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

FORM 10-K

(Mark One)

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

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For transition period from _____ to _____.
Commission File Number: 001-37841

Kadmon Holdings, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**27-3576929**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
450 East 29th Street, New York, NY	**10016**
(Address of principal executive offices)	(Zip Code)

(212) 308-6000
(Registrant's telephone number, including area code)
Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of exchange on which registered
Common Stock, par value $0.001 per share	**The New York Stock Exchange**

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

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

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

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

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted and posted 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 and post such files). YES ☒ NO ☐

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or 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 Exchange Act). Yes ☐ No ☒

As of June 30, 2018, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of its voting and non-voting common equity held by non-affiliates was approximately $256,736,155 based upon the closing price of the registrant's common stock on June 30, 2018.

The number of shares of the registrant's common stock outstanding as of March 1, 2019 was 126,909,522.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of Kadmon Holdings, Inc.'s definitive proxy statement for the 2019 Annual Meeting of Shareholders are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

Kadmon Holdings, Inc.

Table of Contents

REFERENCES TO KADMON

In this Annual Report on Form 10-K, unless otherwise stated or the context otherwise requires:

- references to the "Company," "Kadmon," "we," "us" and "our" following the date of the Corporate Conversion (July 26, 2016) refer to Kadmon Holdings, Inc. and its consolidated subsidiaries;
- references to the "Company," "Kadmon," "we," "us" and "our" prior to the date of the Corporate Conversion refer to Kadmon Holdings, LLC and its consolidated subsidiaries; and
- references to the "Corporate Conversion" or "corporate conversion" refer to all of the transactions related to the conversion of Kadmon Holdings, LLC into Kadmon Holdings, Inc., including the conversion of all of the outstanding membership units of Kadmon Holdings, LLC into shares of common stock of Kadmon Holdings, Inc. effected on July 26, 2016. See Note 1, "Organization—Corporate Conversion and Initial Public Offering," of the notes to our audited consolidated financial statements included in this Annual Report on Form 10-K for more information.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this Annual Report on Form 10-K may be forward-looking statements. Statements regarding our future results of operations and financial position, business strategy and plans and objectives of management for future operations, including, among others, statements regarding future capital expenditures and debt service obligations, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expects,” “plans,” “anticipates,” “could,” “intends,” “targets,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions.

Forward-looking statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. We believe that these factors include, but are not limited to, the following:

- the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- our reliance on the success of our product candidates;
- the timing or likelihood of regulatory filings and approvals;
- our ability to expand our sales and marketing capabilities;
- the commercialization of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights and proprietary technology of third parties;
- cost associated with defending or enforcing, if any, intellectual property infringement, misappropriation or
- other intellectual property violation, product liability and other claims;
- regulatory and governmental policy developments in the United States, Europe and other jurisdictions;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the potential benefits of strategic collaboration agreements and our ability to enter into strategic arrangements;
- our ability to maintain and establish collaborations or obtain additional grant funding;
- the rate and degree of market acceptance, if any, of our product candidates, if approved;
- developments relating to our competitors and our industry, including competing therapies;
- our ability to effectively manage our anticipated growth;
- our ability to attract and retain qualified employees and key personnel;
- our ability to achieve cost savings and benefits from our efforts to streamline our operations and to not harm our business with such efforts;
- our expectations regarding the period during which we qualify as an emerging growth company under the Jumpstart Our Business Startups Act (JOBS Act);
- statements regarding future revenue, hiring plans, expenses, capital expenditures, capital requirements and share performance;
- litigation, including costs associated with prosecuting or defending pending or threatened claims and any adverse outcomes or settlements not covered by insurance;
- our expected use of cash and cash equivalents and other sources of liquidity;
- our ability to amend or refinance the 2015 Credit Agreement due July 1, 2020;
- the future trading price of the shares of our common stock and impact of securities analysts’ reports on these prices;
- the future trading price of our investments and our potential inability to sell those securities; and
- other risks and uncertainties, including those listed under the caption “Risk Factors.”

The forward-looking statements in this Annual Report on Form 10-K are only predictions, and we may not actually achieve the plans, intentions or expectations included in our forward-looking statements. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements.

PART 1

Item 1. Business

Overview

We are a fully integrated biopharmaceutical company engaged in the discovery, development and commercialization of small molecules and biologics to address significant unmet medical needs, with a focus on autoimmune, inflammatory and fibrotic diseases as well as immuno-oncology. Below is a brief description of our lead product candidates:

- ***Autoimmune, Inflammatory and Fibrotic Diseases.*** We are developing oral small molecule inhibitors of Rho-associated coiled-coil kinase (ROCK) to treat autoimmune, inflammatory and fibrotic diseases. Research by Kadmon and several academic institutions has demonstrated that inhibition of ROCK can regulate aberrant immune responses and fibrotic processes.
  - ***KD025***. KD025, our most advanced product candidate, is an oral small molecule inhibitor of Rho-associated coiled-coil kinase 2 (ROCK2). We are conducting an open-label registration trial of KD025 for the treatment of chronic graft-versus-host disease (cGVHD), a complication arising from allogeneic hematopoietic stem cell transplantation. The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation and Orphan Drug Designation to KD025 for the treatment of cGVHD.

    We plan to initiate a double-blind, placebo-controlled Phase 2 clinical trial of KD025 for the treatment of systemic sclerosis (a subtype of scleroderma), an immune and fibrotic disorder sharing several pathological complications with cGVHD, in the first half of 2019.

    We are conducting a Phase 2 proof-of-concept clinical trial of KD025 for the treatment of idiopathic pulmonary fibrosis (IPF). Initial findings from this trial demonstrated clinical benefit and tolerability of KD025 in IPF. We anticipate that data from this trial will support the ongoing development of our novel ROCK inhibitors for the treatment of fibrotic diseases, including IPF.
  - ***KD045.*** KD045 is a pan-ROCK inhibitor in development for fibrotic diseases and is the lead product candidate from our internal effort to identify and develop next-generation ROCK inhibitors. KD045 inhibited key fibrotic processes in multiple *in vivo* pharmacology models, including models of bleomycin-induced lung fibrosis, renal fibrosis and liver fibrosis. We expect to complete an IND submission and initiate a clinical trial of KD045 in the second half of 2019.
- ***Immuno-oncology.*** We have a biologics research platform focused on the development of IL-15-containing fusion proteins for the treatment of cancer.
  - ***KD033.*** KD033 is an anti-PD-L1/IL-15 fusion protein and is the most advanced product candidate from our IL-15-fused biologics platform. KD033 significantly inhibited tumor growth in many mouse syngeneic models including PD-L1-expressing models that are resistant to approved immunotherapies. In these models, KD033 has demonstrated long-lasting responses through the induction of immune system memory. We expect to complete an IND submission and initiate a clinical trial of KD033 in the second half of 2019.
- ***Generic Product Candidate for Wilson's Disease.*** We have developed KD034, a generic to Syprine (trientine hydrochloride), for the treatment of Wilson's disease, a genetic liver disease.
  - ***KD034.*** We have submitted Abbreviated New Drug Applications (ANDAs) to the FDA for bottled KD034 capsules as well as for KD034 in proprietary blister packaging that offers room temperature stability, which we believe has the potential to address shortcomings of the currently marketed trientine hydrochloride. We are continuing dialogue with the FDA regarding the potential approval of KD034. We intend to use Kadmon Pharmaceuticals, LLC (Kadmon Pharmaceuticals), our specialty-focused commercial operation, to market our KD034 product candidates, if approved.

Kadmon Pharmaceuticals markets and distributes pharmaceutical products in a variety of therapeutic areas. We do not currently depend on commercial revenues from Kadmon Pharmaceuticals to support our non-commercial operations. Our commercial infrastructure, including the regulatory, compliance, quality and chemistry, manufacturing and controls (CMC) teams of Kadmon Pharmaceuticals, currently supports the development of our clinical-stage product candidates. We plan to leverage our commercial infrastructure to commercialize our product candidates, if approved.

Our Strategy

Our goal is to develop innovative therapies for significant unmet medical needs. Our key strategies to achieve this goal are listed below:

- ***Advance KD025 for the treatment of autoimmune and inflammatory diseases.*** We are conducting a registration trial of KD025 in cGVHD and expect to complete enrollment and potentially meet the study's primary endpoint in the second half of 2019. We also plan to initiate a Phase 2 clinical trial of KD025 in systemic sclerosis in the first half of 2019. In addition, we are conducting a proof-of-concept clinical trial of KD025 in IPF and anticipate that date from trial will support the rationale for our ongoing development of KD045, our pan-ROCK inhibitor, for the treatment of fibrotic diseases.
- ***Develop KD045 for the treatment of fibrotic diseases.*** We plan to complete an IND submission and initiate a first-in-human clinical trial of KD045, our pan-ROCK inhibitor, in the second half of 2019.
- ***Develop KD033 for the treatment of cancer.*** We plan to complete an IND submission initiate a first-in-human clinical trial of KD033, our anti-PD-L1/IL-15 fusion protein, in the second half of 2019.
- ***Leverage our research platforms to develop new product candidates in the areas of fibrosis, autoimmunity and immuno-oncology.*** In addition to KD045 and KD033, we are using our small molecule and biologics research platforms to develop new therapies in the areas of fibrosis, autoimmunity and immuno-oncology.

Our Clinical-Stage Pipeline

ROCK Inhibitors for Autoimmune, Inflammatory and Fibrotic Diseases

ROCK is an "on" switch in cells that regulates cell movement, shape and differentiation. Two ROCK isoforms exist: ROCK1 and ROCK2, and dysregulation of ROCK is implicated in many chronic diseases. Kadmon's research has demonstrated that inhibition of ROCK can regulate aberrant immune responses and fibrotic processes.

Kadmon's ROCK portfolio includes a ROCK2-selective inhibitor, KD025, for the treatment of autoimmune and inflammatory diseases, and KD045, a ROCK inhibitor for the treatment of fibrotic diseases.

A central goal in the study of autoimmune and inflammatory diseases is to develop therapies that down-regulate pro-inflammatory immune responses while preserving the immune system's ability to fight infections and tumors. Our research has demonstrated that selective ROCK2 inhibition rebalances the immune system. In clinical and preclinical studies, KD025 down-regulated pro-inflammatory responses driven by T helper 17 (Th17) cells through the down-regulation of STAT3, a key transcription factor and regulator of the inflammatory pathway. ROCK2 inhibition concurrently increased regulatory T cells (Tregs) through activation of STAT5, a controller of regulatory cell function, helping to resolve inflammation with a minimal effect on the rest of the immune response.

In fibrotic diseases, research by Kadmon and others has demonstrated that ROCK signaling is up-regulated throughout the fibrotic process, regardless of initiating factor, affecting macrophage infiltration, endothelial cell activation and fibroblast to myofibroblast differentiation. These processes result in the deposition of excess collagen and creation of scar tissue. We believe that ROCK inhibition has the potential to halt these processes to successfully treat fibrotic diseases.

KD025 Clinical Program

To date, more than 450 subjects have been dosed with KD025 for autoimmune, inflammatory or fibrotic diseases or as healthy volunteers. KD025 has been well tolerated and demonstrated clinical activity.

KD025 for the Treatment of Chronic Graft-Versus-Host Disease

Medical Need: Chronic Graft-Versus-Host Disease

cGVHD is a major cause of morbidity and mortality after allogeneic hematopoietic cell transplantation (HCT) in patients that suffered from hematologic malignancies. Clinically, cGVHD is a multiorgan syndrome involving tissue inflammation and fibrosis that often results in permanent organ dysfunction. Approximately 14,000 people are living with cGVHD in the United States, with approximately 5,200 new patients per year. Preclinical research has demonstrated that IL-21 and IL-17, two pro-inflammatory cytokines, play a key role in cGVHD pathogenesis.

KD025 in Chronic Graft-Versus-Host Disease

KD025 has demonstrated clinical activity and tolerability in an ongoing Phase 2 clinical trial in patients with steroid-dependent or steroid-refractory cGVHD with 1-3 prior lines of treatment for the disease (KD025-208). Three cohorts of patients, (KD025 200 mg QD (n=17), KD025 200 mg BID (n=16) and KD025 400 mg QD (n=21)), were enrolled sequentially following a safety assessment of the previous cohort. KD025 achieved Overall Response Rates (ORRs) of approximately 60% across all three cohorts. Responses were observed across all affected organ systems, including in organs with fibrotic disease. Responses were durable, and patients reported improvements in quality of life and were also able to reduce and/or completely discontinue doses of corticosteroids and other immunosuppressants. Pharmacodynamics (PD) data showed a decrease in Th17 cells and an increase in Treg cells during KD025 treatment, consistent with KD025 mechanism of action. KD025 was well tolerated, with no treatment-related serious adverse events and no apparent increased risk of infection.

Ongoing Registration Trial of KD025 in Chronic Graft-Versus-Host Disease (KD025-213)

We are conducting an open-label, two-arm registration clinical trial of KD025 in patients with cGVHD who have received two or more prior lines of systemic therapy. Patients are randomized to receive KD025 200 mg QD or 200 mg BID (63 patients per arm). Either KD025 dose may be considered by the FDA for registration. The primary endpoint is the ORR, defined as the percentage of patients who meet the 2014 National Institutes of Health (NIH) Consensus Conference overall response criteria of Complete Response (CR) or Partial Response (PR). During a Type C meeting in March 2018, the FDA provided guidance to Kadmon on how to design a pivotal study of KD025 in cGVHD. The FDA granted Breakthrough Therapy Designation to KD025 in cGVHD in October 2018. We plan to continue our dialogue with regulatory authorities throughout 2019 to obtain further guidance on a regulatory pathway to approval for KD025 in cGVHD.

KD025 for the Treatment of Systemic Sclerosis

Medical Need: Systemic Sclerosis

Systemic sclerosis (a subtype of scleroderma) is a chronic multi-system disease characterized by skin thickening and internal organ fibrosis. Approximately 75,000 to 100,000 people in the United States are living with systemic sclerosis. There are no FDA-approved targeted therapies for systemic sclerosis.

KD025 in Systemic Sclerosis

In the first half of 2019, we plan to initiate a double-blind, placebo-controlled Phase 2 clinical trial of KD025 in systemic sclerosis, a disease in which KD025 has demonstrated potential in preclinical models. The trial will randomize 60 patients to receive KD025 200 mg QD, KD025 200 mg BID or placebo (20 patients per arm) for 24 weeks. The primary endpoint is the change in Combined Response Index for Systemic Sclerosis (CRISS) score, a measure of improvement in systemic sclerosis, at 24 weeks.

KD025 for the Treatment of Idiopathic Pulmonary Fibrosis

Medical Need: Idiopathic Pulmonary Fibrosis (IPF)

IPF is a progressive fibrotic disease of the lungs, with a median survival of three to five years from the time of diagnosis. Approximately 128,000 people in the United States are living with IPF, with 48,000 new cases diagnosed annually. IPF is thought to be caused by repetitive environmental injury to the lining of the lung airways and the resulting abnormal wound-healing responses.

KD025 in IPF

Independent research from academic institutions has demonstrated that ROCK signaling is increased in idiopathic pulmonary fibrosis in humans as well as in murine lung samples. In our preclinical research, KD025 reduced fibrosis in multiple preclinical models, including lung fibrosis in a bleomycin mouse model system. These data suggest that ROCK inhibition has therapeutic potential in IPF by blocking key fibrotic processes mediated by ROCK.

Ongoing Phase 2 Clinical Trial of KD025 in Idiopathic Pulmonary Fibrosis (KD025-207)

We are conducting a randomized, open-label, Phase 2 clinical trial to examine the safety, tolerability and activity of KD025 in IPF patients who have received or been offered pirfenidone and/or nintedanib. The study enrolled 39 patients randomized 2:1 to receive KD025 at 400 mg QD or best supportive care (BSC). The primary efficacy endpoint is a measure of lung function, the forced vital capacity (FVC), at 24 weeks. In initial data announced in 2018, KD025 demonstrated clinical benefit in IPF patients, with a median decline in FVC of 48 mL at week 24, compared to a median decline of 175 mL in patients treated with BSC. KD025 was well tolerated, with no drug-related SAEs.

In 2018, we expanded the KD025-207 study to enroll approximately 40 additional patients. We expect this data to support the development of KD045, Kadmon's ROCK inhibitor, for the treatment of fibrotic diseases, including IPF.

KD045

Kadmon is developing next-generation ROCK inhibitors for the treatment of fibrotic diseases. A key challenge in the development of ROCK inhibitors is to develop potent, selective oral therapies. Earlier-generation ROCK inhibitors target the majority of the AGC kinase family and lack specificity or potency to effectively target ROCK. Using innovative medicinal chemistry, computational and structure-based design approaches, we have identified and developed proprietary, next-generation inhibitors with enhanced potency and AGC-kinase selectivity to specifically target ROCK. We have selected our lead candidate from this effort, KD045, for clinical development.

KD045 inhibited key fibrotic processes in multiple *in vivo* pharmacology models, including in models of bleomycin-induced lung fibrosis, renal fibrosis and liver fibrosis. KD045 has been shown to selectively target ROCK, exhibiting a favorable safety profile compared to earlier-generation ROCK inhibitors. We plan to complete an IND submission and initiate a clinical trial of KD045 in the second half of 2019.

KD033

We have an in-house novel phage display library able to generate fully human monoclonal antibodies against many protein targets. This platform is run by an experienced group of scientists with an outstanding antibody development track record. Prior to joining Kadmon, this team was involved in the development of multiple commercially successful antibodies including Erbitux (cetuximab) and Cyramza (ramucirumab). Our scientists are developing monoclonal antibodies as well as fusion proteins and bispecific antibodies that we believe represent the next generation of cancer immunotherapies.

Our most advanced candidate from the biologics platform, KD033, is a novel anti PD-L1/IL-15 fusion protein designed to stimulate an immune response directed to the tumor microenvironment. Recombinant IL-15 alone, which stimulates cancer-fighting immune effector cells, is not well tolerated when administered systemically. We have developed KD033 as a novel approach to overcome this challenge by fusing IL-15 to an anti-PD-L1 antibody to direct IL-15 activity specifically to the tumor microenvironment, which is designed to promote efficacy and induce durable responses while potentially increasing tolerability.

Preclinical data demonstrated that a single dose of KD033 inhibited tumor growth across multiple *in vivo* syngeneic tumor models. KD033 induced a strong immune response with a single treatment, resulting in mice that remained tumor-free following several tumor re-challenges. Furthermore, KD033 in combination with anti-PD-1 therapy demonstrated synergistic activity, providing clinical rationale for administering KD033 in combination with other immune checkpoint inhibitors. KD033 has demonstrated significant tumor inhibition in murine models that are resistant to approved immunotherapies (PD-L1, PD-1 or CTLA-4 antibodies), suggesting that KD033 may deliver promising clinical outcomes in cancer patients resistant

or refractory to immuno-oncology monotherapy. We have presented encouraging preclinical data on KD033 at scientific conferences. We plan to complete an IND submission and initiate a clinical trial of KD033 in the second half of 2019.

KD034 Clinical Program

KD034 represents our formulations of trientine hydrochloride for the treatment of Wilson's disease.

Medical Need: Wilson's disease

Wilson's disease is a genetic disorder characterized by an inability to excrete copper, leading to severe hepatic, neurologic, psychiatric and/or ophthalmic abnormalities. Approximately 10,000 people in the United States are diagnosed with Wilson's disease.

Currently approved Wilson's disease therapies include penicillamine, which has a high rate of serious and sometimes fatal adverse events. Severe adverse effects requiring drug discontinuation of penicillamine occur in approximately 30% of patients. Trientine hydrochloride, currently marketed under the brand name Syprine, is used as therapy for patients intolerant of penicillamine. The currently marketed trientine hydrochloride products require cold storage, potentially impacting patient compliance. Since Wilson's disease requires lifelong management and as the consequences of discontinuing therapy can be fatal, well-tolerated, effective and convenient therapies are needed.

KD034 Development Program for Wilson's disease

We are developing a bottled generic 250 mg capsule formulation of trientine hydrochloride that is identical to Syprine. We are also developing a generic 250 mg capsule formulation in a blister packaging that offers room temperature stability, which we believe has the potential to address shortcomings of currently available trientine hydrochloride.

We have submitted ANDAs for both formulations of KD034 and are in dialogue with the FDA regarding regulatory approval. We intend to use Kadmon Pharmaceuticals, our specialty-focused commercial organization, to market these formulations, if approved.

Other Clinical Programs

KD025 for the Treatment of Moderate to Severe Psoriasis

Based on clinical data from our completed Phase 2 clinical study of KD025 in psoriasis (KD025-206), in 2016 we initiated a randomized, double-blind, placebo-controlled Phase 2 clinical study of KD025 in moderate to severe psoriasis, an autoimmune disease. While enrollment continues in this study, we have prioritized the development of KD025 in the indications of cGVHD and systemic sclerosis.

Tesevatinib for the Treatment of Polycystic Kidney Disease

Tesevatinib is an oral tyrosine kinase inhibitor (TKI) in development for the treatment of polycystic kidney disease (PKD), a genetic kidney disorder. We are developing tesevatinib to treat autosomal dominant PKD (ADPKD) and autosomal recessive PKD (ARPKD). To date, more than 300 subjects have received at least one dose of tesevatinib for the treatment of ADPKD, cancer or as healthy volunteers in clinical pharmacology studies.

In 2017, we initiated a randomized, placebo-controlled Phase 2 clinical trial of tesevatinib in ADPKD and a Phase 1 clinical trial of tesevatinib in ARPKD. In 2016, the FDA granted orphan drug designation to tesevatinib for the treatment of patients with ARPKD. These trials are ongoing and continue to enroll patients.

Medical Need: Polycystic Kidney Disease

PKD is the most prevalent monogenic disease, with approximately 600,000 patients in the United States and 12.5 million patients worldwide, affecting more individuals than all other monogenic diseases combined. There are two forms of the disease: ADPKD, which presents in adulthood, and ARPKD, a rare autosomal recessive form affecting infants. ADPKD and ARPKD demonstrate significant elevation in molecular signaling cascades frequently implicated in cancer cell growth, including EGFR and Src family kinases.

Our Drug Discovery Platforms

Drug Discovery Platforms

We have two drug discovery platforms that support our pipeline of clinical-stage product candidates: small molecules and biologics. We are developing novel therapies in the areas of fibrosis, autoimmune disease and immuno-oncology.

Research and Development

Research and development expenses consist primarily of costs incurred for the development of our product candidates. For the years ended December 31, 2018, 2017 and 2016, we recognized $49.0 million, $40.8 million and $35.8 million, respectively, in research and development expenses. For further detail about our research and development activities, refer to the research and development sections in “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in this Annual Report on Form 10-K.

Sales and Marketing

Kadmon Pharmaceuticals is our marketing and sales organization focused on specialty pharmaceuticals. Kadmon Pharmaceuticals markets and distributes products in a variety of therapeutic areas. We do not currently place significant value on our commercial operations from a revenue-generation standpoint, as revenues from such operations do not currently support our research and development efforts. We leverage our commercial infrastructure to support the development of our clinical-stage product candidates by providing quality assurance, compliance, regulatory and pharmacovigilance among other capabilities. We believe our commercial infrastructure will be most advantageous to us in the future, in connection with the anticipated commercialization of our pipeline product candidates, if approved.

Kadmon Pharmaceuticals is a fully integrated commercial organization encompassing managed care and specialty pharmacy account directors, experienced regulatory, quality, compliance and CMC teams, marketing experts and sales specialists. Kadmon Pharmaceuticals has long-standing relationships with specialty pharmacies. The specialty pharmacies through which we distribute our products are fully independent of Kadmon. We do not have any ownership interest in or affiliations with any specialty pharmacy, nor do we consolidate the financial results of any specialty pharmacies with our own.

Investment in MeiraGTx

On June 12, 2018, MeiraGTx Holdings plc (“MeiraGTx”) completed its initial public offering (the “MeiraGTx IPO”) whereby it sold 5,000,000 shares of common stock at $15.00 per share. Upon completion of the MeiraGTx IPO, we owned approximately 13.0% of MeiraGTx’s issued and outstanding common stock and we no longer have the ability to exert significant influence over MeiraGTx’s operations. We discontinued the equity method of accounting for the investment in MeiraGTx on June 12, 2018 and determined the remaining investment to be an equity security accounted for in accordance with ASC 321. As our investment in MeiraGTx common stock has a readily determinable market value, we recorded an unrealized gain of $40.5 million during the second quarter of 2018 related to the fair value of our ownership of common stock of MeiraGTx. As of December 31, 2018, we owned approximately 12.9% of the issued and outstanding common stock of MeiraGTx, with a fair value of $34.1 million.

Strategic Collaborations and License Agreements

Symphony Evolution, Inc.

In August 2010, we entered into a license agreement with Symphony Evolution, Inc. (Symphony), under which Symphony granted to us an exclusive, worldwide, royalty-bearing, sublicensable license under certain Symphony patents, copyrights and technology to develop, make, use, sell, import and export of tesevatinib (formerlyXL647) and the related technology in the field of oncology and non-oncology.

We are the licensee of granted patents in Australia, Canada, Europe, Japan and the United States. The patents claim tesevatinib as a composition-of-matter, as well as use of tesevatinib to treat certain cancers. A pending U.S. application supports additional composition-of-matter claims and methods of synthesis. The last to expire U.S. patent in this family has a term that ends in May 2026 based on a calculated Patent Term Adjustment (PTA) and without regard to any potential Patent Term Extension (PTE), which could further extend the term by an additional five years.

We are the licensee of a second family of granted patents in China and Europe, as well as applications in Canada, Eurasia, Japan, Taiwan and the United States. These patents and applications disclose the use of tesevatinib to treat PKD. The

last to expire U.S. patent in this family would have a term that ends in 2031, though this term could be extended by obtaining a PTA and/or PTE.

The license agreement includes a series of acquisition and worldwide development milestone payments totaling up to $218.4 million, and $14.1 million of these payments and other fees have been paid as of December 31, 2018. Additionally, the license agreement includes commercial milestone payments totaling up to $175.0 million, none of which have been paid as of December 31, 2018, contingent upon the achievement of various sales milestones, as well as single-digit sales royalties. The royalty term expires with the last to expire patent.

Our agreement with Symphony will expire upon the expiration of the last to expire patent within the licensed patents. We may terminate the agreement at any time upon six months written notice to Symphony. Either party may terminate the agreement for any material breach by the other party that is not cured within a specified time period. Symphony may terminate the agreement if we challenge the licensed patents. Either party may terminate the agreement upon the bankruptcy or insolvency of the other party.

Nano Terra, Inc.

In April 2011, in connection with the acquisition of Surface Logix, Inc. (SLx) by Nano Terra, Inc. (Nano Terra), our subsidiary Kadmon Corporation entered into a joint venture with SLx through the formation of NT Life Sciences, LLC (NT Life), whereby Kadmon Corporation contributed $0.9 million at the date of formation in exchange for a 50.0% interest in NT Life. Contemporaneously with our entry into the joint venture, we entered into an exclusive sub-license agreement with NT Life and SLx, under which NT Life granted us rights to certain patents and know-how it licensed from SLx relating to KD025 (formerly SLx-2119). Under this agreement, NT Life granted to us an exclusive, worldwide, royalty-bearing, sublicensable license (under the patents and know how it licensed from SLx) to make, have made, use, sell, offer for sale, import and export certain products, including KD025. NT Life also granted to us a worldwide, non-exclusive, non-transferable, sublicensable license under certain SLx platform technology to make, have made, use, sell, offer for sale, import and export the products.

The initial purpose of the joint venture with SLx was to develop assets licensed to us from SLx and to define the royalty obligations with respect to certain products not exclusively licensed to us. The joint venture is, however, currently inactive. We expect that the joint venture will become active and develop certain intellectual property in the future.

Regarding KD025, we are the sublicensee of granted patents in the United States, as well as applications in Australia, Canada, Europe, Japan and the United States, which claim KD025 as a composition-of-matter, as well as use of KD025 to treat certain diseases. The last to expire U.S. patent in this family has a term that ends in October 2029 based on a calculated PTA and without regard to any potential PTE, which could further extend the term by an additional five years.

In consideration for the rights granted to us by NT Life, we agreed to assume certain of Nano Terra's payment obligations, which are limited to the royalty percentages discussed in this paragraph, under the Agreement and Plan of Merger dated April 8, 2011, by and among Nano Terra, NT Acquisition, Inc., SLx, and Dion Madsen, as the Stockholder Representative of SLx (Merger Agreement). Pursuant to these obligations, we are required to pay to the Stockholder Representative a royalty based on a percentage of net sales of licensed products in the mid-single digits, subject to specified deductions and adjustments. We are also required to pay to NT Life a 10.0% royalty on the net sales remaining after giving effect to the royalty payment to the Stockholder Representative. Pursuant to the assumption of Nano Terra's payment obligations, if we further assign or sublicense our rights to any licensed product to certain third parties, we are also required to pay to the Stockholder Representative a portion of any sublicensing revenue relating to such licensed product ranging from the low twenty percents to the low forty percents, subject to specified deductions and adjustments. We are also required to pay to NT Life any remaining sublicensing revenue after giving effect to the foregoing sublicense revenue payment to the Stockholder Representative.

Unless earlier terminated, our agreement with NT Life will, with respect to a licensed product, end on a country-by-country and licensed product-by-licensed product basis upon the latest of (a) the expiration or invalidation of the last valid claim of a licensed patent right covering such licensed product in such country and (b) the expiration or termination of payment obligations with respect to such licensed product in such country under the Merger Agreement. The agreement will, with respect to the licensed SLx platform technology, end on a country-by-country basis upon the expiration or invalidation of the last valid claim of a licensed patent right covering such SLx platform technology. We may terminate the agreement at any time upon six months' written notice to NT Life and if we provide such notice, NT Life may accelerate such termination upon thirty days' prior written notice. Either party may terminate the agreement for any material breach by the other party that is not cured within a specified time period. NT Life may terminate the agreement if we challenge the licensed patents. Either party may terminate the agreement upon the bankruptcy or insolvency of the other party. The agreement shall terminate in the event we are dissolved.

In addition, the agreement shall terminate on a licensed product-by-licensed product basis in the event such licensed product reverts to the Stockholder Representative because of a failure to satisfy the diligence requirements as set forth in the Merger Agreement. More specifically, pursuant to our sub-license agreement with NT Life and SLx, we agreed to assume certain of Nano Terra's diligence obligations under the Merger Agreement such that we are obligated to use commercially reasonable efforts to develop the licensed products, including KD025. With respect to KD025, our diligence obligations do not expire until the completion of a certain specified Phase 2 clinical trial of KD025 in oncology. If, prior to the expiration of our diligence obligations, we fail to comply with such diligence obligations for any licensed product, including KD025, the Stockholder Representative may require Nano Terra to assign all assets of SLx, including intellectual property, relating to such licensed product to an entity designated by such Stockholder Representative, subject to Nano Terra's and our rights to contest such assignment. If such an assignment takes place, our sublicense rights to such intellectual property for such licensed product will terminate.

If the agreement is terminated, among other things, we will be required to cease all development and commercialization of the licensed products, including KD025, all licenses granted to us will terminate and we are obligated to grant NT Life a perpetual, irrevocable, worldwide, exclusive license under certain intellectual property owned or controlled by us that relate to the licensed products to develop and commercialize such licensed products.

Dyax Corp. (acquired by Shire Plc in January 2016 and acquired by Takeda Pharmaceutical Co. Ltd in 2018)

In July 2011, we entered into a license agreement with Dyax Corp. ("Dyax") for the rights to use the Dyax Antibody Libraries, Dyax Materials and Dyax Know-How (collectively "Dyax Property"). The agreement terminated on September 22, 2015, but we had a right to a commercial license of any research target within two years of expiration of the agreement. We exercised this right to a commercial license of two targets in September 2017, resulting in a license fee payable to Shire Plc of $1.5 million, which was recorded to research and development expense for the year end December 31, 2017. The agreement includes the world-wide, non-exclusive, royalty-free, non-transferable licenses to be used in the research field, without the right to sublicense. Additionally, we have the option to obtain a sublicense for use in the commercial field if any research target is obtained.

On September 13, 2012 we entered into a separate license agreement with Dyax whereby we obtained from Dyax the exclusive, worldwide license to use research, develop, manufacture and commercialize DX-2400 in exchange for payment of $0.5 million. All payments associated with this agreement were recorded as research and development expense at the time the agreement was executed. The DX-2400 license requires the Company to make additional payments contingent on the achievement of certain development milestones (such as receiving certain regulatory approvals and commencing certain clinical trials) and sales targets. None of these targets have been achieved and, as such, no assets or liabilities associated with the milestones have been recorded in the accompanying consolidated financial statements for the year ended December 31, 2018. The DX-2400 license also includes royalty payments commencing on the first commercial sale of any licensed product, which had not occurred as of December 31, 2018 and 2017. On April 2, 2018, we gave notice of our intent to terminate this agreement effective six months from the date of notice and the agreement terminated on October 2, 2018.

Jinghua Pharmaceutical Group Co., Ltd.

In November 2015, we entered into a collaboration and license agreement with Jinghua. Under this agreement, we granted to Jinghua an exclusive, royalty-bearing, sublicensable license under certain of our intellectual property and know-how to use, develop, manufacture, and commercialize certain monoclonal antibodies in China, Hong Kong, Macau and Taiwan.

In partial consideration for the rights granted to Jinghua under the agreement, we received an upfront payment of $10.0 million in the form of an investment in our Class E redeemable convertible membership units. We are eligible to receive from Jinghua a royalty equal to a low double-digit percentage of net sales of product in the territory. In addition to such payments, we are eligible to receive milestone payments for the achievement of certain development milestones, totaling up to $40.0 million. We earned a $2.0 million milestone payment in March 2016, which was recorded as license and other revenue during the year ended December 31, 2016. We earned a $2.0 million milestone payment in February 2017, which was recorded as license and other revenue during the year ended December 31, 2017. No revenue was recognized for the year ended December 31, 2018. We are also eligible to receive a portion of sublicensing revenue from Jinghua ranging from a percentage in the low double-digits to the low thirties based on the development stage of a product. No royalty or sublicensing revenue was received from Jinghua during the three years ended December 31, 2018.

Our agreement with Jinghua will continue on a product-by-product and country-by-country basis until the later of 10 years after the first commercial sale of the product in such country or the date on which there is no longer a valid claim covering the licensed antibody contained in the product in such country. Either party may terminate the agreement for any

material breach by the other party that is not cured within a specified time period or upon the bankruptcy or insolvency of the other party.

Our Intellectual Property

The proprietary nature of, and protection for, our product candidates, their methods of use, and our technologies are an important part of our strategy to discover and develop small molecules and biologics that address areas of significant unmet medical needs in inflammatory and fibrotic diseases, genetic diseases, and in the area of immuno-oncology. We are the owner or exclusive licensee of patents and applications relating to certain of our product candidates, and are pursuing additional patent protection for them and for our other product candidates and technologies. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Additionally, we maintain copyrights and trademarks, both registered and unregistered.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important products, product candidates, technologies, inventions and know-how related to our business and our ability to defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain the proprietary position of our development programs. We actively seek to protect our proprietary information, including our trade secrets and proprietary know-how, by requiring our employees, consultants, advisors and partners to enter into confidentiality agreements and other arrangements upon the commencement of their employment or engagement. The chart below identifies which of our product candidates are covered by patents and patent applications that we own or license, the relevant expiration periods and the major jurisdictions. Additional patent applications have been filed to extend the patent life on some of these products, but there can be no assurance that these will issue as filed.

Product Candidate	Description/ Indications	US Patent Numbers	Patent Expiration(0)	Patent Type	Major Jurisdictions	Claim Type
KD025	ROCK2 Inhibitor/cGVHD	15,303,420	2035	Utility	CA, CN, EA, EP, JP, US	Method of Use
KD025	ROCK2 Inhibitor/Fibrosis	8,357,693 8,916,576	2029+	Utility	CA, CN, EA, EP, JP, US	Composition of Matter/Method of Use
Tesevatinib	Multi-kinase Inhibitor/Oncology	7,576,074 8,658,654	2026+	Utility	AU, CA, EP, JP, US	Composition of Matter/Method of Use
Tesevatinib	Multi-kinase Inhibitor/Polycystic Kidney Disease	9,364,479	2031*	Utility	CA, CN, EA, EP, TW, US	Method of Use
KD033	Monoclonal Antibody, Fusion Protein/Immunotherapry,Oncology	Pending	2035*	Utility	US, CN, TBD	Composition of Matter/Method of Use
KD034	Chelating Agent/Wilson's Disease	Pending	2036*	Provisional	US, TBD	Formulation
KD035	VEGFR2 Monoclonal Antibody/Oncology, Angiogenesis	10,023,640	2033*	Utility	CN, EA, EP, JP, US	Composition of Matter/Method of Use
Ribavirin	Nucleoside Inhibitor/Hepatitis	6,720,000 7,538,094 7,723,310	2028+	Utility	US	Composition of Matter
Metabolic Inhibitors	Metabolic Inhibitors/Viral Infection	9,029,413	2028*	Utility	CA, EP, JP, US	Method of Use
GLUT Inhibitors	Glucose Uptake Inhibitors/Immunological and Infectious Diseases	Pending	2036*	Provisional	US, TBD	Method of Use
Anti-PD-L1/VEGFR2	Bispecific Antibody/Immunotherapy/Oncology	Pending	2037*	Provisional	US, TBD	Composition of Matter/Method of Use

(0) Indicates the expiration date of a main patent within a patent family.

\+ Indicates the expiration date of a granted patent for which a Patent Term Adjustment (PTA) has been fixed by the United States Patent and Trademark Office. The date may be lengthened by a Patent Term Extension (PTE) upon regulatory approval.

* Indicates the calculated expiration date of a pending patent application based solely on a twenty-year term from the international filing date, without regard to the outcome of patent prosecution or obtaining a PTA and/or PTE.

Manufacturing and Supply

We currently do not own or operate manufacturing facilities for the production of our product candidates. We currently outsource to a limited number of external service providers the production of all active pharmaceutical ingredients (API), drug substances and drug products, and we expect to continue to do so to meet the preclinical and clinical requirements of our product candidates. We do not have long-term agreements with these third parties. We have framework agreements with most of our external service providers, under which they generally provide services to us on a short-term,

project-by-project basis. We have long-term relationships with our manufacturing and supply chain partners for our commercial products.

Currently, our drug substance or API raw materials for our product candidates can be supplied by multiple source suppliers. Our API drug raw material for our ribavirin portfolio of products is approved to be supplied by a single source, which we believe has the capacity and quality control to meet ongoing demands. We typically order raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. The contract manufacturing organizations that we use to manufacture our product candidates and our ribavirin portfolio are obligated to operate under current Good Manufacturing Practice regulations (cGMP) conditions.

Competition

We compete directly with companies that focus on cGVHD, systemic sclerosis, and IPF and companies dedicating their resources to novel forms of therapies for these indications. We also face competition from academic research institutions, governmental agencies and other various public and private research institutions. With the proliferation of new drugs and therapies in these areas, we expect to face increasingly intense competition as new technologies become available. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining top qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, dosing convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, less expensive, more convenient or easier to administer, or have fewer or less severe effects than any products that we may develop. Our competitors also may obtain FDA, European Medicines Agency (EMA) or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Even if our product candidates achieve marketing approval, they may be priced at a significant premium over competitive products if any have been approved by then.

There are a number of currently marketed therapies and products in late-stage clinical development to treat cGVHD, systemic sclerosis and IPF, including:

cGVHD	Systemic Sclerosis	IPF
Imbruvica (ibrutinib)	Lenabasum	Esbriet (pirfenidone)
Rituxan (rituximab)	Ofev (nintedanib)	Ofev (nintedanib)
Corticosteroids	Mycophenolate mofetil	
Calcineurin inhibitors	Cyclosporine	
Jakafi (Ruxolitinib)		

Certain products in development may provide efficacy, safety, dosing convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain marketing approval.

Government Regulation

Government Regulation and Product Approval

Government authorities in the United States and in other countries extensively regulate, among other things, the research, development, testing, manufacture (including manufacturing changes), quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, export and import of products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial resources.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act (FDCA), and in the case of biologics, also the Public Health Service Act (PHS Act), and various implementing regulations. Most biological products meet the FDCA's definition of "drug" and are subject to FDA drug requirements, supplemented by biologics requirements.

Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices regulations;
- submission to the FDA of an Investigational New Drug Application (IND), which must become effective before human clinical studies may begin;
- approval by an independent institutional review board (IRB), at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical studies according to "good clinical practices" (GCP) regulations, to establish the safety and efficacy of the proposed drug or biologic for its intended use;
- preparation and submission to the FDA of a New Drug Application (NDA) or Biologics License Application (BLA);
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP to assure that the facilities, methods, and controls are adequate to preserve the drug's identity, strength, quality, and purity; and
- FDA review and approval of the NDA or BLA.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

Once a pharmaceutical or biological product candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as animal studies. When a sponsor wants to proceed to test the product candidate in humans, it must submit an IND in order to conduct clinical trials.

An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, to the FDA as part of the IND. The sponsor must also include a protocol detailing, among other things, the objectives of the initial clinical study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the initial clinical study lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions related to a proposed clinical study and places the study on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical studies due to safety concerns or non-compliance, and may be imposed on all product candidates within a certain pharmaceutical class.

The FDA also can impose partial clinical holds, for example, prohibiting the initiation of clinical studies of a certain duration or for a certain dose.

All clinical studies must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. These regulations include the requirement that all research subjects provide informed consent in writing before their participation in any clinical study. Further, an IRB must review and approve the plan for any clinical study before it commences at any institution, and the IRB must conduct continuing review and reapprove the study at least annually. An IRB considers, among other things, whether the risks to individuals participating in the clinical study are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the clinical study and the consent form that must be provided to each clinical study subject or his or her legal representative and must monitor the clinical study until completed.

Each new clinical protocol and any amendments to the protocol must be submitted for FDA review, and to the IRBs for approval. Protocols detail, among other things, the objectives of the clinical study, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health (NIH), for public dissemination on their ClinicalTrials.gov website.

Human clinical studies are typically conducted in three sequential phases that may overlap or be combined:

- *Phase 1.* The product is initially introduced into a small number of healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain early evidence on effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product is suspected or known to be unavoidably toxic, the initial human testing may be conducted in patients.

- *Phase 2.* Involves clinical studies in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage and schedule.

- *Phase 3.* Clinical studies are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical studies are intended to establish the overall risk/benefit relationship of the product and provide an adequate basis for product labeling.

Progress reports detailing the results of the clinical studies must be submitted at least annually to the FDA and safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events. Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical study at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Concurrent with clinical studies, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

United States Review and Approval Processes

Assuming successful completion of the required clinical testing, the results of product development, preclinical studies and clinical studies, along with descriptions of the manufacturing process, analytical tests conducted on the drug, proposed labeling and other relevant information, are submitted to the FDA as part of an NDA for a new drug, or a BLA for a biological drug product, requesting approval to market the product.

The submission of an NDA or BLA is subject to the payment of a substantial application user fee although a waiver of such fee may be obtained under certain limited circumstances. For example, the agency will waive the application fee for the first human drug application that a small business or its affiliate submits for review. The sponsor of an approved NDA or BLA is also subject to annual product and establishment user fees. For FDA fiscal year 2018 the application fee for an

application with clinical data was $2,421,495. Sponsors are also subject to a prescription drug program fee. For fiscal 2018, the prescription drug program fee was $304,162.

In addition, under the Pediatric Research Equity Act of 2003 (PREA), an NDA or BLA applications (or supplements to applications) for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the applicant has obtained a waiver or deferral.

In 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) amended the FDCA to require that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan (PSP), within sixty days of an End-of-Phase 2 meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of data or full or partial waivers. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical studies, and/or other clinical development programs.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy (REMS) to mitigate any identified or suspected serious risks. The REMS could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA reviews all NDAs and BLAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an application for filing. In this event, the application must be re-submitted with the additional information. The re-submitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant. For biologics, the applicant must demonstrate that the product is safe, pure, and potent (interpreted to include effectiveness), and that the facilities designed for its production meet standards to ensure the product will consistently be safe, pure, and potent.

The FDA may approve an NDA or BLA only if the methods used in, and the facilities and controls used for, the manufacture processing, packing, and testing of the product are adequate to ensure and preserve its identity, strength, quality, and purity. Drug cGMPs are established in 21 C.F.R. Parts 210 and 211, and biologic drug products must meet the drug standards as well as the supplemental requirements in 21 C.F.R. Part 600 et seq.

Before approving an NDA or BLA, the FDA often will inspect the facility or facilities where the product is or will be manufactured.

The FDA may refer the NDA or BLA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. An advisory committee is a panel of experts, including clinicians and other scientific experts, who provide advice and recommendations when requested by the FDA. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations when making decisions.

Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to ensure that clinical data supporting the submission were developed in compliance with GCP.

The approval process is lengthy and difficult and the FDA may refuse to approve an NDA or BLA if the applicable regulatory criteria are not satisfied, or may require additional clinical data or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical studies are not always conclusive and the FDA may interpret data differently than an applicant interprets the same data.

After the FDA's evaluation of an application, the FDA may issue an approval letter, or, in some cases, a complete response letter to indicate that the review cycle is complete and that the application is not ready for approval. A complete response letter generally contains a statement of specific conditions that must be met to secure final approval of the application and may require additional clinical or preclinical testing for the FDA to reconsider the application. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical studies. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the application, addressing all of the deficiencies identified in the letter, or withdraw the application or request an opportunity for a hearing.

Even with submission of additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require post-approval studies, including Phase 4 clinical studies, to further assess safety and effectiveness after approval and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

ANDAs and Section 505(b)(2) New Drug Applications

Most drug products obtain FDA marketing approval pursuant to an NDA or BLA (described above) for innovator products, or an ANDA for generic products. Relevant to ANDAs, the Hatch-Waxman amendments to the FDCA established a statutory procedure for submission and FDA review and approval of ANDAs for generic versions of branded drugs previously approved by the FDA (such previously approved drugs are also referred to as listed drugs). Because the safety and efficacy of listed drugs have already been established by the brand company (sometimes referred to as the innovator), the FDA does not require a demonstration of safety and efficacy of generic products. However, a generic manufacturer is typically required to conduct bioequivalence studies of its test product against the listed drug. The bioequivalence studies for orally administered, systemically available drug products assess the rate and extent to which the API is absorbed into the bloodstream from the drug product and becomes available at the site of action. Bioequivalence is established when there is an absence of a significant difference in the rate and extent for absorption of the generic product and the listed drug. For some drugs (e.g., locally acting drugs like topical anti-fungals), other means of demonstrating bioequivalence may be required by the FDA, especially where rate and/or extent of absorption are difficult or impossible to measure. In addition to the bioequivalence data, an ANDA must contain patent certifications and chemistry, manufacturing, labeling and stability data.

The third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on the FDA's findings of safety and efficacy of an existing product, or published literature, in support of its application. Section 505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The applicant may rely upon the FDA's findings with respect to certain preclinical or clinical studies conducted for an approved product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA certain patents of the applicant or that are held by third parties whose claims cover the applicant's product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in the Orange Book. Any subsequent applicant who files an ANDA seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must make one of the following certifications to the FDA concerning patents: (1) the patent information concerning the reference listed drug product has not been submitted to the FDA; (2) any such patent that was filed has expired; (3) the date on which such patent will expire; or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. This last certification is known as a paragraph IV certification. A notice of the paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA or 505(b)(2) application refers. The applicant may also elect to submit a "section viii" statement certifying that its

proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent.

If the reference NDA holder or patent owners assert a patent challenge directed to one of the Orange Book listed patents within 45 days of the receipt of the paragraph IV certification notice, the FDA is prohibited from approving the application until the earlier of 30 months from the receipt of the paragraph IV certification expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired as described in further detail below. Thus approval of a Section 505(b)(2) NDA or ANDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA or Section 505(b)(2) applicant.

Expedited Programs

Fast Track Designation

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs (including biological drug products) are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition for which there is no effective treatment and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a Fast Track product concurrently with, or at any time after, submission of an IND, and the FDA must determine if the product candidate qualifies for Fast Track designation within 60 days of receipt of the sponsor's request.

The FDA may initiate review of sections of a Fast Track drug's NDA or BLA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of each portion of the NDA or BLA and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the application is submitted. Additionally, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical study process.

Accelerated Approval

Under the FDA's accelerated approval regulations, the FDA may approve a drug or biologic for a serious or life-threatening illness that fills an unmet medical need, providing a meaningful therapeutic benefit to patients over existing treatments, based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. In clinical studies, a surrogate endpoint is a marker, such as a measurement of laboratory or clinical signs of a disease or condition that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of post-approval clinical studies sometimes referred to as Phase 4 studies to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated approval regulations are subject to prior review by the FDA.

Breakthrough Designation

The FDASIA amended the FDCA to require the FDA to expedite the development and review of a breakthrough therapy. A drug or biologic product can be designated as a breakthrough therapy if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A sponsor may request that a drug or biologic product be designated as a breakthrough therapy concurrently with, or at any time after, the submission of an IND, and the FDA must determine if the product candidate qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor's request. If so designated, the FDA shall act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather preclinical and clinical data is as efficient as practicable, involving senior managers and experienced review staff in a cross-disciplinary review, assigning a cross-disciplinary project

lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor, and taking steps to ensure that the design of the clinical studies is as efficient as practicable.

Priority Review

Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of 10 months after the FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Post-Approval Requirements

Drugs and biologics manufactured or distributed pursuant to FDA approvals are subject to extensive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping (including certain electronic record and signature requirements), periodic reporting, product sampling and distribution, advertising and promotion and reporting of certain adverse experiences, deviations, and other problems with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. Further, manufacturers must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Manufacturers and certain other entities involved in the manufacturing and distribution of approved products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, sterilization, packaging, labeling, storage and shipment of the product. Manufacturers must establish validated systems to ensure that products meet specifications and regulatory standards, and test each product batch or lot prior to its release.

Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

The FDA may impose a number of post-approval requirements as a condition of approval of an application. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

The FDA may withdraw a product approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, problems with manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on the product or even complete withdrawal of the product from the market.

Potential implications include required revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs/BLAs or supplements to approved NDAs/BLAs, or suspension or revocation of product license approvals;

- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs and biologics may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription drugs and biologics is subject to the Prescription Drug Marketing Act (PDMA), which regulates the distribution of the products and product samples at the federal level, and sets minimum standards for the registration and regulation of distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations, guidances and policies are often revised or reinterpreted by the agency in ways that may significantly affect our business and our product candidates. It is impossible to predict whether further legislative or FDA regulation or policy changes will be enacted or implemented and what the impact of such changes, if any, may be.

Patent Term Restoration

Depending upon the timing, duration and specifics of FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term effectively lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA/BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension. Extensions are not granted as a matter of right and the extension must be applied for prior to expiration of the patent and within a 60-day period from the date the product is first approved for commercial marketing. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for Patent Term Extensions, defined as the length of the regulatory review of products covered by our granted patents, for some of our currently owned or licensed applications and patents to add patent life beyond their current expiration dates. Such extensions will depend on the length of the regulatory review; however, there can be no assurance that any such extension will be granted to us.

Marketing Exclusivity

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

Pediatric exclusivity is another type of exclusivity in the United States. Pediatric exclusivity, if granted, provides an additional six months to the term of any existing regulatory exclusivity, including the non-patent exclusivity periods described above. This six-month exclusivity may be granted based on the voluntary completion of a pediatric clinical study in accordance with an FDA-issued "Written Request" for such a clinical study.

With respect to biologics, the Patient Protection and Affordable Care Act, as amended by the Healthcare and Education Reconciliation Act (collectively, the PPACA) signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCIA), which created an abbreviated licensure pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. To date, only one biosimilar has been licensed under the BPCIA in the United States (in September 2015), with many more well into the process for approval. Numerous biosimilars have already been approved in Europe. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars, although there has been significant litigation and questions over interpretation of such guidelines.

Biosimilarity, which requires that the product be "highly similar" and there be no clinically significant differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

The BPCIA is complex and only beginning to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and meaning of the BPCIA is subject to significant uncertainty.

Orphan Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs (including biological drug products) intended to treat a rare disease or condition—generally a disease or condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that costs of research and development of the drug for the indication can be recovered by sales of the drug in the United States. Orphan drug designation must be requested before submitting an NDA or BLA.

After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first applicant to receive FDA approval for a particular active ingredient to treat a particular disease or condition with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA/BLA application user fee.

During the exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease or condition, except in limited circumstances, such as if the second applicant demonstrates the clinical superiority of its product to the product with orphan drug exclusivity through a demonstration of superior safety, superior efficacy, or a major contribution to patient care, or if the manufacturer of the product with orphan exclusivity is not able to assure sufficient quantities of the product. "Same drug" means a drug that contains the same identity of the active moiety if it is a drug composed of small molecules, or of the principal molecular structural features if it is composed of macromolecules and is intended for the same use as a previously approved drug, except that if the subsequent drug can be shown to be clinically superior to the first drug, it will not be considered to be the same drug. Drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States, sales of Ribasphere RibaPak and any products for which we may receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations.

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. The process for determining whether a payor will provide coverage for a biologic or drug may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Some of the additional requirements and restrictions on coverage and reimbursement levels imposed by third-party payors influence the purchase of healthcare services and products. Third-party payors may limit coverage to specific biologics and drugs on an approved list, or formulary, which might not include all of the FDA-approved biologics or drugs for a particular indication, or place biologics and drugs at certain formulary levels that result in lower reimbursement levels and higher cost-sharing obligation imposed on patients. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Further, one payor's determination to provide coverage does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement may differ significantly from payor to payor.

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

The U.S. government and state legislatures have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and coverage and requirements for substitution of generic products for branded prescription drugs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could exclude or limit our drugs and product candidates from coverage and limit payments for pharmaceuticals.

In addition, we expect that the increased emphasis on managed care and cost containment measures in the United States by third-party payors and government authorities to continue and will place pressure on pharmaceutical pricing and coverage. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other Healthcare Laws and Compliance Requirements

Healthcare providers, physicians, and third-party payors often play a primary role in the recommendation and prescription of any currently marketed products and product candidates for which we may obtain marketing approval. Our current and future arrangements with healthcare providers, physicians, third-party payors and customers, and our sales, marketing and educational activities, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations (at the federal and state level) that may constrain our business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval.

In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that govern certain of our operations include the following, but are not limited to:

a) federal and state laws relating to the Medicare and Medicaid programs and any other federal healthcare program;
b) federal and state laws relating to healthcare fraud and abuse, including, without limitation, the federal Anti-Kickback Statute (42 U.S.C. § 1320a-7b(b)), the federal False Claims Act (31 U.S.C. §§ 3729 et seq.), the False Statements Statute, (42 U.S.C. § 1320a-7b(a)), the Exclusion Laws (42 U.S.C. § 1320a-7), the federal Physician Payment Sunshine Act (42 U.S.C. § 1320a-7h), the Drug Supply Chain Security Act (21 U.S.C. § 351 et seq.), the Anti-Inducement Statute (42 U.S.C. § 1320a-7a(a)(5)), the Civil Monetary Penalties Law (42 U.S.C. § 1320a-7a) and criminal laws relating to healthcare fraud and abuse, including but not limited to 18 U.S.C. §§ 286, 287 and 1001, and the Health Insurance Portability and Accountability Act of 1996, or HIPAA, (Pub.L. 104-191);
c) state laws relating to Medicaid or any other state healthcare or health insurance programs;
d) federal or state laws relating to billing or claims for reimbursement submitted to any third party payor, employer or similar entity, or patient;
e) any other federal or state laws relating to fraudulent, abusive or unlawful practices connected in any way with the provision or marketing of healthcare items or services, including laws relating to the billing or submitting of claims for reimbursement for any items or services reimbursable under any state, federal or other governmental healthcare or health insurance program or any private payor; and
f) federal and state laws relating to health information privacy and security, including HIPAA, and any rules or regulations promulgated thereunder, and the Health Information Technology for Economic and Clinical Health Act, enacted as part of the American Recovery and Reinvestment Act of 2009 and any regulations promulgated thereunder.

If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government healthcare programs, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, private qui tam actions brought by individual whistleblowers in the name of the government or refusal to allow us to enter into supply contracts, including government contracts 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.

Foreign Regulation of Drugs and Biologics

In order to market any product outside of the United States, we will need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding development, approval, commercial sales and distribution of our products, and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products, if approved. Whether or not we obtain FDA approval for a product, we must obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Employees

As of December 31, 2018, we employed 116 people, including 66 in research and development, 15 in commercial operations and 35 in a general and administrative capacity, including executive officers. We also engage a number of

temporary employees and consultants. None of our employees is represented by a labor union with respect to his or her employment with us. We have not experienced any work stoppages, and we consider our relations with our employees to be good.

Facilities

Our corporate headquarters are located in New York, New York, and consist of approximately 35,771 square feet of space under a lease that expires in October, 2025. In addition, we also have locations in Warrendale, Pennsylvania; Cambridge, Massachusetts and Monmouth Junction, New Jersey. We believe that our facilities are adequate for our current needs and for the foreseeable future.

Corporate Information

We were established in September 2010 as a Delaware limited liability company under the name Kadmon Holdings, LLC. In July 2016, we converted to a Delaware corporation pursuant to a statutory conversion and changed our name to Kadmon Holdings, Inc. We completed our IPO in August 2016. Our common stock is currently listed on The New York Stock Exchange under the symbol “KDMN.” We are an “emerging growth company” under the Jumpstart Our Business Startups Act of 2012, and therefore we are subject to reduced public company reporting requirements. Our principal executive offices are located at 450 East 29th Street, New York, New York 10016, and our telephone number is (212) 308-6000. Our website address is www.kadmon.com. The information on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K or any other filings we make with the U.S. Securities and Exchange Commission (SEC).

Available Information

We make available on or through our website certain reports and amendments to those reports that we file with, or furnish to, the SEC in accordance with the Securities Exchange Act of 1934, as amended, or the Exchange Act. These include our Annual Reports on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC. Our website address is www.kadmon.com. Copies of this information may be obtained at the SEC’s Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding our filings, at www.sec.gov. The information on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K or any other filings we make with the SEC.

Item 1A. Risk Factors

Described below are various risks and uncertainties that may affect our business. These risks and uncertainties are not the only ones we face. You should recognize that other significant risks and uncertainties may arise in the future, which we cannot foresee at this time. Also, the risks that we now foresee might affect us to a greater or different degree than expected. Certain risks and uncertainties, including ones that we currently deem immaterial or that are similar to those faced by other companies in our industry or business in general, may also affect our business. If any of the risks described below actually occur, our business, financial condition or results of operations could be materially and adversely affected.

Risks Related to Our Financial Position

We have incurred substantial losses since our inception, anticipate that we will continue to incur losses for the foreseeable future and may not achieve or sustain profitability. We expect to continue to incur significant expenses related to the development of our clinical product candidates for at least the next several years, and we anticipate that our expenses will increase substantially as a result of multiple initiatives.

Since inception, we have incurred substantial operating losses. Our consolidated net loss was $54.3 million, $79.8 million and $208.8 million for the years ended December 31, 2018, 2017 and 2016, respectively. The decrease in net loss for the year ended December 31, 2018 compared to the same period in 2017 is primarily driven by a $34.1 million non-cash unrealized gain related to our investment in MeiraGTx common stock, which no longer qualifies for the equity method of accounting following the completion of MeiraGTx's initial public offering in June 2018. Our accumulated deficit was $269.6 million and $237.4 million at December 31, 2018 and 2017, respectively. The decrease in accumulated deficit at December 31, 2018 compared to December 31, 2017 is primarily driven by the company's adoption of FASB ASC 606, Revenue from Contracts with Customers ("ASC 606"), on January 1, 2018 using the modified retrospective method by recognizing the cumulative effect of initially applying ASC 606 as an adjustment of $24.0 million to the opening balance of stockholders' equity at January 1, 2018.

To date, we have financed our clinical development operations primarily through issuance of common stock in our IPO, a private placement of our common stock and warrants to purchase common stock, private placements of our membership units, debt financing, public registered offerings of our common stock and warrants to purchase common stock and, to a lesser extent, through equipment lease financings. We expect to continue to incur significant expenses related to the development of our clinical product candidates for at least the next several years. We anticipate that our expenses will increase substantially as we:

- initiate or continue our clinical trials related to our most advanced product candidates;
- continue the research and development of our other product candidates;
- seek to discover additional product candidates;
- seek regulatory approvals for our product candidates;
- scale up our sales, marketing and distribution infrastructure and product sourcing capabilities to commercialize additional products we may acquire or license from others or for which we may develop and obtain regulatory approval; and/or
- scale up our operational, financial and management information systems and personnel, including personnel to support our product development and planned additional commercialization efforts.

In the absence of substantial revenue from the sale of our products and products that we distribute, or from other sources (the amount, timing, nature or source of which cannot be predicted), we expect our substantial losses to continue and we may need to discontinue operations. Our ability to generate sufficient revenues from our existing products or from any of our product candidates in development, and to transition to profitability and generate consistent positive cash flow is uncertain. We may continue to incur losses and negative cash flow and may never transition to profitability or positive cash flow.

Our level of indebtedness could adversely affect our business and limit our ability to plan for, or respond to, changes in our business.

Since our inception, we have incurred substantial indebtedness in order to fund acquisitions, research and development activities and the operations of our commercial pharmaceutical business. At December 31, 2018, we had approximately $28.0 million outstanding under our senior secured non-convertible term loan (the 2015 Credit Agreement),

which has a maturity date of July 1, 2020. In addition, we have incurred recurring losses from operations and have an accumulated deficit of $269.6 million at December 31, 2018.

Our level of indebtedness could adversely affect our business by, among other things:

- requiring us to dedicate a substantial portion of our cash from operations and from financings to payments on our indebtedness, thereby reducing the availability of our cash for other purposes, including research and development, investment in our commercial operations and business development efforts;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate, thereby placing us at a disadvantage to our competitors that may have less debt;
- limiting our flexibility in consolidating our corporate operations due to certain covenants that require us to maintain minimum liquidity in our business; and/or
- increasing our vulnerability to adverse economic and industry conditions.

We may not be able to generate sufficient cash to pay our indebtedness, and we may be forced to take other actions to satisfy our payment obligations under our indebtedness, which may not be successful.

Our ability to make scheduled payments on, or to refinance, our debt obligations depends on our future performance, which will be affected by financial, business and economic conditions and other factors. We will not be able to control many of these factors, such as economic conditions in the industry in which we operate and competitive pressures. Our cash flow and cash on hand may not be sufficient to allow us to pay principal and interest on our debt and to meet our other obligations. If our cash flow and other capital resources are insufficient to timely fund our debt service obligations, we may be forced to reduce or delay investments and capital expenditures, or to sell assets, seek additional capital or restructure or refinance our indebtedness. These alternative measures may not be successful and may not permit us to meet our scheduled debt service obligations. In addition, the terms of existing or future debt agreements may restrict our ability to pursue any of these alternatives.

Our 2015 Credit Agreement, as amended, matures on July 1, 2020. We may not be able to comply with the covenants under the 2015 Credit Agreement, as amended, or refinance our debt under this facility before the maturity date, in which event our ability to continue our operations would be materially and adversely impacted.

Our 2015 Credit Agreement, as amended, matures on July 1, 2020. Pursuant to the 2015 Credit Agreement, as amended, we are required to comply with a minimum liquidity covenant and certain ongoing developmental milestones. A failure to comply with these covenants would be an event of default, which, if not cured or waived, could result in the acceleration of the debt under our 2015 Credit Agreement, as amended. No assurances can be given that we will be able to comply with these covenants or that we will be able to amend the 2015 Credit Agreement, as amended, to further extend the maturity date or refinance this debt on or before the maturity date.

Subsequent debt financing, if available at all, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we are unable to comply with our covenants under these facilities, refinance our debt under these facilities or negotiate an extension of such facilities prior to their maturity dates, the lenders thereunder may accelerate our indebtedness and exercise the remedies available to them as secured creditors, including foreclosure on our tangible and intangible property that we have pledged as security. In that event, our ability to continue our operations may be materially and adversely impacted. If we raise additional funds through marketing and distribution arrangements or collaborations, strategic alliances or licensing arrangements with third parties, we may be required to pledge certain assets, grant licenses on terms that may not be favorable to us or relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We will need additional funding in the future, which may not be available to us, and this may force us to delay, reduce or eliminate our product development programs or commercialization efforts.

We will need to expend substantial resources for research and development and commercialization of our marketed products, including costs associated with:

- clinical trials for our product candidates;
- discovery of additional product candidates;

- life-cycle management of our marketed products;
- the continued commercialization of our commercial products; and/or
- preparing for potential commercialization of our late-stage product candidates and, if one or more of those product candidates receive(s) regulatory approval, to fund the launch of that (those) product(s).

We do not expect that our existing cash, cash equivalents and restricted cash will be sufficient to enable us to fund the completion of development and commercialization of any of our product candidates. We do not have any additional committed external source of funds. Additionally, our revenues may fall short of our projections or be delayed, or our expenses may increase, which could result in our capital being consumed significantly faster than anticipated. Our expenses may increase for many reasons, including:

- clinical trial-related expenses for our product candidates;
- the potential launch and marketing of our late-stage product candidates; and/or
- manufacturing scale-up for commercialization of our late-stage product candidates.

To the extent that we need to raise additional capital through the sale of equity or convertible debt securities, investors in our common stock will be diluted, and the terms of any newly issued securities may include liquidation or other preferences that adversely affect the value of our common stock.

Our independent registered public accounting firm has expressed doubt about our ability to continue as a going concern.

Our independent registered public accounting firm has included an explanatory paragraph in its report as of and for the year ended December 31, 2018 expressing substantial doubt in our ability to continue as a going concern based on certain covenants associated with our 2015 Credit Agreement and our recurring and continuing losses from operations. The 2015 Credit Agreement contains certain developmental milestones that must be achieved by December 31, 2019, which are considered to be outside of the Company's control. As such, if achievement of the developmental milestones does not occur as anticipated before December 31, 2019, we may need to use our cash and cash equivalents to repay the outstanding principle under the 2015 Credit Agreement, which could, under the exclusive remedies set forth in the 2015 Credit Agreement, include a termination of the Commitments (as defined in the 2015 Credit Agreement) or a declaration by the Lender that the Loan (as defined in the 2015 Credit Agreement) be due and payable in whole or part, together with any applicable fees and/or interest thereon. In the event that we had to repay the outstanding principle under the 2015 Debt Agreement, we would likely need to raise additional capital to fund continued operations. Additionally, we expect to incur further losses and negative cash flows over the next several years as we develop our business, and we will require significant additional funding to continue operations. These factors individually and collectively raise substantial doubt about the Company's ability to continue as a going concern. Our consolidated financial statements as of December 31, 2018 did not include any adjustments that might result from the outcome of this going concern uncertainty and have been prepared under the assumption that we will continue to operate as a going concern for the next twelve months, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. If we are unable to continue as a going concern, we may be unable to meet our debt obligations, which could result in an acceleration of our obligation to repay such amounts, and we may be forced to liquidate our assets. In such a scenario, the values we receive for our assets in liquidation or dissolution could be significantly lower than the values reflected in our financial statements. The reaction of investors to the inclusion of a going concern statement by our independents auditors and our potential inability to continue as a going concern may materially adversely affect our stock price and our ability to raise new capital or to enter into strategic alliances. The explanatory paragraph regarding our ability to continue as a going concern in the report and opinion of our independent registered public accounting firm for the year ended December 31, 2018 is an event of default under the 2015 Credit Agreement. The Company entered into a sixth waiver agreement to the 2015 Credit Agreement in March 2019 under which the lenders under the 2015 Credit Agreement agreed to refrain from exercising certain rights under the 2015 Credit Agreement, including the declaration of a default and to forbear from acceleration of any repayment rights with respect to existing covenants.

We are or have been party to certain litigation, which could adversely affect our business, results of operations and financial condition.

We are party to, or have been party to, various litigation claims and legal proceedings. We believe that the plaintiffs' claims in recent litigations had no merit. However, litigation is inherently uncertain, and any adverse outcome(s) could negatively affect our business, results of operations and financial condition. In addition, litigation can involve significant management time and attention and be expensive, regardless of outcome. During the course of litigation, there may be announcements of the results of hearings and motions and other interim developments related to the litigation. If securities analysts or investors regard these announcements as negative, the trading price of our shares of common stock may decline. In addition, we evaluate these litigation claims and legal proceedings to assess the likelihood of unfavorable outcomes and to estimate, if possible, the amount of potential losses. Based on these assessments and estimates, we establish reserves or disclose the relevant litigation claims or legal proceedings, as appropriate. These assessments and estimates are based on the information available to management at the time and involve a significant amount of management judgment. Actual outcomes or losses may differ materially from our current assessments and estimates. See Note 16, "Contingencies" of the notes to our audited consolidated financial statements included in this Annual Report on Form 10-K for more information.

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

We have incurred substantial losses during our history and may never achieve profitability. To the extent that we continue to generate losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. As of December 31, 2018, we had unused federal and state net operating loss ("NOL") carry-forwards of approximately $460.3 million and $404.3 million, respectively, which may be applied against and reduce future taxable income. At December 31, 2018, we have fully reserved the deferred tax asset related to our NOL carry-forwards as reflected in our audited consolidated financial statements. These NOL carry-forwards expire at various dates through December 31, 2037, with the exception of approximately $44.0 million of the federal NOL carry-forwards, which will not expire.

The use of our NOL carry-forwards may, however, be subject to limitations as a result of an ownership change. A corporation undergoes an "ownership change," in general, if a greater than 50% change (by value) in its equity ownership by one or more five-percent stockholders (or certain groups of non-five-percent stockholders) over a three-year period occurs. After such an ownership change, the corporation's use of its pre-change NOL carry-forwards and other pre-change tax attributes to offset its post-change income is subject to an annual limitation determined by the equity value of the corporation on the date the ownership change occurs multiplied by a rate determined monthly by the Internal Revenue Service. This rate for March 2019 equals 2.39 percent. We experienced ownership changes under Section 382 of the Code in 2010, 2011 and 2016, but we did not reduce the gross deferred tax assets related to the NOL carry-forwards because the limitations do not hinder our ability to potentially utilize all of the NOL carry-forwards.

We are likely to experience another ownership change in the future, possibly in 2019, as a result of future shifts in our stock ownership, which may include shifts in our stock ownership as a result of any future equity offerings. A renewed ownership change will likely materially and substantially reduce our ability to fully utilize our NOL carry-forwards and, consequently, will likely reduce the gross deferred tax assets related to our NOL carry-forwards. If an ownership change occurred and if we earned net taxable income, our ability to use our pre-change NOLs to offset U.S. federal taxable income would be subject to these limitations, which could potentially result in increased future tax liability compared to the tax liability we would incur if our use of NOL carry-forwards were not so limited. In addition, for state income, franchise and similar tax purposes, there may be periods during which the use of NOL carry-forwards is suspended or otherwise limited, which could accelerate or permanently increase our state income, franchise or similar taxes.

The market price of our investment in MeiraGTx may be volatile and fluctuate substantially, which could result in significant changes to the fair value of our investment and limit our ability to sell those securities.

As of December 31, 2018, we own approximately 12.9% of MeiraGTx. Common stock of MeiraGTx began trading on the Nasdaq Global Select Market on June 7, 2018 under the symbol "MGTX." The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated or disproportionate to the operating performance of particular companies. Broad market and industry factors may negatively affect the market price of MeiraGTx common stock, regardless of its actual operating performance. Further, a decline in the financial markets and related factors beyond our control or the control of MeiraGTx may cause the price of MeiraGTx to decline rapidly and unexpectedly. In addition, MeiraGTx may require significant additional capital to continue its planned operations. To raise capital, MeiraGTx may sell equity securities, convertible securities or other securities in one or more transactions, which may result in material dilution of our investment in MeiraGTx and result in additional volatility in the fair value of our investment in MeiraGTx.

As a result of this volatility, the fair value of our investment in MeiraGTx may be significantly and adversely affected. Investments in common stock of companies traded on public markets, including our MeiraGTx investment, are reflected on our balance sheet at fair value based on the closing price of the shares owned on the last trading day before the date of the balance sheet. Fluctuations in the underlying bid price of the shares result in unrealized gains or losses. In accordance with FASB ASC 321, Investments – Equity Securities, we recognize these fluctuations in value as other expense (income). Accordingly, a decline in the trading price of MeiraGTx would require us to recognize unrealized losses, which could result in significant harm to our financial position and adversely affect the price of our common stock.

Furthermore, as a result of this volatility, we may not be able to sell our common stock of MeiraGTx at prices we find attractive, or we may be required to recognize realized losses if we sell MeiraGTx common stock. For investments sold, we recognizes the gains and losses attributable to these investments as realized gains or losses in other expense (income). Based on the level of our ownership of MeiraGTx, we may be considered an affiliate of MeiraGTx, and our shares of MeiraGTx may be subject to volume, manner of sale and other limitations under Rule 144 of the Securities Act, which may limit our ability to sell our shares of MeiraGTx at prices or volumes that we find attractive.

Risks Related to Our Clinical Development Pipeline

Clinical development is a lengthy and expensive process with a potentially uncertain outcome. Our long-term success depends upon the successful development and commercialization of our product candidates. To obtain regulatory approval to market our products, preclinical studies and costly and lengthy clinical trials are required. The conduct of preclinical studies and clinical trials is subject to numerous risks and results of the studies and trials are highly uncertain.

We currently have no internally clinically-developed products approved for sale and we cannot guarantee that we will ever develop such products. To date, we have invested a significant portion of our efforts and financial resources in the acquisition and development of our product candidates. Our long-term success depends upon the successful development, regulatory approval and commercialization of these product candidates. If we fail to obtain regulatory approval to market and sell our product candidates, or if approval is delayed, we will be unable to generate revenue from the sale of these products, our potential for generating positive cash flow will be diminished and the capital necessary to fund our operations will be increased. Two of our product candidates, KD025 and tesevatinib, are in clinical trials and we have additional product candidates in preclinical development for which we expect to initiate clinical trials in the second half of 2019. While we have submitted ANDAs to the FDA for bottled KD034 capsules as well as for KD034 in proprietary blister packaging that offers room temperature stability, we are continuing dialogue with the FDA regarding the potential approval of KD034 and such approval may not be granted. In December 2018 we received Complete Response Letter's (CRLs) from the FDA in relation to our ANDA submissions for bottled KD034 and our KD034 proprietary blister packaging. The FDA issues CRLs to communicate that is has completed a review cycle of an application and to request additional information for review and approval. The CRLs we received in December 2018 included minor deficiencies as defined by the FDA, asked for additional information and did not request additional clinical trials. We plan to resubmit our ANDAs to address the FDA CRLs. Our business depends significantly on the successful development, regulatory approval and commercialization of our product candidates, which may never occur.

We cannot be certain as to what type and how many clinical trials the FDA, or equivalent foreign regulatory agencies, will require us to conduct before we may successfully gain approval to market any of our product candidates. Prior to approving a new drug or biologic, the FDA generally requires that the effectiveness of the product candidate (which is not typically fully investigated until Phase 3) be demonstrated in two adequate and well-controlled clinical trials. In some situations, the FDA approves drugs or biologics on the basis of a single well-controlled clinical trial establishing effectiveness. However, if the FDA or the EMA determines that our Phase 3 clinical trial results do not demonstrate a statistically significant, clinically significant benefit with an acceptable safety profile, or if the FDA or EMA requires us to conduct additional Phase 3 clinical trials in order to gain approval, we will incur significant additional development costs and commercialization of these products would be prevented or delayed and our business would be adversely affected.

Our ongoing clinical trials may be subject to delays or setbacks for a variety of common and unpredictable reasons.

We may experience unforeseen delays or setbacks in our ongoing clinical trials, such as trial initiation timing, trial redesign or amendments, timing and availability of patient enrollment or successful trial completion. Such delays and setbacks are common and unpredictable in pharmaceutical drug development. Clinical trials can be delayed for a variety of reasons, including delays related to:

- regulatory objections to commencing a clinical trial, continuing a clinical trial that is underway, or proceeding to the next phase of investigation, including inability to reach agreement with the FDA or non-U.S. regulators regarding the scope or design of our clinical trials or for other reasons such as safety concerns that might be identified through preclinical testing and animal studies or clinical trials, at any stage;
- reaching agreement on acceptable terms with prospective contract research organizations (CROs), and clinical trial sites (the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites);
- failure of CROs or other third-party contractors to comply with contractual and regulatory requirements or to perform their services in a timely or acceptable manner;
- difficulty identifying and engaging qualified clinical investigators;
- obtaining institutional review board (IRB) approval at each site;
- difficulty recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including meeting the enrollment criteria for our study and competition from other clinical trial programs for the same indication as product candidates we seek to commercialize;
- having patients complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- inability to retain patients in clinical trials due to the treatment protocol, personal issues, side effects from the therapy or lack of efficacy, particularly for those patients receiving a placebo;
- withdrawal of clinical trial sites from our clinical trials as a result of changing standards of care or the ineligibility of a site to participate in our clinical trials;
- adding new clinical trial sites;
- inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indication as our product candidates;
- changes in applicable regulatory policies and regulations;
- insufficient data to support regulatory approval;
- difficulty in maintaining contact with subjects during or after treatment, which may result in incomplete data; or
- manufacturing sufficient quantities of the product candidate for use in clinical trials.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Furthermore, we rely on clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including:

- failure by us, CROs or clinical investigators to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- failed inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety or efficacy issues or any determination that a clinical trial presents unacceptable health risks;
- failure to demonstrate a benefit from using a drug; or
- lack of adequate funding to continue the clinical trial due to unforeseen costs resulting from enrollment delays, requirements to conduct additional trials and studies, increased expenses associated with the services of our CROs and other third parties, changes in governmental regulations or administrative actions, or other reasons.

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

If serious adverse events or other undesirable side effects are identified during the use of product candidates in investigator-sponsored trials, it may adversely affect our development of such product candidates.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt non-clinical studies and clinical trials, or could make it more difficult for us to enroll patients in our clinical trials. If serious adverse events or other undesirable side effects, or unexpected characteristics of our product candidates are observed in investigator-sponsored trials, further clinical development of such product candidate may be delayed or we may not be able to continue development of such product candidate at all, and the occurrence of these events could have a material adverse effect on our business. Undesirable side effects caused by our product candidates could also result in the delay or denial of regulatory approval by the FDA or other regulatory authorities or in a more restrictive label than we expect.

The regulatory approval processes of the FDA and similar foreign authorities are lengthy, time consuming, expensive and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. It is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;

- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support a submission for regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and/or
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

In addition, even if we were to obtain approval, regulatory authorities may:

- approve any of our product candidates for fewer or more limited indications than we request;
- may not approve the price we intend to charge for our products;
- may grant approval contingent on the performance of costly post-marketing clinical trials; or
- may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate.

If we do not achieve our projected development goals in the timeframes we announce and expect, or we face significant competition from other biotechnology and pharmaceutical companies, the commercialization of our products may be delayed, our operating results may be lower that we expect, the credibility of our management may be adversely affected and, as a result, the value of our common stock may decline.

Even if we obtain regulatory approval for our product candidates, they may never be successfully launched or become profitable, in which case our business, prospects, operating results and financial condition may be materially harmed.

In order to successfully launch our product candidates and have them become profitable, we anticipate that we will have to dedicate substantial time and resources and hire additional personnel to expand and enhance our commercial infrastructure, which will at a minimum include the following:

- ensure the quality of the product candidate manufactured by our suppliers and by us;
- expand our sales and marketing force;
- expand and enhance programs and other procedures to educate physicians and drive physician adoption of our product candidates;
- create additional policies and procedures, and hire additional personnel to carry out those policies and procedures, to ensure customer satisfaction with our products;
- obtain reimbursement for hospitals and physicians; and/or
- expand and enhance our general and administrative operations to manage our anticipated growth in operations and to support public company activities.

Because of the numerous risks and uncertainties associated with launch and profitability of our product candidates, we are unable to predict the extent of any future losses, or when we will become profitable, if ever.

Our product candidates may have undesirable side effects that may delay or prevent marketing approval or, if approval is obtained, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales.

Undesirable or unexpected side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval

by the FDA or other comparable foreign authorities. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

- we could be sued and held liable for harm caused to patients;
- sales of the product may decrease significantly; and/or
- our reputation may suffer.

In addition, a regulatory agency may:

- suspend or withdraw approvals of such product;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed by us, our collaborators or our potential future collaborators;
- require additional warnings on the label;
- require that we create a medication guide outlining the risks of such side effects for distribution to patients;
- issue warning letters;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require us or our collaborators to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- impose other civil or criminal penalties;
- impose restrictions on operations, including costly new manufacturing requirements; and/or
- seize or detain products or require a product recall.

Non-compliance may also result in potential whistleblower lawsuits and the potential for liability under the False Claims Act or other laws and regulations, as discussed above. Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

The results of previous clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or non-U.S. regulatory authorities.

Clinical failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we or any of our current and future collaborators may decide, or regulators may require us, to conduct additional clinical or preclinical testing. In addition, data obtained from tests are susceptible to varying interpretations, and regulators may not interpret data as favorably as we do, which may delay, limit or prevent regulatory approval.

We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek regulatory approvals for their commercial sale. Success in early clinical trials does not mean that future larger registration clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and non-U.S. regulatory authorities despite having progressed through initial clinical trials. Product candidates that have shown promising results in early clinical trials may still suffer significant setbacks in subsequent registration clinical trials.

Similarly, the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and preliminary and interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials.

Further, at various points during the course of the preclinical and clinical trial process, companies must assess both the statistical and clinical significance of trial results. In this context, "statistical significance" refers to the likelihood that a result or relationship is caused by something other than random chance or error. Statistical significance is measured by a "p-value," which indicates the probability value that the results observed in a study were due to chance alone. A p-value of < 0.05 is generally considered statistically significant, meaning that the probability of the results occurring by chance alone is less than five percent. The lower the p-value, the less likely that the results observed were random. "Clinical significance," on the other hand, is a qualitative assessment of the results observed. Where we use the term "clinically significant," we have not necessarily made a formal statistical assessment of the probability that the change in patient status was attributable to the study drug as opposed to chance alone, nor does such a statement necessarily mean that study endpoints have been met or the protocol has been completed. A clinically significant effect is one that is determined to have practical importance for patients and physicians, and includes benefits that are often defined by peer-reviewed literature as having a meaningful impact on a patient's condition. An effect that is statistically significant may or may not also be clinically significant. When a study fails to result in statistical significance, the FDA may not consider such study to serve as substantial evidence of safety and effectiveness required for approval. Even if a study results in statistical significance, the FDA may also consider clinical significance in evaluating a marketing application. For example, the FDA typically requires more than one pivotal clinical study to support approval of a new drug. However, the FDA has indicated that approval may be based on a single study in limited situations in which a trial has demonstrated a clinically significant effect. In either case, the clinical or statistical significance of a particular study result in no way guarantees that FDA or other regulators will ultimately determine that the drug being investigated is safe and effective.

In addition, the design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to design and execute a clinical trial to support regulatory approval.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any Phase 1, Phase 2, Phase 3 or other clinical trials we or any of our collaborators may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

Further, our product candidates may not be approved even if they achieve their primary endpoints in Phase 3 clinical trials or registration trials. The FDA or other non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal Phase 3 clinical trial that has the potential to result in the FDA or other agencies' approval. In addition, any of these regulatory authorities may also approve a product candidate for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. The FDA or other non-U.S. regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our product candidates.

We may not be successful in our efforts to use and expand our drug discovery platforms to build a pipeline of product candidates.

A key element of our strategy is to leverage our drug discovery platforms to identify and develop new product candidates for additional diseases with significant unmet medical needs. Although our research and development efforts to date have contributed to the development of product candidates directed at inflammatory and fibrotic diseases, oncology and genetic diseases, we may not be able to develop product candidates that are safe and effective. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we do not continue to successfully develop and begin to commercialize product candidates, we will face difficulty in obtaining product revenues in future periods, which could result in significant harm to our financial position and adversely affect the price of our common stock.

Biologics carry particular risks and uncertainties, which could have a negative impact on future results of operations.

Through our drug discovery platform, we are currently engaged in the development of novel highly active fusion proteins for immunotherapy in various indications. The successful development, testing, manufacturing and commercialization of biologics is a long, expensive and uncertain process. There are particular risks and uncertainties with biologics, including:

- There may be limited access to and supply of normal and diseased tissue samples, cell lines, pathogens, bacteria, viral strains and other biological materials. In addition, government regulations in multiple jurisdictions, such as the United States and the European Union, could result in restricted access to, or transport or use of, such materials. If we lose access to sufficient sources of such materials, or if tighter restrictions are imposed on the use of such materials, we may not be able to conduct research activities as planned and may incur additional development costs.

- The development, manufacturing and marketing of biologics are subject to regulation by the FDA, the EMA and other regulatory bodies. These regulations are often more complex and extensive than the regulations applicable to other pharmaceutical products. For example, in the United States, a BLA including both preclinical and clinical trial data and extensive data regarding the manufacturing procedures is required for human vaccine candidates and FDA approval is required for the release of each manufactured commercial lot.

- Manufacturing biologics, especially in large quantities, is often complex and may require the use of innovative technologies to handle living micro-organisms. Each lot of an approved biologic must undergo thorough testing for identity, strength, quality, purity and potency. Manufacturing biologics requires facilities specifically designed for and validated for this purpose, and sophisticated quality assurance and quality control procedures are necessary. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes.

- Biologics are frequently costly to manufacture because production ingredients are derived from living animal or plant material, and most biologics cannot be made synthetically. In particular, keeping up with the demand for vaccines may be difficult due to the complexity of producing vaccines.

- The use of biologically derived ingredients can lead to allegations of harm, including infections or allergic reactions, or closure of product facilities due to possible contamination.

Any of these events could result in substantial costs and result in a material adverse effect on our business and results of operations.

We face substantial competition, which may result in others discovering, developing and commercializing products before or more successfully than our products and product candidates.

The development and commercialization of new therapeutics is highly competitive. We face competition (from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide) with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future. We compete directly with companies that focus on cGVHD, systemic sclerosis, and IPF and companies dedicating their resources to novel forms of therapies for these indications. We also face competition from academic research institutions, governmental agencies and other various public and private research institutions. Many of these competitors are attempting to develop therapeutics for our target indications. With the proliferation of new drugs and therapies in these areas, we expect to face increasingly intense competition as new technologies become available. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

There are products already approved for many of the diseases we are targeting. Many of these approved products are well established therapies and are widely accepted by physicians, patients and third-party payors. This may make it difficult for us to achieve our business strategy of replacing existing therapies with our product candidates. Our commercial operations face significant direct competition and our competitors may develop products that are safer, more effective, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

Many of our competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our product candidates for which we intend to seek approval may face competition sooner than anticipated, and for biologics there is additional uncertainty as the relevant law is relatively new and there is limited precedent.

Although we plan to pursue all available FDA exclusivities for our product candidates, we may face competition sooner than anticipated. Market and data exclusivity provisions under the Federal Food, Drug, and Cosmetic Act (FDCA) can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity, running from the time of NDA approval. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the five-year exclusivity period for a new chemical entity, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company that references the previously approved drug. However, the FDA may accept an ANDA or 505(b)(2) NDA for review after four years if it contains a certification of patent invalidity or non-infringement.

The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example (for new indications, dosages, strengths or dosage forms of an existing drug). This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product.

Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (PPACA), signed into law on March 23, 2010, includes a subtitle called the BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor’s own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on our most promising research programs and product candidates. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize our products outside of the United States, which would limit our ability to realize their full market potential.

None of our product candidates are approved for sale in any jurisdiction, including international markets, and we have limited experience in obtaining regulatory approval in international markets. In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays.

In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of our products will be harmed. As described above, such effects include the risks that:

- any current or future product candidates we may seek to develop may not generate preclinical or clinical data that are deemed sufficient by regulators in a given jurisdiction;
- product candidates may not be approved for all indications requested, or any indications at all, in a given jurisdiction which could limit the uses of any future product candidates we may seek to develop and have an adverse effect on product sales and potential royalties; or
- such approval in a given jurisdiction may be subject to limitations on the indicated uses for which the product may be marketed or require costly post-marketing follow-up studies.

Foreign regulators may have requirements for marketing authorization holders or distributors to have a legal or physical presence in that country. Consideration of and compliance with these requirements may result in additional time and expense before we can pursue or obtain marketing authorization in foreign jurisdictions. If we do receive approval in other countries, we may enter into sales and marketing arrangements with third parties for international sales of any approved products.

The environment in which our regulatory submissions may be reviewed changes over time, which may make it more difficult to obtain regulatory approval of any of our product candidates.

The environment in which our regulatory submissions are reviewed changes over time. Average review times at the FDA for NDAs and BLAs fluctuate, and we cannot predict the review time for any submission with any regulatory authorities. Review times can be affected by a variety of factors, including budget and funding levels and statutory, regulatory and policy changes. Moreover, in light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of Risk Evaluation and Mitigation Strategies that may, for instance, restrict distribution of drug or biologic products. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials. Data from preclinical studies and clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense, a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

In addition, data obtained from preclinical studies and clinical trials are subject to different interpretations, which could delay, limit or prevent regulatory review or approval of our product candidates. Changes in FDA personnel responsible for review of our submissions could also impact the manner in which our data are viewed. Further, regulatory attitudes toward the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information (including on other products), policy changes and agency funding, staffing

and leadership. We do not know whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects.

We have received breakthrough therapy designation for our product candidate KD025 for the treatment of patients with chronic graft-versus-host disease (cGVHD) and may seek breakthrough therapy designation by the FDA for any of our other product candidates, but there is no assurance that we will request or receive such designation, and, in any event, even if we do receive such designation, it may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval in the United States.

We have applied for breakthrough therapy designation for our product candidate KD025 and, in October 2018, the FDA granted breakthrough therapy designation to KD025 for the treatment of patients with cGVHD after failure of two or more lines of systemic therapy. We may apply for breakthrough therapy designation for some of our other product candidates. The FDA is authorized to designate a product candidate as a breakthrough therapy if it finds that the product is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Products designated as breakthrough therapies by the FDA may also be eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for KD025 in cGVHD, or for any of our other product candidates may not result in a faster development process, review or approval compared to product candidates without the breakthrough therapy designation and, in any event, does not assure ultimate approval by the FDA. In addition, the FDA may later decide that KD025 in cGVHD or such other product candidates that may in the future receive breakthrough therapy designation no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

We may seek Fast Track, Accelerated Approval and/or Priority Review designation of some of our product candidates. There is no assurance that the FDA will grant such designations and, even if it does grant any such designation for one of our product candidates, that designation may not ultimately lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval in the United States.

We may seek Fast Track, Accelerated Approval and/or Priority Review designation and review for our product candidates. We have not, at this point, had any specific discussions with the FDA about the potential for any of our product candidates to take advantage of these potential pathways. The FDA has broad discretion whether or not to grant any of these designations, so even if we believe a particular product candidate is eligible for such a designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw any such designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, any such designation does not have any impact on the likelihood that a product candidate will ultimately be granted marketing approval in the United States.

KD025 has received orphan drug designation for the treatment of cGVHD, and we plan to seek orphan product designation for certain of our other product candidates for certain indications, and we may be unable to obtain orphan product designation, and even if we do, we may be unable to maintain the benefits associated with orphan product designation, including the potential for marketing exclusivity. Moreover, if our competitors are able to obtain orphan product designation and the associated exclusivity for their products that are competitors with our product candidates, the applicable regulatory authority may be prohibited from approving our products for a significant period of time.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as having a prevalence of less than 200,000 affected individuals in the United States or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers. In the European Union, EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the European Union. Additionally, orphan designation is granted for products intended for the diagnosis,

prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biologic product. In October 2017, the FDA granted orphan drug designation to KD025 for the treatment of cGVHD.

Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for the same indication for that time period, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. The applicable period is seven years in the United States and 10 years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Moreover, even if we obtain orphan designation, we may not be the first to obtain marketing approval of our product candidate for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, while we intend to seek orphan drug designation for our product candidates, we may never receive such designations.

Independent clinical investigators or CROs that we engage may not devote sufficient time or attention to conducting our clinical trials or may not be able to repeat their past success.

We expect to continue to depend on independent clinical investigators and may depend on CROs to conduct some of our clinical trials. CROs may also assist us in the collection and analysis of data. There is a limited number of third-party service providers that specialize or have the expertise required to achieve our business objectives. Identifying, qualifying and managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. These investigators and CROs, if any, will not be our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. If independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if their performance is substandard, it may delay or compromise the prospects for approval and commercialization of any product candidates that we develop. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. Further, the FDA requires that we comply with standards, commonly referred to as cGCP for conducting, recording and reporting clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial subjects are protected. Failure of clinical investigators or CROs to meet their obligations to us or comply with cGCP procedures could adversely affect the clinical development of our product candidates and harm our business.

We may not be able to attract collaborators or external funding for the development and commercialization of our product candidates.

Our product development programs and potential commercialization of our product candidates will require substantial additional capital to fund expenses. As part of our ongoing strategy, we may seek additional collaborative arrangements with pharmaceutical and biotechnology companies or other third parties or external funding for certain of our development programs and/or seek to expand existing collaborations to cover additional commercialization and/or development activities. We have a number of research programs and early-stage clinical development programs. At any time, we may determine that in order to continue development of a product candidate or program or successfully commercialize a drug we need to identify a collaborator or amend or expand an existing collaboration. Potentially, and depending on the circumstances, we may desire that a collaborator either agree to fund portions of a drug development program led by us, or agree to provide all the funding and directly lead the development and commercialization of a program. We face significant competition in seeking appropriate collaborators. Collaborations are complex and time-consuming to negotiate and document. We may also be restricted under existing collaboration agreements from entering into agreements on certain terms with other potential collaborators. No assurance can be given that any efforts we make to seek additional collaborative arrangements will be successfully completed on acceptable terms, a timely basis or at all.

If we are unable to negotiate favorable collaborations, we may have to curtail the development of a particular product candidate, reduce or delay its development program and its potential commercialization, reduce the scope of our sales or marketing activities, and/or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we will not be able to bring our product candidates to market and generate product revenue.

Risks Related to Our Marketed Products and Product Candidates

Historically, our revenue has depended upon sales of our ribavirin marketed product portfolio. However, in 2019 and beyond, our revenue will likely depend on sales from other products.

Historically, our revenue has depended upon sales of our ribavirin portfolio of products. The treatment of chronic HCV infection rapidly changed as multiple ribavirin-free treatment regimens, including novel direct-acting antivirals, have entered the market and become the new standard of care. As a result, sales of our ribavirin portfolio of products contributed insignificantly in 2018 and we expect sales of our ribavirin portfolio of products to contribute insignificantly in 2019 and beyond. No meaningful revenue was generated from sales of our other products for the years ended December 31, 2017 and 2016. For the year ended December 31, 2018 our sales revenue was primarily generated from sales of our other products, including Camber products tertrabenazine and valganciclovir.

We cannot be certain how profitable, if at all, the commercialization of our marketed products will be.

To become and remain profitable, we must compete effectively against other therapies with our products or any of our product candidates for which we obtain marketing approval, as well as developing and eventually commercializing product candidates with significant market potential. This will require us to be successful in a range of challenging activities, including discovering product candidates, completing preclinical testing and clinical trials for our product candidates and obtaining regulatory approval for these line extensions and product candidates, in addition to the manufacturing, marketing and selling of those products for which we may obtain regulatory approval. We may never succeed in these activities and may never generate revenues that are significant or large enough to achieve profitability.

In addition to the risks discussed elsewhere in this section, our ability to continue to generate revenues from our commercialized products will depend on a number of factors, including, but not limited to:

- achievement of broad market acceptance and coverage by third-party payors for our products;
- the effectiveness of our collaborators' efforts in marketing and selling our products;
- our ability to successfully manufacture, or have manufactured, commercial quantities of our products at acceptable cost levels and in compliance with regulatory requirements;
- our ability to maintain a cost-efficient organization and, to the extent we seek to do so, to collaborate successfully with additional third parties;
- our ability to expand and maintain intellectual property protection for our products successfully;
- the efficacy and safety of our products; and/or
- our ability to comply with regulatory requirements, which are subject to change.

Because of the numerous risks and uncertainties associated with our commercialization efforts, we may not be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. A failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Our inability to accurately estimate demand for our products, the uptake of new products or the timing of fluctuations in the inventories maintained by customers makes it difficult for us to accurately forecast sales and may cause our financial results to fluctuate.

We are unable to accurately estimate demand for our products, including uptake from new products, as demand is dependent on a number of factors. We sell products primarily to wholesalers and specialty pharmacies. These customers maintain and control their own inventory levels by making estimates to determine end user demand. Our customers may not be effective in matching their inventory levels to actual end user demand. As a result, changes in inventory levels held by our

customers can cause our operating results to fluctuate unexpectedly. Adverse changes in economic conditions or other factors may cause our customers to reduce their inventories of our products, which would reduce their orders from us, even if end user demand has not changed. If our inventory exceeds demand from our customers and exceeds its shelf life, we will be required to destroy unsold inventory and write off its value. As our inventory and distribution channels fluctuate from quarter to quarter, we may continue to see fluctuations in our earnings and a mismatch between prescription demand for our products and our revenues.

If we discover safety issues with any of our products or if we fail to comply with continuing U.S. and applicable foreign regulations, commercialization efforts for the product could be negatively affected, the approved product could be subject to withdrawal of approval or sales could be suspended, and our business could be materially harmed.

Our products are subject to continuing regulatory oversight, including the review of additional safety information. Drugs are more widely used by patients once approval has been obtained and therefore side effects and other problems may be observed after approval that were not seen or anticipated, or were not as prevalent or severe, during pre-approval clinical trials or nonclinical studies. The subsequent discovery of previously unknown problems with a product, or public speculation about adverse safety events, could negatively affect commercial sales of the product, result in restrictions on the product or lead to the withdrawal of the product from the market.

If we or our collaborators fail to comply with applicable continuing regulatory requirements, we or our collaborators may be subject to fines, suspension or withdrawal of regulatory approvals for specific products, product recalls and seizures, injunctions, consent decrees or other operating restrictions and/or criminal prosecutions. In addition, the manufacturers we engage to make our products and the manufacturing facilities in which our products are made are subject to periodic review and inspection by the FDA and foreign regulatory authorities. If problems are identified during the review or inspection of these manufacturers or manufacturing facilities, it could result in our inability to use the facility to make our product or a determination that inventories are not safe for commercial sale.

If physicians, nurses, pharmacists, patients, the medical community and/or third-party payors do not accept our drugs or product candidates, we may be unable to generate significant revenue in future periods.

Our drugs may not gain or maintain market acceptance among physicians, nurses, pharmacists, patients, the medical community and/or third-party payors. Effectively marketing our products and any of our product candidates, if approved, requires substantial efforts and resources, both prior to launch and after approval; and marketing efforts are subject to numerous regulatory restrictions as well as fraud and abuse laws. The demand for our drugs and degree of market acceptance of our product candidates will depend on a number of factors including:

- limitations or warnings contained in the approved labeling for any of our drugs or product candidates;
- changes in the standard of care for the targeted indications for any of our drugs or product candidates;
- lower demonstrated efficacy, safety and/or tolerability compared to other drugs;
- prevalence and severity of adverse events;
- lack of cost-effectiveness;
- limited or lack of reimbursement and coverage from government authorities, managed care plans and other third-party payors;
- a decision to wait for the approval of other therapies in development that have significant perceived advantages over our drug;
- the clinical indications for which the product is approved;
- adverse publicity about any of our drugs or product candidates or favorable publicity about competitive products;
- the timing or market introduction of any approved products as well as competitive products;
- the extent to which our drugs and product candidates are approved for inclusion on formularies of hospitals and manages care organizations;
- whether our drugs and product candidates are designated under physician treatment guidelines as first-line therapies or as a second- or third-line therapies for particular diseases;

- convenience and ease of administration;
- availability of alternative therapies at similar or lower cost, including generic and over-the-counter products;
- other potential advantages of alternative treatment methods;
- ineffective sales, marketing and/or distribution support; and/or
- potential product liability claims.

If any of our drugs or product candidates fails to maintain or achieve, as applicable, market acceptance, we will not be able to generate significant revenue in future periods.

Failure to comply with FDA promotional rules may subject us to withdrawal, and correction, of related product promotion, seizure of product and other administrative or enforcement actions as well as the potential for ancillary liability under the False Claims Act (False Claims Act) and/or product liability litigation.

The FDA regulates the promotion of our products, which may only be promoted within their approved indication for use. Promotional materials and activity must be presented with fair balance of the risks and benefits of any product in a manner which is not otherwise inaccurate or misleading. The FDCA and the FDA's implementing regulations require that manufacturers label, advertise and promote their products with appropriate safety warnings and adequate directions for their FDA-approved use. However, the FDA does not have the legal authority to regulate the practice of medicine. Although physicians are permitted, based on their medical judgment, to prescribe products for indications other than those approved by the FDA, manufacturers are prohibited from promoting their products for such off-label uses.

If the FDA determines that our promotional materials, training or other activities constitute off-label promotion, it could request that we modify our training or promotional materials or other activities or subject us to regulatory enforcement actions, including the issuance of a warning letter, injunction, seizure, civil fine and criminal penalties. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may also lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws. The FDA or other regulatory authorities could also request that we enter into a consent decree or a corporate integrity agreement, or seek a permanent injunction against us under which specified promotional conduct is monitored, changed or curtailed.

Although recent decisions of the United States Supreme Court, the U.S. Court of Appeals for the Second Circuit and the U.S. District Court for the Southern District of New York have clarified that the United States may not, consistent with the First Amendment, restrict or punish a pharmaceutical manufacturer's truthful and non-misleading speech promoting the lawful use of an approved drug, there are still significant risks in this area. It is unclear how these court decisions will impact the FDA's enforcement practices, and there is likely to be substantial disagreement and difference of opinion regarding whether any particular statement is truthful and not misleading.

In the past we have been subject to enforcement action relating to allegations of improper promotion of our products, and we may be subject to such action in the future.

If we cannot successfully manage the promotion of our currently marketed products, and product candidates, if approved, we could become subject to significant liability which would materially adversely affect our business and financial condition. It is also possible that other federal, state or foreign enforcement authorities, or private parties, might take action if they believe that an alleged improper promotion led to inappropriate use of one of our products and/or the submission and payment of claims for an off-label use, which could result in significant fines or penalties under other statutory provisions, such as the False Claims Act and similar laws. Even if it is later determined that we were not in violation of these laws, we may face negative publicity, incur significant expenses defending our actions and have to divert significant management resources from other matters. In addition, there are a number of specific FDA requirements related to drug labeling and advertising, and failure to adhere to these requirements could result in our products being deemed "misbranded."

The manufacture of pharmaceutical products is a highly exacting and complex process, and if our suppliers encounter problems manufacturing our products, our business could suffer.

The manufacture of pharmaceutical products is a highly exacting and complex process, due in part to strict regulatory requirements. Problems may arise during manufacturing for a variety of reasons, including equipment malfunction, failure to follow specific protocols and procedures, problems with raw materials, delays related to the construction of new facilities or the expansion of existing facilities, including those intended to support future demand for our products, changes in manufacturing production sites and limits to manufacturing capacity due to regulatory requirements, changes in the types of products produced, physical limitations that could inhibit continuous supply, man-made or natural

disasters and environmental factors. If problems arise during the production of a batch of product, that batch of product may have to be discarded and we may experience product shortages or incur added expenses. This could, among other things, lead to increased costs, lost revenue, damage to customer relationships, time and expense spent investigating the cause and, depending on the cause, similar losses with respect to other batches or products. If problems are not discovered before the product is released to the market, recall and product liability costs may also be incurred.

Risks Related to Government and Regulatory Agencies

If we engage in research or commercial activities involving any of our products or pipeline assets in a manner that violates federal or state healthcare laws, including fraud and abuse laws, false claims laws, disclosure laws, government price reporting and healthcare information privacy and security laws or other similar laws, we may be subject to corporate or individual civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Our business operations and activities are subject to extensive federal, state and local fraud and abuse and other healthcare laws and regulations, such as the False Claims Act and the federal Anti-Kickback Statute, the Foreign Corrupt Practices Act (FCPA), federal Physician Payment Sunshine Act, the federal Drug Supply Chain Security Act, federal Civil Monetary Penalty statute, the PPACA program integrity requirements, patient privacy laws and regulation, criminal laws relating to healthcare fraud and abuse, including but not limited to the Health Insurance Portability and Accountability Act, federal consumer protection and unfair competition laws, federal government price reporting laws and state law equivalents of each of these. These laws and regulations constrain, among other things, the business or financial arrangements and relationships through which we may research and develop any product candidate, as well as market, sell and distribute any approved products.

In addition, any sales of our products or product candidates, if approved, commercialized outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

We have entered into consulting agreements, scientific advisory board and other financial arrangements with physicians, including some who prescribe our products and may prescribe our product candidates, if approved. Compensation for some of these arrangements includes the provision of stock options. While these arrangements were structured to comply with all applicable laws, including state and federal anti-kickback laws, to the extent applicable, regulatory agencies may view these arrangements as prohibited arrangements that must be restructured, or discontinued, or for which we could be subject to other significant penalties. Moreover, while we do not submit claims and our customers make the ultimate decision on how to submit claims, we may provide reimbursement guidance and support to our customers and patients. If a government authority were to conclude that we provided improper advice to our customers and/or encouraged the submission of false claims for reimbursement, we could face action against by government authorities.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. The sales and marketing practices of our industry are the subject of immense scrutiny from federal and state government agencies. Despite sequestration measures, governmental enforcement funding continues at robust levels and enforcement officials are interpreting fraud and abuse laws broadly. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are subject to a variety of interpretations. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources, divert our management's attention from the operation of the business, and generate negative publicity, which could harm our business. If our past or present operations are found to be in violation of any such laws or any other governmental regulations that may apply to us, we may be subject to, without limitation, civil, criminal and administrative penalties, damages, monetary fines, disgorgement, exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and/or the curtailment or restructuring of our operations. If we were to be excluded from federal healthcare programs, it would mean that no federal healthcare program payment could be made for any of our products.

Our commercial success depends on adequate reimbursement and coverage from third-party commercial and government payors for our products, and changes to coverage or reimbursement policies, as well as healthcare reform measures, may materially harm our sales and potential revenue.

Most patients rely on reimbursement from third-party payors, including government programs (such as Medicare and Medicaid) and private payor healthcare and insurance programs to pay for their medical needs, including any drugs we may market. Coverage and reimbursement for our products can differ significantly from payor to payor. Even when we

obtain coverage and reimbursement for our products, we may not be able to maintain adequate coverage and reimbursement in the future.

There is significant uncertainty related to the third-party coverage and reimbursement of newly approved products. We intend to seek approval to market our product candidates in the United States, Europe and other selected foreign jurisdictions. Market acceptance and commercial success of our product candidates in both domestic and international markets will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for any of our product candidates.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products to each third-party payor separately, with no assurance that coverage and adequate reimbursement will be obtained or applied consistently. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. Additionally, coverage may be more limited than the purposes for which the product is approved by the FDA or similar regulatory authorities outside of the United States. Assuming that coverage is obtained for a given product, the resulting reimbursement rates might not be adequate or may require co-payments that patients find unacceptably high. Patients, physicians, and other healthcare providers may be less likely to prescribe, dispense or use, as applicable, our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

Government payors and other third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and the amount of reimbursement. Coverage decisions may depend upon clinical and economic standards that disfavor new drug or biologic products when more established or lower-cost therapeutic alternatives are already available or subsequently become available. Based upon a number of factors, including clinical and economic standards, our products may not qualify for coverage and reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor’s determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective;
- neither experimental nor investigational;
- prescribed by a practitioner acting within the scope of license and health plan participation agreements;
- documented adequately in the patient’s medical record;
- dispensed by a participating pharmacy; and/or
- logged and documented appropriately by the dispensing pharmacy.

The market for our products will depend significantly on access to third-party payors’ drug formularies 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. If coverage and reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

In the United States, our products may be subject to discounts from list price and rebate obligations. Third-party payors have from time to time refused to include our products in their formularies, limit the type of patients for whom coverage will be provided, or restrict patient access to our products through formulary control or otherwise, in favor of less-costly generic versions of ribavirin or other treatment alternatives. Any change in formulary coverage, treatment paradigm, reimbursement levels, discounts or rebates offered on our products may impact our anticipated revenues.

In the United States, governmental and commercial third-party payors are developing increasingly sophisticated methods of controlling healthcare costs. We believe that pricing pressure for our products will continue, and future coverage and reimbursement will likely be subject to increased restrictions. For example, the PPACA, which has already imposed significant healthcare cost containment measures, also encourages the development of comparative effectiveness research and

any adverse findings for our products from such research may reduce the extent of coverage and reimbursement for our products. The PPACA created the Patient-Centered Outcomes Research Institute to review the effectiveness of treatments and medications in federally-funded healthcare programs. The PCORI publishes the results of its studies. An adverse finding result may result in a treatment or product being removed from Medicare or Medicare coverage.

Managed care organizations continue to seek price discounts and in some cases, to impose restrictions on the coverage of particular drugs. Government efforts to reduce Medicaid expenses may lead to increased use of managed care organizations by Medicaid programs, which may result in managed care organizations influencing prescription decisions for a larger segment of the population, which could constrain pricing, formulary position or reimbursement for our products. Economic pressure on state budgets may also have a similar impact on Medicaid coverage and reimbursement.

In certain countries in the European Union and some other international markets, governments provide healthcare at low-cost to consumers and regulate pharmaceutical pricing, patient eligibility or reimbursement levels to control costs for the government-sponsored healthcare system. We expect to see strong efforts to reduce healthcare costs in our international markets, including: patient access restrictions; suspensions on price increases; prospective and possibly retroactive price reductions, mandatory discounts and rebates, and other recoupments; recoveries of past price increases; and greater importation of drugs from lower-cost countries to higher-cost countries. In addition, certain countries set prices by reference to the prices in other countries where our products are marketed. Thus, our inability to secure adequate prices in a particular country may not only limit the marketing of our products within that country, but may also adversely affect our ability to obtain acceptable prices in other markets.

Healthcare reform measures could hinder or prevent our product candidates' commercial success, if approved, and could increase our costs.

In both the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is a significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding individual access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in 2010, the PPACA was enacted, which was intended to expand healthcare coverage within the United States, primarily through the imposition of health insurance mandates on employers and individuals, strengthening of program integrity measures and enforcement authority, and expansion of the Medicaid program. The PPACA substantially changes the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Several provisions of the new law, which have varying effective dates, may affect us and will likely increase certain of our costs. In this regard, the PPACA includes the following provisions:

- an annual, non-deductible 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 that began in 2011;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- an extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extensions;
- changes to the Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to 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;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;

- a new requirement to annually report drug samples that manufacturers and distributors provide to licensed practitioners or to pharmacies of hospitals or other healthcare entities;
- a licensure framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- creation of the Independent Payment Advisory Board which has the authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs.

The reforms imposed by the new law will significantly impact the pharmaceutical industry; however, the full effects of the PPACA cannot be known until these provisions are implemented and the CMS and other federal and state agencies issue and finalize all applicable regulations or guidance. We will continue to evaluate the PPACA, the implementation of regulations or guidance related to various provisions of the PPACA by federal agencies, as well as trends and changes that may be encouraged by the legislation and that may potentially have an impact on our business over time. The cost of implementing more detailed record keeping systems and otherwise complying with these regulations could substantially increase our costs. The changes to the way our products are reimbursed by the CMS could reduce our revenues. Both of these situations could adversely affect our results of operations. There have been judicial and Congressional challenges to certain aspects of the PPACA, and we expect there will be additional challenges and amendments to the PPACA in the future. Significant uncertainty exists regarding the effect of the PPACA, particularly in light of the recent election and campaign pledges to repeal or reform the PPACA.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes included aggregate reductions to Medicare payments to providers and suppliers of up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 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 and suppliers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws and future healthcare reform laws may result in additional reductions in Medicare and other healthcare funding.

There also have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels and elsewhere directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. In May 2018, President Trump announced a Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs. On October 25, 2018, President Trump announced certain actions that are intended to reduce the prices Medicare will pay for drugs.

The Trump Administration has also taken executive actions to undermine or delay implementation of the PPACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the PPACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the PPACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

More recently, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the PPACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the PPACA.

In addition, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Additional changes could be made to governmental healthcare programs that could significantly impact the success of our products or product candidates. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any products for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and/or
- the availability of capital.

Government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our current and future products.

International operations are also generally subject to extensive price and market regulations and there are many proposals for additional cost-containment measures, including proposals that would directly or indirectly impose additional price controls or reduce the value of our intellectual property portfolio or may make it economically unsound to launch our products in certain countries. We cannot predict the extent to which our business may be affected by these or other potential future legislative or regulatory developments. Future price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our current and future products, which would adversely affect our revenue and results of operations.

Additionally, in some countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various European Union member states and parallel distribution or arbitrage between low-priced and high-priced member states, can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct additional clinical trials that compare the cost-effectiveness of our product candidates to other available therapies, which is time-consuming and costly. If reimbursement of our product candidates is unavailable or limited in scope or amount in a particular country, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability of our products in such country.

Guidelines and recommendations published by government agencies, professional societies, and private foundations and organizations can reduce the use of our products and product candidates, if approved.

Government agencies promulgate regulations and guidelines applicable to certain drug classes which may include our products and product candidates that we are developing. In addition, from time to time, professional societies, practice management groups, private health/science foundations and organizations publish guidelines or recommendations directed to certain healthcare and patient communities. These recommendations may relate to such matters as usage, dosage, route of administration and use of concomitant therapies. Regulations or guidelines suggesting the reduced use of certain drug classes which may include our products and product candidates that we are developing or the use of competitive or alternative products as the standard of care to be followed by patients and healthcare providers could result in decreased use of our product candidates or negatively impact our ability to gain market acceptance and market share.

We could be adversely affected by violations of the FCPA and similar worldwide anti-bribery laws.

We are subject to the FCPA, which generally prohibits companies and their intermediaries from making payments to non-U.S. government officials for the purpose of obtaining or retaining business or securing any other improper advantage. We are also subject to anti-bribery laws in the jurisdictions in which we operate. Although we have policies and procedures designed to ensure that we, our employees and our agents comply with the FCPA and other anti-bribery laws, there is no assurance that such policies or procedures will protect us against liability under the FCPA or other laws for actions taken by our agents, employees and intermediaries with respect to our business or any businesses that we acquire. We do business in a number of countries in which FCPA violations have recently been enforced. Failure to comply with the FCPA, other anti-bribery laws or other laws governing the conduct of business with foreign government entities, including local laws, could disrupt our business and lead to severe criminal and civil penalties, including imprisonment, criminal and civil fines, loss of our export licenses, suspension of our ability to do business with the federal government, denial of government reimbursement for our products and/or exclusion from participation in government healthcare programs. Other remedial

measures could include further changes or enhancements to our procedures, policies, and controls and potential personnel changes and/or disciplinary actions, any of which could have a material adverse effect on our business, financial condition, results of operations and liquidity. We could also be adversely affected by any allegation that we violated such laws.

If our processes and systems are not compliant with regulatory requirements, we could be subject to restrictions on marketing our products or could be delayed in submitting regulatory filings seeking approvals for our product candidates.

We have a number of regulated processes and systems that are required to obtain and maintain regulatory approval for our drugs and product candidates. These processes and systems are subject to continual review and periodic inspection by the FDA and other regulatory bodies. If compliance issues are identified at any point in the development and approval process, we may experience delays in filing for regulatory approval for our product candidates, or delays in obtaining regulatory approval after filing. Any later discovery of previously unknown problems or safety issues with approved drugs or manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on such drugs or manufacturing processes, withdrawal of drugs from the market, the imposition of civil or criminal penalties or a refusal by the FDA and/or other regulatory bodies to approve pending applications for marketing approval of new drugs or supplements to approved applications, any of which could have a material adverse effect on our business. Given the number of high profile adverse safety events associated with certain drug products, regulatory authorities may require, as a condition of approval, costly risk evaluation and mitigation strategies, which may include safety surveillance, restricted distribution and use, patient education, enhanced labeling, expedited reporting of certain adverse events, pre-approval of promotional materials and restrictions on direct-to-consumer advertising. For example, any labeling approved for any of our product candidates may include a restriction on the term of its use, or it may not include one or more intended indications. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs during the period of product development, clinical trials and regulatory review and approval, as well as increased costs to assure compliance with any new post-approval regulatory requirements. Any of these restrictions or requirements could force us or our collaborators to conduct costly studies.

In addition, we are a party to agreements that transfer responsibility for complying with specified regulatory requirements, such as packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information on the product or compliance with manufacturing requirements, to our collaborators and third-party manufacturers. Approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to current good manufacturing practices (cGMP). As such, we and our contract manufacturers, which we are responsible for overseeing and monitoring for compliance, are subject to continual review and periodic inspections to assess compliance with cGMP. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. The FDA may hold us responsible for any deficiencies or noncompliance of our contract manufacturers in relation to our product candidates and commercial products. If our collaborators or third-party manufacturers do not fulfill these regulatory obligations, any drugs we market or for which we or they obtain approval may be deemed adulterated, which carries significant legal implications, and may be subject to later restrictions on manufacturing or sale, which could have a material adverse effect on our business.

Risks Related to Our Intellectual Property Rights

If we are unable to obtain and maintain patent protection for our products and product candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and product candidates similar or identical to ours, and our ability to successfully commercialize our products and product candidates may be adversely affected.

Our commercial success will depend, in part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to our products and product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our products and product candidates that are important to our business. We cannot be certain that patents will be issued or granted with respect to applications that are currently pending or that we apply for in the future with respect to one or more of our products and product candidates, or that issued or granted patents will not later be found to be invalid and/or unenforceable.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, collaboration partners, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

We may license patent rights that are valuable to our business from third parties, in which event we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or medicines underlying such licenses. We cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties also apply to patent rights we own.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued, and even if issued, the patents may not meaningfully protect our products or product candidates, effectively prevent competitors and third parties from commercializing competitive products or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative products in a non-infringing manner. Changes in the patent laws, implementing regulations or interpretation of the patent laws in the United States and other countries may also diminish the value of our patents or narrow the scope of our patent protection.

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States, and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. For those countries where we do not have granted patents, we may not have any ability to prevent the unauthorized use or sale of our proprietary medicines and technology or to prevent third parties from selling or importing products made using our inventions in and into the United States and other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our intellectual property rights may not be effective or sufficient to prevent them from competing.

We may not be aware of all third-party intellectual property rights potentially relating to our product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore we cannot be certain that we were the first to make the inventions claimed in our owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, prior to March 2013, in the United States, the first to make the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. Beginning in March 2013, the United States transitioned to a first-inventor-to-file system in which, assuming the other requirements for patentability are met, the first-inventor-to-file a patent application will be entitled to the patent. We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office (U.S. PTO) or become involved in opposition, derivation, revocation, reexamination, post-grant and *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. Participation in these proceedings can be very complex, expensive and may divert our management's attention from our core business. Furthermore, an adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize medicines without infringing third-party patent rights.

Even if our patent applications do issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical products, or limit the duration of the patent protection of our products and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Patent protection may not be available for some of our products or the processes under which they are used or manufactured.

Issued patents covering one or more of our products could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Although we have conducted due diligence on patents we have exclusively in-licensed, the outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the U.S. PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings,and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our products and product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse impact on our business.

Third-party claims of intellectual property infringement, misappropriation or other violation may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and *inter partes* reexamination proceedings before the U.S. PTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization and may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product unless we obtained a license under the applicable patents, or until such patents expire.

Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all. Even if we or our future strategic collaborators were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property and it could require us to make substantial licensing and royalty payments.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

Most of our competitors are larger than we are and have substantially greater resources and may be able to sustain the costs of complex patent litigation longer than we could. The uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our internal research

programs, in-license needed technology or enter into strategic collaborations that would help us bring our product candidates to market.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our 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 or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An adverse result in 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.

An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those 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. There could also 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, it could have a material adverse effect on the price of our common stock.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to patents, we rely on trade secrets, technical know-how and proprietary information concerning our business strategy in order to protect our competitive position in medical research and development. Trade secrets are difficult to protect, and it is possible that our trade secrets and know-how will over time be disseminated within the industry through independent development and intentional or inadvertent disclosures.

We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, collaboration partners, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets. Our agreements with research and development collaboration partners contain contractual limitations regarding the publication and public disclosure of data and other information generated during the course of research. Despite these efforts, any of these parties may breach the agreements and intentionally or inadvertently disclose or use our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches.

Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets or the equivalent knowledge, methods and know-how were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business, or permit us to maintain our competitive advantage. For example:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or collaboration partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or collaboration partners might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantages or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and/or
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employees' former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may also have, in the future, ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

If we do not obtain patent term extension for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, third parties may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

Risks Related to Our Dependence on Third Parties

We expect to continue to contract with third-party suppliers for the production of our commercial product portfolio as well as our developmental product candidates for clinical trial use and, if approved, for commercialization.

We currently employ third parties for the manufacturing of our commercial products and product candidates. This increases the risk that we will not have sufficient quantities of our products or product candidates within the timeframe and at an acceptable cost which could delay, prevent or impair our development or commercialization efforts. Additionally, we may not be able to quickly respond to changes in customer demand which could harm our business as a result of the inability to supply the market or an excess of inventory that we are unable to sell.

The facilities used by our contract manufacturers to manufacture our product candidates must adhere to FDA requirements, and are subject to inspections that may be conducted after we submit our marketing applications to the FDA in connection with review of our application, and on an ongoing basis relevant to postmarketing compliance. Although we are subject to regulatory responsibility for the quality of products manufactured by our contract manufacturers and oversight of their activities, we do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements, known as cGMPs, for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will be subject to enforcement action, and if substantial noncompliance is identified and not corrected, they may be precluded from manufacturing product for the United States or other markets. In addition, although the FDA will hold us responsible for due diligence in the selection of, and oversight in the operations of, our contract manufacturers, we do not have direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority identified significant compliance concerns with our contract manufacturers, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products or product candidates, if approved.

We have agreements with third-party manufacturers for the provision of active pharmaceutical ingredient (API), drug product manufacturing and packaging of our commercial products. Reliance on third-party manufacturers carries additional risks, such as not being able to comply with cGMP or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

We still currently rely on one third-party supplier for the ribavirin API and tetrabenazine. In the event that any of these third-party manufacturers fail regulatory compliance, fail to meet quality assurance specifications or experience an unavoidable extraordinary event, our business could be adversely affected.

Any products that we may develop may compete with other product candidates and commercialized products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure or refusal to supply on the part of our existing or future suppliers could delay clinical development, marketing approval or commercialization of our products. If our current suppliers cannot perform as agreed, we may be required to replace one or more of these suppliers. Although we believe that there are a

number of potential long-term replacements to each supplier, we may incur added costs and delays in identifying and qualifying any such replacements.

We rely on third parties to store and distribute supplies for our clinical trials and for the manufacture of our product candidates. Any performance failure on the part of our existing or future distributors could delay clinical development or regulatory approval or our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We have acquired or in-licensed many of our products from external sources and may owe milestones or royalties based on the achievement of future successes or penalties if certain diligence requirements are not met.

In certain cases, our license or acquisition agreements require us to conduct research or clinical trials within a specified time frame, or we may owe a penalty or lose the right to the product for development. If we do not conduct the necessary research or clinical trials within the specified time frame, we may be required to pay cash penalties to extend the time frame during which studies may be conducted, our licensors may exercise a right to have the product returned or may have the right to terminate the agreement, in which event we would not be able to market products covered by such agreement.

On some of the products we have licensed, we may be obligated in future periods to make significant development and commercial milestone payments as well as royalties. As a result, we may have to raise additional capital (which would likely cause our equity holders to experience dilution) to cover the required milestone payments. The milestone payments and royalties we may owe on the sale of our products may reduce the overall profitability of our operations and if we are unable to sell sufficient product to cover the costs of these milestone payments, our operating profitability, business and value of our equity securities may be adversely impacted.

We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others. We are party to intellectual property license agreements with third parties and expect to enter into additional license agreements in the future. Our current license agreements impose, and we expect that future license agreements will impose, various diligence, development, commercialization, payment and other obligations. If we fail to comply with our obligations under these agreements, the licensor may have the right to terminate the license agreement or may exercise a right to have the intellectual property that we license returned. For example, under our exclusive sub-license agreement for KD025 with NT Life and SLx, if we fail to comply with our diligence obligations, the former owners of the intellectual property licensed under such agreement may require us and our licensors to return such intellectual property, in which case our license to such intellectual property would terminate. Any termination of these licenses could result in the loss of significant rights and could have a material adverse effect on our ability to commercialize our product candidates, including KD025 .

Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including those relating to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- whether we are complying with our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates; and/or
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our collaboration partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

We depend, in part, on our licensors to file, prosecute, maintain, defend and enforce patents and patent applications that are material to our business.

In certain of our license agreements, the patents relating to our product candidates are controlled by certain of our licensors. Such licensors generally have rights to file, prosecute, maintain and defend the patents we have licensed from such licensors. We generally have the first right to enforce our patent rights, although our ability to settle such claims often requires the consent of the licensor. If our licensors or any future licensees having rights to file, prosecute, maintain or defend our patent rights fail to conduct these activities for patents or patent applications covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using or selling competing products. We cannot be certain that such activities by our licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights.

Pursuant to the terms of the license agreements with some of our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and, even if we are permitted to pursue such enforcement or defense, we cannot ensure the cooperation of our licensors. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. Even if we are not a party to these legal actions, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. In addition, even when we have the right to control patent prosecution of licensed patents and patent applications, enforcement of licensed patents, or defense of claims asserting the invalidity of those patents, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to or after our assuming control.

We rely in part on third parties to conduct our clinical trials and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We do not independently conduct clinical trials of our product candidates. We rely on third parties, such as medical institutions and clinical investigators, and may in the future rely on other third parties, to perform this function. Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. We remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, we, along with medical institutions and clinical investigators, are required to comply with “good clinical practices” or “GCP,” which is an international ethical and scientific quality standard for designating, recording and reporting trials that involve the participation of human subjects, and which is implemented via regulations and guidelines enforced by, among others, the FDA, the EMA, the Competent Authorities of the Member States of the European Economic Area (EEA), and comparable foreign regulatory authorities for all of our products in clinical development. GCP is designed to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of patients in clinical trials are protected. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs, study sites, or clinical investigators fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials and create other regulatory and litigation exposure, which would among other things delay the regulatory approval process.

We face risks in connection with existing and future collaborations with respect to the development, manufacture and commercialization of our products and product candidates.

The risks that we face in connection with our current and any future collaborations include the following:

- Our collaborators may change the focus of their development and commercialization efforts or may have insufficient resources to effectively develop our product candidates. The ability of some of our products and product candidates to reach their potential could be limited if collaborators decrease or fail to increase development or commercialization efforts related to those products or product candidates.

- Any future collaboration agreements may have the effect of limiting the areas of research and development that we may pursue, either alone or in collaboration with third parties.

- Collaborators may develop and commercialize, either alone or with others, drugs that are similar to or competitive with the drugs or product candidates that are the subject of their collaborations with us.

Our collaboration agreements are subject to termination under various circumstances.

Risks Related to Our Operations

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

The biopharmaceutical industry has experienced a high rate of turnover of management personnel in recent years. Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities. This may limit their availability to us.

In order to induce valuable employees to continue their employment with us, we have provided equity incentives that vest over time. The value to employees of equity incentives that vest over time is significantly affected by the success of our operations and clinical trials for our product candidates, much of which is beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies.

Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Our employment arrangements generally provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, financial condition and prospects. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

On October 24, 2018, we reported that Konstantin Poukalov, our Executive Vice President, Chief Financial Officer (“CFO”) and Principal Accounting Officer (“PAO”), notified us of his intent to resign, effective immediately. In connection with his resignation, we initiated a search for a replacement CFO. Upon the effectiveness of Mr. Poukalov’s resignation, Harlan W. Waksal, M.D., our President and Chief Executive Officer, served as acting Principal Financial Officer and Kyle Carver, the Company’s Controller, was appointed PAO. On February 11, 2019, we announced that Steven Meehan, who had previously served on the board of directors of the Company, had been appointed as the Company’s Executive Vice President and Chief Financial Officer.

We may not be able to attract or retain qualified management and scientific personnel in the future due to the intense competition for a limited number of qualified personnel among biopharmaceutical, biotechnology, pharmaceutical and other businesses and institutions. Many of the other companies and institutions that we compete with for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than what we have to offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize product candidates will be limited.

Our employees, independent contractors, principal investigators, agents, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk that our employees, independent contractors, principal investigators, agents, consultants, commercial partners and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent failures to:

- comply with regulations by the FDA and other similar foreign regulatory bodies;
- provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies;
- comply with manufacturing standards;

- comply with federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the United States and similar foreign laws;
- report financial information or data accurately; and/or
- disclose unauthorized activities to us.

In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, including off-label uses of our products, structuring and commission(s), certain customer incentive programs, patient assistance programs, and other business arrangements generally. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Ethics. However, it is not always possible to identify and deter misconduct by employees and other third-parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs or other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

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

We face an inherent risk of product liability as a result of the clinical testing of our product candidates, whether by us, on our behalf or by unaffiliated third parties or investigators, and will face an even greater risk for any products that we commercialize. For example, we may be sued if any product we develop or sell allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates, if approved, or our other marketed products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or products that we may develop or sell;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management’s time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenues from product sales; and/or
- the inability to commercialize our product candidates or our marketed products.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry an aggregate of $10.0 million of product liability insurance, which we believe is adequate for our commercial products and our clinical trials. Although we maintain such insurance, any claim that may be brought against us could result in a court

judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our operating results are subject to significant fluctuations.

Our quarterly revenues, expenses and net income (loss) have fluctuated in the past and are likely to fluctuate significantly in the future due to the timing of charges and expenses that we may encounter. In recent periods, for instance, we have recorded charges that include:

- unrealized gain (losses) on investments in equity securities;
- gains (losses) related to the change in fair value of financial instruments
- financing related costs and expenses; and
- milestone payments under license and collaboration agreements.

Our quarterly revenues, expenses and net income (loss) may fluctuate significantly from quarter to quarter and year to year, such that a period to period comparison of our results of operations may not be a good indication of our future performance.

If we are unable to successfully implement our strategic plan, our business may be materially harmed.

We plan to continue to develop and commercialize novel drugs for significant unmet medical needs while we continue to market our commercial products to eligible patients to generate revenue. Absent a successful launch of one or more of our product candidates, we expect our total revenue to decline significantly. In order to maintain a strong financial position, we are focusing our investment on development programs for our most advanced product candidates. In an effort to mitigate our drug development risk and improve our chance of ultimate commercial success, we are developing multiple product candidates in a variety of disease indications. There can be no assurance that our development programs will be successful or that our research programs will result in drugs that we can successfully develop and commercialize.

Our business may become subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Some of our suppliers and collaborative and clinical trial relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- differing regulatory requirements for drug approvals in foreign countries;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country’s or region’s political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;

- difficulties associated with staffing and managing foreign operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and/or
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

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

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

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

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

If we acquire or license technologies, products or product candidates, we will incur a variety of costs and may never realize benefits from the transaction.

If appropriate opportunities become available, we might license or acquire technologies, resources, drugs or product candidates. We might never realize the anticipated benefits of such a transaction, and we may later incur impairment charges related to assets acquired in any such transaction. In particular, due to the risks inherent in drug development, we may not successfully develop or obtain marketing approval for the product candidates we acquire. Future licenses or acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, the creation of contingent liabilities, impairment expenses related to goodwill, and impairment or amortization expenses related to other intangible assets, which could harm our financial condition.

We will need to grow our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

At December 31, 2018, we had 116 full-time employees. As our development and commercialization plans and strategies develop, we expect to expand our employee base for managerial, operational, sales, marketing, financial and other resources. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of their attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations which may result in weaknesses in our infrastructure, give rise to operational errors, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of existing and additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our

ability to generate and/or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates and compete effectively with others in our industry will depend, in part, on our ability to effectively manage any future growth.

We depend on information technology and a failure of those systems could adversely affect our business.

We rely on sophisticated information technology systems to operate our business. These systems are potentially vulnerable to malicious intrusion, random attack, loss of data privacy, or breakdown. Although we have invested in the protection of our data and information technology and also monitor our systems on an ongoing basis, there can be no assurance that these efforts will prevent breakdowns or breaches in our information technology systems that could adversely affect our business.

We may be subject to security breaches or other cybersecurity incidents that could compromise our information and expose us to liability.

We routinely collect and store sensitive data (such as intellectual property, proprietary business information and personally identifiable information) for the Company, its employees and its suppliers and customers. We make significant efforts to maintain the security and integrity of our computer systems and networks and to protect this information. We have not experienced any known attacks on our information technology systems that have resulted in any material system failure, accident or security breach to date. However, like other companies in our industry, our networks and infrastructure may be vulnerable to cyber-attacks or intrusions, including by computer hackers, foreign governments, foreign companies or competitors, or may be breached by employee error, malfeasance or other disruption. Any such breach could result in unauthorized access to (or disclosure of) sensitive, proprietary or confidential information of ours, our employees or our suppliers or customers, and/or loss or damage to our data. If personal information or protected health information is improperly accessed, tampered with or disclosed as a result of a security breach, we may incur significant costs to notify and mitigate potential harm to the affected individuals, and we may be subject to sanctions and civil or criminal penalties if we are found to be in violation of the privacy or security rules under HIPAA or other similar federal or state laws protecting confidential personal information. Any such unauthorized access, disclosure, or loss of information could cause competitive harms, result in legal claims or proceedings, liability under laws that protect the privacy of personal information, and/or cause reputational harm.

Risks Related to Our Common Stock

We expect that our stock price will fluctuate significantly.

The trading prices of the securities of pharmaceutical and biotechnology companies have been highly volatile. The trading price of our common stock also may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this “Risk Factors” section, these factors include:

- adverse results or delays in the planned clinical trials of our product candidates or any future clinical trials we may conduct, or changes in the development status of our product candidates;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority’s review of such filings, including without limitation the FDA’s issuance of a “refusal to file” letter or a request for additional information;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our products and product candidates, including clinical trial requirements for approvals;
- our inability to obtain or delays in obtaining adequate product supply for any approved product or inability to do so at acceptable prices;
- failure to commercialize our product candidates or if the size and growth of the markets we intend to target fail to meet expectations;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our product candidates;

- introductions or announcements of new products offered by us or significant acquisitions, strategic collaborations, joint ventures or capital commitments by us, our collaborators or our competitors and the timing of such introductions or announcements;
- our ability or inability to effectively manage our growth;
- changes in the structure of healthcare payment systems;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- market conditions in the pharmaceutical and biotechnology sectors or the economy generally;
- our ability or inability to raise additional capital through the issuance of equity or debt or collaboration arrangements and the terms on which we raise it;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; and/or
- significant lawsuits, including patent or stockholder litigation.

The stock market in general, and market prices for the securities of biopharmaceutical companies like ours in particular, have from time to time experienced volatility that often has been unrelated to the operating performance of the underlying companies. These broad market and industry fluctuations may adversely affect the market price of our common stock, regardless of our operating performance. Stock prices of many pharmaceutical companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies. In several recent situations when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results.

If securities or industry analysts do not publish research reports about our business, or if they issue an adverse opinion about our business, our stock price and trading volume could decline.

The trading market for our common stock may be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have, and may never obtain research coverage by securities and industry analysts. If no or few analysts commence research coverage of us, or one or more of the analysts who cover us issues an adverse opinion about our company, our stock price would likely decline. If one or more of these analysts ceases research coverage of us or fails to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Future sales of our common stock or securities convertible into our common stock in the public market could cause our stock price to fall.

Our stock price could decline as a result of sales of a large number of shares of our common stock or securities convertible into our common stock or the perception that these sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

Certain holders of our shares have rights requiring us to file registration statements covering the sale of their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, subject to certain conditions. Shares issued upon the exercise of stock options outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market stand-off and lock-up agreements, Rule 144 and Rule 701 under the Securities Act, as well as, to the extent applicable, under the registration statement on Form S-8 that we have filed.

Once we register the offer and sale of shares for the holders of registration rights and shares to be issued under our equity incentive plans, they can be freely sold in the public market upon issuance or resale (as applicable).

In addition, in the future, we may issue additional shares of common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock. In addition, any future testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement.

We are required, pursuant to Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting beginning with our annual report on Form 10-K for the fiscal year ending December 31, 2018. However, for as long as we are an "emerging growth company" under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an emerging growth company for up to five years following the date of our IPO. An independent assessment of the effectiveness of our internal controls could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

The holders of the convertible preferred stock will be entitled to be paid a liquidation preference, which under some circumstances will include a substantial premium.

In the event of a liquidation (as defined in the certificate of designations governing our convertible preferred stock), certain bankruptcy events or a failure to make any payment due on our or our subsidiaries' indebtedness after giving effect to any applicable cure period, the holders of the convertible preferred stock will be entitled to payment of a liquidation preference. The liquidation preference for each share of convertible preferred stock will equal the greater of (i) (A) (I) the original purchase price per share of convertible preferred stock plus dividend arrearages thereon in cash *plus* (II) any dividends accrued and unpaid thereon from the last dividend payment date to the date of the final distribution to such holder *plus* (B) in the majority of the events identified in the previous sentence, a premium equal to 20.2% of the amount described in clause (i)(A) of this sentence at such time or (ii) an amount per share of convertible preferred stock equal to the amount which would have been payable or distributable if each share of convertible preferred stock been converted into shares of our common stock immediately before the liquidation event.

Until the holders of the convertible preferred stock have been paid their liquidation preference in full, no payment will be made to any holder of common stock. If our assets, or the proceeds from their sale, distributable among the holders of the convertible preferred stock are not sufficient to pay the liquidation preference in full and the liquidating payments on any parity securities, then those assets or proceeds will be distributed among the holders of the convertible preferred stock and those parity securities on a pro rata basis. In that case, there would be no assets or proceeds remaining to be distributed to holders of our common stock, which would have a material adverse effect on the trading price of our common stock.

The holders of the convertible preferred stock are entitled to have their shares of convertible preferred stock redeemed at a substantial premium in certain events

Our convertible preferred stock is redeemable if we or our significant subsidiaries are the subject of certain bankruptcy events and upon the failure to make payments of amounts due on our or any of our subsidiaries' indebtedness after giving effect to any applicable cure period. Upon the occurrence of any of these events, the holders of our convertible preferred stock shall, in their sole discretion, be entitled to receive an amount equal to the original purchase price per share of convertible preferred stock plus dividend arrearages thereon *plus* any dividends accrued and unpaid thereon from the last dividend payment date to, but excluding, the date of such redemption *plus* the premium described under "The holders of the convertible preferred stock will be entitled to be paid a liquidation preference, which under some circumstances will include a substantial premium." If we were to become obligated to redeem all or a substantial portion of the outstanding convertible preferred stock, that could have a material adverse effect on the trading price of our common stock.

Shares of our convertible preferred stock are convertible into shares of our common stock and, upon conversion, will dilute your percentage of ownership.

Concurrently with the closing of our IPO, we issued 30,000 shares of our convertible preferred stock pursuant to an exchange agreement with holders of our Senior Convertible Term Loan. Holders of the convertible preferred stock shall be entitled to receive a cumulative dividend at an annual rate of 5% of the sum of the original purchase price per share of convertible preferred stock plus any dividend arrearages. In addition, holders of the convertible preferred stock shall be entitled to receive dividends paid or payable on our common stock with respect to the number of shares of our common stock into which each share of convertible preferred stock is then convertible at the then applicable conversion price. Shares of our convertible preferred stock are convertible at any time at the option of the holder into shares of our common stock at a conversion price equal to their original purchase price plus any accrued but unpaid dividends. At December 31, 2018, 3,519,303 shares of our common stock are issuable upon conversion of our convertible preferred stock. This issuance of common stock upon the conversion will dilute the percentage ownership of holders of our common stock by approximately 3.1% as of December 31, 2018. The dilutive effect of the conversion of these securities may adversely affect our ability to obtain additional equity financing.

Holders of the convertible preferred stock may exert substantial influence over us and may exercise their control in a manner adverse to your interests.

So long as shares of our convertible preferred stock remain outstanding, without the consent of at least a majority of the then outstanding shares of the convertible preferred stock, we may not (i) authorize or approve the issuance of any convertible preferred stock, senior securities or parity securities (or, in each case, any security convertible into, or convertible or exchangeable therefor or linked thereto) or authorize or create or increase the authorized amount of any convertible preferred stock, senior securities or parity securities (or, in each case, any security convertible into, or convertible or exchangeable therefor or linked thereto); (ii) authorize or approve the purchase or redemption of any parity securities or junior securities; (iii) amend, alter or repeal any of the provisions of the certificate of designations, our certificate of incorporation or our by-laws in a manner that would adversely affect the powers, designations, preferences and rights of the convertible preferred stock; (iv) contract, create, incur, assume or suffer to exist any indebtedness or guarantee any such indebtedness with an aggregate value of more than $5,000,000 (subject to certain exceptions); or (v) agree to take any of the above actions. The holders of convertible preferred stock will have one vote for each share of common stock into which such holders' shares could then be converted at the time, and with respect to such vote, will have voting rights and powers equal to the voting rights and powers of the holders of our common stock.

The certificate of designations governing the convertible preferred stock also provides that no amendment or waiver of any provision of the certificate of designations or our charter or bylaws shall, without the prior written consent of all holders of the convertible preferred stock who are known to us to hold, together with their affiliates, more than 5% of the convertible preferred stock then outstanding (i) reduce any amounts payable or that may become payable to holders of the convertible preferred stock; (ii) postpone the payment date of any amount payable to holders of the convertible preferred stock or waive or excuse any payment; (iii) modify or waive the conversion rights of the convertible preferred stock in a manner that would adversely affect any holder of the convertible preferred stock; or (iv) change any of the voting-related provisions or any other provision of the certificate of designations specifying the number or percentage of holders of the convertible preferred stock which are required to waive, amend or modify any rights under the certificate of designations or make any determination or grant any consent under that document.

We will require additional capital in the future, which may not be available to us. Issuances of our equity securities to provide this capital may dilute your ownership in us.

We will need to raise additional funds through public or private debt or equity financings in order to:

- take advantage of expansion opportunities;
- acquire complementary products, product candidates or technologies;
- develop new products or technologies; and/or
- respond to competitive pressures.

Any additional capital raised through the issuance of our equity securities may dilute your percentage ownership interest in us. Furthermore, any additional financing we may need may not be available on terms favorable to us or at all. The unavailability of needed financing could adversely affect our ability to execute our business strategy. See "—Risks Related to Our Financial Position—Our 2015 Credit Agreement, as amended, matures on July 1, 2020. We may not be able to comply with the covenants under the 2015 Credit Agreement, as amended, or refinance our debt under this facility before the

maturity date, in which event our ability to continue our operations would be materially and adversely impacted" for more information.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

Our executive officers, directors and holders of 5% or more of our capital stock, together with their respective affiliates, beneficially owned 53.0% of our capital stock as of March 1, 2019, of which 2.7% is beneficially owned by our executive officers. Accordingly, our executive officers, directors and principal stockholders are able to determine the composition of the board of directors, retain the voting power to approve all matters requiring stockholder approval, including mergers and other business combinations, and continue to have significant influence over our operations. This concentration of ownership could have the effect of delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us that you may believe are in your best interests as one of our stockholders. This in turn could have a material adverse effect on our stock price and may prevent attempts by our stockholders to replace or remove the board of directors or management.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us difficult, limit attempts by our stockholders to replace or remove our current management and adversely affect our stock price.

Provisions of our certificate of incorporation and bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our stock. Among other things, our certificate of incorporation and bylaws:

- permit the board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that all vacancies, including newly-created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum; and
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be taken by written consent.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any stockholder owning in excess of 15.0% of our outstanding stock for a period of three years following the date on which the stockholder obtained such 15.0% equity interest in us.

We will continue to incur significant costs by being a public company.

As a public company, we incur significant legal, accounting and other expenses, including costs associated with public company reporting requirements. We also incur costs associated with corporate governance requirements, including requirements of the SEC and the New York Stock Exchange (NYSE). We expect these rules and regulations to continue to increase our legal and financial compliance costs and to make some activities more time-consuming and costly. We also expect that these rules and regulations may continue to make it more difficult and expensive for us to obtain director and officer liability insurance and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as executive officers. We are currently evaluating and monitoring developments with respect to these rules, and we cannot predict or estimate the amount of additional costs we may incur or the timing of such costs.

When we cease to be an "emerging growth company" and when our independent registered public accounting firm is required to undertake an assessment of our internal control over financial reporting, the cost of our compliance with Section 404 will correspondingly increase. Moreover, if we are not able to comply with the requirements of Section 404 applicable to us in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

We are an "emerging growth company," as defined in the JOBS Act, and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and we take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies" including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive because we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We will take advantage of these reporting exemptions until we are no longer an "emerging growth company." We will remain an "emerging growth company" until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.0 billion or more, (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of our IPO, (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

Our management has broad discretion in using cash and cash equivalents and our other capital resources.

We expect to continue to use our cash and cash equivalents and our other capital resources to fund the clinical development of our pipeline and for general corporate purposes. Our management has broad discretion in the application of our cash and cash equivalents and our other capital resources and could spend the funds in ways that do not improve our results of operations or enhance the value of our equity. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, diminish available cash flows available to service our debt, cause the value of our equity to decline and delay the development of our product candidates. Pending their use, we may invest cash and cash equivalents and our other capital resources in a manner that does not produce income or that loses value.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of existing or any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our equity securities will likely be your sole source of gain for the foreseeable future.

Future sales and issuances of equity securities, convertible securities or other securities could result in additional dilution of the percentage ownership of holders of our common stock.

We expect that additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell equity securities, convertible securities or other securities in one or more transactions at prices and in a manner we determine from time to time. If we sell equity securities, convertible securities or other securities in more than one transaction, investors in such future offerings may be materially diluted by subsequent sales. Such sales would also likely result in material dilution to our existing equity holders, and new investors could gain rights, preferences and privileges senior to those of holders of our existing equity securities.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We have three primary operating locations which are occupied under long-term leasing arrangements. In October 2010, Kadmon Corporation, LLC entered into a corporate headquarters and laboratory lease in New York, New York, expiring in February 2021 and opened a secured letter of credit with a third party financial institution in lieu of a security deposit for $2.0 million. Since inception, there have been six amendments to this lease agreement, which have altered office and laboratory capacity and extended the lease term through October 2025. We have the ability to extend portions of the lease on the same terms and conditions as the current lease, except that the base rent will be adjusted to the fair market rental rate for the building based on the rental rate for comparable space in the building at the time of extension.

We are party to an operating lease in Warrendale, Pennsylvania (our specialty-focused commercial operation), which expires on September 30, 2019, with a five-year renewal option. Rental payments under the renewal period will be at market rates determined from the average rentals of similar tenants in the same industrial park.

In August 2015, we entered into an office lease agreement in Cambridge, Massachusetts (our clinical office) effective January 2016 and expiring in April 2023. We opened a secured letter of credit with a third party financial institution in lieu of a security deposit for $91,000.

For additional information, see Contractual Obligations and Commitments in Part II, Item 7 of this Annual Report on Form 10-K.

Item 3. Legal Proceedings

Please refer to Note 16, “Contingencies,” of the notes to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a discussion related to our legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our common stock has been listed on the NYSE under the symbol "KDMN" since our initial public offering, or IPO, of our common stock on July 27, 2016. Prior to that time, there was no public market for our common stock.

Holders of Record

On March 1, 2019, there were approximately 239 stockholders of record of our common stock and the closing price of our common stock was $2.86 per share as reported by the NYSE. Since many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Dividend Policy

We currently expect to retain all future earnings, if any, for use in the operation and expansion of our business and repayment of debt. We have never declared nor paid any dividends on our common stock and do not anticipate paying cash dividends to holders of our common stock in the foreseeable future. In addition, the 2015 Credit Agreement, as amended, as well as any future borrowings, will restrict our ability to pay dividends. See "Risk Factors—Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain." Any determination to pay dividends on our common stock in the future will be at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements and covenants in our existing financing arrangements and any future financing arrangements. Holders of the convertible preferred stock are entitled to receive a cumulative dividend at an annual rate of 5% of the original purchase price per share of convertible preferred stock, when and as declared by our board of directors and to the extent of funds legally available for the payment of dividends. Holders of the convertible preferred stock are also entitled to participate in all dividends declared and paid to holders of our common stock on an "as if" converted basis.

Purchases of Equity Securities by the Issuer of Affiliated Purchasers

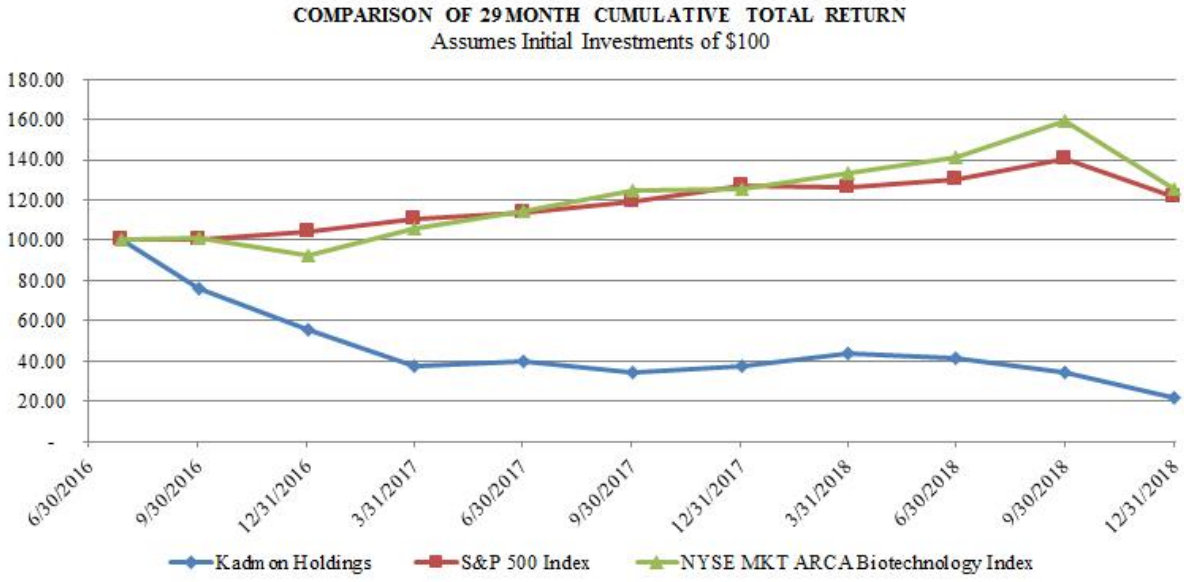
None.

Securities Authorized for issuance under our Equity Compensation Plans

The information called for by this item will be included in our definitive proxy statement with respect to our 2019 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

Stock Performance Graph

The following graph illustrates a comparison from July 27, 2016, which is the date our common stock first began trading on the NYSE, through December 31, 2018, of the total cumulative stockholder return on our common stock, the Standard & Poor's 500 Stock Index (S&P 500 Index) and the NYSE MKT ARCA Biotechnology Index. The graph assumes that $100 was invested at the market close on July 27, 2016 in the common stock of Kadmon Holdings, Inc., the S&P 500 Index and the NYSE MKT ARCA Biotechnology Index and data for the S&P 500 Index and the NYSE MKT ARCA Biotechnology Index assumes reinvestments of dividends. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns. This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



Item 6. Selected Financial Data.

The following selected financial data are derived from the consolidated financial statements. The data presented below should be read in conjunction with our consolidated financial statements, the notes to the consolidated financial statements, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this Annual Report on Form 10-K. The consolidated statement of operations data for the years ended December 31, 2018, 2017 and 2016, and the consolidated balance sheet data at December 31, 2018 and 2017, are derived from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Years Ended December 31,		
	2018	2017	2016
	(in thousands, except per share data)		
Statement of Operations Data:			
Total revenue	$ 1,396	$ 12,264	$ 26,055
Cost of sales	412	1,332	3,485
Write-down of inventory	270	1,654	385
Gross profit	714	9,278	22,185
Research and development	48,966	40,777	35,840
Selling, general and administrative	37,644	37,057	105,880
Gain on settlement of payable	—	—	(4,131)
Total operating expenses	86,610	77,834	137,589
Loss from operations	(85,896)	(68,556)	(115,404)
Total other expense (income)	(31,120)	11,339	93,009
Net loss	(54,252)	(79,774)	(208,755)
Deemed dividend on convertible preferred stock	2,011	1,918	21,733
Net loss attributable to common stockholders	(56,263)	(81,692)	(230,488)
Basic and diluted net loss per share of common stock	$ (0.58)	$ (1.42)	$ (9.74)
Weighted average basic and diluted shares of common stock outstanding	97,609,000	57,405,331	23,674,512

	December 31,	
	2018	2017
	(in thousands)	
Balance Sheet Data:		
Cash and cash equivalents	$ 94,740	$ 67,517
Other current assets	4,196	2,496
Investment, equity securities	34,075	—
Other noncurrent assets	11,650	13,539
Total assets	144,661	83,552
Current liabilities	24,018	56,644
Other long term liabilities	4,752	25,150
Secured term debt – net of current portion and discount	27,480	—
Total liabilities	56,250	81,794
Total stockholders' equity	88,411	1,758

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in, or implied by, the forward-looking statements contained in the following discussion and analysis.

Overview

We are a fully integrated biopharmaceutical company engaged in the discovery, development and commercialization of small molecules and biologics to address significant unmet medical needs, with a near-term clinical focus on autoimmune, inflammatory and fibrotic diseases. Our team, which has a proven track record of successful drug development and commercialization, identifies and develops novel candidates from our small molecule and biologics platforms as well as develops our in-licensed product candidates. By retaining global commercial rights to our lead product candidates, we believe that we have the ability to progress these candidates ourselves while maintaining flexibility for commercial and licensing arrangements. We expect to continue to progress our clinical candidates and have further clinical trial data to report throughout 2019.

Our operations to date have been focused on developing first-in-class innovative therapies for indications with significant unmet medical needs while leveraging our commercial infrastructure. We have never been profitable and had an accumulated deficit of $269.6 million at December 31, 2018. Our net losses were $54.3 million, $79.8 million and $208.8 million for the years ended December 31, 2018, 2017 and 2016, respectively. Although our commercial business generates revenue, we expect to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, our additional product candidates, hire additional personnel and initiate commercialization of any products that receive regulatory approval. We anticipate that our expenses will increase substantially if, or as, we:

- invest significantly to further develop our most advanced product candidates, including KD025 and tesevatinib;
- initiate clinical trials of KD045 and KD033 and preclinical studies for our other product candidates;
- seek regulatory approval for our product candidates that successfully complete clinical trials;
- continue to invest in our research platforms;
- seek to identify additional product candidates;
- scale up our sales, marketing and distribution infrastructure and product sourcing capabilities;
- acquire or in-license other product candidates and technologies;
- scale up our operational, financial and management information systems and personnel, including personnel to support our product development;
- make milestone or other payments under any in-license agreements; or
- maintain, expand and protect our intellectual property portfolio;

On July 26, 2016, prior to the closing of our IPO we completed a corporate conversion transaction whereby we converted from a Delaware limited liability company into a Delaware corporation and changed our name to Kadmon Holdings, Inc., which we refer to herein as the "Corporate Conversion." As required by the Second Amended and Restated Limited Liability Company Agreement of Kadmon Holdings, LLC, the Corporate Conversion was approved by our board of directors. In connection with the Corporate Conversion, holders of our outstanding units received one share of common stock for every 6.5 membership units held immediately prior to the Corporate Conversion, and options and warrants to purchase units became options and warrants to purchase one share of common stock for each unit underlying such options or warrants immediately prior to the Corporate Conversion, at the same aggregate exercise price in effect prior to the Corporate Conversion.

MeiraGTx IPO

On June 12, 2018, MeiraGTx Holdings plc ("MeiraGTx") completed its initial public offering (the "MeiraGTx IPO") whereby it sold 5,000,000 shares of common stock at $15.00 per share. Upon completion of the MeiraGTx IPO, we owned approximately 13.0% of MeiraGTx's issued and outstanding common stock and we no longer have the ability to exert significant influence over MeiraGTx's operations. We discontinued the equity method of accounting for the investment in MeiraGTx on June 12, 2018 and determined the remaining investment to be an equity security accounted for in accordance with ASC 321. As our investment in MeiraGTx common stock has a readily determinable market value, we recorded an unrealized gain of $40.5 million during the second quarter of 2018 related to the fair value of our ownership of common stock of MeiraGTx. As of December 31, 2018, we owned approximately 12.9% of the issued and outstanding common stock of MeiraGTx with a fair value of $34.1 million recorded as a noncurrent investment in equity securities as depending on certain circumstances, we may, at times, be deemed an affiliate of MeiraGTx. The fair value of our investment in MeiraGTx is subject to market conditions and may be volatile and fluctuate substantially. See "Risk Factors—Risks Related to Our Financial Position—The market price of our investment in MeiraGTx may be volatile and fluctuate substantially, which could result in significant changes to the fair value of our investment and limit our ability to sell those securities."

Fourth and Fifth Amendments to 2015 Credit Agreement

On June 12, 2018, we entered into the fourth amendment (the "Fourth Amendment") to our senior secured non-convertible term loan (the "2015 Credit Agreement"). Pursuant to the Fourth Amendment, the maturity date of the 2015 Credit Agreement was extended to August 31, 2018 (the "Extension Period"). We repaid $4.7 million of the outstanding principal on June 18, 2018, representing all amounts due under the 2015 Credit Agreement to GoldenTree Credit Opportunities, LP, GoldenTree Credit Opportunities, Ltd, GoldenTree Insurance Fund Series Interests of the SALI Multi-Series Fund, LP, GT NM, LP, and San Bernardino County Employees' Retirement Association. All other material terms of the 2015 Credit Agreement remained the same during the Extension Period, including a minimum liquidity covenant.

On August 15, 2018, we entered into the fifth amendment (the "Fifth Amendment") to our 2015 Credit Agreement. Pursuant to the Fifth Amendment, the maturity date of the Credit Agreement was extended to July 1, 2020 and principal payments have been deferred until January 31, 2020. Beginning on January 31, 2020, equal principal payments of $750,000 per month will be due until the maturity date. Additionally, the parties amended certain covenants under the 2015 Credit Agreement to require us to meet certain developmental milestones by December 31, 2019. All other material terms of the 2015 Credit Agreement remain the same, including a minimum liquidity covenant.

2018 Public Offering

In June 2018, we raised $113.2 million ($105.8 million net of $7.4 million of underwriting discounts and other offering expenses payable by us) from the issuance of 34,303,030 shares of common stock at a price of $3.30 per share ("2018 Public Offering").

Components of Statement of Operations

Revenue

Our revenue is substantially derived from sales of our portfolio of products, including our ribavirin portfolio of products and Camber products tetrabenazine and valganciclovir. We also recognize service revenue from our transition services and sublease agreements with MeiraGTx. No meaningful revenue has been generated from sales of our other products. Revenue in 2017 and 2016 also includes the recognition of upfront licensing fees and milestone payments received primarily from our license agreements with AbbVie and Jinghua.

Cost of Sales

Cost of sales consists of product costs, including ingredient costs and costs of contract manufacturers for production, and shipping and handling of the products. Also included are costs related to quality release testing and stability testing of the products. Other costs included in cost of sales are packaging costs, warehousing costs and certain allocated costs related to management, facilities and other expenses associated with supply chain logistics.

Research and development expenses

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- license fees related to our license and collaboration agreements;
- research and development-based employee-related expenses, including salaries, benefits, travel and other compensation expenses;
- expenses incurred under our agreements with contract research organizations that conduct nonclinical and preclinical studies, and clinical sites and consultants that conduct our clinical trials;
- costs associated with regulatory filings;
- costs of laboratory supplies and the acquisition, development and manufacture of preclinical and clinical study materials and study drugs; and
- allocated facility-related expenses.

Our research and development expenses may vary substantially from period to period based on the timing of our research and development activities, including timing of initiation of clinical trials and enrollment of patients in clinical trials. We do not allocate personnel-related costs, including share-based compensation, costs associated with broad technology platform improvements and other indirect costs to specific product candidates. We do not allocate these costs to specific product candidates because they are deployed across multiple overlapping projects under development, making it difficult to specifically and accurately allocate such costs to a particular product candidate.

The successful development of our product candidates is highly uncertain and subject to numerous risks including, but not limited to:

- the scope, rate of progress and expense of our research and development activities;
- clinical trial results;
- the scope, terms and timing of regulatory approvals;
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- the cost, timing and our ability to acquire sufficient clinical and commercial supplies for any product candidates and products that we may develop; and
- the risks disclosed in the section entitled “Risk Factors” in this Annual Report on Form 10-K.

A change in the outcome of any of these variables could mean a significant change in the expenses and timing associated with the development of any product candidate.

Selling, general and administrative expenses

Selling, general and administrative expenses consist primarily of salaries and related costs for non-research personnel, including stock-based compensation and travel expenses for our employees in executive, operational, finance, legal, commercial, regulatory, pharmacovigilance and human resource functions. Other selling, general and administrative expenses include facility-related costs, business insurance, director compensation, accounting and legal services, consulting costs and programs and marketing costs to support the commercial business.

Other income (expense)

Other income (expense) is comprised of interest income earned on cash and cash equivalents and restricted cash and interest expense on our outstanding indebtedness, including paid-in-kind interest on our convertible debt during 2016 until the consummation of our initial public offering and non-cash interest related to the write-off and amortization of debt discount, debt premium and deferred financing costs associated with our indebtedness. Our gains and losses on our investment in MeiraGTx, as well as, gains and losses arising from changes in fair value of our financial instruments are recognized in other income (expense) in the consolidated statements of operations. Such financial instruments include warrant liabilities for which the exercise price was contingent on our per share price in a qualified public offering. The change in fair value is based upon the fair value of the underlying security at the end of each reporting period, as calculated using the Black-Scholes option pricing model, in the case of certain warrant liabilities, and a binomial model, in the case of certain warrant liabilities.

In addition, we operate in currencies other than the U.S. dollar to fund research and development and commercial activities performed by various third-party vendors. The translation of these currencies into U.S. dollars results in foreign currency gains or losses, depending on the change in value of these currencies against the U.S. dollar. These gains and losses are included in other income (expense).

Income taxes

Prior to the Corporate Conversion, we were a limited liability company but taxed as a C corporation for federal and state tax purposes. On July 26, 2016, we converted from a limited liability company to a Delaware corporation pursuant to a statutory conversion. At December 31, 2018 and 2017, we had a deferred tax liability of $0.4 million and $0.9 million, respectively, and a full valuation allowance for our deferred tax assets.

As of December 31, 2018, we have unused federal and state net operating loss (“NOL”) carry-forwards of $460.3 million and $404.3 million, respectively, that may be applied against and reduce future taxable income. We recorded a valuation allowance to fully offset the gross deferred tax asset, because it is more likely than not that we will not realize future benefits associated with these deferred tax assets at December 31, 2018 and 2017. These NOL carry-forwards expire at various dates through December 31, 2037, with the exception of approximately $44.0 million of federal net operating loss carry-forwardsm which will not expire.

The use of our NOL carry-forwards may, however, be subject to limitations as a result of an ownership change. A corporation undergoes an “ownership change,” in general, if a greater than 50% change (by value) in its equity ownership by one or more five-percent stockholders (or certain groups of non-five-percent stockholders) over a three-year period occurs. After such an ownership change, the corporation’s use of its pre-change NOL carry-forwards and other pre-change tax attributes to offset its post-change income is subject to an annual limitation determined by the equity value of the corporation on the date the ownership change occurs multiplied by a rate determined monthly by the Internal Revenue Service. This rate for March 2019 equals 2.39 percent. We experienced ownership changes under Section 382 of the Code in 2010, 2011 and 2016, but we did not reduce the gross deferred tax assets related to the NOL carry-forwards because the limitations do not hinder our ability to potentially utilize all of the NOL carry-forwards.

We are likely to experience another ownership change in the future, possibly in 2019, as a result of future shifts in our stock ownership, which may include shifts in our stock ownership as a result of any future equity offerings. A renewed ownership change will likely materially and substantially reduce our ability to fully utilize our NOL carry-forwards and, consequently, will likely reduce the gross deferred tax assets related to our NOL carry-forwards. If an ownership change occurred and if we earned net taxable income, our ability to use our pre-change NOLs to offset U.S. federal taxable income would be subject to these limitations, which could potentially result in increased future tax liability compared to the tax liability we would incur if our use of NOL carry-forwards were not so limited. In addition, for state income, franchise and similar tax purposes, there may be periods during which the use of NOL carry-forwards is suspended or otherwise limited, which could accelerate or permanently increase our state income, franchise or similar taxes.

Critical Accounting Policies and Significant Judgments and Estimates

Management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP"). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reporting amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to investments, goodwill, fair value of financial instruments, share-based compensation and accrued expenses. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. While our significant accounting policies are more fully described in Note 2, "Summary of Significant Accounting Policies" of the notes to our audited consolidated financial statements in Part IV, Item 15 of this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgements and estimates used in the preparation of our financial statements.

Share-based compensation expense

We are required to estimate the grant-date fair value of stock options and stock appreciation rights issued to employees and recognize this cost over the period these awards vest. We estimate the fair value of each stock option granted using the Black-Scholes option pricing model. The Black-Scholes model requires the input of assumptions, including the expected stock price volatility, the calculation of expected term and the fair value of the underlying common stock on the date of grant, among other inputs. Generally, we have issued stock options that vest over time. For these awards, we record compensation cost on a straight-line basis over the vesting period. We calculate the fair value of the award on the grant date, which is the date the award is authorized by the board of directors and the employee has an understanding of the terms of the award.

Prior to our IPO, we were a privately held company with no active public market for our Class A units. Therefore, our management had estimated the fair value of our Class A units at various dates considering our most recently available third-party valuations of Class A units and management's assessment of additional objective and highly subjective factors that it believed were relevant. The consummation of our IPO on August 1, 2016 established a public trading market for shares of our common stock; therefore it is no longer necessary for management to estimate the fair value of our equity in connection with our accounting for granted stock options. In the absence of a public trading market for shares of our common stock, we applied the fair value recognition provisions of FASB ASC Topic 718, "Compensation—Stock Compensation." ASC 718 requires all unit-based payments to employees and directors, including unit option grants and modifications to existing unit options, to be recognized in the statements of operations based on their fair values. We recognize compensation expense over the period during which the recipient renders the required services using the straight-line, single option method.

As there had been no public market for our Class A units prior to our IPO, the estimated fair value of our Class A units had been determined contemporaneously by our board of directors utilizing independent third-party valuations prepared in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, also known as the Practice Aid for financial reporting purposes. We performed contemporaneous valuations of our Class A units concurrently with the achievement of significant milestones or with major financing events, with the last prior to the initial public offering completed as of September 30, 2015 ($32.50). In conducting these valuation analyses, we considered all objective and subjective factors that we believed to be relevant for each valuation conducted, including:

- recent equity financings and the related valuations;
- industry information such as market size and growth;
- market capitalization of comparable companies and the estimated value of transactions such companies have engaged in; and/or
- macroeconomic conditions.

On July 13, 2016, the compensation committee of our board of directors approved an option award for Dr. Harlan W. Waksal, increasing the number of options (giving effect to the Corporate Conversion) subject to his original option grant. The number of shares subject to this option award was equal to the difference between the 769,231 options originally granted to Dr. Harlan W. Waksal and 5% of our outstanding common equity determined on a fully diluted basis on the IPO date, which amounted to 1,630,536 options. The effective date of the new option award was the IPO date of July 26, 2016. The exercise price per share of common stock subject to the new incremental options awarded was equal to the price per share of common stock at the IPO date of $12.00. The option award is subject to the same vesting schedule applicable to the original option grant such that all options awarded will vest on August 4, 2017. In consideration for the new option award, Dr. Harlan W. Waksal committed to perform an additional year of service through August 4, 2018 in connection with receipt of the additional option shares. This modification resulted in a $12.4 million charge, of which the incremental value of the previously vested portion of the awards totaling $8.3 million was expensed during the third quarter of 2016 and the remaining amount of the unvested portion totaling $4.1 million was recognized over the remaining service period through August 4, 2018.

On July 13, 2016, the compensation committee of our board of directors approved the amendment of all outstanding option awards issued under our 2011 Equity Incentive Plan whereby, effective upon pricing of our IPO, the exercise price (on a post-Corporate Conversion, post-split basis) was adjusted to equal the price per share of our common stock in the IPO. Options to purchase an aggregate of approximately 1.6 million shares of our Class A units were modified. The vesting schedule of such awards was not modified. The modification resulted in a $4.0 million charge, of which the incremental value of the previously vested portion of the awards totaling $1.8 million was expensed immediately during the third quarter of 2016 and the remaining $2.2 million was recognized over the remaining vesting periods of each award, ranging from one to three years.

A total of 9,750 units were granted under the 2014 Long-Term Incentive Plan (“LTIP”) at December 31, 2018 and 2017. The compensation expense for these awards was recognized upon consummation of our IPO on August 1, 2016 and was recorded as additional paid in capital. No compensation expense had been recorded prior to this date. We utilized a Monte-Carlo simulation to determine the fair value of the awards granted under the LTIP of $22.6 million, which was recorded during the third quarter of 2016 as these awards are not forfeitable. The LTIP is payable upon the fair market value of our common stock exceeding 333% of the $6.00 grant price ($20.00) per share prior to December 7, 2024. The holders of the LTIP have no right to demand a particular form of payment, and we reserve the right to make payment in the form of cash or common stock.

We granted 1,040,000 stock appreciation rights to three executive employees on December 8, 2017. No stock appreciation rights were granted under the 2016 Equity Plan prior to 2017. The weighted-average fair value of the stock appreciation rights granted was $2.42 and was estimated at the date of grant using the Black-Scholes option-pricing model with the following assumptions: risk-free interest rate of 2.22%, expected term of 6 years, expected volatility of 74.92%, share price of $3.64, strike price of $3.64 and a dividend rate of 0%.

Compensation expense for stock appreciation rights is recognized on a straight-line basis over the awards’ requisite service period. Total unrecognized compensation cost related to stock appreciation rights was $1.3 million and $2.5 million at December 31, 2018 and 2017, respectively. The unrecognized compensation cost at December 31, 2018 is expected to be recognized over a weighted-average period of 1.9 years. No stock appreciation rights were exercised during the years ended December 31, 2018 or 2017.

We granted 1,597,500 nonqualified performance-based stock options (“Performance Options”) to three executive employees on April 3, 2018. No Performance Options were granted under the 2016 Equity Plan prior to 2018. Each Performance Option was granted with an exercise price of $4.06 per share and does not contain any voting rights. The weighted-average fair value of the Performance Options granted was $2.71 and was estimated at the date of grant using the Black-Scholes option-pricing model with the following assumptions: risk-free interest rate of 2.67%, expected term of 6.0 years, expected volatility of 74.50%, and a dividend rate of 0%.

Compensation expense for the Performance Options is recognized on a straight-line basis over the awards’ requisite service period. The Performance Options vest upon the satisfaction of both a service condition and the satisfaction of one or more performance conditions, therefore we initially determined which outcomes are probable of achievement. We believe that the three-year service condition (explicit service period) and all three performance conditions (implicit service periods) will be satisfied. The requisite service period would be three years as that is the longest period of both the explicit service period and the implicit service periods. Total unrecognized compensation expense related to unvested Performance Options was $1.8 million at December 31, 2018. The unrecognized compensation cost is expected to be recognized over a weighted-average period of 1.5 years. No Performance Options were exercised during the year ended December 31, 2018.

The assumptions relating to the valuation of our options granted for the years ended December 31, 2018, 2017 and 2016 are shown below. The table does not include Performance Options.

	Years Ended		
	December 31, 2018	December 31, 2017	December 31, 2016
Weighted average fair value of grants	$1.69	$2.44	$7.12
Expected volatility	72.94% - 75.92%	74.48% - 74.92%	74.98% - 79.35%
Risk-free interest rate	2.44% - 2.90%	1.87% - 2.22%	1.15% - 2.20%
Expected life	5.5 - 6.0 years	5.5 - 6.0 years	5.0 - 6.0 years
Expected dividend yield	0%	0%	0%

The following table summarizes by grant date the number of shares subject to options granted since January 1, 2016, the per share exercise price of the options, the fair value of common stock underlying the options on date of grant and the per share estimated fair value of the options:

Grant Date	Number of Shares Subject to Options Granted	Per Share Exercise Price of Options	Fair Value of Common Stock per Share on Date of Option Grant	Per Share Estimated Fair Value of Options
July 26, 2016	1,630,536	$ 12.00	$ 12.00	$ 7.60
December 15, 2016	3,227,924	$ 4.66	$ 4.66	$ 3.06
February 9, 2017	10,000	$ 3.82	$ 3.82	$ 2.48
June 29, 2017	275,000	$ 4.12	$ 4.12	$ 2.63
December 8, 2017	2,568,000	$ 3.64	$ 3.64	$ 2.42
February 19, 2018	2,000	$ 3.63	$ 3.63	$ 2.42
March 16, 2018	3,077	$ 4.48	$ 4.48	$ 2.05
April 3, 2018	1,597,500	$ 4.06	$ 4.06	$ 2.71
April 10, 2018	40,000	$ 4.22	$ 4.22	$ 2.83
May 9, 2018	2,000	$ 3.96	$ 3.96	$ 2.66
June 25, 2018	33,847	$ 3.88	$ 3.88	$ 1.67
July 27, 2018	200,000	$ 3.35	$ 3.35	$ 2.16
December 14, 2018	1,829,500	$ 2.47	$ 2.47	$ 1.62

Expenses Accrued Under Contractual Arrangements with Third Parties; Accrued Clinical Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing expenses, we estimate the time period over which services will be performed and the level of effort to be expended in each period, which is based on an established protocol specific to each clinical trial. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual accordingly. 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 us reporting amounts that are too high or too low in any particular period.

Investment in Equity Securities

Equity securities consist of investments in common stock of companies traded on public markets (see Note 10 of the notes to our audited consolidated financial statements in Part IV, Item 15 of this Annual Report on Form 10-K). These shares are carried on the Company’s balance sheet at fair value based on the closing price of the shares owned on the last trading

day before the balance sheet of this report. Fluctuations in the underlying bid price of the shares result in unrealized gains or losses. In accordance with FASB ASC 321, Investments – Equity Securities ("ASC 321"), the Company recognizes these fluctuations in value as other expense (income). For investments sold, the Company recognizes the gains and losses attributable to these investments as realized gains or losses in other expense (income).

The Company's total investment balance in equity securities totaled $34.1 million at December 31, 2018, all of which related to our investment in MeiraGTx's common stock. The Company did not maintain any investments in equity securities at December 31, 2017.

Recent Accounting Pronouncements

See Note 2 "Summary of Significant Accounting Policies," of the notes to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a summary of recently issued and adopted accounting pronouncements.

Results of Operations

	Years Ended December 31,		
	2018	2017	2016
	(in thousands)		
Revenues			
Net sales	$ 691	$ 5,257	$ 18,514
License and other revenue	705	7,007	7,541
Total revenue	1,396	12,264	26,055
Cost of sales	412	1,332	3,485
Write-down of inventory	270	1,654	385
Gross profit	714	9,278	22,185
Operating expenses:			
Research and development	48,966	40,777	35,840
Selling, general and administrative	37,644	37,057	105,880
Gain on settlement of payable	—	—	(4,131)
Total operating expenses	86,610	77,834	137,589
Loss from operations	(85,896)	(68,556)	(115,404)
Other expense	(31,120)	11,339	93,009
Income tax expense (benefit)	(524)	(121)	342
Net loss	$ (54,252)	$ (79,774)	$ (208,755)
Deemed dividend on convertible preferred stock and Class E redeemable convertible units	2,011	1,918	21,733
Net loss attributable to common stockholders	$ (56,263)	$ (81,692)	$ (230,488)

Comparison of the years ended December 31, 2018 and 2017

Revenues

Total revenue decreased by 88.6%, or approximately $10.9 million, from $12.3 million in the year ended December 31, 2017 to $1.4 million for the year ended December 31, 2018. The decrease in total revenue was primarily attributable to the decline in sales of our ribavirin portfolio products. Total revenue also included sales of Camber products of $0.5 million and $1.2 million for the years ended December 31, 2018 and 2017, respectively. Total revenue for the year ended December 31, 2017 included a $2.0 million milestone payment earned pursuant to a license agreement entered into with Jinghua to develop products using human monoclonal antibodies while no such revenue was recognized for the year ended December 31, 2018. We recognized previously deferred revenue from our license and collaboration agreements amounting to $4.4 million for the year ended December 31, 2017, while no such revenue was recognized for the year ended December 31, 2018 due to the Company's adoption of ASC 606 (see Note 2 "Summary of Significant Accounting Policies," of the notes to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K). Service and sublease revenue from MeiraGTx was $0.6 million during each of the years ended December 31, 2018 and 2017.

Foreign product sales represented approximately 1.4% and 26.9% of total product sales for the years ended December 31, 2018 and 2017, respectively, the majority of which were sales in the Netherlands and Ireland.

Sales from our ribavirin portfolio continued to decline in 2018, from $4.2 million for the year ended December 31, 2017 to $0.1 million for the year ended December 31, 2018 as the treatment landscape for chronic HCV infection has rapidly evolved, with multiple ribavirin-free treatment regimens, including novel direct-acting antivirals, having entered the market and becoming the new standard of care. As a result, sales of our ribavirin portfolio of products were insignificant in 2018 we expect our ribavirin portfolio of products to contribute insignificantly to revenue in 2019 and beyond.

Cost of sales

Cost of sales was $0.4 million and $1.3 million for the years ended December 31, 2018 and 2017, respectively, which relates primarily to the sales volume of our ribavirin portfolio of products and Camber products.

Write-down of inventory

We recognized $0.3 million and $1.7 million of inventory write-downs during the years ended December 31, 2018 and 2017, respectively, of our Ribasphere inventory based on our expectation that such inventory will not be sold prior to reaching its product expiration date.

Research and development expenses

Research and development expenses increased by 20.1%, or approximately $8.2 million, to $49.0 million, including $3.1 million of non-cash items, for the year ended December 31, 2018 from $40.8 million, including $2.7 million of non-cash items, for the year ended December 31, 2017. The increase in research and development expense was primarily related to direct external costs of developing our product candidates across multiple projects. For the years ended December 31, 2018 and 2017, we recognized $10.1 million and $5.5 million, respectively, for KD025; $5.0 million and $7.6 million, respectively, in development expenses for tesevatinib; $1.5 million and $1.0 million, respectively, for KD034; $9.6 million and $6.8 million, respectively, for other product candidates such as KD033 and KD045; and $22.8 million and $19.8 million, respectively, was related to unallocated internal and external costs of developing our product candidates across multiple projects.

Selling, general and administrative expenses

Selling, general and administrative expenses increased by 1.3%, or approximately $0.5 million, to $37.6 million, including $8.8 million of non-cash items, for the year ended December 31, 2018 from $37.1 million, including $11.5 million of non-cash items, for the year ended December 31, 2017. While selling, general and administrative expense remained consistent for the year ended December 31, 2018 as compared to year ended December 31, 2017, the slight increase is primarily related to consulting costs related to an ERP upgrade of $0.8 million, partially offset by a decrease in depreciation expense of $0.3 million related to fixed assets which have become fully depreciated during 2017 and 2018.

Other expense (income)

The following table provides components of other expense (income):

	Years Ended December 31,	
	2018	2017
	(in thousands)	
Interest expense	$ 3,565	$ 3,720
Amortization of deferred financing costs and debt discount	1,054	2,242
Change in fair value of financial instruments	(1,525)	(2,096)
Unrealized gain on equity securities	(34,075)	—
Loss on equity method investment	1,242	7,599
Interest income	(1,307)	(132)
Other expense (income)	(74)	6
Other expense (income)	**$ (31,120)**	**$ 11,339**

For the year ended December 31, 2018, other income consisted primarily of a change in the fair value of financial instruments of $1.5 million, unrealized gains related to our investment in MeiraGTx common stock of $34.1 million, interest income of $1.3 million, partially offset by interest expense and other costs related to our debt of $4.6 million and loss on equity method investment of $1.2 million for the year ended December 31, 2018.

For the year ended December 31, 2017, other expense consisted primarily of interest expense and other costs related to our debt of $6.0 million and a loss on equity method investment in MeiraGTx of $7.6 million, partially offset by a change in the fair value of financial instruments of $2.1 million.

Income taxes

The Tax Cuts and Jobs Act (the “Act”) was enacted in December 2017. In accordance with the Act, the Company determined it necessary to reduce the recorded deferred tax liability by $0.6 million during the second quarter of 2018 to allow naked credit deferred tax liabilities to be used as a source of taxable income in the future. The change in deferred tax liability has been recognized as income tax benefit in the consolidated financial statements of operations for the year ended December 31, 2018.

For the year ended December 31, 2017, we recorded an income tax benefit of $0.1 million related to a $0.4 million adjustment to the deferred tax liability, net of $0.3 million of income tax expense related to a $2.0 million milestone payment received from Jinghua.

Deemed Dividend

At our IPO, we issued 30,000 shares of convertible preferred stock which accrues dividends at a rate of 5% and converts into shares of our common stock at a 20% discount to the price per share of our common stock of $12.00 in the IPO.

We accrued dividends on the 5% convertible preferred stock of $1.6 million and $1.5 million for the years ended December 31, 2018 and 2017, respectively. The Company calculated a deemed dividend of $0.4 million and $0.4 million on the $1.6 million and $1.5 million of accrued dividends during the year ended December 31, 2018 and 2017, respectively, which is a beneficial conversion feature. Approximately $1.6 million and $1.4 million of accrued dividends that were payable on June 30, 2018 and June 30, 2017, respectively, was added to the stated liquidation preference amount of the 5% convertible preferred stock on those respective dates. The stated liquidation preference of the 5% convertible preferred stock totaled $33.0 million at December 31, 2018.

Comparison of the years ended December 31, 2017 and 2016

Revenues

Total revenue decreased by 53.0%, or approximately $13.8 million, from $26.1 million in the year ended December 31, 2016 to $12.3 million for the year ended December 31, 2017. The decrease in total revenue was primarily attributable to the decline in sales of our ribavirin portfolio products. Total revenue includes a $2.0 million milestone payment earned pursuant to a license agreement entered into with Jinghua to develop products using human monoclonal antibodies for each of the years ended December 31, 2017 and 2016. We recognized previously deferred revenue from our license and collaboration agreements amounting to $4.4 million for each of the years ended December 31, 2017 and 2016. Service revenue from our affiliate MeiraGTx Limited (MeiraGTx) was $0.6 million and $1.0 million during the years ended December 31, 2017 and 2016, respectively.

Foreign product sales represented approximately 26.9% and 8.6% of total product sales for the years ended December 31, 2017 and 2016, respectively, the majority of which were sales in the Netherlands and Ireland.

Sales from our ribavirin portfolio continued to decline in 2017, from $17.0 million for the year ended December 31, 2016 to $4.2 million for the year ended December 31, 2017 as the treatment landscape for chronic HCV infection has rapidly evolved, with multiple ribavirin-free treatment regimens, including novel direct-acting antivirals, having entered the market and becoming the new standard of care. As a result, sales of our ribavirin portfolio of products were insignificant in 2018.

We recognized revenue of $1.0 million and $0.6 million from sales of tetrabenazine during the years ended December 31, 2017 and 2016, respectively. We recognized revenue of $0.2 million and $0.9 million from sales of valganciclovir during the years ended December 31, 2017 and 2016, respectively. No meaningful revenue was generated from sales of our other products for the years ended December 31, 2017 and 2016.

Cost of sales

Cost of sales was $1.3 million and $3.5 million for the years ended December 31, 2017 and 2016, respectively, which relates primarily to the sales volume of our ribavirin portfolio of products.

Write-down of inventory

We recognized $1.7 million and $0.4 million of inventory write-downs during the years ended December 31, 2017 and 2016, respectively, of our Ribasphere inventory based on our expectation that such inventory will not be sold prior to reaching its product expiration date.

Research and development expenses

Research and development expenses increased by 14.0%, or approximately $4.9 million, to $40.8 million, including $2.7 million of non-cash items, for the year ended December 31, 2017 from $35.8 million, including $3.0 million of non-cash items, for the year ended December 31, 2016. The increase in research and development expense was primarily related to direct external costs of developing our product candidates across multiple projects. For the years ended December 31, 2017 and 2016, we recognized $5.5 million and $2.2 million, respectively, for KD025; $7.6 million and $4.8 million, respectively, in development expenses for tesevatinib; $1.0 million and $1.6 million, respectively, for KD034; $6.8 million and $1.4 million, respectively, for other product candidates; and $19.8 million and $25.8 million, respectively, was related to unallocated internal and external costs of developing our product candidates across multiple projects.

In June 2016, research and development expenses, and selling, general and administrative expenses were revised to conform to the current presentation with regard to our method of allocating a portion of facility-related expenses to research and development expenses to more accurately reflect the effort spent on research and development. We reclassified $2.2 million from selling, general and administrative expense to research and development expense for the year ended December 31, 2016.

Selling, general and administrative expenses

Selling, general and administrative expenses decreased by 65.0%, or approximately $68.9 million, to $37.1 million, including $11.5 million of non-cash items, for the year ended December 31, 2017 from $105.9 million, including $69.1 million of non-cash items, for the year ended December 31, 2016. The decrease in selling, general and administrative expenses is primarily related to a decrease in share-based compensation of $34.6 million, of which $22.0 million is related to the Company's 2014 Long Term Incentive Plan, $1.8 million is related to the repricing of employee options, $8.3 million is related to an option grant to our Chief Executive Officer and $2.5 million is related to lower share-based compensation for employee options, as well as, a decrease of $3.0 million in severance expense primarily related to the separation agreement with Dr. Samuel D. Waksal, salary and salary-related expenses of $5.6 million related to a reduction in headcount, legal expense of $4.1 million primarily related to legal settlements entered into during 2016, amortization of intangible assets of $15.2 million due to the intangible asset being fully amortized at December 31, 2016, royalty expense of $1.0 million and consulting fees of $3.0 million resulting from the expiration of an advisory agreement entered into in April 2015.

Gain on settlement of payable

Gain on settlement of payable is primarily related to a gain of $3.9 million resulting from the mutual termination agreement entered into with Valeant during the first quarter of 2016.

Other expense

The following table provides components of other expense:

	Years Ended December 31,	
	2017	2016
	(in thousands)	
Interest expense	$ 3,720	$ 3,782
Interest expense - beneficial conversion feature	—	45,915
Interest paid-in-kind	—	14,695
Write-off of deferred financing costs and debt discount	—	3,820
Amortization of deferred financing costs and debt discount	2,242	4,422
Loss on extinguishment of debt	—	11,176
Change in fair value of financial instruments	(2,096)	(4,380)
Loss on equity method investment	7,599	13,625
Interest income	(132)	(38)
Other expense (income)	6	(8)
Other expense	**$ 11,339**	**$ 93,009**

For the year ended December 31, 2017, other expense consisted primarily of interest expense and other costs related to our debt of $6.0 million and a loss on equity method investment in MeiraGTx of $7.6 million, partially offset by a change in the fair value of financial instruments of $2.1 million.

For the year ended December 31, 2016, other expense consisted primarily of interest expense and other costs related to our debt of $72.6 million, a loss on extinguishment of debt of $11.2 million related to the exchange agreements dated as of June 8, 2016 and a loss on equity method investment in MeiraGTx of $13.6 million, partially offset by a change in the fair value of financial instruments of $4.4 million.

Income taxes

Historically we were a limited liability company taxed as a C corporation for federal and state tax purposes. On July 26, 2016, we effected the Corporate Conversion whereby we converted from a Delaware limited liability company to a Delaware corporation pursuant to a statutory conversion. We recorded an income tax benefit of $0.1 million for the year ended December 31, 2017 related to a $0.4 million adjustment to the deferred tax liability, net of $0.3 million of income tax expense related to a $2.0 million milestone payment received from Jinghua. We recorded income tax expense of $0.3 million for the year ended December 31, 2016, related to a $2.0 million milestone payment received from Jinghua.

Deemed Dividend

We calculated a deemed dividend on the Class E redeemable convertible units of $13.4 million in August 2016, which equaled a 15% discount to the price per share of our common stock of $12.00 in the IPO upon conversion to common stock at our IPO due to a beneficial conversion feature. The Class E redeemable convertible units converted into common stock at our IPO resulting in no Class E redeemable convertible units outstanding at both December 31, 2017 and 2016.

At our IPO, we issued 30,000 shares of convertible preferred stock which accrues dividends at a rate of 5% and converts into shares of our common stock at a 20% discount to the price per share of our common stock of $12.00 in the IPO. We calculated a deemed dividend on the convertible preferred stock of $7.5 million in August 2016, which equals the 20% discount to the price per share of our common stock in the IPO of $12.00, a beneficial conversion feature. We also accrued dividends on the convertible preferred stock of $1.5 million and $0.6 million for the years ended December 31, 2017 and 2016, respectively. Approximately $1.4 million of accrued dividends that were payable on June 30, 2017 was added to the stated liquidation preference amount of the 5% convertible preferred stock, which totaled $31.4 million at December 31, 2017.

Liquidity and Capital Resources

Overview

We had an accumulated deficit of $269.6 million, working capital of $74.9 million, and cash and cash equivalents of $94.7 million at December 31, 2018. Net cash used in operating activities was $71.2 million, $64.1 million and $53.0 million for the years ended December 31, 2018, 2017 and 2016.

In June 2018, we raised $113.2 million ($105.8 million net of $7.4 million of underwriting discounts and other offering expenses payable by us) from the issuance of 34,303,030 shares of common stock at a price of $3.30 per share ("2018 Public Offering").

We entered into a Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor") in August 2017 under which we may sell up to $40.0 million in shares of its common stock in one or more placements at prevailing market prices for its common stock (the "ATM Offering"). As of December 31, 2018, we had not sold any shares of common stock under the ATM Offering. Subsequent to December 31, 2018 and through January 9, 2019, we sold 13,778,705 shares of common stock at a weighted average price of $2.17 per share through the ATM Offering and received total gross proceeds of $29.9 million ($29.0 million net of $0.9 million of commissions payable by us).

Going Concern

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America, which contemplate our continuation as a going concern. We have not established a source of revenues sufficient to cover our operating costs, and as such, have been dependent on funding operations through the issuance of debt and sale of equity securities. Since inception, we have experienced significant loses and incurred negative cash flows from operations. We expect to incur further losses over the next several years as we develop our business. We have spent, and expect to continue to spend, a substantial amount of funds in connection with implementing our business strategy, including our planned product development efforts, preparation for our planned clinical trials, performance of clinical trials and our research and discovery efforts.

Our cash and cash equivalents available at December 31, 2018 was $94.7 million and in January 2019, we raised $29.0 million in net proceeds through the ATM Offering. As such, should we meet our development milestones contained in the 2015 Credit Agreements, the cash and cash equivalents available at February 2019 are expected to fund operations into the second quarter of 2020 and enable us to advance our planned Phase 2 clinical studies for KD025, advance certain of our other pipeline product candidates, including KD033 and KD045, and provide for other working capital purposes. Although cash and cash equivalents will be sufficient to fund the foregoing, cash and cash equivalents will not be sufficient to enable us to meet our long-term expected plans, including commercialization of clinical pipeline products, if approved, or initiation or completion of future registrational studies. Following the completion of our ongoing and planned clinical trials, we will likely need to raise additional capital to fund continued operations, starting in the second quarter of 2020. We have no commitments for any additional financing and may not be successful in our efforts to raise additional funds or achieve profitable operations. Any amounts raised will be used for further development of our product candidates, to provide financing for marketing and promotion, to secure additional property and equipment, and for other working capital purposes.

If we are unable to obtain additional capital (which is not assured at this time), our long-term business plan may not be accomplished and we may be forced to curtail or cease operations. Further, the 2015 Credit Agreement contains certain developmental milestones that must be achieved by December 31, 2019, which are considered to be outside of our control. As such, if achievement of the developmental milestones does not occur as anticipated by December 31, 2019, we may need to use our cash and cash equivalents to fund certain repayment commitments as any such non-compliance could, under the exclusive remedies set forth in the 2015 Credit Agreement, trigger a termination of the Commitments (as defined in the 2015 Credit Agreement) or a declaration by the Lender that the Loan (as defined in the 2015 Credit Agreement) be due and payable in whole or part, together with any applicable fees and/or interest thereon. In the event that we had to repay the outstanding principle under the 2015 Debt Agreement, we would likely need to raise additional capital to fund continued operations. These factors individually and collectively raise substantial doubt about our ability to continue as a going concern. The accompanying financial statements do not include any adjustments or classifications that may result from our possible inability to continue as a going concern. The explanatory paragraph regarding our ability to continue as a going concern in the report and opinion of our independent registered public accounting firm for the year ended December 31, 2018 is an event of default under the 2015 Credit Agreement. We entered into a sixth waiver agreement to the 2015 Credit Agreement in March 2019 under which the lenders under the 2015 Credit Agreement agreed to refrain from exercising certain rights under the 2015 Credit Agreement, including the declaration of a default and to forbear from acceleration of any repayment rights with respect to existing covenants.

Sources of Liquidity

Since our inception through December 31, 2018, we have raised net proceeds from the issuance of equity and debt. At December 31, 2018, we had $28.0 million of outstanding loans under the 2015 Credit Agreement. Pursuant to the Fifth Amendment, principal payments owed under the 2015 Credit Agreement, in the amount of $750,000 per month, were deferred until January 31, 2020. As of the date hereof, we are not in default under the terms of the 2015 Credit Agreement. See Note 5, "Debt" of the notes to our audited consolidated financial statements included in this Annual Report on Form 10-K for more information.

The following table sets forth the primary sources and uses of cash and cash equivalents for each period set forth below:

	Year Ended December 31,		
	2018	2017	2016
	(in thousands)		
Net cash provided by (used in):			
Operating activities	$ (71,227)	$ (64,098)	$ (52,950)
Investing activities	(864)	(479)	(539)
Financing activities	99,314	96,001	68,084
Net increase in cash, cash equivalents and restricted cash	$ 27,223	$ 31,424	$ 14,595

Operating Activities

The net cash used in operating activities was $71.2 million for the year ended December 31, 2018, and consisted primarily of a net loss of $54.3 million adjusted for $21.6 million in non-cash items, including unrealized gain on equity securities of $34.1 million, change in fair value of financial instruments of $1.5 million, and change in deferred tax liability of $0.5 million, offset by depreciation and amortization of fixed assets of $1.5 million, write-down of inventory of $0.3 million, amortization of deferred financing costs, debt discount, and debt premium of $1.1 million, loss on equity method investment of $1.2 million, and share-based compensation expense of $10.4 million, as well as, a net increase in operating assets and liabilities of $4.7 million. The net loss, adjusted for non-cash items, was primarily driven by selling, general and administrative expenses of $28.8 million, research and development expense related to the advancement of our clinical product candidates of $45.9 million and interest paid on our debt of $3.6 million, partially offset by the net sales less cost of sales primarily from Camber products of $0.3 million.

The net cash used in operating activities was $64.1 million for the year ended December 31, 2017, and consisted primarily of a net loss of $79.8 million adjusted for $23.2 million in non-cash items, including depreciation and amortization of fixed assets of $1.8 million, write-down of inventory of $1.7 million, amortization of deferred financing costs, debt discount, and debt premium of $2.2 million, loss on equity method investment of $7.6 million and share-based compensation expense of $12.4 million, as well as, a net decrease in operating assets and liabilities of $7.5 million. The net loss, adjusted for non-cash items, was primarily driven by selling, general and administrative expenses of $25.6 million, research and development expense related to the advancement of our clinical product candidates of $38.1 million and interest paid on our debt of $3.7 million, partially offset by the net sales less cost of sales primarily from our ribavirin portfolio of products and Camber products of $3.9 million and milestone revenue from our license agreement with Jinghua amounting to $2.0 million.

The net cash used in operating activities was $53.0 million for the year ended December 31, 2016, and consisted primarily of a net loss of $208.8 million adjusted for $157.2 million in non-cash items, including the amortization of intangible assets of $15.2 million, depreciation and amortization of fixed assets of $2.3 million, amortization and write-off of deferred financing costs and debt discount of $8.2 million, loss on extinguishment of debt of $11.2 million, fair value of units issued to third parties to settle obligations of $7.4 million, gain on settlement of payables of $4.1 million, paid-in-kind interest expense of $14.7 million, loss on equity method investment of $13.6 million, beneficial conversion feature expense on convertible debt and warrants of $45.9 million and share-based compensation expense of $47.2 million, as well as a net decrease in operating assets and liabilities of $1.8 million. The net loss, adjusted for non-cash items, was primarily driven by selling, general and administrative expenses of $36.8 million, research and development expense related to the advancement of our clinical product candidates of $32.8 million and interest paid on our debt of $3.7 million partially offset by the net sales less cost of sales primarily from our ribavirin portfolio of products of $15.0 million and milestone revenue from our license agreement with Jinghua amounting to $2.0 million

Investing Activities

Net cash used in investing activities was $0.9 million for the year ended December 31, 2018, consisting of costs related to the purchase of property and equipment, primarily related to lab equipment and in-house software purchased to support our internal clinical data management group. Net cash used in investing activities was $0.5 million for both the years ended December 31, 2017 and 2016 consisting of costs related to leasehold improvements at our clinical office in Cambridge, Massachusetts and the purchase of property and equipment, primarily related to in-house software purchased to support our internal clinical data management group.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2018 was $99.3 million, consisting primarily of net proceeds from the issuance of common stock in our 2018 Public Offering of $105.8 million, partially offset by principal payments on our secured term debt of $6.6 million.

Net cash provided by financing activities for the year ended December 31, 2017 was $96.0 million, consisting primarily of proceeds from the issuance of common stock and warrants to purchase common stock in our public offering of $75.1 million, net of underwriting fees, commissions and other offering costs and expenses and proceeds from the issuance of common stock and warrants to purchase common stock in our private placement of $20.9 million, net of placement agent fees and other offering costs and expenses.

Net cash provided by financing activities for the year ended December 31, 2016 was $68.1 million, consisting primarily of proceeds from the issuance of common stock in our IPO of $69.8 million, net of underwriting discounts and commissions, and net proceeds from the issuance of Class E redeemable convertible units of $5.5 million, partially offset by payment of offerings costs of $3.3 million and repayment of the related party loan of $3.0 million.

Future Funding Requirements

We expect our expenses to increase compared to prior periods in connection with our ongoing activities, particularly as we continue research and development, continue and initiate clinical trials and seek regulatory approvals for our product candidates. In anticipation of regulatory approval for any of our product candidates, we expect to incur significant pre-commercialization expenses related to product sales, marketing, distribution and manufacturing.

The expected use of our cash and cash equivalents at December 31, 2018 represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of, and results from, clinical trials, the potential need to conduct additional clinical trials to obtain approval of our product candidates for all intended indications, as well as any additional collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of our existing cash and cash equivalents. In addition, we anticipate the need to raise additional funds from the issuance of additional equity, and our management will retain broad discretion over the allocation of those funds as well.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2018:

	Payments due by period (in thousands)				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
Secured term debt	$ 28,046	$ —	$ 28,046	$ —	$ —
Interest expense[1]	4,921	3,359	1,562	—	—
Operating leases[2]	29,223	4,672	8,381	8,439	7,731
Total[3]	$ 62,190	$ 8,031	$ 37,989	$ 8,439	$ 7,731

(1) Interest expense reflects our obligation to make cash interest payments in connection with our 2015 Credit Agreement at a rate of 11.750%.

(2) Operating lease obligations primarily reflect our obligation to make payments in connection with leases for our corporate headquarters and commercial headquarters distribution center.

(3) This table does not include: (a) milestone payments totaling $215.9 million which may become payable to third parties under license agreements as the timing and likelihood of such payments are not known with certainty; (b) any royalty payments to third parties as the amounts, timing and likelihood of such payments are not known with certainty; and (c) contracts that are entered into in the ordinary course of business which are not material in the aggregate in any period presented above.

Off-balance Sheet Arrangements

During the periods presented we did not have, and we do not currently have, any off-balance sheet arrangements, as defined under the SEC rules.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Market Risk - Investment in Equity Securities

We are exposed to market risk and changes in the fair value of our investments in equity securities. As of December 31, 2018, we have an equity securities investment balance of $34.1 million relating to our common stock ownership of MeiraGTx. These shares are carried on the Company's balance sheet at fair value based on the closing price of the shares owned on the last trading day before the balance sheet date. Fluctuations in the underlying bid price of the shares could result in material gains or losses and as such, the full investment balance at December 31, 2018 is subject to the risk of a decline in the stock price of MeiraGTx.

On June 12, 2018, MeiraGTx completed its initial public offering (the "MeiraGTx IPO") whereby it sold 5,000,000 shares of common stock at $15.00 per share. The shares began trading on the Nasdaq Global Select Market on June 7, 2018 under the symbol "MGTX."

Interest Rate Risk

We are exposed to market risk and changes in interest rates. As of December 31, 2018, we had cash and cash equivalents of $94.7 million, consisting of cash and money market accounts. Due to the short-term duration of our investment portfolio, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

As of December 31, 2018, we had total debt payable of $27.5 million, which is variable-rate debt. Based on our variable-rate debt outstanding as of December 31, 2018, a 100 basis point change versus the market interest rates available on December 31, 2018 would result in approximately an additional $0.4 million of interest expense through maturity of our variable-rate debt in July 2020.

Customer Concentrations

There were no material customer concentrations for the year ended December 31, 2018. For the years ended December 31, 2017 and 2016, sales to AbbVie accounted for approximately 21% and 27% of our aggregate net sales, respectively. For the years ended December 31, 2017 and 2016, sales to Richmond Pharmaceuticals, Inc. accounted for approximately 8% and 14% of our aggregate net sales, respectively. There were no net accounts receivable outstanding from these customers at December 31, 2018, while net accounts receivable from these customers totaled $0.1 million at December 31, 2017.

Supplier Concentrations

We may be exposed to supplier concentration risk. Due to requirements of the FDA and other factors, we are generally unable to make immediate changes to our supplier arrangements. Manufacturing services related to each of our pharmaceutical products are primarily provided by a single source. Our raw materials are also provided by a single source for each product. Management attempts to mitigate this risk through long-term contracts and inventory safety stock.

Item 8. Financial Statements and Supplementary Data

Our financial statements, together with the report of our independent registered public accounting firm, appear beginning on page 93 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

Not applicable.

Item 9A. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934, as amended, is (1) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

At December 31, 2018, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended). Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, at December 31, 2018, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) of the Exchange Act). Internal control over financial reporting is a process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that accurately and fairly reflect in reasonable detail the transactions and dispositions of the assets of our company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- Provide reasonable assurances regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material adverse effect on our financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2018 based on the criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO 2013. Based on our evaluation under the criteria set forth in Internal Control - Integrated Framework issued by the COSO, our management concluded our internal control over financial reporting was effective as of December 31, 2018.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal quarter ended December 31, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item (other than the information set forth in the next paragraph in this Item 10) will be included in our definitive proxy statement with respect to our 2018 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer, or persons performing similar functions, and third-party consultants. We have posted a current copy of the code on our website, *www.kadmon.com*. In addition, we intend to post on our website all disclosures that are required by law or the NYSE listing standards concerning any amendments to, or waivers from, any provision of the code. The reference to our website does not constitute incorporation by reference of the information contained at or available through our website.

Item 11. Executive Compensation

The information called for by this item will be included in our definitive proxy statement with respect to our 2019 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information called for by this item will be included in our definitive proxy statement with respect to our 2019 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item will be included in our definitive proxy statement with respect to our 2019 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be included in our definitive proxy statement with respect to our 2018 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

The financial statements listed in the Index to Financial Statements beginning on page 93 are filed as part of this Annual Report on Form 10-K.

No financial statement schedules have been filed as part of this Annual Report on Form 10-K because they are not applicable, not required or because the information is otherwise included in our financial statements or notes thereto.

The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately following our financial statements. The Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary

None.

Kadmon Holdings, Inc.

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Kadmon Holdings, Inc.
New York, New York

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Kadmon Holdings, Inc. (the "Company") and subsidiaries as of December 31, 2018 and 2017, the related consolidated statements of operations, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with accounting principles generally accepted in the United States of America.

Change in Accounting Principle

As discussed in Note 2 to the financial statements, on January 1, 2018 the Company adopted new accounting guidance related to revenue from contracts with customers. Our opinion is not modified with respect to this matter.

Going Concern Uncertainty

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has incurred recurring losses from operations and expects such losses to continue in the future. Additionally, as more fully described in Note 1 to the consolidated financial statements, the Company's debt agreement is subject to covenants that could accelerate the repayment of that debt if breached. These factors raise substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ BDO USA, LLP

We have served as the Company's auditor since 2010.

New York, New York

March 7, 2019

Kadmon Holdings, Inc.
Consolidated balance sheets
(in thousands, except share amounts)

	December 31,	
	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$ 94,740	$ 67,517
Accounts receivable, net	1,690	325
Accounts receivable from affiliates	—	861
Inventories, net	925	201
Prepaid expenses and other current assets	1,581	1,109
Total current assets	98,936	70,013
Fixed assets, net	3,654	4,292
Goodwill	3,580	3,580
Restricted cash	2,116	2,116
Investment, equity securities	34,075	—
Investment, at cost	2,300	3,542
Other noncurrent assets	—	9
Total assets	$ 144,661	$ 83,552
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 9,986	$ 8,008
Accrued expenses	13,508	8,577
Deferred revenue	—	4,400
Fair market value of financial instruments	524	1,952
Secured term debt - current	—	33,707
Total current liabilities	24,018	56,644
Deferred revenue	—	19,617
Deferred rent	4,290	4,347
Deferred tax liability	415	939
Other long term liabilities	47	247
Secured term debt – net of current portion and discount	27,480	—
Total liabilities	56,250	81,794
Commitments and contingencies (Note 15 and 16)		
Stockholders' equity:		
Convertible Preferred Stock, $0.001 par value; 10,000,000 shares authorized at December 31, 2018 and December 31, 2017; 30,000 shares issued and outstanding at December 31, 2018 and December 31, 2017	42,231	40,220
Common Stock, $0.001 par value; 200,000,000 shares authorized at December 31, 2018 and December 31, 2017; 113,130,817 and 78,643,954 shares issued and outstanding at December 31, 2018 and December 31, 2017, respectively	113	79
Additional paid-in capital	315,710	198,856
Accumulated deficit	(269,643)	(237,397)
Total stockholders' equity	88,411	1,758
Total liabilities and stockholders' equity	$ 144,661	$ 83,552

See accompanying notes to consolidated financial statements

Kadmon Holdings, Inc.
Consolidated statements of operations
(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2018	2017	2016
Revenues			
Net sales	$ 691	$ 5,257	$ 18,514
License and other revenue	705	7,007	7,541
Total revenue	1,396	12,264	26,055
Cost of sales	412	1,332	3,485
Write-down of inventory	270	1,654	385
Gross profit	714	9,278	22,185
Operating expenses:			
Research and development	48,966	40,777	35,840
Selling, general and administrative	37,644	37,057	105,880
Gain on settlement of payable	—	—	(4,131)
Total operating expenses	86,610	77,834	137,589
Loss from operations	(85,896)	(68,556)	(115,404)
Other expense (income):			
Interest income	(1,307)	(132)	(38)
Interest expense	4,619	5,962	72,634
Loss on extinguishment of debt	—	—	11,176
Change in fair value of financial instruments	(1,525)	(2,096)	(4,380)
Loss on equity method investment	1,242	7,599	13,625
Unrealized gain on equity securities	(34,075)	—	—
Other expense (income)	(74)	6	(8)
Total other expense (income)	(31,120)	11,339	93,009
Loss before income tax expense	(54,776)	(79,895)	(208,413)
Income tax expense (benefit)	(524)	(121)	342
Net loss	$ (54,252)	$ (79,774)	$ (208,755)
Deemed dividend on convertible preferred stock and Class E redeemable convertible units	2,011	1,918	21,733
Net loss attributable to common stockholders	$ (56,263)	$ (81,692)	$ (230,488)
Basic and diluted net loss per share of common stock	$ (0.58)	$ (1.42)	$ (9.74)
Weighted average basic and diluted shares of common stock outstanding	97,609,000	57,405,331	23,674,512

See accompanying notes to consolidated financial statements

Kadmon Holdings, Inc.
Consolidated statements of stockholders' equity (deficit)
(in thousands, except unit and share amounts)

	Convertible units		Stockholders' equity (deficit)										
	Class E redeemable convertible units		Class A	Class B	Class C	Class D	Preferred stock		Common stock		Additional paid-in	Accumulated	
	Units	Amount	Units	Units	Units	Units	Shares	Amount	Shares	Amount	capital	Deficit	Total
Balance, January 1, 2016	4,969,252	$ 58,856	53,946,001	1	1	4,373,674	—	$ —	—	$ —	$ 372,936	$ (643,845)	$(270,909)
Issuance of Class A units to settle obligation	—	—	25,000	—	—	—	—	—	—	—	125	—	125
Issuance of Class E units to settle obligation	1,170,437	13,460	—	—	—	—	—	—	—	—	—	—	—
Equity raised through issuance of Class E units, net	478,266	5,500	—	—	—	—	—	—	—	—	—	—	—
Accretion of Class E units fee discount and repayment premium	—	5,812	—	—	—	—	—	—	—	—	(5,812)	—	(5,812)
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	47,217	—	47,217
Issuance of Class A units related to option exercises	—	—	7,200	—	—	—	—	—	—	—	41	—	41
Issuance of common stock to settle obligation	—	—	—	—	—	—	—	—	208,334	1	2,499	—	2,500
Common stock issued in initial public offering, net of commissions and underwriting discounts	—	—	—	—	—	—	—	—	6,250,000	6	69,744	—	69,750
Initial public offering costs	—	—	—	—	—	—	—	—	—	—	(3,739)	—	(3,739)
Beneficial conversion feature on Class E units	—	—	—	—	—	—	—	—	—	—	13,431	(13,431)	—
Cumulative effect of change in accounting principle - ASU 2016-09 forfeiture adjustment	—	—	—	—	—	—	—	—	—	—	1,990	(1,990)	—
Corporate conversion from Kadmon Holdings, LLC to Kadmon Holdings, Inc.	—	—	—	—	—	—	—	—	—	—	(720,618)	720,618	—
Corporate conversion to common stock	(6,617,955)	(83,628)	(53,978,201)	(1)	(1)	(4,373,674)	—	—	19,585,865	19	83,607	—	83,626
Conversion of convertible debt to common stock	—	—	—	—	—	—	—	—	19,034,467	19	182,712	—	182,731
Beneficial conversion feature on convertible debt	—	—	—	—	—	—	—	—	—	—	45,683	—	45,683
Conversion of convertible debt to convertible preferred stock	—	—	—	—	—	—	30,000	30,000	—	—	—	—	30,000
Beneficial conversion feature on convertible preferred stock	—	—	—	—	—	—	—	7,660	—	—	—	(7,660)	—
Accretion of dividends on convertible preferred stock	—	—	—	—	—	—	—	642	—	—	—	(642)	—
Reclassification of warrants to equity	—	—	—	—	—	—	—	—	—	—	1,716	—	1,716
Beneficial conversion feature on warrants	—	—	—	—	—	—	—	—	—	—	634	—	634
Net loss	—	—	—	—	—	—	—	—	—	—	—	(208,755)	(208,755)
Balance, December 31, 2016	—	$ —	—	—	—	—	30,000	$38,302	45,078,666	$ 45	$ 92,166	$ (155,705)	$ (25,192)
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	12,354	—	12,354
Common stock issued for warrant exercises	—	—	—	—	—	—	—	—	11,839	—	37	—	37
Common stock issued under ESPP plan	—	—	—	—	—	—	—	—	10,594	—	30	—	30
Common stock issued in private placement, net	—	—	—	—	—	—	—	—	6,767,855	7	19,209	—	19,216
Common stock and warrants issued in public offering, net	—	—	—	—	—	—	—	—	26,775,000	27	75,060	—	75,087
Beneficial conversion feature on convertible preferred stock	—	—	—	—	—	—	—	384	—	—	—	(384)	—
Accretion of dividends on convertible preferred stock	—	—	—	—	—	—	—	1,534	—	—	—	(1,534)	—
Net loss	—	—	—	—	—	—	—	—	—	—	—	(79,774)	(79,774)
Balance, December 31, 2017	—	$ —	—	—	—	—	30,000	$40,220	78,643,954	79	$ 198,856	$ (237,397)	$ 1,758
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	10,391	—	10,391
Common stock issued in public offering, net	—	—	—	—	—	—	—	—	34,303,030	34	105,727	—	105,761
Common stock issued for warrant exercises	—	—	—	—	—	—	—	—	131,834	—	588	—	588
Common stock issued under ESPP plan	—	—	—	—	—	—	—	—	51,999	—	148	—	148

Cumulative effect of change in accounting principle - ASC 606 adoption	—	—	—	—	—	—	—	—	—	—	—	24,017	24,017
Beneficial conversion feature on convertible preferred stock	—	—	—	—	—	—	—	402	—	—	—	(402)	—
Accretion of dividends on convertible preferred stock	—	—	—	—	—	—	—	1,609	—	—	—	(1,609)	—
Net loss	—	—	—	—	—	—	—	—	—	—	—	(54,252)	(54,252)
Balance, December 31, 2018	—	$ —	—	—	—	—	30,000	$42,231	113,130,817	113	$ 315,710	$ (269,643)	$ 88,411

See accompanying notes to consolidated financial statements

Kadmon Holdings, Inc.
Consolidated statements of cash flows
(in thousands)

	Years Ended December 31,		
	2018	2017	2016
Cash flows from operating activities:			
Net loss	$ (54,252)	$ (79,774)	$ (208,755)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization of fixed assets	1,534	1,822	2,280
Amortization of intangible asset	—	—	15,223
Write-down of inventory	270	1,654	385
Loss on extinguishment of debt / conversion of debt	—	—	11,176
Write-off of deferred financing costs and debt discount	—	—	3,820
Amortization of deferred financing costs	228	509	1,304
Amortization of debt discount	1,170	2,297	3,118
Amortization of debt premium	(344)	(564)	—
Share-based compensation	10,391	12,354	47,217
Bad debt expense	1	3	6
Change in fair value of financial instruments	(1,525)	(2,096)	(4,380)
Loss on equity method investment	1,242	7,599	13,625
Unrealized gain on equity securities	(34,075)	—	—
Deferred taxes	(524)	(437)	27
Gain on settlement of payable	—	—	(4,131)
Beneficial conversion feature expense on warrants	—	—	1,745
Beneficial conversion feature expense on convertible debt	—	—	44,170
Fair value of units issued to consultants	—	—	3,000
Fair value of shares / units issued in settlement of obligation	—	—	4,360
Paid-in-kind interest	—	—	14,695
Changes in operating assets and liabilities:			
Accounts receivable, net	(505)	21	937
Inventories, net	(994)	95	1,133
Prepaid expenses and other assets	(463)	(134)	(479)
Accounts payable	1,967	1,605	530
Accrued expenses, other liabilities and deferred rent	4,652	(4,652)	544
Deferred revenue	—	(4,400)	(4,500)
Net cash used in operating activities	(71,227)	(64,098)	(52,950)

See accompanying notes to consolidated financial statements

Kadmon Holdings, Inc.
Consolidated statements of cash flows (continued)
(in thousands)

	Years Ended December 31,		
	2018	2017	2016
Cash flows from investing activities:			
Purchases of fixed assets	(864)	(479)	(539)
Net cash used in investing activities	(864)	(479)	(539)
Cash flows from financing activities:			
Proceeds from issuance of common stock and warrants, net	105,761	95,954	—
Proceeds from issuance of ESPP shares	148	30	—
Proceeds from warrant exercises	575	37	—
Payment of financing costs	(596)	(20)	—
Principal payments on secured term debt	(6,574)	—	(380)
Proceeds from issuance of common stock in IPO, net	—	—	69,750
Payments of initial public offering costs	—	—	(3,293)
Payment of financing costs related to debt exchange agreements	—	—	(534)
Repayment of related party loans	—	—	(3,000)
Proceeds from issuance of Class E redeemable convertible units, net	—	—	5,500
Proceeds from exercise of stock options	—	—	41
Net cash provided by financing activities	99,314	96,001	68,084
Net increase in cash, cash equivalents and restricted cash	27,223	31,424	14,595
Cash, cash equivalents and restricted cash, beginning of period	69,633	38,209	23,614
Cash, cash equivalents and restricted cash, end of period	$ 96,856	$ 69,633	$ 38,209
Components of cash, cash equivalents, and restricted cash			
Cash and cash equivalents	94,740	67,517	36,093
Restricted cash	2,116	2,116	2,116
Total cash, cash equivalents, and restricted cash	96,856	69,633	38,209
Supplemental cash flow disclosures:			
Cash paid for interest	$ 3,591	$ 3,689	$ 3,723
Cash paid for taxes	—	356	339
Non-cash investing and financing activities:			
Capitalized lease obligations	32	208	230
Beneficial conversion feature on convertible preferred stock	402	384	7,660
Accretion of dividends on convertible preferred stock	1,609	1,534	642
Fair value of warrants issued in private placement	—	1,651	—
Fair value of modification to lender warrants	111	908	—
Cumulative effect of change in accounting principle - ASC 606 adoption	24,017	—	—
Units issued in settlement of obligation	—	—	11,725
Unpaid financing/offering costs	—	—	56
Cost method investment in affiliate	—	—	1,242
Beneficial conversion feature on Class E units	—	—	13,431
Conversion of Class E units into common stock	—	—	83,628
Conversion of convertible debt into common stock	—	—	176,615
Conversion of convertible debt into convertible preferred stock	—	—	30,000
Reclassification of warrants from liability to equity	—	—	1,716

See accompanying notes to consolidated financial statements

Kadmon Holdings, Inc. and Subsidiaries

Notes to consolidated financial statements

1. Organization

Nature of Business

Kadmon Holdings, Inc. (together with its subsidiaries, "Kadmon" or "Company") is a fully integrated biopharmaceutical company engaged in the discovery, development and commercialization of small molecules and biologics to address significant unmet medical needs, with a near-term clinical focus on autoimmune, inflammatory and fibrotic diseases as well as immuno-oncology. The Company leverages its multi-disciplinary research and clinical development team members to identify and pursue a diverse portfolio of novel product candidates, both through in-licensing products and employing its small molecule and biologics platforms. By retaining global commercial rights to its lead product candidates, the Company believes that it has the ability to develop these candidates while maintaining flexibility for commercial and licensing arrangements. The Company expects to continue to progress its clinical candidates and have further clinical trial events throughout 2019.

Corporate Conversion and Initial Public Offering

On July 26, 2016, in connection with the pricing of the Company's initial public offering ("IPO"), Kadmon Holdings, LLC filed a certificate of conversion, whereby Kadmon Holdings, LLC effected a corporate conversion from a Delaware limited liability company to a Delaware corporation and changed its name to Kadmon Holdings, Inc. As a result of the corporate conversion, accumulated deficit was reduced to zero on the date of the corporate conversion, and the corresponding amount was credited to additional paid-in capital. In connection with this corporate conversion, the Company filed a certificate of incorporation and adopted bylaws, all of which were previously approved by the Company's board of directors and stockholders. Pursuant to the Company's certificate of incorporation, the Company is authorized to issue up to 200,000,000 shares of common stock $0.001 par value per share and 10,000,000 shares of preferred stock $0.001 par value per share. All references in the audited consolidated financial statements to the number of shares and per-share amounts of common stock have been retroactively restated to reflect this conversion.

On August 1, 2016, the Company completed its IPO whereby it sold 6,250,000 shares of common stock at $12.00 per share. The aggregate net proceeds received by the Company from the offering were $66.0 million, net of underwriting discounts and commissions of $5.3 million and offering expenses of $3.7 million. Upon the closing of the IPO, 45,078,666 shares of common stock were outstanding, which includes 19,034,467 shares of common stock as a result of the conversion of the Company's Senior Convertible Term Loan and Second Lien Convert concurrent with the closing of the IPO. The shares began trading on the New York Stock Exchange on July 27, 2016 under the symbol "KDMN."

Liquidity

The Company had an accumulated deficit of $269.6 million, working capital of $74.9 million, and cash and cash equivalents of $94.7 million at December 31, 2018. Net cash used in operating activities was $71.2 million, $64.1 million and $53.0 million for the years ended December 31, 2018, 2017 and 2016. In June 2018, the Company raised $113.2 million ($105.8 million net of $7.4 million of underwriting discounts and other offering expenses payable by the Company) from the issuance of 34,303,030 shares of common stock at a price of $3.30 per share ("2018 Public Offering").

The Company entered into a Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor") in August 2017 under which the Company may sell up to $40.0 million in shares of its common stock in one or more placements at prevailing market prices for its common stock (the "ATM Offering"). Any such sales would be effected pursuant to the Company's registration statement on Form S-3 (File No. 333-222364), declared effective by the SEC on January 10, 2018. As of December 31, 2018, the Company had not sold any shares of common stock under the ATM Offering. Subsequent to December 31, 2018 and through January 9, 2019, the Company sold 13,778,705 shares of common stock at a weighted average price of $2.17 per share through the ATM Offering Program and received total gross proceeds of $29.9 million ($29.0 million net of $0.9 million of commissions payable by the Company) (Note 20). The Company's existing cash and cash equivalents are expected to enable it to advance its planned Phase 2 clinical studies for KD025 and advance certain of its other pipeline product candidates and provide for other working capital purposes.

On June 12, 2018, the Company entered into the fourth amendment to the 2015 Credit Agreement (the "Fourth Amendment") (Note 5). Pursuant to the Fourth Amendment, the maturity date of the 2015 Credit Agreement was extended to August 31, 2018 (the "Extension Period"). The Company repaid $4.7 million of the outstanding principal on June 18, 2018, representing all amounts due under the 2015 Credit Agreement to GoldenTree Credit Opportunities, LP, GoldenTree Credit Opportunities, Ltd, GoldenTree Insurance Fund Series Interests of the SALI Multi-Series Fund, LP, GT NM, LP, and San

Bernardino County Employees' Retirement Association. All other material terms of the 2015 Credit Agreement remained the same during the Extension Period, including a minimum liquidity covenant.

On August 15, 2018, the Company entered into the fifth amendment to the 2015 Credit Agreement (the "Fifth Amendment") (Note 5). Pursuant to the Fifth Amendment, the maturity date of the Credit Agreement was extended to July 1, 2020 and principal payments have been deferred until January 31, 2020. Beginning on January 31, 2020, equal principal payments of $750,000 per month will be due until the maturity date. Additionally, the parties amended certain covenants under the 2015 Credit Agreement to require the Company to meet certain developmental milestones by December 31, 2019. All other material terms of the 2015 Credit Agreement remain the same, including a minimum liquidity covenant. No assurances can be given that the Company will be able to comply with these covenants, meet the development milestones or that the Company will be able to amend the 2015 Credit Agreement to further extend the maturity date or refinance this debt on or before the maturity date.

Management's plans include continuing to finance operations through the issuance of additional equity securities and increasing the commercial portfolio through the development of the current pipeline or through strategic collaborations. Any transactions which occur may contain covenants that restrict the ability of management to operate the business or may have rights, preferences or privileges senior to the Company's common stock and may dilute current stockholders of the Company.

Going Concern

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America, which contemplate continuation of the Company as a going concern. The Company has not established a source of revenues sufficient to cover its operating costs, and as such, have been dependent on funding operations through the issuance of debt and sale of equity securities. Since inception, the Company has experienced significant loses and incurred negative cash flows from operations. The Company expects to incur further losses over the next several years as it develops its business. The Company has spent, and expects to continue to spend, a substantial amount of funds in connection with implementing its business strategy, including its planned product development efforts, preparation for its planned clinical trials, performance of clinical trials and its research and discovery efforts.

The Company's cash and cash equivalents at December 31, 2018 was $94.7 million and during January 2019, the Company raised $29.0 million in net proceeds through the ATM Offering. As such, should the Company meet its development milestones contained in the 2015 Credit Agreements, the cash and cash equivalents available at February 2019 are expected to fund operations into the second quarter of 2020 and enable the Company to advance its planned Phase 2 clinical studies for KD025, advance certain of its other pipeline product candidates, including KD033 and KD045, and provide for other working capital purposes. Although cash and cash equivalents will be sufficient to fund the foregoing, cash and cash equivalents will not be sufficient to enable the Company to meet its long-term expected plans, including commercialization of clinical pipeline products, if approved, or initiation or completion of future registrational studies. Following the completion of its ongoing and planned clinical trials, the Company will likely need to raise additional capital to fund continued operations, starting in the second quarter of 2020. The Company has no commitments for any additional financing and may not be successful in its efforts to raise additional funds or achieve profitable operations. Any amounts raised will be used for further development of the Company's product candidates, to provide financing for marketing and promotion, to secure additional property and equipment, and for other working capital purposes.

If the Company is unable to obtain additional capital (which is not assured at this time), its long-term business plan may not be accomplished and the Company may be forced to curtail or cease operations. Further, the 2015 Credit Agreement contains certain developmental milestones that must be achieved by December 31, 2019, which are considered to be outside of the Company's control. As such, if achievement of the developmental milestones does not occur as anticipated by December 31, 2019, the Company may need to use cash and cash equivalents to fund certain repayment commitments as any such non-compliance could, under the exclusive remedies set forth in the 2015 Credit Agreement, trigger a termination of the Commitments (as defined in the 2015 Credit Agreement) or a declaration by the Lender that the Loan (as defined in the 2015 Credit Agreement) be due and payable in whole or part, together with any applicable fees and/or interest thereon. In the event that the Company had to repay the outstanding principle under the 2015 Debt Agreement, the Company would likely need to raise additional capital to fund continued operations. These factors individually and collectively raise substantial doubt about the Company's ability to continue as a going concern. The accompanying financial statements do not include any adjustments or classifications that may result from the possible inability of the Company to continue as a going concern. The explanatory paragraph regarding the Company's ability to continue as a going concern in the report and opinion of the Company's independent registered public accounting firm for the year ended December 31, 2018 is an event of default under the 2015 Credit Agreement. The Company entered into a sixth waiver agreement to the 2015 Credit Agreement in March 2019 under which the lenders under the 2015 Credit Agreement agreed to refrain from exercising certain rights under the 2015 Credit Agreement, including the declaration of a default and to forbear from acceleration of any repayment rights with respect to existing covenants.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company operates in one segment considering the nature of the Company's products and services, class of customers, methods used to distribute the products and the regulatory environment in which the Company operates.

Principles of Consolidation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). The consolidated financial statements include the accounts of Kadmon Holdings, Inc. and its domestic and international subsidiaries, all of which are wholly owned.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements. Actual results could differ from those estimates.

Company Valuation

To estimate certain expenses and record certain transactions, it was necessary for the Company to estimate the fair value of its membership units. Given the absence of a public trading market prior to the IPO, and in accordance with the American Institute of Certified Public Accountants' Practice Guide, "Valuation of Privately-Held-Company Equity Securities Issued as Compensation", the Company exercised reasonable judgment and considered numerous objective and subjective factors to determine its best estimate of the fair value of its membership units (Note 3).

Revenue Recognition

The Company adopted FASB ASC 606, Revenue from Contracts with Customers ("ASC 606"), on January 1, 2018 using the modified retrospective method for all contracts not completed as of the date of adoption – i.e., by recognizing the cumulative effect of initially applying ASC 606 as an adjustment to the opening balance of stockholders' equity at January 1, 2018. For contracts that were modified before the effective date, the Company reflected the aggregate effect of all modifications when identifying performance obligations and allocating transaction price in accordance with practical expedient ASC 606-10-65-1-(f)-4. The reported results for 2018 reflect the application of ASC 606 guidance while the reported results for 2017 and 2016 were prepared under the guidance of ASC 605, Revenue Recognition ("ASC 605"), which is also referred to herein as the "previous guidance". The adoption of ASC 606 represents a change in accounting principle that will more closely align revenue recognition with the delivery of the Company's services and will provide financial statement readers with enhanced disclosures. Therefore, the comparative information prior to January 1, 2018 has not been adjusted and continues to be reported under ASC 605. The details of significant changes and quantitative impact of the changes are set out below.

The Company recognizes revenue in accordance with ASC 606, the core principle of which is that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled to receive in exchange for those goods or services. To achieve this core principle, five basic criteria must be met before revenue can be recognized: (1) identify the contract with a customer; (2) identify the performance obligations in the contract; (3) determine the transaction price; (4) allocate the transaction price to performance obligations in the contract; and (5) recognize revenue when or as the Company satisfies a performance obligation.

Disaggregation of Revenue

The following table summarizes revenue from contracts with customers for the year ended December 31, 2018 (in thousands):

	Year Ended December 31, 2018
Product sales	$ 691
Other revenue	705
Total revenue	$ 1,396

Product Sales

The Company markets and distributes products in a variety of therapeutic areas, including ribavirin products used as part of a combination treatment for chronic HCV infection (Ribasphere RibaPak and Ribasphere) and tetrabenazine for the treatment of chorea associated with Huntington's disease. These contracts typically include a single promise to deliver a fixed amount of product to the customer with payment due within 30 days of shipment. Revenues are recognized when control of the promised goods is transferred to the customer, in an amount that reflects the consideration the Company expects to be entitled to in exchange for those goods.

As is typical in the pharmaceutical industry, gross product sales are subject to a variety of deductions, primarily representing rebates, chargebacks, returns, and discounts to government agencies, wholesalers, and managed care organizations. These deductions represent management's best estimates of the related reserves and, as such, judgment is required when estimating the impact of these sales deductions on gross sales for a reporting period. If estimates are not representative of the actual future settlement, results could be materially affected.

Other Revenue

The other revenue generated by the Company is primarily related to the transition services agreement and sublease agreement with MeiraGTx Holdings plc ("MeiraGTx") (Note 10). The Company performed various professional services under the transition services agreement that support MeiraGTx. The Company recognizes revenue related to transition services and sublease agreements as they are performed.

Contract Balances

The timing of revenue recognition may differ from the timing of invoicing to customers. Accounts receivable are recorded at the invoiced amount, net of an allowance for doubtful accounts. A receivable is recognized in the period we deliver goods or provide services or when our right to consideration is unconditional. The Company has not recognized any assets for costs to obtain or fulfill a contract with a customer as of December 31, 2018.

Financial Statement Impact of Adopting ASC 606

The Company adopted ASC 606 using the modified retrospective method. The cumulative effect of applying the new guidance to all contracts with customers that were not completed as of January 1, 2018 was recorded as an adjustment to accumulated deficit as of the adoption date as shown in the following table (in thousands):

	As Reported December 31, 2017	Adjustments AbbVie Agreement	Adjusted January 1, 2018
Cash, cash equivalents, and restricted cash	$ 69,633	$ —	$ 69,633
Accounts receivable, net	1,186	—	1,186
Inventories, net	201	—	201
Prepaid expenses and other current assets	1,109	—	1,109
Fixed assets, net	4,292	—	4,292
Goodwill	3,580	—	3,580
Investments at cost	3,542	—	3,542
Other noncurrent assets	9	—	9
Total assets	$ 83,552	$ —	$ 83,552
Accounts payable and accrued expenses	$ 16,585	$ —	$ 16,585
Fair market value of financial instruments - current	1,952	—	1,952
Secured term debt - current	33,707	—	33,707
Deferred revenue, current	4,400	(4,400)	—
Deferred revenue, long term	19,617	(19,617)	—
Other long term liabilities	5,533	—	5,533
Total liabilities	81,794	(24,017)	57,777
Common stock, preferred stock, and additional paid-in capital	239,155	—	239,155
Accumulated deficit	(237,397)	24,017	(213,380)
Total stockholders' equity	1,758	24,017	25,775
Total liabilities and stockholders' equity	$ 83,552	$ —	$ 83,552

The year-end condensed balance sheet data was derived from audited consolidated financial statements, but does not include all disclosures required by GAAP.

Commercial Partnership Agreement with AbbVie Inc. ("AbbVie")

On June 17, 2013, the Company entered into a series of agreements with AbbVie related to certain of the Company's ribavirin products. Pursuant to an asset purchase agreement, as amended, the Company sold marketing authorizations and related assets for ribavirin in certain countries outside the United States. The Company received upfront payments totaling $64.0 million, and could have received additional contingent payments totaling $51.0 million based on the achievement of certain milestones. The Company did not earn any such milestones during the years ended December 31, 2018, 2017 and 2016.

Of the $64.0 million upfront payments, $44.0 million was considered allocable to the domestic licensing arrangement and was recorded as deferred revenue to be recognized over the 10 year term of the agreement. The Company recognized $4.4 million of the upfront consideration as license revenue during each of the years ended December 31, 2017, and 2016. At December 31, 2017, $24.0 million was recorded as deferred revenue, of which $4.4 million was short-term. The Company is required to supply ribavirin products, maintain the marketing authorization for certain ribavirin products and maintain the intellectual property for Ribasphere and RibaPak through the term of the agreements ending December 31, 2020.

The Company's agreements with AbbVie provide AbbVie with access to various forms of intellectual property, as well as supply of product. Under the previous guidance, certain of the upfront payments under the agreements were considered allocable to a 10-year domestic license arrangement and, as a result, the associated revenue was previously deferred and recognized straight line over the life of the agreements. Under ASC 606, the Company has determined that two distinct performance obligations under the domestic license agreement exist, both of which are considered to be completed as of the date of adoption. No other material rights or enforceable rights or obligations exist under the AbbVie agreements. In conjunction with the January 1, 2018 adoption of ASC 606, the Company adjusted its accumulated deficit by $24.0 million, reflecting the recognition of $24.0 million of deferred revenue related to the domestic license agreement with AbbVie.

Income Taxes

The adoption of ASC 606 primarily resulted in an acceleration of revenue as of January 1, 2018, which in turn generated additional deferred tax liabilities that ultimately reduced the Company's net deferred tax asset position. As the Company fully reserves its net deferred tax assets in the jurisdictions impacted by the adoption of ASC 606, this impact was offset by a corresponding reduction to the valuation allowance (Note 19).

Impact of New Revenue Guidance on Financial Statement Line Items

The following table compares the reported condensed consolidated balance sheet as of December 31, 2018 to the pro-forma amounts had the previous guidance been in effect (in thousands):

	As Reported December 31, 2018	Adjustments	Balances without adoption of ASC 606 December 31, 2018	December 31, 2017
Cash, cash equivalents, and restricted cash	$ 96,856	$ —	$ 96,856	$ 69,633
Accounts receivable, net	1,690	—	1,690	1,186
Inventories, net	925	—	925	201
Investment, equity securities	34,075	—	34,075	—
Prepaid expenses and other current assets	1,581	—	1,581	1,109
Fixed assets, net	3,654	—	3,654	4,292
Goodwill	3,580	—	3,580	3,580
Investment, at cost	2,300	—	2,300	3,542
Other noncurrent assets	—	—	—	9
Total assets	$ 144,661	$ —	$ 144,661	$ 83,552
Accounts payable and accrued expenses	$ 23,494	$ —	$ 23,494	$ 16,585
Fair market value of financial instruments - current	524	—	524	1,952
Secured term debt - current	—	—	—	33,707
Deferred revenue, current	—	4,400	4,400	4,400
Deferred revenue, long term	—	15,217	15,217	19,617
Other long term liabilities	4,752	—	4,752	5,533
Secured term debt – net of current portion and discount	27,480	—	27,480	—
Total liabilities	56,250	19,617	75,867	81,794
Common stock, preferred stock, and additional paid-in capital	358,054	—	358,054	239,155
Accumulated deficit	(269,643)	(19,617)	(289,260)	(237,397)
Total stockholders’ equity (deficit)	88,411	(19,617)	68,794	1,758
Total liabilities and stockholders’ equity	$ 144,661	$ —	$ 144,661	$ 83,552

The year-end condensed balance sheet data was derived from audited financial statements, but does not include all disclosures required by GAAP.

Total reported liabilities were $19.6 million less than the pro-forma balance sheet, which assumes the Company had continued to recognize revenues under ASC 605 as of December 31, 2018. This is due to the recognition of the deferred revenue related to the AbbVie agreement upon adoption of ASC 606.

The following summarizes the significant changes on the Company’s condensed consolidated statement of operations for the year ended December 31, 2018 as a result of the adoption of ASC 606 on January 1, 2018, which assumes the Company had continued to recognize revenues under ASC 605 (in thousands, except share and per share amounts):

	As Reported Year Ended December 31, 2018	Adjustments	Balances without adoption of ASC 606 December 31, 2018	Year Ended December 31, 2017	Year Ended December 31, 2016
Net sales	$ 691	$ —	$ 691	$ 5,257	$ 18,514
License and other revenue	705	4,400	5,105	7,007	7,541
Total revenue	1,396	4,400	5,796	12,264	26,055
Cost of sales and write-down of inventory	682	—	682	2,986	3,870
Research and development	48,966	—	48,966	40,777	35,840
Selling, general and administrative	37,644	—	37,644	37,057	105,880

Gain on settlement on payable	—	—	—	—	(4,131)
Total other expense (income)	(31,120)	—	(31,120)	11,339	93,009
Income tax expense (benefit)	(524)	—	(524)	(121)	342
Net income (loss) attributable to common stockholders	$ (54,252)	$ 4,400	$ (49,852)	$ (79,774)	$ (208,755)
Deemed dividend on convertible preferred stock	2,011	—	2,011	1,918	21,733
Net income (loss) attributable to common stockholders	$ (56,263)	$ 4,400	$ (51,863)	$ (81,692)	$ (230,488)
Basic and diluted net income (loss) per share of common stock	$ (0.58)	$ 0.05	$ (0.53)	$ (1.42)	$ (9.74)
Weighted average basic and diluted shares of common stock outstanding	97,609,000	97,609,000	97,609,000	57,405,331	23,674,512

The year-end condensed statement of operations data was derived from audited financial statements, but does not include all disclosures required by GAAP.

The Company's adoption of ASC 606 accelerated the recognition of revenue that was previously deferred under the AbbVie domestic license agreement, resulting in a cumulative effect adjustment to accumulated deficit on January 1, 2018. Therefore no further revenue will be recognized under the AbbVie domestic license agreement. Revenue under this agreement had previously been recognized under license and other revenue.

The adoption of ASC 606 had no impact on the Company's cash flows from operations. The aforementioned adjustments resulted in offsetting shifts in cash flows to net loss and change in deferred revenue.

Transaction Price Allocated to Future Performance Obligations

ASC 606 requires that the Company disclose the aggregate amount of transaction price that is allocated to performance obligations that have not yet been satisfied as of December 31, 2018. The guidance provides certain practical expedients that limit this requirement. The Company has various contracts that meet the following practical expedients provided by ASC 606:

1. The performance obligation is part of a contract that has an original expected duration of one year or less.

2. Revenue is recognized from the satisfaction of the performance obligations in the amount billable to the customer.

3. The variable consideration is allocated entirely to a wholly unsatisfied performance obligation or to a wholly unsatisfied promise to transfer a distinct good or service that forms part of a single performance obligation.

The Company does not have any performance obligations that have not yet been satisfied as of December 31, 2018 and therefore there is no transaction price allocated to future performance obligations under ASC 606.

Foreign Revenue

Foreign product sales represented approximately 1.4%, 26.9% and 8.6% of total product sales for the years ended December 31, 2018, 2017 and 2016, respectively, the majority of which were to the Netherlands and Ireland.

Sales Returns Reserve

Revenue is recognized net of sales returns, which are estimated using the Company's historical experience. The sales returns reserve was less than $0.1 million and $0.6 million at December 31, 2018 and 2017, respectively. Sales returns expense was $0.3 million, $0.6 million and $0.9 million for the years ended December 31, 2018, 2017 and 2016, respectively. Actual results could differ from original estimates resulting in future adjustments to revenue.

Reserve for Wholesaler Chargebacks and Rebates

The Company maintains a reserve for wholesaler chargebacks and rebates to properly reflect the realizable value of accounts receivable. A chargeback represents a contractual allowance provided by the Company to its wholesalers for any variances between wholesale and lower retail prices of the Company's pharmaceutical products. The Company estimates the reserve for wholesaler chargebacks based on wholesaler inventory levels, contract prices and historical experience. Rebate reserves represent contractual allowances based on specific customer contracts. The rebate allowance is estimated as a percentage of specific customer sales. There was no reserve for wholesales chargebacks and rebates at December 31, 2018, while the reserve for wholesaler chargebacks and rebates was $0.2 million at December 31, 2017. Wholesaler chargebacks and rebates expense was less than $0.1 million, $0.3 million and $0.5 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Rebates Payable

The Company issues rebates related to various government programs and buying groups. In these instances, the rebates are paid in cash to the party managing the discount buying program. The estimated rebates earned but unpaid was $0.2 million and $0.3 million at December 31, 2018 and 2017, respectively. Such amounts have been included in accounts payable on the Company's consolidated balance sheets. Rebates expense was less than $0.1 million, $0.7 million and $0.8 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Shipping and Handling Costs

Shipping and handling costs for raw materials and finished goods prior to their sale are classified in cost of sales. Freight charges for shipments to customers are not billed to customers and are included in selling, general and administrative expenses when incurred and were $0.1 million, $0.1 million and $0.2 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Foreign Currencies

The consolidated financial statements are presented in U.S. dollars, the reporting currency of the Company. Gains or losses on transactions denominated in a currency other than the Company's functional currency, which arise as a result of changes in foreign currency exchange rates, are recorded in other income on the consolidated statements of operations. The transaction gains (loss) were less than $0.1 million for each of the years ended December 31, 2018, 2017 and 2016.

Share-based Compensation Expense

The Company recognizes share-based compensation expense in accordance with FASB ASC Topic 718, "Stock Compensation" ("ASC 718"), for all share-based awards made to employees and board members based on estimated fair values.

ASC 718 requires companies to measure the cost of employee services incurred in exchange for the award of equity instruments based on the estimated fair value of the share-based award on the grant date. The expense is recognized over the requisite service period.

All share-based awards to non-employees are accounted for in accordance with FASB ASC Topic 505-50, "Equity Based Payments to Non-Employees," where the value of unit compensation is based on the measurement date, as determined at either a) the date at which a performance commitment is reached, or b) the date at which the necessary performance to earn the equity instruments is complete.

The Company uses a Black-Scholes option-pricing model to value the Company's option awards. Using this option-pricing model, the fair value of each employee and board member award is estimated on the grant date. The fair value is expensed on a straight-line basis over the vesting period. The option awards generally vest pro-rata annually. The expected volatility assumption is based on the volatility of the share price of comparable public companies. The expected life is determined using the "simplified method" permitted by Staff Accounting Bulletin Numbers 107 and 110 (the midpoint between the term of the agreement and the weighted average vesting term). The risk-free interest rate is based on the implied yield on a U.S. Treasury security at a constant maturity with a remaining term equal to the expected term of the option granted. The dividend yield is zero, as the Company has never declared a cash dividend.

In the fourth quarter of 2016, the Company adopted ASU 2016-09, "*Compensation—Stock Compensation*". ASU 2016-09 requires that certain other amendments relevant to the Company be applied using a modified-retrospective transition method by means of a cumulative-effect adjustment to accumulated deficit as of the beginning of the period in which the guidance is adopted. As a result of adopting ASU 2016-09 during the three months ended December 31, 2016, the Company adjusted accumulated deficit for amendments related to an entity-wide accounting policy election to recognize share-based award forfeitures only as they occur rather than an estimate by applying a forfeiture rate. The Company recorded a $2.0 million charge to accumulated deficit as of January 1, 2016 and an associated credit to additional paid-in capital for previously unrecognized share-based compensation expense as a result of applying this policy election. The Company also recorded $0.8 million in additional share-based compensation expense during the fourth quarter of 2016 as a result of applying estimated forfeitures recorded during the nine months ended September 30, 2016.

ASU 2016-09 also requires the recognition of the income tax effects of awards in the consolidated statement of operations when the awards vest or are settled, thus eliminating addition paid-in capital pools. The Company elected to adopt the amendments related to the presentation of excess tax benefits on the consolidated statement of cash flows using a prospective transition method.

Modification of Awards

A change in any of the terms or conditions of the awards is accounted for as a modification of the award. Incremental compensation cost is measured as the excess, if any, of the fair value of the modified award over the fair value of the original award immediately before its terms are modified, measured based on the fair value of the awards and other pertinent factors at the modification date. For vested awards, the Company recognizes incremental compensation cost in the period the modification occurs. For unvested awards, if the award is probable of vesting both before and after the change, the Company recognizes the sum of the incremental compensation cost and the remaining unrecognized compensation cost for the original award on the modification date over the remaining requisite service period. If the fair value of the modified award is lower than the fair value of the original award immediately before modification, the minimum compensation cost the Company recognizes is the cost of the original award.

Research and Development

Innovation is critical to the success of the Company, and drug discovery and development are time-consuming, expensive and unpredictable. The Company has built a pipeline of therapeutic candidates in all stages of development. The focus is on serious diseases where there is a great need and opportunity for innovative medicines. Product candidates and development strategies contemplate both immediate possibilities in medicine, such as reducing toxicity or addressing certain disease resistance and mutation, and future possibilities and medical needs. Included in research and development expense are personnel related costs, expenditures for laboratory equipment and consumables, payments made pursuant to licensing and acquisition agreements, and the cost of conducting clinical trials. Expenses incurred associated with conducting clinical trials include, but are not limited to, dosing of patients with clinical drug candidates, assistance from third party consultants and other industry experts, accumulation and interpretation of data on drug safety and efficacy, and manufacturing of active pharmaceutical ingredients and placebos for use within the clinical trial.

The Company has entered into agreements with third parties to acquire technologies and pharmaceutical product candidates for development (Note 11). Such agreements generally require an initial payment by the Company when the contract is executed, and additional payments upon the achievement of certain milestones. Additionally, the Company may be obligated to make future royalty payments in the event the Company commercializes the pharmaceutical product candidate and achieves a certain sales volume. In accordance with FASB ASC Topic 730-10-55, “Research and Development”, expenditures for research and development, including upfront licensing fees and milestone payments associated with products that have not yet been approved by the FDA, are charged to research and development expense as incurred. Future contract milestone payments will be recognized as expense when achievement of the milestone is determined to be probable. Once a product candidate receives regulatory approval, subsequent license payments are recorded as an intangible asset.

Research and development expense was $49.0 million, $40.8 million and $35.8 million during the years ended December 31, 2018, 2017 and 2016, respectively.

Income Taxes

The Company accounts for income taxes in accordance with the asset and liability method of accounting for income taxes prescribed by FASB ASC Topic 740, “Accounting for Income Taxes” (“ASC 740”). Under the asset and liability method of ASC 740, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax basis and operating loss and tax credit carry-forwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to the taxable income in the years in which those temporary differences are expected to be recovered or settled. Under ASC 740, the effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment dates.

The Company follows FASB ASC Topic 740-10, “Accounting for Uncertainty in Income Taxes”, which prescribes a recognition threshold and measurement attribute for financial statement recognition and measurement of a tax position taken, or expected to be taken, in a tax return. For those benefits to be recognized, a tax position must be more likely than not to be sustained upon examination by taxing authorities. At December 31, 2018 and 2017, the Company had no material uncertain tax positions to be accounted for in the financial statements. The Company recognizes interest and penalties, if any, related to unrecognized tax benefits in interest expense.

Cash and Cash Equivalents

Cash and cash equivalents are comprised of deposits at major financial banking institutions and highly liquid investments with an original maturity of three months or less at the date of purchase. At times, cash balances deposited at

major financial banking institutions exceed the federally insured limit. The Company regularly monitors the financial condition of the institutions in which it has depository accounts and believes the risk of loss is minimal.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentration of credit risk consist of cash and cash equivalents. Cash and cash equivalents are held at financial institutions in the United States. The Company is exposed to credit risk in the event of default by the financial institution to the extent that cash and cash equivalent balances recorded in the balance sheets are in excess of the amounts that are insured by the Federal Deposit Insurance Corporation. The Company has not experienced any losses on its deposits since inception, and management believes that minimal credit risk exists with respect to these financial institutions.

Restricted Cash

The Company has a lease agreement for the premises it occupies in New York. A secured letter of credit in lieu of a lease deposit totaling $2.0 million is secured by restricted cash in the same amount at December 31, 2018 and 2017. The secured letter of credit will remain in place for the life of the related lease, expiring in October 2024 (Note 15). The Company also has a lease agreement for the premises it occupies in Massachusetts. A secured letter of credit in lieu of a lease deposit totaling approximately $0.1 million is secured by restricted cash in the same amount at December 31, 2018 and 2017. The secured letter of credit will remain in place for the life of the related lease, expiring in April 2023 (Note 15).

Allowance for Doubtful Accounts

The Company reviews the collectability of accounts receivable based on an assessment of historical experience, current economic conditions, and other collection indicators. The Company had no allowance for doubtful accounts at December 31, 2018, while the Company recorded an allowance for doubtful accounts of $0.7 million at December 31, 2017. Adjustments to the allowance for doubtful accounts are recorded to selling, general and administrative expenses, and amounted to less than $0.1 million for each the years ended December 31, 2018, 2017 and 2016. When accounts are determined to be uncollectible they are written off against the reserve balance and the reserve is reassessed. When payments are received on reserved accounts they are applied to the customer’s account and the reserve is reassessed.

Inventories

Inventories are stated at the lower of cost or market (on a first-in, first-out basis) using standard costs. Standard costs include an allocation of overhead rates, which include those costs attributable to managing the supply chain and are evaluated regularly. Variances are expensed as incurred.

Investment in Equity Securities

Equity securities consist of investments in common stock of companies traded on public markets (Note 10). These shares are carried on the Company’s balance sheet at fair value based on the closing price of the shares owned on the last trading day before the balance sheet of this report. Fluctuations in the underlying bid price of the shares result in unrealized gains or losses. In accordance with FASB ASC 321, Investments – Equity Securities (“ASC 321”), the Company recognizes these fluctuations in value as other expense (income). For investments sold, the Company recognizes the gains and losses attributable to these investments as realized gains or losses in other expense (income).

The Company’s total investment balance in equity securities totaled $34.1 million at December 31, 2018. The Company did not maintain any investments in equity securities at December 31, 2017.

Investments

The Company follows FASB ASC Topic 323, “Investments—Equity Method and Joint Ventures” (“ASC 323”), in accounting for its investment in a joint venture. In the event the Company’s share of the joint venture’s net losses reduces the Company’s investment to zero, the Company will discontinue applying the equity method and will not provide for additional losses unless the Company has guaranteed obligations of the joint venture or is otherwise committed to provide further financial support for the joint venture. If the joint venture subsequently reports net income, the Company will resume applying the equity method only after its share of that net income equals the share of net losses not recognized during the period the equity method was suspended.

The Company follows FASB ASC Topic 325, “Investments—Other” (“ASC 325”), in accounting for its investment in the stock of another company accounted for as cost method investments. In the event further contributions or additional shares are purchased, the Company will increase the basis in the investment. In the event distributions are made or indications exist that the fair value of the investment has decreased below the carrying amount, the Company will decrease

the value of the investment as considered appropriate. The Company's total cost method investment balance totaled $2.3 million and $3.5 million at December 31, 2018 and 2017, respectively.

For all non-consolidated investments, the Company will continually assess the applicability of FASB ASC Topic 810, "Consolidation" ("ASC 810"), to determine if the investments qualify for consolidation. At December 31, 2018 and 2017, no such investments qualified for consolidation (Note 10).

Fixed Assets

Fixed assets are carried at cost less accumulated depreciation and amortization. Depreciated and amortization of fixed assets is calculated using the straight-line method over their estimated useful lives. Leasehold improvements are amortized over the shorter of their estimated useful lives or the lease term, using the straight-line method. Construction-in-progress and software under development are stated at cost and not depreciated. These items are transferred to fixed assets when the assets are placed into service.

When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the balance sheet and any resulting gain or loss is reflected in operations in the period realized. Expenditures for repairs and maintenance, which do not improve or extend the life of the assets, are expensed as incurred.

Goodwill and Intangible Assets

The Company's goodwill relates to the 2010 acquisition of Kadmon Pharmaceuticals, a Pennsylvania limited liability company that was formed in April 2000. Goodwill is not amortized, but rather is assessed for impairment annually or upon the occurrence of an event that indicates impairment may have occurred, in accordance with FASB ASC Topic 350 "Intangibles—Goodwill and Other". No impairment to goodwill was recorded during the years ended December 31, 2018, 2017 and 2016.

Intangible assets with finite useful lives are amortized over the shorter of their estimated useful lives, the estimated period that the assets will generate revenue, or the statutory or contractual term in the case of patents.

Impairment of Long-Lived Assets

Long-lived assets, including fixed assets and definite-lived intangible assets, are evaluated for impairment periodically, or when events or changes in circumstances indicate that the carrying amount of the assets may not be recoverable. When any such impairment exists, a charge is recorded in the statement of operations to adjust the carrying value of the related assets.

The Company performed a trigger analysis over all other long-lived assets at the lowest identifiable level of cash flows and determined that no impairment triggers existed during the years ended December 31, 2018, 2017 and 2016.

Accounting for Leases

The Company recognizes rent expense for operating leases as of the earlier of the possession date or the lease commencement date. Rental expense, inclusive of rent escalations, rent holidays, concessions and tenant allowances are recognized over the lease term on a straight-line basis. See Note 15 for a further discussion of operating leases.

The Company has entered into capital lease agreements for information technology and laboratory equipment. Amortization expense for capital lease agreements is included in depreciation and amortization of fixed assets. As a result of these leases, the Company capitalized less than $0.1 million, $0.2 million and $0.2 million as office equipment and furniture during the years ended December 31, 2018, 2017 and 2016, respectively. The unamortized portion of capital leases totaled $0.1 million and $0.3 million at December 31, 2018 and 2017, respectively.

Accounting for Contingencies

The Company follows the guidance of FASB ASC Topic 450, "Contingencies" ("ASC 450"), in accounting for contingencies. If some amount within a range of loss is probable and appears at the time to be a better estimate than any other amount within the range, that amount shall be expensed. If a loss is probable, and no amount within the range is a better estimate than any other amount, the estimated minimum amount in the range shall be expensed.

Fair Value of Financial Instruments

The Company follows the provisions of FASB ASC Topic 820, "Fair Value Measurements and Disclosures" ("ASC 820"). This pronouncement defines fair value, establishes a framework for measuring fair value under GAAP and requires expanded disclosures about fair value measurements. ASC 820 emphasizes that fair value is a market-based measurement, not an entity-specific measurement, and defines fair value as the price to sell an asset or transfer a liability in an orderly transaction between market participants at the measurement date. ASC 820 discusses valuation techniques, such as the market approach (comparable market prices), the income approach (present value of future income or cash flow) and the cost approach (cost to replace the service capacity of an asset or replacement cost). These valuation techniques are based upon observable and unobservable inputs. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect the Company's market assumptions. ASC 820 utilizes a fair value hierarchy that prioritizes inputs to fair value measurement techniques into three broad levels. The following is a brief description of those three levels:

- Level 1: Observable inputs such as quoted prices for identical assets or liabilities in active markets.
- Level 2: Observable inputs other than quoted prices that are directly or indirectly observable for the asset or liability, including quoted prices for similar assets or liabilities in active markets; quoted prices for similar or identical assets or liabilities in markets that are not active; and model-derived valuations whose inputs are observable or whose significant value drivers are observable.
- Level 3: Unobservable inputs that reflect the reporting entity's own assumptions.

The fair value of cash and cash equivalents, accounts receivable and accounts payable approximate their carrying amounts due to their short term nature (Note 6).

Loan Modifications and Extinguishments

The Company follows the provisions of FASB ASC Subtopic 470-50 "Debt Modifications and Extinguishments" ("ASC 470-60") and ASC Subtopic 470-60, "Troubled Debt Restructurings by Debtors" ("ASC 470-60"). Under ASC 470-50, an exchange of debt instruments between or a modification of a debt instrument by a debtor and a creditor in a nontroubled debt situation is deemed to have been accomplished with debt instruments that are substantially different if the present value of the cash flows under the terms of the new debt instrument is at least 10 percent different from the present value of the remaining cash flows under the terms of the original instrument. If the terms of a debt instrument are changed or modified and the cash flow effect on a present value basis is less than 10 percent, the debt instruments are not considered to be substantially different, except in the following two circumstances:

- A modification or an exchange affects the terms of an embedded conversion option, from which the change in the fair value of the embedded conversion option (calculated as the difference between the fair value of the embedded conversion option immediately before and after the modification or exchange) is at least 10 percent of the carrying amount of the original debt instrument immediately before the modification or exchange.
- A modification or an exchange of debt instruments adds a substantive conversion option or eliminates a conversion option that was substantive at the date of the modification or exchange.

Under ASC 470-60, a restructuring of a debt constitutes a troubled debt restructuring for purposes of this Subtopic if the creditor for economic or legal reasons related to the debtor's financial difficulties grants a concession to the debtor that it would not otherwise consider.

Warrants and Derivative Liabilities

The Company accounts for its derivative financial instruments in accordance with FASB ASC Topic 815, "Derivatives and Hedging" ("ASC 815"). The Company does not have derivative financial instruments that are hedges. ASC 815 establishes accounting and reporting standards requiring that derivative instruments, both freestanding and embedded in other contracts, be recorded on the balance sheet as either an asset or liability measured at its fair value each reporting period. ASC 815 also requires that changes in the fair value of derivative instruments be recognized currently in the results of operations unless specific criteria are met. For embedded features that are not clearly and closely related to the host instrument, are not carried at fair value, and are derivatives, the feature will be bifurcated and recorded as an asset or liability as noted above, unless the exceptions below are not met. Freestanding instruments that do not meet these exceptions will be accounted for in the same manner.

ASC 815 provides an exception—if an embedded derivative or freestanding instrument is both indexed to the company's own stock and classified in stockholders' equity, it can be accounted for in stockholders' equity. If at least one of

the criteria is not met, the embedded derivative or warrant is classified as an asset or liability and recorded to fair value each reporting period through the income statement.

The Company assesses classification of our warrants and embedded features at each reporting date to determine whether a change in classification is required. The Company's accounting for its embedded warrants are explained further in Note 6.

Recent Accounting Pronouncements

In November 2018, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2018-18, *"Collaborative Arrangements (Topic 808): Clarifying the Interaction Between Topic 808 and Topic 606"*, which requires transactions in collaborative arrangements to be accounted for under ASC 606 if the counterparty is a customer for a good or service (or bundle of goods and services) that is a distinct unit of account. The amendments also preclude entities from presenting consideration from transactions with a collaborator that is not a customer together with revenue recognized from contracts with customers. The ASU is effective for annual or interim periods beginning after December 15, 2019. Early adoption is permitted for entities that have adopted ASC 606. The Company is evaluating the impact of adopting this standard.

In August 2018, the FASB issued ASU No. 2018-15, "*Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract (a consensus of the FASB Emerging Issues Task Force)"*, which requires customers in a cloud computing arrangement that is a service contract to follow the internal-use software guidance in Accounting Standards Codification 350-40 to determine which implementation costs to capitalize as assets. This ASU is effective for annual or any interim periods beginning after December 15, 2019. The Company does not expect the standard to have a significant impact on its consolidated financial statements, as the Company's cloud computing contracts are not material.

In June 2018, the FASB issued ASU No. 2018-07, "*Compensation – Stock Compensation"*, which expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees, except for specific exceptions. This ASU is effective for annual or any interim periods beginning after December 15, 2018. The Company does not expect the standard to have a significant impact on its consolidated financial statements, as the fair value of the Company's awards to nonemployees is immaterial.

In May 2017, the FASB issued ASU No. 2017-09, "*Compensation – Stock Compensation"*, which clarifies the guidance about which changes to the terms and conditions of a share-based payments award require an entity to apply modification accounting in Topic 718. This ASU is effective for annual or any interim periods beginning after December 15, 2017. The Company adopted this standard on January 1, 2018, which did not impact the consolidated financial statements as the Company has not modified the terms and conditions of any share-based payments during the year ended December 31, 2018.

In January 2017, the FASB issued ASU No. 2017-04, "*Intangibles – Goodwill and Other"*, which simplifies the subsequent measurement of goodwill by eliminating "Step 2" from the goodwill impairment test. Instead of performing Step 2 to determine the amount of an impairment charge, the fair value of a reporting unit will be compared with its carrying amount and an impairment charge will be recognized for the value by which the carrying amount exceeds the reporting unit's fair value. ASU 2017-04 is effective for annual or any interim goodwill impairment tests in fiscal years beginning after December 15, 2019. Early adoption is permitted for interim or annual goodwill impairment tests performed on testing dates after January 1, 2017. The Company does not expect the standard to have a significant impact on its consolidated financial statements.

In November 2016, the FASB issued ASU No. 2016-18, "*Statement of Cash Flows (Topic 230): Restricted Cash*". This ASU requires that the statement of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents. Entities will also be required to reconcile such total amounts on the balance sheet and disclose the nature of the restrictions. The Company adopted this standard on January 1, 2018, which did not have a significant impact on its consolidated financial statements as the Company's restricted cash balances are immaterial.

In February 2016, the FASB issued ASU No. 2016 02, "Leases" (ASC 842). ASC 842 amends the existing accounting standards for lease accounting, including requiring lessees to recognize most leases on their balance sheet and disclose key information about leasing arrangements. Current GAAP does not require lessees to recognize assets and liabilities related to operating leases on the balance sheet. In July 2018, the FASB issued ASU No. 2018-10, "Codification Improvements to Topic 842, Leases" and ASU 2018-11, "Leases (Topic 842): Targeted Improvements". These ASU's make improvements and provide clarity to several aspects of the guidance in ASC 842. The new standard establishes a right-of-use model (ROU) that requires a lessee to recognize a ROU asset and lease liability on the balance sheet for all leases with a term

longer than 12 months. Leases will be classified as finance or operating, with classification affecting the pattern and classification of expense recognition in the income statement. The new standard is effective for the Company on January 1, 2019, with early adoption permitted. An entity may choose to use either (1) its effective date or (2) the beginning of the earliest comparative period presented in the financial statements as its date of initial application. The Company has adopted the standard effective January 1, 2019 and has chosen to use the effective date as our date of initial application. Consequently, financial information will not be updated and the disclosures required under the new standard will not be provided for dates and periods prior to January 1, 2019. The new standard provides a number of optional practical expedients in transition. The Company has elected to apply the 'package of practical expedients' which allow us to not reassess i) whether existing or expired arrangements contain a lease, ii) the lease classification of existing or expired leases, or iii) whether previous initial direct costs would qualify for capitalization under the new lease standard. The Company has also elected to apply i) the practical expedient which allows us to not separate lease and non-lease components, and (2) the short-term lease exemption for all leases with an original term of less than 12 months, for purposes of applying the recognition and measurements requirements in the new standard. In preparation for adoption of the standard, the Company has implemented internal controls to enable the preparation of financial information including the assessment of the impact of the standard. The adoption of the new standard is expected to result in the recognition of additional lease liabilities of approximately $27.0 million, and right-of-use assets of approximately $23.0 million as of January 1, 2019 related to the Company's operating leases. The Company does not expect that the new standard will have a material impact to the Company's consolidated statement of operations, consolidated statement of cash flows, or to its covenants under the 2015 Credit Agreement.

3. Stockholders' Equity

Conversion Event

The Class B, C and D units were required to automatically convert into Class A units pursuant to the Company's Second Amended and Restated Limited Liability Company Operating Agreement, as amended (the "Operating Agreement") upon certain defined conversion events including, but not limited to, dissolution of the Company or an underwritten IPO of the Company's equity (each, a "Conversion Event"). The Conversion Event occurred on August 1, 2016, upon consummation of the Company's IPO. The valuation of the Company at the Conversion Event was greater than $45.8 million, which resulted in the Class B and C units receiving $41.7 million of the proceeds of the Conversion Event in the form of equivalent Class A units. The Class D units converted into Class A units such that the holders thereof received $4.2 million of such proceeds. The proceeds in excess of $45.8 million were shared ratably by the other holders of Class A units.

Class A Units

Class A units represented the Company's common stock equivalents. At December 31, 2016, Kadmon I, LLC ("Kadmon I") held approximately 12.1% of the total outstanding common stock of the Company. Kadmon I was a Delaware limited liability company that was formed in August 2009 and was an affiliate of the Company (Note 18). Kadmon I's funds were raised through a private offering of 80% of Kadmon I's total membership interests, the other 20% being owned by certain other members, including members of the Company's board of directors and an executive officer at the time of such offering.

Once each Kadmon I investor has received aggregate distributions equal to four times the amount of their initial investment, their collective ownership percentage in additional distributions would have decreased from 80% to 50%, and the collective ownership percentage for the members of the Company's board of directors, an executive officer and members in Kadmon I, and certain other members who received units would have increased from 20% to 50%. The change in ownership percentages would have required the Company to evaluate whether such changes would result in additional compensation expense. Kadmon I investors had never received any distributions. Accordingly, no additional compensation expense was recognized. On January 23, 2017, Kadmon I, LLC was dissolved and liquidated. Upon dissolution and liquidation, all assets of Kadmon I, LLC which consists solely of the shares of common stock in Kadmon Holdings, Inc., were distributed to the members of Kadmon I, LLC.

During the year ended December 31, 2016, the Company issued 25,000 Class A units to settle third party obligations, for which the Company expensed $0.1 million related to these settlements during the year ended Dcember 31, 2016 and issued 7,200 Class A units as the result of stock option exercises. The Company also recorded an expense of $3.0 million during the year ended December 31, 2016 related to the 1,500,000 Class A units issued in an advisory agreement entered into in April 2015.

The Class A units converted into common stock at the Conversion Event resulting in no Class A units outstanding at December 31, 2018.

Class B Unit

The Class B unit did not participate in distributions from the Company, did not have any preferences in relation to the Class A units, was non-voting, and was non-redeemable. The only right afforded to the Class B unit was the right to convert into Class A units pursuant to the Company's Operating Agreement (see "Conversion Event"). The Class B unit converted into common stock at the Conversion Event resulting in no Class B units outstanding at December 31, 2018.

Class C Unit

The Class C unit did not participate in distributions from the Company, does not have any preferences in relation to the Class A units, is non-voting, and is non-redeemable. The only right afforded to the Class C unit was the right to convert into Class A units pursuant to the Operating Agreement (see "Conversion Event"). The Class C unit converted into common stock at the Conversion Event resulting in no Class C units outstanding at December 31, 2018.

Class D Units

The Class D units did not participate in distributions from the Company, did not have any preferences in relation to the Class A units, were non-voting, and were non-redeemable. The only right afforded to the Class D unit was the right to convert into Class A units pursuant to the Company's Operating Agreement (see "Conversion Event"). The Class D units converted into common stock at the Conversion Event resulting in no Class D units outstanding at December 31, 2018.

Class E Redeemable Convertible Units

One series of Class E redeemable convertible units, the Class E Series E-1 units (the "Class E redeemable convertible units"), was authorized. The Company was able to issue Class E redeemable convertible units with an aggregate Class E original issue price of up to $85 million, calculated in accordance with the terms of the Operating Agreement, of any series without being subject to preemptive rights. The Class E redeemable convertible units had voting rights and powers equal to the Class A units on an as-if converted basis, had a liquidation preference for liquidating distributions and participated in distributions from the Company on an as-converted basis on non-liquidating distributions. In the case of a qualified IPO, the Class E redeemable convertible units automatically converted into Class A units at a conversion price of the lower of 85% of the value of Class A units (or the price per share of common stock of the corporate successor to the Company) or $11.50 per unit. Prior to a qualified IPO, the Class E redeemable convertible units could be converted at $11.50 per unit. A qualified IPO was defined as an offering of the Company's equity interests with gross proceeds to the Company of at least $75 million. At any time after December 31, 2017, Class E redeemable convertible units were redeemable for cash at the option of the holders of at least 80% of all Class E redeemable convertible units at a redemption price equal to 125% of the liquidation preference. After January 1, 2016 all Class E redeemable convertible units began to accrue a liquidation preference (payable in connection with such liquidating distribution from the Company) at a rate of 5% per annum, compounding annually, with such liquidation preference rate increasing by 100 basis points every six months to a maximum of 10%. Redemption was subject to the Company's ability to make such payment under then-existing debt obligations.

Based on the terms of the Class E redeemable convertible units, the fair value of the Class E redeemable convertible units issued was classified as mezzanine capital on the Company's consolidated balance sheet. The Company accreted changes in the redemption value of the Class E redeemable convertible units to paid-in capital using the interest method, as the Company did not have available retained earnings, from the date of issuance to the earliest redemption date.

During the year ended December 31, 2016, the Company raised $5.5 million in gross proceeds, with no transaction costs, through the issuance of 478,266 Class E redeemable convertible units. Dr. Harlan W. Waksal, the Company's President and Chief Executive Officer, certain entities affiliated with GoldenTree Asset Management LP, Bart M. Schwartz, Esq., the Company's former Chairman of the board of directors who resigned effective December 31, 2018, and D. Dixon Boardman, a member of the Company's board of directors subscribed for 86,957, 43,479, 21,740 and 21,740 Class E redeemable convertible units, respectively.

The Company calculated a deemed dividend on the Class E redeemable convertible units of $13.4 million in August 2016, which equals a 15% discount to the IPO price of the Company's common stock of $12.00 per share upon conversion to common stock at the Conversion Event, a beneficial conversion feature. The Class E redeemable convertible units converted into common stock at the Conversion Event resulting in no Class E redeemable convertible units outstanding at December 31, 2018.

5% Convertible Preferred Stock

Our certificate of incorporation permitted the Company's board of directors to issue up to 10,000,000 shares of preferred stock from time to time in one or more classes or series. Concurrently with the closing of the Company's IPO and

pursuant to the terms of the exchange agreement entered into with the holders of the Company's Senior Convertible Term Loan, the Company issued to such holders 30,000 shares of 5% convertible preferred stock, designated as the convertible preferred stock. Each share of convertible preferred stock was issued for an amount equal to $1,000 per share, which is referred to as the original purchase price. Shares of convertible preferred stock with an aggregate original purchase price and initial liquidation preference of $30.0 million were issued to the holders of the Senior Convertible Term Loan in exchange for an equivalent principal amount of the Senior Convertible Term Loan pursuant to the terms of an exchange agreement dated as of June 8, 2016, between the Company and those holders, which is referred to as the exchange agreement.

The shares of 5% convertible preferred stock are entitled to receive dividends, when and as declared by the board of directors and to the extent of funds legally available for the payment of dividends, at an annual rate of 5% of the sum of the original purchase price per share of 5% convertible preferred stock plus any dividend arrearages. Dividends on the 5% convertible preferred stock shall, at the Company's option, either be paid in cash or added to the stated liquidation preference amount for purposes of calculating dividends at the 5% annual rate (until such time as the Company declares and pays the missed dividend in full and in cash, at which time that dividend will no longer be part of the stated liquidation preference amount). Dividends shall be payable annually on June 30 of each year and shall be cumulative from the most recent dividend payment date on which the dividend has been paid or, if no dividend has ever been paid, from the original date of issuance of the 5% convertible preferred stock and shall accumulate from day to day whether or not declared until paid.

The 5% convertible preferred stock converts into shares of the Company's common stock at a 20% discount to the price per share of common stock in the IPO. The Company calculated a deemed dividend on the 5% convertible preferred stock of $7.5 million in August 2016, which equals the 20% discount to the IPO price of the Company's common stock of $12.00 per share, a beneficial conversion feature. The 5% convertible preferred stock, inclusive of accrued and unpaid dividends, is convertible into 3,519,303 and 3,351,717 shares of common stock at December 31, 2018 and 2017, respectively. The Company accrued dividends on the 5% convertible preferred stock of $1.6 million, $1.5 million and $0.6 million for the years ended December 31, 2018, 2017 and 2016, respectively. The Company also calculated a deemed dividend of $0.4 million on the $1.6 million of accrued dividends for the year ended December 31, 2018, $0.4 million on the $1.5 million of accrued dividends for the year ended December 31, 2017, and $0.2 million on the $0.6 million of accrued dividends for the year ended December 31, 2016, which equals the 20% discount to the IPO price of the Company's common stock of $12.00 per share, a beneficial conversion feature. Approximately $1.6 million and $1.4 million of accrued dividends that were payable on June 30, 2018 and June 30, 2017, respectively, were added to the stated liquidation preference amount of the 5% convertible preferred stock. The stated liquidation preference amount on the 5% convertible preferred stock totaled $33.0 million and $31.4 million at December 31, 2018 and December 31, 2017, respectively.

Common Stock

Prior to the IPO, there were no shares outstanding of the Company's common stock, par value $0.001 per share, and no stockholders of record. The Company's certificate of incorporation authorizes the issuance of up to 200,000,000 shares of the Company's common stock. On August 1, 2016, the Company completed its IPO whereby it sold 6,250,000 shares of common stock at $12.00 per share. The aggregate net proceeds received by the Company from the offering were $66.0 million, net of underwriting discounts and commissions of $5.3 million and offering expenses of $3.7 million. At December 31, 2018, 113,130,817 shares of common stock were outstanding.

For the year ended December 31, 2018, the Company raised $113.2 million, $105.8 million net of $7.4 million of underwriting discounts and other offering costs and expenses, from the issuance of 34,303,030 shares of common stock at a price of $3.30 per share ("2018 Public Offering").

For the year ended December 31, 2017, the Company raised $80.4 million in gross proceeds, $75.1 million net of $5.3 million in underwriting fees, commissions and other offering costs and expenses, from the issuance of 26,775,000 shares of common stock and warrants to purchase 10,710,000 shares of common stock at an initial exercise price of $3.35 per share for a term of 5 years from the date of issuance at a combined price of $3.001 per share and accompanying warrant. The Company allocated $57.6 million to the common stock which was recorded as common stock and additional paid in capital and allocated $22.8 million to the warrants which was recorded to additional paid in capital.

The Company also raised $22.7 million in gross proceeds, $20.9 million net of $1.8 million in placement agent fees and other offering costs and expenses, from the issuance of 6,767,855 shares of common stock, at a price of $3.36 per share, and warrants to purchase 2,707,138 shares of common stock at an initial exercise price of $4.50 per share for a term of 13 months from the date of issuance.

Valuation

Prior to the IPO, to estimate certain expenses and record certain transactions, it was necessary for the Company to estimate the fair value of its membership units. Given the absence of a public trading market, and in accordance with the

American Institute of Certified Public Accountants' Practice Guide, "Valuation of Privately-Held-Company Equity Securities Issued as Compensation," the Company exercised reasonable judgment and considered numerous objective and subjective factors to determine its best estimate of the fair value of its membership units. Factors considered included:

- recent equity financings and the related valuations;
- the estimated present value of the Company's future cash flows;
- industry information such as market size and growth;
- market capitalization of comparable companies and the estimated value of transactions such companies have engaged in; and
- macroeconomic conditions.

The Company updated the valuation of Class A units as of September 30, 2015 using a methodology consistent with prior valuations. At the time of the valuation, the Company had issued $92.0 million in second-lien convertible debt, and it was deemed appropriate to place additional weighting on this consideration, as compared to prior valuations. The Company also considered equity raised through the issuance of $15.0 million in Class A units during 2015. The Company assigned no value to the Ribasphere products to reflect changes in market conditions that have resulted in lower sales of the Ribasphere products. As a result of the revised inputs to the analysis, the estimated fair value of each Class A unit was decreased from $39.00 to $32.50 as of September 30, 2015.

4. Net Loss per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common stock outstanding for the period. Because the Company has reported a net loss for all periods presented, diluted net loss per common share is the same as basic net loss per common share for those periods. The following table summarizes the computation of basic and diluted net loss per share attributable to common stockholders of the Company (in thousands, except share and per share amounts):

	Years Ended December 31,		
	2018	2017	2016
Numerator – basic and diluted:			
Net loss attributable to common stockholders	$ (56,263)	$ (81,692)	$ (230,488)
Denominator – basic and diluted:			
Weighted average common stock outstanding used to compute basic and diluted net loss per share	97,609,000	57,405,331	23,674,512
Net loss per share, basic and diluted	**$ (0.58)**	**$ (1.42)**	**$ (9.74)**

The amounts in the table below were excluded from the calculation of diluted net loss per share, due to their anti-dilutive effect:

	Years Ended December 31,		
	2018	2017	2016
Options to purchase common stock	11,054,539	8,496,872	6,437,515
Warrants to purchase common stock	11,999,852	14,722,790	1,328,452
Convertible preferred stock	3,519,303	3,351,717	3,191,843
Total shares of common stock equivalents	**26,573,694**	**26,571,379**	**10,957,810**

5. Debt

The Company is a party to one credit agreement in the following amount (in thousands):

	December 31, 2018	December 31, 2017
Secured term debt due July 1, 2020	$ 28,046	$ 34,620
Total debt before fees and debt discount/premium	28,046	34,620
Less: Deferred financing costs	—	(228)
Debt discount	(566)	(1,030)
Add: Debt premium	—	345
Total debt payable	**$ 27,480**	**$ 33,707**
Debt payable, current portion	$ —	$ 33,707
Debt payable, long-term	$ 27,480	$ —

Secured Term Debt

August 2015 Secured Term Debt

In August 2015, the Company entered into a secured term loan in the amount of $35.0 million with two lenders ("2015 Credit Agreement"). The interest rate on the loan is LIBOR plus 9.375% with a 1% floor. The Company incurred and paid a $0.8 million commitment fee in connection with the loan that will be amortized to interest expense over the term of the agreement. The basic terms of the loan required monthly payments of interest only through the first anniversary date of the loan and require the Company to maintain certain financial covenants requiring the Company to maintain a minimum liquidity amount and minimum revenue levels beginning after June 30, 2016 through August 1, 2016, the date the Company consummated its IPO. Beginning on the first anniversary date of the loan, the Company was required to make monthly principal payments in the amount of $380,000. Any outstanding balance of the loan and accrued interest was to be repaid on June 17, 2018. The secured term loan is collateralized by a first priority perfected security interest in all the tangible and intangible property of the Company.

In conjunction with the 2015 Credit Agreement, warrants to purchase $6.3 million of Class A units were issued to two lenders, of which $5.4 million was recorded as a debt discount and $0.9 million was recorded as loss on extinguishment of debt (Note 6). The debt discount was being amortized over the life of the outstanding term loan using the effective interest method.

Deferred financing costs of $1.3 million were recognized in recording the 2015 Credit Agreement and were amortized to interest expense over the three year term of the agreement. There were no unamortized deferred financing costs at December 31, 2018, and approximately $0.2 million of unamortized deferred financing costs at December 31, 2017. Approximately $0.2 million, $0.5 million and $0.4 million were charged to interest expense during the years ended December 31, 2018, 2017 and 2016, respectively.

The Company entered into a third waiver agreement to the 2015 Credit Agreement in September 2016 to negotiate the amendment and restatement of certain covenants of the Company contained in the 2015 Credit Agreement. In connection with such negotiation, the lenders under the 2015 Credit Agreement had agreed to refrain from exercising certain rights under the 2015 Credit Agreement, including the declaration of a default and to forbear from acceleration of any repayment rights with respect to existing covenants until the parties have consummated the amendment and restatement of such provisions. In addition, certain payments required to be made under the 2015 Credit Agreement had been deferred while the parties negotiated the amendment. The parties executed a second amendment to the 2015 Credit Agreement in November 2016 whereby the Company deferred further principal payments owed under the 2015 Credit Agreement in the amount of $380,000 per month until August 31, 2017. Additionally, the parties amended various clinical development milestones and added a covenant pursuant to which the Company was required to raise $40.0 million of additional equity capital by the end of the second quarter of 2017. All other material terms of the 2015 Credit Agreement, including the maturity date, remain the same.

The Company entered into a fourth waiver agreement to the 2015 Credit Agreement in March 2017 under which the lenders under the 2015 Credit Agreement agreed to refrain from exercising certain rights under the 2015 Credit Agreement, including the declaration of a default and to forbear from acceleration of any repayment rights with respect to existing covenants.

On March 31, 2017, the Company entered into the Third Amendment. Pursuant to this amendment, principal payments owed under the 2015 Credit Agreement, in the amount of $380,000 per month, were deferred until January 31, 2018. Additionally, the parties amended a future capital raising covenant by extending the time period by which the Company was required to raise the remaining $17.0 million of capital by six months, from June 30, 2017 to December 31, 2017, which was satisfied in September 2017. All other material terms of the 2015 Credit Agreement, including the maturity date, remain the same. The clinical development milestone was deemed satisfied in a letter agreement entered into on December 22, 2017 with a majority of lenders under our 2015 Credit Agreement.

The Third Amendment also amended certain terms of the warrants to purchase an aggregate of 617,651 shares of the Company's common stock issued in connection with the 2015 Credit Agreement (the "2015 Warrants"). Pursuant to the Third Amendment, the 2015 Warrants may now only be exercised for cash and the exercise price was reduced from $10.20 per share to $4.50 per share. The redemption feature in the 2015 Warrants was also amended such that the warrant holder may only demand a redemption of the 2015 Warrants upon the occurrence of, and during the continuance of, an event of default. Prior to this amendment, the warrant could be redeemed by the warrant holder at any time after the 51st month.

As a result of the Third Amendment, $0.9 million was recorded as a debt premium at March 31, 2017, inclusive of the fair value of the warrant modification utilizing a Black-Scholes calculation, and was amortized to interest expense over the remaining term of the agreement as the amendment was deemed to be a modification in accordance with ASC 470 (Note 6). Approximately $0.3 million and $0.6 million was recorded as interest expense for the years ended December 31, 2018 and 2017, respectively.

The Company entered into a fifth waiver agreement to the 2015 Credit Agreement in March 2018 under which the lenders under the 2015 Credit Agreement agreed to refrain from exercising certain rights under the 2015 Credit Agreement, including the declaration of a default and to forbear from acceleration of any repayment rights with respect to existing covenants.

The Company entered into the fourth amendment to the 2015 Credit Agreement in June 2018 (the "Fourth Amendment"). Pursuant to the Fourth Amendment, the maturity date of the 2015 Credit Agreement was extended to August 31, 2018 (the "Extension Period"). The Company repaid $4.7 million of the outstanding principal on June 18, 2018, representing all amounts due under the 2015 Credit Agreement to GoldenTree Credit Opportunities, LP, GoldenTree Credit Opportunities, Ltd, GoldenTree Insurance Fund Series Interests of the SALI Multi-Series Fund, LP, GT NM, LP, and San Bernardino County Employees' Retirement Association. All other material terms of the 2015 Credit Agreement remained the same during the Extension Period.

The Company entered into the fifth amendment to the 2015 Credit Agreement in August 2018 (the "Fifth Amendment"). Pursuant to the Fifth Amendment, the maturity date of the Credit Agreement was extended to July 1, 2020 and principal payments have been deferred until January 31, 2020. Beginning on January 31, 2020, equal principal payments of $750,000 per month will be due until the maturity date. Additionally, the parties amended certain covenants under the 2015 Credit Agreement to require the Company to meet certain developmental milestones by December 31, 2019. All other material terms of the 2015 Credit Agreement remain the same, including a minimum liquidity covenant. As of the date hereof, the Company is not in default under the terms of the 2015 Credit Agreement.

The Fifth Amendment also amended the exercise price of a portion of the 2015 Warrants to purchase an aggregate of 529,413 shares of the Company's common stock from $4.50 per warrant share to $3.30 per warrant share. The terms of the remaining 2015 Warrants to purchase an aggregate of 88,238 shares of the Company's common stock remain the same. As amended, if all of the 2015 Warrants are exercised, the Company will receive approximately $2.1 million in cash proceeds.

As a result of the Fifth Amendment, $0.7 million was recorded as a debt discount in August 2018, inclusive of the fair value of the warrant modification utilizing a Black-Scholes calculation, and will be amortized to interest expense over the remaining term of the agreement as the amendment was deemed to be a modification in accordance with ASC 470 (Note 6). Approximately $0.1 million was recorded to interest expense during the year ended December 31, 2018.

The Company entered into a sixth waiver agreement to the 2015 Credit Agreement in March 2019 under which the lenders under the 2015 Credit Agreement agreed to refrain from exercising certain rights under the 2015 Credit Agreement, including the declaration of a default and to forbear from acceleration of any repayment rights with respect to existing covenants. The report and opinion of our independent registered public accounting firm, BDO USA, LLP, for the year ended December 31, 2018 contains an explanatory paragraph regarding our ability to continue as a going concern, which is an event of default under the 2015 Credit Agreement.

The minimum payments required on the outstanding balances of the 2015 Credit Agreement at December 31, 2018 are (in thousands):

	2015 Credit Agreement
2019	$ —
2020	28,046
	$ 28,046

The following table provides components of interest expense and other related financing costs (in thousands):

	Years Ended December 31,		
	2018	2017	2016
Interest expense and other financing costs	$ 3,565	$ 3,720	$ 3,782
Interest expense - beneficial conversion feature	—	—	45,915
Interest paid-in kind	—	—	14,695
Write-off of deferred financing costs and debt discount	—	—	3,820
Amortization of deferred financing costs, debt discount and debt premium	1,054	2,242	4,422
Interest expense	**$ 4,619**	**$ 5,962**	**$ 72,634**

6. Financial Instruments

Equity issued pursuant to Credit Agreements

In connection with the 2015 Credit Agreement, the Company issued the 2015 Warrants as fees to the lenders to purchase an aggregate of $6.3 million of the Company's Class A units. The strike price of the warrants was 85% of the price per unit in an IPO or, if before an IPO, 85% of the deemed per unit equity value as defined in the 2015 Credit Agreement. The warrants were exercisable as of the earlier of an IPO or July 1, 2016. Upon entry into the agreement in August 2015, the warrants issued to an existing lender was recorded to loss on extinguishment of debt of $0.9 million and the warrants issued to the new lender was recorded as a debt discount of $5.4 million and was amortized over the remaining term of the agreement (Note 5) in accordance with ASC 470. Upon consummation of the Company's IPO on August 1, 2016 with a price per share of common stock in the IPO of $12.00, the warrants to purchase Class A units issued to lenders under the 2015 Credit Agreement were exchanged for 617,651 warrants with a strike price of $10.20 per share to purchase the same number of shares of the Company's common stock.

As a result of the Third Amendment, the exercise price of the 2015 Warrants was reduced from $10.20 per share to $4.50 per share. As a result of the The Fifth Amendment, the exercise price of a portion of the 2015 Warrants to purchase an aggregate of 529,413 shares of the Company's common stock was reduced from $4.50 per warrant share to $3.30 per warrant share. The exercise price of the remaining 2015 Warrants to purchase an aggregate of 88,238 shares of the Company's common stock remain the same. Since these warrants are exercisable and are redeemable at the option of the holder upon the occurrence of, and during the continuance of, an event of default, the fair value of the warrants is recorded as a short-term liability of $0.5 million and $1.2 million at December 31, 2018 and December 31, 2017, respectively.

The Company used the Black-Scholes pricing model to value the 2015 warrant liability at December 31, 2018 and 2017 with the following assumptions:

	December 31, 2018	December 31, 2017
Stock Price	$2.08	$3.62
Strike price	$3.30 - $4.50	$4.50
Expected Volatility	72.44%	74.90%
Risk-free interest rate	2.47%	2.20%
Expected term	3.7 years	4.7 years
Expected dividend yield	0%	0%

The decline in fair value of the 2015 Warrants was $(0.8) million, $(1.1) million and $(4.3) million for the years ended December 31, 2018, 2017 and 2016, respectively. None of these instruments have been exercised at December 31, 2018 or December 31, 2017.

In connection with the incurrence of the Senior Convertible Term Loan in 2015, the Company issued three tranches of warrants as fees to the lenders that were redeemable for Class A units. The change in fair value of the warrants was ($0.2) million for the year ended December 31, 2016. Upon consummation of the Company's IPO on August 1, 2016 with a

price per share of common stock in the IPO of $12.00, the warrants to purchase Class A units issued to lenders in the Senior Convertible Term Loan were exchanged for 351,992 warrants with a strike price of $10.20 per share to purchase the same number of shares of the Company's common stock. Since the strike price was determined at IPO, the aggregate fair value of these warrants totaling $1.7 million was reclassified from liability to equity upon consummation of the Company's IPO in August 2016.

Other Warrants

On April 16, 2013, the Company issued warrants with an estimated fair value of $1.4 million for the purchase of 30,000 Class A units at a strike price of $21.24 as consideration for fundraising efforts performed. Upon consummation of the Company's IPO on August 1, 2016 and Corporate Conversion, these warrants to purchase Class A units were exchanged for 46,163 warrants to purchase the same number of shares of the Company's common stock at a strike price of $138.06. None of these warrants have been exercised at December 31, 2018.

In connection with the sale of common stock in March 2017, warrants to purchase 2,707,138 shares of common stock were issued at an exercise price of $4.50 per share. During April 2018, warrants to purchase 119,047 shares of common stock were exercised for which the Company received proceeds of $0.5 million. The remaining 2,588,091 warrants expired in April 2018. These warrants included a cash settlement option requiring the Company to record a liability for the fair value of the warrants at the time of issuance and at each reporting period with any change in the fair value reported as other income or expense. At the time of issuance, approximately $1.6 million was recorded as warrant liability. The decline in the fair value of these warrants was $(0.7) million and $(0.9) million for the years ended December 31, 2018 and 2017, respectively.

In connection with the 2017 Public Offering, the Company issued warrants to purchase 10,710,000 shares of common stock at an initial exercise price of $3.35 per share for a term of 5 years from the date of issuance. As of December 31, 2018, warrants to purchase 10,671,400 shares of common stock were outstanding. The Company assessed the warrants under FASB ASC 480 and determined that the warrants were outside the scope of ASC 480. The Company next assessed the warrants under FASB ASC 815. Under the related guidance, a reporting entity shall not consider a contract to be a derivative instrument if the contract is both (1) indexed to the entity's own stock and (2) classified in stockholders' equity. The Company determined that the warrants were indexed to the Company's stock, as the agreements do not contain any exercise contingencies and the warrants' settlement amount equals the difference between the fair value of the Company's common stock price and the warrant strike price. The Company also assessed the classification in stockholders' equity and determined the warrants met all of the criteria for classification as equity under ASC 815. Based on this analysis, the Company determined that the warrant should be classified as equity and recorded $22.8 million to additional paid in capital, which represents the allocation of the 2017 Public Offering proceeds to the fair value of the warrants at issuance date.

Fair Value of Long-term Debt

The Company maintained a long-term secured debt balance of $27.5 million at December 31, 2018 and had no long-term secured term debt at December 31, 2017. Since the secured debt becomes due on July 1, 2020, it has been recorded as long-term secured debt at December 31, 2018.The underlying agreements for these balances were negotiated with parties that included fully independent third parties, at an interest rate which is considered to be in line with over-arching market conditions. Based on these factors management considers the carrying value of the debt to approximate fair value at December 31, 2018.

Fair Value Classification

The Company held certain liabilities that are required to be measured at fair value on a recurring basis. Fair value guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. These tiers include:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The table below represents the values of the Company's financial instruments at December 31, 2018 and December 31, 2017 (in thousands):

	Fair Value Measurement Using Significant Other Observable Inputs (Level 2)	
Description	December 31, 2018	December 31, 2017
Warrants	$ 524	$ 1,952
Total	**$ 524**	**$ 1,952**

The table below represents a rollforward of the Level 2 financial instruments from January 1, 2017 to December 31, 2018 (in thousands).

	Significant Other Observable Inputs (Level 2)
Balance as of January 1, 2017	**$ 3,305**
Fair value of warrants modified in the Third Amendment	(908)
Issuance of warrants in private placement	1,651
Change in fair value of financial instruments	(2,096)
Balance as of December 31, 2017	**$ 1,952**
Change in fair value of financial instruments	(1,525)
Fair value of warrants modified in the Fifth Amendment	111
Exercise of warrants recorded as liability	(14)
Balance as of December 31, 2018	**$ 524**

The Level 2 inputs used to value our financial instruments were determined using prices that can be directly observed or corroborated in active markets. In August 2016, the warrants issued in connection with the 2015 Credit Agreement were transferred from Level 3 to Level 2 as the Company's securities began trading on the New York Stock Exchange. Although the fair value of this obligation is calculated using the observable market price of Kadmon Holdings Inc. common stock, an active market for this financial instrument does not exist and therefore the Company has classified the fair value of this liability as a Level 2 liability in the table above.

Warrants Outstanding

The following table summarizes information about warrants outstanding at December 31, 2018 and 2017:

	Warrants	Weighted Average Exercise Price
Balance, December 31, 2016	1,328,452	$ 29.70
Granted	13,417,138	3.58
Exercised	(22,800)	3.35
Balance, December 31, 2017	14,722,790	$ 5.94
Exercised	(134,847)	4.21
Forfeited	(2,588,091)	4.50
Balance, December 31, 2018	11,999,852	$ 5.97

7. Inventories

Inventories are stated at the lower of cost or market (on a first-in, first-out basis) using standard costs. Standard costs include an allocation of overhead rates, which include those costs attributable to managing the supply chain and are evaluated regularly. Variances are expensed as incurred.

The Company regularly reviews the expiration date of its inventories and maintains a reserve for inventories that are probable to expire before shipment. Inventories recorded on the Company's consolidated balance sheets are net of a reserve for expirable inventory of $2.2 million and $4.8 million at December 31, 2018 and 2017, respectively. The Company expensed Ribasphere inventory that it believes will not be sold prior to reaching its product expiration date totaling $0.3 million, $1.7 million and $0.4 million during the years ended December 31, 2018, 2017 and 2016, respectively. If the amount and timing of future sales differ from management's assumptions, adjustments to the estimated inventory reserves may be required.

Inventories Produced in Preparation for Product Launches

The Company capitalizes inventories produced in preparation for product launches sufficient to support estimated initial market demand. Typically, capitalization of such inventory begins when positive results have been obtained for the clinical trials that the Company believes are necessary to support regulatory approval, uncertainties regarding ultimate regulatory approval have been significantly reduced and the Company has determined it is probable that these capitalized costs will provide some future economic benefit in excess of capitalized costs. The material factors considered by the Company in evaluating these uncertainties include the receipt and analysis of positive clinical trial results for the underlying product candidate, results from meetings with the relevant regulatory authorities prior to the filing of regulatory applications, and the compilation of the regulatory application. The Company closely monitors the status of each respective product within the regulatory approval process, including all relevant communication with regulatory authorities. If the Company is aware of any specific material risks or contingencies other than the normal regulatory review and approval process or if there are any specific issues identified relating to safety, efficacy, manufacturing, marketing or labeling, the related inventory would generally not be capitalized.

For inventories that are capitalized in preparation of product launch, anticipated future sales, expected approval date and shelf lives are evaluated in assessing realizability. The shelf life of a product is determined as part of the regulatory approval process; however in evaluating whether to capitalize pre-launch inventory production costs, the Company considers the product stability data of all of the pre-approval production to date to determine whether there is adequate expected shelf life for the capitalized pre-launch production costs.

The Company has concluded that KD034, its generic version of trientine hydrochloride, is commercially viable since it is the chemical equivalent of the original drug approved by the U.S. Food and Drug Administration (“FDA”). The Company has submitted two Abrreviated New Drug Application’s with the FDA, and economic benefits of the pre-launch inventory recorded at December 31, 2018 are probable. Accordingly, the pre-launch costs are realizable as the Company expects the inventory will be sold or used prior to expiration. An assessment of likelihood that regulatory approval will not be obtained will be made at each reporting period. If at any time regulatory approval is deemed to not be probable, the inventory will be written down to its net realizable value, which is presumably zero, as the product would have no alternative future use. The Company maintained $0.9 million and $0.1 million of work-in-process inventory related to KD034 at December 31, 2018 and December 31, 2017, respectively.

Inventories are comprised of the following (in thousands):

	December 31, 2018	December 31, 2017
Raw materials	$ —	$ —
Work-in-process	886	80
Finished goods, net	39	121
Total inventories	**$ 925**	**$ 201**

8. Fixed Assets

Fixed assets consisted of the following (in thousands):

	Useful Lives (Years)	December 31, 2018	December 31, 2017
Leasehold improvements	4-8	$ 10,187	$ 10,120
Office equipment and furniture	3-15	1,529	1,488
Machinery and laboratory equipment	3-15	3,247	2,765
Software	1-5	3,831	3,162
Construction-in-progress	—	45	408
		18,839	17,943
Less accumulated depreciation and amortization		(15,185)	(13,651)
Fixed assets, net		$ 3,654	$ 4,292

Depreciation and amortization of fixed assets totaled $1.5 million, $1.8 million and $2.3 million in each of the years ended December 31, 2018, 2017 and 2016, respectively. The construction-in-progress balance was related to costs of unimplemented software still under development. Unamortized computer software costs were $0.7 million and $0.2 million

at December 31, 2018 and 2017, respectively. The amortization of computer software costs amounted to $0.2 million, $0.6 million and $0.7 million during the years ended December 31, 2018, 2017 and 2016, respectively.

During the first quarter of 2017, the Company disposed of $2.1 million of fully depreciated assets. There was no consideration received for the disposal of these assets and the disposal did not have a significant impact on the consolidated financial statements of the Company.

9. Goodwill and Other Intangible Assets

The Company's goodwill relates to the 2010 acquisition of Kadmon Pharmaceuticals, LLC, a Pennsylvania limited liability company that was formed in April 2000. The Company maintains a goodwill balance of $3.6 million at both December 31, 2018 and 2017. There were no changes in the carrying amount of goodwill for the years ended December 31, 2018 and 2017.

In October 2015, the Company determined that the proportional performance method of amortization was more appropriate than straight-line amortization for the Company's Ribasphere product rights intangible asset. The amortization of the Ribasphere product rights intangible asset based on the consumption of the economic benefit (Ribasphere gross profit), became a reliably determinable method of amortization due to the remaining asset useful life being only 1.25 years and the ability to more accurately forecast the Ribasphere market. Accordingly, Kadmon amortized the remaining book value of the intangible asset utilizing the proportional performance method starting October 1, 2015 and ending December 31, 2016.

Amortization expense is included within selling, general and administrative expenses on the Company's consolidated statements of operations. The Company recorded amortization expense related to the intangible asset of $15.2 million for the year ended December 31, 2016. No amortization expense related to the intangible asset was recorded in the year ended years ended December 31, 2018 and 2017, as the Ribasphere product rights intangible asset was fully amortized as of December 31, 2016.

10. Investment in MeiraGTx

In April 2015, the Company executed several agreements which transferred its ownership of Kadmon Gene Therapy, LLC to MeiraGTx. As part of these agreements, the Company also transferred various property rights, employees and management tied to the intellectual property and contracts identified in the agreements to MeiraGTx. At a later date, MeiraGTx ratified its shareholder agreement and accepted the pending equity subscription agreements, which provided equity ownership to various parties. The execution of these agreements resulted in a 48% ownership in MeiraGTx by the Company. After MeiraGTx was deconsolidated or derecognized, the retained ownership interest was initially recognized at fair value and a gain of $24.0 million was recorded based on the fair value of this equity investment. The Company's investment was accounted for under the equity method at zero cost with an estimated fair value at the time of the transaction of $24.0 million. This value was determined based upon the implied value established by the cash raised by MeiraGTx in exchange for equity interests by third parties. During April 2016, the Company received 230,000 shares of MeiraGTx's convertible preferred Class C shares as a settlement for $1.2 million in receivables from MeiraGTx. Under ASC 323, the Class C shares of MeiraGTx do not qualify as common stock or in-substance common stock and the $1.2 million was recorded as a cost method investment. As of March 31, 2018, the Company had no remaining basis in any of the investments in MeiraGTx.

MeiraGTx is an exempted company incorporated under the laws of the Cayman Islands in 2018, and prior to that, they commenced operations as MeiraGTx Limited, a private limited company incorporated under the laws of England and Wales in 2015. MeiraGTx is developing therapies for ocular diseases, including rare inherited blindness, as well as xerostomia following radiation treatment for head and neck cancers and neurodegenerative diseases.

The Company assessed the applicability of ASC 810 to the aforementioned agreements and based on the corporate structure, voting rights and contributions of the various parties in connection with these agreements, determined that MeiraGTx was a variable interest entity, however consolidation was not required as the Company was not the primary beneficiary based upon the voting and managerial structure of the entity.

The Company assessed the recoverability of both the cost method and equity method investment in MeiraGTx at December 31, 2017 and 2016 and identified no events or changes in circumstances that had a significant adverse impact on the fair value of this investment. For the years ended December 31, 2017 and 2016, the Company recorded its share of MeiraGTx's net loss of $7.6 million and $13.6 million, respectively, inclusive of adjustments related to MeiraGTx's 2015 financial statements that resulted in the Company recording a loss on equity method investment of $3.9 million for the year ended December 31, 2016. The Company maintained a 25.6% ownership in MeiraGTx at December 31, 2017, inclusive of C preferred shares issued by MeiraGTx. For accounting purposes, the Company determined that the C preferred shares issued by MeiraGTx are not in-substance common stock. Accordingly, the Company recorded 38.7% of MeiraGTx's losses, which

represents what the Company's percentage would be if only A ordinary shares were outstanding. The Company's maximum exposure associated with MeiraGTx was limited to its initial investment of $24.0 million, which has been written down to zero at December 31, 2017 based on the Company's absorption of MeiraGTx's net losses.

On June 12, 2018, MeiraGTx completed its initial public offering (the "MeiraGTx IPO") whereby it sold 5,000,000 shares of common stock at $15.00 per share. Upon the closing of the MeiraGTx IPO, 27,184,132 shares of common stock were outstanding, which includes the conversion of all C preferred shares into common stock. The shares began trading on the Nasdaq Global Select Market on June 7, 2018 under the symbol "MGTX."

Prior to the MeiraGTx IPO, the Company had no remaining basis in any of the investments held in MeiraGTx. Upon completion of the MeiraGTx IPO, the Company's investment was diluted to a 13.0% ownership in MeiraGTx common stock and no longer has the ability to exert significant influence over MeiraGTx. The Company discontinued the equity method of accounting for the investment in MeiraGTx on June 12, 2018 and determined the remaining investment to be an equity security accounted for in accordance with ASC 321 at the date the investment no longer qualifies for the equity method of accounting. ASC 321 requires the investments to be recorded at cost, less any impairment, plus or minus changes resulting from observable price changes in orderly transactions for the identical or similar investment of the same issuer. As the Company's investment in MeiraGTx common stock has a readily determinable market value, the Company recorded an unrealized gain of $40.5 million in June 2018 related to the fair value of its ownership of common stock of MeiraGTx. As of December 31, 2018, the Company maintains a 12.9% ownership in the common stock of MeiraGTx with a fair value of $34.1 million recorded as a noncurrent investment in equity securities as depending on certain circumstances, the Company may, at times, be deemed to be an affiliate of MeiraGTx. The Company has recorded an unrealized gain on the MeiraGTx common stock investment of $34.1 million for the year ended December 31, 2018. The investment in MeiraGTx is valued using Level 1 inputs which includes quoted prices in active markets for identicial assets in accordance with the fair value hierarchy (Note 6). The Company has not realized any gains related to the investment in common stock of MeiraGTx.

As part of the agreements executed with MeiraGTx in April 2015, the Company entered into a transition services agreement ("TSA") with MeiraGTx which expired in April 2018. Upon expiration of the TSA, the Company continued to provide office space to MeiraGTx. On October 1, 2018, the Company and MeiraGTx entered into a sublease agreement which is effective from October 1, 2018 for a period of two months and will automatically be renewed on a monthly basis unless MeiraGTx provides 30 days prior written notice. The monthly sublease amount is approximately $47,000. As part of the TSA and sublease agreement with MeiraGTx, the Company recognized $0.6 million. $0.6 million and $1.0 million to license and other revenue during the years ended December 31, 2018, 2017 and 2016, respectively. The Company received cash payments of $1.4 million, $0.3 million and $0.2 million from MeiraGTx during 2018, 2017 and 2016, respectively. The Company has no amounts receivable from MeiraGTx at December 31, 2018 and had $0.9 million of amounts receivable from MeiraGTx at December 31, 2017. For the period beginning January 1, 2018 through June 12, 2018, the Company recorded its share of MeiraGTx's net loss under the equity method of accounting of $1.2 million. For the the years ended December 31, 2017 and December 31, 2016, the Company recorded its share of MeiraGTx's net loss under the equity method of accounting of $7.6 million and $13.6 million, respectively.

11. License Agreements

Symphony Evolution, Inc.

In August 2010, the Company entered into a license agreement with Symphony Evolution, Inc. (Symphony), under which Symphony granted to the Company an exclusive, worldwide, royalty-bearing, sublicensable license under certain Symphony patents, copyrights and technology to develop, make, use, sell, import and export XL647 and the related technology in the field of oncology and non-oncology.

The Company is the licensee of granted patents in Australia, Canada, Europe, Japan and the United States. The patents claim tesevatinib as a composition-of-matter, as well as use of tesevatinib to treat certain cancers. A pending U.S. application supports additional composition-of-matter claims and methods of synthesis. The last to expire U.S. patent in this family has a term that ends in May 2026 based on a calculated Patent Term Adjustment (PTA) and without regard to any potential Patent Term Extension (PTE), which could further extend the term by an additional five years.

The Company is the licensee of a second family of granted patents in China and Europe, as well as applications in Canada, Eurasia, Japan, Taiwan and the United States. These patents and applications disclose the use of tesevatinib to treat PKD. The last to expire U.S. patent in this family would have a term that ends in 2031, though this term could be extended by obtaining a PTA and/or PTE.

The license agreement includes a series of acquisition and worldwide development milestone payments totaling up to $218.4 million, and $14.1 million of these payments and other fees have been paid as of December 31, 2018. Additionally, the license agreement includes commercial milestone payments totaling up to $175.0 million, none of which have been paid

as of December 31, 2018, contingent upon the achievement of various sales milestones, as well as single-digit sales royalties. The royalty term expires with the last to expire patent.

The agreement with Symphony will expire upon the expiration of the last to expire patent within the licensed patents. The Company may terminate the agreement at any time upon six months written notice to Symphony. Either party may terminate the agreement for any material breach by the other party that is not cured within a specified time period. Symphony may terminate the agreement if the Company challenges the licensed patents. Either party may terminate the agreement upon the bankruptcy or insolvency of the other party.

All other contingent payments will be expensed as research and development as incurred.

Valeant Pharmaceuticals North America LLC

On February 25, 2014, the Company entered into an agreement with Valeant for the co-promotion of Syprine®, a chelation therapy indicated in the treatment of patients with Wilson's disease who are intolerant of penicillamine. In February 2016, the Company entered into a mutual termination agreement with Valeant. Upon termination, neither party shall have any rights or obligation including any and all past, present and future payments. Additionally, all rights and licenses granted under the agreement were immediately terminated and reverted to the party granting such rights. As a result of the termination, in February 2016 the Company recorded a gain on settlement of the $3.9 million other milestone payable to Valeant in connection with the acquisition of the drug Infergen.

Nano Terra, Inc.

On April 8, 2011, the Company entered into a series of transactions with Nano Terra, Inc. ("Nano Terra"), pursuant to which the Company (i) paid $2.3 million for Nano Terra's Series B Preferred Stock, (ii) entered into a joint venture with Surface Logix, Inc. ("Surface Logix") (Nano Terra's wholly-owned subsidiary) through the formation of NT Life Sciences, LLC ("NT Life"), whereby the Company contributed $0.9 million at the date of formation in exchange for a 50% interest in NT Life and (iii) entered into a sub-licensing arrangement with NT Life and Surface Logix. Pursuant to the sub-licensing arrangement, the Company was granted a worldwide, exclusive license under certain intellectual property owned by Surface Logix to three clinical-stage product candidates, as well as rights to Surface Logix's drug discovery platform, Pharmacomer™ Technology, each of which were licensed by Surface Logix to NT Life. In December 2014, the Company received one share of Nano Terra's Common Stock for every 100 shares of Series B Preferred Stock held by the Company, resulting in approximately a 1% holding in Nano Terra as of December 31, 2018 and 2017. In accordance with ASC 325, "Investments—Other", the Company continues to account for the investment under the cost method.

The primary product candidates are currently in early to mid-stage clinical development for a variety of diseases and target several novel pathways of disease by inhibiting the activity of specific enzymes.

Nano Terra and NT Life are research and development companies, each of which independently maintains intellectual property for the purpose of pursuing medical discoveries. The Company is a minority shareholder of Nano Terra and thereby is unable to exercise significant influence with regard to the entity's daily operations. The Company is represented on the board of managers of NT Life and is a party to decisions which influence the direction of the organization.

Since inception, the Company has continuously assessed the applicability of ASC 810, based on the corporate structure, voting rights and contributions of the various parties in connection with these agreements, and determined that Nano Terra and NT Life are not variable interest entities and not subject to consolidation. On April 8, 2011 the Company recorded its $2.3 million investment in Nano Terra in accordance with ASC 325 and the Company has assessed the recoverability of the investment in Nano Terra as of December 31, 2018 and 2017 and identified no events or changes in circumstances that may have a significant adverse impact on the fair value of this investment. There was no activity of the joint venture during the years ended December 31, 2018, 2017 and 2016 which resulted in income or loss to the Company. The Company's maximum exposure associated with Nano Terra and NT Life is limited to cash contributions made.

Additionally, subject to certain exceptions, the Company must pay to the previous shareholders of Surface Logix from which Nano Terra acquired Surface Logix a mid-single digit percentage royalty of net sales of the applicable licensed products and a percentage that ranges between a low twenty percent and a low forty percent of all sublicensing revenue the Company receives in the event the Company further assigns or sublicenses its rights under the sub-licensing arrangement to certain third parties. In addition, the Company must pay to NT Life a ten percent royalty of any remaining net sales amount of the applicable licensed products and all of such sublicensing revenue after taking into account the royalties and sublicensing revenue paid to the previous shareholders of Surface Logix. No sublicensing revenue or sales were achieved as of December 31, 2018 and 2017.

Dyax Corp. (acquired by Shire Plc in January 2016, acquired by Takeda Pharmaceuticals Co., Ltd. in 2018)

On July 22, 2011 the Company entered into a license agreement with Dyax Corp. ("Dyax") for the rights to use the Dyax Antibody Libraries, Dyax Materials and Dyax Know-How (collectively "Dyax Property"). The agreement terminated on September 22, 2015, but the Company had a right to a commercial license of any research target within two years of expiration of the agreement. The Company exercised its right to a commercial license of two targets in September 2017, resulting in a license fee payable to Shire Plc of $1.5 million which was recorded to research and development expense for the year ended December 31, 2017. The agreement includes the world-wide, non-exclusive, royalty-free, non-transferable license to use the Dyax Property to be used in the research field, without the right to sublicense. Additionally, the Company has the option to obtain a sublicense for use in the commercial field if any research target is obtained.

On September 13, 2012 the Company entered into a separate license agreement with Dyax whereby the Company obtained from Dyax the exclusive, worldwide license to use research, develop, manufacture and commercialize DX-2400 in exchange for a payment of $0.5 million. All payments associated with this agreement were recorded as research and development expense at the time the agreement was executed. The DX-2400 license requires the Company to make additional payments contingent on the achievement of certain development milestones (such as receiving certain regulatory approvals and commencing certain clinical trials) and sales targets. None of these targets have been achieved and, as such, no assets or liabilities associated with the milestones have been recorded in the accompanying consolidated financial statements for the year ended December 31, 2018. The DX-2400 license also includes royalty payments commencing on the first commercial sale of any licensed product, which had not occurred as of December 31, 2018 and 2017. On April 2, 2018, we gave notice of our intent to terminate this agreement effective six months from the date of notice and the agreement terminated on October 2, 2018.

Zydus

In June 2008, the Company entered into an asset purchase agreement with Zydus Pharmaceuticals USA, Inc. ("Zydus") and Cadila Healthcare Limited where the Company purchased all of Zydus' rights, title and interest to high dosages of ribavirin. Under the terms of the agreement, the Company paid a one-time purchase price of $1.1 million. The Company was required to pay a royalty based on net sales of products in the low twenty percents, subject to specified reductions and offsets. In April 2013, the Company entered into an amendment to the asset purchase agreement with Zydus which reduced the royalty payable on net sales of products from the low twenty percents to the mid-teens percents.

In June 2008, the Company also entered into a non-exclusive patent license agreement with Zydus, under which Zydus granted to the Company a non-exclusive, royalty free, fully paid up, non-transferable license under certain Zydus patent rights related to ribavirin. This agreement will expire upon the expiration or termination of a specific licensed patent. Either party may terminate the agreement for any material breach by the other party that is not cured within a specified time period or upon the bankruptcy or insolvency of the other party.

The Company recorded royalty expense of less than $0.1 million, $0.1 million and $1.2 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Jinghua

In November 2015, the Company entered into a license agreement with Jinghua Pharmaceutical Group Co., Ltd. ("Jinghua"). Under this agreement, the Company granted to Jinghua an exclusive, royalty-bearing, sublicensable license under certain of its intellectual property and know-how to use, develop, manufacture, and commercialize certain monoclonal antibodies in China, Hong Kong, Macau and Taiwan.

In partial consideration for the rights granted to Jinghua under the agreement, the Company received an upfront payment of $10.0 million in the form of an equity investment in Class E redeemable convertible units of the Company. The Company is eligible to receive from Jinghua a royalty equal to a percentage of net sales of product in the territory in the low ten percents. In addition to such payments, the Company is eligible to receive milestone payments for the achievement of certain development milestones, totaling up to $40.0 million. The Company earned a $2.0 million milestone payment in

March 2016, which was recorded as license and other revenue during the year ended December 31, 2016. The Company earned a $2.0 million milestone payment in January 2017, which was received in February 2017, and was recorded as license and other revenue during the year ended December 31, 2017.The Company is also eligible to receive a portion of sublicensing revenue from Jinghua ranging from the low ten percents to the low thirty percents based on the development stage of a product. No such revenue was earned during the years ended December 31, 2018, 2017 and 2016

The Company's agreement with Jinghua will continue on a product-by-product and country-by-country basis until the later of ten years after the first commercial sale of the product in such country or the date on which there is no longer a valid claim covering the licensed antibody contained in the product in such country. Either party may terminate the agreement for any material breach by the other party that is not cured within a specified time period or upon the bankruptcy or insolvency of the other party. No patents were licensed to the Company under this agreement.

Camber Pharmaceuticals, Inc.

In February 2016, we entered into a supply and distribution agreement with Camber Pharmaceuticals, Inc. (Camber) for the purposes of marketing, selling and distributing tetrabenazine, a medicine that is used to treat the involuntary movements (chorea) of Huntington's disease. The initial term of the agreement was twelve months. In May 2016, we amended our agreement with Camber to include the marketing, selling and distributing of valganciclovir, a medicine that is used for the treatment of CMV retinitis, a viral inflammation of the retina of the eye, in patients with acquired immunodeficiency syndrome (AIDS) and for the prevention of CMV disease, a common viral infection complicating solid organ transplants, in kidney, heart and kidney pancreas transplant patients. In August 2016, we amended our agreement with Camber to include the marketing, selling and distributing of several other products that have not had meaningful sales to date. In February 2017, we entered into a third amendment to the supply and distribution agreement with Camber extending the initial term of the agreement by an additional twelve months. The supply and distribution agreement with Camber terminated on February 23, 2018.

Under the agreement, as amended, we obtained commercial supplies of the Camber products at a contracted price and distributed them through our existing sales force and commercial network. We retained 100% of the revenue generated from the sale of the Camber products. The Company recognized revenue from the sale of Camber products of $0.5 million, $1.2 million and $1.5 million during the years ended December 31, 2018, 2017 and 2016, respectively.

Oncon and Ras

On May 19, 2016, the Company entered into a development and license agreement with Limited Liability Company Oncon ("Oncon") whereby the Company granted Oncon exclusive licenses for certain antibodies. While Oncon is not considered a related party to Kadmon, a family member of a former executive of Kadmon is a limited, non-controlling partner and minority shareholder in Oncon who is unable to exert significant influence on the policies or operations of Oncon. Upon commercial sale of the licensed antibodies, the Company is eligible to receive a royalty equal to a percentage of net sales in the high-teens. The Company is also eligible to receive a portion of sublicensing revenue from Oncon ranging from the low ten percents to low thirty percents based on the development stage of the product. No such revenue was earned during the years ended December 31, 2018, 2017 and 2016. In connection with the development and license agreement, the Company also entered into an exclusive supply agreement with Limited Liability Company Ras ("Ras") whereby the Company will supply Ras with antibodies under the agreement for Ras to supply to Oncon. Ras is controlled by the family member of a former executive of Kadmon and was a related party to Kadmon until the resignation of the executive on October 24, 2018, at which point Ras ceased to be a related party. There has been no activity between the Company and Ras under the development and license agreement as of December 31, 2018.

On April 20, 2018, the Company entered into a cell bank development and royalty agreement with Oncon whereby the Company would serve as an agent to engage a third party to develop and manufacture a biological product for Oncon. Under the cell bank development agreement, Ras is Oncon's designated recipient of the master cell bank, if and when its development is complete. There has been no activity between the Company and Ras under the cell bank development agreement as of December 31, 2018. In June 2018, the Company received an upfront payment from Oncon totaling $0.8 million which the Company is required to deliver to the third party upon completion of development of the master cell bank. At December 31, 2018, the Company has $0.7 million recorded as an accrued liability for payments still to be made to the third party. Under this agreement, the Company is also to provide expertise and know-how to the development process and is eligible to receive a royalty equal to a percentage of net sales in the low single digit percents upon commercialization of the biological product. The Company is also eligible to receive a portion of sublicensing revenue from Oncon in the low single digit percents. No such revenue was earned during the year ended December 31, 2018.

12. Share-based Compensation

2011 Equity Incentive Plan—Options

The 2011 Equity Incentive Plan was adopted in July 2011. Under this plan, the Company's board of directors was able to grant unit-based awards to certain employees, officers, directors, managers, consultants and advisors. The plan was amended on November 7, 2013 to authorize the grant of a number of options to purchase Class A units equal to 7.5% of the outstanding Class A units calculated on a fully diluted basis. Effective July 26, 2016, no award may be granted under the 2011 Equity Plan. The 2011 Equity Plan was merged with and into the 2016 Equity Incentive Plan, outstanding awards were converted into awards with respect to our common stock and any new awards will be issued under the terms of the 2016 Equity Incentive Plan.

2016 Equity Incentive Plan

The Company's 2016 Equity Incentive Plan (the "2016 Equity Plan"), was approved by the Company's board of directors and holders of the Company's membership units in July 2016. The 2016 Equity Plan was Amended and Restated effective December 5, 2017. It is intended to make available incentives that will assist the Company to attract, retain and motivate employees, including officers, consultants and directors. The Company may provide these incentives through the grant of stock options, stock appreciation rights, restricted stock, restricted stock units, performance shares and units and other cash-based or stock-based awards.

A total of 6,720,000 shares of the Company's common stock was initially authorized and reserved for issuance under the 2016 Equity Plan, which was increased to 8,523,147on January 1, 2017, and to 11,668,905 on January 1, 2018. At December 31, 2018 the number of additional shares available for grant was 614,366. The 2016 Equity Plan provides for annual increases in the number of shares available for issuance under the 2016 Equity Plan on January 1, 2017 and each subsequent anniversary through January 1, 2025, by an amount equal to the smaller of (a) 4% of the number of shares of common stock issued and outstanding on the immediately preceding December 31, or (b) an amount determined by the board of directors. This reserve was increased to include any shares issuable upon exercise of options granted under the Company's 2011 Equity Incentive Plan that expire or terminate without having been exercised in full.

Appropriate adjustments will be made in the number of authorized shares and other numerical limits in the 2016 Equity Plan and in outstanding awards to prevent dilution or enlargement of participants' rights in the event of a stock split or other change in the Company's capital structure. Shares subject to awards which expire or are cancelled or forfeited will again become available for issuance under the 2016 Equity Plan. The shares available will not be reduced by awards settled in cash or by shares withheld to satisfy tax withholding obligations. Only the net number of shares issued upon the exercise of stock appreciation rights or options exercised by means of a net exercise or by tender of previously owned shares will be deducted from the shares available under the 2016 Equity Plan.

The 2016 Equity Plan will be generally administered by the compensation committee of the Company's board of directors. Subject to the provisions of the 2016 Equity Plan, the compensation committee will determine, in its discretion, the persons to whom and the times at which awards are granted, the sizes of such awards and all of their terms and conditions. However, the compensation committee may delegate to one or more of our officers the authority to grant awards to persons who are not officers or directors, subject to certain limitations contained in the 2016 Equity Plan and award guidelines established by the compensation committee. The compensation committee will have the authority to construe and interpret the terms of the 2016 Equity Plan and awards granted under it. The 2016 Equity Plan provides, subject to certain limitations, for indemnification by the Company of any director, officer or employee against all reasonable expenses, including attorneys' fees, incurred in connection with any legal action arising from such person's action or failure to act in administering the 2016 Equity Plan.

Awards may be granted under the 2016 Equity Plan to the Company's employees, including officers, directors or consultants or those of any present or future parent or subsidiary corporation or other affiliated entity. All awards will be evidenced by a written agreement between the Company and the holder of the award and may include any of the following:

- *Stock options.* The Company may grant nonstatutory stock options or incentive stock options as described in Section 422 of the Internal Revenue Code of 1986, as amended (the "Code"), each of which gives its holder the right, during a specified term (not exceeding 10 years) and subject to any specified vesting or other conditions, to purchase a number of shares of our common stock at an exercise price per share determined by the administrator, which may not be less than the fair market value of a share of the Company's common stock on the date of grant.

- *Stock appreciation rights.* A stock appreciation right gives its holder the right, during a specified term (not exceeding 10 years) and subject to any specified vesting or other conditions, to receive the appreciation in the fair market value of the Company's common stock between the date of grant of the award and the date of its exercise. The Company may pay the appreciation in shares of the Company's common stock or in cash.

- *Restricted stock.* The administrator may grant restricted stock awards either as a bonus or as a purchase right at such price as the administrator determines. Shares of restricted stock remain subject to forfeiture until vested, based on such terms and conditions as the administrator specifies. Holders of restricted stock will have the right to vote the shares and to receive any dividends paid, except that the dividends may be subject to the same vesting conditions as the related shares.

- *Restricted stock units.* Restricted stock units represent rights to receive shares of the Company's common stock (or their value in cash) at a future date without payment of a purchase price, subject to vesting or other conditions specified by the administrator. Holders of restricted stock units have no voting rights or rights to receive cash dividends unless and until shares of common stock are issued in settlement of such awards. However, the administrator may grant restricted stock units that entitle their holders to dividend equivalent rights.

- *Performance shares and performance units.* Performance shares and performance units are awards that will result in a payment to their holder only if specified performance goals are achieved during a specified performance period. Performance share awards are rights whose value is based on the fair market value of shares of the Company's common stock, while performance unit awards are rights denominated in dollars. The administrator establishes the applicable performance goals based on one or more measures of business performance enumerated in the 2016 Equity Plan, such as revenue, gross margin, net income or total stockholder return. To the extent earned, performance share and unit awards may be settled in cash or in shares of our common stock. Holders of performance shares or performance units have no voting rights or rights to receive cash dividends unless and until shares of common stock are issued in settlement of such awards. However, the administrator may grant performance shares that entitle their holders to dividend equivalent rights.

- *Cash-based awards and other stock-based awards.* The administrator may grant cash-based awards that specify a monetary payment or range of payments or other stock-based awards that specify a number or range of shares or units that, in either case, are subject to vesting or other conditions specified by the administrator. Settlement of these awards may be in cash or shares of our common stock, as determined by the administrator. Their holder will have no voting rights or right to receive cash dividends unless and until shares of our common stock are issued pursuant to the award. The administrator may grant dividend equivalent rights with respect to other stock-based awards.

The 2016 Equity Plan contains certain change of control provisions that provide for varied acceleration of vesting of outstanding awards, assumption, continuation or substitution of outstanding awards or cash-out of outstanding awards in the event of a change of control. Any awards which are not assumed or continued in connection with a change in control or are not exercised or settled prior to the change in control will terminate effective as of the time of the change in control. The compensation committee may provide for the acceleration of vesting of any or all outstanding awards upon such terms and to such extent as it determines, except that the vesting of all awards held by members of the board of directors who are not employees will automatically be accelerated in full. The 2016 Equity Plan also authorizes the compensation committee, in its discretion and without the consent of any participant, to cancel each or any outstanding award denominated in shares upon a change in control in exchange for a payment to the participant with respect to each share subject to the cancelled award of an amount equal to the excess of the consideration to be paid per share of common stock in the change in control transaction over the exercise price per share, if any, under the award.

The 2016 Equity Plan will continue in effect until it is terminated by the administrator, provided, however, that all awards will be granted, if at all, within 10 years of its effective date. The administrator may amend, suspend or terminate the 2016 Equity Plan at any time, provided that without stockholder approval, the plan cannot be amended to increase the number of shares authorized, change the class of persons eligible to receive incentive stock options, or effect any other change that would require stockholder approval under any applicable law or listing rule.

Total unrecognized compensation expense related to unvested options granted under the Company's share-based compensation plan was $6.8 million and $13.3 million at December 31, 2018 and 2017, respectively. That expense is expected to be recognized over a weighted average period of 1.5 years and 1.9 years as of December 31, 2018 and 2017, respectively. The Company recorded share-based option compensation expense under the 2011 Equity Incentive Plan and 2016 Equity Plan of $10.4 million, $12.4 million and $24.6 million for the years ended December 31, 2018, 2017 and 2016, respectively.

On July 13, 2016, the compensation committee of the Company's board of directors approved the amendment of all outstanding option awards issued under the Company's 2011 Equity Incentive Plan whereby, effective upon pricing of the Company's IPO, the exercise price (on a post-Corporate Conversion, post-split basis) was adjusted to equal the price per share of the Company's common stock in the IPO. The amendment was made to the awards as the original exercise price was substantially higher than the price of the Company's common stock in the IPO as a result of changes in the Company's capital structure that occurred upon IPO. Options to purchase an aggregate of approximately 1.6 million shares of the Company's Class A units were modified. Following this modification, the previously granted options will have the same vesting schedule as the original award and are modified on a one-for-one basis. The modification resulted in a $4.0 million charge, of which the incremental value of the previously vested portion of the awards totaling $1.8 million was expensed immediately during the third quarter of 2016 and the remaining $2.2 million was recognized over the remaining vesting periods of each award.

The following table summarizes information about stock options outstanding, not including performance stock options, at December 31, 2018 and 2017:

	Options Outstanding			
	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Balance, December 31, 2016	6,437,515	$ 8.32	9.28	$ 2,227,268
Granted	2,853,000	3.69		
Exercised	—	—		
Forfeited	(793,643)	6.23		
Balance, December 31, 2017	8,496,872	$ 6.96	8.83	$ —
Granted	2,110,424	2.76		
Exercised	—	—		
Forfeited	(842,757)	4.82		
Balance, December 31, 2018	9,764,539	$ 6.24	7.84	$ —
Options vested and exercisable, December 31, 2018	6,205,765	$ 8.06	6.92	$ —

The aggregate intrinsic value in the table above represents the total pre-tax intrinsic value calculated as the difference between the fair value of the Company's common stock at December 31, 2018 ($2.08 per share), December 31, 2017 ($3.62 per share) and December 31, 2016 ($5.35 per share) and the exercise price, multiplied by the related in-the-money options that would have been received by the option holders had they exercised their options at the end of the fiscal year. This amount changes based on the fair value of the Company's common stock. There were no options exercised during the years ended December 31, 2018 and 2017. There were 1,109 options exercised during the year ended December 31, 2016 that were not in-the-money.

The weighted-average fair value of the stock option awards, not including performance stock options, granted to employees, officers, directors and advisors was $1.69, $2.44 and $7.12 during the years ended December 31, 2018, 2017 and 2016, respectively, and was estimated at the date of grant using the Black-Scholes option-pricing model and the assumptions noted in the following table:

	Years Ended		
	December 31, 2018	December 31, 2017	December 31, 2016
Weighted average fair value of grants	$1.69	$2.44	$7.12
Expected volatility	72.94% - 75.92%	74.48% - 74.92%	74.98% - 79.35%
Risk-free interest rate	2.44% - 2.90%	1.87% - 2.22%	1.15% - 2.20%
Expected life	5.5 - 6.0 years	5.5 - 6.0 years	5.0 - 6.0 years
Expected dividend yield	0%	0%	0%

In December 2015, an option agreement entered into with the Company's Chief Executive Officer was replaced in its entirety by an option agreement dated December 31, 2015 so that the number of units was set to 769,231 unit options valued at $15.2 million which was recognized as compensation expense over the vesting term. These units under this option agreement were issued outside of the 2011 Equity Incentive Plan. The Company expensed $2.9 million, $7.2 million and $5.1 million during the years ended December 31, 2017 and 2016 and the fourth quarter of 2015, respectively. The options vested 1/3 at the grant date, 1/3 in August 2016 and 1/3 in August 2017. While the awards vest over this term they are not exercisable until the occurrence of the Calculation Date. The Calculation Date was deemed to have occurred upon consummation of the Company's IPO on July 26, 2016.

On July 13, 2016, the compensation committee of the Company's board of directors approved an option award for the Company's Chief Executive Officer increasing the number of options (giving effect to the Corporate Conversion) subject to his original option grant. The number of shares subject to this option award shall equal the difference between the 769,231 options originally granted and 5% of the Company's outstanding common equity determined on a fully diluted basis on the IPO date, which amounted to 1,630,536 options. The effective date of the new option award was the IPO date of July 26, 2016. The exercise price per share of common stock subject to the new incremental options awarded was equal to the IPO price per share of common stock at the IPO date of $12.00. The option award was subject to the same vesting schedule applicable to the original option grant such that all options awarded will vest on August 4, 2017. In consideration for the new option award, Dr. Harlan W. Waksal committed to perform an additional year of service in connection with receipt of the additional option shares subject to clawback provisions if the additional service period was not met. The additional year of service was completed on August 4, 2018. This modification resulted in a $12.4 million charge, of which the incremental value of the previously vested portion of the awards totaling $8.3 million was expensed during the third quarter of 2016 and the remaining amount of the unvested portion totaling $4.1 million was recognized over the additional two years of service through August 4, 2018.

Performance Awards

On April 3, 2018 the Company granted 1,597,500 nonqualified performance-based stock options ("Performance Options") to certain executive officers (each, a "Grantee") under the 2016 Equity Plan, which represents the maximum number of Performance Options that may be earned if all three performance milestones (each, a "Performance Goal") are achieved during the three-year period following the Grant Date (the "Performance Period"), as described below. If two of the three Performance Goals are achieved during the Performance Period, two-thirds of the Performance Options may be earned (the "Target" number of Performance Options), and if one of the three Performance Goals are achieved during the Performance Period (the minimum performance threshold for the Performance Options), one-third of the Performance Options is earned. In addition to the achievement of the Performance Goals, the Performance Options are also subject to time-based vesting requirements. Each Performance Option was granted with an exercise price of $4.06 per share and does not contain any voting rights. No Performance Options were granted under the 2016 Equity Plan prior to 2018.

The Performance Options may be earned based on the achievement of three separate Performance Goals related to the Company's operating and research and development activities during the Performance Period, subject to the Grantee's employment through the achievement date. If no Performance Goals are achieved during the Performance Period, the Performance Options will be forfeited. Any Performance Options earned upon the achievement of a Performance Goal will generally vest in three equal installments on specified vesting dates between the date of achievement of the Performance Goal and the third anniversary of the Grant Date based on continued employment; *provided*, that, if the relevant achievement date for a Performance Goal occurs after the second anniversary of the Grant Date, the full vesting of the Options earned will occur on the one year anniversary of the date of achievement of the applicable Performance Goal.

Unvested Performance Options will be forfeited upon the Grantee's termination of employment, unless the Grantee is terminated without cause or resigns for good reason or due to the Grantee's death or disability, in which case earned but

unvested Performance Options will accelerate and vest (and unearned Performance Options will be forfeited). If the Grantee is terminated for cause, all Performance Options, whether earned, unearned, vested or unvested, will be forfeited. If a change in control (as defined in the 2016 Equity Plan) occurs during the Performance Period, the Target number of Performance Options will be deemed earned (if not previously earned), and any unearned Performance Options will be forfeited. In addition, following a change in control (whether such change in control occurs within or after three years following the Grant Date), and subject to the terms of the 2016 Equity Plan, Performance Options earned upon such change in control will vest on the first anniversary of the change in control based on continued employment, and any Performance Options earned prior to the change in control will vest no later than the first anniversary of the change in control based on continued employment; *provided*, that, in each case, any unvested Performance Options will vest upon a Grantee's earlier termination by the Company without cause or resignation for good reason.

The weighted-average fair value of the Performance Options granted was $2.71 and was estimated at the date of grant using the Black-Scholes option-pricing model with the following assumptions: risk-free interest rate of 2.67%, expected term of 6.0 years, expected volatility of 74.50%, and a dividend rate of 0%.

Compensation expense for the Performance Options is recognized on a straight-line basis over the awards' requisite service period. The Performance Options vest upon the satisfaction of both a service condition and the satisfaction of one or more performance conditions, therefore the Company initially determined which outcomes are probable of achievement. The Company believes that the three-year service condition (explicit service period) and all three performance conditions (implicit service periods) will be satisfied. The requisite service period would be three years as that is the longest period of both the explicit service period and the implicit service periods. The first two performance conditions were satisfied during 2018 and the Company expects the third performance condition to be satisfied in 2019.

During the year ended December 31, 2018, 307,500 Performance Options were forfeited. At December 31, 2018, 1,290,000 Performance Options are outstanding with a weighted average remaining contractual life of 9.3 years. Total unrecognized compensation expense related to unvested Performance Options was $1.8 million at December 31, 2018. The unrecognized compensation cost is expected to be recognized over a weighted-average period of 1.5 years. No Performance Options were exercised during the year ended December 31, 2018.

Stock Appreciation Rights

The Company granted 1,040,000 stock appreciation rights under the 2016 Equity Plan to three executive employees during the year ended December 31, 2017. No stock appreciation rights were granted under the 2016 Equity Plan prior to 2017. During the year ended December 31, 2018, 205,000 stock appreciation rights were forfeited. At December 31, 2018, 835,000 stock appreciation rights are outstanding with a weighted average remaining contractual life of 8.9 years. The weighted-average fair value of the stock appreciation rights granted to the three executive officers was $2.42 and was estimated at the date of grant using the Black-Scholes option-pricing model with the following assumptions: risk-free interest rate of 2.22%, expected term of 6.0 years, expected volatility of 74.92%, and a dividend rate of 0%.

Compensation expense for stock appreciation rights is recognized on a straight-line basis over the awards' requisite service period. At December 31, 2018, there was $1.3 million of total unrecognized compensation cost related to stock appreciation rights. The unrecognized compensation cost is expected to be recognized over a weighted-average period of 1.9 years. No stock appreciation rights were exercised during the year ended December 31, 2018.

2014 Long-term Incentive Plan ("LTIP")

The LTIP was adopted in May 2014 and amended in December 2014. Under the LTIP, the Company's board of directors may grant up to 10% of the equity value of the Company including the following types of awards:

- Equity Appreciation Rights Units ("EAR units") whereby the holder would possess the right to a payment equal to the appreciation in value of the designated underlying equity from the grant date to the determination date. Such value is calculated as the product of the excess of the fair market value on the determination date of one EAR unit over the base price specified in the grant agreement and the number of EAR units specified by the award, or, when applicable, the portion thereof which is exercised.

- Performance Awards which become payable on the attainment of one or more performance goals established by the Plan Administrator. No performance period shall end prior to an IPO or Change in Control (the "Determination Date").

The Company's board of directors has the authority, at its discretion, to determine the terms and conditions of any LTIP grant, including vesting schedule.

Certain key employees were granted a total of 1,250 EAR units and 8,500 EAR units with a base price of $6.00/unit, expiring 10 years from the grant date (the "Award") during 2015 and 2014, respectively. Each unit entitles the holder to a payment amount equal to 0.001% of the fair market value of all of the outstanding equity in the Company on a fully diluted basis assuming the exercise of all derivative securities as of the Determination Date. The number of EAR units shall be adjusted to equal a certain percentage of the Company's outstanding common equity securities determined on the first trading date following the Determination Date.

The EAR units vest based on the earlier of (a) the expiration date if an IPO is consummated on or before that date or (b) the date of a change in control that occurs after the submission date of a Form S-1 registration statement to the SEC but prior to the expiration date. The EAR units also vest upon achieving certain predetermined stock price targets subject to continuing service through the date of the Form S-1 submission. The payment amount with respect to the holder's EAR units will be determined using the fair market value of the common stock on the trading date immediately preceding the settlement date. Each payment under the Award will be made in a lump sum and is considered a separate payment. The Company reserves the right to make payment in the form of common stock following the consummation of an IPO or in connection with a change in control, subject to the terms of the LTIP. Any settlement in the form of common stock will be limited to a maximum share allocation. The holder has no right to demand a particular form of payment.

A total of 9,750 units were outstanding under the LTIP at December 31, 2018 and 2017. The compensation expense for this award was recognized upon consummation of the Company's IPO on August 1, 2016 and was recorded as additional paid in capital. No compensation expense had been recorded prior to this date. The Company utilized a Monte-Carlo simulation to determine the fair value of the awards granted under the LTIP of $22.6 million, which was recorded as share-based compensation during the third quarter of 2016 as these awards are not forfeitable. The LTIP is payable upon the fair market value of the Company's common stock exceeding 333% of the $6.00 grant price ($20.00) per share prior to December 7, 2024. The holders of the LTIP have no right to demand a particular form of payment, and the Company reserves the right to make payment in the form of cash or common stock.

2016 Employee Stock Purchase Plan ("2016 ESPP")

The Company's board of directors has adopted and the Company's stockholders have approved the 2016 ESPP. The 2016 ESPP was amended and restated on March 16, 2018. A total of 1,125,000 shares of the Company's common stock were initially available for sale under the 2016 ESPP, which increased to 1,801,180 shares on January 1, 2017 and 2,551,180 shares on January 1, 2018. The Company issued 51,999 shares and 10,594 shares of common stock under the 2016 ESPP during the years ended December 31, 2018 and 2017, respectively. No meaningful compensation expense was recognized for the ESPP during the years ended December 31, 2018, 2017 and 2016. In addition, the 2016 ESPP provides for annual increases in the number of shares available for issuance under the 2016 ESPP on January 1, 2017 and each subsequent anniversary through 2025, equal to the smallest of:

- 750,000 shares;
- 1.5% of the outstanding shares of the Company's common stock on the immediately preceding December 31; or
- such other amount as may be determined by the Company's board of directors.

Appropriate adjustments will be made in the number of authorized shares and in outstanding purchase rights to prevent dilution or enlargement of participants' rights in the event of a stock split or other change in the Company's capital structure. Shares subject to purchase rights which expire or are cancelled will again become available for issuance under the 2016 ESPP.

The compensation committee of the Company's board of directors will administer the 2016 ESPP and have full authority to interpret the terms of the 2016 ESPP. The 2016 ESPP provides, subject to certain limitations, for indemnification by the Company of any director, officer or employee against all reasonable expenses, including attorneys' fees, incurred in connection with any legal action arising from such person's action or failure to act in administering the 2016 ESPP.

All of the Company's employees, including the Company's named executive officers, and employees of any of the Company's subsidiaries designated by the compensation committee are eligible to participate if they are customarily employed by the Company or any participating subsidiary for at least 20 hours per week and more than five months in any calendar year, subject to any local law requirements applicable to participants in jurisdictions outside the United States. However, an employee may not be granted rights to purchase stock under the 2016 ESPP if such employee:

- immediately after the grant would own stock or options to purchase stock possessing 5.0% or more of the total combined voting power or value of all classes of the Company's capital stock; or
- holds rights to purchase stock under all of the Company's employee stock purchase plans that would accrue at a rate that exceeds $25,000 worth of the Company's stock for each calendar year in which the right to be granted would be outstanding at any time.

The 2016 ESPP is intended to qualify under Section 423 of the Code but also permits us to include our non-U.S. employees in offerings not intended to qualify under Section 423. The 2016 ESPP will typically be implemented through consecutive six-month offering periods. The offering periods generally start on the first trading day of April and October of each year. The administrator may, in its discretion, modify the terms of future offering periods, including establishing offering periods of up to 27 months and providing for multiple purchase dates. The administrator may vary certain terms and conditions of separate offerings for employees of the Company's non-U.S. subsidiaries where required by local law or desirable to obtain intended tax or accounting treatment.

The 2016 ESPP permits participants to purchase common stock through payroll deductions of up to 10.0% of their eligible compensation, which includes a participant's regular and recurring straight time gross earnings and payments for overtime and shift premiums, but exclusive of payments for incentive compensation, bonuses and other similar compensation.

Amounts deducted and accumulated from participant compensation, or otherwise funded in any participating non-U.S. jurisdiction in which payroll deductions are not permitted, are used to purchase shares of the Company's common stock at the end of each offering period. The purchase price of the shares will be 85.0% of the lower of the fair market value of the Company's common stock on the first trading day of the offering period or on the last day of the offering period. Participants may end their participation at any time during an offering period and will be paid their accrued payroll deductions that have not yet been used to purchase shares of common stock. Participation ends automatically upon termination of employment with the Company.

Each participant in any offering will have an option to purchase for each full month contained in the offering period a number of shares determined by dividing $2,083 by the fair market value of a share of the Company's common stock on the first day of the offering period and except as limited in order to comply with Section 423 of the Code. Prior to the beginning of any offering period, the administrator may alter the maximum number of shares that may be purchased by any participant during the offering period or specify a maximum aggregate number of shares that may be purchased by all participants in the offering period. If insufficient shares remain available under the plan to permit all participants to purchase the number of shares to which they would otherwise be entitled, the administrator will make a pro rata allocation of the available shares. Any amounts withheld from participants' compensation in excess of the amounts used to purchase shares will be refunded, without interest.

A participant may not transfer rights granted under the 2016 ESPP other than by will, the laws of descent and distribution or as otherwise provided under the 2016 ESPP.

In the event of a change in control, an acquiring or successor corporation may assume the Company's rights and obligations under outstanding purchase rights or substitute substantially equivalent purchase rights. If the acquiring or successor corporation does not assume or substitute for outstanding purchase rights, then the purchase date of the offering periods then in progress will be accelerated to a date prior to the change in control.

The 2016 ESPP will remain in effect until terminated by the administrator. The compensation committee has the authority to amend, suspend or terminate the 2016 ESPP at any time.

13. Accrued Expenses

Short-term accrued expenses at December 31, 2018 and 2017 include the following (in thousands):

	December 31, 2018	December 31, 2017
Commission payable	$ 2,395	$ 2,395
Compensation and benefits	2,894	758
Severance	954	1,122
Research and development	4,847	1,915
Other	2,418	2,387
Total Accrued Expenses	$ 13,508	$ 8,577

Commission Payable

During 2014 and 2015, the Company raised $40.4 million in gross proceeds, $37.2 million net of $3.2 million in transaction costs, through the issuance of 3,514,859 Class E redeemable convertible units. At December 31, 2018 and 2017, $2.4 million remains in accrued liabilities relating to commissions to third parties for Class E redeemable convertible raises during 2015 and 2014.

Severance

Severance balances represent contractual compensation to be paid to former employees. Effective as of February 8, 2016, Dr. Samuel D. Waksal resigned from all positions with the Company and was no longer employed by the Company in any capacity. At December 31, 2018, accrued severance payable to Dr. Samuel D. Waksal totaled $0.1 million, which is recorded as accrued expense. At December 31, 2017, accrued severance payable to Dr. Samuel D. Waksal totaled $1.2 million, of which $1.0 was recorded as accrued expense and $0.2 million was recorded as other long-term liabilities. The separation agreement with Dr. Samuel D. Waksal contained certain supplement conditional payments, none of which have been met at December 31, 2018. The Company has not recorded any expense related to these conditional payments at December 31, 2018 and none of the conditional payments were met as of the expiration of the agreement on February 8, 2019.

Separation Agreement with Dr. Samuel D. Waksal

Dr. Samuel D. Waksal founded the Company in October 2010 and, until August 2014, was the chairman of the Company's board of directors and the Company's Chief Executive Officer. In August 2014, he stepped down as the Company's Chief Executive Officer and became the Company's Chief of Innovation, Science and Strategy.

In connection with his resignation on February 8, 2016, the Company entered into a separation agreement with Dr. Samuel D. Waksal terminating his employment with the Company and providing that he shall perform no further paid or unpaid services for the Company whether as employee, consultant, contractor or any other service provider. The principal provisions of the separation agreement are summarized below.

Severance and Other Payments

The Company agreed to make a series of payments (all subject to withholding taxes) to Dr. Samuel D. Waksal, some of which are contingent, structured as follows:

- a $3.0 million severance payment, of which $0.9 million, $1.0 million and $1.0 million was paid during 2016, 2017, and 2018, respectively, with the remaining $0.1 million payable during 2019. Severance expense totaling $3.1 million, including the cost of Company-paid medical benefits, was recorded during the first quarter of 2016 as these payments are probable and estimable;

- supplemental conditional payments of up to $6.75 million in the aggregate that are payable in 2017 ($2.25 million), 2018 ($2.25 million) and 2019 ($2.25 million) if specified benchmarks related to the valuation of the Company implied by the public offering price in the IPO, the net proceeds to the Company from the IPO and the Company's equity market capitalization on specified dates are achieved and subject to the Company having cash and cash equivalents less payables of $50 million or more on the dates when the Company makes those payments. The supplemental conditional payments that were payable in 2017 and 2018 were not earned and will therefore not be paid. The remaining conditional payment in 2019, although estimable, is not probable at December 31, 2018 and was not met as of the expiration of the agreement on February 8, 2019. The Company

has not recorded any expense related to these conditional payments at December 31, 2018 and the agreement expired on February 8, 2019 with no expense being recorded related to these conditional payments;

- an amount equal to five percent (up to a maximum of $15 million) of any cash received by the Company or guaranteed cash payments (as defined below) payable to the Company pursuant to the first three business development programs that the Company enters into on or before February 8, 2019 to research, develop, market or commercialize the Company's ROCK2 program or the Company's immuno-oncology program. For purposes of the separation agreement, ROCK2 program is defined to mean pathways involving ROCK2 or other pathways effecting inflammation, fibrosis, cancer or neurodegenerative diseases; immunooncology program is defined to mean antibodies or small molecules involved in inducing the immune system to make an anti-tumor response; and guaranteed cash payments is defined to mean payments to the Company of cash contractually provided for pursuant to an agreement entered into by the Company with respect to a business development program, which payments are not subject to the Company's meeting any milestones or thresholds. If the aggregate cash and guaranteed cash payments received by the Company pursuant to any business development program exceed $800 million before the completion of the IPO, the equity market capitalization requirements that must be met for Dr. Samuel D. Waksal to earn the supplemental payments of up to $6.75 million described above shall be deemed fulfilled, regardless of the Company's equity market capitalization at the applicable time. These conditional payments are not estimable or probable at December 31, 2018 The Company has not recorded any expense related to these conditional payments at December 31, 2018 and the agreement expired on February 8, 2019 with no expense being recorded related to these conditional payments.

LTIP EAR Unit Award

In December 2014, Dr. Samuel D. Waksal received an award of EAR units under the 2014 LTIP with a base price of $6.00 per EAR unit. The number of EAR units granted to Dr. Samuel D. Waksal was adjusted to equal 0.75% of our common stock determined on the first trading date following the date of the IPO. Based on the adjustments, the number of shares underlying Dr. Samuel D. Waksal's LTIP award is 1,783,618. The separation agreement provides that:

- by virtue of his separation from the Company, Dr. Samuel D. Waksal acknowledges that he is no longer entitled to vesting at December 16, 2024 date but is eligible to vest based on a change in control or stock price increase, as described herein below;
- the service component included in the vesting condition related to the occurrence of a change of control after an initial public offering but before December 16, 2024 is now satisfied;
- the service component included in the vesting condition related to the occurrence of a 333% increase in the fair market value of each EAR unit from the $6.00 grant price per unit before December 16, 2024 is now satisfied; and
- Dr. Samuel D. Waksal's EAR units shall not be subject to forfeiture, termination or recapture payment for violation of the restrictive covenants contained in the 2014 LTIP.

The compensation expense for this award was recognized upon consummation of the Company's IPO on August 1, 2016 and was recorded as additional paid in capital. No compensation expense had been recorded prior to this date. The Company utilized a Monte-Carlo simulation to determine the fair value of the award granted under the LTIP of $11.6 million, which was recorded during the third quarter of 2016 as this award is not forfeitable.

Covenants

The separation agreement contained customary non-solicitation, non-competition and non-disparagement provisions that continued in effect until the expiration of the agreement on February 8, 2019.

Research and Development

The Company has contracts with third parties for the development of the Company's product candidates. The timing of the expenses varies depending upon the timing of initiation of clinical trials and enrollment of patients in clinical trials. At December 31, 2018 and 2017, accrued research and development expenses for which the Company has not yet been invoiced totaled $4.8 million and $1.9 million, respectively.

14. 401(k) Profit-Sharing Plan

In October 2011, the Company began sponsoring a qualified Tax Deferred Savings Plan (401(k)) for all eligible employees of the Company and its subsidiaries. Participation in the plan is voluntary. Participating employees may defer up to 75% of their compensation up to the maximum prescribed by the Internal Revenue Code. The Company has an obligation to match non-highly compensated employee contributions of up to 6% of deferrals and also has the option to make discretionary matching contributions and profit sharing contributions to the plan annually, as determined by the Company's board of directors. The plan's effective date is October 1, 2011 and incorporates funds converted from the Kadmon Pharmaceuticals Profit Sharing Plan.

The Company expensed employer matching contributions of $0.2 million, $0.2 million and $0.3 million for the years ended December 31, 2018, 2017 and 2016, respectively. The Company made disbursements of $0.2 million and $0.3 million in the years ended December 31, 2018 and 2017, respectively. The Company typically disburses employer matching contributions during the first quarter following the plan year.

15. Commitments

Lease Commitments

The Company has three primary operating locations which are occupied under long-term leasing arrangements. In October 2010, Kadmon Corporation, LLC entered into a corporate headquarters and laboratory lease in New York, New York, expiring in February 2021 and opened a secured letter of credit with a third party financial institution in lieu of a security deposit for $2.0 million. As of December 31, 2016, there were four amendments to this lease agreement, which altered office and laboratory capacity and extended the lease term through October 2024. On August 11, 2017, the Company entered into the fifth and sixth amendments for the corporate headquarters and laboratory lease in New York, New York. Pursuant to the terms of the amendments, the Company surrendered a portion of its laboratory space, made a surrender payment of approximately $1.1 million which equated to the Company's deferred rent liability for the surrendered space, extended the term of the lease for an additional year through October 28, 2025, and received approximately $1.1 million in rent abatement beginning on September 1, 2017, which will be recognized straight-line over the remaining term of the lease. All other material terms of the lease remain intact. Rent expense for this lease amounted to $4.6 million, $5.7 million and $6.4 million for each of the years ended December 31, 2018, 2017 and 2016. During future years, the base rent amount associated with these premises will increase 3.5% annually. The Company has the ability to extend portions of the lease on the same terms and conditions as the current lease, except that the base rent will be adjusted to the fair market rental rate for the building based on the rental rate for comparable space in the building at the time of extension.

The Company is party to an operating lease in Warrendale, Pennsylvania (the Company's specialty-focused commercial operation), which expires on September 30, 2019, with a five-year renewal option. Rental payments under the renewal period will be at market rates determined from the average rentals of similar tenants in the same industrial park. Rental expense for this lease was $0.6 million for each of the years ended December 31, 2018, 2017 and 2016, respectively.

In August 2015, the Company entered into an office lease agreement in Cambridge, Massachusetts (the Company's clinical office) effective January 2016 and expiring in April 2023. The Company opened a secured letter of credit with a third party financial institution in lieu of a security deposit for $0.1 million. Rent expense for this lease was $0.3 million in each of the years ended December 31, 2018, 2017 and 2016.

Future minimum rental payments under noncancellable leases are as follows (in thousands) at December 31, 2018:

Year ending December 31,	Amount
2019	$ 4,672
2020	4,204
2021	4,177
2022	4,286
2023	4,153
Thereafter	7,731
Total	**$ 29,223**

Licensing Commitments

The Company has entered into several license agreements for products currently under development (Note 11). The Company may be obligated in future periods to make additional payments, which would become due and payable only upon the achievement of certain research and development, regulatory, and approval milestones. The specific timing of such milestones cannot be predicted and depends upon future discretionary clinical developments as well as regulatory agency actions which cannot be predicted with certainty (including action which may never occur). These additional contingent milestone payments aggregate to $215.9 million at December 31, 2018. Any payments made prior to FDA approval will be expensed as research and development. Payments made after FDA approval will be capitalized.

Further, under the terms of certain licensing agreements, the Company may be obligated to pay commercial milestones contingent upon the realization of sales revenues and sublicense revenues. Due to the long-range nature of such commercial milestones, they are neither probable at this time nor predictable, and consequently are not included in the additional contingent milestone payment amount.

Employment Agreements

Certain employment agreements provide for routine severance compensation. The Company has recorded a liability for such agreements of $1.0 million and $1.2 million at December 31, 2018 and 2017, respectively (Note 13).

16. Contingencies

The Company is subject to various legal proceedings that arise from time to time in the ordinary course of its business. Although the Company believes that the various proceedings brought against it are without merit, and that it has adequate product liability and other insurance to cover any claims, litigation is subject to many factors which are difficult to predict and there can be no assurance that the Company will not incur material costs in the resolution of legal matters. Should the Company determine that any future obligations will exist, the Company will record expense equal to the amount which is deemed probable and estimable.

Legal Proceedings

The Glodek Litigation

On July 25, 2016, Kevin Glodek filed and served a Summons with Notice against Kadmon Holdings, LLC and Kadmon Holdings, Inc. in the New York State Supreme Court, for the county of New York, for an amount of no less than $2.8 million with interest, plus costs and disbursements. Company counsel demanded a complaint and that complaint was served and filed on September 6, 2016. In the complaint, Glodek alleges fraud, misrepresentation, breach of contract, breach of the implied covenant of good faith and fair dealing, and unjust enrichment, for amounts to be determined at trial, but in no event less than $4 million with interest, plus costs and disbursements. Glodek's claims arise out of a 2015 settlement agreement, in which he released all claims he had against Kadmon Holdings, LLC and Kadmon Holdings, Inc. On September 21, 2016, Glodek filed an Amended Summons and an Amended Complaint adding Mr. Steven N. Gordon and a former executive of the Company as named defendants. All defendants moved (i) to dismiss the Amended Complaint and (ii) for sanctions or, in the alternative, to disqualify Glodek's counsel. Argument on the motions was conducted on January 24, 2017 before the Honorable Anil Singh. On April 18, 2017, the complaint was dismissed in its entirety. Having previously noticed an appeal from that dismissal, Glodek filed his opening appellate brief on July 10, 2018. The defendants filed their brief, which included a cross-appeal seeking sanctions and argument was heard before the Appellate Division on October 26, 2018. On November 20, 2018, the Appellate Division affirmed the lower court's complete dismissal of the compliant. The action terminated on December 20, 2018 and the matter is closed.

17. Concentrations

Major Customers

There were no material customer concentrations for the year ended December 31, 2018. Sales to two major customers aggregate to approximately 29% and 41% of the Company's net sales for the years ended December 31, 2017 and 2016, respectively. There were no net accounts receivable outstanding from these customers at December 31, 2018, while net accounts receivable from these customers totaled $0.1 million at December 31, 2017.

At December 31, 2018, accounts receivable consist primarily of amounts due from a collaboration agreement. The Company's management believes these receivables are fully collectible.

Major Suppliers

Due to FDA requirements and other factors, the Company is generally unable to make immediate changes to its supplier arrangements. Manufacturing services related to each of the Company's pharmaceutical products are primarily provided by a single source. The Company's raw materials are also provided by a single source for each product. Management attempts to mitigate this risk through long-term contracts and inventory safety stock.

18. Related Party Transactions

At December 31, 2016, Kadmon I held approximately 12.1% of the total outstanding common stock of Kadmon Holdings. The sole manager of Kadmon I was an executive officer of the Company. Kadmon I had no special rights or preferences in connection with its investment into Kadmon Holdings, and had the same rights as all other holders of Kadmon Holdings Class A units. On January 23, 2017, Kadmon I, LLC was dissolved and liquidated. Upon dissolution and liquidation, all assets of Kadmon I, LLC which consists solely of the shares of common stock in Kadmon Holdings, Inc., were distributed to the members of Kadmon I, LLC.

During 2014, the Chief Executive Officer provided the Company with short-term, interest-free loans to meet operating obligations. The $3.0 million related party loan with the Chief Executive Officer was repaid in full during the fourth quarter of 2016. During the year ended December 31, 2016, the maximum amount which was outstanding in the aggregate was $3.0 million and was recorded as a related party loan on the Company's balance sheet.

In June 2016, the Company entered into an agreement with 72 KDMN Investments, LLC whereby the Company agreed to extend certain rights to 72 KDMN Investments, LLC which shall survive closing of the IPO, including board of director designation rights and confidentiality rights, subject to standard exceptions. In addition, the Company agreed to provide 72 KDMN Investments, LLC with most favored nation rights which terminated upon the closing of the IPO on August 1, 2016. Andrew B. Cohen, a former member of our board of directors, is an affiliate of 72 KDMN. In January 2017, Mr. Cohen resigned from the Company's board of directors and the Company received notice that 72 KDMN forfeits, relinquishes and waives any and all rights it has to designate a director to the Company's board of directors.

In June 2016, Dr. Harlan W. Waksal, the Company's President and Chief Executive Officer, certain entities affiliated with GoldenTree Asset Management LP, Bart M. Schwartz, the former chairman of the Company's board of directors, 72 KDMN and D. Dixon Boardman, a member of the Company's board of directors, subscribed for 86,957, 43,479, 21,740, 86,957 and 21,740 of the Company's Class E redeemable convertible units, respectively, at a value of $11.50 per unit.

In June 2016, the Company entered into certain agreements with Falcon Flight LLC and one of its affiliates in connection with a settlement of certain claims alleging breaches of a letter agreement between the Company and Falcon Flight LLC relating to a prior investment by Falcon Flight LLC and its affiliate in the Company's securities, which letter agreement was amended and restated as part of this settlement, which, together with a supplemental letter agreement, we refer to as the Falcon Flight Agreement. Subject to certain terms and conditions contained therein, the Falcon Flight Agreement provides Falcon Flight LLC and its affiliate with certain most favored nation rights, information rights, consent rights, anti-dilution protections including the issuance of 1,061,741 additional Class E redeemable convertible membership units with a conversion price equal to any down-round price, a right to designate a member of the Company's board of then managers or observer and notice requirements with respect to any waivers by the underwriters in connection with lock-up agreements, among other things. The aforementioned rights terminated upon the closing of the IPO on August 1, 2016, except for indemnification of Falcon Flight LLC's board designee or observer, which survives termination. In addition, the Company agreed to pay $0.5 million to Falcon Flight LLC within one business day following the consummation of the IPO, and $0.3 million within sixty days following the consummation of the IPO. The Company recorded an estimate for this settlement of approximately $10.4 million in September 2015 and recorded an additional expense of $2.6 million in June 2016 based on the excess of the fair value of this settlement over the $10.4 million previously expensed in 2015.

Two former employees of the Company received $1.25 million each upon the consummation of the IPO, which the Company settled through the issuance of an aggregate of 208,334 shares of its common stock on August 1, 2016.

Certain of the Company's existing institutional investors, including investors affiliated with certain of the Company's directors, purchased an aggregate of 2,708,332 shares of the Company's common stock in its IPO at the IPO price of $12.00 per share, for an aggregate purchase price of $32.5 million, and on the same terms as the shares that were sold to the public generally. Perceptive Advisors, LLC, Third Point Partners, LLC and GoldenTree purchased 1,458,333 shares of the Company's common stock for $17.5 million, 1,041,666 shares of the Company's common stock for $12.5 million and 208,333 shares of the Company's common stock for $2.5 million, respectively.

Certain of the Company's existing institutional investors purchased an aggregate of 21,001,514 shares of our common stock in our public offering that closed on June 11, 2018. Perceptive Advisors LLC purchased 8,000,000 shares of our common stock for $26.4 million, Vivo Capital VIII LLC purchased 7,121,212 shares of our common stock for $23.5 million, Acuta Capital Partners LLC purchased 2,850,000 shares of our common stock for $9.4 million and Puissance Capital Management LP purchased 3,030,302 shares of our common stock for $10.0 million.

19. Income Taxes

The Company files U.S. federal and state tax returns for Kadmon Holdings, Inc. and the required information returns for its international subsidiaries, all of which are wholly owned. The Company recorded an income tax benefit of $0.5 million for the year ended December 31, 2018, related to an adjustment to the deferred tax liability, as explained below. The Company recorded an income tax benefit of $0.1 million for the year ended December 31, 2017, related to a $0.4 million adjustment to the deferred tax liability, as explained below, net of $0.3 million of income tax expense related to a $2.0 million milestone payment received from Jinghua. The Company recorded income tax expense of $0.3 million for the year ended December 31, 2016, related to a $2.0 million milestone payment received from Jinghua.

The Tax Cuts and Jobs Act (the "Act") was enacted in December 2017. The Act reduces the U.S. federal corporate tax rate from 35 percent to 21 percent, requires companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred, limits business interest expense deductions for certain taxpayers, creates new taxes on certain foreign earnings and reduces the orphan drug tax credit. The Company recognized a deferred income tax benefit of $0.4 million for the year ended December 31, 2017 due to the write-down of a deferred tax liability related to the reduction of the corporate income tax rate per the Act.

During the year ended December 31, 2018, in accordance with the Act, the Company determined it necessary to reduce the recorded deferred tax liability by $0.6 million. The deferred tax liability was initially recorded to account for the book vs. tax basis difference related to the goodwill intangible asset, also known as a "naked credit". The deferred tax liability was excluded from sources of future taxable income, as the timing of its reversal cannot be predicted due to the indefinite life of the goodwill. As such, this deferred tax liability cannot be used to offset the valuation allowance. In accordance with the Act, losses generated beginning with the 2018 tax year may be carried forward indefinitely for U.S. federal tax purposes. However, such losses are limited to offset 80% of taxable income in future years. Thus, 80% of the U.S. federal deferred tax liability related to goodwill may be used to offset the valuation allowance, resulting in a reduction of the Company's deferred tax liability of $0.6 million.

The income tax provision consists of the following components (in thousands):

	For the Years Ended December 31,		
	2018	2017	2016
Current tax expense (benefit)			
Foreign	$ —	$ 316	$ 315
Federal	—	—	—
State	—	—	—
Total current tax expense	—	316	315
Deferred tax expense (benefit)			
Federal	(563)	(485)	(15)
State	39	48	42
Total deferred tax benefit	(524)	(437)	27
Total income tax expense (benefit)	**$ (524)**	**$ (121)**	**$ 342**

The income tax expense (benefit) differs from the expense (benefit) that would result from applying federal statutory rates to loss before income taxes as follows (in thousands):

	For the Years Ended December 31,					
	2018		2017		2016	
	Amount	Rate	Amount	Rate	Amount	Rate
Expected federal statutory income tax	$ (11,283)	-21.0%	$ (27,821)	-35.0%	$ (72,945)	-35.0%
State income taxes, net of federal benefits	(3,649)	-6.8%	(8,314)	-10.5%	(9,485)	-4.6%
Change in federal tax rate used for deferred purposes	—	0.0%	112,611	141.7%	200	0.1%
Adjustment to deferred tax assets	8,578	16.0%	15,210	19.1%	—	0.0%
Change in valuation allowance	5,830	10.8%	(91,807)	-115.5%	82,572	39.6%
Income tax expense (benefit)	**$ (524)**	**-1.0%**	**$ (121)**	**-0.2%**	**$ 342**	**0.1%**

Deferred income tax expense (benefit) results primarily from the timing of temporary differences between the tax and financial statement carrying amounts of goodwill. The net deferred tax asset and liability in the accompanying consolidated balance sheets consists of the following components (in thousands):

	For the Years Ended December 31,	
	2018	2017
Deferred tax assets		
Net operating loss carryforward	$ 123,562	$ 112,289
Foreign tax credit carryforward	631	631
Capitalized research and development	73,893	66,500
Share-based compensation	21,319	18,735
Loss on MeiraGTx investments	—	6,294
Organization costs	27	30
Depreciation	838	772
Intangibles	27,769	30,788
163(j) interest limitations	1,252	—
Other	1,335	2,145
Total deferred tax assets	250,626	238,184
Deferred tax liabilities		
Goodwill	(415)	(939)
Unrealized gain on MeiraGTx equity securities investment	(2,393)	—
Change in fair value of financial instruments	(4,112)	—
Total deferred tax liabilities	(6,920)	(939)
Total deferred tax assets, net	243,706	237,245
Valuation allowance	(244,121)	(238,184)
Deferred tax liability	$ (415)	$ (939)

At December 31, 2018, the Company has unused federal and state net operating loss (“NOL”) carry-forwards of $460.3 million and $404.3 million, respectively, that may be applied against future taxable income. These carry-forwards expire at various dates through December 31, 2037, with the exception of approximately $44.0 million of federal net operating loss carry-forwards, which will not expire. The 20-year limitation was eliminated for losses generated after January 1, 2018, giving the taxpayer the ability to carry forward losses indefinitely. However, NOL carry forward arising after January 1, 2018, will now be limited to 80 percent of taxable income.

The use of the Company’s NOL carry-forwards may, however, be subject to limitations as a result of an ownership change. A corporation undergoes an “ownership change,” in general, if a greater than 50% change (by value) in its equity ownership by one or more five-percent stockholders (or certain groups of non-five-percent stockholders) over a three-year period occurs. After such an ownership change, the corporation’s use of its pre-change NOL carry-forwards and other pre-change tax attributes to offset its post-change income is subject to an annual limitation determined by the equity value of the corporation on the date the ownership change occurs multiplied by a rate determined monthly by the Internal Revenue Service. This rate for March 2019 equals 2.39 percent. The Company experienced ownership changes under Section 382 of the Code in 2010, 2011 and 2016, but the Company did not reduce the gross deferred tax assets related to the NOL carry-forwards because the limitations do not hinder the Company’s ability to potentially utilize all of the NOL carry-forwards.

The Company is likely to experience another ownership change in the future, possibly in 2019, as a result of future shifts in stock ownership, which may include shifts in stock ownership as a result of any future equity offerings. A renewed ownership change will likely materially and substantially reduce the Company's ability to fully utilize the NOL carry-forwards and, consequently, will likely reduce the gross deferred tax assets related to the NOL carry-forwards. If an ownership change occurred and if the Company earned net taxable income, our ability to use the pre-change NOLs to offset U.S. federal taxable income would be subject to these limitations, which could potentially result in increased future tax liability compared to the tax liability the Company would incur if the use of NOL carry-forwards were not so limited.

In accordance with ASC 740, "Income Taxes," the Company recorded a valuation allowance to fully offset the gross deferred tax asset, because it is more likely than not that the Company will not realize future benefits associated with these deferred tax assets at December 31, 2018 and 2017. The change in deferred tax liability has been recognized as an income tax benefit in the consolidated statements of operations for the years ended December 31, 2018 and 2017 and as income tax expense for the year ended December 31, 2016.

The Company follows guidance on accounting for uncertainty in income taxes which prescribes a minimum threshold a tax position is required to meet before being recognized in the financial statements. The Company does not have any liabilities as of December 31, 2018 and 2017 to account for potential income tax exposure. The Company is obligated to file income tax returns in the U.S. federal jurisdiction and several U.S. States. Since the Company had losses in the past, all prior years that generated net operating loss carry-forwards are open and subject to audit examination in relation to the net operating loss generated from those years.

20. Subsequent Events

ATM Offering

On August 4, 2017, the Company entered into a Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor") under which the Company may sell up to $40.0 million in shares of its common stock in one or more placements at prevailing market prices for its common stock (the "ATM Offering"). The Company has no obligation to sell any shares under the Sales Agreement, and may at any time suspend solicitation and offers under the Sales Agreement. Any sales would be effected pursuant to the Company's registration statement on Form S-3 (File No. 333-222364), declared effective by the SEC on January 10, 2018. The Company filed a prospectus, dated January 12, 2018, with the SEC in connection with the offer and sale of the shares pursuant to the Sales Agreement.

As of December 31, 2018, the Company had not sold any shares of common stock under the ATM Offering. Subsequent to December 31, 2018 and through January 9, 2019, the Company sold 13,778,705 shares of common stock at a weighted average price of $2.17 per share through the ATM Offering and received total gross proceeds of $29.9 million ($29.0 million net of $0.9 million of commissions payable by the Company).

21. Quarterly Financial Data (unaudited)

The following table presents our unaudited quarterly financial data. Our quarterly results of operations for these periods are not necessarily indicative of our future results of operations.

(in thousands, except per share data)	Three Months Ended December 31,		Three Months Ended September 30,		Three Months Ended June 30,		Three Months Ended March 31,	
	2018	2017	2018	2017	2018	2017	2018	2017
Net sales	$ 58	$ 187	$ 198	$ 1,036	$ 161	$ 1,698	$ 274	$ 2,336
License and other revenue	174	1,277	174	1,241	198	1,259	159	3,230
Total revenue	232	1,464	372	2,277	359	2,957	433	5,566
Cost of sales	51	222	59	277	103	266	199	567
Write-down of inventory	5	(22)	20	933	98	373	147	370
Gross profit	176	1,264	293	1,067	158	2,318	87	4,629
Operating expenses:								
Research and development	17,090	10,499	11,918	11,775	10,178	10,056	9,780	8,447
Selling, general and administrative	10,914	7,916	9,668	9,121	8,812	9,902	8,250	10,118
Total operating expenses	28,004	18,415	21,586	20,896	18,990	19,958	18,030	18,565
Loss from operations	(27,828)	(17,151)	(21,293)	(19,829)	(18,832)	(17,640)	(17,943)	(13,936)
Total other expense	13,651	1,476	(7,494)	1,874	(39,775)	4,674	2,498	3,315
Income tax expense (benefit)	38	(437)	—	—	(562)	—	—	316
Net income (loss)	(41,517)	(18,190)	(13,799)	(21,703)	21,505	(22,314)	(20,441)	(17,567)
Deemed dividend on convertible preferred stock and Class E redeemable convertible units	515	490	515	490	491	469	490	469
Net income (loss) attributable to common stockholders	(42,032)	(18,680)	(14,314)	(22,193)	21,014 [1]	(22,783)	(20,931)	(18,036)
Basic net income (loss) per share of common stock	$ (0.37)	$ (0.24)	$ (0.13)	$ (0.42)	$ 0.25	$ (0.44)	$ (0.27)	$ (0.39)

Diluted net income (loss) per share of common stock	(0.37)	(0.24)	(0.13)	(0.42)	0.24	(0.44)	(0.27)	(0.39)
Weighted average basic shares of common stock outstanding	113,130,817	78,397,156	113,101,776	52,570,880	85,004,107	51,846,521	78,650,143	46,507,435
Weighted average diluted shares of common stock outstanding	113,130,817	78,397,156	113,101,776	52,570,880	90,164,248	51,846,521	78,650,143	46,507,435

(1) Net income attributable to common stockholders for the three months ended June 30, 2018 includes the unrealized gain on equity securities related to the MeiraGTx initial public offering (the “MeiraGTx IPO”) on June 12, 2018. Upon completion of the MeiraGTx IPO, the Company discontinued the equity method of accounting for the investment in MeiraGTx and determined the remaining investment to be an equity security accounted for in accordance with ASC 321. As the Company’s investment in MeiraGTx common stock has a readily determinable market value, the Company recorded an unrealized gain of $40.5 million in June 2018 related to the fair value of its ownership of common stock of MeiraGTx (Note 10).

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
3.1	Certificate of Incorporation of Kadmon Holdings, Inc. (incorporated herein by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37841), filed with the SEC on August 1, 2016).
3.2	Certificate of Designations of Kadmon Holdings, Inc. creating the 5% Convertible Preferred Stock (incorporated herein by reference to Exhibit 3.3 to the Registrant's Current Report on Form 8-K (File No. 001-37841), filed with the SEC on August 1, 2016).
3.3	Bylaws of Kadmon Holdings, Inc. (incorporated herein by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-37841), filed with the SEC on August 1, 2016).
4.1	Form of Kadmon Holdings, Inc.'s Common Stock Certificate (incorporated herein by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-211949), filed with the SEC on July 14, 2016).
4.2	Form of Warrant to Purchase Common Stock issued to investors in Kadmon Holdings, Inc.'s March 8, 2017 financing (incorporated herein by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K Amendment No. 2 (File No. 001-37841), filed with the SEC on March 9, 2017).
4.3	Form of Warrant Agreement dated September 28, 2017 (incorporated herein by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-37841), filed with the SEC on September 28, 2017).
4.4	Form of 2013 Warrant (incorporated by reference to Exhibit 10.46 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
4.5	Form of 2013/2014 Warrant (incorporated by reference to Exhibit 10.47 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
4.6	Form of 2015 Warrant (incorporated by reference to Exhibit 10.48 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.1	Credit Agreement, dated August 28, 2015 between Kadmon Pharmaceuticals, LLC, the guarantors from time to time party thereto, the lenders from time to time party thereto and Perceptive Credit Opportunities Fund, L.P. (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.2	Amendment to Credit Agreement, dated October 27, 2015, by and between Kadmon Pharmaceuticals, LLC, the guarantors from time to time party thereto, the lenders from time to time party thereto and Perceptive (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.3	Amendment # 2 to Credit Agreement, dated November 4, 2016, by and among Kadmon Pharmaceuticals, LLC, the guarantors from time to time party thereto, the lenders from time to time party thereto and Perceptive Credit Holdings, L.P. (incorporated herein by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37841), filed with the SEC on November 9, 2016).
10.4	Amendment #3 to Credit Agreement, dated March 31, 2017 by and among Kadmon Pharmaceuticals, LLC , the guarantors from time to time party thereto, the lenders from time to time party thereto and Perceptive Credit Holdings, L.P. (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37841), filed with the SEC on April 3, 2017).
10.5	First Amended and Restated License Agreement, dated August 13, 2010, by and between Symphony Evolution, Inc. and Kadmon Corporation, LLC (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.6	First Amendment to First Amended and Restated License Agreement, dated December 11, 2012, by and between Symphony Evolution, Inc. and Kadmon Corporation, LLC (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.7	Second Amendment to First Amended and Restated License Agreement, dated March 28, 2013, by and between Symphony Evolution, Inc. and Kadmon Corporation, LLC (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).

10.8	Third Amendment to First Amended and Restated License Agreement, dated October 31, 2013, by and between Symphony Evolution, Inc. and Kadmon Corporation, LLC (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.9	Fourth Amendment to First Amended and Restated License Agreement, dated May 1, 2014, by and between Symphony Evolution, Inc. and Kadmon Corporation, LLC (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.10	Fifth Amendment to First Amended and Restated License Agreement, dated June 11, 2014, by and between Symphony Evolution, Inc. and Kadmon Corporation, LLC (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.11	Sixth Amendment to First Amended and Restated License Agreement, dated September 30, 2014, by and between Symphony Evolution, Inc. and Kadmon Corporation, LLC (incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.12	Sub-license Agreement, dated April 8, 2011, by and among NT Life Sciences, LLC, Kadmon Pharmaceuticals, LLC and Surface Logix, Inc. (incorporated by reference to Exhibit 10.17 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.13	Collaboration and License Agreement, dated November 20, 2015, by and between Kadmon Pharmaceuticals, LLC and Jinghua Pharmaceutical Group Co., Ltd. (incorporated by reference to Exhibit 10.30 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.14	Supply and Distribution Agreement, dated February 23, 2016, by and between Kadmon Pharmaceuticals, LLC and Camber Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.31 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.15	Amendment to Supply and Distribution Agreement, dated May 20, 2016, by and between Kadmon Pharmaceuticals, LLC and Camber Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.32 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.16	Second Amendment to Supply and Distribution Agreement, dated August 23, 2016, by and among Kadmon Pharmaceuticals, LLC and Camber Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.8 to the Registrant's Annual Report on Form 10-K (File No. 001-37841), filed with the SEC on March 22, 2017).
10.17	Third Amendment to Supply and Distribution Agreement, dated February 13, 2017, by and among Kadmon Pharmaceuticals, LLC and Camber Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.17 to the Registrant's Annual Report on Form 10-K (File No. 001-37841), filed with the SEC on March 22, 2017).
10.18	Employment Agreement between Kadmon Corporation, LLC and Harlan W. Waksal, M.D., dated effective as of November 1, 2015 (incorporated by reference to Exhibit 10.33 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.19	Employment Agreement between Kadmon Corporation, LLC and Konstantin Poukalov, effective as of November 1, 2015 (incorporated by reference to Exhibit 10.34 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.20	Employment Agreement between Kadmon Corporation, LLC and Steven N. Gordon, dated and effective as of July 1, 2015 (incorporated by reference to Exhibit 10.35 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.21	Separation Agreement, dated February 3, 2016, by and between Kadmon Holdings, LLC and Samuel D. Waksal, Ph.D. (incorporated by reference to Exhibit 10.36 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.22	Lease Agreement, dated October 28, 2010, by and between ARE-East River Science Park, LLC and Kadmon Pharmaceuticals, LLC (incorporated by reference to Exhibit 10.37 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.23	First Amendment to Lease Agreement, dated July 1, 2011, by and between ARE-East River Science Park, LLC and Kadmon Pharmaceuticals, LLC (incorporated by reference to Exhibit 10.38 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.24	Second Amendment to Lease Agreement, dated November 16, 2011, by and between ARE-East River Science Park, LLC and Kadmon Pharmaceuticals, LLC (incorporated by reference to Exhibit 10.39 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.25	Third Amendment to Lease Agreement, dated January 4, 2013, by and between ARE-East River Science Park, LLC and Kadmon Pharmaceuticals, LLC (incorporated by reference to Exhibit 10.40 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).

10.26	Fourth Amendment to Lease Agreement, dated July 25, 2013, by and between ARE-East River Science Park, LLC and Kadmon Pharmaceuticals, LLC (incorporated by reference to Exhibit 10.41 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.27	Fifth Amendment to Lease Agreement, dated August 11, 2017, by and between ARE-East River Science Park, LLC and Kadmon Corporation, LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37841), filed with the SEC on August 14, 2017).
10.28	Sixth Amendment to Lease Agreement, dated August 11, 2017, by and between ARE-East River Science Park, LLC and Kadmon Corporation, LLC (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-37841), filed with the SEC on August 14, 2017).
10.29	Kadmon Holdings, LLC 2014 Long-Term Incentive Plan, as amended (incorporated by reference to Exhibit 10.43 to the Registrant's Registration Statement on Form S-1 (File No. 333-211949), filed with the SEC on June 10, 2016).
10.30	Form of Indemnification to be entered into by Kadmon Holdings, Inc. and each of its directors, executive officers and certain key employees (incorporated by reference to Exhibit 10.55 to the Registrant's Registration Statement on Form S-1/A (File No. 333-211949), filed with the SEC on July 14, 2016).
10.31	Amended and Restated Kadmon Holdings, Inc. 2016 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.57 to the Registrant's Annual Report on Form 10-K (File No. 001-37841), filed with the SEC on March 6, 2018).
10.32	Form of Stock Appreciation Right Agreement under Amended and Restated Kadmon Holdings, Inc. 2016 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.58 to the Registrant's Annual Report on Form 10-K (File No. 001-37841), filed with the SEC on March 6, 2018).
10.33	Fifth Waiver Agreement to Credit Agreement, dated March 2, 2018, by and among Kadmon Pharmaceuticals, LLC, the guarantors from time to time party thereto, the lenders from time to time party thereto and Perceptive Credit Holdings, L.P. (incorporated herein by reference to Exhibit 10.59 to the Registrant's Annual Report on Form 10-K (File No. 001-37841), filed with the SEC on March 6, 2018).
10.34	Amended and Restated Kadmon Holdings, Inc. 2016 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37841), filed with the SEC on May 8, 2018).
10.35	Form of Subscription Agreement dated June 11, 2018 (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37841), filed with the SEC on June 14, 2018).
10.36	Amendment # 4 to Credit Agreement dated June 12, 2018, by and among Kadmon Pharmaceuticals, LLC, the guarantors from time to time party thereto, the lenders from time to time party thereto and Perceptive Credit Holdings, L.P. (incorporated herein by referend to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37841), filed with the SEC on June 13, 2018.
10.37	Amendment # 5 to Credit Agreement and Amendment to Warrant Certificate, dated August 15, 2018, by and among Kadmon Pharmaceuticals, LLC, the guarantors from time to time party thereto, and Perceptive Credit Holdings, L.P., as collateral representative and lender (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37841), filed with the SEC on August 16, 2018.
10.38	Controlled Equity Offering Sales Agreement, dated August 4, 2017, between the Registrant and Cantor Fitzgerald & Co. (incorporated herein by reference to Exhibit 1.2 to the Registrant's Registration Statement on Form S-3 (File No. 333-219712), filed with the SEC on August 4, 2017.
10.39*	Form of Performance Stock Option Agreement under Amended and Restated Kadmon Holdings, Inc. 2016 Equity Incentive Plan.
10.40*	Separation and Release Agreement between Kadmon Corporation, LLC and Konstantin Poukalov, dated November 30, 2018.
10.41*	Sixth Waiver Agreement to Credit Agreement, dated March 6, 2019, by and among Kadmon Pharmaceuticals, LLC, the guarantors party thereto and Perceptive Credit Holdings, L.P.
21.1*	List of subsidiaries.
23.1*	Consent of independent registered public accounting firm.
31.1*	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of The Sarbanes-Oxley Act of 2002.

31.2*	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of The Sarbanes-Oxley Act of 2002.
32.1**	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2**	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101*	The following materials from the Kadmon Holdings, Inc. Form 10-K for the year ended December 31, 2018, formatted in Extensible Business Reporting Language (XBRL): (i) Consolidated Balance Sheets at December 31, 2018 and 2017, (ii) Consolidated Statements of Operations for the years ended December 31, 2018, 2017 and 2016, (iii) Consolidated Statements of Stockholders' Equity for the years ended December 31, 2018, 2017 and 2016, (iv) Consolidated Statements of Cash Flows for the years ended December 31, 2018, 2017 and 2016, and (v) Notes to the Financial Statements.
*	Filed herewith.
**	Furnished herewith.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Kadmon Holdings, Inc.

Date: March 7, 2019

By: /s/ Harlan W. Waksal
Harlan W. Waksal
President and Chief Executive Officer
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Harlan W. Waksal Harlan W. Waksal	President and Chief Executive Officer (Principal Executive Officer)	March 7, 2019
/s/ Steven Meehan Steven Meehan	Executive Vice President, Chief Financial Officer (Principal Financial Officer)	March 7, 2019
/s/ Kyle Carver Kyle Carver	Principal Accounting Officer, Controller (Principal Accounting Officer)	March 7, 2019
/s/ Tasos Konidaris Tasos Konidaris	Director	March 7, 2019
/s/ Eugene Bauer Eugene Bauer	Director	March 7, 2019
/s/ D. Dixon Boardman D. Dixon Boardman	Director	March 7, 2019
/s/ David E. Cohen David E. Cohen	Director	March 7, 2019
/s/ Cynthia Schwalm Cynthia Schwalm	Director	March 7, 2019
/s/ Susan Wiviott Susan Wiviott	Director	March 7, 2019

KADMON HOLDINGS, INC.
PERFORMANCE STOCK OPTION AGREEMENT

Kadmon Holdings, Inc. (the "***Company***") has granted to the Participant named in the *Notice of Grant of Stock Option* (the "***Grant Notice***") to which this Performance Stock Option Agreement (the "***Option Agreement***") is attached an option (the "***Option***") to purchase certain shares of Stock with the terms and conditions set forth in the Grant Notice and this Option Agreement. The Option has been granted pursuant to, and shall in all respects be subject to, the terms and conditions of the Kadmon Holdings, Inc. 2016 Equity Incentive Plan, as amended (the "***Plan***"), the provisions of which are incorporated herein by reference. By signing the Grant Notice, the Participant: (a) acknowledges receipt of, and represents that the Participant has read and is familiar with, the Grant Notice, this Option Agreement, the Plan and a prospectus for the Plan prepared in connection with the registration with the Securities and Exchange Commission of shares issuable pursuant to the Option (the "***Plan Prospectus***"); (b) accepts the Option subject to all of the terms and conditions of the Grant Notice, this Option Agreement and the Plan; and (c) agrees to accept as binding, conclusive and final all decisions or interpretations of the Committee upon any questions arising under the Grant Notice, this Option Agreement or the Plan.

1. **Definitions and Construction.**

1.1 **Definitions.** Unless otherwise defined herein, capitalized terms shall have the meanings assigned to such terms in the Grant Notice or the Plan.

1.2 **Construction.** Captions and titles contained herein are for convenience only and shall not affect the meaning or interpretation of any provision of this Option Agreement. Except when otherwise indicated by the context, the singular shall include the plural and the plural shall include the singular. Use of the term "or" is not intended to be exclusive, unless the context clearly requires otherwise.

2. **Tax Consequences.**

2.1 **Tax Status of Option.** This Option is intended to be a Nonstatutory Stock Option.

3. **Administration.**

All questions of interpretation concerning the Grant Notice, this Option Agreement, the Plan or any other form of agreement or other document employed by the Company in the administration of the Plan or the Option shall be determined by the Committee. All such determinations by the Committee shall be final, binding and conclusive upon all persons having an interest in the Option, unless fraudulent or made in bad faith. Any and all actions, decisions and determinations taken or made by the Committee in the exercise of its discretion pursuant to the Plan or the Option or other agreement thereunder (other than determining questions of interpretation pursuant to the preceding sentence) shall be final, binding and conclusive upon all persons having an interest in the Option. Any Officer shall have the authority to act on behalf of the Company with respect to any matter, right, obligation, or election which is the responsibility of or which is allocated to the Company herein, provided the Officer has apparent authority with respect to such matter, right, obligation, or election.

4. **Performance Metrics and Service Vesting Conditions.**

4.1 **Performance Goals.** The Option shall be subject to achievement of the Company performance goals set forth in Appendix A attached hereto (each, a "***Performance Goal***") during the three year performance period following the Date of Grant (the "***Performance Period***"). Each Performance Goal shall be deemed achieved only as of the date of achievement of the Performance Goal, as certified by the Committee (each, an "***Achievement Date***"), with the number of shares of Stock underlying the Option eligible to vest on the Applicable Vesting Date (as defined in Section 4.2), if any, determined based on achievement of the applicable Performance Goal (an "***Earned Option***"), as set forth in Appendix A. For the avoidance of doubt, subject to Sections 8 and 9, each Achievement Date must

occur during the Performance Period and if the Achievement Date for any Performance Goal does not occur during the Performance Period, the portion of the Option eligible to be earned upon achievement of the Performance Goal shall terminate in its entirety immediately on the first day following the end of the Performance Period, and Earned Options shall only vest upon an Applicable Vesting Date.

4.2 **Service Vesting.** Subject to Sections 8 and 9, Earned Options attributable to each Performance Goal achieved shall service vest in three equal tranches in accordance with the following conditions (each, an "***Applicable Vesting Date***"), subject to the Participant's continued employment though the Applicable Vesting Date:

(a) The first tranche of an Earned Option shall vest immediately upon the later of the certification of achievement of the relevant Performance Goal and the first anniversary of the Date of Grant (the "***Initial Vesting Date***");

(b) The second tranche of an Earned Option shall vest on the first anniversary of the relevant Achievement Date specified in the Committee certification; and

(c) The third tranche of an Earned Option shall vest on the third anniversary of the Date of Grant (the "***Final Vesting Date***").

Notwithstanding the foregoing, if the relevant Achievement Date for a Performance Goal occurs after the second anniversary of the Date of Grant, the Initial Vesting Date shall be the certification of achievement of the relevant Performance Goal, the second tranche of the Earned Option shall vest on the third anniversary of the Date of Grant and the Final Vesting Date shall be the first anniversary of the Achievement Date. For purposes of this Option Agreement, "***Vested Options***" shall mean any Earned Option that has become vested upon an Applicable Vesting Date, as described in this Section 4.2. For the avoidance of doubt, any Earned Options that do not become Vested Options prior to the termination of the Option (as provided in Section 7) shall terminate in its entirety immediately on the first day following the end of the Final Vesting Date.

5. **Exercise of the Option.**

5.1 **Right to Exercise.** Except as otherwise provided herein, the Option shall be exercisable on and after the Applicable Vesting Date and prior to the termination of the Option (as provided in Section 7) in an amount not to exceed the number shares subject to the Vested Options less the number of shares previously acquired upon exercise of the Option. In no event shall the Option be exercisable for more shares than the Number of Option Shares, as adjusted pursuant to Section 10.

5.2 **Method of Exercise.** Exercise of the Option shall be by means of electronic or written notice (the "***Exercise Notice***") in a form authorized by the Company. An electronic Exercise Notice must be digitally signed or authenticated by the Participant in such manner as required by the notice and transmitted to the Company or an authorized representative of the Company (including a third-party administrator designated by the Company). In the event that the Participant is not authorized or is unable to provide an electronic Exercise Notice, the Option shall be exercised by a written Exercise Notice addressed to the Company, which shall be signed by the Participant and delivered in person, by certified or registered mail, return receipt requested, by confirmed facsimile transmission, or by such other means as the Company may permit, to the Company, or an authorized representative of the Company (including a third-party administrator designated by the Company). Each Exercise Notice, whether electronic or written, must state the Participant's election to exercise the Option, the number of whole shares of Stock for which the Option is being exercised and such other representations and agreements as to the Participant's investment intent with respect to such shares as may be required pursuant to the provisions of this Option Agreement. Further, each Exercise Notice must be received by the Company prior to the termination of the Option as set forth in Section 7 and must be accompanied by full payment of the aggregate Exercise Price for the number of shares of Stock being purchased. The Option shall be deemed to be exercised upon receipt by the Company of such electronic or written Exercise Notice and the aggregate Exercise Price.

5.3 **Payment of Exercise Price.**

(a) ***Forms of Consideration Authorized.*** Except as otherwise provided below, payment of the aggregate Exercise Price for the number of shares of Stock for which the Option is being exercised shall be made (i) in cash, by check or in cash equivalent; (ii) if permitted by the Company and subject to the limitations contained in Section 5.3(b), by means of (1) a Cashless Exercise, (2) a Net-Exercise, or (3) a Stock Tender Exercise; or (iii) by any combination of the foregoing.

(b) ***Limitations on Forms of Consideration.*** The Company reserves, at any and all times, the right, in the Company's sole and absolute discretion, to establish, decline to approve or terminate any program or procedure providing for payment of the Exercise Price through any of the means described below, including with respect to the Participant notwithstanding that such program or procedures may be available to others.

(i) **Cashless Exercise.** A "***Cashless Exercise***" means the delivery of a properly executed Exercise Notice together with irrevocable instructions to a broker in a form acceptable to the Company providing for the assignment to the Company of the proceeds of a sale or loan with respect to shares of Stock acquired upon the exercise of the Option in an amount not less than the aggregate Exercise Price for such shares (including, without limitation, through an exercise complying with the provisions of Regulation T as promulgated from time to time by the Board of Governors of the Federal Reserve System).

(ii) **Net-Exercise.** A "***Net-Exercise***" means the delivery of a properly executed Exercise Notice electing a procedure pursuant to which (1) the Company will reduce the number of shares otherwise issuable to the Participant upon the exercise of the Option by the largest whole number of shares having a Fair Market Value that does not exceed the aggregate Exercise Price for the shares with respect to which the Option is exercised, and (2) the Participant shall pay to the Company in cash the remaining balance of such aggregate Exercise Price not satisfied by such reduction in the number of whole shares to be issued. Following a Net-Exercise, the number of shares remaining subject to the Option, if any, shall be reduced by the sum of (1) the net number of shares issued to the Participant upon such exercise, and (2) the number of shares deducted by the Company for payment of the aggregate Exercise Price.

(iii) **Stock Tender Exercise.** A "***Stock Tender Exercise***" means the delivery of a properly executed Exercise Notice accompanied by (1) the Participant's tender to the Company, or attestation to the ownership, in a form acceptable to the Company of whole shares of Stock having a Fair Market Value that does not exceed the aggregate Exercise Price for the shares with respect to which the Option is exercised, and (2) the Participant's payment to the Company in cash of the remaining balance of such aggregate Exercise Price not satisfied by such shares' Fair Market Value. A Stock Tender Exercise shall not be permitted if it would constitute a violation of the provisions of any law, regulation or agreement restricting the redemption of the Company's stock. If required by the Company, the Option may not be exercised by tender to the Company, or attestation to the ownership, of shares of Stock unless such shares either have been owned by the Participant for a period of time required by the Company (and not used for another option exercise by attestation during such period) or were not acquired, directly or indirectly, from the Company.

5.4 **Tax Withholding.**

(a) ***In General.*** At the time the Option is exercised, in whole or in part, or at any time thereafter as requested by a Participating Company, the Participant hereby authorizes withholding from payroll and any other amounts payable to the Participant, and otherwise agrees to make adequate provision for (including by means of a Cashless Exercise to the extent permitted by the Company), any sums required to satisfy the federal, state, local and foreign tax (including any social insurance) withholding obligations of the Participating Company Group, if any, which arise in connection with the Option. The Company shall have no obligation to deliver shares of Stock until the tax withholding obligations of the Participating Company Group have been satisfied by the Participant.

(b) ***Withholding in Shares.*** The Company shall have the right, but not the obligation, to require the Participant to satisfy all or any portion of a Participating Company's tax withholding obligations upon exercise of the Option by deducting from the shares of Stock otherwise issuable to the Participant upon such exercise a number of whole shares having a fair market value, as determined by the Company as of the date of exercise, not in excess of the amount of such tax withholding obligations determined by the applicable minimum statutory withholding

rates if required to avoid liability classification of the Option under generally accepted accounting principles in the United States.

5.5 **Beneficial Ownership of Shares; Certificate Registration.** The Participant hereby authorizes the Company, in its sole discretion, to deposit for the benefit of the Participant with any broker with which the Participant has an account relationship of which the Company has notice any or all shares acquired by the Participant pursuant to the exercise of the Option. Except as provided by the preceding sentence, a certificate for the shares as to which the Option is exercised shall be registered in the name of the Participant, or, if applicable, in the names of the heirs of the Participant.

5.6 **Restrictions on Grant of the Option and Issuance of Shares.** The grant of the Option and the issuance of shares of Stock upon exercise of the Option shall be subject to compliance with all applicable requirements of federal, state or foreign law with respect to such securities. The Option may not be exercised if the issuance of shares of Stock upon exercise would constitute a violation of any applicable federal, state or foreign securities laws or other law or regulations or the requirements of any stock exchange or market system upon which the Stock may then be listed. In addition, the Option may not be exercised unless (i) a registration statement under the Securities Act shall at the time of exercise of the Option be in effect with respect to the shares issuable upon exercise of the Option or (ii) in the opinion of legal counsel to the Company, the shares issuable upon exercise of the Option may be issued in accordance with the terms of an applicable exemption from the registration requirements of the Securities Act. THE PARTICIPANT IS CAUTIONED THAT THE OPTION MAY NOT BE EXERCISED UNLESS THE FOREGOING CONDITIONS ARE SATISFIED. ACCORDINGLY, THE PARTICIPANT MAY NOT BE ABLE TO EXERCISE THE OPTION WHEN DESIRED EVEN THOUGH THE OPTION IS VESTED. The inability of the Company to obtain from any regulatory body having jurisdiction the authority, if any, deemed by the Company's legal counsel to be necessary to the lawful issuance and sale of any shares subject to the Option shall relieve the Company of any liability in respect of the failure to issue or sell such shares as to which such requisite authority shall not have been obtained. As a condition to the exercise of the Option, the Company may require the Participant to satisfy any qualifications that may be necessary or appropriate, to evidence compliance with any applicable law or regulation and to make any representation or warranty with respect thereto as may be requested by the Company.

5.7 **Fractional Shares.** The Company shall not be required to issue fractional shares upon the exercise of the Option.

6. **Nontransferability of the Option.**

During the lifetime of the Participant, the Option shall be exercisable only by the Participant or the Participant's guardian or legal representative. The Option shall not be subject in any manner to anticipation, alienation, sale, exchange, transfer, assignment, pledge, encumbrance, or garnishment by creditors of the Participant or the Participant's beneficiary, except transfer by will or by the laws of descent and distribution. Following the death of the Participant, the Option, to the extent provided in Section 7, may be exercised by the Participant's legal representative or by any person empowered to do so under the deceased Participant's will or under the then applicable laws of descent and distribution.

7. **Termination of the Option.**

The Option shall terminate after the first to occur of (a) the close of business on the Option Expiration Date, (b) the close of business on the last date for exercising the Option following termination of the Participant's Service as described in Section 8, or (c) as otherwise set forth in this Option Agreement.

8. **Effect of Termination of Service.**

8.1 **Option Exercisability.** The Option shall be exercisable after the Participant's termination of Service only during the applicable time period as determined below and thereafter shall terminate.

(a) ***Termination of Service without Cause or For Good Reason.*** If the Participant's Service is terminated by the Company for any reason other than for Cause or the Participant terminates his or her employment with the Company for Good Reason, (i) any Options that have not become Earned Options due to the failure to achieve the Performance Goal prior to the termination of Service ("***Unearned Options***") shall be cancelled and terminate in their entirety immediately upon such termination of Service and (ii) any Earned Options that have not yet become Vested Options ("***Earned Unvested Options***") shall accelerate and vest, and to the extent unexercised by the Participant immediately prior to the date on which the Participant's Service terminated, may be exercised by the Participant at any time prior to the expiration of the three month anniversary of the date on which the Participant's Service terminated, but in any event no later than the Option Expiration Date.

(b) ***Resignation without Good Reason***. If the Participant terminates his or her employment without Good Reason (i) any Earned Options, Unearned Options and Earned Unvested Options shall be cancelled and terminate in their entirety immediately upon such termination of Service and (ii) any Vested Options unexercised by the Participant immediately prior to the date on which the Participant's Service terminated, may be exercised by the Participant at any time prior to the expiration of the three month anniversary of the date on which the Participant's Service terminated, but in any event no later than the Option Expiration Date.

(c) ***Termination for Cause.*** Notwithstanding any other provision of this Option Agreement to the contrary, if the Participant's Service is terminated for Cause or if, following the Participant's termination of Service and during any period in which the Option otherwise would remain exercisable, the Participant engages in any act that would constitute Cause, all Options (whether Earned or Unearned Options and including Vested Options and Earned Unvested Options) shall terminate in its entirety and cease to be exercisable immediately upon such termination of Service or act.

(d) ***Death or Disability***. If the Participant's Service is terminated due to his or her death or Disability, (i) any Unearned Options shall be cancelled and terminate in their entirety immediately upon such termination of Service and (ii) any Earned Unvested Options shall accelerate and vest, and to the extent unexercised by the Participant immediately prior to the date on which the Participant's Service terminated, may be exercised by the Participant (or the Participant's estate or the person to whom such Option is transferred by will or the applicable law of descent and distribution) at any time prior to the one year anniversary of the date on which the Participant's Service terminated, but in any event no later than the Option Expiration Date.

8.2 **Extension if Exercise Prevented by Law.** Notwithstanding the foregoing, other than termination of the Participant's Service for Cause, if the exercise of the Option within the applicable time periods set forth in Section 8.1 is prevented by the provisions of Section 5.6, the Option shall remain exercisable until the later of (a) thirty (30) days after the date such exercise first would no longer be prevented by such provisions, or (b) the end of the applicable time period under Section 8.1, but in any event no later than the Option Expiration Date.

9. **Effect of Change in Control.**

In the event of a Change in Control occurring within three years after the Date of Grant, to the extent a number of Options have not been earned as of the date of the Change in Control equal to at least two-thirds of the Options granted (the "***Target***"), an additional number of Unearned Options shall be deemed Earned Options such that total Earned Options equals the Target number of Options. In addition, following a Change in Control (whether such Change in Control occurs within or after three years following the Date of Grant), subject to Section 13.2 of the Plan, (x) all Options that become Earned Options, if any, due to the Change in Control shall vest upon the first anniversary of the Change in Control, and (y) all Earned Options with an Achievement Date occurring prior to such Change in Control shall vest upon the earlier of (A) the first anniversary of the Change in Control and (B) the date(s) such Earned Options are eligible to vest in accordance with Section 4.2(b) and (c); *provided*, that all Earned Options that are unvested after the Change in Control shall vest and become immediately exercisable if the Participant's Service is terminated by the Company for any reason other than for Cause or the Participant terminates his or her employment with the Company for Good Reason.

10. **Adjustments for Changes in Capital Structure.**

Subject to any required action by the stockholders of the Company and the requirements of Sections 409A and 424 of the Code to the extent applicable, in the event of any change in the Stock effected without receipt of consideration by the Company, whether through merger, consolidation, reorganization, reincorporation, recapitalization, reclassification, stock dividend, stock split, reverse stock split, split-up, split-off, spin-off, combination of shares, exchange of shares, or similar change in the capital structure of the Company, or in the event of payment of a dividend or distribution to the stockholders of the Company in a form other than Stock (excepting normal cash dividends) that has a material effect on the Fair Market Value of shares of Stock, appropriate and proportionate adjustments shall be made in the number, Exercise Price and kind of shares subject to the Option, in order to prevent dilution or enlargement of the Participant's rights under the Option. For purposes of the foregoing, conversion of any convertible securities of the Company shall not be treated as "effected without receipt of consideration by the Company." Any fractional share resulting from an adjustment pursuant to this Section shall be rounded down to the nearest whole number and the Exercise Price shall be rounded up to the nearest whole cent. In no event may the Exercise Price be decreased to an amount less than the par value, if any, of the stock subject to the Option. The Committee in its sole discretion, may also make such adjustments in the terms of the Option to reflect, or related to, such changes in the capital structure of the Company or distributions as it deems appropriate. All adjustments pursuant to this Section shall be determined by the Committee, and its determination shall be final, binding and conclusive.

11. **Rights as a Stockholder, Director, Employee or Consultant.**

The Participant shall have no rights as a stockholder with respect to any shares covered by the Option until the date of the issuance of the shares for which the Option has been exercised (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company). No adjustment shall be made for dividends, distributions or other rights for which the record date is prior to the date the shares are issued, except as provided in Section 10. If the Participant is an Employee, the Participant understands and acknowledges that, except as otherwise provided in a separate, written employment agreement between a Participating Company and the Participant, the Participant's employment is "at will" and is for no specified term. Nothing in this Option Agreement shall confer upon the Participant any right to continue in the Service of a Participating Company or interfere in any way with any right of the Participating Company Group to terminate the Participant's Service as a Director, an Employee or Consultant, as the case may be, at any time.

12. **Sales.**

The Participant shall dispose of the shares acquired pursuant to the Option only in accordance with the provisions of this Option Agreement.

13. **Legends.**

The Company may at any time place legends referencing any applicable federal, state or foreign securities law restrictions on all certificates representing shares of stock subject to the provisions of this Option Agreement. The Participant shall, at the request of the Company, promptly present to the Company any and all certificates representing shares acquired pursuant to the Option in the possession of the Participant in order to carry out the provisions of this Section.

14. **Miscellaneous Provisions.**

14.1 **Termination or Amendment.** The Committee may terminate or amend the Plan or the Option at any time; provided, however, that except as provided in Section 9 in connection with a Change in Control, no such termination or amendment may have a materially adverse effect on the Option or any unexercised portion thereof without the consent of the Participant unless such termination or amendment is necessary to comply with any applicable law or government regulation. No amendment or addition to this Option Agreement shall be effective unless in writing.

14.2 **Further Instruments.** The parties hereto agree to execute such further instruments and to take such further action as may reasonably be necessary to carry out the intent of this Option Agreement.

14.3 **Binding Effect.** This Option Agreement shall inure to the benefit of the successors and assigns of the Company and, subject to the restrictions on transfer set forth herein, be binding upon the Participant and the Participant's heirs, executors, administrators, successors and assigns.

14.4 **Delivery of Documents and Notices.** Any document relating to participation in the Plan or any notice required or permitted hereunder shall be given in writing and shall be deemed effectively given (except to the extent that this Option Agreement provides for effectiveness only upon actual receipt of such notice) upon personal delivery, electronic delivery at the e-mail address, if any, provided for the Participant by a Participating Company, or upon deposit in the U.S. Post Office or foreign postal service, by registered or certified mail, or with a nationally recognized overnight courier service, with postage and fees prepaid, addressed to the other party at the address of such party set forth in the Grant Notice or at such other address as such party may designate in writing from time to time to the other party.

(a) ***Description of Electronic Delivery.*** The Plan documents, which may include but do not necessarily include: the Plan, the Grant Notice, this Option Agreement, the Plan Prospectus, and any reports of the Company provided generally to the Company's stockholders, may be delivered to the Participant electronically. In addition, if permitted by the Company, the Participant may deliver electronically the Grant Notice and Exercise Notice called for by Section 5.2 to the Company or to such third party involved in administering the Plan as the Company may designate from time to time. Such means of electronic delivery may include but do not necessarily include the delivery of a link to a Company intranet or the Internet site of a third party involved in administering the Plan, the delivery of the document via e-mail or such other means of electronic delivery specified by the Company.

(b) ***Consent to Electronic Delivery.*** The Participant acknowledges that the Participant has read Section 14.4(a) of this Option Agreement and consents to the electronic delivery of the Plan documents and, if permitted by the Company, the delivery of the Grant Notice and Exercise Notice, as described in Section 14.4(a). The Participant acknowledges that he or she may receive from the Company a paper copy of any documents delivered electronically at no cost to the Participant by contacting the Company by telephone or in writing. The Participant further acknowledges that the Participant will be provided with a paper copy of any documents if the attempted electronic delivery of such documents fails. Similarly, the Participant understands that the Participant must provide the Company or any designated third party administrator with a paper copy of any documents if the attempted electronic delivery of such documents fails. The Participant may revoke his or her consent to the electronic delivery of documents described in Section 14.4(a) or may change the electronic mail address to which such documents are to be delivered (if the Participant has provided an electronic mail address) at any time by notifying the Company of such revoked consent or revised e-mail address by telephone, postal service or electronic mail. Finally, the Participant understands that he or she is not required to consent to electronic delivery of documents described in Section 14.4(a).

14.5 **Integrated Agreement.** The Grant Notice, this Option Agreement and the Plan, together with the Superseding Agreement, if any, shall constitute the entire understanding and agreement of the Participant and the Participating Company Group with respect to the subject matter contained herein and supersede any prior agreements, understandings, restrictions, representations, or warranties among the Participant and the Participating Company Group with respect to such subject matter. To the extent contemplated herein, the provisions of the Grant Notice, the Option Agreement and the Plan shall survive any exercise of the Option and shall remain in full force and effect.

14.6 **Applicable Law.** This Option Agreement shall be governed by the laws of the State of Delaware as such laws are applied to agreements between Delaware residents entered into and to be performed entirely within the State of Delaware.

14.7 **Counterparts.** The Grant Notice may be executed in counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

APPENDIX A

The Options shall vest based upon the attainment of the Performance Milestones, and continued employment as set forth below, subject to limited exceptions.

Performance Milestones (which must be achieved in the three years following the Grant Date)	**Performance Milestone**	**Percent of Option Grant Allocated to Milestone**
	1. Successfully securing additional general Company financing of no less than $80 million by the end of 2018, inclusive of debt and equity financing and non-dilutive funding from, or arising out of, a licensing arrangement, business development transaction or similar transaction.	1/3
	2. Initiation of two new Phase 2 clinical studies in areas of ongoing work: a. Chronic graft host disease b. Idiopathic pulmonary fibrosis	1/3
	3. Initiation of Phase 2 clinical trial in an additional indication for KD025 such as scleroderma	1/3
Vesting Upon Achievement of Each Performance Milestone	Each Performance Milestone will be measured independently and will only be deemed achieved as of the date of achievement of the Performance Milestone, as certified by the Committee (the "**Achievement Date**"). Options allocated to each Performance Milestone will become "**Earned Options**" following the Achievement Date.	
	Initial Vesting Date: **1/3 of the Earned Option allocated to such Performance Milestone shall vest immediately on the certification of achievement of the relevant Performance Milestone (provided the Participant remains employed through such date);** *provided* that if the Performance Milestone is achieved prior to the first anniversary of the Date of Grant, 1/3 of the Earned Option subject to such Performance Milestone shall vest on the first anniversary of the Date of Grant (provided the Participant remains employed through such first anniversary date)	
	Second Vesting Date: **1/3 of the Earned Option allocated to such Performance Milestone shall vest on the first anniversary of the relevant Achievement Date specified in the Committee certification (provided the Participant remains employed through this Second Vesting Date)**	
	Final Vesting Date: **1/3 of the Earned Option allocated to such Performance Milestone shall vest on the third anniversary of the Date of Grant (provided the Participant remains employed through this Final Vesting Date)** *provided* that if the Performance Milestone is achieved after the second anniversary of the Date of Grant, 1/3 of the Earned Option shall vest on the relevant Achievement Date specified in the Committee certification, 1/3 of the Earned Option shall vest on the third anniversary of the Date of Grant and 1/3 shall vest on the first anniversary of the Achievement Date (subject to the Participant's continued employment through each vesting date)	

EXHIBIT 10.40

SEPARATION AGREEMENT AND GENERAL RELEASE

This Separation Agreement and General Release (this "Agreement") dated as of November 30, 2018, is entered into by and between Konstantin Poukalov ("Employee" or "you") and Kadmon Corporation, LLC, a Delaware limited liability company (together with Kadmon Holdings, Inc., a Delaware corporation ("Parent"), the "Company"), on behalf of itself and its past and present parent entities, and its or their subsidiaries, divisions, affiliates and related business entities (collectively, the "Company Entities").

SECTION 1. Concluding Employment. Pursuant to your letter of resignation, dated October 24, 2018 (the "Separation Date"), you voluntarily resigned from all employment with the Company and any other positions you may have held as an officer, employee, or otherwise, of any of the other Company Entities. As a result, the Separation Date was the termination date of your employment for purposes of participation in and coverage under all compensation or benefit plans and programs sponsored by or through the Company Entities except as otherwise provided herein. You acknowledge and agree that after the Separation Date you shall not represent, and since the Separation Date you have not represented, yourself as being a director, officer, employee, agent or representative of any Company Entity for any purpose, and you shall not enter the premises of any of the Company Entities at any time. You agree that, as of the date of this Agreement, the Company has made all payments due to you for any earned but unpaid base salary and previously submitted un-reimbursed business expenses (in accordance with usual Company policies, guidelines and practices, including, without limitation, the Company's Business Travel and Expense Policy). You will retain any previously vested benefits (including equity compensation awards) in accordance with the terms of the applicable benefit plan and/or applicable grant or award agreement. For the avoidance of doubt, your vested stock options and vested stock appreciation rights shall be treated as if your termination of employment was without "cause" within the meaning of the Company's 2016 Equity Incentive Plan (the "EIP") (and, for the avoidance of doubt, only for such purposes under the EIP, and not for any other purpose).

SECTION 2. Severance Benefits. In exchange for your execution of a release and waiver of claims against the Released Parties (as defined below) and your compliance with the other terms and conditions of this Agreement, the Company agrees to: (a) pay you severance in the aggregate amount of $600,000 (the "Severance Amount"), which will be subject to all applicable withholding taxes, and will be payable in equal installments, in accordance with the Company's regular payroll schedule, over a one-year period effective as of the Separation Date (the "Severance Period"); and (b) pay on your behalf medical insurance premiums necessary to provide the medical benefits coverage ("Health Insurance") that would otherwise have been provided to you if you remained an employee of the Company during the 12-month period following the first day of the month after the Separation Date (the "Benefit Period"). All payments described in the preceding sentence that would otherwise have been made between the Separation Date through the date of this Agreement shall be made on the next payroll date to occur after the date of this Agreement in accordance with the Company's regular payroll schedule. Notwithstanding anything to the contrary herein, in the event that you (i) materially breach any of your obligations under this Agreement, the Company will immediately cease to have any obligations to make (x) any further severance payments under Section 2(a) above or (y) any further medical insurance premium payments under Section 2(b) above or (ii) become employed by another entity or individual during the Severance Period or the Benefit Period (excluding, for the avoidance of doubt, self-employment), you will notify the Company of the commencement date of such other employment and the Company will reduce each subsequent installment payment of the Severance Amount by the gross wages you receive from such other employment, which you shall inform the Company of as soon as reasonably practicable, after such commencement date. In addition, if you become eligible for Health Insurance by any means during the Benefit Period, you must immediately notify the Company and the Company shall immediately cease making any payments related to Health Insurance as set forth hereunder.

SECTION 3. Acknowledgement. You acknowledge and agree that the payments and other benefits provided pursuant to this Agreement: (a) are in full discharge of any and all liabilities and obligations of the Company to you, monetarily or with respect to employee benefits or otherwise, including but not limited to any and all obligations arising under any alleged written or oral employment agreement (including, without limitation, the Employment Agreement, dated November 1, 2015, by and between you and the Company (the "Employment Agreement")), policy, plan or procedure of the Company and/or any alleged understanding or arrangement between you and the Company and (b) exceeds any payment, benefit or other thing of value to which you might otherwise be entitled under any policy, plan or procedure of the Company and/or any agreement between you and the Company, written, oral or otherwise. You further agree not to seek employment with any of the Company Entities at any time after the Separation Date.

SECTION 4. Release. General Release. You, on behalf of yourself and your agents, heirs, executors, administrators, successors and assigns, hereby RELEASE AND FOREVER DISCHARGE the Company Entities, as well as

any and all of their predecessors, successors and assigns and any and all of their respective past or present directors, officers, employees, investors, shareholders, partners, fiduciaries, agents, trustees, administrators, attorneys and insurers, whether acting as agents for the Company or in their individual capacities (collectively the "Released Parties"), from any and all claims, damages, complaints, grievances, causes of action, suits, liabilities, demands and expenses (including attorneys' fees) of any nature whatsoever, both at law and in equity (except those expressly reserved herein), whether known or unknown, now existing or which may result from the existing state of things, which you now have or ever had against the Released Parties up to and including the date hereof. In particular, without limitation of the foregoing, the Released Parties are specifically released from and held harmless from any and all claims arising out of or related to your employment relationship with the Company Entities, including, without limitation, your separation from such employment. It is your intention that this Section 4 constitute a full and final general release of all such claims and that this release be as broad as possible. This Section 4 does not release or waive any rights or claims that may arise after the date hereof.

(a) Scope of Release. Without limiting the foregoing in any way, your release and waiver includes, but is not limited to, any rights or claims you may have under: the Age Discrimination in Employment Act of 1967 (29 U.S.C. § 621, *et seq.*); Title VII of the Civil Rights Acts of 1964; 42 U.S.C. § 1981; the Family and Medical Leave Act; the Fair Labor Standards Act; the Equal Pay Act; the Rehabilitation Act of 1973 and the Americans with Disabilities Act; the Employee Retirement Income Security Act of 1974; Worker Adjustment and Retraining Notification Act of 1988; the Older Workers Benefit Protection Act; the National Labor Relations Act; claims under the New York State Human Rights Law and the New York City Administrative Code, the Genetic Information Nondiscrimination Act; the Unfair Business Practices Act; and any other federal, state or local laws or regulations concerning employment, the termination thereof or prohibiting employment discrimination, harassment or retaliation. Your release and waiver also includes any claims against the Company or the Released Parties based on contract or tort, claims for defamation, libel, invasion of privacy, intentional or negligent infliction of emotional distress, wrongful termination, constructive discharge, breach of contract, breach of the covenant of good faith and fair dealing, breach of fiduciary duty and fraud. You agree that you shall never file a lawsuit or other complaint challenging the reasonableness, validity or enforceability of this Section 4. You waive and release any claim that you have or may have to reemployment after the Separation Date.

(b) No Lawsuits, Complaints, or Claims. You waive your right to file any charge or complaint against the Company or any of the Released Parties arising out of your employment or separation from such employment or any facts occurring prior to the date hereof before any federal, state or local court or any federal, state or local administrative agency, except where such waivers are prohibited by law. By signing this Agreement you represent that you have not filed any such claims, causes of action or complaints. Notwithstanding the foregoing, you do not waive or release any claim which cannot be validly waived or released by private agreement. Specifically, nothing in this Agreement shall prevent you from filing a charge or complaint with, or from participating in, an investigation or proceeding conducted by the Securities and Exchange Commission (the "SEC"), Equal Employment Opportunity Commission (the "EEOC"), Department of Fair Employment and Housing (the "DFEH") or any other federal, state or local agency charged with the enforcement of any laws applicable to the Company or, directly or indirectly, your employment with the Company. However, you understand that by signing this Agreement, you waive the right to recover any damages or to receive other relief in any claim or suit brought by or through the EEOC, the DFEH or any other state or local deferral agency on your behalf to the fullest extent permitted by law, but expressly excluding any award or other relief available from the SEC. As of the date hereof, you represent and warrant that you have no information that would require you to make any such report, nor have you made any such report, or caused or encouraged any other person to make such a report, as described above in this Section 4. This Agreement is not intended to, and shall not be interpreted in any manner that limits or restricts you from exercising any legally protected whistleblower rights (including pursuant to Section 21F of the Securities Exchange Act of 1934 ("Section 21F")) or receiving an award for information provided to any government agency under any legally protected whistleblower rights. You acknowledge that you have no pending workers' compensation claims and that this Agreement is not related in any way to any claim for workers' compensation benefits, and that you have no basis for such a claim.

(c) Rights Not Relinquished. In executing this Agreement, you shall not relinquish or release (i) any right to any vested benefits under any benefit plans or arrangements maintained by any of the Company Entities and any rights you may have under COBRA, (ii) any available right to indemnification under any applicable directors and officers liability insurance policy, indemnity agreement, applicable state and federal law and the Company's articles of incorporation and bylaws and (iii) your right to enforce this Agreement.

(d) Knowing and Voluntary Execution. By signing this Agreement, you hereby acknowledge and confirm that: (i) you have read this Agreement in its entirety and understands all of its terms; (ii) by this Agreement, you have been advised in writing of the right to consult with an attorney of your choosing before executing this Agreement and have been strongly encouraged and given the opportunity to so consult with an attorney; (iii) you knowingly, freely, and voluntarily assent to all of the terms and conditions set out in this Agreement including, without limitation, the waiver, release, and

covenants contained in it; (iv) you are executing this Agreement, including the waiver and release, in exchange for good and valuable consideration in addition to anything of value to which you are otherwise entitled; (v) you have been given the opportunity to consider the terms of this Agreement for at least 21 days and consult with an attorney of your choice (although you are entitled, at your discretion, to waive any or all of such 21-day period and sign this Agreement sooner, in which case the remainder of such 21-day period shall lapse); and (vi) you understand that the release contained in this Section 4 does not apply to rights and claims that may arise after you sign this Agreement.

(e) Waiver of Relief. You acknowledge and agree that by virtue of the foregoing, you knowingly and voluntarily, following an opportunity to consult with counsel of your choice, have waived any relief available to you (including without limitation, monetary damages, equitable relief and reinstatement) under any of the claims and/or causes of action waived in this Agreement, subject to the exceptions set forth in Section 5(f)(iii). Therefore you agree that you will not accept any award or settlement from any source or proceeding (including but not limited to any proceeding brought by any other person) with respect to any claim or right waived in this Agreement.

SECTION 5. Restrictive Covenants. Non-Compete. You agree that you will not, for 12 months following the Separation Date, directly or indirectly, anywhere in the world, Engage in or Associate with any Competitor (each, as defined below).

(a) Non-Solicit. You agree that you will not, for 12 months following the Separation Date, directly or indirectly, (i) anywhere in the world solicit or make an offer to, or attempt to or participate or assist in any effort to solicit or make an offer to, any Employee of the Company (as defined below) to be employed or to perform services outside of the Company Entities or (ii) seek to encourage or induce any vendor or customer of the Company Entities to cease doing business with, or lessen its business with, any of the Company Entities, or otherwise interfere with or damage (or attempt to interfere with or damage) any of the Company Entities' relationships with its vendors and customers.

(b) Non-Disparagement. You agree not to make any statements or representations, or otherwise communicate, directly or indirectly, in writing, orally, or otherwise, or take any action that may, directly or indirectly, disparage any of the Company Entities, as well as any and all of their predecessors, successors and assigns and any and all of their respective past, present or future directors, officers, employees, investors, shareholders, partners, fiduciaries, agents, trustees, administrators, attorneys and insurers, whether acting as agents for the Company or in their individual capacities (collectively, the "Company Representatives"). For the purposes of this Agreement, the term "disparage" includes, without limitation, comments or statements to the press and/or media, the Company Entities or any individual or entity with whom any of the Company Entities has a business relationship which would adversely affect in any manner (i) the conduct of the business of any of the Company Entities (including, without limitation, any business plans or prospects), (ii) the business reputation of the Company Entities or (iii) the personal reputations of any Company Representative. The Company's directors and executive officers agree not to make any statements or representations, or otherwise communicate, directly or indirectly, in writing, orally, or otherwise, or take any action that may, directly or indirectly, disparage you, and, when describing your separation of employment to third parties, the Company will describe your departure as a resignation, use words consistent in form and substance with the statement contained in Exhibit A or provide an actual copy of Exhibit A; provided, however, that (x) the Company shall have no obligation or liability for the statements, representations or communications of its non-executive officer employees or agents and (y) notwithstanding the foregoing, in the event that the Board of Directors of Parent (the "Board") determines that you have breached any of your obligations under this Section 5(c), the Company and the Company's directors and executive officers shall cease to have any obligations under this Section 5(c). Nothing in this Agreement shall preclude you or the Company's directors and officers from responding truthfully to a valid subpoena, cooperating with a governmental agency in connection with any investigation it is conducting, or taking any action otherwise required or permitted by law, provided that such response does not exceed that required by the law, regulation, or order. You shall promptly provide written notice of any such order to the Company's General Counsel, except as prohibited by law.

(c) Cooperation. You agree that you will cooperate (1) with the Company Entities and their respective counsel in connection with any investigation, administrative proceeding or litigation relating to any matter that occurred during your employment in which you were involved or of which you have knowledge and (2) with the Company Entities with respect to the transition of your duties and authorities to other employees of the Company following the date hereof. The Company will provide you with reasonable compensation for any such cooperation that is provided after the one year anniversary of this Agreement not to exceed $1,095.89 per day; provided, however, that the Company will have no obligation at any time to compensate you for cooperation provided in connection with any currently threatened or pending proceedings or litigation described in subclause (1) above.

(i) You agree that, in the event you are subpoenaed by any person or entity (including, but not limited to, any government agency) to give testimony (in a deposition, court proceeding or otherwise) which in any way relates to your employment by the Company and/or the Company Entities, you will give prompt notice of such request to the Company's General Counsel (or her/his successor or designee), except as prohibited by law, and will make no disclosure until the Company and/or the Company Entities have had a reasonable opportunity to contest the right of the requesting person or entity to such disclosure.

(d) Confidentiality. The terms and conditions of this Agreement are and shall be deemed to be confidential, and shall not be disclosed by you to any person or entity without the prior written consent of the Company, except if required by law or rule of a national securities exchange, and to your accountants, attorneys and/or immediate family, provided that, to the maximum extent permitted by applicable law, rule, code or regulation, they agree to maintain the confidentiality of the Agreement. You further represent that you have not disclosed the terms and conditions of the Agreement, or had any communications regarding the discussions or other deliberative processes of the Board with respect to this Agreement, to anyone other than your attorneys, accountants and/or immediate family. The Company reserves the right to disclose this Agreement, and the terms and conditions thereof, as it determines in its sole discretion.

(e) Confidential Information. You acknowledge that during the course of your employment with the Company Entities, you have had access to information relating to the Company Entities and their respective businesses that is not generally known by persons not employed by the Company Entities and that could not easily be determined or learned by someone outside of the Company Entities that provides the Company Entities with a competitive advantage, or that could be used to the Company Entities' disadvantage by a competitor ("Confidential Information") and that such information constitutes a valuable asset of the Company Entities. You shall not, without the prior written consent of the Company or as required by law, use or disclose or enable anyone else to use or disclose any Confidential Information of the Company Entities (whether or not developed by you), nor shall you have any communications with any outside investors of the Company as of the date hereof regarding the Company Entities and their respective businesses; provided, however, that inadvertent communications with any outside investors regarding the Company Entities and their respective businesses shall not constitute a breach of this Agreement provided that (A) such communications do not include the disclosure of Confidential Information and (B) after you have knowledge of such occurrence, you (x) immediately cease any further infringing communications and (y) report all such inadvertent communications to the Company as soon as reasonably practicable. As used herein, the term "Confidential Information" includes, but is not limited to, (X) all trade secrets, confidential information and know-how, business plans, operations, products, strategies, marketing, sales, inventions, designs, costs, legal strategies, finances, employees, customers, prospective customers, licensees or licensors; information received from third parties under confidential conditions; or other valuable financial, commercial, business, technical or marketing information concerning the Company or any of the products or services made, developed or sold by the Company, but does not include information any of the Company Entities have previously intentionally disclosed to the public or is otherwise in the public domain, and (Y) the Company's tangible and electronic documents and information used to implement, develop, produce, distribute or otherwise commercialize (1) ROCK inhibitor platforms, (2) Wilson disease-based treatments, (3) polycystic kidney disease-based treatments and (4) any of the Company's existing commercial or development programs in place as of the date hereof You agree not to disclose or use such Confidential Information at any time in the future except as may be required by law.

(i) In the event that you are requested pursuant to, or required by, applicable law, rule or regulation of any governmental entity or national securities exchange, or legal process to disclose any Confidential Information, you will promptly notify the Company so that it may seek a protective order or other appropriate remedy, and you will cooperate fully with the Company in protecting Confidential Information to the extent possible under applicable law. In the event that no such protective order or other remedy is obtained, or that the Company does not waive compliance with the terms hereof applicable to such disclosure, the Company nonetheless shall be deemed to consent to the disclosure of, and you will furnish, only that portion of the Confidential Information which you are legally required to disclose and you agree to exercise all reasonable efforts to obtain reliable assurance that confidential treatment will be accorded the information so disclosed.

(ii) Notwithstanding anything in this Agreement to the contrary, nothing in or about this Agreement prohibits you from: (1) filing and, as provided for under Section 21F, maintaining the confidentiality of a claim with the SEC; (2) providing Confidential Information to the SEC, or providing the SEC with information that would otherwise violate this Section 5, to the extent permitted by Section 21F; (3) cooperating, participating or assisting in an SEC investigation or proceeding without notifying the Company; or (4) receiving a monetary award as set forth in Section 21F.

(iii) You acknowledge and agree that, if you are found by a court of competent jurisdiction to have violated the terms and conditions of Section 5(f), you shall be obligated to pay liquidated damages to the Company in an amount equal to the legal fees incurred by the Company in connection with such proceeding. In addition, the Company shall be entitled to obtain equitable relief, including injunctive relief, to enforce this provision and shall be entitled to retain any and all profits related to any commercialization compensation or income earned by or owed to you or your affiliates, directly or indirectly, from any such violation of this Section 5(f).

(f) Return of Property. You represent that, as of the date hereof, you have returned (or have initiated the prompt return) to the Company all property belonging to, procured on behalf of or paid for by the Company Entities during your employment, including but not limited to all proprietary and/or Confidential Information and documents in any form belonging to the Company, cell phone, tablet, keys, card access to the building and office floors, employee handbook, phone cards, electronic files, rolodex or contact lists, computer user name and password, disks drives monitors, computers, servers, storage devices, credit cards and/or voicemail code(s); provided, however, that the Company will return the Company iPhone and one laptop previously used by you following the Company removing all Company software, files and other data as it sees fit.

(g) Other Actions. You agree that, during the Standstill Period (as defined below), without the prior written consent of the Board specifically expressed in a written resolution adopted by a majority vote of the entire Board, you will not directly or indirectly in any manner: (i) engage in any "solicitation" of "proxies" (as such terms are used in the rules of the SEC) or consents to vote any securities of Parent with respect to the election of directors, or become a participant in any election contest with respect to Parent; (ii) seek to influence any person with respect to the voting of any securities of Parent; (iii) otherwise publicly act, alone or in concert with others, to seek to control or influence the management, Board or policies of Parent or initiate or take any action to obtain representation on the Board; (iv) seek representation on the Board; or (v) enter into any agreements with any third party with respect to any of the foregoing. For the avoidance of any doubt, the foregoing should not be construed to limit your ability to vote of any shares of capital stock held by you to the extent not voted in connection with or in furtherance of any action by you in breach of clauses (i)–(v) of the immediately preceding sentence. You acknowledge and agree that, if you are found by a court of competent jurisdiction to have violated the terms and conditions of Section 5(h), you shall be obligated to pay liquidated damages to the Company in the amount of $250,000, plus any legal fees incurred by the Company in successfully proving an entitlement to payment of liquidated damages hereunder. In addition, the Company shall be entitled to obtain equitable relief, including injunctive relief, to enforce this provision.

(h) Prior Acts or Omissions. You represent that, from the Separation Date through the date hereof, you have not performed any act or omission that would otherwise result in a breach of any provision of this Section 5.

(i) Definitions. The following terms have the meanings provided below.

(1) "Competitor" means (a) any entity that is directly engaged in, or owns or controls an interest in any entity that is engaged in, competition with any business area, unit or division of any Company Entity, including, without limitation, the business of implementing, developing, producing, distributing or otherwise commercializing (w) ROCK inhibitor platforms, (x) Wilson disease-based treatments, (y) polycystic kidney disease-based treatments and (z) any of the Company's existing commercial or development programs in place as of the date hereof and (b) any of the Company's current business partners, licensees or collaborators; provided, however, that for the avoidance of doubt, Lyra LLC is not a Competitor.

(2) "Employee of the Company" means any employee of any Company Entity who was employed by any Company Entity at any time in the 12-month period immediately preceding any actual or attempted hiring, solicitation or making of an offer.

(3) "Engage in or Associate with" means any engagement or association, directly or indirectly, with a Competitor as a sole proprietor, owner, employer, director, officer, partner, principal, joint venturer, associate, employee, member, consultant, or contractor. The phrase includes beneficial ownership of one percent or more of any class of outstanding stock of a Competitor.

(4) "Standstill Period" means the period beginning on the date hereof and ending five years from the date of this Agreement.

SECTION 6. Severability. If any provision of this Agreement is held by a court of competent jurisdiction to be illegal, void or unenforceable, such provision shall have no effect; however, the remaining provisions shall be enforced to the maximum extent possible. Further, if a court should determine that any portion of this Agreement is overbroad or unreasonable, such provision shall be given effect to the maximum extent possible by narrowing or enforcing in part that aspect of the provision found overbroad or unreasonable.

SECTION 7. Breach of Agreement. You agree that for any breach of this Agreement the Company may seek all relief available under the law or at equity, including recoupment of the severance payments and benefits provided pursuant to this Agreement. You further acknowledge that any breach of the covenants set forth in this Agreement will cause the Company irreparable harm for which there is no adequate remedy at law, and you therefore consent to the issuance of an injunction in favor of the Company enjoining the breach of any of those covenants by any court of competent jurisdiction.

SECTION 8. Section 409A. Intent to Comply with Section 409A. Notwithstanding anything to the contrary set forth in this Agreement or any other plan, policy, arrangement or agreement with any of the Company Entities (this Agreement and such other plans, policies, arrangements and agreements, collectively the "Company Plans"), it is intended that the provisions of the Company Plans comply with Section 409A of the Internal Revenue Code of 1986, as amended, and the regulations thereunder as in effect from time to time ("Section 409A") and all provisions of the Company Plans shall be construed and interpreted in a manner consistent with the requirements for avoiding taxes or penalties under Section 409A. However, in light of the uncertainty surrounding the proper application of Section 409A, the Company cannot make any representations or guarantees with respect to compliance with such requirements, and neither the Company nor any of the Company Entities will have any obligation to indemnify or otherwise hold you harmless from any or all of such taxes or penalties. Each payment made under this Agreement shall be designated as a "separate payment" within the meaning of Section 409A.

(a) Timing of Reimbursement Payments and Other Benefits. Except as specifically permitted by Section 409A, the benefits and reimbursements provided to you under any Company Plan during any calendar year shall not affect the benefits and reimbursements to be provided to you under any Company Plan in any other calendar year, and the right to such benefits and reimbursements cannot be liquidated or exchanged for any other benefit, in accordance with Treasury Regulation Section 1.409A-3(i)(1)(iv) or any successor thereto. Furthermore, reimbursement payments shall be made to you as soon as practicable following the date that the applicable expense is incurred, but in no event later than the last day of the calendar year following the calendar year in which the underlying expense is incurred, in accordance with Treasury Regulation Section 1.409A-3(i)(1)(iv) or any successor thereto. Notwithstanding anything in this Agreement to the contrary, in the event that you are deemed to be a "specified employee" within the meaning of Section 409A(a)(2)(B)(i), no payments hereunder that are "deferred compensation" subject to Section 409A shall be made to you prior to the date that is six months after your Separation Date or, if earlier, your date of death. Following any applicable six month delay, all such delayed payments will be paid in a single lump sum on the first payroll date following the date that is six months after your Separation Date.

SECTION 9. Miscellaneous. This Agreement is not intended, and shall not be construed, as an admission that any of the Company Entities has violated any federal, state or local law (statutory or decisional), ordinance or regulation, breached any contract or committed any wrong whatsoever against you.

(a) Should any provision of this Agreement require interpretation or construction, it is agreed by the parties that the entity interpreting or construing this Agreement shall not apply a presumption against one party by reason of the rule of construction that a document is to be construed more strictly against the party who prepared the document.

SECTION 10. Assignment. This Agreement is binding upon, and shall inure to the benefit of, the parties and their respective heirs, executors, administrators, successors and assigns. You may not assign this Agreement, or any right, remedy, obligation nor liability arising hereunder, and any attempt to assign this Agreement or any right, remedy, obligation or liability hereunder shall be void *ab initio*.

SECTION 11. Governing Law; Arbitration. This Agreement shall be construed and enforced in accordance with the laws of the State of New York without regard to the principles of conflicts of law.

(a) With the exception of a claim for injunctive relief, for which jurisdiction shall be reserved in the federal and/or state courts in New York County and with respect to which the parties consent to personal jurisdiction, any controversy or claim arising out of or relating to this Agreement or the breach thereof shall be settled by arbitration before a single arbitrator, in accordance with the National Rules for the Resolution of Employment Disputes of the American Arbitration Association then in effect. The decision of the arbitrator shall be final and binding on the parties hereto and

judgment upon the award rendered by the arbitrator may be entered in any court having jurisdiction thereof. To the extent permitted by law, the prevailing party will be entitled to all reasonable attorneys' fees and costs incurred in such arbitration.

SECTION 12. Entire Agreement. You understand that this Agreement constitutes the complete understanding between the Company and you, and supersedes any and all agreements, understandings, and discussions, whether written or oral, between you and any of the Company Entities, including, without limitation, the Employment Agreement; provided, however, that you agree that you shall remain subject to any non-competition agreement; confidentiality agreement, or employee invention agreement that you executed prior to commencing employment with the Company or any of the Company Entities, or during your employment with the Company (including, without limitation, the terms and conditions set forth in Appendix A to the Kadmon Holdings, LLC 2014 Long-Term Incentive Plan, Amended and Restated Award Notification and Grant Agreement – EAR Unit Award). As of the date hereof, you represent and warrant that you have complied with the terms of each of the agreements described in this Section 12 and no breach or default has occurred thereunder as a result of your actions or activities. No other promises or agreements shall be binding unless in writing and signed by both the Company and you after the date hereof.

SECTION 13. Headings and Captions. The headings and captions herein are provided for reference and convenience only. They shall not be considered part of the Agreement and shall not be employed in the construction of the Agreement.

KADMON CORPORATION, LLC

By: /s/ Harlan W. Waksal
Harlan W. Waksal
President and Chief Executive Officer

Date: 11/30/2018

/s/ Konstantin Poukalov
Konstantin Poukalov

Date: 11/30/2018

EXHIBIT 10.41

SIXTH WAIVER AGREEMENT TO CREDIT AGREEMENT

This SIXTH WAIVER AGREEMENT TO CREDIT AGREEMENT, dated as of March 6, 2019 (this "Agreement"), is entered into by and among Kadmon Pharmaceuticals, LLC, a Pennsylvania limited liability company (the "Borrower"), the guarantors party hereto and the lender listed on the signature page hereof under the heading "LENDER". Unless otherwise defined herein or the context otherwise requires, terms used in this Agreement, including its preamble and recitals, have the meanings provided in the Credit Agreement (defined below).

W I T N E S S E T H:

WHEREAS, the Borrower, the Guarantors from time to time party thereto, the Lender and Perceptive Credit Holdings, LP, as Collateral Representative, have entered into that certain Credit Agreement, dated as of August 28, 2015 (as subsequently amended or otherwise modified from time to time, the "Credit Agreement");

WHEREAS, the Borrower has requested that the Lender waive Section 8.01(c) of the Credit Agreement but only to the extent necessary to permit the required report and opinion of BDO USA LLP for fiscal year 2018 (the "2018 Annual Report") to contain a "going concern" or like qualification, exception or explanation (the "Specified Qualification"); and

WHEREAS, upon the request of the Borrower and subject to the terms and conditions set forth herein, the Lender has agreed to waive the requirement set forth in Section 8.01(c) and permit the Specified Qualification only to the extent applicable to fiscal year 2018.

NOW, THEREFORE, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree as follows.

Article I
DEFINITIONS

SECTION 1.1. Certain Terms. The following terms (whether or not underscored) when used in this Agreement, including its preamble and recitals, shall have the following meanings (such definitions to be equally applicable to the singular and plural forms thereof):

"2018 Annual Report" is defined in the second recital.

"Agreement" is defined in the preamble.

"Borrower" is defined in the preamble.

"Credit Agreement" is defined in the first recital.

"Effective Date" is defined in Section 2.1 of this Agreement.

Article II
CERTAIN AMENDMENTS AND MODIFICATION TO the CREDIT AGREEMENT

SECTION 2.1. Partial Waiver of Section 8.01(c) Requirements. Effective as of the date hereof (the "Effective Date"), the Lender hereby agrees to waive the requirements of Section 8.01(c) of the Credit Agreement to the extent, and only to the extent, necessary to permit the 2018 Annual Report to contain the Specified Qualification.

SECTION 2.2. Limited Waiver. Except as expressly so waived or consented to, as applicable, the parties hereto expressly acknowledge and agree that (i) all other terms and provisions of the Credit Agreement and each other Loan Document shall continue in full force and effect in accordance with its terms and (ii) any waivers, consents or other modifications set forth in this Agreement are limited as expressly set forth herein, and shall not be deemed to constitute a waiver of any Default or Event of Default or any future breach of the Credit Agreement or any of the other Loan Documents.

Article III
conditions TO EFFECTIVENESS

SECTION 3.1. Conditions to Effectiveness. This Agreement shall become effective as of the Effective Date upon receipt by the Lender of counterparts of this Agreement duly executed by each of the Obligors and the Lender

Article IV
Representations and Warranties

To induce the Lender to enter into this Agreement, each Obligor represents and warrants to the Collateral Representative and the Lenders as set forth below.

SECTION 4.1. Validity, etc. This Agreement, the Credit Agreement and the other Loan Documents (both before and after giving effect to this Agreement) constitute the legal, valid and binding obligation of such Obligor, enforceable in accordance with its respective terms, subject to the effects of bankruptcy, insolvency, fraudulent conveyance, reorganization, moratorium and other similar laws relating to or affecting creditors' rights generally, general equitable principles (whether considered in a proceeding in equity or at law) and an implied covenant of good faith and fair dealing.

SECTION 4.2. Representations and Warranties, etc. Immediately prior to, on the Effective Date and immediately after giving effect to, this Agreement, the following statements shall be true and correct:

(a) the representations and warranties set forth in each Loan Document shall, in each case, be true and correct in all material respects with the same effect as if then made (unless stated to relate solely to an earlier date, in which case such representations and warranties shall be true and correct in all material respects as of such earlier date); and

(b) no Default or Event of Default shall have then occurred and be continuing.

Article V
Confirmation

SECTION 5.1. Guarantees, Security Interest, Continued Effectiveness. Each Obligor hereby consents to the modifications made to the Loan Documents pursuant to this Agreement and hereby agrees that, after giving effect to this Agreement, each Loan Document to which it is a party is and shall continue to be in full force and effect and the same are hereby ratified in all respects, except that upon the occurrence of the Waiver Effective Date, all references in such Loan Documents to the "Credit Agreement", "Loan Documents", "thereunder", "thereof", or words of similar import shall mean the Credit Agreement and the other Loan Documents, as amended or otherwise modified by this Agreement.

Article VI
Miscellaneous

SECTION 6.1. Cross-References. References in this Agreement to any Article or Section are, unless otherwise specified, to such Article or Section of this Agreement.

SECTION 6.2. Loan Document Pursuant to Credit Agreement. This Agreement is a Loan Document executed pursuant to the Credit Agreement and shall (unless otherwise expressly indicated therein) be construed, administered and applied in accordance with all of the terms and provisions of the Credit Agreement, as amended hereby, including Section 13 thereof.

SECTION 6.3. Successors and Assigns. The provisions of this Agreement shall be binding upon and inure to the benefit of the parties hereto and their respective permitted successors and assigns.

SECTION 6.4. Counterparts. This Agreement may be executed in any number of counterparts, all of which taken together shall constitute one and the same instrument and any of the parties hereto may execute this Agreement by signing any such counterpart.

SECTION 6.5. Governing Law. **THIS AGREEMENT AND THE RIGHTS AND OBLIGATIONS OF THE PARTIES HEREUNDER SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH, THE LAW OF THE STATE OF NEW YORK, WITHOUT REGARD TO PRINCIPLES OF CONFLICTS OF LAWS THAT WOULD RESULT IN THE APPLICATION OF THE LAWS OF ANY OTHER JURISDICTION; PROVIDED THAT SECTION 5-1401 OF THE NEW YORK GENERAL OBLIGATIONS LAW SHALL APPLY.**

SECTION 6.6. Full Force and Effect; Limited Waiver and Consent. Except as expressly amended hereby, the Obligors each jointly and severally agree that all of the representations, warranties, terms, covenants, conditions and other provisions of the Credit Agreement and the other Loan Documents shall remain unchanged and shall continue to be, and shall remain, in full force and effect in accordance with their respective terms. The amendments, consents and other waivers and modifications set forth in this Agreement shall be limited precisely as provided for herein to the provisions expressly amended herein or otherwise modified or waived hereby and shall not be deemed to be an amendment to, waiver of, consent to or modification of any other term or provision of the Credit Agreement or any other Loan Document or of any transaction or further or future action on the part of any Obligor which would require the consent of the Lender under the Credit Agreement or any of the Loan Documents.

SECTION 6.7. No Waiver. Except as otherwise specified herein, this Agreement is not, and shall not be deemed to be, a waiver or consent to any Default or Event of Default, or other non-compliance now existing or hereafter arising under the Credit Agreement and the other Loan Documents.

[Signature pages to follow]

IN WITNESS WHEREOF, each of the parties hereto has caused this Agreement to be duly executed and delivered by a Responsible Officer as of the date first above written.

borrower:

Kadmon PHARMACEUTICALS, LLC

By:

Name: Harlan W. Waksal, M.D

Title: President and Chief Executive Officer

Guarantors:

Kadmon Corporation, LLC

By:

Name: Harlan W. Waksal, M.D

Title: President and Chief Executive Officer

Kadmon Holdings, INC

By:

Name: Harlan W. Waksal, M.D

Title: President and Chief Financial Officer

Kadmon Research Institute, LLC

By:

Name: Harlan W. Waksal, M.D

Title: President and Chief Executive Officer

Three rivers research institute i, LLC

By:

Name: Harlan W. Waksal, M.D.

Title: President and Chief Executive Officer

three rivers biologicS, LLC

By:

Name: Harlan W. Waksal, M.D.

Title: President and Chief Executive Officer

three rivers global pharma, LLC

By:

Name: Harlan W. Waksal, M.D

Title: President and Chief Executive Officer

LENDER:

PERceptive credit holdings, Lp
By: Perceptive Credit Opportunities GP, LLC, its general partner

By
Name:
Title:

By
Name:
Title:

EXHIBIT 21.1

List of Subsidiaries of the Registrant

Name of Subsidiary	Jurisdiction of Organization
Kadmon Corporation, LLC	Delaware
Kadmon Pharmaceuticals, LLC	Pennsylvania

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

Kadmon Holdings, Inc.
New York, New York

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No.333-213748) and Form S-3 (No. 333-222364) of Kadmon Holdings, Inc. of our report dated March 7, 2019, relating to the consolidated financial statements which appears in this Form 10-K. Our report contains an explanatory paragraph regarding the Company's ability to continue as a going concern.

/s/ BDO USA, LLP
New York, New York

March 7, 2019

EXHIBIT 31.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER PURSUANT TO EXCHANGE ACT RULES 13a-14 AND 15d-14, AS ADOPTED PURSUANT TO SECTION 302 OF SARBANES-OXLEY ACT OF 2002

I, Harlan W. Waksal, certify that:

1. I have reviewed this Annual Report on Form 10-K of Kadmon Holdings, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 7, 2019

/s/ Harlan W. Waksal
Harlan W. Waksal
President and Chief Executive Officer

EXHIBIT 31.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER PURSUANT TO EXCHANGE ACT RULES 13a-14 AND 15d-14, AS ADOPTED PURSUANT TO SECTION 302 OF SARBANES-OXLEY ACT OF 2002

I, Steven Meehan, certify that:

1. I have reviewed this Annual Report on Form 10-K of Kadmon Holdings, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 7, 2019

/s/ Steven Meehan
Steven Meehan
Executive Vice President, Chief Financial Officer

EXHIBIT 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Kadmon Holdings, Inc. (the "Company") for the period ended December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Harlan W. Waksal, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

A signed original of this written statement has been provided to Kadmon Holdings, Inc. and will be retained by Kadmon Holdings, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

Dated: March 7, 2019

/s/ Harlan W. Waksal
Harlan W. Waksal
President and Chief Executive Officer

EXHIBIT 32.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Kadmon Holdings, Inc. (the "Company") for the period ended December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Steven Meehan, Executive Vice President, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

A signed original of this written statement has been provided to Kadmon Holdings, Inc. and will be retained by Kadmon Holdings, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

Dated: March 7, 2019

/s/ Steven Meehan
Steven Meehan
Executive Vice President, Chief Financial Officer