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, 2020

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	**Trading Symbol**	**Name of Exchange on Which Registered**
Common Stock, par value $0.001 per share	**ATNX**	**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 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 ExchangeAct.

Large Accelerated Filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report ☒

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 $13.76 of the registrant's common stock as reported on The Nasdaq Global Market on June 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $702 million.

As of February 19, 2021, 93,454,700 shares of common stock of the registrant were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2021 annual meeting of stockholders currently scheduled to be held on June 4, 2021 are incorporated by reference into Part III Items 10, 11, 12, 13 and 14 of this Form 10-K.

SPECIAL NOTE ABOUT FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (the "Annual Report") contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and section 27A of the Securities Act of 1933, as amended (the "Securities Act") and the Private Securities Litigation Reform Act of 1995. 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. 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.

Risk Factors Summary

Risks Related to the COVID-19 Pandemic

- The impact of the COVID-19 pandemic on our business clinical development activities and clinical trials.

Risks Related to Our Financial Position and Need for Additional Capital

- The volatility of our financial results related to our revenue and expenses.
- We will be unable to access funding under certain of our existing financing facilities until Oral Paclitaxel is approved and may be unable to obtain additional capital to finance the development and commercialization of our drug candidates.
- Our inability to refinance, extend, or repay our substantial indebtedness owed to our senior secured lender, would have a material adverse effect on our financial condition and ability to continue as a going concern.
- Our ability to access additional capital is dependent on the fulfillment of certain conditions, which we may not achieve.
- Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates

Risk Related to Clinical Development of Our Proprietary Drug Candidates

- The developmental status of the majority of our primary clinical candidates may make it difficult to evaluate our current business and predict our future performance.
- The novel approach to some of our drug candidates could result in delays in clinical development, and delays in our ability to achieve regulatory approval or commercialization, or market acceptance.

- If clinical trials of our drug candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA, NMPA or other regulatory authorities, as the FDA recently indicated in its Complete Response Letter (CRL) with respect to our NDA for Oral Paclitaxel, we will incur costs and experience delays in the development and commercialization of our drug candidates.

Risks Related to Development, Regulatory Approval and Commercialization

- The regulatory approval processes of the FDA, NMPA and other regulatory authorities are lengthy, time consuming and inherently unpredictable
- The FDA may not accept data from clinical trials outside the U.S.
- Our approved drugs and drug candidates have caused and may cause undesirable adverse events that could delay or prevent their regulatory approval or limit the commercial profile of an approved label.
- Our commercialization of Klisyri® and of any of our drug candidates, if approved, subjects us to ongoing regulatory obligations, which may result in significant additional expenses and we may be subject to penalties.

Risks Related to Commercialization of Klisyri® and Our Drug Candidates

- Any delays in obtaining regulatory approval of our drug candidates, including Oral Paclitaxel, could impact our ability to generate revenue.
- Klisyri® and any of our drug candidates, if approved, may fail to achieve market acceptance
- Orphan drugs target rare diseases and must therefore capture significant market share at high per-patient cost to generate reasonable returns
- Our limited manufacturing experience may materially impact our revenue and financial condition.
- Our limited experience in marketing proprietary drug products could impact our ability to generate sales revenue from such products.
- Klisyri® and any of our drug candidates, if approved, may become subject to unfavorable pricing regulations, third party reimbursement practices or healthcare reform initiatives, which could harm our business
- The use of legal, regulatory, and legislative strategies by both brand and generic competitors, and newly enacted legislation could adversely affect our results of operations.
- Our compounded preparations and the pharmacy compounding industry are subject to regulatory and customer scrutiny

Risks Related to Our Intellectual Property

- A significant portion of our intellectual property portfolio currently comprises pending patent applications.
- We may not be able to successfully protect our intellectual property rights, and claims of infringement by others
- If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.
- 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, we could be required to pay monetary damages or could lose license rights that are important to our business.
- If our licensing and sublicensing activities result in non-compliance with our licensing agreements, our business relationships with our licensing partners may suffer.

Risks Related to Our Reliance on Third Parties

- The reliance on third parties to conduct our preclinical studies and clinical trials may impact our ability to obtain regulatory approval for or commercialize our drug candidates.
- Our dependence on a limited number of API customers and pharmaceutical wholesalers to generate revenue.
- 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 our drug candidates, if approved, which could harm our business if those third parties fail to provide us with sufficient quantities.

Risks Related to Our Industry, Business and Operation

- We are dependent on our key personnel, and the failure to retain our qualified personnel, may impact our business strategy.
- We are substantially dependent on our public-private partnerships and if we or our counterparties fail to meet their obligations of those agreements, it would materially impact our business.
- Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud
- We may have conflicts of interest and transactions with our affiliates and related parties that were not negotiated at arms' length.
- Our internal computer systems, or those used by our contract research organizations (CROs), collaboration partners, third-party service providers or other contractors or consultants, may fail or suffer security breaches.
- If product liability lawsuits are brought against us, we may incur substantial liabilities.
- We have limited insurance coverage, and any claims beyond our insurance coverage may result in substantial costs.
- If our manufacturing facilities are damaged or destroyed or production at such facilities is otherwise interrupted, our business and prospects would be negatively affected.

Risks Related to Government Regulation

- 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.

Risks Related to Our Doing Business in China

- Changes in the political and economic policies of the Chinese government may materially and adversely affect our business.
- There are uncertainties regarding the interpretation and enforcement of laws, rules and regulations in China.
- 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.

Risks Related to Common Stock

- 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.
- Anti-takeover provisions in our charter documents may discourage our acquisition by a third party, which could limit our stockholders' opportunity to sell their shares at a premium.

PART I

Item 1. Business.

Overview

Athenex, Inc., together with its subsidiaries ("Athenex," the "Company," "we," "us" or "our"), is a global biopharmaceutical company dedicated to becoming a leader in the discovery, development and commercialization of next generation drugs for the treatment of cancer. Our mission is to improve the lives of cancer patients by creating more effective, safer and tolerable treatments. We are organized around three platforms, an Oncology Innovation Platform, a Commercial Platform and a Global Supply Chain Platform. Our current clinical pipeline in the Oncology Innovation Platform is derived from four different proprietary technologies: (1) Orascovery, based on a P-glycoprotein ("P-gp") pump inhibitor, (2) Src Kinase inhibition, (3) T-cell Receptor-engineered T-cells ("TCR-T"), and (4) arginine deprivation therapy. We have assembled a strong and experienced leadership team and have established global operations across the pharmaceutical value chain to execute our goal of becoming a global leader in bringing innovative cancer treatments to the market and improving health outcomes.

Significant Developments in the Oncology Innovation Platform

Orascovery Platform

Our Orascovery technology is based on the novel P-gp pump inhibitor molecule, encequidar, formerly known as HM30181A. Oral administration of encequidar in combination with established chemotherapy agents such as paclitaxel, irinotecan, docetaxel, topotecan and eribulin has been shown in our clinical studies to date to improve the absorption of these agents by blocking the P-gp pump in the intestinal wall. Oral paclitaxel and encequidar, formerly known as Oraxol ("Oral Paclitaxel"), is our lead asset in our Orascovery platform. We are also advancing the following clinical candidates for the treatment of solid tumors on this platform: oral irinotecan and encequidar, formerly known as Oratecan ("Oral Irinotecan"); oral docetaxel and encequidar, formerly known as Oradoxel ("Oral Docetaxel"); oral topotecan and encequidar, formerly known as Oratopo ("Oral Topotecan"); and oral eribulin and encequidar, formerly known as Eribulin ORA ("Oral Eribulin").

Significant developments in our Orascovery platform in 2020 include the following:

On February 26, 2021, we received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration ("FDA") regarding our New Drug Application ("NDA") for Oral Paclitaxel for the treatment of metastatic breast cancer. The FDA issues a CRL to indicate that the review cycle for an application is complete and that the application is not ready for approval in its present form. In the CRL, the FDA indicated its concern of safety risk to patients in terms of an increase in neutropenia-related sequelae on the Oral Paclitaxel arm compared with the IV paclitaxel arm in the Phase III study. The FDA also expressed concerns regarding the uncertainty over the results of the primary endpoint of objective response rate (ORR) at week 19 conducted by blinded independent central review (BICR). The agency stated that the BICR reconciliation and re-read process may have introduced unmeasured bias and influence on the BICR. Additionally, the FDA recommended that we conduct a new adequate and well-conducted clinical trial in a patient population with metastatic breast cancer ("MBC") representative of the population in the U.S. The agency determined that additional risk mitigation strategies to improve toxicity, which may involve dose optimization and / or exclusion of patients deemed to be at higher risk of toxicity, are required to support potential approval of the NDA.

We are working to consider the appropriate next steps in the development of Oral Paclitaxel. We plan to request a meeting with the FDA to discuss the FDA's response, engage in a dialogue on the design and scope of a clinical trial to address the agency's requirements and align on the next steps required to obtain approval.

On September 1, 2020, we announced the FDA accepted for filing our NDA for Oral Paclitaxel for the treatment of MBC and granted the application Priority Review. Under the Prescription Drug User Fee Act ("PDUFA"), the FDA set a target action date of February 28, 2021.

On December 9, 2020, we presented updated Phase 3 data on survival and tolerability associated with Oral Paclitaxel in metastatic breast cancer patients at the 2020 San Antonio Breast Cancer Symposium ("SABCS"). Progression free survival (PFS) and overall survival (OS) data presented indicates benefits of Oral Paclitaxel versus IV paclitaxel and supports the superiority of increased overall response rate observed with Oral Paclitaxel. In the intent-to-treat (ITT) population, Oral Paclitaxel showed a benefit on PFS versus IV paclitaxel and showed a trend favoring Oral Paclitaxel on OS versus IV paclitaxel. Oral Paclitaxel demonstrated a median PFS of 8.4 months vs. 7.4 months, hazard ratio (HR) 0.768 (95% CI: 0.584, 1.01), p=0.046. Oral Paclitaxel demonstrated a median OS of 22.7 months vs. 16.5 months, HR 0.794 (95% CI: 0.607, 1.037), p=0.082.

On September 8, 2020, we and Quantum Leap Healthcare Collaborative ("Quantum Leap") jointly announced the launch of two new study arms of the I-SPY 2 TRIAL to evaluate Oral Paclitaxel in combination with GlaxoSmithKline's ("GSK") dostarlimab, an investigational antibody binding PD-1, in the neoadjuvant chemotherapy setting, targeting stage 2/3 HER2+ and HER2- breast cancers. The I-SPY 2 TRIAL, sponsored by Quantum Leap, is a standing Phase 2 randomized, controlled, multicenter platform with a Bayesian adaptive randomization design aimed to rapidly screen and identify promising new treatments in specific subgroups of adults with newly-diagnosed, high-risk (high likelihood of recurrence), locally-advanced breast cancer that is either Stage II or Stage III. GSK will provide dostarlimab. We will provide Oral Paclitaxel. Quantum Leap will be responsible for running the trial.

On May 29, 2020, we presented interim data from an ongoing Phase II clinical trial in which Oral Paclitaxel monotherapy showed encouraging efficacy and tolerability in elderly patients with unresectable cutaneous angiosarcoma, an aggressive malignancy with poor prognosis. The interim results were presented at the American Society of Clinical Oncology (ASCO) 2020 Virtual Scientific Program and reflected data from 22 evaluable patients out of 26 enrolled patients. The interim data showed a clinical benefit rate (CR+PR+SD) of 100% in 22 evaluable patients who reached their first post treatment efficacy evaluation. All 22 patients experienced a reduction in tumor size. Complete responses (CR) were observed in 27.3% of patients (6/22), partial responses (PR) were observed in 22.7% of patients (5/22), and stable disease was observed in 50% of patients (11/22). Oral Paclitaxel has been generally well tolerated in this predominantly elderly population.

We are also evaluating Oral Paclitaxel in combination with other therapies, including anti-VEGF and anti-PD-1 therapies. We are studying Oral Paclitaxel with ramucirumab in a Phase 1b study in patients with advanced gastric cancer who failed previous chemotherapy and the expansion phase of the study has completed enrollment. Our Phase 1/2 study of Oral Paclitaxel in combination with pembrolizumab in patients with advanced solid malignancies is ongoing.

In addition to our lead product candidate, development of our other Orascovery product candidates is ongoing. We are planning Phase 2 studies for both Oral Irinotecan and Oral Docetaxel. A Phase 1 study of Oral Eribulin in patients with solid tumors is ongoing.

Src Kinase Inhibition Platform

Our Src Kinase inhibition platform technology is based on novel small molecule compounds that have multiple mechanisms of action, including the inhibition of the activity of Src Kinase and the inhibition of tubulin polymerization, which may limit the growth or proliferation of cancerous cells. We believe the combination of these mechanisms of action provides a broader range of anti-cancer activity compared to either mechanism of action alone. Our lead product candidate on our Src Kinase inhibition platform is tirbanibulin (formerly known as KX2-391 and KX-01) ointment, which we are advancing for the treatment of actinic keratosis ("AK") as well as psoriasis and skin cancer. Our other clinical candidates and their indications in this platform include tirbanibulin oral for solid and liquid tumors, and KX2-361, formerly known as KX-02, for brain cancers, such as glioblastoma multiforme ("GBM").

Significant developments in our Src Kinase inhibition platform in 2020 include the following:

On December 15, 2020, we announced that the FDA has approved Klisyri® (tirbanibulin) for the topical treatment of AK on the face or scalp. Klisyri is the first FDA approved branded proprietary product for Athenex and was launched in the U.S., led by our partner Almirall S.A ("Almirall") on February 18, 2021. Klisyri will be manufactured by Athenex, highlighting the vertically integrated capabilities of the company ranging from a preclinical lead to a developed product for market launch. The FDA approved Klisyri based on the data from two pivotal, randomized, double-blind, vehicle-controlled Phase 3 studies (KX01-AK-003 and KX01-AK-004) that evaluated the efficacy and safety of Klisyri (tirbanibulin) ointment 1% in 702 adults with AK of the face or scalp. Tirbanibulin demonstrated complete clearance of AK lesions at day 57 in treated face or scalp areas in a significantly higher number of patients compared to vehicle. The most common adverse events were application site pruritus and pain reported by 9% and 10% of treated patients, respectively.

The New England Journal of Medicine published the pivotal Phase 3 trial results on Klisyri® for the topical treatment of AK of the face or scalp in the February 11, 2021 issue.

In March 2020, our partner Almirall announced that the European Medicines Agency (EMA) accepted the filing of a European marketing authorization for tirbanibulin ointment for the treatment of AK.

On February 15, 2021, we entered into the Second Amendment to the 2011 license agreement with PharmaEssentia Corp. ("PharmaEssentia") for tirbanibulin ointment. The Second Amendment expands the territory to include Japan and South Korea and includes a license to use the intellectual property for additional dermatology indications and skin cancer in the existing territories.

The development of our other Src Kinase programs/product candidates is ongoing.

Other Platforms

The other technologies in our Oncology Innovation Platform are our TCR-T immunotherapy technology under which we are advancing TCR affinity-enhancing specific T-cell (TAEST) therapy with our first drug candidate, TCRT-ESO-A2, and our arginine deprivation therapy technology under which we are advancing PT01, also known as Pegtomarginase.

In September 2020, we announced that the FDA allowed our Investigational New Drug (IND) application for TCRT-ESO-A2, an autologous T cell receptor (TCR)-T cell therapy targeting solid tumors that are NY-ESO-1 positive in HLA-A*02:01 positive patients. TCRT-ESO-A2 is being developed by Axis Therapeutics Limited, a joint venture between Athenex and Xiangxue Life Sciences Limited ("XLifeSc"). TCRT-ESO-A2 is similar to TAEST16001, an autologous cell-based therapy being developed simultaneously by XLifeSc for clinical application in China in that both therapies express the same affinity-enhanced TCR.

PT01 targets cancer growth and survival by removing the supply of arginine to cancers that have a disrupted urea cycle. The FDA allowed our IND application for the clinical investigation of PT01 for the treatment of patients with advanced malignancies in 2019. We plan to initiate first human exposure in 2021.

Other Business Developments

Other significant business developments for the Company in 2020 include:

- In September 2020, we completed an underwritten follow-on public offering in which we sold 11,500,000 shares of our common stock, including 1,500,000 shares of common stock pursuant to the underwriters' option to purchase additional shares, at a public offering price of $11.00 per share and received net proceeds of $118.7 million, after deducting underwriting discounts and commissions and offering expenses of $7.9 million.
- In August 2020, we entered into a Revenue Interest Financing Agreement with Sagard Healthcare Royalty Partners, LP ("Sagard"), pursuant to which Sagard has agreed to pay us $50.0 million (the "Product Payment") to provide funding for our development and commercialization of Oral Paclitaxel upon receipt of marketing authorization for Oral Paclitaxel by the U.S. FDA for the treatment of metastatic breast cancer. For additional information, please see "*Liquidity and Capital Resources —Debt and Equity Financings*."
- In June 2020, we entered into a senior secured loan agreement and related security agreements (the "Senior Credit Agreement") with Oaktree Fund Administration, LLC, as administrative agent, and the lenders party thereto (collectively, "Oaktree") to borrow up to $225.0 million in five tranches with a maturity date of June 19, 2026, bearing interest at a fixed annual rate of 11.0%. For additional information, please see "*Liquidity and Capital Resources —Debt and Equity Financings*."
- In March 2020, we entered into a letter agreement with Guangzhou Xiangxue Pharmaceutical Co., Ltd. ("Xiangxue") to amend certain provisions of the license agreement entered into with Xiangxue in December 2019 (the "2019 Xiangxue License"). In June 2020, we entered into a second supplemental agreement to amend certain provisions of the 2019 Xiangxue License to facilitate our receipt of payment from Xiangxue, providing, among other things, that Xiangxue shall be entitled to make the USD $30 million upfront payment in Chinese Renminbi to Chongqing Taihao Pharmaceutical Co. Ltd. ("Taihao"), our wholly owned subsidiary in China. For additional information, please see "*Business—License and Collaboration Agreements—Xiangxue License Agreements*."

Mission and Strategy

We have a comprehensive and experienced leadership team who have come together under one organization to achieve our mission of improving the lives of cancer patients by creating more effective, safer and tolerable treatments. We have the goal of becoming a global leader in bringing innovative cancer treatments to the market and improving health outcomes. To achieve our goal, we have established the following strategic priorities, which, after receipt of a CRL for our NDA for Oral Paclitaxel, are currently under review by management:

Obtain regulatory approval for our product candidates and prepare to commercialize Klisyri and our other approved products in the U.S. and abroad - On February 26, 2021, we received a CRL from the FDA regarding our NDA for our lead product candidate, Oral Paclitaxel, for metastatic breast cancer. We are working to consider the appropriate next steps in the development of Oral Paclitaxel. We plan to request a meeting with the FDA to discuss the FDA's response, engage in a dialogue on the design and scope of a clinical trial to address the agency's requirements and align on the next steps required to obtain approval.

Our goal with Oral Paclitaxel, in the event we decide to continue development after our meeting with the FDA, is to establish it, if approved, as the chemotherapy of choice for patients with MBC and to commercialize Oral Paclitaxel in the U.S. by leveraging our commercialization capabilities in the U.S. We also plan to evaluate marketing options outside of the U.S., including using our internal resources, partnering with others, or out-licensing the product. The FDA has approved Klisyri® (tirbanibulin) for the topical treatment of AK on the face or scalp. Our strategic partner Almirall launched Klisyri in the U.S. on February 18, 2021 and will employ its expertise to support the development of tirbanibulin in Europe. Almirall will also commercialize the product in European countries, including Russia, if approved in those jurisdictions.

Rapidly and concurrently advance our other clinical programs and product candidates - We intend to pursue the fastest feasible pathways to approval of our existing clinical product pipeline. We plan to continue to advance our studies evaluating Oral Paclitaxel in other indications. As part of our label expansion strategy, we intend to pursue those indications where paclitaxel is already indicated by FDA approval or is on National Comprehensive Cancer Network ("NCCN") guidelines, and we also intend to explore combinations with new modalities, such as immunotherapies and targeted therapies. We will continue to advance the development of our other Orascovery product candidates to maximize the value of the Orascovery platform. In addition, we continue to make progress with the development of the clinical program for tirbanibulin. We will also evaluate options to enter into partnerships and collaborations where appropriate.

Enhance and expand our other new technology platforms - We intend to continue expanding and broadening our oncology pipeline. In 2020, the FDA allowed the IND application for TCRT-ESO-A2, which represents Athenex's first T cell therapy product cleared to advance to the first stage of clinical development in the U.S. The FDA also allowed the IND application for the clinical investigation of PT01, an arginine deprivation therapy, for the treatment of patients with advanced malignancies and we plan to initiate first human exposure in 2021. 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.

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., U.K., China, Taiwan and Latin America 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. 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.

Continue to build an integrated business model that leverages our proprietary commercial platform, supply chain and cGMP manufacturing capabilities - 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 tirbanibulin in the U.S. and, if approved, European countries, including Russia. In addition, we currently expect to continue to invest in our CMC development for our product candidates and manufacturing infrastructure, which may involve significant capital expenditures, utilizing current Good Manufacturing Practices ("cGMP") manufacturing facilities from our public/private partnerships in both the China and U.S. markets as a mechanism to build-out our supply chain around the world. We plan to manufacture 503B compounding products at our Dunkirk facility when it is operational later this year, and to also utilize the facility for specialty products and our proprietary drugs in the future.

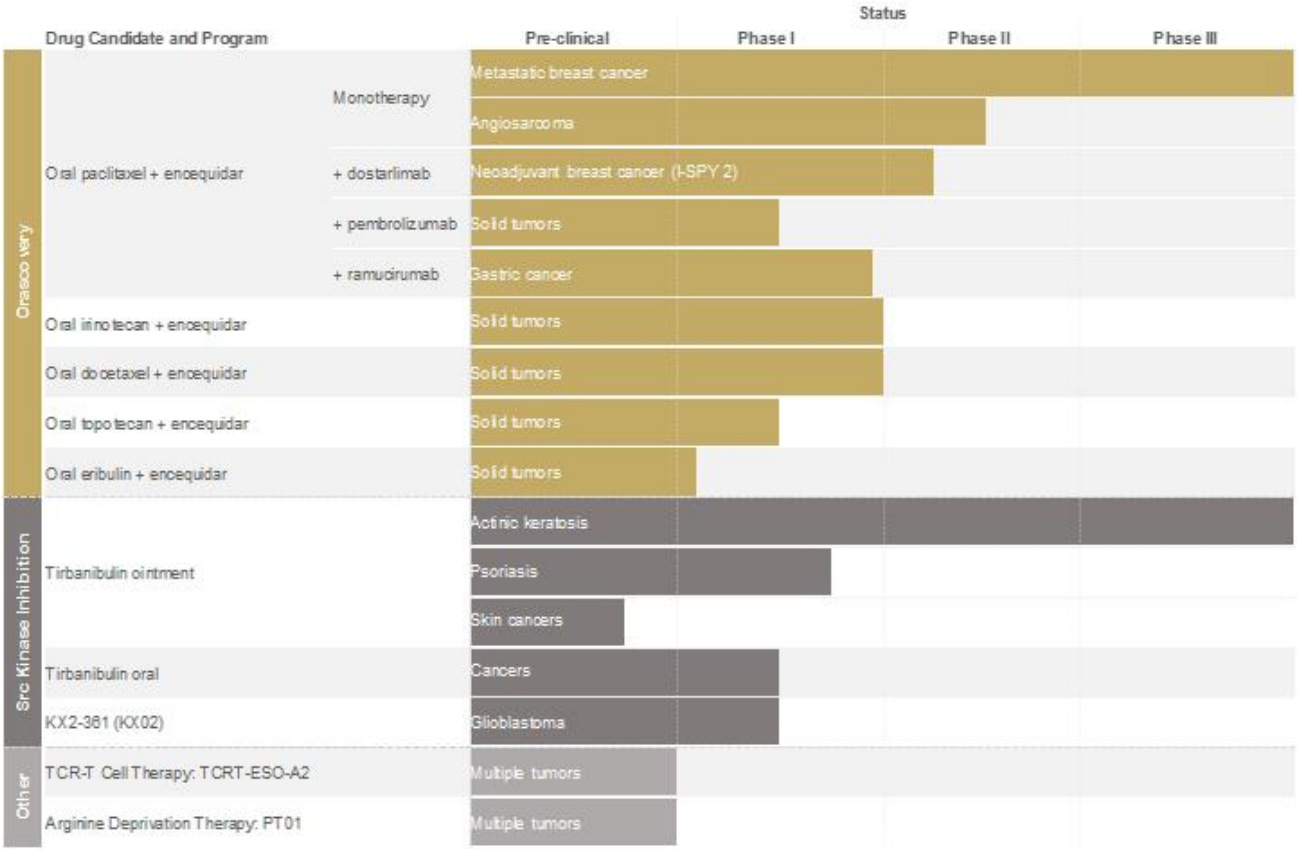
Selectively pursue strategic M&A, licensing or partnership opportunities to complement our existing operations - We continue to pursue strategic acquisitions, licensing and partnership opportunities. We will continue to target opportunities that will complement our existing portfolio and operations to create value for stockholders and support our business strategy and mission.

Operating Segments

We have organized our business model into three platforms: (1) our Oncology Innovation Platform, dedicated to the research and development of our proprietary drugs; (2) our Commercial Platform, focused on the sales and marketing of our specialty drugs and the market development of our proprietary drugs; and (3) our Global Supply Chain Platform, dedicated to providing a stable and efficient supply of APIs for our clinical and commercial efforts. Athenex has global operations with offices and facilities in Buffalo and Clarence, New York; Cranford, New Jersey; Houston, Texas; Chicago, Illinois; Hong Kong; Taipei, Taiwan; multiple locations in Chongqing, China; Manchester, United Kingdom; Guatemala City, Guatemala and Buenos Aires, Argentina.

Our Oncology Innovation Platform

Within our Oncology Innovation Platform, we have four different technologies: (1) Orascovery, based on a P-glycoprotein (P-gp) pump inhibitor, (2) Src Kinase inhibition, (3) TCR-T immunotherapy, and (4) arginine deprivation therapy. The following table summarizes the development status of our current pipeline of product candidates in our Oncology Innovation Platform as of December 31, 2020:



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 CYP and P-gp dual inhibitor technology could expand the breadth of application for our oral enabling platform.

We collaborate with a number of biotechnology pharmaceutical companies, including Hanmi Pharmaceutical Co., Ltd. (“Hanmi”), Eli Lilly and Company (“Lilly”), Almirall, Xiangxue, ZenRx Limited (“ZenRx”) and PharmaEssentia, to support the development of our clinical pipeline globally and explore additional indications. For additional information, please see “*Business—License and Collaboration Agreements*”.

Our Orascovery Platform

Our Orascovery platform technology is based on the novel oral P-gp pump inhibitor molecule, encequidar. The P-gp pump is a plasma membrane efflux protein on the cells which forms a localized drug transport system. In the intestine it limits the oral absorption of a large number of drugs, including widely used P-gp substrate cancer chemotherapeutic drugs such as paclitaxel, irinotecan, docetaxel and eribulin, thus restricting their current dosing to IV administration. We are developing a series of orally administered chemotherapeutic agents using our proprietary P-gp pump inhibitor delivery system. For our lead Orascovery product candidate, Oral Paclitaxel, sequential co-administration of encequidar and oral paclitaxel is designed to facilitate oral absorption of paclitaxel and achieve therapeutic blood levels. Studies conducted to date have indicated that oral administration of paclitaxel in combination with encequidar has lower peak concentrations of paclitaxel in the blood which we believe will result in lower rates of peripheral neuropathy. In addition, oral administration eliminates infusion-related reactions related to IV administration of paclitaxel, which could improve patient tolerability and allow for longer dosing durations to improve efficacy. 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 drugs. In addition to Oral Paclitaxel, we are advancing Oral Irinotecan, Oral Docetaxel, Oral Topotecan and Oral Eribulin as other clinical candidates on this platform.

Chemotherapeutic agents such as paclitaxel, irinotecan, docetaxel and eribulin are clinically proven and widely used. However, these agents have historically been limited to IV administration, which can result in adverse events which are due, in part, to high peak blood concentration levels of the chemotherapeutic drugs. In addition, for some agents, there are infusion-related reactions caused, in part, by solubilizing dilution agents used to facilitate IV administration. A cancer patient's inability to tolerate IV chemotherapies may limit the long-term efficacy of IV anti-cancer therapies. We believe our pipeline products, which leverages our proprietary delivery system will expand the use of these chemotherapeutic agents. We believe that our Orascovery platform overcomes the current challenges of chemotherapeutic agents 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 exposure to the chemotherapeutic agent.

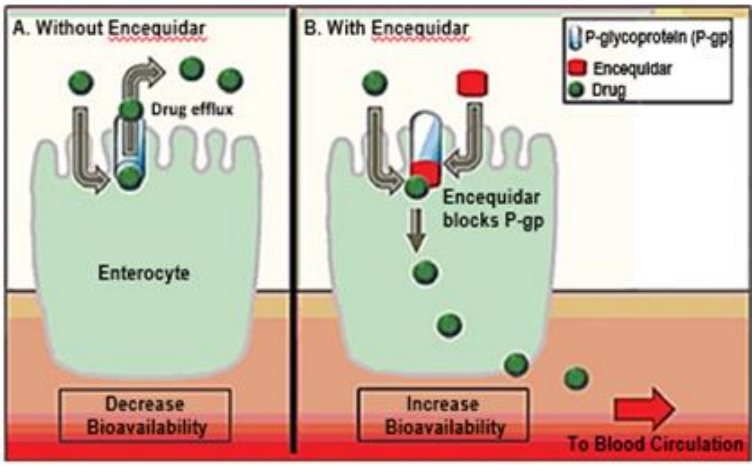
We have historically observed that a novel technology applied to a traditional chemotherapy agent may achieve pricing premiums if data demonstrates superior efficacy and tolerability as compared to current standards of care. We believe our pipeline products will be able to capture a large untapped market 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 immuno-oncology therapy and oral targeted treatments.

Encequidar—Our Novel P-gp Pump Inhibitor

The novel P-gp inhibition molecule, encequidar (formerly known as HM30181A), belongs to a new class of P-gp inhibitor that has high potency, specificity and local action at the intestine cells, and forms the cornerstone of our Orascovery platform. Encequidar is designed to enable the administration of oral dosing formats of paclitaxel, irinotecan, docetaxel, topotecan, and eribulin, each of which is currently under clinical development. The feature that distinguishes encequidar 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. Encequidar 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 encequidar clinical development programs to date, inhibition of gastrointestinal P-gp has been shown to improve 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, encequidar is not expected to cause drug-to-drug interactions other than enhancement of oral absorption of medications which are P-gp substrates.

Mechanism of Action - P-gp Inhibition

Encequidar is a P-gp pump inhibitor and an oral absorption enhancer that prevents the P-gp pump-mediated efflux of chemotherapy agents back into the gastrointestinal tract. P-gp plays an important physiologic role as a transporter protein at multiple barrier sites, including the gastrointestinal tract and the blood brain barrier ("BBB"). 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. Encequidar 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 encequidar) to 41% in rats. As shown in the below chart, encequidar is distinct from previously developed small molecule P-gp inhibitors because it 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 encequidar 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.



Clinical Development

In three separate pharmacokinetics ("PK") studies of encequidar conducted in healthy subjects, a total of 81 individuals received single oral doses of encequidar tablets in single doses of up to 900 mg, and 30 individuals were enrolled in multiple dose cohorts with treatment groups receiving encequidar tablets ranging from 60 to 360 mg per day for five days. Encequidar was well-tolerated, with mostly mild gastrointestinal adverse effects. No serious adverse events ("SAEs") were reported. At the current clinical dose of 15 mg given once daily for up to five days, the Cmax in systemic circulation is low. Drug-drug interaction studies of encequidar with digoxin and dabigatran have been conducted, and the metabolism and routes of excretion in humans has been determined.

Our Orascovery Product Candidates

Oral Paclitaxel and Encequidar

Overview

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 high dose 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 paclitaxel indications, including 175 and 135 mg/m^2 administered as both three and twenty-four hour infusions, respectively, once every three weeks. Over the past number of 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 area under the concentration-time curve (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.

Oral Paclitaxel is our lead drug candidate in our Orascovery Platform and is initially being developed for the treatment of patients with metastatic breast cancer. We conducted a pivotal, randomized Phase 3 study of Oral Paclitaxel monotherapy versus IV paclitaxel monotherapy which met its primary endpoint of confirmed response rate in patients receiving Oral Paclitaxel. On February 26, 2021, we received a CRL from the FDA regarding our NDA for Oral Paclitaxel. We are working to consider the appropriate next steps in the development of Oral Paclitaxel. We plan to request a meeting with the FDA to discuss the FDA's response, engage in a dialogue on the design and scope of a clinical trial to address the agency's requirements and align on the next steps required to obtain approval. Although our plans may change based on our discussions with the FDA, we are also evaluating Oral Paclitaxel (1) as a monotherapy treatment for patients with cutaneous angiosarcoma, (2) in combination with ramucirumab for patients with advanced gastric cancers, (3) in combination with pembrolizumab for advanced solid malignancies including urothelial, gastric or gastroesophageal or non-small cell lung cancer, and (4) in combination with GSK's dostarlimab in the neoadjuvant chemotherapy setting for breast cancer. We have also been working to develop Oral Paclitaxel for additional indications and are exploring potential combinations with immuno-oncology agents.

Overview of Clinical Findings

As of December 31, 2020, five Phase 1, 2 and 3 clinical studies of Oral Paclitaxel have been completed. However, the FDA, in its CRL dated February 26, 2021 has indicated an additional trial and additional risk mitigation strategies to improve toxicity, which may involve dose optimization and / or exclusion of the patients deemed to be at a higher risk of toxicity, are required to support potential approval of the NDA. Oral Paclitaxel (encequidar plus oral paclitaxel) administration has shown to result in overall exposure in the blood approximately equivalent to that achieved with 80 mg/m^2 of IV paclitaxel. We believe oral dosing of paclitaxel can provide a longer drug exposure over a target drug concentration than IV paclitaxel, which may translate to better clinical response. We also observed in a Phase 3 clinical study of 402 metastatic breast cancer patients that Oral Paclitaxel had statistically significantly higher confirmed tumor response rate with lower incidence and severity of neuropathy compared to IV paclitaxel. See "*Our Orascovery Product Candidates— Oral Paclitaxel and Encequidar—Clinical Development by Indication—Metastatic Breast Cancer—Phase 3 Study*" for a further discussion of the results of the Phase 3 study.

We have also completed a randomized two-way crossover study comparing the exposure of paclitaxel after administration of IV paclitaxel 80 mg/m^2 and Oral Paclitaxel 205mg/m^2 daily over three consecutive days. Intensive PK sampling was conducted over each treatment period. Statistical analysis demonstrated that the exposure to paclitaxel, based on the AUC was similar between the two treatments. For Oral Paclitaxel, the AUC was 5033 ng.hr/mL and Cmax was 397 ng/mL. For IV paclitaxel, the AUC was 5595 ng.hr/mL with a Cmax of 2732 ng/mL. The geometric ratio and 90% confidence intervals for AUC was 89.5% (83.9-95.5) falling within the guidelines for equivalence.

Clinical Development by Indication

Metastatic Breast Cancer

Phase 2 Study

We conducted a PK and Phase 2 study of Oral Paclitaxel in patients with metastatic breast cancer who failed previous chemotherapies in Taiwan. The study was a multicenter, single-arm, open-label, PK study of Oral Paclitaxel administered orally for 3 consecutive days weekly for up to 16 weeks. We presented encouraging data on the efficacy of Oral Paclitaxel in the treatment of metastatic breast cancer patients obtained from this Phase 2 study at the 2019 ASCO Annual Meeting. Study results on tumor response showed that there were 6 (27.3%) complete response, 5 (22.7%) partial response, and 11 (50%) stable disease in 22 evaluable patients. Three patients had treatment-related SAEs (grade ≥3 neutropenia) and all patients recovered completely. PK results showed that the AUC of Oral Paclitaxel at week-1 was reproducible at week-4 (3050 to 3594 ng-hr/mL). The results indicated that weekly Oral Paclitaxel can achieve paclitaxel exposure similar to that of weekly IV paclitaxel (80mg/m^2) reported previously and that Oral Paclitaxel appears effective in the treatment of advanced breast cancer patients.

Phase 3 Study

Our Phase 3 pivotal study of Oral Paclitaxel in patients with metastatic breast cancer was a randomized, active-controlled clinical trial comparing Oral Paclitaxel monotherapy against IV paclitaxel monotherapy. The trial randomized subjects in a 2:1 ratio to Oral Paclitaxel, and was designed to compare the safety and efficacy of Oral Paclitaxel with IV paclitaxel. The primary endpoint was ORR (confirmed by scans at two consecutive timepoints) as assessed by RECIST v1.1 criteria, a generally accepted method for assessing tumor response. Blinded assessments of tumor response were made by independent radiologists.

A total of 402 metastatic breast cancer patients were enrolled (Oral Paclitaxel=265 vs. IV paclitaxel=137), which represented the ITT population. Patient demographics were balanced. The prespecified modified ITT ("mITT") population comprised 360 patients (Oral Paclitaxel =235 vs. IV paclitaxel=125), which includes patients who received at least 7 doses of Oral Paclitaxel (the majority of one cycle of treatment) or one dose of IV paclitaxel and excludes patients that did not have tumors that could be evaluated by the central radiologist at baseline. The study was designed with 360 evaluable patients (prespecified mITT population) and was statistically powered to detect a difference of 15% in confirmed ORR at p=0.045 with 80% power at the final analysis.

In the final analysis of the primary endpoint of the study, Oral Paclitaxel (205 mg/m^2 per day 3 days/week) showed a statistically significant improvement in ORR at 40.4% compared to IV paclitaxel (175 mg/m^2 once every 3 weeks) at 25.6%, a difference of 14.8% (p=0.005) favoring Oral Paclitaxel, based on prespecified mITT analysis. Based on ITT analysis, Oral Paclitaxel showed a statistically significant improvement in ORR over IV paclitaxel, with 35.8% ORR, compared to 23.4% for IV paclitaxel, a difference of 12.4% (p=0.011).

Secondary endpoints in the study include PFS and OS. In December 2020, we presented updated PFS and OS data from our Phase 3 study of Oral Paclitaxel in patients with metastatic breast cancer at the 2020 SABCS. In the ITT population, the median PFS showed a benefit for Oral Paclitaxel versus IV paclitaxel (8.4 months vs. 7.4 months, respectively; hazard ratio (HR) = 0.768; 95% confidence interval (CI): 0.584, 1.01; p = 0.046). The median OS data demonstrated a trend favoring Oral Paclitaxel versus IV paclitaxel (22.7 months vs. 16.5 months, respectively; HR = 0.794; 95% CI: 0.607, 1.037; p = 0.082). In the mITT population, the median PFS data showed a benefit for Oral Paclitaxel versus IVP (8.4 vs. 7.4 months, respectively; HR = 0.739; 95% CI: 0.561, 0.974; p = 0.023). Median OS data also showed a benefit for Oral Paclitaxel versus IV paclitaxel (23.3 months vs. 16.3 months, respectively; HR = 0.735; 95% CI: 0.556, 0.972; p = 0.026).

Based on data presented at the 2019 SABCS: 31.1% of IV paclitaxel patients experienced grade 2 or above neuropathy versus 7.6% of Oral Paclitaxel patients. The results also showed lower incidence of alopecia compared to IV paclitaxel, with 28.8% of the Oral Paclitaxel group experiencing alopecia versus 48.2% of the IV paclitaxel group in treatment-emergent adverse events of interest. For other treatment-emergent adverse events of interest, there was a higher incidence of neutropenia with CTCAE grade ≥ 3 (29.9% vs. 28.1%; with Grade 4 14.8% vs 8.9%) and gastro-intestinal side effects, such as diarrhea with CTCAE grade ≥ 3 (5.3% vs. 1.5%) and vomiting or nausea with CTCAE grade ≥ 3 (6.8% vs. 0.7%), in the Oral Paclitaxel group as compared to the IV paclitaxel group.

Based on data presented at the 2020 SABCS: all grades of neuropathy were observed in 22% of Oral Paclitaxel patients versus 64% of IV paclitaxel patients, and grade 3 neuropathy was observed in 2% of Oral Paclitaxel patients versus 15% of IV paclitaxel patients. Also presented were data on the effect of prophylactic treatments on the incidence and severity of gastrointestinal-related adverse events. After approximately 30% of patients were enrolled, the Phase 3 trial protocol was amended to allow patients randomized to the Oral Paclitaxel arm to receive prophylactic pre-medications for gastrointestinal side effects. Overall gastrointestinal (GI)-related adverse events (AEs) were less frequent in the IV paclitaxel arm. GI-related AEs improved in the Oral Paclitaxel arm following the amendment, as measured by lower incidences of grade 2 vomiting before and after amendment (24% vs. 7%) and grade 2 diarrhea before and after amendment (27% vs. 16%).

On February 26, 2021, we received a CRL from the FDA regarding our NDA for Oral Paclitaxel for the treatment of metastatic breast cancer. The FDA issues a CRL to indicate that the review cycle for an application is complete and that the application is not ready for approval in its present form. In the CRL, the FDA indicated its concern of safety risk to patients in terms of an increase in neutropenia-related sequelae on the Oral Paclitaxel arm compared with the IV paclitaxel arm in the Phase III study. The FDA also expressed concerns regarding the uncertainty over the results of the primary endpoint of objective response rate (ORR) at week 19 conducted by BICR. The agency stated that the BICR reconciliation and re-read process may have introduced unmeasured bias and influence on the BICR. Additionally, the FDA recommended that we conduct a new adequate and well-conducted clinical trial in a patient population with MBC representative of the population in the U.S. The agency determined that additional risk mitigation strategies to improve toxicity, which may involve dose optimization and / or exclusion of patients deemed to be at higher risk of toxicity, are required to support potential approval of the NDA. We are working to consider the appropriate next steps in the development of Oral Paclitaxel. We plan to request a meeting with the FDA to discuss the FDA's response, engage in a dialogue on the design and scope of a clinical trial to address the agency's requirements and align on the next steps required to obtain approval.

In the event we continue to pursue Oral Paclitaxel after our meeting with the FDA and ultimately receive regulatory approval from the FDA for MBC, we plan to pursue additional oncology indications where we believe taxanes will remain a foundational treatment and to continue exploring combination therapies.

Angiosarcoma

We have also been developing Oral Paclitaxel for the treatment of angiosarcoma. Angiosarcomas are rare, aggressive and heterogeneous tumors accounting for approximately 2% of all soft tissue sarcomas. Only limited treatment options for advanced disease exist with poor outcomes and low 5-year survival rates.

In the angiosarcoma xenograft model in preclinical studies, oral dosing of Oral Paclitaxel resulted in dose-dependent tumor growth inhibition and subsequent increased survival. Tumor histology revealed that Oral Paclitaxel greatly reduced the formation of cavernous blood-filled neoplastic vessels characteristic of angiosarcoma.

We commenced a study of Oral Paclitaxel monotherapy in the treatment of angiosarcoma in December 2018. At the ASCO 2020 Virtual Scientific Program, we announced interim data from an ongoing Phase 2 clinical trial in which Oral Paclitaxel monotherapy showed encouraging efficacy and tolerability in elderly patients with unresectable cutaneous angiosarcoma, an aggressive malignancy with poor prognosis. The interim results reflect data from 22 evaluable patients out of 26 enrolled patients. The interim data showed a clinical benefit rate (CR+PR+SD) of 100% in 22 evaluable patients who reached their first post treatment efficacy evaluation. All 22 patients experienced reduction in tumor size. Complete responses (CR) were observed in 27.3% of patients (6/22), partial responses (PR) were observed in 22.7% of patients (5/22), and stable disease was observed in 50% of patients (11/22). Oral Paclitaxel has been generally well tolerated in this predominantly elderly population. The study is ongoing.

Other Indications

We are conducting an MTD (maximum tolerated dose) study of Oral Paclitaxel in combination with ramucirumab in patients with advanced gastric cancer in the U.S. and Asia through a clinical trial collaboration with Lilly. We commenced a study of up to 32 patients in a dose escalation part of the trial with a dose expansion of Oral Paclitaxel in combination with a fixed dose of ramucirumab in July 2017.

The objective of our ongoing Phase 1 study is to define the MTD of daily Oral Paclitaxel dosing, starting at 200 mg/m^2 for three days in a week, in combination with ramucirumab, which will be dosed every other week. In the first part of the study, 17 subjects were enrolled at doses ranging from 200-300 mg/m^2. We defined the MTD dose of Oral Paclitaxel as 200 mg/m^2 daily for three consecutive days weekly in combination with ramucirumab. Dose limiting toxicities ("DLTs") included febrile neutropenia, grade 4 neutropenia and grade 3 gastric hemorrhage. The most frequently reported adverse events were vomiting (70%), neutropenia (59%), decreased appetite (53%), nausea (24%) and mucositis (24%). The second part of the study is ongoing.

We have an ongoing Phase 1/2 clinical study to assess the safety, tolerability and activity of Oral Paclitaxel in combination with an anti-programmed cell death protein 1 (anti-PD1) antibody (pembrolizumab) in patients with advanced solid malignancies. Pembrolizumab is a checkpoint inhibitor approved by the FDA. The study is being conducted in patients with urothelial, gastric or gastroesophageal or non-small cell lung cancer that have previously failed treatment with a checkpoint inhibitor. Dose escalation of paclitaxel administered as a flat dose of 270 mg per day for 3 to 5 days per week for 2 of 3 weeks is ongoing.

In September 2020, we and Quantum Leap Healthcare Collaborative announced the launch of two new study arms of the I-SPY 2 TRIAL to evaluate Oral Paclitaxel with GSK's dostarlimab, an investigational antibody binding PD-1, in the neoadjuvant chemotherapy setting. The goal of this study is to evaluate the safety and efficacy of oral paclitaxel plus encequidar with dostarlimab +/- carboplatin in Stage 2/3 HER2- breast cancer patients and plus trastuzumab in HER2+ patients, followed, if needed, by doxorubicin plus cyclophosphamide chemotherapy and surgical resection of breast tissue. The primary objective is to determine whether this regimen increases the probability of pathologic complete response (pCR) over standard neoadjuvant chemotherapy alone for any of the tumor subtypes established at trial entry, and to determine the predictive probability of success in a subsequent Phase 3 trial. The study is ongoing.

Overview of Safety Observations in Oral Paclitaxel Studies

Studies to date have indicated that Oral Paclitaxel does not result in hypersensitivity reactions when given without premedication for hypersensitivity type reactions, in contrast to the premedication requirement for IV paclitaxel, namely steroids and antihistamines. No new toxicity, apart from those typically observed with paclitaxel, was observed. Infusion related reactions, including hypersensitivity type reactions, have not been observed in patients administered Oral Paclitaxel. Additionally, severe toxicities associated with IV administration of paclitaxel, including neuropathy and alopecia, are at a lower incidence and severity for Oral Paclitaxel.

As of December 31, 2020, approximately 14% of patients treated in clinical studies with Oral Paclitaxel experienced SAEs that were considered to be related to the study treatment. The most common were neutropenia in approximately 3.4% of patients and febrile neutropenia in approximately 4.05% of patients; pneumonia in approximately 2.9% of patients; septic shock in approximately 1.6% of patients and sepsis, dehydration in approximately 1% of patients; gastroenteritis, anemia, diarrhea, mucositis, gastrointestinal bleeding, vomiting, nausea and hypokalaemia each in less than one percent of patients. Other serious treatment-related infections were reported in approximately 1.9% of patients. Approximately 2.5% of patients had other treatment-related SAEs (one patient each including rectal bleeding, altered state of consciousness, cardiac arrest, tachycardia, atrial fibrillation, cardiogenic shock, hypotension, pancytopenia, multiorgan failure, renal failure, atrial fibrillation, pleural effusion, supraventricular tachycardia, respiratory failure, hypokalaemia, malnutrition, dyspnoea, cardiac failure, and peripheral sensory neuropathy).

Oral Irinotecan and Encequidar

Overview

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. Oral Irinotecan is intended for oral administration for the treatment of irinotecan-responsive cancers.

Early Clinical Studies

Hanmi conducted three Oral Irinotecan Phase 1 studies, two as monotherapy, and one in combination with capecitabine, 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 Oral Irinotecan 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.

Completed Clinical Studies

In a Phase 1 MTD study (HM-OTE-101), Oral Irinotecan 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 encequidar 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 Oral Irinotecan monotherapy in patients with advanced solid tumors resulted in a disease control rate of 44%.

In a Phase 1 MTD study (HM-OTE-102), Oral Irinotecan 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. The disease control rate was 50% or above at each of the dose levels tested.

In a Phase 1 MTD study (HM-OTE-103), Oral Irinotecan in combination with capecitabine. Oral Irinotecan 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 encequidar in combination with capecitabine at 800-1000 mg/m^2 for fourteen days. The MTD of Oral Irinotecan, in combination with capecitabine at the 1000 mg/m^2 dose was identified at 15 mg/m^2 per day of Oral Irinotecan. In this study of combination of Oral Irinotecan 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.

Current and Planned Clinical Development

A Phase 1 MTD study is being conducted and is currently ongoing. This study is to determine the MTD of Oral Irinotecan, when given once every three weeks, in subjects with advanced malignancies. We have identified a dosing regimen suitable for Phase 2, and Phase 2 studies are being planned.

Overview of Safety Observations in Oral Irinotecan Studies

In our Oral Irinotecan clinical studies to date, the SAEs observed that were deemed to be at least possibly related to Oral Irinotecan include diarrhea, rash, gastrointestinal hemorrhage, anorexia, vomiting, nausea, enteritis, asthenia, neutropenia, increased alanine aminotransferase, increased aspartate aminotransferase, and C diff infection. As the clinical development program is still in its early stages, we do not yet have meaningful statistics on safety, including adverse events, to report.

Oral Docetaxel and Encequidar

Overview

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 Docetaxel will provide therapeutic exposures of the drug and result in the potential for better clinical response with reduced toxicity.

Preclinical Activity and Evaluation

The potential effectiveness of encequidar 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 showed a significant increase upon co-administration of encequidar with docetaxel. In this experiment, docetaxel was formulated in the currently proposed clinical formulation. Oral Docetaxel was also tested in preclinical human prostate cancer murine model and overall, Oral Docetaxel 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 encequidar 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 encequidar, 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 encequidar.

Current and Planned Clinical Studies

A Phase 1 dose escalation U.S. based trial for Oral Docetaxel in patients with various solid tumors with a starting dose of 35 mg/m2 given once every three weeks is ongoing. Another Phase 1 study to identify the absolute bioavailability of Oral Docetaxel in prostate cancer patients is ongoing in New Zealand. Based on Phase 1 results so far, we believe that we can achieve similar exposure to IV docetaxel with one to three days of dosing every three weeks. Alternative schedules such as weekly or 2 of 3 weeks are also being explored. Phase 2 studies are being planned.

Overview of Safety Observations in Oral Docetaxel Studies

We expect that the overall safety profile of Oral Docetaxel will be similar to that of IV docetaxel, with differences related to the route of administration. As with Oral Paclitaxel, premedication has not been required and hypersensitivity type reactions have not been observed. As of December 31, 2020, in our Oral Docetaxel clinical studies, the SAEs observed that were deemed to at least possibly related to Oral Docetaxel include gastrointestinal toxicity; vomiting, nausea and diarrhea in 1 subject.

Oral Topotecan and Encequidar

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, nausea, and vomiting.

In rat oral PK studies, the plasma concentrations of topotecan versus time demonstrated a significant increase upon co-administration with encequidar. 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 encequidar was more active than Oral Topotecan alone following administration at a dose of topotecan 1 mg/kg once daily for five days per week.

A Phase 1 clinical trial in advanced malignancies for Oral Topotecan is ongoing.

We expect that the overall safety profile of Oral Topotecan will be similar to that of IV topotecan, with differences related to the route of administration. As the clinical development program is still in its early stages, we do not yet have meaningful statistics on safety, including adverse events, to report.

Oral Eribulin and Encequidar

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, suggests the potential for an efficacy and safety profile for Oral Eribulin, similar to what we have observed with Oral Paclitaxel and other Orascovery products. 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 application for Oral Eribulin. A Phase 1 study commenced in 2019 to assess the safety, MTD, DLT and absolute bioavailability of Oral Eribulin in subjects with solid tumors. As the clinical development program is still in its early stages, we do not yet have meaningful statistics on safety, including adverse events, to report.

Our Src Kinase Inhibition Platform

Our Src Kinase inhibition platform technology is based on novel small molecule compounds that have multiple mechanisms of action, including the inhibition of the activity of Src Kinase and the inhibition of tubulin polymerization, which may limit the growth or proliferation of cancerous cells. We believe the combination of these mechanisms of action provides a broader range of anti-cancer activity compared to either mechanism of action alone. Our lead product candidate on our Src Kinase inhibition platform is tirbanibulin ointment. Our other clinical candidates in this platform include tirbanibulin oral and KX2-361.

Tirbanibulin

Mechanism of Action

Tirbanibulin, formerly known as KX2-391 or KX-01, is a novel small molecule that we discovered and developed, which demonstrates at least two mechanisms of action (“MOAs”) relevant to the potential control of cancer and hyper-proliferative disorders: (1) Src tyrosine kinase inhibition (non-ATP competitive) and (2) tubulin polymerization inhibition. Src Kinase, a tyrosine kinase protein involved in regulating cell growth, is strongly implicated in metastasis. Inhibiting Src Kinase may limit the growth or proliferation of cancerous cell types. 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 tirbanibulin 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.

Tirbanibulin Ointment

Tirbanibulin is a compound developed under our Src Kinase inhibition platform that, as a free base, has advantageous physical properties for topical ointment formulations.

In December 2020, we announced that the FDA has approved Klisyri® (tirbanibulin), a microtubule inhibitor, for the topical treatment of AK on the face or scalp. We completed two Phase 3 pivotal studies of tirbanibulin ointment for the treatment of AK, in which both Phase 3 studies achieved their primary endpoint of 100% clearance AK lesions at Day 57 within the face or scalp treatment areas. AK or solar keratosis is a chronic and precancerous skin disease that occurs primarily in areas that have been exposed to ultraviolet (UV) radiation for a long period of time. It is usually found on the face, ears, lips, bald scalp, forearms, the posterior part of the hands, and lower legs. AK is the most common pre-cancerous dermatological condition and is the second most common diagnosis made by dermatologists in the U.S.

An additional indication for psoriasis is being evaluated in a Phase 1 clinical trial led by our out-licensing partner PharmaEssentia. We are also evaluating other indications, which could provide additional potential therapeutic utilities for tirbanibulin ointment and could represent significant potential market expansions beyond AK.

Actinic Keratosis

In December 2020, the FDA has approved Klisyri® (tirbanibulin), a microtubule inhibitor, for the topical treatment of AK on the face or scalp. The FDA approved Klisyri based on data from two pivotal, randomized, double-blind, vehicle-controlled Phase 3 trials (KX01-AK-003 and KX01-AK-004) that evaluated the efficacy and safety of tirbanibulin ointment 1% (10mg/g) in adults with AK of the face or scalp. The studies enrolled a total of 702 patients across 62 sites in the U.S. Enrollment of patients was controlled to achieve a 2:1 ratio of facial: scalp treatment areas. Tirbanibulin ointment 1% (10 mg/g) or vehicle (randomized 1:1) was self-administered to 25 cm2 of the face or scalp encompassing 4-8 typical AK lesions, once daily for 5 consecutive days.

Both Phase 3 trials, KX01-AK-003 and KX01-AK-004, achieved their primary endpoint, which was defined as 100% clearance of the AK lesions at day 57 within the face or scalp treatment areas, each study achieving statistical significance ($p<0.0001$) on this endpoint. In the KX01-AK-003 study, complete clearance was observed in 44% of the patients treated with tirbanibulin versus 5% for the vehicle treated groups. In the KX01-AK-004 study, complete clearance was observed in 54% of the patients treated with tirbanibulin and 13% for vehicle treated groups. Furthermore, tirbanibulin also achieved the secondary endpoint of partial (≥75%) clearance of lesions in each trial (68% of patients receiving tirbanibulin versus 16% receiving vehicle in KX01-AK-003, and 76% versus 20% respectively in KX01-AK-004). Both results were again highly statistically significant ($p<0.0001$).

In both trials, patient-reported adverse events were mostly transient mild application-site pruritus and application-site pain. No patients experienced a serious adverse event or discontinuation due to tirbanibulin or vehicle in either clinical trial. Signs of local skin reactions assessed by investigators were mostly mild to moderate erythema, flaking or scaling that peaked at day 8 (maximum mean composite local skin reaction score ≤4.3 out of 18 across both trials) and resolved spontaneously in about 2 weeks.

In March 2020, our partner Almirall announced that the EMA accepted the filing of a European marketing authorization for tirbanibulin ointment for the treatment of AK.

Psoriasis

To date, tirbanibulin ointment has shown encouraging preclinical results in treating psoriasis, a chronic autoimmune skin disease that speeds up the growth cycle of skin cells. Psoriasis causes localized or generalized patches of red papules and plaques, covered with white or silver scales and itching. A Phase 1 clinical trial of tirbanibulin ointment 1% in psoriasis, performed by our partner PharmaEssentia, is ongoing.

We licensed the rights to tirbanibulin to PharmaEssentia for psoriasis and non-malignant skin conditions (excluding AK) in Mainland China, Taiwan, Hong Kong, Macau, Singapore, Malaysia, Japan, and South Korea, as well as the rights for AK in Taiwan. PharmaEssentia is sponsoring this Phase I clinical trial in psoriasis. For additional information, please see "*Business—License and Collaboration Agreements—PharmaEssentia License Agreements*."

Tirbanibulin Oral

We are also developing tirbanibulin in an oral formulation. Tirbanibulin 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 in early studies and to investigate alternative dosing regimens.

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, 44 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, who failed 9 prior therapies, had stable disease for 16 months and a tirbanibulin oral induced a large decrease in the ovarian cancer CA-125 biomarker, which correlates well with clinical response.

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 tirbanibulin oral at 40 mg/dose twice daily until disease progression or unacceptable toxicity. The primary endpoint was 24-week progression-free survival. The designated clinical endpoints were not met with tirbanibulin 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 tirbanibulin. 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 tirbanibulin oral daily.

We are planning further studies to evaluate targeted cancer indications. Hanmi, who we partnered with on tirbanibulin oral up until August 2018, completed a Phase 1b clinical trial in South Korea, combining escalating continuous once daily doses of tirbanibulin with a standard IV paclitaxel treatment of 80 mg/m^2. The study enrolled 23 subjects who received doses of tirbanibulin ranging from 20 through 80 mg/day. The five most frequently reported treatment-related adverse events were neutrophil count decreased (83%), myalgia (61%), decreased appetite (57%), anemia (53%) and peripheral sensory neuropathy (48%). Six subjects experienced serious adverse events: febrile neutropenia (n=3), and pneumonia, sepsis, fever, and neutrophil count decreased (n=1 each). There were no CR or PR in this heavily treated Phase 1 population, but 12 subjects had a best response of stable disease. Dose expansion in part 2 of the study was not conducted.

In our tirbanibulin oral clinical studies to date, the SAEs observed that were deemed to be possibly, likely or definitely related to tirbanibulin 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. As the clinical development program is still in its early stages, we do not yet have meaningful statistics on safety, including adverse events, to report.

KX2-361

KX2-361, formerly known as KX-02, is the second compound we developed using our Src Kinase inhibition platform technology. KX2-361 is a closely related structural analog of tirbanibulin and has been observed to have a similar dual MOA of inhibition of Src activity and microtubule polymerization. Although KX2-361 is an analog of tirbanibulin, it has significantly different physical properties. These properties are designed to allow KX2-361 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 KX2-361 as a novel therapy for unmet medical needs such as brain cancers, including GBM and brain metastases. KX2-361's multiple MOAs along with its ability to cross the BBB, make it a novel molecule for the treatment of brain tumors. The FDA has granted Orphan Drug Designation to KX2-361 for the treatment of gliomas.

Studies of KX2-361 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. KX2-361 produced long-term survival mice, as compared to temozolomide, which extended survival but did not result in any long-term survivors.

In vivo studies in mice have found that the KX2-361 levels in the mouse brain meet or exceed the levels in the plasma at the same time points after oral dosing, indicating that KX2-361 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.

KX2-361 is currently in the early stages of clinical development. In our KX2-361 clinical studies to date, the SAEs observed were thromboembolic events, hyperuricemia and pulmonary embolism. As the clinical development program is still in its early stages, we do not yet have meaningful statistics on safety, including adverse events, to report.

We out-licensed the development and marketing of KX2-361 in Greater China to our partner, Xiangxue. The NMPA allowed the start of a Phase 1 trial of KX2-361 in China, which commenced at the end of 2019 for the treatment of advanced malignant solid tumors. The Phase 1 clinical study in China is a single-center, open-label dose escalation trial that will enroll approximately 36-72 patients with advanced malignant solid tumors who have no standard treatment or standard treatment failed.

Our Other Technology Platforms

TCR-T Immunotherapy

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. 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.

Arginine Deprivation Therapy

PT01, the arginine deprivation therapy product, is based on our pegylated genetically engineered human arginase. It targets cancer growth and survival by interrupting the supply of arginine to cancers with disrupted urea cycles such as melanoma, hepatocellular carcinoma and prostate cancer. Our proprietary arginase biologic product is well suited to deplete arginine from the tumors, while healthy cells, capable of producing their own arginine, are largely unaffected.

Other Research Programs

Proprietary Dual (CYP/P-gp) Inhibitor

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 metabolism 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.

Research and Development

We have drug discovery, drug formulation, clinical and regulatory development and API/drug product manufacturing facilities and capabilities around the world. The U.S. drug discovery, clinical and regulatory 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. We also have research, clinical development and regulatory capabilities in China, the U.K. and Latin America, as well as in Taiwan, where we also have built up data management facility. Our research and development center in Hong Kong concentrates on drug formulation development and evaluation. Our global research and development capabilities and facilities are well integrated with our research and development center in the U.S.

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

Commercialization

For Oral Paclitaxel, our strategy has been to develop and, if we receive approval from the FDA, commercialize Oral Paclitaxel in the U.S. by leveraging our Commercial Platform and sales and marketing capabilities established in the U.S. In terms of commercialization planning efforts, we are further developing and executing strategies around marketing, market access, sales, medical affairs, and policy and patient advocacy. Due to the receipt of the CRL for our NDA for Oral Paclitaxel for the treatment of metastatic breast cancer, we are working to consider the appropriate next steps in the development of Oral Paclitaxel. Athenex plans to request a meeting with the FDA to discuss the FDA's response, engage in a dialogue on the design and scope of a clinical trial to address the agency's requirements and align on the next steps required to obtain approval.

If Oral Paclitaxel is ultimately approved by the FDA, we intend to establish Oral Paclitaxel as the chemotherapy of choice for patients receiving chemotherapy for MBC. We also intend to explore establishing Oral Paclitaxel in other oncology indications where we believe taxanes will continue to be a foundational treatment and continue to explore combination therapies.

We plan to evaluate marketing options outside of the U.S., including using our internal resources, partnering with others, or out-licensing the product.

For Klisyri® (tirbanibulin) in the treatment of AK, 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 tirbanibulin 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 tirbanibulin. On December 15, 2020, we announced that the FDA has approved Klisyri for the topical treatment of AK on the face or scalp. Klisyri is the first FDA approved branded proprietary product for Athenex and was launched in the U.S., led by our partner Almirall on February 18, 2021. Klisyri will be manufactured by Athenex, highlighting the vertically integrated capabilities of the company ranging from a preclinical lead to a developed product for market launch. For additional information, please see "*Business—License and Collaboration Agreements—Almirall License Agreement*." We may also partner with third parties or consider using our internal resources to reach other geographic markets.

Our 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 Platform includes our Specialty Pharmaceuticals business and our manufacture and marketing of products subject to Section 503B of the Federal Food, Drug & Cosmetic Act ("FDCA"). Our Specialty Pharmaceuticals business markets specialty pharmaceuticals, including multi-source oncology and other pharmaceutical products which are therapeutically related to our proprietary portfolio. Our 503B product offerings, which include sterile to sterile products and products from sterilized bulk API, support our offerings in the U.S. oncology market.

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.).

Specialty Pharmaceuticals

Our Specialty Pharmaceuticals business develops and sources products through licensing agreements with various partners, whom we collectively refer to as our Global Partner network. Our team 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 we market in the Specialty Pharmaceutical business. We primarily market the products to the acute hospital and oncology clinics in the U.S. oncology market. As of December 31, 2020, Athenex Pharmaceutical Division ("APD") markets thirty-two products with fifty-eight SKUs. In addition, Athenex Pharma Solutions ("APS") markets six products with nineteen SKUs as of December 31, 2020.

The U.S. Oncology market is highly complex with gatekeepers, influencers and prescribers influencing sales of oncology products. 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 (KOL) physicians, regional cancer centers (as defined by the National Cancer Institute) and the U.S. government. Prescribers include oncologists and dermatologists. 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 these gatekeepers, influencers and prescribers in the oncology market at launch. Through our Commercial Platform, which has established a comprehensive sales and marketing organization, we are able to target and build relationships with gatekeepers, influencers and prescribers in the U.S. Oncology market, enabling us to manage the risks and capture post commercial oncology economics.

Agreements with Suppliers and Marketing Partners

Gland Term Sheets

From August 2016 to May 2017, we entered into four binding term sheets with Gland Pharma Ltd ("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 term sheets 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 term sheets is five years from the launch of each product licensed pursuant to the term sheet, 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.

MAIA Agreement

In December 2018, we entered into a distribution and supply agreement with MAIA Pharmaceuticals ("MAIA") effective as of October 3, 2018 whereby we acquired the exclusive license to a generic version of an approved product, which we began selling in January 2019. 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.

In December 2019, the agreement with MAIA was amended to grant us the license to a branded product which MAIA holds the approved NDA. In connection with this amendment, we agreed to an upfront milestone payment and 56% of the net profits from sales of the licensed product. Additionally, we agreed to increase MAIA's share of the net profits to 70% for both products until certain financial metrics are achieved and shall revert to the initial rates after those metrics are satisfied.

Ingenus Agreements

In September 2020, we entered into an asset purchase and sale agreement with Ingenus Pharmaceuticals, LLC ("Ingenus") whereby we purchased from Ingenus all of their right, title and interest in and to Glycopyrrolate Injection ("Glycopyrrolate") in the U.S. for $2 million and pursuant to which Ingenus transferred to us the ANDA for Glycopyrrolate.

In November 2020, we entered into a co-marketing, manufacturing and supply agreement with Ingenus Cyclophosphamide Injection pursuant to which Ingenus will be our exclusive supplier of the product and granted us a license to market and sell the product to acute care group purchasing organizations (GPOs) and their entire memberships as provided by said GPOs, integrated delivery networks (IDNs) and to hospitals within the U.S. for a purchase price of $1 million. Under the agreement, Athenex is entitled to 25% of the net profits from our sales of the product and we are entitled to a marketing allowance. The agreement has a 3-year term, which may be extended if we mutually agree.

In January 2021, we entered into a manufacture and supply agreement with Ingenus for Arsenic Trioxide Injection pursuant to which Ingenus will be our exclusive supplier of the product and granted us a license to market and sell the product to acute care GPOs and their entire memberships as provided by said GPOs, IDNs and to hospitals within the U.S. Under the agreement, we are entitled to 45% of the net profits from our sales of the product and we are entitled to a marketing allowance. The agreement has a 5-year term, which may be extended if we mutually agree.

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, 2020, the products we sold through our three largest wholesalers in the U.S., which, accounted for 45%, 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 for 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 stockholders. For example, the World Health Organization (WHO) 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, Oral Paclitaxel. 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. ("Polymed") and Chongqing Taihao Pharmaceutical Co. Ltd., or Taihao. Taihao operates a cGMP high potency oncology API plant based in Chongqing, China ("CQ API Facility") and Polymed 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 the manufacturing capacity at the CQ API Facility will be used for the Company's needs in the future, and, therefore, sales to third parties may decrease. Historically, Polymed sold certain of these API products internationally to mostly large multi-national pharmaceutical companies. However, we have experienced a slowdown of commercial operations at our CQ API Facility. We suspended production in May 2019 based on concerns raised by the DEMC related to the location of our plant. We resumed producing API primarily for the Company's use in March 2020 in accordance with local regulatory guidance. We continue to produce API at the CQ API Facility for our ongoing clinical studies and commercial launches of our proprietary drugs. However, we can make no assurances that such production at the CQ API Facility will be able to continue to provide sufficient quantities for clinical studies as well as potential commercial launches of our proprietary drugs.

A new API manufacturing facility in Chongqing, China ("New API Facility") was constructed and commenced operations in January 2021. We expect the facility to expand our API production capabilities to further support our global clinical development needs and ensure the supply of API for commercial launches. We will continue to build out the facility and invest in equipment and expect to incur additional engineering costs. We expect to start producing commercial batches at the New API Facility in the second half of 2021.

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 APS (formerly known as QuaDPharma, LLC), 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 affiliated with the State of New York, for a medical technology research, development, innovation and commercialization alliance (the "Alliance Agreement"). Under the agreement, FSMC agreed to pay up to $25.0 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. Under the agreement, we are obligated to spend $100.0 million in the Buffalo area over the initial 10-year term of the lease and an additional $100.0 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, 2020, we had hired 192 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 Alliance 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 injectable and 503B products and, eventually, our proprietary oncology products for commercial production at this facility. 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 $200.0 million, plus any additional funds available from the previous $25.0 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 $200.0 million, plus about $8.0 million available from the previous $25.0 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 $50.0 million each into an ESD held account. The $50.0 million installment was deposited in the third quarter of 2017 and the remaining $50.0 million installments were made in the first, third, and fourth quarter of 2019. Actual disbursement of such funds occurred as we submitted appropriate documentation verifying that expenditures on the project have been incurred. As of December 31, 2020, the construction was not complete, nor was the lease effective. 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 $78.0 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 around $200.0 million. 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.). The agreement, as amended to date, provides that M+W will be responsible for the design and construction of the Dunkirk facility at a cost estimated about $208.0 million. 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 facility and began ordering equipment for the operation and maintenance of the facility. This manufacturing facility, which was originally planned to be 320,000 square feet, has been expanded to approximately 409,000 square feet to meet our needs and within the terms of the September 2017 agreement. 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 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 an API plant and a formulation 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 and committed to a registration capital requirement of no less than $30.0 million. CQ is responsible for the construction of both facilities according to the U.S. cGMP standards. 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 Chinese Renminbi ("RMB") per square meter of space occupied. We are responsible for the costs of all equipment and technology for the facilities. As of December 31, 2020, the construction of the New API Facility was in the final stage of completion. In January 2021, we accepted the building and the lease became effective. Within six months of our acceptance of the building, we are required to finish equipment installation and testing, and within twelve months, we are required to commence production. 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.

The New API Facility commenced operations in January 2021 and is part of our strategy for vertical integration in order to capture value across the supply chain. We expect the facility will expand our API production capabilities to further support our global clinical development needs and ensure the supply of API for commercial launches.

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 those 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 stockholders.

In May 2019, we suspended operations at our existing API plant in Chongqing, or CQ API Facility, based on the concerns raised by the DEMC related to the location of our plant. As a result of the suspension, we were unable to produce commercial batches of API, which has impacted our revenue. We resumed producing API primarily for the Company's use since March 2020 in accordance with local regulatory guidance. We continue to produce API at the CQ API Facility for our ongoing clinical studies and commercial launches of our proprietary drugs. However, we can make no assurances that such production at the CQ API Facility will be able to continue to provide sufficient quantities for clinical studies as well as commercial launches of our proprietary drugs. We plan to start producing commercial batches at the New API Facility in the second half of 2021.

License and Collaboration Agreements

In-Licenses

Arginase License Agreement

In June 2018, we entered into a license agreement with 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.

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 in June 2018. In September 2019, we made a cash payment of $1.0 million to Polytom upon meeting the first regulatory milestone under the agreement. We may be required to make additional payments to Polytom worth up to $44.0 million of our common stock or of cash upon the occurrence of additional regulatory milestones. Pursuant to the agreement, we have also agreed to pay royalties based on certain percentage of 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.

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 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, one of our directors, has a controlling interest in, and serve on the board of directors of, Avalon.

We made an upfront payment of cash of $0.5 million to HepaPOC upon effectiveness of the HepaPOC License Agreement, and we may be 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. Pursuant to the agreement, we have also agreed to pay royalties based on certain percentage of 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: (1) at least ninety days prior to the expiration date of the patent rights licensed under the agreement or (2) as soon as practically possible in the case of an invalidation claim or (3) at least ninety days prior to the then current expiration date of the agreement thereafter. Notwithstanding the foregoing, after the occurrence of (1) or (2) 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 XLifeSc, a subsidiary of Xiangxue, to establish, operate and manage a joint venture 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 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. 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. In April 2019, Axis made a cash payment of $2.0 million to XLifeSc upon meeting the first regulatory milestone under the agreement. Axis may be required to make additional cash payments to XLifeSc worth up to $108.0 million in aggregate upon the occurrence of certain additional regulatory milestones to be achieved in the U.S., the EU, China and Japan. In addition, XLifeSc is required to pay Axis royalty payments based on certain percentage of aggregate net income generated by 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 (1) upon the occurrence of a liquidity event, if the regulatory approval has already been received, or (2) 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 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.

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 Oral Paclitaxel or Oral Irinotecan 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 (1) our first commercial sale of products using such technology or (2) 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 (1) expiration of the last of Hanmi's patent rights licensed under the agreement or (2) 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 (1) we fail to file an IND application with the FDA for Oral Paclitaxel within six months of the latest of (x) our receipt from Hanmi of all English translations necessary for the filing of an IND application with the FDA, (y) the date we and Hanmi agree that all studies necessary for the filing of an IND application 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 application with the FDA or (2) we fail to commence clinical studies for Oral Paclitaxel within twelve months after the date of approval of an IND application by the FDA.

The 2013 Hanmi Agreement may be terminated by Hanmi if (1) we fail to file an IND application for Oral Paclitaxel with the NMPA within six months after the latest of (w) completion of all Chinese translations necessary for the filing of an IND application with the NMPA, (x) completion of all manufacturing and toxicology studies necessary for the filing of an IND application with the NMPA (y) the date we and Hanmi agree that all studies necessary for the filing of an IND application 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 application with the NMPA or (2) we fail to commence clinical studies for Oral Paclitaxel within twelve months after the date of approval of an IND application 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-Licenses

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 Oral Irinotecan and Oral Paclitaxel in Australia and New Zealand, and a non-exclusive license to manufacture a certain compound but only for use in Oral Irinotecan and Oral Paclitaxel. ZenRx is responsible for all development, manufacturing and commercialization, and the related costs and expenses, of any product candidates resulting from the agreement.

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 Oral Irinotecan and Oral Paclitaxel 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 (1) expiration of the last of our patent rights licensed under the agreement or (2) 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 tirbanibulin or KX-361 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 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.

On February 15, 2021, we entered into the Second Amendment to the 2011 PharmaEssentia Agreement for tirbanibulin ointment. The Second Amendment expands the territory to include Japan and South Korea and includes a license to use the intellectual property for additional dermatology indications and skin cancer in the existing territories. Pursuant to this Second Amendment, we will receive an upfront payment of $0.5 million, milestone payments up to $13.0 million associated with the achievement of certain development and sales milestone, as well as royalties on the sale of tirbanibulin ointment in Japan and South Korea. We will supply PharmaEssentia with the licensed products under a supply arrangement for a separate fee.

The December 2013 agreement, which we refer to as the 2013 PharmaEssentia Agreement, granted an exclusive, sublicensable license for development and commercialization of Oral Paclitaxel and Oral Irinotecan in Taiwan and Singapore. 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 Oral Docetaxel in Singapore, Taiwan and Vietnam. We received $2.0 million from PharmaEssentia upon effectiveness of the amended agreement.

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. During 2020, we recognized and received revenue of $1.0 million upon meeting regulatory milestones. We may be entitled to an aggregate of up to $6.5 million in additional development and regulatory milestone payments related to Oral Docetaxel.

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 (1) expiration of the last of our patent rights licensed under the agreement or (2) 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.

Xiangxue License Agreements

2012 License Agreement

In May 2012, we entered into a license agreement with Xiangxue, which we refer to as the Xiangxue 2012 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-361 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 Xiangxue 2012 License 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. 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 2012 License expires on the earlier of (1) expiration of the last of our patent rights licensed under the agreement or (2) 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 Xiangxue 2012 License, 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 2012 License. The Xiangxue 2012 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.

2019 License Agreement

In December 2019, we entered into an exclusive license agreement with Xiangxue, which we refer to as the 2019 Xiangxue License, in which we granted Xiangxue exclusive rights to develop and commercialize certain licensed products for China, Hong Kong and Macau, including Oral Paclitaxel, Oral Irinotecan, and tirbanibulin ointment for certain indications, including oncological and AK indications, as well as other indications that we and Xiangxue mutually agree to pursue under the 2019 Xiangxue License. The 2019 Xiangxue License contains an option, exercisable by Xiangxue, to license two additional product candidates on terms and conditions to be negotiated separately from the 2019 Xiangxue License. Under the terms and conditions of the 2019 Xiangxue License, we and Xiangxue will be jointly responsible for licensed products in the territory covered by the 2019 Xiangxue License in their permitted fields of use and Xiangxue will be responsible for the commercialization of the licensed products in the territory in their permitted fields of use. Xiangxue agreed to pay us an initial payment of $30.0 million (the "Upfront Payment"), subject to the satisfaction of certain conditions, including the delivery of required regulatory data, which occurred in the first quarter of 2020. The parties further acknowledged certain difficulties Xiangxue has experienced due to the COVID-19 pandemic in making the Upfront Payment. Therefore, in order to facilitate Xiangxue's payment of the Upfront Payment to us, the parties entered into two letter agreements on March 31, 2020 and June 30, 2020, respectively, to amend certain provisions of the 2019 Xiangxue License. In particular, the parties have agreed that, notwithstanding the provisions of the 2019 Xiangxue License Agreement to the contrary, Xiangxue shall be entitled to make the Upfront Payment in Chinese Renminbi to Taihao, our wholly owned subsidiary in China, and that Xiangxue shall remit the gross amount of the Upfront Payment to Taihao with Athenex bearing the responsibility for indirect taxes in connection with license payments made under the 2019 Xiangxue License Agreement rather than Xiangxue. We received the final balance due on the upfront payment of $30.0 million in the third quarter of 2020. In the third quarter of 2020, we recognized revenue for a $10.0 million milestone fee from Xiangxue upon meeting the first regulatory milestone under the 2019 Xiangxue License, and as of February 28, 2021 we received $1.5 million. Consequently, the Company decided to record a provision for the outstanding balance of $8.5 million and $0.4 million related to currency conversion in our financial statements for the three months and year ended December 31, 2020, respectively. We have not yet taken legal action against Xiangxue to enforce the provisions of the 2019 Xiangxue License, but we may exercise all rights and remedies available to us under the terms of the 2019 Xiangxue License and applicable law at any time. We may be eligible to receive future additional payments up to $140.0 million in the event defined regulatory and sales milestones are achieved, a payment of $20.0 million in the event of a change of control or assignment of rights involving Xiangxue (as further defined and subject to the conditions set forth in the 2019 Xiangxue License), and to receive tiered royalties at rates ranging from the low teens to low twenties based on annual net sales of the licensed products in the territory covered by the 2019 Xiangxue License and a percentage of sublicensing revenue. The 2019 Xiangxue License will continue until Xiangxue has no payment obligations under the 2019 Xiangxue License, unless terminated earlier in accordance with the terms of the 2019 Xiangxue License. The 2019 Xiangxue License may be terminated in its entirety upon the mutual agreement of the parties, by Xiangxue for convenience upon requisite notice, or by either party for material breach as set forth in the 2019 Xiangxue License. The 2019 Xiangxue License also will be terminated with respect to any licensed product for Xiangxue's failure to meet agreed upon regulatory milestones with respect to such 2019 Licensed Product.

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 tirbanibulin to treat and prevent skin disorders and diseases in humans (including AK), or the Field, in the licensed territory, which includes the U.S. and substantially all European countries (including Russia and Turkey). 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 tirbanibulin) that we may develop in the future with the same mechanism of action as tirbanibulin 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 tirbanibulin 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 tirbanibulin 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 $30.0 million from Almirall under this agreement. In June 2019, we received milestone payment of $20.0 million, and we expect to receive other near-term payments of up to $5.0 million. We may also be entitled to receive an aggregate of $65.0 million in additional milestone payments, as well as sales milestone payments we estimate will likely total $155.0 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. 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.

Collaboration Agreement

Eli Lilly and Company Agreement

In October 2016, we entered into a Clinical Trial Collaboration and Supply Agreement with Lilly, which we refer to as the Lilly Agreement, under which we and Lilly will conduct a Phase 1b trial of Oral Paclitaxel 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/clinical trial application ("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.

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.

From the inception of Athenex, we have recognized the value of oral chemotherapies, and as a result of the COVID-19 pandemic, there has been increasing interest and demand in both the medical and patient communities for oral therapy options. In 2020, the NCCN issued guidance to support cancer patients and healthcare provider safety. This guidance encouraged switching patients from infusion-based therapies to oral oncolytics, where an oral formulation is available for the same active compound. In addition, we believe there is a significant commercial opportunity in the oral chemotherapy market that allows for several competitors. Based on where paclitaxel is currently being used or is the standard of care, there are opportunities beyond the initial label in MBC that we are pursuing with Oral Paclitaxel, such as in early stage breast cancer, ovarian cancer, lung cancer and gastric cancer. There are also emerging opportunities with important modalities like immunotherapies or targeted therapies. There are other companies working to develop oral therapies in the field of oncology, targeting various tumor types, and these companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes.

Many of the companies, either alone or with strategic partners, against which we are competing or against which we may compete in the future have significantly greater financial, technical and human resources, and clinical, regulatory, commercialization and manufacturing capabilities 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 January 25, 2021, we owned approximately 200 granted patents and over 80 pending patent applications, including six allowed 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. As of January 25, 2021, we have in-licensed patents and technologies in relation to our TCR T-cell therapy. Some of these patents will expire in 2034, excluding any potential patent term adjustments and/or patent term extensions that may be available. We have in-licensed a patent relating to the site-directed PEGylation of arginases and their use as anti-cancer and anti-viral therapies granted in the U.S. and other territories, such as China and Europe. This patent will expire in March 2030, excluding any potential patent term adjustments and/or patent term extensions that may be available. A PCT application has entered national phases in the U.S. and other territories, such as China and Europe covering the compositions and methods for amino acid depletion therapy.

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 U.S. 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 inhibition 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 2040.

Government Regulation and Product Approval

Governmental authorities in the U.S., at the federal, state and local level, and in 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. In order to be lawfully marketed in the U.S., our therapeutic drug candidates and compounded products must comply with either Section 503B (outsourcing facility) or Section 505 (new drug approval) of the FDCA as applicable, and they will be subject to similar premarket requirements in other countries. The process of obtaining regulatory approvals and ensuring compliance with applicable federal, state, local and foreign statutes and regulations requires 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 in accordance with GLPs and other applicable regulations;
- submission to the FDA of an IND application, which must be authorized before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials in accordance with 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 cGMP to assure that the facilities, methods and controls are adequate to assure 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 application. Some nonclinical testing may continue even after the IND application is submitted. In addition to including the results of the nonclinical studies, the IND application 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 application 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 application.

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 endpoints to be evaluated. Each protocol, and any subsequent material amendment to the protocol, must be submitted to the FDA as part of the IND application, 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, with jurisdiction 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.

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 that it is scientifically appropriate to rely on the findings of the studies that were previously conducted by other sponsors to the drug that is the subject of the marketing application.

In addition, the manufacturer of an investigational drug in a Phase 2 or Phase 3 clinical trial for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access to such investigational drug.

The outcome of human clinical trials is 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 application 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 trials that they believe will support the approval of the new therapeutic. A sponsor may 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, 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. An NDA must also contain data to assess the safety and effectiveness of the product for the claimed indication in all relevant pediatric populations. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. 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 program fee for each prescription drug. 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 an NDA, FDA reviews the application 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 has agreed to certain performance goals in the review of NDAs. FDA seeks to review NDAs for standard review products that are not new molecular entities, or NMEs, within ten months of the date the NDA is submitted, while FDA seeks to review NDAs for standard review NMEs within ten months of the date FDA files the NDA. FDA seeks to review NDAs for priority review products that are not NMEs within six months of the date the NDA is submitted, while FDA seeks to review NDAs for priority review NMEs within six months of the date FDA files the NDA. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission. The FDA may refer applications for novel drug products or drug 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, if so, under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully 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 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. 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, with no implication regarding the ultimate approvability of the application or the timing of any such approval, if ever. 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 appeal the decision.

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 of the date that FDA files the NDA as compared to a standard review time of ten months of the date that FDA files the NDA.

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 will require that a sponsor of a product candidate receiving accelerated approval perform post-marketing studies to verify and describe the predicted effect on IMM or other clinical endpoint. The product may be subject to accelerated withdrawal procedures under certain circumstances.

In addition to the Fast Track, accelerated approval and priority review programs discussed above, a sponsor may seek a 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.

Abbreviated New Drug Applications for Generic Drugs and 505(b)(2)NDAs

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. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and effectiveness but where some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. A 505(b)(2) applicant may be able to rely on published literature or on FDA's previous findings of safety and effectiveness for an approved drug. A 505(b)(2) NDA may be submitted for changes to a previously approved drug, including, for example, in the dosage form, route of administration, or indication.

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: (1) the required patent information has not been filed; (2) the listed patent has expired (3) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) 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 application 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. Five- and three-year exclusivity do not affect the submission of a full 505(b)(1) NDA.

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) 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-361 for the treatment of gliomas and Oral Paclitaxel 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 for the same disease or condition 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. Orphan drug exclusivity does not prevent FDA from approving the same drug for a different disease or a different drug for the same 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.

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;
- 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 or consistent with 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 manufacturing 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 cGMP 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 for up to two years after the date of completion of the trial. 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 Outsourcing Facilities

Pharmaceutical drug compounding is a practice in which a licensed pharmacist, a licensed physician, or in the case of an outsourcing facility, a person under the direct supervision of a licensed pharmacist, combines, mixes, or alters ingredients of a drug to create a medication. We are engaged in the compounding of sterile drugs as an outsourcing facility registered with FDA under FDCA Section 503B. Title I of the Drug Quality and Security Act, the Compounding Quality Act, or CQA, allows a facility that compounds sterile drugs to register with FDA as an outsourcing facility. Once registered (which includes payment of an annual fee, among other requirements), an outsourcing facility must meet certain conditions in order to be statutorily exempt from the FDCA's new drug approval requirements, the requirement to label products with adequate directions for use, and certain product tracing and serialization requirements. Under the CQA, a drug must be lawfully compounded in compliance with the provisions set forth in Section 503B including FDA's cGMP regulations and related cGMP guidance for outsourcing facilities in order to remain eligible for the statutory exemptions. The outsourcing facility must also bi-annually report specific information about the products that it compounds, including a list of all of the products it compounded during the previous six months pursuant to Section 503B(b)(2). The source of any bulk substance active ingredient used in compounding must be a Section 510-registered manufacturer, and the substances must be accompanied by a Certificate of Analysis. If the outsourcing facility compounds using bulk drug substances, the bulk drug substances must either appear on FDA's "interim" Category 1 list of bulk substances that may be used in compounding under Section 503B, which are bulk drug substances for which FDA has determined there is a clinical need for use in compounding. Drugs may also be compounded if an FDA-approved drug product appears on FDA's published drug shortage list.

FDA has not yet finalized its list of bulk drug substances for which there is a clinical need. Provided certain conditions are met, FDA will exercise enforcement discretion concerning interim Category 1 substances pending evaluation of the substances for inclusion on FDA's final 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). Outsourcing facilities are prohibited from transferring or otherwise selling compounded drugs through a wholesale distributor, or from compounding drugs that are essentially copies of commercially available, FDA-approved drugs. 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 managed care providers, private health insurers and other organizations as well as government payors such as Medicare, Medicaid, TRICARE and the Department of Veterans Affairs.

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.

Government Programs

Medicaid, the 340B Drug Pricing Program, and Medicare

Federal law requires that a pharmaceutical manufacturer, as a condition of having its products receive federal reimbursement under Medicaid and Medicare Part B, must pay rebates to state Medicaid programs for all units of its covered outpatient drugs dispensed to Medicaid beneficiaries and paid for by a state Medicaid program under either a fee-for-service arrangement or through a managed care organization. This federal requirement is effectuated through a Medicaid drug rebate agreement between the manufacturer and the Secretary of Health and Human Services. The Centers for Medicare & Medicaid Services ("CMS") administers the Medicaid drug rebate agreements, which provide, among other things, that the drug manufacturer will pay rebates to each state Medicaid agency on a quarterly basis and report certain price information on a monthly and quarterly basis. The rebates are based on prices reported to CMS by manufacturers for their covered outpatient drugs. For innovator products, that is, drugs that are marketed under approved NDAs, the basic rebate amount is the greater of 23.1% of the average manufacturer price ("AMP") for the quarter or the difference between such AMP and the best price for that same quarter. The AMP is the weighted average of prices paid to the manufacturer (1) directly by retail community pharmacies and (2) by wholesalers for drugs distributed to retail community pharmacies. The best price is essentially the lowest price available to non-governmental entities. Innovator products are also subject to an additional rebate that is based on the amount, if any, by which the product's current AMP has increased over the baseline AMP, which is the AMP for the first full quarter after launch, adjusted for inflation. For non-innovator products, generally generic drugs marketed under approved abbreviated new drug applications, the basic rebate amount is 13% of the AMP for the quarter. Non-innovator products are also subject to an additional rebate. The additional rebate is similar to that discussed above for innovator products, except that the baseline AMP quarter is the fifth full quarter after launch (for non-innovator multiple source drugs launched on April 1, 2013 or later) or the third quarter of 2014 (for those launched before April 1, 2013).

The terms of participation in the Medicaid drug rebate program impose an obligation to correct the prices reported in previous quarters, as may be necessary. Any such corrections could result in additional or lesser rebate liability, depending on the direction of the correction. In addition to retroactive rebates, if a manufacturer were found to have knowingly submitted false information to the government, federal law provides for civil monetary penalties for failing to provide required information, late submission of required information, and false information.

A manufacturer must also participate in a federal program known as the 340B drug pricing program in order for federal funds to be available to pay for the manufacturer's drugs under Medicaid and Medicare Part B. Under this program, the participating manufacturer agrees to charge certain safety net healthcare providers no more than an established discounted price for its covered outpatient drugs. The formula for determining the discounted price is defined by statute and is based on the AMP and the unit rebate amount as calculated under the Medicaid drug rebate program, discussed above. Manufacturers are required to report pricing information to the Health Resources and Services Administration ("HRSA") on a quarterly basis. HRSA has also issued regulations relating to the calculation of the ceiling price as well as imposition of civil monetary penalties for each instance of knowingly and intentionally overcharging a 340B covered entity.

Federal law also requires that manufacturers report data on a quarterly basis to CMS regarding the pricing of drugs that are separately reimbursable under Medicare Part B. These are generally drugs, such as injectable products, that are administered "incident to" a physician service and are not generally self-administered. The pricing information submitted by manufacturers is the basis for reimbursement to physicians and suppliers for drugs covered under Medicare Part B. As with the Medicaid drug rebate program, federal law provides for civil monetary penalties for failing to provide required information, late submission of required information, and false information.

Medicare Part D provides prescription drug benefits for seniors and people with disabilities. Medicare Part D beneficiaries have a gap in their coverage (between the initial coverage limit and the point at which catastrophic coverage begins) where Medicare does not cover their prescription drug costs, known as the coverage gap. However, by 2020, Medicare Part D beneficiaries will pay 25% of drug costs after they reach the initial coverage limit - the same percentage they were responsible for before they reached that limit - thereby closing the coverage gap. The cost of closing the coverage gap is being borne by innovator companies and the government through subsidies. Each manufacturer of a drug approved under an NDA is required to enter into a Medicare Part D coverage gap discount agreement and provide a 70% discount on those drugs dispensed to Medicare beneficiaries in the coverage gap, in order for its drugs to be reimbursed by Medicare Part D.

Federal Contracting/Pricing Requirements

Manufacturers are also required to make their covered drugs, which are generally drugs approved under NDAs, available to authorized users of the Federal Supply Schedule ("FSS") of the General Services Administration. The law also requires manufacturers to offer deeply discounted FSS contract pricing for purchases of their covered drugs by the Department of Veterans Affairs, the Department of Defense ("DoD"), the Coast Guard, and the Public Health Service (including the Indian Health Service) in order for federal funding to be available for reimbursement or purchase of the manufacturer's drugs under certain federal programs. FSS pricing to those four federal agencies for covered drugs must be no more than the Federal Ceiling Price ("FCP"), which is at least 24% below the Non-Federal Average Manufacturer Price ("Non-FAMP") for the prior year. The Non-FAMP is the average price for covered drugs sold to wholesalers or other middlemen, net of any price reductions.

The accuracy of a manufacturer's reported Non-FAMPs, FCPs, or FSS contract prices may be audited by the government. Among the remedies available to the government for inaccuracies is recoupment of any overcharges to the four specified federal agencies based on those inaccuracies. If a manufacturer were found to have knowingly reported false prices, in addition to other penalties available to the government, the law provides for civil monetary penalties of $100,000 per incorrect item. Finally, manufacturers are required to disclose in FSS contract proposals all commercial pricing that is equal to or less than the proposed FSS pricing, and subsequent to award of an FSS contract, manufacturers are required to monitor certain commercial price reductions and extend commensurate price reductions to the government, under the terms of the FSS contract Price Reductions Clause. Among the remedies available to the government for any failure to properly disclose commercial pricing and/or to extend FSS contract price reductions is recoupment of any FSS overcharges that may result from such omissions.

Tricare Retail Pharmacy Network Program

The DoD provides pharmacy benefits to current and retired military service members and their families through the Tricare healthcare program. When a Tricare beneficiary obtains a prescription drug through a retail pharmacy, the DoD reimburses the pharmacy at the retail price for the drug rather than procuring it from the manufacturer at the discounted FCP discussed above. In order for the DoD to realize discounted prices for covered drugs (generally drugs approved under NDAs), federal law requires manufacturers to pay refunds on utilization of their covered drugs sold to Tricare beneficiaries through retail pharmacies in DoD's Tricare network. These refunds are generally the difference between the Non-FAMP and the FCP and are due on a quarterly basis. Absent an agreement from the manufacturer to provide such refunds, DoD will designate the manufacturer's products as Tier 3 (non-formulary) and require that beneficiaries obtain prior authorization in order for the products to be dispensed at a Tricare retail network pharmacy. However, refunds are due whether or not the manufacturer has entered into such an agreement.

Branded Pharmaceutical Fee

A branded pharmaceutical fee is imposed on manufacturers and importers of branded prescription drugs, generally drugs approved under NDAs. The fee is $2.8 billion in 2019 and subsequent years. This annual fee is apportioned among the participating companies based on each company's sales of qualifying products to or utilization by certain U.S. government programs during the preceding calendar year. The fee is not deductible for U.S. federal income tax purposes. Utilization of generic drugs, generally drugs approved under ANDAs, is not included in a manufacturer's sales used to calculate its portion of the fee.

The ACA

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. CMS will expand Medicaid rebate liability to the territories of the U.S. as well, beginning in 2022, 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.

With regard to the 340B program, 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.

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 & 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.
- The ACA imposed a requirement on manufacturers of branded drugs to provide a discount, now 70%, 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, generic drug pricing is the subject of Congressional inquiries and media attention, and many generic drug manufacturers are the targets of government investigations.

In addition, like branded drug manufacturers, generic drug manufacturers are now required to pay an inflation penalty if price increases on generic drugs exceed the rate of inflation.

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, 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.

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 report payments and other transfers of value they make to U.S. physicians and teaching hospitals (as well as physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, and certified nurse-midwives effective January 1, 2022), 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.

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. Most recently, the Tax Cuts and Jobs Act (the "Tax Reform 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 this legislation will have on the ACA because a decision regarding the constitutionality of the ACA after the repeal of the individual mandate was ultimately appealed to the U.S. Supreme Court. On November 10, 2020, oral arguments were heard in this case. It is unclear when a decision will be made. Additional reforms by the incoming administration 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 Foreign Corrupt Practices Act of 1977 ("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 the People's Republic of China ("PRC" or "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

Foreign investment in China was previously subject to the Catalogue for the Guidance of Foreign Investment Industries (2017 Revision) issued and effective beginning July 28, 2017, and the Special Administrative Measures for the Access of Foreign Investment (2018 Revision) ("Negative List") issued and effective beginning July 28, 2018, which together comprised the encouraged foreign-invested industries catalogue and the special administrative measures for the access of foreign investments to the restricted or the prohibited foreign-invested industries. The latter set out restrictions such as percentage of shareholding and qualifications of senior management. The Catalogue of Industries in which Foreign Investment is Encouraged, and the Negative List are revised yearly, and the most updated revisions were issued on December 27, 2020 (the "2020 Catalogue") and came into effect on January 27, 2021. The most updated Negative List was issued on June 23, 2020 (the "2020 Negative List") and took effect on July 23, 2020, which further reduced restrictions on foreign investment. The manufacturing and production of new anti-cancer drugs, new cardiovascular medicine and new nervous system drugs all fall within the field of industries in which foreign investment is encouraged in the 2020 Catalogue.

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 (NHC) 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 of the PRC (the "State Council") Institutional Reform Proposal promulgated by the Chinese National Congress on March 17, 2018, (1) the State Administration for Market Regulation was established; and the China Food and Drug Administration (CFDA) ceased 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 NHC 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, April 2015, and again in August 2019. 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, and again in March 2019, providing detailed implementing regulations for the revised Chinese Drug Administration Law.

The Chinese Drug Administration Law was newly revised on August 26, 2019 and came into effect on December 1, 2019. As compared to the old law, the current revised Chinese 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.

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, which was revised in 2020, and began to conduct the certification program of GLP. Under the Administrative Provisions on Drug Clinical Test Units, promulgated in November 29, 2019, which replaced 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. According to the newly revised Chinese Drug Administration Law, drug clinical trial institutions shall complete filing with NMPA (approval by NMPA is no longer required). Accordingly, NMPA promulgated the Filing Measures for Drug Clinical Trial Institutions on November 29, 2019, which provides details of the filing procedures and requirements.

Approval for Clinical Trials and Production of New Drugs

According to the Provisions for Drug Registration promulgated by the NMPA in 2007 and revised in January 2020, 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. GMP certification was no longer required from December 2019 and regular and random onsite checking and supervision will be implemented by the relevant authority. 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, July 2013, and March 2017, and Administrative Measures on the Certificate for Animal Experimentation promulgated by the State Science and Technology Commission and other regulatory authorities in December 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 EMA. Multinational companies may need to apply for conducting multi-regional clinical trials, 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, which abolished the Opinions on Implementing a Prioritized Review System to Avoid Drug Review Backlogs. 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 NHC in May 2018, the Chinese government seeks to further simplify and accelerated the clinical trial approval process.

On July 7, 2020, the NMPA promulgated the Announcement on Promulgating Three Documents Including the Working Procedures for the Evaluation of Breakthrough Therapy Designation Drugs (for Trial Implementation), which abolished the Opinions on Encouraging the Prioritized Evaluation and Approval for Drug, and stipulates that sponsors of innovative drug candidates which exhibit clinical benefits for the treatment of life-threatening or other serious conditions for which there is no existing effective prevention and treatment method, or compared with existing treatment methods that have sufficient evidence to show that they have obvious clinical advantages, then any applicant can apply for breakthrough therapeutic drug programs during Phase I and II clinical trials for such drug candidates.

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 Treaty Treatment for Non-Resident Taxpayers promulgated by the Chinese State Administration of Taxation in October 2019 and effective from January 1, 2020, 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.

Pursuant to the Announcement on Continuation of Enterprise Income Tax Policies for Extensive Development in the Western Region issued by the Ministry of Finance, the General Administration of Customs, and the State Administration of Taxation and effective from January 1, 2021, which replaced 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, 2021 to December 31, 2030, 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 60% 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 wastewater 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 RMB is converted into a foreign currency and remitted out of China to pay capital expenses such as the repayment of foreign currency-denominated loans.

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 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 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, and the Foreign Investment Law, which took effect on January 1, 2020 and replaced the Wholly Foreign-owned Enterprise Law, the Cooperative Joint Venture Law, and the Equity Joint Venture Law. 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.

Human Capital

As of December 31, 2020, we had 593 full-time employees and 12 part-time employees. Of these, 244 are engaged in full-time research and development and laboratory operations, 203 are engaged in manufacturing activities and 146 are engaged in full-time selling, general and administrative functions.

As of December 31, 2020, 49% of our personnel were located in the U.S., 42% were located in Asia, 8% were located in Latin America, and 1% in Europe. 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 not experienced any employment related work stoppages, and we consider our relations with our employees to be good.

Supporting our people is a fundamental value for Athenex. We believe the Company’s success depends on its ability to attract, develop and retain key personnel. We monitor our compensation and total reward programs closely and provide a competitive mix of compensation and benefits for all employees. This includes competitive salaries, bonus opportunities for approximately one-third of our employees, and long-term incentives in the form of stock options and other equity types for nearly one-half of our employees. Benefits include opportunities for 401(k) matches, insurance covering health, dental and life, and HSA contributions.

Because of our global presence with locations and employees around the world, Athenex maintains a rich diverse culture. We believe this diversity is an asset and with the skills, experience and industry knowledge of our employees significantly benefit our operations and performance. We believe in a culture of equity, diversity and inclusion. We are also committed to advancing safe and respectful work environments. We recognize and value that our employees can make important contributions to our business based on their individual talents, backgrounds, and expertise, allowing everyone to thrive personally and professionally. We strive for a diverse workforce at every level of the company and its board of directors.

Health and safety in the workplace for our employees and personnel has been of primary importance, particularly with the many issues surrounding COVID-19. The COVID-19 pandemic has underscored the importance of keeping our employees safe and healthy. In response to the pandemic, the Company has taken actions aligned with the Centers for Disease Control and Prevention to protect its workforce so that its workforce can more safely and effectively perform their work. We have invested in systems and technology to allow many employees the ability to work remotely. We have implemented wellness checks for employees including officers and board members. We did not lay off or furlough our work force in response to the COVID-19 pandemic.

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, 2020, 2019, and 2018 and our total assets as of December 31, 2020 and 2019, 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, New York 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, proxy statements and other information with the Securities and Exchange Commission (SEC). Our filings with the SEC are available on the SEC's website at www.sec.gov. You may also access our press releases, financial information and reports filed with the SEC (for example, our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q, our Current Reports on Form 8-K and any amendments to those Forms) on our website under the "Investor Relations" tab. Copies of any documents on our website are available without charge, and reports filed with or furnished to the SEC will be available as soon as reasonably practicable after such materials are electronically filed with or furnished 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 the COVID-19 Pandemic

The COVID-19 pandemic could continue to adversely impact our business, including our commercial operations, clinical development activities and clinical trials.

As a result of the COVID-19 pandemic, we experienced disruptions in production at our CQ API Facility during 2020, and in line with the industry overall, slowed enrollment as well as suspensions of ongoing clinical trials for our earlier stage product candidates, which continued through the fourth quarter of 2020, and disruptions related to our Chairman and Chief Executive Officer falling ill with COVID-19 in January 2021. The future extent of the impact of the COVID-19 pandemic on our business and operations is largely unknown and the situation is fluid. The extent to which our business and operations may be impacted by the pandemic will depend on a number of factors, including (i) the ultimate spread and severity of the outbreaks in the U.S. and globally, (ii) the existence of additional waves of outbreak as containment measures are lifted, (iii) the scope, duration and impact of containment measures on individuals and businesses, and (iv) the timing to market and relative availability of testing and treatment options for COVID-19. If the pandemic worsens or we experience additional waves of outbreak on a local, national or global scale, we may experience a multitude of additional disruptions that could severely impact our business, operations, clinical development activities and planned clinical trials, including without limitation, the following:

- a spread of COVID-19 among our workforce and/or management team, which would result in our reduced capacity to manage our business to the extent key personnel are impacted or our personnel are impacted in significant numbers;
- continued delays or difficulties in clinical trials, which could include extended periods of time in which early stage trials are suspended, sustained difficulties enrolling patients in clinical trials and/or disruptions to ongoing trials based on the attrition of patients as a result of contracting or being exposed to COVID-19, facility closures or limitations on the use of hospitals as clinical trial sites and governmental restrictions on "non-essential" procedures and activities, any of which may further delay our clinical development plans and timelines and also may impact the integrity of our clinical trial data for ongoing trials;
- temporary or long-term disruptions in our supply chains and resulting delays in the delivery of products, services or other materials necessary for our operations;
- interruptions in FDA operations or the operations of comparable foreign regulatory agencies, which may in turn impact our timelines for receiving regulatory approvals and feedback;
- complete or partial shutdowns of the construction efforts at our Dunkirk or PRC facilities or additional production slowdowns or stoppages at our Chongqing facility;
- disruptions due to the increased cybersecurity vulnerabilities caused by remote work and a distributed workforce, including data breaches and data loss;
- interruption or delays in our and our partners ability to meet expected clinical development deadlines or to comply with contractual commitments with respect to the same, including timelines around preclinical studies and planned clinical trials which could in turn delay overall developmental and commercialization timelines; and
- limitations on our ability to engage in face-to-face essential business activities as well as marketing and public relations activities due to the health risks posed by such activities, the widespread cancellation of conferences and events targeting the biotech and medical fields, and restrictions on domestic and international travel, including travel bans and government imposed quarantines.

Each of these disruptions as well as others arising from the COVID-19 pandemic could adversely impact our ability to conduct clinical development activities, planned clinical trials and our business generally, and could have a material adverse impact on our operations and financial condition and results.

The economic disruption from the COVID-19 pandemic may result in material adverse consequences for general economic, financial and business conditions, and could result in increased credit and counterparty risks.

Through our normal business activities, we are subject to significant credit and counterparty risks that arise in the ordinary course of business. These risks have been heightened due to the COVID-19 pandemic and resulting economic turbulence, giving rise to substantial macroeconomic uncertainty. In the event of a sustained economic downturn, our customers, lenders, licensing partners, service providers, and other counterparties may be unable to fully fulfil their respective obligations to us in a timely manner, or at all. In addition, governments that we have partnered with and received grants from in connection with the construction of certain production facilities may be unable to timely fulfil their obligations under such agreements due to the impact of COVID-19 on their financial conditions.

In particular, we are a party to various strategic collaboration and license agreements that are important to our business and to our current and future product candidates. Unfavorable macroeconomic conditions caused by COVID-19 may lead our business partners to delay or curtail planned expenditures under our licensing arrangements, which could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

As a result of COVID-19, we have experienced difficulties in collecting certain license agreement receivables. For instance, we have experienced significant delays in the receipt of payments due from a license partner – see Part 1, Item 2, "*Management Discussion and Analysis*," under the heading "*Recent business updates and COVID-19 related measures*" for further information. If any of these difficulties persist for one or more of our partnerships, we may need to declare a default and terminate a license arrangement, which could delay or impair our ability to develop and commercialize the product candidates in the territories covered by the license agreement. In addition, we may seek replacement partnerships to develop and commercialize these product candidates in the territories covered by the terminated arrangement, the negotiation and entry into which may impact our development timelines and otherwise be on terms less favorable compared to existing contractual terms. This could in turn have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

In addition, a prolonged downturn in macroeconomic conditions or negative trends in the global credit markets could further negatively impact our ability to collect on receivables, including milestone payments, due to us which may increase our concessions and discount rates as well as the length of time until these receivables are collected. An inability to timely collect may lead to an increase in our borrowing requirements, our accounts receivable and potentially lead to increased write-offs, with possible adverse effects on our business, financial condition, results of operations and cash flows.

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 public and 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 2020, 2019 and 2018. For the years ended December 31, 2020, 2019 and 2018, we reported net losses of $148.4 million, $125.5 million and $128.7 million, respectively, and had an accumulated deficit of $713.6 million as of December 31, 2020. 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, including Klisyri (tirbanibulin). Typically, it takes many years to develop a new drug before it is available for treating patients. In addition to our recent receipt of a CRL regarding the NDA for Oral Paclitaxel, 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, payments due pursuant to our financing arrangements, 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 stockholders' 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, as 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 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 financial results are subject to volatility related to our revenue and expenses, and despite beginning to generate revenue from product sales, we have not yet been profitable and may never become profitable.

Our financial results are subject to volatility based on a number of factors, including the timing of milestone licensing fees that we receive or are required to pay, the amount and timing of our debt repayment obligations, the change in product types sold by APD and APS and whether those products are in high demand, our ability to predict the products in high demand in the market, competition in the market for generic drugs. As we currently only have commercialized our API products and recently received approval to commercialize Klisyri, 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, including Oral Paclitaxel and Oral Docetaxel, and specialty products, such as medical testing kits. Our product sales of API totaled $3.6 million, $12.7 million and $18.0 million in the years ended December 31, 2020, 2019 and 2018, respectively. Our specialty products launched in March 2017 and sales totaled $89.6 million, $50.4 million, and $30.4 million for the years ended December 31, 2020, 2019, and 2018, respectively. We have an existing API manufacturing facility in Chongqing, China, where operations were suspended as a result of the COVID-19 outbreak in China but resumed producing API primarily for the Company's use in March 2020 in accordance with local regulatory guidance. Our revenue and gross margins are also subject to fluctuation due to changes in product mix and the expenses we incur to continue our research and development and commercialization efforts.

We expect to continue to incur substantial losses through the projected development and commercialization of our drug candidates. Other than Klisyri, which received FDA approval for commercialization in December 2020, 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 as 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 optimal pricing for products in key global markets;
- 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 as our proprietary drug candidates are approved for commercial sale, we anticipate incurring significant costs associated with the commercial launch of these drugs. In the case of Klisyri, our only approved drug product, we are exclusively dependent on the marketing and sales efforts of our partners to generate revenue, particularly Almirall, which holds the commercialization rights to the U.S. and European markets.

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.

To date, we have financed our operations with the proceeds from debt financings, public and private securities offerings, public-private partnerships, the issuance of convertible notes and public grants. In addition to the significant amounts we will need to expend to complete the additional trial for NDA resubmission and to market and commercialize Oral Paclitaxel, if approved, together with any additional approved products, our drug candidates will require the completion of clinical studies and regulatory review, 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 $131.2 million, $97.5 million and $109.4 million for the years ended December 31, 2020, 2019 and 2018 respectively. We expect to continue to spend substantial amounts on advancing the clinical development of our proprietary drug candidates, supporting the commercialization of Klisyri and any additional proprietary drugs for which we receive regulatory approval, including building our own commercial organizations to address certain markets.

On June 19, 2020, we entered into a 6-year $225.0 million Senior Credit Agreement with Oaktree, bearing interest at a fixed annual rate of 11%. We expect to use borrowings under our Senior Credit Agreement, proceeds from out-licensing arrangements and potential future financing transactions, if necessary, to fund expenditures that are in excess of our operating cash flow and cash on hand, including completing the development and commercialization of our proprietary drug candidates and 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, we will require additional financial resources and personnel to build out operations at our public-private partnership facilities in Chongqing, China and Dunkirk, New York.

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.

We have also incurred debt service obligations under our Senior Credit Agreement and will have minimum payment obligations under our Revenue Interest Financing Agreement entered into with Sagard on August 4, 2020, which could make it more difficult for us to fund our operations. Under the Senior Credit Agreement, we are required to make quarterly interest-only payments until June 19, 2022, after which we are required to make quarterly amortizing payments, with the remaining balance of the principal plus accrued and unpaid interest due at maturity. Beginning on September 17, 2020, we were required to pay a commitment fee on any undrawn commitments equal to 0.6% per annum, payable on each subsequent funding date or the commitment termination date. Under the Revenue Interest Financing Agreement, our receipt of financing is contingent on receiving an FDA approval for Oral Paclitaxel and, in the event we are unable to do so before December 31, 2021, Sagard will have a termination right. In the event we receive approval but do not generate revenues from Oral Paclitaxel sufficient to satisfy minimum payment obligations of $20.0 million by September 30, 2024 and $50.0 million by August 4, 2026, we will in each instance be required to pay Sagard the amount of the shortfall. In addition, if Sagard has not received payments equaling at least $85.0 million by the tenth anniversary of the date the Product Payment is funded, then subject to the Hard Cap, we will be required to pay Sagard an amount such that Sagard will have obtained a 6.0% internal rate of return on the Product Payment (taking into account all other payments received by Sagard from us under the Revenue Interest Financing Agreement). For additional information, please see "*Liquidity and Capital Resources — Debt and Equity Financings*".

We believe that the existing cash and cash equivalents, restricted cash, and short-term investments will fund operations into the second quarter of 2022. The Company's estimates are based on relevant conditions that are known and reasonably knowable at the date of these consolidated financial statements being available for issuance, and are subject to change due to changes in business, industry or macroeconomic conditions. This forecasted cash runway does not contemplate the additional funding we may receive through the Senior Credit Agreement and Revenue Interest Financing Agreement. Further, we do not expect to have further access to additional capital under these facilities due to our receipt of the CRL for Oral Paclitaxel and will need to seek out alternative sources of financing unless and until Oral Paclitaxel is approved by the FDA or we will need to renegotiate these arrangements. We have based this estimate on assumptions that may prove to be wrong, and we could spend our available financial resources much faster than expected and may need to raise additional funds sooner than anticipated. 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 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 under the Senior Credit Agreement when they mature on July 3, 2023 and to continue to fund our operations. We are required to make quarterly interest-only payments until June 19, 2022, after which we are required to make quarterly amortizing payments, with the remaining balance of the principal plus accrued and unpaid interest due 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 agreements restrict the manner in which we conduct our business.

The Senior Credit Agreement contains various covenants that limit, subject to certain exemptions, our ability and/or our certain of our subsidiaries' ability to, among other things, incur additional indebtedness or liens; make investments; consummate business combinations such as mergers and dispositions; prepay other indebtedness; and to declare dividends and other distributions, subject to certain exceptions, including specific exceptions with respect to product commercialization and development activities. In addition, the Senior Credit Agreement contains certain financial covenants, including, among other things, maintenance of minimum liquidity and a minimum revenue test, measured quarterly until the last day of the second consecutive fiscal quarter where the consolidated leverage ratio does not exceed 4.5 to 1, provided that thereafter we cannot allow our consolidated leverage ratio to exceed 4.5 to 1, measured quarterly.

The Senior Credit Agreement requires that we maintain (i) a debt service reserve account with a minimum cash balance equal to the amount required to pay interest on the outstanding loan for a period of the next twelve months and (ii) a minimum liquidity amount in cash or permitted cash equivalent investments of $20.0 million until the date on which the aggregate principal amount of loans outstanding is greater than or equal to $150.0 million (the "First Step-Up Date"), $25.0 million from the First Step-Up Date until the date on which the aggregate principal amount of loans outstanding balance is equal to $225.0 million (the "Second Step-Up Date"), and $30.0 million from the Second Step-up Date until the maturity date. Our obligations under the Senior Credit Agreement are guaranteed by certain of our existing domestic subsidiaries and subsequently acquired or organized subsidiaries subject to certain exceptions. Our obligations under the Senior Credit Agreement and the related guarantees thereunder are secured, subject to customary permitted liens and other agreed upon exceptions, by (i) a pledge of all of the equity interests of our direct subsidiaries, and (ii) a perfected security interest in all of our tangible and intangible assets.

The restrictions contained in our Senior Credit 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.

In addition, the Revenue Interest Financing Agreement imposes various affirmative and negative covenants, including consent and information rights for Sagard.

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

Our ability to comply with the covenants, restrictions and specified financial ratios 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.

Our access to additional capital under the Senior Credit Agreement, Sagard Revenue Interest Financing Agreement and our out-licensing agreements is dependent on the fulfillment of certain conditions, where applicable, and achievement of certain milestones, which we may not achieve.

As of December 31, 2020, we had $150.0 million of indebtedness outstanding under the Senior Credit Agreement, $54.1 million of which was used to repay amounts outstanding under our previous facility with Perceptive and an additional $16.5 million of the upfront loan proceeds held by us as restricted cash in a debt service reserve account, and $12.7 million in fees and expenses incurred in connection with the financing, leaving $66.7 million in available proceeds from the first three tranches after payment of fees and expenses incurred in connection with our entry into the Senior Credit Agreement. Under our Senior Credit Agreement and our out-licensing arrangements, our ability to access additional capital is dependent on our ability to achieve various regulatory and commercial milestones, which we may never achieve. Our Senior Credit Agreement provides that we must meet funding conditions related to the approval and commercialization of Oral Paclitaxel to draw down the remaining $75.0 million of commitments under Senior Credit Agreement. Each of the Senior Credit Agreement and Revenue Interest Financing Agreement also require bringdowns of various representations and warranties as a condition to funding and our access to funding under the Revenue Interest Financing Agreement is dependent on the approval of Oral Paclitaxel. The Revenue Interest Financing Agreement also provides Sagard with a termination right in the event we do not receive a marketing authorization for Oral Paclitaxel by December 31, 2021. Given that the FDA is requiring an additional clinical trial, there is a substantial likelihood that we will not be able to receive FDA approval by this date and we will not be able to access additional funds under our financing arrangements until we receive FDA approval of Oral Paclitaxel. For additional information, please see "*Liquidity and Capital Resources —Debt and Equity Financings —Oaktree Senior Credit Agreement*."

In the event we are unable to meet the above funding conditions and/or achieve the various commercial and regulatory milestones in our out-licensing agreements, we will need to raise additional capital and can provide no assurances that we will be able to do so when needed or on acceptable terms. In the event we are unable to access additional capital we would be forced to delay, reduce or eliminate our research and drug development programs or commercialization efforts. In addition, the failure to meet these conditions and milestones would have broader implications on the value and prospects of our Company and could impair our ability to raise such additional necessary capital, grow our business, retain key employees and continue our operations.

Raising additional capital may cause dilution to our stockholders, 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.

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, 2020, our existing goodwill represented $38.9 million, or 10% of our total assets, as a result of our acquisitions of APS, CDE, Polymed, Taihao and CIDAL. 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

The majority of 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 all of our drug candidates and have not yet established sales and marketing activities necessary for successful commercialization of the drug candidates we plan to commercialize. We are also dependent on the marketing and sales efforts of our partners for the successful commercialization of our approved drug, Klisyri. 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 February 19, 2021, we had a total of 21 planned or ongoing clinical trials for our drug candidates. We have one FDA approved drug product, Klisyri, and have completed, two Phase 3 clinical trials for tirbanibulin ointment 1% for AK, and one Phase 3 clinical trial for Oral Paclitaxel for the treatment of patients with metastatic breast cancer. 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. 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 as previous trials with the same compound, even with the same indication.

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, and 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, as recently indicated by the FDA in its CRL with respect to our NDA for Oral Paclitaxel, that indicated a need for an additional study to examine safety and dosing. Further, once 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, as the FDA recently indicated in its CRL with respect to our NDA for Oral Paclitaxel, or do not otherwise produce positive results, we will incur costs and experience delays in completing, and may 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 manufacture API and clinical products in the event our manufacturing facilities' operations are suspended indefinitely or terminated due to events beyond our control;
- 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 API and our proprietary product candidates. As a result, our business is subject to risks associated with that facility in particular and doing business in China generally, including:

- the possibility of our operations at the Chongqing facility being suspended indefinitely or terminated by an order of the local government due to events beyond our control;
- the impact of the ongoing COVID-19 pandemic on our operations in China;
- the possibility that the costs of building and maintaining the Chongqing facility exceed the revenue we are able to generate from manufacturing API at the facility;
- 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.

Operations at the CQ API Facility in Chongqing, China were suspended as a result of the COVID-19 outbreak in China but resumed producing API primarily for the Company's use in March 2020 in accordance with local regulatory guidance.

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 and may have to use alternate suppliers of API to meet our needs. 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 Development, Regulatory Approval and Commercialization

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. We cannot provide any assurances with respect to the timing for any regulatory approval or if our studies will be considered to be sufficient by regulators, as we recently experienced with our NDA for Oral Paclitaxel. 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. It is possible that none of our other 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 in those territories 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, significantly 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 the U.S. or 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. For marketing approval in Europe, we will seek to obtain marketing approval from the EMA. 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., including in the U.K., China, Taiwan and Latin America. 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. For example, in the CRL we received regarding the NDA for Oral Paclitaxel, the FDA indicated that the participants in a new clinical trial they are recommending should be reflective of the U.S. population. If the FDA does not accept the data from any of our other clinical trials conducted outside the U.S., it would likely result in the need for additional clinical trials, 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, one of our product candidates, Oral Paclitaxel, for which we filed and the FDA accepted an NDA in September 2020 and received a CRL in February 2021, has been in development since 2011. Delays in clinical trials, regulatory approvals or rejections of applications for regulatory approval in the U.S., United Kingdom, Taiwan, New Zealand, China, Latin America, or other jurisdictions may result from many factors, including:

- our inability to obtain sufficient funds required for a clinical trial;
- regulatory requests for, or the requirement of, 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 and retain 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 safety or effectiveness of drug candidates during clinical trials;
- feedback from the FDA, NMPA, IRB, the Data and Safety Monitoring Board (“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 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 candidate;
- 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 during the study or 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 Special Examination and Approval Provisions issued by the NMPA in 2009, the NMPA may conduct special examinations and approve new drug registration applications for drugs which (i) have active ingredients extracted from plants, animals and minerals, etc. and their preparations are not yet marketed in China, and newly discovered Chinese crude drugs and their preparations, (ii) contain chemical drug substances and their preparations and biological products not yet approved for marketing in China or abroad, (iii) are new drugs for the treatment of diseases, including, among others, AIDS, malignant tumors and rare diseases, with significant clinical advantage, and (iv) are new drugs for the treatment of diseases, for which effective therapeutic methods are not available. On May 17, 2018, the NMPA and NHC issued the Announcement on Optimizing the Review and Approval of Drug Registration, which clarifies that a priority review and approval mechanism will be available. The current Chinese Drug Administration Law, which was promulgated on August 26, 2019 and came into effect on December 1, 2019, also stipulates that the government encourages research and development of innovative drugs for serious diseases such as cancer.

On July 7, 2020, the NMPA promulgated the Announcement on Promulgating Three Documents Including the Working Procedures for the Evaluation of Breakthrough Therapy Designation Drugs (for Trial Implementation), which stipulates that sponsors of, innovative drug candidates which exhibit clinical benefits for the treatment of life-threatening or other serious conditions for which there is no existing effective prevention and treatment method, or compared with existing treatment methods that have sufficient evidence to show that they have obvious clinical advantages, may apply for breakthrough therapeutic drug programs during Phase I and II clinical trials for such drug candidates. We cannot be sure that the NMPA will grant such priority treatment to any of our drug candidates.

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 approved drugs and 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 related to our approved drugs or drug candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials that would preclude approval of our drug candidates by the FDA, NMPA, or another regulatory authority or, if approved, could result in a more restrictive label. 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. For example, in the CRL we received from the FDA, the FDA indicated that it had determined that our Oral Paclitaxel Phase III study demonstrated an unacceptable increase in neutropenia-related sequelae and has determined that additional risk mitigation strategies to improve toxicity, which may involve dose optimization and / or exclusion of the patients deemed to be at a higher risk of toxicity, are required to support potential approval of the NDA. 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.

For Klisyri® (tirbanibulin), adverse events reported during clinical trials and identified in the approved prescribing information included erythema, flaking/ scaling, crusting, swelling, vesiculation/pustulation, erosion/ ulceration, application site pruritus, and application site pain, which included pain, tenderness, stinging, and burning sensation at the application site.

In our clinical studies to date, we have observed the following SAEs that were deemed at least possibly related to each of our product candidates:

- Oral Paclitaxel - neutropenia, febrile neutropenia , pneumonia, septic shock, sepsis and other infections, dehydration gastroenteritis, anemia, diarrhea, mucositis, gastrointestinal bleeding, vomiting and nausea, rectal bleeding, altered state of consciousness, hypokalemia, cardiac arrest, tachycardia, atrial fibrillation, cardiogenic shock, hypotension, pancytopenia, multiorgan failure, renal failure, atrial fibrillation, pleural effusion, supraventricular tachycardia, respiratory failure, malnutrition, dyspnea, cardiac failure, and peripheral sensory neuropathy;
- Oral Docetaxel – vomiting, nausea, diarrhea and gastrointestinal toxicity;
- Oral Irinotecan - diarrhea, rash, gastrointestinal hemorrhage, vomiting, nausea, asthenia, neutropenia, anorexia, increased alanine aminotransferase, increased aspartate aminotransferase, enteritis, decreased neutrophil count and clostridium difficile infection;
- Tirbanibulin oral - allergic reaction, bacteremia, rash, syncope, perivascular 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, pain at the base of the neck, pyrexia, chills, rigors, tachypenea, oxygen desaturation, pneumonia, anemia, elevated ALT and AST, dehydration, leukopenia and tremor; and
- KX2-361 - pulmonary embolism; thromboembolic event, hyperuricemia and nausea.

Additionally, if we or others later identify undesirable side effects caused by Klisyri® or one or more of our drug candidates, if approved, 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 or drug candidate, if approved, and could significantly harm our business, results of operations and prospects.

The commercialization of Klisyri® and of any of our drug candidates, if approved, subjects us to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expenses and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drug candidates.

Klisyri® and our drug candidates, if any are approved, are 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 foreign 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 conditions of approval or limitations on the approved indicated uses for which the drug may be marketed, 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 cGMP and GCP 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 drugs, 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 their approved indications and in a manner consistent with the provisions of the approved prescribing information. 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. 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.

Risks Related to Commercialization of Klisyri® and Our Drug Candidates

We depend substantially on the success of our approved product, Klisyri® and our drug candidates. If we are unable to successfully commercialize Klisyri® or experience significant delays in doing so for our other drug candidates, our business will be materially harmed.

Our business and the ability to generate revenue related to product sales depend on the successful commercialization of our approved product Klisyri® and the successful development, regulatory approval and commercialization of any current or future product candidates. Klisyri® has been approved by the FDA in the U.S., but Klisyri® has not received regulatory approval in any other jurisdiction and no sales can be made in any such jurisdiction unless such approval occurs. We have invested a significant portion of our efforts and financial resources in the development of Klisyri®, and our prospects are highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully commercialize these products. The success of Klisyri® and any current or future product candidates depends on several factors, including:

- successfully completing clinical trials;
- receiving and maintaining regulatory approvals from applicable regulatory authorities;
- developing and maintaining effective sales, marketing and distribution capabilities or partnerships to commercialize our products;
- establishing adequate internal manufacturing capacity or arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- establishing commercial markets;

- obtaining coverage and reimbursement from third-party payers; and
- successfully competing with other products;

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize Klisyri® or any current or future product candidates, which could materially harm our business, and we may not be able to earn sufficient revenues and cash flows to continue our operations.

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

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. Some of 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. We recently experienced this uncertainty with the receipt of a CRL for our NDA for Oral Paclitaxel, and the FDA recommended an additional clinical trial be completed and additional risk mitigation strategies to improve toxicity, which may involve dose optimization and / or exclusion of the patients deemed to be at a higher risk of toxicity, to support potential approval of the NDA. 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.

If our NDA for Oral Paclitaxel is not approved by the FDA, this would have a material adverse effect on our business, financial performance and results of operations.

We submitted an NDA for Oral Paclitaxel for the treatment of metastsatic breast cancer. On February 26, 2021, we received a CRL from the FDA regarding our NDA for Oral Paclitaxel. In the CRL, the FDA indicated its concern of safety risk to patients in terms of an increase in neutropenia-related sequelae on the Oral Paclitaxel arm compared with the IV paclitaxel arm in the Phase III study. The FDA also expressed concerns regarding the uncertainty over the results of the primary endpoint of objective response rate (ORR) at week 19 conducted by blinded independent central review (BICR). The agency stated that the BICR reconciliation and re-read process may have introduced unmeasured bias and influence on the BICR. Additionally, the FDA recommended that we conduct a new adequate and well-conducted clinical trial in a patient population with MBC representative of the population in the U.S. We are working to consider the appropriate next steps in the development of Oral Paclitaxel. The agency determined that additional risk mitigation strategies to improve toxicity, which may involve dose optimization and / or exclusion of patients deemed to be at higher risk of toxicity, are required to support potential approval of the NDA. We plan to request a meeting with the FDA to discuss the FDA’s response, engage in a dialogue on the design and scope of a clinical trial to address the agency’s requirements and align on the next steps required to obtain approval. If we pursue the additional trial, it will be at significant cost and if we fail to obtain approval or experience additional delays in obtaining approval, any such decision or delays would have a material impact on our ability to generate revenue from the sales of Oral Paclitaxel. Accordingly, an inability to generate such revenue would have a material effect on our business, financial performance and results of operations.

Any fast track designation or grant of priority review status by the FDA may not actually lead to a faster development or regulatory review or approval process, nor will it assure FDA approval of our product candidates. Additionally, our product candidates may treat indications that do not qualify for priority review vouchers.

We previously received priority review for Oral Paclitaxel in the U.S. and may seek fast track designation or priority review of applications for approval of our product candidate for future indications. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation. If a product candidate offers major advances in treatment, the FDA may designate it eligible for priority review. A priority review designation means that the FDA's goal to review an application is six months, rather than the standard review period of ten months. The FDA has broad discretion whether or not to grant these designations, so even if we believe a particular product candidate is eligible for these designations, we cannot assure you that the FDA would decide to grant them. Even if we do receive fast track designation or priority review, we may not experience a faster development process, review or approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter.

We are dependent on the efforts of Almirall for the commercialization of Klisyri in the U.S. and Europe.

We have entered into collaborations with Almirall and are dependent on the efforts of Almirall for the commercialization of Klisyri in the U.S. and in Europe. The success of this arrangement will depend heavily on the efforts and activities of Almirall. In some situations, we may not be able to influence Almirall's decisions regarding the commercialization of Klisyri or Almirall's level of effort in marketing and selling Klisyri.

Klisyri® and any of our drug candidates, if approved, 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.

Klisyri® and any of our drug candidates, if approved, 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 Klisyri® and our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- the clinical indications for which our drugs are approved;
- physicians, hospitals, cancer treatment centers and patients considering our drugs as a safe and effective treatment;
- the potential and perceived advantages of our drugs 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 drugs 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 drugs;
- obtaining optimal pricing for products in key global markets;
- 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;
- the emergence of new biomarker-driven therapies as alternatives to chemotherapy; and
- the effectiveness of our sales and marketing efforts.

If Klisyri® and any of our drug candidates, if approved, 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.

Our sales force is working to gain market acceptance among physicians, patients, patient advocacy groups, healthcare payers, including pharmacy benefit managers, and others in the medical community. Our partner Almirall is commercializing Klisyri® in the U.S. The commercial success of our products in the U.S. will depend on the degree of such market acceptance. Insurers and other third-party payers may also encourage the use of generic products, either in preference to or prior to the use of brand therapies. The degree of market acceptance of Klisyri® and any current or future product candidates, if approved, will depend on a number of factors, including:

- the market price, affordability and patient out-of-pocket costs, relative to other available products, which are predominantly generics;
- the possibility that third-party payers will not give favorable positions on their formularies or will place restrictions on their use, including through use of step therapy or prior authorization programs;
- the timing of market introduction;
- their effectiveness as compared with currently available products;
- physician willingness to prescribe and patient willingness to adopt them in place of current therapies;
- varying patient characteristics including demographic factors such as age, health, race and economic status;
- changes in the standard of care for the targeted indications;
- the prevalence and severity of any adverse side effects;
- limitations or warnings contained in labeling;
- limitations in the approved clinical indications;
- our success in demonstrating their benefits including relative convenience and ease of initiation, prescription and administration;
- the strength of our selling, marketing and distribution capabilities;
- the quality of our relationships with physicians, patient advocacy groups, third-party payers and others in the medical community;
- the continuous availability of quality manufactured products;
- sufficient third-party coverage or reimbursement; and
- the degree to which the products are subject to material product liability claims

It is possible that we may find it necessary or desirable to provide rebates on Klisyri® or future product candidates, if approved, to customers or third-party payers or to implement patient assistance programs, including co-pay assistance programs, which could affect our profitability. In addition, we do not know how physicians, patients and third-party payers will respond to the pricing of Klisyri® in the U.S. or the pricing of any current or future product candidates in any jurisdiction, if approved.

The market opportunities for our currently marketed or potential products, if approved, are difficult to precisely estimate.

Orphan drugs target rare diseases and must therefore capture significant market share at high per-patient cost to generate reasonable returns.

KX2-361 has obtained Orphan Drug Designation from the FDA and Oral Paclitaxel has obtained Orphan Drug Designations from both the FDA and EC, respectively. As orphan drug candidates target rare diseases with small patient populations, we believe that we would need to capture significant market share to achieve meaningful returns on these product candidates. Further, as is typical of drugs for rare conditions, we would need to establish relatively higher prices in order to generate a return on investment and achieve meaningful gross margins. There can be no assurance that we will be successful in commercializing our orphan drug product candidates, if at all, or that we will be able to generate sufficient revenues from their sales to produce a meaningful return due to the limited market size.

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, an additional cGMP manufacturing facility for our use is substantially complete in Dunkirk, New York, and the construction of a new API facility is complete in Chongqing, China. Our facility in Dunkirk, New York is being built pursuant to an agreement with FSMC. Under the current arrangement, we selected and hired 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 around $208.0 million (including approximately $8.0 million in additional funds that were available from the previous $25.0 million ESD grant), and ESD, not us, will own the facility and equipment. If development of the Dunkirk facility is delayed or not completed it could materially adversely affect our operations and financial results. Our New API Facility in Chongqing was constructed in accordance with an agreement with CQ. Under the current agreement, CQ is responsible for construction of the facility but we are responsible for the costs of all equipment for the facilities. CQ will own the land and buildings, 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 have committed to achieving certain operational, revenue and tax generation milestones within certain time periods once we commence operation. If we are not able to achieve such milestones, CQ will have the opportunity to terminate the agreement and dispose of the plants in its discretion.

Additionally, both the Dunkirk and Chongqing facilities will need to be cGMP validated. The Chongqing facility commenced operations in January of 2021 and the Dunkirk facility is expected to commence operations in the second half of 2021. Validation is a lengthy process that must be completed before we can manufacture under cGMP requirements. We cannot guarantee that the FDA or foreign regulatory agencies will approve the manufacture of any products at these or other facilities, that such facilities will remain in compliance with cGMP regulations, or that such facilities will maintain a compliance status acceptable to the FDA or other regulatory agencies.

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 Klisyri or any of our other product candidates in a timely or economical manner. As with Klisyri or other product candidates 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 and prospects for commercialization 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. In addition, the existing Chongqing API plant's commercial operations were suspended in 2019 based on concerns raised by the DEMC related to the location of our plant. If the FDA, NMPA, DEMC 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, regulatory approval process, 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. For the product candidates and/or territories where we do not have existing partnerships pursuant to which our partners will be responsible for the marketing and sales of such products, 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 sufficient internal sales, marketing and commercial distribution capabilities for these proprietary drug candidates, we will need to pursue additional 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.

Factors that may inhibit our efforts to successfully establish a sales force include:

- an inability to compete with other pharmaceutical companies to recruit, hire, train and retain adequate numbers of effective sales and marketing personnel with requisite knowledge of our target market;
- an inability to effectively manage a geographically dispersed sales and marketing organization in such jurisdictions;
- the inability of sales personnel to obtain access to adequate numbers of physicians to prescribe any future approved products;
- failure to adhere to regulatory requirements governing the sale of products in any jurisdiction;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- a delay in bringing products to market after efforts to hire and train our sales force have already commenced.

In the event we are unable to successfully market and promote our products, our business may be harmed.

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 Klisyri® 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 and commercializing our drug candidates and drugs. 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.

If our competitors market products that are more effective, safer, have fewer side effects or are less expensive than our products or that reach the market sooner than any of our current or future product candidates, if approved, we may not achieve commercial success.

Klisyri® and any of our drug candidates, if approved, may become subject to unfavorable pricing regulations, third party reimbursement practices or healthcare reform initiatives, which could harm our business.

Successful sales of Klisyri® and any 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 entitled 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 our drugs, if and once approved, 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. If we fail to obtain and sustain an adequate level of coverage and reimbursement for Klisyri® or any current or future product candidates, if approved, by third-party payers, potential future sales would be materially adversely affected. There will be no commercially viable market for Klisyri® or any current or future product candidates, if approved, without adequate coverage and reimbursement from third-party payers, and any reimbursement policy may be affected by future healthcare reform measures. Further, we cannot be certain that adequate coverage and reimbursement will be available for either of our products in jurisdictions outside the U.S. or for any current or future product candidates, if approved. Additionally, even if there is a commercially viable market, if the level of coverage or reimbursement is below our expectations, our anticipated revenue and gross margins will be adversely affected.

Third-party payers, such as government or private healthcare insurers and pharmacy benefit managers, carefully review and increasingly question and challenge the coverage of and the prices charged for drugs. Reimbursement rates from private health insurance companies vary depending on the company, the insurance plan and other factors. Reimbursement rates may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. A current trend in the U.S. healthcare industry is toward cost containment. Large public and private payers, managed care organizations, group purchasing organizations and similar organizations are exerting increasing influence on decisions regarding the use of, and reimbursement levels for, particular treatments. Such third-party payers, including Medicare, may question the coverage of, and challenge the prices charged for, medical products and services, and many third-party payers limit coverage of or reimbursement for newly approved healthcare products. In particular, third-party payers may limit the covered indications. Cost-control initiatives in the U.S. healthcare industry could put downward pressure on the price we have established for Klisyri® or any current or future product candidates, if approved, which could result in product revenues being lower than anticipated. If we are unable to show a significant benefit relative to existing generic drugs, Medicare, Medicaid and private payers may not be willing to reimburse for Klisyri® or any current or future product candidates, if approved, which would significantly reduce the likelihood of them gaining market acceptance. Reimbursement systems in international markets vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted.

We believe that U.S. third-party payers consider the efficacy, cost effectiveness, safety and tolerability of Klisyri® and will consider such factors of any current or future product candidates, if approved, and whether use of any such products should be a covered benefit under its health plan in determining whether to approve coverage and reimbursement for such products and at what level. Obtaining these approvals can be a time consuming and expensive process. Our business would be materially adversely affected if we do not obtain or maintain approval for reimbursement of Klisyri® or any current or future product candidates, if approved, from third-party payers on a timely or satisfactory basis or if pricing is set at unsatisfactory levels. Limitations on coverage could also be imposed at the local Medicare carrier level or by fiscal intermediaries. Medicare Part D, which provides a pharmacy benefit to Medicare patients as discussed below, does not require participating prescription drug plans to cover all drugs within a class of products. Our business could be materially adversely affected if Part D prescription drug plans were to limit access to or deny or limit reimbursement of any of our approved products.

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 requires 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 Ministry of Human Resources and Social Security of the PRC (the "MHRSS"), together with other government authorities, has the power to determine the medicines included in the National Reimbursement Drug List (the "NRDL"). In February 2017, the MHRSS released the 2017 NRDL, which was amended in 2019 and 2020. Medicines included in the NRDL are divided into two parts, Part A and Part B. Patients purchasing medicines included in Part A of the NRDL are entitled to reimbursement of the entire amount of the purchase price. Patients purchasing medicines included in Part B of the NRDL are required to pay a certain percentage of the purchase price and obtain reimbursement for the rest of the purchase price. The percentage of reimbursement for Part B medicines differs from region to region in the PRC. The National Healthcare Security Administration requires provincial authorities to increase reimbursement rates step by step.

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.

If and as our drug candidates are approved, we intend to test and market our approved drugs 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, New Zealand and the United Kingdom, and other non-U.S. markets, including certain countries in Latin America, 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.

Risks Related to Compounding

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

Formulations prepared and distributed by outsourcing facilities may contain ingredients found in FDA-approved drugs (i.e., "sterile-to-sterile" compounding) or ingredients that are on FDA's interim or final list of bulk substances that may be used in compounding. Compounded formulations are subject to various statutory and FDA regulatory requirements. Outsourcing facilities are regulated under FDCA Section 503B. Certain compounding pharmacies and outsourcing facilities have experienced both facility and product quality issues and been the subject of negative media coverage in recent years. Such product quality and facility issues have resulted in increased scrutiny of compounding activities from the FDA and state governmental agencies. For example, the FDA has in the past requested that a number of compounding pharmacies and outsourcing facilities recall unexpired drug products and cease sterile compounding operations due to, among other reasons, lack of assurance of sterility. Pharmacies and outsourcing facilities have also, at the request of FDA, suspended sterile production or voluntarily recalled certain sterile compounded products after an FDA inspection of those facilities. As a result, some prescribers and hospital/clinic purchasing agents may be hesitant to prescribe or procure compounded formulations, and some patients may be hesitant to purchase the same.

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, from the FDCA requirement that products be labeled with adequate directions for use, and serialization and product tracing requirements. For example, the facility must register with FDA and produce at least one sterile drug product, and the drugs must be compounded by or under the direct supervision of a licensed pharmacist. The facility must also operate in compliance with FDA's cGMP regulations and FDA's guidance for outsourcing facilities addressing cGMP. If our outsourcing facility or any of our compounded products are found not to satisfy the criteria set forth in Section 503B, the marketing of our products absent Section 503B's exemptions from FDA's new drug approval requirements, adequate directions for use on the product labeling, or without compliance with certain serialization and product tracing requirements could render our products adulterated or misbranded under the FDCA, which could have an adverse effect on our business.

The source of any bulk substance active ingredient used in compounding must be a Section 510 registered manufacturer, and the bulk substance must be accompanied by a Certificate of Analysis. If the outsourcing facility compounds using bulk drug substances, the bulk drug substances must either appear on FDA's "interim" list of bulk substances that may be used in compounding under Section 503B which are those bulk drug substances for which FDA has determined there is a clinical need. Drugs may also be compounded if the FDA-approved drug appear on FDA's published drug shortage list. Provided certain conditions are met, FDA will exercise enforcement discretion concerning use of "interim" Category 1 substances pending evaluation of the substances for inclusion on FDA's final list of bulk drug substances for which there is a clinical need.

FDA has also finalized guidance on determining whether a product is an "essential copy" of a commercially available product, which the FDA has announced it intends to revisit in 2021. If our products were ever determined to be an essential copy of a commercially available product, FDA could engage in enforcement action. 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 final 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.

If a compounded drug formulation provided by our FDA-registered outsourcing facility leads to patient injury or death, results in a product recall, or causes FDA to request the company shut down its sterile compounding operations, we may be exposed to significant liability and reputational harm.

The production, labeling and packaging of compounded drugs is inherently risky. The success of our compounded formulations and facility 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 outsourcing facilities, prove to be, or are alleged or 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 distribution or other 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 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 from the field 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 related to compounded formulations generally, 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 January 25, 2021, we owned approximately 200 granted patents and over 80 pending patent applications, including six allowed patent applications worldwide. 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 or commercializing 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.

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 approximately from 2024 to 2040, 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 and/or pay license maintenance and other fees. We also have 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 tirbanibulin ointments and KX2-361 products, including to Almirall, which has rights to the U.S. and European markets. 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*".

We depend on our agreements with 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 encequidar, 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 encequidar.

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 Oral Paclitaxel and Oral Irinotecan 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 (1) our first commercial sale of products using such technology or (2) 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 (1) expiration of the last of Hanmi's patent rights licensed under the agreement or (2) 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*."

Risks Related to Our Reliance on Third Parties

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. In addition, as a result of our acquisition of CIDAL, our preclinical and clinical programs are largely performed within the Company and we are responsible for conducting clinical trials and complying with applicable laws and regulations, which increases our concentration of risk in the event of business continuity disruptions experienced by CIDAL.

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, or CIDAL experiences business continuity issues, 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, 2018, we generated 10% of our total revenue from our two largest API customers, and generated 30% of our total revenue from the three largest wholesalers in the U.S. market. During the year ended December 31, 2019, we generated 8% of our total revenue from those API customers and generated 45% of our total revenue from the three largest wholesalers in the U.S. market. During the year ended December 31, 2020, we generated less than 1% of our total revenue from those API customers due to the restrictions on our production of commercial batches of API at our existing facility in Chongqing and generated 38% of our total revenue from the three largest wholesalers in the U.S. market.

Additionally, Polymed, our wholly owned subsidiary, prior to the suspension, sold API to third parties for use in those third parties' products, which may be manufactured in cGMP facilities. The decrease in orders by Polymed's customers has impacted Polymed's revenue and, as a result, our overall financial condition. However, we resumed producing API primarily for internal use since March 2020 in accordance with local regulatory guidance. Polymed recently commenced operations at our new API manufacturing facility in Chongqing, China and also develops new compounds and processing techniques.

Once API production for external use resumes, 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. Even if we are able to maintain our relationships with customers, a change in the mix of products those customers purchase and which we are able to produce may affect our gross margin and results of operations.

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.

We partially rely on outside vendors to manufacture supplies and process our drug candidates. With the FDA's approval of Klisyri, we are preparing to manufacture and process drugs on a commercial scale and may not be able to do so for all 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 are further developing our manufacturing facilities, including 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 experience supply chain difficulties or other business continuity issues related to events beyond their control such as fires, floods, earthquakes, hurricanes, epidemics, quarantines, wars, civil unrest, strikes or governmental action; 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, Xiangxue, XLifeSc and Gland and may form or seek strategic alliances, create joint ventures or collaborations, or enter into additional licensing arrangements with third parties, subject to any restrictions imposed by our financing arrangements, 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 stockholders, 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 earlier stage 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, including disputes over amounts payable under the agreements, 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 Eversana Life Science Services (“Eversana”), a managed services provider with a focus on life sciences companies. If we were to lose the availability of Eversana’s services due to a dispute, termination of or inability to renew the contract, or business continuity issues due to events beyond their control such as fires, floods, earthquakes, hurricanes, epidemics, quarantines, wars, civil unrest, strikes or governmental action, 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.

The loss of any member of the Company's senior management, either permanently or for an indeterminate period of time, and/or failure to successfully implement our succession plan to enable the effective transfer of knowledge or to facilitate smooth transitions in leadership could significantly disrupt the management of the Company's business and impair the Company's ability to execute its business strategies. 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, a stockholder of ours. Dr. Lau also serves as the Chief Executive Officer of Axis, a joint venture that we majority own.

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 around $208.0 million, which includes approximately $8.0 million in additional funds not used under the prior $25.0 million grant to construct our North American headquarters and formulation lab in Buffalo, New York, and shall retain ownership of the Dunkirk facility and the equipment. To the extent the costs of constructing the Dunkirk facility exceed approximately $208.0 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 CQ 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. Failure to satisfy our operating commitments could result in our compensating ESD for those minimum commitments.

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, 2020, we had 647 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, particularly with respect to the build out of our marketing and sales team as we begin to commercialize approved products, including key leadership roles;
- managing our internal development and commercialization efforts effectively, including the clinical and FDA or other comparable authority review process for our drug candidates and developing and implementing marketing and sales plans, 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.

We are 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 executive officers, 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 U.S., including regulations 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. In addition to Klisyri, which was approved by the FDA in December 2020, if and as we obtain FDA approval of additional drug candidates and begin commercializing those drugs in the U.S., our potential exposure under U.S. laws will continue to 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 affiliates 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 stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

Subject to any limitations imposed by our financing arrangements, 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;
- integrating global operations and conducting our business in multiple geographic areas, each with its own legal system and regulations;
- 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. As the majority of our workforce works remotely due to the ongoing COVID-19 pandemic, we face heightened risks related to remote work, including strain on our information technology systems, coordination issues and the threat of cyber-security incidents related to unauthorized system access, aggressive social engineering tactics, and attacks on our information technology systems used to conduct our business. 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's 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 or pandemics, 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 as we commercialize our clinical candidates, once approved. For example, we may be sued if our drugs that we 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 us 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 as well as business interruption insurance covering loss of income & extra expenses associated with physical damage to our property. We maintain workers' compensation/employer's liability insurance covering death or work-related injury of employees. We purchase general liability insurance covering certain incidents involving third parties that occur on or in the premises of the company, and products liability insurance covering certain incidents involving third parties resulting from our products. We purchase directors' and officers' liability insurance and employment practices liability 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 creates 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 negative publicity 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 net operating losses ("NOLs") for U.S. federal income tax purposes. Unused NOLs will carry forward to offset future taxable income, if any, until such unused NOLs expire (if ever). NOLs generated after December 31, 2017 are not subject to expiration, but the yearly utilization of such NOLs is limited to 80 percent of taxable income. 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 the equity ownership of one or more stockholders or groups of stockholders who own at least 5% of a corporation's stock over any three-year period), the corporation's ability to use its pre-change NOLs and other pre-change tax attributes to offset its post-change income may be limited. We believe that we have experienced at least one ownership change in the past and may experience one in the future, which may affect our ability to utilize our NOLs. As of December 31, 2020, we had federal NOLs of approximately $184.8 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.

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 for any of our approved drugs.

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:

- the continued suspension of our commercial production of API at our existing Chongqing facility or the termination of operations at the facility by the DEMC;
- plant shutdowns as a result of the ongoing COVID-19 pandemic;
- regulatory holds on operations at the facilities or the loss of permits to operate facilities;
- 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.

If we are unable to perform the clinical testing required to obtain regulatory approval, we will be unable to commercialize our product candidates.

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 Klisyri and any additional 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 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 Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% 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. The Medicare reductions have been extended through 2030 unless additional Congressional action is taken. The Coronavirus Aid, Relief, and Economic Security Act, which was signed into law in March 2020 and is designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare reductions from May 1, 2020 through December 31, 2020, and extended the reductions by one year, through 2030. The Consolidated Appropriations Act, 2021 extended the suspension of the 2% Medicare reductions through March 31, 2021. 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. Most recently, the Tax Reform 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 this legislation will have on the ACA because a decision regarding the constitutionality of the ACA after the repeal of the individual mandate was ultimately appealed to the U.S. Supreme Court. On November 10, 2020, oral arguments were heard in this case. It is unclear when a decision will be made. Additional reforms by the incoming administration 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 the Centers for Medicare & 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, 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 physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, and certified nurse-midwives effective January 1, 2022), 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 civil whistleblower or *qui tam* 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 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 and countries in Latin America, 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.

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 and countries in Latin America, 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

Tensions between the U.S. and China over Hong Kong and any continued heightening of retaliatory policies 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.

We have operations in Hong Kong and expect that a portion of our future revenue will be sourced from licensing partnerships and API sales in China. Accordingly, our operations, financial condition and results of operations are affected by economic, political and legal developments between the U.S. and China. The continued tensions between the U.S. and China over China's June 30, 2020 enactment of a new national security law in Hong Kong has resulted in heightened diplomatic tensions and a number of escalating retaliatory measures by the U.S. and China, including in an executive order signed by former President Trump on July 14, 2020, which ended the special economic status that was afforded to Hong Kong under the United States-Hong Kong Policy Act of 1992, a U.S. ban on investments in businesses linked to China's military, the U.S. announcement of the removal of restrictions on U.S. government official interactions with Taiwan and new rules issued by the Chinese Communist Party that would allow Chinese courts to impose penalties on persons for complying with foreign sanctions that impose prohibitions or restrictions on Chinese economic or trade relationships.

These political tensions between the U.S. and China, together with the uncertainties around the Biden administration's stance with respect to China, create uncertainties for doing business in China, including compliance risks that may arise from retaliatory regulations, restrictions on technology transfers between the countries or measures enacted that further impede our ability to repatriate capital from our subsidiaries in China. The uncertainties caused by continued tensions, together with the risk of escalating retaliatory policies could increase our cost of doing business, adversely affect our business, financial condition and results of operations and may result in our inability to sustain our operations, and growth and expansion strategies with respect to 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, 2017 to December 31, 2018, the RMB depreciated approximately 5.6% against the U.S. dollar. From December 31, 2018 to December 31, 2019, the RMB depreciated approximately 1% against the U.S. dollar. From December 31, 2019 to December 31, 2020, the RMB appreciated approximately 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, and 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, 2019 and 2020, 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, interpretation and implementation of Chinese Foreign Investment Law and Negative List and how they may impact the viability of our current corporate governance.

On March 15, 2019, the National People’s Congress of the PRC promulgated the Foreign Investment Law of the People’s Republic of China (the “FIL”) which became effective on January 1, 2020. Simultaneously, the three foreign investment laws (i.e. the Wholly Foreign-Owned Enterprise Law, the Sino-Foreign Equity Joint Venture Enterprise Law, and the Sino-Foreign Cooperative Joint Venture Enterprise Law) were repealed on January 1, 2020. Pursuant to the FIL, foreign investors shall not invest in any field forbidden by the negative list for access of foreign investment. For any field on the negative list, foreign investors shall conform to the investment conditions provided in the negative list. Fields not included in the negative list shall be managed under the principle that domestic investment and foreign investment shall be treated uniformly. According to the FIL, the organization form and institutional framework shall be subject to the provisions of the Company Law of the People's Republic of China, the Partnership Enterprise Law of the PRC, and other PRC laws. Foreign invested enterprises, which were established in accordance with the aforesaid three foreign investment laws may retain their original organization forms and other aspects for five years after the implementation of the FIL. Specific implementation measures shall be formulated by the State Council.

In June 2017 the National Development and Reform Commission and the Ministry of Commerce jointly issued Catalogue of Industries for Guiding Foreign Investment (2017 Revision), which introduced Special Administrative Measures on Access of Foreign Investment (Negative List). Any industry not listed in the catalogue and Negative List is a permitted industry, and is generally open to foreign investment unless specifically prohibited or restricted by the Chinese laws and regulations. The Negative List is further divided into restricted foreign-invested industries and prohibited foreign-invested industries. The Negative List was further revised in 2018, 2019, and 2020. The most updated Negative List was issued on June 23, 2020 and took effect on July 23, 2020.

The FIL and Negative List may also materially impact our corporate governance practice and increase our compliance costs. For instance, the FIL 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. According to Notice on Further Simplifying and Improving Policies for the Foreign Exchange Administration of Direct Investment, the "Circular 13", which became effective on June 1, 2015, banks shall directly examine and handle foreign exchange registration under domestic direct investment and foreign exchange registration under overseas direct investment, and the SAFE and its branch offices shall indirectly regulate the foreign exchange registration of direct investment through banks. SAFE Circular 37, Circular 13 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 stockholder 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 stockholders are Chinese residents under SAFE Circular 37. These certain stockholders have undertaken to (1) apply to register with local SAFE branch or its delegated commercial bank as soon as possible after exercising their options and (2) 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 stockholders 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, as amended on February 24, 2017 and December 29, 2018, 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. Although the reviewing procedure in Circular 82 was simplified on December 29, 2017, pursuant to Decision of the SAT on Issuing the Catalogues of Tax Departmental Rules and Tax Regulatory Documents Which Are Invalidated, the "de facto management body" test is still valid. 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 stockholders 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 stockholders, 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.

The passage of the Holding Foreign Companies Accountable Act and recent delistings of Chinese telecommunications companies, and the general 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 the passage of the Holding Foreign Companies Accountable Act (the "HFCAA") on December 18, 2020, the delistings of China Mobile Ltd., China Telecom Corp., and China Unicom Hong Kong Ltd. by executive order from the Trump administration on December 31, 2020, and the general 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 and the HFCAA may result in additional delistings of companies with significant China operations from U.S. securities exchanges. 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;
- changes to our acting management team, including as a result of additions, departures and health-related leaves of absence;
- 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 stockholders 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, stockholders 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.

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. In addition, our Senior Credit Agreement with Oaktree and Sagard restricts our and our restricted subsidiaries' ability to pay dividends. 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, subject to the restrictions contained in our financing agreements. 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, restrictions on the form and amount of such dividends in our debt agreements, 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.

There are limitations on the liability of our officers and directors, and we may have to indemnify our officers and directors in certain instances.

Our amended and restated certificate of incorporation limits, to the maximum extent permitted under Delaware law, the personal liability of our directors for monetary damages for breach of their fiduciary duties as directors. The indemnification provisions may require us, among other things, to indemnify such officers and directors against certain liabilities that may arise by reason of their status or service as directors or officers (other than liabilities arising from willful misconduct of a culpable nature), to advance their expenses incurred as a result of certain proceedings against them as to which they could be indemnified. Section 145 of the Delaware General Corporation Law provides that a corporation may indemnify a director, officer, employee or agent made or threatened to be made a party to an action by reason of the fact that he or she was a director, officer, employee or agent of the corporation or was serving at the request of the corporation, against expenses actually and reasonably incurred in connection with such action if he or she acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. Delaware law does not permit a corporation to eliminate a director's duty of care and the provisions of our certificate of incorporation have no effect on the availability of equitable remedies, such as injunction or rescission, for a director's breach of the duty of care.

We believe that our limitation of officer and director liability assists us to attract and retain qualified employees and directors. However, in the event an officer, a director or the board of directors commits an act that may legally be indemnified under Delaware law, we will be responsible to pay for such officer(s) or director(s) legal defense and potentially any damages resulting there from. Furthermore, the limitation on director liability may reduce the likelihood of derivative litigation against directors and may discourage or deter stockholders from instituting litigation against directors for breach of their fiduciary duties, even though such an action, if successful, might benefit our stockholders and us. Limitations of director liability may be viewed as limiting the rights of stockholders, and the broad scope of the indemnification provisions contained in our certificate of incorporation could result in increased expenses.

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 42.4% of our outstanding common stock based on the number shares outstanding as of December 31, 2020. 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, beneficially own in the aggregate approximately 14.6% of our outstanding common stock based on the number shares outstanding as of December 31, 2020. 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 stockholders' 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 stockholders 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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our Oncology Innovation Platform operates in several facilities globally: 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 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 5,500 square feet of office and lab space which represents a portion of the IC Development Centre in Hong Kong under a lease that expires in November 2022 that serves as our Hong Kong headquarters and research and development center. 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. In addition, we occupy approximately 9,900 square feet of office space in multiple locations across Latin America under lease agreements which expire at various dates through October 2022, which serve as clinical research facilities.

Our Commercial Platform is headquartered and operates in 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.

Our Global Supply Chain Platform utilizes several facilities globally: 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 409,000 sq. ft. and is targeted for completion in 2021. See "*Business — Global Supply Chain Platform—Strategic Public-Private Partnerships—New York State Partnership*" for more information. Lastly, Chongqing Sintaho Pharmaceuticals Co., Ltd. ("CQ Sintaho"), a wholly owned subsidiary of the Company, entered into a lease agreement with Chongqing International Biological City Development & Investment Co., Ltd ("CQ D&I"), an affiliate of CQ. Pursuant to the lease agreement with CQ D&I, CQ Sintaho will lease the newly constructed API of 34,517 square meters rent-free, for the first 10-year term, with an option to extend the lease for an additional 10-year term, during which, if CQ Sintaho is profitable, it will pay a monthly rent of 5 Chinese Renminbi per square meter of space occupied. This lease agreement was executed in January 2021. See "*Business – Global Supply Chain Platform—Strategic Public-Private Partnerships—China 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.

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.

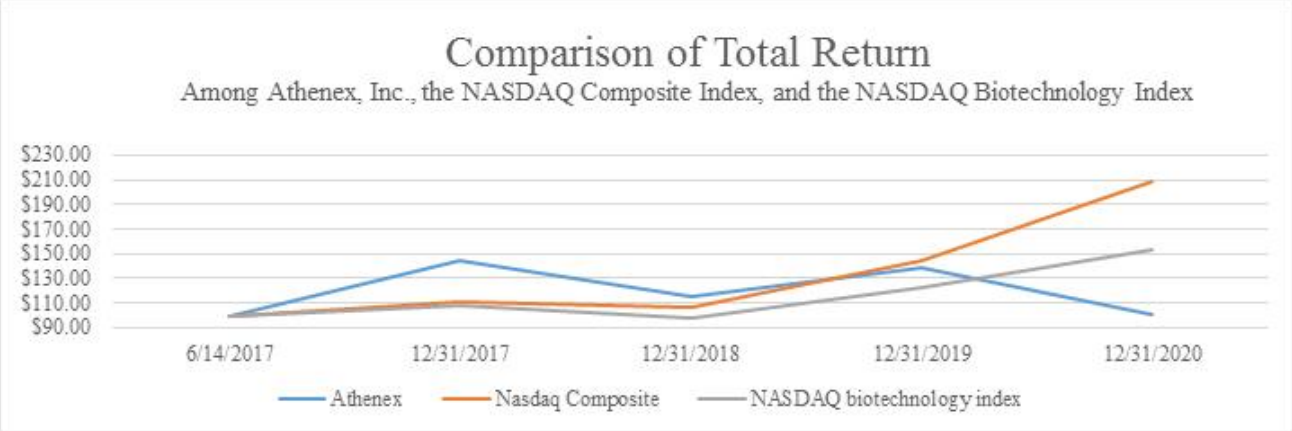
Market for our Common Stock

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 February 19, 2021, there were 97 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, 2020. Such returns are based on historical results and are not intended to suggest future performance.



Cumulative Total Return Comparison

	June 14, 2017	December 31, 2018	December 31, 2019	December 31, 2020
Athenex, Inc.	$ 100.00	$ 115.36	$ 138.82	$ 100.55
NASDAQ Composite	$ 100.00	$ 107.11	$ 144.84	$ 208.05
NASDAQ Biotechnology Index	$ 100.00	$ 98.23	$ 122.20	$ 153.59

This performance graph is not deemed to be "soliciting material" or to be "filed" with the Securities and Exchange Commission ("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, 2020, 2019, and 2018 and the balance sheet data as of December 31, 2020 and 2019 are derived from our audited consolidated financial statements included elsewhere in this Annual 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 U.S., or U.S. GAAP.

	Year Ended December 31,				
	2020	2019	2018	2017	2016
	(In thousands, except share and per share data)				
Statements of Operations and Comprehensive Loss Data:					
Revenue:					
Product sales, net	$ 105,274	$ 80,535	$ 56,394	$ 36,106	$ 19,394
License and other revenue	39,117	20,694	32,706	1,937	1,157
Total revenue	144,391	101,229	89,100	38,043	20,551
Cost of sales	95,355	69,619	47,005	25,122	19,718
Gross profit	49,036	31,610	42,095	12,921	833
Operating expenses:					
Research and development expenses	75,904	84,393	119,905	76,797	60,624
Selling, general, and administrative expenses	96,855	66,749	49,008	46,112	25,956
Total operating expenses	172,759	151,142	168,913	122,909	86,580
Operating loss	(123,723)	(119,532)	(126,818)	(109,988)	(85,747)
Interest expense (net of interest income)	10,345	5,073	1,793	5,912	1,891
Loss on derivative liability	—	—	—	15,411	533
Loss on extinguishment of debt	10,278	—	—	—	—
Income tax expense (benefit)	4,088	928	100	85	(265)
Net loss	(148,434)	(125,533)	(128,711)	(131,396)	(87,906)
Less: net loss attributable to non-controlling interests	(2,255)	(1,784)	(11,271)	(226)	(191)
Net loss attributable to Athenex, Inc.	$ (146,179)	$ (123,749)	$ (117,440)	$ (131,170)	$ (87,715)
Net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted (1)	$ (1.72)	$ (1.67)	$ (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)	85,082,868	74,054,261	64,590,270	49,960,925	40,120,908
Comprehensive loss	$ (146,678)	$ (123,728)	$ (117,950)	$ (130,012)	$ (88,796)

(1) See Note 15 to our audited consolidated financial statements appearing elsewhere in this Annual 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,				
	2020	2019	2018	2017	2016
	(In thousands)				
Selected Balance sheet data:					
Cash, cash equivalents, and restricted cash	$ 86,087	$ 127,674	$ 49,794	$ 39,284	$ 33,125
Short-term investments	138,636	33,139	57,629	11,753	8,628
Goodwill	38,891	38,513	37,495	37,795	37,552
Working capital(1)	229,820	159,398	119,143	38,615	23,904
Total assets	384,329	309,932	231,095	140,413	105,890
Long-term debt	148,587	53,246	46,764	1,981	41,807
Total liabilities	218,981	134,077	102,326	49,691	71,221
Non-controlling interests	(14,427)	(12,370)	(10,586)	685	862
Total stockholders' equity	$ 165,348	$ 175,855	$ 128,769	$ 90,722	$ 34,669

(1) Working capital = total current assets - total current liabilities.

	Year Ended December 31,				
	2020	2019	2018	2017	2016
	(In thousands)				
Selected Cash flow data:					
Net cash used in operating activities	$ (131,243)	$ (97,460)	$ (109,387)	$ (81,512)	$ (47,870)
Net cash (used in) provided by investing activities	(118,972)	7,499	(48,963)	(10,018)	2,659
Net cash provided by financing activities	209,427	167,452	169,035	96,896	35,272
Net effect of foreign exchange rate changes	(799)	389	(175)	793	(431)
Net (decrease) increase in cash, cash equivalents, and restricted cash	(41,587)	77,880	10,510	6,159	(10,370)
Cash, cash equivalents, and restricted cash at beginning of period	127,674	49,794	39,284	33,125	43,495
Cash, cash equivalents, and restricted cash at end of period	$ 86,087	$ 127,674	$ 49,794	$ 39,284	$ 33,125

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 About Forward-Looking Statements" and Part I, Item 1A, "Risk Factors."

Overview and Recent Developments

Overview

We are a global biopharmaceutical company dedicated to becoming a leader in the discovery, development and commercialization of next generation drugs for the treatment of cancer. Our mission is to improve the lives of cancer patients by creating more effective, safer and tolerable treatments. We have assembled a strong and experienced leadership team and have established global operations across the pharmaceutical value chain to execute our goal of becoming a global leader in bringing innovative cancer treatments to the market and improving health outcomes.

We are organized around three operating segments: (1) our Oncology Innovation Platform, dedicated to the research and development of our proprietary drugs; (2) our Commercial Platform, focused on the sales and marketing of our specialty drugs and the market development of our proprietary drugs; and (3) our Global Supply Chain Platform, dedicated to providing a stable and efficient supply of APIs for our clinical and commercial efforts. Our current clinical pipeline in the Oncology Innovation Platform is derived from four different proprietary technologies: (1) Orascovery, based on a P-glycoprotein or P-gp pump, inhibitor, (2) Src Kinase inhibition, (3) T-cell Receptor-engineered T-cells ("TCR-T"), and (4) arginine deprivation therapy.

Significant Developments in the Oncology Innovation Platform

Orascovery Platform

Our Orascovery technology is based on the novel P-gp pump inhibitor molecule, encequidar. Oral administration of encequidar in combination with established chemotherapy agents such as paclitaxel, irinotecan, docetaxel, topotecan and eribulin has been shown in our clinical studies to date to improve the absorption of these agents by blocking the P-gp pump in the intestinal wall. Oral paclitaxel and encequidar, formerly known as Oraxol ("Oral Paclitaxel") is our lead asset in our Orascovery platform. We are also advancing the following clinical candidates for the treatment of solid tumors on this platform: oral irinotecan and encequidar, formerly known as Oratecan ("Oral Irinotecan"); oral docetaxel and encequidar, formerly known as Oradoxel ("Oral Docetaxel"); oral topotecan and encequidar, formerly known as Oratopo ("Oral Topotecan"); and oral eribulin and encequidar, formerly known as Eribulin ORA ("Oral Eribulin").

Significant developments in our Orascovery platform in 2020 include the following:

On February 26, 2021, we received a CRL from the FDA regarding our NDA for Oral Paclitaxel for the treatment of metastatic breast cancer. The FDA issues a CRL to indicate that the review cycle for an application is complete and that the application is not ready for approval in its present form. In the CRL, the FDA indicated its concern of safety risk to patients in terms of an increase in neutropenia-related sequelae on the Oral Paclitaxel arm compared with the IV paclitaxel arm in the Phase III study. The FDA also expressed concerns regarding the uncertainty over the results of the primary endpoint of ORR at week 19 conducted by BICR. The agency stated that the BICR reconciliation and re-read process may have introduced unmeasured bias and influence on the BICR. Additionally, the FDA recommended that we conduct a new adequate and well-conducted clinical trial in a patient population with MBC representative of the population in the U.S. The agency determined that additional risk mitigation strategies to improve toxicity, which may involve dose optimization and / or exclusion of patients deemed to be at higher risk of toxicity, are required to support potential approval of the NDA. We are working to consider the appropriate next steps in the development of Oral Paclitaxel. We plan to request a meeting with the FDA to discuss the FDA's response, engage in a dialogue on the design and scope of a clinical trial to address the agency's requirements and align on the next steps required to obtain approval.

On September 1, 2020, we announced that the FDA accepted for filing our NDA for Oral Paclitaxel for the treatment of metastatic breast cancer ("MBC") and granted the application Priority Review. Under the Prescription Drug User Fee Act ("PDUFA"), the FDA set a target action date of February 28, 2021.

On December 9, 2020, we presented updated Phase 3 data on survival and tolerability associated with Oral Paclitaxel in metastatic breast cancer patients at the 2020 San Antonio Breast Cancer Symposium (SABCS). Progression free survival (PFS) and overall survival (OS) data presented indicates benefits of Oral Paclitaxel versus IV paclitaxel and supports the superiority of increased overall response rate observed with Oral Paclitaxel. In the intent-to-treat (ITT) population, Oral Paclitaxel showed a benefit on PFS versus IV paclitaxel and showed a trend favoring Oral Paclitaxel on OS versus IV paclitaxel. Oral Paclitaxel demonstrated a median PFS of 8.4 months vs. 7.4 months, hazard ratio (HR) 0.768 (95% CI: 0.584, 1.01), p=0.046. Oral Paclitaxel demonstrated a median OS of 22.7 months vs. 16.5 months, HR 0.794 (95% CI: 0.607, 1.037), p=0.082.

On September 8, 2020, we and Quantum Leap Healthcare Collaborative ("Quantum Leap") jointly announced the launch of two new study arms of the I-SPY 2 TRIAL to evaluate Oral Paclitaxel in combination with GlaxoSmithKline's ("GSK") dostarlimab, an investigational antibody binding PD-1, in the neoadjuvant chemotherapy setting, targeting stage 2/3 HER2+ and HER2- breast cancers. The I-SPY 2 TRIAL, sponsored by Quantum Leap, is a standing Phase 2 randomized, controlled, multicenter platform with a Bayesian adaptive randomization design aimed to rapidly screen and identify promising new treatments in specific subgroups of adults with newly-diagnosed, high-risk (high likelihood of recurrence), locally-advanced breast cancer that is either Stage II or Stage III. GSK will provide dostarlimab. We will provide Oral Paclitaxel. Quantum Leap will be responsible for running the trial.

On May 29, 2020, we presented interim data from an ongoing Phase II clinical trial in which Oral Paclitaxel monotherapy showed encouraging efficacy and tolerability in elderly patients with unresectable cutaneous angiosarcoma, an aggressive malignancy with poor prognosis. The interim results were presented at the American Society of Clinical Oncology (ASCO) 2020 Virtual Scientific Program and reflected data from 22 evaluable patients out of 26 enrolled patients. The interim data showed a clinical benefit rate (CR+PR+SD) of 100% in 22 evaluable patients who reached their first post treatment efficacy evaluation. All 22 patients experienced a reduction in tumor size. Complete responses (CR) were observed in 27.3% of patients (6/22), partial responses (PR) were observed in 22.7% of patients (5/22), and stable disease was observed in 50% of patients (11/22). Oral Paclitaxel has been generally well tolerated in this predominantly elderly population.

We are also evaluating Oral Paclitaxel in combination with other therapies, including anti-VEGF and anti-PD-1 therapies. We are studying Oral Paclitaxel with ramucirumab in a Phase 1b study in patients with advanced gastric cancer who failed previous chemotherapy and the expansion phase of the study has completed enrollment. Our Phase 1/2 study of Oral Paclitaxel in combination with pembrolizumab in patients with advanced solid malignancies is ongoing.

In addition to our lead product candidate, development of our other Orascovery product candidates is ongoing. We are planning Phase 2 studies for both Oral Irinotecan and Oral Docetaxel. A Phase 1 study of Oral Eribulin in patients with solid tumors is ongoing.

Our goal with Oral Paclitaxel, in the event we decide to continue development after our meeting with the FDA, is to establish Oral Paclitaxel as the chemotherapy of choice for patients receiving chemotherapy for MBC, although we can provide no assurance that we will be successful in obtaining the FDA's approval to commercialize Oral Paclitaxel. We intend to explore establishing Oral Paclitaxel in other oncology indications where we believe taxanes will continue to be a foundational treatment and continue to explore combination therapies. Our strategy is to develop and, if we receive approval from the FDA, commercialize Oral Paclitaxel in the U.S. by leveraging our Commercial Platform and sales and marketing capabilities established in the U.S. We also plan to evaluate marketing options outside of the U.S., including using our internal resources, partnering with others, or out-licensing the product.

Src Kinase Inhibition Platform

Our Src Kinase inhibition platform technology is based on novel small molecule compounds that have multiple mechanisms of action, including the inhibition of the activity of Src Kinase and the inhibition of tubulin polymerization, which may limit the growth or proliferation of cancerous cells. We believe the combination of these mechanisms of action provides a broader range of anti-cancer activity compared to either mechanism of action alone. Our lead product candidate on our Src Kinase inhibition platform is tirbanibulin ointment, which we are advancing for the treatment of AK as well as psoriasis and skin cancer. Our other clinical candidates and their indications in this platform include tirbanibulin oral for solid and liquid tumors and KX2-361 for brain cancers, such as GBM.

Significant developments in our Src Kinase inhibition platform in 2020 include the following:

On December 15, 2020, we announced that the FDA has approved Klisyri® (tirbanibulin) for the topical treatment of actinic keratosis (AK) on the face or scalp. Klisyri is the first FDA approved branded proprietary product for Athenex and was launched in the U.S., led by our partner Almirall S.A. ("Almirall") on February 18, 2021. Klisyri will be manufactured by Athenex, highlighting the vertically integrated capabilities of the company ranging from a preclinical lead to a developed product for market launch. The FDA approved Klisyri based on the data from two pivotal, randomized, double-blind, vehicle-controlled Phase 3 studies (KX01-AK-003 and KX01-AK-004) that evaluated the efficacy and safety of Klisyri (tirbanibulin) ointment 1% in 702 adults with AK of the face or scalp. Tirbanibulin demonstrated complete clearance of AK lesions at day 57 in treated face or scalp areas in a significantly higher number of patients compared to vehicle. The most common adverse events were application site pruritus and pain reported by 9% and 10% of treated patients, respectively.

The New England Journal of Medicine published the pivotal Phase 3 trial results on Klisyri® for the topical treatment of AK of the face or scalp in the February 11, 2021 issue.

In March 2020, our partner Almirall announced that the European Medicines Agency (EMA) accepted the filing of a European marketing authorization for tirbanibulin ointment for the treatment of AK.

The development of our other Src Kinase programs/product candidates is ongoing.

Other Platforms

The other technologies in our Oncology Innovation Platform are our TCR-T immunotherapy technology under which we are advancing TCR affinity-enhancing specific T-cell (TAEST) therapy with our first T cell therapy product, TCRT-ESO-A2, and our arginine deprivation therapy technology under which we are advancing PT01, also known as Pegtomarginase.

In September 2020, we announced that the FDA allowed our Investigational New Drug (IND) application for TCRT-ESO-A2, an autologous TCR-T cell therapy targeting solid tumors that are NY-ESO-1 positive in HLA-A*02:01 positive patients. TCRT-ESO-A2 is being developed by Axis Therapeutics Limited, a joint venture between Athenex and Xiangxue Life Sciences Limited ("XLifeSc"). TCRT-ESO-A2 is similar to TAEST16001, an autologous cell-based therapy being developed simultaneously by XLifeSc for clinical application in China in that both therapies express the same affinity-enhanced TCR.

PT01 targets cancer growth and survival by removing the supply of arginine to cancers that have a disrupted urea cycle. The FDA allowed our IND application for the clinical investigation of PT01 for the treatment of patients with advanced malignancies in 2019. We plan to initiate first human exposure in 2021.

Recent business updates and *COVID-19 related measures*

Since early 2020, after monitoring developments related to the spread of COVID-19, we have undertaken a number of measures in response to the COVID-19 pandemic, with a goal to prioritize the health and safety of our employees and ensure continuity in our business. These measures included implementing a work-from-home policy at various times and other efforts in accordance with recommendations by local authorities for certain of our personnel across the globe as well as imposing restrictions on travel and in-person meetings to protect the health and safety of our workforce while we continue to advance our clinical programs and operations. We have continued to add additional safety procedures and tools in all our locations. We adhere to all state and federal requirements as the same may be in force from time to time. While our operations in China were disrupted from late January to early March due to the COVID-19 pandemic, during March our Chinese operations returned to normal operation. We have been deemed an "essential business" by New York State and as a result, we have experienced minimal disruptions at our New York-based operations in Clarence and Buffalo. Despite these efforts, we may from time to time experience additional disruptions related to COVID-19. For instance, in January 2021, we experienced disruptions related to our Chairman and Chief Executive Officer falling ill with COVID-19. We have supplied our employees with face coverings and other necessary personal protective equipment and have taken other measures to reduce the risk of the spread of COVID-19 at our work sites. Despite the delay in construction in both Dunkirk facility and API plant due to the pandemic, as of December 31, 2020, both facilities were in the final stage of completion. We accepted the API building and entered into a lease agreement with the local government in January 2021. Dunkirk facility is expected to commence operations in the second half of 2021. We are actively monitoring our operations and supply chain across the globe and are making adjustments to respond to logistical challenges that arise due to COVID-19 where appropriate. Further, we have opened up our production facilities to produce medicines that are used to treat COVID-19 as part of our commitment to contribute to the COVID-19 relief effort.

With respect to our clinical development program, our anticipated timelines for our later-stage product candidates remain largely unaffected by COVID-19. However, for our earlier stage product candidates, in line with the industry overall, we have experienced and expect to continue to experience, slowed enrollment for our clinical trials as well as suspensions in our clinical trials as healthcare resources are diverted to address the COVID-19 pandemic. We remain committed to advancing our pipeline while ensuring the safety of all participants as well as the integrity of the data and will monitor developments with respect to COVID-19 as well as industry and regulatory best practices for continuing clinical development programs during the pandemic, including, if and where appropriate, the use of virtual communications, interviews and visits as well as self-administration and remote monitoring techniques to address health and safety concerns while minimizing disruptions and delays to our clinical development timelines.

We also put in place a number of measures intended to adjust/allocate resources towards prioritizing key business operations such as clinical and regulatory activities for later-stage product candidates and pre-launch commercial activities, and to delay or defray compensation costs in order to preserve our cash on hand and liquidity during a volatile period in the U.S. and global capital markets.

On March 31, 2020, we entered into a letter agreement with Xiangxue Pharmaceutical Co., Ltd. ("Xiangxue") to amend certain provisions of the license agreement entered into with Xiangxue in December 2019 (the "2019 Xiangxue License"). On June 30, 2020, we entered into a second supplemental agreement to amend certain provisions of the 2019 Xiangxue License to facilitate our receipt of payment from Xiangxue, providing, among other things, that notwithstanding the provisions of the 2019 Xiangxue License to the contrary, Xiangxue shall be entitled to make the USD $30 million upfront payment in Chinese Renminbi to Chongqing Taihao Pharmaceutical Co. Ltd. ("Taihao"), our wholly owned subsidiary in China, and we would bear the responsibility for indirect taxes in connection with license payments made under the 2019 Xiangxue License rather than Xiangxue. In the third quarter of 2020, pursuant to the 2019 Xiangxue License, we recognized $9.4 million license revenue, net of $0.6 million value added tax, for a milestone achievement. As of February 28, 2021, we have only received $1.5 million of the $10.0 million milestone achievement. After consideration of historical collection rates, the current financial status of the counterparty, and other macroeconomic factors, we have recorded a provision for its expected credit losses for the outstanding balance of $8.5 million and $0.4 million related to currency conversion in our consolidated financial statements for the three months and year ended December 31, 2020, respectively.

In order to strengthen our short-term liquidity and to ensure financial flexibility, on June 19, 2020, we entered into a senior secured loan agreement and related security agreements (the "Senior Credit Agreement") with Oaktree Fund Administration, LLC, as administrative agent, and the lenders party thereto (collectively, "Oaktree") to borrow up to $225.0 million in five tranches with a maturity date of June 19, 2026, bearing interest at a fixed annual rate of 11.0%. The first three tranches with a combined value of $150.0 million was funded, with a portion of the upfront loan proceeds being used to repay in full our credit facility with Perceptive Advisors LLC and its affiliates ("Perceptive"). The early repayment of the Perceptive facility resulted in a one-time loss on extinguishment of debt of $7.2 million. Additional debt tranches of $75.0 million in aggregate are available, subject to our achievement of certain regulatory and commercial milestones (see *Liquidity and Capital Resources—Debt and Equity Financings—Oaktree Senior Credit Agreement*). In connection with our entry into the Senior Credit Agreement, we granted warrants to Oaktree to purchase up to an aggregate of 908,393 shares of our common stock at a purchase price of $12.63 per share and entered into a registration rights agreement with Oaktree on June 19, 2020, pursuant to which, among other things, we agreed to register for resale the shares of common stock issuable upon exercise of the warrants. On August 6, 2020, we filed with the SEC a Registration Statement on Form S-3 (File No. 333-241665) registering for resale the shares of common stock issuable upon exercise of the warrants.

On August 4, 2020, we entered into a Revenue Interest Financing Agreement with Sagard Healthcare Royalty Partners, LP ("Sagard"), pursuant to which Sagard has agreed to pay us $50.0 million (the "Product Payment") to provide funding for our development and commercialization of Oral Paclitaxel upon receipt of marketing authorization for Oral Paclitaxel by the U.S. FDA for the treatment of MBC. In exchange for the Product Payment, we have agreed to make payments to Sagard equal to 5.0% of our world-wide net sales of Oral Paclitaxel, subject to a hard cap equal to the lesser of 170% of the Product Payment and the Put/Call Price set forth in the Revenue Interest Financing Agreement (the "Hard Cap"). We are required to make certain additional payments to Sagard to the extent Sagard has not received Payments equaling at least $20.0 million by September 30, 2024 and at least $50.0 million by August 4, 2026, in the amount of the applicable shortfall, and, subject to the Hard Cap, if Sagard has not received payments equaling at least $85.0 million by the tenth anniversary of the date the Product Payment is funded, in an amount such that Sagard will have obtained a 6.0% internal rate of return on the Product Payment (see *Note 11 - Debt and Lease Obligations*).

Sagard and its co-investors OPB SHRP Co-Invest Credit Limited and SIMCOE SHRP Co-Invest Credit Ltd. (the "IMCO Investors") also acquired by assignment (the "Assignment") term loans and commitments equal to $50.0 million under the Senior Credit Agreement. In connection with the Assignment, we granted warrants to Sagard and the IMCO Investors to purchase up to an aggregate of 201,865 shares of our common stock at a purchase price of $12.63 per share. As a result of the issuance of the additional warrants, we evaluated the debt modification in accordance with Accounting Standards Codification ("ASC") 470 and concluded that the assigned debt qualified for a partial debt extinguishment of the existing Senior Credit Agreement with Oaktree. Therefore, we recorded a loss on partial extinguishment of debt in the amount of $3.0 million for the three months ended September 30, 2020.

In September 2020, we completed an underwritten follow-on public offering in which we sold 11,500,000 shares of our common stock, including 1,500,000 shares of common stock pursuant to the underwriters' option to purchase additional shares, at a public offering price of $11.00 per share and received net proceeds of $118.7 million, after deducting underwriting discounts and commissions and offering expenses of $7.9 million.

Outlook

We have a comprehensive and experienced leadership team who have come together under one organization to achieve our mission of improving the lives of cancer patients by creating more effective, safer and tolerable treatments. We have the goal of becoming a global leader in bringing innovative cancer treatments to the market and improving health outcomes. To achieve our goal, we have established the following strategic priorities, which, after receipt of a CRL for our NDA for Oral Paclitaxel, are currently under review by management:

Obtain regulatory approval for our product candidates and prepare to commercialize Klisyri and our other approved products in the U.S. and abroad - On February 26, 2021, we received a CRL from the FDA regarding our NDA for our lead product candidate, Oral Paclitaxel, for the treatment of metastatic breast cancer. We are working to consider the appropriate next steps in the development of Oral Paclitaxel. We plan to request a meeting with the FDA to discuss the FDA's response, engage in a dialogue on the design and scope of a clinical trial to address the agency's requirements and align on the next steps required to obtain approval. Our goal with Oral Paclitaxel, in the event we decide to continue development after our meeting with the FDA, is to establish it, if approved, as the chemotherapy of choice for patients with MBC and to commercialize Oral Paclitaxel in the U.S. by leveraging our commercialization capabilities in the U.S. We also plan to evaluate marketing options outside of the U.S., including using our internal resources, partnering with others, or out-licensing the product. The FDA has approved Klisyri® (tirbanibulin) for the topical treatment of AK on the face or scalp. Our strategic partner Almirall launched Klisyri in the U.S. on February 18, 2021 and will employ its expertise to support the development of tirbanibulin in Europe. If approved, Almirall will also commercialize the product in European countries, including Russia.

Rapidly and concurrently advance our other clinical programs and product candidates - We intend to pursue the fastest feasible pathways to approval of our existing clinical product pipeline. We plan to continue to advance our studies evaluating Oral Paclitaxel in other indications. As part of our label expansion strategy, we intend to pursue those indications where paclitaxel is already indicated by FDA approval or is on National Comprehensive Cancer Network guidelines, and we also intend to explore combinations with new modalities, such as immunotherapies and targeted therapies. We will continue to advance the development of our other Orascovery product candidates to maximize the value of the Orascovery platform. In addition, we continue to make progress with the development of the clinical program for tirbanibulin. We will also evaluate options to enter into partnerships and collaborations where appropriate.

Enhance and expand our other new technology platforms - We intend to continue expanding and broadening our oncology pipeline. In 2020, the FDA allowed the IND application for TCRT-ESO-A2, which represents Athenex's first T cell therapy product cleared to advance to the first stage of clinical development in the U.S. The FDA also allowed the IND application for the clinical investigation of PT01, an arginine deprivation therapy, for the treatment of patients with advanced malignancies and we plan to initiate first human exposure in 2021. 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.

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., U.K., China, Taiwan and Latin America 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. 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.

Continue to build an integrated business model that leverages our proprietary commercial platform, supply chain and cGMP manufacturing capabilities - 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 tirbanibulin in the U.S. and if approved, European countries, including Russia. In addition, we currently expect to continue to invest in our CMC development for our product candidates and manufacturing infrastructure, which may involve significant capital expenditures, utilizing U.S. current Good Manufacturing Practices ("cGMP") manufacturing facilities from our public/private partnerships in both the China and U.S. markets as a mechanism to build-out our supply chain around the world. We plan to commence 503B compounding at our Dunkirk facility when it is operational later this year, and to utilize the facility for ointment, injectables, and ultimately our proprietary drugs.

Selectively pursue strategic M&A, licensing or partnership opportunities to complement our existing operations - We continue to pursue acquisitions, licensing and partnership opportunities. We will continue to target opportunities that will complement our existing portfolio and operations to create value for stockholders and support our business strategy and mission.

As we pursue these strategic priorities, we expect to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we seek to:

- Continue to advance our lead programs, Orascovery and Src Kinase inhibition technology platforms, through clinical development;
- Continue to invest in further developing our Commercial Platform ahead of our intended proprietary drug launch of Oral Paclitaxel and other drug candidates upon approval;
- Continue our current preclinical and clinical research program and development activities;
- Continue to invest in our manufacturing facilities;
- Advance the preclinical and clinical research program and development activities of our in-licensed technology platforms, TCR-T immunotherapy and arginine deprivation therapy;
- Seek to identify additional research programs and product candidates within existing platform technologies;
- Attain new drugs and technologies through acquisitions or in-licensing opportunities;
- Hire additional research, development and business personnel;
- Maintain, expand and protect our IP portfolio; and
- Incur additional costs associated with operating as a public company.

Results of Operations

Except where otherwise noted, the following discussion compares fiscal years 2019 and 2020 results. For a discussion on the comparison between fiscal year 2018 and fiscal year 2019 results, see the Management's Discussion and Analysis of Financial Condition and Results of Operations included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, as filed with the SEC and incorporated by reference herein.

Since inception, we have devoted a substantial amount of our resources to research and development of our lead product candidates under our Orascovery, Src Kinase inhibition, TCR-T immunotherapy and arginine deprivation therapy technology platforms, to sales and general administrative costs associated with our operations, and to the development of our specialty drug operations in our Commercial Platform and 503B operations. We have incurred significant net losses since inception. Our net losses were $148.4 million, $125.5 million, and $128.7 million for the years ended December 31, 2020, 2019, and 2018, respectively. As of December 31, 2020 and 2019, we had an accumulated deficit of approximately $713.6 million and $567.5 million, respectively.

We have funded our operations to date primarily from the issuance and sale of our common stock through public offerings, private placements, debt and convertible bonds, and to a lesser extent, through revenue generated from our Global Supply Chain Platform. Our operating activities used $131.2 million, $97.5 million and $109.4 million of cash during the years ended December 31, 2020, 2019, and 2018, respectively. As of December 31, 2020, we had cash and cash equivalents of $69.6 million, restricted cash of $16.5 million, and short-term investments of $138.6 million.

Key Components of Results of Operations

Revenue

We derive our consolidated revenue primarily from (i) the sales of generic injectable products by our Commercial Platform; (ii) 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; (iii) the sales of 503B and API products by our Global Supply Chain Platform; 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,					
	2020		2019		2018	
	(in thousands)	%	(in thousands)	%	(in thousands)	%
Product sales, net	$ 105,274	73%	$ 80,535	80%	$ 56,394	63%
License and other revenue	39,117	27%	20,694	20%	32,706	37%
	$ 144,391		$ 101,229		$ 89,100	

Cost of Sales

Along with sourcing from third-party manufacturers, we manufacture clinical products in our U.S. current Good Manufacturing Practices ("cGMP") facility in New York. Cost of sales primarily includes the cost of finished products, raw materials, labor costs, manufacturing overhead expenses and 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, certain direct costs such as shipping costs, net of costs charged to customers, and sublicense fees related to in-license agreements.

Research and Development Expenses

Research and development ("R&D") expenses primarily consist of the costs associated with in-licensing of product candidates, milestone payments, conducting preclinical studies and clinical trials, activities related to regulatory filings and other R&D activities. The following table sets forth the components of our R&D expenses and the amount as a percentage of total R&D expenses for the periods indicated.

	Year Ended December 31,					
	2020		2019		2018	
	(in thousands)	%	(in thousands)	%	(in thousands)	%
Wages, benefits, and related costs	$ 22,809	30%	$ 19,569	23%	$ 17,715	15%
Clinical trial costs	36,245	48%	45,839	54%	49,572	41%
Preclinical research costs	8,411	11%	8,418	10%	3,699	3%
Drug licensing costs	2,437	3%	8,071	10%	38,037	32%
Other research and development costs	6,002	8%	2,496	3%	10,882	9%
Total research and development costs	$ 75,904		$ 84,393		$ 119,905	

Our current R&D activities mainly relate to the clinical development of our Oncology Innovation Platform.

We expense R&D 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 R&D programs because these costs are deployed across multiple product programs under R&D.

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 R&D 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, including delays caused by the ongoing COVID-19 pandemic, could mean a significant change in the costs and timing associated with the development of that drug candidate.

R&D activities are central to our business model. We expect our R&D expenses to continue to increase for the foreseeable future as we continue to support the clinical trials of Oral Paclitaxel, Oral Irinotecan, Oral Docetaxel, Oral Topotecan, Oral Eribulin, tirbanibulin ointment, tirbanibulin oral and KX2-361, as well as initiate and prepare for additional clinical and preclinical studies, including TCR-T immunotherapy and arginine deprivation therapy program activities. We also expect spending to increase in the R&D 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, regulatory and public health, including the ongoing COVID-19 pandemic, factors beyond our control will likely impact our clinical development programs and plans.

Selling, General and Administrative Expenses

Selling, general and administrative, ("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 include professional fees for legal, patent, consulting, auditing and tax services, as well as other direct and allocated expenses for rent and maintenance of facilities, development of the facility in Dunkirk, New York, insurance and other supplies used in the selling, marketing, general and administrative activities. SG&A expenses also include costs associated with our commercialization efforts for our proprietary drugs, such as market research, brand strategy and development work on market access, scientific publication, product distribution, and patient support.

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 and Interest Income

Interest expense consists primarily of interest on our long-term loans 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 Extinguishment of Debt

The loss on extinguishment of debt is the result of refinancing the senior secured loan agreement with Perceptive with the Senior Credit Agreement with Oaktree, as well as the subsequent assignment of a portion of the Senior Credit Agreement to Sagard. The refinancing of the senior secured loan agreement with Perceptive resulted in an exit fee and the recognition of the unamortized debt discount as a loss on extinguishment of debt in the consolidated statements of operations and comprehensive loss. The assignment of a portion of the Senior Credit Agreement to Sagard qualified as a partial debt extinguishment and resulted in a proportional loss from the existing unamortized debt discount, inclusive of unamortized deferred financing fees.

Results of Operations

Year Ended December 31, 2020 Compared to Year Ended December 31, 2019

The following table sets forth a summary of our consolidated results of operations for the years ended December 31, 2020 and 2019, 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,			
	2020	2019	Change	
	(in thousands)	(in thousands)	(in thousands)	%
Revenue				
Product sales, net	$ 105,274	$ 80,535	$ 24,739	31%
License and other revenue	39,117	20,694	18,423	89%
Total revenue	$ 144,391	$ 101,229	43,162	
Cost of sales	(95,355)	(69,619)	(25,736)	37%
Gross profit	49,036	31,610	17,426	
Research and development expenses	(75,904)	(84,393)	8,489	-10%
Selling, general, and administrative expenses	(96,855)	(66,749)	(30,106)	45%
Interest income	874	1,881	(1,007)	-54%
Interest expense	(11,219)	(6,954)	(4,265)	61%
Loss on extinguishment of debt	(10,278)	—	(10,278)	100%
Income tax expense	(4,088)	(928)	(3,160)	341%
Net loss	(148,434)	(125,533)	(22,901)	
Less: net loss attributable to non-controlling interests	(2,255)	(1,784)	(471)	-26%
Net loss attributable to Athenex, Inc.	$ (146,179)	$ (123,749)	$ (22,430)	

Revenue

Product sales for the year ended December 31, 2020 was $105.3 million, an increase of $24.7 million, or 31%, as compared to $80.5 million for the year ended December 31, 2019. This increase was primarily attributable to a significant increase in specialty product sales of $39.1 million as a result of increased demand for COVID-19 related drugs due to the global health pandemic and the launch of additional products. We experienced an increase in purchases from our existing customers as well as obtaining large, non-recurring orders of specialty products from new customers. Fluctuations in the infection rate and the spread of the global health pandemic and market demand can significantly affect our product sales in the future. If and when the COVID-19 pandemic recedes temporarily or is quelled, we expect to see a significant softening in demand for these products. This increase was partially offset by a decrease in API and 503B products sales of $9.1 million, and $5.0 million, respectively, due to the suspension of production of commercial batches at our old API facility in May 2019, and the discontinued sales of compounded vasopressin drug products in ready-to-use form in August 2019. Contract manufacturing revenue also decreased by $0.3 million during the period.

We recognized $39.1 million and $20.0 million in collaboration and license revenue for the years ended December 31, 2020 and 2019, respectively. During the year ended December 31, 2020, we recognized $37.7 million in license revenue, net of $2.3 million VAT pursuant to the 2019 Xiangxue License to develop and commercialize Oral Paclitaxel, Oral Irinotecan, and tirbanibulin ointment in People's Republic of China ("PRC" or "China"), Hong Kong, and Macau, and $1.0 million in license revenue pursuant to the license agreement we entered into with PharmaEssentia Corp. ("PharmaEssentia") to develop and commercialize Oral Paclitaxel, Oral Irinotecan, and Oral Docetaxel in Taiwan, Singapore, and Vietnam. During the year ended December 31, 2019, we recognized $20.0 million in collaboration and license revenue pursuant to the license agreement entered into with Almirall in December 2017 under which Almirall acquired an exclusive license to research, develop and commercialize tirbanibulin in the U.S., Europe, and Russia.

Cost of Sales

Cost of sales totaled $95.4 million for the year ended December 31, 2020, an increase of $25.7 million, or 37%, as compared to $69.6 million for the year ended December 31, 2019. The increase in our cost of specialty product sales was in-line with the increase in revenue and we continued to incur fixed costs despite decreased production at our old API facility in Chongqing. Additionally, we incurred sublicense fees of $5.8 million on our license revenue for the year ended December 31, 2020.

Research and Development Expenses

R&D expenses totaled $75.9 million for the year ended December 31, 2020, a decrease of $8.5 million, or 10%, as compared to $84.4 million for the year ended December 31, 2019. This was primarily due to a decrease in clinical operations, drug licensing fees, and included the following:

- $9.1 million decrease in clinical studies costs related to the supply of clinical studies and patient costs on Oral Paclitaxel, and tirbanibulin ointment, as all Phase 3 studies wound down, and we filed an NDA with the FDA for Oral Paclitaxel in September 2020 and for tirbanibulin ointment in March 2020;
- $5.6 million decrease in drug development for specialty products, and licensing costs primarily related to TCR-T immunotherapy technology and arginine deprivation therapy technology incurred during the prior year; and
- $0.5 million decrease in regulatory costs in connection with our NDA preparation that began during 2019.

The decrease in these R&D expenses was partially offset by an increase of $3.5 million in medical affairs related to preparing our proprietary drugs for commercialization, API research and development, and a $3.2 million increase related to the expansion of our R&D teams in Latin America and Taiwan.

Selling, General and Administrative Expenses

Selling, general, and administrative expenses totaled $96.9 million for the year ended December 31, 2020, an increase of $30.1 million, or 45%, as compared to $66.7 million for the year ended December 31, 2019. This was primarily due to an increase of $16.7 million primarily related to preparations for the commercialization of our proprietary drugs, if approved, a provision for credit losses of $8.9 million related to our license milestone receivable, an increase of $2.6 million in costs related to the expanded work forces at our manufacturing plants, and an increase of $1.9 million of general, administrative expense, including professional service fees, IT, insurance, and other operating expenses.

Interest Income and Interest Expense

Interest income consisted of interest earned on our short-term investments and decreased by $1.0 million, or 54%, from 2019 to 2020 due a significant decrease in market rates for commercial paper, corporate bonds, and U.S. Treasury securities. Interest expense for the year ended December 31, 2020 totaled $11.2 million, an increase of $4.2 million, or 61%, as compared to $7.0 million for the year ended December 31, 2019, primarily due to increased borrowings. Interest expense in 2020 included interest on borrowings under the credit agreement with Perceptive we entered into in June 2018, and the Senior Credit Agreement with Oaktree we entered into in June 2020 to finance, in part, to repay in full the outstanding loan and fees under the credit agreement with Perceptive. The majority of interest expense in the prior period was incurred from the Perceptive debt.

Loss on Debt Extinguishment

We recognized a $7.2 million loss on the extinguishment of debt related to the termination of the senior secured loan agreement with Perceptive and a $3.0 million loss on the partial extinguishment of debt related to the assignment of a portion of the senior secured loan from Oaktree's co-investors to Sagard during the year ended December 31, 2020.

Income Tax Expense

For the year ended December 31, 2020, we incurred income tax expense of $4.1 million, compared to $0.9 million for the same period in 2019. The increase in income tax expenses was primarily attributable to $3.9 million foreign tax withholding in relation to license revenue recognized in 2020.

Liquidity and Capital Resources

Capital Resources

Since our inception, we have incurred net losses and negative cash flows from our operations. Our cash requirement was primarily cash used for our R&D programs, SG&A costs associated with our operations, the development of our specialty drug operations in our Commercial Platform and 503B operations, and the investment we are making in our pre-launch activities in anticipation of commercializing our proprietary drugs. We incurred net losses of $148.4 million, $125.5 million and $128.7 million for the years ended December 31, 2020, 2019, and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of $713.6 million. Our operating activities used $131.2 million, $97.5 million and $109.4 million of cash during the years ended December 31, 2020, 2019, and 2018, respectively. We intend to continue to advance our various clinical and pre-clinical programs which we expect will lead to increased cash outflow of research and development costs and increase our investments in commercialization activities for our proprietary drugs. In addition, we can provide no assurance that the funding requirements to diversify the product portfolio for specialty drug products in the Commercial Platform and 503B operations will decline in the future. Our principal sources of liquidity as of December 31, 2020 were cash and cash equivalents totaling of $69.6 million, restricted cash of $16.5 million, held in a controlled bank account in connection with the Senior Credit Agreement with Oaktree, and short-term investments totaling $138.6 million, which are generally high-quality investment grade corporate debt securities.

In September 2020, we successfully raised $118.7 million through public offering of our shares, thus alleviated the substantial doubt about our ability to continue as a going concern as of June 30, 2020. We believe that our cash from operations and existing cash, cash equivalents, restricted cash, and short-term investments will enable us to meet our current operational liquidity needs and fund operations into the second quarter of 2022. The Company's estimates are based on relevant conditions that are known and reasonably knowable at the date of these consolidated financial statements being available for issuance, and are subject to change due to changes in business, industry or macroeconomic conditions. This forecasted cash runway does not reflect additional funding available to us through the existing Senior Credit Agreement with Oaktree, or the Revenue Interest Financing Agreement with Sagard. Further, we do not expect to have access to additional capital under these facilities and will need to find alternative sources of financing until such time as Oral Paclitaxel is approved or we will need to renegotiate these arrangements.

Debt and Equity Financings

Public Offering of Stock

In September 2020, we completed an underwritten public offering of 10,000,000 shares of its common stock. We granted the underwriters a 30-day option to purchase up to an additional 1,500,000 shares of common stock, which was exercised in full in September 2020. All shares were offered at a price of $11.00 per share. Net proceeds were $118.7 million, after deducting underwriting discounts and commissions and offering expenses of $7.9 million.

Revenue Interest Financing Agreement

On August 4, 2020, we entered into a Revenue Interest Financing Agreement with Sagard, pursuant to which Sagard has agreed to pay the Company us $50.0 million to provide funding for the Company's development and commercialization of Oral Paclitaxel upon receipt of marketing authorization for Oral Paclitaxel by the U.S. FDA for the treatment of MBC. In exchange for the Product Payment, we have agreed to make payments to Sagard equal to 5.0% of our world-wide net sales of Oral Paclitaxel, subject to a hard cap equal to the lesser of 170% of the Product Payment and the Put/Call Price set forth below (the "Hard Cap"). We are required to make certain additional payments to Sagard to the extent Sagard has not received Payments equaling at least $20.0 million by September 30, 2024 and at least $50.0 million by August 4, 2026. In addition, if Sagard has not received Payments equaling at least $85.0 million by the tenth anniversary of the date the Product Payment is funded (the "Funding Date"), then subject to the Hard Cap, we will be required to pay Sagard an amount such that Sagard will have obtained a 6.0% internal rate of return, calculated on a quarterly basis and calculated from the Funding Date to the tenth anniversary of the Funding Date, on the amount of the Product Payment, taking into account all other payments received by Sagard from us under the Revenue Interest Financing Agreement.

Our obligations under the Revenue Interest Financing Agreement are secured, subject to customary permitted liens and other agreed upon exceptions and subject to an intercreditor agreement with Oaktree, as administrative agent for the lenders under our Senior Credit Agreement, by a perfected security interest in (i) accounts receivable arising from net sales of Oral Paclitaxel and (ii) intellectual property that is claiming or covering Oral Paclitaxel itself or any method of using, making or manufacturing Oral Paclitaxel.

At any time after August 4, 2022, we will have the right, but not the obligation (the "Call Option"), to buy out Sagard's interest in the Payments at a repurchase price (the "Put/Call Price") equal to (a) on or before August 4, 2023, a payment sufficient to generate an internal rate of return of 18.0% of the Product Payment, (b) after August 4, 2023 and on or before August 4, 2024, a payment sufficient to generate an internal rate of return of 16.0% of the Product Payment, (c) after August 4, 2024 and on or before August 4, 2025, a payment sufficient to generate an internal rate of return of 15.0% of the Product Payment, and (d) thereafter, the greater of (i) an amount that, when paid to Sagard, would generate an internal rate of return of 13.0% of the Product Payment, and (ii) an amount equal to the product of the Product Payment and 165%, in the case of each foregoing clause (a) through (d), taking into account all other payments received by Sagard from us under the Revenue Interest Financing Agreement.

The Revenue Interest Financing Agreement contains customary representations and warranties and certain restrictions on our ability to incur indebtedness and grant liens on intellectual property related to Oral Paclitaxel. In addition, the Revenue Interest Financing Agreement provides that if certain events ("Put Option Events") occur, including certain bankruptcy events, non-payment of Payments, a change of control, an out-license or sale of all of the rights in and to Oral Paclitaxel in the U.S. (other than any out-licensing transaction that includes all or substantially all of the U.S. and European development and commercialization rights to Oral Paclitaxel with a pharmaceutical company with global annual revenues for its most recently completed fiscal year that is greater than or equal to $500.0 million attributable to its oncology business) and (subject to applicable cure periods) non-compliance with the covenants in the Revenue Interest Financing Agreement, Sagard may require us to repurchase its interests in the Payments at the Put/Call Price. Our ability to access capital under the agreement is dependent upon receiving regulatory approval for Oral Paclitaxel in the U.S. for the treatment of MBC and Sagard may also terminate the Revenue Interest Financing Agreement if we have not received marketing authorization for Oral Paclitaxel by the FDA for the treatment of metastatic breast cancer by December 31, 2021. Due to our receipt of a CRL for our Oral Paclitaxel NDA requiring an additional clinical trial, we will likely not receive FDA approval before December 31, 2021 and Sagard will have the ability to exercise the termination right absent our renegotiation of this provision.

Sagard and the IMCO Investors also acquired by the Assignment term loans and commitments equal to $50.0 million under the Senior Credit Agreement. In connection with the Assignment, we granted warrants to Sagard and the IMCO Investors to purchase up to an aggregate of 201,865 shares of our common stock at a purchase price of $12.63 per share. As a result of the issuance of the additional warrants, we evaluated the debt modification in accordance with ASC 470 and concluded that the assigned debt qualified for a partial debt extinguishment of the existing Senior Credit Agreement with Oaktree. Therefore, we recorded a loss on partial extinguishment of debt in the amount of $3.0 million for the three months ended September 30, 2020.

Oaktree Senior Credit Agreement

On June 19, 2020 (the "Closing Date"), we entered into the Senior Credit Agreement to borrow up to $225.0 million in five tranches with a maturity date of June 19, 2026, bearing interest at a fixed annual rate of 11.0%, payable quarterly. We are required to make quarterly interest-only payments until the second anniversary of the Closing Date, after which we are required to make quarterly amortizing payments, with the remaining balance of the principal plus accrued and unpaid interest due at maturity. After the date that is 90 days after the Closing Date, we will be required to pay a commitment fee on any undrawn commitments equal to 0.6% per annum, payable on each subsequent funding date and the commitment termination date. We are also required to pay an exit fee at maturity equal to 2.0% of the aggregate principal amount of the loans funded under the Senior Credit Agreement.

The first tranche of $100.0 million was drawn prior to June 30, 2020, with $54.1 million of the proceeds used in part to repay in full the outstanding loan and fees under the credit agreement with Perceptive and an additional $11.0 million of the upfront loan proceeds held by us as restricted cash in a debt service reserve account, and $6.4 million in fees and expenses incurred in connection with the financing, leaving $28.5 million in available proceeds from the first tranche. The second tranche of $25.0 million was drawn prior to September 30, 2020 and the third tranche of $25.0 million was drawn prior to December 31, 2020. Tranche C and E of $75.0 million in the aggregate are available for borrowing from time to time prior to the date that is either 24 or 36 months after the Closing Date, subject to our achievement of certain regulatory and commercial milestones, each as further set forth below:

Tranche	**Funding Condition**	**Tranche Commitment Amount**
Tranche C	The receipt of approval from the FDA of an NDA in respect of the use of Oral Paclitaxel permitting the marketing of Oral Paclitaxel in interstate commerce in the United States to treat metastatic breast cancer.	$25.0 million
Tranche E	The achievement of (A) net sales for the twelve (12) consecutive month period ending on the last day of a fiscal quarter in excess of $200.0 million and (B) net sales attributable to Oral Paclitaxel for such quarter in excess of $40.0 million.	$50.0 million

We may voluntarily prepay the Senior Credit Agreement at any time subject to a prepayment premium which up until the second anniversary of the Closing Date is equal to the amount of interest that would have been paid up to, but not including, the second anniversary date (excluding interest amounts already paid), plus 3.0% of the principal amount of the senior secured loans being repaid. Thereafter, the prepayment premium equals 3.0% of the principal amount of the senior secured loans being repaid and is reduced over time until the fourth anniversary date, after which no prepayment premium is required.

We are required to make mandatory prepayments of the senior secured loans with net cash proceeds from certain asset sales or insurance proceeds or condemnation awards, in each case, subject to certain exceptions and reinvestment rights.

Our obligations under the Senior Credit Agreement are guaranteed by us and certain of our existing domestic subsidiaries and subsequently acquired or organized subsidiaries subject to certain exceptions. Our obligations under the Senior Credit Agreement and the related guarantees thereunder are secured, subject to customary permitted liens and other agreed upon exceptions, by (i) a pledge of all of the equity interests of our direct subsidiaries, and (ii) a perfected security interest in all of our tangible and intangible assets.

The Senior Credit Agreement contains customary representations and warranties and customary affirmative and negative covenants, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of other indebtedness, and dividends and other distributions, subject to certain exceptions, including specific exceptions with respect to product commercialization and development activities. In addition, the Senior Credit Agreement contains certain financial covenants, including, among other things, maintenance of minimum liquidity and a minimum revenue test, measured quarterly until the last day of the second consecutive fiscal quarter where the consolidated leverage ratio does not exceed 4.5 to 1, provided that thereafter we cannot allow our consolidated leverage ratio to exceed 4.5 to 1, measured quarterly. Failure of the Company to comply with the financial covenants will result in an event of default, subject to certain cure rights of the Company. At December 31, 2020, we were in compliance with all applicable covenants.

The Senior Credit Agreement contains events of default which are customary for financings of this type, in certain circumstances subject to customary cure periods. Following an event of default and any cure period, if applicable, Oaktree will have the right upon notice to terminate any undrawn commitments and may accelerate all amounts outstanding under the Senior Credit Agreement, in addition to other remedies available to it as a secured creditor of the Company.

In connection with our entry into the Senior Credit Agreement, we granted warrants to Oaktree to purchase up to an aggregate of 908,393 shares of our common stock at a purchase price of $12.63 per share and entered into a registration rights agreement with Oaktree on June 19, 2020, pursuant to which, among other things, we agreed to register for resale the shares of common stock issuable upon exercise of the warrants of no later than the 45th day following the issuance of the warrants. On August 6, 2020, we filed with the SEC a Registration Statement on Form S-3 (File No. 333-241665) registering for resale the shares of common stock issuable upon exercise of the warrants.

Outlook

We have borrowed and, in the future, may borrow additional capital from institutional and commercial banking sources to fund future growth, including pursuant to the Senior Credit Agreement, or potentially pursuant to new arrangements with different lenders. We may borrow additional funds on terms that may include restrictive covenants, including covenants that further restrict the operation of our business, liens on assets, high effective interest rates, financial performance covenants and repayment provisions that reduce cash resources and limit future access to capital markets. In addition, we expect to continue to opportunistically seek access to the equity capital markets to support our development efforts and operations. To the extent that we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. To the extent that we raise additional funds through collaboration or partnering arrangements, we may be required to relinquish some of our rights to our technologies or rights to market and sell our products in certain geographies, grant licenses on terms that are not favorable to us, or issue equity that may be substantially dilutive to our stockholders.

As of December 31, 2020, we had cash and cash equivalents of $69.6 million, restricted cash of $16.5 million, and short-term investments of $138.6 million. We believe that the existing cash and cash equivalents, restricted cash, and short-term investments will fund operations into the second quarter of 2022. The Company's estimates are based on relevant conditions that are known and reasonably knowable at the date of these consolidated financial statements being available for issuance, and are subject to change due to changes in business, industry or macroeconomic conditions. This forecasted cash runway also does not contemplate the additional funding we may receive through the Senior Credit Agreement and Revenue Interest Financing Agreement. Further, we do not expect to have access to additional capital under these facilities and will need to find alternative sources of financing until such time as Oral Paclitaxel is approved or will need to renegotiate these arrangements. We have based these estimates on assumptions that may prove to be wrong, and it could spend the available financial resources much faster than expected and need to raise additional funds sooner than anticipated.

We expect that our expenses will increase as we continue to fund clinical and preclinical development of our research programs, pre-launch activities of our proprietary drugs, funding of our Commercial Platform and manufacturing facilities, and working capital and other general corporate purposes. We have based our estimates on assumptions that might prove to be wrong, and we might 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 future capital requirements will depend on many factors, some or all of which may be impacted by the COVID-19 pandemic, including:

- Our ability to generate revenue and profits from our Commercial Platform or otherwise;
- The costs, timing and outcome of regulatory reviews and approvals;
- Progress of our drug candidates to progress through clinical development successfully;
- The initiation, progress, timing, costs and results of nonclinical studies and clinical trials for our other programs and potential drug candidates;
- The costs of preparing our Commercial Platform for the commercialization of our proprietary drugs;
- The costs of construction and fit-out of planned drug at both Dunkirk and API manufacturing facilities;
- The number and characteristics of the drug candidates we pursue;
- The costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our IP rights and defending IP 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.

Until 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 Flows

The following table provides information regarding our cash flows for the years ended December 31, 2020, 2019, and 2018:

	Year ended December 31,		
	2020	2019	2018
	(in thousands)		
Net cash used in operating activities	$ (131,243)	$ (97,460)	$ (109,387)
Net cash (used in) provided by investing activities	(118,972)	7,499	(48,963)
Net cash provided by financing activities	209,427	167,452	169,035
Net effect of foreign exchange rate changes	(799)	389	(175)
Net (decrease) increase in cash, cash equivalents, and restricted cash	$ (41,587)	$ 77,880	$ 10,510

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 R&D, regulatory and other clinical trial costs, drug licensing costs, inventory purchases, pre-launch commercialization activities, 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, 2020, operating activities used $131.2 million of cash, which resulted principally from our net loss of $148.4 million, adjusted for non-cash charges of $37.2 million and cash used by our operating assets and liabilities of $20.0 million. Our non-cash charges during the year ended December 31, 2020 primarily consisted of $10.9 million of stock-based compensation, $10.3 million of loss on extinguishment of debt, $9.5 million provision for expected credit losses, $4.5 million of depreciation and amortization, and $1.8 million of amortization of debt discount. Our operating assets increased $16.4 million for accounts receivable mainly related to the contract asset recognized from license revenue in the current period and the increased sales of specialty products during the year ended December 31, 2020 and decreased by $5.7 million for prepaids related to the Dunkirk construction, as it entered into the final stage of completion, and other assets, and $3.8 million for inventory of all drug products. Our operating liabilities decreased by $13.1 million mainly due to a decrease in accrued construction costs and accrued inventory purchases, offset by an increase in accrued selling costs and rebates, an increase in accrued interest, and other operating liabilities.

During the year ended December 31, 2019, operating activities used $97.5 million of cash, which resulted principally from our net loss of $125.5 million, adjusted for non-cash charges of $15.4 million. Cash provided by our operating assets and liabilities was $12.6 million primarily due to increases in accounts payable and accrued expenses. Our net non-cash charges during the year ended December 31, 2019 primarily consisted of $3.8 million in depreciation and amortization expense, $9.9 million in stock-based compensation expense, and $1.0 million in amortization of debt discount.

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 license in fees settled with stock.

Net Cash (Used in) Provided by Investing Activities

In 2020, cash used in investing activities of $119.0 million was primarily attributable to $105.5 million in purchases of short-term investments, net of sales and maturities, $13.3 million in purchasing property and equipment, and $0.2 million in payment for licenses.

In 2019, cash provided by investing activities of $7.5 million was primarily attributable to $24.4 million in sale and maturity of short-term investments, net of purchases, and $0.9 million provided by the acquisition of CIDAL, offset by $13.6 million in purchasing property and equipment, and $4.2 million in payment for licenses.

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 purchases of short-term investments, and $0.1 million in payment for licenses.

Net Cash Provided by Financing Activities

In 2020, cash provided by financing activities was $209.4 million, which primarily consisted of $127.0 million from the sale of common stock and $143.0 million from the draw downs of debt from our Senior Credit Agreement with Oaktree and $2.1 million to fund our new API plant in China, $7.0 million from the issuance of warrants to Oaktree and Sagard, and $1.7 million from the exercise of stock options, partially offset by $54.4 million repayment of the Perceptive loan and other long-term debt, and $7.9 million and $9.4 million issuance costs related to sale of our common stock in our underwritten follow-on public offering and the issuance of the new Oaktree debt and warrants to Oaktree and Sagard, respectively.

In 2019, cash provided by financing activities was $167.5 million, which primarily consisted of net proceeds of $161.1 million from the issuance of our common stock mostly from private placements, net of offering expenses of approximately $1.1 million, and $6.5 million from the issuance of debt to fund our new API plant in China, offset by $1.0 million repayment of debt and finance lease obligations.

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.

Indebtedness

We had $158.1 million and $63.9 million of debt as of December 31, 2020 and 2019, respectively. As of December 31, 2020, this primarily consisted of finance and operating lease obligations, the Senior Credit Agreement entered into with Oaktree during 2020, and a credit agreement with Chongqing Maliu Riverside Development and Investment Co., LTD.

In 2020, we entered into a Senior Credit Agreement with Oaktree to borrow up to $225.0 million in five tranches with a maturity date of June 19, 2026, bearing interest at a fixed annual rate of 11.0%, payable quarterly. We are required to make quarterly interest-only payments until the second anniversary of the Senior Credit Agreement, after which we are also required to make quarterly amortizing payments, with the remaining balance of the principal plus accrued and unpaid interest due at maturity. Ninety days after the date of the Senior Credit Agreement, we will be required to pay a commitment fee on any undrawn commitments equal to 0.6% per annum, payable on each subsequent funding date and the commitment termination date. We are also required to pay an exit fee at maturity equal to 2.0% of the aggregate principal amount of the loans funded under the Senior Credit Agreement.

In 2019, we entered into a credit agreement which amended the existing partnership agreement with Chongqing Maliu Riverside Development and Investment Co., LTD ("CQ"), for a Renminbi ¥50.0 million (USD $7.2 million at December 31, 2019) line of credit to be used for the construction of the new API plant in China. We are required to repay the principal amount with accrued interest within three years after the plant receives cGMP certification, with 20% of the total loan with accrued interest is due within the first twelve months following receiving the certification, 30% of the total loan with accrued interest due within twenty-four months, and the remaining balance with accrued interest due within thirty-six months. Interest accrues at the three-year loan interest rate by the People's Bank of China for the same period on the date of the deposit of the full loan amount. If we fail to obtain the cGMP certification within three years upon the completion and acceptance of the plant, we shall return all renovation costs with the accrued interest to CQ, in a single transaction within the first ten business days of the next day. If we fail to obtain the cGMP certification within three years of the acceptance of the plant, we are required to return all renovation costs with accrued interest to CQ within ten business days. As of December 31, 2020, the balance due to CQ was $7.6 million.

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;
- Our ability to improve margins on our commercial products;
- Fluctuations in working capital; and
- Our ability to raise additional funds.

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;
- Build out of our manufacturing facility in Dunkirk;
- 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 409,000 square foot, ISO Class 5 high potency oral and sterile injectable pharmaceutical manufacturing facility, which is under construction in Dunkirk, New York. We will be able to occupy the space on concessionary terms. In Chongqing, China, funded by the Banan District government, a cGMP API and a GMP pharmaceutical manufacturing plant is being 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. 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. We are responsible for the costs of all equipment and technology for the 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 (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 about $208.0 million. 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. As of December 31, 2020, construction of the Dunkirk manufacturing facility and the new API manufacturing facility in Chongqing was in the final stage of completion. We accepted the API building and entered into a lease agreement with CQ in January 2021 and commenced operations since. We expect Dunkirk facility to commerce operations in the second half of 2021.

Future Capital Requirements

We believe that our existing cash, cash equivalents, restricted cash, and short-term will fund operations into the second quarter of 2022. The Company's estimates are based on relevant conditions that are known and reasonably knowable at the date of these consolidated financial statements being available for issuance, and are subject to change due to changes in business, industry or macroeconomic conditions. This cash runway does not reflect additional funding available to us through our existing Senior Credit Agreement with Oaktree, as administrative agent, or the Revenue Interest Financing Agreement with Sagard. Further, we do not expect to have access to additional capital under these facilities and will need to find alternative sources of financing until such time as Oral Paclitaxel is approved or will need to renegotiate these arrangements. We have based these estimates on assumptions that may prove to be wrong, and it could spend the available financial resources much faster than expected and need to raise additional funds sooner than anticipated. Operations have been funded primarily through the sale of common stock, senior secured loans, and to a lesser extent, from convertible bond financing, revenue, and grant funding. Although we plan to raise additional funds or access additional funding via the Senior Credit Agreement and Revenue Interest Financing, these plans are subject to market conditions which are outside of our control and based on the satisfaction of future milestone funding conditions, and therefore cannot be deemed to be probable. 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.

Contractual Obligations

A summary of our contractual obligations as of December 31, 2020 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	$ 3,454	$ 5,023	$ 3,473	$ 479	$ 12,429
Long-term debt	1,634	22,669	27,919	110,410	162,632
Finance lease obligations	468	523	177	—	1,168
License fees	3,216	—	—	—	3,216
	$ 8,772	$ 28,215	$ 31,569	$ 110,889	$ 179,445

Our operating and finance leases are principally for facilities and equipment. We currently lease office space in the U.S. and foreign countries to support our operations as a global organization. The operating leases in the above table include our several locations with the amounts committed by each location: (1) the rental of our global headquarters in the Conventus Center for Collaborative Medicine in Buffalo, NY; (2) the rental of our research and development facility in the IC Development Centre in Hong Kong; (3) the rental of the Commercial Platform headquarters in Chicago, IL; (4) the rental of our clinical research headquarters in Cranford, NJ; (5) the rental of our clinical data management center in Taipei, Taiwan; (6) the rental of our contract research organization throughout Latin America; (7) the rental of our Global Supply Chain distribution office in Houston, TX; (8) the rental of our Global Supply Chain API manufacturing facility in Chongqing, China; and (9) the rental of other facilities and equipment located mainly in Buffalo, NY. These locations represent $7.2 million, $0.6 million, $2.2 million, $0.2 million, $0.8 million, $0.3 million, $0.4 million, $0.4 million, and $2.6 million, respectively, of the total amounts committed. In addition to the minimum rental commitments on our operating leases we may also be required to pay amounts for taxes, insurance, maintenance and other operating expenses.

The long-term debt includes our senior secured loan, the mortgage assumed in connection with the acquisition of CDE, and the credit agreement with CQ. The finance lease obligations represent three leases of equipment in our 503B manufacturing facility outside of Buffalo, NY. The license fees in the above table represent the amount committed and accrued under in-license agreements for specialty drug products by the Commercial platform.

In addition, we have certain obligations under licensing arrangements with third parties contingent upon achieving various development, regulatory, and commercial milestones. Pursuant to our license agreement with Polytom, we may be required to make payments worth up to $44.0 million of our common stock or cash upon the occurrence of certain regulatory milestones related to a pegylated genetically modified human arginase, and make royalty payments representing a percentage of net sales of the licensed products. Pursuant to our license agreement with Avalon HepaPOC, we may be required to make payments worth up to $4.8 million of our common stock or cash upon the occurrence of certain regulatory and sales milestones related to the meter and strips for conduct of liver function tests in humans taking our oncology drugs and make royalty payments representing a percentage of aggregate net sales of the licensed product. Pursuant to the license agreement with XLifeSc, our 55% owned joint venture Axis Therapeutics Limited, we may be required to make cash payments worth up to $108.0 million upon the occurrence of certain regulatory milestones related to XLifeSc's proprietary TCR-T technology, and make royalty payments representing a percentage of aggregate net income generated by sales of licensed products. Pursuant to our license agreements with Hanmi, we may be required to make equity payment of $24.0 million upon regulatory approval of a product within the Orasovery platform and make tiered royalty payments based on net sales of any product using the licensed intellectual property. These amounts are not included in the table above.

Under our partnerships with New York State and CQ, we are obligated to contribute to the building of manufacturing facilities in Dunkirk, NY and Chongqing, China. Pursuant to our arrangement with New York State, we are committed to bear the costs of the construction of the facility in Dunkirk, NY in excess of approximately $208.0 million, as described in *Capital Expenditures* above. Further, 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 and are 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. Pursuant to our arrangement with CQ, the Finance Bureau of Banan District of Chongqing is responsible for investing in the construction of the API and formulation plants and completing renovation in accordance with U.S. cGMP standards, and we are required to commit capital of no less than $30 million, which can be used as working capital in the normal course of the business. As of December 31, 2020, we had contributed a total of $14.1 million of capital to our subsidiary. The remaining $15.9 million commitment is not included in the table above. We are allowed to lease the facility 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, or, we shall have the option to purchase the land and building. If we do not purchase the land and building after 20 years at the price described above, we shall have the option to lease the land and building with rental fee charged at market price of construction area. We are responsible for the costs of all equipment and technology for the facilities. Neither of these facilities in New York State and Chongqing, China were operational as of December 31, 2020 and the amounts under these agreements described above are not included in the table above.

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

The Company out-licenses certain of its IP to other pharmaceutical companies in specific territories that allow the customer to use, develop, commercialize, or otherwise exploit the licensed IP. In accordance with ASC 606, *Revenue from Contracts with Customers* ("Topic 606"), the Company analyzes the contracts to identify its performance obligations within the contract. Most of the Company's out-license arrangements contain multiple performance obligations and variable pricing. After the performance obligations are identified, the Company determines the transaction price, which generally includes upfront fees, milestone payments related to the achievement of developmental, regulatory, or commercial goals, and royalty payments on net sales of licensed products. The Company considers whether the transaction price is fixed or variable, and whether such consideration is subject to return. Variable consideration is only included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. If any portion of the transaction price is constrained, it is excluded from the transaction price until the constraint no longer exists. The Company then allocates the transaction price to the performance obligation to which the consideration is related. Where a portion of the transaction price is received and allocated to continuing performance obligations under the terms of the arrangement, it is recorded as deferred revenue and recognized as revenue when (or as) the underlying performance obligation is satisfied.

The Company's contracts may contain one or multiple promises, including the license of IP and development services. The licensed IP is capable of being distinct from the other performance obligations identified in the contract and is distinct within the context of the contract, as upon transfer of the IP, the customer is able to use and benefit from it, and the customer could obtain the development services from other parties. The Company also considers the economic and regulatory characteristics of the licensed IP and other promises in the contract to determine if it is a distinct performance obligation. The Company considers if the IP is modified or enhanced by other performance obligations through the life of the agreement and whether the customer is contractually or practically required to use updated IP. The IP licensed by the Company has been determined to be functional IP. The IP is not modified during the license period and therefore, the Company recognizes revenues from any portion of the transaction price allocated to the licensed IP when the license is transferred to the customer and they can benefit from the right to use the IP. The Company recognized $37.7 million in license revenue, net of $2.3 million value added tax ("VAT"), and $1.0 million in license revenue from two of the Company's out-license arrangements for the year ended December 31, 2020. The Company recognized revenue allocated to the licensed IP performance obligation upon transfer of the license of $0.1 million for the year ended December 31, 2019.

Other performance obligations included in most of the Company's out-licensing agreements include performing development services to reach clinical and regulatory milestone events. The Company satisfies these performance obligations at a point-in-time, because the customer does not simultaneously receive and consume the benefits as the development occurs, the development does not create or enhance an asset controlled by the customer, and the development does not create an asset with no alternative use. The Company considers milestone payments to be variable consideration measured using the most likely amount method, as the entitlement to the consideration is contingent on the occurrence or nonoccurrence of future events. The Company allocates each variable milestone payment to the associated milestone performance obligation, as the variable payment relates directly to the Company's efforts to satisfy the performance obligation and such allocation depicts the amount of consideration to which the Company expects to be entitled for satisfying the corresponding performance obligation. The Company re-evaluates the probability of achievement of such performance obligations and any related constraint and adjusts its estimate of the transaction price as appropriate. To date, no amounts have been constrained in the initial or subsequent assessments of the transaction price. The Company did not recognize revenue from other performance obligations included in the Company's out-licensing agreements during the year ended December 31, 2020. The Company recognized revenue allocated to development performance obligations upon transfer to the customer of $20.0 million for the year ended December 31, 2019.

Certain out-license agreements include performance obligations to manufacture and provide drug product in the future for commercial sale when the licensed product is approved. For the commercial, sales-based royalties, the consideration is predominantly related to the licensed IP and is contingent on the customer's subsequent sales to another commercial customer. Consequently, the sales- or usage-based royalty exception would apply. Revenue will be recognized for the commercial, sales-based milestones as the underlying sales occur.

The Company exercises significant judgment when identifying distinct performance obligations within its out-license arrangements, determining the transaction price, which often includes both fixed and variable considerations, and allocating the transaction price to the proper performance obligation. The Company did not use any other significant judgments related to out-licensing revenue during the years ended December 31, 2020 and 2019.

2. Global Supply Chain Platform

The Company's Global Supply Chain Platform manufactures API for use internally in its research and development activities as well as its clinical studies, and for sale to pharmaceutical customers globally. The Company generates additional revenue on this platform, by providing small to mid-scale cGMP manufacturing of clinical and commercial products for pharmaceutical and biotech companies and selling pharmaceutical products under 503B regulations set forth by the U.S. FDA.

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.

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. Upon the sale by the wholesaler to the end-user, the wholesaler will chargeback the difference, if any, between the original list price and price at which the product was sold to the end-user. The Company also offers cash discounts, which approximate 2.3% 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. Further, the Company offers contractual allowances, generally in the form of rebates or administrative fees, to certain wholesale customers, group purchasing organizations ("GPOs"), and end-user customers, consistent with pharmaceutical industry practices. Revenues are recorded net of provisions for variable consideration, including discounts, rebates, GPO allowances, price adjustments, returns, chargebacks, promotional programs and other sales allowances. Accruals for these provisions are presented in the consolidated financial statements as reductions in determining net sales and as a contra asset in accounts receivable, net (if settled via credit) and other current liabilities (if paid in cash). As of December 31, 2020 and 2019, the Company's total provision for chargebacks and other deductions included as a reduction of accounts receivable totaled $12.5 million and $14.4 million, respectively. The Company's total provision for chargebacks and other revenue deductions was $89.3 million, $87.2 million, and $36.5 million for the years ended December 31, 2020, 2019, and 2018, respectively.

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.

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.

Recent Accounting Pronouncements

In the normal course of business, we evaluate all new accounting pronouncements issued by the Financial Accounting Standards Board, 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.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk.

Foreign Currency Exchange Risk

A significant portion of our business is located outside the U.S. 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 2020, 2019, and 2018, approximately 1%, 2% 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. As of December 31, 2020, we had cash and cash equivalents of approximately $16.0 million at our Chinese subsidiaries. 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, ("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 PRC foreign exchange trading system market.

Interest Rate Sensitivity

We had cash and cash equivalents of $69.6 million, restricted cash of $16.5 million, and short-term investments of $138.6 million as of December 31, 2020, 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 U.S. market interest rates is not 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.

Credit Risk

We had cash and cash equivalents of $69.6 million, $127.7 million and $49.8 million and marketable securities of $138.6 million, $33.1 million, and $57.6 million at December 31, 2020, 2019, and 2018, 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, 2020 and 2019, 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, 2020, and the related notes and the consolidated financial statement 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, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with accounting principles generally accepted in the United States of America.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 1, 2021, expressed an unqualified opinion on the Company's internal control over financial reporting.

Change in Accounting Principle

As discussed in Note 2 to the financial statements, effective January 1, 2019, the Company adopted Financial Accounting Standards Board Accounting Standards Update No. 2016-02, *Leases (Topic 842)*, as amended, using the modified retrospective method.

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 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. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or 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.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current-period audit of the financial statements that were communicated or required to be communicated to the audit committee and that (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

License Revenue Recognition – Refer to Notes 2 and 18 (Oncology Innovation Platform) to the financial statements

Critical Audit Matter Description

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 ("ASC 606"), the Company determines each of its performance obligations under the agreements and allocates the transaction price to those obligations accordingly, including the determination as to whether variable consideration within the total transaction price meets the criteria for recognition. 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. For the period ended December 31, 2020, total out-license revenue amounted to $37.7 million.

We identified license revenue recognition as a critical audit matter because of the judgments necessary for management to: identify performance obligations, determine variable consideration, allocate transaction price amongst the identified performance obligations, and determine the timing of recognition for such revenue. Because of the complexity associated with applying the recognition criteria of ASC 606, notably related to the determination as to whether entered license agreements represent functional or symbolic IP, this required extensive audit effort and a high degree of auditor judgment when performing audit procedures and evaluating the results of those procedures.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the recognition of license revenue, included the following, among others:

- We tested the effectiveness of controls over the identification of performance obligations, determination of variable consideration, allocation of transaction price, and determination of timing of license revenue recognition.
- We evaluated the Company's revenue recognition for licenses through the inspection of license agreements and the evaluation of management's revenue recognition analysis corresponding to license agreements to validate that such transactions are being recognized in a manner commensurate with the terms of the established contracts and the relevant accounting guidance. Evaluating the reasonableness of management's accounting conclusions involved:
    - Evaluating the accuracy and completeness of performance obligations identified by management in license agreements. We analyzed the license agreements to determine if the arrangement terms that may have an impact on revenue recognition were identified and properly considered in the evaluation of the accounting for the contract. We also inquired of management and reviewed source documentation to assess whether the performance obligations identified by management are complete, and for those performance obligations identified, that they are both capable of being distinct and are distinct within the context of the contract.
    - Determining the reasonableness of management's determination of the amounts of variable consideration included within total transaction price. We analyzed the nature of performance obligations and the contingencies related to the variable consideration in assessing management's methods in estimating the amount of variable consideration to be included in total transaction price.
    - Testing the estimates utilized by management in allocating total transaction price amongst the performance obligations identified in the license agreements. We evaluated the reasonableness of management's methodology in allocating transaction price amongst the performance obligations and recalculated such allocations to determine that such were accurate.
    - Evaluating whether the performance obligations specific to the license agreements have been satisfied and that the related revenues corresponding to such were appropriately recognized in conjunction with such obligations being met.
    - Assessing the appropriateness of the method of measurement of progress and timing of recognition for amounts in license agreements. We tested the appropriateness of management's recognition method (point-in-time or over-time) for performance obligations by evaluating the manner in which the performance obligations are satisfied, in addition to the determination of whether such agreements were functional versus symbolic IP.

Revenue Chargebacks – Refer to Note 18 (Commercial Platform) to the financial statements

Critical Audit Matter Description

The Company has revenue agreements with certain independent pharmaceutical wholesalers to sell and distribute specialty products. These wholesalers then sell these specialty drug products to an end-user (Hospital, alternative healthcare facility, etc.). In such case, sales are initially recorded at the 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 provision for chargebacks as of December 31, 2020 was $12.6 million, included as a reduction of accounts receivable.

We identified the accrual for chargebacks at the balance sheet date as a critical audit matter because of the judgments necessary for management to estimate the accrual based on estimates of wholesaler inventory stocking levels and of differences between list price and price at which the product was sold to the end-user. Given the volume of transactions subject to potential chargeback at the balance sheet date and the level of uncertainty involved in the estimation of the quantity and mix of products in wholesaler inventory, this matter required a high degree of auditor judgment when performing audit procedures and evaluating the results of those procedures.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to revenue chargebacks included the following, among others:

- We tested the effectiveness of controls over the Company's chargeback estimation process, which included management's control activities in reviewing the estimated wholesaler stock levels and anticipated chargeback claims outstanding.
- We evaluated the reasonableness of the methodology and assumptions applied by management when developing their chargeback estimate. We tested the accuracy and completeness of amounts in the accrual computations, inquired of management, and reviewed source documentation – including wholesaler agreements and inventory schedules to assess that management's methodology included relevant data and assumptions to arrive at a reasonable estimation process in material respects.
- We evaluated whether the methodology and assumptions have been consistently applied, throughout the estimation process, during the course of the year and in a manner consistent with the estimation process in the prior years presented.

We selected a sample of activity of the chargeback accrual at the balance sheet date and performed audit procedures on such sample. Such procedures included: obtaining wholesaler agreements for the samples and recalculating the year-end accrual for the selected transactions; verifying quantities-on-hand with wholesalers for the sample transactions; and performing a retrospective review of payments received subsequent to the balance sheet date to evaluate reasonableness of the Company's estimate of the chargebacks contra asset at the year-end balance sheet date. Additionally, we also performed procedures over the historical accuracy of the chargeback accrual through comparison of initial estimates to actual chargebacks incurred.

/s/ Deloitte & Touche LLP
Williamsville, New York
March 1, 2021

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, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 69,587	$ 127,674
Restricted cash	16,500	—
Short-term investments	138,636	33,139
Accounts receivable, net of chargebacks and other deductions of $12,552 and $14,394, respectively, and provision for credit losses of $9,637 and $124, respectively	23,603	16,689
Inventories	28,846	32,630
Prepaid expenses and other current assets	14,789	20,794
Total current assets	291,961	230,926
Property and equipment, net	34,388	23,153
Goodwill	38,891	38,513
Intangible assets, net	10,218	8,522
Operating lease right-of-use assets, net	7,921	8,818
Other assets	950	—
Total assets	$ 384,329	$ 309,932
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 18,673	$ 23,331
Accrued expenses	38,273	44,307
Current portion of operating lease liabilities	3,185	3,010
Current portion of long-term debt and finance lease obligations	2,010	880
Total current liabilities	62,141	71,528
Long-term liabilities:		
Long-term operating lease liabilities	6,355	7,620
Long-term debt and finance lease obligations	146,577	52,366
Deferred tax liabilities	56	—
Other long-term liabilities	3,852	2,563
Total liabilities	218,981	134,077
Commitments and contingencies (Note 20)		
Stockholders' equity:		
Common stock, par value $0.001 per share, 250,000,000 shares authorized at December 31, 2020 and 2019; 95,066,195 and 83,231,063 shares issued at December 31, 2020 and 2019, respectively; 93,393,275 and 81,558,143 shares outstanding at December 31, 2020 and 2019, respectively	95	83
Additional paid-in capital	901,864	763,648
Accumulated other comprehensive loss	(1,134)	(635)
Accumulated deficit	(713,644)	(567,465)
Less: treasury stock, at cost; 1,672,920 shares at December 31, 2020 and 2019	(7,406)	(7,406)
Total Athenex, Inc. stockholders' equity	179,775	188,225
Non-controlling interests	(14,427)	(12,370)
Total stockholders' equity	165,348	175,855
Total liabilities and stockholders' equity	$ 384,329	$ 309,932

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,		
	2020	2019	2018
Revenue:			
Product sales, net	$ 105,274	$ 80,535	$ 56,394
License and other revenue	39,117	20,694	32,706
Total revenue	144,391	101,229	89,100
Cost of sales	95,355	69,619	47,005
Gross profit	49,036	31,610	42,095
Operating expenses:			
Research and development expenses	75,904	84,393	119,905
Selling, general, and administrative expenses	96,855	66,749	49,008
Total operating expenses	172,759	151,142	168,913
Operating loss	(123,723)	(119,532)	(126,818)
Interest income	(874)	(1,881)	(1,788)
Interest expense	11,219	6,954	3,581
Loss on extinguishment of debt	10,278	—	—
Loss before income tax expense	(144,346)	(124,605)	(128,611)
Income tax expense	4,088	928	100
Net loss	(148,434)	(125,533)	(128,711)
Less: net loss attributable to non-controlling interests	(2,255)	(1,784)	(11,271)
Net loss attributable to Athenex, Inc.	$ (146,179)	$ (123,749)	$ (117,440)
Unrealized (loss) gain on investment, net of income taxes	(5)	(97)	15
Foreign currency translation adjustment, net of income taxes	(494)	118	(525)
Comprehensive loss	$ (146,678)	$ (123,728)	$ (117,950)
Net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted (Note 15)	$ (1.72)	$ (1.67)	$ (1.82)
Weighted-average shares used in computing net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted (Note 15)	85,082,868	74,054,261	64,590,270

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, 2018	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
Sale of common stock, net of costs of $1,103	14,006,575	14	159,963	—	—	—	—	159,977	—	159,977
Equity consideration in connection with acquisition	—	—	748	—	—	—	—	748	—	748
Stock-based compensation cost	—	—	8,219	—	—	—	—	8,219	—	8,219
Restricted stock expense	223,723	—	1,671	—	—	—	—	1,671	—	1,671
Stock options exercised	331,779	—	1,983	—	—	—	—	1,983	—	1,983
Net loss	—	—	—	(123,749)	—	—	—	(123,749)	(1,784)	(125,533)
Other comprehensive loss, net of tax	—	—	—	—	21	—	—	21	—	21
Balance at December 31, 2019	83,231,063	83	763,648	(567,465)	(635)	(1,672,920)	(7,406)	188,225	(12,370)	175,855
Sale of common stock, net of costs of $7,869	11,607,322	11	119,099	—	—	—	—	119,110	—	119,110
Issuance of warrant, net	—	—	6,544	—	—	—	—	6,544	—	6,544
Stock-based compensation cost	—	—	9,833	—	—	—	—	9,833	—	9,833
Restricted stock expense	(10,820)	—	1,017	—	—	—	—	1,017	—	1,017
Stock options exercised	238,630	1	1,723	—	—	—	—	1,724	—	1,724
Non-controlling interests	—	—	—	—	—	—	—	—	198	198
Net loss	—	—	—	(146,179)	—	—	—	(146,179)	(2,255)	(148,434)
Other comprehensive loss, net of tax	—	—	—	—	(499)	—	—	(499)	—	(499)
Balance at December 31, 2020	95,066,195	$ 95	$ 901,864	$ (713,644)	$ (1,134)	(1,672,920)	$ (7,406)	$ 179,775	$ (14,427)	$ 165,348

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,		
	2020	**2019**	**2018**
Cash flows from operating activities:			
Net loss	$ (148,434)	$ (125,533)	$ (128,711)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	4,492	3,817	3,269
Stock-based compensation expense	10,850	9,885	11,011
Loss on extinguishment of debt	10,278	—	—
Provision for credit losses	9,513	—	—
Amortization of debt discount	1,781	1,026	514
Deferred rent expense	—	—	262
Net loss on disposal of assets and impairment charges	222	232	236
Research and development license fees settled with convertible bond and stock	—	—	31,545
Deferred income taxes	56	486	(365)
Changes in operating assets and liabilities, net of effect of acquisition:			
Receivables, net	(16,427)	(3,738)	(4,483)
Prepaid expenses and other assets	5,702	864	(13,966)
Inventories	3,784	(3,844)	(12,226)
Accounts payable and accrued expenses	(13,060)	19,345	3,527
Net cash used in operating activities	(131,243)	(97,460)	(109,387)
Cash flows from investing activities:			
Purchase of property and equipment	(13,256)	(13,572)	(3,321)
Payments for licenses	(214)	(4,175)	(110)
Acquisition activity	—	853	—
Purchases of short-term investments	(161,847)	(74,697)	(113,259)
Sale of short-term investments	56,345	99,090	67,727
Net cash (used in) provided by investing activities	(118,972)	7,499	(48,963)
Cash flows from financing activities:			
Proceeds from sale of stock	126,980	161,080	123,134
Proceeds from issuance of debt	145,126	6,464	50,000
Proceeds from issuance of warrants	7,039	—	—
Costs incurred related to the sale of stock	(7,869)	(1,103)	(5,518)
Costs incurred related to the issuance of debt and warrants	(9,363)	—	(1,993)
Proceeds from exercise of stock options	1,723	1,983	3,956
Investment from non-controlling interest	198	—	—
Repayment of finance lease obligations and long-term debt	(54,407)	(972)	(544)
Net cash provided by financing activities	209,427	167,452	169,035
Net (decrease) increase in cash, cash equivalents, and restricted cash	(40,788)	77,491	10,685
Cash, cash equivalents, and restricted cash beginning of period	127,674	49,794	39,284
Effect of exchange rate changes on cash, cash equivalents, and restricted cash	(799)	389	(175)
Cash, cash equivalents, and restricted cash, end of period (See Note 3)	$ 86,087	$ 127,674	$ 49,794
Supplemental cash flow disclosures			
Interest paid	$ 6,056	$ 4,925	$ 2,977
Income taxes paid	$ 3,066	$ 448	$ 464
Non-cash investing and financing activities:			
Accrued purchases of property and equipment	$ 478	$ 483	$ 340
Accrued cost of debt issuance	$ 750	$ —	$ —
Common stock issued in lieu of licensing cash payment	$ —	$ —	$ 31,545
Property and equipment financed under capital and finance leases	$ 848	$ —	$ —
Accrued purchases of licenses	$ 2,850	$ —	$ 4,175
ROU assets derecognized from modification of operating lease obligations	$ (468)	$ —	$ —
Equity consideration in connection with acquisition	$ —	$ 748	$ —

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 becoming a leader in 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's current clinical pipeline is derived from Orascovery, based on a P-glycoprotein ("P-gp") pump inhibitor, Src Kinase inhibition, T-cell receptor-engineered T-cells ("TCR-T"), and arginine deprivation therapy technology platforms. The Company has assembled a strong and experienced leadership team and has established global operations across the pharmaceutical value chain to execute its goal of becoming a global leader in bringing innovative cancer treatments to the market and improve health outcomes. The Company is primarily engaged in conducting research and development activities through corporate collaborators, in-licensing and out-licensing pharmaceutical compounds and technology, conducting preclinical and clinical testing, recruiting personnel, identifying and evaluating additional drug candidates for potential in-licensing or acquisition, and raising capital to support development and commercialization activities. The Company also conducts commercial sales of specialty products through its wholly owned subsidiary, Athenex Pharmaceutical Division ("APD"), and 503B products through its wholly owned subsidiary, Athenex Pharma Solutions ("APS").

Recent Financing

Public Offering of Stock

In September 2020, the Company completed an underwritten follow-on public offering in which it sold 11,500,000 shares of its common stock, including 1,500,000 shares of common stock pursuant to underwriters' option to purchase additional shares, at a public offering price of $11.00 per share and received net proceeds of $118.7 million, after deducting underwriting discounts and commissions and offering expenses of $7.9 million.

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. The aggregate net proceeds were $68.1 million, net of underwriting discounts and commissions and offering expenses of $4.6 million.

Revenue Interest Financing Agreement and Detachable Warrants

On August 4, 2020, the Company entered into a Revenue Interest Financing Agreement with Sagard Healthcare Royalty Partners, LP ("Sagard"), pursuant to which Sagard agreed to pay the Company $50.0 million (the "Product Payment") to provide funding for the Company's development and commercialization of Oral Paclitaxel upon receipt of marketing authorization for Oral Paclitaxel by the U.S. Food and Drug Administration (FDA) for the treatment of metastatic breast cancer. In exchange for the Product Payment, the Company agreed to make payments to Sagard (the "Payments") equal to 5.0% of its world-wide net sales of Oral Paclitaxel, subject to a hard cap equal to the lesser of 170% of the Product Payment and the Put/Call Price set forth in the Revenue Interest Financing Agreement (the "Hard Cap"). The Company is required to make certain additional payments to Sagard to the extent Sagard has not received Payments equaling at least $20.0 million by September 30, 2024 and at least $50.0 million by August 4, 2026, in the amount of the applicable shortfall, and, subject to the Hard Cap, if Sagard has not received Payments equaling at least $85.0 million by the tenth anniversary of the date the Product Payment is funded, in an amount such that Sagard will have obtained a 6.0% internal rate of return on the Product Payment.

Sagard and its co-investors OPB SHRP Co-Invest Credit Limited and SIMCOE SHRP Co-Invest Credit Ltd. (the "IMCO Investors") also acquired by assignment (the "Assignment") term loans and commitments equal to $50.0 million under the Senior Credit Agreement, as further discussed below. In connection with the Assignment, the Company granted warrants to Sagard and the IMCO Investors to purchase up to an aggregate of 201,865 shares of its common stock at a purchase price of $12.63 per share. As a result of the issuance of the additional warrants, the Company evaluated the debt modification in accordance with ASC 470 and concluded that the assigned debt qualified for a partial debt extinguishment of the existing Senior Credit Agreement (as defined below) with Oaktree. Therefore, the Company recorded a loss on partial extinguishment of debt in the amount of $3.0 million during the year ended December 31, 2020.

Senior Secured Loan Agreement and Detachable Warrants

On June 19, 2020, the Company entered into a senior secured loan agreement and related security agreements (the "Senior Credit Agreement") with Oaktree Fund Administration, LLC as administrative agent, and the lenders party thereto (collectively "Oaktree") to borrow up to $225.0 million in five tranches with a maturity date of June 19, 2026, bearing interest at a fixed annual rate of 11.0%. The first tranche of $100.0 million was drawn by the Company prior to June 30, 2020, with the proceeds used in part to repay in full the outstanding loan and fees under the credit agreement with Perceptive Advisors LLC and its affiliates ("Perceptive"), which resulted in a loss on extinguishment of debt of $7.2 million. The second tranche of $25.0 million was drawn by the Company prior to September 30, 2020 and the third tranche of $25.0 million was drawn by the Company prior to December 31, 2020. Additional debt tranches of $75.0 million in aggregate are available subject to the Company's achievement of certain regulatory and commercial milestones. The Company is required to make quarterly interest-only payments until June 19, 2022, after which the Company is required to make quarterly amortizing payments, with the remaining balance of the principal plus accrued and unpaid interest due at maturity. The loan agreement contains specified financial maintenance covenants. The Company was in compliance with such covenants as of December 31, 2020.

In connection with the Senior Credit Agreement, the Company granted warrants to Oaktree to purchase an aggregate of up to 908,393 shares of the Company's common stock at a purchase price of $12.63 per share. This transaction was accounted for as a detachable warrant at its fair value, using the relative fair value method, which is based on a number of unobservable inputs, and is recorded as an increase to additional paid-in-capital on the consolidated statement of stockholders' equity. The fair value of the warrants was reflected as a discount to the term loan and amortized over the life of the term loan.

Debt and Equity Offering

On July 3, 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 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, 2019 and 2018. On June 19, 2020, the Company paid off all obligations owing under, and terminated, the senior secured loan agreement with Perceptive. 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.

Private Placements

On December 9, 2019, the Company closed a private placement with a group of institutional investors, led by Kingdon Capital Management, LLC (collectively, the "Institutional Investors"), pursuant to which the Company sold an aggregate of 3,945,750 shares of its common stock to the Institutional Investors at a purchase price of $15.30 per share for aggregate net proceeds of $59.4 million, net of offering expenses of approximately $1.0 million. These shares were subsequently registered with the Securities and Exchange Commission ("SEC") on January 28, 2020.

On May 7, 2019, the Company closed a private placement with Perceptive Life Sciences Master Fund, Ltd., Avoro Capital Advisors (formerly known as venBio Select Fund LLC), OrbiMed Partners Master Fund Limited and the Biotech Growth Trust PLC (combined known as OrbiMed), (collectively, the "Investors"), pursuant to which the Company sold an aggregate of 10 million shares of its common stock to the Investors at a purchase price of $10.00 per share for aggregate net proceeds of $99.9 million, net of offering expenses of approximately $0.1 million. These shares were subsequently registered with the SEC on July 23, 2019.

Significant Risks and Uncertainties

The Company has incurred operating losses since its inception and, as a result, as of December 31, 2020 and December 31, 2019 had an accumulated deficit of $713.6 million and $567.5 million, respectively. In September 2020, the Company successfully raised $118.7 million through public offering of its shares, thus alleviated the substantial doubt about the Company's ability to continue as a going concern as of June 30, 2020. As of December 31, 2020, the Company had cash and cash equivalents of $69.6 million, restricted cash of $16.5 million, and short-term investments of $138.6 million. The Company believes that the existing cash and cash equivalents, restricted cash, and short-term investments will fund operations into the second quarter of 2022. The Company's estimates are based on relevant conditions that are known and reasonably knowable at the date of these consolidated financial statements being available for issuance, and are subject to change due to changes in business, industry or macroeconomic conditions. This forecasted cash runway does not reflect additional funding available to the Company through its existing Senior Credit Agreement with Oaktree, as administrative agent, or the Revenue Interest Financing Agreement with Sagard. Further, we do not expect to have access to additional capital under these facilities and will need to find alternative sources of financing until such time as Oral Paclitaxel is approved or will need to renegotiate these arrangements. The Company has based these estimates on assumptions that may prove to be wrong, and it could spend the available financial resources much faster than expected and need to raise additional funds sooner than anticipated. Operations have been funded primarily through the sale of common stock, senior secured loans, and to a lesser extent, from convertible bond financing, revenue, and grant funding. Although the Company plans to raise additional funds or access additional funding via the Senior Credit Agreement and Revenue Interest Financing, these plans are subject to market conditions which are outside of its control and based on the satisfaction of future milestone funding conditions, and therefore cannot be deemed to be probable.

The Company 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, unsuccessful commercialization strategy and launch plans for its proprietary drug candidates, market acceptance of the Company's products, and protection of proprietary technology. If the Company or its partners do not successfully commercialize any of the Company's product candidates, it will be unable to generate sufficient product revenue and might not, if ever, achieve profitability and positive cash flow.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). The accompanying 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

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 clinical research accruals, chargebacks, measurement of acquired assets and assumed liabilities in business combinations, provision for credit losses, inventory reserves, deferred income taxes, the estimated useful life and recoverability of long-lived assets, and the valuation of stock-based awards and other items as appropriate. 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, 2020, a gain of $0.1 million for the year ended December 31, 2019 and a loss of $0.5 million for the year ended December 31, 2018.

Cash, Cash Equivalents, Restricted Cash, and Short-term Investments

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 short-term investments including certificates of deposit. Funds held in foreign accounts that are subject to regulations governing transfers oversees are included within cash and cash equivalents. As of December 31, 2020 and 2019, the Company had $42.5 million and $7.6 million, respectively, at its Chinese subsidiaries, which were subject to Chinese funds transfer limitations, but available for the Company's general use. Restricted cash consists of deposits that are restricted as to their withdrawal or use. Restricted cash primarily include amounts held in a controlled bank account in connection with the Senior Credit Agreement. 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 a provision for credit losses, based upon a history of past write-offs, the age of the receivables, and current credit conditions.

Credit Losses

The Company estimates and records a provision for its expected credit losses related to its financial instruments, including its trade receivables and contract assets recorded under Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 606, *Revenue from Contracts with Customers* ("Topic 606"). The Company considers historical collection rates, current financial status of its customers, macroeconomic factors, and other industry-specific factors when evaluating for current expected credit losses. Forward-looking information is also considered in the evaluation of current expected credit losses. However, because of the short time to the expected receipt of accounts receivable and contract assets, the Company believes that the carrying value, net of excepted losses, approximates fair value and therefore, relies more on historical and current analysis of such financial instruments.

To determine the provision for credit losses for accounts receivable, the Company has disaggregated its accounts receivable by class of customer, as the Company determined that risk profile of its customers is consistent based on the type and industry in which they operate. These customer classes include pharmaceutical wholesalers for specialty product sales, drug manufacturers for active pharmaceutical ingredient (API) sales, and hospitals and end-users for 503B sales. Each class of customer is analyzed for estimated credit losses individually. In doing so, the Company establishes a historical loss matrix, based on the previous collections of accounts receivable by the age of such receivables, and evaluates the current and forecasted financial position of its customers, as available. Further, the Company considers macroeconomic factors and the status of the pharmaceutical industry, including unemployment rates, industry indices, and other factors, to estimate if there are current expected credit losses within its trade receivables based on the trends and the Company's expectation of the future status of such economic and industry-specific factors. The Company believes that its customers, the majority of which are in the pharmaceutical industries with sound financial condition, and therefore, the Company's evaluation of macroeconomic and industry-specific factors did not have a significant impact on the provision for credit losses. As of December 31, 2020 and 2019, the Company recorded a provision for credit losses of $0.7 million and $0.1 million, respectively, for accounts receivable related to the customer classes of pharmaceutical wholesalers, drug manufacturers, and hospitals and end users.

Expected credit losses related to contract assets are evaluated on an individual basis. The Company's contract assets relate to upfront fees or milestone payments due from licensees for which the underlying performance obligations have been satisfied. The Company evaluates the financial status of the licensee and any historical payment activity from them. Macroeconomic and industry-specific factors are considered when estimated current expected credit losses related to contract assets. Contract assets are generally classified as short-term, and the Company is in frequent communication with licensees to establish timely payment terms. If the Company expects that credit losses exist for license-related contract assets, it will record provision for such losses against the contract asset. As of December 31, 2019, the Company determined that credit losses related to its contract assets recognized in connection with its license arrangements were not expected to be significant. In the third quarter of 2020, pursuant to the 2019 Xiangxue License, the Company recognized $9.4 million license revenue, net of $0.6 million value added tax, for a milestone achievement. As of February 28, 2021, the Company only received $1.5 million of the $10.0 million milestone achievement. After consideration of historical collection rates, the current financial status of the counterparty, and other macroeconomic factors, the Company recorded a provision for its expected credit losses for the outstanding balance of $8.5 million and $0.4 million related to currency conversion in its consolidated financial statements for the three months and year ended December 31, 2020, respectively.

Inventories

Prior to the regulatory approval of product candidates, the Company may incur expenses for the manufacture of drug product to support the commercial launch of those products. Until the date at which regulatory approval has been received or is otherwise considered probable, all such costs are recorded as research and development expenses as incurred. Inventories for special products and 503B products are stated at the lower of cost and net realizable value, with approximate cost being determined on a first-in-first-out basis. 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. Reserves for inventory amounted to $6.2 million and $9.0 million as of December 31, 2020 and 2019, respectively.

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

Leases

On January 1, 2019, the Company adopted FASB Accounting Standards Update (“ASU”) No. 2016-02, *Leases (Topic 842)* on a modified retrospective basis and did not restate comparative periods as permitted under the transition guidance. The Company elected the package of practical expedients as permitted, which carries forward the Company’s assessments prior to the date of initial application with respect to lease classifications, initial direct costs as well as whether an existing contract contains a lease. Prior period amounts continue to be reported in accordance with our historic accounting under previous lease guidance, ASC 840, Leases Topic 840 (Topic 840). The Company recognizes operating leases with terms greater than one year as right-of-use (“ROU”) assets and lease liabilities on its consolidated balance sheet. A majority of the Company’s operating leases are for real estate properties used in operations located in the U.S. and Asia. The Company’s finance leases are included in property and equipment, net and long-term debt and finance lease obligations on the consolidated balance sheet. The Company’s finance leases are for manufacturing equipment in the U.S.

The lease liabilities are determined as the present value of future fixed minimum lease payments. In determining the discount rate, the Company uses rates implicit in the lease, or if not readily available, the Company uses an estimated incremental borrowing rate based on yield trends in the biotechnology and healthcare industry and debt instruments held by the Company with stated interest rates. The Company uses the stated rate per lease agreement in determining the finance lease liabilities. The lease term is determined at the commencement date and considers whether it is reasonably certain that the Company will exercise renewal options or termination options. The lease liabilities and ROU asset are amortized over the term of the lease with operating lease expenses being recognized on a straight-line basis over the lease terms.

Leases with an initial lease term of 12 months or less are not recorded on the consolidated balance sheet. Lease expense for these leases is recognized on a straight-line basis over the lease term.

Fair Value of Financial Instruments

The Company has certain financial assets and liabilities recorded at fair value which have been classified as Level 1, 2 or 3 within the fair value hierarchy as described in the accounting standards for fair value measurements. Financial instruments consist of cash and cash equivalents, restricted cash, short-term investments, accounts receivable, other current assets, accounts payable, accrued expenses, and other. These financial instruments 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, each of which represents a separate reporting unit: Oncology Innovation Platform, Commercial Platform, and Global Supply Chain Platform. Each of the three reporting units has discrete financial information that is reviewed by segment managers. Goodwill is assigned to two reporting units: Oncology Innovation Platform and Global Supply Chain Platform. 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, 2020, 2019, and 2018.

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. No impairment charges were recorded during the year ended December 31, 2020. Impairment charges of $0.2 million and $0.3 million were recorded for the years ended December 31, 2019, and 2018, respectively. See Note 6 – *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 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 to identify the 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.

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.

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; 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, 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 short-term investments. The Company deposits its cash equivalents in interest-bearing money market accounts and certificates of deposit and invests in highly liquid U.S. Treasury notes, commercial paper, and corporate bonds. The Company deposits its cash with multiple financial institutions. Cash balances exceed federally insured limits. 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, and research and development facility in China, and therefore is subject to foreign currency fluctuation and regulatory uncertainties.

Recently Adopted Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, *"Measurement of Credit Losses on Financial Instruments"* to improve reporting requirements specific to loans, receivables, and other financial instruments. The new standard requires that credit losses on financial assets, including trade receivables and held-to-maturity debt securities, measured at amortized cost be determined using an expected loss model, instead of the current incurred loss model. In addition, ASC 326 requires that credit losses related to available-for-sale debt securities be recorded through an allowance for credit losses if the Company does not intend to sell or believes that it is more likely than not they will be required to sell, and limited to the amount by which carrying value exceeds fair value. The new standard also requires enhanced disclosure of credit risk associated with financial assets. The Company adopted the standard on January 1, 2020. Based on the composition of our trade receivables, investment portfolio and other financial assets, current economic conditions and historical credit loss activity, the adoption of this standard did not have a material impact on our condensed consolidated financial statements and related disclosures. A significant portion of the Company's accounts receivable is from large pharmaceutical wholesalers in the U.S., and a licensing fee receivable from a public company in the People's Republic of China ("PRC"). The Company's estimate of expected credit losses as of January 1, 2020, using its expected credit loss evaluation process described above, resulted in no adjustments to the provision for credit losses and no cumulative-effect adjustment to retained earnings upon adoption.

3. RESTRICTED CASH

The Company has a restricted cash balance of $16.5 million as of December 31, 2020 held in a controlled bank account in connection with the Senior Credit Agreement, which requires the Company to maintain, in a debt service reserve account, a minimum cash balance equal to twelve months of interest on the outstanding loans under the Senior Credit Agreement.

4. INVENTORIES

Inventories consist of the following (in thousands):

	December 31,	
	2020	2019
Raw materials and purchased parts	$ 6,498	$ 4,176
Work in progress	776	1,870
Finished goods	21,572	26,584
Total inventories	$ 28,846	$ 32,630

5. PROPERTY AND EQUIPMENT, NET

Property and equipment, net, consists of the following (in thousands):

	December 31,	
	2020	2019
Land	$ 1,190	$ 1,117
Equipment	11,353	6,724
Furniture and fixtures	933	578
Computer hardware	4,183	3,142
Leasehold improvements	2,933	2,792
Construction in process	22,514	14,758
Property and equipment, gross	43,106	29,111
Less: accumulated depreciation	(8,718)	(5,958)
Property and equipment, net	$ 34,388	$ 23,153

Depreciation expense amounted to $2.6 million, $2.0 million, and $1.7 million for the years ended December 31, 2020, 2019, and 2018, respectively.

6. GOODWILL AND INTANGIBLE ASSETS, NET

Goodwill

The changes in the carrying amount of goodwill for each reporting unit to which goodwill is assigned for the periods indicated are as follows (in thousands):

	Global Supply Chain	Oncology Innovation Platform	Total
Balance as of January 1, 2019	$ 26,233	$ 11,262	$ 37,495
Goodwill acquired	—	1,018	1,018
Effect of currency translation adjustment	(64)	64	—
Balance as of December 31, 2019	26,169	12,344	38,513
Effect of currency translation adjustment	327	51	378
Balance as of December 31, 2020	$ 26,496	$ 12,395	$ 38,891

Intangible Assets, Net

The Company's identifiable intangible assets, net, consist of the following (in thousands):

	December 31, 2020			
	Cost/Fair Value	Accumulated Amortization	Impairments	Net
Amortizable intangible assets				
Licenses	$ 12,641	$ 5,157	$ —	$ 7,484
Polymed customer list	1,593	1,418	—	175
Polymed technology	3,712	1,685	—	2,027
Indefinite-lived intangible assets:				
CDE in-process research and development (IPR&D)	728	—	—	728
Effect of currency translation adjustment	(196)	—	—	(196)
Total intangibles, net	$ 18,478	$ 8,260	$ —	$ 10,218

	December 31, 2019			
	Cost/Fair Value	Accumulated Amortization	Impairments	Net
Amortizable intangible assets				
Licenses	$ 8,935	$ 3,561	$ —	$ 5,374
Polymed customer list	1,593	1,164	—	429
Polymed technology	3,712	1,297	—	2,415
Product rights	530	360	170	—
Indefinite-lived intangible assets:				
CDE in-process research and development (IPR&D)	728	—	—	728
Effect of currency translation adjustment	(424)	—	—	(424)
Total intangibles, net	$ 15,074	$ 6,382	$ 170	$ 8,522

As of December 31, 2020, licenses at cost include an Orascovery license of $0.4 million and licenses purchased from Gland Pharma Ltd ("Gland") of $4.4 million, a license purchased from MAIA Pharmaceuticals, Inc. ("MAIA") for $4.0 million, a license purchased from Ingenus Pharmaceuticals, LLC ("Ingenus") for $2.0 million, and licenses of other specialty products of $0.7 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 license purchased from Ingenus is being amortized over a period of 5 years, the estimated useful life of the license agreement.

The remaining intangible assets were acquired in connection with the acquisitions of Polymed Therapeutics, Inc. ("Polymed"), Comprehensive Drug Enterprises ("CDE"). Intangible assets are amortized using the straight-line method over their useful lives. 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 ("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). The Company recorded no impairments of IPR&D during the year ended December 31, 2020. During each of the years ended December 31, 2019 and 2018, the Company abandoned projects within IPR&D and therefore, the related balances of $0.2 million and $0.3 million, respectively, were written-off as impaired and were included within research and development expenses in the consolidated statement of operations and comprehensive loss. The weighted-average useful life for all intangible assets was 7.1 years as of December 31, 2020.

The Company recorded $1.8 million, $1.9 million, and $1.6 million of amortization expense for the years ended December 31, 2020, 2019, and 2018, 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, 2020 (in thousands):

Year ending December 31:	Estimated Amortization Expense
2021	$ 2,653
2022	1,834
2023	1,805
2024	1,430
2025	1,388
Thereafter	576
	$ 9,686

7. FAIR VALUE MEASUREMENTS

Financial instruments consist of cash and cash equivalents, restricted cash, short-term investments, an equity investment, accounts receivable, accounts payable, accrued expenses, and debt. Short-term investments and the equity investment are stated at fair value. Cash and cash equivalents, restricted cash, accounts receivable, accounts payable and accrued expenses, 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.

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, 2020, 2019, or 2018.

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, 2020 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	$ 5,615	$ 5,615	$ —	$ —
Short-term investments - certificates of deposit	4,070	—	4,070	—
Short-term investments - U.S. government bonds	5,000	—	5,000	—
Short-term investments - commercial paper	34,860	—	34,860	—
Financial assets included within short-term investments				
Short-term investments - certificates of deposit	20,696	—	20,696	—
Short-term investments - U.S. government bonds	14,998	—	14,998	—
Short-term investments - commercial paper	102,715	—	102,715	—
Available-for-sale investment	227	227	—	—
Total assets	$ 188,181	$ 5,842	$ 182,339	$ —

	Fair Value Measurements at December 31, 2019 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	$ 5,460	$ 5,460	$ —	$ —
Short-term investments - certificates of deposit	15,110	—	15,110	—
Short-term investments - commercial paper	51,017	—	51,017	—
Financial assets included within short-term investments				
Short-term investments - certificates of deposit	10,054	—	10,054	—
Short-term investments - commercial paper	22,835	—	22,835	—
Available-for-sale investment	250	250	—	—
Total assets	$ 104,726	$ 5,710	$ 99,016	$ —

The Company classifies its 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, certificates of deposit, 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 Corp. (“PharmaEssentia”), a company publicly traded on the Taiwan OTC Exchange. As of December 31, 2020 and 2019, the Company’s investment in PharmaEssentia is valued at the reported closing price. This investment is classified as a level 1 investment and is recorded as an available-for-sale investment within short-term investments on the Company’s consolidated balance sheet.

8. ACQUISITIONS

AXIS

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-T 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.

The Company has consolidated the financial statements of Axis into its consolidated financial statements as of and for the years ended December 31, 2020, 2019, and 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.

On September 27, 2019, the Company executed a sponsorship agreement whereby Athenex will sponsor and conduct all Investigation New Drug applications with the U.S. FDA arising from the TCR-T platform. Axis will pay a fee to the Company for these services and will reimburse Athenex for all costs incurred in connection with the work performed. For the years ended December 31, 2020 and 2019, the Company charged Axis $4.0 million and $1.2 million for these expenses, respectively. This amount is included within research and development expenses. The minority interests' portion of these expenses is recorded within net loss attributable to non-controlling interests on the Company's consolidated statements of operations and comprehensive loss.

9. ACCRUED EXPENSES

Accrued expenses consist of the following (in thousands):

	December 31,	
	2020	2019
Accrued selling fees, rebates, and royalties	$ 9,046	$ 1,577
Accrued wages and benefits	6,720	7,541
Accrued construction costs	4,104	22,811
Accrued inventory purchases	3,714	7,194
Accrued interest	3,583	—
Accrued operating expenses	3,222	1,885
Accrued clinical expenses	2,949	2,510
Accrued tax withholdings	1,948	187
Accrued costs for product launch	1,474	—
Deferred revenue	1,147	218
Accrued R&D licensing fees	366	384
Total accrued expenses	$ 38,273	$ 44,307

The accrued construction costs relate to the building of the manufacturing facility in Dunkirk, NY (see Note 13 – *Business and Economic Collaborative Agreements*). This amount, plus an additional $0.5 million paid by the Company is expected to be funded by New York State. Therefore, $4.6 million is recorded within prepaid expenses and other current assets on the Company's consolidated balance sheet as of December 31, 2020.

10. INCOME TAXES

The Company recorded income tax expense of $4.1 million, $0.9 million, and $0.1 million during the years ended December 31, 2020, 2019, and 2018, respectively. 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, 2020.

The components of loss before income tax expense consist of the following (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Domestic	$ (133,929)	$ (109,769)	$ (95,479)
Foreign	(10,417)	(14,836)	(33,132)
	$ (144,346)	$ (124,605)	$ (128,611)

The components of the income tax expense consist of the following (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Current:			
Federal	$ —	$ —	$ —
State	4	23	27
Foreign	4,026	419	455
	4,030	442	482
Deferred:			
Federal	(27,279)	(26,878)	(26,260)
State	(916)	(2,567)	(293)
Foreign	(1,424)	(2,411)	(1,863)
	(29,619)	(31,856)	(28,416)
Change in valuation allowance	29,677	32,342	28,034
	$ 4,088	$ 928	$ 100

The income tax expense differs from the federal statutory rate due to the following:

	Year Ended December 31,		
	2020	2019	2018
Statutory rate	21.0%	21.0%	21.0%
State taxes, net of federal benefit	0.7	2.0	0.2
Foreign rate differential	0.1	0.1	(0.3)
Valuation allowance	(20.3)	(25.9)	(21.6)
Stock-based compensation	(2.6)	—	—
Foreign tax withholdings	(2.3)	(0.2)	—
Other	0.6	1.9	0.6
	(2.8)%	(0.7)%	(0.1)%

Net deferred income tax liabilities consist of the following (in thousands):

	December 31,	
	2020	2019
Intangible assets	$ 11,372	$ 11,348
Property and equipment	51	77
Stock-based compensation	7,148	9,551
Net operating loss carryforwards	106,342	81,630
Tax credit carryforwards	13,528	9,191
Research and development deduction	1,859	1,493
Reserves and accruals	11,472	8,377
Gross deferred income tax assets	151,772	121,667
Less: valuation allowance	(150,864)	(120,805)
Net deferred income tax assets	908	862
Intangible assets	(821)	(862)
Property and equipment	(143)	—
Gross deferred income tax liabilities	(964)	(862)
Net deferred income tax liabilities	$ (56)	$ —

As of December 31, 2020, there exists $448.5 million federal net operating losses and $88.2 million of state net operating losses, respectively. Of the federal net operating losses, $184.8 million expire beginning in 2027 and $263.7 million have an indefinite life. In addition, there exists $34.2 million of foreign net operating losses as of December 31, 2020 which may be carried forward indefinitely.

The valuation allowance for deferred tax assets increased by $29.7 million for the year ended December 31, 2020 and increased by $32.3 million for the year ended December 31, 2019. 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 Company has provided a full valuation allowance against its deferred tax assets as it has determined that it is not more likely than not that recognition of such deferred tax assets will be utilized in the foreseeable future.

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, 2020, 2019, and 2018. The Company recognizes interest and penalties related to unrecognized tax benefits as a component of income tax 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, 2020, 2019, and 2018. The income tax returns for the taxable years 2014 to 2019 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, if any, 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.

On March 27, 2020, President Trump signed the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") into law. The CARES Act includes several significant business tax provisions that, among other things, would eliminate the taxable income limit for certain net operating losses ("NOLs") and allow businesses to carry back NOLs arising in 2018, 2019, and 2020 to the five prior tax years, accelerate refunds of previously generated corporate alternative minimum tax credits, change the business interest limitation under Internal Revenue Code ("IRC") section 163(j) of the IRC from 30 percent to 50 percent, and fix qualified improvement property from the Tax Cuts and Jobs Act of 2017. This recent legislation did not materially affect the Company's income tax position.

11. DEBT AND LEASE OBLIGATIONS

Debt

The Company's debt as of December 31, 2020 and 2019, consists of the following (in thousands):

	December 31,	
	2020	2019
Current portion of mortgage	$ 731	$ 686
Current portion of bank loan	764	—
Current portion of senior secured loan	70	—
Current portion of finance lease obligations	445	194
Current portion of operating lease obligations	3,185	3,010
Long-term portion of finance lease obligations	537	227
Long-term portion of operating lease obligations	6,355	7,620
Chongqing Maliu credit agreement	7,641	5,731
Senior secured loan, net of debt discount and financing fees of $11,601 and $3,592, respectively	138,399	46,408
Total	$ 158,127	$ 63,876

Senior Credit Agreements

During 2018, Perceptive issued a senior secured loan to the Company with a principal value of $50.0 million and a maturity date of June 30, 2023. The loan bore interest at a floating per annum rate equal to LIBOR (with a floor of 2.0%) plus 9.0%. The Company was required to make monthly interest-only payments with a bullet payment of the principal at maturity. On June 19, 2020, the Company paid off all obligations owing under, and terminated, the senior secured loan agreement with Perceptive. The secured interests were terminated in connection with the Company's payoff of all obligations. In connection with the repayment of the Perceptive loan, the Company incurred a $3.8 million prepayment fee, the unamortized debt discount of $3.1 million, and $0.3 million in other charges. The Perceptive debt extinguishment resulted in a $7.2 million loss that was included in loss on extinguishment of debt, in the consolidated statements of operations and comprehensive loss.

On June 19, 2020 ("Closing Date"), the Company entered into the Senior Credit Agreement with Oaktree to borrow up to $225.0 million in five tranches, with a maturity date of June 19, 2026. The first three tranches ("Tranche A", "Tranche B", and "Tranche C") of the term loans with an aggregate principal amount of $150.0 million were drawn by the Company in 2020. A portion of the proceeds of the first tranche was used to repay in full the senior secured loan with Perceptive, including related prepayment fees, unpaid interest, and legal fees. The fourth tranche of $25.0 million ("Tranche D") will be available to the Company from 90 days after the Closing Date through June 20, 2022, subject to the Company's satisfaction of certain regulatory and commercial milestones; and the fifth tranche of $50.0 million ("Tranche E") will be available to the Company from 90 days after the Closing Date through June 19, 2023, also subject to the Company's satisfaction of certain regulatory and commercial milestones. The loan bears interest at a fixed annual rate of 11.0%. The Company is required to make quarterly interest-only payments until June 19, 2022, after which the Company is required to make quarterly amortizing payments, with the remaining balance of the principal plus accrued and unpaid interest due at maturity. Beginning on September 17, 2020, the Company was required to pay a commitment fee on any undrawn commitments equal to 0.6% per annum, payable on each subsequent funding date or the commitment termination date. Prepayments of the loan, in whole or in part, will be subject to early prepayment fee which declines each year until the fourth anniversary date of the Closing Date, after which no prepayment fee is required. Upon the final payment, the Company must also pay an exit fee calculated based on a percentage of the aggregate principal amount of all tranches advanced to the Company, and as of December 31, 2020, the Company has reflected a long-term exit fee liability of $2.0 million within long-term debt and finance lease obligations on the consolidated balance sheet.

The Senior Credit Agreement contains certain representations and warranties, affirmative covenants, negative covenants and conditions that were customarily required for similar financings. The Company is subject to certain financial covenants under the Senior Credit Agreement, including (1) a minimum liquidity amount in cash or permitted cash equivalent investments of $20.0 million from the closing date until the date on which the aggregate principal amount of loans outstanding is greater than or equal to $150.0 million (the "First Step-Up Date"), $25.0 million from the First Step-Up Date until the date on which the aggregate principal amount of loans outstanding balance is equal to $225.0 million (the "Second Step-Up Date"), and $30.0 million from the Second Step-up Date until the maturity date; (2) minimum revenue no less than 50% of target revenue beginning with the fiscal quarter ended on December 31, 2020 and with respect to each such subsequent fiscal quarter prior to the revenue covenant termination date; (3) leverage ratio covenant not to exceed 4.50 to 1.00 as of the last day of any fiscal quarter beginning with the first fiscal quarter following the revenue covenant termination date. At December 31, 2020, the Company was in compliance with all applicable debt covenants.

Revenue Interest Financing Agreement

On August 4, 2020, the Company entered into a Revenue Interest Financing Agreement with Sagard, pursuant to which Sagard agreed to pay the Company $50.0 million to provide funding for the Company's development and commercialization of Oral Paclitaxel upon receipt of marketing authorization for Oral Paclitaxel by the U.S. FDA for the treatment of metastatic breast cancer. In exchange for the Product Payment, the Company agreed to make payments to Sagard equal to 5.0% of its world-wide net sales of Oral Paclitaxel, subject to a hard cap equal to the lesser of 170% of the Product Payment and the Put/Call Price as discussed below and further set forth in the Revenue Interest Financing Agreement. The Company is required to make certain additional payments to Sagard to the extent Sagard has not received Payments equaling at least $20.0 million by September 30, 2024 and at least $50.0 million by August 4, 2026, in the amount of the applicable shortfall, and, subject to the Hard Cap, if Sagard has not received Payments equaling at least $85.0 million by the tenth anniversary of the date the Product Payment is funded, in an amount such that Sagard will have obtained a 6.0% internal rate of return on the Product Payment.

The Company's obligations under the Revenue Interest Financing Agreement are secured, subject to customary permitted liens and other agreed upon exceptions and subject to an intercreditor agreement with Oaktree as administrative agent for the lenders under our Senior Credit Agreement, by a perfected security interest in (i) accounts receivable arising from net sales of Oral Paclitaxel and (ii) intellectual property that is claiming or covering Oral Paclitaxel itself or any method of using, making or manufacturing Oral Paclitaxel.

At any time after August 4, 2022, the Company will have the right, but not the obligation (the "Call Option"), to buy out Sagard's interest in the Payments at a repurchase price (the "Put/Call Price") equal to (a) on or before August 4, 2023, a payment sufficient to generate an internal rate of return of 18.0% of the Product Payment, (b) after August 4, 2023 and on or before August 4, 2024, a payment sufficient to generate an internal rate of return of 16.0% of the Product Payment, (c) after August 4, 2024 and on or before August 4, 2025, a payment sufficient to generate an internal rate of return of 15.0% of the Product Payment, and (d) thereafter, the greater of (i) an amount that, when paid to Sagard, would generate an internal rate of return of 13.0% of the Product Payment, and (ii) an amount equal to the product of the Product Payment and 165%, in the case of each foregoing clause (a) through (d), taking into account all other payments received by Sagard from us under the Revenue Interest Financing Agreement.

The Revenue Interest Financing Agreement contains customary representations and warranties and certain restrictions on our ability to incur indebtedness and grant liens on intellectual property related to Oral Paclitaxel. In addition, the Revenue Interest Financing Agreement provides that if certain events ("Put Option Events") occur, including certain bankruptcy events, non-payment of Payments, a change of control, an out-license or sale of all of the rights in and to Oral Paclitaxel in the U.S. (other than any out-licensing transaction that includes all or substantially all of the U.S. and European development and commercialization rights to Oral Paclitaxel with a pharmaceutical company with global annual revenues for its most recently completed fiscal year that is greater than or equal to $500.0 million attributable to its oncology business) and (subject to applicable cure periods) non-compliance with the covenants in the Revenue Interest Financing Agreement, Sagard may require us to repurchase its interests in the Payments at the Put/Call Price. Sagard may also terminate the Revenue Interest Financing Agreement if the Company has not received marketing authorization for Oral Paclitaxel by the FDA for the treatment of metastatic breast cancer by December 31, 2021.

The Company has evaluated the terms of the Revenue Interest Financing Agreement and concluded that the features of the Product Payment are similar to those of a debt instrument. Accordingly, the Company will account for the transaction as long-term debt. In connection with the debt, the Company granted warrants to Sagard and the IMCO Investors to purchase up to 201,865 shares of its common stock at a purchase price of $12.63 per share. As a result of the issuance of the additional warrants, the Company evaluated the debt modification in accordance with ASC 470 and concluded that the assigned debt qualified for a partial debt extinguishment of the existing Senior Credit Agreement with Oaktree. Therefore, the Company recorded a loss on partial extinguishment of debt in the amount of $3.0 million for the year ended December 31, 2020. The Company will subsequently measure the transaction pursuant to ASC 835 using the effective interest rate method. The Company has elected to apply the prospective method to address changes in the estimated cash flows.

Credit Agreements, Bank Loan and Mortgage

During the first quarter of 2019, the Company was issued an unsecured, subordinated bank loan from China Merchants Bank to fund operations in China. This loan had a principal value of $0.7 million, a maturity date of December 11, 2019, and bore interest at a fixed rate of 5.7% annually. The loan was paid in full as of December 31, 2019.

During the second quarter of 2019, the Company entered into a credit agreement which amended the existing partnership agreement with Chongqing Maliu Riverside Development and Investment Co., LTD ("CQ"), for a Renminbi ¥50.0 million (USD $7.7 million at December 31, 2020) line of credit to be used for the construction of the new API plant in China. The Company is required to repay the principal amount with accrued interest within three years after the plant receives the cGMP certification, with 20% of the total loan with accrued interest is due within the first twelve months following receiving the certification, 30% of the total loan with accrued interest due within twenty-four months, and the remaining balance with accrued interest due within thirty-six months. Interest accrues at the three-year loan interest rate by the People's Bank of China for the same period on the date of the deposit of the full loan amount, which is expected to approximate 4.75% annually. If the Company fails to obtain the cGMP certification within three years upon the acceptance of the plant, it shall return all renovation costs with the accrued interest to CQ in a single transaction within the first ten business days. As of December 31, 2020, the balance due to CQ was $7.6 million.

On May 15, 2020, the Company entered into a credit agreement with China Merchants Bank, enabling the Company to draw up to a Renminbi ¥5.0 million (USD $0.8 million at December 31, 2020) during the period through May 14, 2021. The Company drew the entire available credit in July 2020. This loan has a maturity date of May 14, 2021 and bears interest at a fixed rate of 4.35% annually. The Company is required to make interest and principal payment at maturity.

The mortgage payments, assumed in connection with the acquisition of CDE, extend through December 31, 2021.

Lease Obligations

As described in Note 2 - *Summary of Significant Accounting Policies*, on January 1, 2019, the Company adopted ASU No. 2016-02, *Leases (Topic 842)* on a modified retrospective basis and did not restate comparative periods as permitted under the transition guidance.

The Company has operating leases for office and manufacturing facilities in several locations in the U.S., Asia, and Latin America, and has three finance leases for manufacturing equipment used in its facilities near Buffalo, NY (see Note 20 – *Commitments and Contingencies)*. The components of lease expense are as follows (in thousands):

	Year Ended December 31, 2020	Year Ended December 31, 2019
Operating lease cost	$ 3,041	$ 3,162
Finance lease cost:		
Amortization of assets	238	81
Interest on lease liabilities	73	31
Total net lease cost	$ 3,352	$ 3,274

The Company has elected to exclude short-term leases from its operating lease ROU assets and lease liabilities. Lease costs for short-term leases were not material to the financial statements for the years ended December 31, 2020 and 2019. Variable lease costs for the years ended December 31, 2020 and 2019 were not material to the financial statements.

Supplemental balance sheet information related to leases is as follows (in thousands, except lease term and discount rate):

	December 31, 2020	December 31, 2019
Finance leases:		
Property and equipment, at cost	$ 1,535	$ 688
Accumulated amortization, net	(347)	(109)
Property and equipment, net	$ 1,188	$ 579
Current obligations of finance leases	$ 445	$ 194
Long-term portion of finance leases	537	227
Total finance lease obligations	$ 982	$ 421
Weighted average remaining lease term (in years):		
Operating leases	4.23	5.21
Finance leases	3.40	2.11
Weighted average discount rate:		
Operating leases	12.8%	12.9%
Finance leases	10.4%	5.9%

Supplemental cash flow information related to leases is as follows (in thousands):

	Year Ended December 31, 2020
Cash paid for amount included in the measurements of lease liabilities:	
Operating cash flows from operating leases	$ (3,304)
Operating cash flows from finance leases	(286)
Financing cash flows from finance leases	(73)
ROU assets recognized in exchange for new operating lease obligations	$ 852

Future minimum payments and maturities of leases is as follows (in thousands):

Year ending December 31:	Operating Leases	Finance Leases
2021	$ 3,454	$ 468
2022	2,927	275
2023	2,096	248
2024	2,002	177
2025	1,472	—
Thereafter	478	—
Total lease payments	12,429	1,168
Less: Imputed interest	(2,889)	(186)
Total lease obligations	9,540	982
Less: Current obligations	(3,185)	(445)
Long-term lease obligations	$ 6,355	$ 537

Pursuant to the public-private partnership agreements with the State of New York and CQ, the Company will rent the manufacturing facilities from the government with favorable terms. Both facilities are in the final stage of completion as of December 31, 2020. However, neither lease term had commenced as of December 31, 2020, as neither of the facilities were operational and the Company could not direct the use of the facilities. No lease costs were incurred related to the manufacturing facilities during the year ended December 31, 2020. (See Note 13 – *Business and Economic Collaborative Agreements* and Note 20 – *Commitments and Contingencies)*

The Company exercises judgment in determining the discount rate used to measure the lease liabilities. When rates are not implicit within an operating lease, the Company uses its incremental borrowing rate as its discount rate, which is based on yield trends in the biotechnology and healthcare industry and debt instruments held by the Company with stated interest rates. The Company re-assesses its incremental borrowing rate when new leases arise, or existing leases are modified.

12. RELATED PARTY TRANSACTIONS

During the years ended December 31, 2020, 2019, and 2018, 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 June 2018, the Company entered into two in-licensing agreements with Avalon BioMedical (Management) Limited (“Avalon”) wherein the Company obtained certain IP from Avalon 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, 2020 and 2019, the Company recorded $0 and $1.0 million milestone fee paid to Avalon, respectively, as research and development expenses on its condensed consolidated statement of operations and comprehensive loss. Certain 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, 2020, and, 2019, Avalon held 786,061 shares of the Company’s common stock, which represented approximately 1% of the Company’s total issued shares for both periods. Balances due from Avalon recorded on the condensed consolidated balance sheets were not significant.

In June 2019, the Company entered into an agreement whereby Avalon would hold a 90% ownership interest and the Company would hold a 10% ownership interest of the newly formed entity under the name Nuwagen Limited (“Nuwagen”), incorporated under the laws of Hong Kong. Nuwagen is principally engaged in the development and commercialization of herbal medicine products for metabolic, endocrine, and other related indications. The Company contributed nonmonetary assets in exchange for the 10% ownership interest.

b. The Company earns licensing revenue from PharmaEssentia, an entity in which the Company has an investment classified as available-for-sale (see Note 7 – *Fair Value Measurements*). Funds paid to PharmaEssentia under the license and cost-sharing agreements amounted to $0.4 million in each of the years ended December 31, 2020 and 2019. Pursuant to out-license agreements, the Company received $2.0 million, $0, and $2.3 million for the years ended December 31, 2020, 2019, and 2018, 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 $0.6 million, $2.7 million, and $0.3 million for the years ended December 31, 2020, 2019, and 2018, 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 the Company's IP to develop and commercialize Oral Irinotecan, and Oral Paclitaxel in Australia and New Zealand, and a non-exclusive license to manufacture a certain compound, but only for use in Oral Irinotecan and Oral Paclitaxel. 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. Certain family members of our executive officers work as employees or consultants of 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"). Under the agreement, FSMC agreed to pay up to $25.0 million for the construction of our North American headquarters and formulation lab and equipment in Buffalo, New York. The Company moved into the North American headquarters in October 2015 and is sub-leasing the space from FSMC for a 10-year term, with an option to extend the term for an additional 10 years.

The Company, through its partnership with FSMC, Empire State Development ("ESD"), and The State University of New York ("SUNY") Polytechnic, was to complete the construction of an ISO Class 5 high potency oral and sterile injectable pharmaceutical manufacturing facility in Dunkirk, New York. This manufacturing facility, which was originally planned to be 320,000 square feet, has been expanded to approximately 409,000 square feet to meet the required needs of the Company and within the terms of the September 2017 agreement. On September 4, 2017, the Company entered into a Grant Disbursement Agreement whereby the State agreed to grant up to approximately $208.0 million, which includes approximately $8.0 million in additional funds available from the previous $25.0 million ESD Grant for the Company's corporate offices, to fund the construction of the new pharmaceutical manufacturing facility. 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 hold ownership of the manufacturing and office facilities. Construction of these facilities is in the final stage of completion.

Chongqing Government Department of Economic Development

In October 2015, the Company completed and executed an agreement with the Banan District in Chongqing, China ("CQ") to construct a cGMP API manufacturing plant of approximately 440,000 square feet and a GMP pharmaceutical manufacturing plant of approximately 510,000 square feet 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 the construction costs and hold ownership of the facilities. Pursuant to the agreement, the Company is committed to a registration capital requirement of no less than $30.0 million, which can be used as working capital in the course of the business. As of December 31, 2020, the Company had contributed a total of $14.1 million registration capital to its subsidiary set up under the agreement. The land and buildings will be owned by CQ, and the Company 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 the Company is profitable, it will pay a monthly rent of 5 RMB per square meter of space occupied. In addition, the Company is responsible for the costs of all equipment and technology for the facilities. On January 5, 2021, Chongqing Sintaho Pharmaceutical Co., Ltd. ("CQ Sintaho"), a wholly owned subsidiary of the Company, entered into a lease agreement with Chongqing International Biological City Development & Investment Co., Ltd ("CQ D&I"), an affiliate of CQ. Pursuant to the lease agreement CQ Sintaho will lease the newly constructed API facility of 34,517 square meters rent-free, for the first 10-year term, with an option to extend the lease for an additional 10-year term, during which, if CQ Sintaho is profitable, it will pay a monthly rent of 5 Chinese Renminbi per square meter of space occupied.

In connection with these arrangements with FSMC and the Banan District we have committed to certain operational milestones.

14. STOCK-BASED COMPENSATION

Common Stock Option Plans

The Company has four equity compensation plans, adopted in 2017, 2013, 2007 and 2004 (the "Plans") which, taken together, authorize the grant of up to 16,000,000 shares of common stock to employees, directors, and consultants. On May 23, 2019, the board of directors approved the amendment and restatement of the 2017 Omnibus Incentive Plan (the "2017 Plan"), which increases the number of shares available for issuance under the plan by up to 500,000 shares, subject to the approval of the Company's stockholders at the Company's 2020 annual meeting of stockholders. Additionally, on June 14, 2017, the Company adopted its 2017 Employee Stock Purchase Plan (the "ESPP"), which authorizes the issuance of up to 1,000,000 shares of common stock for future issuances to eligible employees.

Stock Options

The total fair value of stock options vested and recorded as compensation expense during the year ended December 31, 2020, 2019, and 2018 was $9.6 million, $7.9 million, and $9.8 million, respectively. As of December 31, 2020, $18.7 million of unrecognized cost related to non-vested stock options was expected to be recognized over a weighted-average period of approximately 1.90 Years. The total intrinsic value of options exercised was approximately $1.5 million and $2.7 million for the years ended December 31, 2020 and 2019, respectively.

The following table summarizes the status of the Company's stock option activity granted under the Plans and 2017 Plan 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 Plan 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, 2019	10,916,936	$ 8.88	6.87	$ 69,785
Granted	1,970,972	11.46	—	—
Exercised	(238,630)	7.23	—	—
Forfeited and expired	(152,390)	13.31	—	—
Outstanding at December 31, 2020	12,496,888	$ 9.26	5.42	$ 22,463
Vested and exercisable at December 31, 2020	9,126,142	$ 7.89	4.29	$ 28,936

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,		
	2020	2019	2018
Weighted average grant date fair value	$ 6.93	$ 8.06	$ 9.80
Expected dividend yield	—%	—%	—%
Expected stock price volatility	67%	64%	59%
Risk-free interest rate	0.91%	2.60%	2.61%
Expected life of options (in years)	6.2	6.3	6.1

Restricted Stock Awards

The Company granted 131,000 restricted stock awards to employees during the year ended December 31, 2019. Stock-based compensation related to the restricted stock awards amounted to $1.0 million for the year ended December 31, 2020. As of December 31, 2020, $0.3 million of unrecognized cost related to non-vested restricted stock awards were expected to be recognized over a weighted-average period of approximately 1.2 years. No such awards were granted during the year ended December 31, 2020.

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, 2020 to May 31, 2021. The Company expects to offer six-month offering periods after the current period. The 2017 Plan reserved 1,000,000 shares of common stock for issuance under the ESPP. Stock-based compensation related to the ESPP amounted to $0.3 million for each of the years ended December 31, 2020 and 2019 and $0.2 million for the year ended December 31, 2018. The Company issued 50,827, 60,825, and 41,733 shares of common stock to participants during the years ended December 31, 2020, 2019, and 2018, respectively.

Stock-Based Compensation Cost

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, 2020, 2019, and 2018 (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Stock options	$ 9,557	$ 7,887	$ 9,786
Restricted stock expense	1,017	566	1,008
Stock awarded to directors and officers	—	1,105	—
Employee stock purchase plan	276	327	217
Total stock-based compensation expense	$ 10,850	$ 9,885	$ 11,011
Cost of sales	$ 249	$ 248	$ 228
Research and development expenses	3,647	3,251	2,621
Selling, general, and administrative expenses	6,954	6,386	8,162
Total stock-based compensation expense	$ 10,850	$ 9,885	$ 11,011

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,		
	2020	2019	2018
Stock options and other common stock equivalents	12,748,882	10,814,635	10,480,084
Unvested restricted common shares	76,750	45,581	113,260
Total potential dilutive common shares	12,825,632	10,860,216	10,593,344

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, 2018	$ (146)
Foreign currency translation adjustment	(525)
Unrealized gain on investment	15
Balance as of December 31, 2018	(656)
Foreign currency translation adjustment	118
Unrealized loss on investment	(97)
Balance as of December 31, 2019	(635)
Foreign currency translation adjustment	(494)
Unrealized loss on investment	(5)
Balance as of December 31, 2020	$ (1,134)

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. 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. Consequently, the Company has concluded each operating segment to be a reportable segment. The Company's operating segments are as follows:

Oncology Innovation Platform— This 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. It focuses specifically on Orascovery and Src Kinase Inhibition research platforms, and TCR-T immunotherapy and arginine deprivation therapy. This segment operates in the U.S., Taiwan, Hong Kong, mainland China, the United Kingdom, and Latin America.

Global Supply Chain Platform— This operating segment includes APS and Polymed and the construction of the manufacturing facilities in Chongqing, China and Dunkirk, NY. APS is a manufacturing company that supplies sterile injectable drugs to hospital pharmacies across the U.S. APS manufactures products under Section 503B of the Compounding Quality Act within the Federal Food, Drug & Cosmetic Act ("FDCA"). Additionally, APS provides products for the development and manufacturing of the Company's proprietary drug candidates as well as providing the Company with a cGMP analytical services function. Polymed is primarily in the business of marketing and selling API in North America, Europe, and Asia from its locations in Texas and China. Polymed also develops new compounds and processing techniques and is in the final phase of completion of the new API manufacturing facility in Chongqing, China (see Note 13 – *Business and Economic Collaborative Agreements*).

Commercial Platform— This operating segment includes APD and Athenex Oncology, which focus on the manufacturing, distribution, and sales of specialty pharmaceuticals and the pre-launch commercial activities for the Company's proprietary drugs, respectively. This segment provides services and products to external customers based mainly in the U.S.

The Company's Oncology Innovation Platform segment operates and holds long-lived assets located in the U.S., Taiwan, Hong Kong, mainland China, the United Kingdom, and Latin America. The Global Supply Chain Platform segment operates and holds long-lived assets located in the U.S. and China. The Commercial Platform segment operates and holds long-lived assets located in the U.S. 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,		
	2020	2019	2018
Total revenue:			
Oncology Innovation Platform	$ 38,851	$ 20,562	$ 32,776
Global Supply Chain Platform	20,491	33,970	31,274
Commercial Platform	89,572	50,427	30,426
Total revenue for reportable segments	148,914	104,959	94,476
Intersegment revenue	(4,523)	(3,730)	(5,376)
Total consolidated revenue	$ 144,391	$ 101,229	$ 89,100

Intersegment revenue eliminated in the above table reflects sales from the Global Supply Chain Platform to the Oncology Innovation Platform.

	Year Ended December 31,		
	2020	2019	2018
Total revenue by product group:			
Commercial product sales	$ 101,590	$ 67,411	$ 35,640
License fees	38,827	20,100	32,000
API sales	3,599	12,733	17,952
Contract manufacturing revenue	85	391	458
Medical device sales	—	—	2,344
Other revenue	290	594	706
Total consolidated revenue	$ 144,391	$ 101,229	$ 89,100

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,		
	2020	2019	2018
Net loss attributable to Athenex, Inc.:			
Oncology Innovation Platform	$ (89,189)	$ (100,919)	$ (89,912)
Global Supply Chain Platform	(19,400)	(8,575)	(16,858)
Commercial Platform	(37,590)	(14,255)	(10,670)
Total consolidated net loss attributable to Athenex, Inc.	$ (146,179)	$ (123,749)	$ (117,440)

	Year Ended December 31,		
	2020	2019	2018
Total depreciation and amortization			
Oncology Innovation Platform	$ 776	$ 762	$ 690
Global Supply Chain Platform	2,048	1,489	1,603
Commercial Platform	1,668	1,566	976
Total consolidated depreciation and amortization	$ 4,492	$ 3,817	$ 3,269

	December 31,	
	2020	2019
Total assets:		
Oncology Innovation Platform	$ 234,153	$ 194,183
Global Supply Chain Platform	99,087	63,598
Commercial Platform	51,089	52,151
Total assets	$ 384,329	$ 309,932

	Year Ended December 31,		
	2020	2019	2018
Total revenue			
United States	$ 82,362	$ 67,794	$ 37,904
China	39,796	2,105	4,416
United Kingdom	19,289	1,023	—
South Korea	2,354	513	—
Austria	226	4,422	9,569
India	—	3,066	3,457
Spain	—	20,000	30,000
Other foreign countries	364	2,306	3,754
Total consolidated revenue	$ 144,391	$ 101,229	$ 89,100

	December 31,	
	2020	2019
Total property and equipment, net:		
United States	$ 15,511	$ 11,486
China	18,877	11,667
Total property and equipment, net	$ 34,388	$ 23,153

Customer revenue and accounts receivable concentration amounted to the following for the identified periods:

	Year Ended December 31,		
	2020	2019	2018
Percentage of total revenue by customer:			
Customer A	26%	—	—
Customer B	14%	15%	9%
Customer C	14%	16%	12%
Customer D	13%	—	—
Customer E	10%	14%	9%
Customer F	—	20%	34%

	December 31,	
	2020	2019
Percentage of total accounts receivable by customer:		
Customer A	33%	45%
Customer B	23%	31%
Customer C	16%	10%

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. Below is a description of principal activities – separated by reportable segments – from which the Company generates its revenue (See Note 17 – *Business Segment, Geographic, and Concentration Risk Information*).

1. Oncology Innovation Platform

The Company out-licenses certain of its IP to other 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 the contracts to identify its performance obligations within the contract. Most of the Company's out-license arrangements contain multiple performance obligations and variable pricing. After the performance obligations are identified, the Company determines the transaction price, which generally includes upfront fees, milestone payments related to the achievement of developmental, regulatory, or commercial goals, and royalty payments on net sales of licensed products. The Company considers whether the transaction price is fixed or variable, and whether such consideration is subject to return. Variable consideration is only included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. If any portion of the transaction price is constrained, it is excluded from the transaction price until the constraint no longer exists. The Company then allocates the transaction price to the performance obligation to which the consideration is related. Where a portion of the transaction price is received and allocated to continuing performance obligations under the terms of the arrangement, it is recorded as deferred revenue and recognized as revenue when (or as) the underlying performance obligation is satisfied.

The Company's contracts may contain one or multiple promises, including the license of IP and development services. The licensed IP is capable of being distinct from the other performance obligations identified in the contract and is distinct within the context of the contract, as upon transfer of the IP, the customer is able to use and benefit from it, and the customer could obtain the development services from other parties. The Company also considers the economic and regulatory characteristics of the licensed IP and other promises in the contract to determine if it is a distinct performance obligation. The Company considers if the IP is modified or enhanced by other performance obligations through the life of the agreement and whether the customer is contractually or practically required to use updated IP. The IP licensed by the Company has been determined to be functional IP. The IP is not modified during the license period and therefore, the Company recognizes revenues from any portion of the transaction price allocated to the licensed IP when the license is transferred to the customer and they can benefit from the right to use the IP. The Company recognized $37.7 million in license revenue, net of $2.3 million value added tax ("VAT"), and $1.0 million in license revenue from two of the Company's out-license arrangements for the year ended December 31, 2020. The Company recognized revenue allocated to the licensed IP performance obligation upon transfer of the license of $0.1 million for the year ended December 31, 2019.

Other performance obligations included in most of the Company's out-licensing agreements include performing development services to reach clinical and regulatory milestone events. The Company satisfies these performance obligations at a point-in-time, because the customer does not simultaneously receive and consume the benefits as the development occurs, the development does not create or enhance an asset controlled by the customer, and the development does not create an asset with no alternative use. The Company considers milestone payments to be variable consideration measured using the most likely amount method, as the entitlement to the consideration is contingent on the occurrence or nonoccurrence of future events. The Company allocates each variable milestone payment to the associated milestone performance obligation, as the variable payment relates directly to the Company's efforts to satisfy the performance obligation and such allocation depicts the amount of consideration to which the Company expects to be entitled for satisfying the corresponding performance obligation. The Company re-evaluates the probability of achievement of such performance obligations and any related constraint and adjusts its estimate of the transaction price as appropriate. To date, no amounts have been constrained in the initial or subsequent assessments of the transaction price. The Company did not recognize revenue from other performance obligations included in the Company's out-licensing agreements during the year ended December 31, 2020. The Company recognized revenue allocated to development performance obligations upon transfer to the customer of $20.0 million for the year ended December 31, 2019.

Certain out-license agreements include performance obligations to manufacture and provide drug product in the future for commercial sale when the licensed product is approved. For the commercial, sales-based royalties, the consideration is predominantly related to the licensed IP and is contingent on the customer's subsequent sales to another commercial customer. Consequently, the sales- or usage-based royalty exception would apply. Revenue will be recognized for the commercial, sales-based milestones as the underlying sales occur.

The Company exercises significant judgment when identifying distinct performance obligations within its out-license arrangements, determining the transaction price, which often includes both fixed and variable considerations, and allocating the transaction price to the proper performance obligation. The Company did not use any other significant judgments related to out-licensing revenue during the years ended December 31, 2020 and 2019.

2. Global Supply Chain Platform

The Company's Global Supply Chain Platform manufactures API for use internally in its research and development activities as well as its clinical studies, and for sale to pharmaceutical customers globally. The Company generates additional revenue on this platform, by providing small to mid-scale cGMP manufacturing of clinical and commercial products for pharmaceutical and biotech companies and selling pharmaceutical products under 503B regulations set forth by the U.S. FDA.

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.

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. Upon the sale by the wholesaler to the end-user, the wholesaler will chargeback the difference, if any, between the original list price and price at which the product was sold to the end-user. The Company also offers cash discounts, which approximate 2.3% 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. Further, the Company offers contractual allowances, generally in the form of rebates or administrative fees, to certain wholesale customers, group purchasing organizations ("GPOs"), and end-user customers, consistent with pharmaceutical industry practices. Revenues are recorded net of provisions for variable consideration, including discounts, rebates, GPO allowances, price adjustments, returns, chargebacks, promotional programs and other sales allowances. Accruals for these provisions are presented in the consolidated financial statements as reductions in determining net sales and as a contra asset in accounts receivable, net (if settled via credit) and other current liabilities (if paid in cash). As of December 31, 2020 and 2019, the Company's total provision for chargebacks and other deductions included as a reduction of accounts receivable totaled $12.6 million and $14.4 million, respectively. The Company's total provision for chargebacks and other revenue deductions was $89.3 million, $87.2 million, and $36.5 million for the years ended December 31, 2020, 2019, and 2018, respectively.

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, 2020			
	Oncology Innovation Platform	**Global Supply Chain Platform**	**Commercial Platform**	**Consolidated Total**
United States	$ —	$ 12,079	$ 70,283	$ 82,362
China	38,760	1,036	—	39,796
United Kingdom	—	—	19,289	19,289
South Korea	—	2,354	—	2,354
Other Foreign Countries	91	499	—	590
Total Revenue	$ 38,851	$ 15,968	$ 89,572	$ 144,391

	For the Year Ended December 31, 2019			
	Oncology Innovation Platform	Global Supply Chain Platform	Commercial Platform	Consolidated Total
United States	$ —	$ 17,367	$ 50,427	$ 67,794
Spain	20,000	—	—	20,000
Austria	—	4,422	—	4,422
India	—	3,066	—	3,066
China	562	1,543	—	2,105
United Kingdom	—	1,023	—	1,023
Other Foreign Countries	—	2,819	—	2,819
Total Revenue	$ 20,562	$ 30,240	$ 50,427	$ 101,229

	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
Austria	—	9,569	—	9,569
China	2,776	1,640	—	4,416
India	—	3,457	—	3,457
Other Foreign Countries	—	3,754	—	3,754
Total Revenue	$ 32,776	$ 25,898	$ 30,426	$ 89,100

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,	
	2020	2019
Accounts receivable, gross	$ 45,792	$ 31,207
Chargebacks and other deductions	(12,552)	(14,394)
Provision for credit losses	(9,637)	(124)
Accounts receivable, net	$ 23,603	$ 16,689
Deferred revenue	1,147	218
Total contract liabilities	$ 1,147	$ 218

The following tables illustrate accounts receivable by reportable segments (in thousands).

	December 31, 2020			
	Oncology Innovation Platform	Global Supply Chain Platform	Commercial Platform	Consolidated Total
Accounts receivable, gross	$ 10,783	$ 4,074	$ 30,935	$ 45,792
Chargebacks and other deductions	—	(1)	(12,551)	(12,552)
Provision for credit losses	(8,919)	(164)	(554)	(9,637)
Accounts receivable, net	$ 1,864	$ 3,909	$ 17,830	$ 23,603

	December 31, 2019			
	Oncology Innovation Platform	Global Supply Chain Platform	Commercial Platform	Consolidated Total
Accounts receivable, gross	$ 49	$ 1,522	$ 29,636	$ 31,207
Chargebacks and other deductions	—	(1)	(14,393)	(14,394)
Provision for credit losses	—	(114)	(10)	(124)
Accounts receivable, net	$ 49	$ 1,407	$ 15,233	$ 16,689

The Company incurs contract obligations on general customer purchase orders that have been accepted but unfulfilled. Due to the short duration of time between order acceptance and delivery of the related product or service, the Company has determined that the balance related to these contract obligations is generally immaterial at any point in time. The Company monitors the value of orders accepted but unfulfilled at the close of each reporting period to determine if disclosure is appropriate. As of December 31, 2020, $1.0 million and $0.1 million of contract liabilities related to customer deposits were made by customers of the Oncology Innovation Platform and the Global Supply Chain Platform, respectively, and as of December 31, 2019, $0.2 million of contract liabilities related to customer deposits were made by customers of the Global Supply Chain Platform.

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 2020 Quarter Ended			
	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
	(In thousands, except per share data)			
Statements of Operations Data:				
Revenue:				
Product sales	$ 18,547	$ 40,167	$ 24,780	$ 21,780
License and other revenue	28,388	5	10,696	28
Total revenue	46,935	40,172	35,476	21,808
Cost of sales	19,572	33,006	24,510	18,267
Gross profit	27,363	7,166	10,966	3,541
Operating expenses:				
Research and development expenses	17,192	22,015	18,390	18,307
Selling, general, and administrative expenses	25,748	17,486	22,220	31,401
Total operating expenses	42,940	39,501	40,610	49,708
Operating loss	(15,577)	(32,335)	(29,644)	(46,167)
Net loss	(19,718)	(41,051)	(37,268)	(50,397)
Less: net loss attributable to non-controlling interests	(289)	(600)	(462)	(904)
Net loss attributable to Athenex, Inc.	$ (19,429)	$ (40,451)	$ (36,806)	$ (49,493)
Net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted	$ (0.24)	$ (0.50)	$ (0.44)	$ (0.53)

	Fiscal 2019 Quarter Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
	(In thousands, except per share data)			
Statements of Operations Data:				
Revenue:				
Product sales	$ 25,163	$ 22,033	$ 19,237	$ 14,102
License and other revenue	144	164	127	20,259
Total revenue	25,307	22,197	19,364	34,361
Cost of sales	19,902	16,942	17,071	15,704
Gross profit	5,405	5,255	2,293	18,657
Operating expenses:				
Research and development expenses	24,475	18,507	19,588	21,823
Selling, general, and administrative expenses	15,188	17,169	16,283	18,109
Total operating expenses	39,663	35,676	35,871	39,932
Operating loss	(34,258)	(30,421)	(33,578)	(21,275)
Net loss	(36,230)	(32,105)	(34,787)	(22,411)
Less: net loss attributable to non-controlling interests	(997)	(74)	(29)	(684)
Net loss attributable to Athenex, Inc.	$ (35,233)	$ (32,031)	$ (34,758)	$ (21,727)
Net loss per share attributable to Athenex, Inc. common stockholders, basic and diluted	$ (0.53)	$ (0.44)	$ (0.45)	$ (0.28)

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 was recorded as of December 31, 2018 and was derecognized upon adoption ASC 842 on January 1, 2019. 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, 2020, 2019, and 2018.

In July 2015, CDE entered into an agreement to lease facilities in Hong Kong, which expired in November 2019. Under the rental agreement, CDE made 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 $0.3 million, and $0.4 million for the years ended December 31, 2019, and 2018, respectively. In November 2019, CDE entered into an agreement to lease facilities in Hong Kong through November 2022. Rent expense is recognized on a straight-line basis, amounted to $0.1 million for the year ended December 31, 2020.

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 for each of the years ended December 31, 2020, 2019, and 2018. A deferred rent liability for this agreement of $0.3 million was recorded as of December 31, 2018 and was derecognized upon adoption ASC 842 on January 1, 2019. In lieu of a security deposit, an irrevocable letter of credit was issued to the landlord in the amount of $0.2 million.

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 for each of the years ended December 31, 2020, 2019, and 2018.

The Company entered into additional leases for lab space, warehouse facilities, and various equipment in, Houston, TX; Cranford, NJ; Taipei, Taiwan; Latin America; and Buffalo, NY, during 2019 and 2020 which expire at various times through 2026. Rent expense recognized for these operating leases was not material to the financial statements for the years ended December 31, 2020, 2019, and 2018.

Future minimum payments under the non-cancelable operating leases consists of the following as of December 31, 2020 (in thousands):

Year ending December 31:	Minimum payments
2021	$ 3,454
2022	2,927
2023	2,096
2024	2,002
2025	1,472
Thereafter	478
	$ 12,429

Commitments under New York State and Chongqing Partnerships

Under its partnerships with New York State and CQ as described in Note 13 – *Business and Economic Collaborative Arrangements*, the Company is committed to contribute to the building of manufacturing facilities in Dunkirk, NY and Chongqing, China. Pursuant to the arrangement with New York State, the Company is committed to bear the costs of the construction of the facility in Dunkirk, NY in excess of approximately $208.0 million. The Company is 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 elected to extend the lease for an additional 10-year term. The Company is responsible for all operating costs and expenses for the facility and is committed to spending $1.52 billion on operational expenses in the first 10-year term in the facility, and an additional $1.5 billion on operational expenses if elected to extend the lease for a second 10-year term. Pursuant to the arrangement with CQ, the Finance Bureau of Banan District of Chongqing is responsible for investing in the construction of the API and formulation plants and completing renovation in accordance with U.S. cGMP standards. The Company is able to lease the facility rent free, for the first 10-year term, with an option to extend the lease for an additional 10-year term, during which, if the Company is profitable, it will pay a monthly rent of 5 RMB per square meter of space occupied or, it will have the option to purchase the land and building. If the Company does not purchase the land and building after 20 years at the price described above, it will have the option to lease the land and building with rental fee charged at market price of construction area. The Company is responsible for the costs of all equipment and technology for the facilities. Neither of these facilities in New York State and Chongqing, China were completed, and neither leases were effective as of December 31, 2020 (see Note 13 – *Business and Economic Collaborative Agreements*).

Legal Proceedings

From time to time, the Company may become subject to other legal proceedings, claims and litigation arising in the ordinary course of business. In addition, the Company may receive letters alleging infringement of patent or other intellectual property rights. The Company is not currently a party to any other material legal proceedings, nor is it aware of any pending or threatened litigation that, in the Company's opinion, would have a material adverse effect on the business, operating results, cash flows or financial condition should such litigation be resolved unfavorably.

21. SUBSEQUENT EVENTS

In January 2021, the Company entered into a manufacture and supply agreement with Ingenus for Arsenic Trioxide Injection pursuant to which Ingenus will be the Company's exclusive supplier of the product and granted the Company a license to market and sell the product to acute care GPOs and their entire memberships as provided by said GPOs, IDNs and to hospitals within the U.S. Under the agreement, the Company is entitled to 45% of the net profits from its sales of the product and also entitled to a marketing allowance. The agreement has a 5 year term, which may be extended upon mutual agreement (See Commercialization - Our Commercial Platform – Specialty Pharmaceuticals – Ingenus Agreements).

On January 5, 2021, CQ Sintaho entered into a lease agreement with CQ D&I. Under the lease agreement, the provisions of which are consistent with those agreed upon in the 2015 Agreement, CQ Sintaho will lease the newly constructed API facility, or Sintaho API Facility, of 34,517 square meters rent-free, for the first 10-year term, with an option to extend the lease for an additional 10-year term, during which, if CQ Sintaho is profitable, it will pay a monthly rent of 5 RMB per square meter of space occupied (See Note 13 - *Business and Economic Collaborative Agreements - Chongqing Government Department of Economic Development*). The Company will account for this in accordance with ASC 842 and is evaluating the effect on its consolidated financial statements.

On February 15, 2021, the Company entered into a Second Amendment to its 2011 license agreement with PharmaEssentia for tirbanibulin ointment. The Second Amendment expands the territory to include Japan and South Korea and includes a license to use the intellectual property for additional dermatology indications and skin cancer in the existing territories. Pursuant to this Second Amendment, the Company will receive an upfront payment of $0.5 million, milestone payments up to $13.0 million associated with the achievement of certain development and sales milestone, as well as royalties on the sale of tirbanibulin ointment in Japan and South Korea. The Company will supply PharmaEssentia with the licensed products under a supply arrangement for a separate fee. The Company will account for this in accordance with ASC 606 and is evaluating the effect on its consolidated financial statements.

On February 26, 2021, the Company received a CRL from the FDA regarding our NDA for Oral Paclitaxel for the treatment of metastatic breast cancer. The FDA issues a CRL to indicate that the review cycle for an application is complete and that the application is not ready for approval in its present form. In the CRL, the FDA indicated its concern of safety risk to patients in terms of an increase in neutropenia-related sequelae on the Oral Paclitaxel arm compared with the IV paclitaxel arm in the Phase III study. The FDA also expressed concerns regarding the uncertainty over the results of the primary endpoint of ORR at week 19 conducted by BICR. The agency stated that the BICR reconciliation and re-read process may have introduced unmeasured bias and influence on the BICR. Additionally, the FDA recommended that the Company conduct a new adequate and well-conducted clinical trial in a patient population with MBC representative of the population in the U.S. The agency determined that additional risk mitigation strategies to improve toxicity, which may involve dose optimization and / or exclusion of patients deemed to be at higher risk of toxicity, are required to support potential approval of the NDA. The Company is working to consider the appropriate next steps in the development of Oral Paclitaxel. The Company plans to request a meeting with the FDA to discuss the FDA's response, engage in a dialogue on the design and scope of a clinical trial to address the agency's requirements and align on the next steps required to obtain approval.

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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, 2020. 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, 2020, 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, 2020 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

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, 2020, 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, 2020.

Deloitte & Touche LLP, Independent Registered Public Accounting Firm., the independent registered public accounting firm that audited the Company's consolidated financial statements, issued an attestation report on management's effectiveness of the Company's internal control over financial reporting as of December 31, 2020, as stated in their report which is included below.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Athenex, Inc.

Opinion on Internal Control over Financial Reporting

We have audited the internal control over financial reporting of Athenex, Inc. and subsidiaries (the "Company") as of December 31, 2020, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by COSO.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated financial statements as of and for the year ended December 31, 2020, and the related notes and the schedule listed in the Index at Item 15 (collectively referred to as the "financial statements") of the Company and our report dated March 1, 2021 expressed an unqualified opinion on those financial statements.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying *Management's Annual Report on Internal Control Over Financial Reporting*. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed 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. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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.

/s/ Deloitte & Touche LLP

Williamsville, New York
March 1, 2021

Item 9B. Other Information.

None.

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,” and “Delinquent Section 16(a) Reports” contained in our proxy statement related to the 2021 Annual Meeting of Stockholders (Proxy Statement) currently scheduled to be held on June 4, 2021, 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, 2020					
Provision for credit losses	$ 124	$ 9,577 (1)	$ —	$ (64) (1)	$ 9,637
Allowance for chargebacks and other deductions	$ 14,394	$ 90,237 (2)	$ —	$ (92,079) (2)	$ 12,552
Deferred tax asset valuation allowance	$ 120,805	$ —	$ 30,059 (3)	$ —	$ 150,864
December 31, 2019					
Provision for credit losses	$ 9	$ 488 (1)	$ —	$ (373) (1)	$ 124
Allowance for chargebacks and other deductions	$ 13,101	$ 95,100 (2)	$ —	$ (93,807) (2)	$ 14,394
Deferred tax asset valuation allowance	$ 88,455	$ —	$ 32,350 (3)	$ —	$ 120,805
December 31, 2018					
Provision for credit losses	$ 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

(1) Increases in the provision for credit losses consist of our provision for credit losses, which is included within selling, general, and administrative expenses on the consolidated statements of operations and comprehensive loss. Decreases in the provision for credit losses 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.

(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
4.2	Form of Warrant to Purchase Common Stock (Oaktree).	Form 8-K	001-38112	4.1	June 22, 2020
4.3	Form of Warrant to Purchase Common Stock (Sagard and IMCO Investors).	Form 8-K	001-38112	4.1	August 6, 2020
4.4	Description of Securities	Form 10-K	001-38112	4.2	March 2, 2020
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+	Amended and Restated 2017 Omnibus Incentive Plan.	Form 10-Q	001-38112	10.4	August 6, 2020
10.6+	Form of Stock Option Award Agreement pursuant to the 2017 Omnibus Incentive Plan.	Form S-1/A	333-217928	10.5	June 2, 2017
10.7+	Form of Restricted Stock Award Agreement pursuant to the 2017 Omnibus Incentive Plan.				Filed herewith
10.8+	2017 Employee Stock Purchase Plan.	Form S-1/A	333-217928	10.6	June 2, 2017
10.9^	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
10.9.1	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
10.9.2	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
10.9.3	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
10.9.4^	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
10.9.5	Fifth Amendment to License Agreement by and between Athenex, Inc. and Hanmi Pharmaceutical Co. Ltd., effective as of September 4, 2018.	Form 10-K	001-38112	10.45	March 11, 2019

10.10^	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
10.11^	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
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	10.10.1	May 12, 2017
10.12^	License Agreement by and between Kinex Pharmaceuticals, Inc. and PharmaEssentia Corp., effective as of December 16, 2013.	Form 10-Q	001-38112	10.11	May 7, 2020
10.12.1	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
10.12.2^	Second Amendment to License Agreement by and between Athenex, Inc. and PharmaEssentia Corp., effective as of November 27, 2018.	Form 10-Q	001-38112	10.11.2	May 7, 2020
10.13^	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
10.14^	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 10-Q	001-38112	10.13	May 7, 2020
10.15^	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
10.15.1^	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
10.15.3^	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
10.16^	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
10.16.1^	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
10.16.2	Limited Liability Company Agreement of Peterson Athenex Pharmaceuticals, LLC, effective as of October 4, 2016.	Form S-1	333-217928	10.15.2	May 12, 2017
10.17^	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
10.18^	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

10.19	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
10.19.1	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
10.19.2	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
10.20	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
10.21	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
10.21.1	Supplemental Agreement to 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 April 1, 2019 (English translation of original foreign language agreement).	Form 10-Q	001-38112	10.20.1	August 7, 2019
10.22^	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
10.23	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
10.24+	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
10.25+	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
10.26+	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
10.27+	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
10.28+	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+	Employment Agreement between Athenex, Inc. and Randoll Sze dated as of August 20, 2018.	Form 8-K	001-38112	10.1	August 20, 2018
10.30	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

10.30.1	Amendment to Grant Disbursement Agreement by and between the New York State Urban Development Corporation d/b/a Empire State Development and Athenex, Inc., dated as July 24, 2019.	Form 10-Q	001-38112	10.29.1	August 7, 2019
10.31^	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
10.31.1^	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
10.31.2^	Letter Agreement by and between Athenex, Inc., Almirall, S.A. and Aqua Pharmaceuticals LLC, dated as of September 26, 2018.	Form 10-Q	001-38112	10.4	November 14, 2018
10.31.3	Second Amendment to License and Development Agreement by and between Athenex, Inc., Almirall, S.A., and Aqua Pharmaceuticals LLC, dated as of June 18, 2019.	Form 10-Q	001-38112	10.30.2	August 7, 2019
10.32	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
10.32.1	First Amendment to Agreement by and between M+W U.S., Inc. and Athenex, Inc., effective as of March 27, 2018.	Form 10-Q	001-38112	10.31.1	May 9, 2019
10.32.2	Second Amendment to Agreement by and between M+W U.S., Inc. and Athenex, Inc., effective as of October 1, 2018.	Form 10-Q	001-38112	10.31.2	May 9, 2019
10.32.3	Third Amendment to Agreement by and between Exyte U.S., Inc. (f/k/a M+W U.S., Inc.), effective as of January 23, 2019.	Form 10-Q	001-38112	10.31.3	May 9, 2019
10.33^	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
10.34^	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
10.35^	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
10.36**	License Agreement between the Company and Guangzhou Xiangxue Pharmaceutical Co., Ltd., dated December 12, 2019.	Form 8-K	001-38112	10.1	December 16, 2019
10.36.1	Second Supplemental Agreement to License Agreement dated December 12, 2019 by and among Athenex, Inc. and Chongqing Taihao Pharmaceutical Co. Ltd. and Guangzhou Xiangxue Pharmaceutical Co., Ltd., dated June 30, 2020.	Form 8-Q	001-38112	10.5	August 6, 2020
10.37	Share 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
10.38	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	Share Purchase Agreement by and among Athenex, Inc., Perceptive Life Sciences Master Fund, Ltd., venBio Select Fund LLC, OrbiMed Partners Master Fund Limited, and The Biotech Growth Trust PLC, dated as of May 3, 2019.	Form 8-K	001-38112	10.1	May 6, 2019

10.40	Registration Rights Agreement by and among Athenex, Inc., Perceptive Life Sciences Master Fund, Ltd., venBio Select Fund LLC, OrbiMed Partners Master Fund Limited, and The Biotech Growth Trust PLC, dated as of May 7, 2019.	Form S-3	333-232772	4.2	July 23, 2019
10.41	Share Purchase Agreement by and among Athenex, Inc., M. Kingdon Offshore Master Fund, LP, Schonfeld Strategic 460 Fund LLC, Point72 Associates, LLC, J. Goldman Master Fund, L.P., and Avoro Life Sciences Fund LLC, dated as of December 5, 2019.	Form 8-K	001-38112	10.1	December 5, 2019
10.42	Registration Rights Agreement by and among Athenex, Inc., M. Kingdon Offshore Master Fund, LP, Schonfeld Strategic 460 Fund LLC, Point72 Associates, LLC, J. Goldman Master Fund, L.P., and Avoro Life Sciences Fund LLC, dated as of December 9, 2019.	Form S-3	333-236104	4.2	January 28, 2020
10.43	Credit Agreement and Guaranty dated as of June 19, 2020, by and among Athenex, Inc., the subsidiary guarantors from time to time party thereto, the lenders from time to time party thereto, and Oaktree Fund Administration, LLC, as administrative agent.	Form 8-K	001-38112	10.1	June 22, 2020
10.44	Security Agreement dated as of June 19, 2020, by and among Athenex, Inc., the subsidiary guarantors from time to time party thereto, the lenders from time to time party thereto, and Oaktree Fund Administration, LLC, as administrative agent.	Form 10-Q	001-38112	10.2	August 6, 2020
10.45	Registration Rights Agreement by and among Athenex, Inc. and the purchasers named therein, dated as of June 19, 2020.	Form 10-Q	001-38112	10.3	August 6, 2020
10.46	Revenue Interest Financing Agreement dated as of August 4, 2020, by and between Athenex, Inc. and Sagard Healthcare Royalty Partners, LP.	Form 8-K	001-38112	10.1	August 6, 2020
10.47	Security Agreement dated as of August 4, 2020, by and between Athenex, Inc. and Sagard Healthcare Royalty Partners, LP.	Form 10-Q	001-38112	10.2	November 5, 2020
10.48	Intercreditor Agreement dated as of August 4, 2020, by and among Oaktree Fund Administration, LLC, as administrative agent, and Sagard Healthcare Royalty Partners, LP, and as acknowledged by Athenex, Inc.	Form 10-Q	001-38112	10.3	November 5, 2020
10.49	Assignment and Assumption dated as of August 4, 2020, by and among Athenex, Inc, as the borrower, Sagard Healthcare Royalty Partners, LP, OPB SHRP Co-Invest Credit Limited and SIMCOE SHRP Co-Invest Credit Ltd., as assignees, and the affiliates of Oaktree Capital Management, L.P. party thereto as assignors, and the other assignees party thereto.	Form 10-Q	001-38112	10.4	November 5, 2020
10.50**	Asset Purchase and Sale Agreement dated as of September 1, 2020 by and between Athenex Pharmaceutical Division, LLC and Ingenus Pharmaceuticals, LLC.				Filed herewith
10.51**	Co-Marketing, Manufacture and Supply Agreement dated as of November 2, 2020 by and between Athenex Pharmaceutical Division, LLC and Ingenus Pharmaceuticals, LLC.				Filed herewith
10.52**	Manufacture and Supply Agreement dated as of January 15, 2021 by and between Athenex Pharmaceutical Division, LLC and Ingenus Pharmaceuticals, LLC.				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	Inline XBRL Instance Document.	—	—	—	Filed herewith
101.SCHY	Inline XBRL Taxonomy Extension Schema Document.	—	—	—	Filed herewith
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.	—	—	—	Filed herewith
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.	—	—	—	Filed herewith
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.	—	—	—	Filed herewith
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.	—	—	—	Filed herewith
104	Cover Page Interactive Data File	—	—	—	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.

** Certain portions of this exhibit have been omitted (indicated by asterisks) pursuant to Item 601(b) of Regulation S-K of the Securities Act of 1933, as amended, because such omitted information is (i) not material and (ii) would be competitively harmful if publicly disclosed.

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.

Date: March 1, 2021

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 1, 2021
/s/ Randoll Sze Randoll Sze	Chief Financial Officer (Principal Financial and Accounting Officer)	March 1, 2021
/s/ Kim Campbell Kim Campbell	Director	March 1, 2021
/s/ Manson Fok Manson Fok	Director	March 1, 2021
/s/ Jinn Wu Jinn Wu	Director	March 1, 2021
/s/ Benson Tsang Benson Tsang	Director	March 1, 2021
/s/ Robert Spiegel Robert Spiegel	Director	March 1, 2021
/s/ Stephanie Davis Stephanie Davis	Director	March 1, 2021
/s/ Jordan Kanfer Jordan Kanfer	Director	March 1, 2021
/s/ John Moore Vierling John Moore Vierling	Director	March 1, 2021

Exhibit 10.7

Award Number:

ATHENEX, INC. 2017 OMNIBUS INCENTIVE PLAN

RESTRICTED STOCK AWARD AGREEMENT

1. Issuance of Shares. Athenex, Inc., a Delaware corporation (the "Company"), hereby issues to the Grantee (the "Grantee") named in the Notice of Restricted Stock Award (the "Notice"), the Total Number of Shares of Common Stock Awarded set forth in the Notice (the "Shares"), subject to the Notice, this Restricted Stock Award Agreement (the "Restricted Stock Agreement") and the terms and provisions of the Company's 2017 Omnibus Incentive Plan, as amended from time to time (the "Plan"), which are incorporated herein by reference. Unless otherwise defined herein, the terms defined in the Plan shall have the same defined meanings in this Restricted Stock Agreement. All Shares issued under this Restricted Stock Agreement will be deemed issued to the Grantee as fully paid and nonassessable shares, subject to forfeiture as provided in the Notice and this Restricted Stock Agreement, and the Grantee will have the right to vote the Shares at meetings of the Company's stockholders.

2. Transfer Restrictions. The Shares issued to the Grantee under this Restricted Stock Agreement may not be sold, transferred by gift, pledged, hypothecated, or otherwise transferred or disposed of by the Grantee prior to the date when the Shares become vested pursuant to the vesting schedule specified in the Notice (the "Vesting Schedule"). Any attempt to transfer Restricted Shares (as defined in the Notice) in violation of this Section 2 will be null and void and will be disregarded.

3. Additional Securities and Distributions.

(a) Any securities or cash received as the result of ownership of the Restricted Shares (the "Additional Securities"), including, but not by way of limitation, warrants, options and securities received as a stock dividend or stock split, or as a result of a recapitalization or reorganization or other similar change in the Company's capital structure, will be subject to the same conditions and restrictions as the Restricted Shares with respect to which they were issued, including, without limitation, the Vesting Schedule.

(b) The Grantee will be entitled to direct the Company to exercise any warrant or option received as Additional Securities upon supplying the funds necessary to do so, in which event the securities so purchased will constitute Additional Securities, subject to the same conditions and restrictions as the Restricted Shares with respect to which they were issued, including, without limitation, the Vesting Schedule, but the Grantee may not direct the Company to sell any of these warrants or options. However, the Grantee understands and agrees that any Additional Securities received from the Grantees' exercise of any warrant or option received as Additional Securities may be subject to forfeiture under the terms of the Notice, the Plan and this Restricted Stock Agreement and that Company will have no liability to the Grantee resulting from any forfeiture of these Additional Securities.

(c) If Additional Securities consist of a convertible security, the Grantee may exercise any conversion right, and any securities so acquired will constitute Additional Securities, subject to the same conditions and restrictions as the Restricted Shares with respect to which they were issued, including, without limitation, the Vesting Schedule.

4. Taxes.

(a) No Section 83(b) Election. As a condition to receiving the Shares, the Grantee agrees to refrain from making an election pursuant to Section 83(b) of the Code with respect to the Shares.

(b) Tax Liability. The Grantee is ultimately liable and responsible for all taxes owed by the Grantee in connection with the Award, regardless of any action the Company or any Related Entity takes with respect to any tax withholding obligations that arise in connection with the Award. Neither the Company nor any Related Entity makes any representation or undertaking regarding the treatment of any tax withholding in connection with the grant or vesting of the Award or the subsequent sale of Shares subject to the Award. The Company and its Related Entities do not commit and are under no obligation to structure the Award to reduce or eliminate the Grantee's tax liability.

(c) Payment of Withholding Taxes. Prior to any event in connection with the Award (e.g., vesting) that the Company determines may result in any tax withholding obligation, whether United States federal, state, local or non-U.S., including any employment tax obligation (the "Tax Withholding Obligation"), the Grantee must arrange for the satisfaction of the minimum amount of the Tax Withholding Obligation in a manner acceptable to the Company. At any time not less than five (5) business days (or fewer number of business days as determined by the Administrator) before any Tax Withholding Obligation arises (e.g., a vesting date), the Grantee may elect to satisfy the Grantee's Tax Withholding Obligation that the Company determines is sufficient by (i) wire transfer to such account as the Company may direct, (ii) delivery of a certified check payable to the Company, or (iii) such other means as specified from time to time by the Administrator. If the Grantee does not make such arrangements, the Company may, at its sole election, satisfy the Grantee's Tax Withholding Obligation in accordance with clause (i) below.

(i) By Sale of Shares. The Grantee's acceptance of this Award constitutes the Grantee's instruction and authorization to the Company, and any brokerage firm determined acceptable to the Company for this purpose, to sell on the Grantee's behalf a whole number of Shares from those Shares issuable to the Grantee as the Company determines to be appropriate to generate cash proceeds sufficient to satisfy the minimum applicable Tax Withholding Obligation (a "Tax Obligation Sale"). These Shares will be sold on the day the Tax Withholding Obligation arises (e.g., a vesting date) or as soon thereafter as practicable. The Grantee will be responsible for all broker's fees and other costs related to a Tax Obligation Sale, and the Grantee agrees to indemnify and hold the Company harmless from any losses, costs, damages, or expenses relating to any Tax Obligation Sale. To the extent the proceeds of a Tax Obligation Sale exceed the Grantee's minimum Tax Withholding Obligation, the Company agrees to pay the excess in cash to the Grantee. The Grantee acknowledges that the Company or its designee is under no obligation to arrange for a Tax Obligation Sale at any particular price, and that the proceeds of any Tax Obligation Sale may not be sufficient to satisfy the Grantee's minimum Tax Withholding Obligation. Accordingly, the Grantee agrees to pay to the Company or any Related Entity as soon as practicable, including through additional payroll withholding, any amount of the Tax Withholding Obligation that is not satisfied bya Tax Obligation Sale.

The Company or a Related Entity also may satisfy any Tax Withholding Obligation by offsetting any amounts (including, but not limited to, salary, bonus and severance payments) payable to the Grantee by the Company and/or a Related Entity. Furthermore, in the event of any determination that the Company has failed to withhold a sum sufficient to pay all withholding taxes due in connection with the Award, the Grantee agrees to pay the Company the amount of the deficiency in cash within five (5) days after receiving a written demand from the Company to do so, whether or not the Grantee is an employee of the Company at that time.

5. Stop-Transfer Notices. In order to ensure compliance with the restrictions on transfer specified in this Restricted Stock Agreement, the Notice or the Plan, the Company may issue appropriate "stop transfer" instructions to its transfer agent, if any, and, if the Company transfers its own securities, it may make appropriate notations to the same effect in its own records. The Company may issue a "stop transfer" instruction if the Grantee fails to satisfy any Tax Withholding Obligations.

6. Refusal to Transfer. The Company will not be required (i) to transfer on its books any Shares that have been sold or otherwise transferred in violation of any of the provisions of this Restricted Stock Agreement (an "Improper Transfer") or (ii) to treat as owner of any Shares or to accord the right to vote or pay dividends to any purchaser or other transferee of Shares in an Improper Transfer.

7. Restrictive Legends. The Grantee understands and agrees that the Company will cause the legends set forth below, or substantially equivalent legends, to be placed upon any certificate(s) evidencing ownership of the Shares together with any other legends that may be required by the Company or by state or federal securities laws:

THE SHARES REPRESENTED BY THIS CERTIFICATE ARE RESTRICTED BY THE TERMS OF THAT CERTAIN RESTRICTED STOCK AWARD AGREEMENT BETWEEN THE COMPANY AND THE NAMED STOCKHOLDER. THE SHARES REPRESENTED BY THIS CERTIFICATE MAY BE TRANSFERRED ONLY IN ACCORDANCE WITH THE RESTRICTED STOCK AWARD AGREEMENT, A COPY OF WHICH IS ON FILE WITH THE SECRETARY OF THE COMPANY.

8. [Intentionally Omitted.]

9. Entire Agreement: Governing Law. The Notice, the Plan and this Restricted Stock Agreement constitute the entire agreement of the parties with respect to the subject matter of this Restricted Stock Agreement and supersede in their entirety all prior undertakings and agreements of the Company and the Grantee with respect to the subject matter of this Restricted Stock Agreement, and may not be modified adversely to the Grantee's interest except by means of a writing signed by the Company and the Grantee. The Notice, the Plan and this Restricted Stock Agreement are to be construed in accordance with and governed by the internal laws of the State of Delaware without giving effect to any choice of law rule that would cause the application of the laws of any jurisdiction other than the internal laws of the State of Delaware to the rights and duties of the parties. Should any provision of the Notice, the Plan or this Restricted Stock Agreement, including, without limitation, any provision of Section 13 of this Restricted Stock Agreement, be determined for any reason to be illegal, invalid or unenforceable, it is the specific intent of the parties that the provision will be modified to the minimum extent necessary to make it or its application valid and enforceable and will

be enforced to the fullest extent allowed by law and the other provisions of the Notice, the Plan and this Restricted Stock Agreement will nevertheless remain effective and will remain enforceable.

10. Construction. The captions used in the Notice and this Restricted Stock Agreement are inserted for convenience and shall not be deemed a part of the Award for construction or interpretation. Except when otherwise indicated by the context, the singular shall include the plural and the plural shall include the singular. Use of the term "or" is not intended to be exclusive, unless the context clearly requires otherwise.

11. Administration and Interpretation. Any question or dispute regarding the administration or interpretation of the Notice, the Plan or this Restricted Stock Agreement shall be submitted by the Grantee or by the Company to the Administrator. The resolution of such question or dispute by the Administrator shall be final and binding on all persons.

12. Venue and Waiver of Jury Trial. The Company and the Grantee (the "parties") agree that any suit, action, or proceeding arising out of or relating to the Notice, the Plan or this Restricted Stock Agreement shall be brought in the United States District Court for Western District of New York (or should such court lack jurisdiction to hear such action, suit or proceeding, in an appropriate state court in the State of New York) and that the parties shall submit to the jurisdiction of such court. The parties irrevocably waive, to the fullest extent permitted by law, any objection the party may have to the laying of venue for any such suit, action or proceeding brought in such court. **THE PARTIES ALSO EXPRESSLY WAIVE ANY RIGHT THEY HAVE OR MAY HAVE TO A JURY TRIAL OF ANY SUCH SUIT, ACTION OR PROCEEDING**. If any one or more provisions of this Section 13 shall for any reason be held invalid or unenforceable, it is the specific intent of the parties that such provisions shall be modified to the minimum extent necessary to make it or its application valid and enforceable.

13. Notices. Any notice required or permitted hereunder shall be given in writing and shall be deemed effectively given upon personal delivery, upon deposit for delivery by an internationally recognized express mail courier service or upon deposit in the United States mail by certified mail (if the parties are within the United States), with postage and fees prepaid, addressed to the other party at its address as shown in these instruments, or to such other address as such party may designate in writing from time to time to the other party.

14. Language. If the Grantee has received this Restricted Stock Agreement or any other document related to the Plan translated into a language other than English and if the translated version is different than the English version, the English version will control, unless otherwise prescribed by Applicable Law.

15. Nature of Award. In accepting the Award, the Grantee acknowledges and agrees that:

(a) the Plan is established voluntarily by the Company, it is discretionary in nature, and it may be modified, amended, suspended or terminated by the Company at any time, unless otherwise provided in the Plan and this Restricted Stock Agreement;

(b) the Award is voluntary and occasional and does not create any contractual or other right to receive future awards, or benefits in lieu of awards, even if awards have been awarded repeatedly in the past;

(c) all decisions with respect to future awards, if any, will be at the sole discretion of the Company;

(d) the Grantee's participation in the Plan is voluntary;

(e) the Grantee's participation in the Plan shall not create a right to any employment with the Grantee's employer and shall not interfere with the ability of the Company or the employer to terminate the Grantee's employment relationship, if any, at any time;

(f) the Award is not part of normal or expected compensation or salary for any purposes, including, but not limited to, calculating any severance, resignation, termination, redundancy, end of service payments, bonuses, long-service awards, pension or retirement or welfare benefits or similar payments and in no event should be considered as compensation for, or relating in any way to, past services for the Company or any Related Entity;

(g) in the event that the Grantee is not an Employee of the Company or any Related Entity, the Award and the Grantee's participation in the Plan will not be interpreted to form an employment or service contract or relationship with the Company or any Related Entity;

(h) the future value of the Shares is unknown and cannot be predicted with certainty;

(i) in consideration of the Award, no claim or entitlement to compensation or damages shall arise from termination of the Award or diminution in value of the Award or Shares acquired upon vesting of the Award, resulting from termination of the Grantee's Continuous Service by the Company or any Related Entity (for any reason whatsoever and whether or not in breach of local labor laws) and in consideration of the grant of the Award, the Grantee irrevocably releases the Company and any Related Entity from any such claim that may arise; if, notwithstanding the foregoing, any such claim is found by a court of competent jurisdiction to have arisen, then, by signing the Notice, the Grantee shall be deemed irrevocably to have waived his or her right to pursue or seek remedy for any such claim or entitlement;

(j) in the event of termination of the Grantee's Continuous Service (whether or not in breach of local labor laws), the Grantee's right to receive Awards under the Plan and to vest in such Awards, if any, will (except as otherwise provided in the Notice or herein) terminate effective as of the date that the Grantee is no longer providing services and will not be extended by any notice period mandated under local law (e.g., providing services would not include a period of "garden leave" or similar period pursuant to local law); furthermore, in the event of termination of the Grantee's Continuous Service (whether or not in breach of local labor laws), the Administrator shall have the exclusive discretion to determine when the Grantee is no longer providing services for purposes of this Award;

(k) the Company is not providing any tax, legal or financial advice, nor is the Company making any recommendations regarding the Grantee's participation in the Plan or the Grantee's acquisition or sale of the underlying Shares; and

(l) the Grantee is hereby advised to consult with the Grantee's own personal tax, legal and financial advisers regarding the Grantee's participation in the Plan before taking any action related to the Plan.

19. Data Privacy.

(a) The Grantee hereby explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of the Grantee's personal data as described in the Notice and this Restricted Stock Agreement by and among, as applicable, the Grantee's employer, the Company and any Related Entity for the exclusive purpose of implementing, administering and managing the Grantee's participation in the Plan.

(b) The Grantee understands that the Company and the Grantee's employer may hold certain personal information about the Grantee, including, but not limited to, the Grantee's name, home address and telephone number, date of birth, social insurance or other identification number, salary, nationality, job title, any Shares or directorships held in the Company, details of all Awards or any other entitlement to Shares awarded, canceled, vested, unvested or outstanding in the Grantee's favor, for the exclusive purpose of implementing, administering and managing the Plan ("Data").

(c) The Grantee understands that Data will be transferred to any third party assisting the Company with the implementation, administration and management of the Plan. The Grantee understands that the recipients of the Data may be located in the Grantee's country, or elsewhere, and that the recipients' country may have different data privacy laws and protections than the Grantee's country. The Grantee understands that the Grantee may request a list with the names and addresses of any potential recipients of the Data by contacting the Grantee's local human resources representative. The Grantee authorizes the Company and any other possible recipients which may assist the Company (presently or in the future) with implementing, administering and managing the Plan to receive, possess, use, retain and transfer the Data, in electronic or other form, for the sole purpose of implementing, administering and managing the Grantee's participation in the Plan. The Grantee understands that Data will be held only as long as is necessary to implement, administer and manage the Grantee's participation in the Plan. The Grantee understands that the Grantee may, at any time, view Data, request additional information about the storage and processing of Data, require any necessary amendments to Data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing the Grantee's local human resources representative. The Grantee understands, however, that refusal or withdrawal of consent may affect the Grantee's ability to participate in the Plan. For more information on the consequences of the Grantee's refusal to consent or withdrawal of consent, the Grantee understands that the Grantee may contact the Grantee's local human resources representative.

END OF AGREEMENT

Exhibit 10.50

Certain information in this exhibit marked [*] has been excluded from the exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

ASSET PURCHASE AND SALE AGREEMENT

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between

ATHENEX PHARMACEUTICAL DIVISION, LLC

and

INGENUS PHARMACEUTICALS, LLC

THIS ASSET PURCHASE AGREEMENT (this "Agreement") is made and entered into effective as of this 1st day of September, 2020 (the "Effective Date"), by and between Ingenus Pharmaceuticals LLC, a Delaware limited liability company ("Ingenus"), and Athenex Pharmaceutical Division, LLC a Delaware limited liability company ("Buyer") .

WHEREAS, Ingenus owns the Product ANDA (as defined below) for the Product (as defined below) and other assets that are part of the Purchased Assets (as defined below);

WHEREAS, Buyer wishes to purchase the Purchased Assets from Ingenus, all upon the terms and subject to the conditions hereinafter set forth;

NOW, THEREFORE, in consideration of the mutual covenants and conditions hereinafter expressed, Buyer and Ingenus agree as follows:

1. Definitions. For purposes of this Agreement, the following terms have the following meanings:

(a) "Affiliate" means, with respect to any Person that controls. is controlled by, or is under common control with such Person. For purposes of this definition, "control" shall mean (a) in the case of corporate entities, direct or indirect ownership of more than fifty percent (50%) of the stock or shares entitled to vote for the election of directors, or otherwise having the power to control or direct the affairs of such Person; and (b) in the case of non-corporate entities, direct or indirect ownership of more than fifty percent (50%) of the equity interest or the power to direct the management and policies of such noncorporate entities.

(b) "Ancillary Documents" means (i) the Bill of Sale, (ii) evidence, reasonably acceptable to Buyer, that the Purchased Assets are owned, beneficially and of record, by Ingenus, including, without limitation, evidence that the Product ANDA has been assigned to Ingenus by Novast prior to the date hereof.

(c) "ANDA" means an Abbreviated New Drug Application filed with the FDA pursuant to its rules and regulations.

(d) "Assumed Liabilities" shall have the meaning ascribed to the term in Section 3 of this Agreement.

(e) "Bill of Sale" means a bill of sale and assignment and assumption agreement to be executed and delivered by each Party concurrently with the execution of this Agreement, substantially in the form of Exhibit A.

(f) "Business Day" means any day on which commercial banks are not authorized or required to close in New York, New York.

(g) Buyer Indemnified Parties" shall have the meaning ascribed to the term in Section 9(a) of this Agreement.

(h) "cGMP" means standards and methods required to be used in, and the facilities or controls to be used for, the manufacture of a drug, as set forth in FDA regulations in 21 C.F.R. Parts 210 and 21 1.

(i) "Confidential Information" shall have the meaning ascribed to the term in Section 10(d) of this Agreement.

(j) "Encumbrance" means, with respect to any asset, any imperfection of title, mortgage, charge, lien, claim, security interest, easement, right of first refusal, pledge or encumbrance of any nature whatsoever.

(k) "Excluded Assets" shall have the meaning ascribed to the term in Section 2(b) of this Agreement.

(l) "FDA" means the United States Food and Drug Administration, including all divisions under its direct control, or any successor organization thereto.

(m) "Governmental Entity " means any international, national, foreign, provincial, federal, state or local judicial, legislative, executive, administrative or regulatory body or authority.

(n) "Indemnified Parties" shall have the meaning ascribed to the term in Section 9 of this Agreement.

(o) "Indemnifying Party" shall have the meaning ascribed to the term in Section 9 of this Agreement.

(p) "Law" means each federal, state, provincial, municipal, local, or foreign law, statute, ordinance, order, determination, judgment, common law, code, rule, guideline, official standard, requirement or regulation, enacted, enforced, entered, promulgated, or issued by any Governmental Entity.

(q) "Liabilities" means any and all debts, liabilities and obligations, whether accrued or fixed, absolute or contingent, matured or unmatured, or known or unknown, including those arising under applicable Law or governmental action and those arising under any contract, arrangement, commitment or undertaking. or otherwise.

(r) "Losses" shall have the meaning ascribed to the term in Section 7(a) of this Agreement.

(s) "Party" or "Parties" means Ingenus or Buyer or both, as applicable.

(t) "Permitted Encumbrances" means (a) any minor imperfections of title or similar Encumbrance that do not, and would not reasonably be expected to, individually or in the aggregate, materially impair the value or interfere with the use of, the Purchased Assets, (b) Encumbrances for Taxes that are not yet due and payable, or (c) Encumbrances incurred as a result of any facts or circumstances related to Buyer or its Affiliates.

(u) "Person" means any individual, partnership (general or limited), association, corporation, limited liability company, joint venture, trust, estate, limited liability partnership, unincorporated organization, government (or any agency or political subdivision thereof) or other legal person or organization.

(v) "Product" means the Product set forth on Schedule 1 hereto next to the Product ANDA.

(w) "Product ANDA" means the ANDA set forth on Schedule 1 hereto, as filed with the FDA as a generic equivalent to the corresponding RLD, and all amendments, supplements or annual reports thereto.

(x) "Purchased Assets" means (i) the Product ANDA; (ii) any correspondence with the FDA, in each case to the extent relating to the Product ANDAs; (iii) all PADER reports filed for the Product; (iv) reports of all adverse drug experience cases in the United States that were reported to Ingenus for the Products; and (v) all intellectual property rights, of any kind, related to the Purchased Assets.

(y) "Purchase Price" shall have the meaning ascribed to the term in Section 4(a) of this Agreement.

(z) "RLD" or "RLDs" means one or more of the reference listed drugs set forth on Schedule I hereto next to the corresponding Product.

(aa) "Tax(es)" means (a) any and all federal, state, local, or non-U.S. taxes, assessments, charges, duties, fees, imports, levies or other charges from any Governmental Entity (including interest, penalties or additions associated therewith), including income, franchise, capital stock, real property, personal property, tangible, withholding, employment, payroll. social security (or similar tax), social contribution, unemployment compensation, unclaimed property escheat, disability, transfer, sales, bulk sales, use, excise, license, occupation, registration, stamp, premium, environmental, customs duties, alternative or add-on minimum, estimated, gross receipts, value-added, ad valorem, profits, estimated, and all other taxes of any kind for which Ingenus may have any Liability imposed by any Governmental Entity, whether disputed or not, and any charges, interest or penalties imposed by any Governmental Entity, and (b) any Liability in respect of any items described in clause (a) payable by reason of contract, assumption, transferee liability, operation of Law, Treasury Regulations section 1.1 502-6(a) (or any predecessor or successor thereof or any analogous or similar provision under Law) or otherwise.

(bb) "Tax Return" means any report, return, election, notice, estimate. declaration, information statement and other forms and documents (including all schedules, exhibits and other attachments thereto) relating to and filed or required to be filed with a taxing authority in connection with any Taxes (including estimated Taxes).

(cc) "Territory" means the United States of America, including its districts, territories, commonwealths and possessions.

(dd) "Ingenus Indemnified Parties" shall have the meaning ascribed to the term in Section 9(a) of this Agreement.

2. Purchase and Sale.

(a) Upon the terms and subject to the conditions of this Agreement, Ingenus hereby transfers, sells, conveys, assigns and delivers to Buyer, and Buyer hereby purchases, acquires, accepts and assumes, all of Ingenus's right, title and interest within the Territory in, to and under the Purchased Assets, free and clear of all Encumbrances, other than Permitted Encumbrances, for the consideration set forth herein. Concurrently herewith, each of the Parties is executing and delivering to the other the Bill of Sale.

(b) Ingenus and Buyer expressly agree and acknowledge that the Purchased Assets do not include any assets of any kind, nature, character or description (whether real, personal or mixed, whether tangible or intangible, whether absolute, accrued, contingent, fixed or otherwise, and wherever situated) that are not expressly included within the definition of Purchased Assets (the "Excluded Assets"). For purposes hereof, it is agreed that the Excluded Assets include, without limitation, (i) information or data relating to any assets of Ingenus and its Affiliates other than the Purchased Assets and (ii) any and all trademarks, trade names, brand names, logotypes, symbols, service marks, and trade dress, and any registrations or applications for any of the foregoing.

(c) Buyer acknowledges and agrees that Ingenus may retain such copies of all or any part of the documentation that Ingenus delivers to Buyer pursuant to paragraph (a) as are reasonably necessary for archival purposes and for purposes of complying with applicable Law and for legal and regulatory purposes as a seller of pharmaceutical products and that all such retained copies shall be deemed the Confidential Information of the Buyer that shall be subject to the provisions of Section 10.

(d) Assumption of Liabilities and Obligations. Buyer agrees that from and after the Effective Date, Buyer will be responsible for and will pay, perform and/or otherwise discharge when due those Liabilities (including any Liabilities arising in respect of Taxes) arising from and after the Effective Date to the extent directly arising from or related to the Purchased Assets, including, without limitation: (i) Liabilities arising on or after the Effective Date from any patent infringement claim or other lawsuit brought by any third party, the FDA or any other Governmental Entity, in all cases only to the extent that they relate to Product sold by or on behalf of the Buyer and its Affiliates on or after the Effective Date; (ii) Liabilities arising on or after the Effective Date from any FDA or any other Governmental Entity action or notification filed on or after the Effective Date in all cases only to the extent related to the Purchased Assets following the Effective Date; (iii) Liabilities arising on or after the Effective Date from any product liability claims relating to Product sold by or on behalf of Buyer, its Affiliates, agents or assignees on or after the Effective Date; and (iv) state and federal Medicaid/Medicare rebates and payments, and all credits, chargebacks, rebates, discounts, allowances, incentives and similar payments in connection with the sale of Product by or on behalf of Buyer and its Affiliates on or after the Effective Date (collectively, the "Assumed Liabilities"). It is understood and agreed that the "Assumed Liabilities" do not include (a) any Liabilities that arose prior to the Effective Date, including any amounts accrued prior to the Effective Date or that arise from and after the Date that relate to the Purchased Assets or any other Liabilities set forth in clauses (i) through (iv) above in each case that relate to or arise in respect of the period prior to the Date or (b) any Product sold or distributed by or on behalf of Ingenus, Novast or any of their respective Affiliates, which will remain the Liabilities of Ingenus.

3. Assumption of Regulatory Commitments.

(a) From and after the Effective Date, Buyer will be in control of, and responsible for, all costs and Liabilities arising from or related to any commitments or obligations to any Governmental Entity relating to the Product or the Product ANDA, or otherwise related to the Purchased Assets with respect to the period following the Effective Date.

(b) From and after the Effective Date, Buyer will be responsible for communications with any Governmental Entity involving the Product ANDA or any batches of Product manufactured after the Effective Date. Ingenus will forward to Buyer any correspondence received by Ingenus after the Effective Date from the FDA solely to the extent related to the Purchased Assets within one (1) business day of receipt by Ingenus.

(c) From and after the Effective Date, Buyer shall be responsible for all adverse experience reporting to the FDA in respect of the Products; provided, however, that Ingenus shall cooperate with Buyer's requests regarding adverse experience information with respect to the Product to ensure that all adverse experience data and documentation for the Product are transferred to Buyer. Legacy adverse experience data and documentation will be transferred to the Buyer no later than 30 calendar days following the date hereof. Any new adverse experience reports, any follow-up adverse experience reports or medical inquiries received by Ingenus will be forwarded to Buyer in accordance with quality agreement , together with any source documents within one (1) Business Day.

(d) Ingenus covenants and agrees that it shall deliver electronic copies of the ANDA and all materials, information or data related to the manufacture of the Product included therein (including any such information included in the Chemistry, Manufacturing and Controls section of the ANDA), to Buyer by mail or FTP site no later than the earlier of five (5) business days following the date hereof and two (2) days following delivery of FDA Notice of Transfer pursuant to Section 11 below, with complete paper copies thereof to follow by mail no later than 30 days following the Closing Date.

Ingenus shall continue to maintain the drug listing for the Product, including the annual drug listing certifications under 21 C.F.R. 207. Ingenus will work with Buyer to update the drug listing in the event that there are any corrections or labeling updates required under regulations the drug listing will be delisted promptly following the date upon which the last marketed batch of the Product has reached its expiration date.

4. Purchase Price. The Parties covenant and agree as follows:

(a) Purchase Price. In consideration for the transfer of the Purchased Assets to Buyer, upon receipt of the executed Ancillary Documents from Ingenus, on the Effective Date, Buyer shall pay to Ingenus, by wire transfer of immediately available funds into an account designated in writing to the Buyer by Ingenus, the amount of Two Million United States Dollars ($2,000,000.00) (the "Purchase Price"). The Purchase Price shall be paid to Ingenus by Buyer in 10 equal calendar quarterly installments of $200,000 each beginning on the earlier of (i) the end of the first calendar quarter following the Product launch or (ii) March 31, 2021.

(b) The Purchase Price will be allocated among the Purchased Assets as of the Effective Date in accordance with applicable Law and as may be agreed by the Parties. Each of the Parties shall report (and to cause its Affiliates to report) the transactions contemplated by this Agreement in a manner consistent with applicable Law and with the terms of this Agreement, and agrees not to take any position inconsistent therewith in any Tax Return, in any Tax refund claim, in any litigation or otherwise.

(c) All transfer, sales, value added, stamp duty and similar Taxes solely and directly related to payment of the Purchase Price which are payable in connection with the transactions contemplated hereby will be borne by Buyer.

(d) If Buyer is required by Law to withhold Taxes from any amounts due to Ingenus under this Agreement, Buyer shall (a) deduct such Taxes from the amounts due, (b) pay the Taxes to the proper Governmental Authority, and (c) deliver to Ingenus a statement including the amount of Tax withheld and the basis therefore, together with such other information it may have that may be necessary for Ingenus to determine Tax credits available to it. Buyer will work with Ingenus to apply a reduced withholding Tax rate or zero rate to the extent available pursuant to applicable Law.

(e) **Default in Purchase Price Installment Payments by Buyer.** In the event that the Buyer fails to make any installment payment on the Purchase Price as described in section 4(a) above, the Buyer shall be in default of this Agreement. Ingenus shall provide notice of default to the Buyer and the Buyer shall have fifteen (15) days to cure such default. In the event of an uncured default by the Buyer, the Buyer agrees to immediately and without any delay, transfer the Purchased Assets back to Ingenus for one-dollar ($1). Buyer agrees to appoint Ingenus as its attorney-in-fact to execute any such documents as may be reasonably required to transfer the Purchased Assets back to Ingenus, including but not limited to any transfer letters to the FDA.

5. Representations and Warranties: Covenants.

(a) Each of the Parties represents and warrants to the other Party that as of the Effective Date:

i. such Party has the requisite corporate or company power and authority to enter into this Agreement and to consummate the transactions contemplated hereby;

ii. neither the execution and delivery of this Agreement by such Party, nor its performance hereunder, conflicts with or will result in any violation or breach of, or constitutes (with or without due notice or lapse of time or both) a default under any of the terms or conditions of any note, indenture, license, agreement or other instrument or obligation to which it is a party or by which it or any of its properties or assets may be bound; or to its best knowledge, violates any applicable Law;

iii. this Agreement and each Ancillary Document executed by it, is a legal, valid and binding agreement of such Party, enforceable in accordance with its terms, subject to applicable bankruptcy, insolvency, reorganization, moratorium, fraudulent transfer and other similar laws affecting creditors' rights generally from time to time in effect and to general principles ofequity (including concepts ofmateriality, reasonableness, good faith and fair dealing), regardless of whether considered in a proceeding in equity or at law;

iv. there are no claims, suits, actions or other proceedings pending or threatened against such Party at law or in equity before or by any federal, state, municipal or other governmental department, commission, board bureau, agency or instrumentality, domestic or foreign, which may in any way materially adversely affect the performance of such Party's obligations under this Agreement or the transactions contemplated hereby; such Party has not, and will not, directly or indirectly, enter into any contract or any other transaction with any third party that conflicts or derogates from its undertakings hereunder; and

vi. such Party has not been debarred, is not subject to debarment, and will not use, in any capacity in connection with the obligations to be performed under this Agreement, any Person who has been debarred pursuant to Section 346 of the United States Food, Drug and Cosmetic Act.

(b) In addition, Ingenus hereby represents and warrants to Buyer that as of the Effective Date:

i. there is no proceeding, material suit, claim or similar action pending or, to its knowledge threatened against the Product, Product ANDA or Purchased Assets; no proceeding or inquiry is pending, or, to its knowledge, has been threatened or made by any Governmental Entity relating to any Product ANDA;

ii. Ingenus is the owner of record of the Product ANDA;

iii. Ingenus has good and marketable title to the Purchased Assets, free and clear of all Encumbrances other than Permitted Encumbrances, and Ingenus has no knowledge of any Liabilities relating to the Purchased Assets;

(c) All representations and warranties contained in this Section 6 shall survive the Effective Date and shall remain operative and in full force and effect for a period of thirty (30) months following the Effective Date. Notwithstanding anything herein to the contrary, any breach of a representation or warranty that is the subject of a claim that is asserted in writing prior to the time at which it would otherwise terminate pursuant to this paragraph shall survive with respect to such claim or any dispute with respect thereto until the final resolution thereof.

6. EXCEPT AS EXPRESSLY SET FORTH HEREIN, INGENUS IS NOT MAKING AND HEREBY EXPRESSLY DISCLAIMS, ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, TITLE OR NON-INFRINGEMENT. WITHOUT DEROGATING FROM THE GENERALITY OF THE FOREGOING, EXCEPT AS EXPRESSLY SET FORTH HEREIN, BUYER ACKNOWLEDGES AND AGREES THAT INGENUS IS SELLING THE PURCHASED ASSETS ON AN "AS IS" AND "WHERE IS" BASIS AND INGENUS MAKES NO REPRESENTATION OR WARRANTY HEREUNDER WITH RESPECT TO THE PURCHASED ASSETS OR THE PRODUCTS INCLUDING, WITHOUT LIMITATION, ANY GUARANTEE THAT FDA APPROVAL WILL BE OBTAINED, RELATING TO THE MANUFACTURE AND/OR MARKETING OF ANY PRODUCT.

7 Indemnification.

(a) Subject to Section 9, Buyer shall indemnify, defend and hold Ingenus and its Affiliates and their respective officers, directors, employees, agents and subcontractors ("Ingenus Indemnified Parties") harmless from and against any and all Liability, damage, loss, cost or expense (including reasonable attorneys' fees and expenses) ("Losses"), including any claim for personal injury or death, arising out of or resulting from (i) Buyer's material breach of any of its representations or warranties in this Agreement (ii) Buyer's material breach of any of its covenants, agreements or obligations set forth in this Agreement, (iii) Buyer's gross negligence or willful misconduct, and (iv) any and all Assumed Liabilities.

(b) Subject to Section 9, Ingenus shall indemnify, defend and hold Buyer and its Affiliates and their respective officers, directors, employees, agents and subcontractors (“Buyer Indemnified Parties") harmless from and against any and all Losses, including any claim for personal injury or death, arising out of or resulting from (i) Ingenus's material breach of any of its representations or warranties in this Agreement, (ii) Ingenus's material breach of any

covenants, agreements or obligations set forth in this Agreement, (iii) Ingenus's gross negligence or willful misconduct, (iv) any and all Liabilities relating to the Excluded Assets or any other asset that is not a Purchased Asset and any Liabilities other than the Assumed Liabilities.

Buyer Indemnified Parties and Ingenus Indemnified Parties are sometimes referred to herein as "Indemnified Parties".

8. Limitations.

(a) The amount of any Losses for which either Ingenus or Buyer, as the case may be, is liable shall be reduced by the aggregate amount actually recovered under any indemnity agreement, contribution agreement, or any other agreement between any of the Indemnified Parties, on the one hand, and any third party, on the other hand, with respect to such Losses net of any costs associated with the recovery thereof.

(b) Except for claims based on fraud or a breach of Section 12 or to the extent payable in a Third Party Claim, in no event shall either Party or its Affiliates have any liability to the other Party for indirect, incidental, special or consequential damages (including lost profits) of the other arising out of the performance or failure to perform any obligations set forth herein, irrespective of whether attributable to breach of contract, breach of warranty, negligence, strict liability or otherwise; provided that the foregoing does not limit any of the obligations or Liability of either Party or its Affiliates under Section 9 with respect to claims of unrelated third parties.

9. Indemnification Procedure.

(a) In order for an Indemnified Party to be entitled to any indemnification provided for under this Agreement, such Indemnified Party will, within a reasonable period of time following the discovery of the matters giving rise to any Losses shall notify the indemnifying party under Section 8 (the "Indemnifying Party") in writing of its claim for indemnification for such Losses, specifying in reasonable detail the nature of such Losses and the amount of the Loss estimated to accrue therefrom; provided, however, that failure to give such notification will not affect the indemnification provided hereunder, except to the extent the Indemnifying Party will have been prejudiced as a result of such failure. Thereafter, the Indemnified Party will deliver to the Indemnifying Party, within a reasonable period of time after the Indemnified Party's receipt of such request, all information and documentation reasonably requested by the Indemnifying Party with respect to such Losses.

(b) If the indemnification sought pursuant hereto involves a claim made by a third party against the Indemnified Party (a "Third Party Claim"), the Indemnifying Party will be entitled to assume the defense of such Third Party Claim at its own expense with counsel selected by the Indemnifying Party, unless such Third Party Claim seeks an injunction or other equitable relief against the Indemnified Party. Except as provided below, should the Indemnifying Party so elect to assume the defense of a Third Party Claim, the Indemnifying Party will not be liable to the Indemnified Party for any legal expenses subsequently incurred by the Indemnified Part) in connection with the defense thereof. If the Indemnifying Party assumes such defense, the Indemnified Party will have the right to participate in the defense thereof and to employ counsel, at its own expense (which expense shall not constitute a Loss), separate from the counsel employed by the Indemnifying Party, it being understood that the Indemnifying Party will control such defense. The Indemnifying Party will be liable for the reasonable and documented fees and expenses of counsel employed by the Indemnified Party for any period during which the Indemnifying Party has not assumed the defense thereof (other than during any period in which the Indemnified Party will have failed to give notice of the Third Party Claim as provided above). If the Indemnifying Party chooses to defend or prosecute a Third Party Claim, all of the Parties hereto will reasonably cooperate in the defense or prosecution thereof. Such cooperation will include the retention and (upon the Indemnifying Party's request) the provision to the Indemnifying Party of records and information which are reasonably relevant to such Third Party Claim, and making employees available on a mutually convenient basis to provide additional information and explanation of any material provided hereunder. If the Indemnifying Party chooses to defend or prosecute any Third Party Claim, it will defend or prosecute it diligently and the Indemnifying Party will obtain the prior written consent of the Indemnified Party (not to be unreasonably withheld) before entering into any settlement, compromise or discharge of such Third Party Claim if (i) such settlement, compromise or discharge does not relate solely to monetary

damages, (ii) such settlement, compromise or discharge does not expressly unconditionally and completely release the Indemnified Party from all Losses and liabilities with respect to such Third Party Claim and (iii) the Indemnifying Party is not directly paying the full amount of the Losses in connection with such Third Party Claim. Whether or not the Indemnifying Party will have assumed the defense of a Third Party Claim, the Indemnified Party will not admit any liability with respect to, or settle, compromise or discharge, such Third Party Claim without the Indemnifying Party's prior written consent (not to be unreasonably withheld).

(c) Each Indemnified Party shall take, and shall cause its Affiliates to take. all reasonable steps to mitigate any Loss upon becoming aware of any event or circumstance that would reasonably be expected to, or such Indemnified Party believes does, give rise thereto, including incurring costs only to the minimum extent necessary to remedy the breach that gives rise to such Loss (which costs shall be deemed to be Losses); provided, that such failure to use such efforts in accordance with the foregoing shall not relieve the Indemnifying Party of its indemnification obligations under Section 9 except and only to the extent that the Indemnifying Party is prejudiced thereby.

10. Confidentiality. Each of the Parties agrees that:

(a) Except as required by Law or court order or the rules of any applicable stock exchange: (i) it will not disclose any Confidential Information, as defined herein, of the other Party to any third party at any time without the prior written consent of the disclosing Party; (ii) it will not make use of any Confidential Information of the other Party for any purpose other than for the purposes set forth in, or in furtherance of the transactions contemplated by, this Agreement; and (iii) without limitation, it will use all commercially reasonable efforts to prevent unauthorized publication or disclosure by any Person of such Confidential Information. In addition, Buyer shall be entitled to disclose this Agreement to prospective purchasers of the Product ANDA, the purchaser of all or substantially all of the assets or business of the Buyer provided that any such prospective purchaser has executed a non-disclosure agreement that contains provisions at least as restrictive as the provisions set forth in this Section 10.

(b) With respect to any Confidential Information required to be disclosed by law or court order or the rules of any applicable stock exchange by a Party that has received such Confidential Information from another Party, the receiving Party shall promptly notify the disclosing Party as to the requirement or demand for such disclosure and shall reasonably assist the disclosing Party in seeking to limit the scope of such disclosure or ensuring that the same is accorded confidential treatment. Any such disclosure by the receiving Party shall in no event otherwise change, alter or diminish the confidential and/or proprietary, status of such Confidential Information, or treatment as such by the receiving Party, under this Agreement,

(c) All Confidential Information in any form will be returned to the Party who disclosed the Confidential Information within thirty (30) days after written request by the disclosing Party; provided that the Parties may retain: (i) one (1) copy of such Confidential Information with its legal counsel as a record of the receiving Party's ongoing confidentiality obligations under this Agreement and as expressly provided in Section 2(d) hereof (ii) it is held as a backup in electronic form in backup tapes, servers or other sources as a result of receiving Party's normal back up procedures for electronic data, provided that no attempt is made to recover such Confidential Information from back-up tapes, servers or other sources (except for legal or compliance purposes), all of which retained Confidential Information shall remain subject to the restrictions set forth in this Section 11.

(d) For purposes of this Agreement, the term "Confidential Information" means all know-how, trade secrets, formulae, data, inventions, Product ANDA, technology and other information, including financial information, in whatever form, related to the registration, manufacture, sale or marketing of the Products, marketing strategies or business of the disclosing Party, related to this Agreement. Without limiting the generality of the foregoing, subject to Section 12 below, the existence of this Agreement and each of its provisions shall be considered Confidential Information of each Party. Confidential Information shall not include any information that (i) is or becomes public knowledge through no fault of the receiving Party; (ii) rightfully was in the receiving Party's possession at the time of disclosure (as evidenced by written records); (iii) was independently created by the receiving Party (as evidenced by written records) without use or reference to any Confidential Information; or (iv) is received from a third party having the lawful right to disclose the information.

11. FDA Notice of Transfer of Product ANDA. Ingenus shall dispatch a letter to FDA in the form set forth in Exhibit B within three (3) Business Days of the Effective Date, with respect to the Purchased Assets. The letter will indicate that a copy of the Product ANDA and applicable regulatory correspondence has been submitted to Buyer to satisfy the transfer. A copy of the letter shall be provided by Ingenus to Buyer upon submission to the FDA. Within three (3) Business Day of receipt by Buyer of the complete copy of the electronic regulatory file pursuant to Section 4(d), Buyer will dispatch an acceptance letter to the FDA with respect to the Product ANDA.

12. Publicity. The Parties agree that no publicity, release, disclosure or announcement concerning this Agreement or the transactions contemplated hereunder shall be issued without the advance written consent of the other Party, which consent shall not be unreasonably withheld, delayed or conditioned. For releases, disclosures or announcements required by applicable Law, the Party proposing to make the release, disclosure or announcement shall, before making any such release, disclosure or announcement, afford the other Party a reasonable opportunity to review and comment, and the first Party shall give due consideration to the comments of the other Party.

13. Maintenance of Records. Buyer will preserve all books and records included within the Purchased Assets for applicable periods of time required by the FDA and any other applicable Governmental Entity and, subject to the confidentiality restrictions contained herein, make such books and records available for inspection and copying by Ingenus or its agents upon reasonable request and upon reasonable notice.

14. Governing Law. Jurisdiction: Venue: WAIVER OF JURY TRIAL This Agreement shall be governed, interpreted and construed in accordance with the substantive laws of the State of New York, U.S.A., without regard to its conflict of laws principles. Each of the Parties hereby irrevocably submits to the exclusive jurisdiction of the United States District Court for the Southern District of New York over any action or proceeding arising out of or relating to this Agreement, and each hereby waives the defense of any inconvenient forum for the maintenance or such action or proceeding. In addition, it is further agreed that the Parties shall be entitled to enforce specifically the terms of this Agreement in the United States District Court for the Southern District of New York, this entitlement being in addition to any other remedy to which such Party is entitled at law or in equity.

15. THE BUYER AND INGENUS HEREBY WAIVE, TO THE FULLEST EXTEM PERMITTED BY LAW, ANY RIGHT TO TRIAL BY JURY OF ANY CLAIM, DEMAND, ACTION, OR CAUSE OF ACTION (l) ARISING UNDER THIS AGREEMENT OR (Il) IN ANY WAY CONNECTED WITH OR RELATED OR INCIDENTAL TO THE DEALINGS OF THE PARTIES HERETO IN RESPECT OF THIS AGREEMENT OR ANY OF THE TRANSACTIONS RELATED HERETO, IN EACH CASE WHETHER NOW EXISTING OR HEREAFTER ARISING, AND WHETHER IN CONTRACT, TORT, EQUITY, OR OTHERWISE. THE PARTIES TO THIS AGREEMENT EACH HEREBY AGREES AND CONSENTS THAT ANY SUCH CLAIM, DEMAND, ACTION, OR CAUSE OF ACTION SHALL BE DECIDED BY COURT TRIAL WITHOUT A JURY AND THAT THE PARTIES TO THIS AGREEMENT MAY FILE AN ORIGINAL COUNTERPART OF A COPY OF THIS AGREEMENT WITH ANY COURT AS WRITTEN EVIDENCE OF THE CONSEN T' OF THE PARTIES HERETO TO THE WAIVER OF THEIR RIGHT TO TRIAL BY JURY.

16. Notices. All notices and other communications required or permitted to be given or made pursuant to this Agreement shall be in writing signed by the sender and shall be deemed duly given (a) on the date delivered, if personally delivered, (b) on the date sent by telecopier with automatic confirmation by the transmitting machine showing the proper number of pages were transmitted without error, (c) on the Business Day after being sent by Federal Express or another recognized overnight mail service which utilizes a written form of receipt for next day or next Business Day delivery or (d) three (3) Business Days after mailing, if mailed by U.S. postage prepaid certified or registered mail, return receipt requested, in each case addressed to the applicable Party at the address set forth below and each Party agrees to accept service of process on behalf of itself and, with respect to Ingenus, its Affiliates at the applicable address set forth below; provided that a Party may change its address for receiving notice by the proper giving of notice hereunder:

if to Ingenus, to:

Ingenus Pharmaceuticals, LLC
4190 Millenia Boulevard
Orlando, FL 32839 Attention:
Facsimile:

if to Buyer, to:

Athenex , Inc.
Conventus Building
1001 Main Street, Suite 600
Buffalo, NY 14203
Attn: Legal Department
Email: [*]

17. Independent Contractors. The status of the Parties under this Agreement shall be that of independent contractors, without the authority to act on behalf of or bind each other. Nothing in this Agreement shall be construed as establishing a partnership or joint venture relationship between the Parties hereto.

18. Entire Agreement; No Third-Party Beneficiaries. This Agreement (including its Exhibits) constitutes the entire agreement between the Parties with respect to its subject matter, and supersedes all prior agreements, arrangements, dealings or writings between the Parties, both written and oral (including any letter of intent, memorandum of understanding or term sheet), with respect to the subject matter hereof. Except as specifically provided herein, this Agreement is not intended to confer upon any Person other than the parties hereto any rights or remedies hereunder. This Agreement may not be amended or modified except in writing executed by the duly authorized representatives of the Parties.

19. Severability. Should any part or provision of this Agreement be held unenforceable or in conflict with applicable Law, the invalid or unenforceable part or provision shall, provided that it does not affect the essence of this Agreement, be replaced with a revision which accomplished, to the greatest extent possible, the original commercial purpose of such part or provision in a valid and enforceable manner, and the balance of this Agreement shall remain in full force and effect and binding upon the Parties hereto.

20. Assignment. The terms and provisions hereof shall inure to the benefit of, and be binding upon the Parties and their respective successors and permitted assigns. Any Party may assign its rights and obligations under this Agreement without the prior written consent of the other Party, to an Affiliate or to a successor of the assigning Party by reason of merger, sale of all or substantially all of its assets or portion of its business which relates to the Product, or any similar transaction; provided that any such assignee or successor-in-interest assumes all obligations of its assignor under this Agreement. No assignment will relieve any party of its responsibility for the performance of any obligation.

21. Waiver. No waiver of a breach or default hereunder shall be considered valid unless in writing and signed by the Party giving such waiver, and no such waiver shall be deemed a waiver of any subsequent breach or default of the same or similar nature,

22. Further Assurances. Without limitation, each of the Parties shall use its commercially reasonable efforts to take, or cause to be taken, all such further actions and to do, or cause to be done, including by its Affiliates, all things necessary, proper or advisable to consummate and make effective as promptly as possible, the transactions contemplated by this Agreement including, without limitation, notices to the FDA regarding the transfer of the Product ANDA from Ingenus to Buyer. Each Party shall bear its own costs related thereto.

23. Counterparts. This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original but all of which, taken together, shall constitute one and the same instrument. PDF and facsimile signatures shall constitute original signatures.

24. Expenses. Except as otherwise expressly provided herein, each Party shall bear its own costs and expenses, including attorney, accountant, consultant and broker's fees, incurred in connection with the negotiation and execution of this Agreement, the related agreements and the consummation of the transactions contemplated hereby and thereby.

25. Interpretation: Headings. As used in this Agreement, unless the context otherwise requires: words describing the singular number include the plural, and vice versa; words denoting any gender include all genders; the word "including" means "including, without limitation"; and the words "hereof," "herein" and "hereunder," and words of similar import, refer to this Agreement as a whole and not to any particular provision of this Agreement. The headings contained herein are for the sole purpose of convenience of reference, and do not in any way limit or affect the meaning or interpretation of any of the provisions of this Agreement.

[The remainder of this page intentionally left blank.]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first written above.

INGENUS PHARMACEUTICALS, LLC.

By: /s/ Andrew Gellman
Name: Andrew Gellman
Title: President
8/31/2020

ATHENEX PHARMACEUTICAL DIVISION, LLC

By: /s/ Jeffrey Yordon
Name: Jeffrey Yordon
Title: President/COO
8/29/2020

SCHEDULE 1

[*]

Exhibit 10.51

Certain information in this exhibit marked [*] has been excluded from the exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

CO-MARKETING, MANUFACTURE AND SUPPLY AGREEMENT

THIS CO-MARKETING, MANUFACTURE AND SUPPLY AGREEMENT ("**Agreement**") is entered into as of November 2, 2020, ("**Effective Date**") between INGENUS PHARMACEUTICALS LLC, a Delaware, USA limited liability company with a principal place of business at 4190 Millenia Blvd., Orlando, FL 32839 ("**Ingenus**") and ATHENEX PHARMACEUTICAL DIVISION, LLC, a Delaware limited liability company with a principal place of business at 10 Martingale Rd, Suite 230, Schaumburg, IL 60173 ("**Athenex**") (hereinafter each a "**Party**" and collectively referred to as the "**Parties**").

WHEREAS, Ingenus is in the business of developing, manufacturing, marketing and distributing pharmaceutical products.

WHEREAS, Ingenus is the owner of certain NDA (as defined in Section 1) for the Product (as defined in Section 1) and Athenex is desirous of co-marketing and distributing the Product in accordance with the terms and conditions of this Agreement.

WHEREAS, subject to the terms and conditions of this Agreement, (i) Ingenus will grant a license to Athenex on the terms set forth in section 2.2 below; (ii) Ingenus shall also be responsible for manufacturing and supplying the Product to Athenex; (iii) Athenex shall market and sell the Product in Athenex Territory in Athenex's name and Athenex label. Athenex shall, subject to the terms of this Agreement (including, without limitation, Section 5.3(a)), purchase the Product exclusively for sale from Ingenus.

NOW, THEREFORE, the Parties hereby agree as follows:

SECTION 1: DEFINITIONS

Capitalized terms have the meanings set forth or referred to in this Section 1.

1.1 Affiliate. With respect to any Party, any person or entity directly or indirectly controlling, controlled by, or under common control with such Party. For purposes of this definition "control" of a person or entity means the direct or indirect (a) ownership of more than 50% of any class of voting securities such person or entity, (b) power to vote more than 50% of any class of voting securities such person or entity or (c) other power to control the management and policies of such person or entity, whether through the ownership of voting securities, by contract, or otherwise.

1.2 Agreement. This Agreement, together with its exhibits, annexes and attachments, as the same may be amended from time to time in accordance herewith.

1.3 API. The acronym for the active pharmaceutical ingredient contained in the NDA.

1.4 Applicable Law. As to any person or entity, any treaty, constitution, statute, ordinance, law, rule or regulation, guidance issued by any governmental or regulatory authority, or order or other determination of an arbitrator or a court or other governmental or regulatory authority, in each case applicable to or binding upon such person or

entity or any of its property or to which such person or entity or any of its property is subject (including, without limitation, the FD&C Act and cGMPs).

1.5. Athenex Territory. Acute Care GPO's and their entire memberships as provided by said GPOs, IDNs and individual Hospitals within the United States of America, its territories and protectorates. Specifically excluded from the Athenex Territory are the following customers of Acute Care Market: Members of Comprehensive Pharmacy Services (CPS), Cancer Treatment Centers of America (CTCA), University of Pittsburgh Medical Center (UPMC), CHI Health (Nebraska) and Kaiser Permanente.

1.6 Certificate of Analysis. A document generated by Ingenus that is specific for each lot of Product and signed by the applicable quality assurance personnel of Ingenus. Such Certificate of Analysis shall comply with any promulgated Applicable Law.

1.7 cGMPs or GMPs. The acronym for "current Good Manufacturing Practices", as defined in 21 CFR Section 210 and Section 211 et. seq, as amended and in effect from time to time, or such similar term as used under Applicable Law in any country.

1.8 FD&C Act. The U.S. Food, Drug and Cosmetic Act and the rules, regulations and guidance there-under, all as amended and in effect from time to time.

1.9 EXW. The acronym for the delivery term Ex works (named place of delivery) consistent with the use of EXW in Incoterms® 2010, which for purposes of this Agreement means that Product will be made available for pick up by Athenex at Ingenus' Lugano Switzerland facility. This is where the risk and title transfer to the Product is deemed to occur.

1.10 FDA. The United States Food and Drug Administration.

1.11 Failure to Supply Charges. The charges due to the failure to supply Product to customers of Athenex as more fully described in section 5.2(g) of this Agreement.

1.12 GDUFA. The Generic Drug User Fee Act 21 U.S.C. §379j-42 signed into law on July 9, 2012, and as may be amended and in effect from time to time.

1.13 Ingenus Territory. All customers and geographic areas not included in Athenex Territory.

1.14 Marketing Allowance. With respect to a Product for any period, a fee payable to Athenex for (but not limited to) the following costs: sales personnel, sales support personnel, logistics personnel (managing freight and importation activity), administrative personnel (state licensure and Medicaid pricing), Medicaid rebate personnel, chargeback processing personnel, chargeback transactional fees, marketing expenses and pharmacovigilance services. The Marketing Allowance shall be a fixed [*] percent ([*]%) of the Net Sales of the Product.

1.15 Materials. All ingredients and materials used in and/or for the Product from API and excipient procurement through finished-product manufacture and final packaging of the Product, including but not limited to, API, excipients, labeling, and packaging components.

1.16 NDA. The New Drug Application filed by an Affiliate of Ingenus for the Product, of which Ingenus has the full rights to such NDA

1.17 Net Sales. The gross sales of any Products by Athenex or any of its Affiliates or successors in arm's-length transactions with any third party in the Athenex Territory, less the following deductions, to the extent accrued, paid or allowed in accordance with GAAP, with respect to the sale of any Products:

(a) cash discounts, quantity discounts, promotional discounts, stocking or other promotional allowances;

(b) sales and excise taxes, customs, duties, tariffs and any other taxes or government charges, all to the extent added to the sale price and paid or accrued and not refunded in accordance with applicable law (but not including taxes assessed against the income derived from such sale);

(c) rejections, returns, returned goods allowances and the costs of recalls, seizures or destruction of goods, whether voluntarily or pursuant to a governmental request;

(d) retroactive corrections, including price adjustments (including those on customer inventories following price changes) and corrections for billing errors or shipping errors;

(e) chargebacks, rebates, price protection, shelf stock adjustments, administrative fees, and any other allowances actually granted or allowed to any person or entity, including group purchasing organizations, managed health care organizations and to governments, including their agencies, or to trade customers, in each case that are not Affiliates of Athenex, and that are directly attributable to the sale of any Products; and

(f) other payments required by law to be made under Medicaid, Medicare or other government special medical assistance programs.

In no event shall any particular amount, identified above, be deducted more than once in calculating Net Sales (*i.e.*, no "double counting" of reductions). Sales of any Products between Athenex and its Affiliates for resale shall be excluded from the computation of Net Sales, but the subsequent resale of such Products to a Third Party shall be included within the computation of Net Sales. If any of the Products are sold or transferred for consideration other than cash, the Net Sales from such sale or transfer shall be deemed the average sales price for the prior quarter of such Products. Net Sales shall exclude any samples of Products transferred or disposed of at no cost for promotional or educational purposes.

1.17 Net Profits. Net Sales less the sum of the following: (a) the Product Transfer Price, and (b) the Marketing Allowance. If the Net Profits for the Product for a particular calendar quarter is negative, such negative amount shall be carried forward and offset against positive Net Profits amounts for the Product in successive calendar quarters.

1.18 Product. Cyclophosphamide Injection, 500mg/2.5mL and Cyclophosphamide Injection, 1g/5mL as approved under NDA 212501**.**

1.19 Product Launch. The date on which Athenex makes its first sale of Product to an unrelated third party in an arm's length transaction for ultimate use or consumption by the general public in the Athenex Territory.

1.20 Purchase Order. A document, generally in the form of **Exhibit B** hereto, sent by Athenex to Ingenus to purchase a quantity of the Product pursuant to this Agreement.

1.21 Recall. Has the meaning set forth in Section 5.4(d).

[*] Confidential treatment requested; certain information omitted and filed separately with the SEC.

1.22 Specifications. Those chemistry, manufacturing, controls, and other technical parameters for the Product as set forth in the NDA Approval.

1.23 Term. Has the meaning set forth in Section 8.1.

1.24 Transfer Price. The price at which Ingenus shall charge Athenex for the manufacture of the Product, as defined in Section 3.1 and as set forth on Exhibit A.

SECTION 2: NDA OWNERSHIP AND LICENSING

2.1 NDA Ownership. The ownership of the NDA and all related documents, registrations and intellectual property ("**Ingenus Intellectual Property**") belongs to Ingenus and its Affiliates. Athenex has no ownership interest in or claim to any of the Ingenus Intellectual Property or any other Ingenus property and none is granted to Athenex by this Agreement other than those specific licensing rights granted herein.

2.2 Product NDA Licensing. Ingenus grants to Athenex, and Athenex hereby accepts a territory-based license to use Ingenus' intellectual property rights to the Product (including all Ingenus Intellectual Property) for the purpose of commercializing the Product in the Athenex Territory (the "**License**").

As consideration for the License, Athenex will pay a licensing fee of USD $1,000,000 to Ingenus in two installments, as follows: USD $150,000 to be paid within 15 days of execution of this Agreement and USD $850,000 is due to Ingenus on or before Jan 15, 2021. In addition, Athenex will have obligations to Ingenus for Transfer Price payments and Net Profit payments to Ingenus as outlined in Exhibit A to this Agreement

2.3 Regulatory Matters.

(a) Ingenus shall be responsible for registering Athenex under the NDA.

(b) Ingenus will be responsible for interacting with the FDA and obtaining all regulatory approvals and/or variations to the NDA, including without limitation counsel and opinions (if applicable) deemed necessary for successful maintenance of the NDA. Ingenus shall be solely responsible for such costs.

2.4 Ingenus Reserved Sale and Distribution Rights. Ingenus shall retain the rights to sell products to all channels outside of Athenex Territory, as described in this Section. Athenex shall not be entitled to any compensation, remuneration, profit split or otherwise related thereto – which will be outside of the Net Profit Split described in Exhibit A. Likewise, Athenex shall not be responsible for any expenses, costs or otherwise related thereto. Athenex hereby agrees that it shall not sell any Product outside of the Athenex Territory without the express written consent of Ingenus.

2.5 Provisions Regarding Certain Sales. Sales under an Ingenus label in the Athenex Territory will count as Athenex Sales and sales of the Athenex label in Ingenus Territory will count as Ingenus Sales for the purpose of calculating Net Profit payments to Ingenus as outlined in Exhibit A to this Agreement.

Within 15 days of the end of each calendar quarter, Athenex and Ingenus will review the quarters'sales records and communicate its sales in the other Party's territory (i.e. Athenex's sales in the Ingenus Territory and Ingenus's sale in the Athenex Territory) and, with respect to such sales, the Net Profit share shall be as follows:

a. Athenex sales in Ingenus Territory: Athenex will pay 100% of Net Profits to Ingenus less the [*]% Marketing Fee of Contracted Sales payable to Athenex; and
b. Ingenus Sales in Athenex Territory: Ingenus will pay 25% of Net Profits less the [*]% Marketing Fee of Contract Sales payable to Ingenus; and

c. Payments will be due within 45 days of the end of each calendar quarter.

SECTION 3: *TRANSFER PRICE*

3.1 Transfer Price. Athenex Purchase Orders shall state that the purchase of the Product as manufactured and supplied by Ingenus shall be in accordance with the agreed upon Transfer Price, as referenced in **Exhibit A** hereto ("**Transfer Price**"). The Transfer Price may be adjusted in accordance with Section 5.2 (a)(iii) of this Agreement. The Transfer Price excludes all costs relating to freight, transportation related insurance and U.S. Customs or other costs of shipment and logistics, which shall be the sole responsibility of Athenex.

SECTION 4: *INTELLECTUAL PROPERTY LICENSE; INTELLECTUAL PROPERTY LITIGATION*

4.1 Intellectual Property. Ingenus shall solely own all Ingenus Intellectual Property whether patentable or not and technical information created and/or related to Product and/or NDA. Each Party shall be the sole owner of its own intellectual property not related to the Product, and nothing in this Agreement shall be deemed to transfer any incidence of ownership thereto, other than the terms specified in this Agreement.

4.2 Intellectual Property Litigation.

(a) Management of Intellectual Property Litigation. In the event a third party threatens or initiates litigation against Athenex related to the Product, Ingenus or any of their respective Affiliates alleging that the Product, the NDA or any Ingenus Intellectual Property infringes that third party's rights ("**IP Litigation**"), Ingenus shall control such IP Litigation at its own cost. Athenex shall not enter into any settlement agreement or settlement arrangements, voluntary final disposition of any claim, without the prior written consent of Ingenus.

(b) IP Litigation Discovery. Athenex will fully comply with discovery requests and provide reasonable access to Ingenus and/or its designated agents to relevant information within the custody and control of Athenex in order to defend and/or prosecute any IP Litigation. Athenex shall fully cooperate with Ingenus in any reasonable manner with respect to discovery and or other litigation matters.

(c) Indemnification Obligations Not Affected. The Parties' respective rights and obligations pursuant to this Section 4.2 will be subject to, and will not affect, their respective rights and obligations pursuant to Section 9.1, 9.2 and 9.3.

SECTION 5: *MANUFACTURE, PURCHASE, AND DELIVERY*

5.1 Manufacture of Product. Ingenus shall be responsible for the manufacturing, packaging, labeling on the Athenex label (or other private label, as designated by Athenex) and otherwise preparing the Product for Athenex to sell, commercialize and distribute in the Athenex Territory. Athenex shall exclusively purchase all its supply of the Product for sale and distribution in the Athenex Territory from Ingenus.

(a) Product Manufacture.

(i) Ingenus shall be responsible for the timely manufacture and supply of the Product in accordance with Athenex Purchase Orders and Section 5.1(b) of this Agreement.

(ii) Ingenus shall be responsible for procuring all Materials and performing all applicable analytical release testing to process the quantity of Product for which firm Purchase Orders have been issued by Athenex in accordance with the Forecasts.

(iii) At the time of the Product being made available to Athenex for EXW shipment, the Product shall have a minimum shelf-life of 75% of the approved Product expiry dating.

(b) Specifications; Ingenus to inform Athenex of Developments. Ingenus shall ensure the Product is manufactured, packaged, labeled, and supplied according to (i) the master batch record, (ii) the Specifications, (iii) the NDA, (iv) GMPs, (v) the Quality Agreement and (vi) and any further requirements agreed upon by the Parties in writing and or required by the Applicable Law. Ingenus will keep Athenex informed of any development that could materially affect Ingenus' manufacture or supply of the Product.

(c) Stability Testing. Ingenus shall maintain a stability testing program for the Product and provide Athenex with an annual product review thereon. At least one (1) batch and one SKU of each strength shall be included in the annual stability program.

(d) Annual Reports. Ingenus shall be responsible for compiling Annual Reports for the Product for filing with the FDA. Athenex will, without additional costs or charges, provide in a timely manner, any assistance and/or documents within Athenex' custody or control and required by Ingenus to compile and file such Annual Reports, or any other required FDA documentation.

(e) Import and Customs. Ingenus will provide Athenex with a certificate of analysis for the Product which Ingenus will ensure complies with Section 5.1(b) .

5.2. Purchase Orders.

(a) Purchase Orders.

(i) Athenex shall make all purchases hereunder by submitting to Ingenus written Purchase Orders. In the event of a conflict between the terms and conditions of any Purchase Orders and this Agreement, the terms and conditions of this Agreement shall prevail.

(ii) Each Purchase Order shall be in whole batch quantities and have a maximum delivery date of one hundred and twenty (120) days EXW Ingenus' site after the acceptance of the Purchase Order by Ingenus. Ingenus shall be bound to accept all Purchase Orders which are placed in accordance with this Agreement and the Forecast (+/- ten percent (10%)). Ingenus shall accept Purchase Orders, in writing, within five (5) business days as from placement by Athenex. In the absence of express acceptance within the foregoing term, the relevant Purchase Order shall be deemed to have been accepted.

(iii) The initial Transfer Price for the Product purchased under this Agreement is set forth on Exhibit A and will be fixed for one year from the Effective Date of this Agreement. If necessary, from time to time after the initial one-year period noted above, the Parties agree to cooperate in determining a new Transfer Price due to, among other things, market conditions or increases or decreases in cost of Materials. Consent in determining a new Transfer Price will not be unreasonably withheld, delayed or conditioned by a Party, and each Party will provide reasonably requested information and documentation necessary to determine a new Transfer Price. The Parties also may alter the Transfer Price during the initial one-year period only upon mutual agreement in writing by the Parties. In addition, in case that Athenex determines that the Product is not commercially viable at any during the Term, Athenex shall send a notice to Ingenus. The Parties shall then discuss an adjustment of the Transfer Price. If the Parties fail to reach an agreement within a period of sixty (60) days from Athenex notification, Athenex shall have the right to terminate the Agreement as per Section 8.2(e) .

If Ingenus seeks an increase in the Transfer Price, it will provide written notice to Athenex thereof at least ninety (90) days prior to the desired effective date of the proposed increase, specifying the amount of, and reasonably detailed reasons for, the increase. The Parties then will negotiate in good faith to arrive at a mutually agreeable new Transfer Price. Should the Parties fail to reach a mutually acceptable agreement on the requested change

within thirty (30) days, then Ingenus may submit the request under the terms of "Dispute Resolution" as outlined in Section 10 of this Agreement. No change in the Transfer Price and no interruption in the supply of Products shall occur during the negotiations and Dispute Resolution periods, however, any change in the Transfer Price through negotiation or Dispute Resolution shall be retroactive to the date of the requested change by Ingenus.

(b) Authorized Distributors of Record. Ingenus acknowledges that Athenex will supply the Product to certain distributor customers in the Athenex Territory, and Ingenus designates such customers to be authorized distributors of record, having permission to distribute the Product for and on behalf of Athenex. Upon request, Athenex will provide Ingenus with a current list of designated authorized distributors of record.

(c) Payment Terms.

(i) Product. Except as mutually agreed by the Parties, Ingenus will invoice Athenex for the Transfer Price of Product purchased under this Agreement when such Product is made available for delivery EXW at Ingenus' site. Payments are due within forty-five (45) days after invoice receipt.

(ii) Other Amounts. For other amounts hereunder, if a Party is entitled to receive any payment from the other Party pursuant to this Agreement, then the Party to receive Payment shall invoice the Party obligated to make Payment (with each invoice setting forth, in reasonable detail, the amounts invoiced therein and the reason for such invoicing) and each such invoice will be due and payable within forty-five (45) days after invoice receipt.

(iii) Dollars. All monetary amounts set forth herein are in U.S. Dollars ($) and all payments hereunder shall be made in U.S. Dollars. All costs and expenses incurred by Ingenus in foreign currencies that are being passed on to Ingenus in any manner, shall be converted to U.S. Dollars at the conversion rate noted in the Wall Street Journal® as of the date the expense is incurred or as mutually agreed to by the Parties.

(iv) Withholding Taxes. For the avoidance of doubt, all payments made by Athenex to or for the benefit of Ingenus shall be made free and clear of, and without deduction or withholding for or on account of, any present or future taxes, withholdings or similar assessments, now or hereafter imposed, levied, collected, withheld or assessed by any governmental or taxing agency or authority.

(d) Forecasts. Athenex shall provide Ingenus with a 12-month rolling forecast, on a monthly basis (no less than 10 days prior to the beginning of each calendar month) beginning on 180-days preceding the agreed-upon and predicted Product Launch, which sets forth the quantities of the Product Athenex anticipates it will order from Ingenus (each a "**Forecast**"). The first three-months of any Forecast shall be deemed firm orderable quantities upon receipt of Purchase Order. All Purchase Orders shall be full batch size or its multiple.

(e) Rejection.

(i) Athenex may examine and test Product as it sees fit and may reject Product provided hereunder by Ingenus if such Product is defective due to Ingenus' failure to follow, or the Products failure to meet, the requirements set forth in Section 5.1 (b) above (a "**Product Defect**"); provided, however, that Athenex shall give written notice to Ingenus of its rejection of any Product hereunder, together with appropriate documentation for its decision (a "**Rejection Notice**"), within ten (10) days after Athenex' receipt of shipment of such Product. The Rejection Notice shall specify the grounds for rejection. If such Rejection Notice is not received within ten (10) days after Athenex' receipt of any Product, such Product shall be deemed to be accepted by Athenex. However, any Product Defect that would not be discoverable upon a reasonable inspection of a Product in accordance with industry standard incoming inspection practices (a "**Hidden Defect**") will not be deemed accepted by Athenex at any time. As soon as possible but not exceeding the shelf life of any Product, if either Party becomes aware of a Hidden Defect in such Product, it will, within ten (10) business days of becoming aware of such Hidden Defect, notify the other Party in writing about all Product involved (a "**Hidden Defect Rejection Notice**").

(ii) Ingenus may dispute a Rejection Notice or Hidden Defect Rejection Notice by providing written notice to Athenex of the dispute within fifteen (15) days after receipt of such Rejection Notice or Hidden Defect Rejection Notice (as applicable), which notice from Ingenus shall specify, in reasonable detail, the grounds for the dispute.

(iii) If a Rejection Notice or Hidden Defect Rejection Notice for any Product is not disputed by Ingenus as set forth in Section 5.2(e)(ii) above or if, in the event of a rejection dispute between the Parties, the contract laboratory referred to in Section 5.2(e)(iv) below gives a decision in favor of Ingenus, then:

(1) Athenex may withhold all payment for the rejected batch;

(2) where payment for the rejected batch has been made, Ingenus will promptly issue a full credit or pay a full refund (as selected by Athenex) to Athenex for the rejected batch of Product; and

(iv) If there is a dispute between the Parties with respect to the rejection of Product, the Parties will first seek to amicably resolve the dispute among themselves. If after thirty (30) days the Parties believe that the dispute cannot be amicably resolved, then the Parties shall mutually agree on a contract laboratory to conduct further testing of the rejected Product in order for the laboratory to determine whether the rejected Product meets the requirements for rejection set forth in this Section 5.2(e) . The Party whose conclusions are not borne out by the laboratory shall bear the cost of such testing, or as reasonably allocated based upon testing results. If the contract laboratory gives a decision in favor of Ingenus, Athenex shall promptly pay for the Product subject to the dispute, if such payment had not earlier been made. The decision of the contract laboratory, to the extent dispositive of a Product rejection dispute between the Parties, shall be binding upon the Parties with respect to such rejection dispute; any other or further disputes between the Parties with respect to Product conformance with Specifications, other representations and warranties made by a Party herein, or other matters will be addressed in accordance with Sections 9.1, 9.2, 9.3 and 10.2.

5.3. Delivery and Supply Obligations.

(a) Supply. Ingenus shall use commercially reasonable efforts to ensure the Product to be delivered and supplied to Athenex in accordance with this Section 5.3 and the other provisions of this Agreement and all Purchase Orders. If Ingenus does not comply with any of its delivery obligations under this Agreement for any accepted Purchase Order, Athenex may, in Athenex's sole discretion and at Ingenus's sole cost and expense (and without limiting any other rights and remedies available to Athenex including, without limitation, a right to recover damages), (a) approve a revised delivery date, (b) require expedited or premium shipment, or (c) cancel the applicable Purchase Order

(b) Labeling and Packaging. The design, formatting, content and any Specifications for artwork, labels and packaging shall be provided by Athenex. Athenex agrees that such materials, in the form provided by Athenex, will comply with Applicable Laws and the NDA. Ingenus shall be solely responsible for the packaging, labeling, label printing and otherwise preparing for, and actual delivery EXW of the Product to Ingenus in accordance with this Agreement. Athenex shall be solely responsible for all costs in connection with any artwork changes (except those specifically requested by Ingenus) and shipment and logistics/transportation.

(c) Certificate of Analysis. Each delivery of Product hereunder shall be accompanied by a Certificate of Analysis prepared by an authorized representative of Ingenus, certifying that all Product in the shipment has been tested in accordance with the NDA, meets the Specifications and was manufactured in compliance with cGMPs.

5.4 Quality Control and Compliance.

(a) Quality and Complaint Agreements. The Parties agree to enter into a separate quality agreement (as amended or otherwise modified, the "**Quality Agreement**") with respect to the Product promptly after the Effective Date but in any case, prior to Product Launch. Each Party agrees to perform its obligations under the Quality Agreement; however, in the event of a conflict between this Agreement, on the one hand, and the Quality Agreement, on the other hand, the terms of the Quality Agreement will control and be applicable in respect of quality-related matters. For all other matters, this Agreement will control and be applicable.

(b) Compliance With Laws. Each Party agrees to comply with all Applicable Laws, including, without limitation, GDUFA, cGMPs and state licensing laws, in its performance under this Agreement.

(c) Audit and Inspection. During the Term, upon reasonable prior notice by a Party, the other Party shall make open and available its facilities, employees, agents, and documentation related to its performance hereunder and/or the manufacturing of the Product to the requesting Party for audit and inspection. Such audits and inspections are limited to one (1) per calendar year, unless there exists good cause, shall not extend to any records beyond two (2) calendar years prior to the year of the requested audit and inspection, and no accounting period may be audited more than once. In the event there is a conflict between an audit scheduled by Ingenus and one performed by a governmental agency pursuant to Applicable Law ("**Government Audit**"), Ingenus shall use commercially reasonable efforts to permit Ingenus scheduled audit. If the Ingenus audit cannot be conducted simultaneously with the Government Audit, Ingenus shall schedule the Ingenus audit for immediately prior to or after such Government Audit. Each Party shall be permitted to receive a written copy of any audit reports within fifteen (15) days of its written request. Any audit reports generated are subject to the provisions of Section 10.11 (Confidentiality) and may not be shared with any third parties without prior written consent. Each Party will provide to the other Party, within Seven (7) business days after receipt or submission, copies of all correspondences, deficiency letters, 483's, warning letters, responses, and other documents which concern or may concern the Product and/or a Party's ability to perform hereunder.

(d) Recalls. If any Product is recalled or withdrawn pursuant to FDA regulation or other Applicable Laws or because the Parties, in their reasonable discretion determine that a recall is necessary to protect the public health (a "**Recall**") and such (i) Recall is due Ingenus' breach of its obligations under this Agreement, negligence, or willful misconduct ("**Ingenus Conduct**"), then Ingenus will bear all justified costs in connection with the Recall, including, but not limited to, all notification letters, postage, phone calls, faxes, courier charges, and all shipping expenses and (ii) where the Recall is the result of Athenex breach of its obligations under this Agreement, negligence, or willful misconduct ("**Athenex Conduct**"), then Athenex will bear all justified costs in connection with the Recall, including, but not limited to, all notification letters, postage, phone calls, faxes, courier charges, and all shipping expenses. If a Recall is due to the nature of the Product (for example, the FDA deems the Product to be unsafe) and is not due to Ingenus Conduct or Athenex Conduct, then the Parties shall equally bear the cost of the Recall. The Parties agree to cooperate in case of a Recall and provide such information as may be necessary to effectuate the Recall and to satisfy any regulatory requests about the Recall.

(e) Customer Questions and Complaints. Questions or complaints received by Athenex relating to the Product shall be referred to Ingenus no later than Seven (7) days after receipt. Ingenus shall process, investigate and respond to such said questions and complaints.

5.5 Drug Supply Chain Security Act.

(a) Capitalized terms used in this Section 5.5 will have the meanings set forth in the Drug Supply Chain Security Act of 2013, 21. U.S.C. Section 360eee, et seq., and the rules, regulations and guidance there-under, all as amended and in effect from time to time (collectively, the "**DSCSA**").

(b) Ingenus will affix or imprint a Product Identifier to each package, each homogenous case and each pallet of Product provided by Ingenus under this Agreement and these Product Identifiers (serial numbers) will be fully aggregated and communicated electronically in EPCIS format in GS1 EPCIS 1.1 standard.

(c) Each Party will keep and maintain records of its performance under this Section 5.5 for not less than Three (3) years after such records are generated or such longer period as may be required under the DSCSA.

SECTION 6: *REPRESENTATIONS AND WARRANTIES*

6.1 Representations, Warranties and Agreements of Ingenus. Ingenus represents, warrants and agrees as follows:

(a) Due Authorization; Enforceability. Ingenus is duly organized, validly existing and in good standing under the laws of its jurisdiction of formation, is qualified to do business and is in good standing as a foreign corporation in each jurisdiction in which the conduct of its business or the ownership of its properties requires such qualification, and has all requisite power and authority, corporate and otherwise, to conduct its business as now being conducted, to own, lease and operate its own properties and to execute, deliver and perform this Agreement. All requisite action, corporate and otherwise, has been taken to authorize Ingenus' execution, delivery and performance of this Agreement. This Agreement is a legal, valid and binding obligation of Ingenus, enforceable against Ingenus with its terms.

(b) Title. Upon the delivery of any Product to Athenex, good title thereto will pass to Athenex, free and clear of all liens and other encumbrances.

(c) No Conflicts. Neither execution and delivery of this Agreement nor its performance of this Agreement will: (i) constitute a breach of, default under, or violation of (A) any Applicable Law; (B) any agreement or other obligation to which Ingenus is a party or by which it or any of its property is bound; or (C) the rights of any person or entity; or (ii) result in the creation of any right or claim that adversely affects Ingenus' performance pursuant to this Agreement.

(d) Debarment. Neither Ingenus nor any of its officers or employees has been (i) convicted of a felony under the U.S. state or federal law for conduct relating to any drug product, biologic, medical device, new drug application or abbreviated new drug application (including, without limitation, conduct relating to the development, approval or manufacture thereof) or (ii) otherwise debarred under Applicable Law. To Ingenus' best knowledge, it has not and will not use in its performance under this Agreement the services of any person or entity that has been Excluded. Upon request by Ingenus, Ingenus will provide for FDA submission a standard "Debarment Certification".

(e) Generic Drug User Fee Amendments Act Compliance. Ingenus will comply with the requirements of GDUFA that are applicable to Ingenus, including, without limitation, all provisions relating to self-identification. Ingenus will ensure the payment of all applicable GDUFA facility, whether payable by Ingenus or its agent(s) or suppliers and Athenex shall reimburse to Ingenus its proportionate share of such GDUFA fees as reasonably calculated by Ingenus. Ingenus further represents and warrants that at all times, the facility utilized by Ingenus to manufacture the Product is in compliance with all Applicable Law, including but not limited to cGMP and that the facility is an approved facility by the FDA for manufacture of the Product for distribution in the Territory.

(f) Licenses. Ingenus has all licenses, permits and authorizations required for its performance of its obligations under this Agreement hereunder (including, without limitation, the manufacturing, supply and delivery of Product in accordance with this Agreement) and agrees to maintain such licenses, permits and authorizations in full force and effect.

(g) Product. Each delivery of Product hereunder will not be, at the time of delivery, (A) manufactured other than in compliance with Section 5.1 (b) above, (B) not be adulterated, misbranded or otherwise prohibited (within the

meaning of the FD&C Act and all other Applicable Laws), (C) a drug subject to restrictions on sale, purchase, trade or offers to sell, purchase or trade, pursuant to 21 U.S.C. 353 (c)(1) (as amended and in effect from time to time), and/or (D) a drug that has been imported or reimported in violation of Applicable Laws (including, without limitation, 21 U.S.C. Section 381, as amended and in effect from time to time).

6.2 Representations, Warranties and Agreements by Athenex. Athenex represents, warrants and agrees as follows:

(a) Due Authorization; Enforceability. Athenex is duly organized, validly existing and in good standing under the laws of its jurisdiction of formation, is qualified to do business and is in good standing as a foreign corporation in each jurisdiction in which the conduct of its business or the ownership of its properties requires such qualification, and has all requisite power and authority, corporate and otherwise, to conduct its business as now being conducted, to own, lease and operate its properties and to execute, deliver and perform this Agreement. All requisite action, corporate and otherwise, has been taken to authorize Athenex's execution, delivery and performance of this Agreement. This Agreement is a legal, valid and binding obligation of Athenex, enforceable against Athenex with its terms.

(b) No Conflicts. Neither execution and delivery of this Agreement nor its performance of this Agreement will: (i) constitute a breach of, default under, or violation of (A) any Applicable Law; (B) any agreement or other obligation to which Ingenus is a party or by which it or any of its property is bound; or (C) the rights of any person or entity; (ii) infringe the intellectual property rights of any person or entity; or (iii) result in the creation of any right or claim that adversely affects Ingenus' performance pursuant to this Agreement.

(c) Debarment. Neither Athenex nor, to the knowledge of Athenex, any of its officers or employees has been (i) convicted of a felony under the U.S. state or federal law for conduct relating to any drug product, biologic, medical device, new drug application or abbreviated new drug application (including, without limitation, conduct relating to the development, approval or manufacture thereof) or (ii) otherwise debarred under Applicable Law. To Athenex' best knowledge, it has not and will not use in its performance under this Agreement the services of any person or entity that has been Excluded. Upon request by Ingenus, Ingenus will provide for FDA submission a standard "Debarment Certification".

(d) GDUFA Compliance. Athenex will comply (and will cause any agents, subcontractors or other third parties conducting business relating to the NDA on Ingenus' behalf to comply) with the requirements of GDUFA that are applicable to Athenex.

6.3 Warranty Disclaimer. **EXCEPT FOR THE REPRESENTATIONS AND WARRANTIES EXPRESSLY SET FORTH IN THIS AGREEMENT, EACH PARTY HEREBY DISCLAIMS ALL REPRESENTATIONS AND WARRANTIES, INCLUDING, WITHOUT LIMITATION, THE IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE.**

SECTION 7: *CONTRACTS WITH THIRD PARTIES*

7.1 If Ingenus retains, engages or otherwise enters into a relationship with any third party to discharge its performance under this Agreement (including, without limitation, any agents or subcontractors), whether through a new or already existing contract with such third party, then:

(a) Ingenus will ensure that such third party is fully capable of performing the obligations of this Agreement and is in compliance with all the representations and warranties made by Ingenus in this Agreement.

(b) Ingenus will notify Athenex in writing at least 30 days prior to any such third party taking over Ingenus obligations under this Agreement.

(c) No such retention, engagement or other relationship will relieve Ingenus of its obligations pursuant to this Agreement and any conduct of such third party that fails to meet the requirements of this Agreement will constitute a breach of this Agreement by Ingenus.

SECTION 8: *AGREEMENT TERM AND TERMINATION OF AGREEMENT*

8.1 Agreement Term. The Agreement is effective as of the Effective Date and, unless earlier terminated as provided herein, shall continue for an initial term ending the Third (3rd) anniversary of the Effective Date (the "Initial Term"). Upon expiration of this Agreement, the Parties may mutually agree to ex- tend this Agreement in one year increments. Upon the expiration of such Initial Term and each renewal term thereafter, this Agreement will require the mutual written consent of the Parties to be extended. For the avoidance of doubt, any non-renewal or expiration of this Agreement shall constitute a termination of this Agreement for all purposes hereof. When used in reference to this Agreement, "Term" means the period from the Effective Date through the Initial Term and each renewal term until termination or expiration in accordance with the terms of this Agreement.

8.2 Termination.

(a) In the event of a material breach of this Agreement by either Party, the non-breaching Party may provide written notice of such breach to the breaching Party, including a description of the breach, and indicating the non-breaching Party's intent to terminate this Agreement. The breaching Party will have sixty (60) days from its receipt of such notice to cure the breach, provided the breach is capable of being cured within the sixty-day period. If the breaching Party fails to cure the breach within such period, then the non-breaching Party may terminate this Agreement on written notice to the breaching Party.

(b) Either Party may terminate this Agreement, effective immediately upon written notice to the other Party, if the other Party files for bankruptcy, is adjudicated bankrupt, files a petition under insolvency laws, is dissolved or has a receiver appointed for substantially all of its property. Furthermore, if a Party has reason to know that it may cease operations or will be unable to honor its obligations under this Agreement due to its financial condition, it shall provide immediate written notice to the other Party, who may in its sole discretion terminate this Agreement effective immediately upon written notice.

(c) By Ingenus, by providing (A) Athenex 90 days' prior written notice of termination in the case there is (i) a sale of substantially all the assets of Ingenus; (ii) a sale of voting control of Ingenus; (iii) a sale of the Product or; (iv) the sale of the manufacturing site for the Product which is located in Via Cadepiano 24 CH 6917 – Barbengo Lugano Switzerland ("Facility"), (B) returning to Athenex the licensing fee in section 2.1 of $1,000,000 and (C) supplying the Product to Athenex for up to 240 days from the date of receipt of the termination notice at a monthly quantity not to exceed Athenex's average monthly Product sales over the 90 day period immediately preceding the notice.

(d) By Athenex, in case the NDA is cancelled and/or withdrawn by the FDA or if Athenex is otherwise prevented from commercializing the Product in the Territory.

(e) By Athenex, in case that the Parties fail to reach an agreement on the Transfer Price as per Section 5.2. (a)(iii).

8.3 Effect of Termination.

Upon termination for any reason except for breach as per section 8.2 (a) above, Athenex shall purchase from Ingenus (at Ingenus' then-current Transfer Price as provided herein) all of Ingenus' remaining finished goods inventory of any Product and work in process, which were on Athenex Purchase Orders to Ingenus. Ingenus shall deliver to Athenex all such finished goods indicated above.

8.4 Suspension. In addition to the rights of a Party pursuant to Section 8.2(a), either Party may suspend its performance hereunder for as long as the other Party remains in material breach of this Agreement.

8.5 Survival. The following Sections of this Agreement, together with any related defined terms and exhibits and schedules hereto, will survive any termination of this Agreement: 2.1, 4, 5.1(d), 5.2(d),, 5.4(b)(ii), 5.4(b)(iii), 5.4(d), 5.4(e), 5.5 and 6, 8.5, 9, and 10. Termination of this Agreement will not release a Party from any liabilities (including, without limitation, liabilities for breach) that, as of the effective date of such termination, have already accrued or that are based upon any event occurring prior to such termination.

8.6 Remedies Cumulative. Each right or remedy of a Party hereunder is in addition to, and not in lieu of, the other rights and remedies of such Party pursuant to this Agreement and Applicable Law.

SECTION 9: *INDEMNIFICATION; INSURANCE; EXCLUSION OF DAMAGES*

9.1 Indemnification by Ingenus. Ingenus shall, at its sole cost and expense, defend, indemnify and hold Athenex and its Affiliates and their respective officers, directors, agents, and employees (collectively "Athenex Indemnified Parties") harmless from and against any and all third-party losses, claims, liabilities, obligations, expenses and/or damages (including without limitation reasonable attorneys' fees) (collectively, "**Third Party Claim(s)**")) to the extent that such Third Party Claims arise out of or result from: (i) any negligence, recklessness, willful misconduct, or fraud by Ingenus in connection with the execution and/or performance of this Agreement; (ii) any breach of this Agreement by Ingenus; (iii) any allegation of Product liability attributable to the performance or failure to perform hereunder by Ingenus (including without limitation any allegation made that a Product has not been manufactured, or supplied in accordance with Section 5.1(b) or that a Product is defective; (iv) any claim alleging that the Product, the NDA or any other Ingenus Intellectual Property misappropriates or infringes any third party's rights including, without limitation, any IP Litigation; or (v) the subject matter of any claims by Auromedics Pharma LLC and Scidose LLC against against Ingenus, including the action filed in the United States District Court for the District of Delaware on September 16, 2020 by Auromedics Pharma LLC and Scidose LLC against Ingenus; provided, however, that Ingenus shall have no such obligation to indemnify, defend or hold harmless with respect to any Third Party Claim to the extent such Third Party Claim is caused by the negligence, recklessness, willful misconduct or fraud of any Athenex Indemnified Party, or Athenex' breach of this Agreement.

9.2 Indemnification by Athenex. Athenex shall, at its sole cost and expense, defend, indemnify and hold Ingenus and its Affiliates and their respective officers, directors, agents, and employees (collectively "**Ingenus Indemnified Parties**") harmless from and against any and all Third Party Claims to the extent that such Third Party Claims arise out of or result from: (i) any negligence, recklessness, willful misconduct, or fraud by Athenex in connection with the execution and/or performance of this Agreement; (ii) any breach of this Agreement by Athenex; or (iii) any allegation of Product liability attributable to the performance or failure to perform hereunder by Athenex related to the sale, marketing and distribution of Product, provided, however, that Athenex shall have no such obligation to indemnify, defend or hold harmless with respect to any Third Party Claim to the extent such Third Party Claim is caused by the negligence, recklessness, willful misconduct or fraud of any Ingenus Indemnified Party, or Ingenus' breach of this Agreement.

9.3 Indemnification Procedures. If a Party (the "Indemnified Party") believes it is entitled to indemnification and defense pursuant to this Section 9 with respect to a Third Party Claim, it will notify the other Party (the "Indemnifying Party") in writing promptly after it becomes aware of such Third Party Claim (provided that the failure of the Indemnified Party to so provide such notice will not relieve the Indemnifying Party of its obligations under this Section 9, except to the extent the Indemnifying Party is actually prejudiced thereby). Within thirty (30) days after receipt of such notice, the Indemnifying Party will, upon written notice thereof to the Indemnified Party, assume control of the defense of such Third Party Claim with counsel selected by the Indemnifying Party (which may be, at the Indemnifying Party's election, the Indemnifying Party's in-house litigation counsel). If the Indemnifying Party believes that a Third-Party Claim presented to it for indemnification and defense is one as to which the Indemnified Party is not entitled to indemnification and defense under this Section 9, it will so notify the Indemnified Party. The Indemnified Party may participate in such defense with counsel it selects, all at the Indemnified Party's own expense. The Indemnified Party will provide the Indemnifying Party, at the Indemnifying Party's expense, with reasonable assistance and cooperation as reasonably requested by the Indemnifying Party. Without the prior written consent of the Indemnified Party, such consent not to be

unreasonably withheld, delayed or conditioned, the Indemnifying Party will not agree to any settlement of such Third Party Claim or consent to any judgment in respect thereof; further, without the prior written consent of the Indemnifying Party, such consent not to be unreasonably withheld, delayed or conditioned, the Indemnified Party will not agree to any settlement of such Third Party Claim or consent to any judgment in respect thereof.

9.4 Insurance.

(a) Ingenus agrees that prior to any commercial manufacture hereunder, it will obtain and shall at all times during the Term will maintain in full force and effect, at its own cost and expense, insurance sufficient to insure against all liabilities arising pursuant to this Agreement as a result of its performance hereunder, including the following minimum insurance coverages: (i) 'worker's compensation insurance, if applicable, as required by law; (ii) Manufacturing Defect with respect to the Product with minimum coverage of Ten Million Dollars ($10,000,000) per occurrence; and (iii) physical property damage insurance, through the designated freight carrier or otherwise, on all of the Product at all times until receipt by Athenex. Upon request, Ingenus will supply to Athenex its certificate of insurance to evidence such coverage and shall name Ingenus as an additional insured under such coverage.

(b) Athenex agrees that prior to any commercial manufacture hereunder, it will obtain and shall at all times during the Term and for two (2) years thereafter will maintain in full force and effect, at its own cost and expense, insurance sufficient to insure against all liabilities arising pursuant to this Agreement as a result of its performance hereunder, including the following minimum insurance coverages: product liability insurance with respect to the Product with minimum coverage of Ten Million Dollars ($10,000,000) per occurrence. Upon request, Athenex will supply Ingenus with a certificate of insurance to evidence such coverage and name Ingenus as an additional insured.

9.5 Exclusion of Damages. **EXCEPT FOR BREACHES OF CONFIDENTIALITY OBLIGATIONS, NEITHER PARTY WILL BE LIABLE FOR SPECIAL, INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES (INCLUDING, BUT NOT LIMITED TO, LOST PROFITS), WHETHER IN CONTRACT, NEGLIGENCE, STRICT LIABILITY OR OTHERWISE, EVEN IF SUCH PARTY HAS BEEN ADVISED OF OR COULD HAVE FORESEEN THE POSSIBILITY OF SUCH DAMAGES**

SECTION 10: *MISCELLANEOUS*

10.1 Entire Agreement; Amendments. This Agreement constitutes the entire agreement between the Parties with respect to the subject matter hereof and supersedes any prior negotiations, understandings or agreements, whether oral or in writing, concerning the subject matter hereof. This Agreement may not be modified, changed or amended except by an instrument in writing duly executed by the Parties hereto.

10.2 Governing Law and Jurisdiction; Arbitration.

(a) This Agreement shall be governed by and construed in accordance with the laws of the State of New York, United States of America, without reference to its conflict of laws principles.

(b) The Parties will first use their best endeavors to resolve through mutual consultation any dispute, difference or question arising between Parties or their respective representatives or assigns, which may arise out of, in connection with or in relation to this Agreement. Any dispute arising out of or in connection with this contract, including any question regarding its existence, validity or termination, which is not resolved through mutual consultation, shall be referred to and finally resolved by arbitration administered by the American Arbitration Association ("AAA") in accordance with the American Arbitration Rules ("AAA Rules") for the time being in force, which rules are deemed to be incorporated by reference in this clause. The arbitration shall be conducted in English and the venue of arbitration shall be London. The Arbitration shall be conducted by one Arbitrator mutually agreeable to the Parties.

10.3 Severability. If any provision of this Agreement is unenforceable or invalid, no other provision shall be affected thereby, and the remaining provisions shall be construed and reformed to the maximum extent possible and continue with the same effect as if such unenforceable or invalid provision was not a part of this Agreement, it being the intent and agreement of the Parties that this Agreement will be deemed to have been amended by modifying such provision to the extent necessary to render it valid, legal and enforceable while preserving its intent or, if such modification is not possible, by substituting therefore another provision that is legal and enforceable and that achieves the same objective.

10.4 Notices. All notices or communications given pursuant to this Agreement shall be in writing, if to INGENUS addressed to the attention of Matthew J Baumgartner at 4190 Millenia Blvd., Orlando, FL 32839 and if to Athenex, to (i) the attention of John Romano at 10 Martingale Rd Suite 230, Schaum-burg, IL 60173, (ii) with a copy to Teresa Bair, Esq., Legal Affairs, Athenex, Inc., Coventus Building, 1001 Main Street, Suite 600, Buffalo, New York 14203. Notice shall be: (a) hand delivered, (b) sent by prepaid express courier service, or (c) sent by electronic mail (e-mail) or facsimile transmission. A Party may change its address for the receipt of notices and communications hereunder by providing the other Party with written notice thereof given in accordance with this Section 10.4. All notices and communications shall be deemed given when received.

10.5 Waiver. Any waiver or consent hereunder must be in writing and signed by the Party claimed to have so waived or consented. A waiver of or consent hereunder given with respect to any breach or provision of this Agreement will not constitute a waiver of any other breach or provision of this Agreement.

10.6 Relationship of Parties and Other Activities. The Parties hereto are independent contractors and no Party is an employee, agent, partner or joint venture of the other.

10.7 Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments and to do all such other acts, as may be reasonably necessary or appropriate in order to carry out the purposes and intent of this Agreement.

10.8 Execution. This Agreement may be executed in any number of counterparts and by facsimile signature or PDF/email, each of which shall be deemed to be an original as against any Party whose signature appears thereon, and all of which shall together constitute one and the same instrument. This Agreement shall become binding when one or more counterparts hereof, individually or taken together, shall bear the signatures of all of the Parties reflected hereon as the signatories hereto.

10.9 Titles. The titles of the Sections and subsections of this Agreement are for convenience of reference only and are not to be considered in construing the terms and provisions hereof.

10.10 Exhibits All exhibits and schedules to this Agreement, if any, are hereby incorporated by reference into, and made a part of, this Agreement.

10.11 Confidentiality.

(a) During the Term and for three (3) years thereafter, each Party and/or its Affiliates (the “receiving Party”) shall maintain in confidence all information of the other Party and/or its Affiliates (the “disclosing Party”) disclosed hereunder and identified as, or acknowledged to be, or by its nature ought to be considered, Confidential Information (as defined in Section 10.11(b)) of the disclosing Party. The receiving Party will not use the disclosing Party’s Confidential Information in any manner or disclose the disclosing Party’s Confidential Information to anyone, except: (i) for uses and disclosures expressly permitted by this Agreement or necessary for the receiving Party to perform its obligations or exercise its rights hereunder; or (ii) for disclosures to those of the receiving Party’s Affiliates and the officers, directors, employees, agents and subcontractors of the receiving Party or any of its Affiliates (collectively, “Representatives”) to whom disclosure is reasonably necessary in connection with the receiving Party’s activities contemplated by this Agreement, provided that, prior to such disclosure to a Representative, the receiving Party will have advised such Representative of the confidential nature of such Confidential Information and such Representative shall be bound by obligations of confidentiality at least as

restrictive as those of this Section 10.11. The receiving Party will be responsible for any breach of this Section 10.11 arising from the conduct of its Representatives.

(b) As used herein "Confidential Information" of the disclosing Party shall include all confidential or proprietary information disclosed by or on behalf of the disclosing Party hereunder, including, without limitation, information of or regarding the disclosing Party's or its Affiliates' products, advertising, distribution, marketing, strategic plans, costs data, productivity or technological advances, specifications, data, know-how, formulations, technical information, pricing and other transaction terms, customers and suppliers, potential customers and suppliers, and information provided to the disclosing Party on a confidential basis by a third party; in each case whether in written, electronic, oral, visual or another form. The term "Confidential Information" will not include information that the receiving Party establishes (i) is or becomes generally available to the public other than as a result of a disclosure by the receiving Party or any of its Representatives in breach of this Agreement, (ii) is in the receiving Party's lawful possession, on a non-confidential basis, prior to disclosure thereof by or on behalf of the disclosing Party to the receiving Party, (iii) becomes available to the receiving Party on a non-confidential basis from a source other than the disclosing Party, provided that such source is not known to the receiving Party to be bound by an obligation of confidentiality to the disclosing Party with respect to such information or (iv) by contemporaneous written records is independently developed or discovered by the receiving Party without use of or reference to the Confidential Information of the disclosing Party.

(c) If the receiving Party or any of its Representatives becomes required pursuant to Applicable Law, rule or regulation (including, without limitation, subpoena, civil investigative demand, compulsory process or other legal requirement) to disclose any Confidential Information of the disclosing Party, then (i) unless prohibited from doing so by Applicable Law, the receiving Party will promptly notify the disclosing Party in writing thereof and will cooperate with the disclosing Party, at the disclosing Party's expense, in seeking a protective order or confidential treatment and (ii) the receiving Party and its Representatives may disclose such Confidential Information to the extent so required.

(d) The disclosing Party would be irreparably injured by a breach of this Section 10.11 by the receiving Party, and such a breach would not be compensable in money damages. Accordingly, in addition to any other rights and remedies of the disclosing Party pursuant to this Agreement and Applicable Law, the disclosing Party shall be entitled to seek injunctive and other equitable relief with respect to any breach or threatened breach of this Section 10.11 without posting a bond or other surety.

(e) Upon the termination of this Agreement, the receiving Party will, upon written request of the disclosing Party, promptly return to the disclosing Party or destroy all Confidential Information of the disclosing Party in the possession or control of the receiving Party or any of its Representatives; provided that the receiving Party may retain (i) one (1) copy of the disclosing Party's Confidential Information in order to comply with Applicable Law and determine the rights and obligations of the receiving Party pursuant to this Section 10.11, and (ii) any Confidential Information that is located on backup tapes or archival systems created for disaster recovery that are not commonly accessible or that require the Receiving Party to erase or delete information using special programs or techniques, which retained Confidential Information will remain confidential, subject to the terms of this Section 10.11, for as long as it is so retained by the receiving Party, notwithstanding the expiration of the three (3) year period referred to in Section 10.11(a) . The disclosing Party shall be responsible for all expenses relating to the return and/or destruction of such Confidential Information.

10.12 Press Release. Neither Party may issue a press release or issue a statement to the media in any form whatsoever concerning the Product or the Agreement, unless: required by Applicable Law; or the other Party provides its prior written consent thereto, such consent not be unreasonably withheld, delayed or conditioned.

10.13 Assignment. No Party may assign this Agreement or any of its rights, liabilities or obligations hereunder without the prior written consent of the other Party, such consent to not to be unreasonably withheld, delayed or conditioned; provided however, that a Party may, upon written notice to the other Party, assign this Agreement (in whole or in part) to any of its Affiliates, to the purchaser of all or substantially all of its assets or to its successor by merger or stock purchase.

10.14 Force Majeure. No Party shall be responsible for its failure to perform under this Agreement due to any act of God, act of any governmental authority or agency, change in government laws, rules or regulations or orders of courts or of statutory authorities having jurisdiction, act of the public enemy, war, riot, flood, civil commotion, terrorism, insurrection, severe or adverse weather conditions, lack or shortage of electrical power, failure of public transport, strikes or other labor disturbances, epidemics, pandemics or any other cause beyond such Party's reasonable control (each, "**Force Majeure Event**"). If a Party becomes subject to a Force Majeure Event, it will promptly notify the other Party thereof. If a Party becomes subject to a Force Majeure Event that is reasonably expected to continue for more than 120 days, the other Party may, upon written notice and without liability, terminate this Agreement (and, consequently, any issued Purchase Orders that are affected by such Force Majeure Event) as described in section 8.2 (c) above. For the avoidance of doubt, a delay or interruption in performance due to a Force Majeure Event will not constitute a breach of this Agreement.

[Signature Page Follows]

IN WITNESS WHEREOF, Ingenus and Athenex have executed this Agreement by their duly authorized officers as of the latest date set forth above.

ATHENEX PHARMACEUTICAL DIVISION, LLC	**INGENUS PHARMACEUTICALS, LLC.**
By: /s/ Jeffrey Yordon	By: /s/ Samir Mehta
Name: Jeffrey Yordon	Name: Samir Mehta
Position: President/COO	Position: COO

EXHIBIT A: TRANSFER PRICE, VALIDATION CHARGES, AND PROFIT SPLIT.

1. TRANSFER PRICE

[*]

2. NET PROFIT SPLIT:

The Parties agree that they will share (Athenex:[25]%/Ingenus:[75]%) the Net Profits arising from the sale of the Product by Athenex in Athenex Territory under the following terms and conditions:

- Athenex shall receive the Marketing Allowance without sharing with Ingenus.
- Athenex shall not share in the profits on sales of Product by Ingenus, as described in Section 2.5 above.
- Athenex shall calculate the Net Profit from the sale of Product in the Athenex Territory and shall provide such calculation to Ingenus by the 30th day following the end of each calendar quarter.
- Athenex shall pay to Ingenus its share of such calculated Net Profit on or before the 45th day following the end of each calendar quarter.

Certain information in this exhibit marked [*] has been excluded from the exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

MANUFACTURE AND SUPPLY AGREEMENT

MANUFACTURE AND SUPPLY AGREEMENT ("**Agreement**") is entered into as of January 15, 2021, ("**Effective Date**") between INGENUS PHARMACEUTICALS LLC, a Delaware, USA limited liability company with a principal place of business at 4190 Millenia Blvd., Orlando, FL 32839 ("**Ingenus**") and ATHENEX PHARMACEUTICAL DIVISION, LLC, a Delaware limited liability company with a principal place of business at 10 Martingale Rd, Suite 230, Schaumburg, IL 60173 ("**Athenex**") (hereinafter each a "**Party**" and collectively referred to as the "**Parties**").

WHEREAS, Ingenus is in the business of developing, manufacturing, marketing and distributing pharmaceutical products.

WHEREAS, Ingenus is the owner of certain ANDA (as defined in Section 1) for the Product (as defined in Section 1) and Athenex is desirous of co-marketing and distributing the Product in accordance with the terms and conditions of this Agreement.

WHEREAS, subject to the terms and conditions of this Agreement, (i) Ingenus will grant a license to Athenex on the terms set forth in section 2.2 below; (ii) Ingenus shall also be responsible for manufacturing and supplying the Product to Athenex; (iii) Athenex shall market and sell the Product in Athenex Territory in Athenex's name and Athenex label. Athenex shall, subject to the terms of this Agreement (including, without limitation, Section 5.3(a)), purchase the Product exclusively for sale from Ingenus.

NOW, THEREFORE, the Parties hereby agree as follows:

SECTION 1: DEFINITIONS

Capitalized terms have the meanings set forth or referred to in this Section 1.

1.1 Affiliate. With respect to any Party, any person or entity directly or indirectly controlling, controlled by, or under common control with such Party. For purposes of this definition "control" of a person or entity means the direct or indirect (a) ownership of more than 50% of any class of voting securities such person or entity, (b) power to vote more than 50% of any class of voting securities such person or entity or (c) other power to control the management and policies of such person or entity, whether through the ownership of voting securities, by contract, or otherwise.

1.2 Agreement. This Agreement, together with its exhibits, annexes and attachments, as the same may be amended from time to time in accordance herewith.

1.3 API. The acronym for the active pharmaceutical ingredient contained in the ANDA.

1.4 Applicable Law. As to any person or entity, any treaty, constitution, statute, ordinance, law, rule or regulation, guidance issued by any governmental or regulatory authority, or order or other determination of an arbitrator or a court or other governmental or regulatory authority, in each case applicable to or binding upon such person or entity or any of its property or to which such person or entity or any of its property is subject (including, without limitation, the FD&C Act and cGMPs).

1.5. Athenex Territory. Acute Care GPO's and their entire memberships as provided by said GPOs, IDNs and individual Hospitals within the United States of America, its territories and protectorates.

1.6 Certificate of Analysis. A document generated by Ingenus that is specific for each lot of Product and signed by the applicable quality assurance personnel of Ingenus. Such Certificate of Analysis shall comply with any promulgated Applicable Law.

1.7 cGMPs or GMPs. The acronym for "current Good Manufacturing Practices", as defined in 21 CFR Section 210 and Section 211 et. seq, as amended and in effect from time to time, or such similar term as used under Applicable Law in any country.

1.8 FD&C Act. The U.S. Food, Drug and Cosmetic Act and the rules, regulations and guidance there-under, all as amended and in effect from time to time.

1.9 EXW. The acronym for the delivery term Ex works (named place of delivery) consistent with the use of EXW in Incoterms® 2010, which for purposes of this Agreement means that Product will be made available for pick up by Athenex at Ingenus' Lugano Switzerland facility. This is where the risk and title transfer to the Product is deemed to occur.

1.10 FDA. The United States Food and Drug Administration.

1.11 Failure to Supply Charges. The charges due to the failure to supply Product to customers of Athenex as more fully described in section 5.2(g) of this Agreement.

1.12 GDUFA. The Generic Drug User Fee Act 21 U.S.C. §379j-42 signed into law on July 9, 2012, and as may be amended and in effect from time to time.

1.13 Ingenus Territory. All customers and geographic areas not included in Athenex Territory.

1.14 Marketing Allowance. With respect to a Product for any period, a fee payable to Athenex for (but not limited to) the following costs: sales personnel, sales support personnel, logistics personnel (managing freight and importation activity), administrative personnel (state licensure and Medicaid pricing), Medicaid rebate personnel, chargeback processing personnel, chargeback transactional fees, marketing expenses and pharmacovigilance services. The Marketing Allowance shall be a fixed [*] percent ([*]%) of the Net Sales of the Product.

1.15 Materials. All ingredients and materials used in and/or for the Product from API and excipient procurement through finished-product manufacture and final packaging of the Product, including but not limited to, API, excipients, labeling, and packaging components.

1.16 ANDA. The New Drug Application filed by an Affiliate of Ingenus for the Product, of which Ingenus has the full rights to such ANDA

1.17 Net Sales. The gross sales of any Products by Athenex or any of its Affiliates or successors in arm's-length transactions with any third party in the Athenex Territory, less the following deductions, to the extent accrued, paid or allowed in accordance with GAAP, with respect to the sale of any Products:

(a) cash discounts, quantity discounts, promotional discounts, stocking or other promotional allowances;

(b) sales and excise taxes, customs, duties, tariffs and any other taxes or government charges, all to the extent added to the sale price and paid or accrued and not refunded in accordance with applicable law (but not including taxes assessed against the income derived from such sale);

(c) rejections, returns, returned goods allowances and the costs of recalls, seizures or destruction of goods, whether voluntarily or pursuant to a governmental request;

(d) retroactive corrections, including price adjustments (including those on customer inventories following price changes) and corrections for billing errors or shipping errors;

(e) chargebacks, rebates, price protection, shelf stock adjustments, administrative fees, and any other allowances actually granted or allowed to any person or entity, including group purchasing organizations, managed health care organizations and to governments, including their agencies, or to trade customers, in each case that are not Affiliates of Athenex, and that are directly attributable to the sale of any Products; and

(f) other payments required by law to be made under Medicaid, Medicare or other government special medical assistance programs.

In no event shall any particular amount, identified above, be deducted more than once in calculating Net Sales (*i.e.*, no "double counting" of reductions). Sales of any Products between Athenex and its Affiliates for resale shall be excluded from the computation of Net Sales, but the subsequent resale of such Products to a Third Party shall be included within the computation of Net Sales. If any of the Products are sold or transferred for consideration other than cash, the Net Sales from such sale or transfer shall be deemed the average sales price for the prior quarter of such Products. Net Sales shall exclude any samples of Products transferred or disposed of at no cost for promotional or educational purposes.

1.17 Net Profits. Net Sales less the sum of the following: (a) the Product Transfer Price, and (b) the Marketing Allowance. If the Net Profits for the Product for a particular calendar quarter is negative, such negative amount shall be carried forward and offset against positive Net Profits amounts for the Product in successive calendar quarters.

1.19 Product Launch. The date on which Athenex makes its first sale of Product to an unrelated third party in an arm's length transaction for ultimate use or consumption by the general public in the Athenex Territory.

1.20 Purchase Order. A document, generally in the form of **Exhibit B** hereto, sent by Athenex to Ingenus to purchase a quantity of the Product pursuant to this Agreement.

1.21 Recall. Has the meaning set forth in Section 5.4 (d).

1.22 Specifications. Those chemistry, manufacturing, controls, and other technical parameters for the Product as set forth in the ANDA Approval.

1.23 Term. Has the meaning set forth in Section 8.1.

1.24 Transfer Price. The price at which Ingenus shall charge Athenex for the manufacture of the Product, as defined in Section 3.1 and as set forth on Exhibit A.

SECTION 2: ANDA OWNERSHIP AND LICENSING

2.1 ANDA Ownership. The ownership of the ANDA and all related documents, registrations and intellectual property ("**Ingenus Intellectual Property**") belongs to Ingenus and its Affiliates. Athenex has no ownership interest in or claim to any of the Ingenus Intellectual Property or any other Ingenus property and none is granted to Athenex by this Agreement other than those specific licensing rights granted herein.

2.2 Product ANDA Licensing. Ingenus grants to Athenex, and Athenex hereby accepts a territory-based license to use Ingenus' intellectual property rights to the Product (including all Ingenus Intellectual Property) for the purpose of commercializing the Product in the Athenex Territory (the "**License**").

2.3 Regulatory Matters.

(a) Ingenus shall be responsible for registering Athenex under the ANDA.

(b) Ingenus will be responsible for interacting with the FDA and obtaining all regulatory approvals and/or variations to the ANDA, including without limitation counsel and opinions (if applicable) deemed necessary for successful maintenance of the ANDA. Ingenus shall be solely responsible for such costs.

2.4 Ingenus Reserved Sale and Distribution Rights. Ingenus shall retain the rights to sell products to all channels outside of Athenex Territory. Athenex shall not be entitled to any compensation, remuneration, profit split or otherwise related thereto – which will be outside of the Net Profit Split described in Exhibit A. Likewise, Athenex shall not be responsible for any expenses, costs or otherwise related thereto. Athenex hereby agrees that it shall not sell any Product outside of the Athenex Territory without the express written consent of Ingenus.

SECTION 3: *TRANSFER PRICE*

3.1 Transfer Price. Athenex Purchase Orders shall state that the purchase of the Product as manufactured and supplied by Ingenus shall be in accordance with the agreed upon Transfer Price, as referenced in **Exhibit A** hereto ("**Transfer Price**"). The Transfer Price may be adjusted in accordance with Section 5.2 (a)(iii) of this Agreement. The Transfer Price excludes all costs relating to freight, transportation related insurance and U.S. Customs or other costs of shipment and logistics, which shall be the sole responsibility of Athenex.

SECTION 4: *INTELLECTUAL PROPERTY LICENSE; INTELLECTUAL PROPERTY LITIGATION*

4.1 Intellectual Property. Ingenus shall solely own all Ingenus Intellectual Property whether patentable or not and technical information created and/or related to Product and/or ANDA. Each Party shall be the sole owner of its own intellectual property not related to the Product, and nothing in this Agreement shall be deemed to transfer any incidence of ownership thereto, other than the terms specified in this Agreement.

4.2 Intellectual Property Litigation.

(a) Management of Intellectual Property Litigation. In the event a third party threatens or initiates litigation against Athenex related to the Product, Ingenus or any of their respective Affiliates alleging that the Product, the ANDA or any Ingenus Intellectual Property infringes that third party's rights ("**IP Litigation**"), Ingenus shall control such IP Litigation at its own cost. Athenex shall not enter into any settlement agreement or settlement arrangements, voluntary final disposition of any claim, without the prior written consent of Ingenus.

(b) IP Litigation Discovery. Athenex will fully comply with discovery requests and provide reasonable access to Ingenus and/or its designated agents to relevant information within the custody and control of Athenex in order to defend and/or prosecute any IP Litigation. Athenex shall fully cooperate with Ingenus in any reasonable manner with respect to discovery and or other litigation matters.

(c) Indemnification Obligations Not Affected. The Parties' respective rights and obligations pursuant to this Section 4.2 will be subject to, and will not affect, their respective rights and obligations pursuant to Section 9.1, 9.2 and 9.3.

SECTION 5: *MANUFACTURE, PURCHASE, AND DELIVERY*

5.1 Manufacture of Product. Ingenus shall be responsible for the manufacturing, packaging, labeling on the Athenex label (or other private label, as designated by Athenex) and otherwise preparing the Product for Athenex to sell, commercialize and distribute in the Athenex Territory. Athenex shall exclusively purchase all its supply of the Product for sale and distribution in the Athenex Territory from Ingenus.

(a) Product Manufacture.

(i) Ingenus shall be responsible for the timely manufacture and supply of the Product in accordance with Athenex Purchase Orders and Section 5.1(b) of this Agreement.

(ii) Ingenus shall be responsible for procuring all Materials and performing all applicable analytical release testing to process the quantity of Product for which firm Purchase Orders have been issued by Athenex in accordance with the Forecasts.

(iii) At the time of the Product being made available to Athenex for EXW shipment, the Product shall have a minimum shelf-life of 75% of the approved Product expiry dating.

(b) Specifications; Ingenus to inform Athenex of Developments. Ingenus shall ensure the Product is manufactured, packaged, labeled, and supplied according to (i) the master batch record, (ii) the Specifications, (iii) the ANDA, (iv) GMPs, (v) the Quality Agreement and (vi) and any further requirements agreed upon by the Parties in writing and or required by the Applicable Law. Ingenus will keep Athenex informed of any development that could materially affect Ingenus' manufacture or supply of the Product.

(c) Stability Testing. Ingenus shall maintain a stability testing program for the Product and provide Athenex with an annual product review thereon. At least one (1) batch and one SKU of each strength shall be included in the annual stability program.

(d) Annual Reports. Ingenus shall be responsible for compiling Annual Reports for the Product for filing with the FDA. Athenex will, without additional costs or charges, provide in a timely manner, any assistance and/or documents within Athenex' custody or control and required by Ingenus to compile and file such Annual Reports, or any other required FDA documentation.

(e) Import and Customs. Ingenus will provide Athenex with a certificate of analysis for the Product which Ingenus will ensure complies with Section 5.1(b).

5.2. Purchase Orders.

(a) Purchase Orders.

(i) Athenex shall make all purchases hereunder by submitting to Ingenus written Purchase Orders. In the event of a conflict between the terms and conditions of any Purchase Orders and this Agreement, the terms and conditions of this Agreement shall prevail.

(ii) Each Purchase Order shall be in whole batch quantities and have a maximum delivery date of one hundred and twenty (120) days EXW Ingenus' site after the acceptance of the Purchase Order by Ingenus. Ingenus shall be bound to accept all Purchase Orders which are placed in accordance with this Agreement and the Forecast (+/- ten percent (10%)). Ingenus shall accept Purchase Orders, in writing, within five (5) business days as from placement by Athenex. In the absence of express acceptance within the foregoing term, the relevant Purchase Order shall be deemed to have been accepted.

(iii) The initial Transfer Price for the Product purchased under this Agreement is set forth on Exhibit A and will be fixed for one year from the Effective Date of this Agreement. If necessary, from time to time after the initial one-year period noted above, the Parties agree to cooperate in determining a new Transfer Price due to, among other things, market conditions or increases or decreases in cost of Materials. Consent in determining a new Transfer Price will not be unreasonably withheld, delayed or conditioned by a Party, and each Party will provide reasonably requested information and documentation necessary to determine a new Transfer Price. The Parties also may alter the Transfer Price during the initial one-year period only upon mutual agreement in writing by the Parties. In addition, in case that Athenex determines that the Product is not commercially viable at any during the Term, Athenex shall send a notice to Ingenus. The Parties shall then discuss an adjustment of the Transfer Price. If the Parties fail to reach an agreement within a period of sixty (60) days from Athenex notification, Athenex shall have the right to terminate the Agreement as per Section 8.2(e).

If Ingenus seeks an increase in the Transfer Price, it will provide written notice to Athenex thereof at least ninety (90) days prior to the desired effective date of the proposed increase, specifying the amount of, and reasonably detailed reasons for, the increase. The Parties then will negotiate in good faith to arrive at a mutually agreeable new Transfer Price. Should the Parties fail to reach a mutually acceptable agreement on the requested change within thirty (30) days, then Ingenus may submit the request under the terms of "Dispute Resolution" as outlined in Section 10 of this Agreement. No change in the Transfer Price and no interruption in the supply of Products shall occur during the negotiations and Dispute Resolution periods, however, any change in the Transfer Price through negotiation or Dispute Resolution shall be retroactive to the date of the requested change by Ingenus.

(b) Authorized Distributors of Record. Ingenus acknowledges that Athenex will supply the Product to certain distributor customers in the Athenex Territory, and Ingenus designates such customers to be authorized distributors of record, having permission to distribute the Product for and on behalf of Athenex. Upon request, Athenex will provide Ingenus with a current list of designated authorized distributors of record.

(c) Payment Terms.

(i) Product. Except as mutually agreed by the Parties, Ingenus will invoice Athenex for the Transfer Price of Product purchased under this Agreement when such Product is made available for delivery EXW at Ingenus' site. Payments are due within forty-five (45) days after invoice receipt.

(ii) Other Amounts. For other amounts hereunder, if a Party is entitled to receive any payment from the other Party pursuant to this Agreement, then the Party to receive Payment shall invoice the Party obligated to make Payment (with each invoice setting forth, in reasonable detail, the amounts invoiced therein and the reason for such invoicing) and each such invoice will be due and payable within forty-five (45) days after invoice receipt.

(iii) Dollars. All monetary amounts set forth herein are in U.S. Dollars ($) and all payments hereunder shall be made in U.S. Dollars. All costs and expenses incurred by Ingenus in foreign currencies that are being passed on to Ingenus in any manner, shall be converted to U.S. Dollars at the conversion rate noted in the Wall Street Journal® as of the date the expense is incurred or as mutually agreed to by the Parties.

(iv) Withholding Taxes. For the avoidance of doubt, all payments made by Athenex to or for the benefit of Ingenus shall be made free and clear of, and without deduction or withholding for or on account of, any present or future taxes, withholdings or similar assessments, now or hereafter imposed, levied, collected, withheld or assessed by any governmental or taxing agency or authority.

(d) Forecasts. Athenex shall provide Ingenus with a 12-month rolling forecast, on a monthly basis (no less than 10 days prior to the beginning of each calendar month) beginning on 180-days preceding the agreed-upon and predicted Product Launch, which sets forth the quantities of the Product Athenex anticipates it

will order from Ingenus (each a "**Forecast**"). The first three-months of any Forecast shall be deemed firm orderable quantities upon receipt of Purchase Order. All Purchase Orders shall be full batch size or its multiple.

(e) Rejection.

(i) Athenex may examine and test Product as it sees fit and may reject Product provided hereunder by Ingenus if such Product is defective due to Ingenus' failure to follow, or the Products failure to meet, the requirements set forth in Section 5.1 (b) above (a "**Product Defect**"); provided, however, that Athenex shall give written notice to Ingenus of its rejection of any Product hereunder, together with appropriate documentation for its decision (a "**Rejection Notice**"), within ten (10) days after Athenex' receipt of shipment of such Product. The Rejection Notice shall specify the grounds for rejection. If such Rejection Notice is not received within ten (10) days after Athenex' receipt of any Product, such Product shall be deemed to be accepted by Athenex. However, any Product Defect that would not be discoverable upon a reasonable inspection of a Product in accordance with industry standard incoming inspection practices (a "**Hidden Defect**") will not be deemed accepted by Athenex at any time. As soon as possible but not exceeding the shelf life of any Product, if either Party becomes aware of a Hidden Defect in such Product, it will, within ten (10) business days of becoming aware of such Hidden Defect, notify the other Party in writing about all Product involved (a "**Hidden Defect Rejection Notice**").

(ii) Ingenus may dispute a Rejection Notice or Hidden Defect Rejection Notice by providing written notice to Athenex of the dispute within fifteen (15) days after receipt of such Rejection Notice or Hidden Defect Rejection Notice (as applicable), which notice from Ingenus shall specify, in reasonable detail, the grounds for the dispute.

(iii) If a Rejection Notice or Hidden Defect Rejection Notice for any Product is not disputed by Ingenus as set forth in Section 5.2(e)(ii) above or if, in the event of a rejection dispute between the Parties, the contract laboratory referred to in Section 5.2(e)(iv) below gives a decision in favor of Ingenus, then:

(1) Athenex may withhold all payment for the rejected batch;

(2) where payment for the rejected batch has been made, Ingenus will promptly issue a full credit or pay a full refund (as selected by Athenex) to Athenex for the rejected batch of Product; and

(iv) If there is a dispute between the Parties with respect to the rejection of Product, the Parties will first seek to amicably resolve the dispute among themselves. If after thirty (30) days the Parties believe that the dispute cannot be amicably resolved, then the Parties shall mutually agree on a contract laboratory to conduct further testing of the rejected Product in order for the laboratory to determine whether the rejected Product meets the requirements for rejection set forth in this Section 5.2(e). The Party whose conclusions are not borne out by the laboratory shall bear the cost of such testing, or as reasonably allocated based upon testing results. If the contract laboratory gives a decision in favor of Ingenus, Athenex shall promptly pay for the Product subject to the dispute, if such payment had not earlier been made. The decision of the contract laboratory, to the extent dispositive of a Product rejection dispute between the Parties, shall be binding upon the Parties with respect to such rejection dispute; any other or further disputes between the Parties with respect to Product conformance with Specifications, other representations and warranties made by a Party herein, or other matters will be addressed in accordance with Sections 9.1, 9.2, 9.3 and 10.2.

5.3. Delivery and Supply Obligations.

(a) Supply. Ingenus shall use commercially reasonable efforts to ensure the Product to be delivered and supplied to Athenex in accordance with this Section 5.3 and the other provisions of this Agreement and all Purchase Orders. If Ingenus does not comply with any of its delivery obligations under this Agreement

for any accepted Purchase Order, Athenex may, in Athenex's sole discretion and at Ingenus's sole cost and expense (and without limiting any other rights and remedies available to Athenex including, without limitation, a right to recover damages), (a) approve a revised delivery date, (b) require expedited or premium shipment, or (c) cancel the applicable Purchase Order

(b) Labeling and Packaging. The design, formatting, content and any Specifications for artwork, labels and packaging shall be provided by Athenex. Athenex agrees that such materials, in the form provided by Athenex, will comply with Applicable Laws and the ANDA. Ingenus shall be solely responsible for the packaging, labeling, label printing and otherwise preparing for, and actual delivery EXW of the Product to Ingenus in accordance with this Agreement. Athenex shall be solely responsible for all costs in connection with any artwork changes (except those specifically requested by Ingenus) and shipment and logistics/transportation.

(c) Certificate of Analysis. Each delivery of Product hereunder shall be accompanied by a Certificate of Analysis prepared by an authorized representative of Ingenus, certifying that all Product in the shipment has been tested in accordance with the ANDA, meets the Specifications and was manufactured in compliance with cGMPs.

5.4 Quality Control and Compliance.

(a) Quality and Complaint Agreements. The Parties agree to enter into a separate quality agreement (as amended or otherwise modified, the "**Quality Agreement**") with respect to the Product promptly after the Effective Date but in any case, prior to Product Launch. Each Party agrees to perform its obligations under the Quality Agreement; however, in the event of a conflict between this Agreement, on the one hand, and the Quality Agreement, on the other hand, the terms of the Quality Agreement will control and be applicable in respect of quality-related matters. For all other matters, this Agreement will control and be applicable.

(b) Compliance With Laws. Each Party agrees to comply with all Applicable Laws, including, without limitation, GDUFA, cGMPs and state licensing laws, in its performance under this Agreement.

(c) Audit and Inspection. During the Term, upon reasonable prior notice by a Party, the other Party shall make open and available its facilities, employees, agents, and documentation related to its performance hereunder and/or the manufacturing of the Product to the requesting Party for audit and inspection. Such audits and inspections are limited to one (1) per calendar year, unless there exists good cause, shall not extend to any records beyond two (2) calendar years prior to the year of the requested audit and inspection, and no accounting period may be audited more than once. In the event there is a conflict between an audit scheduled by Ingenus and one performed by a governmental agency pursuant to Applicable Law ("**Government Audit**"), Ingenus shall use commercially reasonable efforts to permit Ingenus scheduled audit. If the Ingenus audit cannot be conducted simultaneously with the Government Audit, Ingenus shall schedule the Ingenus audit for immediately prior to or after such Government Audit. Each Party shall be permitted to receive a written copy of any audit reports within fifteen (15) days of its written request. Any audit reports generated are subject to the provisions of Section 10.11 (Confidentiality) and may not be shared with any third parties without prior written consent. Each Party will provide to the other Party, within Seven (7) business days after receipt or submission, copies of all correspondences, deficiency letters, 483's, warning letters, responses, and other documents which concern or may concern the Product and/or a Party's ability to perform hereunder.

(d) Recalls. If any Product is recalled or withdrawn pursuant to FDA regulation or other Applicable Laws or because the Parties, in their reasonable discretion determine that a recall is necessary to protect the public health (a "**Recall**") and such (i) Recall is due Ingenus' breach of its obligations under this Agreement, negligence, or willful misconduct ("**Ingenus Conduct**"), then Ingenus will bear all justified costs in connection with the Recall, including, but not limited to, all notification letters, postage, phone calls,

faxes, courier charges, and all shipping expenses and (ii) where the Recall is the result of Athenex breach of its obligations under this Agreement, negligence, or willful misconduct ("**Athenex Conduct**"), then Athenex will bear all justified costs in connection with the Recall, including, but not limited to, all notification letters, postage, phone calls, faxes, courier charges, and all shipping expenses.If a Recall is due to the nature of the Product (for example, the FDA deems the Product to be unsafe) and is not due to Ingenus Conduct or Athenex Conduct, then the Parties shall equally bear the cost of the Recall. The Parties agree to cooperate in case of a Recall and provide such information as may be necessary to effectuate the Recall and to satisfy any regulatory requests about the Recall.

(e) Customer Questions and Complaints. Questions or complaints received by Athenex relating to the Product shall be referred to Ingenus no later than Seven (7) days after receipt. Ingenus shall process, investigate and respond to such said questions and complaints.

5.5 Drug Supply Chain Security Act.

(a) Capitalized terms used in this Section 5.5 will have the meanings set forth in the Drug Supply Chain Security Act of 2013, 21. U.S.C. Section 360eee, et seq., and the rules, regulations and guidance there-under, all as amended and in effect from time to time (collectively, the "**DSCSA**").

(b) Ingenus will affix or imprint a Product Identifier to each package, each homogenous case and each pallet of Product provided by Ingenus under this Agreement and these Product Identifiers (serial numbers) will be fully aggregated and communicated electronically in EPCIS format in GS1 EPCIS 1.1 standard.

(c) Each Party will keep and maintain records of its performance under this Section 5.5 for not less than Three (3) years after such records are generated or such longer period as may be required under the DSCSA.

SECTION 6: *REPRESENTATIONS AND WARRANTIES*

6.1 Representations, Warranties and Agreements of Ingenus. Ingenus represents, warrants and agrees as follows:

(a) Due Authorization; Enforceability. Ingenus is duly organized, validly existing and in good standing under the laws of its jurisdiction of formation, is qualified to do business and is in good standing as a foreign corporation in each jurisdiction in which the conduct of its business or the ownership of its properties requires such qualification, and has all requisite power and authority, corporate and otherwise, to conduct its business as now being conducted, to own, lease and operate its own properties and to execute, deliver and perform this Agreement. All requisite action, corporate and otherwise, has been taken to authorize Ingenus' execution, delivery and performance of this Agreement. This Agreement is a legal, valid and binding obligation of Ingenus, enforceable against Ingenus with its terms.

(b) Title. Upon the delivery of any Product to Athenex, good title thereto will pass to Athenex, free and clear of all liens and other encumbrances.

(c) No Conflicts. Neither execution and delivery of this Agreement nor its performance of this Agreement will: (i) constitute a breach of, default under, or violation of (A) any Applicable Law; (B) any agreement or other obligation to which Ingenus is a party or by which it or any of its property is bound; or (C) the rights of any person or entity; or (ii) result in the creation of any right or claim that adversely affects Ingenus' performance pursuant to this Agreement.

(d) Debarment. Neither Ingenus nor any of its officers or employees has been (i) convicted of a felony under the U.S. state or federal law for conduct relating to any drug product, biologic, medical device, new drug application or abbreviated new drug application (including, without limitation, conduct relating to the

development, approval or manufacture thereof) or (ii) otherwise debarred under Applicable Law. To Ingenus' best knowledge, it has not and will not use in its performance under this Agreement the services of any person or entity that has been Excluded. Upon request by Ingenus, Ingenus will provide for FDA submission a standard "Debarment Certification".

(e) Generic Drug User Fee Amendments Act Compliance. Ingenus will comply with the requirements of GDUFA that are applicable to Ingenus, including, without limitation, all provisions relating to selfidentification. Ingenus will ensure the payment of all applicable GDUFA facility, whether payable by Ingenus or its agent(s) or suppliers and Athenex shall reimburse to Ingenus its proportionate share of such GDUFA fees as reasonably calculated by Ingenus. Ingenus further represents and warrants that at all times, the facility utilized by Ingenus to manufacture the Product is in compliance with all Applicable Law, including but not limited to cGMP and that the facility is an approved facility by the FDA for manufacture of the Product for distribution in the Territory.

(f) Licenses. Ingenus has all licenses, permits and authorizations required for its performance of its obligations under this Agreement hereunder (including, without limitation, the manufacturing, supply and delivery of Product in accordance with this Agreement) and agrees to maintain such licenses, permits and authorizations in full force and effect.

(g) Product. Each delivery of Product hereunder will not be, at the time of delivery, (A) manufactured other than in compliance with Section 5.1 (b) above, (B) not be adulterated, misbranded or otherwise prohibited (within the meaning of the FD&C Act and all other Applicable Laws), (C) a drug subject to restrictions on sale, purchase, trade or offers to sell, purchase or trade, pursuant to 21 U.S.C. 353 (c)(1) (as amended and in effect from time to time), and/or (D) a drug that has been imported or reimported in violation of Applicable Laws (including, without limitation, 21 U.S.C. Section 381, as amended and in effect from time to time).

6.2 Representations, Warranties and Agreements by Athenex. Athenex represents, warrants and agrees as follows:

(a) Due Authorization; Enforceability. Athenex is duly organized, validly existing and in good standing under the laws of its jurisdiction of formation, is qualified to do business and is in good standing as a foreign corporation in each jurisdiction in which the conduct of its business or the ownership of its properties requires such qualification, and has all requisite power and authority, corporate and otherwise, to conduct its business as now being conducted, to own, lease and operate its properties and to execute, deliver and perform this Agreement. All requisite action, corporate and otherwise, has been taken to authorize Athenex's execution, delivery and performance of this Agreement. This Agreement is a legal, valid and binding obligation of Athenex, enforceable against Athenex with its terms.

(b) No Conflicts. Neither execution and delivery of this Agreement nor its performance of this Agreement will: (i) constitute a breach of, default under, or violation of (A) any Applicable Law; (B) any agreement or other obligation to which Ingenus is a party or by which it or any of its property is bound; or (C) the rights of any person or entity; (ii) infringe the intellectual property rights of any person or entity; or (iii) result in the creation of any right or claim that adversely affects Ingenus' performance pursuant to this Agreement.

(c) Debarment. Neither Athenex nor, to the knowledge of Athenex, any of its officers or employees has been (i) convicted of a felony under the U.S. state or federal law for conduct relating to any drug product, biologic, medical device, new drug application or abbreviated new drug application (including, without limitation, conduct relating to the development, approval or manufacture thereof) or (ii) otherwise debarred under Applicable Law. To Athenex' best knowledge, it has not and will not use in its performance under this Agreement the services of any person or entity that has been Excluded.Upon request by Ingenus, Ingenus will provide for FDA submission a standard "Debarment Certification".

(d) GDUFA Compliance. Athenex will comply (and will cause any agents, subcontractors or other third parties conducting business relating to the ANDA on Ingenus' behalf to comply) with the requirements of GDUFA that are applicable to Athenex.

6.3 Warranty Disclaimer. **EXCEPT FOR THE REPRESENTATIONS AND WARRANTIES EXPRESSLY SET FORTH IN THIS AGREEMENT, EACH PARTY HEREBY DISCLAIMS ALL REPRESENTATIONS AND WARRANTIES, INCLUDING, WITHOUT LIMITATION, THE IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE.**

SECTION 7: *CONTRACTS WITH THIRD PARTIES*

7.1 If Ingenus retains, engages or otherwise enters into a relationship with any third party to discharge its performance under this Agreement (including, without limitation, any agents or subcontractors), whether through a new or already existing contract with such third party, then:

(a) Ingenus will ensure that such third party is fully capable of performing the obligations of this Agreement and is in compliance with all the representations and warranties made by Ingenus in this Agreement.

(b) Ingenus will notify Athenex in writing at least 30 days prior to any such third party taking over Ingenus obligations under this Agreement.

(c) No such retention, engagement or other relationship will relieve Ingenus of its obligations pursuant to this Agreement and any conduct of such third party that fails to meet the requirements of this Agreement will constitute a breach of this Agreement by Ingenus.

SECTION 8: *AGREEMENT TERM AND TERMINATION OF AGREEMENT*

8.1 Agreement Term. The Agreement is effective as of the Effective Date and, unless earlier terminated as provided herein, shall continue for an initial term ending the Fifth (5th) anniversary of the Effective Date (the "Initial Term"). Upon expiration of this Agreement, the Parties may mutually agree to extend this Agreement in one year increments. Upon the expiration of such Initial Term and each renewal term thereafter, this Agreement will require the mutual written consent of the Parties to be extended. For the avoidance of doubt, any non-renewal or expiration of this Agreement shall constitute a termination of this Agreement for all purposes hereof. When used in reference to this Agreement, "Term" means the period from the Effective Date through the Initial Term and each renewal term until termination or expiration in accordance with the terms of this Agreement.

8.2 Termination.

(a) In the event of a material breach of this Agreement by either Party, the non-breaching Party may provide written notice of such breach to the breaching Party, including a description of the breach, and indicating the non-breaching Party's intent to terminate this Agreement. The breaching Party will have sixty (60) days from its receipt of such notice to cure the breach, provided the breach is capable of being cured within the sixty-day period. If the breaching Party fails to cure the breach within such period, then the non-breaching Party may terminate this Agreement on written notice to the breaching Party.

(b) Either Party may terminate this Agreement, effective immediately upon written notice to the other Party, if the other Party files for bankruptcy, is adjudicated bankrupt, files a petition under insolvency laws, is dissolved or has a receiver appointed for substantially all of its property. Furthermore, if a Party has reason to know that it may cease operations or will be unable to honor its obligations under this Agreement due to its financial condition, it shall provide immediate written notice to the other Party, who may in its sole discretion terminate this Agreement effective immediately upon written notice.

(c) By Ingenus, by providing (A) Athenex 90 days' prior written notice of termination in the case there is (i) a sale of substantially all the assets of Ingenus; (ii) a sale of voting control of Ingenus; (iii) a sale of the Product or; (iv) the sale of the manufacturing site for the Product which is located in Via Cadepiano 24 CH 6917 – Barbengo Lugano Switzerland ("Facility"), and (B) supplying the Product to Athenex for up to 240 days from the date of receipt of the termination notice at a monthly quantity not to exceed Athenex's average monthly Product sales over the 90 day period immediately preceding the notice.

(d) By Athenex, in case the ANDA is cancelled and/or withdrawn by the FDA or if Athenex is otherwise prevented from commercializing the Product in the Territory.

(e) By Athenex, in case that the Parties fail to reach an agreement on the Transfer Price as per Section 5.2. (a)(iii).

8.3 Effect of Termination.

Upon termination for any reason except for breach as per section 8.2 (a) above, Athenex shall purchase from Ingenus (at Ingenus' then-current Transfer Price as provided herein) all of Ingenus' remaining finished goods inventory of any Product and work in process, which were on Athenex Purchase Orders to Ingenus. Ingenus shall deliver to Athenex all such finished goods indicated above.

8.4 Suspension. In addition to the rights of a Party pursuant to Section 8.2(a), either Party may suspend its performance hereunder for as long as the other Party remains in material breach of this Agreement.

8.5 Survival. The following Sections of this Agreement, together with any related defined terms and exhibits and schedules hereto, will survive any termination of this Agreement: 2.1, 4, 5.1(d), 5.2(d),, 5.4(b)(ii), 5.4(b)(iii), 5.4(d), 5.4(e), 5.5 and 6, 8.5, 9, and 10. Termination of this Agreement will not release a Party from any liabilities (including, without limitation, liabilities for breach) that, as of the effective date of such termination, have already accrued or that are based upon any event occurring prior to such termination.

8.6 Remedies Cumulative. Each right or remedy of a Party hereunder is in addition to, and not in lieu of, the other rights and remedies of such Party pursuant to this Agreement and Applicable Law.

SECTION 9: *INDEMNIFICATION; INSURANCE; EXCLUSION OF DAMAGES*

9.1 Indemnification by Ingenus. Ingenus shall, at its sole cost and expense, defend, indemnify and hold Athenex and its Affiliates and their respective officers, directors, agents, and employees (collectively "Athenex Indemnified Parties") harmless from and against any and all third-party losses, claims, liabilities, obligations, expenses and/or damages (including without limitation reasonable attorneys' fees) (collectively, "**Third Party Claim(s)**")) to the extent that such Third Party Claims arise out of or result from: (i) any negligence, recklessness, willful misconduct, or fraud by Ingenus in connection with the execution and/or performance of this Agreement; (ii) any breach of this Agreement by Ingenus; (iii) any allegation of Product liability attributable to the performance or failure to perform hereunder by Ingenus (including without limitation any allegation made that a Product has not been manufactured, or supplied in accordance with Section 5.1(b) or that a Product is defective; or (iv) any claim alleging that the Product, the ANDA or any other Ingenus Intellectual Property misappropriates or infringes any third party's rights including, without limitation, any IP Litigation; provided, however, that Ingenus shall have no such obligation to indemnify, defend or hold harmless with respect to any Third Party Claim to the extent such Third Party Claim is caused by the negligence, recklessness, willful misconduct or fraud of any Athenex Indemnified Party, or Athenex' breach of this Agreement.

9.2 Indemnification by Athenex. Athenex shall, at its sole cost and expense, defend, indemnify and hold Ingenus and its Affiliates and their respective officers, directors, agents, and employees (collectively "**Ingenus Indemnified Parties**") harmless from and against any and all Third Party Claims to the extent that such Third Party Claims

arise out of or result from: (i) any negligence, recklessness, willful misconduct, or fraud by Athenex in connection with the execution and/or performance of this Agreement; (ii) any breach of this Agreement by Athenex; or (iii) any allegation of Product liability attributable to the performance or failure to perform hereunder by Athenex related to the sale, marketing and distribution of Product, provided, however, that Athenex shall have no such obligation to indemnify, defend or hold harmless with respect to any Third Party Claim to the extent such Third Party Claim is caused by the negligence, recklessness, willful misconduct or fraud of any Ingenus Indemnified Party, or Ingenus' breach of this Agreement.

9.3 Indemnification Procedures. If a Party (the "Indemnified Party") believes it is entitled to indemnification and defense pursuant to this Section 9 with respect to a Third Party Claim, it will notify the other Party (the "Indemnifying Party") in writing promptly after it becomes aware of such Third Party Claim (provided that the failure of the Indemnified Party to so provide such notice will not relieve the Indemnifying Party of its obligations under this Section 9, except to the extent the Indemnifying Party is actually prejudiced thereby). Within thirty (30) days after receipt of such notice, the Indemnifying Party will, upon written notice thereof to the Indemnified Party, assume control of the defense of such Third Party Claim with counsel selected by the Indemnifying Party (which may be, at the Indemnifying Party's election, the Indemnifying Party's in-house litigation counsel). If the Indemnifying Party believes that a Third-Party Claim presented to it for indemnification and defense is one as to which the Indemnified Party is not entitled to indemnification and defense under this Section 9, it will so notify the Indemnified Party. The Indemnified Party may participate in such defense with counsel it selects, all at the Indemnified Party's own expense. The Indemnified Party will provide the Indemnifying Party, at the Indemnifying Party's expense, with reasonable assistance and cooperation as reasonably requested by the Indemnifying Party. Without the prior written consent of the Indemnified Party, such consent not to be unreasonably withheld, delayed or conditioned, the Indemnifying Party will not agree to any settlement of such Third Party Claim or consent to any judgment in respect thereof; further, without the prior written consent of the Indemnifying Party, such consent not to be unreasonably withheld, delayed or conditioned, the Indemnified Party will not agree to any settlement of such Third Party Claim or consent to any judgment in respect thereof.

9.4 Insurance.

(a) Ingenus agrees that prior to any commercial manufacture hereunder, it will obtain and shall at all times during the Term will maintain in full force and effect, at its own cost and expense, insurance sufficient to insure against all liabilities arising pursuant to this Agreement as a result of its performance hereunder, including the following minimum insurance coverages: (i) 'worker's compensation insurance, if applicable, as required by law; (ii) Manufacturing Defect with respect to the Product with minimum coverage of Ten Million Dollars ($10,000,000) per occurrence; and (iii) physical property damage insurance, through the designated freight carrier or otherwise, on all of the Product at all times until receipt by Athenex. Upon request, Ingenus will supply to Athenex its certificate of insurance to evidence such coverage and shall name Ingenus as an additional insured under such coverage.

(b) Athenex agrees that prior to any commercial manufacture hereunder, it will obtain and shall at all times during the Term and for two (2) years thereafter will maintain in full force and effect, at its own cost and expense, insurance sufficient to insure against all liabilities arising pursuant to this Agreement as a result of its performance hereunder, including the following minimum insurance coverages: product liability insurance with respect to the Product with minimum coverage of Ten Million Dollars ($10,000,000) per occurrence. Upon request, Athenex will supply Ingenus with a certificate of insurance to evidence such coverage and name Ingenus as an additional insured.

9.5 Exclusion of Damages. **EXCEPT FOR BREACHES OF CONFIDENTIALITY OBLIGATIONS, NEITHER PARTY WILL BE LIABLE FOR SPECIAL, INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES (INCLUDING, BUT NOT LIMITED TO, LOST PROFITS), WHETHER IN CONTRACT, NEGLIGENCE, STRICT LIABILITY OR OTHERWISE, EVEN IF SUCH PARTY HAS BEEN ADVISED OF OR COULD HAVE FORESEEN THE POSSIBILITY OF SUCH DAMAGES**

SECTION 10: *MISCELLANEOUS*

10.1 Entire Agreement; Amendments. This Agreement constitutes the entire agreement between the Parties with respect to the subject matter hereof and supersedes any prior negotiations, understandings or agreements, whether oral or in writing, concerning the subject matter hereof. This Agreement may not be modified, changed or amended except by an instrument in writing duly executed by the Parties hereto.

10.2 Governing Law and Jurisdiction; Arbitration.

(a) This Agreement shall be governed by and construed in accordance with the laws of the State of New York, United States of America, without reference to its conflict of laws principles.

(b) The Parties will first use their best endeavors to resolve through mutual consultation any dispute, difference or question arising between Parties or their respective representatives or assigns, which may arise out of, in connection with or in relation to this Agreement. Any dispute arising out of or in connection with this contract, including any question regarding its existence, validity or termination, which is not resolved through mutual consultation, shall be referred to and finally resolved by arbitration administered by the American Arbitration Association (“AAA”) in accordance with the American Arbitration Rules ("AAA Rules") for the time being in force, which rules are deemed to be incorporated by reference in this clause. The arbitration shall be conducted in English and the venue of arbitration shall be London. The Arbitration shall be conducted by one Arbitrator mutually agreeable to the Parties.

10.3 Severability. If any provision of this Agreement is unenforceable or invalid, no other provision shall be affected thereby, and the remaining provisions shall be construed and reformed to the maximum extent possible and continue with the same effect as if such unenforceable or invalid provision was not a part of this Agreement, it being the intent and agreement of the Parties that this Agreement will be deemed to have been amended by modifying such provision to the extent necessary to render it valid, legal and enforceable while preserving its intent or, if such modification is not possible, by substituting therefore another provision that is legal and enforceable and that achieves the same objective.

10.4 Notices. All notices or communications given pursuant to this Agreement shall be in writing, if to INGENUS addressed to the attention of Matthew J Baumgartner at 4190 Millenia Blvd., Orlando, FL 32839 and if to Athenex, to (i) the attention of John Romano at 10 Martingale Rd Suite 230, Schaumburg, IL 60173, (ii) with a copy to Teresa Bair, Esq., Legal Affairs, Athenex, Inc., Coventus Building, 1001 Main Street, Suite 600, Buffalo, New York 14203. Notice shall be: (a) hand delivered, (b) sent by prepaid express courier service, or (c) sent by electronic mail (e-mail) or facsimile transmission. A Party may change its address for the receipt of notices and communications hereunder by providing the other Party with written notice thereof given in accordance with this Section 10.4. All notices and communications shall be deemed given when received.

10.5 Waiver. Any waiver or consent hereunder must be in writing and signed by the Party claimed to have so waived or consented. A waiver of or consent hereunder given with respect to any breach or provision of this Agreement will not constitute a waiver of any other breach or provision of this Agreement.

10.6 Relationship of Parties and Other Activities. The Parties hereto are independent contractors and no Party is an employee, agent, partner or joint venture of the other.

10.7 Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments and to do all such other acts, as may be reasonably necessary or appropriate in order to carry out the purposes and intent of this Agreement.

10.8 Execution. This Agreement may be executed in any number of counterparts and by facsimile signature or PDF/email, each of which shall be deemed to be an original as against any Party whose signature appears thereon,

and all of which shall together constitute one and the same instrument. This Agreement shall become binding when one or more counterparts hereof, individually or taken together, shall bear the signatures of all of the Parties reflected hereon as the signatories hereto.

10.9 Titles. The titles of the Sections and subsections of this Agreement are for convenience of reference only and are not to be considered in construing the terms and provisions hereof.

10.10 Exhibits All exhibits and schedules to this Agreement, if any, are hereby incorporated by reference into, and made a part of, this Agreement.

10.11 Confidentiality.

(a) During the Term and for three (3) years thereafter, each Party and/or its Affiliates (the "receiving Party") shall maintain in confidence all information of the other Party and/or its Affiliates (the "disclosing Party") disclosed hereunder and identified as, or acknowledged to be, or by its nature ought to be considered, Confidential Information (as defined in Section 10.11(b)) of the disclosing Party. The receiving Party will not use the disclosing Party's Confidential Information in any manner or disclose the disclosing Party's Confidential Information to anyone, except: (i) for uses and disclosures expressly permitted by this Agreement or necessary for the receiving Party to perform its obligations or exercise its rights hereunder; or (ii) for disclosures to those of the receiving Party's Affiliates and the officers, directors, employees, agents and subcontractors of the receiving Party or any of its Affiliates (collectively, "Representatives") to whom disclosure is reasonably necessary in connection with the receiving Party's activities contemplated by this Agreement, provided that, prior to such disclosure to a Representative, the receiving Party will have advised such Representative of the confidential nature of such Confidential Information and such Representative shall be bound by obligations of confidentiality at least as restrictive as those of this Section 10.11. The receiving Party will be responsible for any breach of this Section 10.11 arising from the conduct of its Representatives.

(b) As used herein "Confidential Information" of the disclosing Party shall include all confidential or proprietary information disclosed by or on behalf of the disclosing Party hereunder, including, without limitation, information of or regarding the disclosing Party's or its Affiliates' products, advertising, distribution, marketing, strategic plans, costs data, productivity or technological advances, specifications, data, know-how, formulations, technical information, pricing and other transaction terms, customers and suppliers, potential customers and suppliers, and information provided to the disclosing Party on a confidential basis by a third party; in each case whether in written, electronic, oral, visual or another form. The term "Confidential Information" will not include information that the receiving Party establishes (i) is or becomes generally available to the public other than as a result of a disclosure by the receiving Party or any of its Representatives in breach of this Agreement, (ii) is in the receiving Party's lawful possession, on a non-confidential basis, prior to disclosure thereof by or on behalf of the disclosing Party to the receiving Party, (iii) becomes available to the receiving Party on a non-confidential basis from a source other than the disclosing Party, provided that such source is not known to the receiving Party to be bound by an obligation of confidentiality to the disclosing Party with respect to such information or (iv) by contemporaneous written records is independently developed or discovered by the receiving Party without use of or reference to the Confidential Information of the disclosing Party.

(c) If the receiving Party or any of its Representatives becomes required pursuant to Applicable Law, rule or regulation (including, without limitation, subpoena, civil investigative demand, compulsory process or other legal requirement) to disclose any Confidential Information of the disclosing Party, then (i) unless prohibited from doing so by Applicable Law, the receiving Party will promptly notify the disclosing Party in writing thereof and will cooperate with the disclosing Party, at the disclosing Party's expense, in seeking a protective order or confidential treatment and (ii) the receiving Party and its Representatives may disclose such Confidential Information to the extent so required.

(d) The disclosing Party would be irreparably injured by a breach of this Section 10.11 by the receiving Party, and such a breach would not be compensable in money damages. Accordingly, in addition to any other rights and remedies of the disclosing Party pursuant to this Agreement and Applicable Law, the disclosing Party shall be entitled to seek injunctive and other equitable relief with respect to any breach or threatened breach of this Section 10.11 without posting a bond or other surety.

(e) Upon the termination of this Agreement, the receiving Party will, upon written request of the disclosing Party, promptly return to the disclosing Party or destroy all Confidential Information of the disclosing Party in the possession or control of the receiving Party or any of its Representatives; provided that the receiving Party may retain (i) one (1) copy of the disclosing Party's Confidential Information in order to comply with Applicable Law and determine the rights and obligations of the receiving Party pursuant to this Section 10.11, and (ii) any Confidential Information that is located on backup tapes or archival systems created for disaster recovery that are not commonly accessible or that require the Receiving Party to erase or delete information using special programs or techniques, which retained Confidential Information will remain confidential, subject to the terms of this Section 10.11, for as long as it is so retained by the receiving Party, notwithstanding the expiration of the three (3) year period referred to in Section 10.11(a). The disclosing Party shall be responsible for all expenses relating to the return and/or destruction of such Confidential Information.

10.12 Press Release. Neither Party may issue a press release or issue a statement to the media in any form whatsoever concerning the Product or the Agreement, unless: required by Applicable Law; or the other Party provides its prior written consent thereto, such consent not be unreasonably withheld, delayed or conditioned.

10.13 Assignment. No Party may assign this Agreement or any of its rights, liabilities or obligations hereunder without the prior written consent of the other Party, such consent to not to be unreasonably withheld, delayed or conditioned; provided however, that a Party may, upon written notice to the other Party, assign this Agreement (in whole or in part) to any of its Affiliates, to the purchaser of all or substantially all of its assets or to its successor by merger or stock purchase.

10.14 Force Majeure. No Party shall be responsible for its failure to perform under this Agreement due to any act of God, act of any governmental authority or agency, change in government laws, rules or regulations or orders of courts or of statutory authorities having jurisdiction, act of the public enemy, war, riot, flood, civil commotion, terrorism, insurrection, severe or adverse weather conditions, lack or shortage of electrical power, failure of public transport, strikes or other labor disturbances, epidemics, pandemics or any other cause beyond such Party's reasonable control (each, "**Force Majeure Event**"). If a Party becomes subject to a Force Majeure Event, it will promptly notify the other Party thereof. If a Party becomes subject to a Force Majeure Event that is reasonably expected to continue for more than 120 days, the other Party may, upon written notice and without liability, terminate this Agreement (and, consequently, any issued Purchase Orders that are affected by such Force Majeure Event) as described in section 8.2 (c) above. For the avoidance of doubt, a delay or interruption in performance due to a Force Majeure Event will not constitute a breach of this Agreement.

[Signature Page Follows]

IN WITNESS WHEREOF, Ingenus and Athenex have executed this Agreement by their duly authorized officers as of the latest date set forth above.

ATHENEX PHARMACEUTICAL DIVISION, LLC	**INGENUS PHARMACEUTICALS, LLC.**
By: /s/ Jeffrey Yordon Name: Jeffrey Yordon Position: President/COO 1/16/2021	By: /s/ Samir Mehta Name: Samir Mehta Position: COO

EXHIBIT A: TRANSFER PRICE, VALIDATION CHARGES, AND PROFIT SPLIT.

1. TRANSFER PRICE

[*]

2. NET PROFIT SPLIT:

The Parties agree that they will share (Athenex:[45]%/Ingenus:[55]%) the Net Profits arising from the sale of the Product by Athenex in Athenex Territory under the following terms and conditions:

- Athenex shall receive the Marketing Allowance without sharing with Ingenus.
- Athenex shall not share in the profits on sales of Product by Ingenus, as described in Section 2.4 above.
- Athenex shall calculate the Net Profit from the sale of Product in the Athenex Territory and shall provide such calculation to Ingenus by the 30th day following the end of each calendar quarter.
- Athenex shall pay to Ingenus its share of such calculated Net Profit on or before the 45th day following the end of each calendar quarter.

Exhibit 21.1

SUBSIDIARIES OF ATHENEX, INC.

Subsidiary Companies	Jurisdiction of Incorporation
Athenex API Limited	Hong Kong
Athenex Belgium	Belgium
Athenex Biomedical International Holdings Limited	Hong Kong
ATHENEX CIDAL HOLDINGS I, S.A.	Panama
ATHENEX CIDAL HOLDINGS II, S.A.	Panama
ATHENEX CIDAL PANAMA, S.A.	Panama
Athenex Cidal Columbia S.A.S.	Columbia
Athenex Cidal Argentina S.A.U.	Argentina
Athenex Cidal Chile SpA	Chile
Athenex Cidal Costa Rica S.A.	Costa Rica
Athenex Cidal Peru, S.A.C.	Peru
Athenex Cidal Ecuador ATHENEXCUA S.A.	Ecuador
Athenex Cidal Guatemala S.A.	Guatemala
Athenex Euro Limited	United Kingdom
Athenex HK Innovative Limited	Hong Kong
Athenex Manufacturing China Limited	British Virgin Islands
Athenex Pharma Solutions, LLC	Delaware
Athenex Pharmaceuticals Co., Ltd.	Taiwan
Athenex Pharmaceutical Division, LLC	Delaware
Athenex Pharmaceuticals (China) Limited	Hong Kong
Athenex Pharmaceuticals (Chongqing) Limited	People’s Republic of China
Athenex Pharmaceuticals (Hong Kong) Limited	Hong Kong
Athenex Pharmaceuticals International Holdings Limited	Hong Kong
Athenex Pharmaceuticals LLC	Delaware
Athenex R&D LLC	Delaware
Athenex Therapeutics Limited	Hong Kong
AtheSino Holdings Limited	British Virgin Islands
Atis Science and Technology Company Limited	Hong Kong
Axis Therapeutics Limited	Hong Kong
Bioksy Investments Ltd.	British Virgin Islands
Chongqing MJ Medical Devices Co., Ltd.	People’s Republic of China
Chongqing MJ Medical Sciences Co., Ltd.	People’s Republic of China
Chongqing Taihao Pharmaceutical Co., Ltd.	People’s Republic of China
Chongqing Sintaho Pharmaceutical Co., Ltd.	People’s Republic of China
Comprehensive Drug Enterprises Limited	Hong Kong
Excel Bloom Limited	British Virgin Islands
Maxinase Life Sciences Limited	Hong Kong
Meridian East Limited	British Virgin Islands
MJ Medical Gel Systems Limited	Hong Kong
Nuwagen Limited*	Hong Kong
Peterson Athenex Pharmaceuticals, LLC*	Delaware
Polymed Therapeutics, Inc.	Texas
Renascence Therapeutics Limited*	Hong Kong

* Minority-owned

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-227492, 333-232772, 333-236104, and 333-241665 on Form S-3 and No. 333-218984 and 333-241666 on Form S-8 of our reports dated March 1, 2021, relating to the financial statements of Athenex, Inc. and subsidiaries (the "Company") and the effectiveness of the Company's internal control over financial reporting, appearing in this Annual Report on Form 10-K for the year ended December 31, 2020.

/s/ Deloitte & Touche LLP

Williamsville, New York
March 1, 2021

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 1, 2021

/s/ Johnson Y.N. Lau
Name: Johnson Y.N. Lau
Title: Chief Executive Officer and Board Chairman
(Principal Executive Officer)

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 1, 2021

/s/ Randoll Sze
Name: Randoll Sze
Title: Chief Financial Officer
(Principal Financial and Accounting Officer)

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, 2020, 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 1, 2021

/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)