlled, studies were designed as pivotal Phase 3 efficacy and safety studies to support the registration of KX2-391 (or KX-01) as field therapy for AK of the face and scalp. The studies, each conducted at 31 centers in the U.S., enrolled a total of 702 subjects. KX2-391, or vehicle ointment, was applied once daily for five days. In addition to the clinical activity of KX2-391, the LSR profile was within expectations, in line with the Phase 2 study reported at the annual American Academy of Dermatology (AAD) meeting in February 2018 in San Diego. Both studies are still on-going to complete the one-year follow-up of the patients who had complete responses. We will be submitting a request to the FDA for a pre-new drug application (NDA) submission meeting to discuss the data and regulatory submission timelines.

In December 2017, we entered into a license agreement with Almirall S.A. (Almirall), pursuant to which we granted to Almirall an exclusive, sublicensable license of certain of our intellectual property for the development and commercialization of topical products containing KX-01 for the treatment of AK in the United States and substantially all European countries. We believe this partnership validates the potential of this candidate and that this partnership is an important step in the development and commercialization of KX-01 develop and commercialize this product. For additional information, please see “Business—License and Collaboration Agreements—Almirall License Agreement.”

T-cell Receptor-engineered T-cells (TCR-T) Platform

In 2018 we commenced development of T-cell Receptor Engineered T-Cells (TCR-T) pursuant to a new in-license. The TCR-T immunotherapy technology harnesses and enhances the patient's immune cells to target and eliminate cancer. It is a cell-based therapy that takes advantage of unique attributes of T-cell receptor (TCR) mediated target recognition and provides a potent and selective TCR-T directed response against cancer cells. The preliminary results of pilot studies in China, in which patients received T-cell receptor affinity enhanced specific T-cell therapy (TAEST), showed encouraging clinical signals in terms of efficacy and safety. For additional information, please see "Business—License and Collaboration Agreements—TCR-T License Agreement."

Arginine Deprivation Therapy Platform

In 2018 we commenced development of Arginine Deprivation Therapy pursuant to a new in-license. The Arginine Deprivation Therapy product, based on a pegylated genetically engineered human arginase, targets cancer growth and survival by interrupting the supply of an essential amino acid, arginine, to a proportion of cancers with disrupted urea cycle. Our proprietary arginase biologic product is designed to deplete arginine from tumors with disrupted urea cycle, while healthy cells, capable of producing their own argininеare largely unaffected.

In addition to our existing portfolio of clinical candidates, our research and development teams are evaluating additional applications of our novel technology platforms. For example, our novel Cytochrome P450 (CYP) and P-gp dual inhibitor technology could expand the breadth of application for our oral enabling platform.

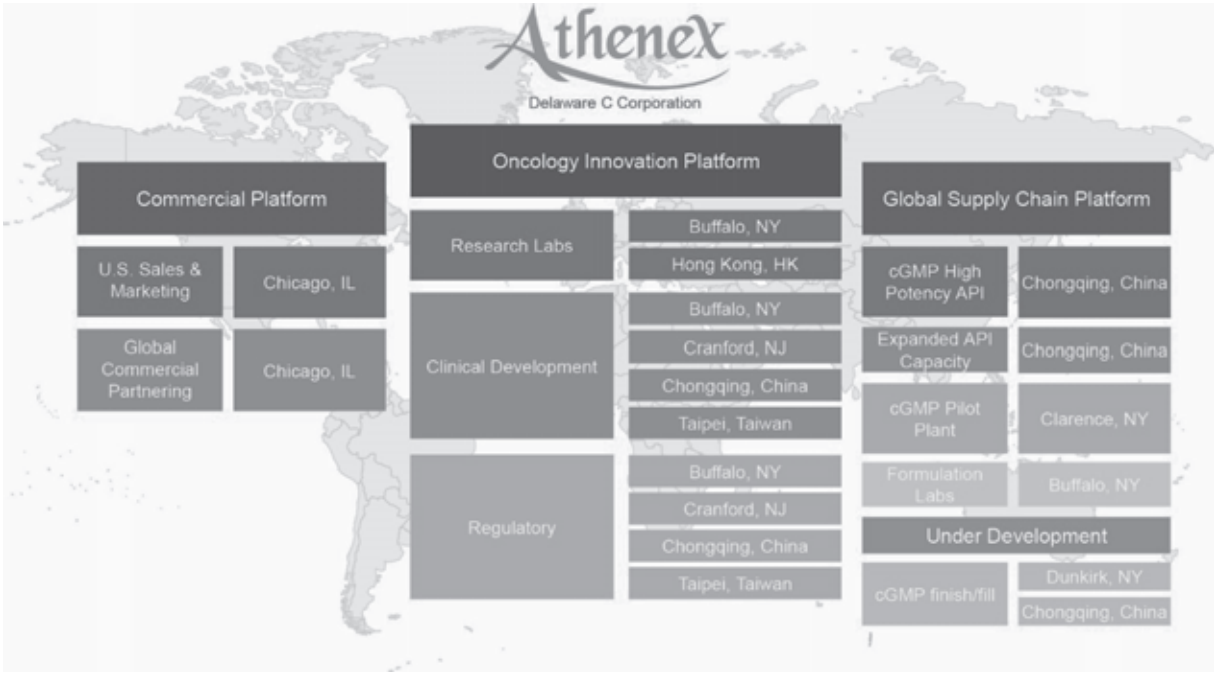
The following pipeline chart sets forth certain information concerning our key innovative drug product candidates:

Program	Drug Candidate	Indication	Major Territories Owned	Pre-Clinical	Phase 1	Phase 2	Phase 3
Orascovery (P-gp + chemo-therapeutic agents)	Oraxol	Breast cancer	Worldwide, except Korea				
	Oraxol with ramucirumab*	Gastric cancer	Worldwide, except Korea				
	Oratecan	Solid tumors	Worldwide, except Korea				
	Oradoxel	Solid tumors	Worldwide, except Korea				
	Oratopo	Solid tumors	Worldwide, except Korea				
	Eribulin ORA	Solid tumors	Worldwide, except Korea				
Src Kinase Inhibition	KX-01 Ointment	Actinic Keratosis	Partnered in U.S. and Europe				
		Psoriasis	Worldwide, except China				
		Skin cancers	Worldwide				
	KX-01 Oral	Liquid tumors	Worldwide				
		Ovarian cancer	Worldwide				
	KX-02 Oral	Glioblastoma	Worldwide, except China				
Dual Inhibition	ATNX-04 (CYP / P-gp)	Multiple tumors	Worldwide				
Cellular Immunotherapy	TCR-T Immunotherapy	Multiple Tumors	Worldwide, except China				
Pegylated Modified Human Arginase	Pegtomarginase	Multiple Tumors	Worldwide				

* Collaboration with Eli Lilly and Company, makers of ramucirumab

To date, we and our partners have conducted, or are conducting, clinical trials across sites in the U.S., South Korea, New Zealand, Taiwan, Argentina, Chile, Colombia, Ecuador, Guatemala, Honduras, the Dominican Republic, Peru and China.

In advance of the launch of our proprietary product candidates in the U.S., our commercial team has begun to market oncology and oncology symptom-related products to fund our infrastructure build-out. We believe it is important to minimize supply chain disruptions for high potency oncology active pharmaceutical ingredients. We have thus internalized key components of the supply chain that we believe are integral to minimizing the associated risks. We have organized our business model into three segments - Oncology Innovation Platform, Commercial Platform and Global Supply Chain Platform - with operations in both the U.S. and China. Our global operations across the three segments are shown below:



Our Global Supply Chain Platform manufactures active pharmaceutical ingredients, or API, for use internally in our research and development and clinical studies and for sale to pharmaceutical customers globally. The platform includes Polymed Therapeutics, Inc. and Chongqing Taihao Pharmaceutical Co Ltd, collectively Polymed. Our Commercial Platform currently markets eighteen APIs produced by our Global Supply Chain Platform in the specialty and generic market segment in the U.S., twenty-four products by the Athenex Pharmaceutical Division, or APD, and six products subject to Section 503B of the Federal Food, Drug and Cosmetic Act (FDCA) through our FDA registered outsourcing facility. Our Commercial Platform is expected to launch an additional thirteen products in the first half of 2019.

Our leadership team has been carefully assembled to capture the global commercial market opportunities in novel drug development. Our executive officers are seasoned leaders with complementary skill sets across global pharmaceutical research and development, operations, supply chain and manufacturing, capital markets and mergers and acquisitions. We believe this characteristic is unique for a U.S. based company, and we believe we will be able to utilize this strength to create long term value for cancer patients, our employees and our shareholders. Our team is excited about the prospects of creating new paradigms in the treatment of cancer in developed markets and also driving our product candidates to emerging markets where patient access to treatments has historically been limited.

Strategy and Mission

We have a comprehensive and experienced leadership team who have come together under one organization to achieve our mission. Our mission is to improve the lives of cancer patients by creating more effective, safer and tolerable treatments. To achieve our mission, we intend to execute the following strategies:

Rapidly and concurrently advance our clinical product candidates.

We intend to pursue the fastest feasible pathways to approval of our existing novel oral absorption technology. We have recently completed enrollment of patients in a Phase 3 clinical trial of Oraxol, which is comprised of a combination of our novel investigational absorption-enhancing tablet, HM30181A, with the oral capsule formulation of paclitaxel. We believe that if we demonstrate the safety and effectiveness of our oral absorption technology with Oraxol, the other drug candidates paired with this technology will face a more efficient development process. In addition, we presented our Phase 2 clinical study data for KX-01 ointment at the AAD meeting, and we completed patient enrollment for both Phase 3 clinical studies of KX-01 ointment for AK in February 2018. In July 2018, we announced that both of our Phase 3 pivotal efficacy studies achieved their primary endpoint of 100% clearance of AK lesions at Day 57 within the face or scalp treatment areas. An IND for Eribulin has been allowed, and Phase 1 trials are expected to commence in early 2019. We identified potential dosing regimens for Oratecan and Oradoxel Phase 2 development, which we are planning to initiate in 2019. For Oratecan, we believe that we can identify a Phase 2 dose that will produce similar exposure to SN38 as a labeled dose of IV irinotecan. For Oradoxel, we believe that we can achieve similar exposure to IV docetaxel with one or two days of dosing every three weeks. Preliminary results from our joint TAEST Phase 1 pilot study in China indicate positive clinical efficacy and safety results. We plan to file an IND for pegtomarginase, an Arginine Deprivation Therapy product, in the first half of 2019.

Leverage our global research and development operations to continue development of an oncology-focused product pipeline.

We have research and development operations in the U.S. and China that are focused on advancing our existing product pipeline and on developing additional novel clinical drug product candidates in order to replenish our development pipeline as other candidates mature. We have developed a core competency in oral absorption technology and apply that skill to develop new methods of drug discovery and to identify new pipeline candidates, such as our oral eribulin IND program. In addition, we may leverage our research and development capabilities to partner with others for the development of new pipeline candidates. We believe that we can create substantial long-term value by pursuing a robust, ongoing research and development program.

Build a proprietary commercial platform and selectively leverage collaborative relationships to achieve global drug sales, marketing and distribution.

We built our U.S. commercial operation in preparation for future FDA approvals of our proprietary product candidates. We believe that our experienced product commercialization team can build an infrastructure that leverages both our global facilities and collaborative relationships to achieve global distribution of any products approved by the FDA and regulatory authorities in other jurisdictions, as applicable, in a timely and cost-effective manner. Our strategic partner Almirall will employ its expertise to support the development in Europe and also to commercialize KX2-391 in the US and European countries, including Russia.

Continue to build-out our supply chain and cGMP manufacturing capabilities.

Our internal supply chain is uniquely suited to execute in both the U.S. and China, two of the world's largest pharmaceutical markets. We intend to utilize current Good Manufacturing Practices, or cGMP, manufacturing facilities from our public/private partnerships in both the China and U.S. markets as a mechanism to access both important markets and minimize supply disruptions. We intend to manufacture certain of our proprietary drugs and our partnered drugs commercialized around the world. Additionally, we expect that the expansion of our existing cGMP high potency API facilities will provide us with more flexibility and control over high potency APIs as our drugs become commercialized. Our goal is to continue expanding this infrastructure and to leverage it to maintain future financial flexibility by optimizing our financial commitments and capital expenditures, which we believe will create value for shareholders.

Selectively pursue strategic M&A or licensing opportunities to complement our existing operations.

We continue to pursue acquisitions and in-licensing opportunities. Through in-licensing, we acquired an Arginine Deprivation Therapy, Pegtomarginase, which is an enzyme capable of depleting some tumors of a key resource for their growth and survival, the amino acid arginine. In addition, our newly formed entity, Axis Therapeutics, in-licensed the worldwide (excluding mainland China) rights of all the intellectual properties and know-how of a TCR-T Cellular Immunotherapy. We will continue to target opportunities that will complement our existing portfolio and operations to create value for shareholders and support our business strategy and mission.

Operating Segments

We operate in three segments, including our Oncology Innovation Platform, dedicated to the research and development of the Company's proprietary drugs; our Commercial Platform, focused on the sales and marketing of the Company's specialty drugs and the market development of our proprietary drugs; and our Global Supply Chain Platform, dedicated to providing a stable and efficient supply of active pharmaceutical ingredients for our clinical and commercial efforts.

Oncology Innovation Platform

Our Orascovery Research Platform

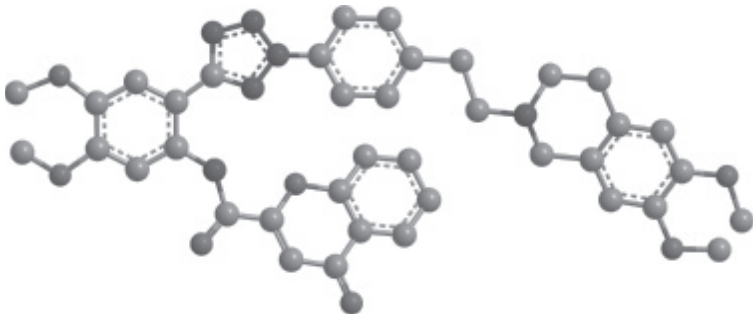
We are developing a series of orally administered chemotherapeutic agents using our proprietary P-gp pump inhibitor delivery system. The technology is designed to enable the oral administration of many cancer agents, which currently are only given by IV due to poor oral absorption. Oral administration of certain cytotoxic chemotherapies can potentially overcome several key challenges in IV administration of those molecules. We believe that our Orascovery platform overcomes these challenges by allowing more frequent dosing over longer periods of time, which we believe will lead to better tolerability and allow for higher total dosage and longer time exposure to the chemotherapeutic agent. Further, we believe additional agents like immuno-oncology and targeted therapy can be better optimized with longer administration of oral chemotherapy agents.

Chemotherapeutic agents such as paclitaxel, irinotecan, docetaxel, topotecan and eribulin are clinically proven and widely used but have historically been limited to IV administration. The combined worldwide revenue of marketed formulations of these agents was estimated to be $1.9 billion in 2015 and is expected to grow at a CAGR of 9.6% to reach $3.6 billion by 2022. We believe our pipeline products, which leverage our proprietary delivery system that enables oral administration of these chemotherapeutic agents, will substantially expand the use of these chemotherapeutic agents. Additionally, we believe that there is a substantial opportunity for our products to be used in combination with targeted therapies. Furthermore, as shown by Abraxane, novel technology applied to a traditional chemotherapy agent may achieve pricing premiums if data demonstrates superior efficacy and tolerability as compared to current standards of care. We believe our pipeline products will be able to capture a large untapped market and achieve significantly larger market potential than the revenue generated by existing formulations, due to (1) increasing adoption of oral therapy due to patient preference, (2) the potential for improved response rates through greater exposure (based on our predictive model), (3) the potential for improved tolerability (based on our predictive model) and (4) the possibility to expand the market through combination therapies with immune-oncology therapy and oral targeted treatments, of which, 39% are already oral.

The table below shows certain clinical trials for our major Orascovery drug candidates.

	Protocol	Phase	Indication	Location	Status
ORAXOL	HM-OXL-101	I	Solid Tumor	South Korea	Completed
	HM-OXL-102	I	HM30181A PK, Safety, Tolerability	South Korea	Completed
	HM-OXL-103	I	P-glycoprotein inhibition by HM30181A	South Korea	Completed
	HM-OXL-104	I	Duration of P-glycoprotein inhibition and verify the optimal dose of HM30181AK.	South Korea	Completed
	HM-OXL-201	I/II	Gastric	South Korea	Completed
	ORAX-01-13-US	I	MTD PK	United States	Completed
	ORAX-01-14-NZ	I	Bioavailability PK	New Zealand	Completed
	KX-ORAX-001	III	Breast	South America	Enrollment complete
	KX-ORAX-002	I	Bioequivalence PK	New Zealand/ Taiwan, AUS	Enrolling
	KX-ORAX-003	I	Tolerability PK	New Zealand, Taiwan, US	Enrolling
	KX-ORAX-004	I	MTD PK	United States	Enrolling
	KX-ORAX-005	I	Gastric	Asia-Pacific/ United States	Enrolling
	KX-ORAX-007	I	Breast	Asia-Pacific	Enrollment complete
	KX-ORAX-008	I	Bioavailability PK	Asia-Pacific	Enrolling
	KX-ORAX-010	I	Bioavailability PK	Asia-Pacific United States	Enrolling
	KX-ORAX-011	I	Pembrolizumab/Oraxol Combination/PK	United states	Enrolling
	KX-ORAX-012	I	Food Effect / PK	United Kingdom	Approval pending
	KX-ORAX-013	I	Bioavailability / PK Tablet 90mg vs 30mg	Europe	Under development
HM30181A	KX HM 001	I	Drug to Drug Interaction (Dabigatran)	New Zealand	Enrollment complete
ORATECAN	HM-OTE-101	I	Solid Tumor	South Korea	Completed
	HM-OTE-102	I	Solid Tumor	South Korea	Completed
	HM-OTE-103	I	Solid Tumor	South Korea	Completed
	ORTE-01-14-US	I	MTD PK	United States	Ongoing
	KX-ORTE-001	I	Bioavailability PK	New Zealand	Start pending
ORADOXEL	KX-ORADOX-002	I	Efficacy and Safety	New Zealand	Enrolling
	KX-ORADOX-003	I	MTD PK	United States	Enrolling
ORATOPO	KX-ORATOP-001	I	Solid Tumor	United States, United Kingdom	US enrolling
ERIBULIN ORA	KX-ERB-001	I	Solid Tumor	United States United Kingdom	US approval pending

HM30181A—Our Novel P-gp Pump Inhibitor



Overview

The novel P-gp inhibition by HM30181A forms the cornerstone of our Orascovery platform, and enables the administration of oral dosing formats of paclitaxel (Oraxol), irinotecan (Oratecan), docetaxel (Oradoxel), topotecan (Oratopo) and eribulin (Eribulin ORA), each of which is currently under clinical development. The feature that distinguishes HM30181A from other small molecule P-gp inhibitors is that this novel compound is specific to P-gp, does not interfere significantly with the activity of other related transporters and does not significantly inhibit cytochrome 3A4, an enzyme that is important in the metabolism of commonly used drugs. HM30181A is minimally absorbed following oral administration. This localizes P-gp inhibitory activity in the gastrointestinal tract, limiting the potential for interaction at additional systemic sites where P-gp is expressed. Based on the results of our HM30181A clinical development programs to date, inhibition of gastrointestinal P-gp significantly improves the absorption of chemotherapy agents to achieve systemic exposure profiles which enhance the efficacy and may reduce toxicity of these established chemotherapeutic agents. Based on its pharmacological profile and low systemic absorption, HM30181A is not expected to cause drug-to-drug interactions other than enhancement of oral absorption of medications which are P-gp substrates.

Background—Chemotherapy Treatments

IV paclitaxel is used widely for the treatment of breast, ovarian and lung cancer. Due to its poor solubility, paclitaxel is usually dissolved in ethanol and polyethoxylated castor oil, which is a major cause of IV hypersensitivity reactions. As a result, premedication with steroids and antihistamines is required to minimize these adverse reactions. Additional common toxicities associated with IV administration of paclitaxel include neuropathy, neutropenia and alopecia. These side effects limit dose intensification and often require reduction in dosing.

As a single agent or in combination, IV paclitaxel is administered at a variety of doses and regimens that are approved for therapeutic use for various indications, including 135 and 175 mg/m^2 administered as both three and twenty-four hour infusions once every three weeks. Over the past fifteen years, there has been great interest in dose dense therapy with paclitaxel, switching from the conventional every three-week regimen to administering the drug once weekly. Dose dense treatment with paclitaxel has various advantages that can lead to an increase in the overall exposure, as measured by AUC, over a treatment cycle, while balancing the adverse event profile normally observed, such as neutropenia. This concept is consistent with the hypothesis of maintaining sufficient drug concentrations above a threshold target value for an extended duration.

Based on various clinical trials conducted across multiple tumor types, the weekly regimen of paclitaxel can lead to an increase in response rate, progression free survival, and overall survival. For example, in a clinical trial investigating different dosing schedules of paclitaxel for the treatment of breast cancer in the adjuvant setting, dose-dense paclitaxel given as 80 mg/m^2 weekly led to an improvement in disease-free and overall survival, with a five year survival rate of 81.5% versus 76.9%. In addition, weekly paclitaxel (80 mg/m^2) has a benefit in response rate (42% vs. 29%), time to tumor progression (TTP) (nine vs. five months), and median overall survival (twenty-four vs. twelve months) over conventional 175 mg/m^2 every three weeks.

A recent analysis compiling data from twenty-nine clinical trials of paclitaxel given as monotherapy investigated the relationship between paclitaxel dose and dosing regimen versus safety and efficacy. This average weekly dose from the every three week regimen (175—210 mg/m^2) of paclitaxel produced a response rate of 30%, while the weekly regimen of 80 mg/m^2 showed a response rate of 37%. In another analysis, a trend towards reduced grade 3 neuropathy with weekly paclitaxel was observed. Together, several clinical trials along with analyses, which evaluated efficacy and safety for dose-dense paclitaxel, suggested a trend of larger therapeutic window and a better safety-efficacy profile for weekly paclitaxel.

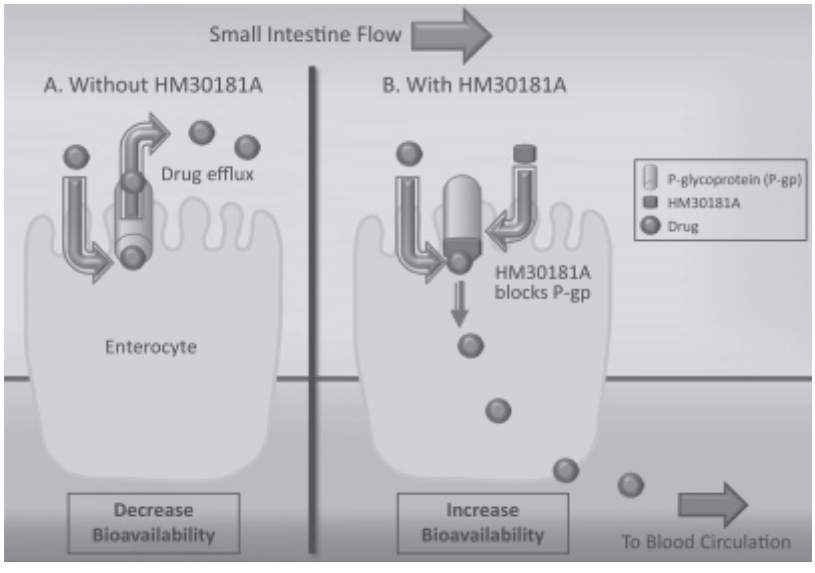
Irinotecan is a potent anticancer drug that is marketed under the trade name Camptosar. Irinotecan is mainly administered to patients with metastatic colorectal cancer (mCRC), but also in glioblastoma, lung, ovarian, cervical, upper gastrointestinal cancer and pancreatic cancer. The active metabolite of Irinotecan, SN38, is a type 1 DNA topoisomerase inhibitor with potent antitumor activity and wide antitumor spectrum. We believe that oral administration of irinotecan will more efficiently generate SN38, resulting in the potential for better clinical response with reduced toxicity. Oratecan is intended for oral administration for the treatment of irinotecan-responsive cancers.

Docetaxel is a potent anticancer drug within the class of antimicrotubule agents that is marketed under the trade name Taxotere. Docetaxel is mainly administered to patients with breast, lung, prostate, gastric and head and neck cancers. Docetaxel has potent activity with a wide antitumor spectrum. As a single-agent therapy, docetaxel is administered by IV infusion over one hour at a dose of 60-100 mg/m^2 for breast cancer and 75 mg/m^2 for non-small cell lung cancer given once every three weeks. Docetaxel is also used in combination with doxorubicin and cyclophosphamide (adjuvant treatment of breast cancer), cisplatin (lung), topical fluorouracil (head and neck and gastric) and prednisone (prostate). Docetaxel causes dose-limiting toxicities that are more common at higher doses. One significant dose-limiting toxicity is fluid retention that we believe is associated (at least in part) with the IV formulation that contains polysorbate 80, a nonionic and emulsifier frequently used in food and cosmetics. Hypersensitivity reactions may also be attributable to IV administration of polysorbate 80. We believe that oral administration of docetaxel with HM30181A will provide therapeutic exposures of the drug and result in the potential for better clinical response with reduced toxicity.

Topotecan is a potent anticancer drug under the class of camptothecins that is marketed under the trade name Hycamtin. Topotecan is mainly administered to patients with lung, ovarian and cervical cancer. Clinical activity has been shown in combination with the taxanes, docetaxel and paclitaxel, for the treatment of a variety of tumors, including lung cancer. Topotecan causes dose-limiting toxicities. These side effects mainly include neutropenia, late onset diarrhea and nausea and vomiting.

Eribulin is an anticancer intravenous drug marketed by Eisai Company under the trade name Halaven. It is used to treat certain patients with breast cancer and liposarcoma. Eribulin is a synthetic derivative of the natural product Halichondrin B. The potent anticancer effects of this agent come primarily from its unique means of targeting microtubule dynamics, a process critical to cell proliferation. The nonclinical demonstration of a favorable PK profile, with lowered peak plasma concentration and longer duration of the drug within the desired plasma concentration range, provides the potential for a better efficacy and an improved safety profile for Eribulin, similar to what we have observed with Oraxol and other Orascovery products. We have also developed a novel and efficient synthetic process for Eribulin with an excellent purity profile.

Mechanism of Action of HM30181A



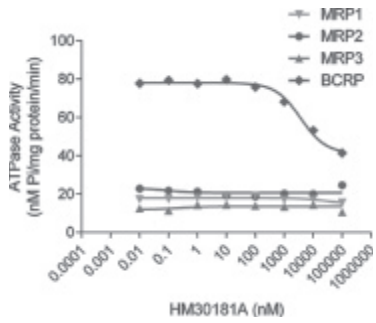
P-gp plays an important physiologic role as a transporter protein at multiple barrier sites, including the gastrointestinal tract and the blood brain barrier. The demonstrated role of P-gp in limiting intestinal absorption of multiple cancer chemotherapies highlighted the potential utility of a small molecule P-gp inhibitor for enabling oral administration of P-gp substrate drugs otherwise restricted to IV dosing. HM30181A was originally identified by Hanmi as a highly selective and potent P-gp inhibitor, capable of elevating the oral bioavailability of paclitaxel from less than 5% (in the absence of HM30181A) to 41% in rats. Unlike previously developed small molecule P-gp inhibitors, HM30181A is designed to not be systemically absorbed in the gastrointestinal tract following oral administration with only small amounts detectable in the plasma even after relatively high doses. This unique property makes

HM30181A a good candidate for co-administration with P-gp substrate drugs, such as paclitaxel, which normally exhibit poor oral bioavailability and are therefore limited to IV routes of dosing.

Preclinical and Clinical Development of HM30181A

In vitro Activity

HM30181A was first discovered as a novel P-gp inhibitor in 2006. A subsequent published study demonstrated selective activity against P-gp, with low nanomolar inhibitory activity reported (IC_{50}=0.6 nM in an *in vitro* assay of P-gp function, where the lower the number, the higher the potency) and more potent than cyclosporin A, tariquidar and elacridar, which are previously tested P-gp inhibitors, as shown in the first figure below. In similar assays, HM30181A did not inhibit the transporter proteins MRP1, MRP2 or MRP3 at the concentrations evaluated and only marginally inhibited breast cancer resistance protein (BCRP) transporter activity (IC50 = 3,717 nM, as shown in the second figure below).



Inhibition concentration against P-gp transporter

Compound	IC50 (nM)
Cyclosporin A	123.1
Tariquidar	44.4
Elacridar	4.9
HM30181A	0.6

Inhibition concentration against transporters

Transporter	IC50 (nM)
MRP1	> 5,000
MRP2	> 5,000
MRP3	> 5,000
BCRP	2,960

In vivo Activity

In preclinical studies, HM30181A demonstrated poor absorption from the gastrointestinal tract following oral administration in rats and dogs. The low systemic exposure to HM30181A may at least partially account for the good tolerability observed thus far in preclinical toxicology studies. In a single dose rat study, no mortality was noted, and there were no test article-related clinical signs or body weight changes and no gross necropsy findings fifteen days after treatment with single oral doses of HM30181A as high as 2,000 mg/kg. Likewise, the highest dose evaluated (200 mg/kg) was well-tolerated in repeat dose studies in both rats and dogs (once daily up to thirteen weeks) with no dose-related mortality.

Multiple preclinical studies have evaluated the *in vivo* pharmacologic effect of HM30181A, generally in the context of a co-administered P-gp substrate such as paclitaxel. In each case, co-administration of HM30181A significantly enhanced systemic exposure of the co-administered substrate. In murine models of human cancer, oral co-administration of HM30181A with oral paclitaxel or docetaxel conferred anti-tumor activity comparable to the IV dosing route.

Clinical Development

HM30181A belongs to a new class of P-gp inhibitor that has high potency, specificity and local action at the intestine cells. Oraxol consists of two drug products, a paclitaxel capsule and a HM30181A tablet. The 15 mg HM30181A tablet has an established room temperature shelf life of thirty-six months. The 30 mg paclitaxel liquid-filled, hard gelatin capsule has an established room temperature shelf life of eighteen months. Oratecan consists of two drug products, an irinotecan tablet and a HM30181A tablet. The irinotecan 20 mg tablet has an established room temperature shelf life of at least eighteen months.

Phase 1 clinical trials showed HM30181A has a good clinical safety profile and was not significantly absorbed systemically in humans. It has been given in amounts of up to 900 mg as a single dose, and up to 360 mg/day for five days without major toxicities. The clinical dose we use currently in our Phase 3 clinical trial is 15 mg/day.

In three separate PK studies of HM30181A conducted in healthy subjects, a total of eighty-one individuals received single oral doses of HM30181A tablets in single doses of up to 900 mg, and thirty individuals were enrolled in multiple dose cohorts with treatment groups receiving HM30181A tablets ranging from 60 to 360 mg per day for five days. HM30181A was well-tolerated, with mostly mild gastrointestinal side effects at high doses. At the current clinical dose of 15 mg given once daily for up to five days, the C_{max} in systemic circulation is low.

Our Orascovery Product Candidates

Oraxol (HM30181A tablet + Oral Paclitaxel)

Overview of Clinical Findings

As of December 31, 2018, four Phase 1 and 2 clinical studies of Oraxol have been completed with no MTD reached. Overall, Oraxol has been well-tolerated by cancer patients. Studies have indicated that anti-cancer activity of paclitaxel may be related to blood exposure in the patient. Oraxol administration results in similar blood concentration of paclitaxel over time as achieved with IV paclitaxel. We believe oral dosing of paclitaxel can provide a longer drug exposure over a target drug concentration than intravenous paclitaxel, which may translate to better clinical response. We have observed anti-cancer activity in a Phase 1/2 study of patients in gastric cancer with Oraxol monotherapy, where the overall survival in the study for 43 subjects was 10.7 months, which compared favorably to historical data for ramucirumab, the only FDA approved drug for second line treatment of gastric cancer, which reported 5.2 months of overall survival in a randomized, placebo controlled Phase 3 clinical study.

Completed Clinical Studies

HM-OXL-101 Phase 1 MTD Study

The Phase 1 MTD study was conducted by Hanmi in South Korea in twenty-four subjects with advanced solid cancer, with a "3+3" design in which cycles were twenty-eight days and dosing with HM30181A tablets and an oral liquid formulation of paclitaxel was given on Days 1, 8, and 15 of each cycle for three cycles. Premedication was not required prior to treatment with Oraxol. Paclitaxel doses evaluated ranged from 60 to 420 mg/m^2. HM30181A doses were half of paclitaxel doses (30 to 210 mg/m^2). The MTD was not reached in this study and dose escalation was stopped after 420 mg/m^2 because the drug exposure at doses above 300 mg/m^2 reached a plateau.

HM-OXL-201 Phase 2 Gastric Cancer Study

The Phase 1/2 gastric cancer study was conducted by Hanmi in South Korea. HM-OXL-201 was an open-label Phase 2, single-arm clinical trial of Oraxol for second line treatment of advanced gastric cancer patients. This trial included dosing Oraxol at 150 mg/m^2 per day, for two consecutive days per week, for 3 weeks out of a 4-week cycle. A total of forty-six subjects enrolled in this study. Oraxol was well-tolerated by gastric cancer patients. The results of the Phase 2 portion of this clinical trial showed treatment with Oraxol resulted in a median overall survival of 10.7 months.

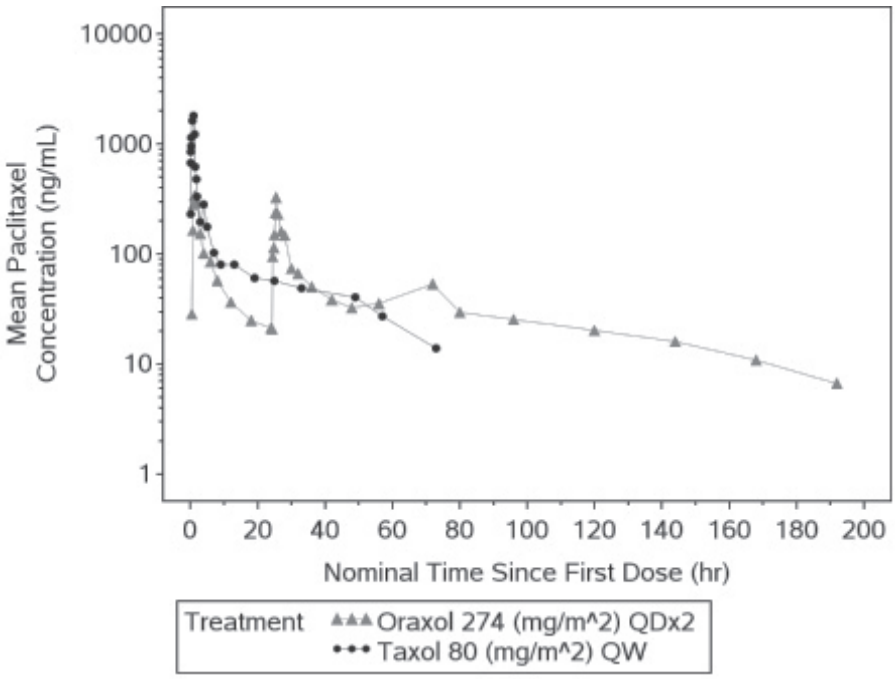
ORAX-01-13-US Phase 1 MTD Study

We conducted this Phase 1 MTD study in the U.S. and it is clinically complete. The objective of this study was to demonstrate the MTD of Oraxol. Study ORAX-01-13-US was a standard "3+3" Phase 1b study to determine the MTD of Oraxol in subjects with advanced malignancies. Oraxol dosing was 270 mg (approximately 150 mg/m^2) per day starting at two days of treatment per week for 3 weeks out of a 4-week cycle. Subjects in subsequent cohorts received 3, 4 or 5 days of treatment per week for 3 weeks out of a 4-week cycle. Premedication was not required prior to Oraxol treatment. A total of thirty-four subjects were enrolled in this study, including ten subjects in an expansion cohort at the highest weekly dose tested (five days per week of dosing). The MTD was not reached in this study, showing daily oral dosing of Oraxol was well-tolerated.

ORAX-01-14-NZ Phase 1 Bioavailability Study

This Phase 1 bioavailability study was conducted by us in conjunction with ZenRX Limited, or ZenRx, in New Zealand and is clinically complete. The objective of this study was to determine the absolute bioavailability of Oraxol and to compare the extent of absorption of Oraxol to that of IV paclitaxel. This study showed that Oraxol can achieve blood paclitaxel concentrations over time that are comparable in total exposure to IV paclitaxel.

The following figure shows the mean plasma concentrations of paclitaxel following intravenous administration of 80 mg/m^2, as compared to oral administrations of 274 mg/m^2 orally dosed daily for two days:



In this study the aggregate Oraxol AUC was 7,052 ng*hr/mL for the 274 mg/m^2 dosing regimen (N=2) versus IV Taxol AUC of 6,628 ng*hr/mL (N=2). Oraxol dose escalation above 274 mg/m^2 did not further increase exposure (N=2). Based on this, we chose a dose regimen of 15 mg HM30181A + 205 mg/m^2 of Oraxol daily over three consecutive days each week for future study, that we believe will produce similar exposure to paclitaxel as 80 mg/m^2 IV Taxol given weekly. In addition, this 3-day dosing regimen is expected to provide a longer time above the target plasma concentration and could lead to better anti-cancer efficacy.

Overview of Safety Observations in the four completed Oraxol Studies

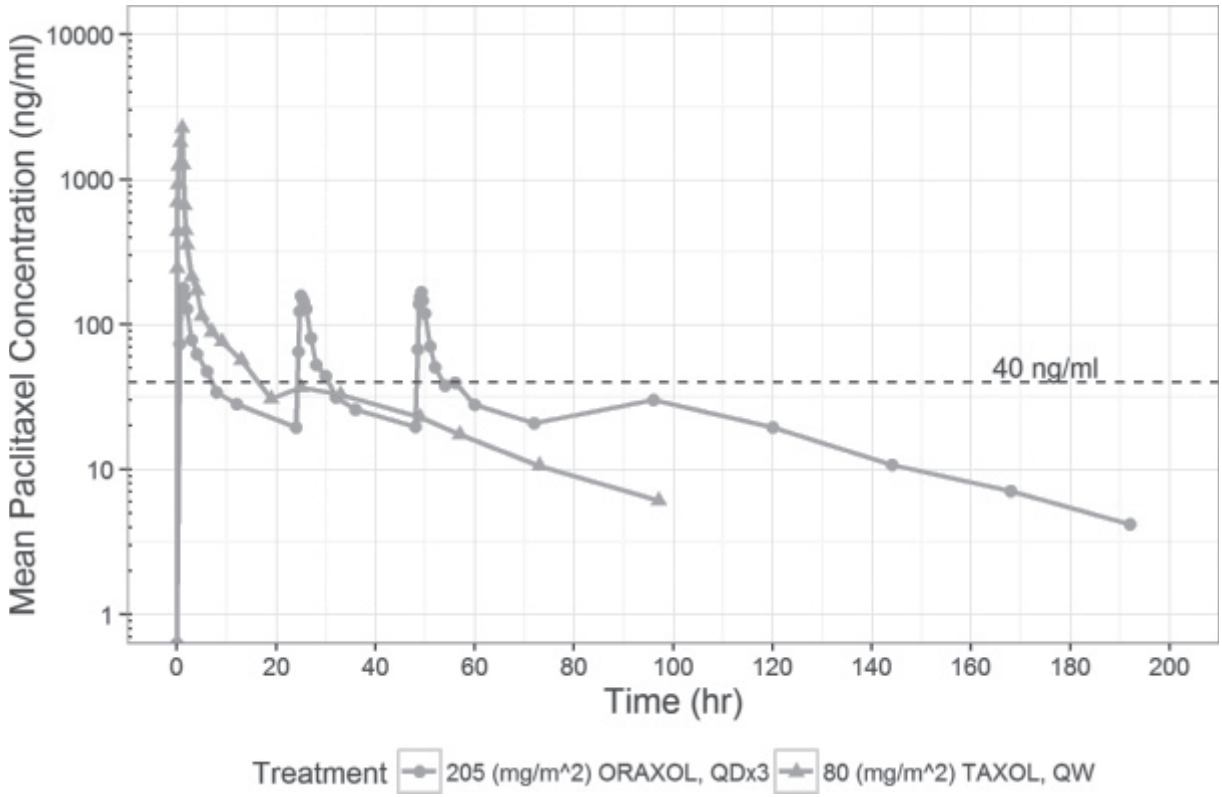
The MTD for Oraxol was not reached in these studies. Oraxol was well-tolerated by cancer patients even when given without premedication for hypersensitivity type reactions, in contrast to the premedication requirement for IV paclitaxel. No hypersensitivity type reactions were observed. No new toxicity, apart from those typically observed with paclitaxel, was observed. Infusion related reactions, including hypersensitivity type reactions, have not been observed. Additionally, severe toxicities associated with IV administration of paclitaxel, including neuropathy, neutropenia and alopecia, are expected to be at a lower incidence and grade for Oraxol.

In our Oraxol clinical studies to date, the serious adverse effects observed that were deemed to be possibly, likely or definitely related to Oraxol include severe neutropenia, febrile neutropenia, sepsis, septic shock, altered state of consciousness, hypokalemia and cardiac arrest, dehydration, pneumonia, death, nausea, vomiting, diarrhea, fatigue, anorexia and acute gastroenteritis.

Current and Planned Clinical Studies

Phase 1 Bioequivalence Study

The Phase 1 AUC bioequivalence study is being conducted by us in conjunction with ZenRx in New Zealand and is currently ongoing. The study of approximately forty patients was designed to compare the area under the curve of Oraxol at the estimated clinical dose to that of IV paclitaxel. We are evaluating the bioavailability, safety and tolerability of the Oraxol Phase 3 dosing regimen of 15 mg HM30181A + 205 mg/m^2 of paclitaxel daily over three consecutive days each week. The following chart shows interim PK results from the first six completed patients, indicating that this dosing regimen could achieve similar exposure to weekly AUC to 80 mg/m^2 of IV paclitaxel:



According to findings from this study, patients treated with Oraxol demonstrated exposure that was comparable to IV paclitaxel and no grade 3 or4 toxicities. These interim results were presented at ESMO Asia 2017 in Singapore.

Phase 1 MTD Study of Oraxol in Combination with Ramucirumab

We are conducting a Phase 1 MTD study of Oraxol in combination with ramucirumab in patients with advanced gastric cancer in the U.S. and Asia through a clinical trial collaboration with Eli Lilly and Company (Lilly). We commenced a study of up to 32 patients in a dose escalation study of Oraxol in combination with a fixed dose of ramucirumab to determine the MTD in July 2017. In a published Lilly-sponsored Phase 3 study comparing ramucirumab in combination with IV paclitaxel to IV paclitaxel alone, the single agent IV paclitaxel arm of the study showed a median overall survival of 7.4 months as compared to 9.6 months with IV paclitaxel in combination with ramucirumab.

The following list shows overall survival rates from the randomized, Phase 3 studies for Lilly's FDA approved drug, ramucirumab, approved in combination with IV paclitaxel for second line treatment of advanced gastric cancer:

Phase 3 clinical study of ramucirumab vs placebo (n=355)	5.2 months ramucirumab 3.8 months placebo
Phase 3 trial of ramucirumab plus IV paclitaxel vs IV paclitaxel (n=665)	9.6 months ramucirumab + IV paclitaxel 7.4 months IV paclitaxel

We conducted a Phase 1/2 study of single agent Oraxol dosing in end-stage gastric cancer patients at 150 mg/m^2 for two consecutive days each week, three weeks on, one week off, resulting in a median overall survival of 10.7 months. The objective of our Phase 1 study is to define the MTD of daily Oraxol dosing, starting at 200 mg/m^2 for three days in a week, three weeks on, one week off, in combination with ramucirumab, which will be dosed every other week. In January 2018, we announced the completion of the first cohort of patients in this study. Of the six patients in the first cohort, the Oraxol and ramucirumab combination treatment was well-tolerated. Grade 4 neutropenia occurred in one patient who fully recovered and there were no patient deaths or neuropathy. Two patients had partial responses (tumor shrinkage of 34-42%) and three patients had stable diseases (with tumor shrinkage of 27% in one patient). Only one patient had progressive disease. Although early, these results are regarded as encouraging compared with previous IV paclitaxel and ramucirumab combination therapy Phase 3 clinical trial results. In December 2018, we announced the completion of the second cohort of patients in this study. The results indicate strong positive signals of efficacy, and the treatment was well-tolerated. This second cohort of patients was given an escalated Oraxol dose of 250 mg/m^2 with the same dosing regimen as the first cohort. Three patients (50%) had partial responses. Grade 3 vomiting occurred in one patient who elected to withdraw from the study and subsequently had complete recovery. We are currently advancing to the third cohort with an escalated dose of 300 mg/m^2 of Oraxol.

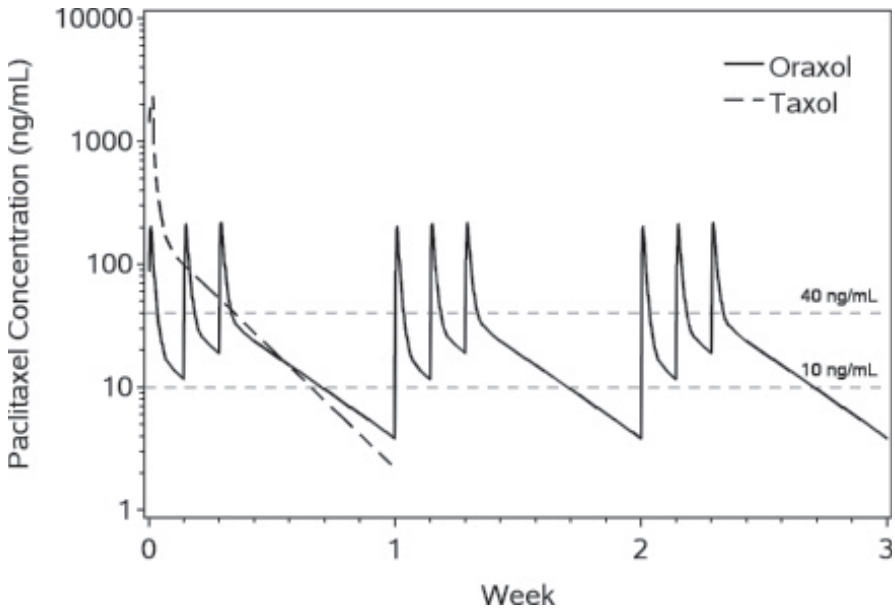
Phase 3 Study for Treatment of Metastatic Breast Cancer

Our Phase 3 study of Oraxol for the treatment of metastatic breast cancer is an open-label, randomized, multicenter study in approximately 360 adult female subjects. The study contains a screening period, a treatment period of 18-21 weeks, and a treatment extension period up to a total of forty-eight weeks. The study is currently being conducted in ten countries in Central and South America and will have up to fifty sites participating. Subjects will be randomized to either Oraxol or IV paclitaxel in a 2:1 ratio. The study is designed with two interim analyses which will be conducted after 90 and 180 evaluable subjects have been treated. Tumor assessments will be performed utilizing Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 guidelines by a blinded central radiologist group in the U.S. The blinded U.S. radiology group will measure tumor response rates with scans at week 10, 16 and week 19. An independent DSMB conducted and reviewed a planned interim analysis of the study in October 2017 and unanimously recommended continuation of the study. In January 2018, we received positive feedback from the FDA on the design of the ongoing Phase 3 trial, which indicated that if the study meets the primary endpoint with an acceptable benefit to risk profile, it could be adequate as a single comparative trial to support registration of Oraxol in the U.S. for the indication of metastatic breast cancer. In August 2018, an independent DSMB conducted and reviewed a second interim analysis of the study. The DSMB congratulated us on the rapid patient recruitment and the promising results achieved. The DSMB recommended that we continue this study and complete the recruitment of patients. In January 2019, we achieved target Phase 3 enrollment of 360 evaluable patients.

Our Oraxol dosing regimen consists of three days consecutive dosing each week of a 15 mg tablet HM30181A one hour before dosing an oral formulation of paclitaxel of 205 mg/m^2. The comparator IV paclitaxel arm is the labeled dosing regimen of 175 mg/m^2 paclitaxel IV one week out of three.

The chart below shows the simulated comparison of one cycle of the labeled dose of IV paclitaxel (Taxol) of 175 mg/m^2 and Oraxol dosed daily at 205 mg/m^2 for three consecutive days per week over a similar three-week period. While the expected aggregate Oraxol AUC over the cycle is similar to IV Taxol at 15,240 as compared to 15,000, the expected time exposure of Oraxol in the patient's blood at a therapeutic level is projected to be longer. For Oraxol, the time above 40 ng/mL is forecasted to equal 108 hours per 3-week cycle as compared to 54 hours for IV Taxol. We believe time exposure of the active pharmaceutical ingredient in the patient's blood is an important consideration in determining efficacy. In addition, the lower C_{max} with Oraxol is believed to be associated with better long-term tolerability of Oraxol.

Simulated PK comparison of Oraxol 205 mg/m^2 QDx3 per week for three weeks vs. IV Taxol 175 mg/m^2 one week out of three weeks cycle:



In summary, we believe Oraxol's longer paclitaxel exposure over time and lower C_{max} (based on our predictive model) as compared to the labeled dose of IV paclitaxel could translate into superior clinical response and improved tolerability.

Other Planned Clinical Development

We initiated a Phase 1/2 clinical study to assess the safety, tolerability and activity of Oraxol in combination with an anti-programmed cell death protein 1 (anti-PD1) antibody (pembrolizumab) in patients with advanced solid malignancies, in collaboration with Mayo Clinic. Pembrolizumab is a checkpoint inhibitor approved by the FDA. The study, KX-ORAX-011, is a Phase 1/2 study being conducted in patients with urothelial, gastric or gastroesophageal or non-small cell lung cancer that have previously failed treatment with a checkpoint inhibitor.

Oraxol is also in development for angiosarcoma, for which the FDA has granted orphan drug status.

Oratecan (HM30181A Tablet + Oral Irinotecan)

Completed Clinical Studies

Hanmi conducted three Oratecan Phase 1 studies, two as monotherapy (HM-OTE-101, HM-OTE-102), and one in combination with capecitabine (HM-OTE-103), in a total of fifty-four Korean patients with advanced solid tumors. The tumor types in these clinical trials were mostly gastric and colorectal cancers. MTD for Oratecan as monotherapy was defined as 100 mg/m^2 per 3-week cycle, either given as once daily for five consecutive days for one week (20 mg/day), or two weeks (10 mg/day), of a 3-week cycle. Anti-cancer activity was observed in these studies.

HM-OTE-101 Phase 1 MTD Oratecan Study

Oratecan was administered to twenty patients with advanced solid tumors on Days 1 to 5 during a 21-day cycle. Irinotecan daily doses ranged from 5 to 30 mg/m^2, and HM30181A doses were 60 mg. MTD was identified at 20 mg/m^2 per day for five days of a 3-week cycle. Adverse events were typical of events seen with IV irinotecan. Common adverse events included nausea (90%), diarrhea (65%), and vomiting (55%). Four subjects had dose-limiting toxicity (DLT) events (diarrhea, neutropenia, nausea/vomiting and AST elevation). At the MTD, the SN-38 C_{max} on Days 1 and 5 were 9 and 12 ng/mL. Estimated SN-38 cycle exposure (AUC) was 373 ng*hr/mL. In this study Oratecan monotherapy in patients with advanced solid tumors resulted in a disease control rate of 44%.

HM-OTE-102 Phase 1 MTD Oratecan Study

Oratecan was given once daily for five consecutive days each week for two weeks during a 21-day cycle to thirteen patients with advanced solid tumors. Irinotecan doses ranged from 5 to 20 mg/m^2. MTD was identified at 10 mg/m^2 per day. Adverse events were similar to those observed following IV irinotecan and included diarrhea, nausea, and anorexia. Five subjects had a DLT in Cycle 1. At the MTD, the resulting SN-38 C_{max} on Days 1 and 12 were 5 and 4 ng/mL. Estimated cycle exposure (AUC) for SN-38 was 423 ng*hr/mL.

The following table shows the rate of control of the disease following administration of Oratecan once daily for five days for two out of every three weeks.

		Disease control rate (DCR)*	
Dose Level	**N**	**# of DCR (%)**	
HM30181A tablet 60 mg + irinotecan HCl tablet 5 mg/m2	3	3	(100%)
HM30181A tablet 60 mg + irinotecan HCl tablet 10 mg/m2	5	3	(60.0%)
HM30181A tablet 60 mg + irinotecan HCl tablet 15 mg/m2	1	1	(100%)
HM30181A tablet 60 mg + irinotecan HCl tablet 20 mg/m2	2	1	(50.0%)
Total	11	8	(72.7%)

* DCR determined by the total number of subjects with complete response, partial response or stable disease, divided by the number of subjects at each dose level.

HM-OTE-103 Phase 1 MTD Study of Oratecan in Combination with Capecitabine

This study was to determine the MTD of Oratecan in combination with capecitabine. Oratecan was administered to twenty-one patients on Days 1 to 5 during a 21-day cycle. Irinotecan doses ranged from 10 to 20 mg/m^2 per day, with HM30181A (15 mg) in combination with capecitabine at 800-1000 mg/m^2 for fourteen days. The MTD of Oratecan, in combination with capecitabine at the 1000 mg/m^2 dose was identified at 15 mg/m^2 per day. Adverse drug reactions in the study included diarrhea, nausea, anorexia and vomiting. At the MTD of 15 mg/m^2, the SN-38 C_{max} on Days 1 and 5 were 6 and 4 ng/mL. Estimated SN-38 cycle exposure (AUC) was 217 ng-hr/mL. In this study of combination of Oratecan with capecitabine in patients with a variety of solid tumors (mostly GI cancers), 10 out of 18 (56%) patients had either stable disease or a partial response.

Overview of Safety Observations in completed Oratecan Studies

In our Oratecan clinical studies to date, the serious adverse effects observed that were deemed to be possibly, likely or definitely related to Oratecan include diarrhea, rash, gastrointestinal hemorrhage, anorexia, vomiting, nausea, enteritis, asthenia, neutropenia, increased alanine aminotransferase and increased aspartate aminotransferase.

Current and Planned Clinical Development

ORTE-01-14-US Phase 1 MTD Study

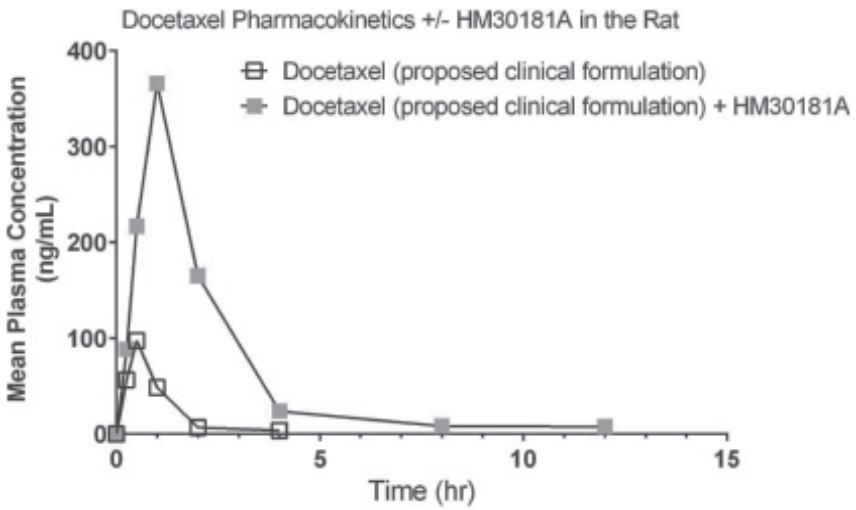
The Phase 1 MTD study is being conducted by us and is currently ongoing. This study is to determine the MTD of Oratecan, when given once every three weeks, in subjects with advanced malignancies. In previous studies, Oratecan was given once daily for five days every three weeks and achieved total cycle SN38 exposure, as measured by AUC, similar to IV administration of irinotecan. This once every 3-week dosing strategy is being evaluated in order to assess if we can further increase SN-38 exposure while avoiding toxicity. Based on Phase 1 results thus far, we believe that we can identify a Phase 2 dose that will produce similar exposure to SN-38 as a labeled dose of IV irinotecan. Phase 2 studies are being planned.

We are currently planning a Phase 1 bioavailability study of Oratecan to be conducted in conjunction with ZenRx in New Zealand. The objective is to determine the absolute bioavailability of Oratecan and to compare the extent of absorption of Oratecan to that of IV irinotecan based on levels of SN38. This study will allow us to determine the exposure of SN38 following Oratecan administration that will be equivalent to the SN38 levels observed with the IV route of administration.

Oradoxel (HM30181A Tablet + Oral Docetaxel)

Preclinical Activity and Evaluation

The potential effectiveness of HM30181A to inhibit the P-gp pump's ability to transport docetaxel out of cells was first observed *in vitro* by an increase in the potency of docetaxel by 1,788-fold in a uterine sarcoma cell line. In rat oral PK studies, the plasma concentrations of docetaxel versus time, shown below, showed a significant increase upon co-administration of HM30181A with docetaxel. In this experiment, docetaxel was formulated in the currently proposed clinical formulation. Oradoxel was tested in preclinical human prostate cancer murine model as shown in the table below. Overall, Oradoxel was more active than docetaxel given orally without a P-gp inhibitor and was similar to the efficacy of IV docetaxel administration. At a dose of 25 mg/kg docetaxel with HM30181A a percent of tumor control of 4.8% was achieved which is comparable to the standard 10 mg/kg IV dosing regimen of docetaxel (2.9%). Without P-gp pump inhibition by HM30181A, oral administration of docetaxel demonstrated less inhibition of tumor growth, with a percent of control of 50.5%, consistent with reduced absorption of oral docetaxel when dosed without HM30181A.



Docetaxel +/- HM30181A in Prostate Cancer Murine Model

Treatment	Mean (±SEM) Tumor Weight (g) on Day 21 Post Treatment	(T/C (%))a
Control	0.348 ± 0.047	(—)
Docetaxel (10 mg/kg, IV)	0.01 ± 0	(2.87%)
Docetaxel (25 mg/kg. Oral) plus HM30181A	0.017 ± 0.003	(4.78%)
Docetaxel (25 mg/kg Oral)	0.176 ±0.035	(50.53%)

[a] Tumor Growth Inhibition is calculated by dividing the group average tumor volume for the treated group by the group average tumor volume for the control group (T/C).

Current and Planned Clinical Studies

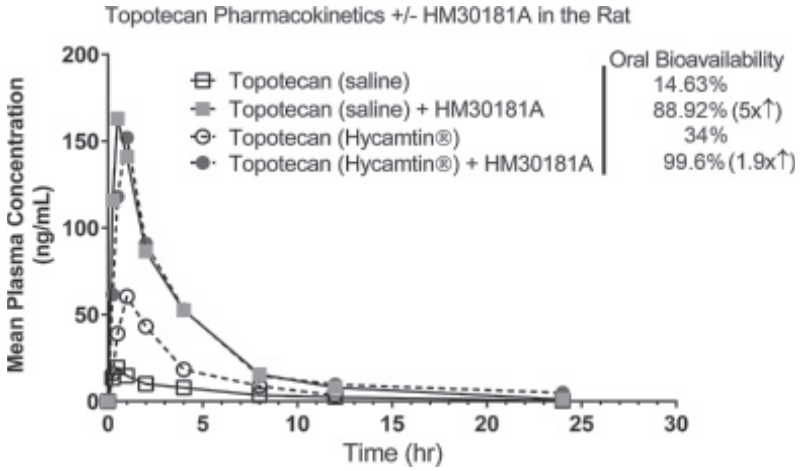
Based on the preclinical mouse efficacy data and rat and dog toxicology data, we expect that oral administration of docetaxel together with HM30181A will be efficacious and well tolerated in the clinic. We believe it may minimize the dose-limiting toxicities associated with docetaxel therapy, such as fluid retention, and allow increasing dosing to obtain superior efficacy.

The FDA authorized us to proceed with a Phase 1 clinical study under an IND in the first quarter of 2016, and we received regulatory allowance for a clinical trial in New Zealand. The ongoing U.S. study is a Phase 1 dose escalation trial for Oradoxel in patients with various solid tumors with a starting dose of 35 mg/m^2 given once every three weeks. In New Zealand, a Phase 1 study is being conducted to identify the absolute bioavailability of Oradoxel in prostate cancer patients. Based on Phase 1 results thus far, we believe that we can achieve similar exposure to IV docetaxel with one or two days of dosing every three weeks. Phase 2 studies are being planned.

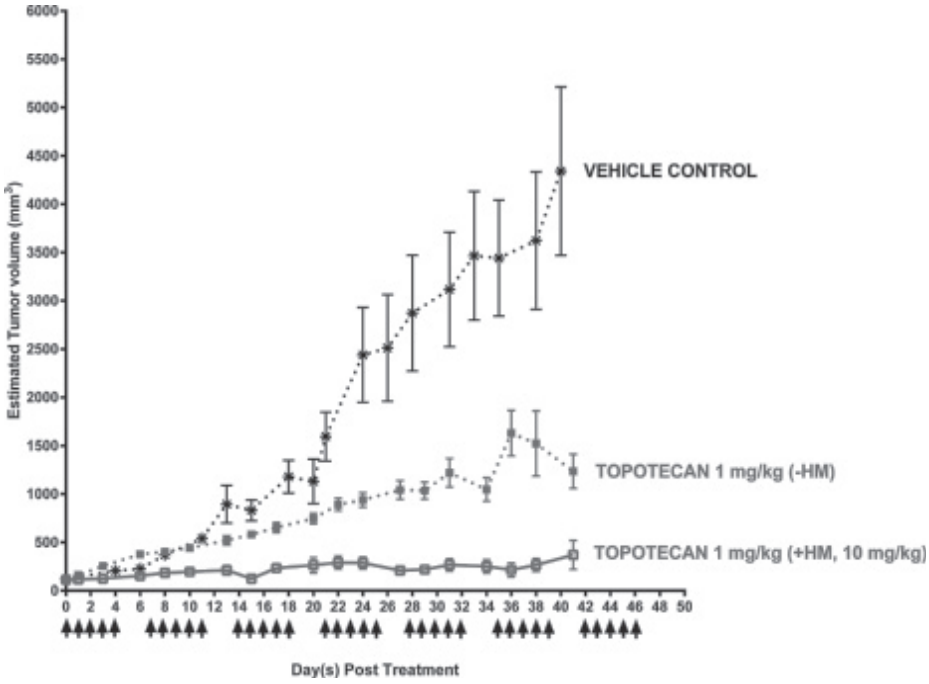
Oratopo (HM30181A Tablet + Oral Topotecan)

Preclinical Activity and Evaluation

In rat oral PK studies, the plasma concentrations of topotecan versus time, shown below, demonstrates a significant increase upon co-administration with HM30181A. This effect is evident when topotecan is formulated in saline or the marketed product, Hycamtin. In preclinical murine models with human tumor transplants, including ovarian cancer, oral topotecan in combination with HM30181A was more active than oral topotecan alone following administration at a dose of topotecan 1 mg/kg once daily for five days per week, as illustrated in the lower chart below.



Topotecan +/- HM30181A in Ovarian Cancer Murine Model



Current and Planned Clinical Studies

IND enabling studies have been conducted. To date, dose-range finding studies along with Good Laboratory Practice, or GLP, compliant toxicology and toxicokinetic studies following single and multiple daily doses are being conducted with oral Topotecan in combination with HM30181A. These studies have been completed to establish the maximum tolerated dose for the 5-day regimen to support our proposed clinical dosing regimen. We filed an IND application for oral topotecan in combination with HM30181A in February 2017, and the FDA authorized us to proceed with a Phase 1 clinical study in March 2017. We are currently enrolling in a Phase 1 clinical trial in advanced malignancies for Oratopo.

Eribulin ORA (HM30181A Tablet + Oral Eribulin)

Eribulin is an intravenous anticancer drug used to treat certain patients with breast cancer and advanced liposarcoma marketed by Eisai Company under the trade name Halaven. Utilizing Athenex's proprietary Orascovery platform with Eribulin, we were able to demonstrate that good oral absorption of Eribulin is possible, based on preclinical studies. In addition, we have developed a novel and efficient synthetic route for the synthesis of eribulin API which we believe will support our development of this candidate. In October 2018, the FDA allowed our IND for oral eribulin co-administered with HM30181A (Eribulin ORA). A Phase 1 study is expected to commence in early 2019.

Our Src Kinase Inhibition Research Platform

The table below shows certain clinical trials for our major Kinase inhibition drug candidates.

Protocol		Phase	Indication	Location	Status
KX01 (Ointment)	KX01-AK-01-US	I	Safety PK	United States	Completed
	KX01-PS-01-TW	I	Psoriasis	Taiwan	Ongoing
	KX01-AK-002	II	Safety PK	United States	Completed
	KX01-AK-003	III	Efficacy	United States	Follow-up ongoing
	KX01-AK-004	III	Efficacy	United States	Follow-up ongoing
	KX01-006	I	RIPT (Sensitization)	United States	Completed
	KX01-007	I	Muse PK	United States	Enrolling
	KX01-008	I	Phototoxicity	United States	Completed
	KX01-009	I	Photoallergy	United States	Completed
KX01 (Oral)	KX01-01-07	I	Solid Tumor	United States	Completed
	KX01-02-09	II	Prostate	United States	Completed
	KX01-03-11	I	Acute Myelogenous Leukemia	United States	Completed
	HM-KX1-101	I	Solid Tumor	South Korea	Completed
	KX01-CA-001	I	Ovarian	United States United Kingdom	Under Development
	KX01-CA-002	I	Liquid Tumor	Taiwan	Under Development
KX02	KX02-01-13	I	MTD PK	United States	Enrollment Closed

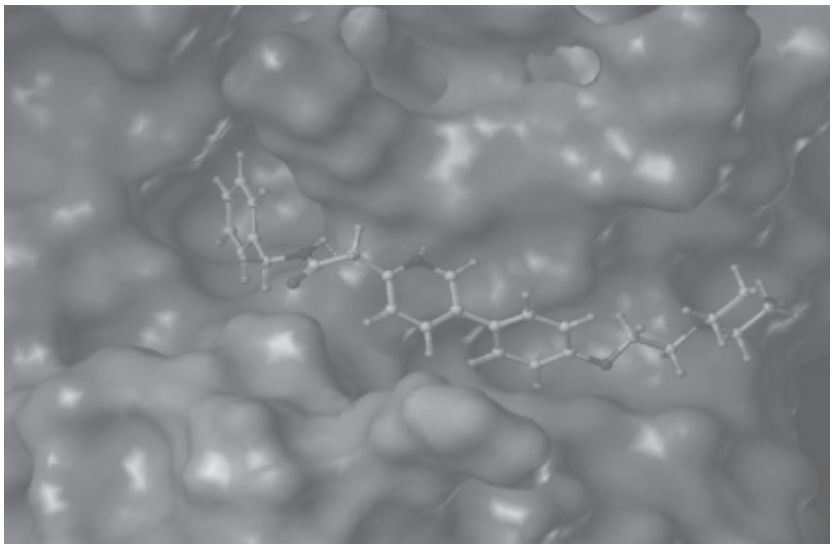
PK and MTD denote pharmacokinetics and maximum tolerated dose, respectively.

KX-01

Mechanism of Action

KX-01 is a novel small molecule, which we discovered and developed, which demonstrates at least two MOAs relevant to the potential control of cancer and hyper-proliferative disorders: Src tyrosine kinase inhibition (non-ATP competitive) and tubulin polymerization inhibition. Src plays a role in regulating multiple aspects of tumor development, growth and metastases, and its inhibition limits such tumor activity. Interfering with tubulin polymerization activity is a clinically validated mechanism for treating cancer. For both targets KX-01 binds at a novel binding site. Taken together, these two MOAs may provide for a potent means of treating cancer and other hyper-proliferative disorders.

The first MOA defined for KX-01 is Src tyrosine kinase inhibition. We have observed the correlation of KX-01 inhibition of Src auto-phosphorylation (a measure of Src activity) and cell growth during the proliferation phase of tumor cells in both c-Src^{527F}/NIH-3T3, a cell line derived from fibroblasts with enhanced Src activity, and HT29, a cell line derived from colon cancer cells. Through *in vitro* tests, KX-01 has been shown to induce caspase 3 cleavage and PARP cleavage, which are both markers for cell death or apoptosis, as well as p53 induction, which is a protein involved in tumor suppression. Unlike most known Src inhibitors, KX-01 is unique in that it is not an ATP competitive inhibitor of Src, but, rather, it is believed to be a substrate competitive inhibitor, which means high specificity for the intended binding target. A computational model for how KX-01 is predicted to bind in the peptide substrate site of Src is depicted in the figure below, as noted in an NMR/paramagnetic probe study conducted and published by Wyeth LLC.



The second MOA defined for KX-01 is inhibition of tubulin polymerization, a step essential for cell growth. We have observed the ability of KX-01 to inhibit tubulin polymerization *in vivo* within tumors in a mouse xenograft and synergistic activity with paclitaxel to interrupt cell proliferation.

The two MOAs of KX-01 are believed to have the potential to control cell growth and proliferation of cancer cell types as well as cell types involved in hyper-proliferative diseases. Specifically, KX-01 has been observed *in vitro* to have potent activity in controlling cell growth in keratinocytes, or skin cells (with IC_{50} = 32 nM). This activity demonstrates the potential of these compounds to control hyper-proliferative diseases of the skin, examples being actinic keratosis and psoriasis.

The following table shows the potential broad-spectrum activity of KX-01 against many cancer types. GI50 represents the concentration of KX-01 that may be used to inhibit 50% of tumor cell growth. The lower the numerical value of GI50 the higher the potency of KX-01.

Human Tumor Cell Line	KX-01 GI50 (nM)	Human Leukemia Cell Line	KX-01 GI50 (nM)
HT29 (Colon)	25	K562 (CML)	13
SKOV-3 (Ovarian)	10	K562R (Gleevec resistant CML)	0.64
PC3-MM2 (Prostate)	9	MOLT-4 (ALL)	13
L3.6pl (Pancreas)	25	CCRF-HSB-2 (ALL)	12
MDA-MB-231 (Breast)	20	Jurkat (Adult T Cell Leukemia)	10
A549 (Lung)	9	Ba/F3 + WT BCR-Abl	85
HuH7 (Liver)	9	Ba/F3 + E225K (Gleevec Resistant)	80
769-P (Kidney)	45	Ba/F3 + T315l (Gleevec & Dasatinib Resistant)	35
SNU-1 (Gastric)	6	KG-1 (AML)	16
		RPMI8226 (Multiple Myeloma)	40
		RL (non-Hodgkin’s lymphoma)	19

Research Background

Topical formulation development studies carried out by our licensing partner, PharmaEssentia, in Taiwan resulted in a formulation believed to be suitable for clinical testing. KX-01 topical formulations were initially tested by PharmaEssentia in psoriasis clinical trials in Taiwan. In parallel, we are evaluating topical KX-01 ointment in the clinic for AK in the U.S. The most common cause of AK is exposure to ultraviolet radiation from the sun or tanning beds. This exposure can lead to oncogenic changes, such as inactivation of p53, and consequential hyper-proliferation of mutated keratinocytes. If left untreated, 10-15% of AKs can progress to skin cancer. KX-01 inhibits the proliferation of keratinocytes and up-regulates p53 so its utility in clinically treating AK is of interest. Phase 2 clinical trials with a KX-01 topical ointment for treating AK have produced encouraging results, and Phase 3 studies have completed recruitment. KX-01 ointment 1% has a room temperature shelf life of at least six months.

KX-01 Ointment for Topical Indications

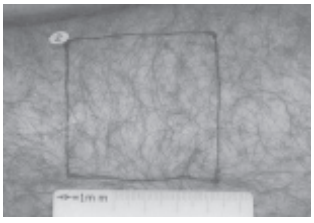
Completed Clinical Study

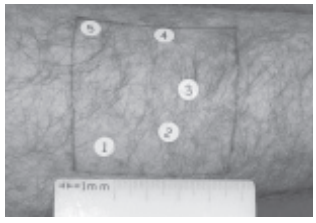
Phase 1 Study

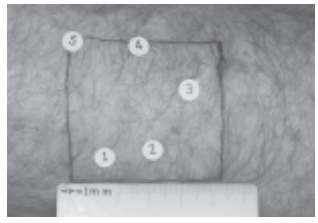
The Phase 1 study of KX-01 ointment for treatment of AK was conducted by us in the U.S. and is clinically complete. This was a four cohort, PK and safety study of three or five days, with treatment of 25 cm^2 or 100 cm^2 applied to the forearm. The results for the Phase 1 studies showed that with 1% KX-01 ointment being applied for five consecutive days in on a 25 cm^2 area of the forearm; 50% (four of eight subjects) had complete response (100% clearance). This was achieved with very good local and systemic tolerability. We believe that the high clearance rate with low skin toxicity compares well to existing treatments on the market.

Clinical data thus far indicate that KX-01 ointment produces a complete response without severe adverse skin reactions in some patients, as shown in the images below:

Skin reaction from KX-01 ointment in a subject who had a 100% response







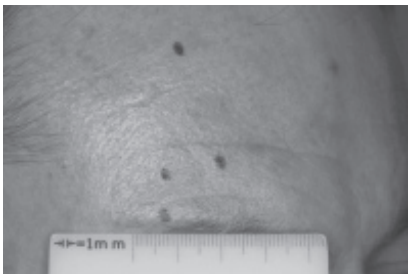
Current and Planned Clinical Development

Phase 2a Study

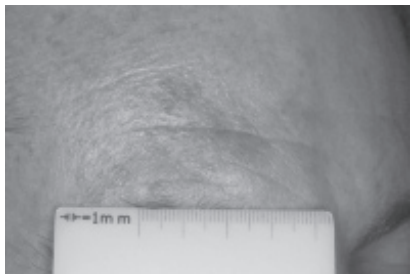
We completed enrollment in 2016 of an approximately 160-patient Phase 2a clinical study in the U.S. of KX-01 ointment for treatment of AK on the face and scalp. This was an open label, two sequential cohort study of approximately eighty patients each with treatment of KX-01 ointment 1% for either three or five days. The primary objective was to evaluate the complete response rate, which was defined as 100% clearance of such patient's AK at Day 57 after treatment. Additionally, we sought to further investigate the findings from the Phase 1 proof of concept study indicating that KX-01 ointment has a favorable side effect profile.

Data from 168 patients in the Phase 2 study shows that the KX-01 dosing regimen used in this study is well-tolerated, with mostly mild and transientLSRs. The five-day treatment cohort achieved a higher overall 100% clearance of actinic keratosis lesions at Day 57 (i.e. eight weeks after the initiation of treatment) than the three-day treatment cohort (43% vs. 32%). In the five-day treatment cohort, twenty-three of forty-four subjects (52%) with actinic keratosis on face and thirteen of forty (33%) on scalp attained 100% clearance at Day 57. LSRs were mild and mostly erythema, flaking or scaling, crusting and swelling with the majority of the LSRs scores of < 2 and resolved rapidly. Only one subject scored 4 in erythema and flaking or scaling, which both resolved rapidly without concomitant medications. Erosions or ulcers and vesicles or pustules were observed in only 15% and 5% of subjects, respectively. No subjects scored ≥ 3 in erosions or ulcers or vesicles or pustules. Treatment related adverse effects were few and predominately mild transient application site pruritus, tenderness and pain. There were no treatment related serious adverse effects or discontinuations. Plasma levels of KX2-391 were low to undetectable.

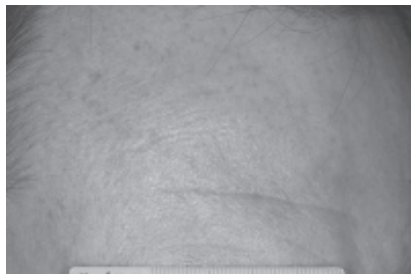
Skin reaction example from KX-01 ointment in a subject who had a 100% response



Day 1



Day 8



Day 57

The images above show the experience of a subject in our Phase 2 study who experienced a 100% response experienced no severe skin reaction. Since skin toxicity is likely to be a significant consideration of clinicians and patients, especially on the face and scalp, we believe that the market is likely to expand for topical treatments options for this pre-cancerous skin condition. To the extent that skin toxicity has been limiting the market, we believe that KX-01 ointment may significantly expand the market as a result of a low skin toxicity.

Phase 3 Studies

We commenced patient enrollment in two Phase 3 studies of KX-01 for treatment of AK on the face and scalp at approximately sixty total sites in the United States in September 2017. Each trial is designed to enroll approximately 300 subjects. We completed patient enrollment for both Phase 3 studies in February 2018 with 702 subjects. The endpoints of these studies are identical to those in the Phase 2 program, although, unlike the Phase 2 study, the two identical Phase 3 clinical trials each include a vehicle-treated control group and a double-blinded study design in which subjects are randomly assigned to receive either the vehicle or the KX-01 ointment. In July 2018, both Phase 3 studies achieved their primary endpoint of 100% clearance of AK lesions at Day 57 within the face or scalp treatment areas, with each study achieving statistical significance ($p<0.0001$). Statistical significance ($p<0.001$) was achieved for both face and scalp subgroups as well. Topline results from the two Phase 3 studies were featured in a late breaker session at the 2019 American Dermatology Annual Meeting in March 2019. Results showed that 44% and 54% of patients in studies KX01-AK-003 and KX-01-AK-004, respectively, achieved 100% AK lesion clearance at Day 57. Compliance rate in these two studies was greater than 99%. There was a statistically significant clearance rate in favor of the KX-01 ointment versus the vehicle in each of the patient subgroups. A 12-month recurrence follow-up period is expected to be complete for the last subject in June 2019, and a final clinical study report for both trials, marking official completion of the Phase 3 study, is expected to be available in the fourth quarter of 2019.

KX-01 Oral

Completed Clinical Studies

KX-01 oral capsules are available in strengths of 20 mg and 80 mg and have a room temperature shelf life of forty-eight months. KX-01 oral has been evaluated in several early dose finding studies against both solid and liquid tumors. Initial clinical results indicate activity against both solid and liquid tumors in patients in clinical studies. We are planning further probe studies to focus our evaluation in certain of those indications where activity was observed.

Phase 1 and Phase 2a U.S. Study—Complete

A Phase 1 clinical trial in solid tumor patients identified the MTD for continuous twice daily oral dosing at 40 mg/dose, with a favorable PK profile, and indications of activity. In this trial, forty-four patients were enrolled in nine dose cohorts. The drug was well-tolerated and the DLTs were mainly elevated levels of AST and ALT, which were readily reversible. Eleven patients had stable disease for at least four months, including patients with ovarian, carcinoid, papillary thyroid, prostate, pancreas and head and neck cancer. An ovarian cancer patient had stable disease for 16 months and a KX-01 oral induced a large decrease in the ovarian cancer CA-125 biomarker, which correlates well with clinical response. As shown in the table below, this patient had failed nine prior drug, and drug combination therapies, showing a clear benefit from KX-01 oral treatment.

Therapy	Duration (months)
Carboplatin, Paclitaxel	5
Gemcitabine, Carboplatin	2
Gemcitabine, Taxotere	2
Doxil	1
Cisplatin, Cyclophosphamide, Epirubicin	4
Tamoxifen	2
Topotecan	3
Abraxane, Avastin	4
Folfox, Avastin	1
KX-01 oral	16

A subsequent Phase 2a clinical study in men with bone-metastatic castration-resistant prostate cancer using the twice daily 40 mg/dose was conducted. Thirty-one patients were dosed with KX-01 oral at 40 mg/dose twice daily until disease progression or unacceptable toxicity. The primary endpoint was 24-week progression-free survival (PFS). The designated clinical endpoints were not met with KX-01 oral at this dose.

A Phase 1b clinical study in elderly acute myeloid leukemia (AML) patients was conducted using once daily dosing. The doses tested were 40, 80, 120, 140 and 160 mg of KX-01. Twenty-four patients were recruited with a median age of 76 years (range 63 to 86 years). Most had been previously treated for their disease, generally with decitabine or azacitidine. The MTD is estimated to be 105 mg of KX-01 oral daily.

Overview of Safety Observations in completed KX-01 Oral Studies

In our KX-01 Oral clinical studies to date, the serious adverse effects observed that were deemed to be possibly, likely or definitely related to KX-01 Oral include allergic reaction, bacteremia, rash, syncope, tremor, dermatitis, neutropenic fever, hyponatremia, hypersensitivity, failure to thrive, lower extremity edema, mucositis, neutropenia, pancytopenia, thrombocytopenia, seizure and motor vehicle accident, embolic stroke, pneumonitis, fever, acute kidney injury, increased bilirubin and albumin levels, decreased blood platelet count, abdominal pain, arm pain, pyrexia, rigors, tachypenea, oxygen desaturation, pneumonia, anemia, elevated ALT and AST, dehydration and leukopenia.

Current and Planned Clinical Development

Our licensing collaborator, Hanmi is completing a Phase 1b clinical trial in South Korea, combining escalating continuous once daily doses of KX-01 with a standard IV paclitaxel treatment of 80 mg/m^2 once weekly for three out of four weeks. This study is clinically completed and awaiting a study report.

KX-02

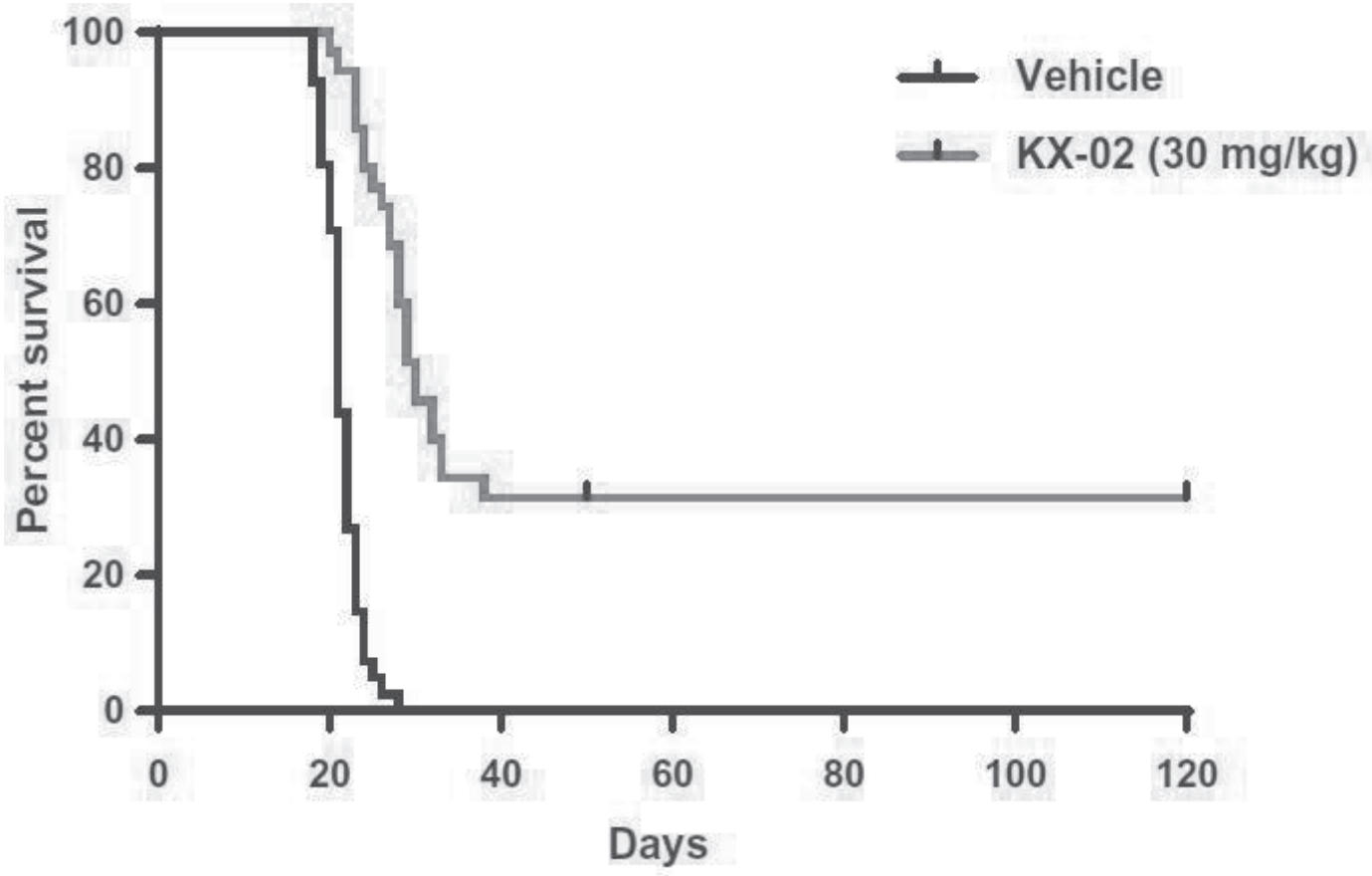
Research Background

KX-02 is a closely related structural analog of KX-01 and has been observed to have a similar dual MOA of inhibition of Src activity and microtubule polymerization. KX-02 was designed to readily cross the blood-brain-barrier (BBB). *In* vitro studies in mice have found that the KX-02 levels in the mouse brain meet or exceed the levels in the plasma at the same time points after oral dosing, indicating that KX-02 readily crosses the BBB. We believe that this ability to cross the BBB provides a rationale for investigating brain cancers and metastases in the brain as potential therapeutic applications, which are traditionally considered to be an unmet medical need.

Preclinical evaluation and activity

In Vivo Activity

Based on preclinical testing which found activity of KX-02 against a number of brain cancer cell lines and BBB penetration by KX-02, KX-02 was tested orally in a mouse GBM tumor model, wherein mouse GBM tumor cells were implanted into the brains of mice with fully-competent immune systems in order to simulate human patients. When compared with temozolomide (TMZ), the current standard of treatment, in one particular study, KX-02 produced long -term survival mice, as compared to TMZ, which extended survival but did not result in any long-term survivors. Across multiple experiments, an average of approximately 30% long term survival mice were produced when dosed with KX-02 at 30 mg/kg once daily, as shown in the figure below.



To visualize tumor growth *in situ*, animals treated with KX-02 were compared to those that had been treated with placebo alone using magnetic resonance imaging (MRI). The KX-02 treated mice that eventually survived long term did not have tumors whereas the placebo mice had large tumors at the time points evaluated.

The potential role of an adaptive immune response in the responses of the mice treated with KX-02 was observed in three ways. First, when the same mouse study was repeated with mice lacking an adaptive immune system, no cures were obtained. Second, when mice that had been cured by KX-02 were re-challenged with mouse GBM cells, they failed to support sustained tumor growth, whereas untreated mice readily showed pernicious tumor growth. Third, a larger infiltration of lymphocytes into brain tumor tissues

was seen in mice treated with KX-02 as compared to those treated with a placebo, and these lymphocytes stained as CD3 and CD8 immune cells. Accordingly, KX-02 also appears to facilitate the immune system's recognition of brain tumor tissues as foreign cells, in addition to its Src and tubulin-targeted activities. In our KX-02 clinical studies to date, the only serious adverse effects observed were thromboembolic events, hyperuricemia and pulmonary embolism.

Current and Planned Clinical Studies

Phase 1 Study

We have completed enrollment in a Phase 1 study in the U.S. of KX-02 for treatment of solid tumors in order to determine the MTD, PK and safety profile. We plan to initiate a new Phase 1 study using an improved oral formulation in 2019.

In 2012, we out-licensed KX-02 to Xiangxue for development and marketing in greater China, and clinical trials are currently being planned. In May 2017, the NMPA allowed an IND to commence clinical trials in China. Based on the approval that has been granted by the NMPA, we expect Xiangxue to commence Phase 1 clinical trials for KX-02 for GBM in China in 2019. We anticipate this partnered clinical program in China will accelerate the development timeline of this candidate.

Our Src Kinase Product Candidates

KX-01

KX-01 is a compound developed under our Src Kinase Inhibition platform that, as a free base, has advantageous physical properties for topical ointment formulations. A topical ointment with KX-01 has shown promising results in a proof of concept clinical trial for AK. We completed enrollment of an approximately 160-patient Phase 2a study of KX-01 for treatment of AK in 2016, and we commenced two Phase 3 studies in September 2017, which completed patient enrollment in February 2018. In July 2018, both Phase 3 studies achieved their primary endpoint of 100% clearance AK lesions at Day 57 within the face or scalp treatment areas. A 12-month recurrence follow-up period is expected to be complete for the last subject in June 2019, and a final clinical study report for both trials, marking official completion of the Phase 3 study, is expected to be available in the fourth quarter of 2019. An additional indication for psoriasis is being evaluated in a Phase 1 clinical trial led by our out-licensing partner PharmaEssentia. Since AK can lead to skin cancers, we are now investigating the initiation of a study in that basal cell carcinoma. These applications provide additional potential therapeutic utilities for KX-01 ointment and could represent significant potential market expansions beyond AK. We are also developing KX-01 in an oral formulation, and we have observed activity against both solid and liquid tumors in patients in clinical studies, and we are planning further studies to focus our upcoming evaluation efforts in targeted indications.

In December 2017, we entered into a license agreement with Almirall, pursuant to which we granted to Almirall an exclusive, sublicensable license of certain of our intellectual property for the development and commercialization of topical products containing KX-01 for the treatment of AK in the U.S. and substantially all European countries. We believe this partnership validates the potential of this candidate and that this partnership is an important step in the development and commercialization of KX-01 develop and commercialize this product. For additional information, please see "Business—License and Collaboration Agreements—Almirall License Agreement." We presented data from our Phase 2 clinical trials at the AAD meeting in February 2018. Both studies are still on-going to complete the one-year follow-up of the patients who had complete responses. We will be submitting a request to the FDA for a pre-NDA submission meeting to discuss the data and regulatory submission timelines.

KX-02

KX-02 is the second compound we developed using our Src Kinase Inhibition platform. Although KX-02 is an analog of KX-01, it has significantly different physical properties. These properties are designated to allow KX-02 freely cross the BBB such that the concentration in the brain is equal to, or somewhat greater than, that in the plasma. This trait is uncommon for oncology drugs and highlights the potential for KX-02 as a novel therapy for unmet medical needs such as brain cancers, including GBM and brain metastases. The FDA has granted Orphan Drug Designation to KX-02 for the treatment of gliomas. KX-02 is a non-ATP competitive Src Kinase inhibitor and tubulin polymerization inhibitor. Studies of KX-02 in preclinical syngeneic mouse GBM models resulted in the complete eradication, without recurrence, of the tumors in an average of approximately 30% of treated mice. KX-02's multiple MOAs along with its ability to cross the BBB, make it a novel molecule for the treatment of brain tumors. KX-02 is currently in the early stages of clinical development. The NMPA allowed the start of a Phase 1 trial in China, which commenced at the end of 2019.

Intranasal Granisetron (GNS)

The development of supportive therapy is complementary to our oncology drug platform. Chemotherapy-induced nausea and vomiting, or CINV, is a common side effect of cytotoxic chemotherapy treatments. Granisetron is a 5-hydroxytryptamine 3, or 5-HT3, receptor antagonist, a class of anti-emetic drugs that are commonly used in the prevention of CINV. Our subsidiary, Comprehensive Drug Enterprises, has developed intranasal formulations of granisetron for further evaluation in the clinic.

Current Therapies and Limitations

Currently, granisetron is dosed in IV, oral and patch forms to treat CINV. We believe these dosing regimens have disadvantages including time to effectiveness, and lack of ability to control the symptoms effectively at home.

Current and Planned Clinical Studies

We believe intranasal delivery will possess a number of advantages for the patient. These advantages may include a rapid delivery of therapeutic drug levels for quick relief of CINV as well as the ability to self-dose outside of the hospital and IV settings while experiencing CINV (when oral administration would be difficult). The intranasal route of administration of GNS leads to more rapid achievement of systemic concentrations of the drug compared to the oral route.

A Phase 1 parallel-group study of GNS was conducted in Taiwan to assess the PK, safety and tolerability of GNS. A total of fifty healthy subjects, 25 male and 25 female, were divided into the following treatment groups: 1 mg Kytril administered IV over thirty seconds to ten patients, 1 mg Kytril tablets administered orally to ten patients, and either 0.5, 1, or 2 mg of intranasal GNS administered to ten patients. The results showed that the drug concentrations were dose proportional following intranasal delivery of GNS and the side effects were acceptable.

We are presently evaluating the market opportunity in various geographies for the development of an intranasal route of delivery in order to determine the clinical development program for this drug candidate.

Our Proprietary Dual (CYP/P-gp) Inhibitor Program

We are developing a proprietary class of “dual” absorption enhancers that are intended to inhibit both the P-gp transporter and the CYP enzymes within the gastrointestinal tract. There are many barriers that limit the oral absorption of drugs in humans. The P-gp transporter is a major barrier to absorption of active chemotherapy drugs. However, certain other drugs with P-gp liabilities may also have liabilities for other barriers such as metabolizing enzymes, such as the cytochrome P450, or CYP, class of enzymes. This intestinal CYP mediated metabolisim can be a contributing factor in limiting oral absorption of certain drugs. This class of dual absorption enhancers has shown potential to significantly improve the oral bioavailability of certain other drugs in laboratory tests and may expand the application of our oral absorption platform to drugs where the CYP barrier to oral absorption is also important. These dual absorption enhancers may lead to better performing next-generation oral medicines in our pipeline of clinical products.

The development of these dual absorption enhancers is at the preclinical stage. Proof of concept, providing increased oral bioavailability in preclinical species, has been obtained with several absorption enhancers and candidate drugs. Currently additional filters such as patentability/freedom to operate, physical-chemical characterization, pre-formulation studies, manufacturing analysis and preliminary toxicity testing are being applied to our first group of lead candidates to facilitate election of an IND candidate.

Our TCR-T Immunotherapy and Arginine Deprivation Therapy Platforms

We commenced the development of two new in-licensed platforms based on our knowledge of absorption biology: TCR-T and Arginine Deprivation Therapy.

TCR-T Immunotherapy

T Cell Receptor Engineered T Cell, or TCR-T, immunotherapy is a cell-based therapy that takes advantage of unique attributes of TCR mediated target recognition and provides a potent and selective TCR-T directed response against cancer cells. Central to this platform is the ability to first identify endogenous TCRs with specificity for a defined tumor antigen and to then enhance the affinity of the TCR to optimize tumor recognition and killing. These High Affinity TCRs can be incorporated into a patient’s own T cells, converting the cells into a potent anti-cancer therapy. Using this technology, we believe the platform has generated engineered T-cells with higher binding affinity, specificity for intended target cells, expression level of the TCR and persistence in patients’ circulation during therapy. Preliminary studies have shown positive clinical signals.

Pegtomarginase

Pegtomarginase, the Arginine Deprivation Therapy product, is based on our pegylated genetically engineered human arginase technology that targets cancer growth and survival by interrupting the supply of arginine to a proportion of cancers with disrupted urea cycles. Our proprietary arginase biologic product is well suited to deplete arginine from the tumors with disrupted urea cycle, while healthy cells, capable of producing their own arginine, are largely unaffected.

Our Research and Development

We are an innovative oncology company with drug discovery, drug formulation, clinical development and API/drug product manufacturing facilities in both the U.S. and China. The U.S. drug discovery, clinical development and formulation research facilities are largely concentrated in Buffalo, New York and Cranford, New Jersey. The range of capabilities at these facilities includes medicinal chemistry, biochemistry, cell biology, formulation, chemical manufacturing and control, quality control, pharmacokinetics/pharmacodynamics (PK/PD) and data management, as well as pharmacovigilance, clinical development and regulatory expertise functions. Animal efficacy, PK/PD and toxicology studies are carried out at various contract research organizations, or CROs, around the world in order to facilitate the drug research and development process.

In China, our research and development center in Hong Kong is integrated with our research and development center in Buffalo. This center concentrates on drug formulation development and evaluation. When we acquired Comprehensive Drug Enterprises, or CDE, in 2015, we added scale to our formulation and research personnel in Hong Kong. The clinical oral formulation of docetaxel is an example of a discovery emanating from our Hong Kong research and development center. Higher strength paclitaxel powder tablet formulations, to be introduced into our future clinical evaluations of the Oraxol drug product, are a second example of the formulation development work being successfully carried out at the Hong Kong research and development center.

Commercial Platform

We believe the value creation potential is higher for biopharmaceutical companies able to commercialize their proprietary products as compared to companies who have a partner to commercialize. The infrastructure investment and build-out of a commercial team prior to regulatory approval is typically costly and requires years of investment. In 2016, we launched a commercial platform in the U.S. to begin building out this infrastructure in advance of our launch of proprietary products. Our commercial team markets and sells a variety of in-licensed pharmaceutical products, which are therapeutically related to our proprietary portfolio.

Using our resources to commercialize products in oncology may create more value for investors than marketing product rights pre-commercialization. We believe commercialization risks can be offset by establishing oncology manufacturing operations (API, Manufacturing, etc.) and commercial operations (Multi-source Oncology, Pharmacy, Hospitals, etc.).

Our Commercial Operations

Target Audiences: U.S. Oncology Market

The U.S. Oncology market is highly complex with Gatekeepers, Influencers and Prescribers influencing sales of oncology products. Launching a commercial operation in preparation for a proprietary drug approval is risky, difficult and expensive. Any commercial oncology organization must be able to market to Gatekeepers, Influencers and Prescribers in the oncology market at launch. Gatekeepers include hospitals (including pharmacies and therapeutics committees), buying groups, oncology managed care organizations, specialty distributors and pharmacists. Influencers in the oncology market include Key Opinion Leader physicians, regional cancer centers (as defined by the National Cancer Institute) and the U.S. government. Prescribers include oncologists and dermatologists.

Key hurdles in establishing Commercial Operations in the oncology market include the unpredictability of timing for FDA approval, the limited time to establish market relationships post approval, competition with companies with broader oncology offerings and identifying key influencers in the local oncology market. Another hurdle is recruiting key senior business leaders since they are responsible for recruiting a successful Oncology Sales and Marketing team. For all these reasons, establishing commercial operations in the oncology market is risky and expensive.

In order to manage the risks and capture post commercial oncology economics, we launched two oncology product lines in 2017—Multisource Oncology products and 503B Compounded Oncology Products. We support these two product lines with a sales and marketing organization to target Gatekeepers. Our National Accounts organization targets Gatekeepers and the U.S. Government for these two oncology product lines. Regional Cancer Centers are targeted for Multisource Oncology and 503B Outsourced Facility products.

503B Outsourced Facility Products

We manufacture certain products in our FDA registered 503B Outsourcing Facility. We use our internal cGMP operations and select- contract manufacturers to make both sterile-to-sterile products and products from sterilized bulk API. For example, we manufacture a ready to use (RTU) vasopressin product that is preservative free. We source certain of our API from our own internal supply chain to make products from sterile API bulk. We also buy API from other sources. For sterile-to-sterile products, we source the sterile vials and bags from national suppliers. This oncology business further expands our offering to the U.S. oncology market.

U.S. Specialty Pharmaceuticals

Our U.S. Specialty Pharmaceuticals business develops and sources products through licensing agreements with various partners, whom we collectively refer to as our Global Partner network. The company has unique commercial expertise in multisource oncology and injectable products and has developed a number of Global Partners that develop and manufacture multisource products for the U.S. market. This Global Partner network supplies the products the company markets in the U.S. Specialty Pharmaceutical business. We launched a commercial oncology business in the U.S. by launching multisource oncology and therapeutically related products supplied by our Global Partner network. We structure collaborations whereby we split the profits with the Global Partners and market the products to the acute hospital and oncology clinics in the U.S. oncology market. This will help the company prepare to launch proprietary oncology products into the U.S. market.

As of December 31, 2018, APD markets twenty-four products with forty-nine SKUs. In addition, Athenex Pharma Solutions (APS) markets six products with sixteen SKUs as of December 31, 2018. Our Commercial Platform is expected to launch an additional thirteen products in the first half of 2019, including eleven products by APD and two products by APS.

Agreements with key Suppliers and Marketing Partners

Gland Agreement

From August 2016 to May 2017, we entered into four binding term sheets with Gland to market twenty-seven of Gland's products. Gland has obtained FDA approval for twenty-two of such products and has filed an abbreviated new drug application, or ANDA, in the U.S. for the remaining five products. For each of the licensed products, we will pay a license fee to Gland. Additionally, during the terms of the agreements we have a profit-sharing arrangement pursuant to which we will pay to Gland between 0% and 60% of the net profits from sales of each of the licensed products, depending on the product. The initial term of each of the Gland license agreements is five years from the launch of each product licensed pursuant to the agreement, subject to automatic renewal for additional two year terms, unless terminated by either party upon provision to the other party at least 90 days' notice in advance of a renewal date.

Pemetrexed, Supply Agreement Term Sheet

In December 2016, we entered into a binding term sheet with Nang-Kuang Pharmaceutical Co., LTD and CANDA NK-2, LLC, two affiliated pharmaceutical suppliers, pursuant to which we will enter into a definitive agreement for exclusive distribution of a generic injectable oncology product for the U.S. market. The ANDA for this product has been filed by the suppliers with the FDA. Upon signing of the term sheet, we were obligated to make a prepayment for a total of $12.0 million.

Under the agreement, we will make two additional product transfer payments, one equal to a premium between 10% and 20% over the cost incurred by the suppliers to produce and ship the product after confirmation of each purchase order of the product and, after receiving such product, we will make the other payments quarterly to the suppliers of between 40% and 60% of the earnings from sales, less certain expenses, of the product.

The initial term of the definitive agreement will begin on the signing date and continue through ten years after the date of our first commercial sale of the product, subject to automatic renewals of successive two-year terms, unless terminated by either party with six months' notice prior to the expiration of the initial term or any renewal term. The agreement will also contain customary termination rights for either party in the event of a material breach of the agreement by the other party or bankruptcy or insolvency. In addition, we will be able to terminate the agreement with 30 days' notice to the suppliers if the net profits from sales of the product, less certain expenses, equals zero or less and the parties cannot agree on reductions to the actual cost of the products.

Amphastar Agreement

In February 2017, we entered into a definitive agreement with Amphastar Pharmaceuticals, Inc. (Amphastar) to acquire fourteen ANDAs and inventory for certain APIs. The agreement requires payments of up to $6.4 million, which has been paid in full as of December 31, 2018. In addition to the payments described above, we have agreed to pay Amphastar a royalty fee equal to 2% of our

net sales relating to the fourteen ANDAs and API inventory transferred to us by Amphastar for a period of ten years from the execution of the agreement.

MAIA Agreement

In December 2018, we entered into a distribution and supply agreement with MAIA Pharmaceuticals effective as of October 3, 2018 whereby we acquired the exclusive license to a generic version of an approved product. The FDA has not yet approved the ANDA for the generic version to which we have an exclusive license. In connection with the execution of this agreement, we agreed to pay an upfront milestone payment in addition to profit sharing of 50% of the net profits from the sales of the licensed product. We also agreed to pay an additional milestone payment to MAIA in the event the FDA approves the ANDA for the licensed product. The initial term of the agreement is for seven years from the launch of the product and is subject to an automatic two-year renewal term unless terminated by either party upon at least 180 days' notice in advance of the renewal date.

Summary of Commercial Strategy & Source of Supply Chain

Product line	Proprietary Oral / Dermal	Multisource / Specialty	503B Products	API
Launch date	To be determined	2017	2017	Ongoing
Commercialization regions	U.S., EU, China	U.S.	U.S.	U.S., EU, China
Manufacturing sites	Clarence, NY, Dunkirk, NY, Chongqing, China	Partner network, Dunkirk, NY, Chongqing, China	Clarence, NY, Dunkirk, NY	Chongqing, China

*EU is European Union

Customers and Product Distribution

We distribute our products primarily through pharmaceutical wholesalers and, to a lesser extent, specialty distributors that focus on particular therapeutic product categories, for use by a wide variety of end-users, including hospitals, integrated delivery networks and alternative site facilities. For the year ended December 31, 2018, the products we sold through our three largest wholesalers, AmerisourceBergen Corp. (Amerisource), Cardinal Health Inc. (Cardinal Health) and McKesson Corp. (McKesson), accounted for approximately 12%, 9% and 9%, respectively, of our total revenue.

We utilize an outside third-party logistics contractor to distribute our U.S. products. Since the inception of the launch of our specialty products, the third-party logistics provider has been handling all aspects of our product logistics efforts and related services to us, including warehousing and shipment services, order-to-cash services, contract administration services and chargeback processing. Our products are warehoused and distributed through a third-party logistics provider located in Memphis, Tennessee. Under our agreement with the third-party logistics provider, we maintain ownership of our finished products until sale to our customers. The initial term of the agreement is three years following the initial delivery date and will automatically renew for successive 12-month periods, unless either we or the other party give notice of intent to terminate at least 90 days in advance of such automatic renewal. We may also have the opportunity to terminate the agreement within 30 days of receiving notice of certain price increases by the third-party logistics provider. The agreement also contains customary termination rights for either party, such as in the event of a breach of the agreement.

Global Supply Chain Platform

We believe it is important to minimize potential disruptions associated with a high potency oncology pharmaceutical supply chain. Therefore, we have begun the process of internalizing key components of the supply chain that we believe are integral to minimizing these risks and retaining value for shareholders. For example, the World Health Organization lists paclitaxel as an essential medicine. Paclitaxel is derived from the bark of the Pacific yew tree and harvestable trees for the starting biomass are globally limited in supply. While current supply of the starting biomass for paclitaxel may be sufficient to meet global paclitaxel API demand, we believe future shortages are possible if we are successful in the commercialization of one of our lead drug candidates, Oraxol. We believe this increased demand could lead to shortages of paclitaxel API potentially leading to market and supply disruptions.

Our research group evaluated the purity and potency of some of the largest global suppliers of paclitaxel API. In 2015, we acquired one of these suppliers, Polymed Therapeutics Inc. and Chongqing Taihao Pharmaceutical Co. Ltd., or Taihao. Taihao is a cGMP manufacturer of high potency oncology API based in Chongqing, China and Polymed Therapeutics Inc. is the U.S. marketing entity for Taihao's API in North America and Europe. Historical production and sales of API by this subsidiary were to third parties.

We anticipate a greater share of Taihao's manufacturing capacity will be used for our internal needs in the future, and, therefore, sales to third parties may decrease. Historically, Polymed Therapeutics Inc. sold certain of these API products internationally to mostly large multi-national pharmaceutical companies. For the years ended December 31, 2018, 3% of our total revenue came from Intas Pharmaceuticals and 6% came from Ebewe Pharmaceuticals.

In 2014, we sought to obtain better control over our manufacturing of high potency oncology drugs used in global clinical studies, and, in the third quarter of 2014 acquired QuaDPharma, one of our suppliers based in Clarence, New York. The number of our clinical studies has grown since the close of the acquisition. We are standardizing and leveraging the acquired cGMP systems and operating procedures in anticipation of developing multi-cGMP large scale manufacturing plants in both the U.S. and China.

Strategic Public-Private Partnerships

New York State Partnership

In May 2015, we entered into an agreement with Fort Schuyler Management Corporation (FSMC) a not-for-profit corporation owned by the State of New York, for a medical technology research, development, innovation and commercialization alliance. Under the agreement, FSMC agreed to pay up to $25 million for the construction of our North American headquarters and formulation lab and equipment in Buffalo, New York. We moved into the North American Headquarters in October 2015 and are sub-leasing the space from FSMC for a 10-year term, with an option to extend the term for an additional 10 years. For the first three years of the lease, we are paying rent to FSMC equal to 35% of FSMC's operating costs for the space and thereafter will pay 100% of FSMC's operating costs for the space for the remainder of the term. Under the agreement, we are obligated to spend $100 million in the Buffalo area over the initial 10-year term of the lease and an additional $100 million during the second 10-year term if we elect to extend the lease. We also committed to hiring 250 permanent employees in the Buffalo area within the first 5 years of completion of the project. As of December 31, 2018, we had hired 162 permanent employees in the Buffalo area. In the event we are unable to hire enough employees in the Buffalo area or meet our other obligations under this agreement, FSMC may terminate the agreement and we may have to renegotiate our lease or relocate our North American headquarters.

Under the same May 2015 agreement, FSMC also agreed to fund the costs of construction of a new manufacturing facility in Dunkirk, New York that we intend to use for large scale 503B compounding and other cGMP-compliant drug manufacturing. Under the current arrangement, we have selected a general contractor for the project, and we will oversee the development of the facility. Empire State Development (ESD), the parent entity of FSMC, is responsible for the costs of construction and all equipment for the facility, up to an aggregate of $200 million, plus any additional funds available from the previous $25 million grant, and FSMC, not us, will own the facility and equipment. We are entitled to lease the facility and all equipment at a rate of $1.00 per year for an initial 10-year term and for the same rate if we elect to extend the lease for an additional 10-year term. We are responsible for all operating costs and expenses for the facility. In exchange, we have committed to spending $1.52 billion on operational expenses in our first 10-year term in the facility, and an additional $1.5 billion on operational expenses if we elect to extend the lease for a second 10-year term. We also committed to hiring 450 employees at our Dunkirk facility within the first 5 years of operations, including hiring at least 300 new employees within 2.5 years of the Dunkirk facility becoming operational. In September 2017, we entered into a grant disbursement agreement with ESD, whereby the State of New York will grant up to $200 million, plus any additional funds available from the previous $25 million ESD grant, to us in order to fund the construction of the Dunkirk facility. The funds will be deposited in four installments of up to $50 million each into an ESD held account, and the first $50 million installment was deposited in the third quarter of 2017. Actual disbursement of such funds to the Company occurs as the Company submits appropriate documentation verifying that expenditures on the project have been incurred. In addition, in July 2017, we entered into a 20-year payment in-lieu of tax agreement for the construction of the Dunkirk facility with the County of Chautauqua Industrial Development Agency (CCIDA), under which we anticipate incurring sales tax exemption savings of approximately $9.1 million during the development of the facility and property tax savings of approximately $78 million over 20 years.

In November 2017, we entered into a project agreement with the CCIDA which sets forth the obligations of the parties in relation to the CCIDA's grant to us of certain sales and use tax exemptions and real property tax exemptions in consideration for our agreement to complete the Dunkirk facility. The project agreement estimates the cost of the Dunkirk project at greater than $208.0 million, which exceeds the $200 million grant committed to by the State of New York, and we will be responsible for the difference. We are obligated to invest no less than $187.2 million in the facility prior to the completion of the project, which sum includes funds committed by the State of New York. The agreement includes commitments to comply with state and local laws in connection with the project. In December 2017, we entered into an agreement with M+W, U.S., Inc. (now renamed Exyte U.S., Inc.), whereby M+W will be responsible for the design and construction of the Dunkirk facility at a cost estimated between $205 million and $210 million, of which up to $200 million will be paid by a grant from the State of New York, with the remaining amount being paid by us. Payments under the December 2017 agreement will be made to M+W over time based upon completion of certain milestones under the agreement, and ESD must approve any payment from the grant funds.

Under the same September 2017 agreement with ESD, we must complete the construction of the facility in Dunkirk, New York in accordance with the final plans and specifications approved in writing by ESD and must maintain our business operations at the facility for a minimum of ten years after its completion. In 2018, we began constructing the 320,000 sq. ft. facility and began ordering equipment for our 503B compounding operations at the site. The September 2017 agreement may be subject to termination if ESD and FSMC perform their obligations under the agreement, and we do not attain and or maintain certain levels of employment or spending for specified periods of time. In such event and in accordance with the May 2015 agreement, any potential liability of us would be capped at the amount of actual ESD spending on the facility in Dunkirk, New York times the percentage of required spending by us which we have not yet incurred.

China Partnership

In October 2015, we entered into an agreement with Chongqing Maliu Riverside Development & Investment Co., Ltd. (CQ), which is wholly owned by the Finance Bureau of Banan district of Chongqing, and is authorized to be responsible for investments, financing, infrastructure construction, operations and management in the Chongqing Maliu Riverside Development Zone. Our agreement with CQ provides for the construction of both a formulation plant and an API plant in China. After entering into the agreement, and pursuant to its terms, we established a China-based subsidiary that is responsible for the operations of both facilities in July 2016. CQ is now responsible for construction of both facilities according to U.S. GMP standards. We expect to begin utilizing the facility in 2019. The land and buildings will be owned by CQ, and we will lease the facilities, rent-free, for the first 10-year term, with an option to extend the lease for an additional 10-year term, during which, if we are profitable, we will pay a monthly rent of 5 RMB per square meter of space occupied. We are responsible for the costs of all equipment for the facilities, and we have committed to occupying and beginning to use the facilities within six months of the completion of construction. We have also committed to achieving certain operational, revenue and tax generation milestones within certain time periods once we commence operations. If we are unable to achieve these milestones, CQ will have the opportunity to terminate the agreement and dispose of the plants in its discretion.

Our goal is to use our public-private partnerships as a capital efficient method for large scale cGMP manufacturing within our supply chain and to facilitate market access in China. We believe our current facilities will be adequate and suitable for our operations for the foreseeable future.

To date, we have utilized a combination of acquisitions and public-private partnerships to internalize certain key components of our manufacturing and supply chain. We expect to continue to use a combination of collaborations and acquisitions to continue to build out elements of our supply chain where needed as a mechanism to minimize execution risk and retain value for our shareholders.

License and Collaboration Agreements

In-Licenses

Arginase License Agreement

In June 2018, we entered into a license agreement with Avalon Polytom (HK) Limited (Polytom), an entity affiliated with Avalon Global Holdings Limited and a related party of the Company, which we refer to as the Arginase License, pursuant to which Polytom granted us an exclusive, sublicensable right and license to develop and commercialize products containing pegylated and cobalt-replaced arginase for the treatment of cancer in humans, apart from ophthalmic uses and use as eye drops, worldwide. Dr. Johnson Lau, our chief executive officer and chairman, and Dr. Manson Fok, one of our directors, collectively have a controlling interest in, and serve on the board of directors of, Avalon Global Holdings Limited. Mr. Song-Yi Zhang, one of our directors, also has a controlling interest in Avalon Global Holdings Limited.

We made an upfront payment of cash of $3.0 million and common stock of $2.0 million to Polytom upon effectiveness of the Arginase License, and we were required to make payments to Polytom worth up to $45.0 million of our common stock or of cash upon the occurrence of certain regulatory and sales milestones. We have also agreed to pay royalty payments ranging from 10% to 12% based on net sales of any products utilizing the intellectual property that is the subject of the Arginase License. Such royalties will be reduced by 40% when competing generic products have 25% of the market share in the applicable country and will be eliminated entirely when competing generic products have 50% of the market share in the applicable country.

The terms of the Arginase License shall extend for a period which may expire on a country-by-country basis upon the earliest to occur of either (i) the expiration of the last of the patent rights licensed under the agreement, or (ii) invalidation of substantially all of the patent rights licensed under the agreement. Notwithstanding the foregoing, after the occurrence of immediately preceding clauses (i) or (ii) , the terms of the Arginase License shall automatically be extended for consecutive one year periods subject to the same terms and conditions set forth in the agreement unless either Polytom or we give written notice of its intention not to extend the

agreement terms: (i) at least ninety days prior to the expiration of the patent rights licensed under the agreement; or (ii) as soon as practically possible in the case of an invalidation claim and at least ninety days prior to the then current expiration date of the agreement. Prior to the expiration of the term of the agreement, both parties may terminate the agreement in whole or in part upon mutual written agreement. Subject to certain conditions, we may also terminate in whole or in part the agreement in our sole discretion upon not less than six months prior written notice of termination at any time. The agreement also contains customary termination rights for either party, such as in the event of a breach of the agreement or the initiation of bankruptcy proceedings by the other party.

HepaPOC License and Supply Agreement

In June 2018, we entered into a license and supply agreement with Avalon HepaPOC Limited (HepaPOC), an entity affiliated with Avalon Global Holdings Limited and a related party of the Company, which we refer to as the HepaPOC License, pursuant to which HepaPOC agreed to exclusively sell to us the meter and consumable strips that can be used to detect galactose concentrations in human blood and granted us an exclusive, sublicensable right and license to use and commercialize the meter and strips for conduct of liver function tests in humans taking our oncology drugs. Dr. Johnson Lau, our chief executive officer and chairman, and Dr. Manson Fok and Mr. Song-Yi Zhang, two of our directors, collectively have a controlling interest in, and/or serve on the board of directors of, Avalon Global Holdings Limited.

We made an upfront payment of cash of $0.5 million to HepaPOC upon effectiveness of the HepaPOC License Agreement, and we were required to make payments to HepaPOC worth up to $4.8 million in our common stock or in cash upon the occurrence of certain regulatory and sales milestones. In addition, we have agreed to pay royalty payments of 5% based on aggregate net sales of any products utilizing the intellectual property that is the subject of the HepaPOC License.

The terms of the HepaPOC License shall extend until the date on which the last of the patent rights licensed under the agreement expires or is invalidated. Notwithstanding the foregoing, the terms of the HepaPOC license shall automatically be extended for consecutive one year periods subject to the same terms and conditions set forth herein (unless agreed otherwise) unless either party gives written notice of its intention not to extend the agreement term: (i) at least ninety days prior to the expiration date of the patent rights licensed under the agreement or (ii) as soon as practically possible in the case of an invalidation claim or (iii) at least ninety days prior to the then current expiration date of the agreement thereafter. Notwithstanding the foregoing, after the occurrence of (i) or (ii) above, the terms of the HepaPOC License shall automatically be extended for consecutive one year periods subject to the same terms and conditions set forth in the agreement unless either HepaPOC or we give written notice of its intention not to extend the agreement terms: (i) at least ninety days prior to the expiration of the patent rights licensed under the agreement or (ii) as soon as practically possible in the case of an invalidation claim and (iii) at least ninety days prior to the then current expiration date of the agreement. Prior to the expiration of the term of the agreement, both parties may terminate the agreement in whole or in part upon mutual written agreement. We may also terminate in whole or in part the agreement in our sole discretion upon not less than six months prior written notice of termination at any time. The agreement also contains customary termination rights for either party, such as in the event of a breach of the agreement or the initiation of bankruptcy proceedings by the other party.

TCR-T License Agreement

In June 2018, we entered into a Share Subscription Agreement with Xiangxue Life Sciences Ltd, or XLifeSc, a wholly-owned subsidiary of Guangzhou Xiangxue Pharmaceutical Co., Ltd. to establish, operate and manage a limited liability company named Axis Therapeutics Limited (Axis) to offer certain goods and services worldwide except in China. Axis is owned 45% by XLifeSc and 55% by us.

In June 2018, Axis entered into a license agreement with XLifeSc, which we refer to as the TCR-T License, pursuant to which XLifeSc granted Axis an exclusive, sublicensable right and license to use XLifeSc's proprietary T-cell Receptor Engineered T-Cells (TCR-T) to develop and commercialize therapeutic products for oncology indications worldwide except in China. Axis is responsible for all development, manufacturing and commercialization, and the related costs and expenses, of any product candidates resulting from the agreement.

In September 2018, we completed the closing process under the Share Subscription Agreement which included an exchange of a 45% ownership interest in Axis to XLifeSc for a license of in-process research and development (IPR&D). Upon effectiveness of the TCR-T License and satisfaction of certain conditions in the license agreement, Axis made an upfront payment of the Company's common stock of $5.0 million to XLifeSc, and Axis was required to make payments to XLifeSc worth up to $110.0 million in aggregate upon the occurrence of certain regulatory and sales milestones to be achieved in the U.S., the EU, China and Japan. In addition, XLifeSc has agreed to pay royalty payments of 10% to Axis based on aggregate net sales of any products using the licensed intellectual property in China.

The term of the TCR-T License will remain in effect until the expiration of the patent rights licensed under the agreement. The agreement will terminate automatically if the shareholders agreement between XLifeSc and us is terminated. The TCR-T License also contains customary termination rights for either party, such as in the event of a breach of the agreement or the initiation of bankruptcy proceedings by the other party.

Hanmi Licensing Agreements

In December 2011 and June 2013, we entered into two separate in-licensing agreements with Hanmi pursuant to which Hanmi granted us licenses to certain patents and know-how with respect to Hanmi's Orascovery Program to research, discover and develop compounds that enhance or increase the oral absorption of active pharmaceutical ingredients.

The December 2011 agreement, which we refer to as the 2011 Hanmi Agreement, granted us an exclusive, sublicensable license for development and commercialization activities utilizing Hanmi's patents and know-how related to the Orascovery Program in a certain territory including North America, South America, the EU, Australia, New Zealand, Russia, Eastern Europe, Taiwan and Hong Kong, and a non-exclusive license to utilize the same intellectual property in manufacturing worldwide for sales inside those territories. The June 2013 agreement, which we refer to as the 2013 Hanmi Agreement, granted us an exclusive, sublicensable license comparable to the 2011 Hanmi Agreement solely for China. The 2011 Hanmi Agreement was amended in November 2012 to add Macau and Singapore to the territory licensed under the agreement; in October 2013 to add Malaysia, Thailand, Vietnam, the Philippines and Indonesia; in March 2015 to add India; in March 2017 to add Japan; and again in September 2018 to all territories in the world apart from the Republic of Korea.

Upon effectiveness of the 2011 Hanmi Agreement we made an upfront payment of $0.25 million to Hanmi, and we will pay Hanmi tiered royalty payments in the teens based on aggregate net sales of any products using the licensed intellectual property in the territory. Such royalties will be reduced if competing generic products gain market share in the applicable country. Depending on when we receive regulatory approval of a product using the intellectual property licensed from Hanmi in the U.S. or Europe, we may be obligated to pay Hanmi a regulatory bonus of $24.0 million to be paid (i) upon the occurrence of a liquidity event, if the regulatory approval has already been received, or (ii) upon receipt of the regulatory approval, if such approval is received after a liquidity event. We were also required to pay Hanmi an exit bonus, in shares of our common stock at a 20% discount to the initial public offering price, of $6.25 million upon the completion of our initial public offering in June 2017 based on a nominal value of $5.0 million. In connection with the March 2015 amendment to the 2011 Hanmi Agreement, we made an upfront payment of $50,000 to Hanmi. Additionally, in connection with the March 2017 amendment to the 2011 Hanmi Agreement, we issued a $7.0 million convertible bond to Hanmi in lieu of an upfront payment. Hanmi elected to convert the $7.0 million principal amount of the convertible bond into 795,455 shares of our common stock, based on the agreed 20% discount to our initial public offering price, in September 2017. In connection with the September 2018 amendment to the 2011 Hanmi Agreement, we made an upfront payment of $40,000 to Hanmi.

Upon effectiveness of the 2013 Hanmi Agreement we made an upfront payment of $0.1 million to Hanmi, and we will pay Hanmi tiered royalty payments in the teens based on net sales of any products using the licensed intellectual property in China. The royalties shall be reduced if competing generic products gain market share in China. We also granted to Hanmi a one-time right of first negotiation to purchase all of our rights in Oraxol or Oratecan under the agreement during development and prior that, at Hanmi's discretion, requires us to negotiate in good faith the sale of our rights under such agreement to Hanmi at a purchase price determined by an internationally-recognized investment banking firm with an office in Hong Kong at any time prior to the earlier of (i) our first commercial sale of products using such technology or (ii) receipt by Hanmi of written notice from our company of the sublicense of the rights in an applicable product to a third party.

Under each agreement, we are responsible for all clinical studies and development and commercialization activities, and the related expenses, resulting from the agreements. Each of the 2011 Hanmi Agreement and the 2013 Hanmi Agreement expires on the earlier of (i) expiration of the last of Hanmi's patent rights licensed under the agreement or (ii) invalidation of Hanmi's patent rights which are the subject of the agreement, provided that the term will automatically be extended for consecutive one year periods unless either party gives notice to the other at least 90 days prior to expiration of the patent rights licensed under the agreement or before the then-current annual expiration date of the agreement. The patent rights licensed to us under the 2011 and 2013 Hanmi Agreements have expiry dates ranging from in 2023 to 2033, unless the terms of such licensed patents are extended in accordance with applicable laws and regulations.

Hanmi may also terminate the 2011 Hanmi Agreement if (i) we fail to file an IND with the FDA for Oraxol within six months of the latest of (x) our receipt from Hanmi of all English translations necessary for the filing of an IND with the FDA, (y) the date we and Hanmi agree that all studies necessary for the filing of an IND with the FDA have been completed or (z) the date of the final study report for the last of any additional studies that are necessary for the filing of an IND with the FDA or (ii) we fail to commence clinical studies for Oraxol within twelve months after the date of approval of an IND by the FDA.

The 2013 Hanmi Agreement may be terminated by Hanmi if (i) we fail to file an IND for Oraxol with the NMPA within six months after the latest of (w) completion of all Chinese translations necessary for the filing of an IND with the NMPA, (x) completion of all manufacturing and toxicology studies necessary for the filing of an IND with the NMPA (y) the date we and Hanmi agree that

all studies necessary for the filing of an IND with the NMPA have been completed or (z) the date of the final study report for the last of any additional studies that are necessary for the filing of an IND with the NMPA or (ii) we fail to commence clinical studies for Oraxol within twelve months after the date of approval of an IND by the NMPA.

Such clinical development milestones in respect of the termination right in both the 2011 Hanmi Agreement, and the 2013 Hanmi Agreement may be extended for twelve months if we reasonably request.

Prior to the expiration of the term of each agreement, we may terminate the agreement in our sole discretion, by providing six months' notice to Hanmi. Subject to certain conditions. The agreements also contain customary termination rights for either party, such as in the event of a breach of the agreement or the initiation of bankruptcy proceedings by the other party or by mutual agreement.

Out-License

Hanmi Licensing Agreements

In April 2011, we entered into a license agreement with Hanmi, which we refer to as the Hanmi Out-License, pursuant to which we granted to Hanmi an exclusive, sublicensable license to use certain of our intellectual property for development and commercialization of products containing KX-01 in certain territory including South Korea, China, Taiwan, Hong Kong, Singapore, Malaysia, Thailand, the Philippines, Indonesia and Vietnam. We also granted to Hanmi a right of first refusal for any KX-01 related formulation or pharmaceutical that we develop and intend to grant an exclusive license for in the territory covered by the Hanmi Out-License. Hanmi was responsible for all development, manufacturing and commercialization, and the related costs and expenses, of any product candidates resulting from the agreement.

We received an upfront payment of $1.5 million from Hanmi upon effectiveness of the agreement, and we were entitled to receive an aggregate of $4.0 million in additional development and regulatory milestone payments. We were also eligible to receive tiered royalty payments in the teens on net sales of each product commercialized by Hanmi utilizing the intellectual property subject to the Hanmi Out-License.

On August 20, 2018, we entered into a mutual letter of termination with Hanmi with respect to the Hanmi Out-License for our KX-01 oral formulation, which terminated the Hanmi Out-License as of the same date. This termination will allow us to continue to explore the potential of the KX-01 oral formulation worldwide.

ZenRx License Agreement

In April 2013, we entered into a license agreement with ZenRx, which we refer to as the ZenRx License, pursuant to which we granted to ZenRx an exclusive, sublicensable license to use certain of our intellectual property to develop and commercialize Oratecan and Oraxol in Australia and New Zealand, and a non-exclusive license to manufacture a certain compound but only for use in Oratecan and Oraxol. ZenRx is responsible for all development, manufacturing and commercialization, and the related costs and expenses, of any product candidates resulting from the agreement.

We received a $50,000 payment from ZenRx upon effectiveness of the agreement, and we may be entitled to receive up to an aggregate of $1.4 million in additional development, regulatory and sales milestone payments. We will also be eligible to receive tiered royalties in the teens on net sales of each product commercialized by ZenRx utilizing the intellectual property that is the subject of the ZenRx License. Such royalties will be reduced by 40% when competing generic products have 30% of the market share in the applicable country and will be eliminated entirely when competing generic products have 60% of the market share in the applicable country.

As an incentive to ZenRx to further development and commercialization of Oratecan and Oraxol in the territory, if ZenRx obtains certain regulatory approvals in the territory prior to regulatory approval of those products in either the U.S. or South Korea, we may be required to make payments to ZenRx, at ZenRx's option, either up to $0.6 million in cash or $0.35 million in cash plus $0.25 million worth of our common stock.

The term of the ZenRx License expires on the earlier of (i) expiration of the last of our patent rights licensed under the agreement or (ii) invalidation of our patent rights which are the subject of the agreement, provided that the term will automatically be extended for consecutive one year periods unless either party gives notice to the other at least 90 days prior to expiration of the patent rights licensed under the agreement or before the then current annual expiration date of the agreement. Prior to the expiration of the term of the agreement, ZenRx may terminate the agreement in its sole discretion, by providing three months' notice to us. Subject to certain conditions, we may also terminate the agreement if ZenRx fails to comply with certain development timelines set forth in the ZenRx License. The agreement also contains customary termination rights for either party, such as in the event of a breach of the agreement or the initiation of bankruptcy proceedings by the other party.

PharmaEssentia License Agreements

In December 2011 and December 2013, we entered into two separate out-licensing agreements with PharmaEssentia, pursuant to which we granted to PharmaEssentia certain licenses to our intellectual property for use in development and commercialization of certain products in specific territories.

The December 2011 agreement, which we refer to as the 2011 PharmaEssentia Agreement, granted an exclusive, sublicensable license to use any pharmaceutical preparation containing KX-01 or KX-02 for use in treating psoriasis or other non-malignant skin conditions in a territory that includes China, Taiwan, Macau, Hong Kong, Singapore and Malaysia. In December 2016, we agreed to amend the 2011 PharmaEssentia Agreement such that the field under the license agreement does not include AK for any country in the territory except Taiwan.

We received a $40,000 payment from PharmaEssentia upon effectiveness of the 2011 PharmaEssentia Agreement, and we may be entitled to an aggregate of up to $1.6 million in additional development and regulatory milestone payments, $0.25 million of which may be paid in the form of PharmaEssentia stock. PharmaEssentia has discretion to offer to make such payment in the form of its stock, and we have discretion as to whether to accept such payment in the form of its stock. We will also be eligible to receive tiered royalties ranging from the high single-digits to teens on net sales of each product commercialized by PharmaEssentia utilizing the intellectual property that is the subject of the 2011 PharmaEssentia Agreement. Such royalties will be reduced by 40% when competing generic products have 30% of the market share in the applicable country and will be eliminated entirely when competing generic products have 60% of the market share in the applicable country.

The December 2013 agreement, which we refer to as the 2013 PharmaEssentia Agreement, granted an exclusive, sublicensable license for development and commercialization of Oraxol and Oratecan in Taiwan and Singapore. Under the agreement, PharmaEssentia may also have the right to expand its license to include China, if Hanmi does not exercise its right of first refusal to such a product candidate under the Hanmi Out-License. In December 2016, we agreed to amend the 2013 PharmaEssentia Agreement to also include Vietnam in the territories covered by the license, provided that, if PharmaEssentia has not completed a submission for regulatory approval in Vietnam by 2021, the rights under the license in Vietnam will be returned to us. In November 2018, we agreed to amend the 2013 PharmaEssentia Agreement to also include a license for development and commercialization of Oradoxel in Singapore, Taiwan and Vietnam. We received $2.0 million from PharmaEssentia upon effectiveness of the amended agreement.

We received a $50,000 payment from PharmaEssentia upon effectiveness of the 2013 PharmaEssentia Agreement and a $0.5 million payment upon the initiation of a 505b2 strategy registration study in the first quarter of 2017, and we may be entitled to an aggregate of up to $1.5 million in additional development, regulatory and sales milestone payments. We may be obligated to pay PharmaEssentia an aggregate of $1.0 million in incentives if PharmaEssentia achieves certain milestones within designated timeframes. We will also be eligible to receive tiered royalties in the mid-teens on net sales of each product commercialized by PharmaEssentia utilizing the intellectual property that is the subject of the 2013 PharmaEssentia Agreement. Such royalties will be reduced by 40% when competing generic products have 30% of the market share in the applicable country and will be eliminated entirely when competing generic products have 60% of the market share in the applicable country. Under the November 2018 amendment to the 2013 PharmaEssentia Agreement, we also received an upfront payment of $2.0 million, and we may be entitled to an aggregate of up to $9.1 million in additional development and regulatory milestone payments related to Oradoxel.

Under each agreement, PharmaEssentia is responsible for all clinical studies and development and commercialization activities, and the related expenses, resulting from the agreements. Each of the 2011 PharmaEssentia Agreement and the 2013 PharmaEssentia Agreement expire on the earlier of (i) expiration of the last of our patent rights licensed under the agreement or (ii) invalidation of our patent rights which are the subject of the agreement, provided that the term will automatically be extended for consecutive one year periods unless either party gives notice to the other at least 90 days prior to expiration of the patent rights licensed under the agreement or before the then current annual expiration date of the agreement.

Prior to the expiration of the term of each agreement, PharmaEssentia may terminate the agreement in its sole discretion, by providing six months' notice to us. Subject to certain conditions, we may also terminate the agreement if PharmaEssentia fails to comply with certain development timelines set out in each of the agreements. The agreements also contain customary termination rights for either party, such as in the event of a breach of the agreement or the initiation of bankruptcy proceedings by the other party.

Guangzhou Xiangxue License Agreement

In May 2012, we entered into a license agreement with Guangzhou Xiangxue New Drug Discovery and Development Company Limited, or Xiangxue, which we refer to as the Xiangxue License, pursuant to which we granted to Xiangxue an exclusive, sublicensable license to use certain of our intellectual property to develop and commercialize products containing KX-02 in all indications for brain tumors in China, Taiwan, Hong Kong and Singapore. Xiangxue is responsible for all development, manufacturing and commercialization, and the related costs and expenses, of any product candidates resulting from the agreement.

We received a $0.75 million payment from Xiangxue upon effectiveness of the agreement and in 2013 received a further $0.75 million payment upon meeting the first regulatory milestone under the agreement. We may be entitled to receive an aggregate of up to $4.5 million in additional development and regulatory milestone payments. We will also be eligible to receive royalties in the teens on net sales of each product commercialized by Xiangxue utilizing the intellectual property that is the subject of the Xiangxue License. Such royalties will be reduced by 40% when competing generic products have 30% of the market share in the applicable country and will be eliminated entirely when competing generic products have 60% of the market share in the applicable country.

The term of the Xiangxue License expires on the earlier of (i) expiration of the last of our patent rights licensed under the agreement or (ii) invalidation of our patent rights which are the subject of the agreement, provided that the term will automatically be extended for consecutive one year periods unless either party gives notice to the other at least 90 days prior to expiration of the patent rights licensed under the agreement or before the then current annual expiration date of the agreement. Prior to the expiration of the term of the agreement, Xiangxue may terminate the agreement in its sole discretion, by providing six months' notice to us. Subject to certain conditions, we may also terminate the agreement if Xiangxue fails to comply with certain development timelines set forth in the Xiangxue License. The agreement also contains customary termination rights for either party, such as in the event of a breach of the agreement or the initiation of bankruptcy proceedings by the other party.

Eli Lilly and Company Agreement

In October 2016, we entered into a Clinical Trial Collaboration and Supply Agreement with Eli Lilly and Company, which we refer to as the Lilly Agreement, under which we and Lilly will conduct a Phase 1b trial of Oraxol in combination with Lilly's ramucirumab in patients with gastric, gastro-esophageal and esophageal cancers. Under the terms of the Lilly Agreement we will act as the sponsor of the study and will hold the IND/CTA relating to the study, while all clinical data generated under the study will be jointly owned by us and Lilly. Other than Lilly's obligation to supply ramucirumab to us, we will be responsible for all other costs associated with the conduct of the study.

The Lilly Agreement will remain in effect until the study contemplated by the agreement has been completed. The agreement also contains customary termination rights for either party, such as in the event of a breach of the agreement by the other party, or in the event a regulatory authority takes any action against or raises any objection to the study.

Almirall License Agreement

In December 2017, we entered into a license agreement with Almirall, which we refer to as Almirall License, pursuant to which we granted to Almirall an exclusive, sublicensable license of certain of our intellectual property for the development and commercialization of topical products containing KX-01 to treat and prevent skin disorders and diseases in humans (including AK), or the Field, in a specified territory, which includes the U.S. and substantially all European countries (including Russia and Turkey), or the Licensed Territory. We also granted Almirall a right of first negotiation to license from us in the territory covered by the Almirall license any compound (other than KX-01) that we may develop in the future with the same mechanism of action as KX-01 for topical treatment of skin disorders and diseases if we decide to collaborate with a third party regarding that newly developed compound. Under the Almirall License, Almirall also grants us an exclusive, sublicensable license to use certain of its intellectual property related to the products containing our licensed KX-01 for use in the Field in order to commercialize such products outside of the Licensed Territory and outside of the Field in the Licensed Territory and to commercialize other products containing KX-01 for indications outside the Field. If we decide to sublicense that license from Almirall for certain additional products or indications, we will negotiate with Almirall to allow them to reasonably participate in the commercial benefit of such sublicense.

In March 2018, we received an upfront payment of $30 million from Almirall under this agreement, and we expect to receive other near-term payments of up to $25 million. We may also be entitled to receive an aggregate of $65 million in additional milestone payments, as well as sales milestone payments we estimate will likely total $155 million. Almirall will reward Athenex with additional sales milestones should the sales exceed the currently projected amounts. In addition, we are eligible to receive tiered royalty payments for a certain period starting at 15% based on annual net sales of the topical products commercialized by Almirall, utilizing the intellectual property subject to the license agreement, with incremental increases in royalty rates commensurate with increased sales. Additionally, under certain circumstances starting after one year following regulatory approval of certain licensed products in the U.S., we would have the option to co-promote such licensed products under pre-negotiated terms and conditions with Almirall.

The term of the Almirall License began in February 2018 when antitrust approval was obtained and continues for the entire life of the licensed topical products on a country-by-country basis. Prior to the expiration of the term of the Almirall License, Almirall may terminate the agreement in its entirety or with regard to a certain territory in its sole discretion by providing six months' notice to us. Almirall may also terminate the agreement upon written notice during a 45-day evaluation period if Almirall does not find certain clinical data we provide to them to be satisfactory, upon which we may license the compound from Almirall in exchange for the previously agreed-upon royalty payments and a one-time upfront fee, pursuant to the first amendment to the Almirall License and

letter agreement we entered into with Almirall in September 2018.We may also be required to reimburse Almirall in the event Almirall provides notice that certain clinical endpoints under the agreement are not met. In addition, Almirall may terminate the agreement effective immediately if the licensed topical products cannot be marketed in the territory due to significant safety concerns, if regulatory approval is finally and irrevocably denied in a territory or if an approved product label is less favorable than the product label submitted to the regulatory authorities in a way that would materially affect the commercial value of the product.

The agreement also contains customary termination rights for both parties, such as in the event of a breach of the agreement or if the other party defaults in performance of its obligations under the agreement.

CJ License Agreement

In December 2018, through our subsidiary Chongqing Taihao Pharmaceutical Co., Ltd. (CT), we entered into a series of agreements to license certain intellectual property to Chongqing Jingdong Junzhuo Pharmaceutical Co., Ltd. (CJ) to exclusively develop and commercialize KX2-391 for the treatment of actinic keratosis and oncology indications in humans in mainland China (excluding Hong Kong, Macau and Taiwan). Via the series of agreements, CJ obtained the exclusive right to promote, market, sell and commercialize in mainland China those topical or oral products that contain our proprietary Src/tubulin inhibitor, KX-01, also known as KX2-391. We have agreed to manufacture the products and to conduct all clinical trials, and CJ was required to use its reasonable best efforts to commercialize the licensed products in mainland China. Under the agreements, CJ has agreed to pay CT (i) an upfront payment of $14.5 million, (ii) certain milestone payments totaling $15 million and (iii) royalty payments based on the amount of sales of the product. These agreements have been terminated by mututal consent of both parties as of March 6, 2019, and we will retain the exclusive right to promote, market, sell and commercialize in mainland China those topical or oral products that contain KX2-391. We are not subject to any termination penalties related to the termination of the license and sublicense agreements.

Competition

The biopharmaceutical industry and the oncology subsector are characterized by rapid evolution of technologies, fierce competition and strong defense of intellectual property. Any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our product candidates, platforms and scientific expertise in the field of biotechnology and oncology provide us with competitive advantages, a wide variety of institutions, including large biopharmaceutical companies, specialty biotechnology companies, academic research departments and public and private research institutions, are actively developing potentially competitive products and technologies. We face substantial competition from biotechnology and biopharmaceutical companies developing oncology products. These competitors generally fall within the following categories:

Oral administration: Taxol, Abraxane, Cynviloq, Camptosar, Onivyde, Taxotere and Hycamtin;

Src Kinase inhibitors: Picato and Temodar.

Many of our competitors, either alone or with strategic partners, have substantially greater financial, technical and human resources than we do. Accordingly, our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance, rendering our treatments obsolete or non-competitive. Accelerated merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical study sites and patient registration for clinical studies, acquiring technologies complementary to, or necessary for, our programs and for sales in the API business. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunity could be substantially limited in the event that our competitors develop and commercialize products that are more effective, safer, less toxic, more convenient or less expensive than our comparable products. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of our products' entry. We believe the factors determining the success of our programs will be the efficacy, safety and convenience of our product candidates and our access to supply of API.

Intellectual Property

We strive to protect and enhance the proprietary technologies, inventions, products and product candidates, methods of manufacture, methods of using our products and product candidates, and improvements thereof that are commercially important to our business. We protect our proprietary intellectual property position by, among others, filing patent applications in the U.S. and in jurisdictions outside of the U.S. covering our proprietary technologies, inventions, products and product candidates, methods, and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how, continuing innovation, and licensing opportunities to develop, strengthen and maintain our proprietary intellectual property position.

As of December 31, 2018, we owned more than 150 granted patents and more than 40 pending patent applications worldwide. In addition, we have in-licensed patents and patent applications relating to our Orascovery platform technology from Hanmi. In our Orascovery platform, the lead compound is covered as composition-of-matter in granted patents in the U.S. and other territories, such as China and Europe. These patents will expire in October 2023 or 2024, excluding any potential patent term adjustments and/or patent term extensions that may be available. The lead compounds in our Src Kinase Inhibition platform are covered as composition-of-matter in granted patents in the US and other territories, including China and Europe. These patents will begin to expire in December 2025, excluding any potential patent term adjustments and/or patent term extensions that may be available.

The term of individual patents depends upon the laws of the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. In the U.S., the term of a patent may be lengthened by patent term adjustment to compensate the patentee for administrative delays by the United States Patent and Trade Office (USPTO) in examining and granting the patent or may be shortened if the patent is terminally disclaimed over an earlier-filed patent. In addition, a patent term may be extended to restore a portion of the term effectively lost as a result of FDA regulatory review. However, the restoration period cannot be longer than five years and cannot extend the remaining term of a patent beyond a total of fourteen years from the date of FDA approval, and only one patent applicable to an approved drug may be extended. Similar extensions as compensation for regulatory delays are available in Europe and other jurisdictions. We intend to seek patent term extensions where these are available. However, there is no guarantee that the applicable authorities, including the FDA in the U.S., will agree with our assessment of whether such extensions should be granted, and we cannot predict the length of the extensions even if they are granted. The actual protection afforded by a patent varies on a claim-by-claim basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. For a granted patent to remain in force most countries require the payment of annuities or maintenance fees, either yearly or at certain intervals during the term of a patent. If an annuity or maintenance fee is not paid, the patent may lapse irrevocably.

Granted patents and pending patent applications related to the SRC Kinase Platform cover such aspects as composition-of-matter claims to our lead product candidates and their analogs, claims to pharmaceutical compositions comprising such candidates and claims to methods of making and method of treatment using such candidates. Not accounting for any patent term adjustment, patent term extension or terminal disclaimer, and, assuming that all annuity and/or maintenance fees are paid, the patents and, if granted, patent applications, will expire from 2025 to 2038.

Government Regulation and Product Approval

Governmental authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, approval, quality control, labeling, packaging, promotion, storage, advertising, distribution, post-approval monitoring, marketing and export and import of products such as those we are developing. Our therapeutic drug candidates and compounded products are regulated by the FDA through either Section 503B of the FDCA or the NDA process in order for them to be legally marketed in the U.S. and will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Government Regulation

In the U.S., the FDA regulates drugs under the FDCA and its implementing regulations. Failure to comply with the applicable U.S. requirements at any time during the product development or approval process, or after approval, may subject an applicant to administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning or untitled letters;
- seizures or administrative detention of product;
- total or partial suspension of production or distribution or
- injunctions, fines, restitution, disgorgement, refusal of government contracts, or civil or criminal penalties.

NDA approval processes

The process required by the FDA before a therapeutic drug product may be marketed in the U.S. generally involves the following:

- completion of extensive nonclinical laboratory tests, animal studies and formulation studies conducted according to GLPs, and other applicable regulations;
- submission to the FDA of an IND, which must be authorized before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCPs, to establish the safety and efficacy of the product candidate for its intended use;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product candidate is produced to assess readiness for commercial manufacturing and conformance to the manufacturing-related elements of the application, to conduct a data integrity audit, and to assess compliance with cGMPs to assure that the facilities, methods and controls are adequate to preserve the product candidate's identity, strength, quality and purity;
- potential FDA audit of the clinical trial sites that generated the data in support of the NDA and
- FDA review and approval of the NDA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical or nonclinical testing stage. Nonclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. Such studies must generally be conducted in accordance with the FDA's GLPs. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some nonclinical testing may continue even after the IND is submitted. In addition to including the results of the nonclinical studies, the IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective thirty days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND and may affect one or more specific studies or all studies conducted under the IND.

The manufacture of investigational drugs for the conduct of human clinical trials is subject to cGMP requirements. Investigational drugs and API imported into the U.S. are also subject to regulation by the FDA relating to their labeling and distribution. Further, the export of investigational drug products outside of the U.S. may be subject to regulatory requirements of the receiving country as well as U.S. export requirements under the FDCA.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP requirements, which include, among other things, the requirements that all research subjects provide their informed consent in writing for their participation in any clinical trial. Investigators must also provide certain information to the clinical trial sponsors to allow the sponsors to make certain financial disclosures to the FDA. Clinical trials must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol, and any subsequent material amendment to the protocol, must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors also must report to the FDA serious and unexpected adverse reactions in a timely manner. Reporting requirements also apply to, among other things, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator's brochure and any findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product candidate. An institutional review board, or IRB, at each institution participating in the clinical trial must review and approve the protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each research subject or the subject's legal representative, monitor the study until completed and otherwise comply with IRB regulations. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries within a certain timeframe for public dissemination on the National Institutes of Health clinicaltrials.gov website.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined.

- Phase 1—The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and elimination. In the case of some therapeutic candidates for severe or life-threatening diseases, such as cancer, especially when the product candidate may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- Phase 2—Clinical trials are performed on a limited patient population intended to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3—Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product labeling.

A pivotal study is a clinical study that adequately meets regulatory agency requirements for the evaluation of a product candidate's efficacy and safety such that it can be used to justify the approval of the product. Generally, pivotal studies are also Phase 3 studies but may be Phase 2 studies, with the agreement of FDA, if the trial design provides a reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need.

In the case of a 505(b)(2) NDA, which is a marketing application in which the sponsor may rely on investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted, some of the above-described studies and nonclinical studies may not be required or may be abbreviated. The applicant may rely upon the FDA's prior findings of safety and efficacy for a previously approved product or on published scientific literature in support of its application. Bridging studies, including clinical studies, may be needed, however, to demonstrate the applicability of the studies that were previously conducted by other sponsors to the drug that is the subject of the marketing application.

Human clinical trials are inherently uncertain and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed or may not be completed at all. The FDA or the sponsor may suspend a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

During the development of a new product candidate, sponsors are given opportunities to meet with the FDA at certain points; specifically, prior to the submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. Sponsors typically use the meeting at the end of Phase 2 to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support the approval of the new therapeutic. If a Phase 3 clinical trial is the subject of discussion at the end of Phase 2 meeting with the FDA, a sponsor may be able to request a Special Protocol Assessment, or SPA, the purpose of which is to reach agreement with the FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim. The agreement will be binding on the FDA and may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA or if the FDA determines that a substantial scientific issue essential to determining the safety or efficacy of the product candidate was identified after the testing began.

Post-approval trials, sometimes referred to as "Phase 4" clinical trials, may be required after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Concurrent with clinical trials, sponsors usually complete additional animal safety studies, develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing commercial quantities of the product candidate in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and the manufacturer must develop methods for testing the quality, purity and potency of the product candidate. Additionally, for NDA products, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its proposed shelf-life.

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a significant user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual product fee for products and an annual establishment fee on facilities used to manufacture prescription drug products. Fee waivers or reductions are available in certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation or where the applicant is a small business submitting its first human therapeutic application for review. Product candidates that are designated as orphan drugs are also not subject to user fees unless the application contains an indication other than an orphan indication.

Within sixty days following submission of the application, the FDA reviews a NDA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to accept any NDA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA. The FDA reviews an NDA, whether the product is safe and effective for its intended use, and in each case, whether the product is being manufactured in accordance with cGMP. The FDA may refer applications for novel products or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations when making decisions.

During the product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, plan is necessary to assure the safe use of the product. If the FDA concludes that a REMS plan is needed, the sponsor of the NDA must submit a proposed REMS plan prior to approval. The FDA has authority to require a REMS plan under the Food and Drug Administration Amendments Act of 2007 (the "FDAAA") when necessary to ensure that the benefits of a drug outweigh the risks. In determining whether a REMS plan is necessary, the FDA must consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. A REMS plan may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the risks, limitations on who may prescribe or dispense the drug or other measures that the FDA deems necessary to assure the safe use of the drug. In addition, the REMS plan must include a timetable to assess the strategy at eighteen months, three years and seven years after the strategy's approval.

The FDA may also require a REMS plan for a drug that is already on the market if it determines, based on new safety information, that a REMS plan is necessary to ensure that the product's benefits outweigh its risks.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are compliant with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements. To assure cGMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

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

Even if a product receives regulatory approval, the approval may be significantly limited to specific indications and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as "Phase 4" clinical trials, designed to further assess a drug's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Expedited Review and Approval

The FDA has various programs, including Fast Track, priority review, accelerated approval and breakthrough therapy designation, which are intended to expedite or simplify the process for reviewing therapeutic candidates, or provide for the approval of a product candidate on the basis of a surrogate endpoint. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product candidate no longer meets the conditions for qualification or that the time period for FDA review or approval will be lengthened. Generally, therapeutic candidates that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of therapeutic candidates to treat serious or life-threatening diseases or conditions and fill unmet medical needs. Priority review is designed to give

therapeutic candidates that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of ten months.

Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated product candidate and expedite review of the application for a product candidate designated for priority review. Accelerated approval, which is described in Subpart H of 21 CFR Part 314, provides for an earlier approval for a new product candidate that is (1) intended to treat a serious or life-threatening disease or condition; (2) generally provides a meaningful advantage over available therapies and (3) demonstrates an effect on either a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, and is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a product candidate receiving accelerated approval perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the product may be subject to accelerated withdrawal procedures.

In the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was signed into law in July 2012, the U.S. Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of therapeutic candidates under accelerated approval. The law required the FDA to issue related guidance and also promulgate confirming regulatory changes. In May 2014, the FDA published a final Guidance for Industry titled "Expedited Programs for Serious Conditions—Drugs and Biologics," which provides guidance on FDA programs that are intended to facilitate and expedite development and review of new therapeutic candidates as well as threshold criteria generally applicable to concluding that a product candidate is a candidate for these expedited development and review programs.

In addition to the Fast Track, accelerated approval and priority review programs discussed above, the FDA's "Expedited Programs" guidance also describes the breakthrough therapy designation. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or conditions, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Drugs designated as breakthrough therapies are eligible for, among other things, the Fast Track designation, intensive guidance on an efficient drug development program and a commitment from FDA to involve senior managers and experienced review staff in a proactive collaborative, cross-disciplinary review.

In December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act included numerous provisions that may be relevant to our product candidates, including provisions designed to speed development of innovative and breakthrough therapies. The Cures Act amends the FDCA and the Public Health Service Act, or PHSA, to reauthorize and expand funding for the National Institutes of Health, or NIH, and to authorize FDA to increase spending on innovation projects. Central to the Cures Act are provisions that enhance and accelerate FDA's processes for reviewing and approving new drugs and supplements to approved NDAs. These include, but are not limited to, provisions that (i) require FDA to establish a program to evaluate the potential use of real world evidence to help to support the approval of a new indication for an approved drug and to help to support or satisfy post-approval study requirements, (ii) provide that FDA may rely upon qualified data summaries to support the approval of a supplemental application with respect to a qualified indication for an already approved drug, (iii) require FDA to issue guidance for purposes of assisting sponsors in incorporating complex adaptive and other novel trial designs into proposed clinical protocols and applications for new drugs, (iv) affirm that FDA should continue to expedite the approval of breakthrough therapies and (v) require FDA to establish a process for the qualification of drug development tools for use in supporting or obtaining FDA approval for investigational use of a drug. The Cures Act also includes a provision which requires certain manufacturers or distributors of an investigational drug to make their policies on the availability of certain expanded access programs publicly available. Because the Cures Act was enacted recently and the FDA may take several years to develop these policies, it is difficult to know whether or how the Cures Act will directly affect our business.

Abbreviated New Drug Applications for Generic Drugs

NDA applicants are required to list with the FDA each patent with claims covering the applicant's product or method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic or 505(b)(2) applicants in support of approval of an ANDA, or a 505(b)(2) application. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown to be bioequivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, pre-clinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA or 505(b)(2) applicant is required to make a certification to the FDA concerning any patents listed for the approved NDA product in the FDA's Orange Book. Specifically, the ANDA or 505(b)(2) applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA labeling does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA or 505(b)(2) application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the ANDA or 505(b)(2) product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or 505(b)(2) application has been received by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within forty-five days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of thirty months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA or 505(b)(2) application will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of fourteen years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application, except that this review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, if available, we intend to apply for restorations of patent term for some of our currently owned patents beyond their current expiration dates, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA; however, there can be no assurance that any such extension will be granted to us.

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA, or a 505(b)(2) NDA, submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant Orphan Drug Designation to therapeutic candidates intended to treat a rare disease or condition, which is generally a disease or condition that affects either (1) fewer than 200,000 individuals in the U.S., or (2) or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a product candidate for this type of disease or condition will be recovered from sales in the U.S. for that product candidate. Orphan Drug Designation must be requested before submitting an NDA. We have received Orphan Drug Designation for KX-02 and Oraxol for the treatment of angiosarcomas. After the FDA grants Orphan Drug Designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan Drug Designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product candidate that has Orphan Drug Designation subsequently receives the first FDA approval for the disease for which it has such designation, the product candidate is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except under limited circumstances, for seven years. Orphan drug exclusivity, however, could also block the approval of one of our therapeutic candidates for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our product candidate is determined to be contained within the competitor's product candidate for the same indication or disease.

Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act (BPCA), certain therapeutic candidates may obtain an additional six months of exclusivity if the sponsor submits information requested in writing by the FDA, referred to as a Written Request, relating to the use of the active moiety of the product candidate in children. Although the FDA may issue a Written Request for studies on either approved or unapproved indications, it may only do so where it determines that information relating to that use of a product candidate in a pediatric population, or part of the pediatric population, may produce health benefits in that population.

In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for most therapeutic candidates, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the product candidate for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product candidate is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the product candidate is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. The law requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. It further requires the FDA to post the PREA Non-Compliance letter and sponsor's response.

As part of the FDASIA, the U.S. Congress made a few revisions to the BPCA and PREA, which were slated to expire on September 30, 2012, and made both laws permanent.

Post-Approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product candidate reaches the market. Later discovery of previously unknown problems with a product candidate may result in restrictions on the product candidate or even complete withdrawal of the product candidate from the market. After approval, some types of changes to the approved product candidate, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. In addition, the FDA may under some circumstances require testing and surveillance programs to monitor the effect of approved therapeutic candidates that have been commercialized, and the FDA under some circumstances has the power to prevent or limit further marketing of a product candidate based on the results of these post-marketing programs.

Any therapeutic candidates manufactured or distributed pursuant to FDA approvals for prescription drugs are subject to continuing regulation by the FDA, including, among other things:

- reporting and record-keeping requirements;
- reporting of adverse experiences with the product candidate;
- providing the FDA with updated safety and efficacy information;
- product sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes and
- complying with FDA promotion and advertising requirements, which include, among other things, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved labeling, limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet.

Therapeutic manufacturers and other entities involved in the manufacture and distribution of approved therapeutic products are required to register their establishments with the FDA and obtain licenses in certain states and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMPs and other laws. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural, substantive and record-keeping requirements. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require FDA approval before being implemented. FDA regulations would also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers used. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed under certain limited circumstances. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs. The government recently released a regulation and policy to expand and enhance the requirements related to registering and reporting the results of which may result in greater enforcement of these requirements in the future.

Regulation of Compounding Pharmacies

Compounding is a practice in which a licensed pharmacist, a licensed physician, or in the case of an outsourcing facility, a person under the supervision of a licensed pharmacists, combines, mixes, or alters ingredients of a drug to create a medication tailored to the needs of an individual patient. We are engaged in the compounding of sterile drugs as an outsourcing facility registered with FDA. The Compounding Quality Act, or CQA, allows an entity that compounds sterile drugs to register as an outsourcing facility. Once registered (including payment of a fee), an outsourcing facility must meet certain conditions in order to be exempt from the FDCA's approval requirements and the requirement to label products with adequate directions for use. Under the CQA, a drug must be compounded in compliance with cGMP by or under the direct supervision of a licensed pharmacist in a facility registered pursuant to Section 503B of the FDCA in order to be so exempt. The outsourcing facility must also report specific information about the products that it compounds, including a list of all of the products it compounded during the previous six months, and information about the compounded products, such as the source of the active ingredients used to compound pursuant to Section 503B(b)(2). If the outsourcing facility compounds using bulk drug substances, the bulk drug substances must either appear on a bulk or clinical need list established by FDA of bulk drug substances for which there is a clinical need, or be used to compound drugs that appear on a list established by FDA of drugs for which there is a shortage. Although FDA has not yet established a list of bulk drug substances for which there is a clinical need, FDA has announced an interim policy pursuant to which bulk drug substances for which there is sufficient supporting information for FDA to evaluate them may be nominated for inclusion on Category 1 list and, provided certain conditions are met, FDA will apply its enforcement discretion to Category 1 substances pending evaluation of the substances for inclusion on FDA's list of bulk drug substances for which there is a clinical need.

In addition, an outsourcing facility must meet other conditions described in the CQA, including reporting adverse events pursuant to Section 503B(b)(5) of the FDCA, and labeling its compounded products with certain information pursuant to Section 503B(a)(10). Registered outsourcing facilities are prohibited from selling compounded drugs through a wholesale distributor, or from compounding drugs that are essentially copies of FDA-approved drugs. Registered outsourcing facilities are subject to FDA inspection, and FDA conducts inspections on a risk-based frequency under Section 503B(b)(4).

Pharmaceutical Coverage, Reimbursement and Pricing

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval or compound. In the U.S., sales of any products for which we may compound or receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities such as Medicare, Medicaid, TRICARE and the Veterans Administration, managed care providers, private health insurers and other organizations.

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Effective in 2010, the Affordable Care Act (ACA) made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP, and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of

solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization as of 2010 and by expanding the population potentially eligible for Medicaid drug benefits. Centers for Medicare and Medicaid Services (CMS) will expand Medicaid rebate liability to the territories of the United States as well, beginning in 2017, if the territories elect to enroll in the Medicaid Drug Rebate Program. In addition, the ACA provides for the public availability of retail survey prices and certain weighted average AMPs under the Medicaid program. The implementation of this requirement by CMS may also provide for the public availability of pharmacy acquisition cost data, which could influence our decisions related to setting product prices and offering related discounts.

In order for a pharmaceutical product to receive federal reimbursement under the Medicare Part B and Medicaid programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. Effective in 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing; although, under the current state of the law, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs when used for the orphan indication. In addition, as 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

The process for determining whether a payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list or formulary which might not include all of the FDA-approved products for a particular indication. Also, third-party payors may refuse to include a particular branded drug on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. However, under Medicare Part D—Medicare's outpatient prescription drug benefit—there are protections in place to ensure coverage and reimbursement for oncology products and all Part D prescription drug plans are required to cover substantially all anti-cancer agents. However, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be available. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of any products, in addition to the costs required to obtain regulatory approvals. Our drug candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover an approved product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The U.S. government and state legislatures have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Further, the ACA, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs reimbursed by Medicaid programs and the extension of Medicaid rebates to Medicaid managed care plans. Several other provisions of the ACA focused on cost containment include:

- The Patient-Centered Outcomes Research Institute, which was established to identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.
- The Independent Payment Advisory Board which, since 2014, has had authority to recommend certain changes to the Medicare program to reduce expenditures by the program when spending exceeds a certain growth rate and such changes could result in reduced payments for prescription drugs. Under certain circumstances, these recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings. However, as of late 2016, the President has yet to nominate anyone to serve on the board.
- The Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.
- Effective in 2011, the ACA imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications.

- Effective in 2011, the ACA imposed a requirement on manufacturers of branded drugs to provide a 50% discount off the negotiated price of branded drugs dispensed to Medicare Part D patients in the coverage gap (i.e., the "donut hole" or the period of consumer payment for prescription medicine costs which lies between the initial coverage limit and the catastrophic—coverage threshold).

The adoption of government controls and measures and tightening of restrictive policies in jurisdictions with existing controls and measures, could also limit payments for pharmaceuticals.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Generic Drugs

Given that we manufacture and market generic drug products, our business may be impacted by laws and policies governing the coverage, pricing and reimbursement of generic drugs. Generic drugs are the same API as initial innovator medicines and are typically more affordable in comparison to the innovator's products. Sales of generic medicines have benefitted from policies encouraging generic substitution and a general increasing acceptance of generic drugs on the part of healthcare insurers, consumers, physicians and pharmacists. However, while the U.S. generics market is one of the largest in the world, the recent trend of rising generic drug prices has drawn scrutiny from the U.S. government. Specifically, beginning in 2014 generic drug pricing became the subject of Congressional inquiries and media attention, and many generic drug manufacturers became the targets of government investigations.

In addition, under amendments to the Medicaid Drug Rebate Statute in 2015, generic drug manufacturers are now required to pay an inflation penalty if price increases on generic drugs exceed the rate of inflation. Specifically, the Bipartisan Budget Act of 2015 (BBA '15) amended section 1927(c)(3) of the Social Security Act to require manufacturers of non-innovator multiple source (N) drugs to pay additional Medicaid rebates if a drug's AMP increases at a rate that exceeds the rate of inflation. Manufacturers of generic drugs must calculate the additional Medicaid rebates for non-innovator drugs beginning with the rebates that are calculated for the first quarter of 2017.

Also, the ACA revised the methodology for setting Medicaid generic drug reimbursement in order to further limit the reimbursement of generic drugs under the Medicaid program. Specifically, effective April 1, 2016, the Federal Upper Limit (FUL), which establishes the government's maximum payment amount for certain generic drugs, is no less than 175% of the weighted average of the most recently reported monthly AMPs for pharmaceutically and therapeutically equivalent multiple source drug products that are available for purchase by retail community pharmacies on a nationwide basis. Similarly, reimbursement for generic drugs is also limited in Medicare Part B, as the Average Sales Price (the metric upon which reimbursement is based or ASP) for multiple-source drugs included within the same multiple-source drug billing and payment code is the volume-weighted average of the various manufacturers' ASPs for those drug products.

Laboratory Testing Services Coverage and Reimbursement

Given that we market medical devices in the form of in vitro diagnostic devices, or IVDs, used in the performance of clinical laboratory tests, currently limited to drugs of abuse, pregnancy and alcohol testing in the U.S., and cardiac marker and infectious disease testing in Asia, our business may be impacted by laws and policies governing the coding, coverage, reimbursement and demand for clinical laboratory services. With regard to the clinical laboratory services performed on Medicare beneficiaries, health care providers utilizing such tests generally either are paid under prospective payment systems for most tests performed on hospital inpatients and outpatients or must bill the Medicare Part B program directly in compliance with applicable coding, coverage and reimbursement rules and accept the amount paid by the Medicare contractor under the Medicare Clinical Laboratory Fee Schedule (CLFS) as payment in full. Currently, Medicare does not require the beneficiary to pay a co-payment for clinical laboratory services paid under the CLFS. Pursuant to Section 216 of-the federal Protecting Access to Medicare Act of 2014 (PAMA), CMS is modernizing the CLFS by creating a market-based reimbursement system which will require clinical laboratories subject to the law to report certain private payor prices and test volumes, and CMS will set new payment rates for CLFS tests based on the weighted median of reported prices, effective January 1, 2018. It is unclear how this new law will affect testing services that use our products at this time, but, as a general matter, CMS has indicated that prices of many clinical laboratory tests will decrease under PAMA. In addition, state Medicaid programs are prohibited from paying more (and in many instances, pay significantly less) than Medicare, and payment is subject to state-specific coverage, reimbursement and laboratory law requirements. Certain state Medicaid programs also require Medicaid recipients to pay co-payment amounts for clinical laboratory services. Likewise, payment by private payors is subject to payor-determined coverage and reimbursement policies that vary considerably and are subject to change without notice. Finally, there is increasing legislative attention to opioid abuse in the United States, including passage of the Comprehensive Addiction and Recovery Act of 2016 which, among other things, strengthens state prescription drug monitoring programs and expands educational efforts for certain populations, which may increase the need for drugs of abuse testing. Changes like these related to clinical laboratory services and any other changes related to coverage or reimbursement may impact the demand for and pricing of some of our products which could adversely affect our ability to operate our business and our financial results.

Reimbursement for Compounded Drugs

Given that we intend to compound and sell compounded products, some of which may include APIs that we manufacture, our business may be impacted by the downstream coverage and reimbursement of compounded products. Generally, federal reimbursement is available for compounded drugs but is typically dependent upon whether the individual ingredients or bulk drug substances that make up the compounded product are FDA-approved. Certain of our API products have not yet received FDA approval.

There is a national payment policy for compounded drugs under Medicare Part B, but the policy is unclear because it does not stipulate whether payment is available for ingredients that are bulk drug substances, which are generally not FDA-approved. Under Medicare Part B, claims for compounded drugs are typically submitted using a billing code for "not otherwise classified drugs," and CMS contractors who process Part B claims may conduct further reviews of outpatient claims to determine whether the drug billed under a nonspecific billing code is a compounded drug and to identify its ingredients in order to make payment decisions. However, CMS contractors who process Part B claims do not always collect information on the FDA-approval status of drug ingredients, and, therefore, payment may be made for ingredients that are not FDA-approved products. Therefore, there is uncertainty as to whether Medicare payments for compounded drugs are consistent with the Medicare Part B policy.

Under Medicare Part D, federal payments are not available for non-FDA-approved products—including bulk drug substances—and inactive ingredients used to make a compounded drug. Insurers that offer Medicare Part D benefits and Part D-only sponsors, generally, pay pharmacies for each ingredient in the compounded drug that is an FDA-approved product and is otherwise eligible for reimbursement under Part D. However, with respect to non-FDA approved bulk drug substances, insurers that offer Medicare Part D benefits and Part D-only sponsors may choose to pay for such bulk substances but may not submit these payments as part of the Part D transaction data CMS uses to determine federal payments to Part D plans.

Healthcare Fraud and Abuse Laws and Compliance Requirements

We are subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales and marketing programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration (a term interpreted broadly to include anything of value, including, for example, gifts, discounts, chargebacks, and credits), directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment to Medicare, Medicaid or other third-party payors that are false or fraudulent, or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money owed to the federal government;
- provisions of the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes, referred to as the "HIPAA All-Payor Fraud Prohibition," that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the federal transparency laws, including the federal Physician Payment Sunshine Act, which was part of the ACA, that require manufacturers of certain drugs and biologics to track and disclose payments and other transfers of value they make to U.S. physicians and teaching hospitals as well as physician ownership and investment interests in the manufacturer, and that such information is subsequently made publicly available in a searchable format on a CMS website;
- provisions of HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state transparency reporting and compliance laws; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and which may not have the same effect, thus complicating compliance efforts.

The ACA broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

The federal False Claims Act prohibits anyone from, among other things, knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services that are false or fraudulent. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. For example, pharmaceutical companies have been prosecuted under the federal False Claims Act in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government

price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. In addition, private individuals have the ability to bring actions under the federal False Claims Act, and certain states have enacted laws modeled after the federal False Claims Act.

Medical Devices

Through our subsidiary Polymed, we currently market in vitro diagnostic rapid test kits used in the performance of clinical laboratory tests (limited to drugs of abuse and pregnancy testing in the U.S.) pursuant to clearance under Section 510(k) of the FDCA by the FDA. These products and our operations are subject to extensive regulation by the FDA and other federal and state authorities in the U.S., as well as comparable authorities in foreign jurisdictions. Our test kits are subject to regulation as medical devices in the U.S. under the FDCA, and related regulations enforced by the FDA. The FDA regulates, among other things, the development, design, non-clinical and clinical research, manufacturing, safety, efficacy, labeling, packaging, storage, installation, servicing, recordkeeping, premarket clearance or approval, import, export, adverse event reporting, advertising, promotion, marketing and distribution of medical devices to ensure that medical devices distributed domestically are safe and effective for their intended uses and otherwise meet the requirements of the FDCA.

In addition, the Clinical Laboratory Improvement Amendments of 1988, or CLIA, established quality standards for laboratory testing to ensure the accuracy, reliability and timeliness of patient test results regardless of where the test was performed. Pursuant to CLIA, the FDA categorizes diagnostic tests into three categories based on their complexity in the testing process and risk of harm in reporting erroneous results: (1) waived tests, (2) moderate complexity tests and (3) high complexity tests. Laboratories that perform only waived tests and hold a Certificate of Waiver under CLIA (including most physician office laboratories) are subject to minimal regulation as compared with laboratories that perform moderate or high complexity tests. To obtain a CLIA waived categorization for diagnostic tests that are intended for home use or for use by laboratories holding a Certificate of Waiver, we must demonstrate to FDA that the tests are simple to use with a low risk of error. Foreign countries may require similar or more onerous approvals to manufacture or market our products or to allow the use of our products in certain settings. Most of our test strips are categorized as CLIA waived, but some of our test strips are categorized as moderate in complexity.

FDA Premarket Clearance and Approval Requirements

Unless an exemption applies, each medical device commercially distributed in the U.S. requires either FDA clearance of a 510(k) premarket notification submission, granting of a *de novo* classification request, or approval of a premarket approval application, or PMA. Under the FDCA, medical devices are classified into one of three classes - Class I, Class II or Class III - depending on the degree of risk associated with each medical device. Class I includes devices with the lowest risk to the patient and are subject to the FDA's general controls for medical devices, which include compliance with the applicable portions of the Quality System Regulation, or QSR, facility registration and product listing, reporting of adverse medical events and truthful and non-misleading labeling, advertising and promotional materials. Class II devices are subject to the FDA's general controls, and special controls as deemed necessary by the FDA to ensure the safety and effectiveness of the device. These special controls can include performance standards, post-market surveillance, patient registries and FDA guidance documents.

Most Class I devices are exempt from the 510(k) requirements. Manufacturers of most Class II devices are required to submit to the FDA a premarket notification under Section 510(k) of the FDCA requesting permission to commercially distribute the device. The FDA's permission to commercially distribute a device subject to a 510(k) premarket notification is generally known as 510(k) clearance. Devices deemed by the FDA to pose the greatest risks, such as life sustaining, life supporting or some implantable devices, or devices that have a new intended use or use advanced technology that is not substantially equivalent to that of a legally marketed device, are placed in Class III, requiring approval of a PMA. Our currently marketed products are Class II devices subject to 510(k) clearance.

510(k) Marketing Clearance and De Novo Pathways

To obtain 510(k) clearance, a premarket notification submission must be submitted to the FDA demonstrating that the proposed device is "substantially equivalent" to a predicate device. A predicate device is a legally marketed device that is not subject to premarket approval, i.e., a device that was legally marketed prior to May 28, 1976 (pre-amendments device) and for which a PMA is not required, a device that has been reclassified from Class III to Class II or I or a device that was found substantially equivalent another device cleared through the 510(k) process. The FDA's 510(k) review process usually takes from three to six months but may take longer. The FDA may require additional information, including clinical data, to make a determination regarding substantial equivalence.

If the FDA agrees that the device is substantially equivalent to a predicate device, it will grant 510(k) clearance to market the device. If the FDA determines that the device is "not substantially equivalent" to a previously cleared device, the device is automatically designated as a Class III device. The device sponsor must then fulfill more rigorous PMA requirements, or can request a risk-based classification determination for the device in accordance with the "de novo" process, which may determine that the new device is of low to moderate risk and that it can be appropriately be regulated as a Class I or II device. If a *de novo* request is granted, the device may be legally marketed and a new classification is established. If the device is classified as Class II, the device may serve as a predicate for future 510(k) submissions.

PMA Approval Pathway

Class III devices require PMA approval before they can be marketed. The PMA process is more demanding than the 510(k) process. In a PMA the manufacturer must demonstrate that the device is safe and effective, and the PMA must be supported by extensive data, including data from preclinical studies and human clinical trials. The FDA will approve the new device for commercial distribution if it determines that the data and information in the PMA constitute valid scientific evidence and that there is reasonable assurance that the device is safe and effective for its intended use(s). The FDA may approve a PMA with post-approval conditions intended to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution and collection of long-term follow-up data from patients in the clinical trial that supported PMA approval or requirements to conduct additional clinical trials post-approval. Failure to comply with the conditions of approval can result in material adverse enforcement action, including withdrawal of the approval.

Our products are not currently subject to PMA requirements. However, we may in the future develop devices that will require the submission of a PMA, or FDA may find that some of our proposed uses are not substantially equivalent to previously cleared and marketed devices, and thus a PMA is required.

Clinical Trials

Clinical trials are almost always required to support a PMA and are sometimes required to support a 510(k) submission. All clinical investigations of devices to determine safety and effectiveness must be conducted in accordance with the FDA's investigational device exemption (IDE) regulations which govern investigational device labeling, prohibit promotion of the investigational device and specify an array of recordkeeping, reporting and monitoring responsibilities of study sponsors and study investigators. If the device presents a "significant risk," to human health, as defined by the FDA, the FDA requires the device sponsor to submit an IDE application to the FDA, which must be approved prior to commencing human clinical trials. A significant risk device is one that presents a potential for serious risk to the health, safety or welfare of a patient and either is implanted, used in supporting or sustaining human life, substantially important in diagnosing, curing, mitigating or treating disease or otherwise preventing impairment of human health or otherwise presents a potential for serious risk to a subject. An IDE application must be supported by appropriate data, such as animal and laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The IDE will automatically become effective thirty days after receipt by the FDA unless the FDA notifies us that the investigation may not begin. If the FDA determines that there are deficiencies or other concerns with an IDE for which it requires modification, the FDA may permit a clinical trial to proceed under a conditional approval.

During a clinical trial, the sponsor is required to comply with applicable FDA requirements, and the clinical investigators are also subject to FDA's regulations. Both must comply with GCPs, which among other things require that informed consent be obtained from each research subject, that the investigational plan and study protocol be followed, that the disposition of the investigational device be controlled and that reporting and recordkeeping requirements are followed. Additionally, after a trial begins, we, the FDA or the IRB could suspend or terminate a clinical trial at any time for various reasons, including a belief that the risks to study subjects outweigh the anticipated benefits. Even if a clinical trial is completed, there can be no assurance that the data generated during a clinical trial will meet the safety and effectiveness endpoints or otherwise produce results that will lead the FDA to grant marketing clearance or approval.

Post-Market Regulation

After a device is cleared or approved for marketing, numerous and pervasive regulatory requirements continue to apply. These include:

- establishment registration and device listing with the FDA;
- QSR requirements, which require manufacturers, including third-party manufacturers, to follow stringent design, testing, control, documentation and other quality assurance procedures during all aspects of the design and manufacturing process;
- labeling regulations and requirements related to promotional activities, including FDA prohibitions against the promotion of investigational products, or "off-label" uses of cleared or approved products;

- clearance or approval of product modifications to 510(k)-cleared devices that could significantly affect safety or effectiveness or that would constitute a major change in intended use of one of our cleared devices;
- medical device reporting requirements, which require that a manufacturer report to the FDA if a device it markets may have caused or contributed to a death or serious injury, or has malfunctioned and the device or a similar device that it markets would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur;
- correction, removal and recall reporting regulations, which require that manufacturers report to the FDA field corrections and product recalls or removals if undertaken to reduce a risk to health posed by the device or to remedy a violation of the FDCA that may present a risk to health;
- the FDA's mandatory recall authority, whereby the agency can order device manufacturers to recall from the market a product that is in violation of governing laws and regulations and
- post-market surveillance activities and regulations, which apply when deemed by the FDA to be necessary to protect the public health or to provide additional safety and effectiveness data for the device.

Our manufacturing processes are required to comply with the applicable portions of the QSR, which cover the methods and the facilities and controls for the design, manufacture, testing, production, processes, controls, quality assurance, labeling, packaging, distribution, installation and servicing of finished devices intended for human use. The QSR also requires, among other things, maintenance of a device master file, device history file and complaint files. As a manufacturer, we and our third-party manufacturers are subject to periodic scheduled or unscheduled inspections by the FDA. Our failure to maintain compliance with the QSR requirements could result in the shut-down of, or restrictions on, our manufacturing operations and the recall or seizure of our product. The discovery of previously unknown problems with our product, including unanticipated adverse events or adverse events of increasing severity or frequency, whether resulting from the use of the device within the scope of its clearance or off-label by a physician in the practice of medicine, could result in restrictions on the device, including the removal of the product from the market or voluntary or mandatory device recalls.

New Legislation and Regulations

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing, marketing, coverage and reimbursement of products regulated by the FDA or other government agencies. In addition to new legislation, FDA and healthcare fraud and abuse and coverage and reimbursement regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. In particular, we expect that the current presidential administration and U.S. Congress will continue to seek to modify, repeal or otherwise invalidate all, or certain provisions of, the ACA. Most recently, the Tax Cuts and Jobs Act was enacted, which, among other things, removes penalties for not complying with the individual mandate to carry health insurance. There is still uncertainty with respect to the impact President Trump's administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold. Such reforms could have an adverse effect on anticipated revenues from therapeutic candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop therapeutic candidates. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

Furthermore, in the U.S., the health care industry is subject to political, economic and regulatory influences. Initiatives to reduce the federal budget and debt and to reform health care coverage are increasing cost-containment efforts. We anticipate that federal agencies, Congress, state legislatures and the private sector will continue to review and assess alternative health care benefits, controls on health care spending, and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit coverage or the amounts that federal and state governments will pay for health care products and services, which could also result in reduced demand for our products or additional pricing pressures and limit or eliminate our spending on development projects and affect our ultimate profitability. We are not able to predict whether further legislative changes will be enacted or whether FDA or healthcare fraud and abuse or coverage and reimbursement regulations, guidance, policies or interpretations will be changed or what the effect of such changes, if any, may be.

Foreign Corrupt Practices Act

The FCPA prohibits any U.S. individual or business from corruptly offering, paying, promising or authorizing the provision of anything of value, directly or indirectly, to any foreign official, foreign political party or official thereof, or candidate for foreign political office to obtain or retain business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with accounting provisions requiring the issuer to maintain books and records that accurately and fairly reflect all transactions of the issuer and its controlled subsidiaries and to devise and maintain an adequate system of internal accounting controls.

Environment

We are subject to inspections by the FDA for compliance with cGMP and other U.S. regulatory requirements, including U.S. federal, state and local regulations regarding environmental protection and hazardous and controlled substance controls, among others. Environmental laws and regulations are complex, change frequently and have tended to become more stringent over time. We have incurred, and may continue to incur, significant expenditures to ensure that we are in compliance with these laws and regulations. We would be subject to significant penalties for failure to comply with these laws and regulations.

China Government Regulation

In China, we operate in an increasingly complex legal and regulatory environment. We are subject to a variety of Chinese laws, rules and regulations affecting many aspects of our business. This section summarizes the principal Chinese laws, rules and regulations relevant to our business and operations.

Foreign Investment in Pharmaceutical Industry

The Foreign Investment Industrial Guidance Catalogue (2017 Version), or the Foreign Investment Catalogue jointly promulgated by the National Development and Reform Commission, or NDRC, and the Ministry of Commerce, or MOFCOM, in June 2017 and effective in July 2017 and replaced the previous versions. The Foreign Investment Catalogue divides foreign investments in the pharmaceutical industry into four categories: encouraged, permitted, restricted or prohibited. In September 2016, the National People's Congress Standing Committee adopted a decision on amending the law of foreign invested companies which became effective from October 1, 2016. Upon the effectiveness of the decision, the establishment of the foreign invested enterprise and its subsequent changes will be required to be filed with the relevant authorities instead of obtaining approvals from relevant commerce authorities, except for the foreign invested enterprises which are subject to the special administrative measures regarding foreign investment entry. In June 2018, NDRC and MOFCOM jointly issued a revised notice, according to which the industries falling within the categories in which foreign investment is prohibited or restricted and those falling within the encouraged category subject to relevant requirements of equity or senior management under the Foreign Investment Catalogue, will be subject to the special administrative measures for foreign investment entry.

General Regulations on China Drug Administration

The pharmaceuticals industry in China is mainly regulated and administrated by the State Administration for Market Regulation, the National Health Commission and the Bureau of National Health Care. Pursuant to the Decision of the First Session of the Thirteenth National People's Congress on the State Council Institutional Reform Proposal promulgated by the Chinese National Congress on March 17, 2018, (1) the State Administration for Market Regulation shall be established; and the CFDA shall cease to exist, while the NMPA was established as a department under the State Administration for Market Regulation.; (2) the National Health and Family Planning Commission shall cease to exist, while the National Health Commission shall be established as a department under the State Council, incorporating duties of supervision and management which had been assigned to relevant departments and (3) the Bureau of National Health Care shall be established as a bureau directly subordinate to the State Council.

The NMPA monitors and supervises the administration of pharmaceutical products, as well as medical devices and equipment. The NMPA's primary responsibility includes evaluating, registering and approving new drugs, generic drugs and imported drugs; approving and issuing permits for the manufacture, export and import of pharmaceutical products and medical appliances; approving the establishment of enterprises for pharmaceutical manufacture and distribution; formulating administrative rules and policies concerning the supervision and administration of pharmaceuticals and handling significant accidents involving these products. The local provincial drug administrative authorities are responsible for supervision and administration of drugs within their respective administrative regions.

The People's Republic of China Drug Administration Law promulgated by the Standing Committee of the National People's Congress in 1984 and the Implementing Measures of the Chinese Drug Administration Law promulgated by the Ministry of Health, or the MOH, in 1989 set forth the legal framework for the administration of pharmaceutical products, including the research, development and manufacturing of drugs.

The Chinese Drug Administration Law was revised in February 2001, December 2013 and again in April 2015, respectively. The purpose of the revisions was to strengthen the supervision and administration of pharmaceutical products and to ensure the quality and safety of those products for human use. The revised Chinese Drug Administration Law applies to entities and individuals engaged in the development, production, trade, application, supervision and administration of pharmaceutical products. It regulates and prescribes a framework for the administration of pharmaceutical preparations of medical institutions and for the development, research, manufacturing, distribution, packaging, pricing and advertisement of pharmaceutical products. Revised Implementing Measures of the Chinese Drug Administration Law promulgated by the State Council took effect in September 2002 and was revised in February 2016, providing detailed implementing regulations for the revised Chinese Drug Administration Law.

The Legislative Affairs Commission of the Standing Committee of the National People's Congress released the Draft Amendments of the Drug Administration Law of China (Draft for Comments) , or the DALDA, on November 1, 2018, to seek comments from the public, and as compared to the current Drug Administration Law, mainly includes the following key highlights:

- The supervision and administration of pharmaceutical products will be improved by emphasizing the responsibility of the enterprise, strengthening the management of drug production process and clarifying the traceability requirements of drug quality and safety;
- The responsibility for drug supervision will be clarified, and the supervision measures will be improved;
- The punishment of illegal behaviors will be aggravated by increasing the fine limit, strengthening the punishment for the relevant personnel of pharmaceutical production enterprises and supplementing the responsibility of the drug marketing authorization holder (MAH);
- The MAH system will be implemented, which will cause the MAH holder to undertake the responsibility of the safety and effectiveness of drugs and to bear legal responsibility during the whole process of development, production, management and use of drugs; and
- The drug approval system will be reformed, including the abolishment of the separation of GMP and GSP certification.

As of the latest practicable date, the DALDA has not been approved by the National People's Congress or its Standing Committee. There is no specific timeline for the official enactment of the DALDA.

Under these regulations, we need to follow related regulations for preclinical research, clinical trials and production of new drugs.

Good Laboratories Practice Certification for Preclinical Research

To improve the quality of preclinical research, the NMPA promulgated the Administrative Measures for Good Laboratories Practice of Preclinical Laboratory in 2003 and began to conduct the certification program of GLP. Under the Certifying Measures for Clinical Test Units, or NMPA Circular 44, promulgated in February 2004, the NMPA decides whether an institution is qualified for undertaking pharmaceutical preclinical research upon the evaluation of the institution's organizational administration, its research personnel, its equipment and facilities and its operation and management of preclinical pharmaceutical projects. If all requirements are met, a GLP Certification will be issued by the NMPA, and the result will be published on the NMPA's website.

Approval for Clinical Trials and Production of New Drugs

According to the Provisions for Drug Registration promulgated by the NMPA in 2007, the Chinese Drug Administration Law, the Provisions on the Administration of Special Examination and Approval of Registration of New Drugs, or the Special Examination and Approval Provisions issued by the NMPA in 2009 and the Circular on Information Publish Platform for Pharmaceutical Clinical Trials issued by the NMPA in 2013, we must comply with the following procedures and obtain several approvals for clinical trials and production of new drugs.

Clinical Trial Application

Upon completion of its preclinical research, a research institution must apply for approval of a CTA before conducting clinical trials. According to the Decision of the NMPA on Adjusting the Approval Procedures of the Administrative Approval Items for Certain Drugs promulgated by the NMPA on March 17, 2017, the decision on the approval of clinical trials of drugs enacted by the NMPA can be made by the Center for Drug Evaluation of the NMPA, or the CDE in the name of the NMPA from May 1, 2017. In July 2018, the NMPA promulgated the Announcement of the State Drug Administration on Adjusting Evaluation and Approval Procedures for Clinical Trials for Drugs, which further adjusted for those who apply for drug clinical trials in China, if an applicant does not receive any negative or questioning opinions from the CDE within sixty days after the date of accepting the application and the payment of the fee, drug clinical trials may be conducted in accordance with the plan being submitted.

Four Phases of Clinical Trials

A clinical development program consists of Phases 1, 2, 3 and 4. Phase 1 refers to the initial clinical pharmacology and safety evaluation studies in humans. Phase 2 refers to the preliminary evaluation of a drug candidate's therapeutic effectiveness and safety for particular indication(s) in patients, provides evidence and support for the design of Phase 3 clinical trial and settles the administrative dose regimen. Phase 3 refers to clinical trials undertaken to confirm the therapeutic effectiveness of a drug. Phase 3 is used to further verify the drug's therapeutic effectiveness and safety on patients with target indication(s), to evaluate overall benefit-risk relationships of the drug and ultimately to provide sufficient evidence for the review of drug registration application. Phase 4 refers to a new drug's post-marketing study to assess therapeutic effectiveness and adverse reactions when the drug is widely used, to

evaluate overall benefit-risk relationships of the drug when used among general population or specific groups and to adjust the administration dose, etc.

New Drug Application

When Phase 1, 2 and 3 of the clinical trials have been completed, the applicant must apply to the NMPA for approval of a new drug application. The NMPA then determines whether to approve the application according to the comprehensive evaluation opinion provided by the CDE of the NMPA. We must obtain approval of a new drug application before our drugs can be manufactured and sold in the Chinese market.

Good Manufacturing Practice

All facilities and techniques used in the manufacture of products for clinical use or for sale in China must be operated in conformity with cGMP guidelines as established by the NMPA. Failure to comply with applicable requirements could result in the termination of manufacturing and significant fines.

Animal Test Permits

According to Regulations for the Administration of Affairs Concerning Experimental Animals promulgated by the State Science and Technology Commission in November 1988, as revised in January 2011 and July 2013, and Administrative Measures on the Certificate for Animal Experimentation promulgated by the State Science and Technology Commission and other regulatory authorities in January 2001, performing experimentation on animals requires a Certificate for Use of Laboratory Animals. Applicants must satisfy the following conditions:

- Laboratory animals must be qualified and sourced from institutions that have Certificates for Production of Laboratory Animals;
- The environment and facilities for the animals' living and propagating must meet state requirements;
- The animals' feed and water must meet state requirements;
- The animals' feeding and experimentation must be conducted by professionals, specialized and skilled workers or other trained personnel;
- The management systems must be effective and efficient and
- The applicable entity must follow other requirements as stipulated by the Chinese laws and regulations.

We obtained a Certificate for Use of Laboratory Animals in 2012 regarding the scope of rats and mice.

Domestic Category 1 New Drugs Are Eligible for Special Examination and Approval

According to the Provisions for Drug Registration, drug registration applications are divided into three different types, namely Domestic New Drug Application, Domestic Generic Drug Application and Imported Drug Application. Drugs fall into one of three categories, namely chemical medicine, biological product or traditional Chinese or natural medicine. The registrations of chemical medicines are divided into six categories, among which, a Category 1 drug is a new drug that has never been marketed in any country. All of our clinical-stage drug candidates qualify as domestic Category 1 new drugs.

In March 2016, the NMPA promulgated the Work Plan for Reforming the Chemical Medicines Registration Classification System, under which, the registrations of chemical medicines are divided into five categories as follows:

Category 1: Innovative drugs that are not marketed both domestically and abroad. These drugs contain new compounds with clear structures and pharmacological effects, and they have clinical value.

Category 2: Modified new drugs that are not marketed both domestically and abroad. With known active components, the drug's structure, phase, prescription manufacturing process, administration route and indication are optimized, and it has obvious clinical advantage.

Category 3: The drugs that are imitated by domestic applicants to original drugs that have been marketed abroad but not domestically. These kinds of drugs are supposed to have the same quality and effects with original drugs. Original drugs are the

foremost drugs that are approved to be marketed domestically and /or abroad with complete and full safety and validity data as marketing evidence.

Category 4: The drugs that are imitated by domestic applicants to original drugs that have been marketed domestically. These kinds of drugs are supposed to have the same quality and effects with original drugs.

Category 5: The drugs that have been marketed abroad are applied to be marketed domestically.

The registration of Category 1 or Category 2 drugs above will be subject to the requirements of Domestic New Drug Application under the Provisions for Drug Registration, Domestic Generic Drug Application will be applicable to Category 3 or Category 4 drugs registration, and Imported Drug Application will be applicable to Category 5 drugs registration. The applicants whose registration applications for chemical medicines have been accepted by the NMPA before the date of promulgation of the Work Plan for Reforming the Chemical Medicines Registration Classification System can choose to continue the applications process according to the Provisions for Drug Registration or to comply with the new categories under the Work Plan for Reforming the Chemical Medicines Registration Classification System

According to the Special Examination and Approval Provisions, the NMPA conducts special examination and approval for new drugs registration application when:

(1) active ingredients and their preparations extracted from plants, animals and minerals, and newly discovered medical materials and their preparations have not been marketed in China;

(2) the chemical raw material medicines as well as the preparations and biological products thereof have not been approved for marketing home and abroad

(3) the new drugs are for treating AIDS, malignant tumors and rare diseases, etc., and have obvious advantages in clinic treatment; or

(4) the new drugs are for treating diseases with no effective methods of treatment.

The Special Examination and Approval Provisions provide that the applicant may file for special examination and approval at the stage of Clinical Trial Application if the drug candidate falls within items (1) or (2), and for drug candidates that fall within items (3) or (4), the application for special examination and approval must be made when filing for production.

The registration of Category 1 or Category 2 drugs above will be subject to the requirements of Domestic New Drug Application under the Provisions for Drug Registration, Domestic Generic Drug Application will be applicable to Category 3 or Category 4 drugs registration and Imported Drug Application will be applicable to Category 5 drugs registration. The applicants whose registration applications for chemical medicines have been accepted by the NMPA before the date of promulgation of the Reform Plan Regarding the Category of the Registration of Chemical Medicines can choose to continue the applications process according to the Provisions for Drug Registration or to comply with the new categories under the Reform Plan Regarding the Category of the Registration of Chemical Medicines.

We believe that certain of our products fall within items (2) and (3) above. Therefore, we may file an application for special examination and approval at the CTA stage, which may enable us to pursue a more expedited path to approval in China and bring therapies to patients more quickly.

The Advantages of Category 1 New Drugs over Category 5 Drugs

Under the Provisions for Drug Registration and the Work Plan for Reforming the Chemical Medicines Registration Classification System, Category 5 drugs are drugs which have already been marketed abroad by multinational companies but are not yet approved in China, and Category 5 drug registration will be subject to the requirements of the Imported Drug Application. Compared with the application for Category 5 drugs, the application for Category 1 domestic new drugs has a more straight-forward registration pathway. According to the Special Examination and Approval Provisions, where a special examination and approval treatment is granted, the application for clinical trial and manufacturing will be handled with priority and with enhanced communication with the CDE, which will establish a working mechanism for communicating with the applicants. If it becomes necessary to revise the clinical trial scheme or make other major alterations during the clinical trial, the applicant may file an application for communication. When an application for communication is approved, the CDE will arrange the communication with the applicant within one month.

In comparison, according to the Provisions for Drug Registration, the registration pathway for Category 5 drugs is complicated and evolving. Category 5 drug applications may be submitted after a company obtains an NDA approval and receive the CPP granted

by a major regulatory authority, such as the FDA or the European Medicines Agency (EMA). Multinational companies may need to apply for conducting multi-regional clinical trials (MRCTs), which means that companies do not have the flexibility to design the clinical trials to fit the Chinese patients and standard-of-care. Category 5 drug candidates may not qualify to benefit from fast track review with priority at the CTA stage. Moreover, a requirement to further conduct local clinical trials can potentially delay market access by several years from its international NDA approval.

Adjustment on the Administration of Imported Drug Registration

On October 10, 2017, the NMPA promulgated the Decision on Adjusting Relevant Matters Concerning the Administration of Imported Drug Registration, effective as of the date of its promulgation, which stipulates that, among others, (1) simultaneous research and application are allowed, meaning that, in the case of a clinical trial concerning a drug subject thereto to be conducted at an international multi-center clinical trial (IMCCT) in China, Phase 1 clinical trials of the drug are allowed simultaneously, and the requirement that the drug subject to the clinical trial need to have been previously registered overseas or to have entered a Phase 2 or Phase 3 clinical trial shall not apply, except for preventative biological products; (2) the drug registration procedure is to be optimized, meaning that, upon the completion of a clinical trial at an IMCCT in China, an applicant may directly file a drug registration application and (3) for a new chemical drug or an innovative therapeutic biological drug for which a clinical trial or market registration is made, in each case as an imported drug, the requirement that such drug has received an overseas license issued by the country or region where the drug's overseas pharmaceutical manufacturer is located shall not apply.

Changes to the Review and Approval Process

In August 2015, the State Council issued a statement, Opinions on Reforming the Review and Approval Process for Pharmaceutical Products and Medical Devices, which contained several potential policy changes that could benefit the pharmaceutical industry:

- A plan to accelerate innovative drug approval with a special review and approval process, with a focus on areas of high unmet medical needs, including drugs for HIV, cancer, serious infectious diseases, orphan diseases and drugs on national priority lists.
- A plan to adopt a policy which would allow companies to act as the marketing authorization holder and to hire contract manufacturing organizations to produce drug products.
- A plan to improve the review and approval of clinical trials, and to allow companies to conduct clinical trials at the same time as they are in other countries and encourage local clinical trial organizations to participate in international multi-center clinical trials.

In November 2015, the NMPA released the Circular Concerning Several Policies on Drug Registration Review and Approval, which further clarified the following policies potentially simplifying and accelerating the approval process of clinical trials:

- A one-time umbrella approval procedure allowing approval of all phases of a new drug's clinical trials at once, rather than the current phase-by-phase approval procedure, will be adopted for new drugs' CTAs.
- A fast track drug registration or clinical trial approval pathway will be available for the following applications: (1) registration of innovative new drugs treating HIV, cancer, serious infectious diseases and orphan diseases; (2) registration of pediatric drugs; (3) registration of geriatric drugs and drugs treating China-prevalent diseases; (4) registration of drugs sponsored by national science and technology grants; (5) registration of innovative drugs using advanced technology, using innovative treatment methods, or having distinctive clinical benefits; (6) registration of foreign innovative drugs to be manufactured locally in China; (7) concurrent applications for new drug clinical trials which are already approved in the U.S. or EU, or concurrent drug registration applications for drugs which have applied for marketing authorization and passed onsite inspections in the U.S. or EU and are manufactured using the same production line in China and (8) clinical trial applications for drugs with urgent clinical need and patent expiry within three years, and marketing authorization applications for drugs with urgent clinical need and patent expiry within one year.

In March 2016, the NMPA issued the Interim Provisions on the Procedures for Drug Clinical Trial Data Verification that provides procedural rules for NMPA's on-site verification of clinical data before drug approvals.

Also in February 2016, the NMPA published the Opinions on Implementing a Prioritized Review System to Avoid Drug Review Backlogs, which introduces a prioritized review and approval pathway to clinical trial applications and registration applications of certain drugs as part of NMPA's ongoing reform of its current drug review and approval system.

The NMPA issued the Procedures for Priority Examination and Approval of Medical Devices (Procedures) on October 25, 2016, which shall come into effect on January 1, 2017. The Procedures, composed of seventeen articles, specify that the priority in examination and approval shall be given, in relation to the applications of registering Class-III domestic, or Class-II and Class-III imported medical devices, when those applications fall within such categories as diagnosis or treatment of rare disease or malignant tumor with significant clinical advantage. According to the Procedures, the medical device technical evaluation center of the NMPA will tentatively decide on the applicants applying for their project given priority examination and approval, names of their products and the reception numbers and disclose such information on its website for a period of no less than five working days. The Procedures provide that for projects given priority in examination and approval, the medical device technical evaluation center shall communicate with applicants in an active way, as required by applicable provisions, in the course of evaluating relevant technologies and may arrange for special talks when necessary; food and drug administrative departments at provincial levels shall take the review of the registered quality management system of medical devices as priority and the NMPA will prioritize their administrative examination and approval.

In December 2017, the NMPA innovations promulgated the Opinions on Encouraging the Prioritized Evaluation and Approval for Drug, the NMPA would prioritize the examination and approval on applications of new drugs in particular cases, including (1) applications of new drugs with significant clinical value satisfying particular conditions; (2) applications of new drugs with significant clinical advantages preventing or treating particular diseases and (3) other particular conditions.

According to the Announcement on Optimizing the Evaluation and Approval of Drug Registration promulgated by the NMPA and the National Health Commission in May 2018, the Chinese government seeks to further simplify and accelerated the clinical trial approval process.

Chinese Enterprise Income Tax Law and Its Implementation

The Chinese Enterprise Income Tax Law (EIT Law) and its implementation rules provide that from January 1, 2008, a uniform income tax rate of 25% is applied equally to domestic enterprises as well as foreign investment enterprises and permit certain High and New Technologies Enterprises (HNTEs) to enjoy preferential enterprise income tax rates subject to these HNTEs meeting certain qualification criteria.

The EIT Law and its implementation rules provide that a withholding tax at the rate of 10% is applicable to dividends and other distributions payable by a Chinese resident enterprise to investors who are “non-resident enterprises” (that do not have an establishment or place of business in China, or that have such establishment or place of business but the relevant dividend or other distribution is not effectively connected with the establishment or place of business). However, pursuant to the Arrangement between the Mainland and Hong Kong Special Administrative Region for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with respect to Taxes on Income effective on December 8, 2006, the withholding tax rate for dividends paid by a Chinese resident enterprise is 5% if the Hong Kong enterprise owns at least 25% of the capital of the Chinese enterprise; otherwise, the dividend withholding tax rate is 10%. According to the Notice of the Chinese State Administration of Taxation on Issues relating to the Administration of the Dividend Provision in Tax Treaties promulgated on February 20, 2009 and effective on the same day, the corporate recipient of dividends distributed by Chinese enterprises must satisfy the direct ownership thresholds at all times during the twelve consecutive months preceding the receipt of the dividends. The Chinese State Administration of Taxation issued the Notice on How to Understand and Identify the Owner of Benefits in the China-HK Tax Agreement on October 27, 2009. Pursuant to these regulations and the Administrative Measures for Tax Treaty Treatment for Non-Resident Taxpayers promulgated by the Chinese State Administration of Taxation in August 2015, non-resident enterprises are required to file information sheets to the competent tax authorities in order to enjoy the favorable treatments under the treaties. However, the relevant tax authorities may check and verify at their discretion, and if a company is deemed to be a pass-through entity rather than a qualified owner of benefits, it cannot enjoy the favorable tax treatments provided in the tax arrangement. In addition, if transactions or arrangements are deemed by the relevant tax authorities to be entered into mainly for the purpose of enjoying favorable tax treatments under the tax arrangement, such favorable tax treatments may be subject to adjustment by the relevant tax authorities in the future.

On July 27, 2011, the Ministry of Finance, the General Administration of Customs, and the State Administration of Taxation issued the Notice on the Relevant Tax Policies for the Implementation of the Strategy of Extensive Development of the Western Regions, under which from January 1, 2011 to December 31, 2020, a reduced enterprise income tax rate of 15% is applicable to the enterprises set up in the western regions as designated by the relevant Chinese regulations with their main business in the encouraged industries. The encouraged industries are those listed in the Catalog of Encouraged Industries in the Western Regions as promulgated by NDRC. To qualify for the reduced tax rate, an enterprise must derive 70% or more of its revenue from the business listed in the Catalog of Encouraged Industries in the Western Regions.

Regulations Relating to Business Tax and Value-added Tax

Pursuant to the Temporary Regulations on Business Tax, which were promulgated by the State Council on December 13, 1993 and effective on January 1, 1994, as amended on November 10, 2008 and effective January 1, 2009, any entity or individual

conducting business in a service industry is generally required to pay business tax at the rate of 5% on the revenues generated from providing such services.

In November 2011, the Ministry of Finance and the State Administration of Taxation (SAT) promulgated the Pilot Plan for Imposition of Value-Added Tax to Replace Business Tax (Pilot Plan). Since January 2012, the SAT has been implementing the Pilot Plan, which imposes value-added tax (VAT) in lieu of business tax for certain industries in Shanghai. The Pilot Plan was expanded to other regions, including Beijing, in September 2012 and was further expanded nationwide beginning August 1, 2013. VAT is applicable at a rate of 6% in lieu of business taxes for certain services, and 17% for the sale of goods and provision of tangible property lease services. VAT payable on goods sold or taxable services provided by a general VAT taxpayer for a taxable period is the net balance of the output VAT for the period after crediting the input VAT for the period. In March 2016, the Ministry of Finance and SAT jointly issued the Notice on Adjustment of Transfer Business Tax to Value Added Tax effective from May 2016, according to which Chinese tax authorities have started imposing VAT on revenues from various service sectors, including real estate, construction, financial services and insurance as well as other lifestyle service sectors, replacing the business tax.

Regulations Relating to Environmental Protection

China has adopted extensive environmental laws and regulations with national and local standards for emissions control, discharge of waste water and storage and transportation, treatment and disposal of waste materials. At the national level, the relevant environmental protection laws and regulations include the Chinese Environmental Protection Law, the Chinese Law on the Prevention and Control of Air Pollution, the Chinese Law on the Prevention and Control of Water Pollution, the Chinese Law on the Promotion of Clean Production, the Chinese Law on the Prevention and Control of Noise Pollution, the Chinese Law on the Prevention and Control of Solid Waste Pollution, the Chinese Recycling Economy Promotion Law, the Chinese Law on Environmental Impact Assessment, the Administrative Regulations on the Levy and Use of Discharge Fees and the Measures for the Administration of the Charging Rates for Pollutant Discharge Fees. In recent years, the Chinese Government has introduced a series of new policies designed to generally promote the protection of the environment. For instance, on November 10, 2016, the General Office of the State Council has released the Implementing Plan for the Permit System for Controlling the Discharge of Pollutants (Plan). The Plan proposes the need of instituting a system for enterprises and public institutions to control their respective total amount of pollutants discharged, which shall be connected with the environmental impact assessment system organically. The Plan also stipulates that it is necessary to regulate the orderly issuance of pollutant discharge permits, to make a name list to manage the permission of pollutant discharge, to promote the administration of such permission system per industry and to impose severer administration and control over enterprises and public institutions located at such places where environment quality fails to reach relevant standards. Furthermore, the Plan requires that a national pollutant discharge permit management information platform shall be established by 2017 to strengthen the information disclosure and social supervision.

Regulations Relating to Foreign Exchange and Dividend Distribution

Foreign Exchange Regulation

The Foreign Exchange Administration Regulations, most recently amended in August 2008, are the principal regulations governing foreign currency exchange in China. Under the Chinese foreign exchange regulations, payments of current account items, such as profit distributions and trade and service-related foreign exchange transactions, may be made in foreign currencies without prior approval from the State Administration of Foreign Exchange (SAFE) by complying with certain procedural requirements. In contrast, approval from or registration with appropriate government authorities is required when Renminbi is (RMB) to be converted into a foreign currency and remitted out of China to pay capital expenses such as the repayment of foreign currency-denominated loans.

In August 2008, SAFE issued the Circular on the Relevant Operating Issues Concerning the Improvement of the Administration of the Payment and Settlement of Foreign Currency Capital of Foreign-Invested Enterprises (SAFE Circular 142), regulating the conversion by a foreign-invested enterprise of foreign currency-registered capital into Renminbi by restricting how the converted RMB may be used. In addition, SAFE promulgated Notice on Issues concerning Further Clarifying and Regulating the Foreign Exchange Administration under Some Capital Accounts (Circular 45) on November 9, 2011 to clarify the application of SAFE Circular 142. Under SAFE Circular 142 and Circular 45, RMB capital converted from foreign currency registered capital of a foreign-invested enterprise may only be used for purposes within the business scope approved by the applicable government authority and may not be used for equity investments within China. In addition, SAFE strengthened its oversight of the flow and use of the RMB capital converted from foreign currency registered capital of foreign-invested enterprises. The use of such RMB capital may not be changed without SAFE's approval, and such RMB capital may not, in any case, be used to repay RMB loans whose proceeds were not used. Furthermore, SAFE promulgated Notice on Issues Concerning Strengthening Administration of Foreign Exchange Services in November 2010, which tightens the regulation over settlement of net proceeds from overseas offerings, such as our initial public offering, and requires, among other things, the authenticity of settlement of net proceeds from offshore offerings to be closely examined and the net proceeds to be settled in the manner described in our prospectus or otherwise approved by our board of directors. Violations of these SAFE regulations may result in severe monetary or other penalties, including confiscation of earnings

derived from such violation activities, a fine of up to 30% of the RMB funds converted from the foreign invested funds or in the case of a severe violation, a fine ranging from 30% to 100% of the RMB funds converted from the foreign-invested funds.

In November 2012, SAFE promulgated the Circular of Further Improving and Adjusting Foreign Exchange Administration Policies on Foreign Direct Investment, which substantially amends and simplifies the current foreign exchange procedure. Pursuant to this circular, the opening of various special purpose foreign exchange accounts, such as pre-establishment expenses accounts, foreign exchange capital accounts and guarantee accounts, the reinvestment of RMB proceeds by foreign investors in China, and remittance of foreign exchange profits and dividends by a foreign-invested enterprise to its foreign shareholders no longer require the approval or verification of SAFE, and multiple capital accounts for the same entity may be opened in different provinces, which was not previously possible. In addition, SAFE promulgated the Circular on Printing and Distributing the Provisions on Foreign Exchange Administration over Domestic Direct Investment by Foreign Investors and the Supporting Documents in May 2013, which specifies that the administration by the SAFE or its local branches over direct investment by foreign investors in China will be conducted by way of registration, and banks must process foreign exchange business relating to the direct investment in China based on the registration information provided by SAFE and its branches.

Under the Circular of the SAFE on Further Improving and Adjusting the Policies for Foreign Exchange Administration under Capital Accounts promulgated by the SAFE on January 10, 2014 and effective from February 10, 2014, administration over the outflow of the profits by domestic institutions has been further simplified. In principle, a bank is no longer required to examine transaction documents when handling the outflow of profits of no more than the equivalent of $50,000 by a domestic institution. When handling the outflow of profits exceeding the equivalent of $50,000, the bank, in principle, is no longer required to examine the financial audit report and capital verification report of the domestic institution, provided that it must examine, according to the principle of transaction authenticity, the profit distribution resolution of the board of directors (or the profit distribution resolution of the partners) relating to this profit outflow and the original copy of its tax record-filing form. After each profit outflow, the bank must affix its seal to and endorsements on the original copy of the relevant tax record-filing form to indicate the actual amount of the profit outflow and the date of the outflow.

On March 30, 2015, SAFE promulgated the Circular on Reforming the Management Approach regarding the Settlement of Foreign Exchange Capital of Foreign-invested Enterprises (SAFE Circular 19), which became effective on June 1, 2015. According to SAFE Circular 19, the foreign exchange capital of foreign-invested enterprises may be settled on a discretionary basis, meaning that the foreign exchange capital in the capital account of a foreign-invested enterprise for which the rights and interests of monetary contribution has been confirmed by the local foreign exchange bureau (or the book-entry registration of monetary contribution by the banks) can be settled at the banks based on the actual operational needs of the foreign-invested enterprise. The proportion of such discretionary settlement is temporarily determined as 100%. The RMB converted from the foreign exchange capital will be kept in a designated account, and if a foreign-invested enterprise needs to make further payment from such account, it still must provide supporting documents and go through the review process with the banks.

Furthermore, SAFE Circular 19 stipulates that the use of capital by foreign-invested enterprises must adhere to the principles of authenticity and self-use within the business scope of enterprises. The capital of a foreign-invested enterprise and capital in RMB obtained by the foreign-invested enterprise from foreign exchange settlement must not be used for the following purposes:

(1) directly or indirectly used for the payment beyond the business scope of the enterprises or the payment prohibited by relevant laws and regulations;

(2) directly or indirectly used for investment in securities, unless otherwise provided by relevant laws and regulations;

(3) directly or indirectly used for granting the entrusted loans in RMB, unless permitted by the scope of business, repaying the inter-enterprise borrowing (including advances by the third party), or repaying the bank loans in RMB that have been sub-lent to the third party and/or

(4) paying the expenses related to the purchase of real estate that is not for self-use, except for the foreign-invested real estate enterprises.

On June 9, 2016, SAFE issued the Notice to Reform and Regulate the Administration Policies of Foreign Exchange Capital Settlement to further reform foreign exchange capital settlement nationwide.

Our Chinese subsidiaries' distributions to the offshore parent and carrying out cross-border foreign exchange activities shall comply with the various SAFE registration requirements described above.

Share Option Rules

Under the Administration Measures on Individual Foreign Exchange Control issued by the People's Bank of China on December 25, 2006, all foreign exchange matters involved in employee share ownership plans and share option plans in which Chinese citizens participate require approval from SAFE or its authorized branch. In addition, under the Notices on Issues concerning the Foreign Exchange Administration for Domestic Individuals Participating in Share Incentive Plans of Overseas Publicly-Listed Companies, commonly known as SAFE Circular 7, or Share Option Rules, issued by the SAFE on February 15, 2012, Chinese residents who are granted shares or share options by companies listed on overseas stock exchanges under share incentive plans are required to (1) register with the SAFE or its local branches; (2) retain a qualified Chinese agent, which may be a Chinese subsidiary of the overseas listed company or another qualified institution selected by the Chinese subsidiary, to conduct the SAFE registration and other procedures with respect to the share incentive plans on behalf of the participants and (3) retain an overseas institution to handle matters in connection with their exercise of share options, purchase and sale of shares or interests and funds transfers. We have made and will to continue to make efforts to comply with these requirements since the completion of our initial public offering in June 2017.

In addition, the State Administration of Taxation has issued certain circulars concerning employee share options or restricted shares, including the Circular of the State Administration of Taxation on Issues Concerning Individual Income Tax in Relation to Share Options, promulgated in August 2009. Under these circulars, the employees working in China who exercise share options or are granted restricted shares will be subject to Chinese individual income tax. The Chinese subsidiaries of such overseas listed companies have obligations to file documents related to employee share options or restricted shares with relevant tax authorities and to withhold individual income taxes of those employees who exercise their share options. If the employees fail to pay or the Chinese subsidiaries fail to withhold their income taxes in accordance with relevant laws and regulations, the Chinese subsidiaries may face fines or sanctions imposed by tax authorities or other Chinese government authorities.

Regulation of Dividend Distribution

The principal laws, rules and regulations governing dividend distribution by foreign-invested enterprises in China are the Company Law of China, as amended, the Wholly Foreign-owned Enterprise Law and its implementation regulations, the Cooperative Joint Venture Law and its implementation regulations and the Equity Joint Venture Law and its implementation regulations. Under these laws, rules and regulations, foreign-invested enterprises may pay dividends only out of their accumulated profit, if any, as determined in accordance with Chinese accounting standards and regulations. Both Chinese domestic companies and wholly-foreign owned Chinese enterprises are required to allocate at least 10% of their respective accumulated after-tax profits each year, if any, to fund certain capital reserve funds until the aggregate amount of these reserve funds have reached 50% of the registered capital of the enterprises. A Chinese company is not permitted to distribute any profits until any losses from prior fiscal years have been offset. Profits retained from prior fiscal years may be distributed together with distributable profits from the current fiscal year.

Labor Laws and Social Insurance

Pursuant to the Chinese Labor Law and the Chinese Labor Contract Law, employers must execute written labor contracts with full-time employees. All employers must comply with local minimum wage standards. Violations of the Chinese Labor Contract Law and the Chinese Labor Law may result in the imposition of fines and other administrative and criminal liability in the case of serious violations.

In addition, according to the Chinese Social Insurance Law, employers like our Chinese subsidiaries in China must provide employees with welfare schemes covering pension insurance, unemployment insurance, maternity insurance, work-related injury insurance, and medical insurance and housing funds.

Rest of the World Regulation

For other countries outside of the U.S. and China, the requirements governing the conduct of clinical trials, drug licensing, pricing and reimbursement vary from country to country. In all cases the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles having their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Employees

As of December 31, 2018, we had 575 full-time employees and 7 part-time employees. Of these, 218 are engaged in full-time research and development and laboratory operations, 228 are engaged in manufacturing activities and 129 are engaged in full-time

selling, general and administrative functions. As of December 31, 2018, 42% of our personnel were located in the U.S. and 58% were located in Asia. We have also engaged and may continue to engage independent consultants and contractors to assist us with our operations. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We have never experienced any employment related work stoppages, and we consider our relations with our employees to be good.

Financial Information

We manage our operations and allocate resources in line with our three distinct reportable segments. Financial information regarding our operations, assets and liabilities, including our net loss for the years ended December 31, 2018, 2017, and 2016 and our total assets as of December 31, 2018 and 2017, is included in our Consolidated Financial Statements in Item 8 of this Annual Report.

Corporate Information

We were originally formed under the laws of the state of Delaware in November 2003 under the name Kinex Pharmaceuticals, LLC. In December 2012, we converted from a limited liability company to a Delaware corporation, Kinex Pharmaceuticals, Inc. In August 2015, we amended and restated our certificate of incorporation to change our name to Athenex, Inc. Our principal executive offices are located at 1001 Main Street, Suite 600, Buffalo, NY 14203, and our telephone number is (716) 427-2950. Our website address is www.athenex.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report, and you should not consider information on our website to be part of this Annual Report.

Available Information

We file Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other information with the Securities and Exchange Commission (SEC). Our filings with the SEC are available free of charge on the SEC's website at www.sec.gov and on our website under the "Investor Relations" tab as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should consider carefully the following risk factors, as well as the other information in this report, including our consolidated financial statements and related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations", before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition and results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred net losses every year since our inception and anticipate that we will continue to incur net losses for the foreseeable future.

Investment in pharmaceutical product development is highly speculative because it entails substantial upfront costs and expenses and significant risk that a drug candidate will fail to gain regulatory approval or become commercially viable. Since our formation, the company has relied on a combination of private securities offerings, public-private partnerships, the issuance of convertible notes and public grants to fund our operations. We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. We have not generated substantial revenue from product sales to date, and we continue to incur significant development and other expenses related to our ongoing operations. As a result, we incurred losses in 2018, 2017 and 2016. For the years ended December 31, 2018, 2017 and 2016, we reported net losses of $117.4 million, $131.2 million and $87.7 million, respectively, and had an accumulated deficit of $443.7 million as of December 31, 2018. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative expenses associated with our operations.

We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, our drug candidates, and begin to commercialize approved drugs, if any. Typically, it takes many years to develop a new drug before it is available for treating patients. 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, our ability to generate revenue and the timing and amount of milestones and other required payments to third parties in connection with our potential future arrangements with third parties. If any of our drug candidates fail in clinical trials or do not gain regulatory approval, or if approved, fail to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses and expected future losses have had, and will continue to have, an adverse effect on our shareholders' equity and working capital.

We expect our research and development expenses to continue to be significant in connection with our continued investment in our drug candidates and our ongoing and planned clinical trials for our drug candidates. Furthermore, if we obtain regulatory approval for our drug candidates, we expect to incur increased selling, general and administrative expenses. In addition, as a public company, we incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses and negative cash flows from operations for the foreseeable future. These losses have had and will continue to have a material adverse effect on our stockholders' equity, financial position, cash flows and working capital.

Our ability to continue as a going concern will require us to obtain additional financing to fund our current operations, which may be unavailable on acceptable terms, or at all.

Our recurring losses from operations and our current operating plans raise substantial doubt about our ability to continue as a going concern. As a result, our independent registered public accounting firm included an explanatory paragraph in its report on our consolidated financial statements as of and for the year ended December 31, 2018 with respect to this uncertainty. Our ability to continue as a going concern will require us to obtain additional financing to fund our current operating plans. We believe that our existing cash and cash equivalents and short-term investments, together with cash to be generated from our operating activities, will be sufficient to fund our current operating plans through at least the fourth quarter of 2019. We have based these estimates, however, on assumptions that may prove to be wrong, and we could spend our available financial resources much faster than we currently expect and need to raise additional funds sooner than we anticipate. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate our research and drug development programs or commercialization efforts.

We have not yet been profitable, despite beginning to generate revenue from product sales, and may never become profitable.

Our ability to generate revenue and become profitable depends upon our ability to successfully complete the development of, and obtain the necessary regulatory approvals for, our proprietary drug candidates, as we currently only have commercialized our API

products, such including paclitaxel and docetaxel, and specialty products, such as medical testing kits. Our product sales of API totaled $18.0 million, $15.4 million and $15.3 million in the years ended December 31, 2018, 2017 and 2016, respectively. Our specialty products launched in March 2017 and sales reached a total of $30.4 million for the year ended December 31, 2018. We expect to continue to incur substantial and increasing losses through the projected development and commercialization of our drug candidates. None of our proprietary drug candidates have been approved for marketing in the U.S., China or any other jurisdiction, and they may never receive such approval. Our ability to achieve revenue and profitability is dependent on our ability to complete the development of our proprietary drug candidates, obtain necessary regulatory approvals, and have our proprietary drugs manufactured and successfully marketed.

Even if we receive regulatory approval of our proprietary drug candidates for commercial sale, we do not know when they will generate revenue, if at all. Our ability to generate revenue from product sales of our drug candidates depends on a number of factors, including our ability to:

- complete research regarding, and non-clinical and clinical development of, our proprietary drug candidates;
- formulate appropriate dosing protocols, drug preparations and capsule encapsulation methods;
- obtain regulatory approvals and marketing authorizations for drug candidates for which we complete clinical trials;
- develop a sustainable and scalable manufacturing processes, including establishing and maintaining commercially viable supply relationships with third parties and establishing our own manufacturing capabilities and infrastructure;
- compliantly launch and commercialize proprietary drug candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor;
- obtain market acceptance of our proprietary drug candidates and their routes of administration as viable treatment options;
- obtain adequate coverage and reimbursement for our proprietary drug candidates from government (including U.S. federal healthcare programs) and private payors;
- identify, assess, acquire and/or develop new proprietary drug candidates;
- address any competing technological and market developments;
- negotiate and maintain favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- maintain, protect and expand our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- successfully commercialize our 503B outsourcing facility products and U.S. specialty pharmaceutical products;
- further develop our API business and
- attract, hire and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of increased expenses, or when, or if, we will be able to achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we are required by the FDA, NMPA or regulatory authorities in other jurisdictions to perform studies in addition to those that we currently anticipate. Even if our proprietary drug candidates are approved for commercial sale, we anticipate incurring significant costs associated with the commercial launch of these drugs.

If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce our operations. Failure to become and remain profitable may adversely affect the market price of our common stock and our ability to raise capital and continue operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will need to obtain additional financing to fund our operations, and if we are unable to obtain such financing, we may be unable to complete the development and commercialization of our drug candidates.

We have financed our operations with a combination of private securities offerings, public-private partnerships, issuance of convertible notes and public grants. In June 2018, we entered into a series of equity and debt financing transactions with Perceptive Advisors LLC and its affiliates (Perceptive) that provided us with an aggregate of $100 million for our research and development activities and other corporate purposes. We entered into a stock purchase agreement with Perceptive, pursuant to which we agreed to sell 2,679,528 shares of common stock at a purchase price of $18.66 per share of common stock. We also entered into a $50.0 million senior secured loan agreement with Perceptive in conjunction with the equity transaction described above. Our drug candidates will require the completion of regulatory review, significant sales and marketing efforts and substantial investment before they can provide us with any product sales revenue. Our operations have consumed substantial amounts of cash since inception. The net cash used for our operating activities was $109.4 million, $81.5 million and $47.9 million for the years ended December 31, 2018, 2017 and 2016 respectively. We expect to continue to spend substantial amounts on advancing the clinical development of our proprietary drug

candidates, launching and commercializing any proprietary drug candidates for which we receive regulatory approval, including building our own commercial organizations to address certain markets.

We will need to obtain additional financing to fund our future operations, including completing the development and commercialization of our proprietary drug candidates. We also need to obtain additional financing to conduct additional clinical trials for the approval of our proprietary drug candidates if requested by regulatory bodies and to complete the development of any additional proprietary drug candidates we might discover. Moreover, our research and development expenses and other contractual commitments are substantial and are expected to increase in the future. In addition, to the extent the costs of constructing the Dunkirk facility exceed $225 million, we will be responsible for those costs.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this "Risk Factors" section. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements will depend on many factors, including, but not limited to:

- the progress, timing, scope and costs of our clinical trials, including the ability to timely enroll patients in our planned and potential future clinical trials;
- the outcome, timing and cost of regulatory approvals by the FDA, NMPA and regulatory authorities in jurisdictions where we seek such approvals, including the possibility that the FDA, NMPA or regulatory authorities may require that we perform more studies than those that we currently expect;
- our ability to secure adequate coverage and reimbursement for our proprietary drug candidates from government (including U.S. federal health care programs) and private payors;
- the number and characteristics of drug candidates that we may in-license and develop;
- our ability to successfully and compliantly launch and commercialize our drug candidates;
- the amount of sales and other revenues from drug candidates that we may commercialize, if any, including the selling prices for such potential products and the availability of adequate reimbursement by third-party payors;
- the amount of rebates or other price concessions we may owe under U.S. federal health care programs that cover and reimburse our proprietary drug candidates;
- the amount and timing of the milestone and royalty payments we receive from our collaborators under our licensing arrangements;
- the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- selling and marketing costs associated with our potential products, including the cost and timing of expanding our marketing and sales capabilities;
- the terms and timing of any potential future collaborations, licensing or other arrangements that we may establish;
- cash requirements of any future acquisitions and/or the development of other drug candidates;
- the costs of operating as a public company;
- the cost and timing of completion of commercial-scale outsourced manufacturing activities and
- the time and cost necessary to respond to technological and market developments.

Until we can generate a sufficient amount of revenue, we may finance future cash needs through public or private equity offerings, debt financings, collaborations and strategic alliances. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. General market conditions or the market price of our common stock may not support capital raising transactions such as an additional public or private offering of our common stock or other securities. In addition, our ability to raise additional capital may be dependent upon our common stock being quoted on The Nasdaq Global Select Market or upon obtaining shareholder approval to issue a sufficient number of shares of our common stock. There can be no assurance that we will be able to satisfy the criteria for continued listing on The Nasdaq Global Select Market or that we will be able to obtain shareholder approval of such stock issuances if it is necessary. If adequate funds are not available to us on acceptable terms, or at all, we may be required to delay or reduce the scope of, or eliminate, one or more of our research or development programs or our commercialization efforts. We may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. In addition, if we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or drug candidates or to grant licenses on terms that may not be favorable to us.

We believe that our existing cash and cash equivalents and short-term investments will not be sufficient to enable us to complete all necessary development or commercially launch our proprietary drug candidates. If we are unable to raise capital when needed or on attractive terms, we will be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts. Our inability to obtain additional funding when needed could seriously harm our business.

We entered into a $50.0 million senior secured loan agreement, which subjects the Company to significant interest rate and credit risk.

On June 29, 2018, the Company entered into a 5-year $50.0 million loan agreement with Perceptive, which closed on July 3, 2018, bearing interest at a floating per annum rate equal to the London Interbank Offering Rate (LIBOR) (with a floor of 2%) plus 9%. Thus, a change in the short-term interest rate environment (especially a material change) could have a material adverse effect on our business, financial condition, cash flows and results of operations and could cause the market value of our common shares to decline. As of December 31, 2018, we did not have any outstanding interest rate swap contracts.

We may not be able to refinance, extend, or repay our substantial indebtedness owed to our senior secured lender, which would have a material adverse effect on our financial condition and ability to continue as a going concern.

We anticipate that we will need to raise a significant amount of debt or equity capital in the future in order to repay our outstanding debt obligations owed to our senior secured lender when they mature on July 3, 2023 and fund our operations. We are required to make monthly interest-only payments with a bullet payment of the principal amount of $50.0 million at maturity. If we are unable to raise sufficient capital to repay these obligations at maturity and we are otherwise unable to extend the maturity dates or refinance these obligations, we would be in default. We cannot provide any assurances that we will be able to raise the necessary amount of capital to repay these obligations or that we will be able to extend the maturity dates or otherwise refinance these obligations. Upon a default on the senior debt, our senior secured lender would have the right to exercise its rights and remedies to collect, which would include foreclosing on our assets. Accordingly, a default would have a material adverse effect on our business and, if our senior secured lender exercises its rights and remedies, we would likely be forced to seek bankruptcy protection.

Covenants in the agreements governing our existing debt agreement restrict the manner in which we conduct our business.

The senior secured loan agreement contains various covenants that limit, subject to certain exemptions, our ability and/or our restricted subsidiaries' ability to, among other things:

- Incur or assume liens or additional debt or provide guarantees in respect of obligations of other persons;
- make loans, investments, or acquisitions;
- engage in any other business other than the business engaged in on the date of the loan agreement;
- pay dividends or make distributions on capital stock by any subsidiary;
- make any unscheduled payments on the Company's existing debt prior to the stated maturity thereof;
- sell assets and capital stock of our subsidiaries;
- enter into certain transactions with affiliates; and
- sell, transfer, license, lease, or dispose of our or our subsidiaries' assets.

The senior secured loan agreement requires that we maintain a minimum aggregate balance of $4.0 million in cash free and clear of all liens and that we meet certain minimum revenue targets for each quarter during which the loan is outstanding. In addition, the loan agreement is secured by substantially all of our assets and is guaranteed by certain of our subsidiaries, including APD, Athenex Pharmaceuticals LLC (AP), and APS.

The restrictions contained in our senior secured loan agreement governing our debt could adversely affect our ability to:

- finance our operations;
- make needed capital expenditures;
- make strategic acquisitions or investments or enter into alliances;
- withstand a future downturn in our business or the economy in general;
- engage in business activities, including future opportunities, that may be in our interest; and
- plan for or react to market conditions or otherwise execute our business strategies.

A breach of any of these covenants could result in a default under the senior secured loan agreement governing our debt. Further, additional indebtedness that we incur in the future may subject us to further covenants. If a default under any such loan agreement is not cured or waived, the default could result in the acceleration of debt, which could require us to repurchase or repay debt prior to the date it is otherwise due and that could adversely affect our financial condition. If we default, Percpetive may seek repayment through our subsidiary guarantors or by executing on the security interest granted pursuant to the loan agreement.

Our ability to comply with the covenants contained in our senior secured loan agreement may be affected by events beyond our control, including prevailing economic, financial, and industry conditions. Even if we are able to comply with all of the applicable covenants, the restrictions on our ability to manage our business in our sole discretion could adversely affect our business by, among other things, limiting our ability to take advantage of financings, mergers, acquisitions, and other corporate opportunities that we believe would be beneficial to us. In addition, our obligations under the loan agreement are secured, on a first-priority basis, and such security interests could be enforced in the event of default by the collateral agent for the loan agreement.

Raising additional capital may cause dilution to our shareholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates.

We may seek additional funding through a combination of equity offerings, debt financings, collaborations and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a holder of our common stock. The incurrence of additional indebtedness or the issuance of certain equity securities could result in increased fixed payment obligations and could also result in certain additional restrictive covenants, such as limitations on our ability to incur additional debt or issue additional equity, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. In addition, issuance of additional equity securities, or the possibility of such issuance, may cause the market price of our common stock to decline. In the event that we enter into collaborations or licensing arrangements in order to raise capital, we may be required to accept unfavorable terms, including relinquishing or licensing to a third party on unfavorable terms our rights to technologies or proprietary drug candidates that we otherwise would seek to develop or commercialize ourselves or potentially reserve for future potential arrangements when we might be able to achieve more favorable terms.

Certain of our executive officers and employees have received grants of stock options and shares of restricted stock, which vest over time. Under certain circumstances, such vesting may be accelerated. The accelerated vesting of stock options and shares of restricted stock could result in dilution to our existing stockholders and lower the market price of our common stock.

An impairment of goodwill could have a material adverse effect on our results of operations.

Acquisitions frequently result in the recording of goodwill and other intangible assets. As of December 31, 2018, our existing goodwill represented $37.5 million, or 16.2% of our total assets, primarily as a result of our acquisitions of QuaDPharma, LLC, CDE, and Polymed Therapeutics, Inc. and Chongqing Taihao Pharmaceutical Co Ltd. Goodwill is not amortized and is subject to impairment testing at least annually using a fair value based approach. The identification and measurement of goodwill impairment involves the estimation of the fair value of our reporting units. The estimates of fair value of reporting units are based on the best information available as of the date of the assessment and incorporate management assumptions about expected future cash flows and other valuation techniques. Future cash flows can be affected by changes in industry or market conditions, among other factors. The recoverability of goodwill is evaluated at least annually or more frequently when events or changes in circumstances indicate that the fair value of a reporting unit has more likely than not declined below its carrying value. We cannot accurately predict the amount and timing of any future impairment of assets, and, going forward, we may be required to take goodwill or other asset impairment charges relating to certain of our reporting units. Any such charges would have an adverse effect on our financial results.

Risks Related to Clinical Development of Our Proprietary Drug Candidates

Our primary clinical candidates are still in the development stage and have not yet received regulatory approval, which may make it difficult to evaluate our current business and predict our future performance.

We are a globally-focused biopharmaceutical company formed in November 2003. Our operations to date have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and conducting preclinical studies and clinical trials of our drug candidates. We have not yet successfully completed large-scale, pivotal clinical trials, or obtained regulatory approvals for our drug candidates and have not yet established sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be accurate. In addition, as a developing business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges.

We are focused on the discovery and development of innovative drugs for the treatment of cancers. The fact that we have not yet, among other things, demonstrated our ability to initiate or complete large-scale clinical trials or manufacture drugs at commercial scale, particularly in light of the rapidly evolving cancer treatment field, may make it difficult to evaluate our current business and predict our future performance. These constraints make any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage companies in rapidly evolving fields as we seek to transition to a company capable of supporting commercial activities. If we do not address these risks and difficulties successfully, our business will suffer. We depend substantially on the success of our proprietary drug candidates, which are in pre-clinical and clinical development.

As of the date of this Annual Report, we had a total of 40 planned, ongoing and completed clinical trials for our drug candidates, including a Phase 2 and two Phase 3 clinical trials for KX-01 ointment and a Phase 3 clinical trial for Oraxol. Our business and the ability to generate revenue related to product sales from our proprietary drug candidates will depend on the successful development, regulatory approval and commercialization for the treatment of patients with our drug candidates, which are still in development, and other drugs we may develop. Clinical development is a lengthy and expensive process with an uncertain outcome. The results of pre-clinical studies and early clinical trials of our drug candidates may not be predictive of the results of later-stage clinical trials. In the case of any trials we conduct, results have in the past, and may in the future, fail to meet the desired safety and efficacy endpoints, or differ from earlier trials due to the larger number of clinical trial sites and additional countries and populations involved in such trials. We have invested a significant portion of our efforts and financial resources in the development of our existing drug candidates. The success of our proprietary drug candidates will depend on several factors, including:

- successful enrollment in, and completion of, clinical studies;
- receipt of regulatory approvals from the FDA, NMPA and other regulatory authorities for our drug candidates;
- establishing commercial manufacturing capabilities, either by using our own facilities or making arrangements with third-party manufacturers;
- conducting our clinical trials compliantly and efficiently, and in many cases, relying on third parties to do so;
- obtaining, maintaining and protecting our intellectual property rights, including patent, trade secrets, know-how and regulatory exclusivity;
- ensuring we do not infringe, misappropriate or otherwise violate the patent, trade secret or other intellectual property rights of third parties;
- competition with other drug candidates and drugs, including existing IV chemotherapy treatments, potential oncology biologics and other oral dosing technologies developed or being developed by competitors and
- continued acceptable safety profile for our drug candidates following regulatory approval, if and when received.

If we do not achieve one or more of these requirements in accordance with our business plans or at all, we could experience significant delays in our ability to obtain approval for and/or to successfully commercialize our drug candidates, which would materially harm our business and we may not be able to generate sufficient revenues and cash flows to continue our operations.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. For example, our current lead product candidate, Oraxol, currently in Phase 3 clinical trials, has been in development by us since 2011. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our drug candidates may not be predictive of the results of later-stage clinical trials. Drug candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, including genetic differences, patient adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. In the case of any trials we conduct, results may differ from early trials due to the larger number of patients, clinical trial sites and additional countries and populations involved in such trials. 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. Our future clinical trial results may not be favorable.

We may not be successful in our efforts to identify or discover additional drug candidates. Due to our limited resources and access to capital, we must and have in the past decided to prioritize development of certain product candidates; these decisions may prove to have been wrong and may adversely affect our business.

To date, we have focused our drug discovery efforts on developing our cancer platform, particularly our Orascovery and Src Kinase Inhibition product candidates. If our cancer platform fails to identify potential drug candidates, our business could be materially harmed. Additionally, our management, at the direction of our board of directors, has discretion in prioritizing which product candidates to develop.

Research programs to pursue the development of our drug candidates for additional indications and to identify new drug candidates and disease targets require substantial technical, financial and human resources whether or not we ultimately are successful. Our research programs may initially show promise in identifying potential indications and/or drug candidates, yet fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications and/or drug candidates;
- potential drug candidates may, after further study, be shown to lack efficacy, have harmful adverse effects or other characteristics that indicate they are unlikely to be effective drugs; or
- it may take greater human and financial resources to identify additional therapeutic opportunities for our drug candidates or to develop suitable potential drug candidates through internal research programs than we possess, thereby limiting our ability to diversify and expand our drug portfolio.

Because we have limited financial and managerial resources, we focus on research programs and drug candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Accordingly, there can be no assurance that we will be able to identify additional therapeutic opportunities for our drug candidates or to develop suitable potential drug candidates through internal research programs, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential drug candidates or other potential programs that ultimately prove to be unsuccessful.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We and our research partners have from time to time and may in the future experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including:

- the availability of a sizeable population of eligible patients;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials for similar therapies or other new therapeutics;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the drug candidate being studied in relation to other available therapies,
- our ability to obtain and maintain patient consents;
- the failure of patients to complete a clinical trial and
- the availability of approved therapies that are similar in mechanism to our drug candidates.

In addition, our clinical trials will compete with other clinical trials for drug candidates that are in the same therapeutic areas as our drug candidates, and this competition will reduce the number and types of patients available to us because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Because the number of qualified clinical investigators is limited, we have conducted and expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites.

Even if we are able to enroll a sufficient number of patients in our clinical trials, delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our drug candidates.

Some of our drug candidates represent a novel approach to cancer treatment, which could result in delays in clinical development, heightened regulatory scrutiny, delays in our ability to achieve regulatory approval or commercialization, or market acceptance by physicians and patients of our drug candidates.

Some of our drug candidates, particularly those developed through our Orascovery platform, represent a departure from more commonly used methods for cancer treatment, and therefore represent a novel approach that carries inherent development risks. For instance, our Orascovery platform intends to facilitate the delivery of chemotherapy agents orally, as opposed to IV, while our Src Kinase inhibitor candidates operate by a new mechanism of action. To develop our Orascovery platform, we must successfully develop oral formulations of the active ingredients and ensure they can be delivered safely and consistently in capsule form. The need to further develop or modify in any way the protocols related to our drug candidates to demonstrate safety or efficacy may delay the clinical program, regulatory approval or commercialization, if approved. Our Src Kinase inhibitor platform is based on a novel molecule with an additional mechanism of action that is not found in other Src Kinase inhibitors. Because of this, unexpected safety and tolerability concerns may arise during the development process.

In addition, potential patients and their doctors may be inclined to use conventional standard-of-care treatments rather than enroll patients in any future clinical trial or to use our product candidates commercially once approved. This may have a material impact on our ability to generate revenues from our drug candidates. Further, given the novelty of the administration of our drug candidates, hospitals and physicians may prefer traditional treatment methods, may be reluctant to adopt the use of our products or may require a substantial amount of education and training, any of which could delay or prevent acceptance of our products by physicians and patients and materially hinder successful commercialization of our drug candidates.

Our products and product candidates may cause undesirable, or an increase in the frequency of, side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, NMPA or other regulatory authorities. Further, if a product candidate receives marketing approval and we or others identify undesirable side effects caused by the product after the approval, or if drug abuse is determined to be a significant problem with an approved product, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as a “Black Box warning” or a contraindication;
- we may be required to change the way the product is distributed or administered, conduct additional clinical trials or change the labeling of the product;
- we may decide to remove the product from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking the product and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing an affected product or product candidate and significantly impact our ability to successfully commercialize or maintain sales of our product or product candidates and generate revenues.

If clinical trials of our drug candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA, NMPA or other regulatory authorities or do not otherwise produce positive results, we may incur costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

We may experience various unexpected events during, or as a result of, clinical trials that could delay or prevent our ability to receive regulatory approval or commercialize our drug candidates, including:

- regulators, IRBs or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon drug development programs;
- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate, enrollment may be insufficient or slower than we anticipate or patients may drop out at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we might have to suspend or terminate clinical trials of our drug candidates for various reasons, including a finding of a lack of clinical response or a finding that participants are being exposed to unacceptable health risks;
- regulators, IRBs or ethics committees may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;
- the cost of clinical trials of our drug candidates may be greater than we anticipate;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate and
- our drug candidates may cause adverse events, have undesirable side effects or other unexpected characteristics, causing us or our investigators to suspend or terminate the trials.

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

- be delayed in obtaining regulatory approval for our drug candidates;
- not obtain regulatory approval at all;
- obtain approval for indications that are not as broad as intended;
- have the drug removed from the market after obtaining regulatory approval;
- be subject to additional post-marketing testing requirements;
- be subject to restrictions on how the drug is distributed or used or
- be unable to obtain reimbursement for use of the drug.

Delays in testing or approvals may result in increases in our drug development costs. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all.

Significant clinical trial delays also could shorten any periods during which we have the exclusive right to commercialize our drug candidates or allow our competitors to bring drugs to market before we do and impair our ability to commercialize our drug candidates and may harm our business and results of operations.

Manufacturing risks, including our inability to manufacture API and clinical products used in the clinical trials of our proprietary product candidates could adversely affect our ability to commercialize our product candidates.

Our business strategy depends on our ability to manufacture API in sufficient quantities and on a timely basis so as to meet our needs to manufacture our product candidates for our clinical trials and to meet consumer demand for our future products, while adhering to product quality standards, complying with regulatory requirements and managing manufacturing costs. We are subject to numerous risks relating to our manufacturing capabilities, including:

- our inability to manufacture API and clinical products in sufficient quantities to meet the needs of our clinical trials or to commercialize our products;
- our inability to secure product components in a timely manner, in sufficient quantities or on commercially reasonable terms;
- our failure to increase production of products to meet demand;
- our inability to modify production lines to enable us to efficiently produce future products or implement changes in current products in response to regulatory requirements;
- difficulty identifying and qualifying alternative suppliers for components in a timely manner and
- potential damage to or destruction of our manufacturing equipment or manufacturing facility.

In addition, we conduct manufacturing operations at our facility in Chongqing, China to manufacture our proprietary product candidates. As a result, our business is subject to risks associated with doing business in China, including:

- adverse political and economic conditions, particularly those negatively affecting the trade relationship between the U.S. and China;
- trade protection measures, such as tariff increases, and import and export licensing and control requirements;
- potentially negative consequences from changes in tax laws;
- difficulties associated with the Chinese legal system, including increased costs and uncertainties associated with enforcing contractual obligations in China;
- potentially lower protection of intellectual property rights;
- unexpected or unfavorable changes in regulatory requirements;
- possible patient or physician preferences for more established pharmaceutical products and medical devices manufactured in the U.S. and
- difficulties in managing foreign relationships and operations generally.

These risks are likely to be exacerbated by our limited experience with our current products and manufacturing processes. If, as we expect, our need for API increases, or demand for our products increase, we will have to invest additional resources to purchase components, hire and train employees and enhance our manufacturing processes. If we fail to increase our production capacity efficiently, our sales may not increase in line with our forecasts and our operating margins could fluctuate or decline. Any of these factors may affect our ability to manufacture our product and could reduce our revenues and profitability.

Risks Related to Obtaining Regulatory Approval for Our Drug Candidates

The regulatory approval processes of the FDA, NMPA and other regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA, NMPA and other regulatory authorities in jurisdictions where we seek such approval is unpredictable but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a drug candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any drug candidate, and it is possible that none of our existing drug candidates or any drug candidates we may discover, in-license or acquire and seek to develop in the future will ever obtain regulatory approval.

Our drug candidates could fail to receive regulatory approval from the FDA, NMPA or another regulatory authority for many reasons, including:

- disagreement with the design or implementation of our clinical trials;
- failure to demonstrate that a drug candidate is safe and effective for its proposed indication;
- failure of clinical trial results to meet the level of statistical significance required for approval;
- failure to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;
- disagreement with our interpretation of data from preclinical studies or clinical trials;
- the insufficiency of data collected from clinical trials of our drug candidates to support the submission and filing of a new drug application, or NDA, or other submission or to obtain regulatory approval;
- the FDA, NMPA or another regulatory authority's finding of deficiencies related to the product, manufacturing processes or facilities of ours or of third-party manufacturers with whom we contract for clinical and commercial supplies and
- changes in approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA, NMPA or a regulatory authority in another jurisdiction may require more information, including additional preclinical or clinical data, to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program. If we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that is not desirable for the successful commercialization of that drug candidate. In addition, if our drug candidate produces undesirable side effects or safety issues, the FDA may require the establishment of REMS, or the NMPA or a regulatory authority may require the establishment of a similar strategy, that may, for instance, restrict distribution of our drug candidates and impose burdensome implementation requirements on us. Any of the foregoing scenarios could materially harm the commercial prospects of our drug candidates.

The approval process for pharmaceutical products outside the U.S. varies among countries and may limit our ability to develop, manufacture and sell our products internationally. Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.

In order to market and sell our products internationally, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and may involve additional testing. We may conduct clinical trials for, and seek regulatory approval to market, our product candidates in countries other than the U.S. and China. Depending on the results of clinical trials and the process for obtaining regulatory approvals in other countries, we may decide to first seek regulatory approvals of a product candidate in countries other than the U.S., or we may simultaneously seek regulatory approvals in the U.S. and other countries. If we seek marketing approval for a product candidate outside the U.S., we will be subject to the regulatory requirements of health authorities in each country in which we seek approval. With respect to marketing authorizations in China, we will be required to seek regulatory approval from the NMPA. The approval procedure varies among regions and countries and may involve additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval.

Obtaining regulatory approvals from health authorities in countries outside the U.S. is likely to subject us to all of the risks associated with obtaining FDA approval described above. In addition, marketing approval by the FDA does not ensure approval by the health authorities of any other country, and marketing approvals by foreign health authorities do not ensure a similar approval by the FDA.

We are conducting, and may in the future conduct, clinical trials for our product candidates in sites outside the U.S. and the FDA may not accept data from trials conducted in such locations.

We have conducted, and may in the future conduct, certain of our clinical trials outside of the U.S. Although the FDA may accept data from clinical trials conducted outside the U.S., acceptance of this data is subject to certain conditions imposed by the FDA. There can be no assurance the FDA will accept data from any clinical trials we conduct outside of the U.S. If the FDA does not accept the data from any of our clinical trials conducted outside the U.S., it would likely result in the need for additional clinical trials in the U.S., which would be costly and time-consuming and could delay or prevent the commercialization of any of our product candidates.

Regulatory approval may be substantially delayed or may not be obtained for one or all of our drug candidates for a variety of reasons.

We may be unable to complete development of our drug candidates on schedule, if at all. The completion of the studies for our drug candidates will require funding beyond our current resources. In addition, if regulatory authorities require additional time or studies to assess the safety or efficacy of our drug candidates, we may not have or be able to obtain adequate funding to complete the necessary steps for approval for any or all of our drug candidates. Preclinical studies and clinical trials required to demonstrate the safety and efficacy of our drug candidates are time consuming and expensive and together take several years or more to complete. For example, our current lead product candidate, Oraxol, currently in Phase 3 clinical trials, has been in development since 2011. Delays in clinical trials, regulatory approvals or rejections of applications for regulatory approval in the U.S., Taiwan, New Zealand, China or other jurisdictions may result from many factors, including:

- our inability to obtain sufficient funds required for a clinical trial;
- regulatory requests for additional analyses, reports, data, non-clinical and preclinical studies and clinical trials;
- regulatory questions regarding interpretations of data and results and the emergence of new information regarding our drug candidates or other products;
- clinical holds, other regulatory objections to commencing or continuing a clinical trial or the inability to obtain regulatory approval to commence a clinical trial in countries that require such approvals;
- failure to reach agreement with the FDA, NMPA or other regulators regarding the scope or design of our clinical trials;
- delay or failure in obtaining authorization to commence a trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- our inability to enroll a sufficient number of patients who meet the inclusion and exclusion criteria in a clinical trial;
- our inability to conduct a clinical trial in accordance with regulatory requirements or our clinical protocols;
- clinical sites and investigators deviating from trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial;
- withdrawal of clinical trial sites from our clinical trials as a result of changing standards of care or the ineligibility of a site to participate in our clinical trials;
- inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indication;
- failure of our third-party clinical trial managers to satisfy their contractual duties or meet expected deadlines;
- delay or failure in adding new clinical trial sites;
- ambiguous or negative interim results, or results that are inconsistent with earlier results;
- unfavorable or inconclusive results of clinical trials and supportive non-clinical studies, including unfavorable results regarding effectiveness of drug candidates during clinical trials;
- feedback from the FDA, NMPA, IRB, DSMB or comparable entities, or results from earlier stage or concurrent preclinical studies and clinical trials, that might require modification to the protocol;
- unacceptable risk-benefit profile or unforeseen safety issues or adverse side effects;
- decision by the FDA, NMPA, IRB, comparable entities or the Company, or recommendation by a DSMB or comparable regulatory entity, to suspend or terminate clinical trials at any time for safety issues or for any other reason;
- failure to demonstrate a benefit from using a drug or biologic;
- lack of adequate funding to continue the clinical trial due to unforeseen costs or other business decisions;

- our inability to reach agreements on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- our inability to obtain approval from IRBs or ethics committees to conduct clinical trials at their respective sites;
- manufacturing issues, including problems with manufacturing or timely obtaining from third parties sufficient quantities of a drug candidate for use in a clinical trial and
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data.

Changes in regulatory requirements and guidance may also occur, and we may need to amend clinical trial protocols submitted to applicable regulatory authorities to reflect these changes. Amendments may require us to resubmit clinical trial protocols to IRBs or ethics committees for re-examination, which may impact the costs, timing or successful completion of a clinical trial.

According to the Provisions for Drug Registration and the Reform Plan Regarding the Category of the Registration of Chemical Medicines promulgated by the NMPA, the registrations of chemical medicines in China are divided into five categories, among which, Category 1 means the registration of innovative drugs that are not marketed either domestically or abroad, and Category 5 for the registration of drugs that have been marketed abroad and are being registered for marketing in China for the first time. Our drug candidates are all new therapeutic agents and we have built both research and development, clinical trial capacities, and commercial manufacturing facilities in China. As a result, we expect all of our current drug candidates to fall within the Category 1 application process but cannot be sure we will be granted or be able to maintain Category 1 designation. We believe the local drug registration pathway, Category 1, is a faster and more efficient path to obtain approval in the Chinese market than the drug registration pathway for imported drugs under Category 5. Category 5 drug candidates may not qualify to benefit from fast track review with priority at the CTA stage. Category 1 drugs receive special examination and approval treatment. The advantages of such treatment include a separate pathway for Category 1 application to queue up for examination by the Center for Drug Evaluation of the NMPA, or the CDE, and a working mechanism for communication with the applicants for discussion of relevant technical issues. The applications for Category 1 drugs are handled with higher priority and enhanced communications with the CDE. Compared with Category 5 drugs, Category 1 drugs are qualified to apply for special examination and approval at both the CTA stage and the production registration application stage. If the special examination and approval are granted at the CTA stage, such treatment will apply to the production registration application stage without further approval. During the CTA stage, reduction or exemption of clinical trial may be available if Category 1 drugs are for orphan diseases or other special diseases. The advantages also include, by providing priority resources, shortening time limits to review and exam applications of Category 1 drugs' clinical trials and of production registration, and to handle document submission and approval process. We cannot be sure that the NMPA will grant such priority treatment to any of our drugs candidates. Please see "Business—Government Regulation and Product Approval—Chinese Government Regulation."

If we experience delays in the completion of, or the termination of, a clinical trial, of any of our drug candidates, the commercial prospects of our drug candidates will be harmed, and our ability to generate revenues from the sale of any of those drug candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our drug candidate development and approval process, and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates.

Our drug candidates have caused and may cause undesirable adverse events or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any regulatory approval.

Undesirable adverse events caused by our drug candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, NMPA or another regulatory authority. Results of our trials could reveal a high and unacceptable severity or prevalence of adverse events. In such an event, our trials could be suspended or terminated and the FDA, NMPA or other regulatory authorities could order us to cease further development of, or deny approval of, our drug candidates for any or all targeted indications. Drug-related adverse events could affect patient recruitment or the ability of enrolled subjects to complete the trial, and could result in potential product liability claims. Any of these occurrences may significantly harm our reputation, business, financial condition and prospects.

In our clinical studies to date, we have observed the following serious adverse effects that were deemed to be possibly, likely or definitely related to each of our product candidates:

- Oraxol - severe neutropenia, febrile neutropenia, sepsis, septic shock, altered state of consciousness, hypokalemia and cardiac arrest, dehydration, pneumonia, death, nausea, vomiting, diarrhea, fatigue, anorexia and acute gastroenteritis;
- Oratecan - diarrhea, rash, gastrointestinal hemorrhage, vomiting, nausea, asthenia, neutropenia, anorexia, increased alanine aminotransferase, increased aspartate aminotransferase and enteritis;
- KX-01 oral - allergic reaction, bacteremia, rash, syncope, dermatitis, neutropenic fever, hyponatremia, failure to thrive, hypersensitivity, lower extremity edema, mucositis, neutropenia, pancytopenia, thrombocytopenia, seizure and motor vehicle accident, embolic stroke, pneumonitis, fever, acute kidney injury, increased bilirubin and albumin levels, decreased blood platelet count, abdominal pain, arm pain, pyrexia, rigors, tachypenea, oxygen desaturation pneumonia, anemia, elevated ALT and AST, dehydration and leukopenia and
- KX-02 - embolism.

Additionally, if one or more of our drug candidates receives regulatory approval, and we or others later identify undesirable side effects caused by such drugs, a number of potentially significant negative consequences could result, including:

- we may suspend marketing of the drug;
- regulatory authorities may withdraw approvals of the drug;
- regulatory authorities may require additional warnings on the label;
- we may be required to develop a REMS for the drug or, if a REMS is already in place, to incorporate additional requirements under the REMS, or to develop a similar strategy as required by a regulatory authority;
- we may be required to conduct post-marketing studies;
- we could be sued and held liable for harm caused to subjects or patients and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular drug candidate, if approved, and could significantly harm our business, results of operations and prospects.

We may seek Orphan Drug Designation for some of our drug candidates, and we may be unsuccessful.

We have received Orphan Drug Designation from the FDA for our proprietary product candidates KX-02 for the treatment of glioma and Oraxol for the treatment of angiosarcomas. As part of our business strategy, we may seek Orphan Drug Designation for our product candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the U.S. and Europe, may designate drugs for relatively small patient populations as orphan drugs or medicines, respectively. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a disease with a patient population of fewer than 200,000 individuals in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S.

Generally, if a drug with an Orphan Drug Designation subsequently receives the first regulatory approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug for the same indication during the period of exclusivity, with certain limited exceptions. Orphan designations for medicines in Europe also benefit from incentives such as reduced fees and protocol assistance. The applicable post-approval exclusivity period is seven years in the U.S. and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for Orphan Drug Designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan Drug Exclusivity may be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain Orphan Drug Exclusivity for a drug candidate, exclusivity may not effectively protect the drug candidate from competition because different drugs can be approved for the same condition and the same drugs can be approved for a different condition but used off-label for any orphan indication we may obtain. Even after an orphan drug is approved, the FDA may subsequently approve a different drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

Even if we receive regulatory approval for our drug candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drug candidates.

If our drug candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy and other post-marketing information, including both federal and state requirements in the U.S. and requirements of regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive requirements of the FDA, NMPA and regulatory authorities, including, in the U.S., ensuring that quality control and manufacturing procedures conform to current cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA or other marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our drug candidates may be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the drug candidate. The FDA may also require a REMS program as a condition of approval of one or more of our drug candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA, NMPA or a regulatory authority approves our drug candidates, we will have to comply with requirements including, for example, submissions of safety and other post-marketing information and reports, registration, and continued compliance with cGMPs and or GCPs for any clinical trials that we conduct post-approval.

The FDA may impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the drug reaches the market. Later discovery of previously unknown problems with our drug candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-marketing studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our drugs, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, untitled or warning letters, or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention, or refusal to permit the import or export of our drug candidates and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA, NMPA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. The policies of the FDA, NMPA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any regulatory approval that we may have obtained, and we may not achieve or sustain profitability.

In addition, if we were able to obtain accelerated approval of any of our drug candidates, the FDA would require us to conduct a confirmatory study to verify the predicted clinical benefit and additional safety studies. Other regulatory authorities outside the U.S., such as the NMPA, may have similar requirements. The results from the confirmatory study may not support the clinical benefit, which would result in the approval being withdrawn. While operating under accelerated approval, we will be subject to certain restrictions that we would not be subject to upon receiving regular approval.

Risks Related to Commercialization of Our Drug Candidates

If we are not able to obtain, or experience delays in obtaining, required regulatory approvals, we will not be able to commercialize our drug candidates, and our ability to generate revenue will be materially impaired.

We currently do not have any proprietary drug candidates that have gained regulatory approval for sale in the U.S., China or any other country, and we cannot guarantee that we will ever obtain regulatory approval for marketable proprietary drugs. Our business is substantially dependent on our ability to complete the development of, obtain regulatory approval for and successfully commercialize drug candidates in a timely manner. We cannot commercialize drug candidates without first obtaining regulatory approval to market each drug from the FDA, NMPA or regulatory authorities in the relevant jurisdictions. Our proprietary drug candidates are currently undergoing various phases of FDA clinical trials. We cannot predict whether these trials and future trials will be successful or whether regulators will agree with our conclusions regarding the preclinical studies and clinical trials we have conducted to date.

Before obtaining regulatory approvals for the commercial sale of any drug candidate for a target indication, we must demonstrate in preclinical studies and well-controlled clinical trials, and, with respect to approval in the U.S., to the satisfaction of the FDA, that the drug candidate is safe and effective for use for that target indication and that the manufacturing facilities, processes and controls are adequate. An NDA must include extensive preclinical and clinical data and supporting information to establish the drug candidate's safety and effectiveness. The NDA must also include significant information regarding the chemistry, manufacturing and controls for the drug. Obtaining approval of an NDA is a lengthy, expensive and uncertain process, and approval may not be obtained. If we submit an NDA to the FDA, the FDA decides whether to accept or reject the submission for filing. We cannot be certain that any submissions will be accepted for filing and review by the FDA.

Regulatory authorities outside of the U.S., such as the regulatory authorities in emerging markets, also have requirements for approval of drugs for commercial sale with which we must comply prior to marketing in those areas. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our drug candidates. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and obtaining regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking non-U.S. regulatory approval could require additional non-clinical studies or clinical trials, which could be costly and time-consuming. The non-U.S. regulatory approval process may include all of the risks associated with obtaining FDA approval and other risks specific to the relevant jurisdiction. For all of these reasons, we may not obtain non-U.S. regulatory approvals on a timely basis, if at all.

If we are unable to obtain regulatory approval for our drug candidates in one or more jurisdictions, or any approval contains significant limitations, our target market will be reduced and our ability to realize the full market potential of our drug candidates will be harmed. Furthermore, if we are not able to obtain, or experience delays in obtaining, required regulatory approvals, we will not be able to commercialize our drug candidates, and our ability to generate revenue will be materially impaired.

Even if any of our drug candidates receives regulatory approval, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our drug candidates receives regulatory approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well established in the medical community, and doctors may continue to rely on these treatments to the exclusion of our drug candidates. In addition, physicians, patients and third-party payors may prefer other novel products to ours, and we may experience difficulties gaining acceptance for our orally administered drug candidates. We are also subject to regulatory restrictions on how we market our drug candidates. If our drug candidates do not achieve an adequate level of acceptance, we may not generate significant product sales revenues, and we may not become profitable. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- the clinical indications for which our drug candidates are approved;
- physicians, hospitals, cancer treatment centers and patients considering our drug candidates as a safe and effective treatment;
- the potential and perceived advantages of our drug candidates over alternative treatments;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA, NMPA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA, NMPA or other regulatory authorities;
- the timing of market introduction of our drug candidates as well as competitive drugs;

- the cost of treatment in relation to alternative treatments;
- the amount of upfront costs or training required for physicians to administer our drug candidates;
- the availability of adequate coverage, reimbursement and pricing by third-party payors and government authorities (including U.S. federal healthcare programs);
- the willingness of patients to pay out-of-pocket in the absence of coverage and reimbursement by third-party payors and government authorities;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies and
- the effectiveness of our sales and marketing efforts.

If our drug candidates are approved but fail to achieve market acceptance among physicians, patients, hospitals, cancer treatment centers or others in the medical community, we will not be able to generate significant revenue. Even if our drugs achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our drugs, are more cost effective or render our drugs obsolete.

We market certain medical devices that, if modified, may be subject to FDA clearance and failure to obtain such clearance could adversely affect our financial condition or results of operations.

Through our subsidiary, Polymed, we currently market in-vitro diagnostic rapid test kits used in the performance of clinical laboratory tests (limited to drugs of abuse and pregnancy testing in the U.S.) under 510(k) clearance by the FDA pursuant to Section 510(k) of the FDCA. These products and our operations are subject to extensive regulation by the FDA and other federal and state authorities in the U.S., as well as comparable authorities in foreign jurisdictions. After a device receives 510(k) marketing clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a major change or modification in its intended use, will require a new 510(k) marketing clearance or, depending on the modification PMA. The FDA requires each manufacturer to determine whether the proposed change requires submission of a 510(k) or a PMA in the first instance, but the FDA can review that decision and disagree with a manufacturer's determination. If the FDA disagrees with a manufacturer's determination, the FDA can require the manufacturer to cease marketing and/or request the recall of the modified device until 510(k) marketing clearance or PMA approval is obtained. Also, in these circumstances, we may be subject to significant regulatory fines or penalties. In the event we make additional product enhancements to our 510(k)-cleared products, we cannot be assured that the FDA would agree with any of our decisions to not submit 510(k) premarket notifications for these modified devices.

Our manufacturing experience is limited and any failure by us to manufacture our products for commercial sale after receiving FDA approval would materially impact our revenue and financial condition.

The manufacture of drugs for commercial sale is subject to regulation by the FDA under cGMP regulations and by other regulators under other laws and regulations. We cannot assure you that we will continue to manufacture our products under cGMP regulations or other laws and regulations in sufficient quantities for commercial sale, or in a timely or economical manner.

Our manufacturing facilities require specialized personnel and are expensive to operate and maintain. Any delay in the regulatory approval or market launch of product candidates to be manufactured in these facilities will require us to continue to operate these expensive facilities and retain specialized personnel, which may increase our expected losses.

Through our public-private partnerships, additional cGMP manufacturing facilities for our use are currently being built in Dunkirk, New York and Chongqing, China. Our facility in Dunkirk, New York is being built pursuant to an agreement with FSMC. Under the current arrangement, we will select and hire contractors for the project and oversee the development of the Dunkirk facility. ESD, the parent entity of FSMC, is responsible for the costs of construction and all equipment for the facility, up to an aggregate of $200 million, and ESD, not us, will own the facility and equipment. We have limited experience in overseeing the development of such a facility and we may not be able to complete the development within the timeframe expected, within the expected budget, or at all. If development of the Dunkirk facility is delayed or not completed it could materially adversely affect our operations and financial results.

Additionally, upon completion, both the Dunkirk and Chongqing facilities will need to be cGMP validated prior to operating. Validation is a lengthy process that must be completed before we can manufacture under cGMP guidelines. We cannot guarantee that the FDA or foreign regulatory agencies will approve any of the other facilities or, once they are approved, that such facilities will remain in compliance with cGMP regulations.

The manufacture of pharmaceutical products is a highly complex process in which a variety of difficulties may arise from time to time. We may not be able to resolve any such difficulties in a timely fashion, if at all. If anything were to interfere with the continuing manufacturing operations in our facilities, it could materially adversely affect our business and financial condition.

Currently, many of our product candidates are manufactured in small quantities for use in clinical trials. We cannot assure you that we will be able to successfully scale up the manufacture of each of our product candidates in a timely or economical manner, or at all. If any of these product candidates are approved by the FDA or other drug regulatory authorities for commercial sale, we will need to manufacture them in larger quantities. If we are unable to successfully scale up our manufacturing capacity, the regulatory approval or commercial launch of such product candidate may be delayed or there may be a shortage in supply of such product candidate.

If we fail to develop manufacturing capacity and experience, fail to continue to contract for manufacturing on acceptable terms, or fail to manufacture our product candidates economically on a commercial scale or in accordance with cGMP regulations, our development programs will be materially adversely affected. This may result in delays in receiving FDA or foreign regulatory approval for one or more of our product candidates or delays in the commercial production of a product that has already been approved. Any such delays could materially adversely affect our business and financial condition.

The manufacture of API is highly regulated by FDA, NMPA and other regulatory bodies and is subject to current good manufacturing practice requirements and to inspection by such regulators, which may result in adverse findings and actions against certain API manufacturing facilities.

API manufacturing facilities are subject to regulation by the applicable regulatory bodies in the place of manufacture as well as the regulatory agency in the country to which the product is exported. For instance, FDA's cGMP regulations apply to these facilities and violation of these, or other, regulations may result in adverse action against the facility, including cessation of manufacturing activities. Our API manufacturing facilities in Chongqing are also subject to regulation by the NMPA. If the FDA, NMPA or other regulators discover a problem at one facility, we may be subject to increased scrutiny and/or adverse actions across our operations, including fines or orders to cease manufacturing, which could have a material impact on our operations, clinical development, business strategy or results of operations.

We have limited experience in marketing proprietary drug products. If we are unable to establish such marketing and sales capabilities or enter into agreements with third parties to market and sell our proprietary drug candidates, we may not be able to generate sales revenue from such products.

We have limited sales, marketing and commercial product experience. We intend to continue to develop our in-house commercial organization and sales force for such products, which will require significant capital expenditures, management resources and time. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel.

If we are unable to establish internal sales, marketing and commercial distribution capabilities for our proprietary drug candidates, we will need to pursue collaborative arrangements for the sales and marketing of our proprietary drugs. However, there can be no assurance that we will be able to establish or maintain such collaborative arrangements, or if we are able to do so, that they will have effective sales forces. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have less control over the marketing and sales efforts of such third parties which may present fraud and abuse and other regulatory considerations, and our revenue from product sales may be lower than if we had commercialized our proprietary drug candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our proprietary drug candidates.

There can be no assurance that we will be able to develop our in-house sales and commercial distribution capabilities or establish or maintain relationships with third-party collaborators to successfully commercialize any proprietary product, and as a result, we may not be able to generate sales revenue from such products.

We face substantial competition, and our competitors may discover, develop or commercialize competing drugs before or more successfully than we do.

The development and commercialization of new drugs is highly competitive. We face competition with respect to our current drug candidates and will face competition with respect to any drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of drugs for the treatment of the types of cancer for which we are developing our drug candidates. Some of these competitive drugs and therapies are based on scientific approaches that are the same as or similar to our approach, and others are

based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we may develop. Our competitors also may obtain approval from the FDA, NMPA or other regulatory authorities for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market and/or slow our regulatory approval.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Even if we are able to commercialize any drug candidates, the drugs may become subject to unfavorable pricing regulations, third party reimbursement practices or healthcare reform initiatives, which could harm our business.

Successful sales of our drug candidates, if approved, depend on the availability of adequate coverage and reimbursement from third-party payors. Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the U.S., and commercial payors are critical to new drug acceptance.

The regulations that govern regulatory approvals, pricing and reimbursement for new therapeutic products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or licensing approval is granted. In some non-U.S. markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a drug in a particular country but be subject to price regulations that delay our commercial launch of the drug and negatively impact the revenues we are able to generate from the sale of the drug in that country. For example, according to the guidance issued in March 2015 by the central government of China, each province will decide which drugs to include in its provincial major illness reimbursement lists and the percentage of reimbursement, based on local funding. Adverse pricing limitations may hinder our ability to recover our investment in one or more drug candidates, even if our drug candidates obtain regulatory approval. For example, in China, according to a statement, *Opinions on reforming the review and approval process for pharmaceutical products and medical devices*, issued by the State Council in August 2015, the enterprises applying for new drug approval will be required to undertake that the selling price of new drug on Chinese mainland market shall not be higher than the comparable market prices of the product in its country of origin or Chinese neighboring markets, as applicable.

Our ability to commercialize any drugs successfully also will depend in part on the extent to which coverage and reimbursement for these drugs and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a drug is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective and
- neither experimental nor investigational.

We cannot be sure that reimbursement will be available for any drug that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Reimbursement may impact the demand for, or the price of, any drug for which we obtain regulatory approval. Obtaining reimbursement for our drugs may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of a physician. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any drug candidate that we successfully develop.

In the U.S., no uniform policy of coverage and reimbursement for drugs exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a drug from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our drugs on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given drug, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of our drugs. However, under Medicare Part D—Medicare's outpatient prescription drug benefit—there are protections in place to ensure coverage and reimbursement for oncology products and all Part D prescription drug plans are required to cover substantially all anti-cancer agents.

The State Council required central and provincial authorities across China to promote a medical insurance program for major illnesses, which targets covering at least 50% of the medical cost as incurred by treating major illnesses but falls out of the coverage of the basic insurance programs. The State Council requires provincial authorities to increase reimbursement rates over the next three years.

We intend to seek approval to market our drug candidates in the U.S., China and other selected jurisdictions. If we obtain approval in one or more non-U.S. jurisdictions for our drug candidates, we will be subject to rules and regulations in those jurisdictions. In some non-U.S. countries, the pricing of drugs and biologics is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining regulatory approval of a drug candidate. In addition, market acceptance and sales of our drug candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our drug candidates and may be affected by existing and future health care reform measures.

We intend to market our drugs, if approved, in a variety of international markets and we are exploring the licensing of commercialization rights or other forms of collaboration worldwide, which exposes us to additional risks of conducting business in additional international markets.

We conduct business operations in regions including the U.S., China, Taiwan and New Zealand, and non-U.S. markets are an important component of our growth strategy. If we fail to obtain licenses or enter into collaboration arrangements with third parties in these markets, or if these parties are not successful, our revenue-generating growth potential will be adversely affected.

Moreover, international business relationships subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations, including:

- initiatives to develop an international sales, marketing and distribution organization may increase our expenses, divert our management's attention from the acquisition or development of drug candidates or cause us to forgo profitable licensing opportunities in these geographies;
- efforts to enter into collaboration or licensing arrangements with third parties in connection with our international sales, marketing and distribution efforts may increase our expenses or divert our management's attention from the acquisition or development of drug candidates;
- changes in a specific country's or region's laws, regulations or political and cultural climate or economic condition;
- differing regulatory requirements for drug approvals and marketing internationally;
- difficulty of effective enforcement of contractual provisions and intellectual property rights in local jurisdictions;
- potentially reduced protection for intellectual property rights;
- potential conflicting third-party patent or other intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements, such as Export Administration Regulations promulgated by the U.S. Department of Commerce and fines, penalties or suspension or revocation of export privileges;
- economic weakness, including inflation or political instability, particularly in non-U.S. economies and markets;
- compliance with tax, employment, immigration and labor laws for employees traveling abroad;
- the effects of applicable non-U.S. tax structures and potentially adverse tax consequences;
- currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incidental to doing business in another country;

- workforce uncertainty and labor unrest, particularly in non-U.S. countries where labor unrest is more common than in the U.S.;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a non-U.S. market with low or lower prices rather than buying them locally;
- failure of our employees and contracted third parties to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

These and other risks may materially adversely affect our ability to obtain or sustain revenue from international markets.

The use of legal, regulatory, and legislative strategies by both brand and generic competitors, including but not limited to "authorized generics" and regulatory petitions, as well as the potential impact of proposed and newly enacted legislation, may increase costs associated with the introduction or marketing of our generic products, could delay or prevent such introduction, and could adversely affect our results of operations.

Our competitors, both branded and generic, often pursue strategies to prevent, delay, or eliminate competition from generic alternatives to branded products. These strategies include, but are not limited to:

- entering into agreements whereby other generic companies will begin to market an authorized generic, a generic equivalent of a branded product, at the same time or after generic competition initially enters the market;
- launching a generic version of their own branded product prior to or at the same time or after generic competition initially enters the market;
- filing petitions with the FDA or other regulatory bodies seeking to prevent or delay approvals, including timing the filings so as to thwart generic competition by causing delays of our product approvals;
- seeking to establish regulatory and legal obstacles that would make it more difficult to demonstrate bioequivalence or to meet other requirements for approval, and/or to prevent regulatory agency review of applications, such as through the establishment of patent linkage (laws and regulations barring the issuance of regulatory approvals prior to patent expiration);
- initiating legislative or other efforts to limit the substitution of generic versions of brand pharmaceuticals;
- filing suits for patent infringement and other claims that may delay or prevent regulatory approval, manufacture, and/or scale of generic products;
- introducing "next-generation" products prior to the expiration of market exclusivity for the reference product, which often materially reduces the demand for the generic or the reference product for which we seek regulatory approval;
- persuading regulatory bodies to withdraw the approval of brand name drugs for which the patents are about to expire and converting the market to another product of the brand company on which longer patent protection exists;
- obtaining extensions of market exclusivity by conducting clinical trials of brand drugs in pediatric populations or by other methods and
- seeking to obtain new patents on particular formulations of drugs or methods of administering drugs for which patent protection on the drug itself is about to expire.

If any other actions by our competitors and other third parties to prevent or delay activities necessary to the approval, manufacture, or distribution of our products are successful, our entry into the market and our ability to generate revenues associated with new products may be delayed, reduced, or eliminated, which could have a material adverse effect on our business, financial condition, results of operations, cash flows and/or share price.

Our compounded preparations and the pharmacy compounding industry are subject to regulatory and customer scrutiny, which may impair our growth and sales.

Formulations prepared and dispensed by compounding pharmacies may contain ingredients found in FDA-approved drugs, and such formulations and the compounding thereof are subject to various FDA regulatory requirements. Outsourcing facilities are regulated under Section 503B. Certain compounding pharmacies have been the subject of widespread negative media coverage in

recent years, and the actions of these pharmacies have resulted in increased scrutiny of compounding pharmacy activities from the FDA and state governmental agencies. For example, the FDA has in the past requested that a number of compounding pharmacies conduct a recall of all non-expired, purportedly sterile drug products and cease sterile compounding operations due to lack of sterility assurance, and additional compounding pharmacies have suspended sterile production or voluntarily recalled certain sterile compounding products after an FDA inspection of the relevant facilities. As a result of this exercise of caution, or due to the absence of FDA approval, though such approval is not required, some physicians may be hesitant to prescribe, and some patients may be hesitant to purchase and use, these compounded formulations.

In addition, an outsourcing facility must meet certain conditions under Section 503B of the FDCA in order for its compounded products to be exempt from the FDCA's premarket approval requirements and from the FDCA requirement that products be labeled with adequate directions for use; for example, the drug must be compounded by or under the direct supervision of a licensed pharmacist, in a facility registered pursuant to Section 503B of the FDCA and in compliance with cGMP. If our outsourcing facility or any of our compounded products are found not to satisfy the criteria of Section 503B, the marketing of our products absent the FDA approval and/or absent adequate directions for use in the product labeling could render our products adulterated or misbranded under the FDCA, which could have an adverse effect on our business. Furthermore, if an outsourcing facility compounds drugs using bulk drug substances, such bulk drug substances must either appear on a list established by the FDA of bulk drug substances for which there is a clinical need or be used to compound drugs that appear on a list established by the FDA of drugs for which there is a shortage. The FDA has not yet placed any bulk drug substances on the clinical list; however, the FDA has announced an interim policy pursuant to which bulk drug substances with sufficient supporting information for FDA to evaluate the bulk drug substances may be nominated for inclusion on a Category 1 list and, provided certain conditions are met, the FDA does not intend to enforce against such outsourcing facilities pending evaluation of the Category 1 substances for inclusion on the FDA's list of bulk drug substances for which there is a clinical need. In addition to a clinical need determination, the FDA has established guidance on determining whether a product is an essential copy of an FDA approved product. If our products were ever determined to be an essential copy of an FDA approved product, administrative or judicial action could be taken. We use bulk drug substances in the preparation of certain of our compounded products. In the event the FDA's evaluation of these bulk drug substances results in a determination not to include such substances on the FDA's list of bulk drug substances for which there is a clinical need, or if FDA were to change its interim policy such that compounding with such bulk drug substances could not proceed while the FDA's evaluation of the substances is pending or until the FDA has issued its list of bulk drug substances for which there is a clinical need, our ability to continue marketing compounded products subject to Section 503B would be impaired, and our business could be harmed.

We use bulk vasopressin to produce a compounded ready to use vasopressin product that is preservative free. If we are able to continue to sell our compounded vasopressin product, revenues from those sales are expected to be used to fund clinical trials for our cancer drugs in development. Vasopressin was nominated on July 27, 2017 and FDA placed it on the 503B Category 1 list. On September 4, 2018, the FDA proposed not to list Vasopressin on its list of bulk substances for which there is a clinical need. We submitted substantial technical, legal and policy comments opposing the FDA's proposed action. On March 4, 2019, the FDA decided in a final action not to list vasopressin on the list of bulk substances for which there is a clinical need. We are currently engaged in litigation regarding FDA's decision not to list vasopressin on the list of bulk drug substances for which there is a clinical need, in which we are seeking a temporary restraining order and preliminary injunction regarding FDA's decision, as well as an order vacating its decision. If we are unsuccessful in obtaining the relief we seek in this litigation, we would have to abandon revenue-generating line of business, which would have a material adverse effect on our business, results of operations, financial condition and cash flows. Vasopressin remained on FDA's Category 1 list until March 4, 2019, when FDA decided in final action published in the *Federal Register* not to list vasopressin on the list of bulk drug substances for which there is a clinical need. Also, on March 4, 2019, Athenex, Inc., APS, and APD filed a complaint against FDA seeking to vacate its decision. In this case, FDA has represented to the court that "until the Court issues a decision on the merits of this action, FDA will not initiate enforcement action against Athenex based solely on Athenex's use of the bulk drug substance vasopressin to compound drugs and distribute those drugs" and the court has incorporated FDA's representation into its published order. Because of the court's order, Athenex will continue to produce and distribute compounded vasopressin during the period that the case is pending and will reevaluate its position after the Court issues its decision on the merits of Athenex's lawsuit. If we are ultimately unsuccessful in overturning FDA's final vasopressin decision, we would have to abandon this revenue-generating line of business, which would have a material adverse effect on our business, results of operations, financial condition and cash flows.

We are also engaged in litigation regarding the legal validity of the Category 1 list. See "Item 3. Legal Proceedings" and the risk factor captioned, "If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time-consuming and could prevent or delay us from developing or commercializing our drug candidates."

If a compounded drug formulation provided through our compounding services leads to patient injury or death or results in a product recall, we may be exposed to significant liabilities and reputational harm.

The production, labeling and packaging of compounded drugs is inherently risky. The success of our compounded formulations and pharmacy operations depends to a significant extent upon perceptions of the safety and quality of our products. We could be adversely affected if our formulations are subject to negative publicity. We could also be adversely affected if any of our formulations

or other products, any similar products sold by other companies, or any products sold by other compounding outsourcing facilities, prove to be, or are asserted to be, harmful to patients. There are a number of factors that could result in the injury or death of a patient who receives one of our compounded formulations, including quality issues, manufacturing or labeling flaws, improper packaging or unanticipated or improper uses of the products, any of which could result from human or other error. Any of these situations could lead to a recall of, or safety alert relating to, one or more of our products. Similarly, to the extent any of the components of approved drugs or other ingredients used by us to produce compounded formulations have quality or other problems that adversely affect the finished compounded preparations, our sales could be adversely affected. In addition, in the ordinary course of business, we may voluntarily retrieve products in response to a customer complaint. Because of our dependence upon medical and patient perceptions, any adverse publicity associated with illness or other adverse effects resulting from the use or misuse of our products, any similar products sold by other companies or any other compounded formulations, could have a material adverse impact on our business, results of operations and financial condition.

Risks Related to Our Intellectual Property

A significant portion of our intellectual property portfolio currently comprises pending patent applications that have not yet been issued as granted patents, and if our pending patent applications fail to issue our business will be adversely affected. If we are unable to obtain and maintain patent protection for our technology and drugs, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the U.S., China and other countries with respect to our proprietary technology and drug candidates. We have sought to protect our proprietary position by filing patent applications in the U.S., China and other countries related to novel technologies and drug candidates that we consider important to our business. As of December 31, 2018, we owned more than 150 granted patents and 40 pending patent applications worldwide, including one pending international patent application under the Patent Cooperation Treaty, or PCT, which we plan to file nationally in the U.S. and other jurisdictions. The process of obtaining patent protection is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. There can be no assurance that our pending patent applications will result in issued patents Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our platforms' product candidates. Third parties may have blocking patents that could be used to prevent us from commercializing our patented technologies, platforms and product candidates and practicing our proprietary technology. There can also be no assurance that a third party will not challenge the validity of our patents or that we will obtain sufficient claim scope in those patents, in view of prior art, to prevent a third party from competing successfully with our drug candidates. We may become involved in interference, inter partes review, post grant review, ex parte reexamination, derivation, opposition or similar other proceedings challenging our patent rights or the patent rights of others. Such challenges may result in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and drug candidates, or limit the duration of the patent protection of our technology and drug candidates. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drug candidates similar or identical to ours.

The patent position of biotechnology and pharmaceutical companies is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Changes in patent laws or the interpretation of patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection. Publications of discoveries in scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until eighteen months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

We may not be able to protect our intellectual property rights throughout the world.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions, due to inconsistent policies regarding the scope of claims allowable in patents. Changes in patent laws and rules, either by legislation, judicial decisions, or regulatory interpretation in the U.S. and other countries may diminish our ability to protect our inventions and enforce our intellectual property rights, and more generally could affect the value of our intellectual property.

In addition, the laws of certain non-U.S. countries do not protect intellectual property rights to the same extent as U.S. federal and state laws do. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing drugs made using our inventions in and into the U.S. or non-U.S. jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own drugs and further, may export

otherwise infringing drugs to non-U.S. jurisdictions where we have patent protection but where enforcement rights are not as strong as those in the U.S. These drugs may compete with our drug candidates and our patent or other intellectual property rights may not be effective or adequate to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain jurisdictions, including China. The legal systems of some countries do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to biopharmaceutical products, which could make it difficult in those jurisdictions for us to stop the infringement or misappropriation of our patents or other intellectual property rights, or the marketing of competing drugs in violation of our proprietary rights. Proceedings to enforce our patent and other intellectual property rights in non-U.S. jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business.

Furthermore, such proceedings could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims of infringement or misappropriation against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and our patent rights relating to our drug candidates could be found invalid or unenforceable if challenged in court or before the U.S. Patent and Trademark Office or comparable non-U.S. authority.

Competitors may infringe our patent rights or misappropriate or otherwise violate our intellectual property rights. To counter infringement or unauthorized use, litigation may be necessary 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. Such litigation can be expensive and time-consuming. Our current and potential competitors may have the ability to dedicate substantially greater resources to enforce and/or defend their intellectual property rights than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, in an infringement proceeding, a court may decide that patent or other intellectual property rights owned by us are invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patent or other intellectual property rights do not cover the technology in question. 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.

If we initiate legal proceedings against a third party to enforce any patent, or any patents that may issue in the future from our patent applications, that relates to one of our drug candidates, the defendant could counterclaim that such patent rights are invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include *ex parte* re-examination, *inter partes* review, post-grant review, derivation and equivalent proceedings in non-U.S. jurisdictions, such as opposition proceedings. Although any party alleging invalidity or unenforceability of our patents has a high burden of proof, nonetheless such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our drug candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware of during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on certain drug candidates. Such a loss of patent protection could have a material adverse impact on our business.

We may be subject to claims challenging the inventorship of our patents and ownership of other intellectual property.

Although we are not currently experiencing any claims challenging the inventorship of our patents or ownership of our intellectual property, we may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as inventors or co-inventors. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our drug candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, we may lose rights such as exclusive ownership of, or right to use, our patent or other intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time-consuming and could prevent or delay us from developing or commercializing our drug candidates.

Our commercial success depends in part on our avoiding infringement of the patents and other intellectual property rights of third parties. There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including litigation in the U.S. courts, *inter partes* review, post grant review, interference and *ex parte* reexamination proceedings before the USPTO or oppositions and other comparable proceedings in non-U.S. jurisdictions. Numerous issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing drug candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our drug candidates or manufacturing processes may give rise to claims of infringement of the patent rights of others.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our drug candidates. Because patent applications can take many years to issue, patent applications that are currently pending may later result in issued patents that our drug candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies that are first publicized or commercialized after the filing date of those patents infringes upon them. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our drug candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to prevent us from commercializing such drug candidate unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent is held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the applicable drug candidate unless we obtain a license, limit our uses, or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all.

Third parties who bring successful claims against us for infringement of their intellectual property rights may obtain injunctive or other equitable relief, which could prevent us from developing and commercializing one or more of our drug candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee resources from our business. In the event of a successful claim of infringement or misappropriation against us, we may have to pay substantial damages, including treble damages and attorneys' fees in the case of willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing drug candidates, which may be impossible or require substantial time and monetary expenditure and undertaking additional preclinical studies, clinical trials or regulatory review. In the event of an adverse result in any such litigation, or even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our drug candidates. We cannot predict whether any required license would be available on commercially reasonable terms, or at all, and we may fail to obtain any of these licenses on commercially reasonable terms, if at all. In the event that we are unable to obtain such a license, we would be unable to further develop and commercialize one or more of our drug candidates, which could harm our business significantly. We may also elect to enter into license agreements in order to settle patent infringement claims or to resolve disputes prior to litigation and any such license agreements may require us to pay royalties and other fees that could significantly harm our business.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical personnel, management personnel, or both from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

In particular, on August 13, 2018, APS and APD, our wholly-owned subsidiaries, filed a complaint for declaratory judgment against Par Pharmaceuticals, Inc., Par Sterile Products, LLC and Endo Par Innovation Company, LLC (together, Par) in the United States District Court for the Western District of New York (the Court), seeking a declaratory judgment from the Court that our compounded vasopressin drug products in ready-to-use form do not infringe on patents that Par has with respect to its Vasostrict® product and that Par's patents are invalid. On October 22, 2018, Par filed a motion to dismiss the complaint on the basis that the Court does not have subject matter jurisdiction. Athenex has opposed Par's motion and that motion is fully briefed and currently pending. Par has not filed a claim for infringement of its patents in this suit, but if Par's motion to dismiss Athenex's patent suit is denied and

the declaratory action proceeds, Par could proceed to lodge a counterclaim for patent infringement. If such an infringement claim were brought and the Court ruled for Par, Athenex could be enjoined from further production of compounded vasopressin within in the United States and sale of compounded vasopressin in or from the United States and for payment of damages to Par for U.S. manufacture or sale of compounded vasopressin that has already taken place.

In addition, on August 13, 2018, APS and APD filed a motion to intervene and seek the dismissal of Par's complaint against the FDA and certain governmental officials in the United States District Court for the District of Columbia. Par has sought declaratory and injunctive relief against the FDA and certain governmental officials that: (i) vasopressin be delisted from Category 1 of the FDA's list of bulk drug substances under evaluation pursuant to Section 503B of the Federal Food, Drug and Cosmetic Act (FDCA), (ii) the expansion of the FDA's enforcement discretion to Category 1 substances, be enjoined; and (iii) that the FDA be enjoined from authorizing the compounding of vasopressin under Section 503B of the FDCA. Our motion to intervene was granted. Par filed a preliminary injunction motion and we and the FDA filed motions for judgment on the pleadings. This action currently stayed. On March 4, 2019, FDA published in the Federal Register its final decision not to include vasopressin on the list of bulk drug substances for which there is a clinical need. Also, on March 4, 2019, Athenex, Inc., APS, and APD filed a complaint against FDA seeking to vacate its decision. In this case, FDA has represented to the Court "until the Court issues a decision on the merits of this action, FDA will not initiate enforcement action against Athenex based solely on Athenex's use of the bulk drug substance vasopressin to compound drugs and distribute those drugs" and the court has incorporated FDA's representation into its published order. Because of the court's order, Athenex will continue to produce and distribute compounded vasopressin during the period that the case is pending and will reevaluate its position after the Court issues its decision on the meirits of Atheenx's lawsuit.

If we are unsuccessful in these legal proceedings, we would need to abandon this revenue-generating unit of our business, which would have a material adverse effect on our business, results of operations, financial condition and cash flows.

If our products conflict with the intellectual property rights of third parties, we may incur substantial liabilities and we may be unable to commercialize products in a profitable manner or at all.

We seek to launch generic pharmaceutical products either where patent protection or other regulatory exclusivity of equivalent branded products has expired, where patents have been declared invalid or where products do not infringe the patents of others. However, at times, we may seek approval to market generic products before the expiration of patents relating to the branded versions of those products, based upon our belief that such patents are invalid or otherwise unenforceable or would not be infringed by our products. Our success depends in part on our ability to operate without infringing the patents and proprietary rights of third parties. The manufacture, use and sale of generic versions of products has been subject to substantial litigation in the pharmaceutical industry. These lawsuits relate to the validity and infringement of patents or proprietary rights of third parties. If our products were found to be infringing the intellectual property rights of a third-party, we could be required to cease selling the infringing products, causing us to lose future sales revenue from such products and face substantial liabilities for patent infringement, in the form of payment for the innovator's lost profits or a royalty on our sales of the infringing product. These damages may be significant and could materially adversely affect our business. Any litigation, regardless of the merits or eventual outcome, would be costly and time consuming and we could incur significant costs and/or a significant reduction in revenue in defending the action and from the resulting delays in manufacturing, marketing or selling any of our products subject to such claims.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Periodic maintenance fees on any issued patent are due to be paid to the USPTO and other patent agencies in several stages over the lifetime of the patent. Although an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment of a patent application or lapse of a patent include failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

The terms of our patents may not be sufficient to effectively protect our drug candidates and business.

In most countries in which we file patent applications, including the U.S., the term of an issued patent is twenty years from the earliest claimed filing date of a non-provisional patent application in the applicable country. With respect to any issued patents in the U.S., we may be entitled to obtain a patent term extension or extend the patent expiration date provided we meet the applicable requirements for obtaining such patent term extensions. Although such extensions may be available, the life of a patent and the protection it affords is by definition limited. Even if patents covering our drug candidates are obtained, we may be open to competition from other companies as well as generic medications once the patent life has expired for a drug. If patents are issued on our currently pending patent applications, the resulting patents will be expected to expire on dates ranging from 2025 to 2038, excluding any potential patent term extension or adjustment. Upon the expiration of our issued patents, we will not be able to assert such patent rights against potential competitors and our business and results of operations may be adversely affected.

In addition, the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies. For these reasons, we may have competition for our technologies, platforms and product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that a related patent may expire before any particular product candidate can be commercialized or that such patent will remain in force for only a short period following commercialization, thereby reducing any significant advantage of the patent.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar legislation in other countries extending the terms of our patents, if issued, relating to our drug candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA regulatory approval for our drug candidates, one or more of our U.S. patents, if issued, may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years as compensation for patent term lost during drug development and the FDA regulatory review process. Patent term extensions, however, cannot extend the remaining term of a patent beyond a total of fourteen years from the date of drug approval by the FDA, and only one patent can be extended for a particular drug.

The application for patent term extension is subject to approval by the USPTO, in conjunction with the FDA. We may not be granted an extension due to, for example, failure to apply within applicable deadlines, failure 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. If we are unable to obtain a patent term extension for a given patent or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our drug will be shortened and our competitors may obtain earlier approval of competing drugs. As a result, our ability to generate revenues could be materially adversely affected.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our drug candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patent rights. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity, and is therefore costly, time-consuming, and inherently uncertain. In addition, the U.S. has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, in *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to naturally-occurring substances are not patentable. Although we do not believe that our issued patents or any patents that may issue from our pending patent applications directed to our drug candidates if issued in their currently pending forms, as well as patent rights licensed by us, will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patent rights. There could be similar changes in the laws of foreign jurisdictions that may impact the value of our patent or our other intellectual property rights.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. We may also be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

In addition to our issued patents and pending patent applications, we rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position and to protect our drug candidates. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties that have access to them, such as our employees, corporate collaborators, outside scientific collaborators, sponsored researchers, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In many cases our confidentiality and other agreements with consultants, outside scientific collaborators, sponsored researchers and other advisors require them to assign to us or grant us licenses to inventions they invent as a result of the work or services they render under such agreements or grant us an option to negotiate a license to use such inventions. However, any of these parties may breach such agreements and disclose our proprietary information, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time-consuming, and the outcome is unpredictable. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us and our competitive position would be harmed.

Furthermore, many of our employees, including our senior management, were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. We are not aware of any threatened or pending claims related to these matters or concerning the agreements with our senior management, but litigation may be necessary in the future to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel. Further, to the extent that our employees, contractors, consultants, collaborators and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in the security of our systems, security measures may be breached, and we may not have adequate remedies for any such breach.

We may not be successful in obtaining or maintaining necessary rights for our development pipeline through acquisitions and in-licenses.

Because our programs may involve additional drug candidates that require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire and maintain licenses or other rights to use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, or other third-party intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license intellectual property rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could be required to pay monetary damages or could lose license rights that are important to our business.

We have entered into license agreements with third parties providing us with rights under various third-party patents and patent applications, including the rights to prosecute patent applications and to enforce patents. Certain of these license agreements impose and, for a variety of purposes, we may enter into additional licensing and funding arrangements with third parties that also may impose diligence, development or commercialization timelines and milestone payment, royalty, insurance and other obligations on us. Certain of these license agreements provide us with the exclusive right to practice technologies in major markets including North America, South America, the EU, Australia, New Zealand, Eastern Europe, China, Taiwan, Hong Kong, Macau and parts of Southeast Asia, although the right to practice the technologies and any inventions arising out of such technologies outside of these territories may be reserved to the licensing company. In addition, under certain of our existing licensing agreements, we are obligated to pay royalties on net product sales of our drug candidates once commercialized, pay a percentage of sublicensing revenues, make other specified payments relating to our drug candidates or pay license maintenance and other fees. We also have diligence and clinical development obligations under certain of these agreements that we are required to satisfy. If we fail to comply with our obligations under our current or future license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any drug or drug candidate that is covered by the licenses or we may face claims for monetary damages or other penalties under these agreements. Such an occurrence could diminish the value of these products and our company. Termination of the licenses provided in these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

In particular, our ability to stop third parties from making, using, selling, offering to sell or importing any of our patented inventions, either directly or indirectly, will depend in part on our success in obtaining, defending, and enforcing patent claims that cover our technology, inventions and improvements. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our platforms and product candidates and the methods used to manufacture those platforms and product candidates. Our issued patents and those that may issue in the future may be challenged, invalidated or circumvented, which could limit our ability to stop competitors from marketing related platforms or product candidates or limit the length of the term of patent protection that we may have for our technologies, platforms and product candidates.

If our licensing and sublicensing activities result in non-compliance with our licensing agreements, our business relationships with our licensing partners may suffer and we may be required to pay monetary damages or rescind or amend existing agreements which are important to our business.

We have entered into agreements with third parties under which we have granted licenses to use certain of our patents and patent applications, including the rights to develop, seek regulatory approval for and sell products using our KX-01 and KX-02 products. We have also entered into similar agreements sublicensing the intellectual property for the Orascovery platform, which we have licensed from Hanmi. We have granted exclusive patent rights to certain of these partners and have granted them certain additional rights with respect to the intellectual property we have licensed to them. From time to time we may engage in other licensing transactions in which we acquire licenses to certain intellectual property or sublicense intellectual property rights. If we fail to comply with or are found to have violated the terms of any of our licenses, we may be required to rescind or amend our license agreements or pay damages to license counterparties or other rightsholders. This may also negatively impact our relationships with our licensing and sublicensing partners for our candidate platforms. For further information regarding the terms of our licenses, please see "Business—License and Collaboration Agreements".

Risks Related to Our Reliance on Third Parties

We depend on our agreements with Hanmi Pharmaceutical Co. Ltd, or Hanmi, to provide rights to the intellectual property relating to certain of our lead product candidates. Any termination or loss of significant rights under those agreements would adversely affect our development or commercialization of our lead product candidates.

We have licensed the intellectual property rights related to HM30181A, an integral part of our current product candidates, from Hanmi pursuant to two license agreements. If, for any reason, our license agreements are terminated or we otherwise lose those rights, it would adversely affect our business. Our license agreements with Hanmi impose on us obligations relating to exclusivity, territorial rights, development, commercialization, funding, payment, diligence, sublicensing, insurance, intellectual property protection and other matters. If we breach any material obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages to Hanmi, and Hanmi may have the right to terminate our license, which could result in us being unable to develop, manufacture and sell our product candidates that incorporate HM30181A.

In addition, under our 2013 license agreement with Hanmi, we have granted Hanmi a one-time right of first negotiation that, at Hanmi's discretion, requires us to negotiate in good faith the sale of our rights in Oraxol and Oratecan under such agreement to Hanmi at a purchase price determined by an internationally-recognized investment banking firm with an office in Hong Kong at any time prior to the earlier of (i) our first commercial sale of products using such technology or (ii) receipt by Hanmi of written notice from our company of the sublicense of the rights in an applicable product to a third party. If Hanmi exercises this right of first negotiation and we reach an agreement to sell our rights under that licensing agreement, our ability to continue to develop certain of our product candidates would be significantly impaired and would adversely affect our business and results of operations.

Each of our license agreements with Hanmi expires on the earlier of (i) expiration of the last of Hanmi's patent rights licensed under the agreement or (ii) invalidation of Hanmi's patent rights which are the subject of the agreement, provided that the term will automatically be extended for consecutive one year periods unless either party gives notice to the other at least ninety days prior to expiration of the patent rights licensed under the agreement or before the then current annual expiration date of the agreement. The patent rights licensed to us under the agreements with Hanmi have expiry dates ranging from 2023 to 2033, unless the terms of such licensed patents are extended in accordance with applicable laws and regulations. Subject to certain conditions, Hanmi may also terminate the license agreements if we fail to comply with certain development milestones set out in each of the agreements. The agreements also contain customary termination rights for either party, such as in the event of a breach of the agreement or the initiation of bankruptcy proceedings by the other party or by mutual agreement. For further information regarding the license terms, right of first negotiation and termination provisions of the Hanmi in-license agreements, please see "Business—License and Collaboration Agreements—In-Licenses —Hanmi Licensing Agreements."

We may rely on third parties to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, perform satisfactorily or operate in compliance with laws and regulations, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed.

We have relied upon and may, in the future, rely upon third-party CROs to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, and regulatory requirements and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCPs, which are regulations and guidelines enforced by the FDA, NMPA and other regulatory authorities for all of our drugs in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, NMPA or regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, non-clinical and preclinical programs. In the event that any of our foreign CROs are impacted by political, social or financial instability, they may be unable to maintain production capacity or compliance with regulatory requirements. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements, environmental, health and safety laws and regulations, or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, our results of

operations and the commercial prospects for our drug candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Our total revenue is highly dependent on a limited number of API customers and pharmaceutical wholesalers, and the loss of, or any significant decrease in business from, any one or more of our major API customers or pharmaceutical wholesalers could adversely affect our financial condition and results of operations.

We have derived a significant portion of our revenue from a limited number of customers, as is typical in the pharmaceutical industry. During the year ended December 31, 2016, prior to the launch of our specialty products, we generated 62% of our total revenue from our two largest API customers, Intas Pharmaceuticals and Ebewe Pharmaceuticals. During the year ended December 31, 2017, we generated 28% of our total revenue from those API customers and generated 28% of our total revenue from the three largest wholesalers in the U.S. market, Amerisource, Cardinal Health, and McKesson (15%, 7%, and 6%, respectively). During the year ended December 31, 2018, we generated 10% of our total revenue from those API customers and generated 30% of our total revenue from the three largest wholesalers in the U.S. market, Amerisource, Cardinal Health, and McKesson (12%, 9%, and 9%, respectively).

There are a number of factors that could cause us to lose major API customers. We do not enter into long-term sales contracts with customers but sell API to them based on short-term purchase orders. Accordingly, these customers may choose to use other suppliers with little or no notice, based upon considerations of price, quality, shipping time, competitive or other reasons. In addition, our API customers use the API to manufacture drugs, and they are subject to regulation and oversight by the FDA and other relevant regulatory agencies. If for any reason, any such customer violates an FDA regulation that results in their being prohibited from manufacturing drugs, they would no longer purchase API from us. Such sanctions or regulatory action against drug manufacturers could happen without notice, and our revenue stream could be adversely affected without notice.

If we are unable to maintain our business relationships with these major API customers and pharmaceutical wholesalers on commercially acceptable terms, it could have a material adverse effect on our financial condition and results of operations.

Additionally, Polymed, our wholly owned subsidiary, sells API to third parties for use in those third parties' products, which may be manufactured in cGMP facilities. In the event Polymed's customers fail to remain in compliance with cGMP regulations, their operations may be adversely impacted, causing them to cancel or cease API orders from Polymed. Any decrease in orders by Polymed's customers may impact Polymed's revenue and, as a result, our overall financial condition.

If our Global Supply Chain Platform is insufficient, we may rely on third parties to manufacture at least a portion of our drug candidate supplies, and for at least a portion of the manufacturing process of our drug candidates, if approved. Our business could be harmed if those third parties fail to provide us with sufficient quantities of product or fail to do so at acceptable quality levels or prices.

Although we currently have a facility that may be used as our clinical-scale manufacturing and processing facility, we partially rely on outside vendors to manufacture supplies and process our drug candidates. We have not yet begun to manufacture or process our drug candidates on a commercial scale and may not be able to do so for any of our drug candidates.

We have limited experience in managing the manufacturing process, and our process may be more difficult or expensive than the approaches currently in use.

Although we do intend to further develop our manufacturing facilities, and those leased to us under our public-private partnerships, we may also use third parties as part of our manufacturing process. Our reliance on third-party manufacturers may expose us to the following risks:

- we may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA, NMPA or other regulatory authorities must approve any manufacturers. This approval would require new testing and cGMP-compliance inspections by FDA, NMPA or other regulatory authorities. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our drugs;
- our manufacturers may have little or no experience with manufacturing our drug candidates and, therefore, may experience quality issues or require a significant amount of support from us in order to implement and maintain the infrastructure and processes required to manufacture our drug candidates;
- our third-party manufacturers might be unable to timely manufacture our drug or produce the quantity and quality required to meet our clinical and commercial needs, if any;
- contract manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately;

- our future contract manufacturers may not perform as agreed, may not devote sufficient resources to our drugs, or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our drugs;
- we may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our drugs;
- our third-party manufacturers could breach or terminate their agreement with us;
- raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects;
- our contract manufacturers and critical reagent suppliers may be subject to inclement weather, as well as natural or man-made disasters and
- our contract manufacturers may have unacceptable or inconsistent product quality success rates and yields.

Each of these risks could delay or prevent the completion of our clinical trials or the approval of any of our drug candidates by the FDA, NMPA or other regulatory authorities, result in higher costs or adversely impact commercialization of our drug candidates. In addition, we will rely on third parties to perform certain specification tests on our drug candidates prior to delivery to patients. If these tests are not conducted appropriately and test data are not reliable, patients could be put at risk of serious harm and the FDA, NMPA or other regulatory authorities could place significant restrictions on our company until deficiencies are remedied.

The manufacture of drug and biological products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls.

Currently, raw materials used in our manufacturing activities, including the pacific yew used in many of the API products we manufacture, are supplied by multiple suppliers. We have agreements for the supply of such raw materials with manufacturers or suppliers that we believe have sufficient capacity to meet our demands. In addition, we believe that adequate alternative sources for such supplies exist. However, there is a risk that, if supplies are interrupted, it would materially harm our business.

Manufacturers of drug and biological products often encounter difficulties in production, particularly in scaling up or out, validating the production process, and assuring high reliability of the manufacturing process (including the absence of contamination). These problems include logistics and shipping, difficulties with production costs and yields, quality control, including stability of the product, product testing, operator error, availability of qualified personnel, as well as compliance with strictly enforced federal, state and non-U.S. regulations. Furthermore, if contaminants are discovered in our supply of our drug candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any stability failures or other issues relating to the manufacture of our drug candidates will not occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to provide our drug candidate to patients in clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to begin new clinical trials at additional expense or terminate clinical trials completely.

If third-party manufacturers fail to comply with pharmaceutical manufacturing regulations, our financial results and financial condition will be adversely affected.

Before a third party can begin commercial manufacture of our drug candidates and potential drugs, contract manufacturers are subject to regulatory inspections of their manufacturing facilities, processes and quality systems. Due to the complexity of the processes used to manufacture drug and biological products and our drug candidates, any potential third-party manufacturer may be unable to initially pass federal, state or international regulatory inspections in a cost effective manner in order for us to obtain regulatory approval of our drug candidates. If our contract manufacturers do not pass their inspections by the FDA, NMPA or other regulatory authorities, our commercial supply of drug product or substance will be significantly delayed and may result in significant additional costs, including the delay or denial of any marketing application for our drug candidates. In addition, drug and biological manufacturing facilities are continuously subject to inspection by the FDA, NMPA and other regulatory authorities, before and after drug approval, and must comply with cGMPs. Our contract manufacturers may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. In addition, contract manufacturers' failure to achieve and maintain high manufacturing standards in accordance with applicable regulatory requirements, or the incidence of manufacturing errors, could result in patient injury, product liability claims, product shortages, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously harm our business, reputation or corporate image. If a third-party manufacturer with whom we contract is unable to comply with manufacturing regulations, we may also be subject to fines, unanticipated compliance expenses, recall or seizure of our drugs, product liability claims, total or partial suspension of production and/or enforcement actions, including injunctions and criminal or civil prosecution. These possible sanctions could materially adversely affect our financial results and financial condition.

Furthermore, changes in the manufacturing process or procedure, including a change in the location where the product is manufactured or a change of a third-party manufacturer, could require prior review by the FDA, NMPA or other regulatory authorities and/or approval of the manufacturing process and procedures in accordance with the FDA or NMPA's regulations, or comparable requirements. This review may be costly and time consuming and could delay or prevent the launch of a product. The new facility will also be subject to pre-approval inspection. In addition, we have to demonstrate that the product made at the new facility is equivalent to the product made at the former facility by physical and chemical methods, which are costly and time consuming. It is also possible that the FDA, NMPA or other regulatory authorities may require clinical testing as a way to prove equivalency, which would result in additional costs and delay.

We have entered into collaborations and may form or seek collaborations or strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such alliances or licensing arrangements.

We have partnered with companies such as Hanmi, Almirall, XLifeSci/Guangzhou Xiangxue Pharmaceuticals and Gland and may form or seek strategic alliances, create joint ventures or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our drug candidates and any future drug candidates that we may develop. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing shareholders, or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our drug candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our drug candidates as having the requisite potential to demonstrate safety and efficacy. If and when we collaborate with a third party for development and commercialization of a drug candidate, we can expect to relinquish some or all of the control over the future success of that drug candidate to the third party.

Further, collaborations involving our drug candidates are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our drug candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to the acquisition of competitive drugs, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, drugs that compete directly or indirectly with our drugs or drug candidates;
- a collaborator with marketing and distribution rights to one or more drugs may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our drug candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable drug candidates and
- collaborators may own or co-own intellectual property covering our drugs that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

As a result, if we enter into collaboration agreements and strategic partnerships or license our drugs, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a drug candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our drug candidates or bring them to market and generate product sales revenue, which would harm our business prospects, financial condition and results of operations.

We have engaged and will continue to rely on a single vendor to manage our order to cash cycle and our distribution activities in the U.S., and the loss or disruption of service from this vendor could adversely affect our operations and financial condition.

Our U.S. customer management, order processing, invoicing, cash application, chargeback and rebate processing and distribution and logistics activities are managed by Dohmen Life Science Services (DLSS), a managed services provider with a focus on life sciences companies. If we were to lose the availability of DLSS's services due to a dispute, termination of or inability to renew the contract, or other factors such as fire, natural disaster or other disruption, such loss could have a material adverse effect on our operations. Although multiple providers of such services exist, there can be no assurance that we could secure another source to handle these transactions on acceptable terms or otherwise to our specifications in the event of a disruption of services at operational centers.

Risks Related to Our Industry, Business and Operation

We are dependent on our key personnel, and if we are not successful in attracting and retaining qualified personnel, we may not be able to successfully implement our business strategy. Additionally, certain members of our leadership may engage in other business ventures that may have interests in conflict with ours.

We are highly dependent on Dr. Lau, our Chief Executive Officer, Dr. Kwan, our Chief Medical Officer and the other principal members of our management and scientific teams. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock option grants that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by changes in the price of our common stock that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements with our key employees, any of our employees could leave our employment at any time, with or without notice.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel or consultants will also be critical to our success. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our discovery and preclinical development and commercialization strategy. The loss of the services of our executive officers or other key employees and consultants could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy.

Furthermore, replacing executive officers and key employees or consultants 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 products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel or consultants on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel.

We may choose to hire part-time employees or use consultants. As a result, certain of our employees, officers, directors and consultants may not devote all of their time to our business, and may from time to time serve as officers, directors and consultants of other companies. These other companies may have interests in conflict with ours. For instance, Dr. Johnson Lau, who serves as our Chief Executive Officer and Chairman, Dr. Manson Fok, who serves on our board of directors, are also directors of Avalon Global Holdings Limited, or Avalon, a shareholder of ours.

We also face competition for the hiring of scientific and clinical personnel from universities and research institutions. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We are substantially dependent on our public-private partnerships and if we or our counterparties fail to meet the obligations of those agreements and we lose the benefits of those partnerships, it would materially impact our development, operations and prospects.

Our long-term public-private partnerships with governments and government agencies, including in certain emerging markets, include agreements to build and/or maintain manufacturing facilities for us. For example, we entered into an agreement with FSMC, whereby FSMC agreed to fund the costs of construction of a new manufacturing facility in Dunkirk, New York. FSMC is responsible for the costs of construction and of all equipment for the facility, up to an amount not to exceed $225 million, and shall retain ownership of the facility and the equipment. To the extent the costs of constructing the Dunkirk facility exceed $225 million, we will be responsible for those costs. We are entitled to lease the facility and all equipment at a rate of $1.00 per year for an initial 10-year term, and for the same rate if we elect to extend the lease for an additional 10-year term. We are responsible for all operating costs and expenses for the facility. In exchange, we have committed to spending $1.52 billion on operational expenses in the Dunkirk facility in our first 10-year term in the facility, and an additional $1.5 billion on operational expenses if we elect to extend the lease for a second 10-year term. We have also committed to hiring 450 permanent employees within the first 5 years at the Dunkirk facility. In addition, in July 2017, we entered into a 20-year payment in-lieu of tax agreement with the CCIDA for the construction of our Dunkirk facility, valued at approximately $9.1 million. We have also entered into similar arrangements with FSMC relating to our headquarters, and Chongqing Maliu Riverside Development & Investment Co., Ltd. relating to a plant in Chongqing, China, under which we have committed to achieving certain operating, revenue and tax generation milestones. If we are unable to comply with our obligations under these arrangements, including the milestones we have committed to achieve, we may lose access to the properties covered by such arrangements which could disrupt our operations and manufacturing activities, cause us to divert resources to finding alternative facilities, which would not have any subsidies, and would have a significant impact on our operations and financial performance. We may also be subject to lawsuits or claims for damages against us if we are unable to comply with our obligations under these arrangements. For example, our potential liability in connection with a failure to comply with the New York State partnership agreements could be as high as $225 million, depending on the amount of funding ESD had contributed to the Dunkirk project at the time of the claim.

Furthermore, there is no guarantee that the counterparties to our public-private partnerships will comply with the terms of the agreements, including that their ability to fund their capital commitments under the agreements may be subject to their ability to raise additional capital and that construction timetables may not be met, nor is there guarantee that the successors to such counterparties will continue to comply with terms of the agreements, regardless of existence of such government stipulations as a guideline released on November 4, 2016 by the State Council of China, which provides that, among others governments and relevant departments at all levels shall strictly keep policy commitments lawfully made to society and administrative counterparties, shall carefully perform all the contracts lawfully entered into with investment subjects in activities like attraction of investment and public-private partnership, shall not breach contracts with such excuses as government transition and replacement of leaders, and shall bear legal and economic liability in event of their infringements and contract breaches. If our public-private partnership counterparties or their successors fail to comply with their obligations under these arrangements, our development programs and prospects will be materially adversely affected. Public-private partnerships are also subject to risks associated with government and government agency counterparties, including risks related to government relations compliance, sovereign immunity, shifts in the political environment, changing economic and legal conditions and social dynamics.

We will need to continue to increase the size and capabilities of our organization, and we may experience difficulties in managing our growth.

As of December 31, 2018, we had 582 employees and consultants and most of our employees are full-time. As our development and commercialization plans and strategies develop, and as we continue to operate as a public company, we must add a significant number of additional managerial, operational, sales, marketing, financial and other personnel. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA or other comparable authority review process for our drug candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our drug candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities. In addition, we expect to incur additional costs in hiring, training and retaining such additional personnel.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our drug candidates and, accordingly, may not achieve our research, development and commercialization goals.

If we fail to maintain effective internal control over financial reporting, we may not be able to accurately report our consolidated financial results.

We cannot assure you that there will not be material weaknesses and significant deficiencies that our independent registered public accounting firm or we will identify in the future. Under standards established by the Public Company Accounting Oversight Board, a deficiency in internal control over financial reporting exists when the design or operation of a control does not allow management or personnel, in the normal course of performing their assigned functions, to prevent or detect misstatements on a timely basis. A material weakness is a deficiency or combination of deficiencies in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected and corrected on a timely basis. As a public company, we also need to establish and maintain effective disclosure and financial controls and make changes in our corporate governance practices including our board and committee practices. If we identify such issues or if we are unable to produce accurate and timely financial statements, our stock price may be adversely affected, and we may be unable to maintain compliance with applicable listing requirements.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon completion of our initial public offering, we became subject to the periodic reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC.

We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected, which would cause us to be unable to produce accurate financial statements and may adversely affect our business.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the laws of the FDA and other similar non-U.S. regulatory authorities; provide true, complete and accurate information to the FDA and other similar non-U.S. regulatory authorities; comply with manufacturing standards we have established; comply with healthcare fraud and abuse and privacy laws in the U.S. and similar non-U.S. fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our drug candidates and begin commercializing those drugs in the U.S., our potential exposure under U.S. laws will increase significantly and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We may have conflicts of interest with our affiliates and related parties, and in the past we have engaged in transactions and entered into agreements with affiliates that were not negotiated at arms' length.

We have engaged, and may in the future engage, in transactions with affiliates and other related parties. These transactions may not have been, and may not be, on terms as favorable to us as they could have been if obtained from non-affiliated persons. While an effort has been made and will continue to be made to obtain services from affiliated persons and other related parties at rates and on terms as favorable as would be charged by others, there will always be an inherent conflict of interest between our interests and those of our affiliates and related parties. Our majority stockholders may economically benefit from our arrangements with related parties. If we engage in related party transactions on unfavorable terms, our operating results will be negatively impacted.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our shareholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

We may evaluate various acquisitions and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing drugs or drug candidates and regulatory approvals and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

Our internal computer systems, or those used by our CROs, collaboration partners, third-party service providers or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of cybersecurity measures, our information technology and Internet based systems, including those of our current and future CROs, collaboration partners, third-party service providers and other contractors and consultants, are vulnerable to damage, interruption, or failure from computer viruses, unauthorized access, intrusion, and other cybersecurity incidents. This could result in the exposure of sensitive data including the loss of trade secrets, intellectual property, personal identifiable or sensitive information of employees, customers, partners, clinical trial patients and others, leading to a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we partially rely on our third-party research institution collaborators for research and development of our drug candidates and other third parties for the manufacture of our drug candidates and to conduct clinical trials, and similar cybersecurity incidents relating to their computer systems could also have a material adverse effect on our business. Certain data security breaches must be reported to affected individuals and the government, and in some cases to the media, under provisions of HIPAA, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, and financial penalties may also apply. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our drug candidates could be delayed.

We are aware of a security breach that occurred in March 2017. That incident occurred when the credentials of an approved consultant were compromised, and the consultant's credentials were used to access the remote desktop server and active directory server of our wholly-owned subsidiary APS. Upon discovery of the breach, we immediately took steps to void the compromised credentials and reset all credentials having access to APS' systems. These particular APS information systems are independent of ours and did not contain any drug candidate, clinical trial or patient-specific data. However, information stored on APS' systems may have been vulnerable during the intrusion. To help mitigate future incidents, we have put in place enhanced security measures required for

access by consultants. Notwithstanding such measures, we cannot be certain that no future security breaches will occur or that future breaches will not result in a material disruption of our development programs and our business operations.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our third-party research institution collaborators, CROs, suppliers and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, acts of war or terrorism, and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. In addition, we partially rely on our third-party research collaborators for conducting research and development of our drug candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. Our ability to obtain clinical supplies of our drug candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. Damage or extended periods of interruption to our corporate, development or research facilities due to fire, natural disaster, power loss, communications failure, unauthorized entry or other events could cause us to cease or delay development of some or all of our drug candidates. Although we maintain property damage and business interruption insurance coverage on these facilities, our insurance might not cover all losses under such circumstances and our business may be seriously harmed by such delays and interruption.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our drug candidates or our 503B products.

We face an inherent risk of product liability as a result of the clinical testing of our drug candidates and will face an even greater risk if we commercialize any of our clinical candidates. For example, we may be sued if our drug candidates that we plan to manufacture, or our 503B products that we currently manufacture or plan to manufacture cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, as applicable, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the drug, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our drug candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our drugs;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management’s time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any drug candidate and
- a decline in the price of our common stock.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of drugs we develop, alone or with collaborators. Although we currently carry clinical trial insurance, which we believe to be adequate for our current operations, the amount of such insurance coverage may not be adequate now, or in the future, and we may be unable to maintain such insurance, or we may not be able to obtain additional or replacement insurance at a reasonable cost, if at all. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Additionally, we may be sued if the products that we commercialize, market or distribute for our partners cause or are perceived to cause injury or are found to be otherwise unsuitable, and may result in:

- decreased demand for those products;
- damage to our reputation;
- costs incurred related to product recalls;
- limiting our opportunities to enter into future commercial partnership and
- a decline in the price of our common stock.

We have limited insurance coverage, and any claims beyond our insurance coverage may result in our incurring substantial costs and a diversion of resources.

We maintain property insurance policies covering physical damage to, or loss of, our buildings and their improvements, equipment, office furniture and inventory. We hold employer's liability insurance generally covering death or work-related injury of employees. We hold public liability insurance covering certain incidents involving third parties that occur on or in the premises of the company. We hold directors and officers liability insurance and business interruption insurance. We do not maintain key-man life insurance on any of our senior management or key personnel. Our insurance coverage may be insufficient to cover any claim for product liability, damage to our fixed assets or employee injuries. Any liability or damage to, or caused by, our facilities or our personnel beyond our insurance coverage may result in our incurring substantial costs and a diversion of resources.

We may increasingly become a target for public scrutiny, including complaints to regulatory agencies, negative media coverage, including social media and malicious reports, all of which could severely damage our reputation and materially and adversely affect our business and prospects.

We focus on the development of drugs used in the treatment of cancers, and such drugs may be the subject of regulatory, watchdog and media scrutiny and coverage, which also the possibility of heightened attention from the public, the media and our participants. In addition, members of our management and board include high-profile public figures who may be the subject of media and public scrutiny and attention. From time to time, these objections or allegations, regardless of their veracity, may result in public protests or negative publicity, which could result in government inquiry or harm our reputation. Corporate transactions we or related parties undertake may also subject us to increased media exposure and public scrutiny. There is no assurance that we would not become a target for public scrutiny in the future or such scrutiny and public exposure would not severely damage our reputation as well as our business and prospects.

In addition, our directors and management have been in the past, and may continue to be, subject to scrutiny by the media and the public regarding their activities in and outside our company, which may result in unverified, inaccurate or misleading information about them being reported by the press. Negative publicity about our directors or management, even if untrue or inaccurate, may harm our reputation.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred operating losses that are treated as taxable losses for U.S. federal income tax purposes. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an ownership change (generally defined as a greater than 50 percentage points change (by value) in its equity ownership over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We believe that we have experienced an ownership change in the past, which may affect our ability to utilize our net operating loss carryforwards. As of December 31, 2018, we had federal net operating loss carryforwards of approximately $253.8 million that could be limited by our past and any future ownership change, which could have an adverse effect on our future results of operations. Similar limitations will apply to our ability to carry forward any unused tax credits to offset future taxable income.

Our business, financial condition and stock price may be adversely affected by volatile global markets and economic conditions.

Our business and operating results could be affected by global economic conditions. When global economic conditions deteriorate or economic uncertainty continues, customers and potential customers may delay or cancellation of plans to purchase our products, governments may reduce healthcare expenditures, and other payors may reduce their reimbursement coverage or reimbursement rates. This uncertainty contributes to volatile global markets generally and may have a negative impact on the market value of our common stock. Our sensitivity to economic cycles and any related fluctuations in the businesses of our customers or potential customers could have a material adverse impact on our business and financial results. Although we are uncertain about the extent to which global financial market disruptions or a slowdown of the U.S. or Chinese economy would impact our business in the long term, there is a risk that our business, results of operations and prospects would be materially and adversely affected by any global economic downturn or the slowdown of the U.S. or Chinese economy.

If our manufacturing facilities are damaged or destroyed or production at such facilities is otherwise interrupted, our business and prospects would be negatively affected.

If our manufacturing facilities or the equipment in them is damaged or destroyed, we may not be able to quickly or inexpensively replace our manufacturing capacity or replace it at all. In the event of a temporary or protracted loss of the facilities or equipment, we might not be able to transfer manufacturing to a third party. Even if we could transfer manufacturing to a third party, the shift would likely be expensive and time-consuming, particularly since the new facility would need to comply with the necessary regulatory requirements and we would need FDA, NMPA or and other comparable regulatory agency approval before selling any drugs manufactured at that facility. Such an event could delay our clinical trials or reduce our product sales if and when we are able to successfully commercialize one or more of our drug candidates.

Any interruption in manufacturing operations at our manufacturing facilities could result in our inability to satisfy the demands of our clinical trials or commercialization. A number of factors could cause interruptions, including:

- equipment malfunctions or failures;
- malfunctions or compromise by third party actors of our technology systems;
- work stoppages;
- damage to or destruction of either facility due to natural disasters;
- regional power shortages;
- product tampering or
- terrorist activities.

Any disruption that impedes our ability to manufacture our drug candidates in a timely manner could materially harm our business, financial condition and operating results.

Currently, we maintain insurance coverage against damage to our property and equipment. However, our insurance coverage may not reimburse us, or may not be sufficient to reimburse us, for any expenses or losses we may suffer. We may be unable to meet our requirements for our drug candidates if there were a catastrophic event or failure of our manufacturing facilities or processes.

Risks Related to Government Regulation

Recently enacted and future legislation may increase the difficulty and cost for us to obtain regulatory approval of and commercialize our drug candidates and affect the prices we may obtain.

In the U.S., China and certain other jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay regulatory approval of our drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any drug candidates for which we obtain regulatory approval.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the MMA only applies to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment

limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

The Affordable Care Act, or ACA, included provisions to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the ACA of importance to our potential drug candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologics;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service Act pharmaceutical pricing program;
- requirements to report payments and other transfers of value made to physicians or teaching hospitals;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted in the U.S. since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year, starting in 2013. In January 2013, the American Taxpayer Relief Act of 2012 was enacted, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding.

We expect that the ACA, as well as other healthcare reform legislative measures that have been since adopted or may be adopted in the future, may result in more rigorous coverage criteria and an additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs. In particular, we expect that the current presidential administration and U.S. Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. Most recently, the Tax Cuts and Jobs Act was enacted, which, among other things, removes penalties for not complying with the individual mandate to carry health insurance. There is still uncertainty with respect to the impact President Trump's administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold. Such reforms could have an adverse effect on anticipated revenues from therapeutic candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop therapeutic candidates. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

Other legislative and regulatory proposals have been made to expand post-approval requirements and restrict coverage and reimbursement and sales and promotional activities, for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether agencies such as the FDA or Centers for Medicare and Medicaid Services will issue new regulations, guidance or interpretations that may impact our drug candidates. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent regulatory approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We are subject, directly or indirectly, to applicable U.S. federal and state anti-kickback, false claims laws, physician payment transparency laws, fraud and abuse laws or similar healthcare and privacy and security laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others play a primary role in the recommendation and prescription of our products and any of our product candidates for which we obtain regulatory approval. Our operations are subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act and physician payment transparency laws and regulations. These laws may impact, among other things, our proposed sales and marketing programs as well as any patient support programs we may consider offering. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, such as the federal False Claims Act which imposes criminal and civil penalties, including civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid or other third-party payors that are false or fraudulent, including failure to timely return an overpayment received from the federal government or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- provisions of HIPAA, which created new federal criminal statutes referred to as the "HIPAA All-Payor Fraud Prohibition," prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- provisions of HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;
- the federal transparency requirements under the ACA, including the provision commonly referred to as the Physician Payments Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the U.S. Department of Health and Human Services information related to all payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members unless a specific exclusion applies; and
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Additionally, we are subject to state and non-U.S. equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor. Many U.S. states have adopted laws similar to the Federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare services reimbursed by any source, not just governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement, we could be subject to penalties.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the ACA, among other things, amends the intent requirement of the federal Anti-Kickback and criminal healthcare fraud statutes. As a result of such amendment, a person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including penalties, fines and/or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U.S. government. In addition, private individuals have the ability to bring actions on behalf of the U.S. government under the Federal False Claims Act as well as under the false claims laws of several states.

Law enforcement authorities are increasingly focused on enforcing these laws, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our drug candidates outside the U.S. will also likely subject us to non-U.S. equivalents of the healthcare laws mentioned above, among other non-U.S. laws.

If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Lastly, political, economic and regulatory influences are subjecting the health care industry in the U.S. to fundamental change. Initiatives to reduce the federal budget and debt and to reform health care coverage are increasing cost-containment efforts. We anticipate that federal agencies, Congress, state legislatures, and the private sector will continue to review and assess alternative health care benefits, controls on health care spending, and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit coverage for or the amounts that federal and state governments will pay for health care products and services, which could also result in reduced demand for our products or additional pricing pressures, and limit or eliminate our spending on development projects and affect our ultimate profitability.

Our business is subject to applicable laws and regulations relating to sanctions, anti-money laundering and anti-bribery practices, the violation of which could adversely affect our operations.

We must comply with all applicable economic sanctions, anti-money laundering and anti-bribery laws and regulations of the U.S. and other foreign jurisdictions where we operate, including China. U.S. laws and regulations applicable to us include the economic trade sanctions laws and regulations administered by the U.S. Department of the Treasury's Office of Foreign Assets Control, or OFAC, as well as certain laws administered by the U.S. Department of State. Our business is also subject to anti-money laundering laws and regulations, including the Proceeds of Crime Act 2002, the Terrorism Act 2000 and the Money Laundering Regulations 2007 in the U.K., the Bank Secrecy Act of 1970, the Money Laundering Control Act of 1986 and the USA PATRIOT Act of 2001 in the U.S. and equivalent or similar legislation in the other countries where we do business. In addition, we are subject to the Foreign Corrupt Practices Act of 1977, or FCPA, and other anti-bribery laws such as the U.K. Bribery Act 2010 that generally prohibit the corrupt provision of anything of value to foreign governments and their officials and political parties for the purpose of influencing official conduct or obtaining or retaining an undue business advantage. Applicable anti-bribery laws also may prohibit commercial bribery.

We have operations, conduct clinical trials, deal with government entities, including hospitals and public health regulators, and have contracts in countries known to experience corruption and commercial bribery. Our activities in these countries, particularly China, create the risk of unauthorized payments or offers of payments by our employees, brokers or agents that could be in violation of various laws, including the FCPA, even though these parties are not always subject to our control and supervision. Corruption, extortion, bribery, pay-offs, theft and other fraudulent practices occur from time-to-time in China, where we conduct business. There is no assurance that our existing safeguards and procedures will be completely effective in ensuring compliance with such laws, and our employees, brokers or agents may engage in conduct for which we may be held responsible. Violations of the FCPA or other anti-

bribery laws may result in severe criminal or civil sanctions, and we may be subject to other liabilities, which could negatively affect our reputation, business, operating results, and financial condition.

Regulations administered by OFAC govern transactions with countries and persons subject to U.S. trade sanctions. We are also subject to U.S. Government restrictions on transactions with specific entities and individuals, including, without limitation, those set forth on the Entity List, the Specially Designated Nationals List, the Denied Persons List, the Unverified List, and the U.S. State Department's lists of debarred parties and sanctioned entities, and we may also be subject to restrictions on transactions with specific entities and individuals subject to the sanctions administered by the United Nations Security Council, the EU, Her Majesty's Treasury, or other relevant sanctions authority. These regulations prohibit us from entering into or facilitating unlicensed transactions with, for the benefit of, or in some cases involving the property and property interests of such persons, governments, or countries designated by the relevant sanctions authority under one or more sanctions regimes. Failure to comply with these sanctions and embargoes may result in material fines, sanctions or other penalties being imposed on us or other governmental investigations. In addition, various state and municipal governments, universities and other investors maintain prohibitions or restrictions on investments in companies that do business involving sanctioned countries or entities.

International economic and trade sanctions are complex and subject to frequent change, including jurisdictional reach and the lists of countries, entities, and individuals subject to the sanctions. Current or future economic and trade sanctions regulations or developments might have a negative impact on our business or reputation, and we may incur significant costs related to current, new, or changing sanctions programs, as well as investigations, fines, fees or settlements, which may be difficult to predict. In addition, companies subject to SEC reporting obligations are required under Section 13 of the Exchange Act to disclose in their periodic reports specified dealings or transactions involving Iran or other individuals and entities targeted by certain sanctions promulgated by OFAC that the reporting company or any of its affiliates engaged in during the period covered by the relevant periodic report. In some cases, Section 13 requires companies to disclose transactions even if they are permissible under U.S. law. The SEC is required to post this notice of disclosure pursuant to Section 13 on its website and report to the President and certain congressional committees regarding such filings.

On January 16, 2016, OFAC issued General License H, which authorized certain transactions relating to Iran. Pursuant to General License H, certain of our non-U.S. subsidiaries may conduct business relating to Iran. SEC guidance to date indicates that activities authorized by General License H generally are not subject to disclosure under Section 13, but should applicable SEC guidance or disclosure requirements change, or should our non-U.S. subsidiaries engage in activities subject to disclosure under Section 13, we may be required to disclose certain Iran-related transactions in future periodic reports with the SEC. Even if such activity is permitted under applicable law, disclosure could harm our reputation and have a negative impact on our business. Our non-U.S. subsidiaries also remain subject to OFAC secondary sanctions governing trade with Iran, and any violations of OFAC secondary sanctions regulations could negatively affect our reputation, business, operating results, and financial condition.

Although we have policies and controls in place that are designed to ensure compliance with these laws and regulations, it is possible that an employee or intermediary could fail to comply with applicable laws and regulations. In such event, we could be exposed to civil penalties, criminal penalties and other sanctions, including fines or other punitive actions, and the government may seek to impose modifications to business practices, including cessation of business activities in sanctioned countries, and modifications to compliance programs, which may increase compliance costs. In addition, such violations could damage our business and/or our reputation. Such criminal or civil sanctions, penalties, other sanctions, and damage to our business and/or reputation could have a material adverse effect on our financial condition and results of operations.

Any failure to comply with applicable regulations and industry standards or obtain various licenses and permits could harm our reputation and our business, results of operations and prospects.

A number of governmental agencies or industry regulatory bodies in the U.S., and in non-U.S. jurisdictions including China, impose strict rules, regulations and industry standards governing pharmaceutical and biotechnology research and development and manufacturing and marketing activities, which apply to us. Our failure to comply with such regulations could result in the termination of ongoing research or manufacturing and marketing, administrative penalties imposed by regulatory bodies or the disqualification of data for submission to regulatory authorities. This could harm our reputation, prospects for future work and operating results. For example, if we were to treat research animals inhumanely or in violation of international standards set out by the Association for Assessment and Accreditation of Laboratory Animal Care, it could revoke any such accreditation and the accuracy of our animal research data could be questioned.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from

these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of or exposure to hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage, use or disposal of biological or hazardous materials.

In addition, we may be required to incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

If we face allegations of noncompliance with the law and encounter sanctions, our reputation, revenues and liquidity may suffer, and our drugs could be subject to restrictions or withdrawal from the market.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues from our drugs. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. Additionally, if we are unable to generate revenues from our product sales, our potential for achieving profitability will be diminished and the capital necessary to fund our operations will be increased.

Risks Related to Our Doing Business in China

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

Certain of our research operations and manufacturing facilities are in China. The pharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, registration, manufacturing, packaging, licensing and marketing of new drugs. In recent years, the regulatory framework in China regarding the pharmaceutical industry has undergone significant changes, and we expect that it will continue to undergo significant changes. Any such changes or amendments may result in increased compliance costs on our business or cause delays in or prevent the successful development or commercialization of our drug candidates in China and reduce the current benefits we believe are available to us from developing and manufacturing drugs in China. Chinese authorities have become increasingly vigilant in enforcing laws in the pharmaceutical industry and any failure by us or our partners to maintain compliance with applicable laws and regulations or obtain and maintain required licenses and permits may result in the suspension or termination of our business activities in China. We believe our strategy and approach is aligned with the Chinese government's policies, but we cannot ensure that our strategy and approach will continue to be aligned.

Fluctuations in exchange rates could result in foreign currency exchange losses, which may adversely affect our financial condition, results of operations and cash flows.

We incur portions of our expenses, and may in the future derive revenues, in currencies other than U.S. dollars, in particular, the RMB. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. For example, a portion of our clinical trial activities are conducted outside of the U.S., and associated costs may be incurred in the local currency of the country in which the trial is being conducted, which costs could be subject to fluctuations in currency exchange rates. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the U.S. dollar. A decline in the value of the U.S. dollar against currencies in countries in which we conduct clinical trials could have a negative impact on our research and development costs.

The value of the RMB against the U.S. dollar and other currencies may fluctuate and is affected by, among other things, changes in political and economic conditions and the foreign exchange policy adopted by China and other non-U.S. governments. Specifically in China, on July 21, 2005, the Chinese government changed its policy of pegging the value of the RMB to the U.S. dollar. Following the removal of the U.S. dollar peg, the RMB 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 RMB and the U.S. dollar remained within a narrow band. Since June 2010, the Chinese government has allowed the RMB to appreciate slowly against the U.S. dollar again, and it has appreciated more than 10% since June 2010. In April 2012, the Chinese government announced that it would allow more RMB exchange rate fluctuation and in August 2015, China's central bank executed a 2% devaluation in the RMB. From December 31, 2016 to December 31, 2017, the RMB appreciated approximately 6.3% against the U.S. dollar. From December 31,

2017 to December 31, 2018, the RMB depreciated approximately 5.6% against the U.S. dollar. It remains unclear what further fluctuations may occur or what impact this will have on the currency and our results of operations.

It is difficult to predict how market forces or China, U.S. or other government policies may impact the exchange rate between the RMB, U.S. dollar and other currencies in the future. There remains significant international pressure on the Chinese government to adopt a more flexible currency policy, which could result in greater fluctuation of the RMB against the U.S. dollar. Substantially all of our revenues are denominated in U.S. dollars and our costs are denominated in U.S. dollars and RMB, and a large portion of our financial assets is denominated in U.S. dollars. Generally, to the extent that we need to convert U.S. dollars into RMB for our operations, appreciation of the RMB against the U.S. dollar would have an adverse effect on the RMB amount we would receive. Conversely, if we decide to convert our RMB into U.S. dollars for other business purposes, appreciation of the U.S. dollar against the RMB would have a negative effect on the U.S. dollar amount we would receive. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows.

Changes in the political and economic policies of the Chinese government may materially and adversely affect our business, financial condition and results of operations and may result in our inability to sustain our growth and expansion strategies.

A significant portion of our operations are in China. Accordingly, our financial condition and results of operations are affected to a large extent by economic, political and legal developments in China.

The Chinese economy differs from the economies of most developed countries in many respects, including the extent of government involvement, level of development, growth rate, control of foreign exchange and allocation of resources. Although the Chinese government has implemented measures emphasizing the utilization of market forces for economic reform, the reduction of state ownership of productive assets, and the establishment of improved corporate governance in business enterprises, a substantial portion of productive assets in China is still owned by the government. In addition, the Chinese government continues to play a significant role in regulating industry development by imposing industrial policies. The Chinese government also exercises significant control over China's economic growth by allocating resources, controlling payment of foreign currency-denominated obligations, setting monetary policy, regulating financial services and institutions and providing preferential treatment to particular industries or companies.

While the Chinese economy has experienced significant growth in the past three decades, growth has been uneven, both geographically and among various sectors of the economy. The Chinese government has implemented various measures to encourage economic growth and guide the allocation of resources. Some of these measures may benefit the overall Chinese economy, but may also have a negative effect on us. Our financial condition and results of operation could be materially and adversely affected by government control over capital investments or changes in tax regulations that are applicable to us and consequently have a material adverse effect on our businesses, financial condition and results of operations.

Tariffs imposed by the U.S. and those imposed in response by other countries, as well as rapidly changing trade relations, could have a material adverse effect on our business and results of operations.

Changes in U.S. and foreign governments' trade policies have resulted in, and may continue to result in, tariffs on imports into and exports from the U.S. Throughout 2018, the U.S. imposed tariffs on imports from several countries, including China. In response, China has proposed and implemented their own tariffs on certain products, which may impact our supply chain and our costs of doing business. If we are impacted by the changing trade relations between the U.S. and China, our business and results of operations may be negatively impacted. Continued diminished trade relations between the U.S. and other countries, including potential reductions in trade with China and others, as well as the continued escalation of tariffs, could have a material adverse effect on our financial performance and results of operations.

There are uncertainties regarding the interpretation and enforcement of laws, rules and regulations in China.

A portion of our operations are conducted in China through our Chinese subsidiaries, and are governed by Chinese laws, rules and regulations. Our Chinese subsidiaries are subject to laws, rules and regulations applicable to foreign investment in China. The Chinese legal system is a civil law system based on written statutes. Unlike the common law system, prior court decisions may be cited for reference but have limited precedential value.

In 1979, the Chinese government began to promulgate a comprehensive system of laws, rules and regulations governing economic matters in general. The overall effect of legislation over the past few decades has significantly enhanced the protections afforded to various forms of foreign investment in China. However, China has not developed a fully integrated legal system, and recently enacted laws, rules and regulations may not sufficiently cover all aspects of economic activities in China or may be subject to

significant degrees of interpretation by Chinese regulatory agencies. In particular, because these laws, rules and regulations are relatively new, and because of the limited number of published decisions and the nonbinding nature of such decisions, and because the laws, rules and regulations often give the relevant regulator significant discretion in how to enforce them, the interpretation and enforcement of these laws, rules and regulations involve uncertainties and can be inconsistent and unpredictable. In addition, the Chinese legal system is based in part on government policies and internal rules, some of which are not published on a timely basis or at all, and which may have a retroactive effect. As a result, we may not be aware of our violation of these policies and rules until after the occurrence of the violation.

Any administrative and court proceedings in China may be protracted, resulting in substantial costs and diversion of resources and management attention. Since Chinese administrative and court authorities have significant discretion in interpreting and implementing statutory and contractual terms, it may be more difficult to evaluate the outcome of administrative and court proceedings and the level of legal protection we enjoy than in more developed legal systems. These uncertainties may impede our ability to enforce the contracts we have entered into and could materially and adversely affect our business, financial condition and results of operations.

Substantial uncertainties exist with respect to the enactment timetable, the final version, interpretation and implementation of draft Chinese Foreign Investment Law and how it may impact the viability of our current corporate governance.

The Ministry of Commerce published a discussion draft of the proposed Foreign Investment Law in January 2015 aiming to, upon its enactment, replace the trio of existing laws regulating foreign investment in China, namely, the Sino-foreign Equity Joint Venture Enterprise Law, the Sino-foreign Cooperative Joint Venture Enterprise Law and the Wholly Foreign-invested Enterprise Law, together with their implementation rules and ancillary regulations. The draft Foreign Investment Law embodies an expected Chinese regulatory trend to rationalize its foreign investment regulatory regime in line with prevailing international practice and the legislative efforts to unify the corporate legal requirements for both foreign and domestic investments. The Ministry of Commerce has solicited comments on this draft and substantial uncertainties exist with respect to its enactment timetable, the final version, interpretation and implementation.

Among other things, the draft Foreign Investment Law expands the definition of foreign investment and introduces the principle of "actual control" in determining whether a company is considered a foreign-invested enterprise, or an FIE. The draft Foreign Investment Law specifically provides that entities established in China but "controlled" by foreign investors will be treated as FIEs, whereas an entity set up in a foreign jurisdiction would nonetheless be, upon market entry clearance by the Ministry of Commerce or its local counterparts, treated as a Chinese domestic investor provided that the entity is "controlled" by Chinese entities and/or citizens. In this connection, "control" is broadly defined in the draft law to cover the following summarized categories: (1) holding 50% of more of the shares, equity or voting rights of the subject entity; (2) holding less than 50% of the voting rights of the subject entity but having the power to secure at least 50% of the seats on the board or other equivalent decision making bodies, or having the voting power to exert material influence on the board, the shareholders' meeting or other equivalent decision making bodies or (3) having the power to exert decisive influence, via contractual or trust arrangements, over the subject entity's operations, financial matters or other key aspects of business operations. Once an entity is determined to be an FIE, it will be subject to the foreign investment restrictions or prohibitions, if the FIE is engaged in the industry listed in the "negative list" which will be separately issued by the State Council later. Unless the underlying business of the FIE falls within the negative list, which calls for market entry clearance by the Ministry of Commerce or its local counterparts, prior approval from the government authorities as mandated by the existing foreign investment legal regime would no longer be required for establishment of the FIE.

The draft Foreign Investment Law, if enacted as proposed, may also materially impact our corporate governance practice and increase our compliance costs. For instance, the draft Foreign Investment Law imposes stringent ad hoc and periodic information reporting requirements on foreign investors and the applicable FIEs. Aside from investment implementation report and investment amendment report that are required at each investment and alteration of investment specifics, an annual report is mandatory, and large foreign investors meeting certain criteria are required to report on a quarterly basis. Any company found to be non-compliant with these information reporting obligations may potentially be subject to fines and/or administrative or criminal liabilities, and the persons directly responsible may be subject to criminal liabilities.

Chinese regulations relating to investments in offshore companies by Chinese residents may subject our future Chinese-resident beneficial owners or our Chinese subsidiaries to liability or penalties, limit our ability to inject capital into our Chinese subsidiaries or limit our Chinese subsidiaries' ability to increase their registered capital or distribute profits.

The SAFE promulgated the Circular on Relevant Issues Concerning Foreign Exchange Control on Domestic Residents' Offshore Investment and Financing and Roundtrip Investment through Special Purpose Vehicles, or SAFE Circular 37, on July 4, 2014, which replaced the former circular, commonly known as SAFE Circular 75, promulgated by SAFE on October 21, 2005. SAFE Circular 37 and other SAFE rules require Chinese residents to register with local branches of SAFE or delegated commercial banks in connection with their direct establishment or indirect control of an offshore entity, for the purpose of overseas investment and financing, with such Chinese residents' legally owned assets or equity interests in domestic enterprises or offshore assets or interests,

referred to in SAFE Circular 37 as a "special purpose vehicle". SAFE Circular 37 further requires amendment to the registration in the event of any significant changes with respect to the special purpose vehicle, such as increase or decrease of capital contributed by Chinese individuals, share transfer or exchange, merger, division or other material events. In the event that a Chinese shareholder holding interests in a special purpose vehicle fails to fulfill the required registration, the Chinese subsidiaries of that special purpose vehicle may be prohibited from making profit distributions to the offshore parent and from carrying out subsequent cross-border foreign exchange activities, and the special purpose vehicle may be restricted in its ability to contribute additional capital into its Chinese subsidiary. Moreover, failure to comply with the various registration requirements described above could result in liability under Chinese law for evasion of foreign exchange controls.

We believe that certain of our shareholders are Chinese residents under SAFE Circular 37. These certain shareholders have undertaken to (i) apply to register with local SAFE branch or its delegated commercial bank as soon as possible after exercising their options and (ii) indemnify and hold harmless us and our subsidiaries against any loss suffered arising from their failure to complete the registration. We do not have control over the shareholders and our other beneficial owners and cannot assure you that all of our Chinese-resident beneficial owners have complied with, and will in the future comply with, SAFE Circular 37 and subsequent implementation rules. The failure of Chinese-resident beneficial owners to register or amend their SAFE registrations in a timely manner pursuant to SAFE Circular 37 and subsequent implementation rules, or the failure of future Chinese-resident beneficial owners of our company to comply with the registration procedures set forth in SAFE Circular 37 and subsequent implementation rules, may subject such beneficial owners or our Chinese subsidiaries to fines and legal sanctions. Furthermore, SAFE Circular 37 is unclear how this regulation, and any future regulation concerning offshore or cross-border transactions, will be interpreted, amended and implemented by the relevant Chinese government authorities, and we cannot predict how these regulations will affect our business operations or future strategy. Failure to register or comply with relevant requirements may also limit our ability to contribute additional capital to our Chinese subsidiaries and limit our Chinese subsidiaries' ability to distribute dividends to us. These risks could in the future have a material adverse effect on our business, financial condition and results of operations.

Any failure to comply with Chinese regulations regarding the registration requirements for employee share option plans may subject the Chinese plan participants or us to fines and other legal or administrative sanctions.

In February 2012, SAFE promulgated the Notices on Issues Concerning the Foreign Exchange Administration for Domestic Individuals Participating in Share Incentive Plans of Overseas Publicly-Listed Companies, commonly known as SAFE Circular 7, or the Share Option Rules, replacing earlier rules promulgated in 2007. Pursuant to these rules, Chinese residents who are granted shares or share options by companies listed on overseas stock exchanges under share incentive plans are required to (1) register with the SAFE or its local branches; (2) retain a qualified Chinese agent, which may be a Chinese subsidiary of the overseas listed company or another qualified institution selected by the Chinese subsidiary, to conduct the SAFE registration and other procedures with respect to the share incentive plans on behalf of the participants and (3) retain an overseas institution to handle matters in connection with their exercise of share options, purchase and sale of shares or interests and funds transfers. We and our executive officers and other employees who are Chinese residents and who have been granted options will be subject to these regulations. Failure to complete the SAFE registrations may subject them to fines, and legal sanctions, and may also limit our ability to contribute additional capital into our Chinese subsidiary and limit our Chinese subsidiary's ability to distribute dividends to us. We also face regulatory uncertainties that could restrict our ability to adopt additional incentive plans for our directors, executive officers and employees under Chinese law. See "Regulation—Regulations Relating to Foreign Exchange and Dividend Distribution—Share Option Rules."

We may be treated as a resident enterprise for Chinese tax purposes under the Chinese Enterprise Income Tax Law, and we may therefore be subject to Chinese income tax on our global income.

Under the Chinese Enterprise Income Tax Law and its implementing rules, both of which came into effect on January 1, 2008, enterprises established under the laws of jurisdictions outside of China with "de facto management bodies" located in China may be considered Chinese tax resident enterprises for tax purposes and may be subject to the Chinese enterprise income tax at the rate of 25% on their global income. "De facto management body" refers to a managing body that exercises substantive and overall management and control over the production and business, personnel, accounting books and assets of an enterprise. The State Administration of Taxation has issued guidance, known as Circular 82 that provides certain specific criteria for determining whether the "de facto management body" of a Chinese-controlled offshore-incorporated enterprise is located in China. Although Circular 82 only applies to offshore enterprises controlled by Chinese enterprises, not those, such as us, controlled by foreign enterprises or individuals, the determining criteria set forth in Circular 82 may reflect the State Administration of Taxation's general position on how the "de facto management body" test should be applied in determining the tax resident status of offshore enterprises, regardless of whether they are controlled by Chinese enterprises. Currently, our management is located in the U.S., and we generate a portion of our revenues within China and a portion outside China. We believe that neither we nor any of our subsidiaries outside of China is a Chinese resident enterprise for Chinese tax purposes. However, the tax resident status of an enterprise is subject to determination by the Chinese tax authorities and uncertainties remain with respect to the interpretation of the term "de facto management body". If we were to be considered a Chinese resident enterprise, we would be subject to Chinese enterprise income tax at the rate of 25% on our global income. In such case, our profitability and cash flow may be materially reduced as a result of our global income being taxed under the Chinese Enterprise Income Tax Law.

Dividends payable to our foreign investors and gains on the sale of our common stock by our foreign investors may become subject to Chinese tax law.

Under the Chinese Enterprise Income Tax Law and its implementing rules issued by the State Council, in general, a 10% Chinese withholding tax is applicable to dividends payable to investors that are non-resident enterprises that do not have an establishment or place of business in China or which have such establishment or place of business but the dividends are not effectively connected with such establishment or place of business, to the extent such dividends are derived from sources within China. Similarly, any gain realized on the transfer of shares of our common stock by such investors is also subject to Chinese tax at a current rate of 10%, subject to any reduction or exemption set forth in relevant tax treaties, if such gain is regarded as income derived from sources within China. If we are deemed a Chinese resident enterprise, dividends paid on our common stock, and any gain realized from the transfer of our common stock, would be treated as income derived from sources within China and would as a result be subject to Chinese taxation. Furthermore, if we are deemed a Chinese resident enterprise, dividends payable to individual investors who are non-Chinese residents and any gain realized on the transfer of common stock by such investors may be subject to Chinese tax at a current rate of 20%, subject to any reduction or exemption set forth in applicable tax treaties. It is unclear whether we or any of our subsidiaries established outside China are considered a Chinese resident enterprise, holders of our common stock would be able to claim the benefit of income tax treaties or agreements entered into between China and other countries or areas. If dividends payable to our non-Chinese investors or gains from the transfer of our common stock by such investors are subject to Chinese tax, the value of your investment in our common stock may decline significantly.

We and our shareholders face uncertainties with respect to indirect transfers of equity interests in Chinese resident enterprises by their non-Chinese holding companies.

Pursuant to a notice, or Circular 698, issued by the State Administration of Taxation, where a non-resident enterprise conducts an "indirect transfer" by transferring the equity interests of a Chinese resident enterprise indirectly via disposing of the equity interests of an overseas holding company, and such overseas holding company is located in a tax jurisdiction that: (1) has an effective tax rate less than 12.5% or (2) does not tax foreign income of its residents, the non-resident enterprise, being the transferor, shall report to the relevant tax authority of the Chinese resident enterprise such indirect transfer. Using a "substance over form" principle, the Chinese tax authority may disregard the existence of the overseas holding company if it lacks a reasonable commercial purpose and was established for the purpose of reducing, avoiding or deferring Chinese tax. As a result, gains derived from such indirect transfer may be subject to Chinese enterprise income tax, currently at a rate of 10%. In 2015, the State Administration of Taxation issued a circular, known as Circular 7, which replaced or supplemented certain previous rules under Circular 698. Circular 7 sets out a wider scope of indirect transfer of Chinese assets that might be subject to Chinese enterprise income tax, and more detailed guidelines on the circumstances when such indirect transfer is considered to lack a bona fide commercial purpose and thus regarded as avoiding Chinese tax. The conditional reporting obligation of the non-Chinese investor under Circular 698 is replaced by a voluntary reporting by the transferor, the transferee or the underlying Chinese resident enterprise being transferred. Furthermore, if the indirect transfer is subject to Chinese enterprise income tax, the transferee has an obligation to withhold tax from the sale proceeds, unless the transferor reports the transaction to the Chinese tax authority under Circular 7. Late payment of applicable tax will subject the transferor to default interest. Gains derived from the sale of shares by investors through a public stock exchange are not subject to the Chinese enterprise income tax pursuant to Circular 7 where such shares were acquired in a transaction through a public stock exchange. Circular 698 was abolished by an announcement promulgated by the State Administration of Taxation in October 2017 and effective from December 1, 2017, or SAT Circular 37, which, among other things, provides specific provisions on matters concerning withholding of income tax of non-resident enterprises at the source.

As newly implemented, there is uncertainty as to the application of Circular 7 and SAT Circular 37, both of which may be determined by the tax authorities to be applicable to our offshore restructuring transactions or sale of the shares of our offshore subsidiaries where non-resident enterprises, being the transferors, were involved. The Chinese tax authorities may pursue such non-resident enterprises with respect to a filing regarding the transactions and request our Chinese subsidiaries to assist in the filing. As a result, we and our non-resident enterprises in such transactions may become at risk of being subject to filing obligations or being taxed under Circular 7, and may be required to expend valuable resources to comply with Circular 7 or to establish that we and our non-resident enterprises should not be taxed under Circular 7, for our previous and future restructuring or disposal of shares of our offshore subsidiaries, which may have a material adverse effect on our financial condition and results of operations.

Restrictions on currency exchange may limit our ability to utilize our revenue effectively.

The Chinese government imposes controls on the convertibility of RMB into foreign currencies and, in certain cases, the remittance of currency out of China. A portion of our revenue may in the future be denominated in RMB. Shortages in availability of foreign currency may then restrict the ability of our Chinese subsidiaries to remit sufficient foreign currency to our offshore entities for our offshore entities to pay dividends or make other payments or otherwise to satisfy our foreign currency denominated obligations. The RMB is currently convertible under the "current account," which includes dividends, trade and service-related foreign exchange transactions, but not under the "capital account", which includes foreign direct investment and loans, including loans we may secure from our onshore subsidiaries. Currently, our Chinese subsidiaries, which are wholly-foreign owned enterprises, may

purchase foreign currency for settlement of "current account transactions," including payment of dividends to us, without the approval of SAFE by complying with certain procedural requirements. However, the relevant Chinese governmental authorities may limit or eliminate our ability to purchase foreign currencies in the future for current account transactions. Since a portion of our future revenue may be denominated in RMB, any existing and future restrictions on currency exchange may limit our ability to utilize revenue generated in RMB to fund our business activities outside of China or pay dividends in foreign currencies to our shareholders, including holders of our common stock. Foreign exchange transactions under the capital account remain subject to limitations and require approvals from, or registration with, SAFE and other relevant Chinese governmental authorities. This could affect our ability to obtain foreign currency through debt or equity financing for our subsidiaries.

Recent litigation and negative publicity surrounding China-based companies listed in the U.S. may result in increased regulatory scrutiny of us and negatively impact the trading price of our common stock and could have a material adverse effect upon our business, including our results of operations, financial condition, cash flows and prospects.

We believe that litigation and negative publicity surrounding companies with operations in China, including concerning the directors and officers of such companies, that are listed in the U.S. have negatively impacted stock prices for such companies. Various equity-based research organizations have published reports on China-based companies after examining, among other things, their corporate governance practices, related party transactions, sales practices and financial statements that have led to special investigations and stock suspensions on national exchanges, including as a result of purported whistle-blowing or leaking by employees or former employees. Any similar scrutiny of us, regardless of its lack of merit, could result in a diversion of management resources and energy, potential costs to defend ourselves against rumors, decreases and volatility in the trading price of our common stock, and increased directors and officers insurance premiums and could have a material adverse effect upon our business, including our results of operations, financial condition, cash flows and prospects.

Risks Related to Our Common Stock

The trading price of our common stock has been and is likely to continue to be volatile, which could result in substantial losses to you.

The trading price of our common stock has been and is likely to continue to be volatile and could fluctuate widely in response to a variety of factors, many of which are beyond our control. In addition, the performance and fluctuation of the market prices of other companies with a portion of their business operations located in China that have listed their securities in the U.S. may affect the volatility in the price of and trading volumes for our common stock. Some of these companies have experienced significant volatility, including significant price declines after their initial public offerings. The trading performances of these companies' securities at the time of or after their offerings may affect the overall investor sentiment towards other companies with significant China operations listed in the U.S. and consequently may impact the trading performance of our common stock.

In addition to market and industry factors, the price and trading volume for our common stock 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 or new products 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 drug candidates or preclinical and clinical development programs;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- variations in our results of operations;

- announcements about our earnings that are not in line with analyst expectations, the risk of which is enhanced because it is our policy not to give guidance on earnings;
- 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;
- announcements made by us or our competitors of new product and service offerings, acquisitions, strategic relationships, joint ventures or capital commitments;
- press reports or other negative publicity, whether or not true, about our business;
- additions to or departures of our management;
- fluctuations of exchange rates between the RMB and the U.S. dollar;
- release or expiry of lock-up or other transfer restrictions on our outstanding common stock;
- sales or perceived potential sales of additional common stock;
- sales of our common stock by us, our executive officers and directors or our shareholders in the future;
- general economic and market conditions and overall fluctuations in the U.S. equity markets;
- changes in accounting principles and
- changes or developments in China or global regulatory environment.

Any of these factors may result in large and sudden changes in the volume and trading price of our common stock. In the past, following periods of volatility in the market price of a company's securities, shareholders have often instituted securities class action litigation against that company. If we were involved in a class action suit, it could divert the attention of management, and, if adversely determined, have a material adverse effect on our financial condition and results of operations.

In addition, the stock market, in general, and small 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 common stock, regardless of our actual operating performance. Further, the current decline in the financial markets and related factors beyond our control may cause our common stock price to decline rapidly and unexpectedly.

We may be subject to securities litigation, which could result in significant legal expenses and settlement or damage awards and could divert management attention.

The price of our common stock may be volatile, and in the past companies that have experienced volatility in the market price of their common stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. We generally, to the extent permitted by law, indemnify our executive officers. Regardless, securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could harm our business.

We are currently an "emerging growth company." As a result of the reduced disclosure requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are currently an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act). For so long as we remain an emerging growth company, we are permitted and intend to rely on some of the exemptions from certain reporting requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include but are not limited to not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a non-binding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We cannot predict whether investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and the price of our common stock may be more volatile.

Because we do not expect to pay dividends in the foreseeable future, you must rely on price appreciation of our common stock for return on your investment, if any.

We intend to retain most, if not all, of our available funds and earnings to fund the development and growth of our business. As a result, we do not expect to pay any cash dividends in the foreseeable future. Therefore, you should not rely on an investment in our common stock as a source for any future dividend income.

Our board of directors has significant discretion as to whether to distribute dividends. Even if our board of directors decides to declare and pay dividends, the timing, amount and form of future dividends, if any, will depend on, among other things, our future results of operations and cash flow, our capital requirements and surplus, the amount of distributions, if any, received by us from our subsidiaries, our financial condition, contractual restrictions and other factors deemed relevant by our board of directors. Accordingly, the return on an investment in our common stock will likely depend entirely upon any future price appreciation of our common stock. There is no guarantee that our common stock will appreciate in value or even maintain its current market price. You may not realize a return on your investment in our common stock and you may even lose your entire investment in our common stock. See "Dividend Policy."

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, the market price for our common stock and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If research analysts do not establish and maintain adequate research coverage or if one or more of the analysts who covers us downgrades our common stock or publishes inaccurate or unfavorable research about our business, the market price for our common stock 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 our common stock to decline significantly.

Our directors, executive officers and principal stockholders have substantial control over us, which could limit your ability to influence the outcome of key transactions, including a change of control.

Our directors, officers and stockholders who own greater than 5% of our outstanding common stock, together with their affiliates, beneficially owned, in the aggregate, approximately 13% of our outstanding common stock based on the number shares outstanding as of March 1, 2019. As a result, these stockholders, if acting together, will be able to influence or control matters requiring approval by our stockholders, including the election of directors and the approval of mergers, acquisitions or other extraordinary transactions. In addition, these stockholders, acting together, would have the ability to control the management and affairs of our company. They may also have interests that differ from yours and may vote in a way with which you disagree and which may be adverse to your interests. This concentration of ownership may have the effect of delaying, preventing or deterring a change of control of our company, could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company and might ultimately affect the market price of our common stock.

In addition, our directors and officers as a group, will beneficially own in the aggregate approximately 19% of our outstanding common stock based on the number shares outstanding as of December 31, 2018. As such, our directors and executive officers could have considerable influence over matters such as approving a potential acquisition of us. Our directors and executive officers' investment in and position in our company could also discourage others from pursuing any potential acquisition of us, which could have the effect of depriving the holders of our common stock of the opportunity to sell their shares at a premium over the prevailing market price.

Anti-takeover provisions in our charter documents may discourage our acquisition by a third party, which could limit our shareholders' opportunity to sell their shares at a premium.

Our amended and restated certificate of incorporation and bylaws include provisions that could limit the ability of others to acquire control of our company, modify our structure or cause us to engage in change-of-control transactions. These provisions could have the effect of depriving our shareholders of an opportunity to sell their shares at a premium over prevailing market prices by discouraging third parties from seeking to obtain control in a tender offer or similar transaction.

We will continue to incur increased costs as a result of operating as a public company, and our management are required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing

requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices including our board and committee practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly.

We will continue to evaluate these rules and regulations on an ongoing basis. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters is located in Buffalo, New York, where we occupy approximately 51,000 square feet of the Conventus Center for Collaborative Medicine, which includes approximately 16,000 square feet of a formulation testing and chemistry lab under a lease that expires in July 2025 and is renewable for an additional 10 years. We also occupy approximately 15,000 square feet of office space in the Woodfield Preserve Office Center in Schaumberg, Illinois under a lease that expires in March 2027 which serves as the headquarters for our Commercial Platform. We occupy approximately 1,300 square feet of office space in Cranford, New Jersey under a lease that expires in February 2025 that serves as our clinical research headquarters. We also occupy approximately 10,672 square fee of office and lab space which represents a portion of the IC Development Centre in Hong Kong under a lease that expires in July 2019 and is renewable annually that serves as our Hong Kong headquarters and research and development center serving our Oncology Innovation Platform. We occupy approximately 6,200 square feet of office space in Taipei, Taiwan under a lease that expires in December 2022 which serves for clinical research and clinical data management.

We occupy space in facilities in Clarence and Amherst, New York and Chongqing, China which provide our manufacturing and packaging capabilities for our proprietary and 503B products and our Active Pharmaceutical Ingredient operations. In addition, pursuant to an agreement with FSMC, FSMC is funding the costs of constructing a new manufacturing facility in Dunkirk, New York, which we will lease. FSMC will retain ownership of the facility and equipment, and we will lease the facility and equipment for $1.00 per year for an initial 10-year term in exchange for meeting certain spending and employment targets in the Dunkirk area during our term in the facility. The manufacturing facility is expected to be 320,000 sq. ft. and is targeted for completion in 2020. See “Item 1.

Business — Global Supply Chain Platform — Strategic Public-Private Partnerships — New York State Partnership” for more information.

We believe that these facilities will be sufficient to meet our current needs.

Item 3. Legal Proceedings.

From time to time we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. Regardless of the outcome, litigation can have an adverse impact on us because of prosecution, defense and settlement costs, unfavorable awards, diversion of management resources and other factors.

On August 13, 2018, Athenex Pharma Solutions and Athenex Pharmaceutical Division, LLC, our wholly-owned subsidiaries, filed a complaint for declaratory judgment against Par Pharmaceuticals, Inc., Par Sterile Products, LLC and Endo Par Innovation Company, LLC (together, Par) in the United States District Court for the Western District of New York (the Court), seeking a declaratory judgment from the Court that our compounded vasopressin drug products in ready-to-use form do not infringe on patents that Par has with respect to its Vasostrict® product and that Par's patents are invalid. On October 22, 2018, Par filed a motion to dismiss the complaint on the basis that the Court does not have subject matter jurisdiction. Athenex has opposed Par's motion and that motion is fully briefed and currently pending. Par has not filed a claim for infringement of its patents in this suit but if Par's motion to dismiss Athenex's patent suit is denied and the declaratory action proceeds, Par could proceed to lodge a counterclaim for patent infringement. If such an infringement claim were brought and the Court ruled for Par, Athenex could be enjoined from further production of compounded vasopressin within in the United States and sale of compounded vasopressin in or from the United States and for payment of damages to Par for U.S. manufacture or sale of compounded vasopressin that has already taken place, which could have a material adverse effect on our business.

In addition, on August 13, 2018, Athenex Pharma Solutions, LLC and Athenex Pharmaceutical Division, LLC filed a motion to intervene and seek the dismissal of Par's complaint against the FDA and certain governmental officials in the United States District Court for the District of Columbia. Par has sought declaratory and injunctive relief against the FDA and certain governmental officials that: (i) vasopressin be delisted from Category 1 of the FDA's list of bulk drug substances under evaluation pursuant to Section 503B of the Federal Food, Drug and Cosmetic Act (FDCA), (ii) the expansion of the FDA's enforcement discretion to Category 1 substances, be enjoined; and (iii) that the FDA be enjoined from authorizing the compounding of vasopressin under Section 503B of the FDCA. Our motion to intervene was granted. Par filed a preliminary injunction motion and we and the FDA filed motions for judgment on the pleadings. This action is currently stayed. On March 4, 2019, FDA published in the Federal Register its final decision not to include vasopressin on the list of bulk drug substances for which there is a clinical need. Also, on March 4, 2019, Athenex, Inc., APS, and APD filed a complaint against FDA seeking to vacate its decision. In this case, FDA has represented to the court that "until the Court issues a decision on the merits of this action, FDA will not initiate enforcement action against Athenex based solely on Athenex's use of the bulk drug substance vasopressin to compound drugs and distribute those drugs" and the court has incorporated FDA's representation into its published order. Because of the court's order, Athenex will continue to produce and distribute compounded vasopressin during the period that the case is pending and will reevaluate its position after the court issues its decision on the merits of Athenex's lawsuit.

On August 14, 2018, we began selling compounded vasopressin injection in ready-to-use premix IV bags. If we are unsuccessful in obtaining the relief we seek in our lawsuit against FDA, or there is an adverse final determination that Par's patent is valid and infringed, we would have to abandon this revenue-generating line of business; such events could have a material adverse effect on our business, results of operations, financial condition and cash flows.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

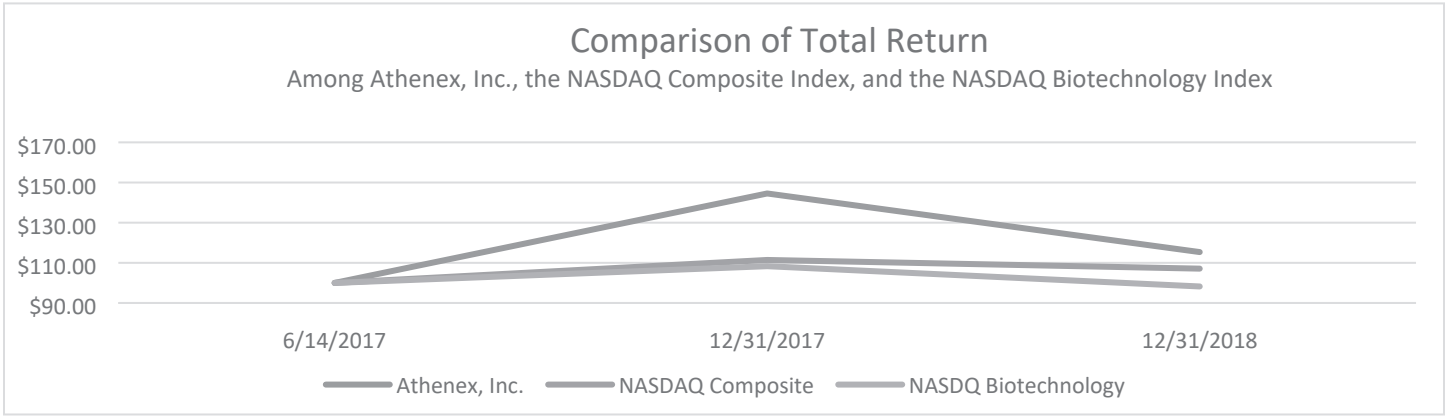
Market for our Common Stock

Our common stock has been listed on the Nasdaq Global Select Market under the symbol "ATNX" since June 14, 2017. Prior to that date, there was no public trading market for our common stock.

As of March 1, 2019, there were 133 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street by brokers and other nominees.

Stock Price Performance Graph

The graph below shows a comparison from June 14, 2017, the date on which our common stock first began trading on the Nasdaq Global Select Market, of the cumulative total return on an assumed investment of $100.00 in cash in our common stock as compared to the same investment in the NASDAQ Composite Index and the NASDAQ Biotechnology Index, all through to December 31, 2018. Such Returns are based on historical results and are not intended to suggest future performance.



Cumulative Total Return Comparison

	June 14, 2017	December 31, 2017	December 31, 2018
Athenex, Inc.	$ 100.00	$ 144.55	$ 115.36
NASDAQ Composite	$ 100.00	$ 111.44	$ 107.11
NASDAQ Biotechnology Index	$ 100.00	$ 108.33	$ 98.23

This performance graph is not deemed to be "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Exchange Act, or incorporated by reference into any of our filings under the Securities Act or the Exchange Act, except as shall be expressly set forth by specific reference to such filing.

Dividend Policy

We have never declared or paid cash or stock dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operations of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends on common stock will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions, any contractual restrictions on dividends, and other factors that our board of directors may deem relevant.

Item 6. Selected Financial Data.

The following selected statements of operations and comprehensive loss data and the cash flow data for the years ended December 31, 2018, 2017, and 2016 and the balance sheet data as of December 31, 2018 and 2017 are derived from our audited consolidated financial statements included elsewhere in this report. You should read this data together with our audited consolidated financial statements and related notes appearing elsewhere in this filing and the information under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative of our future results. Our consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States, or U.S. GAAP.

	Year Ended December 31,		
	2018	2017	2016
	(In thousands, except share and per share data)		
Statements of Operations and Comprehensive Loss Data:			
Revenue:			
Product sales, net	$ 56,394	$ 36,106	$ 19,394
License fees and consulting revenue	32,387	1,105	392
Grant revenue	319	832	765
Total revenue	89,100	38,043	20,551
Costs and operating expenses:			
Cost of sales	47,005	25,122	19,718
Research and development expenses	119,905	76,797	60,624
Selling, general, and administrative expenses	49,008	46,112	25,956
Total costs and operating expenses	215,918	148,031	106,298
Operating loss	(126,818)	(109,988)	(85,747)
Interest expense, net	1,793	5,912	1,891
Loss on derivative liability	—	15,411	533
Income tax (benefit) expense	100	85	(265)
Net loss	(128,711)	(131,396)	(87,906)
Less: net loss attributable to non-controlling interests	(11,271)	(226)	(191)
Net loss attributable to Athenex, Inc.	$ (117,440)	$ (131,170)	$ (87,715)
Net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted [(1)]	$ (1.82)	$ (2.63)	$ (2.19)
Weighted-average shares used in computing net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted [(1)]	64,590,270	49,960,925	40,120,908
Comprehensive loss	$ (117,950)	$ (130,012)	$ (88,796)

(1) See Note 15 to our audited consolidated financial statements appearing elsewhere in this report for a description of the method used to calculate basic and diluted net loss per share attributable to Athenex, Inc. common stockholders and pro forma basic and diluted net loss per share attributable to Athenex, Inc. common stockholders.

	December 31,	
	2018	2017
	(In thousands)	
Selected Balance sheet data:		
Cash and cash equivalents	$ 49,794	$ 39,284
Short-term investments	57,629	11,753
Goodwill	37,495	37,795
Working capital[(1)]	119,143	38,615
Total assets	231,095	140,413
Long-term debt	46,764	1,981
Total liabilities	102,326	49,691
Non-controlling interests	(10,586)	685
Total stockholders' equity	$ 128,769	$ 90,722

	Year Ended December 31,		
	2018	2017	2016
		(In thousands)	
Selected Cash flow data:			
Net cash used in operating activities	$ (109,387)	$ (81,512)	$ (47,870)
Net cash (used in) provided by investing activities	(48,963)	(10,018)	2,659
Net cash provided by financing activities	169,035	96,896	35,272
Net effect of foreign exchange rate changes	(175)	793	(431)
Net increase (decrease) in cash and cash equivalents	10,510	6,159	(10,370)
Cash and cash equivalents at beginning of period	39,284	33,125	43,495
Cash and cash equivalents at end of period	$ 49,794	$ 39,284	$ 33,125

(1) Working capital = total current assets - total current liabilities.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion contains management's discussion and analysis of our financial condition and results of operations and should be read together with the historical consolidated financial statements and the notes thereto included in Part II, Item 8 "Consolidated Financial Statements and Supplementary Data." This discussion contains forward-looking statements that reflect our plans, estimates and beliefs and involve numerous risks and uncertainties, including but not limited to those described in the "Risk Factors" section of this Annual Report. Actual results may differ materially from those contained in any forward-looking statements. You should carefully read "Special Note Regarding Forward-Looking Statements" and Part I, Item 1A, "Risk Factors."

Overview

We are a global clinical stage biopharmaceutical company dedicated to becoming a leader in the discovery and development of next generation drugs for the treatment of cancer. Athenex is organized around three platforms, including an Oncology Innovation Platform, a Commercial Platform and a Global Supply Chain Platform. The Company's current clinical pipeline is derived from four different platform technologies: (1) Orascovery, based on non-absorbed P-glycoprotein inhibitor, (2) Src kinase inhibition, (3) T-cell receptor-engineered T-cells (TCR-T), and (4) Arginine deprivation therapy. We have assembled a leadership team and have established global operations in the U.S. and China across the pharmaceutical value chain to execute our mission to become a global leader in bringing innovative cancer treatments to the market and improve health outcomes.

Our Orascovery platform is based on the novel P-gp pump inhibitor molecule HM30181A, which we in-licensed in 2011 from Hanmi, a major Korean pharmaceutical company focusing on research and development. The P-gp pump is a plasma membrane protein on the cells of the gut which forms a localized drug transport system and prevents oral absorption at therapeutic levels of many well-known, widely used P-gp substrate cancer chemotherapeutic drugs such as paclitaxel, irinotecan and docetaxel, limiting their current delivery to IV. These chemotherapy agents are widely used to treat multiple types of cancer. A cancer patient's inability to tolerate IV chemotherapies has limited the effectiveness of IV anti-cancer therapies. Co-administration of HM30181A with oral chemotherapies, like paclitaxel, facilitates the oral absorption of paclitaxel by blocking P-gp in intestinal cells and enables oral dosing at therapeutic blood levels which have not been successfully and safely achieved to date without the use of HM30181A. We have learned through clinical studies that this technology allows for certain active chemotherapeutic agents to be absorbed into the blood orally as compared to IV and may enable some patients to tolerate a greater number of treatment cycles and duration of treatment time. Oraxol, our leading Orascovery drug candidate is composed of HM30181A co-administered with an oral dosage form of paclitaxel. We have four other major clinical product candidates in this platform, Oratecan, Oradoxel, Oratopo and Eribulin ORA, which include HM30181A co-administered with an oral formulation of the widely used IV-administered chemotherapeutic agents, irinotecan, docetaxel, topotecan and eribulin, respectively. In light of better tolerability of standard chemotherapies delivered orally, combination with immuno-oncology and targeted anti-cancer treatments can be potentially optimized compared to current treatment paradigms.

We are rapidly advancing our lead Orascovery drug candidate, Oraxol. In January 2018, we received positive feedback from the FDA on the design of the ongoing Phase 3 trial, which indicated that if the study meets the primary endpoint with an acceptable benefit to risk profile, it could be adequate as a single comparative trial to support registration of Oraxol in the U.S. for the indication of metastatic breast cancer. Also, in January 2018, the CFDA allowed the IND application for Oraxol. Acceptance of the Oraxol IND by the CFDA allowed us to commence a clinical trial program for Oraxol in China in 2018. In February 2018, the enrollment of patients was on target for the Company to be able to conduct a second interim analysis in the Oraxol KX-ORAX-001 Phase 3 clinical trial in the third quarter of 2018. In April 2018, the FDA granted Orphan Drug status to Oraxol for the treatment of angiosarcomas. In August 2018, we received a positive recommendation by the DSMB of the second interim analysis of the Oraxol 001 Phase 3 Clinical Trial, a randomized controlled clinical trial comparing Oraxol monotherapy against IV paclitaxel monotherapy in patients with metastatic breast cancer. In October 2018, we presented encouraging efficacy and safety data of Oraxol in the treatment of metastatic breast cancer patients obtained from a Phase 2 clinical trial conducted in Taiwan at the ESMO Congress. Results from twenty-four patients with metastatic breast cancer were reported. Eleven patients (45.8%) achieved partial remission (PR), ten patients (41.7%) had stable disease (SD), and three patients had progressive disease (PD). Drug-related serious adverse events consisting of grade 4 neutropenia were observed in three patients and all recovered completely. There was no dose limiting neuropathy observed. In November 2018, we initiated a Phase 1/2 clinical study to assess the safety, tolerability and activity of Oraxol in combination with an anti-PD1 antibody (pembrolizumab) in patients with advanced solid malignancies, in collaboration with Mayo Clinic. In December 2018, our global Phase 1b clinical trial of Oraxol (oral paclitaxel plus HM30181A) plus ramucirumab (monoclonal antibody to VEGF-R2) in gastric cancer patients who failed previous chemotherapies completed the second cohort of patients. In January 2019, the target enrollment of 360 evaluable patients in the Oraxol Phase 3 clinical trial in metastatic breast cancer was achieved.

We have also developed novel small molecule compounds through our Src Kinase Inhibition research platform, which refers to novel small molecule compounds that have differentiated multiple-mechanisms of actions including: (1) the inhibition of the activity of Src Kinase and (2) the inhibition of tubulin polymerization. We believe the combination of the two MOAs provides a broader range of anti-cancer activity compared to either MOA alone. Our three key clinical product candidates in this platform are KX-01 ointments for AK, pre-cancerous lesions, skin cancers and psoriasis; KX-01 oral for solid and liquid tumors and KX-02 for GBM.

We are rapidly advancing our lead candidate in the Src Kinase Inhibition platform, KX-01 ointment, for AK. AK has an estimated prevalence of over 58 million patients and was found in approximately 14% of patients visiting dermatologists in the U.S. while GBM has an incidence of 2 to 3 per 100,000 adults per year and accounts for 52% of all primary brain tumors. If left untreated, 10-15% of AK lesions will develop into skin cancers. Our Phase 1 clinical study and data from our Phase 2 clinical study demonstrated a complete response rate of up to 43% among subjects who received treatment on their faces, with few severe LSRs reported with the dosing regimen studied. Currently available treatments are limited by severe LSRs such as vesiculation, pustulation, erosion and ulceration, with low patient compliance. We believe physicians and patients have avoided topical treatments because of the pronounced side effects of the current treatments such as ingenol mebutate, imiquimod, fluorouracil, and that an ointment product with good clinical activity and a favorable side effect profile could capture substantial new market share for treatment of this condition. Patient enrollment in two Phase 3 studies commenced in September 2017, and the enrollment was completed in February 2018. In July 2018, both of our Phase 3 pivotal efficacy studies achieved their primary endpoint of 100% clearance of AK lesions at Day 57 within the face or scalp treatment areas, with each study achieving statistical significance ($p<0.0001$). Topline results from the two Phase 3 studies were featured in a late breaker session at the 2019 American Dermatology Annual Meeting in March 2019. Results showed that 44% and 54% of patients in studies KX01-AK-003 and KX-01-AK-004, respectively, achieved 100% AK lesion clearance at Day 57. Compliance rate in these two studies was greater than 99%. There was a statistically significant clearance rate in favor of the KX-01 ointment versus the vehicle in each of the patient subgroups.

In 2018, we commenced development of two new in-licensed programs: TCR-T and Arginine Deprivation Therapy. The TCR-T immunotherapy technology harnesses and enhances the patient's own immune cells to target and eliminate cancer. It is a cell-based therapy that takes advantage of unique attributes of TCR mediated target recognition and provides a potent and selective TCR-T directed response against cancer cells. The Arginine Deprivation Therapy product, based on pegylated genetically engineered human arginase, targets cancer growth and survival by interrupting the supply of an essential amino acid, arginine, to a proportion of cancers with disrupted urea cycle. Our proprietary arginase biologic product is well suited to deplete arginine from the tumors with disrupted urea cycle, while healthy cells, capable of producing their own arginine, are largely unaffected.

Since inception, we have devoted substantially all of our resources to research and development of our lead product candidates under our Orascovery and Src Kinase Inhibition research platforms. We have incurred significant net losses since inception. As of December 31, 2018, we had an accumulated deficit of approximately $443.7 million. Our recurring losses from operations and negative cash flows from operations have raised substantial doubt regarding our ability to continue as a going concern, and as a result, our independent registered public accounting firm has noted this in the opinion they issued on our consolidated financial statements for the year ended December 31, 2018. As a result of the acquisitions of QuaDPharma in 2014 and Polymed in 2015, we started to generate revenue from those businesses. Our Commercial Platform also launched sales of generic injectable products in 2017 and 503B products in 2018. Product sales totaled $56.4 million, $36.1 million and $19.4 million for the years ended December 31, 2018, 2017 and 2016, respectively, of which $5.1 million was attributable to 503B products during 2018. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- Continue to advance our lead programs, Orascovery and Src Kinase Inhibition research platforms, through clinical development;
- Continue our current preclinical and clinical research program and development activities;
- Seek to identify additional research programs and product candidate;
- Continue investment in acquiring or in-licensing other drugs and technologies;
- Continue investment in our manufacturing facilities;
- Hire additional research, development and business personnel;
- Maintain, expand and protect our intellectual property portfolio; and
- Incur additional costs associated with operating as a public company.

In June 2017, we completed the initial public offering (IPO) of our common stock pursuant to a registration statement on Form S-1. In the IPO, we sold an aggregate of 6,900,000 shares of our common stock, which included 900,000 shares of common stock purchased by the underwriters upon the full exercise of their options to purchase additional common stock, at a price to the public of

$11.00 per share. We received aggregate cash proceeds of approximately $64.2 million from the initial public offering, net of underwriting discounts and commissions and offering expenses. Upon the IPO, convertible bonds with an aggregate principal value of $68.0 million, and a carrying value of $55.8 million, were converted into 7,727,273 shares of common stock at a 20% discount from the IPO price of $11.00 per share. On September 29, 2017, the remaining convertible bond with a principal value of $7.0 million was converted into 795,455 shares of common stock, at a 20% discount from the IPO price of $11.00 per share.

In January 2018, we completed an underwritten public offering of 4,300,000 shares of common stock at a public offering price of $15.25 per share. In addition, we granted the underwriters a 30-day option to purchase up to an additional 645,000 shares of common stock at the same price. In February 2018, the underwriters partially exercised their option to purchase an additional 465,000 shares of common stock at the offering price of $15.25 per share. Net proceeds from this public offering were - approximately $68.1 million, after deducting underwriting discounts and commissions and offering expenses paid or payable by us of approximately $4.5 million.

On June 29, 2018, we entered into a series of debt and equity financing agreements with Perceptive which provided us capital for our research and development activities and other corporate purposes. In connection with these financing agreements, we received aggregate net proceeds of $97.1 million from the issuance of 2,679,528 shares of common stock at a purchase price of $18.66 per share and from a 5-year $50.0 million senior secured loan bearing interest at a floating per annum rate equal to LIBOR (with a 2% floor) plus 9%, net of fees and offering expenses. The senior secured loan agreement requires that we maintain a minimum aggregate balance of $4.0 million in cash free and clear of all liens and that we meet certain minimum revenue targets for each quarter during which the loan is outstanding. The loan is secured by substantially all of our assets and is guaranteed by certain of our subsidiaries. Our issuance of common stock to Perceptive was exempt from registration under the Securities Act pursuant to Section 4 (a)(2), in addition, pursuant to a registration rights agreement with Perceptive, we were required to register the shares within 90 days after the closing of the transactions. The requirement was fulfilled in September of 2018. In connection with the senior secured loan agreement, the Company granted Perceptive a warrant for the purchase of 425,000 shares of common stock at a purchase price of $18.66 per share.

We have funded our operations to date primarily from the issuance and sale of our common stock, including public and private offerings, convertible bonds and debt. Cash used in operations for the year ended December 31, 2018 was $109.4 million compared with cash used in operations of $81.5 million and $47.9 million for the year ended December 31, 2017 and December 31, 2016, respectively. As of December 31, 2018, we had cash and cash equivalents of $49.8 million and short-term investments of $57.6 million.

We believe that revenue generated from our Global Supply Chain Platform and Commercial Platform will grow at a steady pace in the years ahead. However, due to both unforeseeable factors such as global political and economic changes and foreseeable factors such as market competition, revenue generated from these segments might not be sufficient to meet their operating costs. Therefore, we will continue to require substantial additional capital to continue our clinical development and potential commercialization activities. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our clinical development efforts. We cannot assure you that we will be profitable or generate positive cash flow from operating activities in the next three years, or at all.

Components of Statements of Operations

Revenue

We derive our consolidated revenue primarily from (i) the sales of API and medical devices by our Global Supply Chain Platform; (ii) the sales of generic injectable products and 503B products by our Commercial Platform; (iii) licensing and collaboration projects conducted by our Oncology Innovation Platform, which generates revenue in the form of upfront payments, milestone payments and payments received for providing research and development services for our collaboration projects and for other third parties; and (iv) grant awards from government agencies and universities for our continuing research and development efforts. The following table sets forth the components of our consolidated revenue and the amount as a percentage of total revenue for the periods indicated.

	Year ended December 31,					
	2018		2017		2016	
	(in thousands)	%	(in thousands)	%	(in thousands)	%
Product sales, net	$ 56,394	63%	$ 36,106	95%	$ 19,394	94%
Licensing fees and consulting revenue	32,387	36%	1,105	3%	392	2%
Grant revenue	319	1%	832	2%	765	4%
	$ 89,100		$ 38,043		$ 20,551	

We do not anticipate revenue being generated from sales of our product candidates under development in our Oncology Innovation Platform until we have obtained regulatory approval. We cannot assure you that we will succeed in achieving regulatory approval for our drug candidates as planned, or at all.

Cost of Sales

Along with sourcing from third party manufacturers, we manufacture our clinical products in our cGMP facility in New York and APIs at our cGMP facility in China. Cost of sales primarily includes the cost of finished products, raw materials, labor costs, manufacturing overhead expenses, reserves for expected scrap, as well as transportation costs. Cost of sales also includes depreciation expense for production equipment, changes to our excess and obsolete inventory reserves, and certain direct costs such as shipping costs, net of costs charged to customers.

Research and Development Expenses

Research and development expenses consist of the costs associated with in licensing of product candidates, conducting preclinical studies and clinical trials, activities related to regulatory filings and other research and development activities. The following table sets forth the components of our research and development expenses and the amount as a percentage of total research and development expenses for the periods indicated.

	Year Ended December 31,					
	2018		2017		2016	
	(in thousands)	%	(in thousands)	%	(in thousands)	%
Wages, benefits, and related costs	$ 17,715	15%	$ 12,190	16%	$ 19,531	32%
Clinical trial costs	49,572	41%	31,070	40%	14,438	24%
Preclinical research costs	3,699	3%	3,101	4%	5,449	33%
Drug licensing costs	38,037	32%	22,298	29%	17,690	29%
Other research and development costs	10,882	9%	8,138	11%	3,516	6%
Total research and development costs	$ 119,905		$ 76,797		$ 60,624	

Our current research and development activities mainly relate to the clinical development of the following programs:

Orascovery platform—Comprised of our in-licensed and novel P-gp inhibitor, HM30181A, that is combined with various chemotherapeutic agents and enables them to be absorbed into the blood when given orally:

- Oraxol, combining HM30181A with an oral dosage form of paclitaxel;
- Oratecan, combining HM30181A with an oral dosage form of irinotecan;
- Oradoxel, combining HM30181A with an oral dosage form of docetaxel;
- Oratopo, combining HM30181A with an oral dosage form of topotecan; and
- Oral eribulin, combining HM30181A with an oral dosage form of eribulin.

Src Kinase Inhibition platform—Targets the tyrosine kinase protein in regulating cell growth that leads to blockade of metastasis:

- KX-01 ointment, Src kinase inhibitor that is being topically administered to treat skin cancers and pre-cancers;
- KX-01 oral, Src kinase inhibitor that is being orally administered to treat certain solid and liquid tumors; and
- KX-02, Src kinase inhibitor that is orally administered to treat brain cancer, such as glioblastoma multiforme (GBM).

We expense research and development costs as incurred. We record costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment or clinical site activations. We do not allocate employee related costs, depreciation, rental and other indirect costs to specific research and development programs because these costs are deployed across multiple product programs under research and development.

We cannot determine with certainty the duration, costs and timing of the current or future preclinical or clinical studies of our drug candidates. The duration, costs, and timing of clinical studies and development of our drug candidates will depend on a variety of factors, including:

- The scope, rate of progress, and costs of our ongoing, as well as, any additional clinical studies and other research and development activities;
- Future clinical study results;
- Uncertainties in clinical study enrollment rates;
- Significant and changing government regulation; and
- The timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a drug candidate could mean a significant change in the costs and timing associated with the development of that drug candidate.

Research and development activities are central to our business model. We expect our research and development expenses to continue to increase for the foreseeable future as we continue to support the clinical trials of Oraxol, Oratecan, Oradoxel, Oratopo, oral eribulin, KX-01 ointment, KX-01 oral and KX-02, as well as initiate and prepare for additional clinical and preclinical studies. We also expect spending to increase in the research and development for API, 503B and specialty products. There are numerous factors associated with the successful commercialization of any of our drug candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will likely impact our clinical development programs and plans.

Selling, General and Administrative Expenses

Selling, general and administrative, or SG&A, expenses primarily consist of compensation, including salary, employee benefits and stock-based compensation expenses for sales and marketing personnel, and for administrative personnel that support our general operations such as, executive management, legal counsel, financial accounting, information technology, and human resources personnel. SG&A expenses also includes professional fees for legal, patents, 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. Further, we have incurred additional SG&A expenses in connection with operating as a public company, which may increase further when we are no longer able to rely on the “emerging growth company” exemption pursuant to the JOBS Act.

We anticipate that our SG&A expenses will increase in future periods to support increases in our research and development and commercialization activities. We expect these increases will likely result in increased headcount, increased share compensation charges, expanded infrastructure and increased costs for insurance. We also anticipate increases to legal, compliance, accounting and investor and public relations expenses associated with being a public company.

Interest Expense, Net

Interest expense consists primarily of interest on our long term loan and the amortization of our debt discount. Interest income consists primarily of interest generated from our cash and short term investments in U.S. treasury securities, U.S. agency securities, high rated commercial papers and corporate bonds

Loss on Derivative Liability

The loss results from re-measuring to fair value of the embedded derivative of the convertible bonds as of each balance sheet date. The related remeasurement adjustments are recognized in the consolidated statements of operations and comprehensive loss. The Company records adjustments to the fair value of the derivative liability until the conversion or repayment of the convertible bonds. The derivative liability was no longer outstanding as of December 31, 2018.

Results of Operations

Year Ended December 31, 2018 Compared to Year Ended December 31, 2017

The following table sets forth a summary of our consolidated results of operations for the years ended December 31, 2018 and 2017, together with the changes in those items in dollars and as a percentage. This information should be read together with our consolidated financial statements and related notes included elsewhere in this report. 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,			
	2018	2017	Change	
	(in thousands)	(in thousands)	(in thousands)	%
Revenue	$ 89,100	$ 38,043	$ 51,057	134%
Cost of sales	(47,005)	(25,122)	(21,883)	87%
Research and development expenses	(119,905)	(76,797)	(43,108)	56%
Selling, general, and administrative expenses	(49,008)	(46,112)	(2,896)	6%
Interest expense	(1,793)	(5,912)	4,119	-70%
Unrealized loss on derivative liability	—	(15,411)	15,411	NM
Income tax (benefit) expense	100	85	15	18%
Net loss	(128,711)	(131,396)	2,685	
Less: net loss attributable to non-controlling interests	(11,271)	(226)	(11,045)	NM
Net loss attributable to Athenex, Inc.	$ (117,440)	$ (131,170)	$ 13,730	

Revenue

Revenue for the year ended December 31, 2018 was $89.1 million, an increase of $51.1 million, or 134%, as compared to $38.0 million for the year ended December 31, 2017. The increase was primarily attributable to the $30.0 million license fees related to the collaboration agreement with Almirall, S.A. and the $2.0 million upfront license fees related to our license agreement with PharmaEssentia. Revenue from product sales also increased due to an increase in specialty product revenue of $13.2 million, an increase in 503B revenue of $5.1 million, an increase in API sales of $2.6 million, and an increase in medical device sales of $0.6 million, offset by a decrease in contract manufacturing revenue and other sales of $1.2 million and a decrease in grant revenue of $0.5 million.

Cost of Sales

Cost of sales totaled $47.0 million for the year ended December 31, 2018, an increase of $21.9 million, or 87%, as compared to $25.1 million for the year ended December 31, 2017. The increase in specialty product sales, 503B sales, and API sales increased cost of sales by $15.2 million, $3.7 million, and $3.0 million, respectively. Changes in availability of products and market demand could increase or decrease our revenue and gross profit in the future.

Research and Development Expenses

Research and development expenses totaled $119.9 million for the year ended December 31, 2018, an increase of $43.1 million, or 56%, as compared to $76.8 million for the year ended December 31, 2017. This increase was primarily due to the advancement of our clinical pipeline and additional drug licensing fees, and included the following:

- $18.6 million increase of clinical trial costs with the progression of the Phase 3 trials of KX-01 Ointment and Oraxol;
- $15.7 million increase in drug licensing fees primarily due to a $29.5 million non-cash license fee related to the purchase of T-Cell technology in connection with the establishment of Axis, of which $24.5 million related to the fair value of the IPR&D and $5.0 million related to the Company's common stock issued to XLifeSc. This was offset by a decrease in drug licensing fees paid to Hanmi, Gland and Amphastar;

- $5.4 million increase of employee salary and benefits, which was primarily attributable to hiring more research and development personnel to support our expanding research and clinical activities, including the expansion of our clinical R&D team in Taiwan;
- $2.8 million increase in general product development of 503B products as they were introduced and production was scaled-up to a commercial level and product development of our proprietary products; and
- $0.6 million increase in the cost of preclinical studies as research was performed on an oral formulation of Eribulin.

Selling, General and Administrative Expenses

Selling, general, and administrative expenses totaled $49.0 million for the year ended December 31, 2018, an increase of $2.9 million, or 6%, as compared to $46.1 million for the year ended December 31, 2017. This was primarily due to an increase in operating activities and professional fees and included the following:

- $2.9 million increase in professional fees including legal fees related to the launch of 503B products and consulting fees related to the contruction of the manufacturing facility in Dunkirk, NY; and
- $2.2 million increase in other office expenses including property and sales taxes, insurance expenses, rent and utilities, and others.

These costs were offset by a decrease in employee compensation of $1.6 million from the stock-based compensation incurred in the prior year in connection with our IPO and a decrease in marketing costs of $0.6 million.

Year Ended December 31, 2017 Compared to Year Ended December 31, 2016

The following table sets forth a summary of our consolidated results of operations for the years ended December 31, 2017 and 2016, together with the changes in those items in dollars and as a percentage. This information should be read together with our consolidated financial statements and related notes included elsewhere in this report. 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,			
	2017	2016	Change	
	(in thousands)	(in thousands)	(in thousands)	%
Revenue	$ 38,043	$ 20,551	$ 17,492	85%
Cost of sales	(25,122)	(19,718)	(5,404)	27%
Research and development expenses	(76,797)	(60,624)	(16,173)	27%
Selling, general, and administrative expenses	(46,112)	(25,956)	(20,156)	78%
Interest expense	(5,912)	(1,891)	(4,021)	NM
Loss on derivative liability	(15,411)	(533)	(14,878)	NM
Income tax (expense) benefit	(85)	265	(350)	(132)%
Net loss	(131,396)	(87,906)	(43,490)	49%
Less: net loss attributable to non-controlling interests	(226)	(191)	(35)	18%
Net loss attributable to Athenex, Inc.	$ (131,170)	$ (87,715)	$ (43,455)	

Revenue

Our revenue increased by $17.5 million, or 85%, from the year ended December 31, 2017 to the year ended December 31, 2016, primarily due to an increase from sales primarily of API, of $6.5 million, a portion of which increase was due to the inclusion of Polymed in our consolidated financial statements for the full twelve months of activity in 2016 compared to only seven months of activity in 2015.

Cost of Sales

Our cost of sales similarly increased as a result of the June 1, 2015 acquisition of Polymed. Polymed's cost of sales in 2016 was $14.2 million compared to the seven-month cost of sales of $9.2 million included in the consolidated operating results for the year ended December 31, 2015, a $5.0 million, or 54%, increase. Also, cost of sales at QuaDPharma increased by $1.8 million as a result of increased costs to support the internal production of clinical supplies.

Research and Development Expenses

Our research and development expenses increased by $16.2 million, or 27%, to $76.8 million in the year ended December 31, 2017 from $60.6 million in the year ended December 31, 2016, primarily due to the advancement of our clinical and preclinical pipeline, and included the following:

- $16.6 million increase in the costs of clinical studies, primarily for Oraxol, KX-01 Ointment, and Oratecan;
- $4.6 million increase resulting from drug licensing fees to Hanmi, Gland, and Amphastar;
- $2.7 million increase in general product development and supplies related to 503B products;
- $1.6 million increase in API research and development expenses; and
- $0.3 million increase in the amortization of license fees.

These increases were partially offset by a $7.3 million decrease in compensation expenses due to a shift in focus of certain personnel to support selling, general, and administrative functions and additional R&D stock-based compensation in 2016 associated to the accelerated forgiveness of promissory notes from officers prior to our IPO, as well as a $2.3 million decrease in preclinical study costs as our proprietary drugs entered the clinical stages.

Selling, General and Administrative Expenses

Our selling, general and administrative expenses increased by $20.2 million, or 78%, from $25.9 million in the year ended December 31, 2016 to $46.1 million in the year ended December 31, 2017 primarily due to an increase in employee compensation and selling and marketing costs, and included the following:

- $12.6 million increase in employee and executive compensation, due to the expansion of our sales and marketing force and a shift in focus of certain personnel to general and administrative functions, and stock-based compensation resulting from awards made upon the IPO;
- $3.7 million increase in office expenses, rent and utilities, and other expenses related to the expansion of our business operations;
- $3.1 million increase in selling and marketing costs related to the launch of our generic injectable products and the branding of our proprietary products; and
- $0.8 million increase in professional fees, which included accounting, legal, and consulting fees.

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 $117.4 million, $131.2 million and $87.7 million for the years ended December 31, 2018, 2017, and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of $443.7 million. Our primary use of cash is to fund research and development costs. Our operating activities used $109.4 million, $81.5 million and $47.9 million of cash during the years ended December 31, 2018, 2017, and 2016, respectively. Our principal sources of liquidity as of December 31, 2018 were cash and cash equivalents totaling of $49.8 million and short-term investments totaling $57.6 million, which are generally U.S. government or high quality investment grade corporate debt securities.

In June 2017, we sold an aggregate of 6,900,000 shares of common stock at a price of $11.00 per share for cash proceeds of $64.2 million in our IPO, net of underwriting discounts and commissions of $6.1 million and offering costs of $5.6 million. In January 2018, we completed a second public offering of 4,300,000 shares of common stock at a price of $15.25 per share; and in February 2018, the underwriters exercised their option to purchase an additional 465,000 shares of common stock at the public offering price of $15.25 per share. Net proceeds of the 2018 follow-on offering were approximately $68.1 million, after deducting underwriting discounts and commissions and offering expenses of approximately $4.6 million.

Perceptive Financing

In July 2018, the Company closed a privately placed debt and equity financing deal with Perceptive for gross proceeds of $100.0 million and received aggregate net proceeds of $97.1 million, net of fees and offering expenses. The Company entered into a 5-year senior secured loan for $50.0 million of this financing and issued 2,679,528 shares of its common stock at a purchase price of $18.66 per share for the remaining $50.0 million. The loan matures on the fifth anniversary from the closing date and bears interest at a floating per annum rate equal to LIBOR (with a floor of 2.0%) plus 9.0%. The Company is required to make monthly interest-only

payments with a bullet payment of the principal at maturity. The loan agreement contains specified financial maintenance covenants, including that we maintain a minimum aggregate balance of $4.0 million in cash free and clear of all liens and that we meet certain minimum revenue targets for each quarter during which the loan is outstanding. In addition, the loan agreement is secured by substantially all of our assets and is guaranteed by certain of our subsidiaries, including APD, AP, and APS. In connection with the loan agreement, the Company granted Perceptive a warrant for the purchase of 425,000 shares of common stock at a purchase price of $18.66 per share.

Based on our current operating plan, we expect that our existing cash, cash equivalents and short-term investments as of December 31, 2018, together with cash to be generated from our operating activities, will enable us to fund our operating expenses and capital expenditures requirements at least through the fourth quarter of 2019. We expect that our expenses will increase substantially as we continue to fund clinical development of our Orascovery and Src Kinase Inhibition research programs, new and ongoing research and development activities and working capital and other general corporate purposes. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our drug candidates, we are unable to accurately estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development and commercialization of our drug candidates.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed in the “Risk Factors” section.

Our future capital requirements will depend on many factors, including:

- our ability to generate revenue from our Commercial Platform or otherwise;
- the costs, timing and outcome of regulatory reviews and approvals;
- the ability of our drug candidates to progress through clinical development successfully;
- the initiation, progress, timings, costs and results of nonclinical studies and clinical trials for our other programs and potential drug candidates;
- the number and characteristics of the drug candidate we pursue;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property related claims;
- the extent to which we acquire or in-license other products and technologies; and
- our ability to maintain and establish collaboration arrangements on favorable terms, if at all.

We believe that the existing cash and cash equivalents and short-term investments will not be sufficient to enable us to complete all necessary development or commercially launch our proprietary drug candidates. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, and government grants. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect rights of holders of common stock. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and might require the issuance of warrants, which could potentially dilute the ownership interest of holders of common stock. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we might have to relinquish valuable rights to our technologies, future revenue streams or research programs or to grant licenses on terms that might not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we might be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market products or drug candidates that we would otherwise prefer to develop and market ourselves.

Cash kept in our subsidiaries in China is subject to Chinese regulations restricting transfer of funds overseas. Thus, our Chinese subsidiaries are restricted in their ability to transfer their net assets to us as cash dividends, loans or advances. As of December 31, 2018, we had cash and cash equivalents of approximately $3.2 million at our Chinese subsidiaries. Although we do not currently require any such dividends, loans or advances from our Chinese subsidiaries to fund our operations, should we require additional sources of liquidity in the future, such restrictions may have a material adverse effect on our liquidity and capital resources.

	Year ended December 31,		
	2018	2017	2016
		(in thousands)	
Net cash used in operating activities	$ (109,387)	$ (81,512)	$ (47,870)
Net cash (used in) provided by investing activities	(48,963)	(10,018)	2,659
Net cash provided by financing activities	169,035	96,896	35,272
Net effect of foreign exchange rate changes	(175)	793	(431)
Net increase (decrease) in cash and cash equivalents	$ 10,510	$ 6,159	$ (10,370)

Net Cash Used in Operating Activities

The use of cash in all periods presented resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital. The primary use of our cash in all periods presented was to fund our research and development, regulatory and other clinical trial costs, drug licensing costs, inventory purchases, and other expenditures related to sales, marketing and administration. Our prepaid expenses and other current assets, accounts payable and accrued expense balances in all periods presented were affected by the timing of vendor invoicing and payments.

During the year ended December 31, 2018, operating activities used $109.4 million of cash, which resulted principally from our net loss of $128.7 million, adjusted for non-cash charges of $46.8 million and partially offset by $0.4 million change in deferred income taxes. Cash used in our operating assets and liabilities was $27.1 million. Our net non-cash charges during the year ended December 31, 2018 primarily consisted of $3.3 million in depreciation and amortization expense, $11.0 million in stock-based compensation expense, $0.5 million in amortization of debt discount, and $31.5 million in license fees settled with stock.

During the year ended December 31, 2017, operating activities used $81.5 million of cash, which resulted principally from our net loss of $131.4 million, adjusted for non-cash charges of $54.0 million and partially offset by $0.3 million change in deferred income taxes. Cash used in our operating assets and liabilities was $3.8 million. Our net non-cash charges during the year ended December 31, 2017 primarily consisted of $3.7 million in depreciation and amortization expense, $14.6 million in stock-based compensation expense, $15.4 million in fair value change of derivative liabilities, $3.3 million in amortization of debt discount, $13.3 million license in fees settled with convertible bond and stock and $2.8 million in interest incurred on converted bonds.

During the year ended December 31, 2016, operating activities used $47.9 million of cash, which resulted principally from our net loss of $87.9 million, adjusted for non-cash charges of $24.7 million which was partially offset by $0.5 million change in deferred income taxes. Cash provided from our operating assets and liabilities was $15.8 million. Our net non-cash charges during the year ended December 31, 2016 primarily consisted of $2.0 million in depreciation and amortization expense, $19.5 million in stock-based compensation expense, and $1.0 million in loss on disposal of assets and impairment charges.

Net Cash (Used in) Provided by Investing Activities

In 2018, cash used in investing activities of $49.0 million was primarily attributable to $3.3 million in purchasing property and equipment, $45.5 million in net purchasing short-term investments, and $0.1 million in payment for licenses.

In 2017, cash used in investing activities of $10.0 million was primarily attributable to $5.4 million in purchasing property and equipment, $3.1 million in net purchasing short-term investments and $1.6 million in payment for licenses.

In 2016, cash provided by investing activities was $2.7 million, consisting of $5.5 million in sales of short-term investments and $1.0 million in receipt of refundable deposit, partially offset by $2.7 million in payment for licenses and $1.5 million in purchasing property and equipment.

Net Cash Provided by Financing Activities

In 2018, cash provided by financing activities was $169.0 million, consisting primarily of $123.1 million in proceeds from the sales of common stock in our 2018 follow-on offering and private placement of shares to Perceptive, $50.0 million in proceeds from the issuance of a senior secured loan with Perceptive, and $4.0 million from the exercise of options to purchase common stock, offset by $7.5 million in costs associated with the sale of stock and the issuance of debt and $0.5 million in repayment of capital lease obligations and long-term debt.

In 2017, cash provided by financing activities was $96.9 million, consisting primarily of $75.9 million in net proceeds received from the sales of common stock, $30.0 million from the issuance of convertible bonds and $2.3 million from the exercise of options to purchase common stock, offset by $10.2 million in certain offering costs and $1.2 million in repayment of capital lease obligations and long-term debt.

In 2016, cash provided by financing activities was $35.3 million, consisting primarily of $38.0 million in proceeds from the issuance of convertible bonds and $8.5 million from the sales of common stock, partially offset by $5.9 million in purchase of treasury stock, $3.2 million in payment of contingent consideration, $1.5 million in offering costs and $1.3 million in repayment of capital lease obligation and long-term debt.

Indebtedness

We had $46.8 million and $2.0 million of debt as of December 31, 2018 and 2017, respectively. This consisted of three seller promissory notes that were negotiated as part of the Polymed acquisition and paid in full during 2018, a mortgage under CDE, capital lease obligations, and a senior secured loan entered into with Perceptive during 2018.

The Polymed promissory notes matured on June 1, 2018, and had a 6% stated interest rate during their 36-month term. The outstanding principal on the Polymed promissory notes was $0 and $0.5 million as of December 31, 2018 and December 31, 2017, respectively.

In connection with the acquisition of CDE, we assumed a mortgage liability associated with the manufacturing plant asset in China. The mortgage payments extend through July 30, 2019. The remaining mortgage principal payment of $0.8 million is due in 2019.

In 2018, the Company issued a senior secured loan with a principal value of $50.0 million and a maturity date of June 30, 2023 to Perceptive. The loan bears interest at a floating per annum rate equal to LIBOR (with a floor of 2.0%) plus 9.0%. The Company is required to make monthly interest-only payments with a bullet payment of the principal at maturity. The loan agreement contains specified financial maintenance covenants, including that we maintain a minimum aggregate balance of $4.0 million in cash free and clear of all liens and that we meet certain minimum revenue targets for each quarter during which the loan is outstanding. In addition, the loan agreement is secured by substantially all of our assets and is guaranteed by certain of our subsidiaries, including APD, AP, and APS.

Capital Expenditures

Our liquidity position and capital requirements are subject to a number of factors. For example, our cash inflow and outflow may be impacted by the following:

- Our ability to generate revenue; and
- Fluctuations in working capital.

Our primary short term capital needs, which are subject to change, include expenditures related to:

- Continuous support of the development and research of our proprietary drug products;
- Build out of our new API plant in China and improvements in our existing manufacturing capacity and efficiency;
- New research and product development efforts; and
- Support of our commercialization efforts related to our current and future products.

Although we believe the foregoing items reflect our most likely uses of cash in the short term, we cannot predict with certainty all of our short-term cash uses or the timing or amounts of cash used. If cash generated from operations is insufficient to satisfy our working capital and capital expenditure requirements, we may be required to sell additional equity or debt securities or obtain credit financing. This capital may not be available on satisfactory terms, if at all. Furthermore, any additional equity financing may be dilutive to our stockholders, and debt financing, if available, may include restrictive covenants.

In 2015, we entered into two public-private partnerships. New York State is investing in a 315,000 square foot, ISO Class 5 high potency oral and sterile injectable pharmaceutical manufacturing facility, which will be built in Dunkirk, New York. The estimated cost of the facility will be approximately $200 million, and we will be able to occupy the space on concessionary terms. In Chongqing, China, funded by the Banan District government, a GMP API and a GMP pharmaceutical manufacturing plant will be built, which we

will occupy on concessionary terms. We plan to utilize these plants to manufacture API and the finished drugs in which these API will be used. We do not have significant construction period risks. New York State and the Banan District governments will each fund a majority of the construction costs and hold ownership of the manufacturing and office facilities. In addition, in July 2017 we entered into a 20-year payment in-lieu of tax agreement for the construction of our Dunkirk facility with the CCIDA, valued at approximately $9.1 million. In December 2017, we entered into an agreement with M+W U.S., Inc., or M+W, whereby M+W will be responsible for the design and construction of the Dunkirk facility at a cost estimated between $205 million and $210 million, of which up to $200 million will be paid by a grant from the State of New York, with the remaining amount being paid by us. We are also responsible for the cost of furnishing the facility. Payments under the December 2017 agreement will be made to M+W over time based upon completion of certain milestones under the agreement, and ESD must approve any payment from the grant funds. Construction of the Dunkirk manufacturing facility has begun and is expected to be completed in 2020. Contruction of the API manufacturing facility is expected to be completed in 2019.

Future Capital Requirements

We believe that our existing cash and cash equivalents and short-term investments, together with cash to be generated from our operating activities, will be sufficient to fund our current operating plans through at least the end of 2019. To the extent that we raise additional capital through future equity financings, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through the issuance of debt securities, these securities could contain covenants that would restrict our operations. There can be no assurance that such additional financing, if available, can be obtained on terms acceptable to us. If we are unable to obtain such additional financing, we would need to reevaluate our future operating plans.

Inflation

Inflationary factors, such as increases in our cost of sales and SG&A expenses, may adversely affect our operating results. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, a high rate of inflation in the future may have an adverse effect on our ability to maintain and increase our net income and SG&A expenses as a percentage of our revenue if the selling prices of our products do not increase as much or more than these increased costs.

Contractual Obligations

A summary of our contractual obligations as of December 31, 2018 is as follows:

	Payments Due by Period				Total Amounts Committed
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	
			(in thousands)		
Operating leases	$ 2,943	$ 4,506	$ 3,577	$ 3,099	$ 14,125
Long-term debt	778	—	50,000	—	50,778
Accrued licensing fees	4,828	—	—	—	4,828
Capital leases	182	401	21	—	604
	$ 8,731	$ 4,907	$ 53,598	$ 3,099	$ 70,335

The operating leases include (1) the rental of our global headquarters in the Conventus Center for Collaborative Medicine in Buffalo, NY and (2) the rental of our research and development facility in the IC Development Centre in Hong Kong and (3) the rental of the Commercial Platform headquarters in Chicago, IL and (4) the rental of our clinical research headquarters in Cranford, NJ and (5) the rental of our clinical data management center in Taipei, Taiwan and (6) the rental of our Global Supply Chain distribution office in Houston, TX and (7) the rental of our Global Supply Chain API manufacturing facility in Chongqing, China and (8) the rental of other facilities and equipment located mainly in Buffalo, NY. These locations represent $8.5 million, $0.4 million, $2.4 million, $0.3 million, $0.7 million, $0.4 million, $1.0 million, and $0.4 million, respectively, of the total amounts committed.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities and the disclosure of contingent assets and liabilities at the date of our financial statements and the reported amounts of revenue and expenses during the periods. We evaluate our estimates and judgments on an ongoing basis, including but not limited to, estimating the useful lives of long-lived assets, assessing the impairment of long-lived assets, stock-based compensation expenses, and the realizability of deferred income tax assets. We base

our estimates on historical experience, known trends and events, contractual milestones and other various factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Changes in the accounting estimates are likely to occur from period to period. Actual results could be significantly different from these estimates. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgment and estimates.

Revenue Recognition

1. Oncology Innovation Platform

License fees and consulting revenue

The Company out-licenses certain of its intellectual property ("IP") and provides related consulting services to pharmaceutical companies in specific territories that allow the customer to use, develop, commercialize, or otherwise exploit the licensed IP. In accordance with Accounting Standards Codification Topic 606, the Company determines each of its performance obligations under the agreements and allocates the transaction price to those obligations accordingly. The Company's obligations may include delivering the license of IP (if the license is deemed to be distinct), performing continued research and development on the licensed IP, manufacturing the licensed product, or maintaining the legal protection for the licensed IP throughout the duration of the agreement, among other obligations. Most of the Company's revenue from its out-licensing is recognized at a point-in-time when the performance obligation is satisfied.

Grant revenue

The Company receives grant award funding to support its continuing research and development efforts. The Company considers these grants to be operating revenue as they support the Company's primary operating activities. Revenue is recognized when the underlying performance obligation is satisfied, which is generally when all grant eligibility criteria are met at a point-in-time.

2. Global Supply Chain Platform

The Company's Global Supply Chain Platform manufactures API for use internally in its research and development and clinical studies and for sale to pharmaceutical customers globally. API revenue earned by the Global Supply Platform is recognized when the Company has satisfied its performance obligation, which is the shipment or delivery of drug product. The underlying contracts for these sales are generally purchase orders and the Company recognizes revenue at a point-in-time.

3. Commercial Platform

The Company's Commercial Platform generates revenue by distributing specialty products through independent pharmaceutical wholesalers. The wholesalers then sell to an end-user, normally a hospital, alternative healthcare facility, or an independent pharmacy, at a lower price previously established by the end-user and the Company. Sales are initially recorded at the list price sold to the wholesaler. Because these prices will be reduced for the end-user, the Company records a contra asset in accounts receivable and a reduction to revenue at the time of the sale, using the difference between the list price and the estimated end-user contract price. Upon the sale by the wholesaler to the end-user, the wholesaler will chargeback the difference between the original list price and price at which the product was sold to the end-user and such chargeback is offset against the initial estimated contra asset. The significant estimates inherent in the initial chargeback provision relate to wholesale units pending chargeback and to the ultimate end-user contract selling price. The Company bases the estimate for these factors on product-specific sales and internal chargeback processing experience, as well as estimated wholesaler inventory stocking levels. As of December 31, 2018 and 2017, the Company's chargebacks and other deductions totaled $11.8 million and $3.3 million, respectively, included as a reduction of accounts receivable. The Company's total expenses for chargebacks and other deductions was $33.5 million and $9.8 million for the years ended December 31, 2018 and 2017, respectively.

The Company offers cash discounts, which approximate 2% of the gross sales price, as an incentive for prompt customer payment, and, consistent with industry practice, the Company's return policy permits customers to return products within a window of time before and after the expiration of product dating. The Company expects that its wholesale customers will make prompt payments to take advantage of the cash discounts, and expects customers to use their right of return. Therefore, at the time of sale, product revenue and accounts receivable are reduced by the full amount of the discount offered and the return expected. The Company considers payment performance and historical return rates and adjusts the accrual to reflect actual experience. As of December 31,

2018 and December 31, 2017, the Company's accrual for cash discounts and return accrual included as a reduction of accounts receivable were not material to the consolidated financial statements.

The Company also offers contractual allowances, generally rebates or administrative fees, to certain wholesale customers, group purchasing organizations ("GPOs"), and end-user customers, consistent with pharmaceutical industry practices. Settlement of rebates and fees may generally occur from one to five months from date of sale. The Company provides a provision for contractual allowances at the time of sale based on the historical relationship between sales and such allowances. Contractual allowances are reflected in the consolidated financial statements as a reduction of revenue and as accrued expenses.

The Company estimates the variable transaction price at the time of the sale and recognizes revenue when the performance obligation is satisfied. The underlying contracts for these sales are generally purchase orders and the Company recognizes revenue at a point-in-time.

Research and Development Expenses

Research and development expenses represent costs associated with developing our proprietary drug candidates, our collaboration agreements for such drugs, and our ongoing clinical studies.

Clinical trial costs are a significant component of our research and development expenses. We have a history of contracting with third parties that perform various clinical trial activities on our behalf in the ongoing development of our drug candidates. Expenses related to clinical trials are accrued based on our estimates of the actual services performed by the third parties for the respective period. If the contracted amounts are revised or the scope of a contract is revised, we will modify the accruals accordingly on a prospective basis and will do so in the period in which the facts that give rise to the revision become reasonably certain.

Goodwill

Goodwill is recorded when the purchase price of an acquisition exceeds the fair value of the net tangible and identified intangible assets acquired. Goodwill is allocated to our reporting units based on the relative expected fair value provided by the acquisition. Reporting units may be operating segments as a whole or an operation one level below an operating segment, referred to as a component, or a combination thereof.

We perform an annual impairment assessment on October 1, or more frequently if indicators of potential impairment exist, to determine whether it is more likely than not that the fair value of a reporting unit is less than its carrying value. Impairment test approaches with a weighting of the Discounted Cash Flow (income approach) and Guideline Public Company method (market approach) are utilized. Weighting will most likely be greater for the market approach given the lack of historical results to be able to rely significantly on financial projections. The performance of the goodwill impairment test involves a two-step process. The first step is to estimate the fair value of each reporting unit and compare the fair value to the carrying value. For reporting units in which the step-one impairment assessment concludes that it is more likely than not that the fair value of the reporting unit exceeds the carrying value of the net assets assigned to that reporting unit, goodwill is not considered to be impaired and we do not perform additional analysis. For reporting units in which the step-one impairment assessment concludes that it is more likely than not that the carrying value of the net assets assigned to that reporting unit exceeds the fair value of the reporting unit, we must perform the second step, which is to measure the amount of impairment. We then record the impairment loss equal to the difference between the fair value and the carrying value. None of our reporting units are at risk of failing step one of the impairment test, as the fair value is substantially in excess of the carrying value for each reporting unit.

Off Balance Sheet Arrangements

We do not maintain any off balance sheet partnerships, arrangements, or other relationships with unconsolidated entities or others, often referred to as structured finance or special purpose entities, which are established for the purpose of facilitating off balance sheet arrangements or other contractually narrow or limited purposes.

Impact of Recently Issued Accounting Standards

In the normal course of business, we evaluate all new accounting pronouncements issued by the FASB, SEC, or other authoritative accounting bodies to determine the potential impact they may have on our Consolidated Financial Statements. Refer to Note 2 "Summary of Significant Accounting Policies" of the Notes to Consolidated Financial Statements contained in Item 8 of this report for additional information about these recently issued accounting standards and their potential impact on our financial condition or results of operations.

Jumpstart Our Business Startups Act of 2012 (JOBS Act)

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Subject to certain conditions, as an emerging growth company, we may rely on certain of these exemptions, including without limitation, (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an emerging growth company until the earlier of (a) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (b) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering in June 2017; (c) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (d) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk.

Foreign Currency Exchange Risk

A significant portion of our business is located outside the United States and, as a result, we generate revenue and incur expenses denominated in currencies other that the U.S. dollar, a majority of which is denominated in RMB. In 2018, 2017, and 2016, approximately 2%, 7% and 7%, respectively, of our sales, excluding intercompany sales, were denominated in foreign currencies. As a result, our revenue can be significantly impacted by fluctuations in foreign currency exchange rates. We expect that foreign currencies will represent a lower percentage of our sales in the future due to the anticipated growth of our U.S. business. Our international selling, marketing, and administrative costs related to these sales are largely denominated in the same foreign currencies, which somewhat mitigates our foreign currency exchange risk rate exposure.

Currency Convertibility Risk

A portion of our revenues and expenses, and a portion of our assets and liabilities are denominated in RMB. On January 1, 1994, the Chinese government abolished the dual rate system and introduced a single rate of exchange as quoted daily by the People's Bank of China, or PBOC. However, the unification of exchange rates does not imply that the RMB may be readily convertible into U.S. dollars or other foreign currencies. All foreign exchange transactions continue to take place either through the PBOC or other banks authorized to buy and sell foreign currencies at the exchange rates quoted by the PBOC. Approvals of foreign currency payments by the PBOC or other institutions require submitting a payment application form together with suppliers' invoices, shipping documents and signed contracts.

Additionally, the value of the RMB is subject to changes in central government policies and international economic and political developments affecting supply and demand in the Chinese foreign exchange trading system market.

Interest Rate Sensitivity

We had cash and cash equivalents of $49.8 million and short-term investments of $57.6 million as of December 31, 2018, which consisted primarily of U.S. government or high quality investment grade corporate debt securities. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the instruments in our portfolio, a sudden change in market interest rates would not be expected to have a material impact on our consolidated financial condition or results of operations. We do not believe that our cash or cash equivalents have significant risk of default or illiquidity.

We had a 5-year $50.0 million loan agreement with Perceptive, which closed on July 3, 2018, bearing interest at a floating per annum rate equal to1-Month LIBOR (with a floor of 2%) plus 9%. If 1-Month LIBOR increased by 1%, we would be required to pay Perceptive an additional $0.5 million in interest annually. If 1-Month LIBOR decreased by 1%, we would be required to pay Perceptive $0.5 million less in interest annually.Thus, a change in the short-term interest rate environment (especially a material change) could have a material adverse effect on our business, financial condition, cash flows and results of operations and could cause the market value of our common shares to decline. As of December 31, 2018, we did not have any outstanding interest rate swap contracts.

Credit Risk

We had cash and cash equivalents of $49.8 million, $39.3 million and $33.1 million and marketable securities of $57.6 million, $11.8 million and $8.6 million at December 31, 2018, 2017, and 2016, respectively. Substantially all of our bank deposits are in major financial institutions, which we believe are of high credit quality. The primary objectives of our investment activities are to preserve principle, provide liquidity and maximize income without significant increasing risk.

We make periodic assessments of the recoverability of trade and other receivables and amounts due from related parties. Our historical experience in collection of receivables falls within the recorded allowances, and we believe that we have made adequate provision for uncollectible receivables.

Item 8. Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Athenex, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Athenex, Inc. and subsidiaries (the "Company") as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2018, and the related notes and the schedule listed in the Index at Item 15 (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and negative cash flows from operations that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error of fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Williamsville, New York
March 11, 2019

We have served as the Company's auditor since 2015.

ATHENEX, INC. AND SUBSIDIARIES
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	December 31, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 49,794	$ 39,284
Short-term investments	57,629	11,753
Accounts receivable, net of chargebacks and other deductions of $13,101 and $3,711, respectively, and allowance for doubtful accounts of $9 and $84, respectively	12,951	8,468
Inventories	28,787	16,561
Prepaid expenses and other current assets	21,658	7,692
Total current assets	170,819	83,758
Property and equipment, net	11,447	9,651
Goodwill	37,495	37,795
Intangible assets, net	10,848	8,572
Deferred income tax asset	486	121
Other long-term assets	—	516
Total assets	$ 231,095	$ 140,413
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 12,997	$ 16,659
Accrued expenses	37,718	26,978
Current portion of long-term debt - related parties	—	491
Current portion of long-term debt	961	1,015
Total current liabilities	51,676	45,143
Long-term liabilities:		
Deferred compensation	2,825	2,313
Deferred rent	2,022	1,760
Capital lease obligation	422	475
Long-term debt	45,381	—
Total liabilities	102,326	49,691
Commitments and contingencies (Note 20)		
Stockholders' equity:		
Common stock, par value $0.001 per share, 250,000,000 shares authorized at December 31, 2018 and 2017; 68,668,986 and 59,894,362 shares issued at December 31, 2018 and 2017, respectively; 66,996,066 and 58,221,442 shares outstanding at December 31, 2018 and 2017, respectively	69	60
Additional paid-in capital	591,064	423,805
Accumulated other comprehensive loss	(656)	(146)
Accumulated deficit	(443,716)	(326,276)
Less: treasury stock, at cost; 1,672,920 shares at December 31, 2018 and 2017	(7,406)	(7,406)
Total Athenex, Inc. stockholders' equity	139,355	90,037
Non-controlling interests	(10,586)	685
Total stockholders' equity	128,769	90,722
Total liabilities and stockholders' equity	$ 231,095	$ 140,413

The accompanying notes are an integral part of these consolidated financial statements.

ATHENEX, INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share data)

	Year Ended December 31,		
	2018	2017	2016
Revenue:			
Product sales, net	$ 56,394	$ 36,106	$ 19,394
License fees and consulting revenue	32,387	1,105	392
Grant revenue	319	832	765
Total revenue	89,100	38,043	20,551
Costs and operating expenses:			
Cost of sales	47,005	25,122	19,718
Research and development expenses	119,905	76,797	60,624
Selling, general, and administrative expenses	49,008	46,112	25,956
Total costs and operating expenses	215,918	148,031	106,298
Operating loss	(126,818)	(109,988)	(85,747)
Interest expense, net	1,793	5,912	1,891
Loss on derivative liability	—	15,411	533
Loss before income tax (benefit) expense	(128,611)	(131,311)	(88,171)
Income tax (benefit) expense	100	85	(265)
Net loss	(128,711)	(131,396)	(87,906)
Less: net loss attributable to non-controlling interests	(11,271)	(226)	(191)
Net loss attributable to Athenex, Inc.	$ (117,440)	$ (131,170)	$ (87,715)
Unrealized gain (loss) on investment, net of income taxes	15	(26)	(33)
Foreign currency translation adjustment, net of income taxes	(525)	1,184	(1,048)
Comprehensive loss	$ (117,950)	$ (130,012)	$ (88,796)
Net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted (Note 15)	$ (1.82)	$ (2.63)	$ (2.19)
Weighted-average shares used in computing net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted (Note 15)	64,590,270	49,960,925	40,120,908

The accompanying notes are an integral part of these consolidated financial statements.

ATHENEX, INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands, except share data)

	Common Stock		Additional paid-in capital	Accumulated deficit	Accumulated other comprehensive loss	Treasury Stock		Total Athenex, Inc. stockholders' equity	Non-controlling interests	Total stockholders' equity
	Shares	Amount				Shares	Amount			
Balance at January 1, 2016	40,330,124	$ 40	$ 206,679	$ (107,391)	$ (223)	(422,328)	$ (1,545)	$ 97,560	$ 484	$ 98,044
Issuance of common stock	1,133,332	1	8,499	—	—	—	—	8,500	—	8,500
Issuance of common stock in connection with satisfaction of contingent consideration	315,810	1	2,842	—	—	—	—	2,843	—	2,843
Stock-based compensation cost	—	—	10,977	—	—	—	—	10,977	—	10,977
Vesting of restricted stock	50,000	—	8,534	—	—	—	—	8,534	—	8,534
Repurchase of common stock	—	—	—	—	—	(1,234,592)	(5,861)	(5,861)	—	(5,861)
Stock options and warrants exercised	513,440	—	50	—	—	—	—	50	—	50
Non-controlling interests	—	—	—	—	—	—	—	—	569	569
Net loss	—	—	—	(87,715)	—	—	—	(87,715)	(191)	(87,906)
Other comprehensive loss, net of tax	—	—	—	—	(1,081)	—	—	(1,081)	—	(1,081)
Balance at December 31, 2016	42,342,706	42	237,581	(195,106)	(1,304)	(1,656,920)	(7,406)	33,807	862	34,669
Sale of common stock, net of costs and discounts of $11,706	6,900,000	7	64,187	—	—	—	—	64,194	—	64,194
Conversion of bonds	8,522,728	9	98,920	—	—	—	—	98,929	—	98,929
Stock-based compensation cost	400,000	—	12,431	—	—	—	—	12,431	—	12,431
Research and development licensing fee satisfied with stock	568,182	1	6,249	—	—	—	—	6,250	—	6,250
Vesting of restricted stock	421,982	—	2,160	—	—	—	—	2,160	—	2,160
Stock options and warrants exercised	738,764	1	2,277	—	—	—	—	2,278	—	2,278
Repurchase of common stock	—	—	—	—	—	(16,000)	—	—	—	—
Non-controlling interests	—	—	—	—	—	—	—	—	49	49
Net loss	—	—	—	(131,170)	—	—	—	(131,170)	(226)	(131,396)
Other comprehensive income, net of tax	—	—	—	—	1,158	—	—	1,158	—	1,158
Balance at December 31, 2017	59,894,362	60	423,805	(326,276)	(146)	(1,672,920)	(7,406)	90,037	685	90,722
Sale of common stock, net of costs and discounts of $5,518	7,486,261	7	117,609	—	—	—	—	117,616	—	117,616
Issuance of warrant	—	—	3,140	—	—	—	—	3,140	—	3,140
Stock-based compensation cost	—	—	10,003	—	—	—	—	10,003	—	10,003
Vesting of restricted stock	240,000	1	1,007	—	—	—	—	1,008	—	1,008
Stock options and warrants exercised	673,230	1	3,955	—	—	—	—	3,956	—	3,956
Research and development licensing fee satisfied with stock	375,133	—	31,545	—	—	—	—	31,545	—	31,545
Net loss	—	—	—	(117,440)	—	—	—	(117,440)	(11,271)	(128,711)
Other comprehensive loss, net of tax	—	—	—	—	(510)	—	—	(510)	—	(510)
Balance at December 31, 2018	68,668,986	$ 69	$ 591,064	$ (443,716)	$ (656)	(1,672,920)	$ (7,406)	$ 139,355	$ (10,586)	$ 128,769

The accompanying notes are an integral part of these consolidated financial statements.

ATHENEX, INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year ended December 31,		
	2018	**2017**	**2016**
Cash flows from operating activities:			
Net loss	$ (128,711)	$ (131,396)	$ (87,906)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	3,269	3,673	2,026
Stock-based compensation expense	11,011	14,591	19,511
Change in fair value of contingent consideration	—	—	53
Loss on derivative liability	—	15,411	533
Amortization of debt discount	514	3,349	889
Deferred rent expense	262	856	649
Net loss on disposal of assets and impairment charges	236	80	1,034
Research and development license fees settled with convertible bond and stock	31,545	13,250	—
Interest incurred on converted bonds	—	2,759	—
Deferred income taxes	(365)	(327)	(491)
Changes in operating assets and liabilities:			
Receivables, net	(4,483)	(5,691)	1,055
Prepaid expenses and other assets	(13,966)	(4,537)	(359)
Inventories	(12,226)	(12,321)	(984)
Accounts payable and accrued expenses	3,527	18,791	16,120
Net cash used in operating activities	(109,387)	(81,512)	(47,870)
Cash flows from investing activities:			
Proceeds from sale of property and equipment	—	—	335
Purchase of property and equipment	(3,321)	(5,440)	(1,487)
Receipts of refundable deposit	—	110	1,000
Payments for licenses	(110)	(1,550)	(2,700)
Purchases of short-term investments	(113,259)	(55,282)	(9,750)
Sale of short-term investments	67,727	52,144	15,261
Net cash (used in) provided by investing activities	(48,963)	(10,018)	2,659
Cash flows from financing activities:			
Proceeds from sale of stock	123,134	75,900	8,500
Proceeds from issuance of convertible bonds	—	30,000	38,000
Proceeds from issuance of debt	50,000	—	—
Costs incurred related to the sale of stock	(5,518)	(10,168)	(1,537)
Costs incurred related to the issuance of debt	(1,993)	—	—
Proceeds from exercise of stock options	3,956	2,278	50
Investment from non-controlling interest	—	49	569
Repayment of capital lease obligations and long-term debt	(544)	(1,163)	(1,265)
Payment of contingent consideration	—	—	(3,184)
Purchase of treasury stock	—	—	(5,861)
Net cash provided by financing activities	169,035	96,896	35,272
Net increase (decrease) in cash and cash equivalents	10,685	5,366	(9,939)
Cash and cash equivalents, beginning of period	39,284	33,125	43,495
Effect of exchange rate changes on cash and cash equivalents	(175)	793	(431)
Cash and cash equivalents, end of period	$ 49,794	$ 39,284	$ 33,125
Supplemental cash flow disclosures			
Interest paid	$ 2,977	$ 109	$ 144
Income taxes paid	$ 464	$ 244	$ 329
Non-cash investing and financing activities:			
Accrued purchases of property and equipment	$ 340	$ 156	$ 348
Cost of equity raise in accounts payable and accrued expenses	$ —	$ 188	$ 264
Convertible bond issued in lieu of licensing cash payment	$ —	$ 7,000	$ —
Common stock issued in lieu of licensing cash payment	$ 31,545	$ 6,250	$ —
Common stock issued upon the conversion of bonds and derivative liability	$ —	$ 98,929	$ —
Property and equipment financed under capital lease	$ —	$ 688	$ —
Accrued purchases of licenses	$ 4,175	$ —	$ 343
Stock issued in connection with the acquisition of Polymed	$ —	$ —	$ 2,500

The accompanying notes are an integral part of these consolidated financial statements.

1. COMPANY AND NATURE OF BUSINESS

Description of Business

Athenex, Inc. (the "Company" or "Athenex"), originally under the name Kinex Pharmaceuticals LLC ("Kinex"), formed in November 2003, commenced operations on February 5, 2004, and operated as a limited liability company until it was incorporated in the State of Delaware under the name Kinex Pharmaceuticals, Inc. on December 31, 2012. The Company changed its name to Athenex, Inc. on August 26, 2015.

Athenex is a global biopharmaceutical company dedicated to the discovery, development and commercialization of novel therapies for the treatment of cancer. The Company's mission is to improve the lives of cancer patients by creating more effective, safer and tolerable treatments. The Company has generated its clinical product candidates through its Orascovery and Src Kinase Inhibition research platforms, which are based on their understanding of human absorption biology and novel kinase binding selection, respectively. The Company has assembled a leadership team and have established global operations in the U.S. and China across the pharmaceutical value chain to execute its mission to become a global leader in bringing innovative cancer treatments to the market and improve health outcomes. The Company's primary activities since commencement have been conducting research and development internally and through corporate collaborators, in-licensing and out-licensing pharmaceutical compounds and technology, and conducting clinical trials.

As of December 31, 2018, the Company had cash and cash equivalents of $49.8 million and short-term investments of $57.6 million. The Company expects that its existing cash and cash equivalents and short-term investments, together with cash to be generated from the operating activities, are sufficient to fund our current operating plans through at least the end of 2019.

Significant Risks and Uncertainties

The Company has incurred operating losses and negative cash flows from operations since its inception and, as a result, as of December 31, 2018 and 2017 had an accumulated deficit of $443.7 million and $326.3 million, respectively. Operations have been funded primarily through the sale of common stock and, to a lesser extent, from convertible bond financing and grant funding. The Company will require significant additional funds to conduct clinical trials and to fund its operations. There can be no assurances, however, that additional funding will be available on favorable terms, or at all. If adequate funds are not available, the Company may be required to delay, modify, or terminate its research and development programs or reduce its planned commercialization efforts. The Company believes that it will be able to obtain additional working capital through equity financings or other arrangements to fund operations, including additional public offerings; however, there can be no assurance that such additional financing, if available, can be obtained on terms acceptable to the Company. If the Company is unable to obtain such additional financing, the Company will need to reevaluate future operating plans. Accordingly, there is substantial doubt regarding the Company's ability to continue as a going concern.

These consolidated financial statements have been prepared on a going concern basis, which implies the Company will continue to realize its assets and discharge its liabilities in the normal course of the business. The Company's recurring losses from operations and negative cash flows from operations have raised substantial doubt regarding its ability to continue as a going concern. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

The Company has a senior secured loan agreement which contains various covenants. A breach of any of these covenants could result in a default. If a default under any such loan agreement is not cured or waived, the default could result in the acceleration of debt, which could require us to repurchase or repay debt prior to the date it is otherwise due. If we default, the lender may seek repayment through our subsidiary guarantors or by executing on the security interest granted pursuant to the loan agreement.

Athenex is subject to a number of risks similar to other biopharmaceutical companies, including, but not limited to, the lack of available capital, possible failure of preclinical testing or clinical trials, inability to obtain marketing approval of product candidates, competitors developing new technological innovations, market acceptance of the Company's products, and protection of proprietary technology. If the Company does not successfully commercialize or partner any of its product candidates, it will be unable to generate sufficient product revenue and might not, if ever, achieve profitability.

Initial Public Offering

On June 13, 2017, the Company's Registration Statement on Form S-1 (File No. 333-217928) relating to the initial public offering ("IPO") of its common stock was declared effective by the Securities and Exchange Commission ("SEC"). Pursuant to such Registration Statement, the Company sold an aggregate of 6,900,000 shares of its common stock at a price of $11.00 per share for cash proceeds of $64.2 million, net of underwriting discounts and commissions of $6.1 million and offering costs of $5.6 million.

On June 14, 2017, the day of the IPO, convertible bonds with an aggregate principal value of $68.0 million, and a carrying value of $55.8 million, were converted into 7,727,273 shares of common stock. The IPO closed on June 19, 2017. On September 29, 2017, the remaining convertible bond with a principal value of $7.0 million was converted into 795,455 shares of common stock, at a 20% discount from the IPO price of $11 per share.

Follow-On Offering

In January 2018, the Company completed an underwritten public offering of 4,300,000 shares of its common stock. The Company granted the underwriters a 30-day option to purchase up to an additional 645,000 shares of common stock. In February 2018, the underwriters partially exercised their option, purchasing an additional 465,000 shares of common stock. All shares were offered by the Company at a price of $15.25 per share. Net proceeds were $68.1 million, after deducting underwriting discounts and commissions and offering expenses of $4.6 million.

Debt and Equity Offering

On July 3, 2018, the Company closed a privately placed debt and equity financing deal with Perceptive Advisors LLC and its affiliates ("Perceptive") for gross proceeds of $100.0 million and received aggregate net proceeds of $97.1 million, net of fees and offering expenses. The Company entered into a 5-year senior secured loan for $50.0 million of this financing and issued 2,679,528 shares of its common stock at a purchase price of $18.66 per share for the remaining $50.0 million. The loan matures on the fifth anniversary from the closing date and bears interest at a floating per annum rate equal to London Interbank Offering Rates ("LIBOR") (with a floor of 2.0%) plus 9.0%. The Company is required to make monthly interest-only payments with a bullet payment of the principal at maturity. The loan agreement contains specified financial maintenance covenants. The Company was in compliance with such covenants as of December 31, 2018. In connection with the loan agreement, the Company granted Perceptive a warrant for the purchase of 425,000 shares of common stock at a purchase price of $18.66 per share. This was accounted for as a detachable warrant at its fair value and is recorded as an increase to additional paid-in-capital on the consolidated statement of stockholders' equity for the year ended December 31, 2018. A corresponding debt discount was recorded as a reduction of the related debt in the consolidated balance sheet as of December 31, 2018.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Principles of Consolidation

These consolidated financial statements reflect the accounts and operations of the Company and those of its subsidiaries in which the Company has a controlling financial interest. Intercompany transactions and balances have been eliminated.

Use of Estimates

These consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities as of the date of the consolidated financial statements and the reported amount of revenue and expenses during the reporting period. Such management estimates include those relating to assumptions used in contract research accruals, measurement of acquired assets and assumed liabilities in business combinations, allowance for doubtful accounts, inventory reserves, the valuation of the derivative liability, income taxes, the estimated useful life and recoverability of long-lived assets, and the valuation of stock-based awards. Actual results could differ from those estimates.

Functional Currency

Assets and liabilities of subsidiaries that prepare financial statements in currencies other than the U.S. dollar are translated using rates of exchange as of the balance sheet date and the statements of operations and comprehensive loss are translated at the average rates of exchange for each reporting period. The Company recorded a foreign currency translation loss in accumulated other comprehensive loss of $0.5 million for the year ended December 31, 2018, a gain of $1.2 million for the year ended December 31, 2017 and a loss of $1.0 million for the years ended December 31, 2016.

Cash, Cash Equivalents, and Marketable Securities

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. The Company deposits its cash primarily in checking, money market accounts, as well as certificates of deposit. The Company generally does not enter into investments for trading or speculative purposes, rather to preserve its capital for the purpose of funding operations.

Accounts Receivable, net

Accounts receivable are recorded at the invoiced amount. On a periodic basis, the Company evaluates its accounts receivable and establishes an allowance for doubtful accounts, based upon a history of past write-offs, the age of the receivables, and current credit conditions.

Inventories

Inventories for clinical trials are stated at the lower of cost and net realizable value, with approximate cost being determined on a first-in-first-out basis. Active pharmaceutical ingredient ("API") inventory is stated at the lower of cost and net realizable value, with approximate cost being determined on a weighted average basis.

The Company provides inventory write-downs based on excess and obsolete inventories determined primarily by future demand forecasts. The write-down is measured as the difference between the cost of the inventory and market, based upon assumptions about future demand, and is charged to the provision for inventory, which is a component of cost of sales. At the point of the loss recognition, a new, lower cost basis for that inventory is established, and subsequent changes in facts and circumstances do not result in the restoration or increase in that newly established cost basis.

Property and Equipment, net

Property and equipment are recorded at cost or acquisition date fair value in a business acquisition. Depreciation is recorded over the estimated useful lives of the related assets using the straight-line method. Leasehold improvements are amortized on a straight-line basis over the shorter of the useful life or term of the lease. Upon retirement or disposal, the cost and related accumulated depreciation are removed from the consolidated balance sheets and the resulting gain or loss is recorded to general and administrative expense in the consolidated statements of operations and comprehensive loss. Routine expenditures for maintenance and repairs are expensed as incurred.

Estimated useful lives for property and equipment are as follows:

Property and Equipment	Estimated Useful Life
Land	Not depreciated
Equipment	5 - 8 years
Furniture and fixtures	5 years
Computer hardware	3 years
Leasehold improvements	Lesser of estimated useful life or remaining lease term
Construction in process	Not depreciated

Fair Value of Financial Instruments

Financial instruments consist of cash and cash equivalents, short-term investments, marketable securities, an investment, accounts receivable, accounts payable, accrued liabilities, and long-term debt. Cash and cash equivalents, short-term investments, accounts receivable, accounts payable and accrued liabilities, and debt, are stated at their carrying value, which approximates fair value due to the short time to the expected receipt or payment date of such amounts.

Goodwill

The Company tests goodwill for impairment annually on October 1st, the Company's annual goodwill impairment measurement date, or more frequently if a triggering event occurs. The Company has three operating segments: Oncology Innovation Platform, Commercial Platform, and Global Supply Chain Platform which has two components: Polymed and QuaDPharma. Accordingly, the Company has four reporting units: Oncology Innovation Platform, Commercial Platform, Polymed, and QuaDPharma, all of which have discrete financial information that are reviewed by segment managers. Goodwill is assigned to three reporting units: Oncology

Innovation Platform, Polymed, and QuaDPharma. Goodwill impairment exists when the fair value of goodwill is less than its carrying value. The Company concluded that there was no impairment of goodwill for the years ended December 31, 2018, 2017, and 2016.

Intangible Assets, net

Intangible assets arising from a business acquisition are recognized at fair value as of the acquisition date. The Company amortizes intangible assets using the straight-line method. When the straight-line method of amortization is utilized, the estimated useful life of the intangible asset is shortened to assure the recognition of amortization expense corresponds with the expected cash flows. Other purchased intangibles, including certain licenses, are capitalized at cost and amortized on a straight-line basis over the license life, when a future economic benefit is probable and measurable. If a future economic benefit is not probable or measurable, the license costs are expensed as incurred within research and development expenses.

Impairment of Long-Lived Assets

The Company reviews the recoverability of its long-lived assets, excluding goodwill, when events or changes in circumstances occur that indicate that the carrying value of the asset may not be recoverable. The assessment of possible impairment is based on the ability to recover the carrying value of the assets from the expected future cash flows (undiscounted and without interest expense) of the related operations. If these cash flows are less than the carrying value of such assets, an impairment loss for the difference between the estimated fair value and carrying value is recorded. Impairment charges of $0.3 million, $0.1 million and $0.3 million were recorded for the years ended December 31, 2018, 2017, and 2016 respectively. See Note 5—*Goodwill and Intangible Assets, net* for additional details.

Treasury Stock

The Company records treasury stock activities at the cost of the acquired stock. The Company's accounting policy upon the formal retirement of treasury stock is to deduct the par value from common stock and to reflect any excess of cost over par value as a reduction to additional paid-in capital (to the extent created by previous issuances of the stock) and then accumulated deficit.

Revenue Recognition

Effective January 1, 2018, the Company adopted Accounting Standards Codification ("ASC"), Topic 606, "*Revenue from Contracts with Customers*," using the modified retrospective transition method. Under this method, the Company was required to evaluate the impacts of implementing the standard on existing contracts on the date of the adoption, accounting for those contracts in accordance with Topic 606. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identifies the contract(s) with a customer; (ii) identifies the performance obligations in the contract; (iii) determines the transaction price; (iv) allocates the transaction price to the performance obligations in the contract; and (v) recognizes revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For a complete discussion of accounting for product sales, license fees and consulting revenue, and grant revenue, see Note 18 – *Revenue Recognition*. The Company did not record an adjustment to revenue upon adoption.

Research and Development Expenses

Costs for research and development ("R&D") of products, including payroll, contractor expenses, and supplies, are expensed as incurred. Clinical trial and other development costs incurred by third parties are expensed as the contracted work is performed. Where contingent milestone payments are due to third parties under research and development arrangements, the obligations are recorded when the milestone results are probable of being achieved.

Deferred Rent

Rent expense is recognized on a straight-line basis over the term of the lease. Lease incentives, including rent holidays provided by lessors and rent escalation provisions, are accounted for as deferred rent.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Changes in unrealized gains and losses on investments and foreign currency translation adjustments represent the differences between the Company's net loss and comprehensive loss.

Stock-Based Compensation

Awards granted to employees

The Company recognizes stock-based compensation based on the grant date fair value of stock options granted to employees, officers, and directors. The Company used the Black-Scholes option pricing model to calculate the grant date fair value of stock options. The Black-Scholes option pricing model requires inputs for risk-free interest rate, dividend yield, volatility, fair value of common stock, and expected lives of the stock options. The risk-free rate for periods within the expected life of the stock option is based on the U.S. Treasury yield curve in effect at the time of the grant. No dividend yield is used, consistent with the Company's history. Expected volatility is based on historical volatilities of the stock prices of peer biopharmaceutical companies. The fair value of common stock is based on the quoted market price of the Company's common stock on grant date. The Company uses the simplified method for determining the expected lives of stock options. The Company recognizes compensation expenses based on the grant date fair value of stock options on a straight-line basis over the requisite service period, which is generally the vesting period.

Stock grants

The Company grants common stock to key officers and directors and records the fair value of these grants, based on the fair value of the common stock on the grant date, as compensation expense throughout the requisite service period.

Awards granted to non-employees

The Company has accounted for equity instruments issued to non-employees in accordance with the provisions of ASC 718, *Compensation—Stock Compensation*, and ASC 505, *Equity*. 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 expense is recognized in the same manner as if the Company had paid cash for the services provided by the non-employees.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Deferred income tax assets and liabilities are recognized for the estimated future tax consequences attributable to temporary differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred income tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. Deferred income tax expense or benefit is the result of changes in the deferred income tax assets and liabilities. Valuation allowances are established when necessary to reduce deferred income tax assets where, based upon the available evidence, management concludes that it is more-likely-than not that the deferred income tax assets will not be realized. In evaluating its ability to recover deferred income tax assets, the Company considers all available positive and negative evidence, including its operating results, ongoing tax planning and forecasts of future taxable income on a jurisdiction-by-jurisdiction basis. Because of the uncertainty of the realization of the deferred income tax assets, the Company has recorded a valuation allowance against its deferred income tax assets.

Reserves are provided for tax benefits for which realization is uncertain. Such benefits are only recognized when the underlying tax position is considered more likely than not to be sustained on examination by a taxing authority, assuming they possess full knowledge of the position and facts. Interest and penalties related to uncertain tax positions are recognized in income tax expense (benefit); however, the Company currently has no interest or penalties related to income taxes.

Segment and Geographic Information

The Company's chief operating decision-maker, its Chief Executive Officer, reviews its operating results on an aggregate basis and at the operating segment level for purposes of allocating resources and evaluating financial performance. The Company has three business platforms which are the operating segments: (1) Oncology Innovation Platform, for the discovery and development of cancer supportive therapies, (2) Commercial Platform, the manufacturing and selling of commercial pharmaceutical products, and (3) Global Supply Chain Platform, the cGMP manufacturing and marketing of API, medical devices, and clinical products. Each operating

segment has a segment manager who is held accountable for operations and operating results. Accordingly, the Company operates in three reportable segments.

Concentration of Credit Risk, Other Risks and Uncertainties

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents and investments. The Company deposits its cash equivalents in interest-bearing money market accounts and certificates of deposit. Although the Company deposits the cash with multiple financial institutions, cash balances may occasionally be in excess of the amounts insured by the Federal Deposit Insurance Corporation. The primary focus of the Company's investment strategy is to preserve capital and meet liquidity requirements. The Company's investment policy addresses the level of credit exposure by limiting the concentration in any one corporate issuer and establishing a minimum allowable credit rating. The Company also has significant assets and liabilities held in its overseas manufacturing facility in China, Taihao, and therefore is subject to foreign currency fluctuation.

Recent Accounting Pronouncements Not Yet Adopted

In February 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2016-02, "Leases (Topic 842)", which requires lessees to recognize leases on-balance sheet and disclose key information about leasing arrangements. The new standard establishes a right-of-use model ("ROU") that requires a lessee to recognize a ROU asset representing the right to use the underlying asset over the lease term and lease liability on the balance sheet for all leases with a term longer than 12 months. Lease obligations are to be measured at the present value of lease payments and accounted for using the effective interest method. Leases will be classified as finance or operating, with classification affecting the pattern and classification of expense recognition in the income statement. For finance leases, the leased asset is depreciated on a straight-line basis and recorded separately from the interest expense in the income statement resulting in higher expense in the earlier part of the lease term. For operating leases, the depreciation and interest expense components are combined, recognized evenly over the term of the lease, and presented as a reduction to operating income. The ASU requires that assets and liabilities be presented or disclosed separately and classified appropriately as current and noncurrent. The ASU further requires additional disclosure of certain qualitative and quantitative information related to lease agreements. In July 2018, the FASB issued new guidance that provided for a new optional transition method that allows entities to initially apply the new leases standard at the adoption date and recognize a cumulative-effect adjustment to opening retained earnings. Under this approach, comparative periods are not restated.

The Company adopted the new lease standard on January 1, 2019 and used the effective date as our date of initial application. Consequently, financial information will not be updated and the disclosures required under the new standard will not be provided for dates and periods before January 1, 2019. The processes that are in final refinement related to our full implementation of the standard include: i) finalizing our estimates related to the applicable incremental borrowing rate at January 1, 2019 and ii) process enhancements for refining our financial reporting procedures to develop the additional required qualitative and quantitative disclosures required beginning in 2019.

The new standard provides a number of optional practical expedients in transition. The Company has elected the package of practical expedients permitted under the transition guidance within the new standard, which allows the Company (1) to not reassess whether any expired or existing contracts are or contain leases, (2) to not reassess the lease classification for any expired or existing leases, and (3) to not reassess initial direct costs for any existing leases In preparation for adoption of the standard, the Company has implemented internal controls to enable the preparation of financial information. Further, the Company has made an accounting policy election to keep leases with an initial term of twelve months or less off the balance sheet. The Company will recognize those lease payments in the consolidated statement of operations and comprehensive loss over the lease term.

The standard will have a material impact on our consolidated balance sheets, but is not expected to have a material impact on our consolidated statements of operations and comprehensive loss. The most significant impact will be the recognition of ROU assets and lease liabilities for operating leases. The Company expects that adoption of the standard will result in the recognition of additional ROU assets ranging between $7.5 million to $10.0 million and a ROU liability ranging between $9.5 million to $12.0 million as of January 1, 2019. The difference relates to the de-recognition of the Company's current deferred rent balance of $2.0 million.

In June 2018, the FASB issued ASU No. 2018-07, "*Compensation – Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting,"* which expands the scope of Topic 718, "*Compensation – Stock Compensation,"* which only included share-based payments to employees, to include share-based payments issued to nonemployees for goods and services. The ASU is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. The Company will only need to remeasure liability-classified awards that have not yet been settled as of the date of adoption, and equity-classified awards for which a measurement date has not been established through a cumulative-effect adjustment to retained

earnings as of the beginning of the fiscal year of adoption. The Company does not expect that the adoption of this standard will have a material effect on its consolidated financial statements.

Recently Adopted Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, "*Revenue from Contracts with Customers (Topic 606)*", which requires an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. The ASU has replaced most historical revenue recognition guidance in U.S. GAAP when it became effective. The Company adopted this standard on January 1, 2018 using the modified retrospective transition method. The Company did not record a cumulative catch-up adjustment upon adoption, as there was no effect on the timing or amount of revenue recognized for existing contracts that were not completed as of the implementation date. Refer to Note 18 – *Revenue Recognition* for more information on the effect of this ASU.

In November 2016, the FASB issued ASU 2016-18, "*Statement of Cash Flows (Topic 230): Restricted Cash*." The primary purpose of this ASU is to reduce the diversity in practice that exists in the classification and presentation of changes in restricted cash on the statement of cash flows. This ASU will require that a statement of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash or cash equivalents. Therefore, amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The Company adopted this standard on January 1, 2018 and the adoption of this ASU did not impact the Company's consolidated financial statements.

In May 2017, the FASB issued ASU 2017-09, "*Stock Compensation—Scope of Modification Accounting*," which provides guidance as to when a modification of a share-based award must be accounted for. In general, if a modification of the terms and conditions of an award does not change the fair value of the award (or calculated value or intrinsic value, if used instead of fair value), does not change the vesting conditions of the award, and does not change the classification of the award as an equity instrument or a liability instrument, then an entity need not account for the modification. The new rules are applied prospectively to awards modified after the adoption date. The Company adopted this standard on January 1, 2018 and the adoption of this ASU did not impact the Company's consolidated financial statements.

3. INVENTORIES

Inventories consist of the following (in thousands):

	December 31,	
	2018	2017
Raw materials and purchased parts	$ 4,092	$ 1,471
Work in progress	3,166	1,877
Finished goods	21,529	13,213
Total inventories	$ 28,787	$ 16,561

4. PROPERTY AND EQUIPMENT, NET

Property and equipment, net, consists of the following (in thousands):

	December 31,	
	2018	2017
Land	$ 1,132	$ 1,196
Equipment	6,236	5,123
Furniture and fixtures	640	975
Computer hardware	2,118	1,395
Leasehold improvements	1,380	1,326
Construction in process	3,826	3,225
Property and equipment, gross	15,332	13,240
Less: accumulated depreciation	(3,885)	(3,589)
Property and equipment, net	$ 11,447	$ 9,651

Depreciation expense amounted to $1.7 million, $2.1 million, and $1.2 million for the years ended December 31, 2018, 2017, and 2016, respectively.

5. GOODWILL AND INTANGIBLE ASSETS, NET

Goodwill

The changes in the carrying amount of goodwill for each reporting unit with goodwill for the periods indicated are as follows (in thousands):

	APS	Polymed	Oncology Innovation Platform	Total
Balance as of January 1, 2017	$ 4,586	$ 21,592	$ 11,374	$ 37,552
Effect of currency translation adjustment	—	332	(89)	243
Balance as of December 31, 2017	4,586	21,924	11,285	37,795
Effect of currency translation adjustment	—	(277)	(23)	(300)
Balance as of December 31, 2018	$ 4,586	$ 21,647	$ 11,262	$ 37,495

Intangible Assets, Net

The Company's identifiable intangible assets, net, consist of the following (in thousands):

	December 31, 2018			
	Cost/Fair Value	Accumulated Amortization	Impairments	Net
Amortizable intangible assets				
Licenses	$ 8,935	$ 2,060	$ —	$ 6,875
Polymed customer list	1,593	938	—	655
Polymed technology	3,712	999	—	2,713
Product rights	530	263	—	267
Indefinite-lived intangible assets:				
CDE in-process research and development (IPR&D)	1,026	—	298	728
Effect of currency translation adjustment	(390)	—	—	(390)
Total intangibles, net	$ 15,406	$ 4,260	$ 298	$ 10,848

	December 31, 2017			
	Cost/Fair Value	Accumulated Amortization	Impairments	Net
Amortizable intangible assets				
Licenses	$ 4,650	$ 1,173	$ —	$ 3,477
Polymed customer list	1,593	675	—	918
Polymed technology	3,712	762	—	2,950
Product rights	530	132	—	398
Indefinite-lived intangible assets:				
CDE in-process research and development (IPR&D)	1,106	—	80	1,026
Effect of currency translation adjustment	(197)	—	—	(197)
Total intangibles, net	$ 11,394	$ 2,742	$ 80	$ 8,572

As of December 31, 2018, licenses at cost include an Orascovery license of $0.4 million and licenses purchased from Gland Pharma Ltd ("Gland") of $4.5 million, and a license purchased from MAIA Pharmaceuticals, Inc ("MAIA") for $4.0 million. The Orascovery license with Hanmi Pharmaceuticals Co. Ltd. ("Hanmi") was purchased directly from Hanmi and is being amortized on a straight-line basis over a period of 12.75 years, the remaining life of the license agreement at the time of purchase.

The licenses purchased from Gland are being amortized on a straight-line basis over a period of 5 years, the remaining life of the license agreement at the time of purchase. The license purchased from MAIA is being amortized over a period of 7 years, the remaining life of the license agreement at the time of purchase.

The remaining intangible assets were acquired in connection with the acquisitions of Athenex Pharma Solutions ("APS" or "Athenex Pharma Solutions,"), Polymed Therapeutics, Inc. ("Polymed"), and Comprehensive Drug Enterprises ("CDE"). Intangible assets are amortized using an economic consumption model over their useful lives. The APS customer list is amortized on a straight-line basis over 7 years. The Polymed customer list and technology are amortized on a straight-line basis over 6 and 12 years,

respectively. The CDE in-process research and development, or IPR&D, will not be amortized until the related projects are completed. IPR&D is tested annually for impairment, unless conditions exist causing an earlier impairment test (e.g., abandonment of project). During the year ended December 31, 2018, the Company abandoned a project within IPR&D and therefore, the related balance of $0.3 million was written-off as impaired and is included within research and development expenses in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2018. During the year ended December 31, 2017, an impairment charge of $0.1 million was recorded within research and development expenses due to the impairment of a project within CDE's IPR&D. During the year ended December 31, 2016, impairment charges of $0.2 million and $0.1 million were recorded within research and development costs and selling, general, and administrative costs, respectively, in the 2016 consolidated statement of operations and comprehensive loss. The charge of $0.2 million was due to the impairment of CDE's IPR&D. The charge of $0.1 million was due to the impairment of the APS customer list. This was due to the business model change of APS from a contract manufacturer to a facility primarily producing FDA shortage products under 503B regulations, which changed the Company's anticipated use of the customer list. The weighted-average useful life for all intangible assets was 7.85 years as of December 31, 2018.

The Company recorded $1.6 million, $1.6 million, and $0.8 million of amortization expense for the years ended December 31, 2018, 2017, and 2016, respectively.

The Company expects amortization expense related to its finite-lived intangible assets for the next 5 years and thereafter to be as follows as of December 31, 2018 (in thousands):

Year ending December 31:	Estimated Amortization Expense
2019	$ 2,216
2020	2,216
2021	1,763
2022	995
2023	965
Thereafter	2,355
	$ 10,510

6. FAIR VALUE MEASUREMENTS

ASC 820, *Fair Value Measurements*, establishes a framework for measuring fair value. That framework provides a fair value hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (level 1 measurements) and the lowest priority to unobservable inputs (level 3 measurements). The three levels of the fair value hierarchy under the ASC 820 are described as follows:

Level 1—Inputs to the valuation methodology are unadjusted quoted prices for identical assets or liabilities in active markets that the plan has the ability to access.

Level 2—Inputs to the valuation methodology include:

- Quoted prices for similar assets or liabilities in active markets;
- Quoted prices for identical or similar assets or liabilities in inactive markets;
- Inputs other than quoted prices that are observable for the asset or liability;
- Inputs that are derived principally from or corroborated by observable market data by correlation or other means; and
- If the asset or liability has a specified (contractual) term, the level 2 input must be observable for substantially the full term of the asset or liability.

Level 3—Inputs to the valuation methodology are unobservable, supported by little or no market activity, and that are significant to the fair value measurement.

Transfers between levels, if any, are recorded as of the beginning of the reporting period in which the transfer occurs; there were no transfers between Levels 1, 2 or 3 of any financial assets or liabilities during the years ended December 31, 2018, 2017, or 2016.

The following tables represent the fair value hierarchy for those assets and liabilities that the Company measures at fair value on a recurring basis (in thousands):

	Fair Value Measurements at December 31, 2018 Using:			
	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Financial assets included within cash and cash equivalents				
Money market funds	$ 25	$ 25	$ —	$ —
Short-term investments - commercial paper	5,396	—	5,396	—
Financial assets included within short-term investments				
Short-term investments - commercial paper	36,544	—	36,544	—
Short-term investments - corporate notes	16,699	—	16,699	—
Short-term investments - U.S. government bonds	3,998	—	3,998	—
Available-for-sale investment	388	388	—	—
Total assets	$ 63,050	$ 413	$ 62,637	$ —

	Fair Value Measurements at December 31, 2017 Using:			
	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Financial assets included within cash and cash equivalents				
Money market funds	$ 13,804	$ 13,804	$ —	$ —
Short-term investments - commercial paper	5,740	—	5,740	—
Short-term investments - corporate notes	2,824	—	2,824	—
Short-term investments - U.S. government bonds	2,495	—	2,495	—
Financial assets included within short-term investments				
Short-term investments - commercial paper	9,242	—	9,242	—
Short-term investments - U.S. government bonds	2,511	—	2,511	—
Available-for-sale investment	328	328	—	—
Total assets	$ 36,944	$ 14,132	$ 22,812	$ —

The Company classifies its certificates of deposit and money market funds within Level 1 because it uses quoted market prices to determine their fair value. The Company classifies its commercial paper, corporate notes, and U.S. government bonds within Level 2 because it uses quoted prices for similar assets or liabilities in active markets and each has a specified term and all level 2 inputs are observable for substantially the full term of each instrument.

The Company owns 68,000 shares of PharmaEssentia, a company publicly traded on the Taiwan OTC Exchange. As of December 31, 2018 and 2017, the Company's investment in PharmaEssentia is valued at the reported closing price. This investment is classified as a level 1 investment.

7. ASSET ACQUISITION

On June 29, 2018, the Company entered into a Share Subscription Agreement ("SSA") for Axis Therapeutics Limited ("Axis"), a subsidiary of the Company jointly owned by Athenex and Xiangxue Life Sciences Limited ("XLifeSc"). Under the SSA, Athenex contributed $30.0 million cash for a 55% ownership interest in Axis and XLifeSc contributed a license for IPR&D of certain immunotherapy technology for a 45% ownership interest in Axis. Also, on June 29, 2018, through a license agreement entered into between XLifeSc and Axis, XLifeSc granted Axis an exclusive, sublicensable worldwide (excluding mainland China) right and license to use its proprietary TCR-engineered T Cell therapy to develop and commercialize products for oncology indications ("TCR-T License"). Upon effectiveness of the TCR-T License and satisfaction of certain conditions of the license agreement, the Company issued 267,952 shares of its common stock equal to $5.0 million to XLifeSc. On September 14, 2018, Athenex completed the $30.0 million cash injection to Axis and all the closing conditions under the SSA were fulfilled.

The Company has consolidated the financial statements of Axis into its consolidated financial statements as of and for the year ended December 31, 2018 using the voting interest model. The nonmonetary exchange of 45% of the shares of Axis for the IPR&D from XLifeSc has been accounted for as an asset acquisition that does not constitute a business under ASC 805. Therefore, the acquisition of IPR&D was expensed as research and development expense at its fair value. The Company determined that the fair value of the equity issued to XLifeSc was $24.5 million for the IPR&D, considering the $30.0 million contribution made by the Company for its 55% ownership interest and the arms-length nature of the transaction. Accordingly, the Company recorded an expense of $24.5 million within research and development expenses on its consolidated statements of operations and comprehensive loss for the year ended December 31, 2018.

8. ACCRUED EXPENSES

Accrued expenses consist of the following (in thousands):

	December 31,	
	2018	2017
Accrued wages and benefits	$ 5,061	$ 3,817
Accrued clinical expenses	2,653	3,826
Accrued operating expenses	8,128	1,529
Deferred revenue	190	1,202
Accrued cost of equity raise	—	186
Accrued R&D licensing fees	4,827	5,729
Accrued inventory purchases	—	6,835
Accrued tax withholdings	—	357
Accrued selling fees and rebates	423	788
Accrued construction costs	16,436	2,709
Total accrued expenses	$ 37,718	$ 26,978

The accrued construction costs relate to the building of the manufacturing facility in Dunkirk, NY (refer to Note 13 – *Business and Economic Collaborative Agreements*). The Company expects to be reimbursed by the State for these costs.

9. INCOME TAXES

On December 22, 2017, the Tax Cuts and Jobs Act (Tax Reform Act) was signed into law. This legislation significantly changes U.S. tax law by, among other things, lowering corporate income tax rates, implementing a territorial tax system and imposing a repatriation tax on deemed repatriated earnings of foreign subsidiaries. The Tax Reform Act permanently reduces the U.S. corporate income tax rate from a maximum of 35% to a flat 21% rate, effective January 1, 2018.

Deferred income tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to reverse. As a result of the reduction in the U.S. corporate income tax rate from 35% to 21% under the Tax Reform Act, the Company revalued its net U.S. deferred income tax liabilities at December 31, 2017. The Company has reduced its income tax expense from continuing operations by approximately $34.1 million due to the revaluation of U.S. deferred tax liabilities, offset by an increase in the valuation allowance. The valuation allowance for deferred tax assets increased by $28.1 million for the year ended December 31, 2018 and decreased by $1.9 million for the year ended December 31, 2017. The change in the valuation allowance was due to an increase of deferred tax assets mainly for additional net operating losses and tax credit carryforwards.

The Tax Reform Act provided for a one-time deemed mandatory repatriation of post-1986 undistributed foreign subsidiary earnings and profits ("E&P") through the year ended December 31, 2017. The one-time transition tax is based on the Company's total post-1986 earnings and profits for which it has previously deferred from U.S. income taxes. The Company did not record a provisional amount in income tax expense for the transition tax as it has accumulated losses in its foreign subsidiaries, and thus was not subject to the transition tax.

While the Tax Reform Act provides for a territorial tax system, beginning in 2018, it also includes two new U.S. tax base erosion provisions - the global intangible low-taxed income ("GILTI") provisions and the base-erosion and anti-abuse tax ("BEAT") provisions.

The GILTI provisions require the Company to include in its U.S. income tax return foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets. The Company does not expect that it will be subject to incremental U.S. tax on GILTI income beginning in 2018. In the event that the Company is subject to this tax, it has elected to recognize the tax on GILTI as a period expense in the period the tax is incurred.

The BEAT provisions in the Tax Reform Act eliminates the deduction of certain base-erosion payments made to related foreign corporations, and impose a minimum tax if greater than regular tax. The Company does not expect to be impacted by this tax based on annual gross receipts threshold for 2018.

On December 22, 2017, the Securities and Exchange Commission issued Staff Accounting Bulletin ("SAB") No. 118 to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Reform Act. The Company has recognized the provisional tax impacts related to the revaluation of deferred tax assets and liabilities and included these amounts in its consolidated financial statements for the year ended December 31, 2018. For the year ended December 31, 2018, the Company completed its analysis of the Tax Reform Act. In addition to the amounts reported above, the Company recognized an addition $0.3 million income tax expense from continuing operations for adjustments to deferred tax assets pertaining to executive compensation, offset by a valuation allowance.2018

The Company recorded an income tax expense of $0.1 million during each of the years ended December 31, 2018 and 2017 and an income tax benefit of $0.3 million for the year ended December 31, 2016. The current and prior year income tax expense is attributable to foreign withholding taxes. The Company and its other subsidiaries were in a cumulative loss position as of December 31, 2018.

The components of loss before income tax expense (benefit) consist of the following (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Domestic	$ (95,479)	$ (125,770)	$ (83,714)
Foreign	(33,132)	(5,541)	(4,457)
	$ (128,611)	$ (131,311)	$ (88,171)

The components of the income tax expense (benefit) consist of the following (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Current:			
Federal	$ —	$ 64	$ —
State	27	(92)	61
Foreign	455	440	165
	482	412	226
Deferred:			
Federal	(26,260)	(3,222)	(26,386)
State	(293)	5,799	(4,165)
Foreign	(1,863)	(874)	(848)
	(28,416)	1,703	(31,399)
Change in valuation allowance	28,034	(2,030)	30,908
	$ 100	$ 85	$ (265)

The income tax (expense) benefit differs from the federal statutory rate due to the following:

	Year Ended December 31,		
	2018	2017	2016
Statutory rate	21.0%	34.0%	34.0%
State taxes, net of federal benefit	0.2	(4.3)	5.4
Foreign rate differential	(0.3)	(0.6)	(0.8)
Federal income tax rate change	—	(25.9)	—
Valuation allowance	(21.6)	1.5	(35.1)
Other	0.6	(4.8)	(3.2)
	(0.1)%	(0.1)%	0.3%

Deferred tax assets (liabilities) consist of the following (in thousands):

	December 31,	
	2018	2017
Intangible assets	$ 10,273	$ 8,923
Property and equipment	238	70
Stock-based compensation	7,508	6,489
Net operating loss carryforwards	60,362	44,008
Other	11,482	2,014
Gross deferred income tax assets	89,863	61,504
Less: valuation allowance	(88,455)	(60,379)
Net deferred income tax assets	1,408	1,125
Intangible assets	(922)	(1,004)
Gross deferred income tax liabilities	(922)	(1,004)
Net deferred income tax assets	$ 486	$ 121

As of December 31, 2018, there exists $253.8 million federal net operating losses and $48.3 million of state net operating losses, respectively. Of the federal net operating losses, $184.8 million expire beginning in 2027 and $69.0 million have an indefinite life. In addition, there exists $19.9 million of foreign net operating losses as of December 31, 2018 which may be carried forward indefinitely.

The Company considers whether any positions taken on the Company's income tax returns would be considered uncertain tax positions that may require the recognition of a liability. The Company has concluded that there are no material uncertain tax positions as of December 31, 2018, 2017, and 2016. The Company recognizes interest and penalties related to unrecognized tax benefits as a component of income benefit in the consolidated statement of operations and comprehensive loss. There were no amounts recognized for interest and penalties related to unrecognized tax benefits during the years ended December 31, 2018, 2017, and 2016. The income tax returns for the taxable years 2012 to 2017 in the U.S., China, and Hong Kong remain open and subject to income tax audits.

Provision has not been made for U.S. taxes on undistributed earnings of foreign subsidiaries. Those earnings have been and will continue to be indefinitely reinvested.

Under the provisions of Section 382 of the Internal Revenue Code ("IRC"), net operating loss and credit carryforwards and other tax attributes may be subject to limitation if there has been a significant change in ownership of the Company, as defined by the IRC. Changes in ownership of our common stock could result in limitations on net operating loss carryforwards.

10. DEFERRED COMPENSATION

The Company has a non-qualified deferred compensation plan for certain key employees. In connection with the agreements between the Company and certain members of management, the employees have agreed to defer a portion of their salary to the future which is payable upon their retirement or separation of service with the Company. The deferred compensation accrues interest at 4% annually which is included with the total balance due. The Company incurred $0.5 million, $0.6 million, and $0.7 million of deferred compensation expense included within research and development expenses ($0.1 million, $0 million, and $0.4 million) and selling, general, and administrative expenses ($0.4 million, $0.6 million, and $0.3 million) during the years ended December 31, 2018, 2017, and 2016, respectively. The Company paid $0.1 million and $0.5 million of deferred compensation associated with the separation of key employees in 2018 and 2017, respectively. The related liability as of December 31, 2018 and 2017 totaled $2.8 million and $2.3 million, respectively.

11. DEBT

The Company's debt as of December 31, 2018 and 2017, consists of the following (in thousands):

	December 31,	
	2018	2017
Current portion of promissory notes to related parties	$ —	$ 491
Current portion of mortgage	779	835
Current portion of capital lease obligation	182	180
Long-term portion of promissory notes to related parties	—	—
Long-term portion of capital lease obligation	422	475
Senior secured loan, net of debt discount and financing fees of $4,619	45,381	—
Total	$ 46,764	$ 1,981

The promissory notes had a 36 month maturity beginning on July 1, 2015 and ended on June 1, 2018 with a 6% stated interest rate. The promissory notes were paid in full during 2018. The mortgage payments extend through July 30, 2019. Future minimum principal payments on these promissory notes and mortgage consist of $0.8 million due in the year ending December 31, 2019.

During 2018, the Company issued a senior secured loan with a principal value of $50.0 million and a maturity date of June 30, 2023. The loan bears interest at a floating per annum rate equal to LIBOR (with a floor of 2.0%) plus 9.0%. The Company is required to make monthly interest-only payments with a bullet payment of the principal at maturity.

12. RELATED PARTY TRANSACTIONS

During the years ended December 31, 2018, 2017, and 2016, the Company entered into transactions with individuals and other companies that have financial interests in the Company. Related party transactions included the following:

a. In 2015, CDE signed an agreement with Avalon BioMedical (Management) Limited and its subsidiaries ("Avalon") under which Avalon would receive certain administrative services and would occupy space at CDE's research location. Avalon would reimburse CDE for these administrative services as incurred and pay CDE a percentage of the total rent payment based on its staff headcount occupying the Hong Kong research and development facility (See Note 20—*Commitments and Contingencies*). Members of the Company's board and management collectively have a controlling interest in Avalon. The Company does not hold any interest in Avalon and does not have any obligations to absorb losses or any rights to receive benefits from Avalon. As of December 31, 2018 and December 31, 2017, Avalon held 786,061 and 678,880 shares of the Company's common stock, respectively, which represented approximately 1% of the Company's total issued shares for both periods. Balances due from Avalon recorded on the consolidated balance sheets were not significant.

   In June 2018, the Company entered into two in-licensing agreements with Avalon wherein the Company obtained certain intellectual property from Avalon in an effort to develop and commercialize the underlying products. Under these agreements the Company is required to pay upfront fees and future milestone payments and sales-based royalties. During the year ended December 31, 2018, the Company recorded $5.5 million of upfront fees, consisting of $3.5 million in cash and $2.0 million in equity, as research and development expense on its 2018 consolidated statement of operations and comprehensive loss. During the year ended December 31, 2018, 107,181 shares of common stock were issued to Avalon at a price of $18.66 per share, the closing price of the stock on the date the agreement was executed, in connection with the license agreements.

b. The Company receives consulting and licensing revenue from PharmaEssentia, a company in which Athenex has an investment classified as available-for-sale (see Note 6 —*Fair Value Measurements*). Revenue recorded and cost-sharing funds received from PharmaEssentia amounted to $2.3 million, $0.5 million, and $0 for the years ended December 31, 2018, 2017, and 2016, respectively.

c. The Company receives certain clinical development services from ZenRx Limited and its subsidiaries ("ZenRx"), a company for which one of our executive officers serves on the board of directors. In connection with such services, the Company made payments to ZenRx of $0.3 million, $0.6 million, and less than $0.1 million for the years ended December 31, 2018, 2017, and 2016, respectively. In April 2013, the Company entered into a license agreement with ZenRx pursuant to which the Company granted an exclusive, sublicensable license to use certain of our intellectual property to develop and commercialize Oratecan and Oraxol in Australia and New Zealand, and a non-exclusive license to manufacture a certain compound, but only for use in Oratecan and Oraxol. ZenRx is responsible for all development, manufacturing and commercialization, and the related costs and expenses, of any product candidates resulting from the agreement. No revenue was earned from this license agreement in the periods presented in these consolidated financial statements.

d. The Company received consulting services from RSJ Consulting LLC ("RSJ"), a limited liability company for which one of our executive officers serves as the principal. Services incurred from RSJ amounted to $0, $0.1 million, and $0.2 million for the years ended December 31, 2018, 2017, and 2016, respectively.

e. The Company purchases certain pharmaceutical ingredients from Chongqing Taisheng Biotechnology Co., Ltd. ("Taisheng"), a company which is owned by one of our executive officers. Purchases from Taisheng amounted to $0 for the years ended December 31, 2018 and 2017 and $0.2 million for the year ended December 31, 2016. No amounts were owed to Taisheng as of December 31, 2018 and 2017.

f. During the first quarter of 2017, the Company issued and sold $4.0 million in convertible bonds to two related parties. One of the holders of more than 5% of our outstanding common stock as of the IPO date and a director of the Company each purchased $2.0 million in convertible bonds. In June 2017, these bonds were converted into 2,727,273 shares of common stock.

g. Certain family members of our executive officers perform consulting services to the Company. Such services were not significant to the consolidated financial statements.

13. BUSINESS AND ECONOMIC COLLABORATIVE AGREEMENTS

New York State

On May 1, 2015, the Company executed an agreement for a medical technology research, development, innovation, and commercialization alliance with Fort Schuyler Management Corporation ("FSMC"), a not-for-profit corporation existing under the laws of the State of New York (the "State"). The Company expects that $25 million be invested by the State to build new corporate offices including a formulation lab with related equipment for the Company.

The Company, through its partnership with FSMC, Empire State Development ("ESD"), and The State University of New York ("SUNY") Polytechnic, plans to build a 315,000 square foot, ISO Class 5 high potency oral and sterile injectable pharmaceutical manufacturing facility in Dunkirk, New York. On September 4, 2017, the Company entered into a Grant Disbursement Agreement whereby the State agreed to grant up to $200 million, plus any additional funds available from the previous $25 million ESD Grant for the Company's corporate offices, to fund the construction of the new pharmaceutical manufacturing facility. If construction costs exceed $225 million, the Company is responsible for funding those construction costs. The Company is also responsible for the costs of furnishing the facility. The Company is entitled to lease the facility and all equipment purchased with grant funds at a rate of $1.00 per year for an initial 10-year term, and for the same rate if the Company elects to extend the lease for an additional 10-year term. In exchange, the Company committed to spending $1.52 billion on operational expenses in the facility in its first 10-year term, and an additional $1.50 billion on operational expenses if the Company elects to extend the lease for a second 10-year term. The State will fund a majority of the construction costs and hold ownership of the manufacturing and office facilities. Construction of these facilities has begun and is expected to be completed in 2020.

Chongqing Government Department of Economic Development

In October 2015, the Company completed and executed an agreement with the Banan District in Chongqing, China to construct one GMP API and one GMP pharmaceutical manufacturing plant on Banan sites identified and selected by the Company's management. Under the terms of the agreement, Banan will provide the funding for the land and construction of the manufacturing plants according to Athenex specifications and the Company will equip the plant. This agreement allows the Company to expand its existing high potency oncology active pharmaceutical ingredient manufacturing capacity as well as its drug manufacturing capacity in China. The Company does not have significant construction period risks and the Banan District will fund a majority of the construction costs and hold ownership of the facilities. Construction of these facilities has begun and is expected to be completed in 2019.

In connection with these arrangements with FSMC and the Banan District we have committed to certain operational milestones. If we are unable to comply with such, we may lose access to these properties.

14. STOCK-BASED COMPENSATION

Common Stock Option Plans

The Company has three common stock option plans adopted in 2013, 2007 and 2004 (the "Plans") which authorize the grant of up to 11,800,000 common stock options to employees, directors, and consultants. Additionally, on June 14, 2017, the Company adopted its 2017 Omnibus Incentive Plan and 2017 Employee Stock Purchase Plan (the "2017 Plans"). Under the 2017 Plans, 5,200,000 shares of common stock were reserved for future issuance to employees, directors, and consultants, including 1,000,000 reserved for the Employee Stock Purchase Plan ("ESPP"), which was established at the time of the IPO.

Stock Options

The total fair value of stock options vested and recorded as compensation expense during the year ended December 31, 2018, 2017, and 2016 was $9.8 million, $8.0 million, and $11.0 million, respectively. As of December 31, 2018, $17.4 million of unrecognized cost related to non-vested stock options was expected to be recognized over a weighted-average period of approximately 1.8 years. The total intrinsic value of options exercised was approximately $6.7 million and $4.2 million for the years ended December 31, 2018 and 2017, respectively.

The following table summarizes the status of the Company's stock option activity granted under the Plans and 2017 Plans to employees, directors, and consultants (in thousands, except stock option amounts and exercise price): Stock options granted have a contractual term of 10 years and generally vest over a 2-4 year period. A limited number of stock options vest immediately in certain circumstances. The following table summarizes the status of the Company's stock option activity granted under the Plans and 2017 Plans to employees, directors, and consultants (in thousands, except stock option amounts):

	Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at December 31, 2017	10,176,643	$ 7.19	6.83	$ 88,615
Granted	1,449,650	17.12	—	
Exercised	(673,230)	5.85	—	
Forfeited	(257,513)	11.85	—	
Expired	(7,900)	9.97	—	
Outstanding at December 31, 2018	10,687,650	$ 8.51	6.87	$ 44,688
Vested and exercisable at December 31, 2018	7,889,450	$ 6.53	5.56	$ 48,618

The Company determines the fair value of stock option awards on the grant date using the Black-Scholes option pricing model, which is impacted by assumptions regarding a number of highly subjective variables. The following table summarizes the weighted-average assumptions used as inputs to the Black-Scholes option pricing model during the periods indicated:

	Year Ended December 31,		
	2018	2017	2016
Weighted average grant date fair value	$ 9.80	$ 7.01	$ 5.53
Expected dividend yield	—%	—%	—%
Expected stock price volatility	59%	66%	65%
Risk-free interest rate	2.61%	1.74%	1.29%
Expected life of options (in years)	6.1	6.2	6.0

Restricted Stock

Restricted stock grants cliff vest on the anniversaries of their grant dates. During the year ended December 31, 2018, 240,000 restricted shares were vested and as of December 31, 2018, no restricted shares remained unvested.

Employee Stock Purchase Plan

The ESPP is available to eligible employees as defined in the plan document. Under the ESPP, shares of the Company's common stock may be purchased at a discount (15%) of the lesser of the closing price of the Company's common stock on the first trading or the last trading day of the offering period. The current offering period extends from December 1, 2018 to May 31, 2019. The Company expects to continue to offer 6-month offering periods after the current period. The 2017 Plans reserved 1,000,000 shares of common stock for issuance under the ESPP. Stock-based compensation related to the ESPP amounted to $0.2 million for the year ended December 31, 2018 and $0 for all preceding periods. On November 30, 2018, the Company issued 41,733 shares of common stock to participants in connection with the first offering period spanning July 1, 2018 to November 30, 2018.

Stock-Based Compensation Expense

The components of stock-based compensation and the amounts recorded within research and development expenses and selling, general, and administrative expenses in the Company's consolidated statements of operations and comprehensive loss consisted of the following for the years ended December 31, 2018, 2017, and 2016 (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Stock options	$ 9,786	$ 8,031	$ 10,977
Restricted stock expense	1,008	2,160	8,534
Stock awarded to directors and officers	—	4,400	—
Employee stock purchase plan	217	—	—
Total stock-based compensation expense	$ 11,011	$ 14,591	$ 19,511
Cost of sales	$ 228	$ 137	$ —
Research and development expenses	2,621	2,030	8,573
Selling, general, and administrative expenses	8,162	12,424	10,938
Total stock-based compensation expense	$ 11,011	$ 14,591	$ 19,511

15. NET LOSS PER SHARE ATTRIBUTABLE TO ATHENEX, INC. COMMON STOCKHOLDERS

Basic net loss per share is calculated by dividing net loss attributable to Athenex, Inc. common stockholders by the weighted-average number of common shares issued, outstanding, and vested during the period. Diluted net loss per share is computed by dividing net loss attributable to Athenex, Inc. common stockholders by the weighted-average number of common share and common shares equivalents for the period using the treasury-stock method. For the purposes of this calculation, warrants for common stock and stock options are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

The following weighted average outstanding shares of common stock equivalents were excluded from the calculation of diluted net loss per share attributable Athenex, Inc. to common stockholders for the periods presented because including them would have been antidilutive:

	Year Ended December 31,		
	2018	2017	2016
Stock options and other common stock equivalents	10,480,084	9,534,658	9,624,689
Unvested restricted common shares	113,260	393,408	948,484
Total potential dilutive common shares	10,593,344	9,928,066	10,573,173

16. ACCUMULATED OTHER COMPREHENSIVE LOSS

The components and changes of accumulated other comprehensive loss, net of related income tax effects, are as follows (in thousands):

Balance as of January 1, 2016	$ (223)
Foreign currency translation adjustment	(1,048)
Unrealized loss on investment	(33)
Balance as of December 31, 2016	(1,304)
Foreign currency translation adjustment	1,184
Unrealized loss on investment	(26)
Balance as of December 31, 2017	(146)
Foreign currency translation adjustment	(525)
Unrealized gain on investment	15
Balance as of December 31, 2018	$ (656)

17. BUSINESS SEGMENT, GEOGRAPHIC, AND CONCENTRATION RISK INFORMATION

The Company has three operating segments, which are organized based mainly on the nature of the business activities performed and regulatory environments in which they operate. The Company also considers the types of products from which the reportable segments derive their revenue (only applicable to two reportable segments). Each operating segment has a segment manager who is held accountable for operations and has discrete financial information that is regularly reviewed by the Company's chief operating decision-maker. The Company's operating segments are as follows:

Oncology Innovation Platform—This primary operating segment performs research and development on certain of the Company's proprietary drugs, from the preclinical development of its chemical compounds, to the execution and analysis of its several clinical trials. This segment focuses specifically on the oral absorption cancer drug platform, the Src Kinase inhibitors, and the transmucosal drug delivery system. This segment performs research in the United States, Taiwan, Hong Kong, and mainland China.

Global Supply Chain Platform—This operating segment includes QuaDPharma and Polymed. QuaDPharma manufactures and sell pharmaceutical products under 503B regulations set forth by the U.S. Food and Drug Administration ("FDA"). QuaDPharma is also a contract manufacturing company that provides small to mid-scale cGMP manufacturing of clinical and commercial products for pharmaceutical and biotech companies. QuaDPharma also performs microbiological and analytical testing for raw material and formulated products. Polymed markets and sells API and medical devices in North America, Europe, and Asia from its locations in Texas and mainland China. Polymed also develops new compounds, processing techniques, and manufactures API at Taihao, a cGMP facility in Chongqing, China. The pharmaceutical manufacturing facilities being built in the Banan District in Chongqing, China (see Note 13—*Business and Economic Collaborative Agreements*) will be included within this segment and the Company anticipates that this segment will support the Oncology Innovation Platform segment when drugs in development are approved for market.

Commercial Platform—This operating segment includes Athenex Pharmaceutical Division, a newly-formed component that is focused on the manufacturing, distribution, and sales of generic pharmaceuticals. This segment provides services and products to external customers based mainly in the United States.

The segments operate in North America and Asia. The Company's Oncology Innovation Platform segment operates and holds long-lived assets located in the United States, Taiwan, Hong Kong, and mainland China. The Global Supply Chain Platform segment operates and holds long-lived assets located in the United States and China. The Commercial Platform segment operates and holds long-lived assets located in the United States. For geographic segment reporting, product sales have been attributed to countries based on the location of the customer.

Segment information is as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Net loss attributable to Athenex, Inc.:			
Oncology Innovation Platform	$ (89,912)	$ (108,563)	$ (64,837)
Global Supply Chain Platform	(16,858)	(7,179)	(11)
Commercial Platform	(10,670)	(15,428)	(22,867)
Total consolidated net loss attributable to Athenex, Inc.	$ (117,440)	$ (131,170)	$ (87,715)

	Year Ended December 31,		
	2018	2017	2016
Total revenue:			
Oncology Innovation Platform	$ 32,776	$ 1,411	$ 998
Global Supply Chain Platform	31,274	28,427	26,581
Commercial Platform	30,426	17,218	—
Total revenue for reportable segments	94,476	47,056	27,579
Intersegment revenue	(5,376)	(9,013)	(7,028)
Total consolidated revenue	$ 89,100	$ 38,043	$ 20,551

Intersegment revenue eliminated in the above table reflects sales from the Global Supply Chain Platform to the Oncology Innovation Platform.

	Year Ended December 31,		
	2018	2017	2016
Total revenue by product group:			
API sales	$ 17,952	$ 15,351	$ 15,331
Medical device sales	2,344	1,747	2,338
Contract manufacturing revenue	458	1,360	1,497
Commercial product sales	35,640	17,648	228
License fees and consulting revenue	32,387	1,105	392
Grant revenue	319	832	765
Total consolidated revenue	$ 89,100	$ 38,043	$ 20,551

Intersegment revenue is recorded by the selling segment when it is realized or realizable and all revenue recognition criteria are met. Upon consolidation, all intersegment revenue and related cost of sales are eliminated from the selling segment's ledger.

	Year Ended December 31,		
	2018	2017	2016
Total depreciation and amortization			
Oncology Innovation Platform	$ 690	$ 482	$ 195
Global Supply Chain Platform	1,603	2,272	1,644
Commercial Platform	976	919	187
Total consolidated depreciation and amortization	$ 3,269	$ 3,673	$ 2,026

	December 31,	
	2018	2017
Total assets:		
Oncology Innovation Platform	$ 135,878	$ 65,966
Global Supply Chain Platform	58,816	51,128
Commercial Platform	36,401	23,319
Total assets	$ 231,095	$ 140,413

	Year Ended December 31,		
	2018	2017	2016
Total revenue			
United States	$ 37,904	$ 19,933	$ 3,573
India	3,457	8,479	7,803
Austria	9,569	3,962	5,197
China	4,416	2,803	2,338
Spain	30,000	—	—
Taiwan	—	500	—
Other foreign countries	3,754	2,366	1,640
Total consolidated revenue	$ 89,100	$ 38,043	$ 20,551

	December 31,	
	2018	2017
Total property and equipment, net:		
United States	$ 6,549	$ 5,305
China	4,898	4,346
Total property and equipment, net	$ 11,447	$ 9,651

Customer revenue and accounts receivable concentration amounted to the following for the identified periods:

	Year Ended December 31,		
	2018	2017	2016
Percentage of total revenue by customer:			
Customer A	34%	—	—
Customer B	12%	15%	—
Customer C	6%	9%	24%
Customer D	4%	19%	38%

	December 31,	
	2018	2017
Percentage of total accounts receivable by customer:		
Customer A	18%	18%
Customer B	16%	10%
Customer C	12%	26%
Customer D	—	13%

18. REVENUE RECOGNITION

The Company records revenue in accordance with ASC, Topic 606 "*Revenue from Contracts with Customers*." Under Topic 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which it expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of Topic 606, the entity performs the following five steps: (i) identifies the contract(s) with a customer; (ii) identifies the performance obligations in the contract; (iii) determines the transaction price; (iv) allocates the transaction price to the performance obligations in the contract; and (v) recognizes revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. Following is a description of principal activities – separated by reportable segments – from which the Company generates its revenue.

1. Oncology Innovation Platform

License fees and consulting revenue

The Company out-licenses certain of its intellectual property ("IP") and provides related consulting services to pharmaceutical companies in specific territories that allow the customer to use, develop, commercialize, or otherwise exploit the licensed IP. In accordance with Topic 606, the Company analyzes each of its out-licensing contracts with customers to identify each of the performance obligations within the contract. Each out-license may contain multiple performance obligations. The Company has determined that each of its out-license agreements with customers are classified as functional licenses and are capable of being distinct, because the IP that is licensed carries standalone value and is not expected to be altered through the life of the agreement. Therefore, for each of its out-licensing agreements, the Company has determined that the execution of the license and delivery of the IP to the licensee is a distinct performance obligation. As such, the Company records revenue at a point-in-time for its out-licensing if any of the transaction price is allocated to the obligation, including up-front licensing fee payments. The Company's classification of each out-licensing as such requires significant judgment to be used by management. The Company considers the economic and regulatory characteristics of the licensed IP to determine if it has standalone value on the date of the licensing, which would make the licensing distinct and dictate that the Company recognizes any transaction price allocated to the license performance obligation at a point-in-time. Revenue recognized at a point-in-time for the execution of a distinct licensing of IP amounted to $32.0 million and $0.5 million for the years ended December 31, 2018 and 2017, respectively.

Other performance obligations included in the Company's out-licensing agreements include reaching milestone development and regulatory events by performing research and development activities. The Company reached one milestone event during each of the years ended December 31, 2018 and 2017 resulting in $2.0 million and $0.5 million of revenue recognized, respectively. The Company recorded the associated milestone payment portions of transaction prices as revenue at a point-in-time. Certain out-licensing agreements include performance obligations to manufacture and provide drug product in the future when the licensed product is approved for commercial sale. To date, the Company has not satisfied any of these performance obligations as none of its drugs have been approved by the regulatory agencies in each of the licensed territories.

In addition to the multiple performance obligations, the Company's out-licensing agreements include variable consideration. After the performance obligations are identified, the Company determines each portion of the transaction price, which generally includes upfront fees, milestone payments, and royalty payments. The Company begins by allocating the payments set forth in the agreement to the performance obligation to which the consideration is related. Then, the Company considers whether or not that transaction price is fixed, variable, or subject to return. If any portion of the transaction price is constrained by more than one performance obligation, the Company allocated that portion of the transaction price to the performance obligation that will be satisfied later and will not recognize revenue until it is fully satisfied and the constraint on the transaction price no longer exists. There are no other significant methods employed to allocate the transaction price to performance obligations in a contract. The Company exercises significant judgment when allocating the variable transaction prices to the proper performance obligations, considering if any of those payments are refundable or are contingent on any future events.

Grant revenue

The Company receives grant award funding to support its continuing research and development efforts. The Company considers these grants to be operating revenue as they support the Company's primary operating activities. Revenue is recognized when the underlying performance obligation is satisfied, which is generally when all grant eligibility criteria are met at a point-in-time.

2. Global Supply Chain Platform

The Company's Global Supply Chain Platform manufactures and sells pharmaceutical products under 503B regulations set forth by the FDA. The Global Supply Chain Platform also manufactures API for use internally in its research and development and clinical studies and for sale to pharmaceutical customers globally. API revenue earned by the Global Supply Platform is recognized when the Company has satisfied its performance obligation, which is the shipment or the delivery of drug products. The underlying contracts for these sales are generally purchase orders and the Company recognizes revenue at a point-in-time. Any remaining performance obligations related to product sales are the result of customer deposits and are reflected in the deferred revenue contract liability balance.

The Company also generates revenue, to a lesser extent, by providing small to mid-scale cGMP manufacturing of clinical and commercial products for pharmaceutical and biotech companies.

3. Commercial Platform

The Company's Commercial Platform generates revenue by distributing specialty products through independent pharmaceutical wholesalers. The wholesalers then sell to an end-user, normally a hospital, alternative healthcare facility, or an independent pharmacy, at a lower price previously established by the end-user and the Company. Sales are initially recorded at the list price sold to the wholesaler. Because these prices will be reduced for the end-user, the Company records a contra asset in accounts receivable and a reduction to revenue at the time of the sale, using the difference between the list price and the estimated end-user contract price. Upon the sale by the wholesaler to the end-user, the wholesaler will chargeback the difference between the original list price and price at which the product was sold to the end-user and such chargeback is offset against the initial estimated contra asset. The significant estimates inherent in the initial chargeback provision relate to wholesale units pending chargeback and to the ultimate end-user contract selling price. The Company bases the estimate for these factors on product-specific sales and internal chargeback processing experience, as well as estimated wholesaler inventory stocking levels. As of December 31, 2018 and 2017, the Company's chargebacks and other deductions totaled $11.8 million and $3.3 million, respectively, included as a reduction of accounts receivable. The Company's total expense for chargebacks and other deductions was $33.5 million and $9.8 million for the years ended December 31, 2018 and 2017, respectively.

The Company offers cash discounts, which approximate 2.0% of the gross sales price, as an incentive for prompt customer payment, and, consistent with industry practice, the Company's return policy permits customers to return products within a window of time before and after the expiration of product dating. The Company expects that its wholesale customers will make prompt payments to take advantage of the cash discounts, and expects customers to use their right of return. Therefore, at the time of sale, product revenue and accounts receivable are reduced by the full amount of the discount offered and the return expected. The Company considers payment performance and historical return rates and adjusts the accrual to reflect actual experience. As of December 31, 2018 and 2017, the Company's accrual for cash discounts and return accrual included as a reduction of accounts receivable were not material to the consolidated financial statements.

The Company also offers contractual allowances, generally rebates or administrative fees, to certain wholesale customers, group purchasing organizations ("GPOs"), and end-user customers, consistent with pharmaceutical industry practices. Settlement of rebates and fees may generally occur from one to five months from date of sale. The Company provides a provision for contractual allowances at the time of sale based on the historical relationship between sales and such allowances. Contractual allowances are reflected in the consolidated financial statements as a reduction of revenue and accounts receivable or as accrued expenses.

The Company exercises significant judgment in its estimates of the variable transaction price at the time of the sale and recognizes revenue when the performance obligation is satisfied. Factors that determine the final net transaction price include chargebacks, fees for service, cash discounts, rebates, returns, warranties, and other factors. The Company estimates all of these variables based on historical data obtained from previous sales finalized with the end-user customer on a product-by-product basis. At the time of sale, revenue is recorded net of each of these deductions. Through the normal course of business, the wholesaler will sell the product to the end-user, determining the actual chargeback, return products, and take advantage of cash discounts, charge fees for services, and claim warranties on products. The final transaction price per product is compared to the initial estimated net sale price and reviewed for accuracy. The final prices and other factors are immediately included in the Company's historical data from which it will estimate the transaction price for future sales. The underlying contracts for these sales are generally purchase orders including a single performance obligation, generally the shipment or delivery of products and the Company recognizes this revenue at a point-in-time.

Disaggregation of revenue

The following represents the Company's revenue for its reportable segment by country, based on the locations of the customer (in thousands).

	For the Year Ended December 31, 2018			
	Oncology Innovation Platform	**Global Supply Chain Platform**	**Commercial Platform**	**Consolidated Total**
United States	$ —	$ 7,478	$ 30,426	$ 37,904
Spain	30,000	—	—	30,000
India	—	3,457	—	3,457
Austria	—	9,569	—	9,569
China	2,776	1,640	—	4,416
Other Foreign Countries	—	3,754	—	3,754
Total Revenue	$ 32,776	$ 25,898	$ 30,426	$ 89,100

	For the Year Ended December 31, 2017			
	Oncology Innovation Platform	Global Supply Chain Platform	Commercial Platform	Consolidated Total
United States	$ —	$ 2,715	$ 17,218	$ 19,933
Taiwan	500	—	—	500
India	—	8,479	—	8,479
Austria	—	3,962	—	3,962
China	911	1,892	—	2,803
Other Foreign Countries	—	2,366	—	2,366
Total Revenue	$ 1,411	$ 19,414	$ 17,218	$ 38,043

	For the Year Ended December 31, 2016			
	Oncology Innovation Platform	Global Supply Chain Platform	Commercial Platform	Consolidated Total
United States	$ 63	$ 3,510	$ —	$ 3,573
India	—	7,803	—	7,803
Austria	—	5,197	—	5,197
China	935	1,403	—	2,338
Other Foreign Countries	—	1,640	—	1,640
Total Revenue	$ 998	$ 19,553	$ —	$ 20,551

The Company also disaggregates its revenue by product group which can be found in Note 17 – *Business Segment, Geographic, and Concentration Risk Information.*

Contract balances

The following table provides information about receivables and contract liabilities from contracts with customers. The Company has not recorded any contract assets from contracts with customers (in thousands).

	December 31,	
	2018	2017
Accounts receivable, gross	$ 26,061	$ 12,263
Chargebacks and other deductions	(13,101)	(3,711)
Allowance for doubtful accounts	(9)	(84)
Accounts receivable, net	$ 12,951	$ 8,468
Deferred revenue	190	1,202
Total contract liabilities	$ 190	$ 1,202

The following tables illustrate accounts receivable by reportable segments (in thousands).

	December 31, 2018			
	Oncology Innovation Platform	Global Supply Chain Platform	Commercial Platform	Consolidated Total
Accounts receivable, gross	$ —	$ 7,814	$ 18,247	$ 26,061
Chargebacks and other deductions	—	—	(13,101)	(13,101)
Allowance for doubtful accounts	—	(9)	—	(9)
Accounts receivable, net	$ —	$ 7,805	$ 5,146	$ 12,951

	December 31, 2017			
	Oncology Innovation Platform	Global Supply Chain Platform	Commercial Platform	Consolidated Total
Accounts receivable, gross	$ 49	$ 4,553	$ 7,661	$ 12,263
Chargebacks and other deductions	—	—	(3,711)	(3,711)
Allowance for doubtful accounts	—	(84)	—	(84)
Accounts receivable, net	$ 49	$ 4,469	$ 3,950	$ 8,468

As of December 31, 2018, $0.2 million of the deferred revenue balance relates to customer deposits made by customers of the Global Supply Chain Platform.

As of December 31, 2017, the $1.2 million contract liability related to customer deposits made by customers of the Global Supply Chain Platform. The Company satisfied its performance obligations allocated to these contract liabilities during the year ended December 31, 2018.

There were no other material changes to contract balances during the year ended December 31, 2018.

Practical expedients used

During the adoption of ASC 606, the Company applied the practical expedient in paragraph 606-10-10-4, the *Portfolio Approach*. This allowed the Company to apply the new revenue standard to a portfolio of contracts with similar characteristics because it reasonably expected that the effects on the financial statements of applying the guidance to the portfolio would not differ materially from applying the guidance to the individual contracts within that portfolio. The Company used this to determine the cumulative catch-up required under the modified retrospective transaction method. The Company used the portfolio approach for product sales under the Global Supply Chain Platform and product sales under the Commercial Platform. The Company did not use this approach for its out-licensing contracts, because each of those contracts have unique economic characteristics.

The Company applies the practical expedient in paragraph 606-10-50-14 and does not disclose information about remaining performance obligations related to the license of IP. This practical expedient is applied because the out-licensing agreements include sales-based royalties in exchange for the license of IP accounted for in accordance with Topic 606 and there is significant uncertainty surrounding the future variable consideration that could be received.

19. SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)

The following tables present our unaudited quarterly results of operations for each quarter within the two most recent fiscal years. This unaudited quarterly information has been prepared on the same basis as our audited consolidated financial statements and, in the opinion of management, the statement of operations data includes all adjustments, consisting of normal recurring adjustments, necessary for the fair presentation of the results of operations for these periods. The results of operations for any quarter are not necessarily indicative of the results of operations for any future periods.

	Fiscal 2018 Quarter Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
	(In thousands, except per share data)			
Statements of Operations Data:				
Revenue:				
Product sales	$ 12,605	$ 11,471	$ 13,309	$ 19,009
License fees and consulting revenue	25,091	91	5,096	2,109
Grant revenue	140	3	23	153
Total revenue	37,836	11,565	18,428	21,271
Costs and operating expenses:				
Costs of sales	11,326	9,443	11,965	14,271
Research and development expenses[2]	21,303	26,572	51,202	20,828
Selling, general, and administrative expenses	13,080	12,817	11,493	11,618
Total costs and operating expenses	45,709	48,832	74,660	46,717
Operating loss	(7,873)	(37,267)	(56,232)	(25,446)
Net loss	(7,339)	(36,950)	(57,260)	(27,162)
Less: net loss attributable to non-controlling interests	(41)	(91)	(11,090)	(49)
Net loss attributable to Athenex, Inc.	$ (7,298)	$ (36,859)	$ (46,170)	$ (27,113)
Net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted	$ (0.12)	$ (0.58)	$ (0.70)	$ (0.41)

	Fiscal 2017 Quarter Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
	(In thousands, except per share data)			
Statements of Operations Data:				
Revenue:				
Product sales	$ 3,900	$ 4,416	$ 13,662	$ 14,128
License fees and consulting revenue	598	98	60	349
Grant revenue	83	81	272	396
Total revenue	4,581	4,595	13,994	14,873
Costs and operating expenses:				
Cost of sales	2,839	4,137	8,082	10,064
Research and development expenses	26,408	17,597	11,944	20,848
Selling, general, and administrative expenses	9,799	13,632	10,364	12,317
Total costs and operating expenses	39,046	35,366	30,390	43,229
Operating loss	(34,465)	(30,771)	(16,396)	(28,356)
Net loss [1]	(41,025)	(38,668)	(23,308)	(28,395)
Less: net loss attributable to non-controlling interests	(37)	(43)	(34)	(112)
Net loss attributable to Athenex, Inc.	$ (40,988)	$ (38,625)	$ (23,274)	$ (28,283)
Net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted	$ (1.01)	$ (0.88)	$ (0.41)	$ (0.49)

Note (1): Results for the quarters ended March 31, June 30, and September 30, 2017 include interest expense and losses on derivative liabilities related to convertible notes.

Note (2): Research and development expenses for the quarter ended September 30, 2018 includes $29.5 million of non-cash license fees related to the purchase of T-Cell technology in connection with the establishment of Axis.

20. COMMITMENTS AND CONTINGENCIES

Rental and lease commitments

In August 2015, the Company entered into a lease agreement with FSMC to occupy a portion of the Conventus Center for Collaborative Medicine in Buffalo, NY. A deferred rent liability for this agreement of $1.7 million and $1.5 million was recorded as of December 31, 2018 and 2017, respectively. Total rent expense related to this location, recognized on a straight-line basis, was $1.0 million for the each of the years ended December 31, 2018, 2017, and 2016.

In July 2015, CDE entered into an agreement to lease facilities in Hong Kong. Under the rental agreement, CDE will make monthly payments of less than $0.1 million for three years beginning on July 1, 2015. Total rent expense related to this location, recognized on a straight-line basis, amounted to $0.4 million, $0.4 million, and $0.3 million for the years ended December 31, 2018, 2017, and 2016, respectively.

In October 2016, the Company's Commercial Platform entered into an agreement to lease office space in Chicago, IL. Under the lease agreement, the Company will make monthly payments based on an escalating scale over ten years. Total rent expense related to this location, recognized on a straight-line basis, amounted to $0.3 million, less than $0.2 million, and $0.1 for the years ended December 31, 2018, 2017, and 2016, respectively. The Company has recorded a deferred rent liability of $0.3 million as of December 31, 2018 and 2017. In lieu of a security deposit, an irrevocable letter of credit was issued to the landlord in the amount of $0.3 million.

The Company entered into a lease agreement expiring in 2025 to lease office space in Cranford, New Jersey that serves as its clinical research headquarters. Rent expense is recognized on a straight-line basis and amounted to $0.1 million for each of the years ended December 31, 2018, 2017, and 2016, respectively.

The Company entered into a lease agreement expiring in 2025 to lease office space in Taipei, Taiwan which serves for clinical research and clinical data management. Rent expense is recognized on a straight-line basis and amounted to less than $0.1 million for each of the years ended December 31, 2018, 2017, and 2016, respectively.

The Company leases its manufacturing and office facilities in Chongqing, China, where it produces API and performs research and development. Rent expense is recognized on a straight-line basis and amounted to $0.6 million ended December 31, 2018, 2017, and 2016.

The Company entered into additional leases for lab space, warehouse facilities, and various equipment, mainly in Buffalo, NY, during 2018 and 2019. Rent expense recognized for these operating leases was not material to the financial statements for the years ended December 31, 2018, 2017, and 2016.

Future minimum payments under the non-cancelable operating leases consists of the following as of December 31, 2018 (in thousands):

Year ending December 31:	Minimum payments
2019	$ 2,943
2020	2,466
2021	2,040
2022	1,902
2023	1,675
Thereafter	3,099
	$ 14,125

Legal Proceedings

On August 13, 2018, Athenex Pharma Solutions and Athenex Pharmaceutical Division, LLC, our wholly-owned subsidiaries, filed a complaint for declaratory judgment against Par Pharmaceuticals, Inc., Par Sterile Products, LLC and Endo Par Innovation Company, LLC (together, Par) in the United States District Court for the Western District of New York (the Court), seeking a declaratory judgment from the Court that our compounded vasopressin drug products in ready-to-use form do not infringe on patents that Par has with respect to its Vasostrict® product and that Par's patents are invalid. On October 22, 2018, Par filed a motion to dismiss the complaint on the basis that the Court does not have subject matter jurisdiction. Athenex has opposed Par's motion and that motion is fully briefed and currently pending. Par has not filed a claim for infringement of its patents in this suit but if Par's motion to

dismiss Athenex's patent suit is denied and the declaratory action proceeds, Par could proceed to lodge a counterclaim for patent infringement. If such an infringement claim were brought and the Court ruled for Par, Athenex could be enjoined from further production of compounded vasopressin within in the United States and sale of compounded vasopressin in or from the United States and for payment of damages to Par for U.S. manufacture or sale of compounded vasopressin that has already taken place, which could have a material adverse effect on our business.

In addition, on August 13, 2018, Athenex Pharma Solutions, LLC and Athenex Pharmaceutical Division, LLC filed a motion to intervene and seek the dismissal of Par's complaint against the FDA and certain governmental officials in the United States District Court for the District of Columbia. Par has sought declaratory and injunctive relief against the FDA and certain governmental officials that: (i) vasopressin be delisted from Category 1 of the FDA's list of bulk drug substances under evaluation pursuant to Section 503B of the Federal Food, Drug and Cosmetic Act (FDCA), (ii) the expansion of the FDA's enforcement discretion to Category 1 substances, be enjoined; and (iii) that the FDA be enjoined from authorizing the compounding of vasopressin under Section 503B of the FDCA. Our motion to intervene was granted. Par filed a preliminary injunction motion and we and the FDA filed motions for judgment on the pleadings. This action is currently stayed. On March 4, 2019, FDA published in the Federal Register its final decision not to include vasopressin on the list of bulk drug substances for which there is a clinical need. Also on March 4, 2019, Athenex, Inc., APS, and APD filed a complaint against FDA seeking to vacate its decision; FDA has represented to the Court in this case that "until the Court issues a decision on the merits of this action, FDA will not initiate enforcement action against Athenex based solely on Athenex's use of the bulk drug substance vasopressin to compound drugs and distribute those drugs.".

On August 14, 2018, we began selling compounded vasopressin injection in ready-to-use premix IV bags. If we are unsuccessful in obtaining the relief we seek in our lawsuit against FDA, or there is an adverse final determination that Par's patent is valid and infringed, we would have to abandon this revenue-generating line of business; such events could have a material adverse effect on our business, results of operations, financial condition and cash flows.

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Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Board Chairman (Principal Executive Officer) and our Chief Financial Officer (Principal Financial and Accounting Officer), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2018. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act means controls and other procedures of a company that are designed to ensure that information required to be disclosed by the company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well-designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2018, our Chief Executive Officer and Board Chairman (Principal Executive Officer) and our Chief Financial Officer (Principal Financial and Accounting Officer) concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Annual Report on Internal Control over Financial Reporting

This annual report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by our registered public accounting firm pursuant to exemptions provided to issuers that qualify as an "emerging growth company," as defined in Section 2(a) of the Securities Act of 1933, or the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. However, for as long as we remain an "emerging growth company" as defined in the JOBS Act, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

As of December 31, 2018, management assessed the effectiveness of our internal control over financial reporting based on the framework established in "Internal Control—Integrated Framework" issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) (2013 Framework). Based on this evaluation, management has determined that our internal control over financial reporting was effective as of December 31, 2018.

Item 9B. Other Information.

Termination of Hanmi Out-License

On August 20, 2018, we entered into a mutual letter of termination with Hanmi with respect to the Hanmi Out-License for our KX-01 oral formulation, which terminated the out-licensing agreement as of the same date. This termination will allow us to continue to explore the potential of the KX-01 oral formulation worldwide. We are also party to in-licensing agreements with Hanmi as described below and in "Item 1. Business — License and Collaboration Agreements — In-Licenses — Hanmi Licensing Agreements." A copy of the mutual letter of termination is filed as an exhibit to this Annual Report on Form 10-K.

Amendment of 2011 Hanmi Agreement

On September 4, 2018, we entered into the fifth amendment to the December 2011 in-licensing agreement with Hanmi, which provided for Athenex to pursue worldwide development of the Orascovery Program, except for Korea. Hanmi retained the right to oversee the development of the Orascovery Program and related regulatory efforts in Korea. Going forward, we will have the opportunity to develop the Orascovery Program in the Middle East, North Africa and South Africa territories. In connection with entering into this amendment, we agreed to pay Hanmi $40,000. A copy of this amendment is filed as an exhibit to this Annual Report on Form 10-K.

Changes in Named Executive Officer Compensation.

On March 27, 2018, our Board of Directors approved the compensation of our executive officers for the year ended December 31, 2018, including their annual salaries, cash bonus awards and equity-based compensation. For 2018, the Board of Directors approved an annual salary for Johnson Lau of $500,000, along with a cash bonus of up to $400,000, the amount of which will be based solely on the discretion of the Board of Directors. The Board of Directors approved a base salary for Jeffrey Yordon of $400,000, along with a cash bonus of up to $320,000, the amount of which will be based solely on the discretion of the Board of Directors. The Board of Directors approved a base salary for Rudolf Kwan of $320,000, along with a cash bonus of up to $192,000, the amount of which will be based solely on the discretion of the Board of Directors. Messrs. Lau, Yordon and Kwan were also granted 250,000, 100,000 and 120,000 time-vesting options to purchase Common Stock, respectively, which vest in four equal annual installments beginning on the anniversary of the grant date of March 27, 2018.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item is incorporated by reference from the sections captioned "Election of Directors," "Executive Officers," "Corporate Governance Matters," "Code of Business Conduct and Ethics," "Section 16(a) Beneficial Ownership Reporting Compliance" contained in our proxy statement related to the 2019 Annual Meeting of Stockholders (Proxy Statement) currently scheduled to be held on June 11, 2019, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 11. Executive Compensation.

The information required by this Item is incorporated by reference from the information under the sections captioned "Executive Compensation," "Director Compensation" and "Compensation Committee Interlocks and Insider Participation" in the Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item is incorporated by reference from the information under the sections captioned "Executive Compensation", "Equity Compensation Plan Information" and "Security Ownership of Certain Beneficial Owners and Management" contained in the Proxy Statement.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item is incorporated by reference from the information under the sections captioned "Certain Relationships and Related Party Transactions" and "Corporate Governance Matters" in the Proxy Statement.

Item 14. Principal Accounting Fees and Services.

The information required by this Item is incorporated by reference from the information under the section captioned "Audit Committee Report" in the Proxy Statement.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) The following documents are filed as part of this report.

1. Financial Statements.

The financial statements of the Company and the related report of the Company's independent registered public accounting firm thereon have been filed under Item 8 hereof.

2. Financial Statement Schedules.

Schedule II—Valuation and Qualifying Accounts

Activity in the following valuation and qualifying accounts consisted of the following (in thousands):

Col. A Description	Col. B Balance at Beginning of Period	Col. C - Additions: Charged to Costs & Expenses	Col. C - Additions: Charged to Other Accounts - Describe	Col. D Deductions - Describe	Col. E Balance at End of Period
December 31, 2018					
Allowance for doubtful accounts	$ 84	$ 28 (1)	$ —	$ (103) (1)	$ 9
Allowance for chargebacks and other deductions	$ 3,711	$ 36,102 (2)	$ —	$ (26,712) (2)	$ 13,101
Deferred tax asset valuation allowance	$ 60,379	$ —	$ 28,076 (3)	$ —	$ 88,455
December 31, 2017					
Allowance for doubtful accounts	$ 155	$ 662 (1)	$ —	$ (733) (1)	$ 84
Allowance for chargebacks and other deductions	$ —	$ 3,834 (2)	$ —	$ (123) (2)	$ 3,711
Deferred tax asset valuation allowance	$ 62,308	$ —	$ (1,929) (3)	$ —	$ 60,379
December 31, 2016					
Allowance for doubtful accounts	$ 478	$ 267 (1)	$ —	$ (590) (1)	$ 155
Deferred tax asset valuation allowance	$ 31,400	$ —	$ 30,908 (3)	$ —	$ 62,308

(1) Increases in the allowance for doubtful accounts consist of our provision for bad debts, which is included within selling, general, and administrative expenses on the consolidated statements of operations and comprehensive loss. Decreases in the allowances for doubtful accounts consist of the write-off of specific accounts and the recovery of previously reserved receivables.

(2) Increases in the allowance for chargebacks and other deductions consist of our provision for chargebacks, cash discounts, returns, fees, and other credits, which are a deduction from product sales on the consolidated statements of operations and comprehensive loss. Decreases in the allowances for chargebacks and other deduction consist of the collection of the underlying accounts and advances received on chargebacks.

(3) Increases and decreases in the valuation allowance for deferred income tax assets offset the increases and decreases in our gross deferred tax assets, based on the expected realization of those future tax benefits.

Item 16. Form 10-K Summary.

None.

(b) Exhibits.

Exhibit Number	Exhibit Title	Incorporated by Reference (Unless Otherwise Indicated)			
		Form	File	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Company, effective as of June 19, 2017.	Form 8-K	001-38112	3.1	June 22, 2017
3.2	Amended and Restated Bylaws of the Company, effective as of June 19, 2017.	Form 8-K	001-38112	3.2	June 22, 2017
4.1	Specimen Common Stock Certificate.	Form S-1	333-217928	4.1	May 12, 2017
10.1+	Form of Director and Officer Indemnification Agreement.	Form S-1	333-217928	10.1	May 12, 2017
10.2+	First Amended and Restated 2004 Common Unit Option Plan and Form of Unit Option Agreement.	Form S-1	333-217928	10.2	May 12, 2017
10.3+	First Amended and Restated 2007 Common Unit Option Plan and Form of Unit Option Agreement.	Form S-1	333-217928	10.3	May 12, 2017
10.4+	2013 Common Stock Option Plan and Form of Common Stock Option Agreement.	Form S-1	333-217928	10.4	May 12, 2017
10.5+	2017 Omnibus Incentive Plan and Form of Stock Option Award Agreement.	Form S-1/A	333-217928	10.5	June 2, 2017
10.6+	2017 Employee Stock Purchase Plan.	Form S-1/A	333-217928	10.6	June 2, 2017
10.7^	License Agreement by and between Hanmi Pharmaceutical Ltd. and Kinex Pharmaceuticals, LLC, effective as of December 16, 2011.	Form S-1	333-217928	10.7	May 12, 2017
10.7.1	First Amendment to License Agreement by and between Kinex Pharmaceuticals, LLC and Hanmi Pharmaceutical Co., Ltd., effective as of November 9, 2012.	Form S-1	333-217928	10.7.1	May 12, 2017
10.7.2	Second Amendment to License Agreement by and between Kinex Pharmaceuticals, LLC and Hanmi Pharmaceutical Ltd., effective as of October 21, 2013.	Form S-1	333-217928	10.7.2	May 12, 2017
10.7.3	Third Amendment to License Agreement by and between Kinex Pharmaceuticals, Inc. and Hanmi Pharmaceutical Ltd., effective as of March 3, 2015.	Form S-1	333-217928	10.7.3	May 12, 2017
10.7.4^	Fourth Amendment to License Agreement by and between Athenex, Inc. and Hanmi Pharmaceutical Co. Ltd., effective as of March 7, 2017.	Form S-1	333-217928	10.7.4	May 12, 2017
10.8^	License Agreement by and among Hanmi Pharmaceutical Co., Ltd., Kinex Therapeutics (HK) Limited, and Kinex Pharmaceuticals, Inc., effective as of June 28, 2013.	Form S-1	333-217928	10.8	May 12, 2017
10.9^	License Agreement by and between Kinex Pharmaceuticals, LLC and Hanmi Pharmaceutical Ltd., effective as of April 2011.	Form S-1	333-217928	10.9	May 12, 2017
10.10^	License Agreement by and between Kinex Pharmaceuticals, LLC and PharmaEssentia Corp., effective as of December 8, 2011.	Form S-1	333-217928	10.10	May 12, 2017

Exhibit Number	Exhibit Title	Incorporated by Reference (Unless Otherwise Indicated)			
		Form	File	Exhibit	Filing Date
10.10.1	First Amendment to License Agreement by and between Athenex, Inc. and PharmaEssentia Corp., effective as of December 23, 2016.	Form S-1	333-217928	10.10.1	May 12, 2017
10.11^	License Agreement by and between Kinex Pharmaceuticals, Inc. and PharmaEssentia Corp, effective as of December 16, 2013.	Form S-1	333-217928	10.11	May 12, 2017
10.11.1	First Amendment to License Agreement by and between Athenex, Inc. and PharmaEssentia Corp., effective as of December 23, 2016.	Form S-1	333-217928	10.11.1	May 12, 2017
10.12^	License Agreement by and between Kinex Pharmaceuticals, Inc. and ZenRx Limited, effective as of April 25, 2013.	Form S-1	333-217928	10.12	May 12, 2017
10.13^	License Agreement by and between Kinex Pharmaceuticals, LLC and Guangzhou Xiangxue New Drug Discovery and Development Company Limited, effective as of May 6, 2012.	Form S-1	333-217928	10.13	May 12, 2017
10.14^	Binding Term Sheet for License by and between Athenex Pharmaceutical Division, LLC and Gland Pharma Limited, effective as of August 1, 2016.	Form S-1	333-217928	10.14	May 12, 2017
10.14.1^	Binding Term Sheet for License by and between Athenex Pharmaceutical Division, LLC and Gland Pharma Limited, effective as of August 26, 2016.	Form S-1	333-217928	10.14.1	May 12, 2017
10.14.2^	Binding Term Sheet for License by and between Athenex Pharmaceutical Division, LLC and Gland Pharma Limited, effective as of February 22, 2017.	Form S-1	333-217928	10.14.2	May 12, 2017
10.14.3^	Binding Term Sheet for License by and between Athenex Pharmaceutical Division, LLC and Gland Pharma Limited, effective as of May 5, 2017.	Form S-1/A	333-217928	10.14.3	June 2, 2017
10.15^	Joint Venture Agreement by and between SunGen Pharma LLC and Athenex Pharmaceutical Division, effective as of September 22, 2016.	Form S-1	333-217928	10.15	May 12, 2017
10.15.1^	Addendum to Joint Venture Agreement by and between SunGen Pharma LLC and Athenex Pharmaceutical Division, LLC, effective November 29, 2016.	Form S-1	333-217928	10.15.1	May 12, 2017
10.15.2	Limited Liability Company Agreement of Peterson Athenex Pharmaceuticals, LLC.	Form S-1	333-217928	10.15.2	May 12, 2017
10.16^	Service Agreement by and between Dohmen Life Science Services, LLC and Athenex Pharmaceutical Division, LLC, effective as of August 9, 2016.	Form S-1	333-217928	10.16	May 12, 2017
10.17^	Clinical Trial Collaboration and Supply Agreement by and among Athenex, Inc., Eli Lilly and Company and ImClone LLC, effective as of October 24, 2016.	Form S-1	333-217928	10.17	May 12, 2017
10.18	Agreement for Medical Technology Research, Development, Innovation, and Commercialization Alliance by and between Fort Schuyler Management Corporation and Kinex Pharmaceuticals, Inc., effective as of May 1, 2015.	Form S-1	333-217928	10.18	May 12, 2017

Exhibit Number	Exhibit Title	Incorporated by Reference (Unless Otherwise Indicated)			
		Form	File	Exhibit	Filing Date
10.18.1	First Amendment to Agreement for Medical Technology Research, Development, Innovation, and Commercialization Alliance by and between Fort Schuyler Management Corporation and Kinex Pharmaceuticals, Inc., effective as of July 21, 2015.	Form S-1	333-217928	10.18.1	May 12, 2017
10.18.2	Second Amendment to Agreement for Medical Technology Research, Development, Innovation, and Commercialization Alliance by and between Fort Schuyler Management Corporation and Athenex, Inc., effective as of June 22, 2016.	Form S-1	333-217928	10.18.2	May 12, 2017
10.19	Sublease Agreement by and between Fort Schuyler Management Corporation and Kinex Pharmaceuticals, Inc., effective as of July 21, 2015.	Form S-1	333-217928	10.19	May 12, 2017
10.20	Athenex Pharmaceutical Base Project Located in the Chongqing Maliu Riverside Development Zone Agreement with Chongqing Maliu Riverside Development and Investment Co., Ltd., effective as of October 16, 2015 (English translation of original foreign language agreement).	Form S-1	333-217928	10.20	May 12, 2017
10.21^	Binding Term Sheet for License, Supply and Distribution Agreement by and among Athenex API Limited, Nang-Kuang Pharmaceutical Co., LTD and CANDA NK-2, LLC, effective as of December 29, 2016.	Form S-1	333-217928	10.21	May 12, 2017
10.22	Asset Purchase Agreement by and between Athenex, Inc. and Amphastar Pharmaceuticals, Inc., dated February 1, 2017.	Form S-1	333-217928	10.22	May 12, 2017
10.23+	Amended and Restated Employment Agreement by and between Johnson Lau and Kinex Pharmaceuticals, Inc., effective as of June 1, 2015.	Form S-1	333-217928	10.23	May 12, 2017
10.24+	Employment Agreement by and between Kinex Polymed Hong Kong Ltd. and William Zuo, PhD, effective as of June 1, 2015.	Form S-1	333-217928	10.24	May 12, 2017
10.25+	Employment Agreement by and between Athenex, Inc. and Dr. Rudolf Min-Fun Kwan, effective as of February 21, 2017.	Form S-1	333-217928	10.25	May 12, 2017
10.26+	Employment Agreement by and between Athenex, Inc. and Dr. Simon Pedder, effective as of February 20, 2017.	Form S-1	333-217928	10.26	May 12, 2017
10.27+	Employment Agreement by and between Athenex, Inc. and J. Nick Riehle, effective as of February 21, 2017.	Form S-1	333-217928	10.27	May 12, 2017
10.28+	Employment Agreement by and between Athenex, Inc. and Jeffrey Yordon, effective as of February 21, 2017.	Form S-1	333-217928	10.28	May 12, 2017
10.29	Grant Disbursement Agreement by and between New York State Urban Development Corporation d/b/a Empire State Development and Athenex, Inc., dated September 4, 2017.	Form 10-Q	001-38112	10.30	November 9, 2017
10.30^	License and Development Agreement by and between Athenex, Inc., Almirall, S.A. and Aqua Pharmaceuticals LLC., dated as of December 11, 2017.	Form 8-K	001-38112	10.1	December 15, 2017
10.31	Standard Form of Agreement by and between M+W U.S., Inc. and Athenex, Inc. on December 29, 2017.	Form 10-K	001-38112	10.32	March 26, 2018

Exhibit Number	Exhibit Title	Incorporated by Reference (Unless Otherwise Indicated)			
		Form	File	Exhibit	Filing Date
10.32+	Transition Agreement by and between Athenex, Inc. and James Zukin, dated April 27, 2018.	Form 8-K	001-38112	10.33	April 30, 2018
10.33	Stock Purchase Agreement dated as of June 29, 2018 by and between Athenex, Inc. and Perceptive Life Sciences Master Fund, Ltd.	Form 8-K	001-38112	10.1	July 2, 2018
10.34	Senior Secured Term Loan Agreement dated as of June 30, 2018 by and between Athenex, Inc. and Perceptive Advisors LLC.	Form 8-K	001-38112	10.2	July 2, 2018
10.35^	License Agreement dated as of June 29, 2018 by and between Xiangxue Life Sciences Ltd. and Axis Therapeutics Limited.	Form 8-K	001-38112	10.3	July 2, 2018
10.36^	License Agreement dated as of June 29, 2018 by and between Athenex Therapeutics Limited and Avalon Polytom (HK) Limited Pegtomarginase.	Form 8-K	001-38112	10.4	July 2, 2018
10.37^	License and Supply Agreement dated as of June 29, 2018 by and between Athenex Therapeutics Limited and Avalon HepaPOC Limited Galactose Meter and Strip.	Form 8-K	001-38112	10.5	July 2, 2018
10.38	Registration Rights Agreement dated as of July 3, 2018 by and between Athenex, Inc. and Perceptive Life Sciences Master Fund Ltd.	Form 10-Q	001-38112	10.7	August 14, 2018
10.39+	Employment Agreement between the Company and Randoll Sze dated as of August 20, 2018.	Form 8-K	001-38112	10.1	August 20, 2018
10.40^	First Amendment to License and Development Agreement by and between Athenex, Inc., Almirall, S.A., and Aqua Pharmaceuticals LLC, dated as of September 26, 2018.	Form 10-Q	001-38112	10.3	November 14, 2018
10.41^	Letter Agreement by and between Athenex, Inc., Almirall, S.A. and Aqua Pharamceuticals LLC dated as of September 26, 2018.	Form 10-Q	001-38112	10.4	November 14, 2018
10.42^	License Agreement dated as of December 30, 2018 by and between Athenex, Inc. and Chongqing Taihao Pharmaceutical Co. Ltd.	Form 8-K	001-38112	10.1	January 3, 2019
10.43^	Sublicense Agreement dated as of December 30, 2018 by and among Chongqing Taihao Pharmaceutical Co. Ltd., Chongqing Jingdong Junzhuo Pharmaceutical Co., Ltd. and Athenex, Inc.	Form 8-K	001-38112	10.2	January 3, 2019

Exhibit Number	Exhibit Title	Incorporated by Reference (Unless Otherwise Indicated)			
		Form	File	Exhibit	Filing Date
10.44	Mutual Letter of Termination of the License Agreement by and between Kinex Pharmaceuticals, LLC and Hanmi Pharmaceutical Ltd., effective as of August 20, 2018.	—	—	—	Filed herewith
10.45	Fifth Amendment to License Agreement by and between Athenex, Inc. and Hanmi Pharmaceutical Co. Ltd., effective as of September 4, 2018.	—	—	—	Filed herewith
10.46^^	Second Amendment to License Agreement by and between Athenex, Inc. and PharmaEssentia Corp., effective as of November 27, 2018.	—	—	—	Filed herewith
21.1	Subsidiaries of Athenex, Inc.	—	—	—	Filed herewith
23.1	Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm.	—	—	—	Filed herewith
24.1	Power of Attorney (included on signature page hereto).	—	—	—	Filed herewith
31.1	Certification of the Chief Executive Officer and Board Chairman (Principal Executive Officer) pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
31.2	Certification of the Chief Financial Officer (Principal Financial and Accounting Officer) pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
32.1	Certification of the Chief Executive Officer and Board Chairman (Principal Executive Officer) and Chief Financial Officer (Principal Financial and Accounting Officer) pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
101.INS	XBRL Instance Document.	—	—	—	Filed herewith
101.SCHY	XBRL Taxonomy Extension Schema Document.	—	—	—	Filed herewith
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.	—	—	—	Filed herewith
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.	—	—	—	Filed herewith
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.	—	—	—	Filed herewith
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.	—	—	—	Filed herewith

+ Indicates management contract or compensatory plan.

^ Confidential treatment has been granted for certain confidential portions of this exhibit pursuant to Rule 406 under the Securities Act. In accordance with Rule 406, these confidential portions have been omitted from this exhibit and filed separately with the Securities and Exchange Commission.

^^ Confidential treatment is requested for certain confidential portions of this exhibit pursuant to Rule 406 under the Securities Act. In accordance with Rule 406, these confidential portions have been omitted from this exhibit and filed separately with the Commission.

SIGNATURES

Pursuant to the requirements of Sections 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

ATHENEX, INC.

By: /s/ Johnson Y.N. Lau
Johnson Y.N. Lau
Chief Executive Officer and Board Chairman

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Randoll Sze and Teresa Bair, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Johnson Y.N. Lau Johnson Y.N. Lau	Chief Executive Officer and Board Chairman (Principal Executive Officer)	March 11, 2019
/s/ Randoll Sze Randoll Sze	Chief Financial Officer (Principal Financial and Accounting Officer)	March 11, 2019
/s/ Kim Campbell Kim Campbell	Director	March 11, 2019
/s/ Manson Fok Manson Fok	Director	March 11, 2019
/s/ Jinn Wu Jinn Wu	Director	March 11, 2019
/s/ Song-Yi Zhang Song-Yi Zhang	Director	March 11, 2019
/s/ Sheldon Trainor-Degirolamo Sheldon Trainor-Degirolamo	Director	March 11, 2019
/s/ Benson Tsang Benson Tsang	Director	March 11, 2019

Exhibit 31.1

CERTIFICATION PURSUANT TO
SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Johnson Y.N. Lau, certify that:

1. I have reviewed this Annual Report on Form 10-K of Athenex, Inc. (the registrant);

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2019

/s/ Johnson Y.N. Lau

Name: Johnson Y.N. Lau

Title: Chief Executive Officer and Board Chairman

(Principal Executive Officer)

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Exhibit 31.2

CERTIFICATION PURSUANT TO
SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Randoll Sze, certify that:

1. I have reviewed this Annual Report on Form 10-K of Athenex, Inc. (the registrant);

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2019

/s/ Randoll Sze

Name: Randoll Sze

Title: Chief Financial Officer

(Principal Financial and Accounting Officer)

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Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In accordance with 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Johnson Y.N. Lau, Chief Executive Officer and Board Chairman (Principal Executive Officer) of Athenex, Inc. (the "registrant"), and Randoll Sze, Chief Financial Officer of the registrant (Principal Financial and Accounting Officer), each hereby certifies that, to the best of their knowledge:

1. The registrant's Annual Report on Form 10-K for the period ended December 31, 2018, to which this Certification is attached as Exhibit 32.1 (the "Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition of the registrant at the end of the period covered by the Report and results of operations of the registrant for the period covered by the Report.

Date: March 11, 2019

/s/ Johnson Y.N. Lau

Name: Johnson Y.N. Lau
Title: Chief Executive Officer and Board Chairman
(Principal Executive Officer)

/s/ Randoll Sze

Name: Randoll Sze
Title: Chief Financial Officer
(Principal Financial and Accounting Officer)

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Board of Directors

Johnson Y.N. Lau, M.D., Director
Chief Executive Officer and Chairman of the Board, Athenex, Inc.

Kim Campbell, Director
Founding Principal, Peter Lougheed Leadership College at the University of Alberta

Stephanie Davis, Director
Senior Client Partner, Korn Ferry

Manson Fok, Director
Chairman, Virtus Medical Group
Dean, Faculty of Health Sciences, Macau University of Science and Technology

Jordan Kanfer, Director
Managing Director of Convertible and Equity Research, Opti Capital

John Tiong Lu Koh, Director
Senior Advisor, Global Counsel

Benson Kwan Hung Tsang, Director
Founder, Benita Consulting Company

John Moore Vierling, Ph.D., Director
Tenured Professor of Medicine and Surgery and Chief of Hepatology, Baylor College of Medicine

Jinn Wu, Ph.D., Director
Scientific Strategic Advisor, WuXi AppTec Group

Executive Officers

Johnson Y.N. Lau, M.D., Chief Executive Officer

Randoll Sze, Chief Financial Officer

Jeffrey Yordon, Chief Operating Officer and President, Athenex Pharmaceutical Division

Rudolf Kwan, M.B.B.S., Chief Medical Officer

Simon Pedder, Ph.D., Chief Business and Strategy Officer, Proprietary Products

William Zuo, Ph.D., President, China Division

Financial Reports

Copies of the Company's Annual Report on Form 10-K as filed with the Securities and Exchange Commission are available at www.athenex.com or on request, free of charge, by calling (716) 427-2950 or emailing IR@athenex.com.

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