

MANNKIND CORP
Form 10-K
February 26, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2018

or

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

For the transition period from to

Commission file number: 000-50865

MannKind Corporation

(Exact name of registrant as specified in its charter)

Delaware	13-3607736
(State or other jurisdiction of	(I.R.S. Employer
incorporation or organization)	Identification No.)
30930 Russell Ranch Road, Suite 300	

Westlake Village, California	91362
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code

(818) 661-5000

Securities registered pursuant to Section 12(b) of the Act:

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Title of Class	Name of Each Exchange on Which Registered
Common Stock, par value \$0.01 per share	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act:

None

(Title of Class)

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 15(d) of the Securities Exchange Act of 1934. Yes No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

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

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

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

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company
	Emerging growth company

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

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

As of June 29, 2018, the aggregate market value of the voting stock held by non-affiliates of the registrant, computed by reference to the last sale price of such stock as of such date on the Nasdaq Global Market, was approximately \$252,751,851.

As of February 14, 2019, there were 187,342,566 shares of the registrant's Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement (the "Proxy Statement") for the 2019 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than April 30, 2019 are incorporated by reference in Part III of this Annual Report on Form 10-K.

MANNKIND CORPORATION

Annual Report on Form 10-K

For the Fiscal Year Ended December 31, 2018

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Forward-Looking Statements

Statements in this report that are not strictly historical in nature are “forward-looking statements” within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward-looking statements by terms such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “goal,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would,” and similar words. These statements are intended to identify forward-looking statements, though not all forward-looking statements contain these identifying words. These statements may include, but are not limited to, statements regarding: our ability to successfully market, commercialize and achieve market acceptance for Afrezza or any other product candidates or therapies that we may develop; our ability to manufacture sufficient quantities of Afrezza and obtain insulin supply as needed; our ability to successfully commercialize our Technosphere drug delivery platform; our estimates for future performance; our estimates regarding anticipated operating losses, future revenues, capital requirements and our needs for additional financing; the progress or success of our research, development and clinical programs, including the application for and receipt of regulatory clearances and approvals; our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others; and scientific studies and the conclusions we draw from them. These statements are only predictions or conclusions based on current information and expectations and involve a number of risks and uncertainties. The underlying information and expectations are likely to change over time. Actual events or results may differ materially from those projected in the forward-looking statements due to various factors, including, but not limited to, those set forth under the caption “Risk Factors” and elsewhere in this report. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements. Except as required by law, we undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

Afrezza ® and Technosphere ® are our trademarks in the United States. We have also applied for or have registered company trademarks in other jurisdictions. This document also contains trademarks and service marks of other companies that are the property of their respective owners.

PART I

Item 1. Business

Unless the context requires otherwise, the words “MannKind,” “we,” “Company,” “us” and “our” refer to MannKind Corporation and its subsidiaries.

We are a biopharmaceutical company focused on the development and commercialization of inhaled therapeutic products for patients with diseases such as diabetes and pulmonary arterial hypertension. Our only approved product, Afrezza (insulin human) Inhalation Powder, is a rapid-acting inhaled insulin that was approved by the U.S. Food and Drug Administration (“FDA”) in June 2014. Afrezza became available by prescription in U.S. retail pharmacies in February 2015. According to the Centers for Disease Control and Prevention, 30.3 million people in the United States had diabetes in 2015. Globally, the International Diabetes Federation has estimated that approximately 425.0 million people had diabetes in 2017 and approximately 629.0 million people will have diabetes by 2045.

Afrezza

Afrezza is a rapid-acting inhaled insulin used to improve glycemic control in adults with diabetes. The product consists of a dry powder formulation of human insulin delivered from a small portable inhaler. Administered at the beginning of a meal, Afrezza dissolves rapidly upon inhalation to the lung and delivers insulin quickly to the bloodstream. The first measurable effects of Afrezza occur approximately 12 minutes after administration.

From August 2014 until April 2016, Sanofi-Aventis U.S. LLC (“Sanofi”) was responsible for commercial, regulatory and development activities associated with Afrezza pursuant to a license and collaboration agreement between us and Sanofi (the “Sanofi License Agreement”). The Sanofi License Agreement terminated effective April 2016 and, after a transition period during which Sanofi continued to fulfill orders for Afrezza, we assumed responsibility for worldwide development and commercialization of Afrezza in July 2016.

Currently, we promote Afrezza to endocrinologists and certain high-prescribing primary care physicians through our specialty sales force. To support our sales efforts, we have implemented several patient and physician support programs, including a co-pay assistance and product savings program, direct purchase and our MannKind Cares program that supports providers and patients who have questions about insurance coverage, prescription cost and product use. We have also entered into a number of rebate or other agreements with various payors and pharmacy benefit managers that are intended to facilitate more favorable insurance coverage for Afrezza.

In the future, we may seek to supplement our sales force through a co-promotion arrangement with a third party that has an underutilized primary care sales force, that can be used to promote Afrezza to greater number of primary care physicians in the United States. Internationally, our strategy is to establish regional partnerships in foreign jurisdictions where there are commercial opportunities, subject to receipt of the necessary foreign regulatory approvals. In May 2017 we entered into a supply and distribution agreement with Biomm S.A. to pursue regulatory approval and commercialization of Afrezza in Brazil. In May 2018, we entered into a similar agreement with Cipla Ltd. (“Cipla”) for the regulatory approval and commercialization of Afrezza in India. Our partners have not yet commenced commercialization in their respective territories.

We continue to conduct clinical studies of Afrezza, including an open-label pharmacokinetics (PK) and multiple-dose safety and tolerability dose-titration trial of AFREZZA in pediatric patients with type 1 diabetes. The first cohort (patients aged 13-17) in this study was completed in September 2018. Patients in the second cohort (ages 8-12) are currently being recruited and dosed. During the past year, we also supported a collaborative clinical trial with investigators at the Barbara Davis Center for Diabetes, University of Colorado Denver that examined the effect of

Afrezza on post-prandial glucose excursions and glucose time-in-range using continuous glucose monitors. We have additional collaborative clinical studies that are underway at this time. As part of the approval of Afrezza, the FDA required us to conduct a five-year, randomized, controlled trial in 8,000-10,000 patients with type 2 diabetes to assess the potential serious risk of pulmonary malignancy with AFREZZA use. We have not yet agreed with the FDA on the final study design for this long-term study.

Technosphere Platform

We believe there are additional opportunities for our proprietary Technosphere and inhaler technologies for the delivery of active pharmaceutical ingredients (“API”). We believe that our proprietary Technosphere formulation technology represents a versatile drug delivery platform that may allow the oral inhalation of a wide range of API. We have successfully prepared Technosphere formulations of anionic and cationic drugs, hydrophobic and hydrophilic drugs, proteins, peptides and small molecules. Technosphere powders are based on our proprietary excipient, fumaryl diketopiperazine, which is a pH-sensitive organic molecule that self-assembles into small particles under acidic conditions. Certain drugs, such as insulin or treprostinil, can be loaded onto these particles by combining a solution of the drug with a solution or suspension of Technosphere material, which is then dried to powder form. The resulting powder has a consistent and narrow range of particle sizes with good aerodynamic properties that enable efficient delivery deep into the lungs. Technosphere powders dissolve quickly when the particles contact the moist lung surface with its neutral pH, releasing the drug molecules to diffuse across a thin layer of cells into the arterial circulation, bypassing the liver to provide excellent systemic exposure.

We have also created an innovative line of breath-powered, dry powder inhalers. Our inhalers are easy to use, cost-effective and can be produced in both a reusable (chronic treatment) and a single-use (acute treatment) format. Both the reusable and single use inhaler formats use the same internal air-flow design. Being breath-powered, our inhalers require only the patient's inhalation effort to deliver the powder. To administer the inhalation powder, a patient loads a cartridge into our inhaler and inhales through the mouthpiece. Upon inhalation, the dry powder is lifted out of the cartridge and broken (or de-agglomerated) into small particles. The inhalers are engineered to produce an aggressive airstream to de-agglomerate the powder while keeping the powder moving slowly. This slow-moving powder effectively navigates the patient's airways for delivery into the lung with minimal deposition at the back of the throat. Our inhalers show very little change in performance (i.e., efficient cartridge emptying) over a wide range of inhalation efforts.

We advanced an inhaled formulation of treprostinil (internally designated "TreT") into clinical development, completing a Phase 1 dose-escalation study in June 2018. In September 2018, we announced a license and collaboration agreement with United Therapeutics Corporation ("United Therapeutics" or "UT"), pursuant to which UT became responsible for global development, regulatory and commercial activities with respect to TreT (the "UT License Agreement"). We will manufacture clinical supplies and initial commercial supplies of TreT, whereas long-term commercial supplies may be manufactured by UT. In September 2018, we also signed a research agreement with UT (the "UT Research Agreement") pursuant to which we will evaluate the feasibility of preparing a dry powder formulation of an additional API for the treatment of pulmonary hypertension. In addition to our activities under the UT License Agreement and the UT Research Agreement, we intend to advance additional dry-powder candidates into formulation feasibility and preclinical studies during the next 12-18 months. Our internal product development efforts are supplemented by a collaboration and license agreement with Receptor Life Sciences ("Receptor"), which we entered into in January 2016, pursuant to which Receptor is responsible for the development, manufacture and commercialization of inhaled formulations of certain cannabinoid compounds utilizing our technology. To date, Receptor has conducted formulation studies with a range of different API and has informed us of their plans to commence preclinical development of the most promising powder candidate(s) during 2019.

To aid in the development of our oral inhalation products, we have created a number of innovative tools such as a novel inhalation profiling apparatus that uses miniature sensors to assess the drug delivery process at the level of an individual inhaler. This apparatus provides real-time data regarding patient usage and delivery system performance that is transmitted to a user interface, such as a smartphone application. We are currently evaluating the desirability of developing this apparatus further for use as a training tool in physician offices or as a connected care device that will allow patients to integrate dosing information with other health data, such as blood glucose levels from a self-managed glucose meter or a continuous glucose monitor.

Manufacturing and Supply

We manufacture Afrezza in our Danbury, Connecticut facility, where we formulate the Afrezza inhalation powder, fill it into plastic cartridges and then blister package the cartridges and seal the blister cards inside a foil overwrap. These overwraps are then packaged into cartons along with inhalers and printed material by a third-party packager.

The quality management systems of our Connecticut facility have been certified to be in conformance with the ISO 13485 and ISO 9001 standards. Our facility is inspected on a regular basis by the FDA, most recently in June 2018. We were also inspected by ANVISA (Brazil National Health Surveillance Agency) in May 2018. Neither of the regulatory inspections in 2018 gave rise to any inspectional observations (known as "483s" in the United States). The FDA and other foreign jurisdictions are expected to conduct additional inspections of our facility from time to time.

We believe that our Connecticut facility has enough capacity to satisfy the current commercial demand for Afrezza. In addition, the facility includes expansion space to accommodate additional filling lines and other equipment, allowing

production capacity to be increased based on the reasonably foreseeable demand for Afrezza over the next several years. We are also utilizing some of this expansion space to create production space for TreT in order to supply UT.

Currently, the only source of insulin that we have qualified for Afrezza is manufactured by Amphastar France Pharmaceuticals S.A.S. (“Amphastar”). In April 2014, we entered into a supply agreement with Amphastar (the “Insulin Supply Agreement”) to purchase certain annual minimum quantities with an initial aggregate purchase commitment of €120.1 million which, after taking into account contract amendments, extends through December 31, 2024 with the ability to renew for an additional two years with certain restrictions. On December 24, 2018 we amended the agreement to extend the term for an additional one year through December 31, 2024 with certain restrictions. As of December 31, 2018, there was €85.8 million remaining in aggregate purchase commitments under this agreement. See additional information in Note 14 – Commitments and Contingencies to the consolidated financial statements for further information related to the Insulin Supply Agreement.

Currently, we purchase the raw material for our proprietary excipient, FDKP (fumaryl diketopiperazine), which is the primary component of our Technosphere technology platform, from a major chemical manufacturer with facilities in Europe and North America.

We have a supply agreement with the contract manufacturer that produces the plastic-molded parts for our inhaler and the corresponding cartridges. We expect to be able to qualify an additional vendor of plastic-molding contract manufacturing services, if warranted by demand. We assemble the inhalers at our Connecticut facility.

We also have an agreement with the contractor that performs the final packaging of Afrezza overwraps, inhalers and printed material into patient kits. We expect to be able to qualify an additional vendor of packaging services, if warranted by demand.

Intellectual Property

Our success will depend in large measure on our ability to continue enforcing our intellectual property rights, effectively maintain our trade secrets and avoid infringing the proprietary rights of third parties. Our policy is to file patent applications on what we deem to be important technological developments that might relate to our product candidates or methods of using our product candidates and to seek intellectual property protection for all inventions in the United States, Europe, Japan and, depending on the nature of the invention, selected other jurisdictions. We have obtained, are seeking, and will continue to seek patent protection on the compositions of matter, methods and devices flowing from our research and development efforts.

Our Technosphere drug delivery platform, including Afrezza, enjoys patent protection relating to the powder, its manufacture, and its use for pulmonary delivery of drugs. We have additional patent coverage relating to the treatment of diabetes using Afrezza. We have also been granted patent coverage for our inhalers and associated cartridges. Overall, Afrezza is protected by over 570 issued patents in the United States and selected jurisdictions around the world, the longest-lived of which will expire in 2032. We also have over 160 applications pending that may provide additional protection for Afrezza if and when they are allowed. Our entire portfolio consists of approximately 930 issued patents and 280 patent applications that provide protection for our drug delivery platform, Technosphere-based products, the inhalation-profiling apparatus and development tools. Currently, our longest-lived issued patent will expire in 2034. We expect to file further patent applications as our research and development efforts continue.

The field of pulmonary drug delivery is crowded and a substantial number of patents have been issued in these fields. In addition, because patent positions can be highly uncertain and frequently involve complex legal and factual questions, the breadth of claims obtained in any application or the enforceability of issued patents cannot be confidently predicted. Further, there can be substantial delays in commercializing pharmaceutical products, which can partially consume the statutory period of exclusivity through patents.

In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, either in the United States or abroad. Statutory differences in patentable subject matter may limit the protection we can obtain on some of our inventions outside of the United States. For example, methods of treating humans are not patentable in many countries outside of the United States. These and other issues may limit the patent protection we are able to secure internationally. Consequently, we do not know whether any of our pending or future patent applications will result in the issuance of patents or, to the extent patents have been issued or will be issued, whether these patents will be subjected to further proceedings limiting their scope, will provide significant proprietary protection or competitive advantage, or will be circumvented or invalidated. Furthermore, patents already issued to us or our pending applications may become subject to disputes that could be resolved against us. In addition, in certain countries, including the United States, applications are generally published 18 months after the application's priority date. In any event, because publication of discoveries in scientific or patent literature often trails behind actual discoveries, we cannot be certain that we were the first inventor of the subject matter covered by our pending patent applications or that we were the first to file patent applications on such inventions.

If third parties file patent applications, or are issued patents claiming technology also claimed by us in pending applications, we may be required to participate in interference proceedings in the United States Patent and Trademark Office ("USPTO") to determine priority of invention. We may also be required to participate in interference proceedings involving our issued patents. We also rely on trade secrets and know-how, which are not protected by patents, to maintain our competitive position. We require our officers, employees, consultants and advisors to execute proprietary

information and invention and assignment agreements upon commencement of their relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of our relationship must be kept confidential, except in specified circumstances. These agreements also provide that all inventions developed by the individual on behalf of us must be assigned to us and that the individual will cooperate with us in connection with securing patent protection on the invention if we wish to pursue such protection. There can be no assurance, however, that these agreements will provide meaningful protection for our inventions, trade secrets or other proprietary information in the event of unauthorized use or disclosure of such information.

We also execute confidentiality agreements with outside collaborators. However, disputes may arise as to the ownership of proprietary rights to the extent that outside collaborators apply technological information to our projects that are developed independently by them or others, or apply our technology to outside projects, and there can be no assurance that any such disputes would be resolved in our favor. In addition, any of these parties may breach the agreements and disclose our confidential information or our competitors might learn of the information in some other way. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to or independently developed by a competitor, our business, results of operations and financial condition could be adversely affected.

Competition

The pharmaceutical and biotechnology industries are highly competitive and characterized by rapidly evolving technology and intense research and development efforts. We compete with companies, including major global pharmaceutical companies, and other institutions that have substantially greater financial, research and development, marketing and sales capabilities and have substantially greater experience in undertaking preclinical and clinical testing of products, obtaining regulatory approvals and marketing and selling biopharmaceutical products. We face competition based on, among other things, product efficacy and safety, the timing and scope of regulatory approvals, product ease of use and price.

Diabetes Treatments

We believe that Afrezza has important competitive advantages in the delivery of insulin when compared with currently known alternatives. However, new drugs or further developments in alternative drug delivery methods may provide greater therapeutic benefits, or comparable benefits at lower cost, than Afrezza. There can be no assurance that existing or new competitors will not introduce products or processes competitive with or superior to our product candidates.

We have set forth below more detailed information about certain of our competitors. The following is based on information currently available to us.

Rapid-acting (Injected) Insulin

Currently, we believe that Afrezza has a unique pharmacokinetic profile, i.e., with the first measureable effects occurring approximately 12 minutes after administration, reaching peak effects within 35 or 45 minutes after administration of a 4 or 12 unit dose, respectively. There are several formulations of “rapid-acting” insulin analogs that reach their maximum glucose-lowering effect within one to three hours after injection. The principal products in this category are insulin lispro, which is marketed by Eli Lilly & Company as Humalog® and by Sanofi as Admelog®; insulin aspart, which is marketed by Novo Nordisk A/S as Novolog® and as Fiasp ®; and insulin glulisine, which is marketed by Sanofi as Apidra®.

Inhaled Insulin Delivery Systems

Our drug delivery platform competes with other inhaled delivery systems, including the Dance-501 being developed by Dance Biopharm. Holdings Inc. Dance-501 is a liquid formulation of recombinant human insulin for administration with a small handheld electronic inhaler that is currently being studied in Phase 2 trials.

Government Regulation and Product Approval

The FDA and comparable regulatory agencies in state, local and foreign jurisdictions impose substantial requirements upon the clinical development, manufacture and marketing of medical devices and new drug and biologic products. These agencies, through regulations that implement the Federal Food, Drug and Cosmetic Act, as amended (“FDCA”), and other regulations, regulate research and development activities and the development, testing, manufacture, labeling, storage, shipping, approval, recordkeeping, advertising, promotion, sale and distribution of such products. In addition, if any of our products are marketed abroad, they will also be subject to export requirements and to regulation by foreign governments. The regulatory approval process is generally lengthy, expensive and uncertain. Failure to comply with applicable FDA and other regulatory requirements can result in sanctions being imposed on us or the manufacturers of our products, including hold letters on clinical research, civil or criminal fines or other penalties, product recalls, or seizures, or total or partial suspension of production or injunctions, refusals to permit products to be

imported into or exported out of the United States, refusals of the FDA to grant approval of drugs or to allow us to enter into government supply contracts, withdrawals of previously approved marketing applications and criminal prosecutions.

The steps typically required before an unapproved new drug or biologic product for use in humans may be marketed in the United States include:

• Preclinical studies that include laboratory evaluation of product chemistry and formulation, as well as animal studies to assess the potential safety and efficacy of the product. Certain preclinical tests must be conducted in compliance with good laboratory practice regulations. Violations of these regulations can, in some cases, lead to invalidation of the studies, or requiring such studies to be repeated. In some cases, long-term preclinical studies are conducted while clinical studies are ongoing.

• Submission to the FDA of IND (Investigational New Drug Application), which must become effective before human clinical trials may commence. The results of the preclinical studies are submitted to the FDA as part of the IND. Unless the FDA objects and places a clinical hold, the IND becomes effective 30 days following receipt by the FDA, although the FDA may place trials on hold at any time if it believes the risks to subjects outweigh the potential benefits.

• Approval of clinical protocols by independent institutional review boards (“IRBs”) at each of the participating clinical centers conducting a study. The IRBs consider, among other things, ethical factors, the potential risks to individuals participating in the trials and the potential liability of the institution. The IRB also approves the consent form signed by the trial participants.

• Adequate and well-controlled human clinical trials to establish the safety and efficacy of the product. Clinical trials involve the administration of the drug to healthy volunteers or to patients under the supervision of a qualified medical investigator according to an approved protocol. The clinical trials are conducted in accordance with protocols that detail the objectives of the study, the parameters to be used to monitor participant safety and efficacy or other criteria to be evaluated. Each protocol is submitted to the FDA as part of the IND. Human clinical trials are typically conducted in the following four sequential phases that may overlap or be combined:

• In Phase 1, the drug is initially introduced into a small number of individuals and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. Phase 1 clinical trials are often conducted in healthy human volunteers and such cases do not provide evidence of efficacy. In the case of severe or life-threatening diseases, the initial human testing is often conducted in patients rather than healthy volunteers. Because these patients already have the target disease, these studies may provide initial evidence of efficacy that would traditionally be obtained in Phase 2 clinical trials. Consequently, these types of trials are frequently referred to as Phase 1/2 clinical trials. The FDA receives reports on the progress of each phase of clinical testing and it may require the modification, suspension or termination of clinical trials if it concludes that an unwarranted risk is presented to patients or healthy volunteers.

• Phase 2 involves clinical trials in a limited patient population to further identify any possible adverse effects and safety risks, to determine 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 to further test for safety in an expanded patient population at geographically dispersed clinical study sites. Phase 3 clinical trials usually include a broader patient population so that safety and efficacy can be substantially established. Phase 3 clinical trials cannot begin until Phase 2 evaluation demonstrates that a dosage range of the product may be effective and has an acceptable safety profile.

• Phase 4 clinical trials are performed if the FDA requires, or a company pursues, additional clinical trials after a product is approved. These clinical trials may be made a condition to be satisfied after a drug receives approval. The results of Phase 4 clinical trials can confirm the effectiveness of a product and can provide important safety information to augment the FDA’s voluntary adverse event reporting system.

• Concurrent with clinical trials and preclinical studies, companies also must develop information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with the FDA’s current good manufacturing practices (“cGMPs”), requirements for drug products as well as the quality system regulation for medical devices, or QSR. The manufacturing process must be capable of consistently producing quality batches of the product and the manufacturer must develop methods for testing the quality, purity and potency of the final products. Additionally, appropriate packaging must be selected and tested and chemistry stability studies must be conducted to demonstrate that the product does not undergo unacceptable deterioration over its shelf-life.

• Submission to the FDA of a new drug application (“NDA”) based on the clinical trials. The results of product development, preclinical studies and clinical trials are submitted to the FDA in the form of an NDA for approval of the marketing and commercial shipment of the product. Under the Pediatric Research Equity Act, NDAs are required to include an assessment, generally based on clinical study data, of the safety and efficacy of drugs for all relevant pediatric populations. The statute provides for waivers or deferrals in certain situations.

In its review of an NDA, the FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. Before approving an NDA, the FDA may inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with cGMPs and will also inspect clinical trial sites for integrity of data supporting safety and efficacy. The FDA will issue either an approval of the NDA or a Complete Response Letter, detailing the deficiencies and information required in order for reconsideration of the NDA.

Medical products containing a combination of new drugs, biological products, or medical devices are regulated as “combination products” in the United States. A combination product generally is defined as a product comprised of components from two or more regulatory categories (e.g., drug/device, device/biologic, drug/biologic). Each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a new drug, biologic, or device. The testing and approval process requires substantial time, effort and financial resources. Data that we submit are subject to varying interpretations, and the FDA and comparable regulatory authorities in foreign jurisdictions may not agree that our product candidates have been shown to be safe and effective. We cannot be certain that any approval of our investigational products will be granted on a timely basis, if at all. For an approved product such as Afrezza, we are subject to continuing regulation by the FDA, including post marketing study commitments or requirements, record-keeping requirements, reporting of adverse experiences with the product, submitting other periodic reports, drug sampling and distribution requirements, notifying the FDA and gaining its approval of certain manufacturing or labeling changes, and complying with certain electronic records and signature requirements. Prior to and following approval, if granted, all manufacturing sites are subject to inspection by the FDA

and other national regulatory bodies and must comply with cGMP, QSR and other requirements enforced by the FDA and other national regulatory bodies through their facilities inspection program. In addition, our drug-manufacturing facilities located in Connecticut and the facilities of our insulin supplier, the supplier(s) of FDKP and the supplier(s) of our cartridges are subject to federal registration and listing requirements and, if applicable, to state licensing requirements. A failure, including those of our suppliers, to obtain and maintain applicable federal registrations or state licenses, or to meet the inspection criteria of the FDA or the other national regulatory bodies, would disrupt our manufacturing processes and would harm our business. In complying with standards set forth in these regulations, manufacturers must continue to expend time, money and effort in the area of production and quality control to ensure full compliance. Numerous device regulatory requirements apply to the device part of a drug-device combination. These include:

- product labeling regulations;
- general prohibition against promoting products for unapproved or “off-label” uses;
- corrections and removals (e.g., recalls);
- establishment registration and device listing;
- general prohibitions against the manufacture and distribution of adulterated and misbranded devices; and
- the Medical Device Reporting regulation, which requires that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if it were to recur.

Further, the supplier we contract with to manufacture our inhaler and cartridges is subject to QSRs, which requires manufacturers to follow elaborate design, testing, control, documentation and other quality assurance procedures during the manufacturing process of medical devices, among other requirements.

Failure to adhere to regulatory requirements at any stage of development, including the preclinical and clinical testing process, the review process, or at any time afterward, including after approval, may result in various adverse consequences. These consequences include action by the FDA or another national regulatory body that has the effect of delaying approval or refusing to approve a product; suspending or withdrawing an approved product from the market; seizing or recalling a product; or imposing criminal penalties against the manufacturer. In addition, later discovery of previously unknown problems may result in restrictions on a product, its manufacturer, or the NDA holder, or market restrictions through labeling changes or product withdrawal. Also, new government requirements may be established or current government requirements may be changed at any time, which could delay or prevent regulatory approval of our products under development. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

In addition, the FDA imposes a number of complex regulations on entities that advertise and promote drugs, which include, among other requirements, standards for and regulations of direct-to-consumer advertising, industry sponsored scientific and educational activities, and promotional activities involving the Internet, and restrictions on off-label promotion. The FDA has very broad enforcement authority under the FDCA, and failure to comply with these regulations can result in penalties, including the issuance of a warning letter requirements for corrective advertising to healthcare providers, a requirement that future advertising and promotional materials be pre-cleared by the FDA, and state and federal civil and criminal investigations and prosecutions.

Products manufactured in the United States and marketed outside the United States are subject to certain FDA regulations, as well as regulation by the country in which the products are to be sold. We also would be subject to foreign regulatory requirements governing clinical trials and drug product sales if products are studied or marketed abroad. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries usually must be obtained prior to the marketing of the product in those countries. The approval process varies from jurisdiction to jurisdiction and the time required may be longer or shorter than that

required for FDA approval.

There can be no assurance that the current regulatory framework will not change or that additional regulation will not arise at any stage of our product development or marketing that may affect approval, delay the submission or review of an application or require additional expenditures by us. There can be no assurance that we will be able to obtain necessary regulatory clearances or approvals on a timely basis, if at all, for any of our product candidates under development, and delays in receipt or failure to receive such clearances or approvals, the loss of previously received clearances or approvals, or failure to comply with existing or future regulatory requirements could have a material adverse effect on our business and results of operations.

In addition to the foregoing, we are subject to numerous federal, state and local laws relating to such matters as laboratory practices, the experimental use of animals, the use and disposal of hazardous or potentially hazardous substances, controlled drug substances, privacy of individually identifiable healthcare information, safe working conditions, manufacturing practices, environmental protection and fire hazard control.

Healthcare Regulatory and Pharmaceutical Pricing

Government coverage and reimbursement policies both directly and indirectly affect our ability to successfully commercialize our approved products, and such coverage and reimbursement policies will be affected by future healthcare reform measures. Third-party payors, like government health administration authorities, private health insurers and other organizations that provide healthcare coverage, generally decide which drugs they will pay for and establish reimbursement levels for covered drugs. In particular, in the United States, private third-party payors often provide reimbursement for products and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such products and services. In the United States, the European Union and other potentially significant markets for our product candidates, government authorities and other third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower average selling prices. Further, the increased emphasis on managed healthcare in the United States will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. Recently, in the United States there has been heightened governmental scrutiny of the manner in which drug manufacturers set prices for their marketed products. Pricing pressures can arise from rules and practices of managed care organizations, judicial decisions and governmental laws and regulations related to Medicare, Medicaid, healthcare reform, pharmaceutical reimbursement policies and pricing in general.

The United States and some foreign jurisdictions have enacted or are considering a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives, including, most recently, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, “PPACA”), enacted in March 2010.

The PPACA substantially changed the way healthcare is financed by both governmental and private insurers. Among other cost containment measures, PPACA established: an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents; a new Medicare Part D coverage gap discount program; and a new formula that increased the rebates a manufacturer must pay under the Medicaid Drug Rebate Program. There have been judicial and congressional challenges to certain aspects of PPACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the PPACA. President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal portions or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the PPACA have been signed into law. The Tax Cuts and Jobs Act of 2017 (“Tax Act”) includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amends the PPACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole”. In July 2018, CMS published a final rule permitting further collections and payments to and from certain PPACA qualified

health plans and health insurance issuers under the PPACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the “individual mandate” was repealed by Congress as part of the Tax Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the PPACA will impact the PPACA.

Other legislative changes have been proposed and adopted in the United States since PPACA. For example, through the process created by the Budget Control Act of 2011, there are automatic reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, following passage of the BBA, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers. In the future, there are likely to be additional proposals relating to the reform of the U.S. health care system, some of which could further limit the prices we are able to charge for our products, or the amounts of reimbursement available for our products. If drug products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

Moreover, in the United States, there have been several congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, at the federal level, the Trump administration released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have stated that they continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, if a drug product is reimbursed by Medicare, Medicaid or other federal or state healthcare programs, we must comply with, among others, the federal civil and criminal false claims laws, including the civil False Claims Act, as amended, the federal Anti-Kickback Statute, as amended, and similar state laws. Similarly, if a drug product is reimbursed by Medicare or Medicaid, pricing and rebate programs must comply with, as applicable, the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Medicare Prescription Drug Improvement and Modernization Act of 2003.

The Physician Payments Sunshine Act within PPACA, and its implementing regulations, require certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) to (i) report information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and (ii) report annually certain ownership and investment interests held by physicians and their immediate family members.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. The federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), as amended by the Health Information Technology and Clinical Health Act (“HITECH”), and their respective implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA’s privacy and security standards directly applicable to “business associates” — independent contractors or agents of covered entities, which include certain healthcare providers, health plans, and healthcare clearinghouses, that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys’ fees and costs associated with pursuing federal civil actions. State laws also govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. The recently adopted European General Data Protection Regulation, or GDPR, contains new provisions specifically directed at the processing of health information, higher sanctions and extra-territoriality measures that are intended to bring non-EU companies under the data security and privacy legal framework specified in the regulation. We anticipate that over time we may expand our business operations to include operations in the EU, including potentially conducting preclinical and clinical trials. With such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including the GDPR

Additionally, California recently enacted legislation that has been dubbed the first “GDPR-like” law in the United States. Known as the California Consumer Privacy Act (“CCPA”), it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. When it goes into effect on January 1, 2020, the CCPA will require covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. Legislators have stated that amendments will be proposed to the CCPA before it goes into effect, but it remains unclear what, if any, modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA will likely impact (possibly significantly) our business activities and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

Also, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, that apply regardless of the payer. Additional state laws require pharmaceutical companies to implement a comprehensive compliance program and/or limit expenditure for, or payments to, individual medical or health professionals.

We may incur significant costs to comply with these laws and regulations now or in the future. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including significant criminal, civil and administrative penalties, damages, fines, individual imprisonment, disgorgement, exclusion from government healthcare programs, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Ethical Business Practices and Sustainability

Safety of Clinical Trial Participants

Safe clinical trials play a crucial role in the development of new products and our continuing prosperity. We take numerous steps to maximize the safety of our clinical trial participants.

The health of subjects in clinical trials is a priority for us and we are committed to conducting clinical trials according to uniformly high ethical standards. We apply those standards to trials that we sponsor and conduct directly as well as those conducted on our behalf by clinical research organizations. We conduct trials in accordance with all applicable laws, the standards of International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines and following the ethical principles that have their origin in the Declaration of Helsinki.

We require that a three-stage informed consent process be implemented in all trials to ensure that participants understand the risks and benefits of the procedures, how personal medical data is collected and used, and that participation in the trial is voluntary, among other information. We retain documentation that all participants in our trials have provided informed consent.

We monitor clinical trials through audits and inspections conducted by us and by third parties. These inspections verify that our policies, good clinical practices and applicable laws are being adhered to.

Our ability to ensure the safety of clinical trial participants is critical to securing regulatory approval and continued product development success. Moreover, our inability to conduct safe and effective clinical trials could increase our development costs over time. We will continue to hold ourselves to high standards in our oversight and management of clinical trials.

Ethical Marketing

We require that our employees abide by our Code of Business Conduct and Ethics, our policy on interactions with healthcare professionals and patients, U.S. federal and state laws and applicable foreign laws. We are committed to protecting the health and well-being of patients by ensuring that medically sound knowledge of the benefits and risks of our products is understood and communicated thoroughly and accurately to patients, physicians and global health authorities.

Our policy on interactions with healthcare professionals and patients prohibits off-label promotion of our products. All sales staff received compliance training upon hire and on an annual basis. We also routinely monitor sales calls. Any case where we promote off-label use of our products has the potential to have a material adverse effect on our reputation, sales and liabilities. We expect that consistent enforcement of, and training on, our Code of Business Conduct and Ethics and our policy on interactions with healthcare professionals and patients will help us to limit the incidence of off-label promotion.

Drug Safety

The safety of our products at all stages – from clinical trials to the administration and use and through to safe disposal – is a key area of attention for us. We acknowledge, however, that there are inherent risks associated with the use of drug products. We attempt to minimize these through stringent adherence to quality control procedure and proactive recall processes whenever a safety concern is identified. To date, we have not issued a recall for any product.

In addition, by mid-2018, all sales packs of Afrezza that we placed in the distribution chain are serialized in accordance with the requirements of the Drug Quality and Security Act (“DQSA”). The Drug Supply Chain Security Act (“DSCSA”), included in the DQSA, requires drug manufacturers to assign a unique identifier to each sales pack (and each aggregate of such sales pack, such as a case or pallet), which then remains on such pack or aggregate through the whole supply chain until its consumption or destruction. This system is intended to improve detection and removal of drugs that may be counterfeit, stolen, contaminated, or otherwise harmful from the drug supply chain.

Corruption and Bribery

Our Code of Business Conduct and Ethics includes clear guidelines on anti-bribery and anti-corruption practices. Currently, we have very limited operations outside the United States; however, as we expand our global reach through collaborations or through our own growth, we acknowledge that certain regions may pose a higher risk for corrupt practices. We intend to continue our internal training programs and oversight over collaborators on anti-bribery, anti-corruption and other unethical practices in order to reduce these risks.

Bribing healthcare professionals to use or recommend our products can create adverse publicity and damage our ability to use a critical channel of influence. We have adopted and implement PhRMA’s Code on Interactions with Healthcare Professionals as part of our policy on interactions with healthcare professionals and patients. We believe that training on, and enforcement of, these codes will limit the incidence of unethical interactions between our personnel and healthcare professionals.

Long-Lived Assets

Our long-lived assets are located in the United States and totaled \$25.6 million and \$26.9 million as of December 31, 2018 and 2017, respectively.

Employees

Our human capital helps us develop and commercialize new products, conduct clinical trials and navigate government regulations. Our ability to recruit, develop and retain highly skilled talent is a significant determinant of our success. Our Code of Business Conduct and Ethics codifies our commitment to diversity and to providing equal opportunity and a positive working environment in all aspects of employment. We also have policies setting forth our expectations for nondiscrimination and a harassment-free work environment.

As of December 31, 2018, we had 225 full-time employees, of which 79 were engaged in manufacturing, 19 in research and development, 39 in general and administrative and 88 in selling and marketing. Seventeen of these employees had a Ph.D. degree and/or M.D. degree and were engaged in activities relating to research and development, manufacturing, quality assurance or business development.

None of our employees are subject to a collective bargaining agreement. We believe relations with our employees are good.

Occupational Health and Safety

Hazardous materials are inherent in our operations, and it is not possible to eliminate completely the risk of accidental exposure from our operations. We have established procedures to comply with governmental regulations regarding workplace safety, including training employees to enable them to recognize risks and empower them to learn, discover, work safely, and to minimize injuries, illnesses, environmental impact and regulatory risks. In 2018, our total illness and injury incidence rate was 0.9 compared to the 2017 industry average of 1.6, as reported by the U.S. Department of Labor, and our DART (days away/restricted or job transfer) incident rate was 0.9 per 100 employees compared to the 2017 industry average of 1.0. We will continue our efforts to ensure a high level of workplace safety.

Corporate Information

We were incorporated in the State of Delaware on February 14, 1991. Our principal executive offices are located at 30930 Russell Ranch Road, Suite 300, Westlake Village, California 91362, and our telephone number at that address is (818) 661-5000. MannKind Corporation and the MannKind Corporation logo are our service marks and trademarks. Our website address is <http://www.mannkindcorp.com>. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The contents of these websites are not incorporated into this Annual Report. Further, our references to the URLs for these websites are intended to be inactive textual reference only.

Scientific Advisors

We seek advice from a number of leading scientists and physicians on scientific, technical and medical matters. These advisors are leading scientists in the areas of pharmacology, chemistry, immunology and biology. Our scientific advisors are consulted regularly to assess, among other things:

- our research and development programs;
- the design and implementation of our clinical programs;
- our patent and publication strategies;
- market opportunities from a clinical perspective;
- new technologies relevant to our research and development programs; and
- specific scientific and technical issues relevant to our business.

A current listing of our scientific advisors is maintained on our corporate website at www.mankindcorp.com.

Executive Officers of the Registrant

The following table sets forth our current executive officers and their ages:

Name	Age	Position(s)
Michael E. Castagna, Pharm.D.	42	Chief Executive Officer
Steven B. Binder	56	Chief Financial Officer
David M. Kendall, M.D	57	Chief Medical Officer
Joseph Kocinsky	55	Chief Technology Officer
James P. McCauley, Jr.	53	Chief Commercial Officer
Elizabeth G. Ingram	53	Chief Marketing Officer
Stuart A. Tross, Ph.D.	52	Chief People and Workplace Officer
David B. Thomson, Ph.D., J.D.	52	General Counsel and Secretary
Rosabel R. Alinaya	58	Senior Vice President, Investor Relations and Treasury
Courtney Barton	36	Vice President, Chief Compliance and Privacy Officer

Michael E. Castagna, Pharm.D. has been our Chief Executive Officer since May 2017 and was our Chief Commercial Officer from March 2016 until May 2017. From November 2012 until he joined us, Dr. Castagna was at Amgen, Inc., where he initially served as Vice President, Global Lifecycle Management and was most recently Vice President, Global Commercial Lead for Amgen's Biosimilar Business Unit. From 2010 to 2012, he was Executive Director, Immunology, at Bristol-Myers Squibb Company ("BMS"), an innovative global biopharmaceutical company. Before BMS, Dr. Castagna served as Vice President & Head, Biopharmaceuticals, North America, at Sandoz, a division of Novartis. He has also held positions with commercial responsibilities at EMD (Merck) Serono, Pharmasset and DuPont Pharmaceuticals. He received his pharmacy degree from the University of the Sciences-Philadelphia College of Pharmacy, a Pharma D. from Massachusetts College of Pharmacy & Sciences and an MBA from The Wharton School of Business at the University of Pennsylvania.

Steven B. Binder has been our Chief Financial Officer since July 2017. Before joining us, since 2013 Mr. Binder served as Vice President and Chief Financial Officer of the International Group of Stryker Corporation, a leading global medical technology company, based in Singapore. Prior to Stryker, Mr. Binder served in a series of senior leadership roles at BMS. His last four positions at BMS were Vice President, Finance roles over different geographic operating units: United States (2012-2013), Europe (2008-2011), AsiaPacific (2005-2007), and Japan (2003-2005). Prior to his international experience, Mr. Binder served in three senior leadership roles for Oncology Therapeutics Network, a U.S. based independent subsidiary of BMS: Vice President, Strategic Development (2001-2003), Vice President, Customer Operations (2000-2001), and Chief Financial Officer (1997-2000). Before Oncology Therapeutics Network, Mr. Binder progressed through three finance and accounting roles for BMS Worldwide Medicines Group after joining the company in 1992. Before BMS, he worked for Deloitte & Touche LLP in a series of auditing roles with increasing responsibility over an eight year period beginning in 1984. Mr. Binder received a B.S. degree in Accounting and Business Administration from Muhlenberg College and is a Certified Public Accountant.

David M. Kendall, M.D. has been our Chief Medical Officer since February 2018. His career includes over 30 years of experience in diabetes and metabolism research, clinical management, research, and policy advocacy. Most recently, he served as Research Physician and Vice President of Global Medical Affairs for Lilly Diabetes from 2011

to 2018, and during that time was responsible for all medical affairs activities and guided research and development strategy across multiple geographies. In this role, he worked to re-establish Lilly Diabetes as a world class medical organization and added to his extensive experience with both injected and mealtime insulins, as well as devices and continuous glucose monitors. Prior to joining Eli Lilly, Dr. Kendall served as Chief Scientific and Medical Officer at the American Diabetes Association, where he was responsible for all medical affairs, medical education, research, outcomes, and medical policy activities. Earlier in his career, Dr. Kendall served as Medical Director at the International Diabetes Center (1997-2009), Executive Director of Medical Affairs at Amylin Pharmaceuticals from 2005 to 2008, and as a consultant in endocrinology at the Park Nicollet Clinic (1994-1997). He received his M.D. and completed his Post Graduate Medical Training at the University of Minnesota, and earned a B.A. in Biology from St. Olaf College.

Joseph Kocinsky has been our Chief Technology Officer since October 2015. Mr. Kocinsky has over 30 years experience in the pharmaceutical industry in technical operations and product development. Prior to joining us in 2003, he held a variety of technical and management positions with increased responsibility at Schering-Plough Corp. Mr. Kocinsky holds a bachelor's degree in chemical engineering and an master's degree in Biomedical Engineering from New Jersey Institute of Technology and an master's degree in Business Administration from Seton Hall University.

James P. McCauley, Jr. has been our Chief Commercial Officer since July 2017. Prior to joining us, he spent twelve years at Astellas Pharma in a series of senior sales and compliance leadership roles of increasing responsibility. Prior to Astellas, Mr. McCauley was a member of the U.S. commercialization team and held a sales leadership role with Yamanouchi Pharma before the merger of Yamanouchi and Fujisawa Pharma to create Astellas in 2005. Before that, Mr. McCauley spent thirteen years with DuPont Pharmaceuticals and one year with BMS which acquired DuPont Pharmaceuticals in 2001. At DuPont and BMS, Mr. McCauley held a series of leadership roles across the sales, contracting and pricing, and clinical areas. Throughout his various career moves, Mr. McCauley has developed deep commercial expertise serving both specialty and primary care healthcare providers. He received an MBA from the Kellogg School of Management at Northwestern University, a J.D. from the South Texas College of Law, and a B.A. in Economics from the University of Notre Dame.

Elizabeth G. Ingram has been our Chief Marketing Officer since June 2018. Her career includes over twenty years of experience in marketing and market access, delivering strategic planning, and execution of contract, health economics, sales and marketing programs. Most recently, she served as Senior Vice President — Managed Market at Dexcom in 2017, Vice President — Head of Market Access at Sanofi from 2014 to 2016, Vice President – Market Access Strategy at Bristol Myers Squibb from 2012 to 2014, and various roles of increasing responsibility at Novo Nordisk Pharmaceuticals from 2006 to 2012. Ms. Ingram obtained a Bachelor of Science degree from East Carolina University and a Master's degree from University of South Carolina-Columbia.

Stuart A. Tross, Ph.D. has been our Chief People and Workplace Officer since December 2016, with responsibilities for human resources, information technology, corporate communications and west coast facilities. From 2006 to 2016 he served in various roles of increasing responsibility at Amgen, Inc., most recently as Senior Vice President and Chief Human Resources Officer responsible for human resources and security on a global basis. From 1998 to 2006 he served in a series of leadership roles at BMS, most recently as Vice President and Global Head of Human Resources for Mead Johnson Company. Stuart received a B.S. degree from Cornell University and M.Sc. and Ph.D. degrees in Industrial-Organizational Psychology from the Georgia Institute of Technology.

David B. Thomson, Ph.D., J.D. has been our General Counsel and Corporate Secretary since January 2002. Prior to joining us, he practiced corporate/commercial and securities law at a major Toronto law firm. Earlier in his career, Dr. Thomson was a post-doctoral fellow at the Rockefeller University. Dr. Thomson obtained his B.S degree, M Sc. degree and Ph.D. from Queens University and obtained his J.D. from the University of Toronto.

Rosabel R. Alinaya has been our Senior Vice President, Investor Relations and Treasury since July 2017. Ms. Alinaya also served as Principal Accounting Officer from January 2016 to July 2017 with responsibility for finance, accounting, tax, treasury, investor relations and risk management. Previously, she was our Vice President, Finance since March 2011 after serving as our Corporate Controller since June 2003. Ms. Alinaya began her career at Deloitte & Touche LLP, graduating from California State University, Northridge with a B.S. in Accounting Information Systems. Ms. Alinaya is also a member of the American Institute of Certified Public Accountants and the California Society of Certified Public Accountants.

Courtney Barton has been our Vice President, Chief Compliance Officer since March 2017. From December 2015 until she joined us, she served as Chief Compliance Officer for Anacor Pharmaceuticals, Inc. Prior to that, Ms. Barton served in compliance and privacy roles for Kythera Biopharmaceuticals, Inc. from November 2014 to November 2015, Allergan, Inc. from September 2013 to October 2014, Bausch & Lomb, Inc. from September 2006 to September 2013 and Winn-Dixie Stores, Inc. from August 2003 to August 2006. She has also held positions with Merrill Lynch and Janus, including an international appointment. Ms. Barton holds B.A. degrees in Political Science and International Relations from Syracuse University and is a Certified Compliance and Ethics Professional (CCEP) and Certified Information Privacy Professional (CIPP US/E).

Item 1A. Risk Factors

You should consider carefully the following information about the risks described below, together with the other information contained in this Annual Report before you decide to buy or maintain an investment in our common stock. We believe the risks described below are the risks that are material to us as of the date of this Annual Report. Additional risks and uncertainties that we are unaware of, may also become important factors that affect us. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of the money you paid to buy our common stock.

RISKS RELATED TO OUR BUSINESS

We will need to raise additional capital to fund our operations, and there is substantial doubt about our ability to continue as a going concern.

This report includes disclosures stating that our existing cash resources and our accumulated stockholder's deficit raise substantial doubt about our ability to continue as a going concern. We will need to raise additional capital, whether through the sale of equity or debt securities, additional strategic business collaborations, the establishment of other funding facilities, licensing arrangements, asset sales or other means, in order to support our ongoing activities, including the commercialization of Afrezza and the development of our product candidates, and to avoid defaulting under the financial covenant in our Facility Agreement with Deerfield Private Design Fund II, L.P. and Deerfield Private Design International II, L.P. (collectively, "Deerfield") dated July 1, 2013 (as amended, the "Facility Agreement"), which requires us to maintain at least \$25.0 million in cash and cash equivalents as of the last day of each fiscal quarter (other than December 31, 2018, when we were required to have at least \$20.0 million in cash and cash equivalents). It may be difficult for us to raise additional funds on favorable terms, or at all. As of December 31, 2018, we had cash and cash equivalents of \$71.2 million and a stockholders' deficit of \$175.1 million. The extent of our additional funding requirements will depend on a number of factors, including:

- the degree to which Afrezza is commercially successful;
- the degree to which we are able to generate revenue from our Technosphere drug delivery platform, including through our collaborations;
- the costs of developing and commercializing Afrezza on our own in the United States, including the costs of expanding our commercialization capabilities;
- the demand by any or all of the holders of our debt instruments to require us to repay or repurchase such debt securities if and when required;
- our ability to repay or refinance existing indebtedness, and the extent to which our notes with conversion options or any other convertible debt securities we may issue are converted into or exchanged for shares of our common stock;
- the rate of progress and costs of our clinical studies and research and development activities;
- the costs of procuring raw materials and operating our manufacturing facility;
- our obligation to make milestone payments to Deerfield;
 - our success in establishing additional strategic business collaborations or other sales or licensing of assets, and the timing and amount of any payments we might receive from any such transactions;
- actions taken by the FDA and other regulatory authorities affecting Afrezza and our product candidates and competitive products;
- the emergence of competing technologies and products and other market developments;
- the costs of preparing, filing, prosecuting, maintaining and enforcing patent claims and other intellectual property rights or defending against claims of infringement by others;
- the level of our legal and litigation expenses; and
- the costs of discontinuing projects and technologies, and/or decommissioning existing facilities, if we undertake any such activities.

We have raised capital in the past through the sale of equity and debt securities and we may in the future pursue the sale of additional equity and/or debt securities, or the establishment of other funding facilities including asset-based borrowings. There can be no assurances, however, that we will be able to raise additional capital in the future on acceptable terms, or at all. Issuances of additional debt or equity securities or the issuance of common stock upon conversion of outstanding convertible debt securities or upon the exercise of our currently outstanding warrants for shares of our common stock could impact the rights of the holders of our common stock and will dilute their ownership percentage. Moreover, the establishment of other funding facilities may impose restrictions on our operations. These restrictions could include limitations on additional borrowing and specific restrictions on the use of our assets, as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments.

We may also raise additional capital by pursuing opportunities for the licensing or sale of certain intellectual property and other assets. We cannot offer assurances, however, that any strategic collaboration, sales of securities or sales or licenses of assets will be available to us on a timely basis or on acceptable terms, if at all. We may be required to enter into relationships with third parties to develop or commercialize products or technologies that we otherwise would have sought to develop independently, and any such relationships may not be on terms as commercially favorable to us as might otherwise be the case.

In the event that sufficient additional funds are not obtained through strategic collaboration opportunities, sales of securities, funding facilities, licensing arrangements, borrowing arrangements and/or asset sales on a timely basis, we may be required to reduce expenses through the delay, reduction or curtailment of our projects, or further reduction of costs for facilities and administration. Moreover, if we do not obtain such additional funds, there will continue to be substantial doubt about our ability to continue as a going concern and increased risk of insolvency and up to total loss of investment to our stockholders and other security holders. As of the date hereof, we have not obtained a solvency opinion or otherwise conducted a valuation of our properties to determine whether our debts exceed the fair value of our property within the meaning of applicable solvency laws. If we are or become insolvent, holders of our common stock or other securities may lose the entire value of their investment.

We cannot provide assurances that changed or unexpected circumstances will not result in the depletion of our capital resources more rapidly than we currently anticipate. There can be no assurances that we will be able to raise additional capital in sufficient amounts or on favorable terms, or at all. If we are unable to raise adequate additional capital when required or in sufficient amounts or on terms acceptable to us, we may have to delay, scale back or discontinue one or more product development programs, curtail our commercialization activities, significantly reduce expenses, sell assets (potentially at a loss), enter into relationships with third parties to develop or commercialize products or technologies that we otherwise would have sought to develop or commercialize independently, cease operations altogether, pursue an acquisition of our company at a price that may result in up to a total loss on investment for our stockholders, file for bankruptcy or seek other protection from creditors, or liquidate all of our assets. In addition, if we default under the Facility Agreement, Deerfield could foreclose on substantially all of our assets.

Our prospects are heavily dependent on the successful commercialization of our only approved product, Afrezza. The continued commercialization and development of Afrezza will require substantial capital that we may not be able to obtain.

We have expended significant time, money and effort in the development of our only approved product, Afrezza. We anticipate that in the near term our prospects and ability to generate significant revenues will heavily depend on our ability to successfully commercialize Afrezza in the United States. In addition, we anticipate that revenues from our existing or future licensing arrangements for our Technosphere platform technology that involve license, milestone, royalty or other payments to us will depend on our ability to achieve the performance obligations specified in such arrangements.

Successful commercialization of Afrezza is subject to many risks, including some that are outside our control. There are numerous examples of unsuccessful product launches, second launches that underperform original expectations and other failures to fully exploit the market potential of drug products, including by pharmaceutical companies with more experience and resources than us. We ultimately may be unable to gain market acceptance of Afrezza for a variety of reasons, including the treatment and dosage regimen, potential adverse effects, relative pricing compared with alternative products, the availability of alternative treatments and lack of coverage or adequate reimbursement. We will need to maintain and enhance our commercialization capabilities in order to successfully commercialize Afrezza in the United States, and we may not have sufficient resources to do so. The market for skilled commercial personnel is highly competitive, and we may not be able to retain and find and hire all of the personnel we need on a timely basis or retain them for a sufficient period. In addition, Afrezza is a novel insulin therapy with a distinct time-action profile and non-injectable administration, and we are therefore required to expend significant time and resources to train our sales force to be credible, persuasive and compliant with applicable laws in marketing Afrezza for the treatment diabetes to physicians and to ensure that a consistent and appropriate message about Afrezza is being delivered to our potential customers. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate potential customers about the benefits of Afrezza and its proper administration, our efforts to successfully commercialize Afrezza could be put in jeopardy, which would negatively impact our ability to generate product revenues.

If we are unable to maintain payor coverage of, and adequate reimbursement for Afrezza, physicians may limit how much or under what circumstances they will prescribe or administer Afrezza. As a result, patients may decline to purchase Afrezza, which would have an adverse effect on our ability to generate revenues.

We are responsible for the NDA for Afrezza and its maintenance. We may fail to comply with maintenance requirements, including timely submitting required reports. Furthermore, we are responsible for the conduct of the remaining required post-approval trials of Afrezza. Our financial and other resource constraints may result in delays or adversely impact the reliability and completion of these trials.

If we fail to achieve commercialize success with Afrezza in the United States, our business, financial condition and results of operations will be materially and adversely affected.

We expect that our results of operations will fluctuate for the foreseeable future, which may make it difficult to predict our future performance from period to period.

Our operating results have fluctuated in the past and are likely to do so in future periods. Some of the factors that could cause our operating results to fluctuate from period to period include the factors that will affect our funding requirements described above under “Risk Factors — We will need to raise additional capital to fund our operations, and there is substantial doubt about our ability to continue as a going concern.”

We believe that comparisons from period to period of our financial results are not necessarily meaningful and should not be relied upon as indications of our future performance.

If we do not obtain regulatory approval of Afrezza in foreign jurisdictions, we will not be able to market Afrezza in any jurisdiction outside of the United States, which could limit our commercial revenues. We may not be successful in establishing or maintaining regional partnerships or other arrangements with third parties for the commercialization of Afrezza outside of the United States.

While Afrezza has been approved in the United States by the FDA for glycemic control in adult patients with diabetes, we have not yet obtained approval in any other jurisdiction. In order to market Afrezza outside of the United States, we must obtain regulatory approval in each applicable foreign jurisdiction, and we may never be able to obtain such approvals. The research, testing, manufacturing, labeling, approval, sale, import, export, marketing, and distribution of pharmaceutical products outside the United States are subject to extensive regulation by foreign regulatory authorities, whose regulations differ from country to country. We will be required to comply with different regulations and policies of the jurisdictions where we seek approval for Afrezza, and we have not yet identified all of the requirements that we will need to satisfy to submit Afrezza for approval for other jurisdictions. This will require additional time, expertise and expense, including the potential need to conduct additional studies or development work for other jurisdictions beyond the work that we have conducted to support the NDA for Afrezza.

Our current strategy for the future commercialization of Afrezza outside of the United States, subject to receipt of the necessary regulatory approvals, is to seek and establish regional partnerships in foreign jurisdictions where there are commercial opportunities. It may be difficult to find or maintain collaboration partners that are able and willing to devote the time and resources necessary to successfully commercialize Afrezza. Collaborations with third parties may require us to relinquish material rights, including revenue from commercialization, agree to unfavorable terms or assume material ongoing development obligations that we would have to fund. These collaboration arrangements are complex and time-consuming to negotiate, and if we are unable to reach agreements with third-party collaborators, we may fail to meet our business objectives and our financial condition may be adversely affected. We may also face significant competition in seeking collaboration partners, especially in the current market, and may not be able to find a suitable collaboration partner in a timely manner on acceptable terms, or at all. Any of these factors could cause delay or prevent the successful commercialization of Afrezza in foreign jurisdictions and could have a material and adverse impact on our business, financial condition and results of operations and the market price of our common stock and other securities could decline.

We may not be successful in our efforts to develop and commercialize our product candidates.

We have sought to develop our product candidates through our internal research programs. All of our product candidates will require additional research and development and, in some cases, significant preclinical, clinical and other testing prior to seeking regulatory approval to market them. Accordingly, these product candidates will not be commercially available for a number of years, if at all. Further research and development on these programs will require significant financial resources. Given our limited financial resources and our focus on development and commercialization of Afrezza, we will likely not be able to advance these programs unless we are able to enter into collaborations with third parties to fund these programs or to obtain funding to enable us to continue these programs.

A significant portion of the research that we have conducted involves new technologies, including our Technosphere platform technology. Even if our research programs identify product candidates that initially show promise, these candidates may fail to progress to clinical development for any number of reasons, including discovery upon further research that these candidates have adverse effects or other characteristics that indicate they are unlikely to be effective. In addition, the clinical results we obtain at one stage are not necessarily indicative of future testing results. If we fail to develop and commercialize our product candidates, or if we are significantly delayed in doing so, our

ability to generate product revenues will be limited to the revenues we can generate from Afrezza.

We have a history of operating losses, we expect to incur losses in the future and we may not generate positive cash flow from operations in the future.

We are not currently profitable and have rarely generated positive net cash flow from operations. As of December 31, 2018, we had an accumulated deficit of \$2.9 billion. The accumulated deficit has resulted principally from costs incurred in our research and development programs, the write-off of goodwill, inventory and property, plant and equipment, and general operating expenses. We expect to make substantial expenditures and to incur increasing operating losses in the future in order to continue the commercialization of Afrezza. In addition, under the amended Insulin Supply Agreement with Amphastar, we agreed to purchase certain annual minimum quantities of insulin through 2024. As of December 31, 2018, there was €85.8 million remaining in aggregate purchase commitments under this agreement. We may not have the necessary capital resources on hand in order to service this contractual commitment.

Our losses have had, and are expected to continue to have, an adverse impact on our working capital, total assets and stockholders' equity. Our ability to achieve and sustain positive cash flow from operations and profitability depends heavily upon successfully commercializing Afrezza, and we cannot be sure when, if ever, we will generate positive cash flow from operations or become profitable.

We have a substantial amount of debt, and we may be unable to make required payments of interest and principal as they become due.

As of December 31, 2018, we had \$101.7 million principal amount of outstanding debt, consisting of:

- \$18.7 million principal amount of senior convertible notes bearing interest at 5.75% per annum, with interest payable in cash semiannually in arrears on February 15 and August 15 of each year, and maturing on October 23, 2021;
- \$9.0 million principal amount of Facility Financing Obligation due and payable in July 2019 and bearing interest at 9.75% per annum (the “2019 notes”). Interest is payable in cash quarterly in arrears in the last business day of March, June, September and December of each year;
- \$2.5 million principal amount of Facility Financing Obligation due and payable in May 2019 and bearing interest at 8.75% per annum.

• \$71.5 million principal amount of indebtedness under a loan arrangement (“the Mann Group Loan Arrangement”) bearing interest at a fixed rate of 5.84% per annum compounded quarterly beginning April 1, 2018 and maturing on July 1, 2021, all of which is convertible at a conversion price per share of \$4.00. Interest is due and payable quarterly in arrears on the first day of each calendar quarter for the preceding quarter, except that interest payments are subject to deferral under a subordination agreement with Deerfield until our payment obligations to Deerfield have been satisfied in full.

There can be no assurance that we will have sufficient resources to make any required repayments of principal under the terms of our indebtedness when required. Further, if we undergo a fundamental change, as that term is defined in the indentures governing the terms of the senior convertible notes, or certain Major Transactions as defined in the Facility Agreement in respect of the Facility Financing Obligation, the holders of the respective debt securities will have the option to require us to repurchase all or any portion of such debt securities at a repurchase price of 100% of the principal amount of such debt securities to be repurchased plus accrued and unpaid interest, if any. While we have been able to timely make our required interest payments to date, we cannot guarantee that we will be able to do so in the future. If we fail to pay interest on the senior convertible notes, 2019 notes, or Tranche B notes, or if we fail to repay or repurchase the senior convertible notes, 2019 notes, Tranche B notes, or the loans under The Mann Group Loan Arrangement when required, we will be in default under the instrument for such debt securities or loans, and may also suffer an event of default under the terms of other borrowing arrangements that we may enter into from time to time. Any of these events could have a material adverse effect on our business, results of operations and financial condition, up to and including the note holders initiating bankruptcy proceedings or causing us to cease operations altogether.

The agreements governing our indebtedness contain covenants that we may not be able to meet and place restrictions on our operating and financial flexibility.

Our obligations under the Facility Agreement, including any indebtedness under the Facility Financing Obligation, and the Milestone Rights Purchase Agreement (the “Milestone Agreement”) with Deerfield and Horizon Santé FLML SÁRL (collectively, the “Milestone Purchasers”) are secured by substantially all of our assets, including our intellectual property, accounts receivables, equipment, general intangibles, inventory (excluding insulin inventory) and investment property, and all of the proceeds and products of the foregoing. The Facility Agreement includes customary representations, warranties and covenants by us, including restrictions on our ability to incur additional indebtedness, grant certain liens, engage in certain mergers and acquisitions, make certain distributions and make certain voluntary prepayments. Events of default under the Facility Agreement include: our failure to timely make payments due under the Facility Financing Obligation; inaccuracies in our representations and warranties to Deerfield; our failure to comply with any of our covenants under any of the Facility Agreement, Milestone Agreement or certain other related security agreements and documents entered into in connection with the Facility Agreement, subject to a cure period with respect to most covenants; our insolvency or the occurrence of certain bankruptcy-related events; certain judgments against us; the suspension, cancellation or revocation of governmental authorizations that are reasonably

expected to have a material adverse effect on our business; the acceleration of a specified amount of our indebtedness; our cash and cash equivalents falling below \$25.0 million as of the end of each fiscal quarter after December, 31, 2018. There have been no events of default under the Facility Financing Obligation. If we fail to timely pay accrued interest under The Mann Group Loan Arrangement when required, we will be in default under The Mann Group Loan Arrangement. If one or more events of default under the Facility Agreement occurs and continues beyond any applicable cure period, the holders of the Facility Financing Obligation may declare all or any portion of the Facility Financing Obligation to be immediately due and payable. The Milestone Agreement includes customary representations and warranties and covenants by us, including restrictions on transfers of intellectual property related to Afrezza. The milestones are subject to acceleration in the event we transfer our intellectual property related to Afrezza in violation of the terms of the Milestone Agreement.

There can be no assurance that we will be able to comply with the covenants under any of the foregoing agreements, and we cannot predict whether the holders of the Facility Financing Obligation would demand repayment of the outstanding balance of the Facility Financing Obligation as applicable or exercise any other remedies available to such holders if we were unable to comply with these covenants. The covenants and restrictions contained in the foregoing agreements could significantly limit our ability to respond to changes in our business or competitive activities or take advantage of business opportunities that may create value for our stockholders and the holders of our other securities. In addition, our inability to meet or otherwise comply with the covenants under these agreements could have an adverse impact on our financial position and results of operations and could result in an event of default under the terms of our other indebtedness, including our indebtedness under the senior convertible notes. In the event of certain future defaults under the foregoing agreements for which we are not able to obtain waivers, the holders of the senior convertible notes and Facility Financing Obligation may accelerate all of our repayment obligations, and, with respect to the Facility Financing Obligation, take control of our pledged assets, potentially requiring us to renegotiate the terms of our indebtedness on terms less favorable to us, or to immediately cease operations. If we enter into additional debt arrangements, the terms of such additional arrangements could further restrict our operating and financial flexibility. In the event we must cease operations and liquidate our assets, the rights of any holders of our outstanding secured debt would be senior to the rights of the holders of our unsecured debt and our common stock to receive any proceeds from the liquidation.

If we do not achieve our projected development goals in the timeframes we expect, our business, financial condition and results of operations will be harmed and the market price of our common stock and other securities could decline.

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical studies and the submission of regulatory filings. From time to time, we publicly announce the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions. The actual timing of the achievement of these milestones can vary dramatically from our estimates, in many cases for reasons beyond our control, depending on numerous factors, including:

- the rate of progress, costs and results of our clinical studies and preclinical research and development activities;
- our ability to identify and enroll patients who meet clinical study eligibility criteria;
- our ability to access sufficient, reliable and affordable supplies of components used in the manufacture of our product candidates;
- the costs of expanding and maintaining manufacturing operations, as necessary;
- the extent to which our clinical studies compete for clinical sites and eligible subjects with clinical studies sponsored by other companies; and
- actions by regulators.

In addition, if we do not obtain sufficient additional funds through sales of securities, strategic collaborations or the license or sale of certain of our assets on a timely basis, we may be required to reduce expenses by delaying, reducing or curtailing our development of product candidates. If we fail to commence or complete, or experience delays in or are forced to curtail, our proposed clinical programs or otherwise fail to adhere to our projected development goals in the timeframes we expect (or within the timeframes expected by analysts or investors), our business, financial condition and results of operations will be harmed and the market price of our common stock and other securities may decline.

Afrezza or our product candidates may be rendered obsolete by rapid technological change.

The rapid rate of scientific discoveries and technological changes could result in Afrezza or one or more of our product candidates becoming obsolete or noncompetitive. Our competitors may develop or introduce new products that render our technology or Afrezza less competitive, uneconomical or obsolete. Our future success may depend not only on our ability to develop our product candidates, but also our ability to improve them and to improve Afrezza in order to keep pace with emerging industry developments. We cannot assure you that we will be able to do so.

We also expect to face competition from universities and other non-profit research organizations. These institutions carry out a significant amount of research and development in various areas of unmet medical need. These institutions are becoming increasingly aware of the commercial value of their findings and are more active in seeking patent and other proprietary rights as well as licensing revenues.

Continued testing of Afrezza or our product candidates may not yield successful results, and even if it does, we may still be unable to commercialize our product candidates.

Forecasts about the effects of the use of drugs, including Afrezza, over terms longer than the clinical studies or in much larger populations may not be consistent with the earlier clinical results. For example, with the approval of Afrezza, the FDA has required a five-year, randomized, controlled trial with type 2 diabetes, the primary objective of which is to compare the incidence of pulmonary malignancy observed with Afrezza to that observed in a standard of care control group. If long-term use of a drug results in adverse health effects or reduced efficacy or both, the FDA or other regulatory agencies may terminate our or any future marketing partner's ability to market and sell the drug, may narrow the approved indications for use or otherwise require restrictive product labeling or marketing, or may require

further clinical studies, which may be time-consuming and expensive and may not produce favorable results.

Our research and development programs are designed to test the safety and efficacy of our product candidates through extensive nonclinical and clinical testing. We may experience numerous unforeseen events during, or as a result of, the testing process that could delay or impact commercialization of any of our product candidates, including the following:

- safety and efficacy results obtained in our nonclinical and early clinical testing may be inconclusive or may not be predictive of results that we may obtain in our future clinical studies or following long-term use, and we may as a result be forced to stop developing a product candidate or alter the marketing of an approved product;
- the analysis of data collected from clinical studies of our product candidates may not reach the statistical significance necessary, or otherwise be sufficient to support FDA or other regulatory approval for the claimed indications;
- after reviewing clinical data, we or any collaborators may abandon projects that we previously believed were promising; and
- our product candidates may not produce the desired effects or may result in adverse health effects or other characteristics that preclude regulatory approval or limit their commercial use once approved.

As a result of any of these events, we, any collaborator, the FDA, or any other regulatory authorities, may suspend or terminate clinical studies or marketing of the drug at any time. Any suspension or termination of our clinical studies or marketing activities may harm our business, financial condition and results of operations and the market price of our common stock and other securities may decline.

If our suppliers fail to deliver materials and services needed for the production of Afrezza in a timely and sufficient manner or fail to comply with applicable regulations, and if we fail to timely identify and qualify alternative suppliers, our business, financial condition and results of operations would be harmed and the market price of our common stock and other securities could decline.

For the commercial manufacture of Afrezza, we need access to sufficient, reliable and affordable supplies of insulin, our Afrezza inhaler, the related cartridges and other materials. Currently, the only source of insulin that we have qualified for Afrezza is manufactured by Amphastar. We must rely on our suppliers, including Amphastar, to comply with relevant regulatory and other legal requirements, including the production of insulin and FDKP in accordance with the FDA's cGMP for drug products, and the production of the Afrezza inhaler and related cartridges in accordance with QSRs. The supply of any of these materials may be limited or any of the manufacturers may not meet relevant regulatory requirements, and if we are unable to obtain any of these materials in sufficient amounts, in a timely manner and at reasonable prices, or if we encounter delays or difficulties in our relationships with manufacturers or suppliers, the production of Afrezza may be delayed. Likewise, if Amphastar ceases to manufacture or is otherwise unable to deliver insulin for Afrezza, we will need to locate an alternative source of supply and the production of Afrezza may be delayed. If any of our suppliers is unwilling or unable to meet its supply obligations and we are unable to secure an alternative supply source in a timely manner and on favorable terms, our business, financial condition, and results of operations may be harmed and the market price of our common stock and other securities may decline.

If we fail as an effective manufacturing organization or fail to engage third-party manufacturers with this capability, we may be unable to support commercialization of this product.

We use our Danbury, Connecticut facility to formulate Afrezza inhalation powder, fill plastic cartridges with the powder, package the cartridges in blister packs, and place the blister packs into foil pouches. We utilize a contract packager to assemble the final kits of foil-pouched blister packs along with inhalers and the package insert. The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, especially in scaling up initial production. These problems include difficulties with production costs and yields, quality control and assurance and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. If we engage a third-party manufacturer, we would need to transfer our technology to that third-party manufacturer and gain FDA approval, potentially causing delays in product delivery. In addition, our third-party manufacturer may not perform as agreed or may terminate its agreement with us.

Any of these factors could cause us to delay or suspend production, could entail higher costs and may result in our being unable to obtain sufficient quantities for the commercialization of Afrezza at the costs that we currently anticipate. Furthermore, if we or a third-party manufacturer fail to deliver the required commercial quantities of the product or any raw material on a timely basis, and at commercially reasonable prices, sustainable compliance and acceptable quality, and we were unable to promptly find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volume and quality on a timely basis, we would likely be unable to meet demand for Afrezza and we would lose potential revenues.

If Afrezza or any other product that we develop does not become widely accepted by physicians, patients, third-party payors and the healthcare community, we may be unable to generate significant revenue, if any.

Afrezza, and other products that we may develop in the future, may not gain market acceptance among physicians, patients, third-party payors and the healthcare community. Failure to achieve market acceptance would limit our ability to generate revenue and would adversely affect our results of operations.

The degree of market acceptance of Afrezza and other products that we may develop in the future depends on many factors, including the:

- Approved labeling claims;
- Effectiveness of efforts by us or any future marketing partner to support and educate physicians about the benefits and advantages of Afrezza or our other products, and the perceived advantages and disadvantages of competitive products;
- Willingness of the healthcare community and patients to adopt new technologies;
- Ability to manufacture the product in sufficient quantities with acceptable quality and cost;
- Perception of patients and the healthcare community, including third-party payors, regarding the safety, efficacy and benefits compared to competing products or therapies;
- Convenience and ease of administration relative to existing treatment methods;
 - Coverage and reimbursement, as well as pricing relative to other treatment therapeutics and methods; and
- Marketing and distribution support.

Because of these and other factors, Afrezza and any other product that we develop may not gain market acceptance, which would materially harm our business, financial condition and results of operations.

If third-party payors do not cover Afrezza or any of our product candidates for which we receive regulatory approval, Afrezza or such product candidates might not be prescribed, used or purchased, which would adversely affect our revenues.

Our future revenues and ability to generate positive cash flow from operations may be affected by the continuing efforts of government and other third-party payors to contain or reduce the costs of healthcare through various means. For example, in certain foreign markets the pricing of prescription pharmaceuticals is subject to governmental control. In the United States, there have been several congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have stated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that there will continue to be a number of federal and state proposals to implement similar and/or additional governmental controls. We cannot be certain what legislative proposals will be adopted or what actions federal, state or private third-party payors may take in response to any drug pricing and reimbursement reform proposals or legislation. Such reforms may limit our ability to generate revenues from sales of Afrezza or other products that we may develop in the future and achieve profitability. Further, to the extent that such reforms have a material adverse effect on the business, financial condition and profitability of any future marketing partner for Afrezza, and companies that are prospective collaborators for our product candidates, our ability to commercialize Afrezza and our product candidates under development may be adversely affected.

In the United States and elsewhere, sales of prescription pharmaceuticals still depend in large part on the availability of coverage and adequate reimbursement to the consumer from third-party payors, such as government health administration authorities and private insurance plans. Third-party payors are increasingly challenging the prices charged for medical products and services. The market for Afrezza and our product candidates for which we may receive regulatory approval will depend significantly on access to third-party payors’ drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. In addition, because each third-party payor individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming and costly process. We may be required to provide scientific and clinical support for the use of any product to each third-party payor separately with no assurance that approval would be obtained. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. Even if we succeed in bringing more products to market, we cannot be certain that any such products would be considered cost-effective or that coverage and adequate reimbursement to the consumer would be available. Patients will be unlikely to use our products unless coverage is provided and reimbursement is

adequate to cover a significant portion of the cost of our products.

In addition, in many foreign countries, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition for Afrezza or any of our other product candidates that receives marketing approval from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

If we or any future marketing partner is unable to obtain coverage of, and adequate payment levels reimbursement for, Afrezza or any of our other product candidates that receive marketing approval from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our and any future marketing partner's ability to successfully commercialize Afrezza and our ability to successfully commercialize any of our other product candidates that receives regulatory approval and impact our profitability, results of operations, financial condition, and prospects.

Healthcare legislation may make it more difficult to receive revenues.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals in recent years to change the healthcare system in ways that could impact our ability to sell our products profitably. For example, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, (“PPACA”) became law in the United States. PPACA substantially changed the way healthcare is financed by both governmental and private insurers and significantly affects the healthcare industry. Among the provisions of PPACA of importance to us are the following:

- An annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- A 2.3% medical device excise tax on certain transactions, including many U.S. sales of medical devices, which currently includes and we expect will continue to include U.S. sales of certain drug-device combination products, which has been suspended for calendar years 2016 through 2019;
- An increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- A licensure framework for follow-on biological products;
- Expansion of healthcare fraud and abuse laws, including the False Claims Act and the federal 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 now offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D;
- Extension of manufacturers’ Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- Expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers’ Medicaid rebate liability;
- Expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- Requirements to report annually to the Centers for Medicare & Medicaid Services (“CMS”) certain financial arrangements with physicians and teaching hospitals, as defined in PPACA and its implementing regulations, including reporting any “payments or transfers of value” made or distributed to prescribers, teaching hospitals and other healthcare providers and reporting any ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations during the preceding calendar year;
- A requirement to annually report drug samples that certain manufacturers and authorized 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.

Some of the provisions of the PPACA have yet to be fully implemented, while certain provisions have been subject to judicial and congressional challenges, as well as efforts by the Trump administration to repeal or replace certain aspects of the PPACA. President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the PPACA have been signed into law. The Tax Cuts and Jobs Act of 2017 (“Tax Act”) includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees,

including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the PPACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans. In July 2018, CMS published a final rule permitting further collections and payments to and from certain PPACA qualified health plans and health insurance issuers under the PPACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the “individual mandate” was repealed by Congress as part of the Tax Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the PPACA will impact the PPACA and our business.

In addition, other legislative changes have been proposed and adopted since PPACA was enacted. For example, on August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013, and, following passage of the BBA, will stay in effect through 2027 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012 (the "ATRA"), which, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. These new laws and initiatives may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations.

Further, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

We expect that PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private third-party 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 products.

If we or any future marketing partner fails to comply with federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

As a biopharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations, including those pertaining to fraud and abuse and patients' rights are and will be applicable to our business. For example, we could be subject to healthcare fraud and abuse and 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, among others:

- The federal Anti-Kickback Statute (as amended by PPACA, which modified the intent requirement of the federal Anti-Kickback Statute so that a person or entity no longer needs to have actual knowledge of the Statute or specific intent to violate it to have committed a violation), which constrains our business activities, including our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities by prohibiting, among other things, knowingly and willfully soliciting, receiving, offering or paying remuneration,

directly or indirectly, to induce, or in return for, either the referral of an individual or the purchase 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, including without limitation the False Claims Act, and civil monetary penalties laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other federal healthcare programs that are false or fraudulent, and knowingly making, or causing to be made, a false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government, and under PPACA, 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 federal false claims laws;

• HIPAA, which created new federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program or falsifying, concealing, or covering up a material fact in connection with the delivery of or payment for health care benefits;

• HIPAA, as amended by HITECH, and their respective implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information on entities subject to the law, such as certain healthcare providers, health plans, and healthcare clearinghouses and their respective business associates that perform services for them that involve the creation, use, maintenance or disclosure of, individually identifiable health information. In addition, in May 2018, the European Union, or EU, adopted European General Data Protection Regulation, or GDPR, which contains new

provisions specifically directed at the processing of health information, higher sanctions and extra-territoriality measures intended to bring non-EU companies under the regulation. We anticipate that over time we may expand our business operations to include additional operations in the EU, including potentially conducting preclinical and clinical trials. With such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including the GDPR;

California recently enacted legislation that has been dubbed the first “GDPR-like” law in the United States. Known as the California Consumer Privacy Act (“CCPA”), it will create new individual privacy rights for consumers (as that word is broadly defined in the law) and place increased privacy and security obligations on entities handling personal data of consumers or households. When it goes into effect on January 1, 2020, the CCPA will require covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. Legislators have stated that amendments will be proposed to the CCPA before it goes into effect, but it remains unclear what, if any, modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA will likely impact (possibly significantly) our business activities and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information;

The federal Physician Payments Sunshine Act under PPACA, which requires certain manufacturers of drugs, devices, biologics, and medical supplies to report annually to CMS information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;

State and foreign 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, and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; state laws that require pharmaceutical companies to comply with the industry’s voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to healthcare providers and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state laws that require drug manufacturers to report information related to payments and other transfer of value to physicians and other healthcare providers and entities. Because of the breadth of these laws and the narrowness of available statutory exceptions and regulatory safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. To the extent that Afrezza or any of our product candidates that receives marketing approval is ultimately sold in a foreign country, we may be subject to similar foreign laws and regulations. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil, criminal and administrative penalties, damages, fines, individual imprisonment, disgorgement, exclusion from U.S. federal or state healthcare programs, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could materially adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management’s attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the United States, we could be subject to additional reimbursement requirements, fines, sanctions and exposure under other laws which could have a material adverse effect on our business, results of operations and financial condition.

We participate in the Medicaid Drug Rebate Program, as administered by CMS, and other federal and state government pricing programs in the United States, and we may participate in additional government pricing programs in the future. These programs generally require us to pay rebates or otherwise provide discounts to government payors in connection with drugs that are dispensed to beneficiaries/recipients of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing that we report on a monthly and quarterly basis to the government agencies that administer the programs. Pricing requirements and rebate/discount calculations are complex, vary among products and programs, and are often subject to interpretation by governmental or regulatory agencies and the courts. The requirements of these programs, including, by way of example, their respective terms and scope, change frequently. Responding to current and future changes may increase our costs, and the complexity of compliance will be time consuming. Invoicing for rebates is provided in arrears, and there is frequently a time lag of up to several months between the sales to which rebate notices relate and our receipt of those notices, which further complicates our ability to accurately estimate and accrue for rebates related to the Medicaid program as implemented by individual states. Thus, there can be no assurance that we will be able to identify all factors that may cause our discount and rebate payment obligations to vary from period to period, and our actual results may differ significantly from our estimated allowances for discounts and rebates. Changes in estimates and assumptions may have a material adverse effect on our business, results of operations and financial condition.

In addition, the Office of Inspector General of the Department of Health and Human Services and other Congressional, enforcement and administrative bodies have recently increased their focus on pricing requirements for products, including, but not limited to the methodologies used by manufacturers to calculate average manufacturer price (“AMP”) and best price (“BP”) for compliance with reporting requirements under the Medicaid Drug Rebate Program. We are liable for errors associated with our submission of pricing data and for any overcharging of government payors. For example, failure to submit monthly/quarterly AMP and BP data on a timely basis could result in a civil monetary penalty. Failure to make necessary disclosures and/or to identify overpayments could result in allegations against us under the False Claims Act and other laws and regulations. Any required refunds to the U.S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition. In addition, in the event that the CMS were to terminate our rebate agreement, no federal payments would be available under Medicaid or Medicare for our covered outpatient drugs.

If product liability claims are brought against us, we may incur significant liabilities and suffer damage to our reputation.

The testing, manufacturing, marketing and sale of Afrezza and any clinical testing of our product candidates expose us to potential product liability claims. A product liability claim may result in substantial judgments as well as consume significant financial and management resources and result in adverse publicity, decreased demand for a product, injury to our reputation, withdrawal of clinical studies volunteers and loss of revenues. We currently carry worldwide product liability insurance in the amount of \$10.0 million. Our insurance coverage may not be adequate to satisfy any liability that may arise, and because insurance coverage in our industry can be very expensive and difficult to obtain, we cannot assure you that we will seek to obtain, or be able to obtain if desired, sufficient additional coverage. If losses from such claims exceed our liability insurance coverage, we may incur substantial liabilities that we may not have the resources to pay. If we are required to pay a product liability claim our business, financial condition and results of operations would be harmed and the market price of our common stock and other securities may decline.

If we lose any key employees or scientific advisors, our operations and our ability to execute our business strategy could be materially harmed.

We face intense competition for qualified employees among companies in the biotechnology and biopharmaceutical industries. Our success depends upon our ability to attract, retain and motivate highly skilled employees. We may be unable to attract and retain these individuals on acceptable terms, if at all. In addition, in order to commercialize Afrezza successfully, we may be required to expand our work force, particularly in the areas of manufacturing and sales and marketing. These activities will require the addition of new personnel, including management, and the development of additional expertise by existing personnel, and we cannot assure you that we will be able to attract or retain any such new personnel on acceptable terms, if at all.

The loss of the services of any principal member of our management, commercial and scientific staff could significantly delay or prevent the achievement of our scientific and business objectives. All of our employees are “at will” and we currently do not have employment agreements with any of the principal members of our management, commercial or scientific staff, and we do not have key person life insurance to cover the loss of any of these individuals. Replacing key employees may be difficult and time-consuming because of the limited number of individuals in our industry with the skills and experience required to develop, gain regulatory approval of and commercialize products successfully.

We have relationships with scientific advisors at academic and other institutions to conduct research or assist us in formulating our research, development or clinical strategy. These scientific advisors are not our employees and may have commitments to, and other obligations with, other entities that may limit their availability to us. We have limited

control over the activities of these scientific advisors and can generally expect these individuals to devote only limited time to our activities. Failure of any of these persons to devote sufficient time and resources to our programs could harm our business. In addition, these advisors are not prohibited from, and may have arrangements with, other companies to assist those companies in developing technologies that may compete with Afrezza or our product candidates.

If our internal controls over financial reporting are not considered effective, our business, financial condition and market price of our common stock and other securities could be adversely affected.

Section 404 of the Sarbanes-Oxley Act of 2002 requires us to evaluate the effectiveness of our internal controls over financial reporting as of the end of each fiscal year, and to include a management report assessing the effectiveness of our internal controls over financial reporting in our annual report on Form 10-K for that fiscal year. Section 404 also requires our independent registered public accounting firm to attest to, and report on, our internal controls over financial reporting.

Our management, including our Chief Executive Officer and our Chief Financial Officer, does not expect that our internal controls over financial reporting will prevent all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud involving a company have been, or will be, detected. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and we cannot assure you that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected. A material weakness in our internal controls has been identified in the past, and we cannot assure you that we or our independent registered public accounting firm will not identify a material weakness in our internal controls in the future. A material weakness in our internal controls over financial reporting would require management and our independent registered public accounting firm to evaluate our internal controls as ineffective. If our internal controls over financial reporting are not considered effective, we may experience a loss of public confidence, which could have an adverse effect on our business, financial condition and the market price of our common stock and other securities.

Changes or modifications in financial accounting standards, including those related to revenue recognition, may harm our results of operations.

From time to time, the Financial Accounting Standards Board ("FASB"), either alone or jointly with other organizations, promulgates new accounting principles that could have an adverse impact on our financial position, results of operations or reported cash flows. In May 2014, the FASB issued Accounting Standards Update (ASU) No. 2014-09, Revenue from Contracts with Customers (Topic 606), which was subsequently clarified by additional ASUs. The standard requires a company to recognize revenue to depict the transfer of goods or services when transferred to customers in the amount that reflects the consideration it expects to be entitled to receive in exchange for those goods or services. We adopted the new standard for the year beginning January 1, 2018. We had the option to apply the new standard either retrospectively for all prior reporting periods presented (full retrospective) or retrospectively with the cumulative effect of initially applying the new standard recognized at the date of initial application (modified retrospective). We have elected to apply the new standard using the modified retrospective approach with the cumulative effect of initial application recognized as of January 1, 2018 and the cumulative effect adjustment was a \$1.7 million decrease to the opening balance of accumulated deficit. Any difficulties in implementing this standard, or in adopting or implementing any other new accounting standard, and to update or modify our internal controls as needed on a timely basis, could result in our failure to meet our financial reporting obligations, which could result in regulatory discipline and harm investors' confidence in us. Finally, if we were to change our critical accounting estimates, including those related to the recognition of collaboration revenue and other revenue sources, our operating results could be significantly affected.

Our ability to use net operating losses to offset future taxable income may be subject to limitations.

As of December 31, 2018, we had federal and state net operating loss carryforwards of \$2.1 billion and \$2.4 billion, respectively. The federal and state net operating loss carryforwards have begun to expire. These net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward

indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. In addition, under Section 382 of the Code and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. As a result of our initial public offering, an ownership change within the meaning of Section 382 occurred in August 2004. As a result, federal net operating loss and credit carry forwards of approximately \$216.0 million and are subject to an annual use limitation of approximately \$13.0 million. The annual limitation is cumulative and therefore, if not fully utilized in a year, can be utilized in future years in addition to the Section 382 limitation for those years. We have not completed an IRC Section 382 analysis regarding the limitation of net operating loss carryforwards and other tax attributes since the August 2004 change in ownership in connection with our initial public offering. There is a risk that changes in ownership have occurred since our initial public offering. If a change in ownership were to have occurred after the initial public offering, net operating loss carryforwards and other tax attributes could be further limited or restricted. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

We may undertake internal restructuring activities in the future that could result in disruptions to our business or otherwise materially harm our results of operations or financial condition.

From time to time we may undertake internal restructuring activities as we continue to evaluate and attempt to optimize our cost and operating structure in light of developments in our business strategy and long-term operating plans. These activities may result in write-offs or other restructuring charges. There can be no assurance that any restructuring activities that we undertake will achieve the cost savings, operating efficiencies or other benefits that we may initially expect. Restructuring activities may also result in a loss of continuity, accumulated knowledge and inefficiency during transitional periods and thereafter. In addition, internal restructurings can require a significant amount of time and focus from management and other employees, which may divert attention from commercial operations. If we undertake any internal restructuring activities and fail to achieve some or all of the expected benefits therefrom, our business, results of operations and financial condition could be materially and adversely affected.

We and certain of our executive officers and directors have been named as defendants in ongoing securities lawsuits that could result in substantial costs and divert management's attention.

Following the public announcement of Sanofi's election to terminate the Sanofi License Agreement and the subsequent decline in our stock price, two motions were submitted to the district court at Tel Aviv, Economic Department for the certification of a class action against MannKind and certain of our officers and directors. In general, the complaints allege that MannKind and certain of our officers and directors violated Israeli and U.S. securities laws by making materially false and misleading statements regarding the prospects for Afrezza, thereby artificially inflating the price of its common stock. The plaintiffs are seeking monetary damages. In November 2016, the district court dismissed one of the actions without prejudice. In the remaining action, the district court ruled in October 2017 that U.S. law will apply to this case. The plaintiff has appealed this ruling, and following an oral hearing before the Supreme Court of Israel, has decided to withdraw his appeal. Subsequently, in November 2018, Mannkind filed a motion to dismiss the certification motion. At a case conference in February 2019, the court directed the parties to negotiate a procedure for determining whether the plaintiff can distinguish the claims in the Israeli litigation from those in a U.S. case against us based on the same events (which was dismissed by the U.S. district court for the Central District of California in August 2016). We will continue to vigorously defend against the claims advanced. If we are not successful in our defense, we could be forced to make significant payments to or other settlements with our stockholders and their lawyers, and such payments or settlement arrangements could have a material adverse effect on our business, operating results or financial condition. Even if such claims are not successful, the litigation could result in substantial costs and significant adverse impact on our reputation and divert management's attention and resources, which could have a material adverse effect on our business, operating results and financial condition.

Our operations might be interrupted by the occurrence of a natural disaster or other catastrophic event.

We expect that at least for the foreseeable future, our manufacturing facility in Danbury, Connecticut will be the sole location for the manufacturing of Afrezza. It will also serve as the initial production facility for TreT. This facility and the manufacturing equipment we use would be costly to replace and could require substantial lead time to repair or replace. We depend on our facilities and on collaborators, contractors and vendors for the continued operation of our business, some of whom are located in other countries. Natural disasters or other catastrophic events, including interruptions in the supply of natural resources, political and governmental changes, severe weather conditions, wildfires and other fires, explosions, actions of animal rights activists, terrorist attacks, volcanic eruptions, earthquakes and wars could disrupt our operations or those of our collaborators, contractors and vendors. We might suffer losses as a result of business interruptions that exceed the coverage available under our and our contractors' insurance policies or for which we or our contractors do not have coverage. For example, we are not insured against a terrorist attack. Any natural disaster or catastrophic event could have a significant negative impact on our operations and financial results. Moreover, any such event could delay our research and development programs or cause interruptions in our commercialization of Afrezza.

We deal with hazardous materials and must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development and commercialization of Afrezza work involves the controlled storage and use of hazardous materials, including chemical and biological materials. In addition, our manufacturing operations involve the use of a chemical that may form an explosive mixture under certain conditions. Our operations also produce hazardous waste products. We are subject to federal, state and local laws and regulations (i) governing how we use, manufacture, store, handle and dispose of these materials (ii) imposing liability for costs of cleaning up, and damages to natural resources from past spills, waste disposals on and off-site, or other releases of hazardous materials or regulated substances, and (iii) regulating workplace safety. Moreover, the risk of accidental contamination or injury from hazardous materials cannot be completely eliminated, and in the event of an accident, we could be held liable for

any damages that may result, and any liability could fall outside the coverage or exceed the limits of our insurance. Currently, our general liability policy provides coverage up to \$1.0 million per occurrence and \$2.0 million in the aggregate and is supplemented by an umbrella policy that provides a further \$20.0 million of coverage; however, our insurance policy excludes pollution liability coverage and we do not carry a separate hazardous materials policy. In addition, we could be required to incur significant costs to comply with environmental laws and regulations in the future. Finally, current or future environmental laws and regulations may impair our research, development or production efforts or have an adverse impact on our business, results of operations and financial condition.

When we purchased the facilities located in Danbury, Connecticut in 2001, a soil and groundwater investigation and remediation was being conducted by a former site operator (the responsible party) under the oversight of the Connecticut Department of Environmental Protection, which is not completed. The responsible party will make all filings necessary to achieve closure for the environmental remediation conducted at the site, and has agreed to indemnify us for any future costs and expenses we may incur that are directly related to the final closure. If we are unable to collect these future costs and expenses, if any, from the responsible party, our business, financial condition and results of operations may be harmed.

We are increasingly dependent on information technology systems, infrastructure and data security.

We are increasingly dependent upon information technology systems, infrastructure and data security. Our business requires manipulating, analyzing and storing large amounts of data. In addition, we rely on an enterprise software system to operate and manage our business. Our business therefore depends on the continuous, effective, reliable and secure operation of our computer hardware, software, networks, Internet servers and related infrastructure. The multitude and complexity of our computer systems and the potential value of our data make them inherently vulnerable to service interruption or destruction, malicious intrusion and random attack. Likewise, data privacy or security breaches by employees or others may pose a risk that sensitive data including intellectual property, trade secrets or personal information belonging to us or our customers or other business partners may be exposed to unauthorized persons or to the public. Our systems are also potentially subject to cyber-attacks, which can be highly sophisticated and may be difficult to detect. Such attacks are often carried out by motivated, well-resourced, skilled and persistent actors including nation states, organized crime groups and “hacktivists.” Cyber-attacks could include the deployment of harmful malware and key loggers, a denial-of-service attack, a malicious website, the use of social engineering and other means to affect the confidentiality, integrity and availability of our information technology systems, infrastructure and data. Our key business partners face similar risks and any security breach of their systems could adversely affect our security status. While we continue to invest in the protection of our critical or sensitive data and information technology, there can be no assurance that our efforts will prevent or detect service interruptions or breaches in our systems that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us.

Changes in funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

RISKS RELATED TO GOVERNMENT REGULATION

Our product candidates must undergo costly and time-consuming rigorous nonclinical and clinical testing and we must obtain regulatory approval prior to the sale and marketing of any product in each jurisdiction. The results of this testing or issues that develop in the review and approval by a regulatory agency may subject us to unanticipated delays or prevent us from marketing any products.

Our research and development activities, as well as the manufacturing and marketing of Afrezza and our product candidates, are subject to regulation, including regulation for safety, efficacy and quality, by the FDA in the United States and comparable authorities in other countries. FDA regulations and the regulations of comparable foreign regulatory authorities are wide-ranging and govern, among other things:

- product design, development, manufacture and testing;
- product labeling;
- product storage and shipping;
- pre-market clearance or approval;
- advertising and promotion; and
- product sales and distribution.

The requirements governing the conduct of clinical studies and manufacturing and marketing of Afrezza and our product candidates outside the United States vary widely from country to country. Foreign approvals may take longer to obtain than FDA approvals and can require, among other things, additional testing and different clinical study designs. Foreign regulatory approval processes include essentially all of the risks associated with the FDA approval processes. Some of those agencies also must approve prices of the products. Approval of a product by the FDA does not ensure approval of the same product by the health authorities of other countries. In addition, changes in regulatory policy in the United States or in foreign countries for product approval during the period of product development and regulatory agency review of each submitted new application may cause delays or rejections.

Clinical testing can be costly and take many years, and the outcome is uncertain and susceptible to varying interpretations. We cannot be certain if or when regulatory agencies might request additional studies, under what conditions such studies might be requested, or what the size or length of any such studies might be. The clinical studies of our product candidates may not be completed on schedule, regulatory agencies may order us to stop or modify our research, or these agencies may not ultimately approve any of our product candidates for commercial sale. The data collected from our clinical studies may not be sufficient to support regulatory approval of our product candidates. Even if we believe the data collected from our clinical studies are sufficient, regulatory agencies have substantial discretion in the approval process and may disagree with our interpretation of the data. Our failure to adequately demonstrate the safety and efficacy of any of our product candidates would delay or prevent regulatory approval of our product candidates, which could prevent us from achieving profitability.

Questions that have been raised about the safety of marketed drugs generally, including pertaining to the lack of adequate labeling, may result in increased cautiousness by regulatory agencies in reviewing new drugs based on safety, efficacy, or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Such regulatory considerations may also result in the imposition of more restrictive drug labeling or marketing requirements as conditions of approval, which may significantly affect the marketability of our drug products.

If we do not comply with regulatory requirements at any stage, whether before or after marketing approval is obtained, we may be fined or forced to remove a product from the market, subject to criminal prosecution, or experience other adverse consequences, including restrictions or delays in obtaining regulatory marketing approval.

Even if we comply with regulatory requirements, we may not be able to obtain the labeling claims necessary or desirable for product promotion. We may also be required to undertake post-marketing studies. For example, as part of the approval of Afrezza, the FDA required that we complete a clinical trial to evaluate the potential risk of pulmonary malignancy with Afrezza. To date, we have not enrolled any subjects in this trial.

In addition, if we or other parties identify adverse effects after any of our products are on the market, or if manufacturing problems occur, regulatory approval may be withdrawn and a reformulation of our products, additional clinical studies, changes in labeling of, or indications of use for, our products and/or additional marketing applications may be required. If we encounter any of the foregoing problems, our business, financial condition and results of operations will be harmed and the market price of our common stock and other securities may decline.

We are subject to stringent, ongoing government regulation.

The manufacture, marketing and sale of Afrezza are subject to stringent and ongoing government regulation. The FDA may also withdraw product approvals if problems concerning the safety or efficacy of a product appear following approval. We cannot be sure that FDA and United States Congressional initiatives or actions by foreign regulatory bodies pertaining to ensuring the safety of marketed drugs or other developments pertaining to the pharmaceutical industry will not adversely affect our operations. For example, stability failure of Afrezza could lead to product recall or other sanctions.

We also are required to register our establishments and list our products with the FDA and certain state agencies. We and any third-party manufacturers or suppliers must continually adhere to federal regulations setting forth requirements, known as cGMP (for drugs) and QSR (for medical devices), and their foreign equivalents, which are enforced by the FDA and other national regulatory bodies through their facilities inspection programs. In complying with cGMP and foreign regulatory requirements, we and any of our potential third-party manufacturers or suppliers will be obligated to expend time, money and effort in production, record-keeping and quality control to ensure that our products meet applicable specifications and other requirements. QSR requirements also impose extensive testing,

control and documentation requirements. State regulatory agencies and the regulatory agencies of other countries have similar requirements. In addition, we will be required to comply with regulatory requirements of the FDA, state regulatory agencies and the regulatory agencies of other countries concerning the reporting of adverse events and device malfunctions, corrections and removals (e.g., recalls), promotion and advertising and general prohibitions against the manufacture and distribution of adulterated and misbranded devices. Failure to comply with these regulatory requirements could result in civil fines, product seizures, injunctions and/or criminal prosecution of responsible individuals and us. Any such actions would have a material adverse effect on our business, financial condition and results of operations.

FDA and comparable foreign regulatory authorities subject Afrezza and any approved drug product to extensive and ongoing regulatory requirements concerning the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCP requirements for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems, 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, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, 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 approvals;
product seizure or detention, or refusal to permit the import or export of our product candidates; and
injunctions or the imposition of civil or criminal penalties.

The FDA and other regulatory authorities impose significant restrictions on approved products through regulations on advertising, promotional and distribution activities. This oversight encompasses, but is not limited to, direct-to-consumer advertising, healthcare provider-directed advertising and promotion, sales representative communications to healthcare professionals, promotional programming and promotional activities involving the Internet. Regulatory authorities may also review industry-sponsored scientific and educational activities that make representations regarding product safety or efficacy in a promotional context. The FDA and other regulatory authorities may take enforcement action against a company for promoting unapproved uses of a product or for other violations of its advertising and labeling laws and regulations. Enforcement action may include product seizures, injunctions, civil or criminal penalties or regulatory letters, which may require corrective advertising or other corrective communications to healthcare professionals. Failure to comply with such regulations also can result in adverse publicity or increased scrutiny of company activities by the U.S. Congress or other legislators. Certain states have also adopted regulations and reporting requirements surrounding the promotion of pharmaceuticals. Failure to comply with state requirements may affect our ability to promote or sell our products in certain states.

We are required to comply with FDA regulations concerning the advertising and promotion of Afrezza. Failure to comply with these regulations can result in the receipt of warning letters and further liability if off-label promotion is involved. For example, in October 2018, we received a warning letter from the FDA's Office of Prescription Drug Promotion related to a particular post on our Afrezza Facebook page. The warning letter stated that the post in question failed to adequately disclose the risks associated with the use of Afrezza. As a result, we inactivated all Afrezza social media accounts (including Facebook, Instagram and Twitter) and conducted a review to determine whether any additional postings may contain content similar to the post in question. We have responded to the warning letter and will continue to work with the FDA to address their concerns.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States 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 marketing approval that we may have obtained and we may not achieve or sustain profitability.

Our suppliers are subject to FDA inspection.

We depend on suppliers for insulin and other materials that comprise Afrezza, including our Afrezza inhaler and cartridges. Each supplier must comply with relevant regulatory requirements and is subject to inspection by the FDA. Although we conduct our own inspections and review and/or approve investigations of each supplier, there can be no assurance that the FDA, upon inspection, would find that the supplier substantially complies with the QSR or cGMP requirements, where applicable. If we or any potential third-party manufacturer or supplier fails to comply with these requirements or comparable requirements in foreign countries, regulatory authorities may subject us to regulatory action, including criminal prosecutions, fines and suspension of the manufacture of our products.

If we are required to find a new or additional supplier of insulin, we will be required to evaluate the new supplier's ability to provide insulin that meets regulatory requirements, including cGMP requirements as well as our specifications and quality requirements, which would require significant time and expense and could delay the manufacturing and commercialization of Afrezza.

Reports of side effects or safety concerns in related technology fields or in other companies' clinical studies could delay or prevent us from obtaining regulatory approval for our product candidates or negatively impact public perception of Afrezza or any other products we may develop.

If other pharmaceutical companies announce that they observed frequent adverse events in their studies involving insulin therapies, we may be subject to class warnings in the label for Afrezza. In addition, the public perception of Afrezza might be adversely affected, which could harm our business, financial condition and results of operations and cause the market price of our common stock and other securities to decline, even if the concern relates to another company's products or product candidates.

There are also a number of clinical studies being conducted by other pharmaceutical companies involving compounds similar to, or potentially competitive with, our product candidates. Adverse results reported by these other companies in their clinical studies could delay or prevent us from obtaining regulatory approval or negatively impact public perception of our product candidates, which could harm our business, financial condition and results of operations and cause the market price of our common stock and other securities to decline.

RISKS RELATED TO INTELLECTUAL PROPERTY

If we are unable to protect our proprietary rights, we may not be able to compete effectively, or operate profitably.

Our commercial success depends, in large part, on our ability to obtain and maintain intellectual property protection for our technology. Our ability to do so will depend on, among other things, complex legal and factual questions, and it should be noted that the standards regarding intellectual property rights in our fields are still evolving. We attempt to protect our proprietary technology through a combination of patents, trade secrets and confidentiality agreements. We own a number of domestic and international patents, have a number of domestic and international patent applications pending and have licenses to additional patents. We cannot assure you that our patents and licenses will successfully preclude others from using our technologies, and we could incur substantial costs in seeking enforcement of our proprietary rights against infringement. Even if issued, the patents may not give us an advantage over competitors with alternative technologies.

For example, the coverage claimed in a patent application can be significantly reduced before a patent is issued, either in the United States or abroad. Statutory differences in patentable subject matter may limit the protection we can obtain on some of our inventions outside of the United States. For example, methods of treating patients are not patentable in many countries outside of the United States. These and other issues may limit the patent protection we are able to secure internationally. Consequently, we do not know whether any of our pending or future patent applications will result in the issuance of patents or, to the extent patents have been issued or will be issued, whether these patents will be subjected to further proceedings limiting their scope, will provide significant proprietary protection or competitive advantage, or will be circumvented or invalidated.

In addition, in certain countries, including the United States, applications are generally published 18 months after the application's priority date. In any event, because publication of discoveries in scientific or patent literature often trails behind actual discoveries, we cannot be certain that we were the first inventor of the subject matter covered by our pending patent applications or that we were the first to file patent applications on such inventions. Assuming the other requirements for patentability are met, in the United States prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act ("AIA"), or the Leahy-Smith Act, the United States moved to a first inventor to file system. In general, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, the term of a patent is limited and, as a result, the patents protecting our products expire at various dates. For example, various patents providing protection for the powder component of Afrezza have terms extending into 2020, 2026, 2028, 2029 or 2030. In addition, patents providing protection for our inhaler and cartridges have terms extending into 2023, 2031 or 2032. Our method of treatment claims extend into 2026, 2029, 2030 or 2031. As and when these different patents expire, Afrezza could become subject to increased competition. As a consequence, we may not be able to recover our development costs.

An issued patent is presumed valid unless it is declared otherwise by a court of competent jurisdiction. However, the issuance of a patent is not conclusive as to its validity or enforceability and it is uncertain how much protection, if any, will be afforded by our patents. A third party may challenge the validity or enforceability of a patent after its issuance by various proceedings such as oppositions in foreign jurisdictions, or post grant proceedings, including, oppositions, re-examinations or other review in the United States. In some instances we may seek re-examination or reissuance of our own patents. If we attempt to enforce our patents, they may be challenged in court where they could be held invalid, unenforceable, or have their breadth narrowed to an extent that would destroy their value.

We also rely on unpatented technology, trade secrets, know-how and confidentiality agreements. We require our officers, employees, consultants and advisors to execute proprietary information and invention and assignment agreements upon commencement of their relationships with us. These agreements provide that all inventions developed by the individual on behalf of us must be assigned to us and that the individual will cooperate with us in connection with securing patent protection on the invention if we wish to pursue such protection. We also execute confidentiality agreements with outside collaborators. There can be no assurance, however, that our inventions and assignment agreements and our confidentiality agreements will provide meaningful protection for our inventions, trade secrets, know-how or other proprietary information in the event of unauthorized use or disclosure of such information. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to or independently developed by a competitor, our business, results of operations and financial condition could be adversely affected.

If we become involved in lawsuits to protect or enforce our patents or the patents of our collaborators or licensors, we would be required to devote substantial time and resources to prosecute or defend such proceedings.

Competitors may infringe our patents or the patents of our collaborators or licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover its technology. A court may also decide to award us a royalty from an infringing party instead of issuing an injunction against the infringing activity. An adverse determination of any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings brought by the USPTO, may be necessary to determine the priority of inventions with respect to our pre-AIA patent applications or those of our collaborators or licensors. Additionally, the Leahy-Smith Act has greatly expanded the options for post-grant review of patents that can be brought by third parties. In particular Inter Partes Review (“IPR”), available against any issued United States patent (pre-and post-AIA), has resulted in a higher rate of claim invalidation, due in part to the much reduced opportunity to repair claims by amendment as compared to re-examination, as well as the lower standard of proof used at the USPTO as compared to the federal courts. With the passage of time an increasing number of patents related to successful pharmaceutical products are being subjected to IPR. Moreover, the filing of IPR petitions has been used by short-sellers as a tool to help drive down stock prices. We may not prevail in any litigation, post-grant review, or interference proceedings in which we are involved and, even if we are successful, these proceedings may result in substantial costs and be a distraction to our management. Further, we may not be able, alone or with our collaborators and licensors, to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, the market price of our common stock and other securities may decline.

If our technologies conflict with the proprietary rights of others, we may incur substantial costs as a result of litigation or other proceedings and we could face substantial monetary damages and be precluded from commercializing our products, which would materially harm our business and financial condition.

Biotechnology patents are numerous and may, at times, conflict with one another. As a result, it is not always clear to industry participants, including us, which patents cover the multitude of biotechnology product types. Ultimately, the courts must determine the scope of coverage afforded by a patent and the courts do not always arrive at uniform conclusions.

A patent owner may claim that we are making, using, selling or offering for sale an invention covered by the owner’s patents and may go to court to stop us from engaging in such activities. Such litigation is not uncommon in our industry.

Patent lawsuits can be expensive and would consume time and other resources. There is a risk that a court would decide that we are infringing a third party’s patents and would order us to stop the activities covered by the patents, including the commercialization of our products. In addition, there is a risk that we would have to pay the other party damages for having violated the other party’s patents (which damages may be increased, as well as attorneys’ fees ordered paid, if infringement is found to be willful), or that we will be required to obtain a license from the other party in order to continue to commercialize the affected products, or to design our products in a manner that does not infringe a valid patent. We may not prevail in any legal action, and a required license under the patent may not be available on acceptable terms or at all, requiring cessation of activities that were found to infringe a valid patent. We also may not be able to develop a non-infringing product design on commercially reasonable terms, or at all.

Moreover, certain components of Afrezza may be manufactured outside the United States and imported into the United States. As such, third parties could file complaints under 19 U.S.C. Section 337(a)(1)(B) (a “337 action”) with the International Trade Commission (the “ITC”). A 337 action can be expensive and would consume time and other resources. There is a risk that the ITC would decide that we are infringing a third party’s patents and either enjoin us from importing the infringing products or parts thereof into the United States or set a bond in an amount that the ITC considers would offset our competitive advantage from the continued importation during the statutory review period.

The bond could be up to 100% of the value of the patented products. We may not prevail in any legal action, and a required license under the patent may not be available on acceptable terms, or at all, resulting in a permanent injunction preventing any further importation of the infringing products or parts thereof into the United States. We also may not be able to develop a non-infringing product design on commercially reasonable terms, or at all.

Although we do not believe that Afrezza infringes any third-party patents, we have identified certain patents having claims that may trigger an allegation of infringement in connection with the commercial manufacture and sale of Afrezza. If a court were to determine that Afrezza was infringing any of these patent rights, we would have to establish with the court that these patents are invalid or unenforceable in order to avoid legal liability for infringement of these patents. However, proving patent invalidity or unenforceability can be difficult because issued patents are presumed valid. Therefore, in the event that we are unable to prevail in a non-infringement or invalidity action we will have to either acquire the third-party patents outright or seek a royalty-bearing license. Royalty-bearing licenses effectively increase production costs and therefore may materially affect product profitability. Furthermore, should the patent holder refuse to either assign or license us the infringed patents, it may be necessary to cease manufacturing the product entirely and/or design around the patents, if possible. In either event, our business, financial condition and results of operations would be harmed and our profitability could be materially and adversely impacted.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, the market price of our common stock and other securities may decline.

In addition, patent litigation may divert the attention of key personnel and we may not have sufficient resources to bring these actions to a successful conclusion. At the same time, some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. An adverse determination in a judicial or administrative proceeding or failure to obtain necessary licenses could prevent us from manufacturing and selling our products or result in substantial monetary damages, which would adversely affect our business, financial condition and results of operations and cause the market price of our common stock and other securities to decline.

We may not obtain trademark registrations for our potential trade names.

We have not selected trade names for some of our product candidates in our pipeline; therefore, we have not filed trademark registrations for such potential trade names for our product candidates, nor can we assure that we will be granted registration of any potential trade names for which we do file. No assurance can be given that any of our trademarks will be registered in the United States or elsewhere, or once registered that, prior to our being able to enter a particular market, they will not be cancelled for non-use. Nor can we give assurances, that the use of any of our trademarks will confer a competitive advantage in the marketplace.

Furthermore, even if we are successful in our trademark registrations, the FDA has its own process for drug nomenclature and its own views concerning appropriate proprietary names. It also has the power, even after granting market approval, to request a company to reconsider the name for a product because of evidence of confusion in the marketplace. We cannot assure you that the FDA or any other regulatory authority will approve of any of our trademarks or will not request reconsideration of one of our trademarks at some time in the future.

RISKS RELATED TO OUR COMMON STOCK

We may not be able to generate sufficient cash to service all of our indebtedness. We may be forced to take other actions to satisfy our obligations under our indebtedness or we may experience a financial failure.

Our ability to make scheduled payments on or to refinance our debt obligations will depend on our financial and operating performance, which is subject to the commercial success of Afrezza, the extent to which we are able to successfully develop and commercialize our Technosphere drug delivery platform and any other product candidates that we develop, prevailing economic and competitive conditions, and to certain financial, business and other factors beyond our control. We cannot assure you that we will maintain a level of cash flows from operating activities sufficient to permit us to pay the principal, premium, if any, and interest on our indebtedness. If our cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay capital expenditures, sell assets or operations, seek additional capital or restructure or refinance our indebtedness. We cannot assure you that we would be able to take any of these actions, that these actions would be successful and permit us to meet our scheduled debt service obligations or that these actions would be permitted under the terms of our future debt agreements. In the absence of sufficient operating results and resources, we could face substantial liquidity problems and might be required to dispose of material assets or operations to meet our debt service and other obligations. We may not be able to consummate those dispositions or obtain sufficient proceeds from those dispositions to meet our debt service and other obligations when due.

Future sales of shares of our common stock in the public market, or the perception that such sales may occur, may depress our stock price and adversely impact the market price of our common stock and other securities.

If our existing stockholders or their distributees sell substantial amounts of our common stock in the public market, the market price of our common stock could decrease significantly. The perception in the public market that our existing stockholders might sell shares of common stock could also depress the market price of our common stock and

the market price of our other securities. Any such sales of our common stock in the public market may affect the price of our common stock or the market price of our other securities.

In the future, we may sell additional shares of our common stock to raise capital. In addition, a substantial number of shares of our common stock is reserved for: issuance upon the exercise of stock options and the vesting of restricted stock unit awards and the purchase of shares of common stock under our employee stock purchase program. We cannot predict the size of future issuances or the effect, if any, that they may have on the market price for our common stock. The issuance or sale of substantial amounts of common stock, or the perception that such issuances or sales may occur, could adversely affect the market price of our common stock and other securities.

Our stock price is volatile and may affect the market price of our common stock and other securities.

Between January 1, 2016 and December 31, 2018, our closing stock price as reported on The Nasdaq Global Market has ranged from \$0.71 to \$10.80, adjusted for the 1-for-5 reverse stock split that occurred during this period. The trading price of our common stock is likely to continue to be volatile. The stock market, particularly in recent years, has experienced significant volatility particularly with respect to pharmaceutical and biotechnology stocks, and this trend may continue.

The volatility of pharmaceutical and biotechnology stocks often does not relate to the operating performance of the companies represented by the stock. Our business and the market price of our common stock may be influenced by a large variety of factors, including:

- our ability to obtain marketing approval for Afrezza outside of the United States and to find collaboration partners for the commercialization of Afrezza in foreign jurisdictions;
- our future estimates of Afrezza sales, prescriptions or other operating metrics;
- our ability to successfully commercialize other products (in addition to Afrezza) based on our Technosphere drug delivery platform;
- the progress of preclinical and clinical studies of our product candidates and of post-approval studies of Afrezza required by the FDA;
- the results of preclinical and clinical studies of our product candidates;
- general economic, political or stock market conditions, especially for emerging growth and pharmaceutical market sectors;
- legislative developments;
- announcements by us, our collaborators, or our competitors concerning clinical study results, acquisitions, strategic alliances, technological innovations, newly approved commercial products, product discontinuations, or other developments;
- the availability of critical materials used in developing and manufacturing Afrezza or other product candidates;
- developments or disputes concerning our relationship with any of our current or future collaborators or third party manufacturers;
- developments or disputes concerning our patents or proprietary rights;
- the expense and time associated with, and the extent of our ultimate success in, securing regulatory approvals;
- announcements by us concerning our financial condition or operating performance;
- changes in securities analysts' estimates of our financial condition or operating performance;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;
- our ability, or the perception of investors of our ability, to continue to meet all applicable requirements for continued listing of our common stock on The Nasdaq Stock Market, and the possible delisting of our common stock if we are unable to do so;
- the status of any legal proceedings or regulatory matters against or involving us or any of our executive officers and directors; and
- discussion of Afrezza, our other product candidates, competitors' products, or our stock price by the financial and scientific press, the healthcare community and online investor communities such as chat rooms. In particular, it may be difficult to verify statements about us and our investigational products that appear on interactive websites that permit users to generate content anonymously or under a pseudonym and statements attributed to company officials may, in fact, have originated elsewhere.

Any of these risks, as well as other factors, could cause the market value of our common stock and other securities to decline.

If we fail to continue to meet all applicable listing requirements, our common stock may be delisted from the Nasdaq Global Market, which could have an adverse impact on the liquidity and market price of our common stock.

Our common stock is currently listed on The Nasdaq Global Market, which has qualitative and quantitative listing criteria. If we are unable to meet any of the Nasdaq listing requirements in the future, such as the corporate governance requirements, the minimum closing bid price requirement, or the minimum market value of listed securities requirement, Nasdaq could determine to delist our common stock. A delisting of our common stock could adversely affect the market liquidity of our common stock, decrease the market price of our common stock, adversely affect our ability to obtain financing for the continuation of our operations and result in the loss of confidence in our company. In 2016, we received a notice of non-compliance from the Listing Qualifications Department of the Nasdaq Stock Market with respect to the \$1.00 minimum closing bid price requirement. Although we regained compliance with the minimum closing bid price requirement after effecting a reverse stock split in March 2017, there can be no assurance that we will be able to meet the minimum closing bid price requirement or other listing requirements in the future.

If other biotechnology and biopharmaceutical companies or the securities markets in general encounter problems, the market price of our common stock and other securities could be adversely affected.

Public companies in general, including companies listed on The Nasdaq Global Market, have experienced price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. There has been particular volatility in the market prices of securities of biotechnology and other life sciences companies, and the market prices of these companies have often fluctuated because of problems or successes in a given market segment or because investor interest has shifted to other segments. These broad market and industry factors may cause the market price of our common stock and other securities to decline, regardless of our operating performance. We have no control over this volatility and can only focus our efforts on our own operations, and even these may be affected due to the state of the capital markets.

In the past, following periods of large price declines in the public market price of a company's securities, securities class action litigation has often been initiated against that company. Litigation of this type could result in substantial costs and diversion of management's attention and resources, which would hurt our business. Any adverse determination in litigation could also subject us to significant liabilities.

The future sale of our common stock or the exchange or conversion of our convertible debt into, or exercise of our outstanding warrants for, common stock could negatively affect the market price of our common stock and other securities.

As of February 14, 2019, we had 187,342,566 shares of common stock outstanding. Substantially all of these shares are available for public sale, subject in some cases to volume and other limitations. If our common stockholders sell substantial amounts of common stock in the public market, or the market perceives that such sales may occur, the market price of our common stock and other securities may decline. Likewise the issuance of additional shares of our common stock upon the exchange or conversion of some or all of our senior convertible notes or notes payable to related party or upon issuance of our outstanding warrants, could adversely affect the market price of our common stock and other securities. In addition, the existence of these notes may encourage short selling of our common stock by market participants, which could adversely affect the market price of our common stock and other securities.

In addition, we will need to raise substantial additional capital in the future to fund our operations. If we raise additional funds by issuing equity securities or additional convertible debt, the market price of our common stock and other securities may decline.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

We are incorporated in Delaware. Certain anti-takeover provisions under Delaware law and in our certificate of incorporation and amended and restated bylaws, as currently in effect, may make a change of control of our company more difficult, even if a change in control would be beneficial to our stockholders or the holders of our other securities. Our anti-takeover provisions include provisions such as a prohibition on stockholder actions by written consent, the authority of our board of directors to issue preferred stock without stockholder approval, and supermajority voting requirements for specified actions. In addition, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits stockholders owning 15% or more of our outstanding voting stock from merging or combining with us in certain circumstances. These provisions may delay or prevent an acquisition of us, even if the acquisition may be considered beneficial by some of our stockholders. In addition, they may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for

appointing the members of our management.

Because we do not expect to pay dividends in the foreseeable future, you must rely on stock appreciation for any return on any investment in our common stock.

We have paid no cash dividends on any of our capital stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, we do not expect to pay any cash dividends in the foreseeable future, and payment of cash dividends, if any, will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Pursuant to the Facility Agreement, we are subject to contractual restrictions on the payment of dividends. There is no guarantee that our common stock will appreciate or maintain its current price. You could lose the entire value of any investment in our common stock.

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Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

In 2001, we acquired a facility in Danbury, Connecticut that included two buildings comprising approximately 190,000 square feet encompassing 17.5 acres. In September 2008, we completed the construction of approximately 140,000 square feet of new manufacturing space providing us with two buildings totaling approximately 328,000 square feet, housing our research and development, manufacturing and certain administrative functions for Afrezza. We believe the Connecticut facility will have sufficient space to satisfy commercial demand for Afrezza. Our obligations under the Facility Agreement and the Milestone Agreement are secured by our facility in Danbury, Connecticut and other assets. At the end of December 31, 2018, we leased a total of approximately 24,475 square feet of office space in Westlake Village, California pursuant to a lease that expires in January 2023. This facility contains our principal executive offices.

Item 3. Legal Proceedings

Following the public announcement of Sanofi's election to terminate the Sanofi License Agreement and the subsequent decline in our stock price, two motions were submitted to the district court at Tel Aviv, Economic Department for the certification of a class action against MannKind and certain of our officers and directors. In general, the complaints allege that MannKind and certain of our officers and directors violated Israeli and U.S. securities laws by making materially false and misleading statements regarding the prospects for Afrezza, thereby artificially inflating the price of its common stock. The plaintiffs are seeking monetary damages. In November 2016, the district court dismissed one of the actions without prejudice. In the remaining action, the district court ruled in October 2017 that U.S. law will apply to this case. The plaintiff has appealed this ruling, and following an oral hearing before the Supreme Court of Israel, has decided to withdraw his appeal. Subsequently, in November 2018, we filed a motion to dismiss the certification motion in limine. In December 2018, the district court ordered that the motion to dismiss will be heard during a pretrial hearing set for February 2019. The Court also granted our motion to postpone its response to the merits of the certification motion until after the resolution of the motion to dismiss. We will continue to vigorously defend against the claims advanced.

We are also subject to legal proceedings and claims which arise in the ordinary course of our business. As of the date hereof, we believe that the final disposition of such matters will not have a material adverse effect on our financial position, results of operations or cash flows. We maintain liability insurance coverage to protect our assets from losses arising out of or involving activities associated with ongoing and normal business operations.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for the Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Common Stock Market

Our common stock has been traded on The Nasdaq Global Market under the symbol “MNKD” since July 28, 2004. The following table sets forth for the quarterly periods indicated, the high and low sales prices for our common stock as reported by The Nasdaq Global Market (adjusted for the Reverse Stock Split effected March 3, 2017).

	High	Low
Year ended December 31, 2018		
First quarter	\$4.05	\$2.18
Second quarter	\$2.45	\$1.59
Third quarter	\$3.04	\$0.98
Fourth quarter	\$2.19	\$0.94
Year ended December 31, 2017		
First quarter	\$3.61	\$1.44
Second quarter	\$1.88	\$0.67
Third quarter	\$2.35	\$1.09
Fourth quarter	\$6.96	\$2.01

The closing sales price of our common stock on The Nasdaq Global Market was \$1.39 on February 14, 2019 and there were 105 registered holders of record as of that date.

Performance Measurement Comparison

The material in this section is not “soliciting material,” is not deemed “filed” with the SEC and shall not be incorporated by reference by any general statement incorporating by reference this Annual Report on Form 10-K into any of our filings under the Securities Act, or the Exchange Act, except to the extent we specifically incorporate this section by reference.

The following graph illustrates a comparison of the cumulative total stockholder return (change in stock price plus reinvested dividends) of our common stock with (i) The Nasdaq Composite Index and (ii) The Nasdaq Biotechnology Index. The graph assumes a \$100 investment, on December 31, 2013, in (i) our common stock, (ii) the securities comprising The Nasdaq Composite Index and (iii) the securities comprising The Nasdaq Biotechnology Index.

The comparisons in the graph are required by the SEC and are not intended to forecast or be indicative of possible future performance of our common stock.

Dividend Policy

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operation and expansion of our business. Accordingly, we do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors. In addition, under the terms of the Facility Agreement, we are restricted from distributing any of our assets or declaring and distributing a dividend to our stockholders.

Recent Sales of Unregistered Securities

None.

Item 6. Selected Financial Data

The following data has been derived from our audited financial statements, including the consolidated balance sheets at December 31, 2018 and 2017 and the related consolidated statements of operations for each of the three years ended December 31, 2018, 2017 and 2016 and related notes appearing elsewhere in this report. The consolidated statement of operations data for the years ended December 31, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016, 2015 and 2014 are derived from our audited consolidated financial statements that are not included in this report. Items that significantly impact the comparability among the periods presented include the following:

- Long-lived asset, inventory impairments, and recognition of loss on purchase commitments in 2015,
- Recognition of revenue, related costs and gain on extinguishment of debt related to the collaboration with Sanofi in 2016,
- Recognition of revenue related to commercial sales of Afrezza in 2016 and 2017; and
- Recognition of revenue related to UT License Agreement and Research Agreement.

The selected financial data set forth below should be read in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and the audited consolidated financial statements, and the notes thereto, and other financial information included herein this Annual Report on Form 10-K, which provide additional information about the items noted above that significantly affect the comparability among the periods presented.

	Year Ended December 31,				
	2018	2017	2016	2015	2014
	(In thousands, except per share amounts)				
Statement of Operations Data:					
Revenue:					
Total net revenue	\$27,859	\$11,745	\$174,758	\$—	\$—
(Loss) income from operations	(76,595)	(108,189)	67,260	(344,655)	(179,627)
Net (loss) income	(86,975)	(117,333)	125,664	(368,445)	(198,382)
Net (loss) income per share - basic	(0.60)	(1.13)	1.37	(4.54)	(2.57)
Net (loss) income per share - diluted	(0.60)	(1.13)	1.36	(4.54)	(2.57)
Shares used to compute basic net (loss) income per share	144,136	104,245	92,053	81,233	77,045
Shares used to compute diluted net (loss) income per share	144,136	104,245	92,085	81,233	77,045

	December 31,				
	2018	2017	2016	2015	2014
	(In thousands)				
Balance Sheet Data:					
Cash and cash equivalents	\$71,157	\$43,946	\$22,895	\$59,074	\$120,841
Total assets	107,705	84,575	107,063	126,412	394,439
Facility financing obligation	11,298	52,745	71,339	74,582	72,995
Note payable to related party	72,089	79,666	49,521	49,521	49,521
Accrued interest — note payable to related party	6,835	2,347	9,281	6,380	3,486
Senior convertible notes	19,099	24,411	27,635	27,613	99,355
Sanofi loan facility and loss share obligation	—	—	—	62,371	3,034
Accumulated deficit	(2,940,000)	(2,854,898)	(2,737,565)	(2,863,229)	(2,494,784)
Total stockholders’ deficit	(175,082)	(214,732)	(183,593)	(350,329)	(73,770)

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and notes thereto included in this Annual Report on Form 10-K.

Overview

We are a biopharmaceutical company focused on the development and commercialization of inhaled therapeutic products for patients with diseases such as diabetes and pulmonary arterial hypertension. Our only approved product, Afrezza, is a rapid-acting inhaled insulin that was approved by the FDA in June 2014 to improve glycemic control in adult patients with diabetes. Afrezza became available by prescription in United States retail pharmacies in February 2015.

As of December 31, 2018, we had an accumulated deficit of \$2.9 billion and a stockholders' deficit of \$175.1 million. We had net income (losses) of approximately \$(87.0) million, \$(117.3) million and \$125.7 million in the years ended December 31, 2018, 2017 and 2016, respectively. We have funded our operations primarily through the sale of equity securities and convertible debt securities, borrowings under The Mann Group Loan Arrangement, receipt of a \$45.0 million upfront payment under the UT License Agreement, receipt of upfront and milestone payments under the Sanofi License Agreement and borrowings under a senior secured revolving promissory note and a guaranty and security agreement that we entered into with an affiliate of Sanofi in September 2014 in connection with the Sanofi License Agreement (the "Sanofi Loan Facility"), which provided us with a secured loan facility of up to \$175.0 million to fund our share of net losses under the Sanofi License Agreement, which was terminated in 2016. As discussed below in "Liquidity and Capital Resources", if we are unable to obtain additional funding, there is substantial doubt about our ability to continue as a going concern.

Our business is subject to significant risks, including but not limited to our need to raise additional capital to fund our operations, our ability to successfully commercialize Afrezza and manufacture sufficient quantities of Afrezza, competition from other products and technologies and uncertainties associated with obtaining and enforcing patent rights. Additional significant risks include the risks inherent in clinical trials and the regulatory approval process for our product candidates, which in some cases depends upon the efforts of our partners.

Critical Accounting Policies

The preparation of our consolidated financial statements is in accordance with accounting principles generally accepted in the United States of America (GAAP). The preparation of our consolidated financial statements requires management to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues, and expenses and related disclosure of contingent assets and liabilities. We consider an accounting estimate to be critical to the consolidated financial statements if (i) the estimate is complex in nature or requires a high degree of judgment and (ii) different estimates and assumptions were used, the results could have a material impact on the consolidated financial statements. On an ongoing basis, we evaluate our estimates and the application of our policies. We base our estimates on historical experience, current conditions and on various other assumptions that we believe are 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. Actual results may differ from these estimates under different assumptions or conditions.

We consider our critical accounting policies to be those related to revenue recognition and gross-to-net adjustments, inventory costing and recoverability, recognized loss on purchase commitments, impairment of long-lived assets, milestone rights liability, clinical trial expenses, stock-based compensation and accounting for income taxes. These critical accounting policies are also considered significant accounting policies and are more fully described in Note 2 —

Summary of Significant Accounting Policies of the Notes to Consolidated Financial Statements included in Part II, Item 8 — Financial Statements and Supplementary Data.

Revenue Recognition – Net Revenue – Commercial Product Sales – On January 1, 2018, we adopted Accounting Standards Codification (“ASC”) Topic 606 - Revenue from Contracts with Customers (“the new revenue guidance”). We recognize revenue on product sales when the Customer obtains control of the Company's product, in an amount that reflects the consideration which the Company expects to be entitled in exchange for those goods or services. Product revenues are recorded net of applicable reserves for variable consideration, including discounts, rebates, allowances and fees. For further detail refer to Note 2 – Summary of Significant Accounting Policies.

Prior to January 1, 2018, we invoiced our customers upon shipment of Afrezza to them and record an accounts receivable, with a corresponding liability for deferred revenue equal to the gross invoice price net of estimated gross-to-net adjustments. We were required to reliably estimate returns in a very narrow range in order to recognize revenue upon shipment. While we can currently estimate returns within a range, it is not sufficiently precise to meet the requirements. Accordingly, we deferred recognition of revenue and the related estimated discounts and allowances on Afrezza product shipments until the right of return no longer existed, which occurs at the earlier of the time Afrezza is dispensed through patient prescriptions or expiration of the right of return. Through December 31, 2017, we recognized revenue based on Afrezza prescriptions dispensed, as estimated by syndicated data provided by a third party. We also analyzed additional data points to ensure that such third-party data is reasonable, including data related to inventory movements within the channel and ongoing prescription demand. In addition, the costs of Afrezza associated with the deferred revenue were recorded as deferred costs until such time as the related deferred revenue is recognized. As of December 31, 2017, prior to the adoption of Topic 606, the ending balance for net deferred revenue, was \$3.0 million on the Company's consolidated balance sheets, which is presented net of \$1.5 million in gross-to-net revenue adjustments.

Revenue Recognition – Collaborations and Services — We enter into licensing or research agreements under which we license certain rights to our product candidates to third parties or provide research services to third-parties. The terms of these arrangements may include but are not limited to, payment to us of one or more of the following: nonrefundable, up-front license fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services we provide; and royalties on net sales of licensed products and sublicenses of the rights. As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. We use key assumptions to determine the stand-alone selling price, which may include development timelines, reimbursement rates for personnel costs, discount rates, and probabilities of technical and regulatory success. Given that significant estimates depend on the development plan, these estimates could change and impact the revenue recognition. Consideration received that does not meet the requirements to satisfy the revenue recognition criteria is recorded as deferred revenue in the accompanying consolidated balance sheets based on our best estimate of when such revenue will be recognized. Current deferred revenue consists of amounts that are expected to be recognized as revenue in the next 12 months. Amounts that we expect will not be recognized within the next 12 months are classified as long-term deferred revenue.

Inventory Costing and Recoverability — We determine the cost of inventory using the first-in, first-out or FIFO method. We capitalize inventory costs associated with our product's based on judgement that future economic benefits are expected to be realized. Inventories are stated at the lower of cost or net realizable value. We analyzed our inventory levels to identify inventory that may expire or has a cost basis in excess of its estimated realizable value. We performed an assessment of projected sales to evaluate the lower of cost or net realizable value and the potential excess inventory on hand at December 31, 2018, 2017 and 2016. As a result of these assessments, we recorded inventory write-offs of \$2.2 million and \$3.0 million in the years ended December 31, 2018 and 2017, respectively. There were no write-offs for the year ended December 31, 2016.

Recognized Loss on Purchase Commitments — We assess whether losses on long term purchase commitments should be accrued. Losses that are expected to arise from firm, non-cancellable, commitments for future purchases of inventory items are recognized unless recoverable. The loss on the purchase commitment balance is reduced as material is received. The balance of recognized loss on purchase commitments is primarily associated with insulin purchases. As of December 31, 2018 and 2017 the balance was \$98.3 million and \$109.3 million, respectively.

Impairment of Long-Lived Assets — We evaluate long lived assets for impairment at least on a quarterly basis and whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. An impairment loss would be indicated when estimated undiscounted future cash flows from the use and eventual disposition of an asset group, which are identifiable and largely independent of the cash flows of other asset groups, are less than the carrying amount of the asset group.

In connection with our quarterly assessment of impairment indicators, we recorded no impairments for the year ended December 31, 2018. We recorded \$0.2 million and \$1.2 million for the year ended December 31, 2017 and 2016, respectively. For further information see Note 4 — Property and Equipment of the Notes to Consolidated Financial Statements included in “Part II, Item 8 — Financial Statements and Supplementary Data”.

Milestone Rights Liability — In connection with the execution of the Facility Agreement, we also entered into the Milestone Agreement which requires the Company to make contingent payments to the Milestone Purchasers, totaling up to \$90.0 million, of which \$75.0 million remain payable as of December 31, 2018, upon the Company achieving specified commercialization milestones (the “Milestone Rights”). We evaluated the Milestone Rights and determined that such rights do not meet the definition of a freestanding derivative. Since we have elected not to apply the fair value option, we recorded the rights at the initial fair value. Upon the achievement of a milestone event, the milestone payment will be allocated between (i) a reduction of the initial liability and (ii) a return on investment and the gain or

loss is recognized at the time the milestone event is achieved. The estimated fair value of the Milestone Rights was calculated using the income approach in which the cash flows associated with the specified contractual payments were adjusted for both the expected timing and the probability of achieving the milestones discounted to present value using a selected market discount rate (Level 3 in the fair value hierarchy).

Clinical Trial Expenses — Our clinical trial accrual process seeks to account for expenses resulting from our obligations under contract with vendors, consultants, and clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to us under such contracts. Our objective is to reflect the appropriate trial expenses in our financial statements by matching period expenses with period services and efforts expended. In the event that we do not identify certain costs that have begun to be incurred or we underestimate or overestimate the level of services performed or the costs of such services, our reported expenses for a period would be too low or too high. The date on which certain services commence, the level of services performed on or before a given date and the cost of the services are often judgmental. We make these judgments based upon the facts and circumstances known to us in accordance with generally accepted accounting principles.

Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in our reporting amounts that are too high or too low for any particular period.

Stock-Based Compensation — Share-based payments to employees, including grants of stock options, restricted stock units, performance-based awards and the compensatory elements of employee stock purchase plans, are recognized in the consolidated statements of operations based upon the fair value of the awards at the grant date subject to an estimated forfeiture rate. We use the Black-Scholes option valuation model to estimate the grant date fair value of employee stock options and the compensatory elements of employee stock purchase plans. Restricted stock units are valued based on the market price on the grant date. We evaluate stock awards with performance conditions as to the probability that the performance conditions will be met and estimates the date at which the performance conditions will be met in order to properly recognize stock-based compensation expense over the requisite service period.

Accounting for Income Taxes — Our management must make judgments when determining our provision for income taxes, our deferred tax assets and liabilities and any valuation allowance recorded against our net deferred tax assets. At December 31, 2018 and December 31, 2017, respectively, we had established a valuation allowance of \$665.4 million and \$654.3 million against all of our net deferred tax asset balances, due to uncertainties related to the realizability of our deferred tax assets as a result of our history of operating losses. The valuation allowance is based on our estimates of taxable income by jurisdiction in which we operate and the period over which our deferred tax assets will be recoverable. In the event that actual results differ from these estimates or we adjust these estimates in future periods, we may need to change the valuation allowance, which could materially impact our financial position and results of operations.

On December 22, 2017, the Tax Cuts and Jobs Act of 2017 (the “Act”) was signed into law making significant changes to the Internal Revenue Code of 1986, as amended. The changes include, but are not limited to, a corporate tax rate decrease from 35% to 21% effective for tax years beginning after December 31, 2017, a one-time transition tax on the mandatory deemed repatriation of cumulative foreign earnings as of December 31, 2017, and expanded limits on employee remuneration. In 2017, we recorded provisional amounts for certain enactment-date effects of the Act by applying the guidance in SAB 118 because we had not yet completed our enactment-date accounting for these effects. In 2018 and 2017, we did not record tax expense related to the enactment-date effects of the Act as we maintained a full valuation allowance and we estimated a deficit in post-1986 earnings and profits from its foreign subsidiaries. At December 31, 2018, we have now completed the accounting for all of the enactment-date income tax effects of the Act. During 2018, we did not recognize adjustments to the provisional amounts recorded at December 31, 2017 as all changes were off-set by the valuation allowance.

Results of Operations

Years ended December 31, 2018 and 2017

Revenues

The following table provides a comparison of the revenue categories for the years ended December 31, 2018 and 2017 (dollars in thousands):

	Year Ended December 31,			
	2018	2017	\$ Change	% Change
Net revenue - commercial product sales:				
Gross revenue from product sales	\$30,242	\$12,572	\$17,670	141
Wholesaler distribution fees, rebates and	(12,966)			

chargebacks, product returns and other

discounts